

C2 対称ジラクトン骨格を基盤とした三次元構造
多様性指向型マクロライドライブラリーの開発研究

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略語

Ac	acetyl
aq	aqueous
Bu	butyl
CSA	camphor-10-sulfonic acid
DDQ	2,3-dichloro-5,6-dicyano- <i>p</i> -benzoquinone
DIBAL-H	diisobutylaluminum hydride
DIPEA	diisopropylethylamine
DMAP	<i>N,N</i> -dimethyl-4-aminopyridine
Ee	enantiomer excess
eq	equivalent
ESI	electrospray ionization
HRMS	high-resolution mass spectrometry
IR	infrared
Me	methyl
MS	mass spectrometry
MS4A	molecular sieves 4Å
NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser effect spectroscopy
Ph	phenyl
PMB	<i>p</i> -methoxybenzyl
Pyr.	Pyridine
ROESY	Rotating Overhauser enhancement and Exchange Spectroscopy
TBAF	tetra- <i>n</i> -butylammonium fluoride
TBS	<i>tert</i> -butyldimethylsilyl
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TLC	thin-layer chromatography
TMS	trimethylsilyl
UV	ultraviolet

I. 序論

第一章 マクロライド天然物

「マクロライド (macrolide)」は大環状ラクトン骨格と糖を 1 つ以上有し、抗菌活性を示す化合物群の総称として、R. B. Woodward が 1957 年にその定義を提唱した¹⁾。狭義には抗生物質としてのマクロライドを指し、これは 12, 14, 16 員環ラクトン骨格に 1~3 個のデオキシ糖やアミノ糖が結合した化学構造を有する抗菌活性物質である (狭義のマクロライド)。しかし、現在ではマクロライドは中員環および大環状ラクトン構造を含む化合物の総称として広い概念 (広義のマクロライド) で用いられており、作用の異なる多くの物質が含まれる。

マクロライド類の中で最も代表的な天然物の一つは 1952 年米国の J. M. McGuire らにより *Streptomyces erythreus* の産生物質から発見された erythromycin²⁾である。翌年の 1953 年日本に導入され、臨床で応用されて以来半世紀以上経つが幅広い抗菌スペクトルと強力な活性を持つため、現在でも非常に注目を集めている。Erythromycin はわが国で抗生物質の臨床開発が系統的に行われはじめた最初の抗生物質であり、特にペニシリンの効かない感染症に対しては重篤な副作用もなく、今でも安心して使用できる抗生物質の一つである。また、erythromycin A (EM A) (1)以外のマクロライドも興味深い生物活性を示す天然物や誘導体が報告されている。例えば、16 員環マクロライド抗生物質の leucomycin A₃ (josamycin) (2)³⁾や免疫抑制作用を示す tacrolimus (FK-506) (3)⁴⁾などがある (Figure 1)。現在、8~62 員環構造を持つきわめて多種多様な生物活性を持つものが報告されており、その数は 2000 種以上になる。その中でも、14 員環マクロライドが最も多く、2005 年の時点において 806 種類あると報告されている (Figure 2)⁵⁾。

多様な生物活性を示すマクロライド天然物は長年医薬品開発においては重要なリード化合物として用いられ、創薬研究に貢献してきた。そして、誘導体合成研究や全合成研究、新規マクロライド天然物の探索など広く研究され続けている。近年では新たな研究分野であるケミカルバイオロジーあるいはケミカルゲノミクス研究においても重要なターゲット分子の一つとして、多くの研究者を魅了している。2001 年に完了したゲノム解析以後、低分子有機化合物と標的タンパク質間の相互作用を分子レベルで解明し、新たな創薬標的の探索あるいは検証に結びつけようとする試みが行われており、大環状化合物であるマクロライドの働きが大いに期待されている。

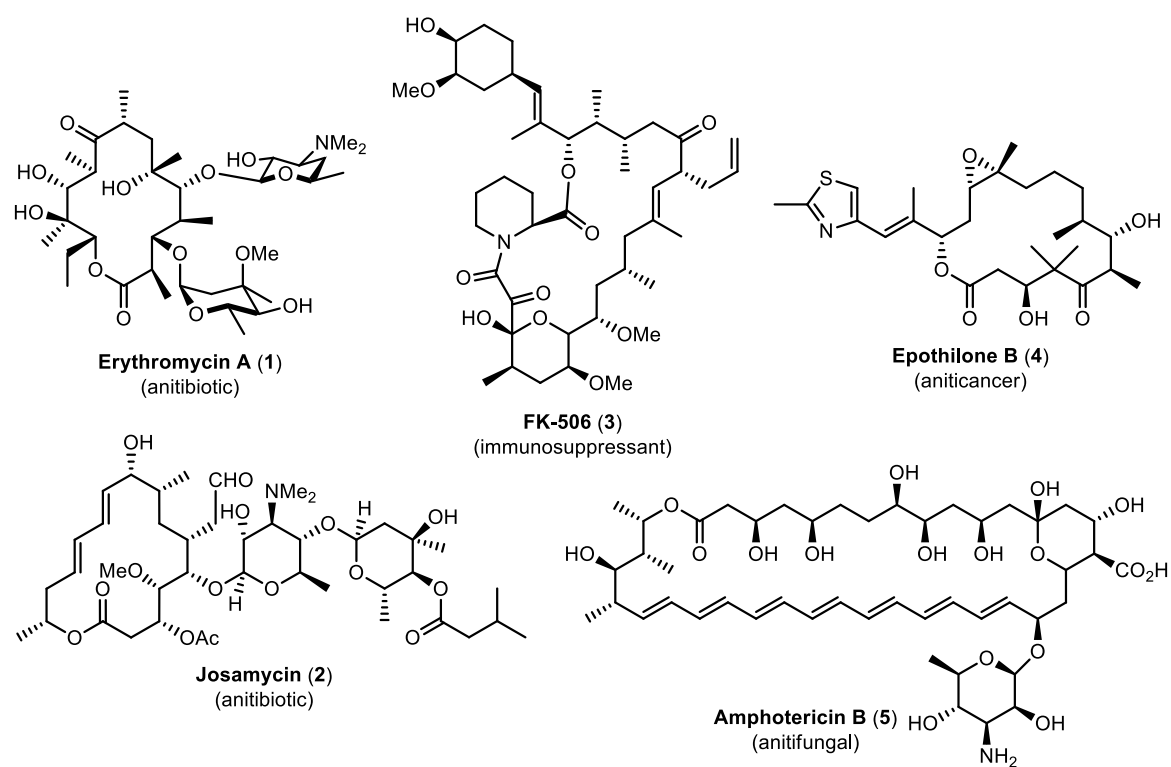
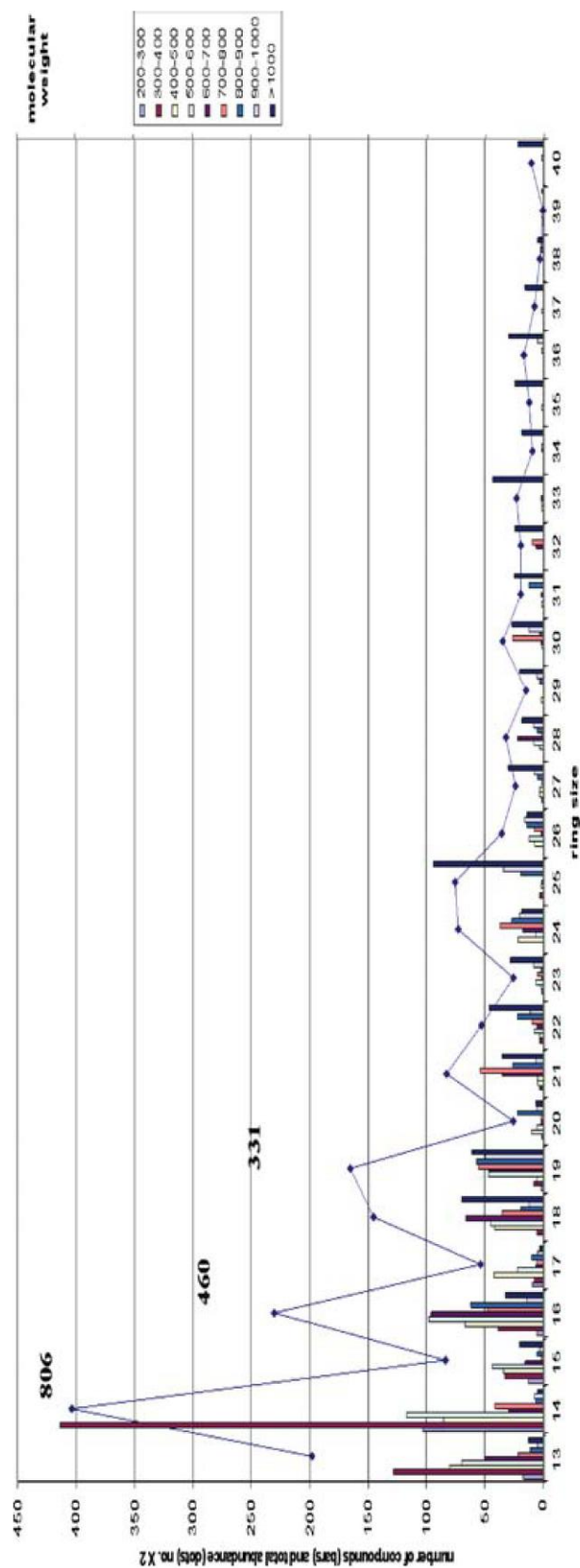


Figure 1. The representative macrolide natural products.



[Reference] Wessjohann, L. A.; Ruijter, E.; Garcia-Rivera, D.; Brandt, W. *Mol. Diversity* **2005**, 9, 171-186.

Figure 2. Distribution (number of compounds) of 100 D molecular weight ranges (bar) and total number of natural macrocycles (line connected dots) of a given ring size. The scale for the total count (abundance) is twice the scale for weight distribution given at the ordinate.

第二章 14 員環マクロライド類と生物活性

マクロライド類は前章で述べたように多くの天然物が存在し、様々な生物活性を示す。その中から、薬として使用されているものやそのリード化合物となっているものなど存在する。マクロライド類の中でも、天然由来の 14 員環マクロライド化合物は報告数が多く、生物活性も多種多様に富んでいる⁶⁾。代表的な天然物としては、前述した erythromycin A (EM A) (1)がある。また、その他に rustmicin (8)⁷⁾や sekothrixide (7)⁸⁾、migrastatin (6)⁹⁾などが存在し、それぞれ抗真菌活性、抗ガン活性を有することが報告されている (Figure 3)。その他の 14 員環大環状化合物としては clonostachydiol (9)¹⁰⁾や fluvirucin A₁ (10)¹¹⁾などがある。Clonostachydiol (9)は駆虫活性を示し、fluvirucin A₁ (10)は抗ウイルス活性を示すことが報告されている。

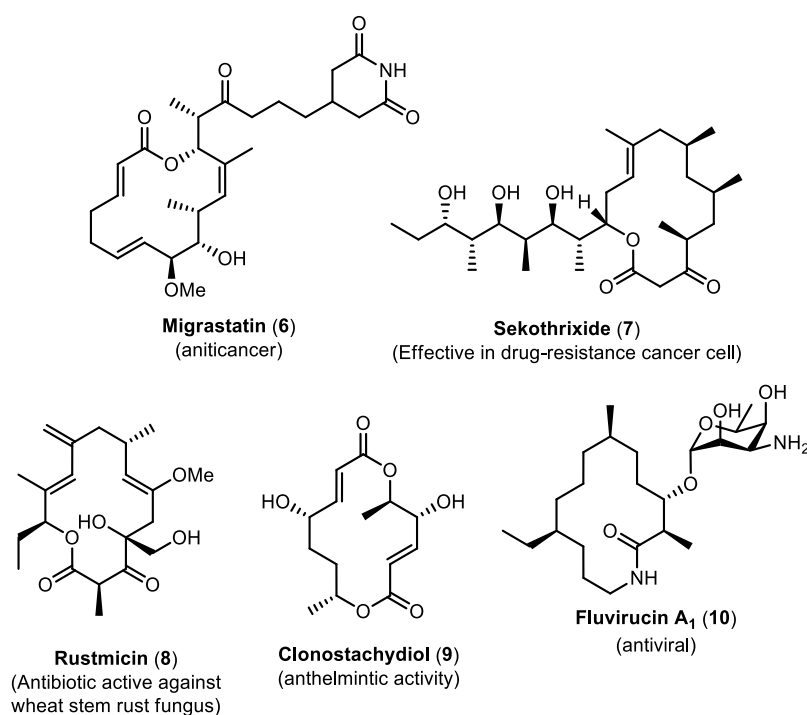


Figure 3. 14-Membered ring macrolide natural products.

さらに 14 員環マクロライド天然物を用いた誘導体合成は盛んに行われ、より高活性な化合物の創製が達成されている。例えば、抗菌剤として広く使用されている EM A (1)は多数の半合成により、新規マクロライド抗生物質を生み出してきた。EM A (1)は Kurath らによって酸性条件下における分解機構が研究され、C6 位のヒドロキシ基が C9 位のカルボニル基とヘミアセタールを形成することでその抗菌作用が失活することが明らかとなった。この知見を基にヘミアセタール化を防ぐため 9 位カルボニル基のアミノ化や 6 位ヒドロキシ基のアルキル化などを行い、酸への安定性の改善を目指した誘導体合成が多くなされた。その中の一つである azithromycin (AZM) (11)¹²⁾は Beckmann 転位によりラクトン骨格にメチル置換窒素を導入した 15 員環マクロライドであり、酸に安定かつ組織への移行性が良好で、細胞内滞留時間が長いこと高い薬物濃度が維持されるという薬物動態的な特徴を持つ。さらに、グラム陰性菌

への抗菌活性も増強されており、EM A (1)が示さなかったインフルエンザ菌に対しても抗菌活性を示す。また、大正製薬が創製し臨床で汎用されている clarithromycin (CAM) (12)¹³⁾は EM A から半合成された誘導体で、6 位の水酸基をメチル化したものである。酸に対する安定性は改善され、EM A と同様な抗菌スペクトルを持つ強い抗菌活性を示し、さらに血中濃度も高く、組織移行性にも優れている。また、副作用である消化器障害も軽減されており、プロトンポンプ阻害剤や amoxicillin と併用して *Helicobacter pylori* 除菌療法に用いられる。これら誘導体は第二世代マクロライドと位置づけられている。

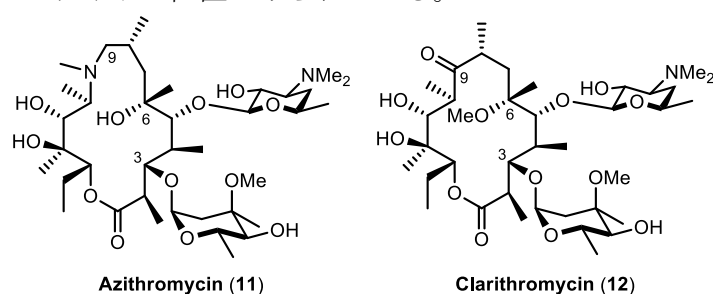


Figure 4. Second-generation macrolide antibiotics.

しかし、第二世代マクロライドが広く用いられはじめた 90 年代より呼吸器感染症の重要原因菌である肺炎球菌によるマクロライド系抗生物質に対する耐性化が問題視されてきた。1967 年にオーストラリアにおいてペニシリン耐性肺炎球菌が初めて報告されて以来、肺炎球菌の薬剤耐性化が進行し 1970 年代後半から 1980 年代にかけて、欧州を中心にペニシリン耐性肺炎球菌が増加した。さらには、1990 年代の半ばから薬剤高度耐性株が出現し、臨床上大きな問題となっている。2000 年以後の薬剤耐性菌はペニシリン系抗菌薬のみでなくセフェム系抗菌薬に対しても広く耐性を示すことが特徴であり、現在では約 31.3%が β -ラクタム系抗菌薬耐性株である。また、約 77.9%にマクロライド耐性遺伝子の発現が認められるなど、多剤耐性化が問題である。マクロライド耐性肺炎球菌の主な耐性メカニズムとして作用部位の変性や薬剤排出亢進などが挙げられる。

このような背景のもと、既存のマクロライド耐性菌に有効な新規マクロライドの開発が早急に進められた。この時、EM A (1)の誘導体として天然型より C6 位ヒドロキシ基をメチル化した後、ラクトン骨格の C3 位にあるクラジノースを除去し、生じた水酸基を酸化してカルボニル基へと変換することでマクロライド耐性菌にも有効なマクロライド（第三世代マクロライド）として、ケトライドと呼ばれる化合物が合成された。この誘導体は天然型と比較して若干の抗菌力の低下が見られたが、マクロライド耐性菌に対して有効な活性を示した。さらにマクロライド耐性菌に対する抗菌力の向上を目的としてさらなる EM A (1)の誘導化が進められ、前述の C3 位ケトン体の 11, 12 位の水酸基を環状カルバモイルとした telithromycin (13)¹⁴⁾や cethromycin (14)¹⁵⁾が合成された (Figure 5)。これらの化合物はマクロライド耐性菌、感受性菌の両方に強い抗菌活性を示すことが見出されている。

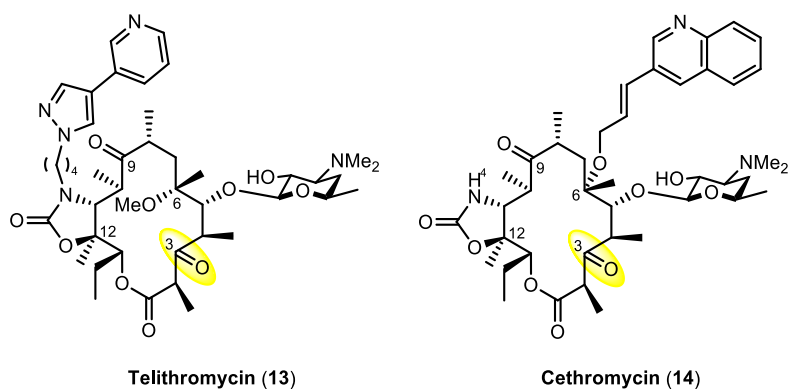


Figure 5. Third-generation macrolide antibiotics.

その他に Danishefsky らはがん細胞の転移を抑制する 14 員環マクロライド天然物 migrastatin (6) の類縁体合成を行い、その中に天然物を超えるがん転移阻害活性を示すマクロラクタム体 **15a**、大環状ケトン体 **15d**、などを見出している¹⁶⁾。具体的には、Danishefsky らは DTS (Diversity Total Synthesis) を指向した合成経路をオレフィンメタセシス反応によるマクロラクトン骨格構築を鍵工程とすることで確立し、migrastatin (6) の全合成および誘導体合成を達成している (Figure 6)。こうして見出された大環状ケトン体 **15d** は分子標的としてアクチン線維の束化タンパク質である fascin を同定するのに用いられ、fascin のアクチン結合活性阻害作用ががん細胞の転移を阻害する分子メカニズムであることを示すに至っている¹⁷⁾。大環状ケトン体 **15d** と fascin との X 線共結晶構造解析により、その結合様式も明らかにされている (Figure 7)。

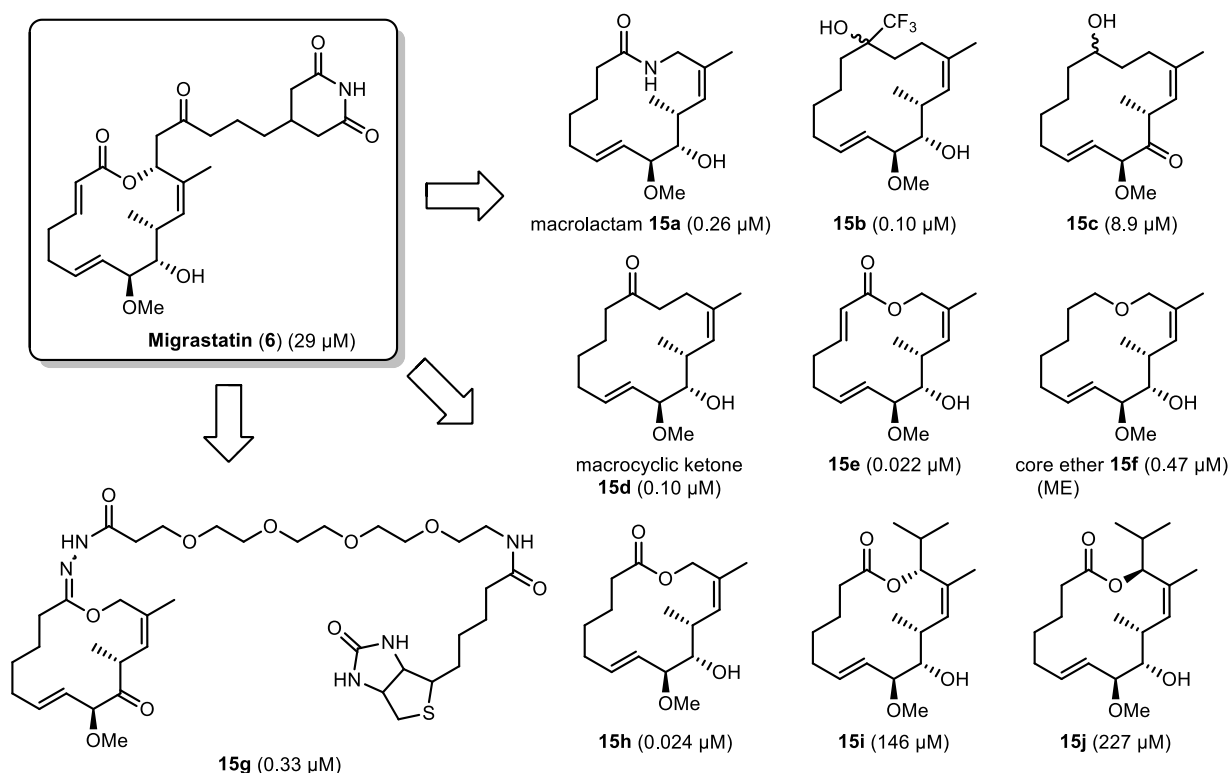


Figure 6. Migrastatin (6) and migrastatin analogs **15a-j**.

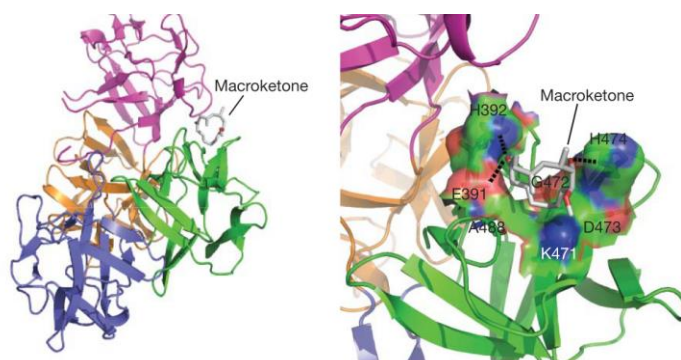
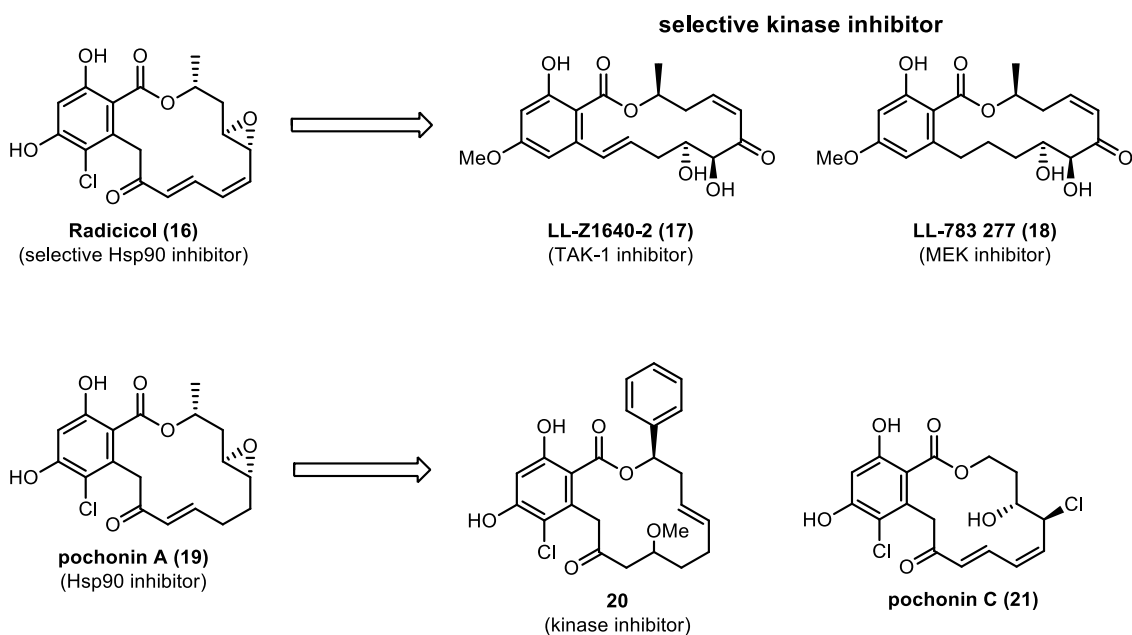


Figure 7. X-ray crystal structures of the complex of fascin and macrocyclic ketone **15d**.

さらに、Winssinger らはベンゼン環を含んだマクロライド骨格を有する天然物 radicicol A (**16**)とその類縁体 **17**, **18**、さらには類似した骨格を持つ天然物 pochonin A (**19**)などが置換基や骨格の違いによりキナーゼ阻害活性や Hsp90 阻害活性などを示すことを見出している (Scheme 1)¹⁸⁾。



Scheme 1. Radicicol (**16**), pochonin A (**19**), analogs **17**, **18**, **20** and pochonin C (**21**).

前述したように 14 員環マクロライドは非常に魅力的かつ有用な生物活性を示す天然物あるいは誘導体が多数報告され、それに伴って多くの有用な生物活性に関する知見も報告されている。当研究室も 14 員環マクロライド、特に EMA に関して以前から誘導体合成研究を行ってきた。そして、EMA の新作用として消化管収縮運動促進作用、すなわちモチリン様作用に興味を持ち、誘導体合成研究を経て多くの知見を見出している¹⁹⁾。具体的には、この作用

は 14 員環マクロライドにのみ発現し、12, 16 員環マクロライドではこの活性は見られないこと、EMA のラクトン骨格、3'位のジメチルアミノ基を化学変換することにより抗菌活性の消失とともにモチリン作用が増強することを見出している。これらの知見を基に強力なモチリン様作用を有した EM A 誘導体の合成が達成され、これら誘導体の総称としてモチライドという名称を大村らは提唱した。後に EM A 誘導体がモチリン受容体のアゴニストであることも明らかにされている²⁰⁾。

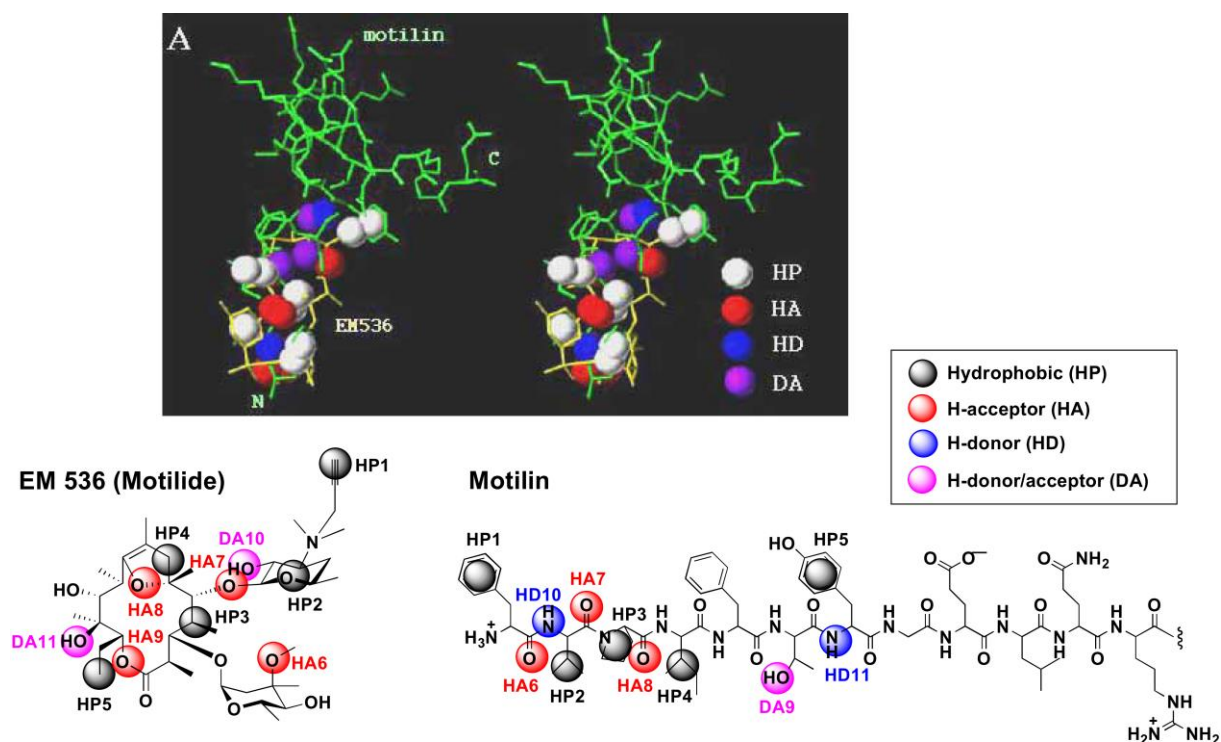
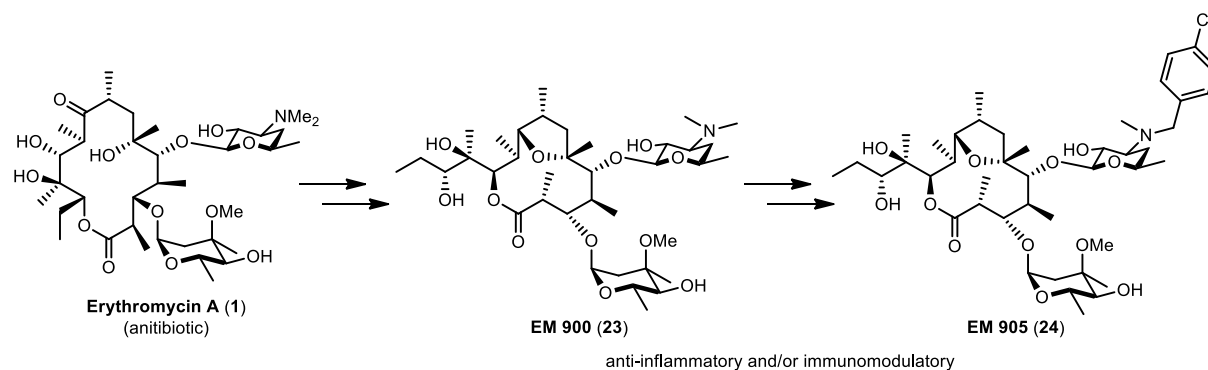


Figure 8. Comparison of structures of motilide EM536 (22) and motilin.

モチリン様作用を有した EM A 誘導体の他に、当研究室では EM A を構造変換することにより新たなマクロライド抗炎症物質の創製に成功している。難治性のびまん性汎細気管支炎 (DPB) が、EM A の少量長期投与によって改善することが日本医大の工藤らにより 1984 年に明らかにされた²¹⁾。びまん性汎細気管支炎とは、代表的な難治性呼吸器疾患であり強い呼吸器障害をきたし最近まで予後不良の疾患とされてきた。しかし、EMA の少量長期投与による治療法 (以下、EM 治療法) の登場により DPB の初診時からの 5 年後の生存率、年間死亡数は大幅に改善された。DPB に対する EM 療法の作用機序は、当初 EM A の肺移行性の高さから抗菌作用による抗炎症作用であると考えられてきたが、今日では EM A 本来の抗菌作用によるものではないと考えられている。現在も多く研究者により作用の本質の解明が進められているが、慢性気道炎症の場をとりまく免疫炎症細胞を介した抗炎症作用であることを示唆する症例などが得られている。そして、14 員環マクロライドが免疫制御および抗炎症作用を示し、慢性呼吸器疾患の治療に有用であることから筆者らのグループでは抗炎症作用のみを有するマクロライドの開発に着手し、感染研の赤川らが確立したモノサイトのマクロファージへの分化誘導促進作用²²⁾に着目し、様々な誘導体合成を進めてきた。その結果、様々な誘

導体の合成・活性評価を経て、抗菌活性とモチリン様活性が消失し、かつモノサイトのマクロファージへの分化誘導作用が **EM A** よりも約 30 倍増強した **EM 905 (24)** の創製を達成した。さらに **EM 905** はラットを用いた難治性の大腸炎モデルに実験において顕著な炎症抑制効果を示すことも見出した²³⁾。



Scheme 2. Erythromycin A (**EM A**), **EM900 (23)** and **EM905 (24)**.

14 員環マクロライドは骨格変換や官能基変換することで天然物を超えるあるいは天然物と異なる生物活性を持つ化合物が多く創製されている。このような背景を踏まえ、筆者は 14 員環マクロライド骨格が創薬リードテンプレートとして有用であると考えた。すなわち、化学合成と化学変換が容易に可能な 14 員環マクロライド骨格を設計し、それをテンプレートとして利用した新規物質の合成あるいはライブラリーの構築を行うことで新たな生物活性物質を見出すことができるだろうと考えた。

さらに近年では創薬ターゲットの一つとして蛋白質-蛋白質相互作用 (**PPI**) に注目が集まりつつある²⁴⁾。**PPI** は無数にある生体内での情報伝達において重要な役割を担っており、特定の **PPI** のみを阻害あるいは調節することでその経路を有する疾病を治療することが可能となる。標的分子に対して特異的に作用する薬は非常に有用であるが、**PPI** を低分子化合物で阻害することは酵素阻害剤や受容体の調整剤を標的とするよりも一般的に難しいと言われている。これは **PPI** に必要な蛋白質表面積が比較的大きいことに起因していること、**PPI** 表面は一般的に平らで低分子化合物が結合可能なポケット構造を持つものが少ないためである。そのため、**PPI** を阻害する低分子では蛋白質と同様に三次元的に相互作用し得る必要があると考えられ、質の高い創薬ライブラリーすなわち三次元的多様性を備える革新的なライブラリーの開発が求められている。マクロライドはフレキシブルな骨格やその他の特徴により、標的蛋白質と特異的に作用し、**PPI** を阻害あるいは調節することが大いに期待できる。従って、三次元構造多様性を指向した新たなマクロライドライブラリーを構築することは **PPI** 阻害剤を創出する上で有用なツールになり得る。

これまで述べたように 14 員環マクロライド骨格は創薬リードとして非常に魅力的であり、様々な生物活性を示す可能性が大いに期待できる分子である。しかしながら、筆者の知る限り **EM A** のように多様な生物活性について研究、応用されている 14 員環マクロライド化合物はなく、また 14 員環マクロライドライブラリーについても天然物の誘導体合成以外はほとんど報告例がない。さらに、誘導体合成で標的とされる生物活性は天然物が示すものがほとん

どである。従って、14 員環マクロライド類は非常に魅力的かつ有用な分子だが、未だ広く展開させる余地が十分にあると言える。そのことから、筆者は 14 員環マクロライド類の創薬リードテンプレートとしての価値と多様な生物活性について興味を持ち、新たな創薬研究展開を目指し、合成研究を行った。

第三章 多様性志向型合成法 (Diversity-Oriented Synthesis) と化合物ライブラリー戦略

前章では 14 員環マクロライドとその生物活性について述べた。本章では多様性指向型合成と化合物ライブラリーについて述べていく。

世界中の大学や研究所、多くの企業は独自の化合物ライブラリーを保有している。これらが保有する化合物ライブラリーは創薬研究において非常に重要なリード化合物探索の生命線である。例えば、新たな感染症やその他の病気が世界的に流行した場合、迅速に既存の化合物ライブラリーを用いた HTS (High Throughput Screening) を通してリード化合物探索を行うことが新薬開発において最初に行われることである。近年は HTS の発展により、一度に多くの化合物の活性評価を素早く行うことができるようになってきた。スクリーニングが高速化されたこととヒット率の向上が相まって、多くの化合物あるいは広いケミカルスペースを網羅した化合物ライブラリーが求められるようになってきた。

近年、S. L. Schreiber により提唱された多様性指向型合成法 (Diversity-Oriented Synthesis, DOS)²⁵⁾の考えに基づき、様々な手法で多様なケミカルライブラリーの構築が世界中で研究されている。この DOS は短工程で一つの物質から骨格自体に多様性を持たせた天然物様の化合物群を合成するアプローチ法である。様々な多成分縮合反応やメタセシス反応、カップリング反応が開発され複雑な骨格あるいは多様な置換基を持つ化合物も短工程かつ簡便に合成できるようになってきたことから、幅広く浸透し現在のライブラリー開発研究における基盤となっている。多様性志向型合成におけるライブラリー構築において、そのターゲット分子あるいは骨格の多くは天然物自体あるいは天然物に類似したものが選ばれてきた。天然物は古くから化合物ソースとして利用されており、FDA で承認されている薬の約 40% が天然物由来であると言われている。天然物が創薬研究とライブラリー戦略で重要となる理由は、その生物活性の多様さと構造の複雑さからである。天然物が持つ複雑な骨格は多くの場合豊富な sp^3 炭素を有しており、従来の合成低分子では埋められなかったケミカルスペースを十分に満たすライブラリーの構築へと導くテンプレートになり得ると言える。化合物ライブラリーを構築する上で DOS の考えを基に様々な戦略が発想されている。例として、DTS (Diversity Total Synthesis), FOS (Function-Oriented Synthesis), TOS (Target-Oriented Synthesis) などがある (Figure 9)²⁶⁾。DTS とは、共通の合成中間体から天然物自体を含む多様性に富んだアナログ体を合成する手法である。近年では共通中間体から天然物類縁体や少し異なる骨格を有する天然物類を合成した報告もある²⁷⁾。

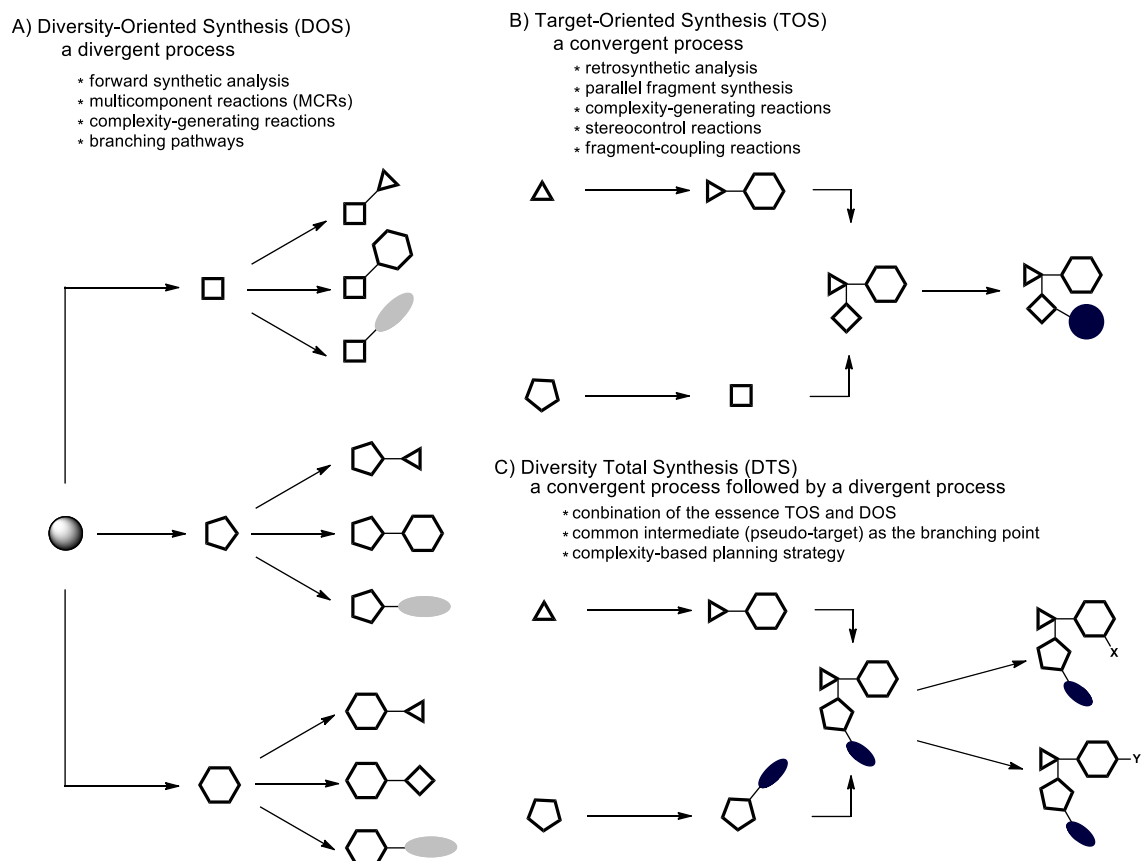
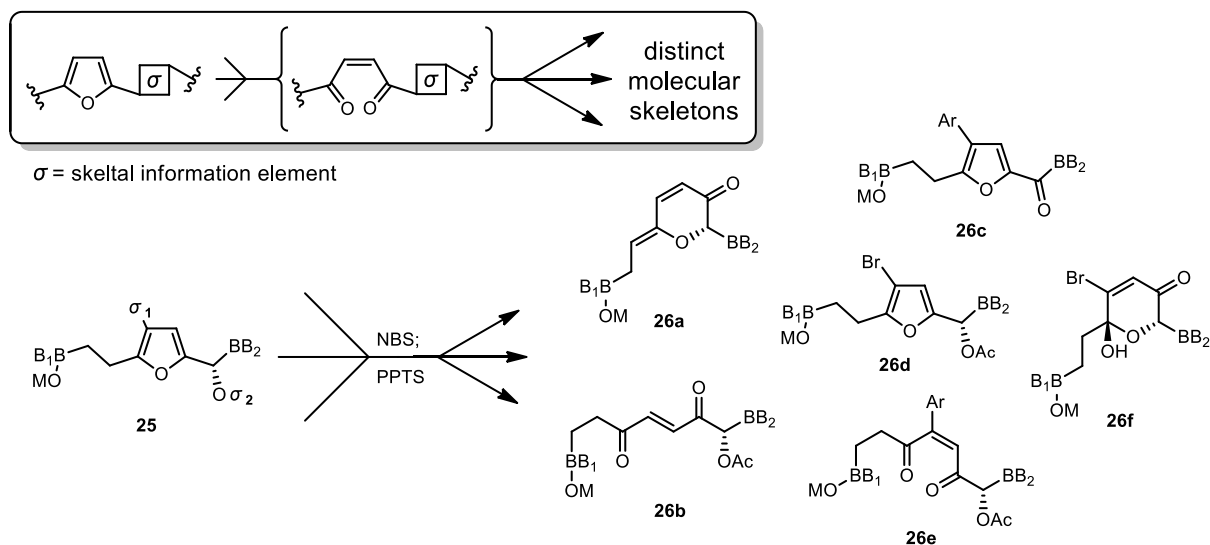
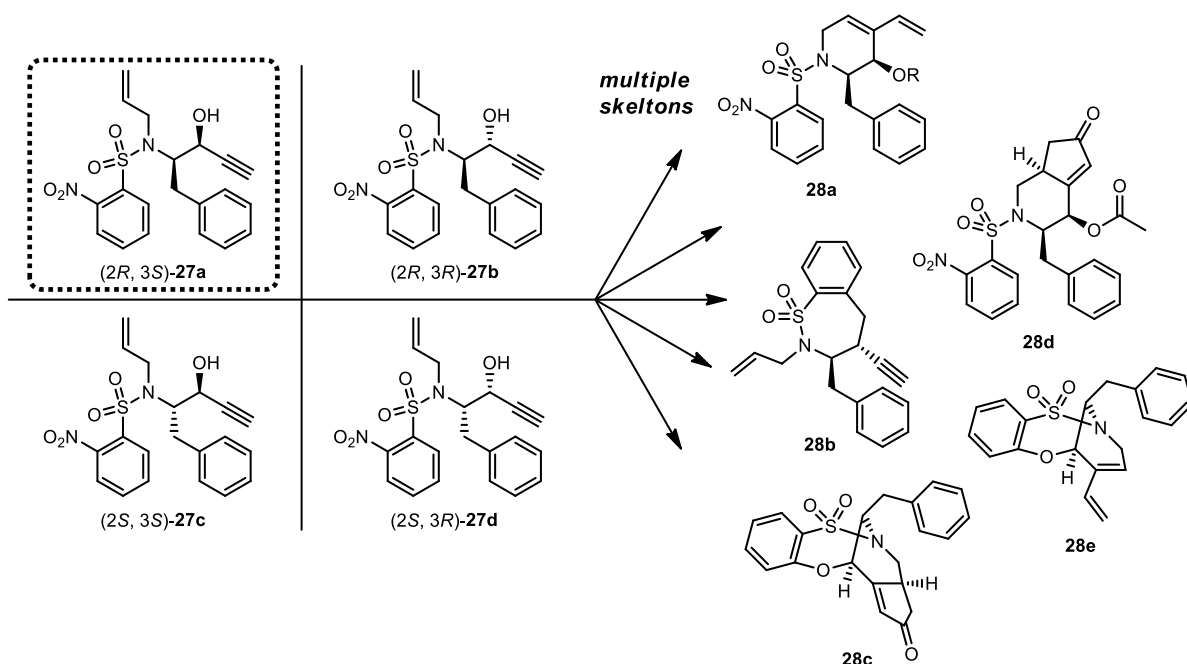


Figure 9. Diversity-Oriented Synthesis (DOS), TOS and DTS.

DOS を提唱したハーバード大学の S. L. Schreiber らはその戦略を軸に様々な化合物ライブラリーの構築を行ってきた²⁸⁾。その中で彼らは骨格多様性と官能基多様性、さらには立体化学多様性を指向した合成経路あるいは手法を開発し、数多くの多様性に富んだ分子とそのライブラリーを創製している (**Scheme 3 and 4**)。

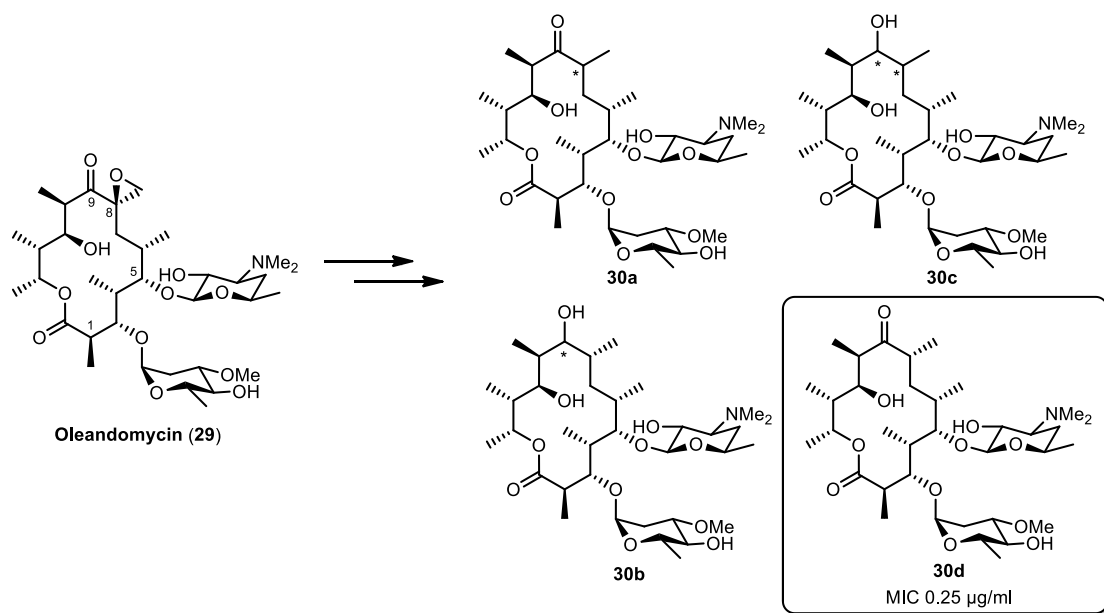


Scheme 3. The σ -element-based approach for generating skeletal diversity.



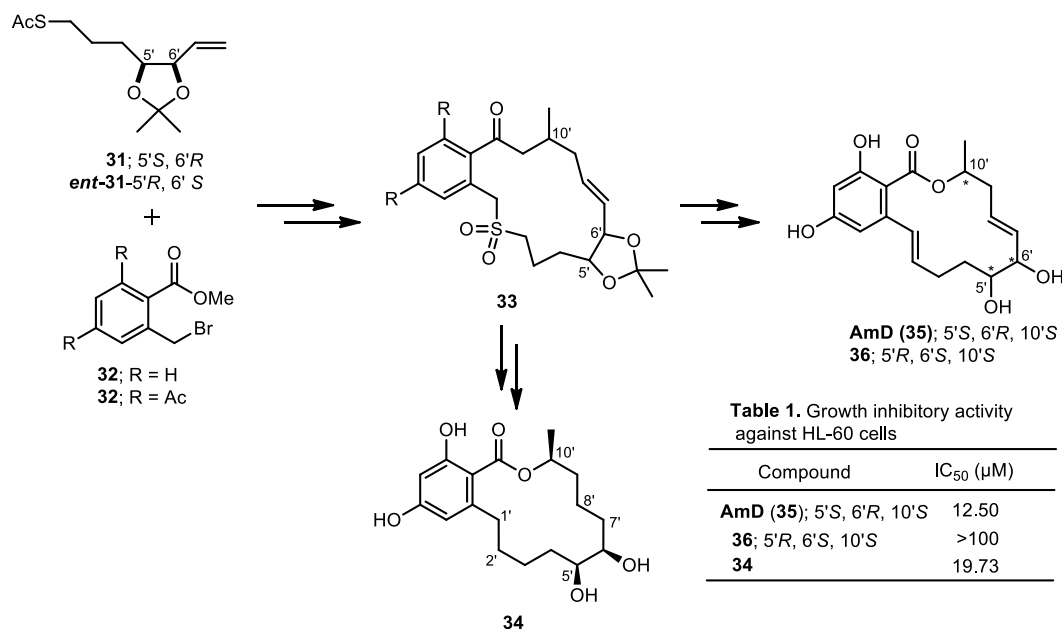
Scheme 4. The skeletal diversity of compound **28a-e**.

前述したように、現在までに Schreiber をはじめとした多くの有機合成化学者、創薬化学者達が DOS などの戦略に基づき、様々な化合物ライブラリーの開発に取り組んできた²⁹⁾。その中で、化合物の立体化学について着目した多様性指向型合成やライブラリーの構築さらには立体化学構造活性相関 (StereoStructure-Activity Relationships, SSAR)に関する研究も盛んに行われてきた³⁰⁾。例えば、G. Kragol らは oleandomycin (**29**)について C8 と C9 位の立体化学に関する異性体を数種合成し、その生物活性を評価している (Scheme 5)³¹⁾。その結果、*S. pneumoniae* に対して MIC 0.25 ($\mu\text{g/ml}$)の値を示す誘導体 **30d** と IL-6 inhibition (50 μM) 61%, 69%の値を示す誘導体を見出している。



Scheme 5. Stereochemistry on the biological activity of oleandomycin derivatives.

また、J. E. Harvey らは 14 員環マクロライド天然物である aigialomycin D (**35**) に関して全合成と誘導体合成を行い、それを生物活性評価を行っている (Scheme 6, Table 1)。その結果、5'位と 6'位の水酸基の立体化学が生物活性に大きく影響することを見出しており、計算化学により三次元コンフォメーションを算出してその違いが活性に大きく影響していることを見出している (Figure 10)³²⁾。

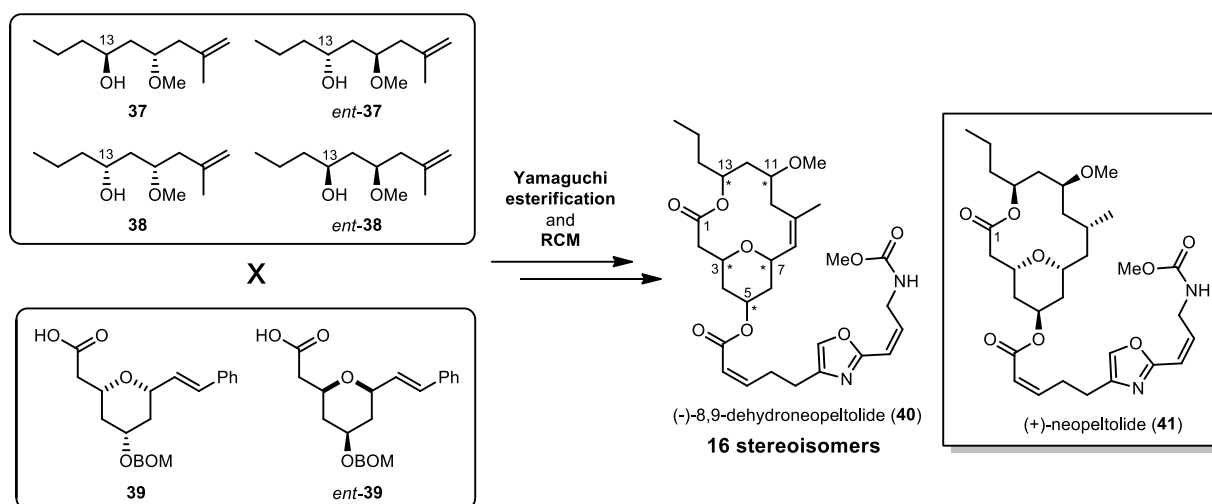


Scheme 6. The synthesis of aigialomycin D (**35**) and analogues **34**, **36**.



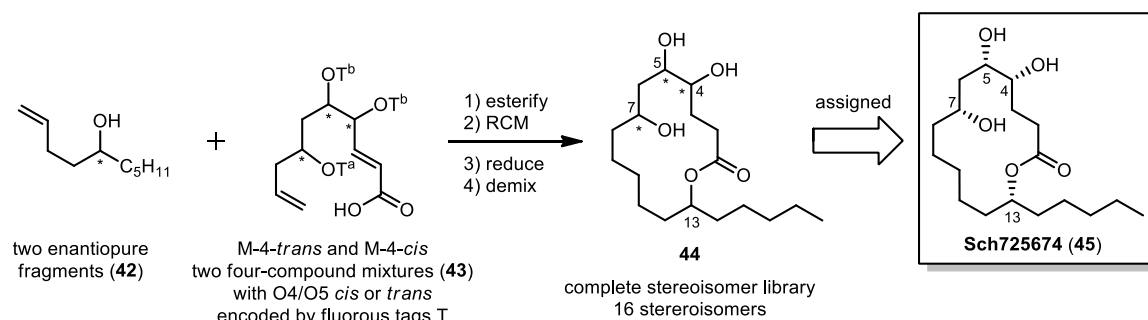
Figure 10. Lowest energy conformations of compounds AmD (**35**) and **36**. (1; AmD, 2; **36**)

さらに、いくつかの研究グループはマクロライド天然物の全合成研究に加え、多くの立体異性体を合成することで立体化学多様性ライブラリーを構築している。例えば、不破、佐々木らは天然物 neopeltolide (**41**) においてオレフィンメタセシスを鍵反応とした合成経路を確立し、その全合成を達成した³³⁾。そして、確立した合成経路を基に Scheme 7 に示す 4 種の立体異性体と 2 種の立体異性体をカップリングさせることで 8,9-dehydroneopeltolide (**40**) について 16 種類の立体異性体を合成している。それらは生物活性評価を行い、強い抗腫瘍活性を示す誘導体を見出している。



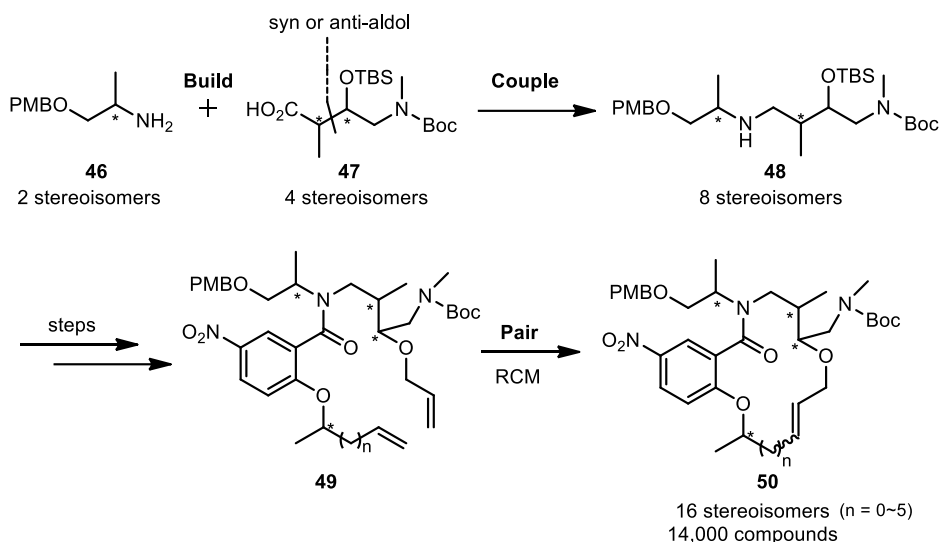
Scheme 7. The synthesis of (-)-8,9-dehydroneopeltolides (40).

また、D. P. Curran らはフルオラスケミストリーを応用した新たな合成手法によりマクロライド天然物 Sch725674 (45) の立体化学の異なるすべてのジアステレオマー体を合成している (Scheme 8)³⁴。そして、ライブラリーから天然物の NMR と一致するものを見出し、Sch725674 (45) の絶対立体構造を決定している。



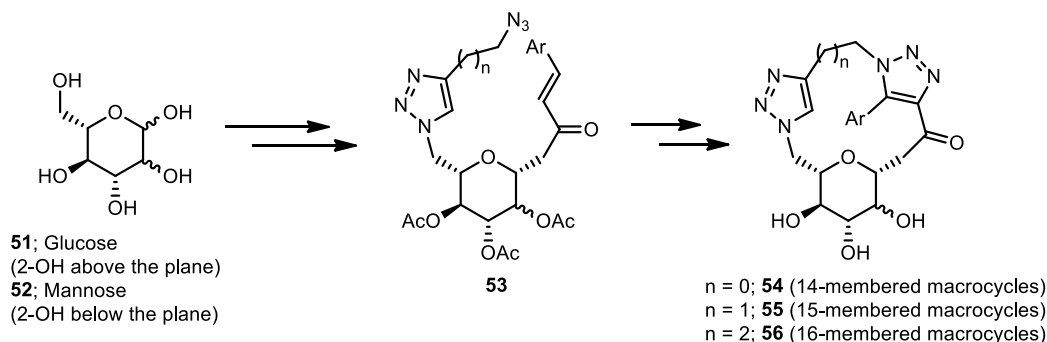
Scheme 8. The synthesis of 16 stereoisomers 44 of Sch725674 (45).

マクロライド天然物以外に関しても DOS の戦略に基づいた立体化学多様性を指向した大環状化合物ライブラリーの開発研究がなされている。最も一般的であろう手法の一つとして build/couple/pair (B/C/P) アプローチが挙げられる。L. A. Marcaurelle のグループはこのアプローチにより、RCM により環化することで 13~18 員環マクロラクタムを合成し、14,000 個の化合物ライブラリーを構築している (Scheme 9)³⁵。



Scheme 9. DOS of 16 stereoisomers **50** of macrolactams via BCP approach.

さらに、Click Chemistry によりトリアゾール環を包括した大環状化合物の合成も容易であることから、これを利用したライブラリーの構築研究も報告されている³⁶⁾。R. S. Ampapathi と R. P. Tripathi らは、アジドとアルキンまたはアルケンのトリアゾール化を利用し、14-16 員環の大環状化合物の創製を行っている (**Scheme 10**)。そして、コンフォメーション解析により三次元構造の違いを考察し、生物活性評価についてもヒト乳がん細胞 (MCF-7 cell line) に対する成長阻害活性を示し、抗腫瘍効果が見出されている (**Figure 11**)。



Scheme 10. The synthesis of macrocyclic glycoconjugates **54-56**.

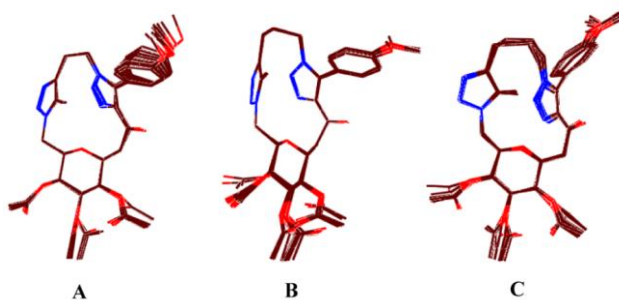
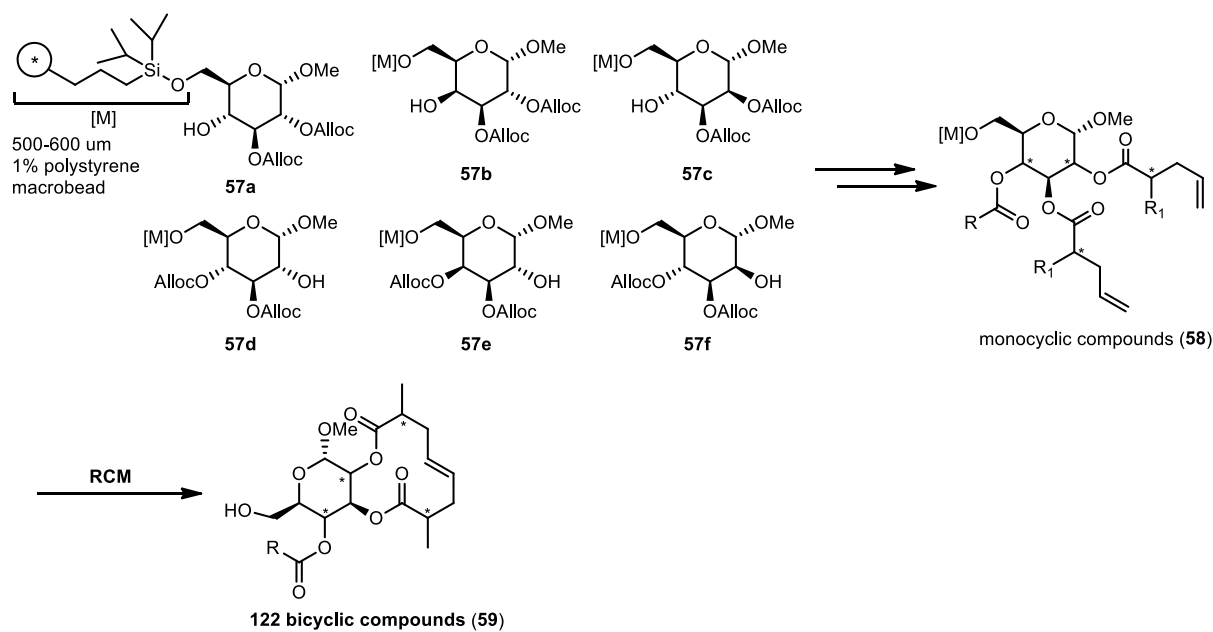


Figure 11. Restrained MD structures of macrocycles. 15 lowest energy structures superimposed of 14-membered macrocycles (A), 15-membered macrocycles (B), 16-membered macrocycles (C).

また、S. L. Schreiber らは 12 員環マクロジオライド骨格を含むビスクロ化合物をマイクロビーズを利用した合成方法により、立体化学多様性を実現したライブラリーを構築している (Scheme 11)³⁷。合成したモノシクロ化合物群 (58) とビスクロ化合物群 (59) を Multidimensional screening で 40 種類の生物活性試験を並行して行ったところ、そのヒット率はモノシクロ化合物群に比べてビスクロ化合物群の方が約 2 倍近く高い結果となったと報告している。



Scheme 11. Relationship of stereochemical and skeletal diversity of small molecules.

前述したように、S. L. Schreiber が DOS を提唱してから十数年しか経っていないが、多くの有機合成化学者により多種多様な合成手法とケミカルライブラリーが開発されている。また、Schreiber らのグループは自身の戦略と構築したケミカルライブラリーからこれまでに Vorinostat (Zolinza®; Merck) (60) や Romidepsin (Istodax®; Celgene) (61) などの FDA 承認された新薬の創製に貢献しており (Figure 12)³⁸、DOS と多様なケミカルライブラリーの有用性を証明している。

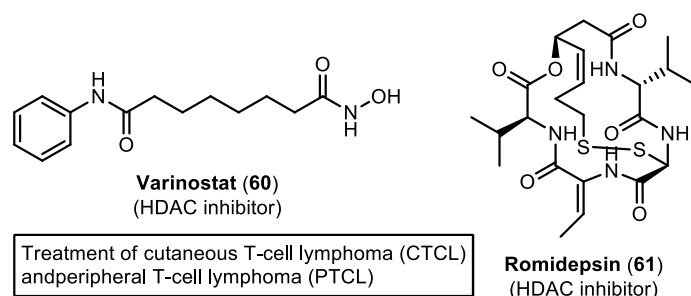


Figure 12. New anti-cancer drugs have been approved by FDA.

北里研究所も独自の天然物ライブラリーを保有しており、その中にもマクロライド天然物は数多くある。さらに長年マクロライドに関する研究を続けてきたことから、北里研究所で単離した kitasamycin や avermectin などの天然物を基盤にした誘導体合成により、約 2000 種類以上のマクロライド化合物を保有している。そして、抗 MRSA 活性や単球分化誘導作用などの生物活性を試験してきた。その結果、EM 誘導体や SPM 誘導体が有する抗 MRSA 活性や EMA 誘導体が有する単球分化誘導作用の発現や増強などの知見を明らかにしてきた。

しかし、北里研究所が保有するマクロライドライブラリーはほとんどが天然物からの誘導体である。天然物からの誘導体は時間の短縮や手間の少なさといったメリットがあるが、同時に、既に定まった構造からの修飾であるため誘導化の範囲はそれほど広がらない、大量供給が難しい場合があるというデメリットも存在する。特に天然物において大幅な化学変換が困難であることは十分なケミカルスペースを網羅したライブラリー構築を行うためには解決すべき問題点である。そこで、天然型からの誘導化ではなく、全ての骨格を含めて全合成的に非天然型の化合物を創製し、ライブラリーの構築を行うことを考えた。すなわち、筆者は博士後期課程の研究テーマとして三次元構造多様性を指向したライブラリーの構築と新たな生物活性物質の創製を最終目標とし、独自に設計したテンプレートによるマクロライドの合成およびライブラリーの構築を発想し、着手することにした。

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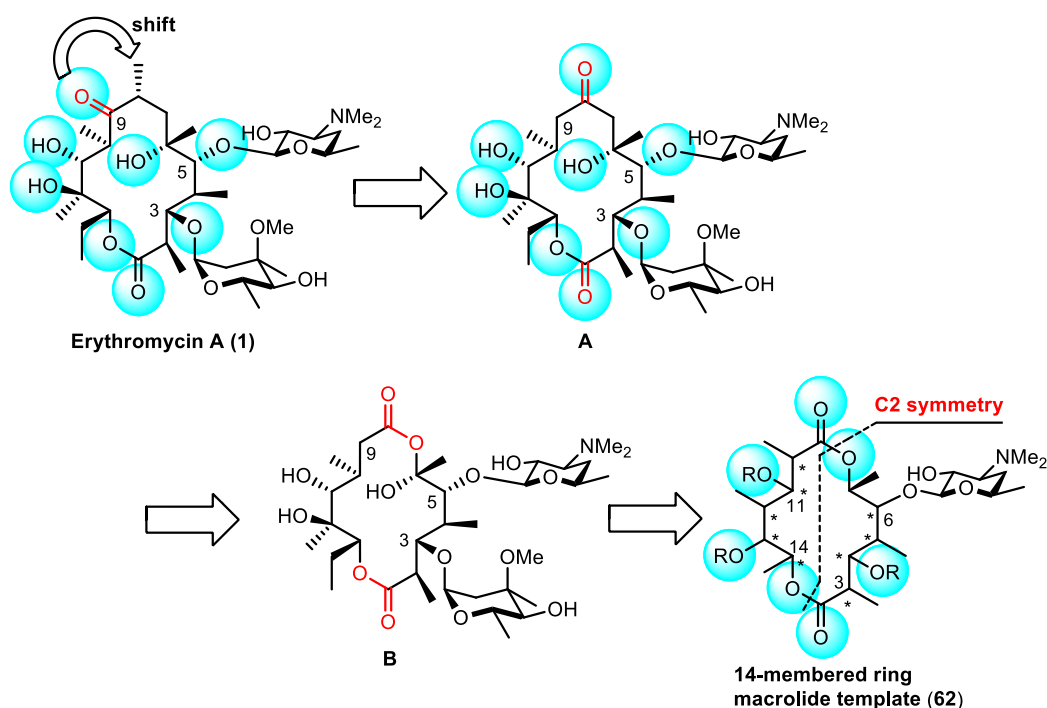
II. 本論

第一章 エリスロマイシンを模倣した C2 対称マクロジオリドテンプレートの設計と三次元構造多様性を指向した合成戦略

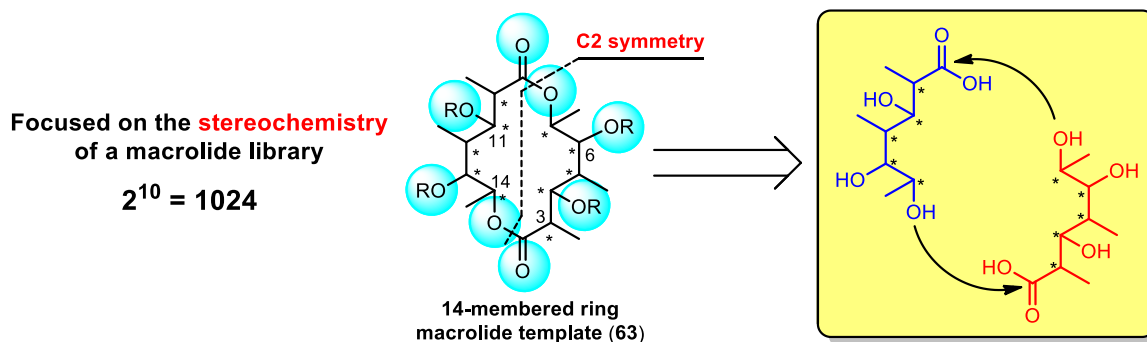
序論で述べた通り、14 員環マクロライド骨格を創薬リードテンプレートと考え、三次元構造多様性を指向したライブラリーの構築研究に着手した。三次元構造多様性を目指したライブラリーを構築する上で、筆者はまず合成標的かつライブラリーの基盤となるテンプレートの設計を行った。テンプレートで重要となるファクターは、合成の簡便さ、多様性の豊富さ、生物活性を示す可能性であると考え、天然物である erythromycin A (**1**)に着目した。すなわち、多様な生物活性を示す erythromycin A (**1**)をモチーフとして新たなテンプレートを発想することとした (Scheme 12)。

まず、erythromycin A (**1**)を基盤として 9 位にあるカルボニル基を隣の 8 位へとシフトさせた。これにより、14 員環マクロライド骨格上に二つのカルボニル基が向かい合う形 (**A**)となり、これを基点とすることで C2-symmetric な構造 (**B**)へと導くことができると考えた。すなわち、14 員環骨格を C2 対称とすることで簡便な合成が可能になると考え、新たにマクロジオリド骨格をテンプレートとして発想した。次に、三次元構造多様性を持たせるべく骨格上の置換基をメチル基と水酸基のみにすることとした。特に、エステル基を除いた骨格上にできる限り多くの sp^3 炭素を含むように置換基を配置した。さらに生物活性の発現を指向すべく、モチーフの erythromycin A (**1**)の酸素原子の数に着目した。テンプレートのマクロジオリドにも同数の酸素原子を似たような位置に配置させることでこれらが水素結合のドナーやアクセプターとして働き、多様な生物活性が発現しうることを期待した。さらに、erythromycin A (**1**)などの抗生物質と同様にアミノ糖を配置することで抗菌活性の発現も期待した。以上をふまえ、C2 対称ジラクトン骨格を持ったマクロライドテンプレートを新たに発想した。

設計したテンプレートは C2 対称骨格マクロジオリドであることから、二つのハーフユニットを組み合わせることで簡便な合成が可能であると考えられ、骨格上には 10 個の不斉炭素原子を有することから三次元的にフレキシブルな構造であるといえる (Scheme 13)。10 個の不斉炭素を有するため、立体化学の組み合わせにより理論上 $2^{10} = 1024$ 通りの立体異性体、すなわちマクロライド誘導体が考えられる。また、水酸基を 4 個有しており、マクロジオリドテンプレートライブラリーを構築後に様々な化学修飾を行うことでより多様性を実現したマクロライドライブラリーの構築ができると考えた。



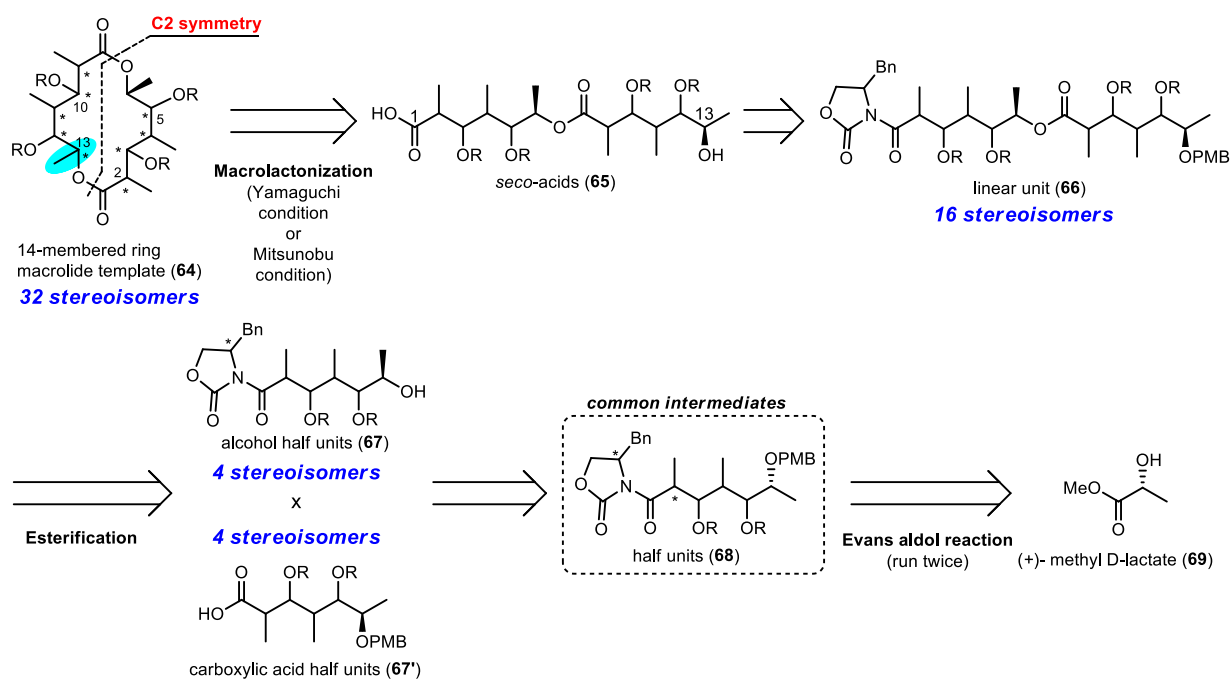
Scheme 12. Design of a new macrolide template (**62**) inspired by erythromycin A.



Scheme 13. The convergent construction of C2-symmetric macrodiolide skeleton.

ライブラリーを構築するための基盤となるテンプレートの設計は **Scheme 12** に示した。次にこれを基盤とし、独自のマクロライドライブラリーの構築を行うため、合成戦略とライブラリーの構築法について着手した。設計したテンプレートは理論上 1024 通りの異性体が合成可能であるが、実際に三次元コンフォメーションの多様性が生じていることを確認するためにまず 32 種の異なる立体化学異性体のマクロジオライドテンプレートの合成を試みることにした。32 種の立体異性体の合成計画を以下に示す (**Scheme 14**)。マクロジオライドテンプレート **64** はセコ酸 **65** からマクロラクトン化で環化させることで合成できると考えた。その際、山口法と光延法の二つの条件により環化させることにした。これは環化する際に、反応メカニズムが異なることから、13 位の立体化学の反転を伴うか伴わないかにより 2 種の立体異性体マクロジオライドテンプレートをつくり分けることができると考えた。環化前駆体と

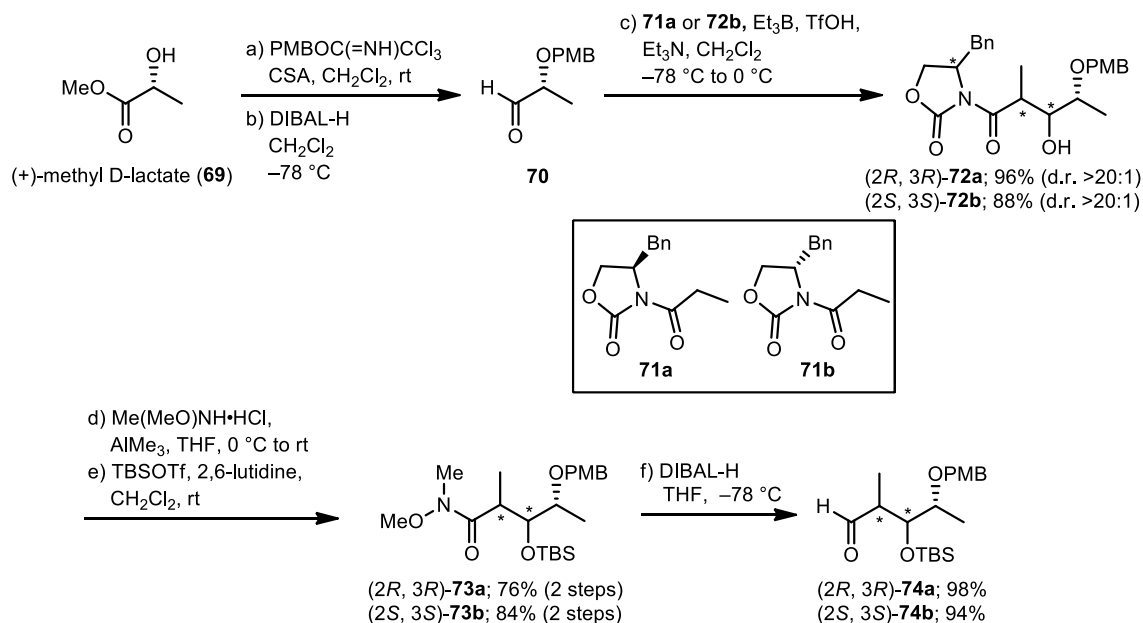
なるセコ酸 **65** はリニアユニット **66** から導けるとし、そのリニアユニット **66** は二つのハーフユニットのアルコール **67** とカルボン酸 **67'** を縮合することで合成できると考えた。これにより、様々なハーフユニットを調製することで多様性に富んだ合成が可能になる。また、縮合させるハーフユニット **68** はそれぞれの立体化学を制御することを考え、二度の Evans aldol 反応により増炭していくことで、市販の(+)-乳酸メチル **69** から合成できるとした。



Scheme 14. The stereochemical divergent approach to 32 stereoisomers using a 14-membered ring macrolide template.

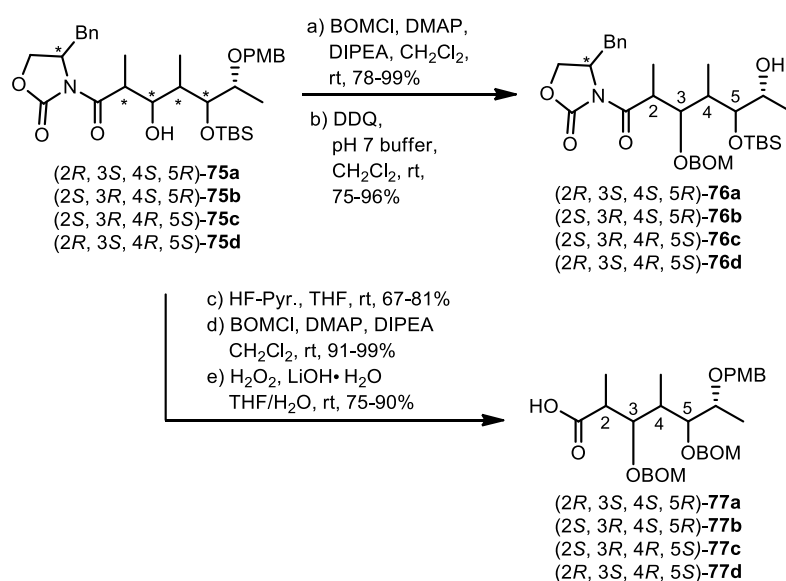
第二章 立体化学多様性を指向したマクロジオリドテンプレートライブラリーの構築

次に実際の合成とライブラリーの構築へと着手した。市販されている(+)-乳酸メチル **69** を出発原料とし、トリクロロアセトイミデートを用いた水酸基の PMB 保護、エステル基の DIBAL-H 還元を経て既知化合物であるアルデヒド体 **70**¹⁾へと導いた。続いて、一度目の Evans aldol 反応²⁾により 2 種の立体の異なるアルドール成績体 **72a, b** を合成した。2 種のアルドール成績体のうち片方の(2*S*, 3*S*)-**72b** は既知化合物³⁾であるため、論文に報告されている ¹H, ¹³C NMR と旋光度を比較した。その結果、NMR と旋光度ともに良い一致を示したため目的のアルドール成績体 **72b** が合成できたことを確認した。続いて、得られたアルドール成績体 **72a, 72b** をそれぞれワインレブアミド化した後、二級水酸基を TBS 基により保護した。ワインレブアミド化反応の精製時、望みの生成物と副生成物であるオキサゾリジノンのスポットが TLC 上で重なっており、シリカゲルカラムクロマトグラフィーによる精製で分離することができなかった。そこで精製せずに次の反応に進むこととし、TBSOTf を過剰量用いて水酸基の保護を行った。合成した TBS 保護体 **73a** および **73b** はそれぞれシリカゲルカラムクロマトグラフィーにより単離精製することができ、それぞれを 2 工程収率 76%, 84%で得ることができた。続いて、DIBAL-H 還元によりアルデヒド体 **74a, 74b** へと導き、それぞれ収率 98%, 94%で合成した。



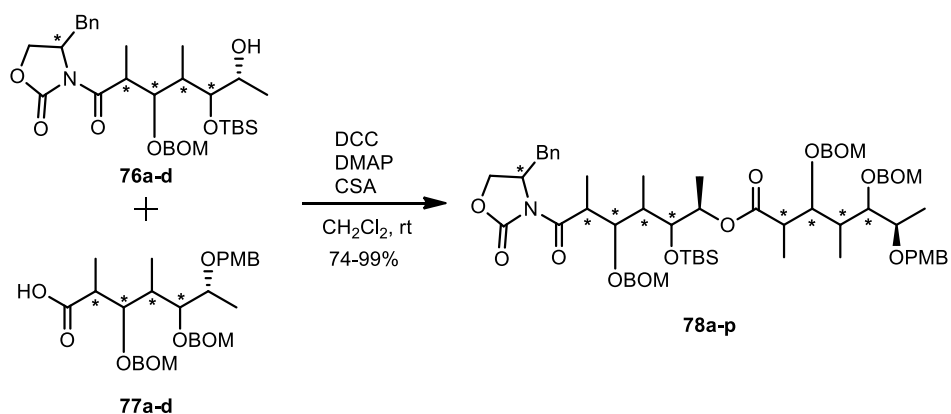
Scheme 15. The synthesis of aldehydes **74a, 74b**.

合成したアルデヒド体 **74a, 74b** を用いて、二度目の Evans aldol 反応を試みた。キラル補助基であるオキサゾリジノン **71a, 71b** を用いた *syn*-アルドール反応であることから生成するハーフユニットは 4 種類となる。実際に反応を試みた結果、それぞれの異なる立体化学を持つハーフユニット **75a-d** を高収率、高選択的に合成することができた。ハーフユニット **75a-d** の立体化学、構造、収率などを Table 2 にまとめて示す。



Scheme 16. The synthesis of alcohols **76a-d** and carboxylic acids **77a-d**.

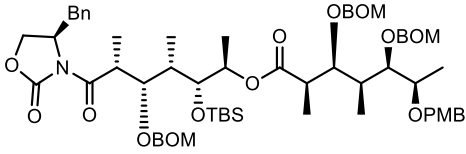
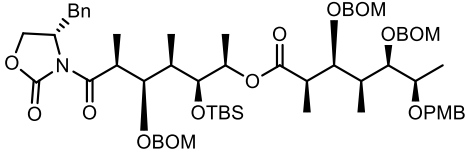
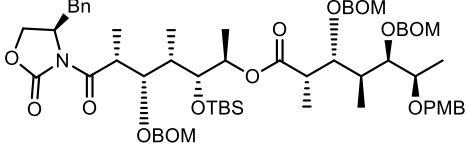
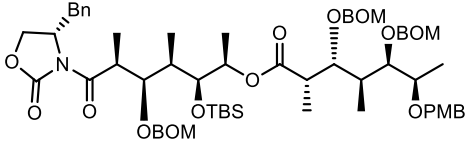
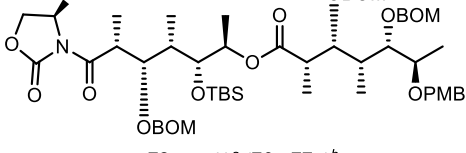
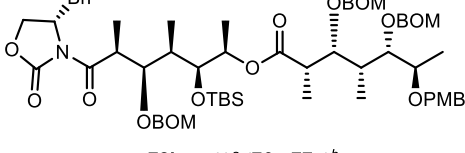
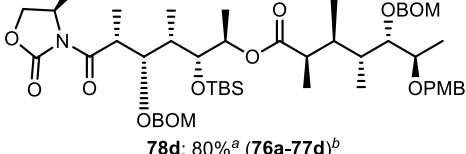
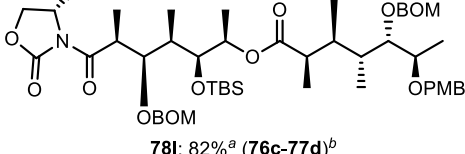
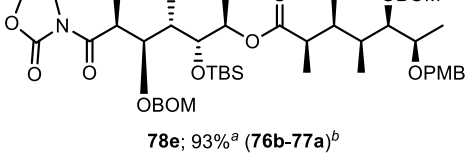
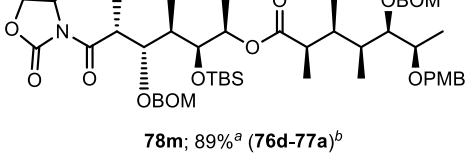
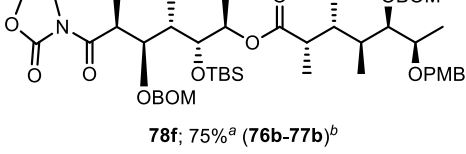
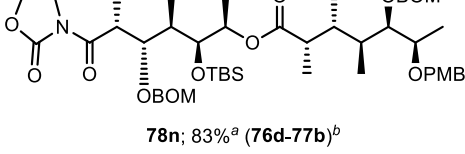
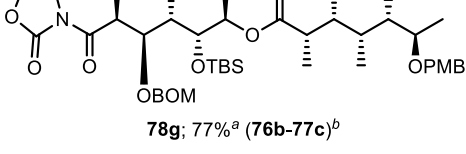
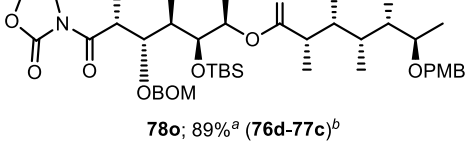
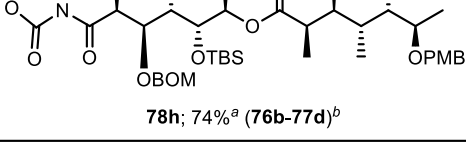
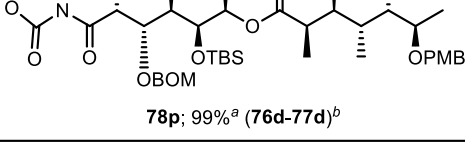
異なる立体化学を持つアルコール体を 4 種 (**76a-d**)、カルボン酸体を 4 種 (**77a-d**) 合成したため、これらを可能な限り組み合わせた 16 種の異なる立体化学を持つリニアユニットの合成を試みた。その結果、DCC, DMAP, CSA 条件下の Keck エステル化⁴⁾によりそれぞれの組み合わせのリニアユニット **78a-p** を良好な収率 (74-99%) で得ることができた (Scheme 17, Table 3)。



Scheme 17. The synthesis of linear units **78a-p** via Keck esterification.

Table 3. The yields and structures of linear units **78a-p**.

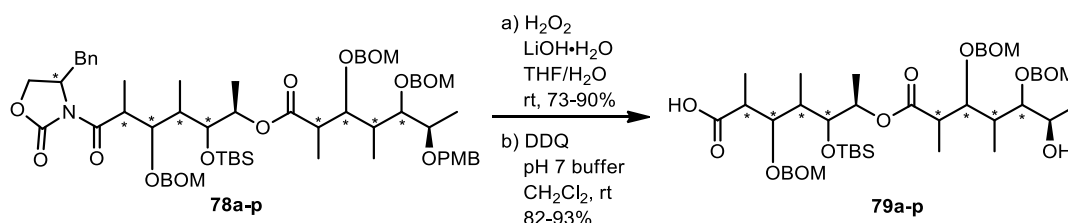
Compound; % Yield (Alcohols **76**-Carboxylic acids **77**)

 78a ; 83% ^a (76a-77a) ^b	 78i ; 97% ^a (76c-77a) ^b
 78b ; 82% ^a (76a-77b) ^b	 78j ; 79% ^a (76c-77b) ^b
 78c ; 74% ^a (76a-77c) ^b	 78k ; 77% ^a (76c-77c) ^b
 78d ; 80% ^a (76a-77d) ^b	 78l ; 82% ^a (76c-77d) ^b
 78e ; 93% ^a (76b-77a) ^b	 78m ; 89% ^a (76d-77a) ^b
 78f ; 75% ^a (76b-77b) ^b	 78n ; 83% ^a (76d-77b) ^b
 78g ; 77% ^a (76b-77c) ^b	 78o ; 89% ^a (76d-77c) ^b
 78h ; 74% ^a (76b-77d) ^b	 78p ; 99% ^a (76d-77d) ^b

^a; Isolated yield.

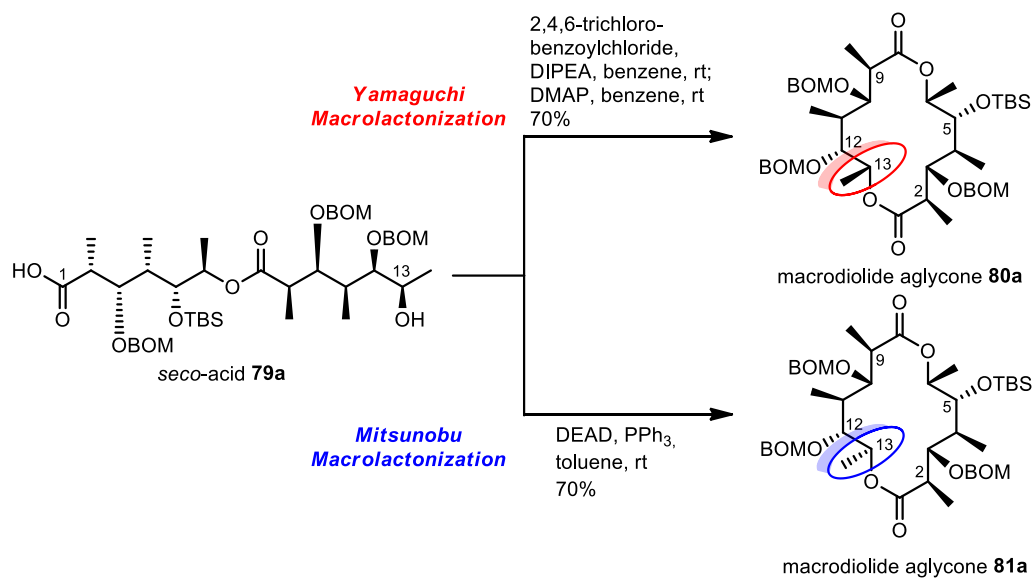
^b; The number of parenthesis indicates alcohols **76** and carboxylic acids **77**.

Keck エステル化により合成したそれぞれのリニアユニット **78a-p** を系内で発生させた LiOOH を用いたイミド選択的加水分解によりキラル補助基であるオキサゾリジノンの除去を行いカルボン酸へと変換した⁵⁾。続いて DDQ により PMB 基の除去を行うことで対応するセコ酸 **79a-p** へと導いた。

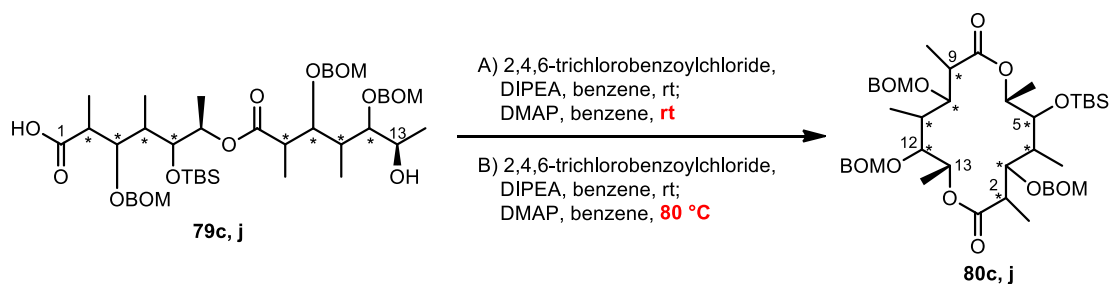


Scheme 18. The synthesis of *seco*-acids **79a-p**.

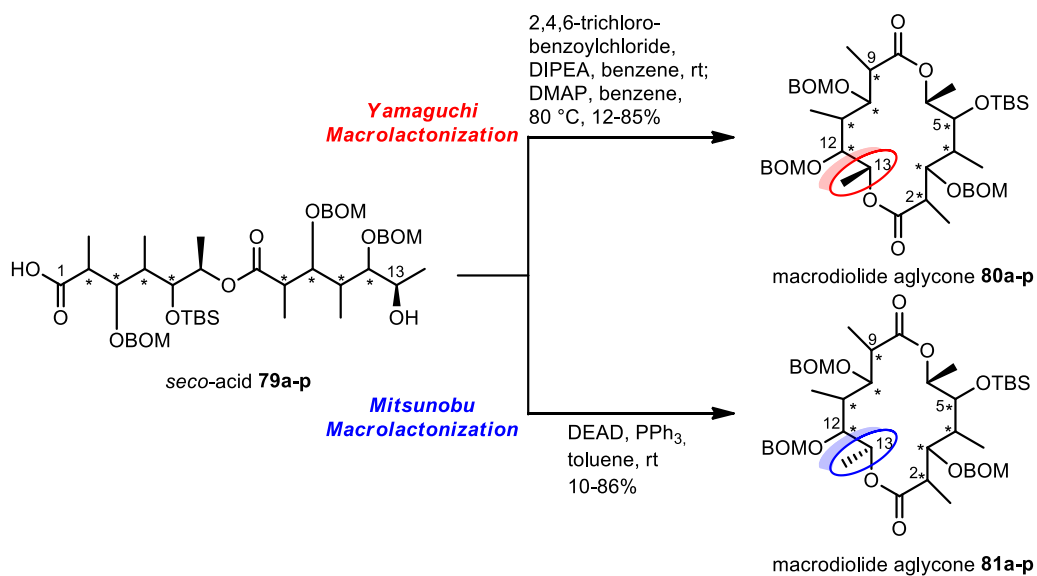
環化前駆体、すなわち 16 種のセコ酸が合成できたため、次にマクロラクトン化を行い対応するマクロジオライドの合成を試みた。マクロラクトン化の反応条件は山口法⁶⁾と光延法⁷⁾を選択した。前述した通り、この二つは反応メカニズムが異なるためマクロラクトン化させることで、1 つのセコ酸から 2 種類の立体異性体をつくり分けることができる。すなわち、山口マクロラクトン化では 13 位の立体化学が保持されたまま環化反応が進行するが、光延マクロラクトン化では 13 位の立体化学が反転して環化反応が進行する。これにより、16 種のセコ酸から 32 種のマクロジオライドが合成可能であると考え、実際の合成を行った。最初にセコ酸 **79a** を用いて山口マクロラクトン化を行ったところ、室温条件下においてマクロジオライド **80a** を収率 70% で得ることができた (**Scheme 19**)。また、光延マクロラクトン化の場合も良好な収率でマクロジオライド **81a** を得ることができた。一方、立体異性体であるその他のセコ酸を用いて同様に山口マクロラクトン化を行ったところ、室温条件下では環化反応が進行しなかった (**Scheme 20, A**)。そこで反応条件を室温から 80 °C まで昇温して環化を試みたところ、反応の進行が確認でき目的のマクロジオライドを得ることができた (**Scheme 20, B**)。そのため、山口マクロラクトン化では加熱条件 (80 °C) を最適条件とし、その他のマクロジオライドの合成を行った (**Scheme 21**)。その収率と合成したマクロジオライドの構造を **Table 4** にまとめて示した。一方、光延マクロラクトン化は室温条件下で環化が進行し、対応するマクロジオライドをそれぞれ合成することができた。その収率と対応するマクロジオライドの構造を **Table 5** にまとめて示した。これにより、16 種のセコ酸 **79a-p** から 32 種のマクロジオライドの合成し、マクロジオライドテンプレートライブラリーの構築を達成した。



Scheme 19. The macrolactonization of *seco*-acid **79a**.

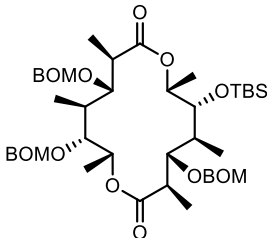
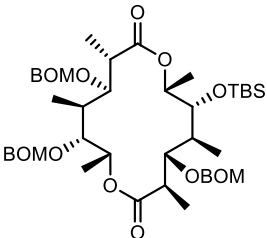
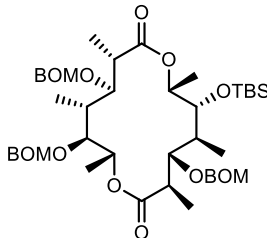
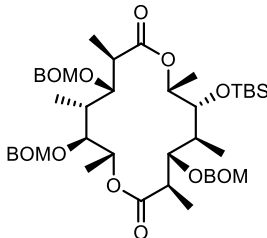
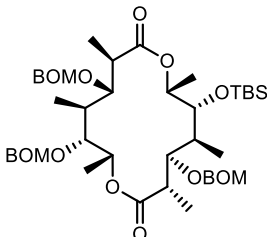
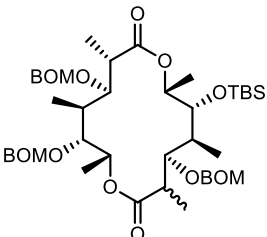
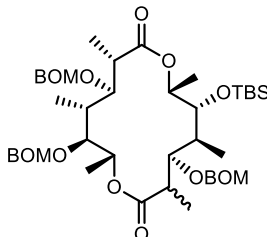
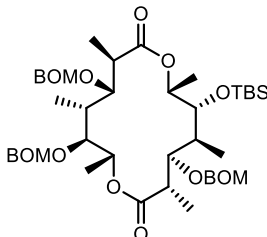
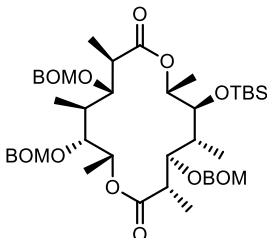
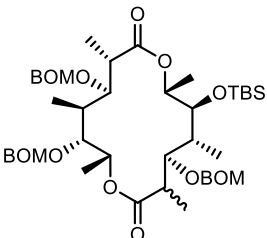
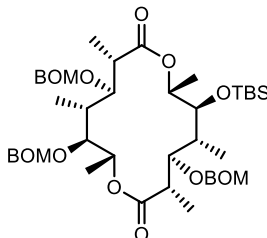
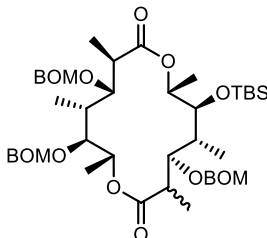
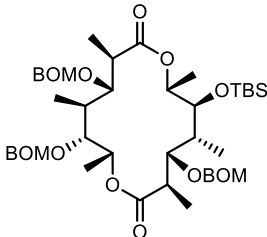
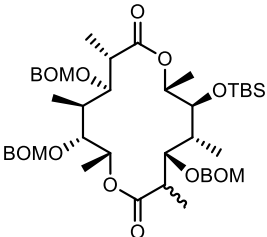
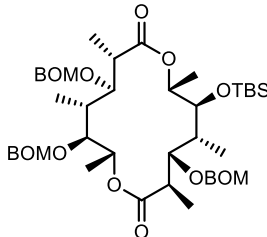
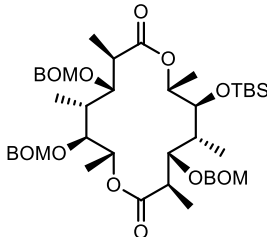


Scheme 20. The macrolactonization of *seco*-acids **79c, j**.



Scheme 21. Yamaguchi macrolactonization and Mitsunobu macrolactonization.

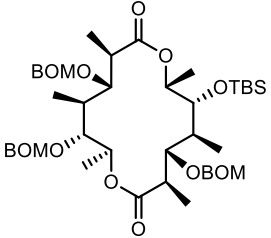
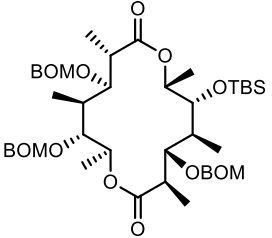
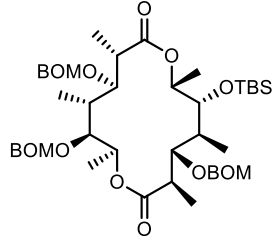
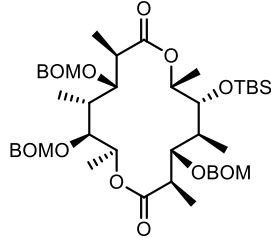
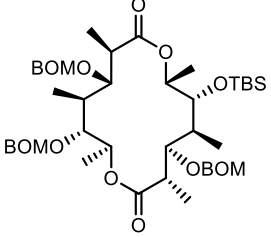
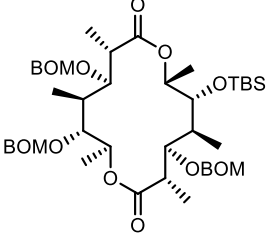
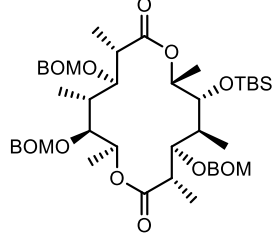
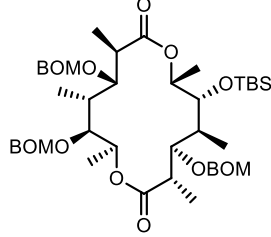
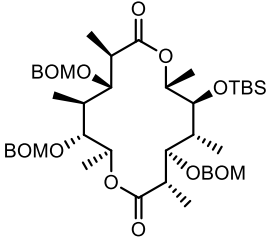
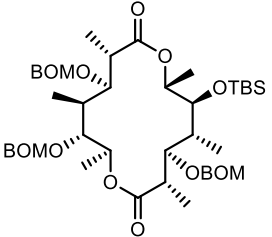
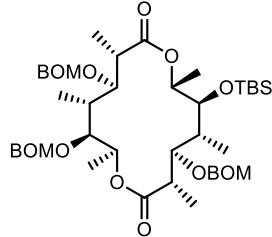
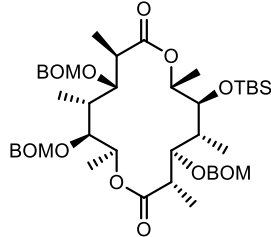
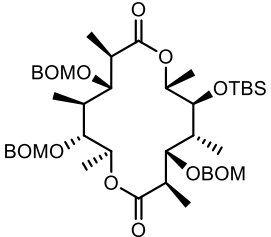
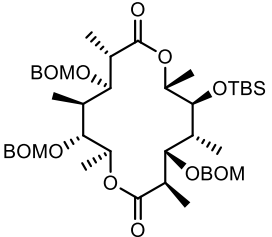
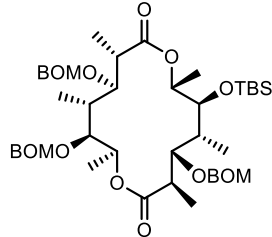
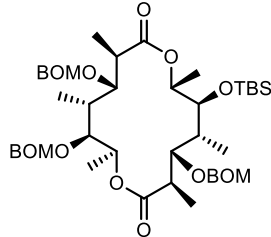
Table 4. The synthesis of macrodiolides **80a-p** by Yamaguchi macrolactonization.

macrodiolide aglycone; % yield			
 <p>80a; 67%^a stereochemistry; (2<i>R</i>, 3<i>S</i>, 4<i>S</i>, 5<i>R</i>, 6<i>R</i>, 9<i>R</i>, 10<i>S</i>, 11<i>S</i>, 12<i>R</i>, 13<i>R</i>)</p>	 <p>80b; 85%^a stereochemistry; (2<i>R</i>, 3<i>S</i>, 4<i>S</i>, 5<i>R</i>, 6<i>R</i>, 9<i>S</i>, 10<i>R</i>, 11<i>S</i>, 12<i>R</i>, 13<i>R</i>)</p>	 <p>80c; 82%^a stereochemistry; (2<i>R</i>, 3<i>S</i>, 4<i>S</i>, 5<i>R</i>, 6<i>R</i>, 9<i>S</i>, 10<i>R</i>, 11<i>R</i>, 12<i>S</i>, 13<i>R</i>)</p>	 <p>80d; 73%^a stereochemistry; (2<i>R</i>, 3<i>S</i>, 4<i>S</i>, 5<i>R</i>, 6<i>R</i>, 9<i>R</i>, 10<i>S</i>, 11<i>R</i>, 12<i>S</i>, 13<i>R</i>)</p>
 <p>80e; 47%^a stereochemistry; (2<i>S</i>, 3<i>R</i>, 4<i>R</i>, 5<i>S</i>, 6<i>R</i>, 9<i>R</i>, 10<i>S</i>, 11<i>S</i>, 12<i>R</i>, 13<i>R</i>)</p>	 <p>80f; 23% (2:1)^b stereochemistry; (3<i>R</i>, 4<i>S</i>, 5<i>R</i>, 6<i>R</i>, 9<i>S</i>, 10<i>R</i>, 11<i>S</i>, 12<i>R</i>, 13<i>R</i>)</p>	 <p>80g; 34% (1:1)^b stereochemistry; (3<i>R</i>, 4<i>S</i>, 5<i>R</i>, 6<i>R</i>, 9<i>S</i>, 10<i>R</i>, 11<i>R</i>, 12<i>S</i>, 13<i>R</i>)</p>	 <p>80h; 63%^a stereochemistry; (2<i>S</i>, 3<i>R</i>, 4<i>S</i>, 5<i>R</i>, 6<i>R</i>, 9<i>R</i>, 10<i>S</i>, 11<i>R</i>, 12<i>S</i>, 13<i>R</i>)</p>
 <p>80i; 29%^a stereochemistry; (2<i>S</i>, 3<i>R</i>, 4<i>R</i>, 5<i>S</i>, 6<i>R</i>, 9<i>R</i>, 10<i>S</i>, 11<i>S</i>, 12<i>R</i>, 13<i>R</i>)</p>	 <p>80j; 12% (2:1)^b stereochemistry; (3<i>R</i>, 4<i>R</i>, 5<i>S</i>, 6<i>R</i>, 9<i>S</i>, 10<i>R</i>, 11<i>S</i>, 12<i>R</i>, 13<i>R</i>)</p>	 <p>80k; 48%^a stereochemistry; (2<i>S</i>, 3<i>R</i>, 4<i>R</i>, 5<i>S</i>, 6<i>R</i>, 9<i>S</i>, 10<i>R</i>, 11<i>R</i>, 12<i>S</i>, 13<i>R</i>)</p>	 <p>80l; 38% (1:1)^b stereochemistry; (3<i>R</i>, 4<i>R</i>, 5<i>S</i>, 6<i>R</i>, 9<i>R</i>, 10<i>S</i>, 11<i>R</i>, 12<i>S</i>, 13<i>R</i>)</p>
 <p>80m; 34%^a stereochemistry; (2<i>R</i>, 3<i>S</i>, 4<i>R</i>, 5<i>S</i>, 6<i>R</i>, 9<i>R</i>, 10<i>S</i>, 11<i>S</i>, 12<i>R</i>, 13<i>R</i>)</p>	 <p>80n; 13% (2:1)^b stereochemistry; (3<i>S</i>, 4<i>R</i>, 5<i>S</i>, 6<i>R</i>, 9<i>S</i>, 10<i>R</i>, 11<i>S</i>, 12<i>R</i>, 13<i>R</i>)</p>	 <p>80o; 16%^a stereochemistry; (2<i>R</i>, 3<i>S</i>, 4<i>R</i>, 5<i>S</i>, 6<i>R</i>, 9<i>S</i>, 10<i>R</i>, 11<i>R</i>, 12<i>S</i>, 13<i>R</i>)</p>	 <p>80p; 68%^a stereochemistry; (2<i>R</i>, 3<i>S</i>, 4<i>R</i>, 5<i>S</i>, 6<i>R</i>, 9<i>R</i>, 10<i>S</i>, 11<i>R</i>, 12<i>S</i>, 13<i>R</i>)</p>

^a; isolated yield.

^b; epimerization was occurred, and yield was calculated as a mixture.

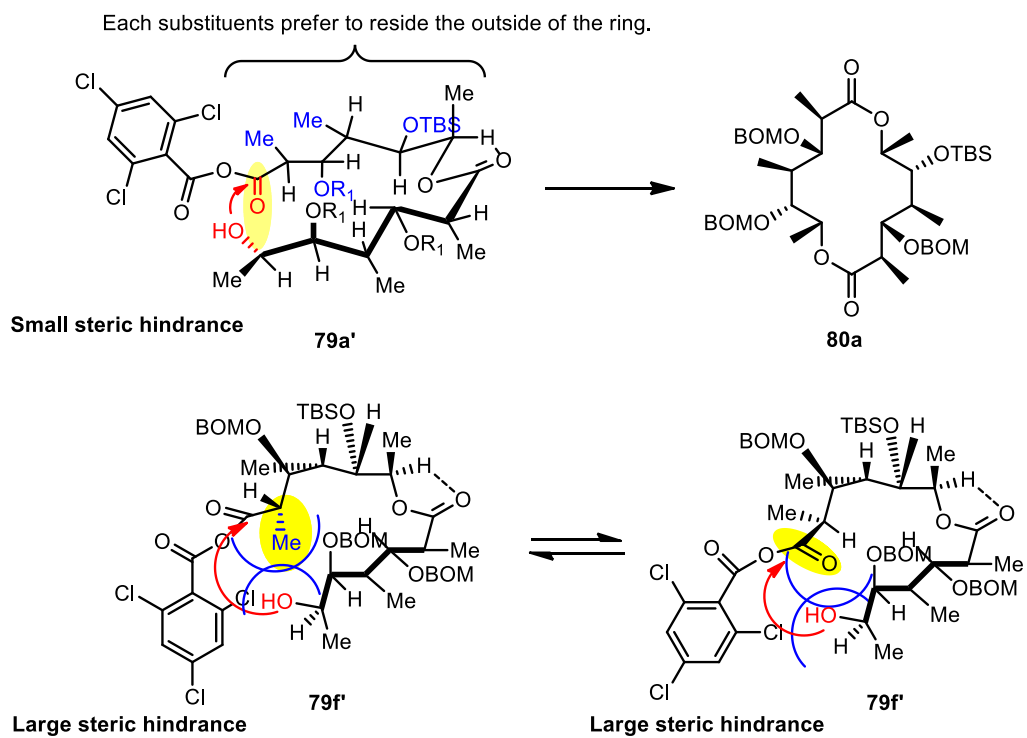
Table 5. The synthesis of macrodiolides **81a-p** by Mitsunobu macrolactonization.

macrodiolide aglycone; % yield			
 <p>81a; 70%^a stereochemistry; (2R, 3S, 4S, 5R, 6R, 9R, 10S, 11S, 12R, 13S)</p>	 <p>81b; 86%^a stereochemistry; (2R, 3S, 4S, 5R, 6R, 9S, 10R, 11S, 12R, 13S)</p>	 <p>81c; 54%^a stereochemistry; (2R, 3S, 4S, 5R, 6R, 9S, 10R, 11R, 12S, 13S)</p>	 <p>81d; 49%^a stereochemistry; (2R, 3S, 4S, 5R, 6R, 9R, 10S, 11R, 12S, 13S)</p>
 <p>81e; 73%^a stereochemistry; (2S, 3R, 4S, 5R, 6R, 9R, 10S, 11S, 12R, 13S)</p>	 <p>81f; 38%^a stereochemistry; (2S, 3R, 4S, 5R, 6R, 9S, 10R, 11S, 12R, 13S)</p>	 <p>81g; 27%^a stereochemistry; (2S, 3R, 4S, 5R, 6R, 9S, 10R, 11R, 12S, 13S)</p>	 <p>81h; 27%^a stereochemistry; (2S, 3R, 4S, 5R, 6R, 9R, 10S, 11R, 12S, 13S)</p>
 <p>81i; 50%^a stereochemistry; (2S, 3R, 4R, 5S, 6R, 9R, 10S, 11S, 12R, 13S)</p>	 <p>81j; 59%^a stereochemistry; (2S, 3R, 4R, 5S, 6R, 9S, 10R, 11S, 12R, 13S)</p>	 <p>81k; 10%^a stereochemistry; (2S, 3R, 4R, 5S, 6R, 9S, 10R, 11R, 12S, 13S)</p>	 <p>81l; 22%^a stereochemistry; (2S, 3R, 4R, 5S, 6R, 9R, 10S, 11R, 12S, 13S)</p>
 <p>81m; 79%^a stereochemistry; (2R, 3S, 4R, 5S, 6R, 9R, 10S, 11S, 12R, 13S)</p>	 <p>81n; 66%^a stereochemistry; (2R, 3S, 4R, 5S, 6R, 9S, 10R, 11S, 12R, 13S)</p>	 <p>81o; 64%^a stereochemistry; (2R, 3S, 4R, 5S, 6R, 9S, 10R, 11R, 12S, 13S)</p>	 <p>81p; 49%^a stereochemistry; (2R, 3S, 4R, 5S, 6R, 9R, 10S, 11R, 12S, 13S)</p>

^a; isolated yield.

以前から全合成研究においてマクロラクトン化ではしばしば反応が進行しない、低収率であるなどの重大な問題が生じることが知られている⁸⁾。これらの原因の一つとして、基質の立体障害や反応点の距離などが挙げられる。例えば、官能基の少ない長鎖のセコ酸は分子全体が安定な直線構造をとるために末端に位置する反応点の接近が妨げられ環化が進行しにくいことが知られている。筆者が合成したセコ酸はメチル基と水酸化がそれぞれ異なる立体化学を持つ基質であるため、反応点が近づきにくいまたは置換基の立体障害の影響を受ける基質が存在し、その場合は環化反応が進行しづらいことは十分にあり得る。実際に合成したマクロジオリドの収率も大きく差が見られ、マクロラクトン化において基質の立体化学の影響が大きいことが分かる。また、セコ酸 **79f**, **79g**, **79j**, **79l**, **79n** を用いた山口マクロラクトン化では **C2** 位においてエピメリ化が起これ、マクロジオリドはジアステレオ混合物として得られた。これは活性エステルである混合酸無水物が生成した際にカルボニル基の α 水素の酸性度が高くなり、エノール化が起こることでエピメリ化したと考えられる。**Table 4, 5** の結果からマクロジオリドの左部分が half unit **75b** の立体化学の場合は特に環化がしづらく、エピメリ化が進行してしまったのではないかといえる (**Scheme 22**)。一方、マクロジオリドの右部分が half unit **75a** の立体化学の場合、対応するマクロジオリド **80a-80d**, **81a-81d** を良好な収率で得ることができている (**Table 4, 5**)。これはかさ高い TBS 基とメチル基と水酸基の立体化学が環化の際のコンフォメーションに良い影響、すなわち反応点が接近しやすいコンフォメーションをとるためだと考えられる (**Scheme 22**)。

合成したマクロジオリドは ^1H , ^{13}C NMR ピークの値が異なるため、容易に区別することができる。また、マクロジオリドの立体化学の違いにより室温下では NMR スペクトルがブロードして観測されるものがあつたため、いくつかの基質において加熱条件下で NMR の測定を行った。これにより、NMR ピークがシャープになる、あるいは観測できるようになった。



Scheme 22. The conformation of a *seco*-acids **79a** and **79f** under Yamaguchi condition.

第三章 計算化学を用いたマクロライドテンプレートとライブラリーの三次元構造多様性の考察

前章では、32種の立体化学の異なるマクロライドテンプレートライブラリーを構築する戦略と実際の合成について述べた。本章では、構築したライブラリーについて三次元的多様性を示すため、アミノ糖を導入したと仮定し、それぞれマクロライドの最安定配座を計算化学により求め、その多様性の視覚化・考察を行った。また、実際にエリスロマイシンと類似したコンフォメーションを持つ新規マクロライドの合成を行い、そのコンフォメーション解析から溶液中の安定配座を求め、計算化学より算出した最安定配座との比較を行った。

設計した C2 対称マクロライドテンプレートは erythromycin A (**1**) を模倣したため、抗菌活性の発現に必須であるアミノ糖を同様の位置 (C5 位) に導入することで抗菌活性の発現が大いに期待できる (Figure 14)。マクロライド系抗生物質の作用機序は X 線共結晶構造解析によりその詳細が明らかとされている⁹⁾。Erythromycin A (**1**) は Figure 13 に示すようにリボソームとの X 線共結晶構造が解かれており、マクロラクトン環自体とそのカルボニル基や水酸基、そしてアミノ糖の水酸基の相互作用が重要であることが分かっている (Figure 13)。このことから、設計したマクロライドの三次元構造が erythromycin A (**1**) と類似し、アミノ糖であるデソサミン部位を持つ化合物であれば抗菌活性が発現するだろうと考えた。次に三次元構造が erythromycin A (**1**) と類似したマクロライドをテンプレートライブラリーの中から選定した。そして、計算化学を用いて算出したマクロライド **82** の最安定配座と erythromycin A の真空中の最安定配座を重ね合わせ比較を行ったところ、活性に重要であるとされるアミノ糖部位がほぼ一致することが分かった (Figure 15)。そこで設定したマクロライド **82** と同様の立体化学を有するテンプレートから、アミノ糖であるデソサミンを C5 位に立体選択的に導入した新規マクロライド **82** の合成を実際に試みた。

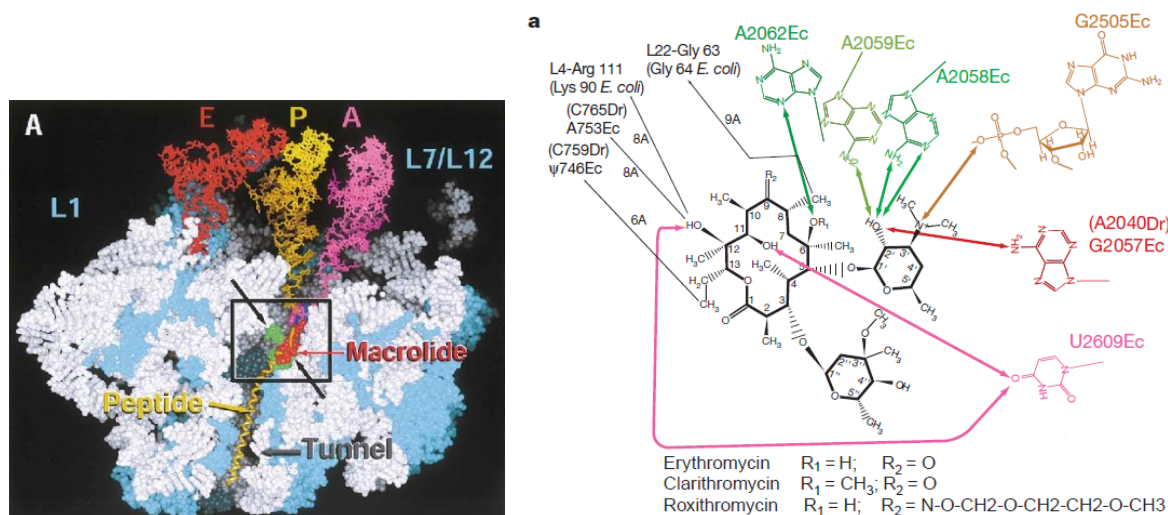


Figure 13. X ray cocrystallized structure of complex of the 50S ribosome with macrolide.

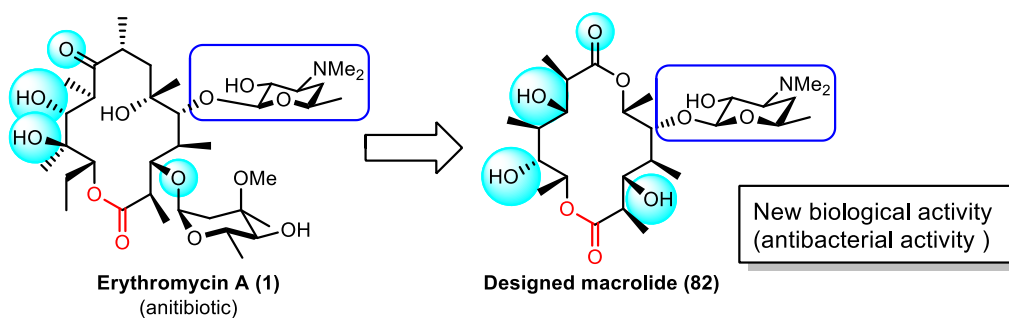


Figure 14. Designed macrolide **82** inspired by erythromycin A (**1**).

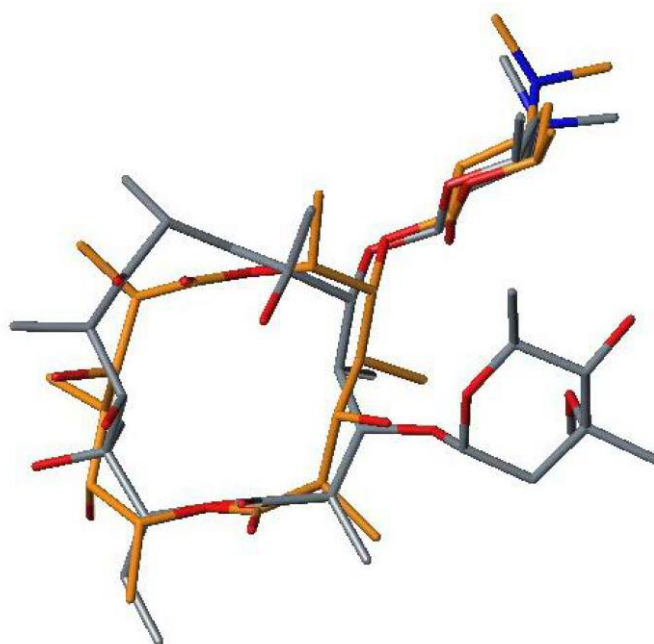
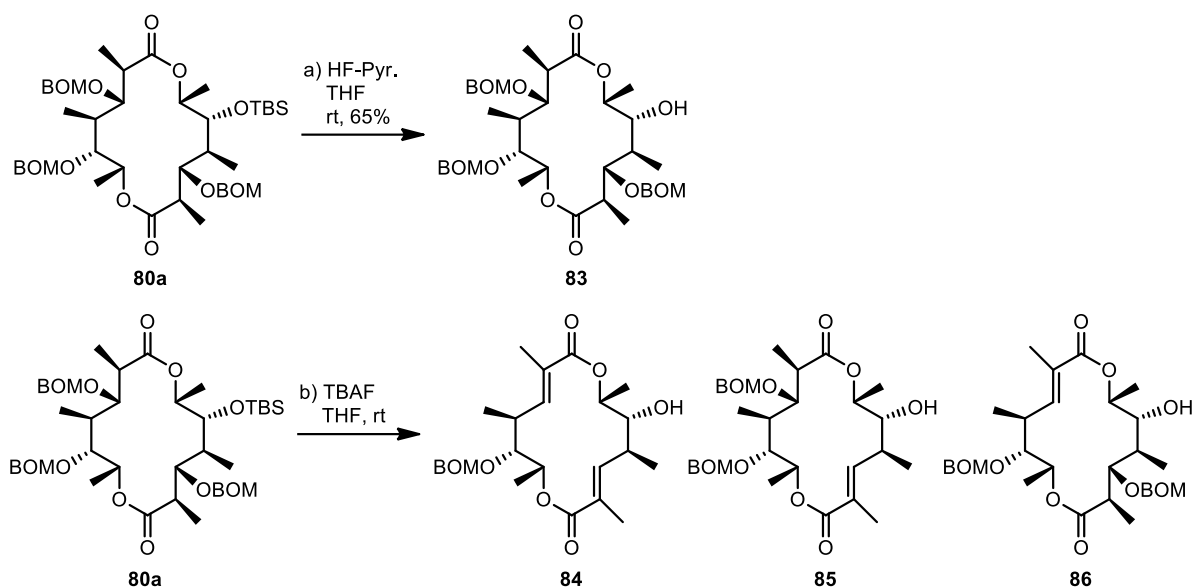


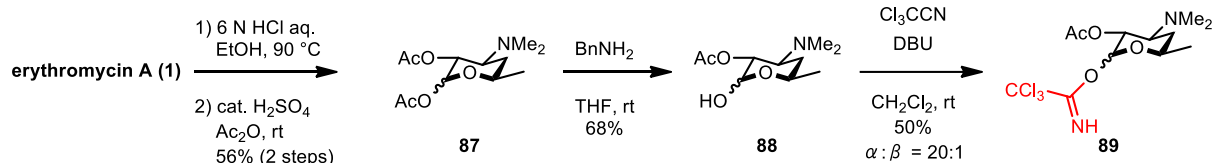
Figure 15. Superimposition of erythromycin A (gray) and designed macrolide **82** (orange).

構築ライブラリー中から一つの化合物をターゲットとして選定し、糖を導入した新たなマクロライドの合成を実際に試みた。最初にマクロジオライド **80a** に対して TBS 基の除去を試みた。BOM 基を分子内に共存することからフッ素試薬である TBAF を用いたところ、原料の消失は確認できたが目的の生成物を得ることができなかった。副生成物は混合物として得られたが、BOM 基が β -脱離した脱保護体の混合物 **84**, **85**, **86** であると ^1H NMR から確認できた。そこで、次に HF-pyr. による脱保護を試みた。その結果、 β -脱離は起こらず、TBS 基が除去されたマクロジオライド **83** を収率 65% で得ることができた (Scheme 23)。



Scheme 23. The removal of TBS group from macrodiolide aglycone **80a**.

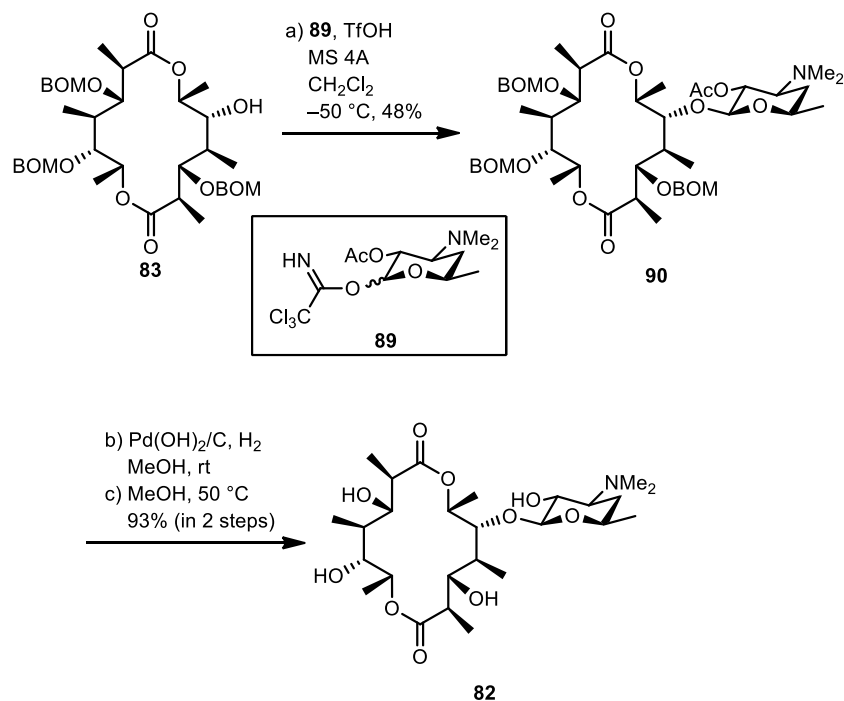
脱保護体を得ることができたため、続いてアミノ糖の導入を試みた。立体選択的に糖を導入するために Schmidt グリコシル化^{3), 10)}による導入を考えた。Schmidt グリコシル化ではイミデートを調製する必要があるため、既知の方法に従い、導入するデソサミンのトリクロロアセトイミデート **89** の調製を行った (**Scheme 24**)。Erythromycin A (**1**)とエタノールの混合液中に 6N HCl aq.を加え、加熱還流することでアミノ糖の酸加水分解を行い、続いて過剰量の無水酢酸と触媒量の硫酸を加えアセチル化を行うことでビスアセチルデソサミン **87** を合成した。次にベンジルアミンを用いてアノマー位の水酸基のみを脱保護し、DBU、トリクロロアセトニトリルを用いてトリクロロアセトイミデート化することでトリクロロアセトイミデート **89**¹¹⁾を合成した。



Scheme 24. The preparation of trichloroacetimidate **89** from EM A (**1**).

次に合成した脱保護体 **83** とトリクロロアセトイミデート **89** を用いて Schmidt グリコシル化反応を行った。既に報告されている反応条件¹²⁾を参考として、TfOH, molecular sieves 4 Å, CH₂Cl₂, -50 °C 条件下 Schmidt グリコシル化反応を行った。反応はスムーズに進行し、目的のマクロライド **90** を中程度の収率 48%で得ることに成功した (**Scheme 25**)。アミノ糖の立体

選択性は β 体のみが選択的に得られたことを ^1H NMRのカップリング定数から確認している($J_{1,2}=7.5\text{ Hz}$)。次に得られた配糖体に対して Pearlman 触媒を用いて BOM 基の除去を行い、続いてメタノール中 $50\text{ }^\circ\text{C}$ で加熱することでアセチル基の除去を行うことで目的のマクロライド **82** の合成を達成した。



Scheme 25. The synthesis of a new macrolide **82** via Schmidt glycosylation.

Erythromycin A を模倣したマクロライド **82** の合成が完了したため、次にその分子の三次元コンフォメーション解析を行うことで計算化学による最安定配座と一致するかを調査した。コンフォメーション解析については既知の手法¹³⁾に従い、高分解能 NMR による測定結果を基に解析を行った。具体的には、 ^1H NMR の H-H カップリング定数により二面角拘束条件を決定し、ROESY の測定結果から水素原子間直線距離 (距離拘束条件) を設定し、計算化学により算出した数千個の配座から拘束条件を満たすものを絞り込んでいくことで三次元構造を導き出した。合成したマクロライド **82** (Figure 16) について実際の NMR 測定を行い、その測定・解析結果を Table 6, 7 にまとめて示す。

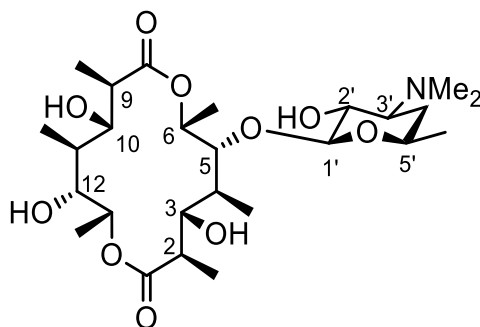


Figure 16. The structure of Macrolide **82**.

Table 6. Vicinal coupling constants and torsional constants

Torsional angle	$^3J_{\text{HH}}$, Hz	Torsional constrains
H2-C2-C3-H3	10.3	$180^\circ \pm 40^\circ$
H5-C5-C6-H6	2.9	$-90^\circ \pm 40^\circ$ or $90^\circ \pm 40^\circ$
H9-C9-C10-H10	10.3	$180^\circ \pm 40^\circ$
H11-C11-C12-H12	9.7	$180^\circ \pm 40^\circ$
H2'-C2'-C3'-H3'	10.3	$180^\circ \pm 40^\circ$
H4'b (ppm)-C4'-C5'-H5'	3.0	$-90^\circ \pm 40^\circ$ or $90^\circ \pm 40^\circ$

Table 7. Distance constrains obtained by the 2D-ROESY experiments^a

Atom A	Atom B	The upper bound, Å
H2	4MeC	6.0
H3	H4	3.5
H3	H6	2.7
H3	2MeC	6.0
H5	6MeC	6.0
H5	H6	2.7
H5	H1'	2.7
H9	11MeC	4.5
H10	H12	5.0
H10	H13	2.7
H10	9MeC	6.0
H12	H13	3.5
H12	13MeC	4.5

^aAccording to the procedure of reference 14, Distance constrains were extracted.

Table 6、**7** に示したように 6 個の二面角拘束条件と 13 個の距離拘束条件を NMR 解析より得られた。続いて、CAMDAS で合成したマクロライド **82** の三次元コンフォメーションを算出し、得られた条件を満たす配座を絞り込んだところ、候補として 10 種類の配座を得ることができた。算出された 10 種類の配座を重ね合わせた図を **Figure 17** に示す。また、候補配座として算出されたそれぞれのコンフォメーションを **Figure 18** に示す。重ね合わせた結果、マクロジオリド骨格部分は全ての配座においてほとんど一致していることが分かった。そのため、合成したマクロライドの三次元コンフォメーションは解析できたと言える。そして、

10 種類の配座の中で最もエネルギーが低い配座をメタノール溶液中の最安定コンフォメーションとし、計算化学により算出した最安定配座との比較を行った。2 つの配座を重ね合わせた図とそれぞれの配座の図を **Figure 19** に示す。

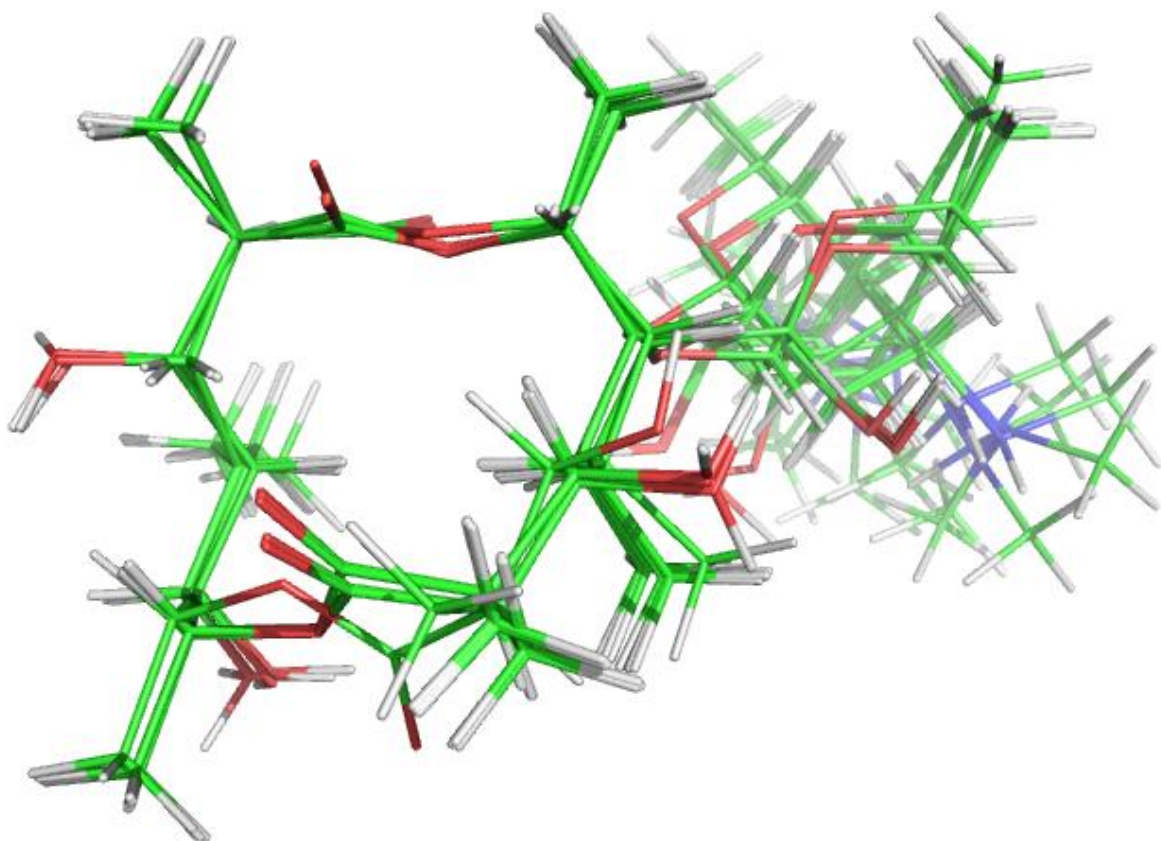


Figure 17. Determined the three-dimensional (3D) solution structure of macrolide **82**.

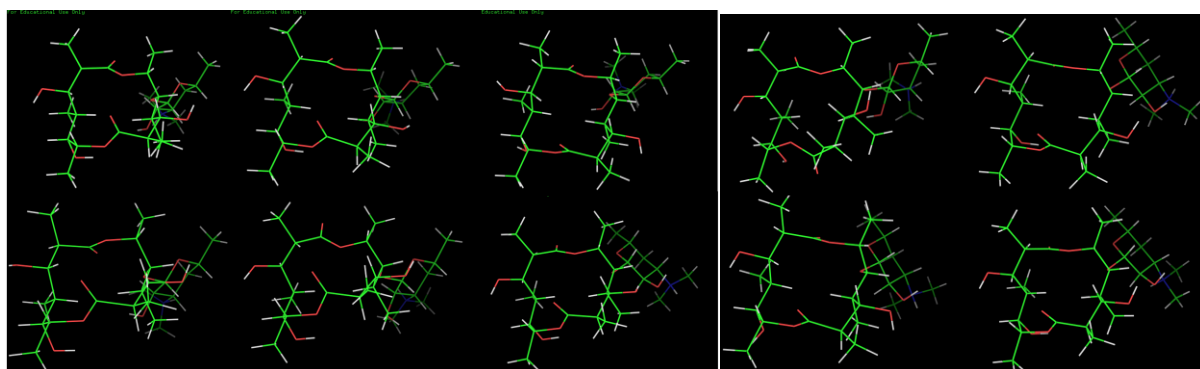


Figure 18. Each three-dimensional (3D) solution structure of macrolide **82**.

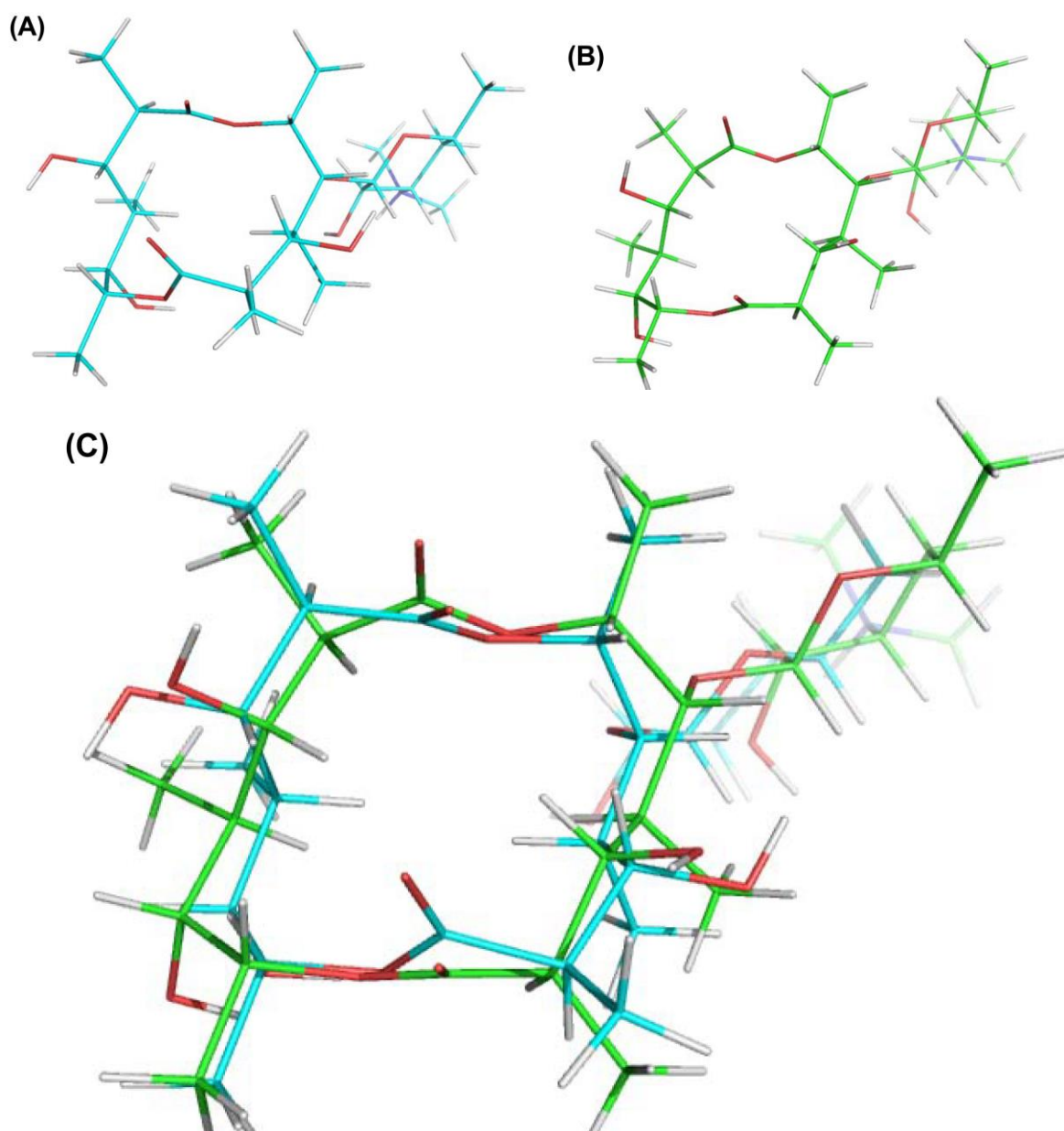


Figure 19. The conformation of macrolide **82**. (A) The conformation determined by NMR analysis of synthesized macrolide **82**. (B) The most stable conformation of macrolide **82**. (C) Superimposition of (A) and (B).

合成したマクロライド **82** における実際の溶液中の配座と計算化学により算出した真空中の最安定配座は多少の違いはあるものの、マクロジオライド骨格部の置換基の位置や向き、マクロラクトン環の形についてはほぼ一致していると言える。このように実際の溶液中のコンフォメーションと計算化学により算出したコンフォメーションが一致することから、このマクロライドの立体異性体の三次元コンフォメーションについて計算化学を利用することで高い精度で予想できることが分かる。計算化学により設計した化合物の三次元構造が予測できることは非常に有用であり、*in silico* 創薬などの展開が大いに期待できる。

次に構築したマクロライドテンプレートライブラリーについてアミノ糖であるデノサミンを導入したと仮定し、三次元多様性について計算化学を用いて考察を行った。テンプレートライブラリーの 32 種類全てにおいてアミノ糖を導入した場合の化合物を想定し、CAMDAS (Conformational Analyzer with Molecular Dynamic and Sampling)プログラム¹⁵⁾を用いて真空中の最安定配座を算出した。CAMDAS とは、広野らにより開発された自動配座解析プログラムであり、Chem 3D を用いて構築した分子モデルについて 1200°K という高温条件の仮定の下で分子動力学 (Molecular Dynamics: MD)シミュレーションを行い、この時にとり得るコンフォメーションの中で低いエネルギーの配座を複数抽出するものである。CAMDAS により計算を行う際、真空条件かつ分子力場の静電相互作用項を無視する中性力場を用いた。算出した 32 種類の最安定配座を重ね合わせた図を **Figure 20, 21** に示す。また、32 種類のマクロライドの構造と最安定配座は実験項にそれぞれ記載した (IV. 実験項、p 61-69)。

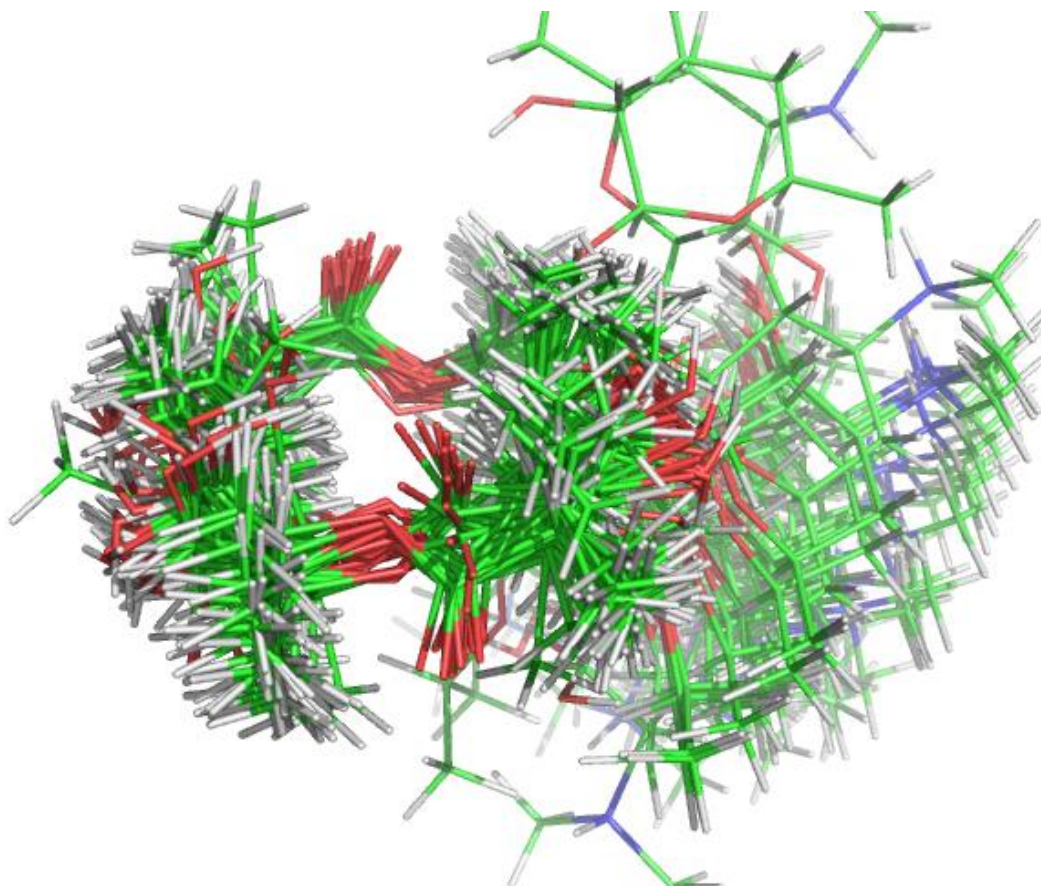


Figure 20. Conformations of our designed macrolide stereoisomers by the CAMDAS program
(Shown a side view of conformations).

重ね合わせた図から、マクロライドの三次元コンフォメーションは多様性に富んでいることが視覚的に分かる。具体的にはアミノ糖の位置が大きく異なり、マクロラクトン骨格上のメチル基や水酸基、さらにはカルボニル基の位置や向きに違いが見られる。また、マクロラクトン環の形にも違いが生じていることが分かる。従って、想定したマクロライドライブラ

リーは十分な三次元的多様性を有しているといえる。このことから、構築したライブラリーを利用することで十分な三次元構造を実現した新たな誘導体合成およびライブラリーの構築が可能であり、構築したマクロジオリドテンプレートライブラリーの有用性を示していると考えている

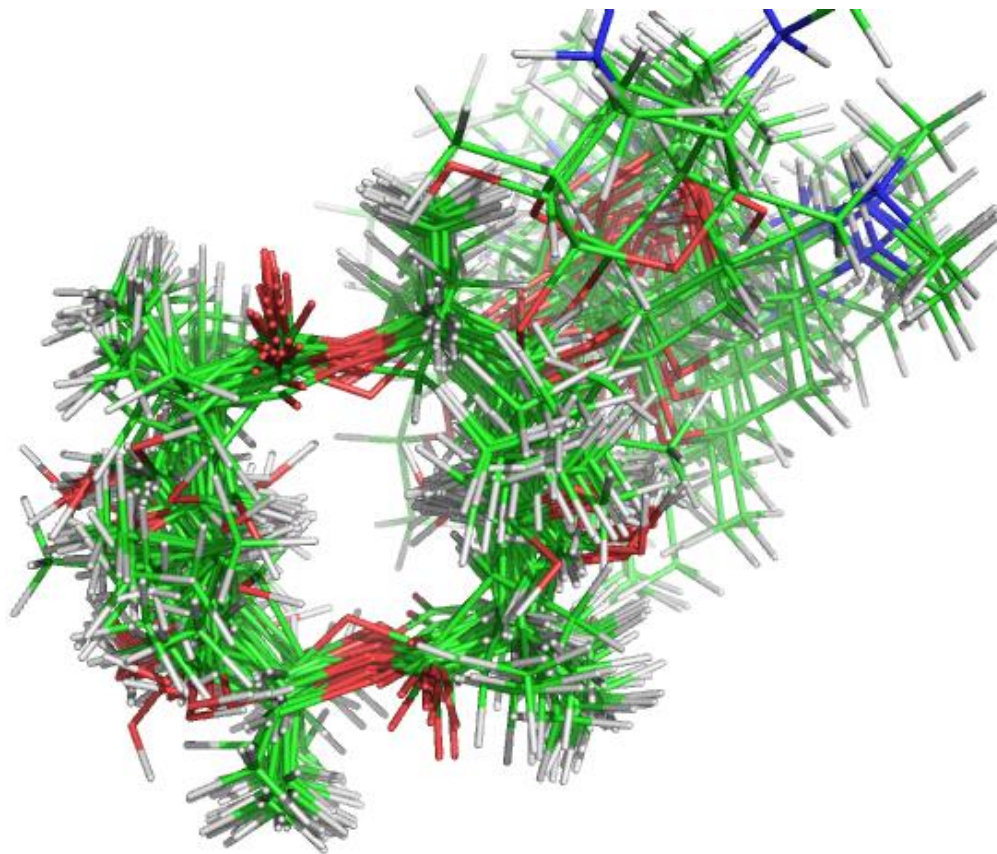


Figure 21. Conformations of our designed macrolide stereoisomers by the CAMDAS program (Figure as seen from above).

立体化学の異なるマクロライドのコンフォメーションに違いが生じていることから、算出した最安定配座についてクラスター解析を行い、三次元構造の類似性に基づいていくつかのグループに分類した (**Figure 22-28**)。その結果、7つのグループに分類することができた。分類したグループ 1 からグループ 4 までにほとんど化合物が属しており、マクロラクトン環部位とカルボニル基の向きに顕著な違いが見られる。また、カルボニル基の向きは二つ隣にある水素原子の立体化学の影響を受けていることがわかる。すなわち、カルボニル基はその水素原子と水素結合で結ばれており、水素原子の向きと同じ方向にカルボニル基が向くことが法則としてあるといえる。しかしながら、その他の置換基の立体化学と分子のコンフォメーションに関する因果関係は見出せず、構造式から三次元構造を予測することは非常に困難である。従って、合成したマクロライド **82** の三次元構造が計算化学で得られた最安定配座と非常に近いものであったことはマクロライドライブラリーの三次元構造を予測に役立ち、様々な創薬展開の機会を与えるだろうといえる。

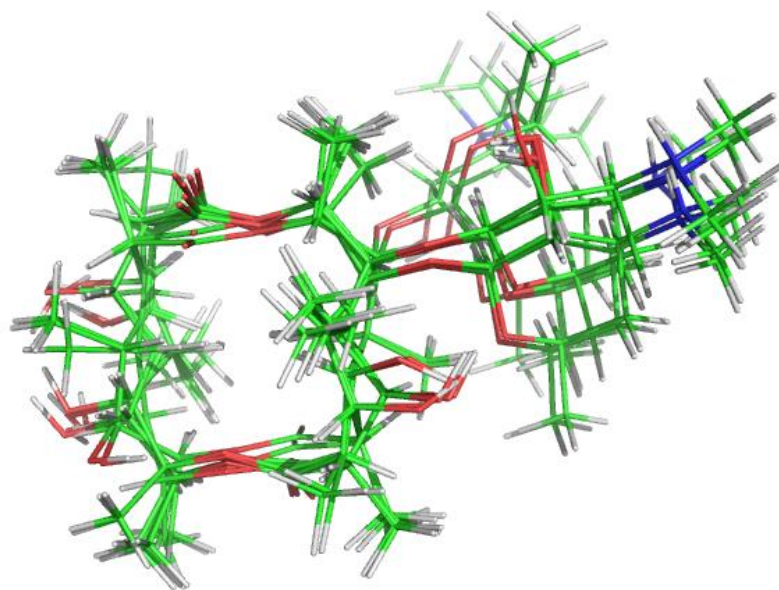


Figure 22. Group 1.

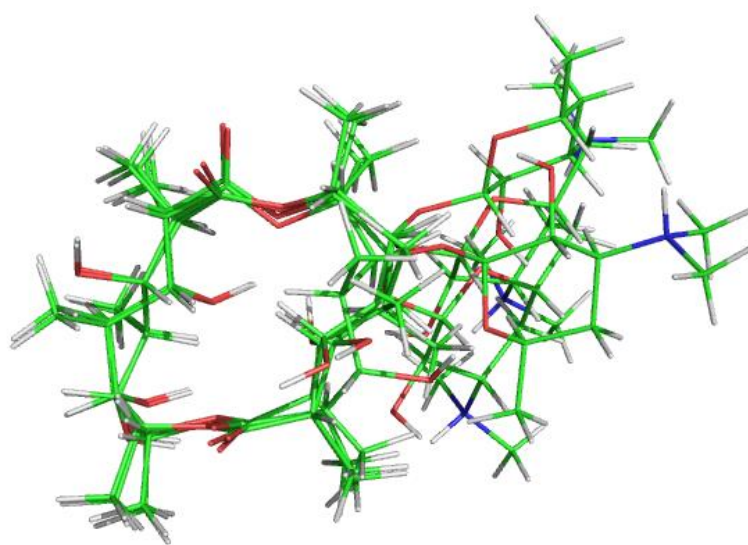


Figure 23. Group 2.

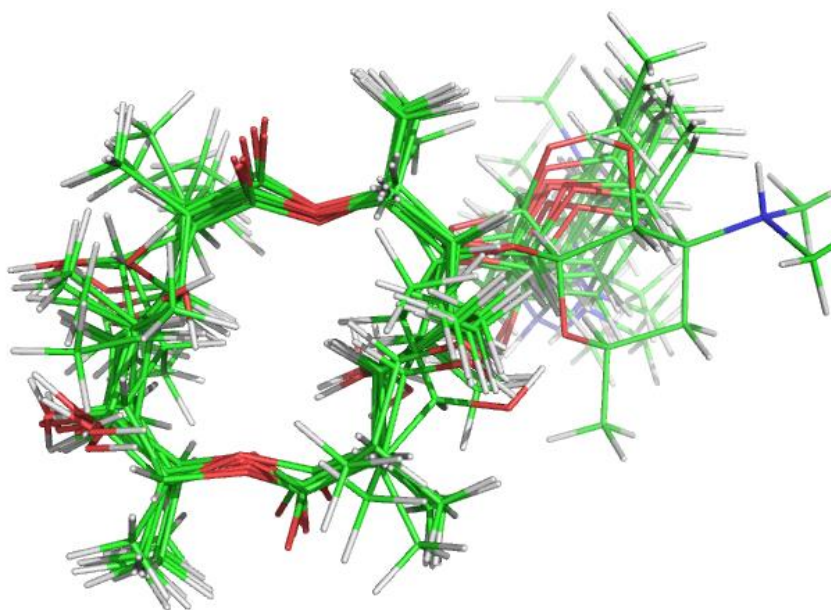


Figure 24. Group 3.

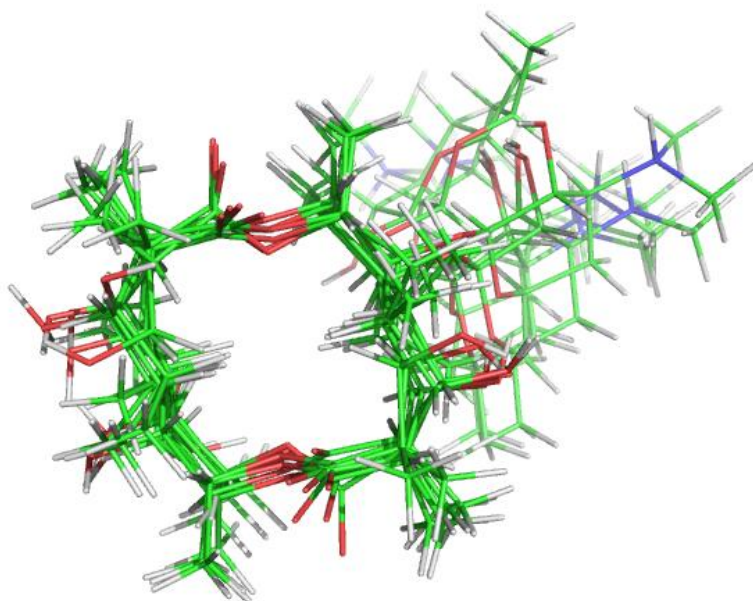


Figure 25. Group 4.

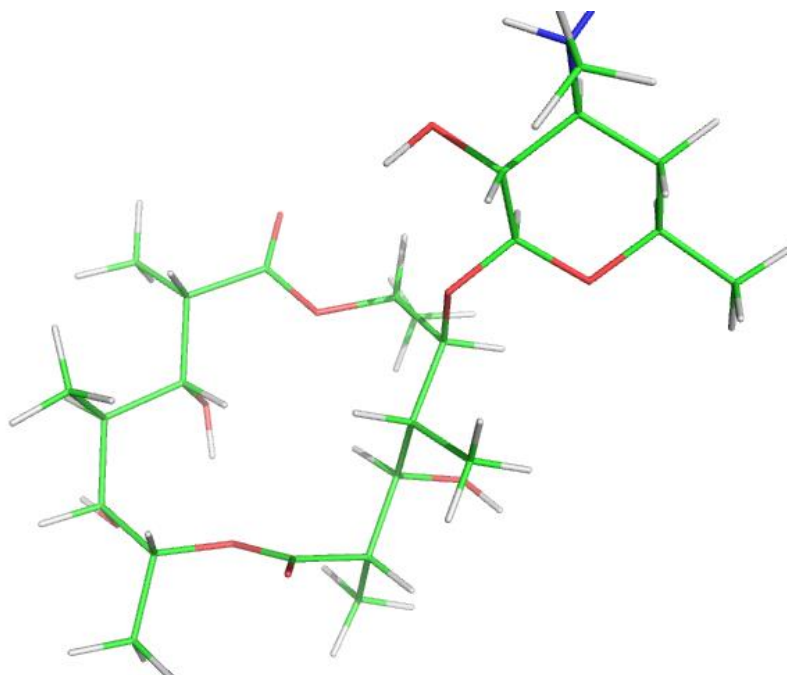


Figure 26. Group 5.

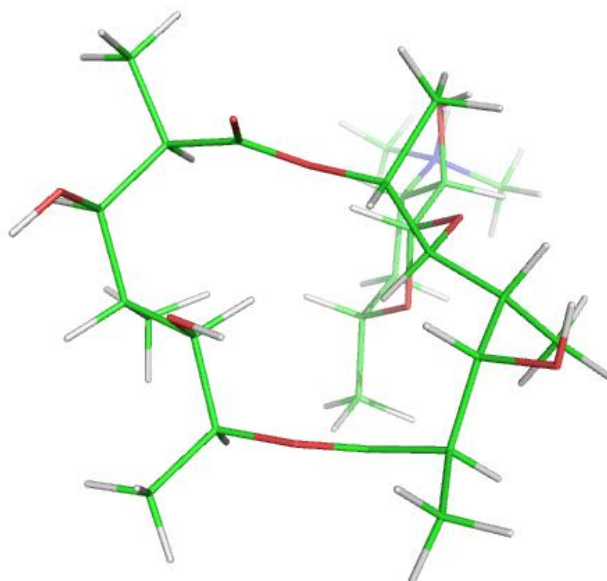


Figure 27. Group 6.

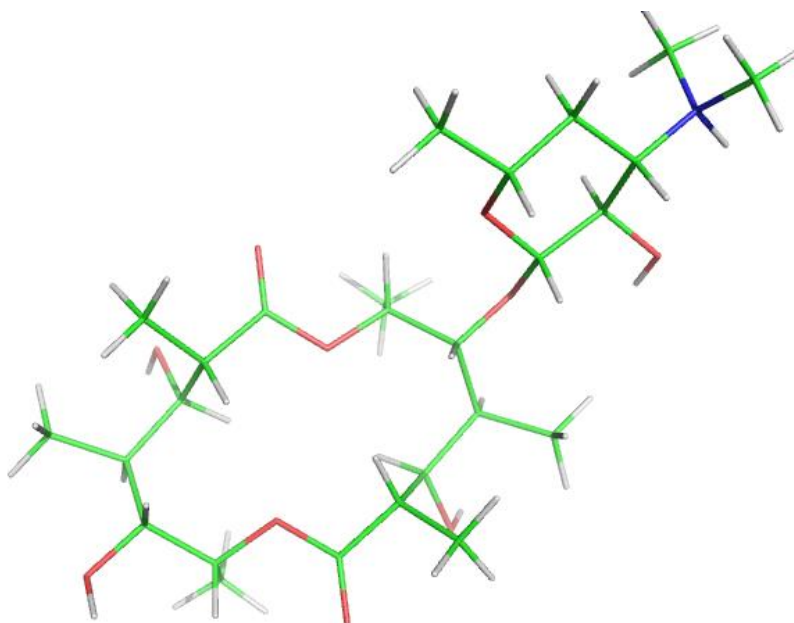


Figure 28. Group 7.

これまで視覚的に三次元構造多様性が生じていることを考察してきた。次に三次元構造多様性を数値の観点からも考察を試みた。近年、質の高いライブラリーの構築を行うため、様々な指標も考えられてきた。創薬開発で有名なものとしてリピンスキーの法則¹⁶⁾がある。あるいは Van der Waals に基づく表面積などの化合物の特徴を記述子として数値化し、それらを組み合わせて主成分分析したりされている。また、近年では化合物が有する sp^3 炭素の数に着目し、 F_{sp^3} の数値によりそのライブラリーを評価する方法も報告されている¹⁷⁾。具体的には、 sp^3 炭素が多いほど開発可能性は高く、平面性が高いような分子すなわち sp^2 , sp 炭素が多い場合は臨床試験でドロップしやすいなどが報告されている。同時に F_{sp^3} の数値が高いことは三次元構造多様性が高いことも示唆されている。

以下に F_{sp^3} を求める式を示す。

$$F_{sp^3} = \text{number of } sp^3\text{-hybridized carbons/total carbon count.} \quad (1)$$

算出した F_{sp^3} の値は分子内に内在する sp^3 炭素の比率であるため、化合物の三次元あるいは立体構造の指標になり得ると言える。また、実際に天然物や薬として承認されている化合物群に対してその値が求められている (**Figure 29**)。

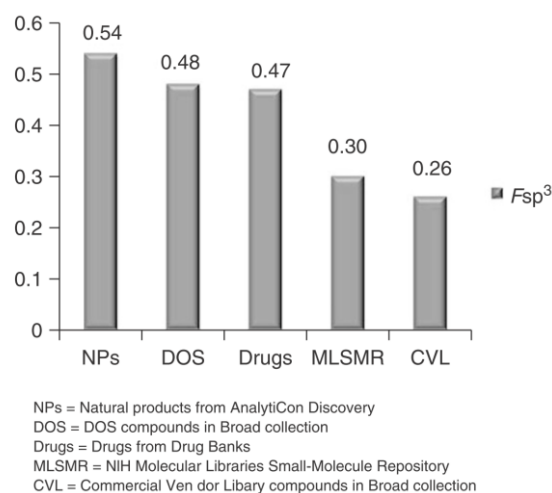


Figure 29. Complexity analysis of different compound collections as measured by F_{sp^3} .¹⁸⁾

合成したマクロジオライドテンプレートライブラリーとアミノ糖を導入したマクロライドライブラリーの両方について F_{sp^3} の値を式 (1)より算出した。その結果を以下に示す。

マクロジオライドテンプレートライブラリー	$F_{sp^3} = 28/48 = 0.583$
マクロライドライブラリー	$F_{sp^3} = 24/26 = 0.923$

この結果と **Figure 29** を比較すると、テンプレートライブラリーは天然物群の F_{sp^3} の値に近く、マクロライドライブラリーは極めて高い F_{sp^3} の値を示していることが分かる。従って、設計したマクロジオライドテンプレートは有用なマルチ創薬テンプレートとして利用することが可能であり、構築したライブラリーは広い多様性を持つことが示唆されたため、有用なツールとして新たな創薬展開が大いに期待できる。

第四章 新規マクロライドとマクロジオリドの生物活性評価と考察

筆者はこれまでに新規マクロライド化合物を1種とマクロジオリドテンプレートを32種合成してきた。構築したライブラリーは様々な活性試験へと供給することで有用な生物活性が、あるいは有用なリード化合物が見出されることが大いに期待できる、今回、実際に合成した化合物について抗菌活性試験を行ったので、その結果について述べていく。

マクロライド系抗生物質の抗菌活性は、細菌のリボソーム内にある50Sサブユニットに結合してタンパク質の合成を阻害することで発現する。具体的には、23S rRNAのドメインVに存在するペプチジルトランスフェラーゼ領域のA2058・A2059に結合し、ペプチジルトランスフェラーゼ反応を阻害していると考えられている (Figure 30)¹⁹。この詳細な作用機序はマクロライドとリボソームサブユニットの共結晶のX線構造解析により解明され、マクロライドがリボソームのペプチドトンネル内に入り込んでいることが分かった。すなわち、マクロライドはペプチドトンネルを塞ぐことでペプチドの伸長を阻害し、タンパク質の合成を阻害している。前章で述べたように、合成したマクロジオリドテンプレートに対してアミノ糖を導入することで、他のマクロライド抗生物質と同様にリボソームと結合しタンパク質の合成を阻害するだろうと考えた。すなわち、合成した新規マクロライド **82** は抗菌活性を示すと考え、活性試験を行った。また、構築したテンプレートライブラリーについても同様に抗菌活性試験を行った。

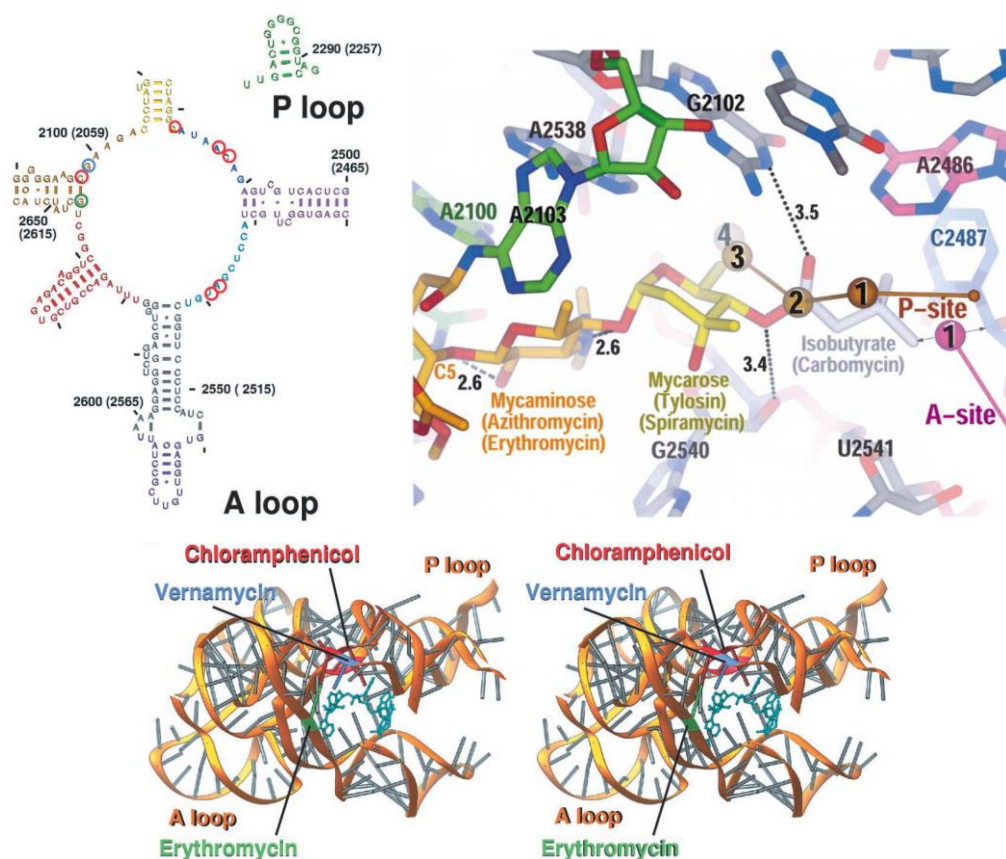


Figure 30. Erythromycin A とリボソーム内の結合部位.

菌株\物質		VCM	82	93	80a	81d	81a	81m	80p	81e	80o	81o	94	SK-89	
1	<i>Staphylococcus aureus</i> FDA209P	1	>64	128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	1
2	<i>Staphylococcus aureus</i> Smith	2	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	2
3	MRSA Low resistance	1	>64	128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	3
4	MRSA High resistance	1	>64	128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	4
5	MRSA 70	0.5	>64	64	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	5
6	MRSA 92-1191	2	>64	128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	6
7	<i>Staphylococcus aureus</i> Macrolide resistance ①	1	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	7
8	<i>Staphylococcus aureus</i> Macrolide resistance ②	1	>64	128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	8
9	MRSA Mu50	8	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	9
10	MRSA LZD-resistant strain⑥	2	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	10
11	<i>Staphylococcus epidermidis</i>	2	>64	128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	11
12	<i>Micrococcus luteus</i> ATCC9341	1	64	64	>128	>128	>128	>128	>128	>128	>128	>128	64	>128	12
13	<i>Enterococcus faecalis</i> ATCC29212	4	>64	128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	13
14	<i>Enterococcus faecalis</i> NCTC12201 (VanA)	>128	>64	128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	14
15	<i>Enterococcus faecium</i> NCTC12204 (VanA)	>128	>64	64	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	15
16	<i>Escherichia coli</i> NIHJ JC-2	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	16
17	<i>Citrobacter freundii</i> ATCC8090	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	17
18	<i>Klebsiella pneumoniae</i> NCTC9632	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	18
19	<i>Proteus mirabilis</i> IFO3849	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	19
20	<i>Proteus vulgaris</i> OX-19	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	20
21	<i>Morganella morganii</i> IID Kono	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	21
22	<i>Serratia marcescens</i> IFO12648	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	22
23	<i>Enterobacter cloacae</i> IFO13535	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	23
24	<i>Enterobacter aerogenes</i> NCTC10006	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	24
25	<i>Pseudomonas aeruginosa</i> 46001	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	25
26	<i>Pseudomonas aeruginosa</i> E-2	>128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	26
27	<i>Acinetobacter calcoaceticus</i> IFO12552	128	>64	>128	>128	>128	>128	>128	>128	>128	>128	>128	>64	>128	27

Table 8. Biological activity (MIC) of synthesized macrolides.

その結果、合成した新規マクロライドとマクロジオライドは抗菌活性を示さないことが分かった。マクロジオライドテンプレートはアミノ糖を持たないために抗菌活性を示さなかったと考えられるが、**erythromycin A** を模倣した形となる新規マクロライドは何故抗菌活性を示さなかったのか。これについては以下の 3 つの理由が考えられる。一つ目は、マクロジオライド骨格自体が抗菌活性を示さないことが考えられる。二つ目は、リボソーム内に入り込まない、あるいはリボソーム内でタンパク質の合成を阻害するように配位しないことが考えられる。三つ目は、**erythromycin A** と構造を比較して 3 位にクラジノースを持たないため、その影響により活性を示さないことが考えられる。

一つ目に挙げたマクロジオライド骨格の抗菌活性に関しては、次のような例が報告されている。塩野義製薬の大原、久米らが **erythromycin A** から数種類の 15 員環マクロジオライド誘導体へと導き、その抗菌活性評価を行ったところ、**erythromycin A** よりも抗菌活性が減少している²⁰⁾。

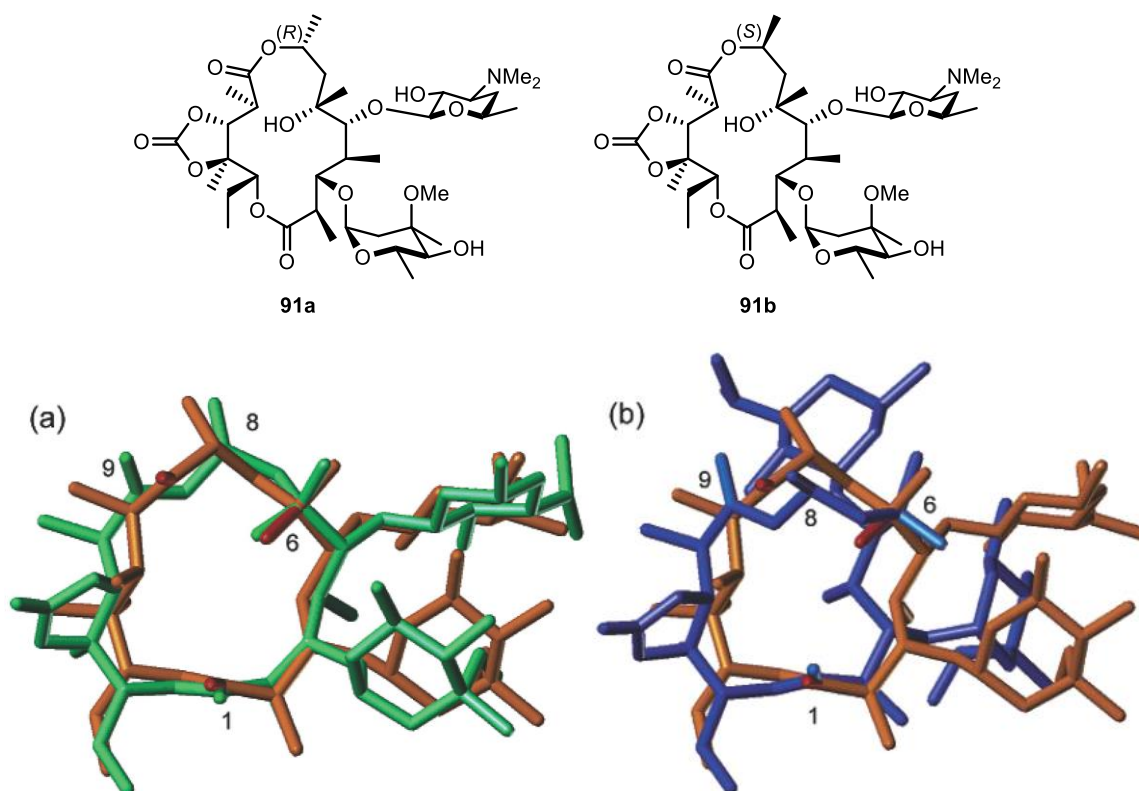


Figure 31. 91a (緑)、91b (青)と **erythromycin A** (オレンジ)の三次元構造の比較.

15 員環マクロジオライドが抗菌活性を示すことから、合成した 14 員環マクロライドのマクロジオライド骨格が抗菌活性を示さなかった理由ではないといえる。さらに、**Figure 31** からも抗菌活性の発現にはマクロラクトン環とアミノ糖が適切な位置にあることが重要であることが示唆されている。次に細菌のリボソーム内に入りこまないことに関してだが、これについては抗菌活性試験の結果だけでは判断ができなかった。一方のタンパク質合成を阻害す

るようにリボソームと結合していないのではないかということについては、erythromycin A と類似したコンフォメーションであれば同様に結合し、阻害しうると考えている。既に合成したマクロライド **82** の溶液中の三次元コンフォメーションは解析し、決定している。そこで、erythromycin A がリボソームと結合している場合のコンフォメーションとの比較を行った。既に X 線共結晶構造が報告されていることから、*Escherichia coli* のリボソームと結合した場合の erythromycin A のコンフォメーションを選び²¹⁾、その比較を行った (**Figure 32**)。

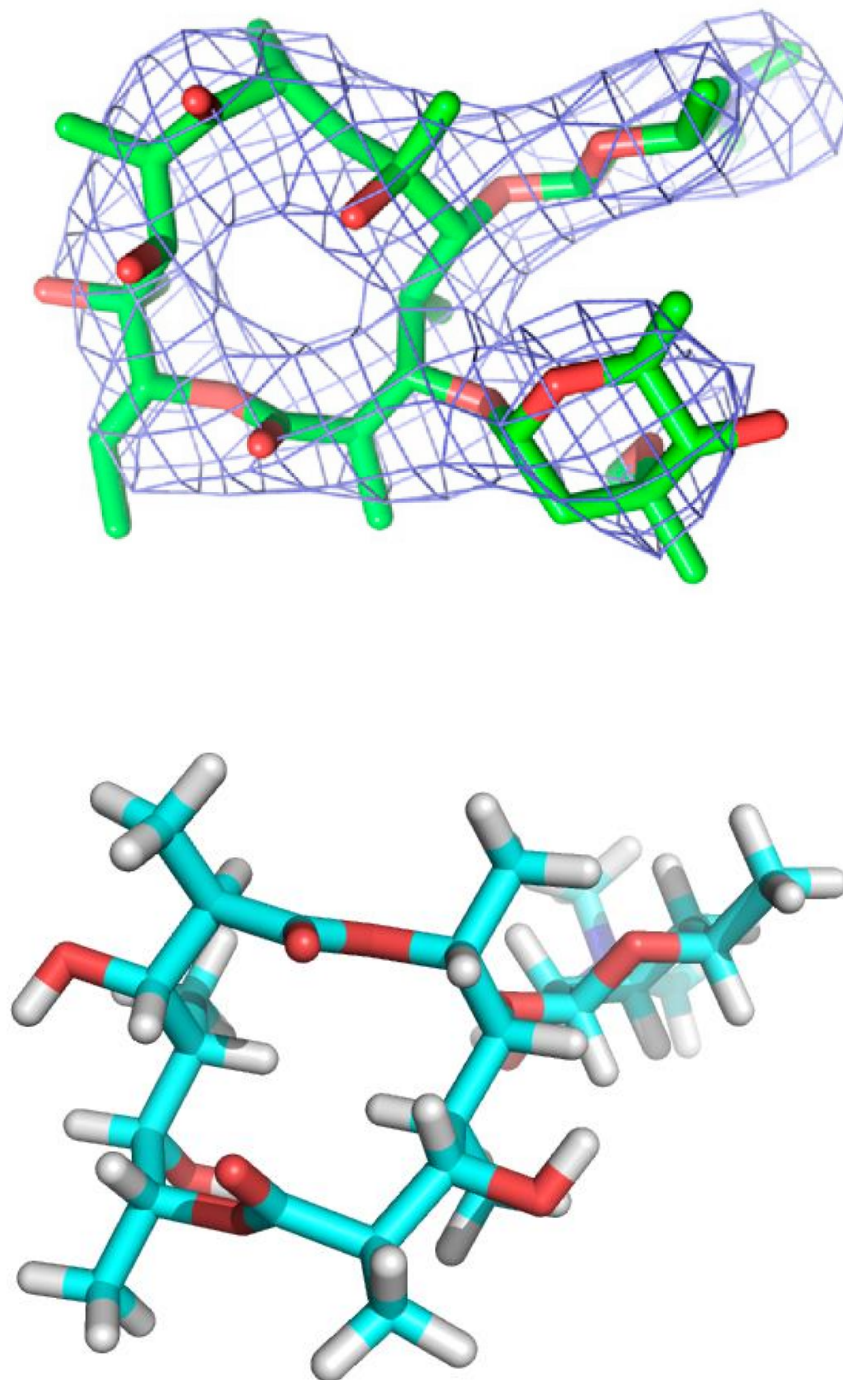


Figure 32. The conformation of erythromycin A bound to the *Escherichia coli* ribosome (green). The conformation determined by NMR analysis of synthesized macrolide **82** (blue).

上記の図から、合成したマクロライド **82** のコンフォメーション (Blue) はリボソームと結合している erythromycin A (Green) と多少の違いが見られるが、アミノ糖であるデソサミン、カルボニル基や水酸基の位置などは非常に近いといえる。そのため、マクロラクトン環の広がりによって違いが見られるがマクロライド **82** もリボソーム内に結合したらタンパク質合成を阻害すると考えられる。その一方で分子の広がり、すなわち分子表面積が重要であることも考えられる。その場合には新たな置換基を導入することで分子構造を大きくする、あるいはリボソームとより強くアフィニティを稼ぐ置換基を導入することで抗菌活性の発現が期待できるといえる。

最後にクラジノースの有無についてであるが、X 線共結晶構造からは 3 位のクラジノースとリボソームとの相互作用は見られない。しかし、以前からマクロライド抗生物質は 1 個あるいは 2 個の糖をはずすと活性が低下することが知られている。特に erythromycin A は 3 位のクラジノースを脱糖し水酸基へと変換した場合は抗菌活性が失われてしまう。実際に合成した 3 位が水酸基の EMA 誘導体 **92** は抗菌活性を示さなかった。このことから、今回合成したマクロライドが抗菌活性を示さなかった理由は 3 位が水酸基であるためだと考えられる。すなわち、設計したマクロジオリドもマクロライド抗生物質と同様の傾向があると考えられることができる。そのため、3 位の水酸基を化学変換することで抗菌活性が発現するだろうといえる。例えば、3 位の水酸基を酸化しケトライドに変換することで telithromycin や cethromycin のように抗菌活性が発現することが予想される。あるいは、アミノ糖を導入したマクロライドライブラリーの中には 3 位が水酸基の場合でも抗菌活性を示す化合物が見出される可能性もあると考えている。

また、本研究中に合成した化合物について抗トリパノソーマや抗マラリア活性など北里研究所内で試験可能な様々な生物活性について評価を行った。その結果、今回ほとんどの化合物は有用な生物活性を示さなかったが、2 種のマクロライドが新たに殺虫活性を示すことを見出した (Figure 33, Table 9)。

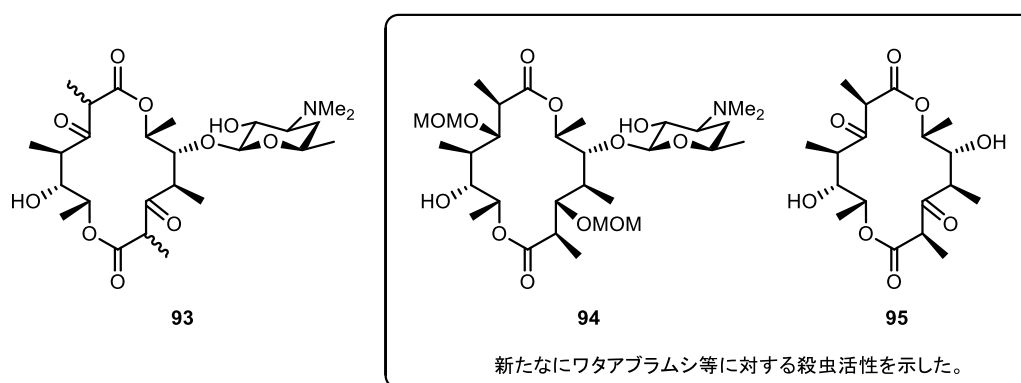
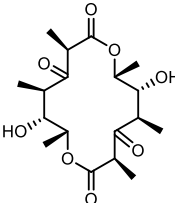
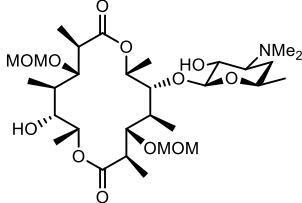
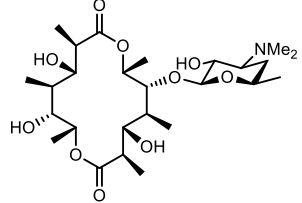
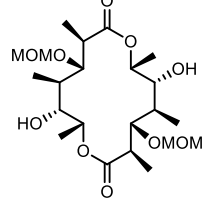
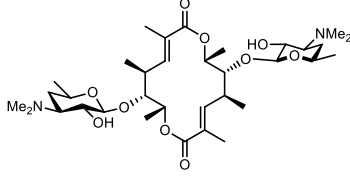


Figure 33. Synthesized macrolides and new biological activity.

新規生物活性物質の創製あるいは探索は今後の課題であるが、マクロジオリドテンプレートライブラリーを利用した新たなケミカルライブラリーを構築するとともに、多様な活性

試験を並行して行っていくことで創薬リードとなりうる有用なマクロライド化合物を見出すことができると考えている。

Table 9. Biological activity (insecticidal activity) of synthesized macrolides.

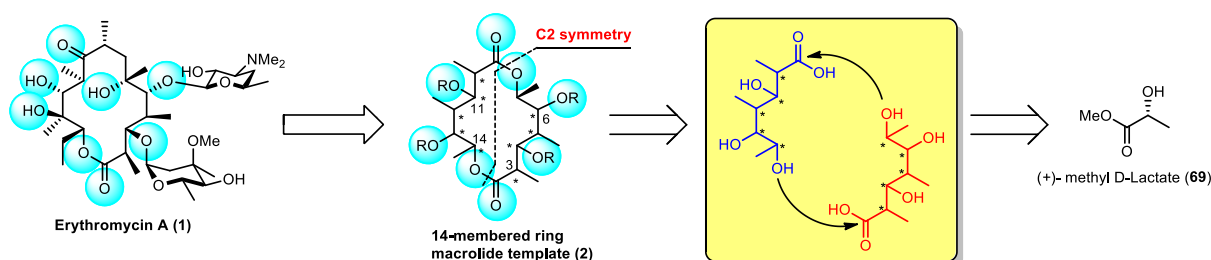
構造式	試験濃度 (ppm)	コナガ幼虫 食用散布 処理 3 日後 死中率 (%)	ワタアブラムシ 食用散布 処理 3 日後 死中率 (%)	処理量 (μ g/苗)
 <p>95</p>	100 20 5	0 0	80 50 (90**) 45 (57**)	20
 <p>94</p>	100 20 5	20 (90*) 0	80 (89**) 44 (56**)	20
	100 20 5	0	0	20
	100 20 5	0	0	20
	100 20 5	10	10 44 (61**)	20
対照薬剤'	0.078	Spinosad 100	Imidacloprid 100	0.13

*苦悶中を含む。 **処理 6 日後調査結果。

III. 総括

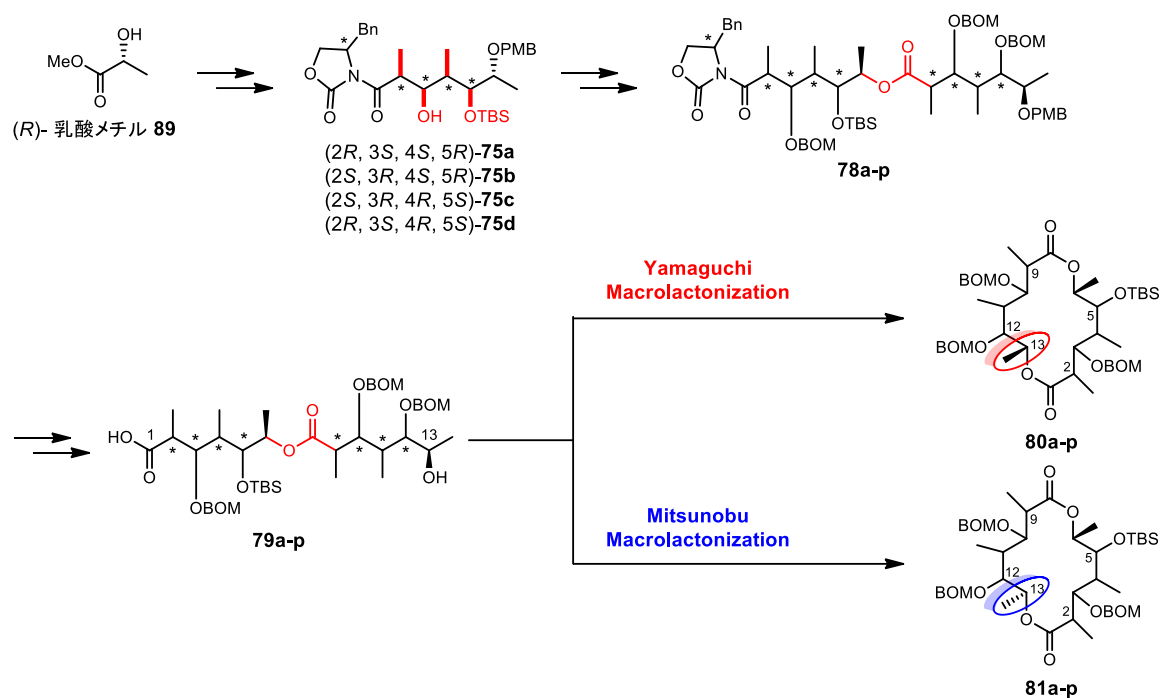
筆者は博士後期課程において「C2 対称ジラクトン骨格を基盤とした三次元構造多様性指向型マクロライドライブラリーの開発研究」に取り組み、erythromycin A をモチーフとした新たな C2 対称テンプレートを設計し、三次元構造多様性を指向した独自のマクロライドライブラリーの構築を行った。

第一章では、erythromycin A (**1**)を模倣したマクロジオライドテンプレートの設計と三次元構造多様性を指向したライブラリーの構築戦略について述べた。三次元構造多様性を指向した C2 対称マクロジオライド骨格を持つ独自のテンプレートを設計した。設計したテンプレートの合成戦略として三次元構造多様性を指向し、その戦略に基づき 32 種の異なる立体化学を持つマクロジオライドテンプレートの立体化学分岐的な合成を計画した。



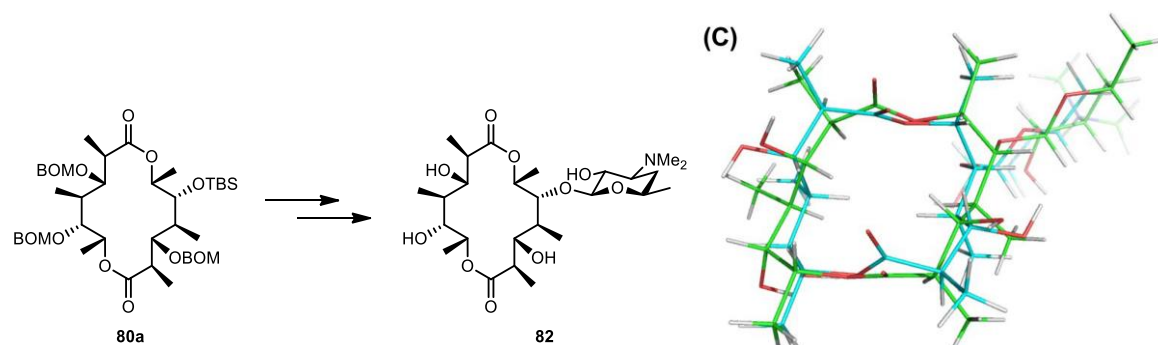
Scheme 26. The design and synthetic plan of 14-membered ring macrolide template.

第二章では、設計したマクロジオライドテンプレートを合成標的として実際にその合成およびマクロジオライドライブラリーの構築を行った。出発原料を市販されているキラルな乳酸メチルとし、二度の Evans aldol 反応により立体化学を制御したハーフユニットを合成した。合成したハーフユニットをそれぞれ組み合わせることで 16 種の立体化学異性体となるリニアユニットを合成し、マクロラクトン化で山口法と光延法の 2 種類の条件を用いることで 32 種の立体異性体となるマクロジオライドテンプレートの合成を達成した。



Scheme 27. The stereochemically divergent synthesis of macrodiolide aglycones **80a-p** and **81a-p**.

第三章では、合成したマクロジオライドテンプレートライブラリーから erythromycin A (**1**) に三次元配座が類似したものを選び、実際に合成を試みた。そして、シュミットグリコシル化反応によりアミノ糖を導入した新規マクロライドを合成した後、コンフォメーション解析を行うことで三次元構造を明らかにし、計算化学による最安定配座との比較を行った。さらに、構築したマクロジオライドライブラリーにアミノ糖を導入した場合を仮定し、CAMDAS を利用することで最安定配座を求め、その三次元構造多様性について考察を行い、多様性と有用性を確認した。



Scheme 28. The synthesis of new macrolide **82** and three-dimensional (3D) solution structure of **82** in MeOH-*d*₄ solution.

第四章では、合成したマクロジオリドテンプレートと新規マクロライド **82** の生物活性評価と考察を行った。合成したマクロジオリドとマクロライド **82** は抗菌活性を示さない結果が得られ、これについて erythromycin A やその他の誘導体と比較し考察を行った。そして、マクロライド **82** は 3 位に水酸基を持つことが抗菌活性を発現しなかった大きな理由であると考え、クラジノースあるいは 3 位の化学変換の重要性がマクロジオリド骨格においても示唆されることが分かった。さらに、種々の生物活性試験の結果から新たに殺虫活性を示すマクロライド化合物を見出すことに成功した。今後も多くの生物活性評価を行うことで、新たなリード化合物の創製が大いに期待できる。

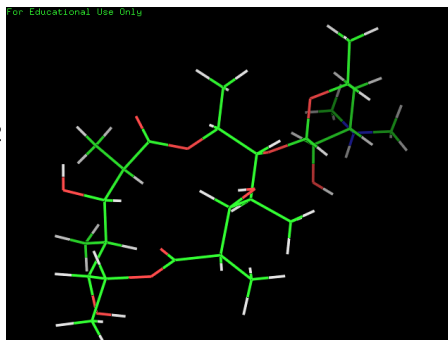
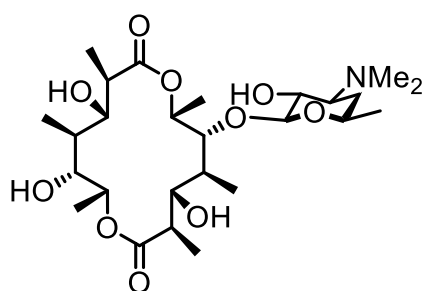
また、本研究で設計したマクロライドテンプレートは骨格上に水酸基を 4 つ有している。今後はそれらに種々の化学修飾を行うことで新たなマクロライドライブラリーの構築とともに、リンカーを介しケミカルプローブやタグを導入した分子を創製し、タンパク質相互作用のネットワーク解析あるいは標的タンパク質の同定などへの応用展開も大いに期待される。

[Reference]

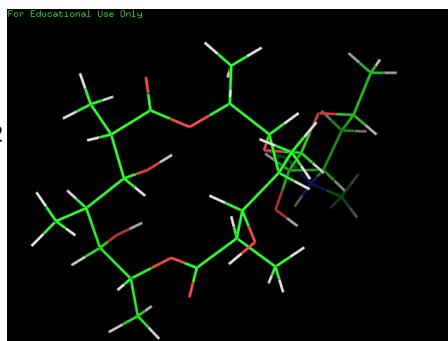
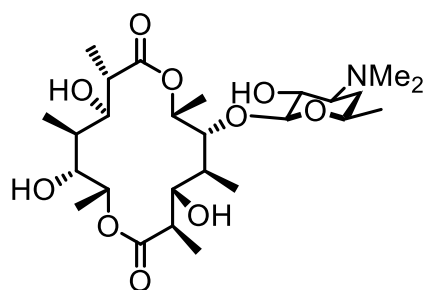
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IV. 実験項・データ項

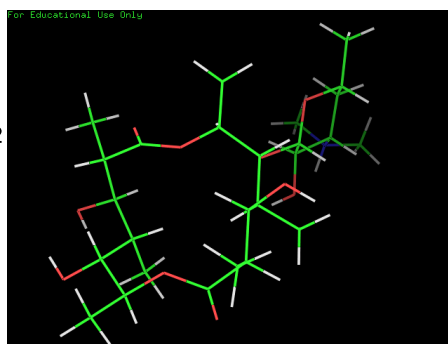
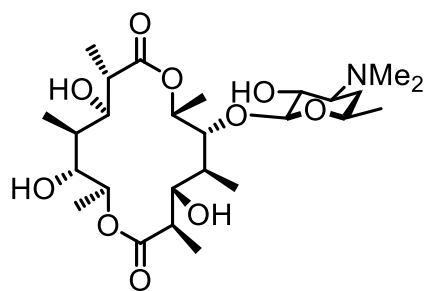
第一章 Conformation of macrolides



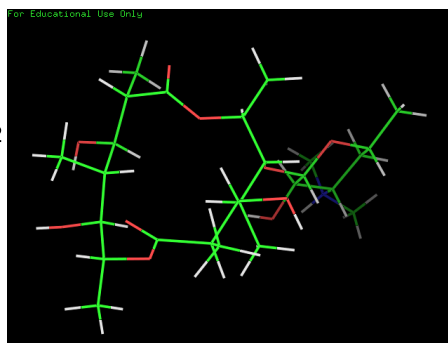
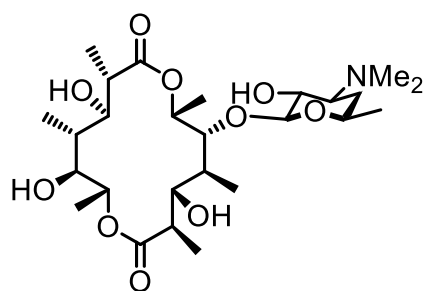
Macrolide **82** (Macrolide 01)



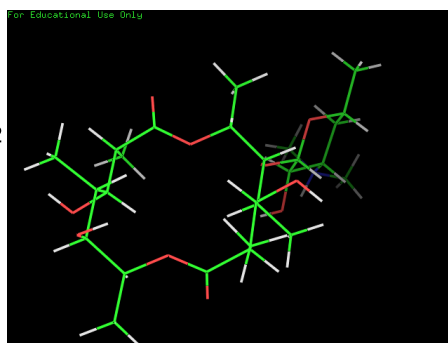
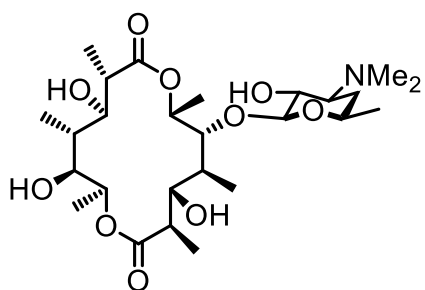
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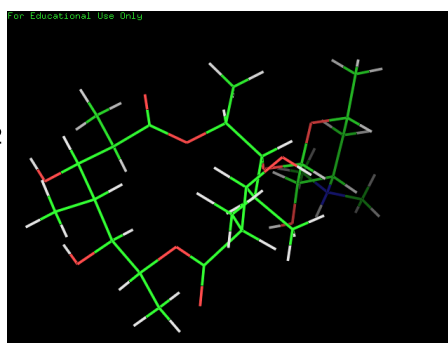
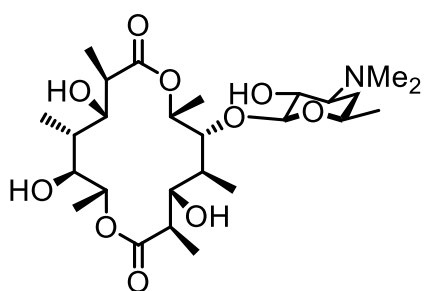
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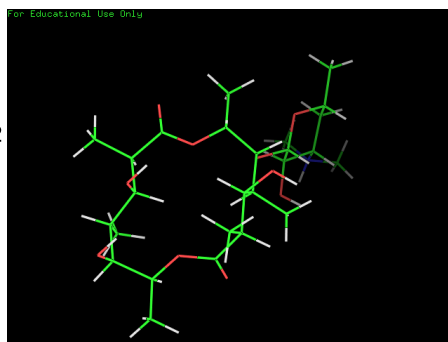
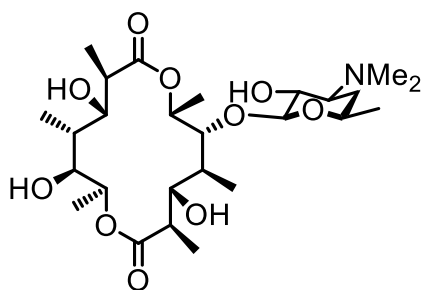
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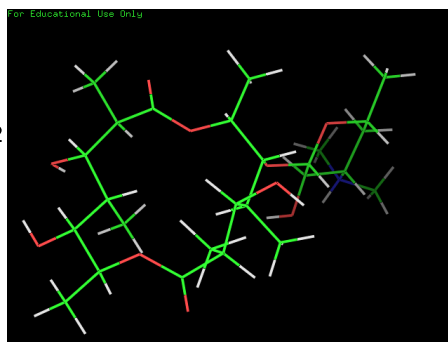
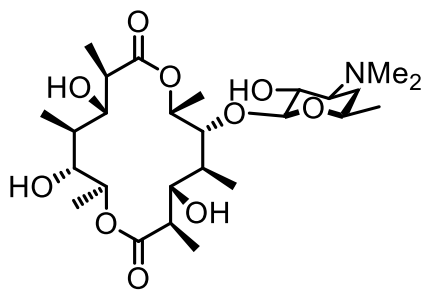
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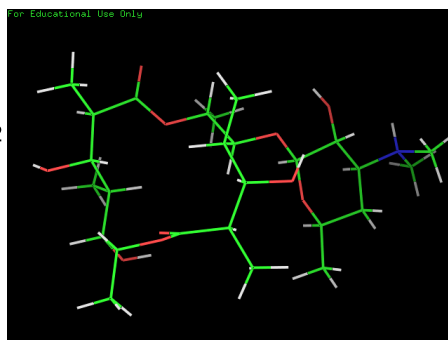
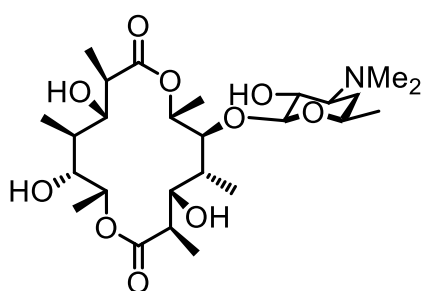
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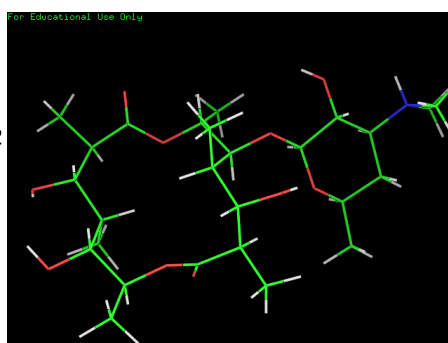
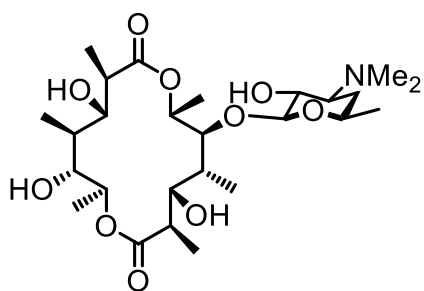
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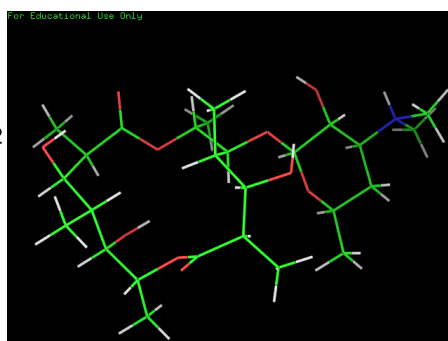
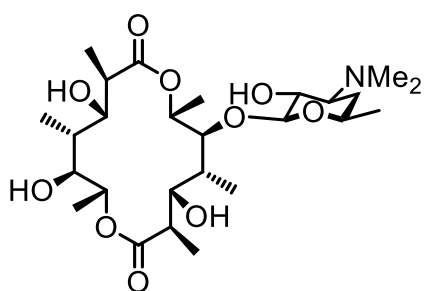
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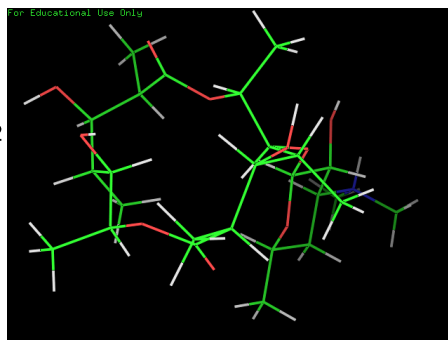
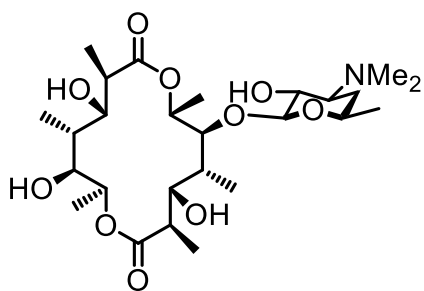
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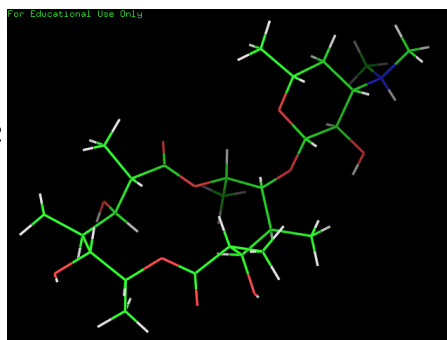
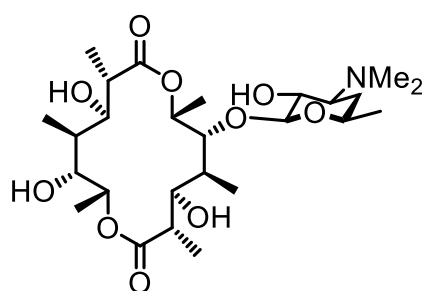
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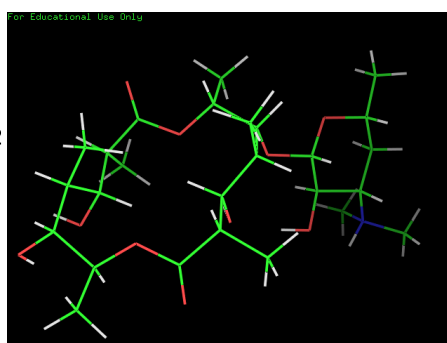
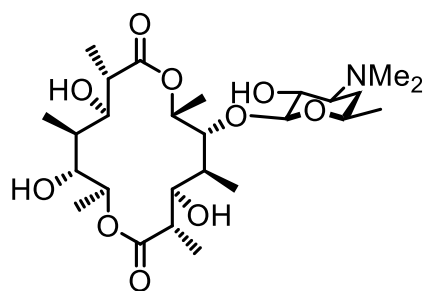
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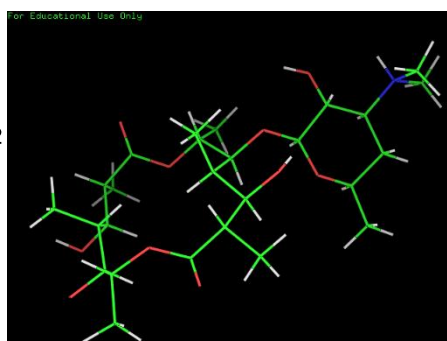
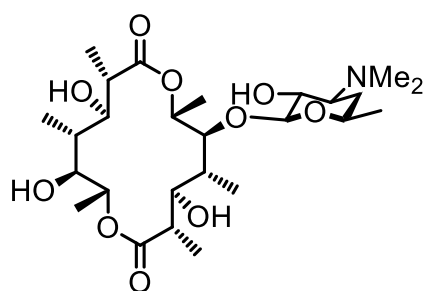
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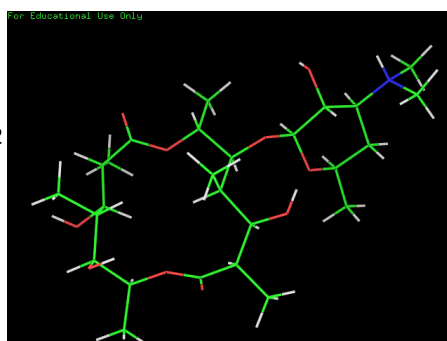
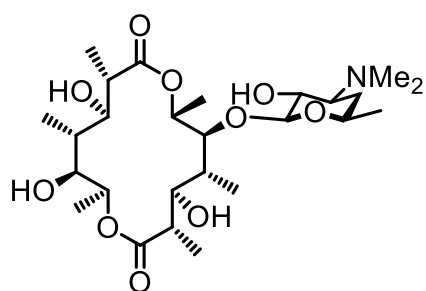
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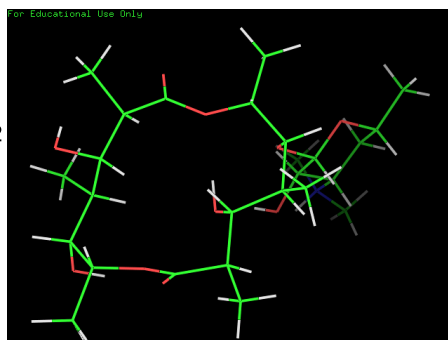
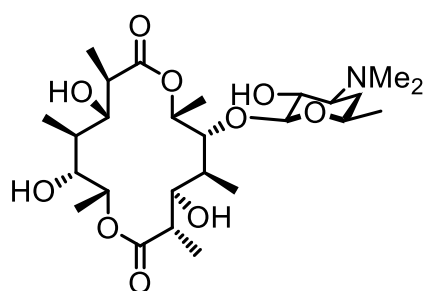
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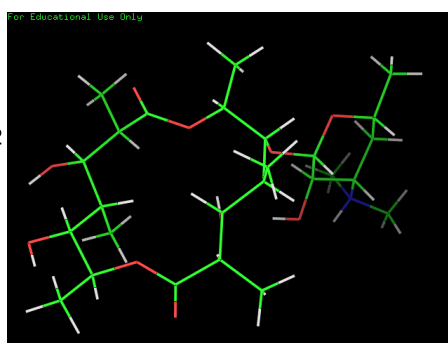
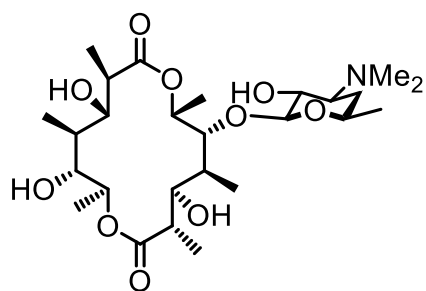
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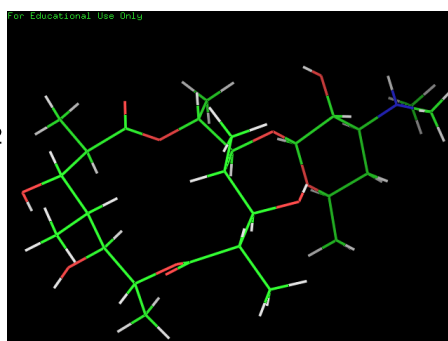
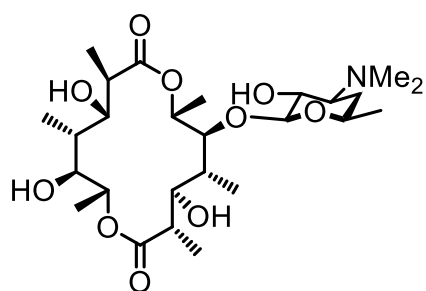
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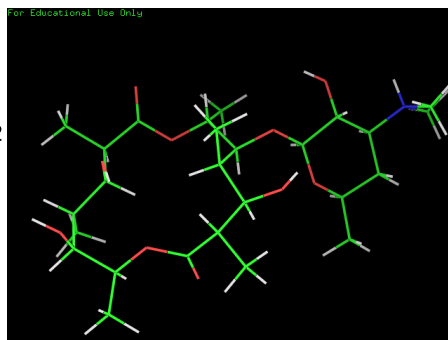
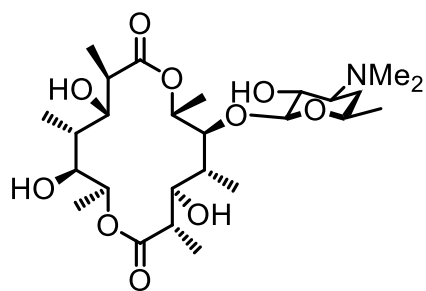
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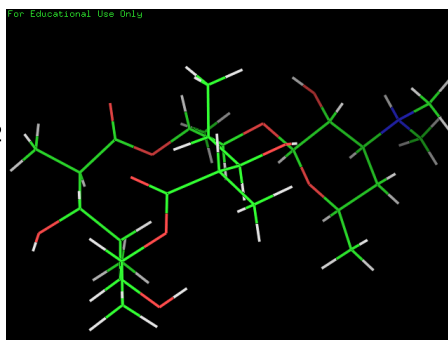
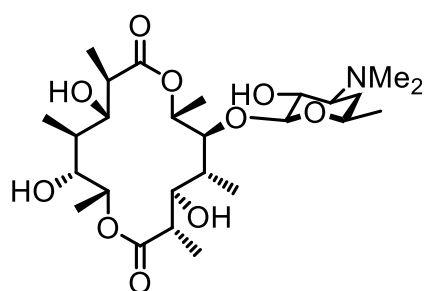
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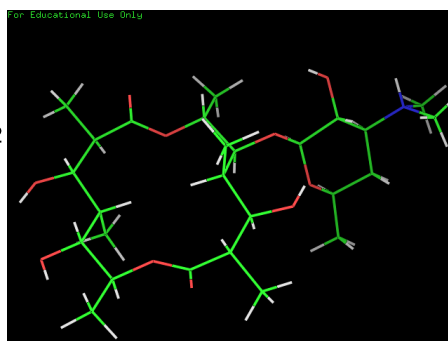
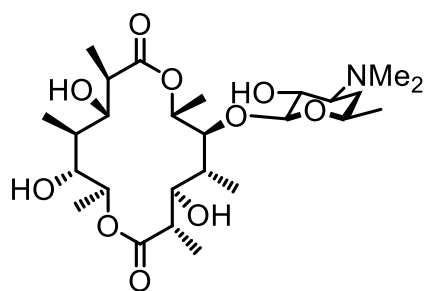
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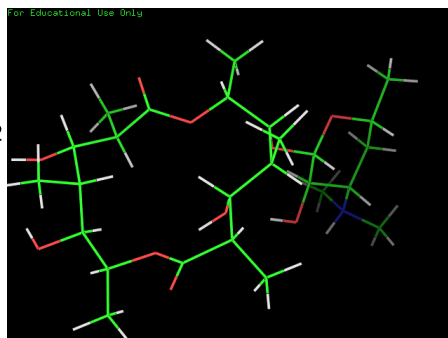
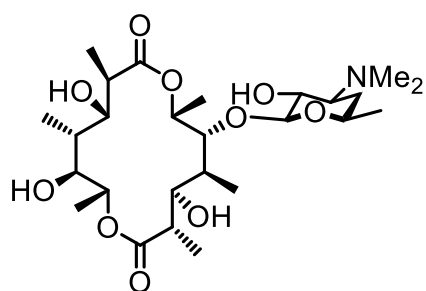
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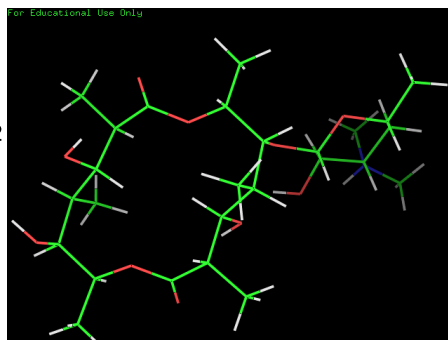
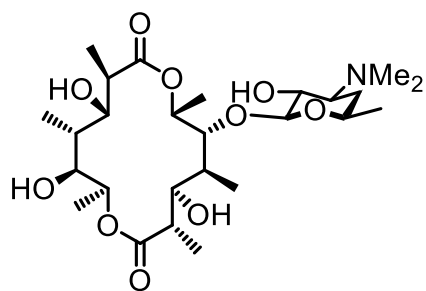
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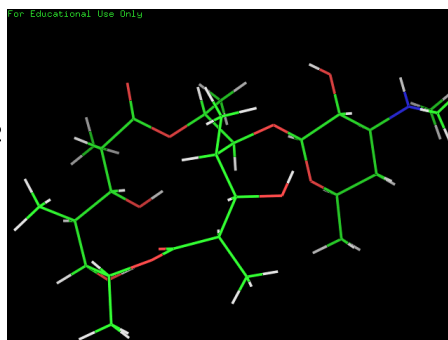
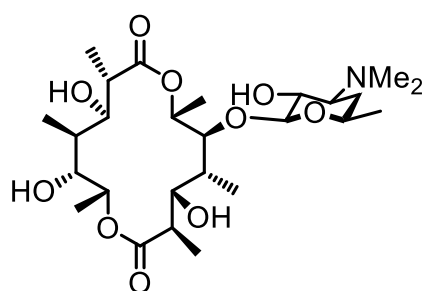
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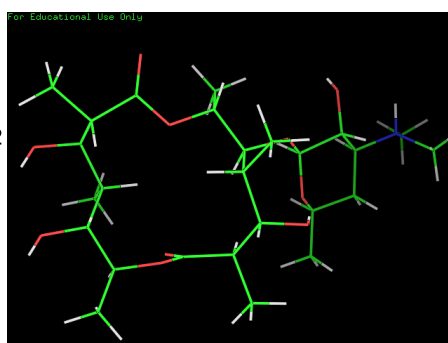
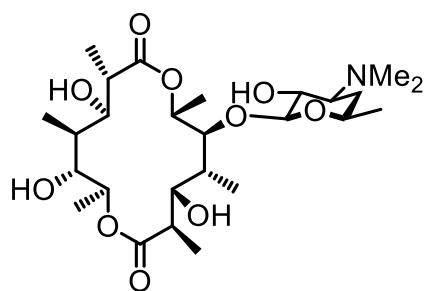
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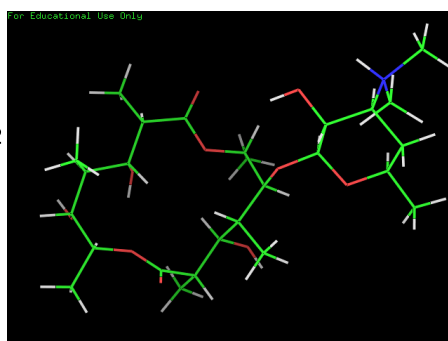
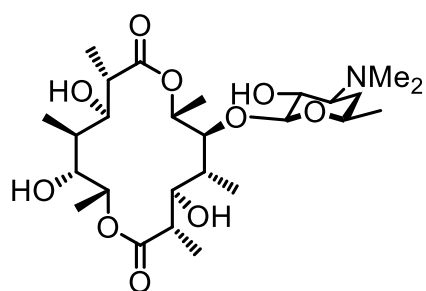
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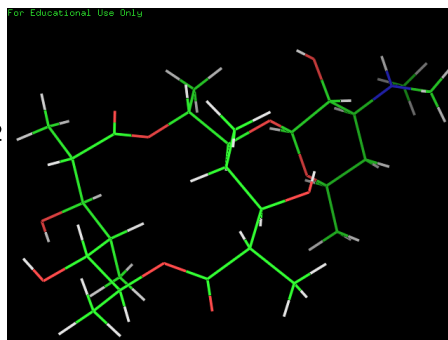
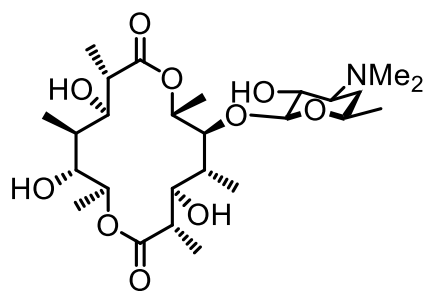
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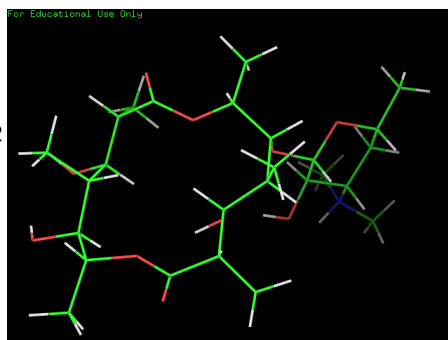
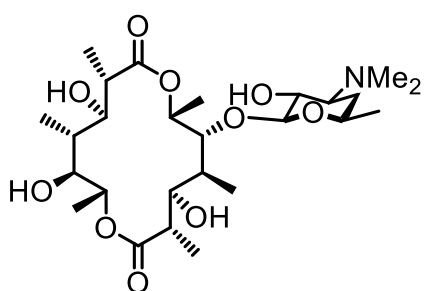
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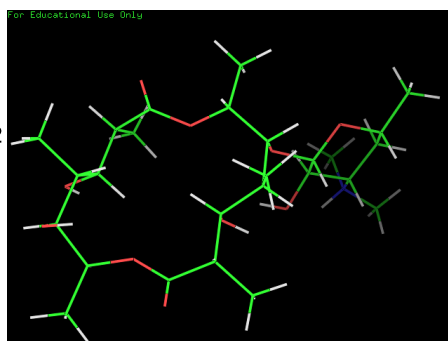
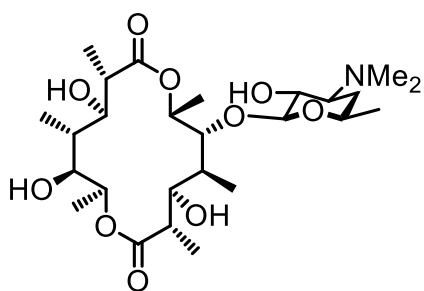
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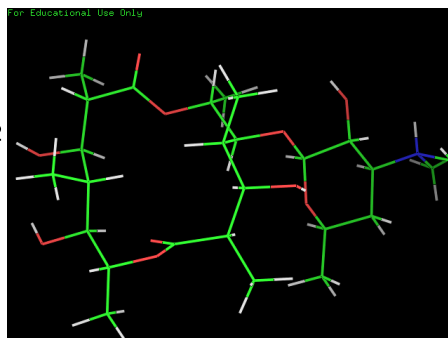
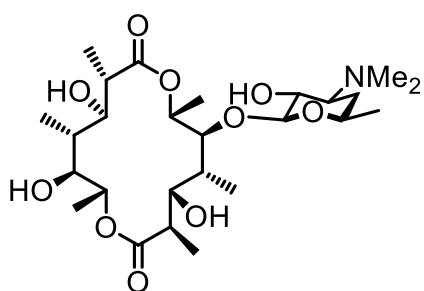
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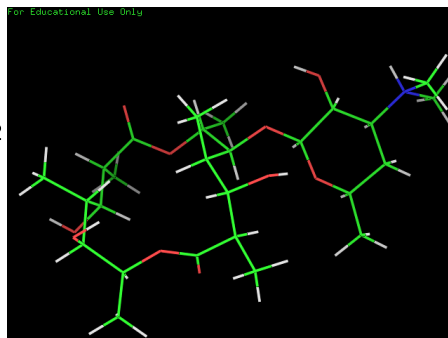
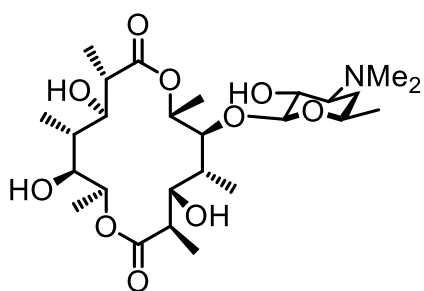
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Macrolide 30



Macrolide 31



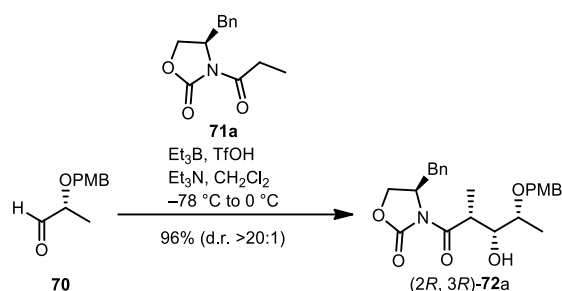
Macrolide 32

第二章 Experimental data

General techniques

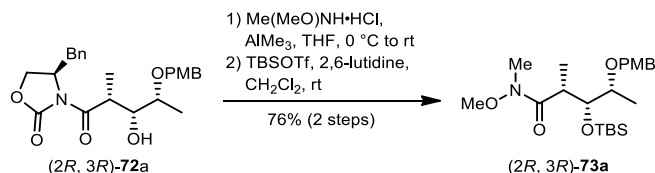
Unless otherwise stated, reactions were carried out under a nitrogen atmosphere. Dry dichloromethane (CH_2Cl_2), tetrahydrofuran (THF), benzene, toluene and hexane were purchased from Kanto Chemical Co., Inc. Pre-coated silica gel plates with a fluorescent indicator were used for analytical (Merck Millipore, TLC silica gel 60 F₂₅₄) and preparative thin layer chromatography (Merck Millipore, PLC silica gel 60 F₂₅₄, 0.5 mm). Silica gel 60N, spherical neutral, for flash chromatography (Kanto Chemical Co., Inc., particle size 40-50 μm , Cat. No. 37563-84) was used for flash column chromatography. ^1H NMR spectra were recorded on 500 MHz spectrometers and ^{13}C NMR spectra were recorded on 125 MHz spectrometers on JEOL ECA-500 (500 MHz). The chemical shifts are expressed in ppm downfield from internal solvent peaks CDCl_3 (7.26 ppm, ^1H NMR, 77.0 ppm, ^{13}C NMR), CD_3OD (3.31 ppm, ^1H NMR, 49.0 ppm, ^{13}C NMR) and coupling constant (J values) are given in Hertz. The coupling patterns are expressed by s (singlet), d (doublet), dd (double doublet), ddd (double double doublet), dt (double triplet), t (triplet), q (quartet), dq (double quartet), m (multiplet), br (broadened), complex m, app (appearance). The all infrared (IR) spectra were measured on a Horiba FT-710 spectrometer using a diamond horizontal ATR accessory. High- and low-resolution mass spectra were measured on JEOL JMS-700 MStation and JEOL JMS-T100LP. Optical rotations were measured with a Jasco P-1010 polarimeter.

4.1. (*R*)-4-Benzyl-3-[(2'*R*,3'*R*,4'*R*)-3'-hydroxy-4'-[(4-methoxybenzyl)oxy]-2'-methylpentanoyl] oxazolidin-2-one (**72a**);



To a solution of Et₃B in hexane (1.04 M, 105 mL, 109 mmol) was added TfOH (9.7 mL, 111 mmol) under N₂ at 0 °C. After stirring for 1 h at 40 °C, to the solution mixture was added a solution of (*R*)-(-)-4-benzyl-3-propionyloxazolidin-2-one **71a** (22.8 g, 97.7 mmol) in CH₂Cl₂ (60 mL) and Et₃N (29.0 mL, 209 mmol) at 0 °C. Then, the mixture was cooled to -78 °C and to this mixture was slowly added a solution of aldehyde **70** (16.0 g, 82.4 mmol) in CH₂Cl₂ (65 mL). After stirring for 30 min, the mixture was warmed to 0 °C and stirred for 1 h. The reaction mixture was quenched with phosphate buffer solution in water (100 mL, pH = 7.0) and MeOH/30% aq. H₂O₂ solution in water (v/v, 2/1, 90 mL) at 0 °C. Resulted two layers were separated and the aqueous phase was extracted with CHCl₃ (50 mL ×3). The combined organic layers were washed with water and brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 5/1, 3/1 to 2/1) to afford aldol product **72a** (33.9 g, 96%) as a colorless oil; [α]_D²² -48.6 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 3448, 1780, 1692, 1385, 1246, 1211, 1105, 1039, 754; ¹H NMR (500 MHz, CDCl₃) δ 7.32 (m, 2H), 7.27 (d, *J* = 6.3 Hz, 1H), 7.23 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.58 (d, *J* = 11.5 Hz, 1H), 4.41 (m, 1H), 4.30 (d, *J* = 11.5 Hz, 1H), 4.07 (dd, *J* = 8.6, 1.7 Hz, 1H), 3.99 (dd, *J* = 8.3, 8.3 Hz, 1H), 3.89 (dq, *J* = 6.9, 6.9 Hz, 1H), 3.79 (m, 1H), 3.75 (s, 3H), 3.53 (m, 1H), 3.20 (dd, *J* = 13.2, 2.9 Hz, 1H), 2.70 (dd, *J* = 13.2, 9.7 Hz, 1H), 2.52 (d, *J* = 6.9 Hz, 1H), 1.29 (d, *J* = 6.9 Hz, 3H), 1.29 (d, *J* = 6.3 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.3, 159.0, 152.7, 135.1, 130.1, 129.6 (C ×2), 129.3 (C ×2), 128.7 (C ×2), 127.2, 113.6 (C ×2), 74.9, 74.1, 69.9, 65.8, 55.1, 55.1, 40.2, 37.5, 15.2, 12.8; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₂₄H₂₉NO₆Na, 450.1893; found: 450.1902.

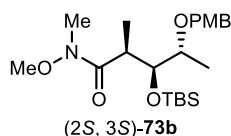
4.2. (2*R*,3*R*,4*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-*N*-methoxy-4-[(4-methoxybenzyl)oxy]-*N*,2-dimethylpentamide (**73a**);



To a suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (11.7g, 120 mmol) in THF (100 mL) was added AlMe₃ (1.06 M in hexane, 116 mL, 123 mmol) under N₂ at 0 °C. After stirring for 1 h, the reaction mixture was warmed to room temperature and stirred for 30 min. The mixture was then cooled to 0 °C and a

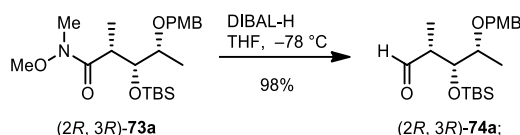
solution of aldol product **72a** (20.5 g, 48.0 mmol) in THF (60 mL) was added. The reaction mixture was warmed to room temperature, and stirred for 13 h. The reaction was quenched with aq. 1N HCl (80 mL) and resulted two layers were separated and the aqueous phase was extracted with CH₂Cl₂ (40 mL ×3). The combined organic layers were washed with water and brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was used in the next reaction without further purification.

To a solution of crude mixture in CH₂Cl₂ (120 mL) was added 2,6-lutidine (18.0 mL, 155 mmol) under N₂. Then the mixture was cooled to 0 °C and TBSOTf (25.8 mL, 112 mmol) was added. After stirring for 4 h, the reaction mixture was quenched with aq. 1N HCl (60 mL). Resulted two layers were separated and the aqueous phase was extracted with CH₂Cl₂ (40mL ×3). The combined organic layers were washed with water and brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 6/1, 4/1 to 3/1) to afford Weinreb amide **73a** (15.5 g, 76%) as a colorless oil; $[\alpha]_D^{24} +24.2$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹; 2935, 2362, 1658, 1514, 1466, 1383, 1252, 1095, 1043, 835, 777; ¹H NMR (500 MHz, CDCl₃) δ 7.24 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 7.5 Hz, 2H), 4.44 (d, *J* = 11.5 Hz, 1H), 4.32 (d, *J* = 11.5 Hz, 1H), 4.20 (dd, *J* = 8.6, 4.6 Hz, 1H), 3.78 (s, 3H), 3.61 (s, 3H), 3.55 (m, 1H), 3.18 (app brs, 1H), 2.97 (s, 3H), 1.19 (d, *J* = 6.3 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.03 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 176.8, 158.9, 131.0, 129.3 (C ×2), 113.4 (C ×2), 76.95, 72.7, 70.7, 61.2, 55.2, 35.0, 32.2, 25.8 (C ×3), 18.1, 15.6, 14.0, -4.5, -4.6; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₂₂H₃₉NO₅SiNa, 448.2495; found: 448.2494.



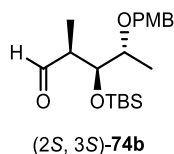
(2S,3S,4R)-3-[(*tert*-Butyldimethylsilyl)oxy]-*N*-methoxy-4-[(4-methoxybenzyl)oxy]-*N*,2-dimethylpentanamide (**73b**); According to the procedure of **4.2.**, aldol product **72b** (26.3 g, 61.5 mmol) was converted to **73b** (22.0 g, 84%) as a colorless oil; $[\alpha]_D^{27} +5.8$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹ 2931, 2893, 2854, 1658, 1250, 1041, 833, 756; ¹H NMR (500 MHz, CDCl₃) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.40 (d, *J* = 12.0 Hz, 1H), 4.09 (dd, *J* = 8.6, 2.3 Hz, 1H), 3.79 (s, 3H), 3.62 (s, 3H), 3.34 (m, 1H), 3.11 (s, 3H), 2.97 (app brs, 1H), 1.18 (d, *J* = 7.5 Hz, 3H), 1.11 (d, *J* = 6.3 Hz, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 176.5, 158.8, 131.0, 129.3 (C ×2), 113.4 (C ×2), 76.6, 75.4, 70.1, 61.4, 55.2, 38.6, 32.1, 26.1 (C ×3), 18.4, 15.0, 14.6, -3.8, -4.6; HRMS-ESI (*m/z*); [M + Na]⁺ Calcd for C₂₂H₃₉NO₅SiNa, 448.2495; found 448.2488.

4.3. (2R,3R,4R)-3-[(*tert*-Butyldimethylsilyl)oxy]-4-(4-methoxybenzyl)oxy-2-methylpentanal (**74a**);



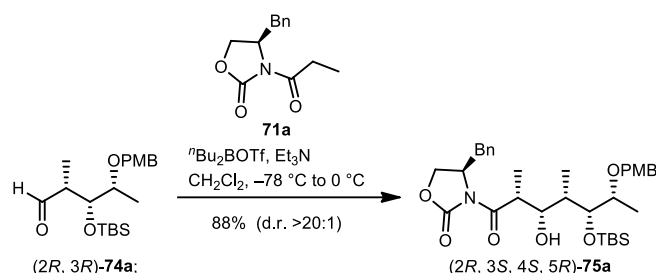
To a solution of Weinreb amide **73a** (22.1 g, 51.9 mmol) in THF (100 mL) was added DIBAL-H (1.0 M in hexane, 110 mL, 110 mmol) under N₂ at -78 °C. After stirring for 1 h, the reaction was quenched with sat. aq. Rochelle's salt (150 mL) and stirred for 1 h at room temperature. Resulted two layers were separated and

the aqueous phase was extracted with EtOAc (50 mL \times 3). The combined organic layers were washed with water and brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 7/1 to 4/1) to afford aldehyde **74a** (18.6 g, 98%) as a colorless oil; $[\alpha]_D^{24}$ -26.4 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹ 2954, 2931, 2885, 2854, 1720, 1512, 1250, 1088, 1034, 833, 771; ¹H NMR (500 MHz, CDCl₃) δ 9.72 (d, *J* = 1.7 Hz, 1H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.46 (d, *J* = 11.5 Hz, 1H), 4.34 (d, *J* = 11.5 Hz, 1H), 3.98 (dd, *J* = 5.7, 4.0 Hz, 1H), 3.80 (s, 3H), 3.55 (dq, *J* = 6.3, 4.0 Hz, 1H), 2.55 (m, 1H), 1.18 (d, *J* = 6.3 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 203.2, 159.1, 130.2, 129.3 (C \times 2), 113.6 (C \times 2), 75.2, 74.6, 70.3, 55.2, 48.9, 25.8 (C \times 3), 18.0, 14.6, 10.2, -4.5 , -4.8 ; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₂₀H₃₄O₄SiNa, 389.2124; found: 389.2132.



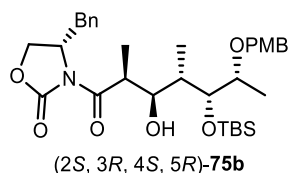
(2S,3S,4R)-3-[(*t*-Butyldimethylsilyl)oxy]-4-(4-methoxybenzyl)oxy-2-methylpentanal (**74b**); According to the procedure of **4.3.**, **73b** (17.3 g, 40.6 mmol) was converted to **74b** (14.0 g, 94%) as a colorless oil; $[\alpha]_D^{27}$ -1.5 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹ ; 2954, 2931, 2885, 2854, 1720, 1512, 1466, 1250, 1103, 1034, 833; ¹H NMR (500 MHz, CDCl₃) δ 9.69 (s, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 4.53 (d, *J* = 11.5 Hz, 1H), 4.36 (d, *J* = 11.5 Hz, 1H), 4.07 (dd, *J* = 6.3, 3.4 Hz, 1H), 3.80 (s, 3H), 3.44 (m, 1H), 2.73 (dq, *J* = 6.9, 3.4 Hz, 1H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.87 (s, 9H), 0.08 (s, 3H), -0.01 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 204.6, 159.2, 130.3, 129.4 (C \times 2), 113.7 (C \times 2), 75.9, 74.5, 70.5, 55.2, 49.9, 25.9 (C \times 3), 18.1, 16.2, 7.9, -4.1 , -4.2 ; HRMS-ESI (*m/z*); [M + Na]⁺ Calcd for C₂₀H₃₄O₄SiNa, 389.2124; found 389.2119.

4.4. (*R*)-4-Benzyl-3-[(2'*R*,3'*S*,4'*S*,5'*R*,6'*R*)-5-[(*tert*-butyldimethylsilyl)oxy]-3-hydroxy-6-(4-methoxybenzyloxy)-2, 4-dimethylheptanoyl} oxazolidin-2-one (**75a**);

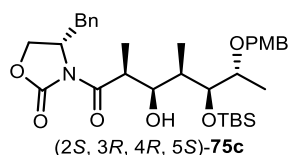


To a solution of (*R*)-(-)-4-benzyl-3-propionyloxazolidin-2-one **71a** (7.08 g, 30.4 mmol) in CH₂Cl₂ (55 mL) was added Et₃N (9.0 mL, 64.9 mmol) and ^{*n*}Bu₂BOTf (1.0 M in CH₂Cl₂ solution, 40 mL, 40.0 mmol) under N₂ at 0 °C. After stirring for 40 min, the solution was cooled to -78°C and a solution of aldehyde **74a** (8.77 g, 23.9 mmol) in CH₂Cl₂ (45 mL) was added. The reaction mixture was stirred at -78°C for 1 h. Then the mixture was allowed to warm to 0 °C and stirred for 1 h. The reaction mixture was quenched with phosphate buffer solution in water (90 mL, pH = 7.0) and MeOH/30% H₂O₂ solution in water (v/v, 2/1, 81 mL). After stirring for 1 h, resulted two layers were separated and the aqueous phase was extracted with CH₂Cl₂ (40 mL \times 3). The

combined organic layers were washed with water and brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 8/1, 6/1 to 3/1) to afford aldol product **75a** (12.6 g, 88%) as a colorless oil; [α]_D²⁶ -42.3 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹; 3564, 2939, 2893, 2854, 1774, 1697, 1381, 1242, 1211, 1026, 833, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.33 (m, 2H), 7.29–7.25 (complex m, 3H), 7.21 (d, *J* = 7.5 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.68 (m, 1H), 4.61 (d, *J* = 11.5 Hz, 1H), 4.40 (d, *J* = 11.5 Hz, 1H), 4.22 (m, 1H), 4.16 (d, *J* = 5.2 Hz, 2H), 3.97 (dq, *J* = 6.9, 6.9 Hz, 1H), 3.79 (s, 3H), 3.65 (dd, *J* = 5.7, 5.2 Hz, 1H), 3.57 (m, 1H), 3.23 (dd, *J* = 13.2, 3.3 Hz, 1H), 3.21 (d, *J* = 3.9 Hz, 1H), 2.78 (dd, *J* = 13.2, 9.2 Hz, 1H), 1.81 (m, 1H), 1.34 (d, *J* = 6.9 Hz, 3H), 1.26 (d, *J* = 6.3 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.85 (s, 9H), 0.01 (s, 3H), -0.05 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 176.7, 159.1, 152.6, 135.0, 130.3, 129.4 (C \times 2), 129.1 (C \times 2), 128.8 (C \times 2), 127.3, 113.7 (C \times 2), 77.5, 75.9, 71.8, 70.2, 65.8, 55.1, 54.9, 40.1, 37.9, 37.5, 25.8 (C \times 3), 18.1, 14.1, 13.4, 10.2, -4.3, -5.0; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₃₃H₄₉NO₇SiNa, 622.3176; found: 622.3181.

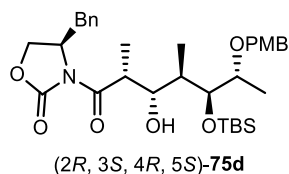


(*S*)-4-Benzyl-3-[(2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-5-[(*t*-butyldimethylsilyl)oxy]-3-hydroxy-6-(4-methoxybenzyloxy)-2,4-dimethylheptanoyl] oxazolidin-2-one (**75b**); According to the procedure of **4.4.**, **74a** (5.76 g, 15.7 mmol) was converted to **75b** (8.39 g, 89%) as a colorless oil; [α]_D²⁶ +11.6 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹; 3533, 3062, 3032, 2931, 2893, 2854, 1774, 1705, 1381, 1242, 1203, 1095, 1026, 833, 733; ¹H NMR (500 MHz, CDCl₃) δ 7.32 (m, 2H), 7.28–7.25 (complex m, 3H), 7.20 (d, *J* = 6.9 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.62 (m, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.44 (d, *J* = 11.5 Hz, 1H), 4.08 (d, *J* = 9.2 Hz, 1H), 3.97–3.92 (complex m, 3H), 3.88 (app q, *J* = 6.9 Hz, 1H), 3.76 (s, 3H), 3.59 (brs, 1H), 3.55 (dq, *J* = 6.3, 6.3 Hz, 1H), 3.31 (dd, *J* = 13.2, 2.3 Hz, 1H), 2.74 (dd, *J* = 13.2, 9.7 Hz, 1H), 1.87 (m, 1H), 1.21 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.3 Hz, 3H), 0.89–0.87 (complex m, 12H), 0.07 (s, 3H), 0.00 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 177.0, 158.8, 153.0, 135.3, 131.0, 129.4 (C \times 2), 128.9 (C \times 2), 128.7 (C \times 2), 127.2, 113.5 (C \times 2), 76.5, 75.4, 72.5, 70.2, 66.0, 55.5, 55.2, 40.1, 37.8, 37.7, 26.0 (C \times 3), 18.2, 15.6, 11.5, 8.5, -4.4, -4.7; HRMS-ESI (*m/z*); [M + Na]⁺ Calcd for C₃₃H₄₉NO₇SiNa, 622.3176; found 622.3166.



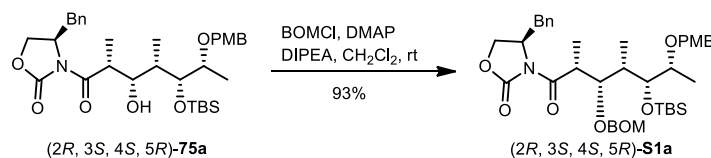
(*S*)-4-Benzyl-3-[(2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-5-[(*t*-butyldimethylsilyl)oxy]-3-hydroxy-6-(4-methoxybenzyloxy)-2,4-dimethylheptanoyl] oxazolidin-2-one (**75c**); According to the procedure of **4.4.**, **74b** (4.03 g, 11.0 mmol) was converted to **75c** (5.84 g, 89%) as a colorless oil; [α]_D²⁶ +26.0 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹; 3548, 3062, 2931, 2893, 2854, 1782, 1697, 1512, 1458, 1381, 1242, 1211, 1034, 833, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.34 (m, 2H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.67 (m, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.17 (d, *J* = 5.2 Hz, 2H), 3.99–3.93

(complex m, 2H), 3.79 (s, 3H), 3.70 (dd, $J = 4.0, 4.0$ Hz, 1H), 3.58 (m, 1H), 3.24 (dd, $J = 13.2, 3.4$ Hz, 1H), 2.79–2.73 (complex m, 2H), 1.85 (m, 1H), 1.29 (d, $J = 6.3$ Hz, 3H), 1.19 (d, $J = 6.3$ Hz, 3H), 1.02 (d, $J = 6.9$ Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 177.1, 159.0, 152.7, 135.0, 130.8, 129.4 (C $\times 2$), 129.2 (C $\times 2$), 128.9 (C $\times 2$), 127.4, 113.6 (C $\times 2$), 76.9, 76.8, 72.7, 70.5, 66.0, 55.2, 55.0, 40.6, 38.9, 37.7, 26.1 (C $\times 3$), 18.4, 15.7, 13.1, 9.9, -3.7 , -4.4 ; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{49}\text{NO}_7\text{SiNa}$, 622.3176; found 622.3174.



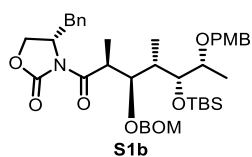
(*R*)-4-Benzyl-3-[(2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-5-[(*t*-butyldimethylsilyl)oxy]-3-hydroxy-6-(4-methoxybenzyloxy)-2,4-dimethylheptanoyl] oxazolidin-2-one (**75d**); According to the procedure of **4.4.**, **74b** (9.94 g, 27.1 mmol) was converted to **75d** (13.8 g, 85%) as a colorless oil; $[\alpha]_{\text{D}}^{30} -38.3$ (c 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3556, 3016, 2931, 2893, 2854, 1782, 1697, 1512, 1458, 1389, 1241, 1211, 1095, 1034, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.33 (m, 2H), 7.29–7.25 (complex m, 3H), 7.21 (d, $J = 7.5$ Hz, 2H), 6.87 (d, $J = 8.0$ Hz, 2H), 4.70 (m, 1H), 4.51 (d, $J = 11.5$ Hz, 1H), 4.40 (d, $J = 11.5$ Hz, 1H), 4.22–4.15 (complex m, 2H), 4.01 (dd, $J = 5.7, 1.2$ Hz, 1H), 3.90–3.86 (complex m, 2H), 3.80 (s, 3H), 3.62 (brs, 1H), 3.58 (dq, $J = 5.7, 5.7$ Hz, 1H), 3.31 (dd, $J = 13.2, 2.9$ Hz, 1H), 2.78 (dd, $J = 13.2, 9.7$ Hz, 1H), 1.96 (m, 1H), 1.23 (d, $J = 5.7$ Hz, 3H), 1.20 (d, $J = 6.9$ Hz, 3H), 0.90 (s, 9H), 0.85 (d, $J = 6.9$ Hz, 3H), 0.10 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 177.0, 159.0, 153.0, 135.3, 130.8, 129.4 (C $\times 2$), 129.3 (C $\times 2$), 128.9 (C $\times 2$), 127.3, 113.7 (C $\times 2$), 76.4, 76.1, 72.4, 70.4, 66.1, 55.5, 55.2, 40.1, 38.2, 37.7, 26.0 (C $\times 3$), 18.2, 16.9, 11.2, 8.5, -4.2 , -4.4 ; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{49}\text{NO}_7\text{SiNa}$, 622.3176; found 622.3180.

4.5. (*R*)-4-Benzyl-3-[(2'*R*,3'*S*,4'*R*,5'*R*,6'*R*)-3'-[(benzyloxy)methoxy]-5'-[(*tert*-butyldimethylsilyl)oxy]-6'-[(4-methoxybenzyloxy)-2',4'-dimethylheptanoyl] oxazolidin-2-one (**S1a**);



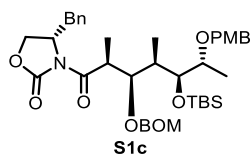
To a solution of Evans aldol product **75a** (3.06 g, 5.10 mmol) in CH_2Cl_2 (7.0 mL) was added DMAP (638 mg, 5.22 mmol) and DIPEA (22.0 mL, 129 mmol) under N_2 at room temperature. Then BOMCl (10.5 mL, 76.4 mmol) was added to the mixture at 0°C . After stirring for 5 h at room temperature, the reaction was quenched with H_2O (20 mL) at 0°C . The resulting mixture was diluted with CH_2Cl_2 (10 mL) and resulted two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (15 mL $\times 3$). The combined organic layers were washed with water and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/ $\text{EtOAc} = 5/1$ to $3/1$) to afford **S1a** (3.42 g, 93%) as a colorless oil; $[\alpha]_{\text{D}}^{27} -33.7$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 2939, 2893, 2854, 1774, 1697, 1512, 1458, 1381, 1242, 1088, 1026, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.23 (complex m, 10H), 7.11 (d,

$J = 6.9$ Hz, 2H), 6.84 (d, $J = 8.6$ Hz, 2H), 4.82 (d, $J = 6.9$ Hz, 1H), 4.81 (d, $J = 6.9$ Hz, 1H), 4.69 (d, $J = 12.0$ Hz, 1H), 4.58 (d, $J = 12.0$ Hz, 1H), 4.54 (d, $J = 11.5$ Hz, 1H), 4.47 (d, $J = 11.5$ Hz, 1H), 4.35 (m, 1H), 4.12–4.05 (complex m, 2H), 4.01 (dd, $J = 9.2, 2.3$ Hz, 1H), 3.93 (dd, $J = 8.0, 8.0$ Hz, 1H), 3.88 (dd, $J = 5.2, 4.0$ Hz, 1H), 3.78 (s, 3H), 3.55 (m, 1H), 3.23 (dd, $J = 13.2, 3.4$ Hz, 1H), 2.70 (dd, $J = 13.2, 9.7$ Hz, 1H), 2.02 (m, 1H), 1.28 (d, $J = 6.3$ Hz, 3H), 1.16 (d, $J = 6.3$ Hz, 3H), 0.96 (d, $J = 6.9$ Hz, 3H), 0.86 (s, 9H), 0.03 (s, 3H), -0.05 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.4, 158.8, 153.0, 138.2, 135.3, 131.1, 129.4 (C $\times 2$), 129.0 (C $\times 2$), 128.8 (C $\times 2$), 128.2 (C $\times 2$), 127.4, 127.3 (C $\times 2$), 127.1, 113.5 (C $\times 2$), 96.7, 81.2, 77.4, 73.1, 70.2, 70.1, 65.8, 55.5, 55.2, 41.5, 37.7, 37.4, 25.9 (C $\times 3$), 18.2, 14.0, 12.5, 11.3, -4.4 , -4.5 ; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{41}\text{H}_{57}\text{NO}_8\text{SiNa}$, 742.3751; found: 742.3744.



(*S*)-4-Benzyl-3-((2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-3'-[(benzyloxy)methoxy]-5'-[(*tert*-butyldimethylsilyl)oxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl} oxazolidin-2-one (**S1b**);

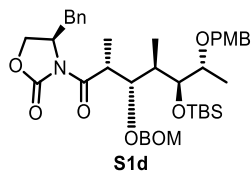
According to the procedure of **4.5.**, **75b** (2.99 g, 4.98 mmol) was converted to **S1b** (3.36 g, 94%) as a colorless oil; $[\alpha]_{\text{D}}^{27} +10.7$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 3031, 2931, 2885, 2854, 1782, 1705, 1381, 1242, 1088, 1034, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.36 (complex m, 2H), 7.33–7.22 (complex m, 8H), 7.01 (d, $J = 8.0$ Hz, 2H), 6.86 (d, $J = 8.6$ Hz, 2H), 4.85 (s, 2H), 4.74 (d, $J = 12.0$ Hz, 1H), 4.52–4.49 (complex m, 2H), 4.40 (d, $J = 12.0$ Hz, 1H), 4.20 (m, 1H), 4.09 (m, 1H), 4.00 (m, 1H), 3.93 (dd, $J = 9.2, 1.7$ Hz, 1H), 3.86 (m, 1H), 3.82–3.79 (complex m, 4H), 3.50 (dq, $J = 6.3, 6.3$ Hz, 1H), 3.23 (dd, $J = 13.2, 2.3$ Hz, 1H), 2.63 (dd, $J = 13.2, 10.3$ Hz, 1H), 1.96 (m, 1H), 1.27 (d, $J = 6.9$ Hz, 3H), 1.15 (d, $J = 6.3$ Hz, 3H), 0.98 (d, $J = 6.9$ Hz, 3H), 0.88 (s, 9H), 0.02 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.6, 158.8, 153.1, 138.2, 135.6, 131.0, 129.3 (C $\times 2$), 128.8 (C $\times 2$), 128.7 (C $\times 2$), 128.3 (C $\times 2$), 127.6 (C $\times 2$), 127.5, 127.0, 113.5 (C $\times 2$), 96.9, 81.9, 78.1, 73.7, 70.6, 69.6, 65.9, 55.7, 55.2, 40.4, 38.8, 37.3, 26.0 (C $\times 3$), 18.5, 14.6, 10.6, 9.9, -3.8 , -4.9 ; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{41}\text{H}_{57}\text{NO}_8\text{SiNa}$, 742.3751; found 742.3728.



(*S*)-4-Benzyl-3-((2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-3'-[(benzyloxy)methoxy]-5'-[(*tert*-butyldimethylsilyl)oxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl} oxazolidin-2-one (**S1c**);

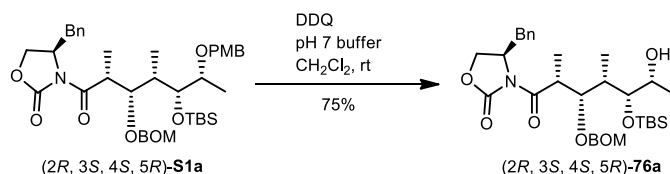
According to the procedure of **4.5.**, **75c** (5.02 g, 8.37 mmol) was converted to **S1c** (4.72 g, 78%) as a colorless oil; $[\alpha]_{\text{D}}^{24} +48.1$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 3032, 2939, 2893, 2854, 1782, 1689, 1512, 1458, 1381, 1211, 1034, 833, 733; ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.31 (complex m, 6H), 7.30–7.27 (complex m, 2H), 7.24 (d, $J = 8.6$ Hz, 2H), 7.17 (d, $J = 6.9$ Hz, 2H), 6.84 (d, $J = 8.6$ Hz, 2H), 4.78 (s, 2H), 4.68 (s, 2H), 4.53 (m, 1H), 4.51 (d, $J = 11.5$ Hz, 1H), 4.43 (d, $J = 11.5$ Hz, 1H), 4.13–4.07 (complex m, 3H), 3.90–3.87 (complex m, 2H), 3.79 (s, 3H), 3.75 (m, 1H), 3.23 (dd, $J = 13.2, 3.4$ Hz, 1H), 2.75 (dd, $J = 13.2, 9.7$ Hz, 1H), 1.66 (m, 1H), 1.28 (d, $J = 6.9$ Hz, 3H), 1.15 (d, $J = 6.3$ Hz, 3H), 1.01 (d, $J = 7.5$ Hz, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.3, 158.8, 152.8, 137.9, 135.1, 131.2, 129.4 (C $\times 2$), 129.2 (C $\times 2$), 128.9

(C × 2), 128.3 (C × 2), 127.5, 127.5 (C × 2), 127.3, 113.5 (C × 2), 96.4, 80.9, 76.1, 75.5, 70.2, 70.1, 65.9, 55.3, 55.2, 41.5, 40.0, 37.5, 26.2 (C × 3), 18.6, 14.2, 13.2, 11.4, −3.7, −4.4; HRMS-ESI (m/z); $[M + Na]^+$ Calcd for $C_{41}H_{57}NO_8SiNa$, 742.3751; found 742.3735.



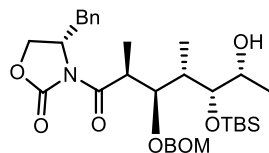
(*R*)-4-Benzyl-3-[(2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-3'-[(benzyloxy)methoxy]-5'-[(*tert*-butyldimethylsilyl)oxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl] oxazolidin-2-one (**S1d**); According to the procedure of **4.5**, **75d** (2.27 g, 3.78 mmol) was converted to **S1d** (2.21 g, 81%) as a colorless oil; $[\alpha]_D^{26}$ −17.0 (*c* 0.50, $CHCl_3$); IR (neat)/ cm^{-1} : 3032, 2931, 2893, 2854, 1782, 1697, 1381, 1242, 1095, 1026, 833, 748; 1H NMR (500 MHz, $CDCl_3$) δ 7.31–7.17 (complex m, 10H), 6.99 (d, J = 6.9 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 4.74 (d, J = 7.5 Hz, 1H), 4.70 (d, J = 7.5 Hz, 1H), 4.63 (d, J = 12.0 Hz, 1H), 4.48 (d, J = 11.5 Hz, 1H), 4.47 (d, J = 12.0 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 4.25 (m, 1H), 3.97–3.91 (complex m, 2H), 3.87 (m, 1H), 3.82 (dd, J = 8.0, 3.4 Hz, 1H), 3.77 (dd, J = 4.0, 2.3 Hz, 1H), 3.73 (s, 3H), 3.43 (m, 1H), 3.18 (dd, J = 13.2, 2.9 Hz, 1H), 2.61 (dd, J = 13.2, 10.3 Hz, 1H), 1.96 (m, 1H), 1.20 (d, J = 6.9 Hz, 3H), 1.12 (d, J = 6.3 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H), 0.85 (s, 9H), 0.01 (s, 3H), −0.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.4, 158.9, 153.0, 137.9, 135.5, 131.1, 129.3 (C × 2), 129.0 (C × 2), 128.8 (C × 2), 128.3 (C × 2), 127.7 (C × 2), 127.6, 127.1, 113.6 (C × 2), 96.9, 83.4, 77.8, 74.4, 70.6, 70.6, 66.0, 55.9, 55.2, 40.6, 38.8, 37.4, 26.1 (C × 3), 18.5, 15.5, 10.8, 10.1, −3.7, −4.0; HRMS-ESI (m/z); $[M + Na]^+$ Calcd for $C_{41}H_{57}NO_8SiNa$, 742.3751; found 742.3731.

4.6. (*R*)-4-Benzyl-3-[(2'*R*,3'*S*,4'*S*,5'*R*,6'*R*)-3'-((benzyloxy)methoxy)-5'-[(*tert*-butyldimethylsilyl)oxy]-6'-hydroxy-2',4'-dimethylheptanoyl] oxazolidin-2-one (**76a**);



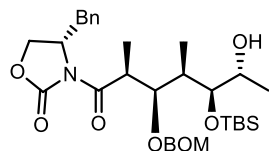
To a solution of PMB ether **S1a** (3.26 g, 4.53 mmol) in CH_2Cl_2 /pH 7.0 phosphate buffer solution in water (v/v, 4/3, 35 mL) was added DDQ (1.94 g, 8.55 mmol) at room temperature. The heterogeneous solution was stirred for 3 h. Then the reaction was quenched with sat. aq. $NaHCO_3$ (50 mL). Resulted two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (25 mL × 3). The combined organic layers were washed with water and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 5/1 to 3/1) to afford alcohol **76a** (2.03 g, 75%) as a colorless oil; $[\alpha]_D^{25}$ −59.1 (*c* 1.00, $CHCl_3$); IR (neat)/ cm^{-1} : 3548, 3510, 3062, 2931, 2893, 2854, 1782, 1689, 1381, 1211, 1026, 748; 1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.25 (complex m, 8H), 7.17 (d, J = 6.9 Hz, 2H), 4.85 (s, 2H), 4.73 (d, J = 12.0 Hz, 1H), 4.64 (d, J = 12.0 Hz, 1H), 4.60 (m, 1H), 4.19–4.08 (complex m, 4H), 3.93 (dq, J = 6.9, 2.9 Hz, 1H), 3.60 (dd, J = 8.0, 2.9 Hz, 1H), 3.22 (dd, J = 13.2, 2.3 Hz, 1H), 2.75 (dd, J = 13.2, 9.7 Hz, 1H), 2.60 (brs, 1H), 1.88 (m, 1H), 1.31 (d, J = 6.3 Hz, 3H), 1.16 (d, J = 6.9 Hz, 3H), 0.99 (d, J = 6.9 Hz,

3H), 0.91 (s, 9H), 0.08 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.4, 152.8, 137.5, 135.0, 129.3 ($\text{C} \times 2$), 128.8 ($\text{C} \times 2$), 128.3 ($\text{C} \times 2$), 127.6, 127.2 ($\text{C} \times 3$), 96.5, 80.8, 76.1, 69.9, 68.6, 65.9, 55.2, 41.5, 39.3, 37.5, 26.0 ($\text{C} \times 3$), 19.6, 18.2, 14.3, 11.3, -3.8, -4.1; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{33}\text{H}_{49}\text{NO}_7\text{Na}$, 622.3176; found 622.3170.



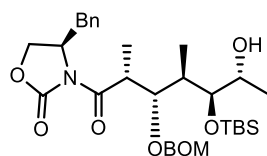
(2S, 3R, 4S, 5R)-**76b**

(*S*)-4-Benzyl-3-[(2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-3'-(benzyloxy)methoxy-5'-[(*tert*-butyldimethylsilyl)oxy]-6'-hydroxy-2',4'-dimethylheptanoyl] oxazolidin-2-one (**76b**); According to the procedure of **4.6.**, **S1b** (3.28 g, 4.56 mmol) was converted to **76b** (2.24 g, 82%) as a colorless oil; $[\alpha]_{\text{D}}^{26} +21.7$ (c 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3525, 3032, 2931, 2885, 2854, 1774, 1705, 1381, 1242, 1203, 1095, 1026, 833, 733; ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.24 (complex m, 8H), 7.03 (d, $J = 6.3$ Hz, 2H), 4.82 (d, $J = 7.5$ Hz, 1H), 4.75 (d, $J = 7.5$ Hz, 1H), 4.71 (d, $J = 11.5$ Hz, 1H), 4.51 (d, $J = 11.5$ Hz, 1H), 4.30 (m, 1H), 4.00 (dd, $J = 10.0, 1.7$ Hz, 1H), 3.98–3.93 (complex m, 4H), 3.70 (m, 1H), 3.66 (dd, $J = 6.3, 1.2$ Hz, 1H), 3.24 (dd, $J = 13.2, 3.4$ Hz, 1H), 2.66 (dd, $J = 13.2, 9.7$ Hz, 1H), 1.96 (d, $J = 4.6$ Hz, 1H), 1.81 (m, 1H), 1.23 (d, $J = 6.9$ Hz, 3H), 1.15 (d, $J = 6.3$ Hz, 3H), 0.94 (d, $J = 7.5$ Hz, 3H), 0.91 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.3, 153.2, 137.9, 135.4, 129.3 ($\text{C} \times 2$), 128.7 ($\text{C} \times 2$), 128.3 ($\text{C} \times 2$), 127.6 ($\text{C} \times 3$), 127.0, 96.9, 82.7, 76.1, 70.7, 70.2, 66.1, 55.9, 40.7, 39.5, 37.3, 26.0 ($\text{C} \times 3$), 19.7, 18.5, 10.5, 9.3, -3.9, -4.0; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{49}\text{NO}_7\text{SiNa}$, 622.3176; found 622.3184.



(2S, 3R, 4R, 5S)-**76c**

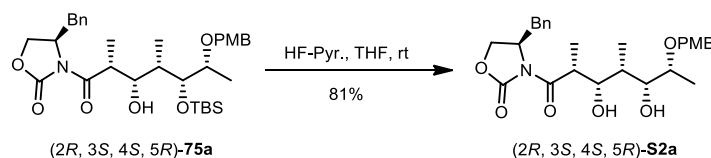
(*S*)-4-Benzyl-3-[(2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-3'-(benzyloxy)methoxy-5'-[(*t*-butyldimethylsilyl)oxy]-6'-hydroxy-2',4'-dimethylheptanoyl] oxazolidin-2-one (**76c**); According to the procedure of **4.6.**, **S1c** (4.42 g, 6.14 mmol) was converted to **76c** (3.31 g, 90%) as a colorless oil; $[\alpha]_{\text{D}}^{27} +90.7$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3556, 3032, 2931, 2885, 2854, 1774, 1697, 1381, 1211, 1026, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.25 (complex m, 8H), 7.15 (d, $J = 6.9$ Hz, 2H), 4.85 (d, $J = 6.9$ Hz, 1H), 4.83 (d, $J = 6.9$ Hz, 1H), 4.68 (d, $J = 12.6$ Hz, 1H), 4.66 (d, $J = 12.6$ Hz, 1H), 4.50 (m, 1H), 4.12–4.01 (complex m, 4H), 3.94 (dd, $J = 6.3, 3.4$ Hz, 1H), 3.71 (m, 1H), 3.22 (dd, $J = 13.2, 2.9$ Hz, 1H), 2.73 (dd, $J = 13.2, 9.7$ Hz, 1H), 1.81 (m, 1H), 1.74 (m, 1H), 1.30 (d, $J = 6.9$ Hz, 3H), 1.16 (d, $J = 6.3$ Hz, 3H), 1.01 (d, $J = 7.5$ Hz, 3H), 0.91 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.1, 152.9, 137.7, 135.0, 129.3 ($\text{C} \times 2$), 128.8 ($\text{C} \times 2$), 128.3 ($\text{C} \times 2$), 127.5, 127.3 ($\text{C} \times 2$), 127.2, 96.3, 80.5, 76.96, 70.1, 69.5, 65.9, 55.3, 41.5, 39.4, 37.4, 26.0 ($\text{C} \times 3$), 18.3, 16.9, 13.7, 11.3, -4.0, -4.3; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{49}\text{NO}_7\text{SiNa}$, 622.3176; found 622.3167.



(2R, 3S, 4R, 5S)-**76d**

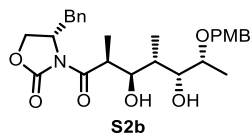
(*R*)-4-Benzyl-3-{(2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-3'-(benzyloxy)methoxy-5'-[(*t*-butyldimethylsilyl)oxy]-6'-hydroxy-2',4'-dimethylheptanoyl} oxazolidin-2-one (**76d**); According to the procedure of **4.6.**, **S1d** (2.48 g, 3.44 mmol) was converted to **76d** (1.98 g, 96%) as a colorless oil; $[\alpha]_D^{27} -32.4$ (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3548, 3032, 3032, 2931, 2885, 2854, 1774, 1697, 1381, 1242, 1203, 1095, 1026, 833, 771, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.37–7.23 (complex m, 8H), 7.05 (d, *J* = 7.5 Hz, 2H), 4.79 (d, *J* = 7.5 Hz, 1H), 4.75 (d, *J* = 7.5 Hz, 1H), 4.68 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.35 (m, 1H), 4.04–3.96 (complex m, 3H), 3.87 (dd, *J* = 9.2, 2.9 Hz, 1H), 3.84 (m, 1H), 3.76 (m, 1H), 3.25 (dd, *J* = 13.2, 3.4 Hz, 1H), 2.68 (dd, *J* = 13.2, 9.7 Hz, 1H), 2.03–1.94 (complex m, 2H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.17 (d, *J* = 6.3 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.3, 153.1, 137.8, 135.4, 129.3 (C \times 2), 128.8 (C \times 2), 128.4 (C \times 2), 127.7 (C \times 2), 127.6, 127.1, 97.1, 83.5, 74.6, 71.2, 70.7, 66.1, 55.9, 40.7, 38.0, 37.4, 25.9 (C \times 3), 18.3, 18.3, 11.2, 9.5, -4.0, -4.2; HRMS-ESI (*m/z*); [M + Na]⁺ Calcd for C₃₃H₄₉NO₇SiNa, 622.3176; found 622.3167.

4.7. (*R*)-4-Benzyl-3-{(2'*R*,3'*S*,4'*S*,5'*R*,6'*R*)-3',5'-dihydroxy-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl} oxazolidin-2-one (**S2a**);

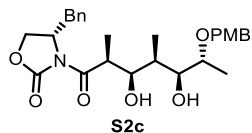


To a solution of 70% HF·Pyr (4.00 mL) in THF (15 mL) was added a solution of aldol product **75a** (2.10 g, 3.50 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 36 h. The reaction was diluted with CH₂Cl₂ (15 mL) and quenched by the addition of cold sat. aq. NaHCO₃ (40 mL). Then the mixture was poured into water (20 mL) and resulted two layers were separated and the aqueous phase was extracted with CH₂Cl₂ (20 mL \times 3). The combined organic layers were washed with water and brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 5/1 to 3/1) to afford a diol **S2a** (1.30 g, 81%) as a colorless oil; $[\alpha]_D^{26} -60.5$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 3533, 3062, 2978, 2939, 2877, 1774, 1689, 1381, 1242, 1211, 1034, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.33 (dd, *J* = 7.5, 6.9 Hz, 2H), 7.29 (d, *J* = 6.9 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 2H), 7.21 (d, *J* = 6.9 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 4.68 (m, 1H), 4.61 (d, *J* = 10.9 Hz, 1H), 4.35 (d, *J* = 10.9 Hz, 1H), 4.23–4.16 (complex m, 2H), 4.09 (dd, *J* = 5.2, 4.2 Hz, 1H), 3.98 (dq, *J* = 6.9, 6.9 Hz, 1H), 3.81 (s, 3H), 3.60 (app d, *J* = 8.0 Hz, 1H), 3.50 (m, 1H), 3.24 (dd, *J* = 13.8, 3.4 Hz, 1H), 2.77 (dd, *J* = 13.8, 9.7 Hz, 1H), 1.70 (m, 1H), 1.33 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.3 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 176.9,

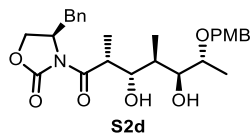
159.3, 152.7, 135.0, 130.1, 129.4 (C ×2), 129.4 (C ×2), 129.0 (C ×2), 127.4, 113.9 (C ×2), 77.9, 76.8, 75.0, 70.8, 66.0, 55.3, 55.0, 40.3, 37.7, 35.9, 15.1, 13.4, 6.9; HRMS-ESI (m/z); $[M+Na]^+$ calcd for $C_{27}H_{35}NO_7Na$, 508.2311; found: 508.2298.



(*S*)-4-Benzyl-3-((2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-3',5'-dihydroxy-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl) oxazolidin-2-one (**S2b**); According to the procedure of **4.7.**, **75b** (4.96 g, 8.27 mmol) was converted to **S2b** (2.88 g, 72%) as a colorless oil; $[\alpha]_D^{26} +21.5$ (c 2.00, $CHCl_3$); IR (neat)/ cm^{-1} : 3564-3410 (br), 3024, 2970, 2931, 2839, 1774, 1689, 1512, 1458, 1381, 1242, 1211, 1034, 980, 818, 748; 1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.31 (complex m, 2H), 7.28 (d, J = 6.9 Hz, 1H), 7.25 (d, J = 8.6 Hz, 2H), 7.20 (d, J = 6.9 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.65 (m, 1H), 4.60 (d, J = 11.5 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 4.19–4.15 (complex m, 2H), 3.97–3.92 (complex m, 2H), 3.80 (dd, J = 8.6, 2.3 Hz, 1H), 3.79 (s, 3H), 3.53 (m, 1H), 3.25 (dd, J = 13.2, 2.9 Hz, 1H), 2.78 (dd, J = 13.2, 9.2 Hz, 1H), 1.76 (m, 1H), 1.30 (d, J = 6.9 Hz, 3H), 1.13 (d, J = 5.7 Hz, 3H), 0.93 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 159.2, 152.8, 135.1, 130.2, 129.4 (C ×2), 129.3 (C ×2), 128.9 (C ×2), 127.4, 113.8 (C ×2), 76.8, 74.5, 73.9, 70.6, 66.1, 55.2, 55.2, 40.2, 37.7, 36.0, 15.3, 11.3, 10.1; HRMS-ESI (m/z); $[M + Na]^+$ Calcd for $C_{27}H_{35}NO_7Na$, 508.2311; found 508.2314.



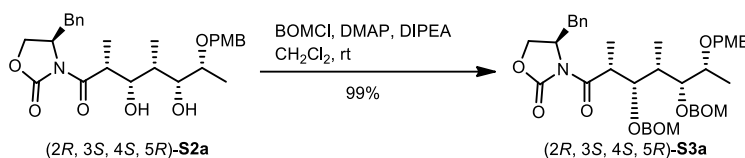
(*S*)-4-Benzyl-3-((2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-3',5'-dihydroxy-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl) oxazolidin-2-one (**S2c**); According to the procedure of **4.7.**, **75c** (3.67 g, 6.12 mmol) was converted to **S2c** (1.98 g, 67%) as a colorless oil; $[\alpha]_D^{27} +29.5$ (c 1.00, $CHCl_3$); IR (neat)/ cm^{-1} : 3518-3425 (br), 2978, 2931, 2885, 1774, 1689, 1512, 1381, 1242, 1211, 1080, 748; 1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.31 (complex m, 2H), 7.28 (m, 1H), 7.23 (d, J = 8.6 Hz, 2H), 7.19 (d, J = 7.2 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 4.61 (m, 1H), 4.56 (d, J = 11.5 Hz, 1H), 4.33 (d, J = 11.5 Hz, 1H), 4.14–4.08 (complex m, 2H), 4.03–3.98 (complex m, 2H), 3.74 (s, 3H), 3.67 (m, 1H), 3.52 (m, 1H), 3.21 (dd, J = 13.2, 3.4 Hz, 1H), 3.11 (dd, J = 11.5, 3.4 Hz, 1H), 2.78 (dd, J = 13.8, 9.2 Hz, 1H), 2.02 (m, 1H), 1.30 (d, J = 6.3 Hz, 3H), 1.28 (d, J = 5.7 Hz, 3H), 0.93 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9, 158.9, 153.0, 134.9, 130.5, 129.2 (C ×2), 129.0 (C ×2), 128.8 (C ×2), 127.2, 113.5 (C ×2), 76.95, 75.3, 74.7, 70.0, 66.0, 55.1, 55.0, 40.7, 37.4, 36.2, 15.7, 12.7, 7.1; HRMS-ESI (m/z); $[M + Na]^+$ Calcd for $C_{27}H_{35}NO_7Na$, 508.2311; found 508.2288.



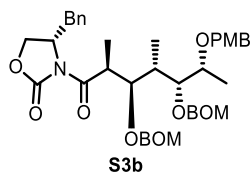
(*R*)-4-Benzyl-3-((2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-3',5'-dihydroxy-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl) oxazolidin-2-one (**S2d**); According to the procedure of **4.7.**, **75d** (8.07 g, 13.5 mmol) was converted to **S2d** (4.51 g, 69%) as a colorless oil; $[\alpha]_D^{27} -38.8$ (c 1.00, $CHCl_3$); IR (neat)/ cm^{-1} : 3456, 3001, 2970, 2939, 1766, 1743, 1689, 1373, 1211, 1080, 748; 1H NMR (500 MHz, $CDCl_3$) δ 7.33 (m, 2H), 7.28 (d, J = 7.5 Hz, 1H), 7.20 (d, J = 8.6 Hz, 2H), 7.15 (d, J = 6.9 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 4.52 (d, J = 10.9 Hz, 1H), 4.45 (m, 1H), 4.28 (d, J = 10.9 Hz, 1H), 4.01 (dd, J = 9.2, 2.3 Hz, 1H), 3.98 (m, 1H), 3.90–3.85 (complex m, 2H), 3.82 (m, 1H), 3.73 (s, 3H), 3.52 (m, 1H), 3.37 (app brs, 1H), 3.18 (dd, J = 13.8, 3.4 Hz, 1H), 2.75 (app

brs, 1H), 2.72 (dd, $J = 13.8, 9.2$ Hz, 1H), 2.07 (m, 1H), 1.30 (d, $J = 6.9$ Hz, 3H), 1.27 (d, $J = 5.7$ Hz, 3H), 0.94 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 176.9, 159.0, 152.9, 135.0, 130.5, 129.3 ($\text{C} \times 2$), 129.2 ($\text{C} \times 2$), 128.7 ($\text{C} \times 2$), 127.1, 113.5 ($\text{C} \times 2$), 76.0, 75.0, 74.1, 70.3, 65.9, 55.1, 55.1, 40.3, 37.5, 35.2, 16.2, 12.2, 10.6; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{27}\text{H}_{35}\text{NO}_7\text{Na}$, 508.2311; found 508.2310.

4.8. (*R*)-4-Benzyl-3-[(2'*R*,3'*S*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl] oxazolidin-2-one (**S3a**);

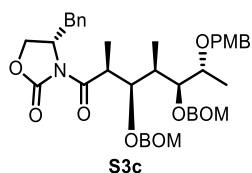


To a solution of diol **S2a** (1.21 g, 2.49 mmol) in CH_2Cl_2 (12 mL) was added DMAP (632 mg, 5.17 mmol) and DIPEA (17 mL, 100 mmol) under N_2 at room temperature. BOMCl (7.0 mL, 51.0 mmol) was then added at 0 °C. After stirring for 6 h at room temperature, the reaction was quenched with H_2O (20 mL) at 0 °C. Then, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and resulted two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (15 mL $\times 3$). The combined organic layers were washed with water and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 5/1 to 3/1) to afford a BOM ether **S3a** (1.79 g, 99%) as a colorless oil; $[\alpha]_{\text{D}}^{23} -42.6$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3024, 2978, 2939, 2885, 1774, 1697, 1381, 1211, 1026, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.23 (complex m, 15H), 7.07 (d, $J = 6.9$ Hz, 2H), 6.83 (d, $J = 8.6$ Hz, 2H), 4.90 (d, $J = 7.5$ Hz, 1H), 4.88 (d, $J = 7.5$ Hz, 1H), 4.88 (d, $J = 6.9$ Hz, 1H), 4.85 (d, $J = 6.9$ Hz, 1H), 4.69 (d, $J = 12.0$ Hz, 1H), 4.66 (d, $J = 11.5$ Hz, 1H), 4.64 (d, $J = 12.0$ Hz, 1H), 4.60 (d, $J = 11.5$ Hz, 1H), 4.56 (d, $J = 11.5$ Hz, 1H), 4.47 (d, $J = 11.3$ Hz, 1H), 4.20–4.11 (complex m, 2H), 4.06 (dd, $J = 5.2, 5.2$ Hz, 1H), 3.91 (dd, $J = 8.9, 2.0$ Hz, 1H), 3.80–3.75 (complex m, 4H), 3.73–3.68 (complex m, 2H), 3.19 (dd, $J = 13.4, 3.2$ Hz, 1H), 2.66 (dd, $J = 13.2, 9.8$ Hz, 1H), 2.05 (m, 1H), 1.28 (d, $J = 6.9$ Hz, 3H), 1.19 (d, $J = 6.3$ Hz, 3H), 1.08 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.3, 158.9, 153.1, 138.2, 138.1, 135.3, 131.1, 129.3 ($\text{C} \times 2$), 129.1 ($\text{C} \times 2$), 128.7 ($\text{C} \times 2$), 128.3 ($\text{C} \times 2$), 128.2 ($\text{C} \times 2$), 127.7 ($\text{C} \times 2$), 127.5 ($\text{C} \times 2$), 127.5 ($\text{C} \times 2$), 127.1, 113.5 ($\text{C} \times 2$), 97.4, 96.4, 82.5, 80.7, 76.2, 70.8, 70.4, 70.3, 65.8, 55.4, 55.2, 41.0, 37.8, 37.4, 15.9, 12.4, 10.8; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{43}\text{H}_{51}\text{NO}_9\text{Na}$, 748.3462; found 748.3453.

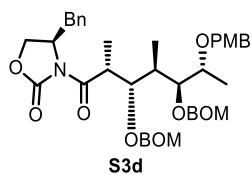


(*S*)-4-Benzyl-3-[(2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl] oxazolidin-2-one (**S3b**); According to the procedure of **4.8.**, **S2b** (2.66 g, 5.48 mmol) was converted to **S3b** (3.70 g, 93%) as a colorless oil; $[\alpha]_{\text{D}}^{26} +47.5$ (c 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 3032, 2978, 2939, 2893, 1774, 1705, 1373, 1242, 1095, 1026, 733; ^1H NMR (500 MHz, CDCl_3) δ 7.31 (m, 2H), 7.28–7.16 (complex m, 13H), 6.86 (d, $J = 7.2$ Hz, 2H), 6.81 (d, $J = 8.0$ Hz, 2H), 5.08 (d, $J = 6.9$ Hz, 1H), 5.02 (d, $J = 6.9$ Hz, 1H), 4.86 (d, $J = 7.5$ Hz, 1H), 4.80–4.76 (complex m, 2H), 4.69 (d, $J =$

12.0 Hz, 1H), 4.53–4.47 (complex m, 2H), 4.41 (d, J = 11.5 Hz, 1H), 4.33 (d, J = 11.5 Hz, 1H), 4.04–3.98 (complex m, 2H), 3.88 (m, 1H), 3.73 (s, 3H), 3.70–3.66 (complex m, 2H), 3.61 (m, 1H), 3.42 (dd, J = 8.0, 8.0 Hz, 1H), 3.12 (dd, J = 13.2, 2.9 Hz, 1H), 2.49 (dd, J = 13.2, 10.3 Hz, 1H), 1.79 (m, 1H), 1.20 (d, J = 6.9 Hz, 3H), 1.12 (d, J = 6.3 Hz, 3H), 1.00 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.7, 159.0, 153.3, 138.3, 138.3, 135.5, 130.7, 129.2 (C \times 2), 129.1 (C \times 2), 128.6 (C \times 2), 128.2 (C \times 2), 128.1 (C \times 2), 127.4 (C \times 2), 127.3, 127.1 (C \times 3), 126.9, 113.7 (C \times 2), 97.9, 96.6, 82.5, 81.3, 77.9, 71.2, 70.9, 69.5, 65.8, 55.7, 55.2, 40.9, 38.5, 37.1, 16.5, 10.1, 9.0; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{43}\text{H}_{51}\text{NO}_9\text{Na}$, 748.3462; found 748.3440.



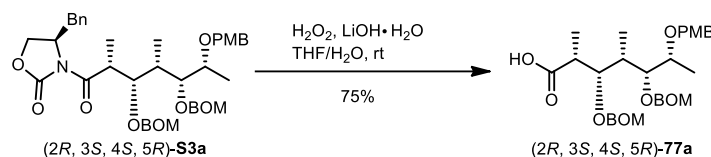
(*S*)-4-Benzyl-3- $\{$ (2',3'*R*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl $\}$ oxazolidin-2-one (**S3c**); According to the procedure of **4.8.**, **S2c** (860 mg, 1.77 mmol) was converted to **S3c** (1.18 g, 92%) as a colorless oil; $[\alpha]_{\text{D}}^{27} +16.9$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 3032, 2978, 2939, 2885, 1774, 1689, 1381, 1242, 1211, 1026, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.34–7.23 (complex m, 13H), 7.19 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 7.5 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 4.99 (d, J = 6.9 Hz, 1H), 4.86 (d, J = 6.9 Hz, 1H), 4.82 (d, J = 6.9 Hz, 1H), 4.78 (d, J = 6.9 Hz, 1H), 4.73 (d, J = 11.5 Hz, 1H), 4.66 (s, 2H), 4.57 (d, J = 11.5 Hz, 1H), 4.49 (d, J = 11.5 Hz, 1H), 4.40 (d, J = 11.5 Hz, 1H), 4.39 (m, 1H), 4.14 (dq, J = 6.9, 6.9 Hz, 1H), 4.02 (dd, J = 9.2, 2.3 Hz, 1H), 3.94 (dd, J = 6.3, 4.6 Hz, 1H), 3.89 (dd, J = 8.0, 8.0 Hz, 1H), 3.85–3.80 (complex m, 2H), 3.79 (s, 3H), 3.20 (dd, J = 13.8, 2.9 Hz, 1H), 2.72 (dd, J = 13.2, 9.7 Hz, 1H), 1.87 (m, 1H), 1.28 (d, J = 6.9 Hz, 3H), 1.23 (d, J = 6.3 Hz, 3H), 1.09 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.4, 158.9, 153.0, 138.2, 137.9, 135.2, 131.0, 129.4 (C \times 2), 129.1 (C \times 2), 128.8 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 127.7 (C \times 2), 127.7 (C \times 2), 127.4, 127.2, 126.9, 113.6 (C \times 2), 96.6, 96.6, 81.1 (C \times 2), 75.8, 70.4, 70.3, 70.3, 65.9, 55.4, 55.2, 41.2, 38.4, 37.5, 14.6, 13.3, 10.9; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{43}\text{H}_{51}\text{NO}_9\text{Na}$, 748.3462; found 748.3453.



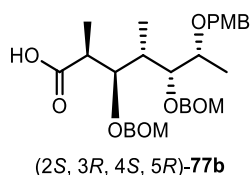
(*R*)-4-Benzyl-3- $\{$ (2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl $\}$ oxazolidin-2-one (**S3d**); According to the procedure of **4.8.**, **S2d** (2.75 g, 5.66 mmol) was converted to **S3d** (3.74 g, 91%) as a colorless oil; $[\alpha]_{\text{D}}^{26} -41.0$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 3032, 2939, 2893, 1774, 1705, 1381, 1242, 1095, 1034, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.22 (complex, m, 15H), 6.97 (d, J = 7.5 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.01 (d, J = 6.9 Hz, 1H), 4.87 (d, J = 6.9 Hz, 1H), 4.84 (d, J = 6.9 Hz, 1H), 4.82 (d, J = 6.9 Hz, 1H), 4.78 (d, J = 12.6 Hz, 1H), 4.71 (d, J = 12.0 Hz, 1H), 4.60 (d, J = 12.6 Hz, 1H), 4.57 (d, J = 11.5 Hz, 1H), 4.46 (d, J = 12.0 Hz, 1H), 4.42 (d, J = 11.5 Hz, 1H), 4.16 (m, 1H), 4.00–3.95 (complex m, 2H), 3.83–3.77 (complex m, 4H), 3.73 (dd, J = 5.7, 1.7 Hz, 1H), 3.65–3.58 (complex m, 2H), 3.20 (dd, J = 13.2, 2.9 Hz, 1H), 2.59 (dd, J = 13.2, 10.3 Hz, 1H), 2.13 (m, 1H), 1.28 (d, J = 6.9 Hz, 3H), 1.24 (d, J = 5.7 Hz, 3H), 1.00 (d, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.9, 159.0, 153.3, 138.2, 138.1, 135.5, 130.7, 129.3 (C \times 4), 128.7 (C \times 2), 128.2 (C \times 2), 128.2 (C \times 2), 127.5

(C × 2), 127.4, 127.3 (C × 2), 127.3, 126.9, 113.7 (C × 2), 97.7, 95.6, 83.4, 80.6, 75.7, 70.8, 70.5, 69.7, 65.9, 55.8, 55.2, 41.0, 37.6, 37.3, 16.2, 10.4, 9.9; HRMS-ESI (*m/z*); [M + Na]⁺ Calcd for C₄₃H₅₁NO₉Na, 748.3462; found 748.3458.

4.9. (2*R*,3*S*,4*S*,5*R*,6*R*)-3,5-Bis[(benzyloxy)methoxy]-6-(4-methoxybenzyl)oxy-2,4-dimethylheptanoic acid (**77a**);

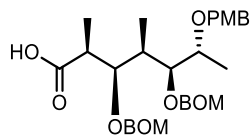


To a solution of 30% H₂O₂ solution in water (25 mL) in H₂O (15 mL) was added LiOH · H₂O (489 mg, 11.7 mmol) at 0 °C. After stirring for 15 min, a solution of BOM ether **S3a** (1.71 g, 2.36 mmol) in THF (25 mL) was added at 0 °C. Then the mixture was allowed to warm to room temperature and stirred for 4 h. The reaction was quenched with sat. aq. NaHCO₃ (25 mL). Resulted two layers were separated and the aqueous phase was extracted with CHCl₃ (25 mL × 3). The combined organic layers were washed with water and brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 4/1 to 3/1) to afford carboxylic acid **77a** (1.00 g, 75%) as a colorless oil; [α]_D²⁵ +3.1 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 3224–3170 (br), 3062, 2978, 2939, 2885, 1705, 1512, 1458, 1250, 1026, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.33–7.25 (complex m, 10H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.94 (d, *J* = 6.9 Hz, 1H), 4.84 (d, *J* = 6.9 Hz, 1H), 4.77 (d, *J* = 6.9 Hz, 1H), 4.73 (d, *J* = 6.9 Hz, 1H), 4.70 (d, *J* = 12.6 Hz, 1H), 4.61 (d, *J* = 12.6 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.40 (d, *J* = 11.5 Hz, 1H), 4.08 (dd, *J* = 7.5, 3.4 Hz, 1H), 3.78 (s, 3H), 3.69 (dq, *J* = 6.3, 6.3 Hz, 1H), 3.50 (dd, *J* = 6.3, 4.0 Hz, 1H), 2.94 (dq, *J* = 6.9, 3.4 Hz, 1H), 1.96 (m, 1H), 1.16 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.3 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 180.0, 159.0, 137.9, 137.8, 130.5, 129.3 (C × 2), 128.3 (C × 4), 127.7 (C × 2), 127.7 (C × 2), 127.5 (C × 2), 113.7 (C × 2), 96.3, 96.2, 81.6 (C × 2), 76.8, 71.0, 70.2, 70.1, 55.2, 41.8, 37.2, 15.9, 10.6, 10.4; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₃₃H₄₂O₈Na, 589.2777; found 589.2782.



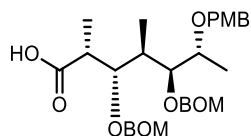
(2*S*,3*R*,4*S*,5*R*,6*R*)-3,5-bis[(Benzyloxy)methoxy]-6-(4-methoxybenzyloxy)-2,4-dimethylheptanoic acid (**77b**); According to the procedure of **4.9.**, **S3b** (1.30 g, 1.79 mmol) was converted to **77b** (892 mg, 88%) as a colorless oil; [α]_D²⁸ +15.6 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 3263–3170 (br), 3062, 3032, 2970, 2939, 2885, 1705, 1512, 1458, 1250, 1095, 1026, 733; ¹H NMR (500 MHz, CDCl₃) δ 7.32–7.29 (complex m, 4H), 7.27–7.22 (complex m, 8H), 6.86 (d, *J* = 8.0 Hz, 2H), 4.94 (d, *J* = 6.9 Hz, 1H), 4.91 (d, *J* = 6.3 Hz, 1H), 4.83 (d, *J* = 6.9 Hz, 1H), 4.77 (d, *J* = 6.3 Hz, 1H), 4.73 (m, 1H), 4.56 (d, *J* = 12.6 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.45 (d, *J* = 11.5 Hz, 1H), 4.20 (dd, *J* = 9.2, 2.3 Hz, 1H), 3.85 (dd, *J* = 6.9, 1.7 Hz, 1H), 3.80 (s, 3H), 3.65 (dq, *J* = 6.3, 6.3 Hz, 1H), 2.69 (dq, *J* = 6.9, 1.7 Hz, 1H), 1.82 (m, 1H), 1.18 (d,

$J = 7.5$ Hz, 3H), 1.16 (d, $J = 6.3$ Hz, 3H), 0.94 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 179.7, 159.0, 137.9, 137.9, 130.8, 129.3 (C $\times 2$), 128.3 (C $\times 2$), 128.2 (C $\times 2$), 127.9 (C $\times 2$), 127.7 (C $\times 2$), 127.5, 127.4, 113.7 (C $\times 2$), 96.7, 96.6, 82.0, 81.2, 77.7, 71.1, 70.1, 70.1, 55.2, 41.2, 37.7, 16.3, 10.9, 9.1; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{42}\text{O}_8\text{Na}$, 589.2777; found 589.2782.



(2*S*, 3*R*, 4*R*, 5*S*)-**77c**

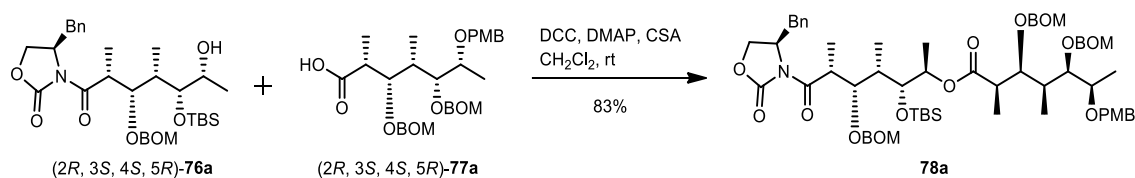
(2*S*, 3*R*, 4*R*, 5*S*, 6*R*)-3,5-bis[(Benzyloxy)methoxy]-6-(4-methoxybenzyloxy)-2,4-dimethylheptanoic acid (**77c**); According to the procedure of **4.9.**, **S3c** (1.06 g, 1.46 mmol) was converted to **77c** (686 mg, 83%) as a colorless oil; $[\alpha]_{\text{D}}^{27} -22.8$ (c 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3217–3163 (br), 3062, 3032, 2978, 2939, 2893, 1705, 1512, 1250, 1026, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.32–7.25 (complex m, 10H), 7.20 (d, $J = 8.6$ Hz, 2H), 6.83 (d, $J = 8.6$ Hz, 2H), 4.91 (d, $J = 6.9$ Hz, 1H), 4.83 (d, $J = 6.9$ Hz, 1H), 4.77–4.72 (complex m, 3H), 4.67–4.61 (complex m, 2H), 4.58 (d, $J = 12.6$ Hz, 1H), 4.49 (d, $J = 11.5$ Hz, 1H), 4.38 (d, $J = 11.5$ Hz, 1H), 3.93 (m, 1H), 3.78 (s, 3H), 3.73–3.68 (complex m, 2H), 2.87 (m, 1H), 1.98 (m, 1H), 1.22 (d, $J = 6.3$ Hz, 3H), 1.20 (d, $J = 6.9$ Hz, 3H), 1.09 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.7, 158.9, 137.9, 137.6, 130.6, 129.1 (C $\times 2$), 128.3 (C $\times 4$), 127.7 (C $\times 4$), 127.5, 127.5, 113.6 (C $\times 2$), 96.2, 95.5, 81.3, 80.6, 75.5, 70.3, 70.2, 70.0, 55.1, 42.6, 38.2, 14.9, 11.7, 11.0; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{42}\text{O}_8\text{Na}$, 589.2777; found 589.2764.



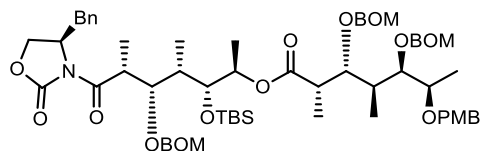
(2*R*, 3*S*, 4*R*, 5*S*)-**77d**

(2*R*, 3*S*, 4*R*, 5*S*, 6*R*)-3,5-bis[(Benzyloxy)methoxy]-6-(4-methoxybenzyloxy)-2,4-dimethylheptanoic acid (**77d**); According to the procedure of **4.9.**, **S3d** (1.31 g, 1.80 mmol) was converted to **77d** (917 mg, 90%) as a colorless oil; $[\alpha]_{\text{D}}^{28} -17.3$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3217–3140 (br), 3062, 3016, 2978, 2939, 2885, 1705, 1512, 1458, 1250, 1219, 1103, 1026, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.32–7.23 (complex m, 12H), 6.86 (d, $J = 8.0$ Hz, 2H), 4.82–4.77 (complex m, 4H), 4.70 (d, $J = 12.0$ Hz, 1H), 4.59–4.53 (complex m, 4H), 4.40 (d, $J = 11.5$ Hz, 1H), 4.10 (app d, $J = 9.2$ Hz, 1H), 3.84 (app d, $J = 5.7$ Hz, 1H), 3.80 (s, 3H), 3.60 (dq, $J = 6.3$, 6.3 Hz, 1H), 2.70 (m, 1H), 2.06 (m, 1H), 1.20 (d, $J = 6.3$ Hz, 3H), 1.19 (d, $J = 6.9$ Hz, 3H), 0.87 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.8, 159.0, 137.9, 137.8, 130.8, 129.2 (C $\times 2$), 128.3 (C $\times 2$), 128.2 (C $\times 2$), 127.8 (C $\times 2$), 127.7 (C $\times 2$), 127.5, 127.4, 113.7 (C $\times 2$), 96.4, 96.0, 82.2, 81.2, 75.5, 70.3, 70.0, 69.9, 55.2, 41.4, 36.9, 16.2, 10.9, 9.0; HRMS-ESI (m/z); $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{33}\text{H}_{42}\text{O}_8\text{Na}$, 589.2777; found 589.2760.

4.10. (2'*R*, 3'*R*, 4'*S*, 5'*S*, 6'*R*)-7-[(*R*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*R*, 3*S*, 4*S*, 5*R*, 6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78a**);

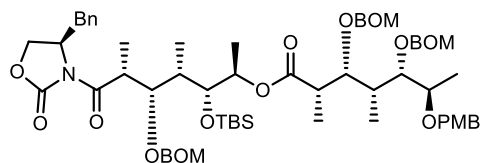


To a solution of alcohol **76a** (335 mg, 558 μmol) and carboxylic acid **77a** (355 mg, 626 μmol) in CH_2Cl_2 (2.5 mL) was added DMAP (45.2 mg, 370 μmol) and CSA (38.7 mg, 167 μmol) under N_2 . The mixture was cooled to 0 $^\circ\text{C}$ and added DCC (310 mg, 1.50 mmol). After stirring for 21 h at room temperature, the reaction was quenched with H_2O (5.0 mL). Resulted two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (10 mL \times 3). The combined organic layers were washed with water and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/ EtOAc = 6/1 to 4/1) to afford a **78a** (532 mg, 83%) as a colorless oil; $[\alpha]_{\text{D}}^{24} -21.3$ (*c* 1.00, CHCl_3); IR (neat)/ cm^{-1} : 2954, 2885, 1782, 1712, 1373, 1234, 1026, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.21 (complex m, 20H), 7.08 (d, *J* = 6.9 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 5.00 (m, 1H), 4.87 (d, *J* = 6.9 Hz, 1H), 4.82 (d, *J* = 6.9 Hz, 1H), 4.80 (s, 2H), 4.79 (s, 2H), 4.69–4.64 (complex m, 4H), 4.57 (d, *J* = 12.6 Hz, 1H), 4.57 (d, *J* = 12.6 Hz, 1H), 4.49 (d, *J* = 11.5 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.39 (m, 1H), 4.18 (dd, *J* = 5.2, 5.2 Hz, 1H), 4.05–3.93 (complex m, 4H), 3.83 (dd, *J* = 4.6, 4.0 Hz, 1H), 3.77 (s, 3H), 3.72 (dq, *J* = 6.3, 6.3 Hz, 1H), 3.57 (dd, *J* = 5.2, 5.2 Hz, 1H), 3.18 (dd, *J* = 13.2, 2.9 Hz, 1H), 2.94 (m, 1H), 2.66 (dd, *J* = 13.8, 9.7 Hz, 1H), 2.01 (m, 1H), 1.96 (m, 1H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.25 (d, *J* = 7.5 Hz, 3H), 1.17–1.14 (complex m, 6H), 1.07 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.0, 174.3, 159.0, 153.0, 138.2, 138.0, 138.0, 135.3, 130.8, 129.4 (C \times 2), 129.3 (C \times 2), 128.8 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 128.2 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.5, 127.4, 127.4, 127.3 (C \times 2), 127.2, 113.6 (C \times 2), 96.5, 96.3, 96.1, 81.5, 80.9, 80.9, 76.9, 73.0, 73.0, 70.9, 70.2, 70.0 (C \times 2), 65.9, 55.5, 55.2, 42.7, 41.4, 38.6, 37.4 (C \times 2), 25.9 (C \times 3), 18.3, 15.9, 15.5, 12.5, 12.0, 11.1, 10.7, –4.1, –4.2; HRMS-ESI (*m/z*); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{66}\text{H}_{89}\text{NO}_{14}\text{SiNa}$, 1170.5950; found 1170.5949.



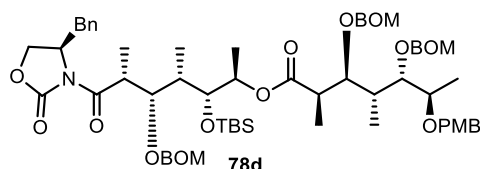
(2'*R*,3'*R*,4'*S*,5'*S*,6'*R*)-7-[(*R*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*S*,3*R*,4*S*,5*R*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78b**); According to the procedure of **4.10.**, **76a** (812 mg, 1.35 mmol) and **77b** (825 mg, 1.46 mmol) were converted to **78b** (1.27 g, 82%) as a colorless oil; $[\alpha]_{\text{D}}^{27} -25.4$ (*c* 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3024, 2939, 2885, 2862, 1782, 1728, 1697, 1458, 1381, 1250, 1095, 1026, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.37–7.24 (complex m, 20H), 7.09 (d, *J* = 6.3 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.06 (m, 1H), 4.96 (d, *J* = 6.3 Hz, 1H), 4.94 (d, *J* = 6.3 Hz, 1H), 4.91 (d, *J* = 6.9 Hz, 1H), 4.81 (d, *J* = 6.9 Hz, 1H), 4.80 (s, 2H), 4.76 (d, *J* = 12.6 Hz, 1H), 4.69 (d, *J* = 12.6 Hz, 1H), 4.69–4.54 (complex m, 5H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.40 (m, 1H), 4.18 (dd, *J* = 9.2, 1.7 Hz, 1H), 4.05–3.93 (complex m, 5H), 3.84 (dd, *J* = 5.7, 4.0 Hz, 1H), 3.80 (s, 3H), 3.68 (dq, *J* = 6.3, 6.3 Hz, 1H), 3.16 (dd, *J* = 13.2, 2.9 Hz, 1H), 2.82 (dq, *J* = 6.9, 1.7 Hz,

1H), 2.65 (dd, $J = 13.2, 9.7$ Hz, 1H), 1.94 (m, 1H), 1.87 (m, 1H), 1.30 (d, $J = 6.3$ Hz, 3H), 1.21 (d, $J = 7.2$ Hz, 3H), 1.20 (d, $J = 6.6$ Hz, 3H), 1.15 (d, $J = 6.3$ Hz, 3H), 0.99 (d, $J = 7.5$ Hz, 3H), 0.98 (d, $J = 7.5$ Hz, 3H), 0.90 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.0, 174.4, 158.9, 152.9, 138.1 (C $\times 2$), 137.9, 135.2, 130.8, 129.3 (C $\times 2$), 129.2 (C $\times 2$), 128.7 (C $\times 2$), 128.3 (C $\times 2$), 128.2 (C $\times 2$), 128.1 (C $\times 2$), 127.7 (C $\times 2$), 127.6 (C $\times 2$), 127.5, 127.4 (C $\times 3$), 127.3, 127.1, 113.6 (C $\times 2$), 96.4, 96.3, 96.1, 82.2, 80.8, 80.6, 77.7, 72.8, 72.6, 71.0, 70.2, 69.9, 69.6, 65.8, 55.4, 55.1, 41.3 (C $\times 2$), 38.2, 37.8, 37.4, 25.9 (C $\times 3$), 18.2, 16.5, 14.6, 13.1, 11.0 (C $\times 2$), 9.0, -4.3, -4.3; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{66}\text{H}_{89}\text{NO}_{14}\text{SiNa}$, 1170.5950; found 1170.5965.



78c

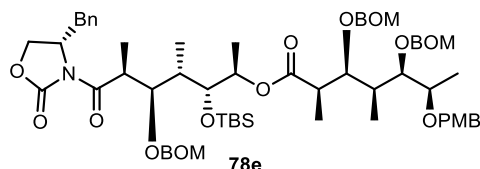
(2',3',4',5',6'R)-7-[(R)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*S*,3*R*,4*R*,5*S*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78c**); According to the procedure of **4.10.**, **76a** (914 mg, 1.52 mmol) and **77c** (929 mg, 1.64 mmol) were converted to **78c** (1.29 g, 74%) as a colorless oil; $[\alpha]_{\text{D}}^{26} -24.5$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3032, 2939, 2885, 2862, 1782, 1728, 1697, 1458, 1381, 1250, 1095, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.22 (complex m, 18H), 7.17 (d, $J = 8.6$ Hz, 2H), 7.09 (d, $J = 6.9$ Hz, 2H), 6.81 (d, $J = 8.6$ Hz, 2H), 5.04 (dq, $J = 6.3, 3.4$ Hz, 1H), 4.93 (d, $J = 6.9$ Hz, 1H), 4.83 (d, $J = 6.9$ Hz, 1H), 4.80–4.71 (complex m, 5H), 4.69 (d, $J = 12.0$ Hz, 1H), 4.66 (d, $J = 12.0$ Hz, 1H), 4.63–4.57 (complex m, 4H), 4.48–4.41 (complex m, 2H), 4.38 (d, $J = 10.9$ Hz, 1H), 4.05 (dq, $J = 6.9, 6.9$ Hz, 1H), 4.01–3.91 (complex m, 3H), 3.85 (dd, $J = 5.2, 5.2$ Hz, 1H), 3.80 (dd, $J = 6.3, 3.4$ Hz, 1H), 3.78–3.73 (complex m, 4H), 3.16 (dd, $J = 13.2, 2.9$ Hz, 1H), 2.90 (dq, $J = 6.9, 6.9$ Hz, 1H), 2.67 (dd, $J = 13.2, 9.7$ Hz, 1H), 1.93–1.86 (complex m, 2H), 1.28 (d, $J = 6.9$ Hz, 3H), 1.24 (d, $J = 6.9$ Hz, 3H), 1.19 (d, $J = 5.7$ Hz, 3H), 1.16 (d, $J = 6.9$ Hz, 3H), 1.11 (d, $J = 6.9$ Hz, 3H), 0.96 (d, $J = 6.9$ Hz, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.0, 174.7, 158.9, 152.9, 138.0, 137.8, 137.8, 135.2, 130.8, 129.3 (C $\times 2$), 129.1 (C $\times 2$), 128.8 (C $\times 2$), 128.3 (C $\times 2$), 128.3 (C $\times 4$), 127.8 (C $\times 2$), 127.7 (C $\times 2$), 127.5, 127.5, 127.5, 127.3 (C $\times 2$), 127.2, 113.6 (C $\times 2$), 96.4, 96.3, 95.9, 81.7, 81.1, 80.7, 75.7, 73.3, 72.6, 70.3, 70.3, 70.1, 69.9, 65.8, 55.3, 55.2, 42.9, 41.4, 38.5 (C $\times 2$), 37.4, 26.0 (C $\times 3$), 18.2, 15.4, 14.8, 13.4, 12.2, 11.1, 11.1, -4.0, -4.1; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{66}\text{H}_{89}\text{NO}_{14}\text{SiNa}$, 1170.5950; found 1170.5932.



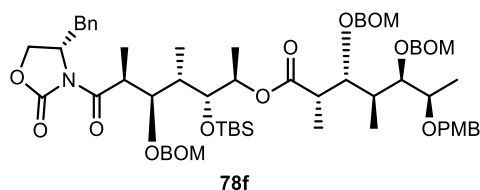
78d

(2',3',4',5',6'R)-7-[(R)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*R*,3*S*,4*R*,5*S*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78d**); According to the procedure of **4.10.**, **76a** (825 mg, 1.38 mmol) and **77d** (834 mg, 1.47 mmol) were converted to **78d** (1.47 g, 93%) as a colorless oil; $[\alpha]_{\text{D}}^{27} -16.2$ (c

1.00, CHCl₃); IR (neat)/cm⁻¹; 3023, 2939, 2885, 2862, 1782, 1697, 1458, 1381, 1242, 1095, 1026, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.23 (complex m, 20H), 7.09 (d, *J* = 6.9 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.06 (dq, *J* = 6.9, 3.4 Hz, 1H), 4.84 (s, 2H), 4.82–4.77 (complex m, 3H), 4.78 (d, *J* = 6.3 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.63 (s, 2H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.54 (d, *J* = 11.5 Hz, 1H), 4.45–4.41 (complex m, 2H), 4.14 (dd, *J* = 8.6, 2.3 Hz, 1H), 4.06 (m, 1H), 4.04–4.02 (complex m, 2H), 3.99–3.96 (complex m, 2H), 3.81 (dd, *J* = 6.3, 3.4 Hz, 1H), 3.78 (s, 3H), 3.67 (dq, *J* = 6.3, 6.3 Hz, 1H), 3.20 (dd, *J* = 13.2, 2.9 Hz, 1H), 2.78 (dq, *J* = 6.9, 2.3 Hz, 1H), 2.68 (dd, *J* = 13.8, 9.7 Hz, 1H), 2.05 (m, 1H), 1.92 (m, 1H), 1.29 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.12 (d, *J* = 6.3 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.1, 174.5, 158.9, 153.0, 138.0 (C ×2), 137.8, 135.2, 131.0, 129.3 (C ×2), 129.1 (C ×2), 128.8 (C ×2), 128.3 (C ×2), 128.2 (C ×2), 128.2 (C ×2), 127.7 (C ×2), 127.7 (C ×2), 127.5, 127.4, 127.4, 127.3 (C ×2), 127.2, 113.6 (C ×2), 96.4, 96.3, 96.0, 81.9, 80.9, 80.7, 76.1, 73.2, 72.6, 70.3, 70.0, 70.0, 69.8, 65.9, 55.4, 55.2, 41.8, 41.4, 38.6, 37.4, 36.7, 25.9 (C ×3), 18.3, 16.2, 15.5, 13.1, 11.3, 11.1, 9.7, -4.0, -4.2; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₆₆H₈₉NO₁₄SiNa, 1170.5950; found 1170.5953.

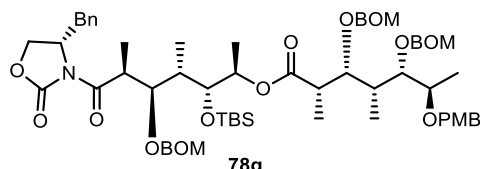


(2'*R*,3'*R*,4'*S*,5'*R*,6'*S*)-7-[(*S*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*R*,3*S*,4*S*,5*R*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyloxy)oxy]-2,4-dimethylheptanoate (**78e**); According to the procedure of **4.10.**, **76b** (740 mg, 1.23 mmol) and **77a** (893 mg, 1.58 mmol) were converted to **78e** (1.54 g, 93%) as a colorless oil; [α]_D²⁶ +1.5 (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹; 3062, 3032, 2939, 2885, 2862, 1782, 1705, 1381, 1242, 1095, 1026, 833, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.37–7.23 (complex m, 20H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 4.89 (d, *J* = 6.9 Hz, 1H), 4.87–4.74 (complex m, 5H), 4.73 (d, *J* = 7.5 Hz, 1H), 4.70–4.66 (complex m, 3H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 10.9 Hz, 1H), 4.41 (d, *J* = 11.5 Hz, 1H), 4.22 (m, 1H), 4.16 (dd, *J* = 5.7, 5.7 Hz, 1H), 3.99 (app d, *J* = 5.7 Hz, 1H), 3.96–3.89 (complex m, 3H), 3.85 (dd, *J* = 9.7, 1.7 Hz, 1H), 3.79 (s, 3H), 3.75 (m, 1H), 3.59 (dd, *J* = 5.2, 5.2 Hz, 1H), 3.23 (dd, *J* = 13.2, 3.4 Hz, 1H), 2.90 (m, 1H), 2.64 (dd, *J* = 13.2, 10.3 Hz, 1H), 2.04 (m, 1H), 1.91 (m, 1H), 1.26 (d, *J* = 7.5 Hz, 3H), 1.24 (d, *J* = 6.9 Hz, 3H), 1.19 (d, *J* = 6.3 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.10 (s, 3H), 0.05 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 174.9, 174.3, 159.0, 153.2, 138.2, 138.0, 137.9, 135.5, 130.7, 129.3 (C ×2), 129.3 (C ×2), 128.7 (C ×2), 128.3 (C ×2), 128.3 (C ×2), 128.2 (C ×2), 127.6 (C ×6), 127.5, 127.5, 127.4, 127.0, 113.6 (C ×2), 97.7, 96.5, 96.0, 83.6, 81.5, 81.1, 76.5, 74.3, 71.0, 70.9, 70.9, 70.2, 70.0, 66.1, 56.0, 55.2, 42.9, 40.7, 38.2, 37.3, 37.2, 25.8 (C ×3), 18.3, 15.8, 15.4, 12.1, 10.7, 10.4, 8.6, -3.9, -4.5; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₆₆H₈₉NO₁₄SiNa, 1170.5950; found 1170.5968.



78f

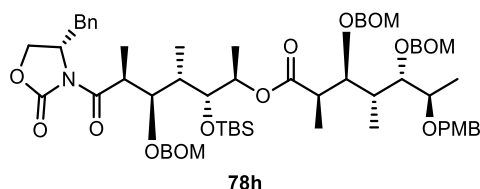
(2'*R*,3'*R*,4'*S*,5'*R*,6'*S*)-7-[(*S*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*S*,3*R*,4*S*,5*R*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78f**); According to the procedure of **4.10.**, **76b** (183 mg, 305 μmol) and **77b** (213 mg, 376 μmol) were converted to **78f** (263 mg, 75%) as a colorless oil; $[\alpha]_{\text{D}}^{23} +4.6$ (*c* 0.50, CHCl_3); IR (neat)/ cm^{-1} : 3032, 2939, 2885, 2862, 1782, 1728, 1705, 1458, 1381, 1242, 1203, 1095, 1026, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.34–7.23 (complex m, 20H), 6.95 (d, *J* = 7.5 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 4.93 (d, *J* = 6.3 Hz, 1H), 4.90 (d, *J* = 6.3 Hz, 1H), 4.87 (d, *J* = 6.9 Hz, 1H), 4.81 (d, *J* = 11.5 Hz, 1H), 4.79 (d, *J* = 12.6 Hz, 1H), 4.73–4.51 (complex m, 9H), 4.45 (d, *J* = 10.9 Hz, 1H), 4.24 (d, *J* = 12.0 Hz, 1H), 4.20–4.13 (complex m, 2H), 3.94–3.87 (complex m, 4H), 3.82 (dd, *J* = 9.7, 2.3 Hz, 1H), 3.80 (s, 3H), 3.65 (dq, *J* = 6.3, 6.3 Hz, 1H), 3.22 (dd, *J* = 13.2, 2.9 Hz, 1H), 2.70 (m, 1H), 2.62 (dd, *J* = 13.2, 10.3 Hz, 1H), 1.88–1.80 (complex m, 2H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 5.7 Hz, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.08 (d, *J* = 6.3 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.11 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.9, 174.5, 159.0, 153.2, 138.0, 138.0, 137.9, 135.6, 130.8, 129.3 (C \times 2), 129.2 (C \times 2), 128.7 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 128.2 (C \times 2), 127.7 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.6, 127.5, 127.4, 127.0, 113.7 (C \times 2), 97.7, 96.5, 96.4, 83.5, 81.9, 81.0, 77.8, 74.3, 71.1, 71.0, 70.9, 70.3, 69.6, 66.1, 56.0, 55.2, 41.5, 40.8, 38.0, 37.9, 37.2, 25.8 (C \times 3), 18.4, 16.5, 14.9, 11.0, 10.3, 9.0, 8.5, -4.1, -4.4; HRMS-ESI (*m/z*); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{66}\text{H}_{89}\text{NO}_{14}\text{SiNa}$, 1170.5950; found 1170.5923.



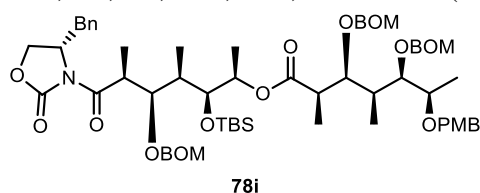
78g

(2'*R*,3'*R*,4'*S*,5'*R*,6'*S*)-7-[(*S*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*S*,3*R*,4*R*,5*S*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78g**); According to the procedure of **4.10.**, **76b** (412 mg, 687 μmol) and **77c** (423 mg, 746 μmol) were converted to **78g** (610 mg, 77%) as a colorless oil; $[\alpha]_{\text{D}}^{30} -4.8$ (*c* 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 2939, 2893, 2862, 1782, 1705, 1458, 1381, 1242, 1095, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.23 (complex m, 18H), 7.18 (d, *J* = 8.6 Hz, 2H), 6.99 (d, *J* = 7.5 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 4.93 (d, *J* = 6.9 Hz, 1H), 4.84 (d, *J* = 6.9 Hz, 1H), 4.81–4.67 (complex m, 8H), 4.63 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 11.5 Hz, 1H), 4.39 (d, *J* = 12.0 Hz, 1H), 4.38 (d, *J* = 10.9 Hz, 1H), 4.24 (m, 1H), 4.00–3.90 (complex m, 4H), 3.87–3.83 (complex m, 2H), 3.78 (s, 3H), 3.77–3.73 (complex m, 2H), 3.24 (dd, *J* = 13.2, 2.9 Hz, 1H), 2.80 (dq, *J* = 6.9, 6.9 Hz, 1H), 2.65 (dd, *J* = 13.2, 10.3 Hz, 1H), 1.92–1.84 (complex m, 2H), 1.24 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 7.5 Hz, 3H), 1.20 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.12 (s, 3H), 0.06 (s,

3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.0, 174.8, 159.0, 153.2, 138.1, 138.0, 137.8, 135.5, 130.8, 129.3 ($\text{C} \times 2$), 129.1 ($\text{C} \times 2$), 128.7 ($\text{C} \times 2$), 128.3 ($\text{C} \times 2$), 128.3 ($\text{C} \times 4$), 127.8 ($\text{C} \times 2$), 127.7 ($\text{C} \times 2$), 127.6 ($\text{C} \times 2$), 127.6, 127.5, 127.5, 127.0, 113.6 ($\text{C} \times 2$), 97.5, 96.3, 95.9, 83.4, 81.4, 80.8, 75.7, 74.5, 71.2, 70.9, 70.3, 70.3, 70.0, 66.1, 56.0, 55.2, 43.0, 40.7, 38.5, 38.2, 37.3, 25.8 ($\text{C} \times 3$), 18.4, 15.2, 14.7, 12.3, 11.0, 10.4, 8.7, -4.0, -4.4; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{66}\text{H}_{89}\text{NO}_{14}\text{SiNa}$, 1170.5950; found 1170.5948.

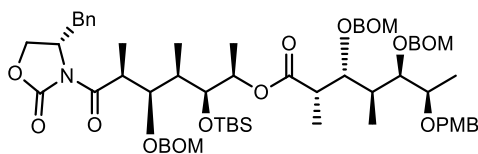


(2'*R*,3'*R*,4'*S*,5'*R*,6'*S*)-7-[(*S*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*R*,3*S*,4*R*,5*S*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyloxy)-2,4-dimethylheptanoate (**78h**); According to the procedure of **4.10.**, **76b** (744 mg, 1.24 mmol) and **77d** (747 mg, 1.32 mmol) were converted to **78h** (1.06 g, 74%) as a colorless oil; $[\alpha]_{\text{D}}^{28}$ -4.2 (c 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3032, 2939, 2885, 2862, 1782, 1705, 1512, 1458, 1381, 1242, 1095, 1026, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.33–7.21 (complex m, 20H), 6.98 (d, J = 7.5 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 4.86–4.78 (complex m, 5H), 4.73 (s, 2H), 4.68 (d, J = 11.5 Hz, 1H), 4.65–4.61 (complex m, 3H), 4.56 (d, J = 12.0 Hz, 1H), 4.55 (d, J = 11.5 Hz, 1H), 4.42 (d, J = 11.7 Hz, 1H), 4.39 (d, J = 12.0 Hz, 1H), 4.22 (m, 1H), 4.11 (dd, J = 8.9, 2.3 Hz, 1H), 3.98–3.90 (complex m, 5H), 3.83 (dd, J = 9.2, 1.2 Hz, 1H), 3.79 (s, 3H), 3.64 (dq, J = 5.7, 5.7 Hz, 1H), 3.22 (dd, J = 13.4, 2.9 Hz, 1H), 2.66–2.60 (complex m, 2H), 2.05 (m, 1H), 1.89 (m, 1H), 1.23–1.21 (complex m, 9H), 1.13 (d, J = 6.9 Hz, 3H), 0.95 (d, J = 6.9 Hz, 3H), 0.90–0.88 (complex m, 12H), 0.09 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.0, 174.6, 158.9, 153.2, 138.0, 138.0, 137.9, 135.5, 130.9, 129.3 ($\text{C} \times 2$), 129.1 ($\text{C} \times 2$), 128.7 ($\text{C} \times 2$), 128.3 ($\text{C} \times 2$), 128.3 ($\text{C} \times 2$), 128.2 ($\text{C} \times 2$), 127.7 ($\text{C} \times 2$), 127.7 ($\text{C} \times 2$), 127.6 ($\text{C} \times 2$), 127.6, 127.4 ($\text{C} \times 2$), 127.0, 113.6 ($\text{C} \times 2$), 97.6, 96.4, 96.1, 83.6, 81.7, 80.9, 75.9, 74.3, 70.9 ($\text{C} \times 2$), 70.3, 70.0, 69.8, 66.1, 56.0, 55.2, 42.0, 40.7, 38.1, 37.2, 36.8, 25.8 ($\text{C} \times 3$), 18.3, 16.2, 15.3, 11.4, 10.6, 9.7, 8.7, -4.1, -4.4; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{66}\text{H}_{89}\text{NO}_{14}\text{SiNa}$, 1170.5950; found 1170.5934.



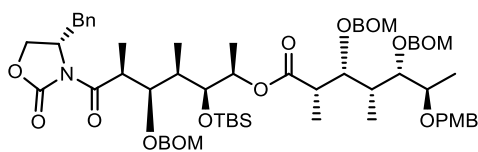
(2'*R*,3'*S*,4'*R*,5'*R*,6'*S*)-7-[(*S*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*R*,3*S*,4*S*,5*R*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyloxy)-2,4-dimethylheptanoate (**78i**); According to the procedure of **4.10.**, **76c** (555 mg, 0.925 mmol) and **77a** (569 mg, 1.00 mmol) were converted to **78i** (1.03 g, 97%) as a colorless oil; $[\alpha]_{\text{D}}^{27}$ +25.2 (c 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 3032, 2939, 2885, 1782, 1720, 1697, 1458, 1381, 1250, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.33–7.23 (complex m, 20H), 7.13 (d, J = 6.9 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 5.18 (dq, J = 6.3, 1.7 Hz, 1H), 4.85 (d, J = 6.9 Hz, 1H), 4.82–4.77 (complex m, 4H), 4.72 (d, J = 6.9 Hz, 1H), 4.67 (d, J = 12.0 Hz, 1H), 4.66 (d, J = 12.0 Hz, 1H), 4.62 (s, 2H), 4.58 (d, J = 12.0 Hz, 1H), 4.54 (d, J = 12.0 Hz, 1H), 4.51 (d, J = 11.5 Hz, 1H), 4.49–4.43 (complex m, 2H), 4.18 (dd, J = 5.7, 5.7 Hz, 1H), 4.06 (d, J = 4.6 Hz, 2H),

4.03 (dq, $J = 6.9, 6.9$ Hz, 1H), 3.95 (dd, $J = 6.3, 3.4$ Hz, 1H), 3.88 (dd, $J = 7.7, 2.3$ Hz, 1H), 3.77 (s, 3H), 3.74 (dq, $J = 6.3, 6.3$ Hz, 1H), 3.61 (dd, $J = 5.2, 5.2$ Hz, 1H), 3.21 (dd, $J = 13.2, 2.9$ Hz, 1H), 2.87 (dq, $J = 6.9, 6.9$ Hz, 1H), 2.69 (dd, $J = 13.8, 9.7$ Hz, 1H), 2.04 (m, 1H), 1.70 (m, 1H), 1.29 (d, $J = 6.9$ Hz, 3H), 1.24 (d, $J = 7.5$ Hz, 3H), 1.19 (d, $J = 6.9$ Hz, 3H), 1.18 (d, $J = 6.3$ Hz, 3H), 1.07 (d, $J = 6.9$ Hz, 3H), 0.98 (d, $J = 6.9$ Hz, 3H), 0.92 (s, 9H), 0.12 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.1, 174.6, 159.0, 152.9, 138.2, 138.1, 138.0, 135.2, 130.8, 129.4 (C \times 2), 129.3 (C \times 2), 128.8 (C \times 2), 128.2 (C \times 6), 127.7 (C \times 2), 127.6 (C \times 2), 127.5 (C \times 2), 127.4 (C \times 3), 127.2, 113.6 (C \times 2), 96.6, 96.5, 95.9, 81.4, 80.9, 80.8, 76.5, 74.8, 73.2, 70.9, 70.2, 70.0, 69.9, 65.9, 55.3, 55.2, 42.9, 41.8, 40.1, 37.5, 37.3, 26.1 (C \times 3), 18.5, 15.6, 13.6, 13.6, 13.0, 11.1, 10.7, -3.9, -4.2; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{66}\text{H}_{89}\text{NO}_{14}\text{SiNa}$, 1170.5950; found 1170.5943.



78j

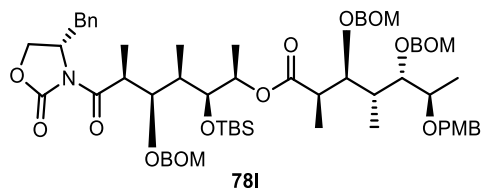
(2'*R*,3'*S*,4'*R*,5'*R*,6'*S*)-7-[(*S*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*S*,3*R*,4*S*,5*R*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78j**); According to the procedure of **4.10.**, **76c** (834 mg, 1.39 mmol) and **77b** (842 mg, 1.49 mmol) were converted to **78j** (1.25 g, 79%) as a colorless oil; $[\alpha]_{\text{D}}^{27} +33.2$ (c 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 2939, 2885, 2862, 1782, 1728, 1697, 1458, 1381, 1211, 1026, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.22 (complex m, 20H), 7.13 (d, $J = 6.9$ Hz, 2H), 6.84 (d, $J = 8.6$ Hz, 2H), 5.16 (app q, $J = 6.9$ Hz, 1H), 4.92 (d, $J = 6.9$ Hz, 1H), 4.90 (d, $J = 6.3$ Hz, 1H), 4.88 (d, $J = 6.3$ Hz, 1H), 4.82 (s, 2H), 4.77 (d, $J = 6.9$ Hz, 1H), 4.70 (d, $J = 12.6$ Hz, 1H), 4.67 (d, $J = 12.0$ Hz, 1H), 4.64 (d, $J = 12.6$ Hz, 2H), 4.58 (d, $J = 12.0$ Hz, 1H), 4.55–4.45 (complex m, 3H), 4.44 (d, $J = 11.5$ Hz, 1H), 4.12 (dd, $J = 9.2, 2.3$ Hz, 1H), 4.09–4.06 (complex m, 2H), 4.03 (dq, $J = 6.9, 6.9$ Hz, 1H), 3.93 (dd, $J = 6.9, 2.9$ Hz, 1H), 3.86 (d, $J = 7.5$ Hz, 1H), 3.84 (dd, $J = 8.0, 1.2$ Hz, 1H), 3.79 (s, 3H), 3.64 (dq, $J = 6.3, 6.3$ Hz, 1H), 3.22 (dd, $J = 13.2, 3.4$ Hz, 1H), 2.69 (dd, $J = 13.2, 9.7$ Hz, 1H), 2.62 (dq, $J = 6.9, 2.3$ Hz, 1H), 1.80 (m, 1H), 1.59 (m, 1H), 1.27 (d, $J = 6.9$ Hz, 3H), 1.16 (d, $J = 5.7$ Hz, 3H), 1.16 (d, $J = 6.9$ Hz, 3H), 1.10 (d, $J = 6.3$ Hz, 3H), 0.93 (d, $J = 6.9$ Hz, 3H), 0.92 (d, $J = 6.9$ Hz, 3H), 0.89 (s, 9H), 0.06 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.1, 174.3, 159.0, 152.9, 138.2, 138.1, 138.1, 135.2, 130.9, 129.4 (C \times 2), 129.2 (C \times 2), 128.8 (C \times 2), 128.2 (C \times 2), 128.2 (C \times 2), 128.2 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.4, 127.4, 127.4 (C \times 2), 127.3, 127.2, 113.6 (C \times 2), 97.1, 96.5, 96.3, 82.2, 80.9, 80.7, 77.8, 74.6, 72.9, 71.0, 70.3, 70.2, 69.5, 65.9, 55.3, 55.2, 41.7, 41.4, 40.1, 37.9, 37.5, 26.1 (C \times 3), 18.5, 16.5, 13.9, 12.9, 11.1, 10.8, 9.1, -4.0, -4.3; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{66}\text{H}_{89}\text{NO}_{14}\text{SiNa}$, 1170.5950; found 1170.5948.



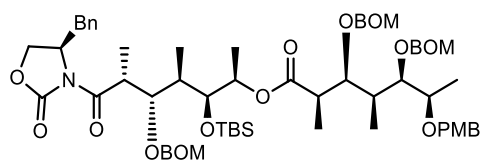
78k

(2'*R*,3'*S*,4'*R*,5'*R*,6'*S*)-7-[(*S*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-

butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*S*,3*R*,4*R*,5*S*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78k**); According to the procedure of **4.10.**, **76c** (570 mg, 0.951 mmol) and **77c** (593 mg, 1.05 mmol) were converted to **78k** (894 mg, 82%) as a colorless oil; $[\alpha]_D^{28} +29.2$ (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3062, 3032, 2939, 2885, 2862, 1782, 1720, 1697, 1381, 1250, 1103, 1026, 833, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.25 (complex m, 18H), 7.18–7.14 (complex m, 4H), 6.81 (d, *J* = 8.6 Hz, 2H), 5.23 (dq, *J* = 6.3, 1.7 Hz, 1H), 4.99 (d, *J* = 6.9 Hz, 1H), 4.85 (d, *J* = 6.9 Hz, 1H), 4.83–4.73 (complex m, 6H), 4.67 (d, *J* = 12.6 Hz, 1H), 4.63 (d, *J* = 12.0 Hz, 1H), 4.61 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 12.6 Hz, 1H), 4.54 (m, 1H), 4.46 (d, *J* = 11.5 Hz, 1H), 4.40 (d, *J* = 11.5 Hz, 1H), 4.14–4.05 (complex m, 3H), 3.97 (dd, *J* = 6.9, 2.9 Hz, 1H), 3.89–3.86 (complex m, 2H), 3.81–3.73 (complex m, 5H), 3.23 (dd, *J* = 13.2, 3.4 Hz, 1H), 2.79–2.70 (complex m, 2H), 1.74 (m, 1H), 1.66 (m, 1H), 1.31 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 5.7 Hz, 3H), 1.20 (d, *J* = 6.3 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.93 (s, 9H), 0.11 (s, 3H), 0.07 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.1, 174.7, 158.9, 152.9, 138.2, 137.9, 137.7, 135.1, 131.0, 129.4 (C \times 2), 129.0 (C \times 2), 128.9 (C \times 2), 128.3 (C \times 4), 128.2 (C \times 2), 127.8 (C \times 2), 127.7 (C \times 2), 127.6, 127.5, 127.4 (C \times 2), 127.4, 127.3, 113.6 (C \times 2), 96.8, 96.5, 95.9, 81.6, 81.0, 80.0, 76.0, 74.8, 72.9, 70.3, 70.2, 70.1, 70.1, 65.9, 55.3, 55.2, 43.6, 41.7, 40.0, 38.7, 37.5, 26.1 (C \times 3), 18.5, 14.2, 14.0, 13.8, 13.2, 11.2, 10.9, –4.0, –4.2; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₆₆H₈₉NO₁₄SiNa, 1170.5950; found 1170.5963.

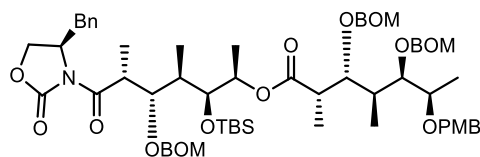


(2'*R*,3'*S*,4'*R*,5'*R*,6'*S*)-7-[(*S*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*R*,3*S*,4*R*,5*S*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78l**); According to the procedure of **4.10.**, **76c** (845 mg, 1.41 mmol) and **77d** (822 mg, 1.45 mmol) were converted to **78l** (1.52 g, 94%) as a colorless oil; $[\alpha]_D^{27} +21.2$ (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3032, 2931, 2885, 2862, 1782, 1697, 1381, 1250, 1103, 1026, 833, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.34–7.21 (complex m, 20H), 7.13 (d, *J* = 6.9 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.14 (m, 1H), 4.85 (s, 2H), 4.81–4.75 (complex m, 4H), 4.68–4.54 (complex m, 7H), 4.46 (m, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.10–3.99 (complex m, 4H), 3.95–3.88 (complex m, 2H), 3.90 (dd, *J* = 7.5, 2.3 Hz, 1H), 3.79 (s, 3H), 3.68 (dq, *J* = 6.3, 6.3 Hz, 1H), 3.21 (dd, *J* = 13.2, 2.9 Hz, 1H), 2.69 (dd, *J* = 13.2, 9.7 Hz, 1H), 2.65 (m, 1H), 2.05 (m, 1H), 1.69 (m, 1H), 1.28 (d, *J* = 7.2 Hz, 3H), 1.24–1.19 (complex m, 6H), 1.17 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.93–0.90 (complex m, 12H), 0.12 (s, 3H), 0.06 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.0, 174.6, 158.9, 152.9, 138.1, 138.0, 137.9, 135.2, 131.0, 129.4 (C \times 2), 129.1 (C \times 2), 128.8 (C \times 2), 128.3 (C \times 2), 128.2 (C \times 4), 127.8 (C \times 2), 127.7 (C \times 2), 127.4 (C \times 5), 127.2, 113.6 (C \times 2), 96.6, 96.5, 96.1, 82.4, 80.9, 80.8, 76.1, 74.6, 73.6, 70.3, 70.1 (C \times 2), 69.8, 65.9, 55.3, 55.2, 42.0, 41.8, 40.1, 37.5, 37.0, 26.1 (C \times 3), 18.5, 16.3, 13.6, 13.4, 11.4, 11.2, 10.0, –3.9, –4.2; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₆₆H₈₉NO₁₄SiNa, 1170.5950; found 1170.5932.



78m

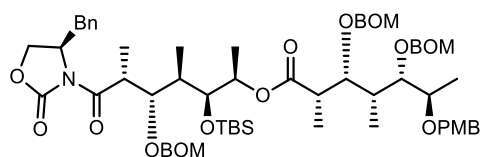
(2',3',4',5',6'R)-7-[(R)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*R*,3*S*,4*S*,5*R*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78m**); According to the procedure of **4.10.**, **76d** (841 mg, 1.40 mmol) and **77a** (870 mg, 1.54 mmol) were converted to **78m** (1.43 g, 89%) as a colorless oil; $[\alpha]_D^{29} -15.2$ (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹; 3062, 3023, 2939, 2885, 2862, 1782, 1705, 1458, 1381, 1095, 1026, 833, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.34–7.23 (complex m, 20H), 7.02 (d, *J* = 7.5 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 4.88–4.71 (complex m, 7H), 4.67–4.60 (complex m, 4H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.30 (m, 1H), 4.09 (dd, *J* = 5.2, 5.2 Hz, 1H), 4.00–3.94 (complex m, 3H), 3.90 (m, 1H), 3.86 (d, *J* = 8.6 Hz, 1H), 3.78 (s, 3H), 3.73 (m, 1H), 3.60 (dd, *J* = 4.6, 4.6 Hz, 1H), 3.23 (d, *J* = 12.6 Hz, 1H), 2.88 (dq, *J* = 6.9, 6.9 Hz, 1H), 2.66 (dd, *J* = 12.6, 10.9 Hz, 1H), 2.02 (m, 1H), 1.90 (m, 1H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.19 (d, *J* = 6.3 Hz, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.07 (d, *J* = 6.3 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.2, 174.4, 159.0, 153.1, 138.1, 137.9, 137.9, 135.4, 130.7, 129.3 (C ×2), 129.3 (C ×2), 128.7 (C ×2), 128.3 (C ×2), 128.2 (C ×2), 128.2 (C ×2), 127.6 (C ×6), 127.5, 127.4, 127.4, 127.0, 113.6 (C ×2), 97.0, 96.3, 96.0, 83.0, 81.3, 81.1, 76.3, 73.7, 73.1, 70.8, 70.6, 70.1, 70.0, 66.0, 55.8, 55.1, 42.9, 40.6, 39.0, 37.3, 37.1, 25.9 (C ×3), 18.4, 15.9, 15.6, 12.7, 10.7, 10.4, 9.4, -3.9, -4.0; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₆₆H₈₉NO₁₄SiNa, 1170.5950; found 1170.5925.



78n

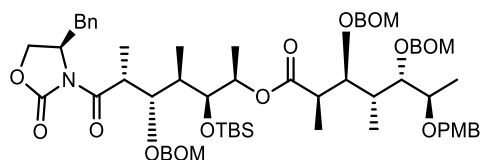
(2',3',4',5',6'R)-7-[(R)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*S*,3*R*,4*S*,5*R*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78n**); According to the procedure of **4.10.**, **76d** (821 mg, 1.37 mmol) and **77b** (877 g, 1.55 mmol) were converted to **78n** (1.49 g, 94%) as a colorless oil; $[\alpha]_D^{27} -9.8$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹; 3062, 3024, 2939, 2885, 2862, 1782, 1720, 1697, 1458, 1381, 1250, 1103, 1026, 833, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.21 (complex m, 20H), 7.06 (d, *J* = 7.5 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 4.90 (d, *J* = 6.3 Hz, 1H), 4.87 (d, *J* = 6.3 Hz, 1H), 4.86 (d, *J* = 6.3 Hz, 1H), 4.84–4.81 (complex m, 2H), 4.77 (d, *J* = 6.9 Hz, 1H), 4.73 (d, *J* = 6.9 Hz, 1H), 4.68 (d, *J* = 12.6 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 12.6 Hz, 1H), 4.56 (d, *J* = 12.6 Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 11.5 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.44–4.40 (complex m, 2H), 4.13 (dd, *J* = 8.3, 8.3 Hz, 1H), 4.07 (dd, *J* = 9.2, 1.7 Hz, 1H), 4.01 (dd, *J* = 8.6, 1.7 Hz, 1H), 3.97 (m, 1H), 3.93 (m, 1H), 3.82 (app d, *J* = 6.9 Hz, 1H), 3.79–3.76 (complex m, 4H), 3.62 (dq, *J* = 6.3, 6.3 Hz, 1H), 3.21 (dd, *J* = 13.2, 2.9 Hz, 1H), 2.68 (dd, *J* = 13.2, 10.3 Hz, 1H), 2.62 (m, 1H),

1.85–1.75 (complex m, 2H), 1.24 (d, $J = 6.9$ Hz, 3H), 1.14 (d, $J = 6.3$ Hz, 3H), 1.12 (d, $J = 6.9$ Hz, 3H), 1.04 (d, $J = 6.3$ Hz, 3H), 0.98 (d, $J = 6.9$ Hz, 3H), 0.92–0.89 (complex m, 12H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.9, 174.4, 159.0, 153.3, 138.0 (C \times 2), 137.9, 135.5, 130.8, 129.3 (C \times 2), 129.2 (C \times 2), 128.7 (C \times 2), 128.3 (C \times 2), 128.2 (C \times 2), 128.2 (C \times 2), 127.7 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.5, 127.4 (C \times 2), 127.0, 113.6 (C \times 2), 96.4, 96.4, 96.3, 82.0, 81.1, 80.7, 77.7, 73.6, 73.6, 71.0, 70.3, 70.2, 69.6, 66.1, 55.6, 55.2, 41.4, 40.1, 39.7, 37.8, 37.6, 26.0 (C \times 3), 18.4, 16.5, 13.9, 11.5, 11.0, 10.8, 9.1, –4.0, –4.3; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{66}\text{H}_{89}\text{NO}_{14}\text{SiNa}$, 1170.5950; found 1170.5940.



78o

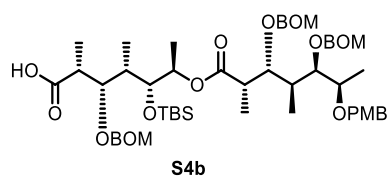
(2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-7-[(*R*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*S*,3*R*,4*R*,5*S*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-[(4-methoxybenzyl)oxy]-2,4-dimethylheptanoate (**78o**); According to the procedure of **4.10.**, **76d** (500 mg, 834 μmol) and **77c** (520 mg, 918 μmol) were converted to **78o** (852 mg, 89%) as a colorless oil; $[\alpha]_{\text{D}}^{29}$ –12.4 (c 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 3032, 2939, 2862, 1782, 1720, 1705, 1458, 1381, 1242, 1095, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.24 (complex m, 18H), 7.17 (d, $J = 8.6$ Hz, 2H), 7.08 (d, $J = 6.9$ Hz, 2H), 6.81 (d, $J = 8.6$ Hz, 2H), 4.97 (d, $J = 6.9$ Hz, 1H), 4.86 (dq, $J = 6.3, 3.4$ Hz, 1H), 4.84 (d, $J = 6.9$ Hz, 1H), 4.82 (d, $J = 6.9$ Hz, 1H), 4.79–4.70 (complex m, 5H), 4.67 (d, $J = 12.0$ Hz, 1H), 4.63 (d, $J = 12.0$ Hz, 1H), 4.58 (d, $J = 12.0$ Hz, 1H), 4.56 (d, $J = 12.0$ Hz, 1H), 4.46 (d, $J = 11.5$ Hz, 1H), 4.42 (m, 1H), 4.38 (d, $J = 11.5$ Hz, 1H), 4.08–3.96 (complex m, 3H), 3.91 (dd, $J = 7.5, 2.9$ Hz, 1H), 3.85 (dd, $J = 3.4, 3.4$ Hz, 1H), 3.82 (dd, $J = 7.5, 3.4$ Hz, 1H), 3.80–3.77 (complex m, 5H), 3.24 (dd, $J = 13.2, 3.4$ Hz, 1H), 2.76 (dq, $J = 6.9, 6.9$ Hz, 1H), 2.71 (dd, $J = 13.2, 10.3$ Hz, 1H), 1.87 (m, 1H), 1.76 (m, 1H), 1.27 (d, $J = 6.9$ Hz, 3H), 1.21 (d, $J = 7.5$ Hz, 3H), 1.20 (d, $J = 6.3$ Hz, 3H), 1.16 (d, $J = 6.3$ Hz, 3H), 1.12 (d, $J = 6.9$ Hz, 3H), 1.01 (d, $J = 6.9$ Hz, 3H), 0.92 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.6, 174.7, 158.9, 153.2, 138.2, 137.8, 137.7, 135.5, 130.9, 129.3 (C \times 2), 129.0 (C \times 2), 128.8 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 127.8 (C \times 2), 127.7 (C \times 2), 127.6, 127.6, 127.4, 127.1, 113.6 (C \times 2), 96.6, 96.4, 95.9, 82.2, 81.3, 80.2, 75.8, 73.8, 73.2, 70.5, 70.3, 70.2, 70.1, 66.1, 55.8, 55.2, 43.4, 40.2, 39.5, 38.6, 37.5, 26.0 (C \times 3), 18.4, 14.9, 14.2, 13.5, 11.0, 10.9, 10.7, –4.0, –4.1; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{66}\text{H}_{89}\text{NO}_{14}\text{SiNa}$, 1170.5950; found 1170.5934.



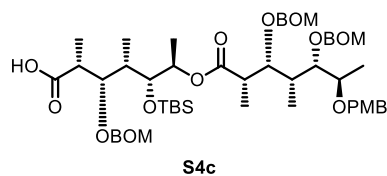
78p

(2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-7-[(*R*)-4''-Benzyl-2''-oxazolidin-3''-yl]-5'-[(benzyloxy)methoxy]-3'-[(*tert*-butyldimethylsilyl)oxy]-4',6'-dimethyl-7'-oxoheptan-2'-yl (2*R*,3*S*,4*R*,5*S*,6*R*)-3,5-bis[(benzyloxy)methoxy]-6-

$J = 6.9$ Hz, 3H), 1.00 (d, $J = 6.9$ Hz, 3H), 0.91 (s, 9H), 0.08 (s, 3H), -0.05 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 176.2, 174.3, 159.0, 137.9, 137.5, 137.3, 130.4, 129.6 (C $\times 2$), 128.4 (C $\times 2$), 128.3 (C $\times 2$), 128.3 (C $\times 2$), 128.2 (C $\times 2$), 127.7 (C $\times 2$), 127.7, 127.6, 127.5, 127.4 (C $\times 2$), 113.6 (C $\times 2$), 96.7, 96.5, 95.2, 82.7, 81.5, 80.6, 75.9, 74.3, 71.0, 70.6, 70.2, 69.9, 69.6, 55.2, 43.9, 42.3, 38.9, 37.3, 26.0 (C $\times 3$), 18.3, 17.0, 15.8, 13.7, 11.6, 10.7, 10.7, -3.5 , -3.8 ; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5259.

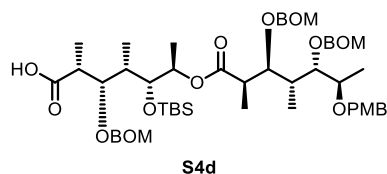


(2*R*,3*S*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*S*,5'*R*,6'*R*}-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4b**); According to the procedure of **4.11.**, **78b** (1.07 g, 0.932 mmol) was converted to **S4b** (773 mg, 84%) as a colorless oil; $[\alpha]_{\text{D}}^{27} +0.59$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3248-3140 (br), 3062, 3032, 2939, 2885, 1736, 1512, 1458, 1381, 1250, 1095, 1026, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.34–7.24 (complex m, 15H), 7.21 (d, $J = 8.6$ Hz, 2H), 6.83 (d, $J = 8.6$ Hz, 2H), 5.00 (m, 1H), 4.93 (d, $J = 5.7$ Hz, 1H), 4.86 (d, $J = 5.7$ Hz, 1H), 4.79 (d, $J = 6.9$ Hz, 1H), 4.74–4.70 (complex m, 3H), 4.68 (d, $J = 12.6$ Hz, 1H), 4.62–4.56 (complex m, 4H), 4.53 (d, $J = 12.0$ Hz, 1H), 4.52 (d, $J = 10.9$ Hz, 1H), 4.42 (d, $J = 10.9$ Hz, 1H), 4.13 (dd, $J = 8.6$, 1.7 Hz, 1H), 4.05 (dd, $J = 5.2$, 5.2 Hz, 1H), 3.81 (app d, $J = 7.5$ Hz, 1H), 3.79 (s, 3H), 3.68 (dd, $J = 5.2$, 5.2 Hz, 1H), 3.63 (dq, $J = 6.3$, 6.3 Hz, 1H), 2.68 (m, 1H), 2.64 (m, 1H), 1.93 (m, 1H), 1.78 (m, 1H), 1.16 (d, $J = 6.9$ Hz, 3H), 1.16–1.14 (complex m, 6H), 1.07 (d, $J = 6.3$ Hz, 3H), 0.96 (d, $J = 6.9$ Hz, 3H), 0.91 (d, $J = 6.9$ Hz, 3H), 0.87 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 177.2, 174.1, 159.0, 137.9, 137.6, 137.4, 130.7, 129.3 (C $\times 2$), 128.4 (C $\times 4$), 128.2 (C $\times 2$), 127.9 (C $\times 2$), 127.8 (C $\times 2$), 127.7, 127.6 (C $\times 3$), 127.4, 113.7 (C $\times 2$), 96.8, 96.4, 96.0, 81.9, 81.6, 80.7, 77.8, 72.9, 72.6, 71.1, 70.3, 70.0, 69.7, 55.2, 43.3, 41.4, 38.0, 37.8, 25.9 (C $\times 3$), 18.1, 16.5, 14.4, 12.1, 10.8, 10.7, 8.9, -4.3 , -4.4 ; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5242.

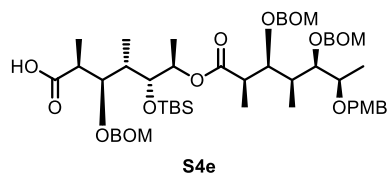


(2*R*,3*S*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*R*,5'*S*,6'*R*}-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4c**); According to the procedure of **4.11.**, **78c** (1.12 g, 0.975 mmol) was converted to **S4c** (763 mg, 79%) as a colorless oil; $[\alpha]_{\text{D}}^{27} -6.7$ (c 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3263-3163 (br), 3062, 2939, 2885, 2862, 1728, 1458, 1381, 1196, 1095, 1026, 833; ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.24 (complex m, 15H), 7.19 (d, $J =$

8.0 Hz, 2H), 6.83 (d, $J = 8.6$ Hz, 2H), 4.95 (dq, $J = 5.7, 5.7$ Hz, 1H), 4.91 (d, $J = 6.9$ Hz, 1H), 4.83 (d, $J = 6.9$ Hz, 1H), 4.76–4.64 (complex m, 7H), 4.61–4.58 (complex m, 3H), 4.50 (d, $J = 11.5$ Hz, 1H), 4.38 (d, $J = 11.5$ Hz, 1H), 3.89 (dd, $J = 5.7, 5.7$ Hz, 1H), 3.84 (dd, $J = 5.7, 5.7$ Hz, 1H), 3.78 (s, 3H), 3.75–3.69 (complex m, 3H), 2.83 (dq, $J = 6.3, 6.3$ Hz, 1H), 2.70 (dq, $J = 6.3, 6.3$ Hz, 1H), 1.96–1.89 (complex m, 2H), 1.22 (d, $J = 5.7$ Hz, 3H), 1.18 (d, $J = 6.9$ Hz, 3H), 1.18 (d, $J = 6.3$ Hz, 3H), 1.12 (d, $J = 6.9$ Hz, 3H), 1.09 (d, $J = 6.9$ Hz, 3H), 1.00 (d, $J = 7.5$ Hz, 3H), 0.88 (s, 9H), 0.09 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.0, 174.6, 159.0, 137.7, 137.6, 137.6, 130.6, 129.2 (C \times 2), 128.3 (C \times 4), 128.3 (C \times 2), 127.9 (C \times 2), 127.8 (C \times 2), 127.6, 127.6 (C \times 3), 127.5, 113.7 (C \times 2), 96.2, 96.1, 95.4, 81.7, 81.5, 80.8, 75.7, 73.2, 73.1, 70.4, 70.3, 70.0, 70.0, 55.2, 42.7, 42.7, 38.4, 38.0, 25.9 (C \times 3), 18.2, 15.2, 15.0, 11.9, 11.6, 11.0, 10.7, -4.0 , -4.4 ; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5242.

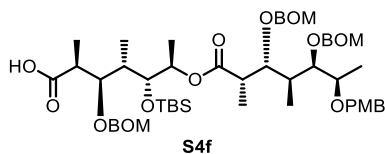


(2*R*,3*S*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*R*,5'*S*,6'*R*}-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4d**); According to the procedure of **4.11.**, **78d** (1.47 g, 1.28 mmol) was converted to **S4d** (765 mg, 60%) as a colorless oil; $[\alpha]_{\text{D}}^{27} -17.4$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3224–3132 (br), 3062, 2931, 2885, 2862, 1705, 1512, 1458, 1250, 1095, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.33–7.26 (complex m, 15H), 7.24 (d, $J = 8.6$ Hz, 2H), 6.84 (d, $J = 8.6$ Hz, 2H), 5.00 (dq, $J = 6.3, 3.4$ Hz, 1H), 4.87 (d, $J = 6.3$ Hz, 1H), 4.84–4.82 (complex m, 2H), 4.79 (d, $J = 6.9$ Hz, 1H), 4.76 (s, 2H), 4.68–4.61 (complex m, 4H), 4.58 (d, $J = 12.0$ Hz, 1H), 4.58 (d, $J = 12.0$ Hz, 1H), 4.53 (d, $J = 11.5$ Hz, 1H), 4.44 (d, $J = 11.5$ Hz, 1H), 4.07 (dd, $J = 6.9, 3.4$ Hz, 1H), 3.90 (dd, $J = 5.2, 2.9$ Hz, 1H), 3.87 (dd, $J = 5.7, 5.2$ Hz, 1H), 3.78 (s, 3H), 3.69 (dd, $J = 5.7, 3.4$ Hz, 1H), 3.67 (m, 1H), 2.73 (dq, $J = 6.9, 6.9$ Hz, 1H), 2.69 (dq, $J = 6.9, 3.4$ Hz, 1H), 2.04 (m, 1H), 1.90 (m, 1H), 1.21–1.18 (complex m, 9H), 1.10 (d, $J = 6.3$ Hz, 3H), 0.99 (d, $J = 6.9$ Hz, 3H), 0.95 (d, $J = 6.9$ Hz, 3H), 0.90 (s, 9H), 0.08 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.0, 174.6, 159.0, 137.7, 137.8, 137.6, 130.8, 129.2 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 127.9 (C \times 2), 127.8 (C \times 2), 127.6, 127.5 (C \times 4), 113.6 (C \times 2), 96.4, 95.9, 95.6, 81.6, 81.3, 80.5, 76.2, 73.8, 72.5, 70.4, 70.0 (C \times 2), 69.8, 55.2, 42.7, 41.7, 38.3, 37.3, 25.9 (C \times 3), 18.3, 16.0, 15.9, 12.2, 11.7, 10.9, 10.7, -4.0 , -4.0 ; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5264.

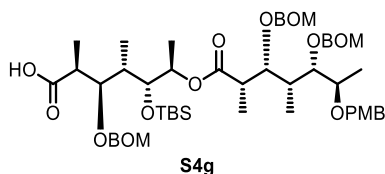


(2*S*,3*R*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*S*,5'*R*,6'*R*}-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4e**); According to the procedure of **4.11.**, **78e** (1.05 g, 0.913 mmol) was converted to **S4e** (746 mg, 83%) as a colorless oil; $[\alpha]_{\text{D}}^{27} -1.7$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3286–3163 (br), 3062, 3032, 2939, 2885, 2862,

1712, 1512, 1458, 1250, 1088, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.32–7.25 (complex m, 15H), 7.22 (d, J = 8.6 Hz, 2H), 6.81 (d, J = 8.6 Hz, 2H), 4.90–4.85 (complex m, 2H), 4.82–4.77 (complex m, 3H), 4.73 (m, 1H), 4.68 (d, J = 12.0 Hz, 1H), 4.66–4.52 (complex m, 6H), 4.49 (d, J = 10.9 Hz, 1H), 4.42 (d, J = 10.9 Hz, 1H), 4.14 (dd, J = 6.3, 5.2 Hz, 1H), 4.01–3.97 (complex m, 2H), 3.77 (s, 3H), 3.71 (m, 1H), 3.56 (dd, J = 5.2, 5.2 Hz, 1H), 2.88 (m, 1H), 2.67 (m, 1H), 2.00–1.93 (complex m, 2H), 1.21 (d, J = 6.9 Hz, 3H), 1.18–1.13 (complex m, 9H), 1.06 (d, J = 6.9 Hz, 3H), 0.90–0.87 (complex m, 12H), 0.07 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 179.7, 174.3, 159.0, 138.0, 138.0, 137.8, 130.7, 129.4 (C \times 2), 128.3 (C \times 6), 127.8 (C \times 2), 127.7 (C \times 4), 127.5 (C \times 3), 113.6 (C \times 2), 96.5, 96.1, 95.9, 82.4, 81.6, 81.1, 76.6, 74.0, 71.2, 70.9, 70.2, 70.0, 70.0, 55.2, 42.6, 40.9, 37.7, 37.3, 25.9 (C \times 3), 18.3, 15.8, 15.3, 11.9, 11.3, 10.8, 9.2, –4.1, –4.4; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5247.

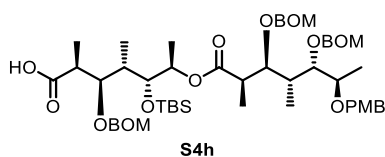


(2*S*,3*R*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4f**); According to the procedure of **4.11.**, **78f** (1.14 g, 0.989 mmol) was converted to **S4f** (748 mg, 76%) as a colorless oil; $[\alpha]_{\text{D}}^{27}$ –1.1 (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3240–3086 (br), 3062, 2939, 2885, 2862, 1705, 1512, 1458, 1250, 1095, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.31–7.22 (complex m, 17H), 6.84 (d, J = 8.6 Hz, 2H), 4.91 (d, J = 6.9 Hz, 1H), 4.89 (d, J = 6.9 Hz, 1H), 4.84–4.80 (complex m, 2H), 4.75 (d, J = 6.9 Hz, 1H), 4.69 (d, J = 12.6 Hz, 1H), 4.67–4.51 (complex m, 7H), 4.44 (d, J = 12.6 Hz, 1H), 4.41 (d, J = 12.6 Hz, 1H), 4.12 (dd, J = 9.2, 2.3 Hz, 1H), 4.00 (dd, J = 5.7, 1.7 Hz, 1H), 3.95 (dd, J = 9.2, 1.7 Hz, 1H), 3.86 (app d, J = 6.9 Hz, 1H), 3.79 (s, 3H), 3.63 (dq, J = 6.3, 6.3 Hz, 1H), 2.67 (dq, J = 6.9, 1.7 Hz, 1H), 2.62 (m, 1H), 1.84–1.78 (complex m, 2H), 1.16 (d, J = 6.9 Hz, 3H), 1.14 (d, J = 6.3 Hz, 3H), 1.13 (d, J = 6.9 Hz, 3H), 1.05 (d, J = 6.3 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H), 0.87 (s, 9H), 0.81 (d, J = 6.9 Hz, 3H), 0.08 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 179.9, 174.4, 159.0, 138.1, 137.9, 137.7, 130.8, 129.2 (C \times 2), 128.3 (C \times 2), 128.2 (C \times 2), 128.2 (C \times 2), 127.7 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.5, 127.5, 127.4, 113.7 (C \times 2), 96.4, 96.4, 96.2, 82.7, 81.9, 81.0, 77.7, 73.6, 71.1, 70.8, 70.3, 70.0, 69.7, 55.2, 41.4, 41.0, 37.9, 37.1, 25.9 (C \times 3), 18.2, 16.5, 14.7, 11.4, 11.0, 9.1, 8.8, –4.2, –4.3; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5249.

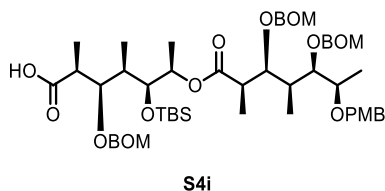


(2*S*,3*R*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4g**); According to the procedure of **4.11.**, **78g** (511 mg, 0.445 mmol) was converted to **S4g** (306 mg, 69%) as a colorless oil; $[\alpha]_{\text{D}}^{24}$ –11.1 (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3278–3147 (br), 3062, 3016, 2939, 2893,

2862, 1712, 1458, 1381, 1250, 1088, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.34–7.24 (complex m, 15H), 7.19 (dd, J = 8.6, 2.9 Hz, 2H), 6.83 (dd, J = 8.6, 2.3 Hz, 2H), 4.93 (m, 1H), 4.85–4.81 (complex m, 2H), 4.78–4.57 (complex m, 9H), 4.54–4.47 (complex m, 2H), 4.39 (dd, J = 11.5, 2.9 Hz, 1H), 4.06 (dd, J = 5.2, 5.2 Hz, 1H), 4.00 (m, 1H), 3.85 (m, 1H), 3.80–3.73 (complex m, 5H), 2.81 (m, 1H), 2.63 (m, 1H), 1.92–1.82 (complex m, 2H), 1.23 (m, 3H), 1.20–1.14 (complex m, 9H), 1.11 (m, 3H), 0.90 (s, 9H), 0.87 (d, J = 6.9 Hz, 3H), 0.11 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.2, 174.7, 159.0, 138.0, 137.8, 137.7, 130.7, 129.1 (C \times 2), 128.3 (C \times 4), 128.2 (C \times 2), 127.8 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.5, 127.5 (C \times 2), 113.6 (C \times 2), 96.3, 96.1, 95.8, 82.6, 81.4, 80.7, 75.8, 73.9, 71.0, 70.4, 70.3, 70.0 (C \times 2), 55.2, 42.9, 41.0, 38.5, 37.3, 25.9 (C \times 3), 18.2, 15.1, 14.7, 12.2, 11.5, 11.0, 9.1, –4.2, –4.3; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5257.

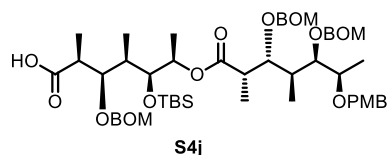


(2*S*,3*R*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4h**); According to the procedure of **4.11.**, **78h** (1.34 g, 1.17 mmol) was converted to **S4h** (693 mg, 60%) as a colorless oil; $[\alpha]_{\text{D}}^{28}$ –9.5 (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3217–3147 (br), 3062, 3032, 2939, 2885, 2862, 1512, 1458, 1381, 1250, 1095, 1026, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.34–7.23 (complex m, 17H), 6.86 (d, J = 8.6 Hz, 2H), 4.88 (m, 1H), 4.85 (s, 2H), 4.80 (s, 2H), 4.78 (d, J = 6.9 Hz, 1H), 4.72 (d, J = 6.9 Hz, 1H), 4.69–4.62 (complex m, 3H), 4.60–4.53 (complex m, 4H), 4.44 (d, J = 11.5 Hz, 1H), 4.12 (dd, J = 8.6, 2.3 Hz, 1H), 4.07 (dd, J = 5.2, 1.2 Hz, 1H), 4.03 (dd, J = 9.2, 1.7 Hz, 1H), 3.96 (dd, J = 5.2, 1.7 Hz, 1H), 3.80 (s, 3H), 3.66 (dq, J = 5.7, 5.7 Hz, 1H), 2.68–2.62 (complex m, 2H), 2.06 (m, 1H), 1.89 (m, 1H), 1.23 (d, J = 6.9 Hz, 3H), 1.22 (d, J = 7.5 Hz, 3H), 1.17 (d, J = 6.9 Hz, 3H), 1.14 (d, J = 6.9 Hz, 3H), 0.92–0.87 (complex m, 15H), 0.11 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 179.7, 174.5, 159.0, 137.9, 137.9, 137.7, 130.9, 129.1 (C \times 2), 128.3 (C \times 6), 127.8 (C \times 2), 127.7 (C \times 2), 127.7 (C \times 2), 127.5, 127.5 (C \times 2), 113.6 (C \times 2), 96.4, 96.1, 95.9, 82.5, 81.8, 80.7, 76.0, 74.1, 71.2, 70.3, 70.1 (C \times 2), 69.8, 55.2, 41.9, 40.8, 37.7, 36.8, 25.9 (C \times 3), 18.3, 16.1, 15.3, 11.4, 11.3, 9.9, 9.0, –4.2 (C \times 2); HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5257.

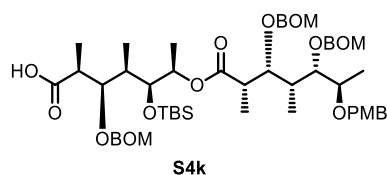


(2*S*,3*R*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4i**); According to the procedure of **4.11.**, **78i** (55.8 mg, 48.6 μmol) was converted to **S4i** (33.8 mg, 70%) as a colorless oil; $[\alpha]_{\text{D}}^{27}$ +1.0 (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3271–3147 (br), 3062, 2931, 2893, 2862, 1712,

1512, 1458, 1381, 1250, 1157, 1095, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.33–7.23 (complex m, 17H), 6.82 (d, J = 8.6 Hz, 2H), 4.95 (m, 1H), 4.86 (d, J = 6.9 Hz, 1H), 4.81–4.78 (complex m, 3H), 4.74 (d, J = 6.9 Hz, 1H), 4.72 (d, J = 6.9 Hz, 1H), 4.66–4.59 (complex m, 4H), 4.57 (d, J = 12.6 Hz, 1H), 4.54 (d, J = 12.0 Hz, 1H), 4.50 (d, J = 11.5 Hz, 1H), 4.42 (d, J = 11.5 Hz, 1H), 4.13 (dd, J = 5.2, 5.2 Hz, 1H), 3.89 (dd, J = 5.2, 5.2 Hz, 1H), 3.77 (s, 3H), 3.75–3.70 (complex m, 2H), 3.58 (dd, J = 4.9, 4.9 Hz, 1H), 2.86 (dq, J = 6.3, 6.3 Hz, 1H), 2.77 (dq, J = 6.9, 6.9 Hz, 1H), 1.98 (m, 1H), 1.82 (m, 1H), 1.22 (d, J = 6.9 Hz, 3H), 1.18 (d, J = 7.5 Hz, 3H), 1.17 (d, J = 6.3 Hz, 3H), 1.15 (d, J = 6.3 Hz, 3H), 1.06 (d, J = 6.9 Hz, 3H), 0.97 (d, J = 6.9 Hz, 3H), 0.90 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.6, 174.4, 159.0, 138.0, 137.9, 137.6, 130.7, 129.4 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 4), 127.7 (C \times 4), 127.7 (C \times 2), 127.6, 127.5, 127.5, 113.6 (C \times 2), 96.5, 96.4, 95.9, 81.5, 81.3, 81.1, 76.4, 74.9, 73.2, 70.9, 70.2, 70.2, 70.0, 55.2, 42.8, 42.5, 39.6, 37.3, 26.0 (C \times 3), 18.4, 15.6, 15.1, 12.7, 12.0, 10.9, 10.7, –4.0, –4.2; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5255.

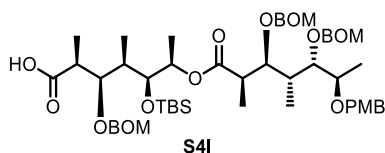


(2*S*,3*R*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4j**); According to the procedure of **4.11.**, **78j** (1.14 g, 0.996 mmol) was converted to **S4j** (814 mg, 83%) as a colorless oil; $[\alpha]_{\text{D}}^{28}$ +6.6 (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3248-3163 (br), 3062, 2939, 2885, 2862, 1705, 1512, 1458, 1250, 1103, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.34–7.23 (complex m, 17H), 6.85 (d, J = 8.6 Hz, 2H), 4.95–4.89 (complex m, 4H), 4.79 (d, J = 6.9 Hz, 1H), 4.78 (d, J = 7.5 Hz, 1H), 4.75 (d, J = 6.9 Hz, 1H), 4.72 (d, J = 12.6 Hz, 1H), 4.64 (d, J = 12.6 Hz, 1H), 4.63 (d, J = 12.0 Hz, 1H), 4.63 (d, J = 12.0 Hz, 1H), 4.58 (d, J = 12.0 Hz, 1H), 4.53 (d, J = 10.9 Hz, 1H), 4.50 (d, J = 12.0 Hz, 1H), 4.45 (d, J = 11.5 Hz, 1H), 4.14 (dd, J = 9.7, 2.3 Hz, 1H), 3.85 (app d, J = 8.0 Hz, 1H), 3.83 (dd, J = 5.2, 5.2 Hz, 1H), 3.80 (s, 3H), 3.70 (dd, J = 5.7, 2.9 Hz, 1H), 3.65 (dq, J = 6.3, 6.3 Hz, 1H), 2.78 (dq, J = 6.9, 5.7 Hz, 1H), 2.63 (dq, J = 6.9, 1.7 Hz, 1H), 1.81 (m, 1H), 1.71 (m, 1H), 1.18 (d, J = 6.9 Hz, 3H), 1.17 (d, J = 6.3 Hz, 6H), 1.08 (d, J = 6.3 Hz, 3H), 0.96 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 6.9 Hz, 3H), 0.90 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 179.6, 174.2, 159.0, 138.1, 137.9, 137.7, 130.8, 129.2 (C \times 2), 128.3 (C \times 4), 128.2 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.6 (C \times 2), 127.5, 127.4, 127.4, 113.7 (C \times 2), 96.7, 96.7, 96.3, 82.4, 81.2, 80.8, 77.8, 74.6, 73.0, 71.1, 70.3, 70.2, 69.5, 55.2, 42.5, 41.4, 39.3, 37.8, 26.0 (C \times 3), 18.4, 16.5, 13.8, 12.0, 11.1, 10.8, 9.0, –4.0, –4.4; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5252.

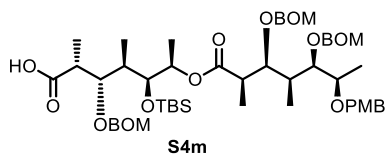


(2*S*,3*R*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic

acid (**S4k**); According to the procedure of **4.11.**, **78k** (769 mg, 0.670 mmol) was converted to **S4k** (567 mg, 86%) as a colorless oil; $[\alpha]_D^{27} +3.7$ (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3263-3201 (br), 3062, 2939, 2893, 2862, 1720, 1512, 1458, 1381, 1250, 1157, 1026, 833, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.24 (complex m, 15H), 7.18 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 5.04 (dq, *J* = 6.3, 2.9 Hz, 1H), 4.98 (d, *J* = 6.9 Hz, 1H), 4.80–4.71 (complex m, 7H), 4.65–4.58 (complex m, 4H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.40 (d, *J* = 11.5 Hz, 1H), 3.91 (dd, *J* = 5.7, 5.2 Hz, 1H), 3.85–3.78 (complex m, 6H), 3.75 (dd, *J* = 5.7, 2.9 Hz, 1H), 2.85–2.72 (complex m, 2H), 1.85–1.75 (complex m, 2H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.3 Hz, 3H), 1.20 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.13 (d, *J* = 7.5 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.93 (s, 9H), 0.10 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 180.1, 174.6, 158.9, 138.1, 137.7, 137.6, 130.9, 129.0 (C \times 2), 128.3 (C \times 4), 128.2 (C \times 2), 127.8 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.6 (C \times 2), 127.4, 113.6 (C \times 2), 96.5, 96.4, 95.8, 81.5, 81.1, 80.2, 75.8, 74.7, 72.8, 70.3, 70.2, 70.2, 70.0, 55.2, 43.4, 42.7, 39.5, 38.6, 26.0 (C \times 3), 18.4, 14.4, 14.2, 13.4, 12.1, 11.1, 10.9, -4.0, -4.2; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₅₆H₈₀O₁₃SiNa, 1011.5266; found 1011.5255.

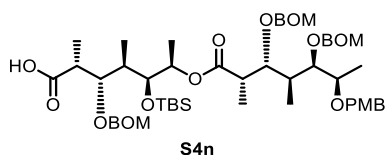


(2*S*,3*R*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*R*,5'*S*,6'*R*}-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4l**); According to the procedure of **4.11.**, **78l** (1.44 g, 1.25 mmol) was converted to **S4l** (1.04 g, 84%) as a colorless oil; $[\alpha]_D^{28} -0.55$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 3232-3116 (br), 3232-3116 (br), 3062, 3032, 2939, 2885, 2862, 1705, 1512, 1458, 1250, 1103, 1026, 833, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.31–7.22 (complex m, 17H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.97 (m, 1H), 4.83 (s, 2H), 4.76 (s, 2H), 4.73 (d, *J* = 6.9 Hz, 1H), 4.70 (d, *J* = 6.9 Hz, 1H), 4.63–4.52 (complex m, 7H), 4.42 (d, *J* = 11.5 Hz, 1H), 4.06 (dd, *J* = 8.6, 2.3 Hz, 1H), 3.91 (app d, *J* = 5.2 Hz, 1H), 3.88 (dd, *J* = 5.2, 5.2 Hz, 1H), 3.77 (s, 3H), 3.74 (m, 1H), 3.67 (dq, *J* = 6.3, 6.3 Hz, 1H), 2.76 (dq, *J* = 6.3, 6.3 Hz, 1H), 2.63 (dq, *J* = 6.9, 2.3 Hz, 1H), 2.04 (m, 1H), 1.80 (m, 1H), 1.22 (d, *J* = 6.3 Hz, 3H), 1.19 (d, *J* = 7.5 Hz, 3H), 1.17 (d, *J* = 7.5 Hz, 3H), 1.15 (d, *J* = 6.3 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.92–0.89 (complex m, 12H), 0.10 (s, 3H), 0.08 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 180.1, 174.4, 158.9, 138.0, 137.8, 137.6, 130.9, 129.1 (C \times 2), 128.3 (C \times 2), 128.2 (C \times 4), 127.8 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.5, 127.5, 127.4, 113.6 (C \times 2), 96.3, 96.3, 95.9, 82.3, 81.1, 80.7, 76.0, 74.8, 73.3, 70.3, 70.1 (C \times 2), 69.8, 55.2, 42.6, 42.0, 39.5, 37.0, 26.0 (C \times 3), 18.4, 16.2, 14.6, 11.8, 11.3, 11.1, 10.1, -3.9, -4.3; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₅₆H₈₀O₁₃SiNa, 1011.5266; found 1011.5257.

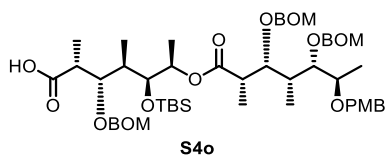


(2*R*,3*S*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*S*,5'*R*,6'*R*}-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4m**); According to the procedure of **4.11.**, **78m** (1.26 g, 1.10 mmol) was converted to **S4m** (946 mg,

87%) as a colorless oil; $[\alpha]_D^{27} -9.2$ (c 2.00, CHCl_3); IR (neat)/ cm^{-1} : 3286-3132 (br), 3062, 3032, 2939, 2885, 2862, 1728, 1512, 1458, 1250, 1088, 1026, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.33–7.24 (complex m, 17H), 6.82 (d, $J = 8.6$ Hz, 2H), 4.91 (dq, $J = 5.7, 5.7$ Hz, 1H), 4.85 (d, $J = 6.9$ Hz, 1H), 4.82–4.70 (complex m, 5H), 4.66 (d, $J = 12.6$ Hz, 1H), 4.63 (s, 2H), 4.57 (d, $J = 11.5$ Hz, 1H), 4.57 (s, 2H), 4.50 (d, $J = 11.5$ Hz, 1H), 4.44 (d, $J = 11.5$ Hz, 1H), 4.05 (dd, $J = 5.7, 5.7$ Hz, 1H), 3.96 (dd, $J = 7.5, 3.4$ Hz, 1H), 3.91 (dd, $J = 4.1, 4.1$ Hz, 1H), 3.77 (s, 3H), 3.74 (dq, $J = 5.7, 5.7$ Hz, 1H), 3.58 (dd, $J = 5.2, 5.2$ Hz, 1H), 2.83 (dq, $J = 6.9, 6.9$ Hz, 1H), 2.66 (dq, $J = 6.9, 3.4$ Hz, 1H), 1.99 (m, 1H), 1.89 (m, 1H), 1.22 (d, $J = 6.9$ Hz, 3H), 1.17 (d, $J = 6.3$ Hz, 3H), 1.16 (d, $J = 6.9$ Hz, 3H), 1.14 (d, $J = 6.9$ Hz, 3H), 1.08 (d, $J = 6.9$ Hz, 3H), 0.91–0.86 (complex m, 12H), 0.10 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.6, 174.4, 159.0, 137.9, 137.9, 137.7, 130.5, 129.5 ($\text{C} \times 2$), 128.3 ($\text{C} \times 6$), 127.8 ($\text{C} \times 2$), 127.7 ($\text{C} \times 2$), 127.7 ($\text{C} \times 2$), 127.5 ($\text{C} \times 3$), 113.6 ($\text{C} \times 2$), 96.3, 95.9, 95.7, 82.0, 81.4, 81.2, 76.0, 73.6, 73.3, 70.8, 70.2, 70.0, 69.9, 55.2, 43.2, 41.0, 39.1, 37.3, 26.1 ($\text{C} \times 3$), 18.5, 15.6, 15.4, 13.2, 10.9, 10.7, 10.5, -3.9, -4.0; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5249.

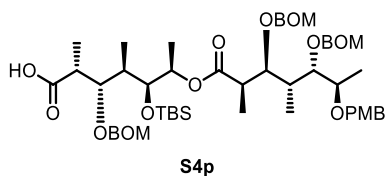


(2*R*,3*S*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4n**); According to the procedure of **4.11.**, **78n** (1.39 mg, 1.21 mmol) was converted to **S4n** (953 mg, 80%) as a colorless oil; $[\alpha]_D^{27} +5.9$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3263-3155 (br), 3062, 3032, 2978, 2939, 2893, 2862, 1736, 1458, 1373, 1242, 1103, 1026, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.32–7.22 (complex m, 17H), 6.83 (d, $J = 8.6$ Hz, 2H), 4.94 (dq, $J = 6.3, 4.0$ Hz, 1H), 4.91–4.87 (complex m, 2H), 4.84 (d, $J = 6.3$ Hz, 1H), 4.77–4.74 (complex m, 2H), 4.71 (d, $J = 7.5$ Hz, 1H), 4.68 (d, $J = 12.6$ Hz, 1H), 4.62–4.59 (complex m, 2H), 4.58–4.54 (complex m, 3H), 4.52 (d, $J = 11.5$ Hz, 1H), 4.44 (d, $J = 11.5$ Hz, 1H), 4.11 (dd, $J = 8.6, 2.9$ Hz, 1H), 3.97–3.93 (complex m, 2H), 3.86 (app d, $J = 6.9$ Hz, 1H), 3.79 (s, 3H), 3.64 (dq, $J = 6.9, 6.9$ Hz, 1H), 2.69–2.62 (complex m, 2H), 1.83 (m, 1H), 1.78 (m, 1H), 1.17 (d, $J = 7.2$ Hz, 3H), 1.16 (d, $J = 6.9$ Hz, 3H), 1.13 (d, $J = 6.9$ Hz, 3H), 1.09 (d, $J = 6.3$ Hz, 3H), 0.93 (d, $J = 6.9$ Hz, 3H), 0.90–0.87 (complex m, 12H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.1, 174.4, 159.0, 138.0, 137.9, 137.7, 130.8, 129.2 ($\text{C} \times 2$), 128.3 ($\text{C} \times 4$), 128.2 ($\text{C} \times 2$), 127.8 ($\text{C} \times 2$), 127.7 ($\text{C} \times 2$), 127.6 ($\text{C} \times 2$), 127.5, 127.4, 127.4, 113.6 ($\text{C} \times 2$), 96.3, 96.2, 95.8, 82.1, 81.9, 80.6, 77.7, 73.9, 73.2, 71.0, 70.1, 70.0, 69.7, 55.2, 41.5, 41.1, 38.5, 37.8, 26.0 ($\text{C} \times 3$), 18.4, 16.5, 15.1, 11.4, 11.0, 9.7, 9.3, -4.1, -4.1; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{56}\text{H}_{80}\text{O}_{13}\text{SiNa}$, 1011.5266; found 1011.5252.



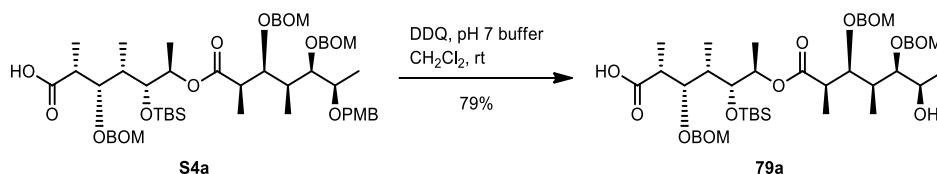
(2*R*,3*S*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-

methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4o**); According to the procedure of **4.11.**, **78o** (609 mg, 0.530 mmol) was converted to **S4o** (446 mg, 85%) as a colorless oil; $[\alpha]_D^{26} +1.1$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 3255-3163 (br), 3062, 3024, 2939, 2885, 2862, 1720, 1512, 1458, 1381, 1250, 1095, 1026, 833, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.25 (complex m, 15H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 5.00–4.91 (complex m, 2H), 4.85 (d, *J* = 6.3 Hz, 1H), 4.81–4.71 (complex m, 6H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.61–4.56 (complex m, 3H), 4.48 (d, *J* = 10.9 Hz, 1H), 4.41 (d, *J* = 10.9 Hz, 1H), 4.04–3.99 (complex m, 2H), 3.88–3.80 (complex m, 3H), 3.79 (s, 3H), 2.79 (m, 1H), 2.67 (m, 1H), 1.85–1.74 (complex m, 2H), 1.24–1.21 (complex m, 6H), 1.19–1.16 (complex m, 6H), 1.14 (d, *J* = 6.3 Hz, 3H), 0.92 (s, 9H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.11 (s, 3H), 0.06 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 180.6, 174.6, 158.9, 138.1, 137.6, 137.6, 130.9, 129.0 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 4), 127.8 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.6, 127.5, 127.4, 113.6 (C \times 2), 96.4, 95.9 (C \times 2), 82.4, 81.3, 80.1, 75.9, 73.8, 73.0, 70.3, 70.2, 70.1, 69.9, 55.2, 43.4, 41.2, 38.7, 38.2, 26.0 (C \times 3), 18.3, 15.8, 14.1, 13.7, 11.2, 10.9, 8.9, –4.0, –4.1; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₅₆H₈₀O₁₃SiNa, 1011.5266; found 1011.5242.

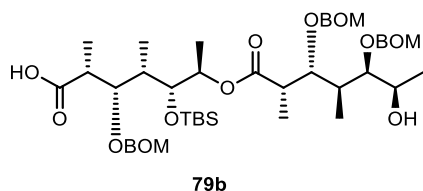


(2*R*,3*S*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-[(4-methoxybenzyl)oxy]-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**S4p**); According to the procedure of **4.11.**, **78p** (1.08 g, 0.941 mmol) was converted to **S4p** (845 mg, 91%) as a colorless oil; $[\alpha]_D^{29} -11.5$ (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3271-3163 (br), 3062, 2939, 2885, 2862, 1712, 1512, 1458, 1250, 1095, 1026, 833, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.33–7.24 (complex m, 17H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.97 (dq, *J* = 6.3, 3.4 Hz, 1H), 4.92 (d, *J* = 6.9 Hz, 1H), 4.82 (d, *J* = 6.9 Hz, 1H), 4.80–4.76 (complex m, 3H), 4.74 (d, *J* = 6.9 Hz, 1H), 4.69–4.65 (complex m, 3H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.58 (s, 2H), 4.55 (d, *J* = 11.5 Hz, 1H), 4.49 (d, *J* = 11.5 Hz, 1H), 4.01 (dd, *J* = 7.5, 4.0 Hz, 1H), 3.91 (dd, *J* = 5.7, 5.7 Hz, 1H), 3.89–3.87 (complex m, 2H), 3.79 (s, 3H), 3.75 (dq, *J* = 5.7, 5.7 Hz, 1H), 2.70–2.64 (complex m, 2H), 2.07 (m, 1H), 1.91 (m, 1H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.21 (d, *J* = 7.5 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.3 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 178.4, 174.4, 159.0, 137.7, 137.6, 137.5, 130.9, 129.2 (C \times 2), 128.3 (C \times 6), 127.9 (C \times 4), 127.8 (C \times 2), 127.6, 127.6 (C \times 2), 113.6 (C \times 2), 95.6, 95.5, 95.5, 81.8, 81.4, 80.6, 76.1, 73.7, 73.6, 70.5, 70.1, 69.9, 69.8, 55.2, 42.0, 40.9, 39.2, 37.4, 26.1 (C \times 3), 18.5, 16.0, 14.5, 11.7, 11.5, 11.4, 11.1, –3.8, –4.0; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₅₆H₈₀O₁₃SiNa, 1011.5266; found 1011.5260.

4.12. (2*R*,3*S*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79a**);

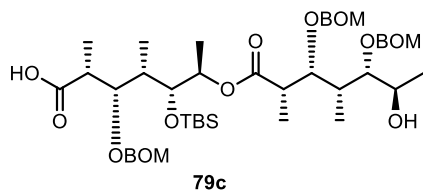


A solution of PMB ether **S4a** (193 mg, 195 μ mol) in CH_2Cl_2 (5.5 mL) and pH 7.0 phosphate buffer solution in water (5.0 mL) at room temperature was added to DDQ (130 mg, 573 μ mol). The heterogeneous solution was stirred for 3 h. Then the reaction was quenched with sat. aq. NaHCO_3 (30 mL). Resulted two layers were separated and the aqueous phase was extracted with CHCl_3 (15 mL \times 3). The combined organic layers were washed with water and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/ EtOAc = 5/1 to 3/1) to afford *seco*-acid **79a** (134 mg, 79%) as a colorless oil; $[\alpha]_{\text{D}}^{25}$ -29.2 (*c* 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3448, 3293-3170 (br), 3062, 3032, 2939, 2893, 1728, 1458, 1381, 1026, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.25 (complex m, 15H), 5.04 (dq, J = 6.3, 1.7 Hz, 1H), 4.86 (d, J = 6.9 Hz, 1H), 4.84 (d, J = 6.9 Hz, 1H), 4.81 (d, J = 6.9 Hz, 1H), 4.80 (d, J = 6.9 Hz, 1H), 4.79 (d, J = 6.9 Hz, 1H), 4.75 (d, J = 6.9 Hz, 1H), 4.72 (d, J = 12.0 Hz, 1H), 4.71 (d, J = 12.0 Hz, 1H), 4.68 (d, J = 12.0 Hz, 1H), 4.65 (d, J = 12.0 Hz, 1H), 4.58 (d, J = 12.0 Hz, 1H), 4.58 (d, J = 12.0 Hz, 1H), 4.06 (m, 1H), 4.00 (dd, J = 5.7, 4.6 Hz, 1H), 3.78 (m, 1H), 3.71 (dd, J = 8.0, 1.7 Hz, 1H), 3.43 (dd, J = 6.9, 4.0 Hz, 1H), 2.76–2.69 (complex m, 2H), 1.86 (m, 1H), 1.82 (m, 1H), 1.24 (d, J = 6.9 Hz, 3H), 1.20 (d, J = 6.9 Hz, 3H), 1.14 (d, J = 6.3 Hz, 3H), 1.13 (d, J = 6.3 Hz, 3H), 1.06 (d, J = 7.5 Hz, 3H), 0.99 (d, J = 6.9 Hz, 3H), 0.91 (s, 9H), 0.08 (s, 3H), -0.04 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 177.1, 174.8, 137.5, 137.4, 137.2, 128.4 ($\text{C} \times 2$), 128.4 ($\text{C} \times 4$), 127.8 ($\text{C} \times 2$), 128.8, 127.8 ($\text{C} \times 2$), 127.7, 127.6, 127.4 ($\text{C} \times 2$), 96.6, 96.4, 96.0, 85.8, 81.5, 79.9, 74.1, 71.5, 70.4, 70.1, 69.9, 67.8, 43.6, 43.2, 38.8, 38.8, 26.0 ($\text{C} \times 3$), 19.3, 18.3, 16.7, 13.6, 13.0, 10.6, 10.3, -3.7 , -3.9 ; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{72}\text{O}_{12}\text{SiNa}$, 891.4691; found 891.4690.

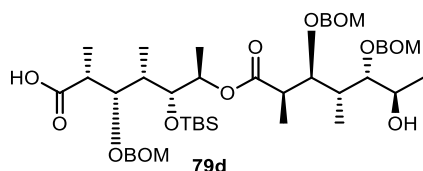


(2*R*,3*S*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79b**); According to the procedure of **4.12.**, **S4b** (661 mg, 668 μ mol) was converted to **79b** (496 mg, 85%) as a colorless oil; $[\alpha]_{\text{D}}^{27}$ -6.1 (*c* 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3464, 3155-3093 (br), 2939, 2885, 2862, 1728, 1458, 1381, 1196, 1149, 1026, 833, 733; ^1H NMR (500 MHz, CDCl_3) δ 7.34–7.25 (complex m, 15H), 4.99 (dq, J = 6.3, 4.6 Hz, 1H), 4.90 (d, J = 6.9 Hz, 1H), 4.82 (d, J = 6.9 Hz, 1H), 4.76–4.72 (complex m, 3H), 4.70 (d, J = 6.9 Hz, 1H), 4.67 (d, J = 6.9 Hz, 1H), 4.62 (d, J = 12.6 Hz, 1H), 4.61 (d, J = 11.5 Hz, 1H), 4.59–4.56 (complex m, 2H), 4.54 (d, J = 12.0 Hz, 1H), 4.01–3.98 (complex m, 2H), 3.83 (dq, J = 6.3, 6.3 Hz, 1H), 3.70 (dd, J = 4.6, 4.6 Hz, 1H), 3.66 (dd, J = 7.5, 1.2 Hz, 1H), 2.71 (dq, J = 6.9, 6.9 Hz, 1H), 2.66 (dq, J = 6.9, 2.3 Hz, 1H), 1.92 (m, 1H), 1.78 (m, 1H), 1.19 (d, J = 6.9 Hz, 3H), 1.15 (d, J = 6.3 Hz, 6H), 1.14 (d, J = 6.9 Hz, 3H), 1.00 (d, J = 6.9 Hz, 3H), 0.88 (s, 9H), 0.87 (d, J = 6.9 Hz, 3H), 0.08 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.8,

174.3, 137.6, 137.5, 136.9, 128.5 (C ×2), 128.4 (C ×4), 128.0 (C ×2), 127.9, 127.8 (C ×2), 127.7, 127.6, 127.6 (C ×2), 96.7, 96.3, 96.1, 87.2, 82.1, 81.1, 73.1, 73.1, 70.4, 70.1, 70.0, 69.0, 42.6, 41.5, 38.3, 38.1, 25.9 (C ×3), 18.9, 18.2, 15.1, 11.7, 10.9, 10.5, 9.2, -4.2, -4.3; HRMS-ESI (m/z); $[M+Na]^+$ calcd for $C_{48}H_{72}O_{12}SiNa$, 891.4691; found 891.4669.

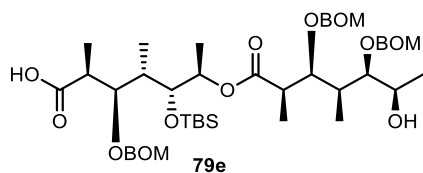


(2*R*,3*S*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79c**); According to the procedure of **4.12.**, **S4c** (701 mg, 708 μ mol) was converted to **79c** (558 mg, 91%) as a colorless oil; $[\alpha]_D^{27} +23.2$ (c 1.00, $CHCl_3$); IR (neat)/ cm^{-1} : 3479, 3286-3170 (br), 3032, 2978, 2939, 2885, 1728, 1458, 1373, 1257, 1157, 1026, 741; 1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.25 (complex m, 15H), 5.01 (m, 1H), 4.93 (d, J = 6.9 Hz, 1H), 4.77 (s, 2H), 4.77–4.71 (complex m, 3H), 4.68–4.57 (complex m, 6H), 3.99 (m, 1H), 3.85–3.81 (complex m, 2H), 3.70 (dd, J = 5.2, 4.6 Hz, 1H), 3.56 (dd, J = 5.7, 1.7 Hz, 1H), 2.79 (m, 1H), 2.74 (dq, J = 6.9, 6.9 Hz, 1H), 1.92 (m, 1H), 1.77 (m, 1H), 1.20 (d, J = 6.9 Hz, 3H), 1.20 (d, J = 6.9 Hz, 3H), 1.18 (d, J = 6.3 Hz, 3H), 1.12 (m, 3H), 1.04 (m, 3H), 1.02 (d, J = 7.5 Hz, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0, 174.4, 137.6, 137.6, 136.8, 128.5 (C ×2), 128.3 (C ×4), 128.0, 127.9 (C ×2), 127.7 (C ×2), 127.6, 127.6, 127.5 (C ×2), 96.9, 96.4, 95.6, 87.0, 81.9, 80.9, 73.7, 72.6, 70.3, 70.2, 70.0, 68.4, 42.9, 42.6, 39.1, 38.4, 25.9 (C ×3), 18.2, 17.0, 15.4, 12.6, 12.1, 11.3, 10.8, -3.9, -4.2; HRMS-ESI (m/z); $[M+Na]^+$ calcd for $C_{48}H_{72}O_{12}SiNa$, 891.4691; found 891.4694.

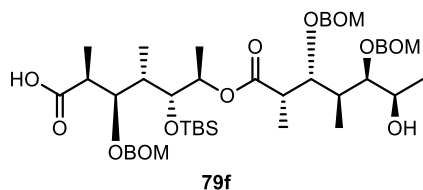


(2*R*,3*S*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79d**); According to the procedure of **4.12.**, **S4d** (719 mg, 727 μ mol) was converted to **79d** (555 mg, 88%) as a colorless oil; $[\alpha]_D^{25} -10.4$ (c 2.00, $CHCl_3$); IR (neat)/ cm^{-1} : 3456, 3240-3140 (br), 3032, 2939, 2885, 2862, 1720, 1458, 1381, 1250, 1157, 1026, 841, 748; 1H NMR (500 MHz, $CDCl_3$) δ 7.39–7.26 (complex m, 15H), 5.11 (app q, J = 6.3 Hz, 1H), 4.97 (d, J = 6.9 Hz, 1H), 4.94 (d, J = 6.9 Hz, 1H), 4.82–4.69 (complex m, 7H), 4.59 (d, J = 12.0 Hz, 2H), 4.57 (d, J = 12.0 Hz, 1H), 4.20 (dd, J = 5.2, 1.2 Hz, 1H), 4.17 (dq, J = 6.3, 2.3 Hz, 1H), 3.83 (dd, J = 8.6, 2.3 Hz, 1H), 3.70 (d, J = 8.6 Hz, 1H), 3.47 (dd, J = 7.5, 1.7 Hz, 1H), 2.74 (dq, J = 7.5, 7.5 Hz, 1H), 2.57 (dq, J = 7.5, 1.2 Hz, 1H), 2.08 (m, 1H), 1.91 (m, 1H), 1.26 (d, J = 7.2 Hz, 3H), 1.24 (d, J = 7.5 Hz, 3H), 1.20 (d, J = 6.3 Hz, 3H), 1.13 (d, J = 6.3 Hz, 3H), 1.07 (d, J = 6.9 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H), 0.93 (s, 9H), 0.09 (s, 3H), -0.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 174.8, 137.8, 137.5, 136.7, 128.5 (C ×2), 128.3 (C ×2), 128.3 (C ×2), 128.0, 128.0 (C ×2), 127.7 (C ×2), 127.6, 127.5, 127.3 (C ×2), 96.7, 96.6, 95.5, 87.5, 81.1, 77.2, 74.6, 71.0, 70.3, 69.8 (C ×2), 67.2, 43.0, 40.1, 39.5, 38.7, 26.0 (C ×3), 18.3, 16.8 (C ×2), 13.9, 12.4, 12.0,

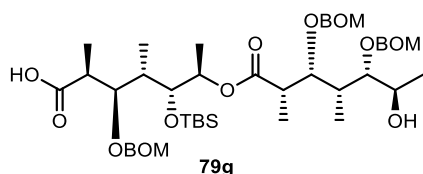
10.9, −3.4, −3.9; HRMS-ESI (m/z); $[M+Na]^+$ calcd for $C_{48}H_{72}O_{12}SiNa$, 891.4691; found 891.4683.



(2*S*,3*R*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79e**); According to the procedure of **4.12.**, **S4e** (688 mg, 695 μ mol) was converted to **79e** (565 mg, 93%) as a colorless oil; $[\alpha]_D^{25}$ −14.7 (c 1.00, $CHCl_3$); $[\alpha]_D^{29}$ −18.9 (c 2.00, $CHCl_3$); IR (neat)/ cm^{-1} : 3440, 3248–3116 (br), 3032, 2939, 2893, 1712, 1458, 1381, 1250, 1149, 1026, 833, 748; 1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.23 (complex m, 15H), 4.89 (d, J = 7.5 Hz, 1H), 4.85 (dq, J = 6.3, 6.3 Hz, 1H), 4.80–4.70 (complex m, 6H), 4.66 (d, J = 12.0 Hz, 1H), 4.62–4.53 (complex m, 4H), 4.07–3.98 (complex m, 3H), 3.93 (dq, J = 6.3, 6.3 Hz, 1H), 3.32 (dd, J = 5.2, 5.2 Hz, 1H), 2.71 (dq, J = 6.3, 6.3 Hz, 1H), 2.64 (m, 1H), 1.93–1.85 (complex m, 2H), 1.22 (d, J = 6.9 Hz, 3H), 1.17 (d, J = 6.3 Hz, 3H), 1.16 (d, J = 6.9 Hz, 3H), 1.14 (d, J = 6.3 Hz, 3H), 1.03 (d, J = 6.9 Hz, 3H), 0.91–0.85 (complex m, 12H), 0.09 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.9, 174.5, 137.7, 137.6, 137.1, 128.4 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 127.8, 127.8 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 3), 127.5, 96.6, 96.2, 96.1, 87.2, 82.5, 80.9, 74.4, 71.3, 70.4, 70.2, 70.0, 68.0, 42.8, 40.9, 38.3, 37.8, 25.9 (C \times 3), 18.8, 18.3, 15.5, 12.1, 11.4, 10.3, 9.1, −4.2, −4.2; HRMS-ESI (m/z); $[M+Na]^+$ calcd for $C_{48}H_{72}O_{12}SiNa$, 891.4691; found 891.4675.

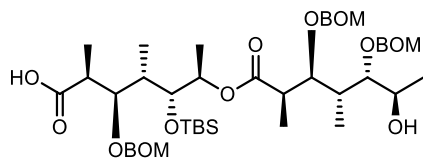


(2*S*,3*R*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79f**); According to the procedure of **4.12.**, **S4f** (705 mg, 712 μ mol) was converted to **79f** (561 mg, 91%) as a colorless oil; $[\alpha]_D^{27}$ −6.7 (c 2.00, $CHCl_3$); IR (neat)/ cm^{-1} : 3456, 3317–3155 (br), 3062, 2978, 2939, 2893, 2862, 1728, 1458, 1381, 1203, 1095, 1026, 833, 748; 1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (complex m, 15H), 4.90–4.84 (complex m, 2H), 4.83 (d, J = 6.9 Hz, 1H), 4.75 (d, J = 6.9 Hz, 1H), 4.73–4.69 (complex m, 4H), 4.62 (d, J = 12.0 Hz, 1H), 4.58 (d, J = 12.0 Hz, 1H), 4.56 (d, J = 12.0 Hz, 1H), 4.52 (d, J = 12.6 Hz, 1H), 4.51 (d, J = 12.0 Hz, 1H), 4.06 (app d, J = 5.7 Hz, 1H), 4.02 (dd, J = 9.2, 1.7 Hz, 2H), 3.84 (dq, J = 6.3, 6.3 Hz, 1H), 3.69 (dd, J = 8.0, 1.2 Hz, 1H), 2.69–2.61 (complex m, 2H), 1.88–1.76 (complex m, 2H), 1.17 (d, J = 6.9 Hz, 3H), 1.16 (d, J = 6.3 Hz, 3H), 1.16 (d, J = 6.9 Hz, 3H), 1.15 (d, J = 6.9 Hz, 3H), 0.91–0.88 (complex m, 12H), 0.87 (d, J = 6.9 Hz, 3H), 0.11 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.4, 174.4, 137.6, 137.5, 136.9, 128.4 (C \times 2), 128.3 (C \times 2), 128.2 (C \times 2), 127.9 (C \times 2), 127.8, 127.7 (C \times 2), 127.6 (C \times 3), 127.5, 96.7, 96.3, 96.0, 87.3, 82.4, 82.0, 74.1, 71.2, 70.4, 70.0, 69.9, 68.8, 41.4, 41.0, 38.2, 37.5, 25.9 (C \times 3), 18.7, 18.3, 15.3, 11.3, 10.3, 9.0, 8.6, −4.2, −4.2; HRMS-ESI (m/z); $[M+Na]^+$ calcd for $C_{48}H_{72}O_{12}SiNa$, 891.4691; found 891.4693.



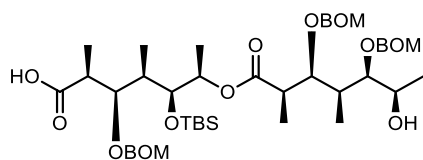
79g

(2*S*,3*R*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79g**); According to the procedure of **4.12.**, **S4g** (279 mg, 282 μ mol) was converted to **79g** (230 mg, 94%) as a colorless oil; $[\alpha]_D^{26} +22.6$ (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3417, 3232-3163 (br), 3032, 2939, 2893, 1720, 1458, 1381, 1250, 1157, 1026, 833, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.24 (complex m, 15H), 4.90 (d, *J* = 6.9 Hz, 1H), 4.82 (dq, *J* = 6.3, 6.3 Hz, 1H), 4.79–4.71 (complex m, 5H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.61–4.57 (complex m, 3H), 4.54 (d, *J* = 12.6 Hz, 1H), 4.05–4.01 (complex m, 2H), 3.99 (dd, *J* = 8.0, 2.9 Hz, 1H), 3.79 (dd, *J* = 6.9, 3.4 Hz, 1H), 3.56 (dd, *J* = 7.5, 2.9 Hz, 1H), 2.75 (dq, *J* = 6.9, 6.9 Hz, 1H), 2.63 (dq, *J* = 6.9, 2.9 Hz, 1H), 1.87 (m, 1H), 1.75 (m, 1H), 1.20 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 7.5 Hz, 3H), 1.17 (d, *J* = 5.7 Hz, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.91–0.88 (complex m, 12H), 0.10 (s, 3H), 0.06 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 179.6, 174.6, 137.7, 137.6, 137.1, 128.5 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 127.9, 127.8 (C \times 2), 127.7 (C \times 2), 127.7, 127.6 (C \times 2), 127.5, 96.9, 96.1, 96.0, 87.2, 82.4, 81.0, 74.1, 71.1, 70.2 (C \times 2), 70.0, 67.8, 42.9, 41.1, 39.0, 37.5, 25.9 (C \times 3), 18.3, 17.0, 15.1, 13.4, 11.6, 11.0, 9.6, -4.2, -4.3; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₂O₁₂SiNa, 891.4691; found 891.4686.



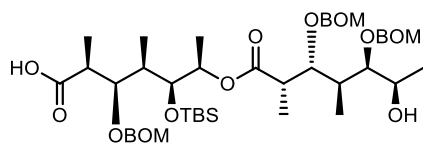
79h

(2*S*,3*R*,4*S*,5*R*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79h**); According to the procedure of **4.12.**, **S4h** (507 mg, 513 μ mol) was converted to **79h** (387 mg, 87%) as a colorless oil; $[\alpha]_D^{25} +9.3$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 3448, 3410-3309 (br), 3062, 2939, 2893, 1712, 1458, 1250, 1026, 833, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.24 (complex m, 15H), 4.88 (m, 1H), 4.85 (d, *J* = 6.9 Hz, 1H), 4.82–4.70 (complex m, 6H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.62–4.52 (complex m, 4H), 4.05–4.00 (complex m, 3H), 3.89 (dq, *J* = 6.3, 4.0 Hz, 1H), 3.78 (dd, *J* = 4.0, 3.4 Hz, 1H), 2.70–2.62 (complex m, 2H), 1.97–1.89 (complex m, 2H), 1.22 (d, *J* = 7.5 Hz, 3H), 1.20 (d, *J* = 6.3 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.91–0.89 (complex m, 12H), 0.10 (s, 3H), 0.06 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 179.9, 174.5, 137.7, 137.7, 137.3, 128.4 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 127.8 (C \times 2), 127.8, 127.7 (C \times 2), 127.6 (C \times 2), 127.6, 127.5, 96.3, 96.2, 96.0, 84.0, 82.2, 81.5, 74.1, 71.0, 70.2, 70.1, 70.0, 69.2, 41.8, 40.8, 37.6, 37.6, 25.9 (C \times 3), 18.2, 18.2, 15.1, 12.0, 11.5, 10.8, 9.3, -4.3, -4.3; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₂O₁₂SiNa, 891.4691; found 891.4686.



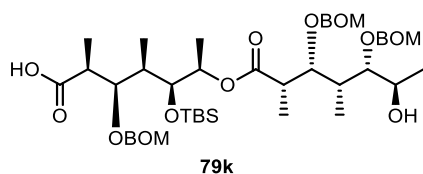
79i

(2*S*,3*R*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79i**); According to the procedure of **4.12.**, **S4i** (253 mg, 256 μ mol) was converted to **79i** (162 mg, 73%) as a colorless oil; $[\alpha]_D^{25}$ -12.9 (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3425, 3255-3132 (br), 3062, 3032, 2939, 2885, 2862, 1705, 1458, 1250, 1157, 1103, 1025, 1026, 833, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.25 (complex m, 15H), 5.02 (dq, *J* = 6.3, 3.4 Hz, 1H), 4.84 (d, *J* = 6.9 Hz, 1H), 4.80–4.74 (complex m, 5H), 4.70 (d, *J* = 11.5 Hz, 1H), 4.68 (d, *J* = 11.5 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 12.6 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.58 (d, *J* = 12.0 Hz, 1H), 3.99 (dd, *J* = 6.3, 4.6 Hz, 1H), 3.93 (m, 1H), 3.89 (dd, *J* = 5.7, 5.7 Hz, 1H), 3.74 (dd, *J* = 5.2, 3.4 Hz, 1H), 3.36 (dd, *J* = 5.2, 5.2 Hz, 1H), 2.77 (dq, *J* = 6.9, 6.9 Hz, 1H), 2.71 (dq, *J* = 6.9, 6.9 Hz, 1H), 1.91 (m, 1H), 1.84 (m, 1H), 1.22 (d, *J* = 7.5 Hz, 3H), 1.21 (d, *J* = 7.5 Hz, 3H), 1.18 (d, *J* = 6.3 Hz, 3H), 1.13 (d, *J* = 6.3 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 178.8, 174.4, 137.6, 137.5, 137.2, 128.4 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 127.8, 127.8 (C \times 2), 127.7 (C \times 2), 127.7 (C \times 3), 127.6, 96.6, 96.2 (C \times 2), 86.7, 81.1, 80.9, 74.9, 73.5, 70.3, 70.1 (C \times 2), 68.0, 43.3, 42.9, 39.7, 38.4, 26.0 (C \times 3), 19.0, 18.3, 14.8, 13.2, 12.3, 11.1, 10.2, -4.0, -4.3; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₂O₁₂SiNa, 891.4691; found 891.4701.



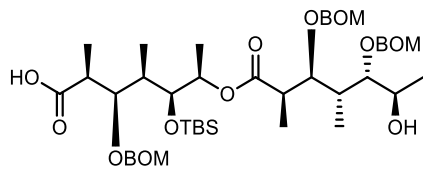
79j

(2*S*,3*R*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*S*,5'*R*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79j**); According to the procedure of **4.12.**, **S4j** (774 mg, 783 μ mol) was converted to **79j** (596 mg, 88%) as a colorless oil; $[\alpha]_D^{25}$ -3.0 (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3456, 3271-3232 (br), 3039, 2939, 2893, 2862, 1728, 1458, 1381, 1250, 1157, 1026, 833, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.24 (complex m, 15H), 5.05 (m, 1H), 4.88 (d, *J* = 6.9 Hz, 1H), 4.81–4.71 (complex m, 4H), 4.69 (d, *J* = 6.9 Hz, 1H), 4.67 (d, *J* = 7.2 Hz, 1H), 4.62–4.58 (complex m, 3H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.02 (dd, *J* = 9.2, 1.2 Hz, 1H), 3.87 (dd, *J* = 5.7, 5.7 Hz, 1H), 3.82 (m, 1H), 3.73 (m, 1H), 3.65 (app d, *J* = 8.0 Hz, 1H), 2.78 (dq, *J* = 6.9, 6.9 Hz, 1H), 2.57 (dq, *J* = 6.9, 2.3 Hz, 1H), 1.80–1.71 (complex m, 2H), 1.20 (dd, *J* = 6.9, 1.7 Hz, 3H), 1.17–1.13 (complex m, 9H), 0.99 (dd, *J* = 6.9, 1.2 Hz, 3H), 0.91 (s, 9H), 0.84 (d, *J* = 7.5 Hz, 3H), 0.05 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 179.6, 174.2, 137.7, 137.5, 136.9, 128.5 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 127.9 (C \times 2), 127.9, 127.8 (C \times 2), 127.6, 127.6, 127.5 (C \times 2), 96.7 (C \times 2), 96.4, 87.4, 82.2, 81.2, 74.9, 72.9, 70.4, 70.2, 69.9, 68.8, 42.7, 41.3, 39.5, 38.2, 26.0 (C \times 3), 18.8, 18.4, 13.9, 12.4, 11.1, 10.2, 9.0, -3.9, -4.3; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₂O₁₂SiNa, 891.4691; found 891.4708.



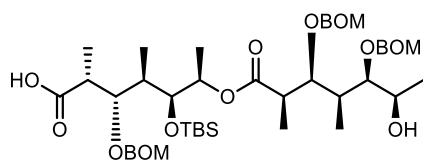
79k

(2*S*,3*R*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79k**); According to the procedure of **4.12.**, **S4k** (510 mg, 515 μ mol) was converted to **79k** (406 mg, 91%) as a colorless oil; $[\alpha]_D^{25} +38.8$ (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3417, 3247-3155 (br), 3032, 2931, 2885, 2862, 1720, 1458, 1381, 1250, 1157, 1026, 833, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.25 (complex m, 15H), 5.07 (dq, *J* = 6.3, 2.9 Hz, 1H), 4.91 (d, *J* = 6.9 Hz, 1H), 4.81 (d, *J* = 6.9 Hz, 1H), 4.77 (d, *J* = 6.9 Hz, 1H), 4.77 (s, 2H), 4.74 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 6.9 Hz, 1H), 4.62–4.57 (complex m, 4H), 4.09 (dq, *J* = 6.3, 2.3 Hz, 1H), 3.89 (dd, *J* = 5.2, 5.2 Hz, 1H), 3.80 (dd, *J* = 8.6, 2.3 Hz, 1H), 3.74 (dd, *J* = 6.3, 2.9 Hz, 1H), 3.58 (dd, *J* = 8.6, 2.3 Hz, 1H), 2.78 (dq, *J* = 6.3, 6.3 Hz, 1H), 2.70 (dq, *J* = 7.5, 7.5 Hz, 1H), 1.78 (m, 1H), 1.69 (m, 1H), 1.22 (d, *J* = 7.5 Hz, 3H), 1.20 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 0.09 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 179.7, 174.5, 137.6, 137.5, 137.1, 128.4 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 127.8, 127.8 (C \times 2), 127.7 (C \times 3), 127.6 (C \times 3), 96.9, 96.4, 96.3, 87.3, 81.0 (C \times 2), 74.8, 72.8, 70.2 (C \times 2), 70.2, 67.5, 43.5, 42.8, 39.5, 39.1, 26.0 (C \times 3), 18.4, 16.9, 14.3, 14.2, 12.4, 11.1, 10.6, -4.0, -4.2; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₂O₁₂SiNa, 891.4691; found 891.4698.



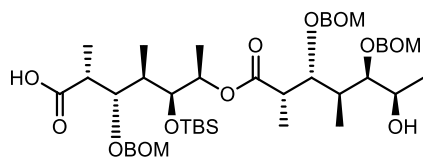
79l

(2*S*,3*R*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79l**); According to the procedure of **4.12.**, **S4l** (922 mg, 932 μ mol) was converted to **79l** (580 mg, 72%) as a colorless oil; $[\alpha]_D^{27} +16.9$ (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3417 (br), 3224-3140 (br), 3070, 2939, 2893, 1712, 1458, 1381, 1250, 1026, 833, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.24 (complex m, 15H), 4.99 (dq, *J* = 6.3, 2.9 Hz, 1H), 4.84 (d, *J* = 6.9 Hz, 1H), 4.77–4.72 (complex m, 5H), 4.71 (d, *J* = 11.5 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.60–4.54 (complex m, 3H), 4.01 (dd, *J* = 7.5, 4.0 Hz, 1H), 3.92 (m, 1H), 3.88 (m, 1H), 3.79–3.75 (complex m, 2H), 2.77 (dq, *J* = 6.9, 6.9 Hz, 1H), 2.67 (dq, *J* = 7.5, 4.0 Hz, 1H), 1.93 (m, 1H), 1.82 (m, 1H), 1.22–1.17 (complex m, 12H), 1.01 (d, *J* = 6.9 Hz, 6H), 0.92 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 179.5, 174.4, 137.6 (C \times 2), 137.3, 128.4 (C \times 2), 128.3 (C \times 4), 127.8 (C \times 2), 127.8 (C \times 3), 127.7 (C \times 2), 127.6, 127.6, 96.3, 96.2 (C \times 2), 83.7, 82.2, 81.2, 74.9, 73.4, 70.2, 70.2, 70.1, 69.2, 42.7, 41.8, 39.6, 37.5, 26.0 (C \times 3), 18.4, 18.3, 14.5, 12.1, 11.9, 11.1, 10.8, -3.9, -4.3; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₂O₁₂SiNa, 891.4691; found 891.4691.



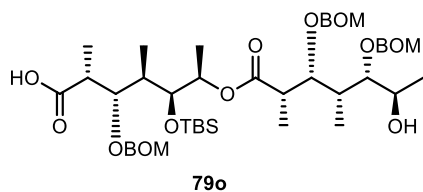
79m

(2*R*,3*S*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*S*,5'*R*,6'*R*}-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79m**); According to the procedure of **4.12.**, **S4m** (855 mg, 864 μ mol) was converted to **79m** (624 mg, 83%) as a colorless oil; $[\alpha]_D^{25}$ -21.6 (c 2.00, CHCl_3); IR (neat)/ cm^{-1} 3410 (br), 3224-3140 (br), 3032, 2939, 2885, 2862, 1728, 1458, 1381, 1250, 1149, 1026, 833, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.25 (complex m, 15H), 5.09 (dq, $J = 6.3, 3.4$ Hz, 1H), 4.82 (d, $J = 6.3$ Hz, 1H), 4.82–4.76 (complex m, 5H), 4.71 (d, $J = 12.0$ Hz, 1H), 4.69 (d, $J = 12.0$ Hz, 1H), 4.63–4.61 (complex m, 2H), 4.58 (d, $J = 11.5$ Hz, 1H), 4.57 (d, $J = 12.0$ Hz, 1H), 3.98 (dq, $J = 6.3, 3.4$ Hz, 1H), 3.93 (dd, $J = 5.7, 5.7$ Hz, 1H), 3.89 (dd, $J = 7.5, 3.4$ Hz, 1H), 3.79 (dd, $J = 6.3, 3.4$ Hz, 1H), 3.40 (dd, $J = 6.9, 3.4$ Hz, 1H), 2.75–2.66 (complex m, 2H), 1.97 (m, 1H), 1.89 (m, 1H), 1.22 (d, $J = 7.5$ Hz, 3H), 1.22 (d, $J = 6.9$ Hz, 3H), 1.16 (d, $J = 6.3$ Hz, 3H), 1.15 (d, $J = 6.3$ Hz, 3H), 1.06 (d, $J = 6.9$ Hz, 3H), 0.98 (d, $J = 7.5$ Hz, 3H), 0.93 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 177.9, 174.5, 137.6, 137.4, 137.3, 128.4 (C $\times 2$), 128.4 (C $\times 2$), 128.3 (C $\times 2$), 127.8 (C $\times 2$), 127.8, 127.7 (C $\times 2$), 127.7 (C $\times 3$), 127.6, 96.6, 96.3, 95.4, 85.3, 80.7, 80.4, 74.0, 73.0, 70.4, 70.1, 69.9, 67.8, 43.9, 41.0, 39.9, 39.0, 26.1 (C $\times 3$), 19.7, 18.5, 14.1, 13.8, 12.5, 11.3, 10.4, -4.0 , -4.0 ; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{72}\text{O}_{12}\text{SiNa}$, 891.4691; found 891.4683.



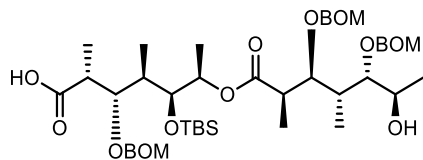
79n

(2*R*,3*S*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*S*,5'*R*,6'*R*}-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79n**); According to the procedure of **4.12.**, **S4n** (819 mg, 828 μ mol) was converted to **79n** (645 mg, 90%) as a colorless oil; $[\alpha]_D^{25}$ -6.5 (c 1.00, CHCl_3); IR (neat)/ cm^{-1} 3440 (br), 3417-3240 (br), 3417, 3062, 2939, 2893, 1728, 1458, 1381, 1095, 1026, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.25 (complex m, 15H), 4.98 (dq, $J = 6.3, 4.0$ Hz, 1H), 4.86 (d, $J = 6.9$ Hz, 1H), 4.82 (d, $J = 6.9$ Hz, 1H), 4.80 (d, $J = 6.9$ Hz, 1H), 4.74 (d, $J = 6.9$ Hz, 1H), 4.73–4.69 (complex m, 3H), 4.65 (d, $J = 12.0$ Hz, 1H), 4.61 (d, $J = 12.0$ Hz, 1H), 4.58 (d, $J = 12.0$ Hz, 1H), 4.56 (d, $J = 12.0$ Hz, 1H), 4.52 (d, $J = 12.0$ Hz, 1H), 4.06–4.01 (complex m, 3H), 3.84 (dq, $J = 6.9, 6.9$ Hz, 1H), 3.69 (dd, $J = 7.5, 1.2$ Hz, 1H), 2.67 (dq, $J = 6.9, 2.3$ Hz, 1H), 2.62 (dq, $J = 6.9, 2.3$ Hz, 1H), 1.84–1.76 (complex m, 2H), 1.19 (d, $J = 6.3$ Hz, 3H), 1.18 (d, $J = 6.3$ Hz, 3H), 1.17 (d, $J = 5.7$ Hz, 3H), 1.16 (d, $J = 6.3$ Hz, 3H), 0.92 (s, 9H), 0.90 (d, $J = 7.5$ Hz, 3H), 0.88 (d, $J = 6.9$ Hz, 3H), 0.11 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.2, 174.3, 137.7, 137.5, 136.9, 128.4 (C $\times 2$), 128.3 (C $\times 2$), 128.2 (C $\times 2$), 128.0 (C $\times 2$), 127.8, 127.8 (C $\times 2$), 127.6, 127.6 (C $\times 2$), 127.5, 96.6, 96.2, 95.9, 87.2, 82.3, 81.8, 74.1, 73.1, 70.3, 69.9, 69.9, 68.7, 41.4, 41.1, 38.4, 38.2, 26.0 (C $\times 3$), 18.7, 18.3, 15.2, 11.3, 10.3, 9.4, 9.0, -4.1 , -4.1 ; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{72}\text{O}_{12}\text{SiNa}$, 891.4691; found 891.4704.



79o

(2*R*,3*S*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*S*,3'*R*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79o**); According to the procedure of **4.12.**, **S4o** (362 mg, 366 μ mol) was converted to **79o** (310 mg, 98%) as a colorless oil; $[\alpha]_D^{26} +39.1$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 3448, 3217-3155 (br), 3032, 2939, 2893, 2862, 1720, 1458, 1381, 1250, 1157, 1026, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.25 (complex m, 15H), 4.93 (m, 1H), 4.91 (d, *J* = 6.9 Hz, 1H), 4.81 (d, *J* = 6.9 Hz, 1H), 4.78–4.76 (complex m, 2H), 4.75 (d, *J* = 12.6 Hz, 1H), 4.72 (d, *J* = 6.9 Hz, 1H), 4.71 (d, *J* = 11.5 Hz, 1H), 4.66 (d, *J* = 6.9 Hz, 1H), 4.61–4.54 (complex m, 4H), 4.09 (dq, *J* = 6.3, 2.3 Hz, 1H), 4.01–3.97 (complex m, 2H), 3.80 (dd, *J* = 8.6, 2.3 Hz, 1H), 3.58 (dd, *J* = 8.7, 2.3 Hz, 1H), 2.73 (dq, *J* = 7.5, 7.5 Hz, 1H), 2.66 (dq, *J* = 6.9, 2.3 Hz, 1H), 1.79 (m, 1H), 1.70 (m, 1H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.18–1.14 (complex m, 9H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.89 (d, *J* = 6.9 Hz, 3H), 0.10 (s, 3H), 0.04 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 180.1, 174.5, 137.6, 137.5, 137.1, 128.5 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 127.9, 127.8 (C \times 2), 127.7 (C \times 2), 127.7 (C \times 3), 127.6, 97.0, 96.2, 95.9, 87.5, 82.4, 80.9, 73.8, 73.0, 70.3, 70.2, 70.0, 67.5, 43.6, 41.2, 39.1, 38.3, 26.0 (C \times 3), 18.3, 16.9, 15.7, 14.5, 11.2, 10.6, 9.1, -4.0, -4.1; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₂O₁₂SiNa, 891.4691; found 891.4695.

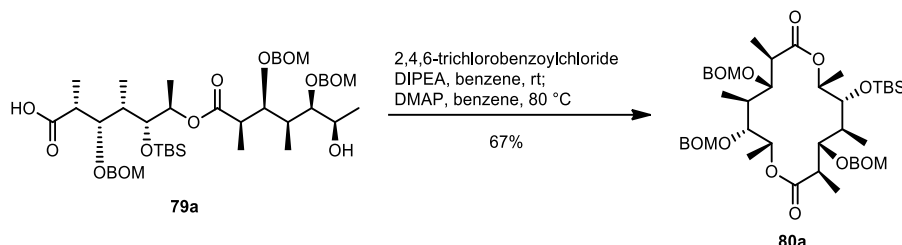


79p

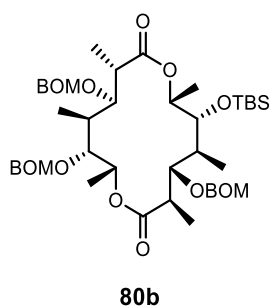
(2*R*,3*S*,4*R*,5*S*,6*R*)-3-[(Benzyloxy)methoxy]-6-({2'*R*,3'*S*,4'*R*,5'*S*,6'*R*)-3',5'-bis[(benzyloxy)methoxy]-6'-hydroxy-2',4'-dimethylheptanoyl}oxy)-5-[(*tert*-butyldimethylsilyl)oxy]-2,4-dimethylheptanoic acid (**79p**); According to the procedure of **4.12.**, **S4p** (172 mg, 198 μ mol) was converted to **79p** (143 mg, 85%) as a colorless oil; $[\alpha]_D^{28} +5.2$ (*c* 2.00, CHCl₃); IR (neat)/cm⁻¹: 3424, 3224-3124 (br), 3062, 2939, 2885, 2862, 1705, 1458, 1389, 1250, 1157, 1095, 1026, 833, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.37–7.27 (complex m, 15H), 5.12 (dq, *J* = 6.3, 2.3 Hz, 1H), 4.99 (d, *J* = 6.9 Hz, 1H), 4.83 (d, *J* = 6.9 Hz, 1H), 4.80–4.77 (complex m, 4H), 4.73 (d, *J* = 6.9 Hz, 1H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.61 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 12.6 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.09 (dq, *J* = 6.3, 2.9 Hz, 1H), 3.99 (dd, *J* = 5.2, 5.2 Hz, 1H), 3.83 (dd, *J* = 8.0, 4.0 Hz, 1H), 3.70 (dd, *J* = 8.0, 2.3 Hz, 1H), 3.47 (dd, *J* = 7.5, 2.3 Hz, 1H), 2.72–2.63 (complex m, 2H), 2.06–1.96 (complex m, 2H), 1.21 (d, *J* = 7.2 Hz, 6H), 1.18 (d, *J* = 6.3 Hz, 3H), 1.12 (d, *J* = 6.3 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.93 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 177.4, 174.7, 137.6, 137.5, 136.7, 128.5 (C \times 2), 128.4 (C \times 4), 128.1 (C \times 2), 128.0, 127.9 (C \times 4), 127.7, 127.7, 96.1, 95.2, 95.1, 85.9, 80.2, 78.9, 74.3, 73.0, 70.1, 69.9, 69.9, 68.0, 40.8, 40.6, 40.5, 39.4, 26.1 (C \times 3), 18.6, 16.8, 14.1, 13.7, 13.0, 11.6, 11.5, -3.8, -4.0; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₂O₁₂SiNa,

891.4691; found 891.4677.

4.13. (3*R*,4*S*,5*S*,6*R*,7*R*,10*R*,11*S*,12*S*,13*R*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80a**);

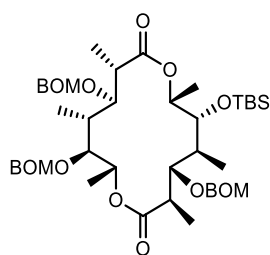


To a solution of *seco*-acid **79a** (30.3 mg, 34.9 μ mol) and DIPEA (120 μ L, 706 μ mol) in benzene (5.0 mL) was added 2,4,6-trichlorobenzoyl chloride (90.0 μ L, 576 μ mol) dropwise under N₂ at 0 °C. Then, the reaction mixture was allowed to warm to room temperature and stirred for 1.5 h. The mixture was diluted with benzene (2.0 mL) and added dropwise over a period of 2 h to a refluxing solution of DMAP (63.9 mg, 523 μ mol) in benzene (4.5 mL). Then, the mixture was stirred for 3 h at 80 °C and quenched with sat. aq. NH₄Cl (3.0 mL) at 0 °C. Resulted two layers were separated and the aqueous phase was extracted with EtOAc (10 mL \times 3). The combined organic layers were washed with water and brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/ EtOAc = 8/1 to 6/1) to afford a macrodiolide aglycone **80a** (19.8 mg, 67%) as a colorless oil; $[\alpha]_D^{24}$ -25.6 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 2939, 2893, 2862, 1728, 1458, 1373, 1165, 1095, 1026, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.25 (complex m, 15H), 5.20 (q, *J* = 6.3 Hz, 1H), 5.09 (q, *J* = 6.3 Hz, 1H), 4.84–4.67 (complex m, 9H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.58 (d, *J* = 12.6 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 3.86 (d, *J* = 9.2 Hz, 1H), 3.75 (d, *J* = 9.7 Hz, 1H), 3.67 (d, *J* = 9.2 Hz, 2H), 2.87–2.75 (complex m, 2H), 1.80 (m, 1H), 1.67 (m, 1H), 1.22–1.18 (complex m, 9H), 1.11 (d, *J* = 6.3 Hz, 3H), 1.06 (d, *J* = 7.5 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.06 (s, 3H), -0.08 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 174.5, 174.2, 138.0, 137.6, 137.5, 128.4 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 127.6, 126.6, 127.5 (C \times 5), 127.3 (C \times 2), 96.8, 96.6, 96.4, 81.6, 81.1, 80.8, 74.4, 70.6, 70.4, 70.2, 70.0, 69.8, 44.6, 44.3, 40.1, 38.8, 26.0 (C \times 3), 18.4, 17.1, 17.0, 14.5, 14.3, 10.7, 9.7, -3.4, -3.9; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4589.



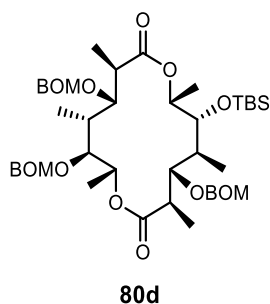
(4*S*,5*S*,6*R*,7*R*,10*S*,11*R*,12*S*,13*R*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80b**); According to the procedure of **4.13.**, **80b** (172 mg, 198 μ mol) was converted to **80b** (143 mg, 85%, diastereo ratio = 5:1) as a colorless oil; IR

(neat)/cm⁻¹ 2939, 2885, 2862, 1728, 1458, 1373, 1168, 1026, 841, 741; Shown ¹H and ¹³C NMR peaks of major product as diastereomer; ¹H NMR (500 MHz, CDCl₃) δ 7.34–7.25 (complex m, 15H), 5.16 (dq, *J* = 6.3, 3.4 Hz, 1H), 5.03 (dq, *J* = 6.3, 2.9 Hz, 1H), 4.81–4.76 (complex m, 3H), 4.74 (d, *J* = 6.9 Hz, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.68–4.66 (complex m, 3H), 4.61–4.54 (complex m, 4H), 4.50 (dd, *J* = 3.7, 3.7 Hz, 1H), 4.08 (m, 1H), 3.77 (dd, *J* = 5.7 3.4 Hz, 1H), 3.70 (dd, *J* = 8.6, 2.9 Hz, 1H), 2.87 (dq, *J* = 6.9, 4.0 Hz, 1H), 2.76 (dq, *J* = 6.9, 6.9 Hz, 1H), 2.34 (m, 1H), 2.01 (m, 1H), 1.32 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.3 Hz, 3H), 1.21 (d, *J* = 6.9 Hz, 3H), 1.13 (d, *J* = 7.5 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 174.7, 173.9, 137.8, 137.7, 137.7, 128.4 (C ×2), 128.3 (C ×3), 128.3, 127.7 (C ×2), 127.7 (C ×3), 127.6, 127.5, 127.5 (C ×2), 96.2, 95.1, 95.0, 81.9, 77.5, 77.1, 74.4, 72.5, 72.4, 70.2, 70.0, 69.8, 45.1, 43.5, 40.6, 37.2, 25.9 (C ×3), 18.1, 14.9 (C ×2), 14.4, 13.4, 12.4, 11.7, -4.2, -4.6; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4583.

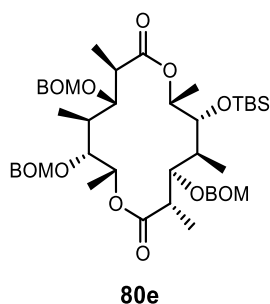


80c

(3*R*,4*S*,5*S*,6*R*,7*R*,10*S*,11*R*,12*R*,13*S*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80c**); According to the procedure of **4.13**, **79c** (186 mg, 214 μmol) was converted to **79c** (149 mg, 82%) as a colorless oil; [α]_D²⁷ +27.0 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹ 2939, 2892, 2862, 1736, 1365, 1211, 1026, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.25 (complex m, 15H), 5.09 (dq, *J* = 6.3, 2.3 Hz, 1H), 4.91 (dq, *J* = 6.3, 6.3 Hz, 1H), 4.84 (d, *J* = 6.9 Hz, 1H), 4.77 (d, *J* = 6.9 Hz, 1H), 4.74–4.66 (complex m, 6H), 4.62–4.58 (complex m, 2H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 11.5 Hz, 1H), 4.39 (dd, *J* = 3.4, 3.4 Hz, 1H), 4.24 (dd, *J* = 4.6, 4.0 Hz, 1H), 3.70 (dd, *J* = 6.3, 4.6 Hz, 1H), 3.67 (dd, *J* = 8.0, 2.9 Hz, 1H), 2.84 (m, 1H), 2.76 (m, 1H), 2.12 (m, 1H), 1.98 (m, 1H), 1.34 (d, *J* = 6.3 Hz, 3H), 1.25 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 6.3 Hz, 3H), 1.17 (d, *J* = 7.5 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 7.5 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 174.7, 174.1, 137.9, 137.8, 137.7, 128.4 (C ×2), 128.3 (C ×2), 128.2 (C ×2), 127.7 (C ×2), 127.6 (C ×2), 127.5 (C ×4), 127.4, 95.4, 95.2, 94.2, 80.4, 79.8, 77.5, 74.8, 73.6, 72.0, 70.2, 70.1 (C ×2), 45.3, 44.3, 41.8, 40.4, 25.9 (C ×3), 18.1, 18.0, 14.9, 12.5, 11.8 (C ×2), 10.7, -4.1, -4.4; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4560.

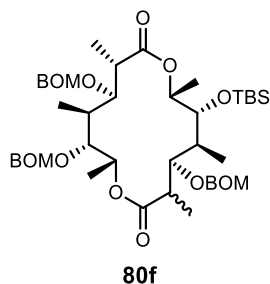


(3*R*,4*S*,5*S*,6*R*,7*R*,10*R*,11*S*,12*R*,13*S*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80d**); According to the procedure of **4.13**, **79d** (59.8 mg, 68.8 μ mol) was converted to **80d** (43.1 mg, 73%) as a colorless oil; $[\alpha]_D^{26}$ -7.9 (*c* 0.50, CHCl₃); IR (neat)/cm⁻¹ 2939, 2885, 1728, 1458, 1373, 1157, 1026, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.26 (complex m, 15H), 5.04 (dq, *J* = 6.9, 1.2 Hz, 1H), 4.91 (d, *J* = 6.9 Hz, 1H), 4.86 (d, *J* = 6.9 Hz, 1H), 4.84–4.79 (complex m, 3H), 4.73 (d, *J* = 6.9 Hz, 1H), 4.71 (d, *J* = 12.6 Hz, 1H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.67–4.61 (complex m, 4H), 4.57 (d, *J* = 12.0 Hz, 1H), 3.94 (dd, *J* = 8.0, 2.9 Hz, 1H), 3.76–3.71 (complex m, 2H), 3.63 (dd, *J* = 5.7, 4.6 Hz, 1H), 2.86 (dq, *J* = 7.5, 7.5 Hz, 1H), 2.79 (dq, *J* = 6.9, 6.9 Hz, 1H), 1.97 (m, 1H), 1.93 (m, 1H), 1.32 (d, *J* = 6.3 Hz, 3H), 1.21 (d, *J* = 6.9 Hz, 3H), 1.20 (d, *J* = 6.3 Hz, 3H), 1.17 (d, *J* = 6.3 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.09 (s, 3H), 0.01 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.7, 174.7, 137.9, 137.8, 137.7, 128.4 (C \times 4), 128.3 (C \times 2), 127.6 (C \times 2), 127.6 (C \times 2), 127.6 (C \times 3), 127.5 (C \times 2), 96.2, 96.2, 95.6, 81.5, 80.4, 79.8, 75.1, 72.0, 70.6, 70.2, 70.0, 70.0, 43.9, 42.6, 40.3, 39.2, 26.0 (C \times 3), 18.3, 17.2, 16.5, 15.6, 12.9, 11.7, 11.7, -3.5 , -4.1 ; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4580.

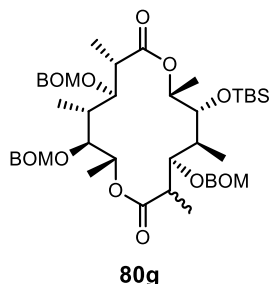


(3*S*,4*R*,5*S*,6*R*,7*R*,10*R*,11*S*,12*S*,13*R*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80e**); According to the procedure of **4.13**, **79e** (108 mg, 124 μ mol) was converted to **80e** (50.0 mg, 47%) as a colorless oil; $[\alpha]_D^{27}$ -8.1 (*c* 0.50, CHCl₃); IR (neat)/cm⁻¹ 3016, 2985, 2954, 2893, 2862, 1728, 1458, 1381, 1257, 1165, 1026, 841, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.26 (complex m, 15H), 5.28 (dq, *J* = 6.3, 2.9 Hz, 1H), 4.91 (dq, *J* = 6.3, 3.4 Hz, 1H), 4.84 (d, *J* = 6.9 Hz, 1H), 4.79 (d, *J* = 6.9 Hz, 2H), 4.71 (d, *J* = 6.9 Hz, 1H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.67 (d, *J* = 7.5 Hz, 1H), 4.65 (d, *J* = 6.9 Hz, 1H), 4.61 (d, *J* = 9.2 Hz, 1H), 4.60 (d, *J* = 10.9 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H),

4.52 (d, $J = 12.0$ Hz, 1H), 4.50–4.48 (complex m, 2H), 4.29 (dd, $J = 6.9, 2.9$ Hz, 1H), 3.69 (dd, $J = 9.2, 3.4$ Hz, 1H), 3.65 (dd, $J = 6.3, 2.9$ Hz, 1H), 3.16 (dq, $J = 6.9, 2.9$ Hz, 1H), 2.86 (dq, $J = 6.9, 3.4$ Hz, 1H), 2.51 (m, 1H), 2.21 (m, 1H), 1.28 (d, $J = 6.3$ Hz, 3H), 1.24 (d, $J = 6.9$ Hz, 3H), 1.22 (d, $J = 6.9$ Hz, 3H), 1.16 (d, $J = 6.9$ Hz, 3H), 1.08 (d, $J = 7.5$ Hz, 3H), 1.00 (d, $J = 6.9$ Hz, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.9, 174.4, 137.8, 137.7, 137.5, 128.5 (C \times 2), 128.4 (C \times 2), 128.4 (C \times 2), 128.0 (C \times 2), 127.8, 127.7 (C \times 3), 127.6 (C \times 3), 95.1, 94.6 (C \times 2), 81.6, 78.9, 77.5, 74.2, 72.1, 70.5, 70.5, 70.0, 69.8, 43.2, 42.5, 38.4, 37.9, 25.8 (C \times 3), 18.0, 16.5, 13.7, 13.1, 12.9, 12.4, 10.6, –4.7, –4.7; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4587.

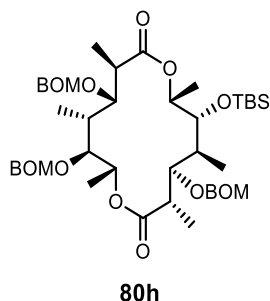


(4*R*,5*S*,6*R*,7*R*,10*S*,11*R*,12*S*,13*R*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80f**); According to the procedure of **4.13.**, **79f** (79.2 mg, 91.1 μmol) was converted to **80f** (17.5 mg, 23%, diastereo ratio = 2:1) as a colorless oil; IR (neat)/ cm^{-1} 2931, 2885, 2862, 1712, 1458, 1381, 1250, 1026, 841, 748; Shown ^1H and ^{13}C NMR peaks of major product as diastereomer; ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.25 (complex m, 15H), 5.19 (m, 1H), 4.93 (m, 1H), 4.84–4.62 (complex m, 9H), 4.60 (d, $J = 11.5$ Hz, 1H), 4.54 (d, $J = 11.5$ Hz, 1H), 4.54 (d, $J = 12.0$ Hz, 1H), 3.67–3.44 (complex m, 4H), 2.66–2.58 (complex m, 2H), 2.34 (m, 1H), 1.58 (brs, 1H), 1.29 (d, $J = 6.9$ Hz, 3H), 1.27–1.21 (complex m, 9H), 1.16 (d, $J = 7.5$ Hz, 3H), 1.09 (d, $J = 6.9$ Hz, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.1, 174.0, 137.7, 137.6, 137.6, 128.4 (C \times 2), 128.4 (C \times 2), 128.4 (C \times 2), 127.9 (C \times 2), 127.8 (C \times 2), 127.8, 127.7 (C \times 2), 127.7, 127.6, 96.1, 95.7, 95.0, 78.2, 75.8, 73.8, 71.2, 70.2, 70.0, 69.8, 42.5, 39.6, 37.6, 35.6, 25.8 (C \times 3), 18.0, 14.2, 13.9, 13.3, 13.0, 12.9, 12.5, –4.3, –4.7; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4577.



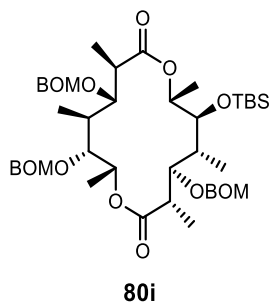
(4*R*,5*S*,6*R*,7*R*,10*S*,11*R*,12*R*,13*S*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80g**); According to the procedure of **4.13.**, **79g** (76.3 mg, 87.7 μmol) was converted to **80g** (25.7 mg, 34%, diastereo ratio = 1:1) as a colorless oil; IR (neat)/ cm^{-1} ; 3032, 2939, 2885, 2862, 1728, 1458, 1381, 1257, 1196, 1026, 841, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.23 (complex m, 15H), 5.37 (dq, $J = 6.9, 4.6$ Hz, 1/2H), 5.08 (dq, $J = 6.6, 2.9$ Hz, 1/2H), 5.00 (dq, $J =$

5.7, 5.7 Hz, 1/2H), 4.83–4.60 (complex m, 19/2H), 4.59–4.49 (complex m, 3H), 4.45 (dd, $J = 4.6, 2.9$ Hz, 1/2H), 4.43 (dd, $J = 9.2, 1.7$ Hz, 1/2H), 4.05 (dd, $J = 4.0, 1.7$ Hz, 1/2H), 4.01 (dd, $J = 7.5, 3.4$ Hz, 1/2H), 3.87 (dd, $J = 7.5, 3.4$ Hz, 1/2H), 3.78 (dd, $J = 4.0, 4.0$ Hz, 1/2H), 3.66 (dd, $J = 5.7, 3.4$ Hz, 1/2H), 3.47 (dd, $J = 9.7, 2.9$ Hz, 1/2H), 3.15 (dq, $J = 6.9, 1.7$ Hz, 1/2H), 2.80 (m, 1/2H), 2.68 (dq, $J = 6.9, 2.9$ Hz, 1/2H), 2.64 (m, 1/2H), 2.44 (m, 1/2H), 2.20 (m, 1/2H), 1.99 (m, 1/2H), 1.91 (m, 1/2H), 1.31–1.20 (complex m, 21/2H), 1.17–1.09 (complex m, 6H), 1.03 (d, $J = 7.5$ Hz, 3/2H), 0.89 (s, 9/2H), 0.87 (s, 9/2H), 0.13 (s, 3/2H), 0.08 (s, 3/2H), 0.06 (s, 3/2H), 0.03 (s, 3/2H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.3 (C \times 1/2), 174.2 (C \times 1/2), 174.2 (C \times 1/2), 174.0 (C \times 1/2), 138.0 (C \times 1/2), 137.9 (C \times 1), 137.8 (C \times 1/2), 137.7 (C \times 1/2), 137.5 (C \times 1/2), 128.5 (C \times 1), 128.4 (C \times 1), 128.3 (C \times 1), 128.3 (C \times 1), 128.3 (C \times 2), 128.0 (C \times 1), 127.9 (C \times 1), 127.8 (C \times 1/2), 127.7 (C \times 2), 127.6 (C \times 1), 127.6 (C \times 1), 127.6 (C \times 1), 127.5 (C \times 1), 127.5 (C \times 1/2), 96.3 (C \times 1/2), 96.0 (C \times 1), 95.7 (C \times 1/2), 95.4 (C \times 1/2), 93.0 (C \times 1/2), 82.3 (C \times 1/2), 80.8 (C \times 1/2), 80.5 (C \times 1/2), 80.2 (C \times 1/2), 78.3 (C \times 1), 78.3 (C \times 1/2), 73.2 (C \times 1), 72.7 (C \times 1/2), 72.1 (C \times 1/2), 71.4 (C \times 1/2), 70.3 (C \times 1/2), 70.1 (C \times 1/2), 70.1 (C \times 1/2), 70.0 (C \times 1/2), 69.9 (C \times 1/2), 69.8 (C \times 1/2), 43.3 (C \times 1/2), 42.3 (C \times 1/2), 42.2 (C \times 1/2), 41.8 (C \times 1), 40.4 (C \times 1), 39.5 (C \times 1/2), 25.9 (C \times 3/2), 25.8 (C \times 3/2), 18.2 (C \times 1/2), 18.0 (C \times 1/2), 17.9 (C \times 1/2), 16.8 (C \times 1/2), 16.1 (C \times 1/2), 14.1 (C \times 1/2), 14.1 (C \times 1/2), 13.5 (C \times 1/2), 12.9 (C \times 1/2), 12.4 (C \times 1/2), 12.0 (C \times 1/2), 10.8 (C \times 1/2), 10.6 (C \times 1/2), 9.7 (C \times 1/2), -4.3 (C \times 1/2), -4.4 (C \times 1/2), -4.4 (C \times 1/2), -4.7 (C \times 1/2); HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4573.

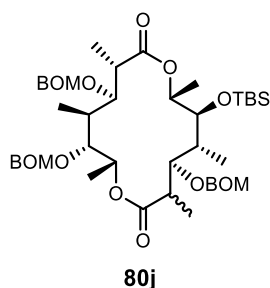


(3*S*,4*R*,5*S*,6*R*,7*R*,10*R*,11*S*,12*R*,13*S*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80h**); According to the procedure of **4.13**, **79h** (128 mg, 147 μmol) was converted to **80h** (79.2 mg, 63%) as a colorless oil; $[\alpha]_{\text{D}}^{24} +32.1$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} 2939, 2877, 1728, 1458, 1373, 1165, 1026, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.27 (complex m, 15H), 4.95 (d, $J = 6.9$ Hz, 1H), 4.90 (dq, $J = 6.3, 3.4$ Hz, 1H), 4.86–4.78 (complex m, 5H), 4.73–4.61 (complex m, 6H), 4.59 (d, $J = 12.0$ Hz, 1H), 4.20 (dd, $J = 4.0, 4.0$ Hz, 1H), 3.82–3.78 (complex m, 2H), 3.69 (dd, $J = 8.0, 3.4$ Hz, 1H), 2.80 (m, 1H), 2.68 (dq, $J = 6.9, 4.0$ Hz, 1H), 2.43 (m, 1H), 1.81 (m, 1H), 1.39 (d, $J = 6.3$ Hz, 3H), 1.27 (d, $J = 6.9$ Hz, 3H), 1.23 (d, $J = 6.3$ Hz, 3H), 1.22 (d, $J = 7.5$ Hz, 3H), 1.08 (d, $J = 7.5$ Hz, 3H), 1.04 (d, $J = 7.5$ Hz, 3H), 0.91 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3 , 60 $^\circ\text{C}$) δ 175.2, 174.3, 137.9, 137.9, 137.8, 128.4 (C \times 2), 128.4 (C \times 2), 128.4 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 3), 127.6 (C \times 4), 96.7, 96.0, 95.0, 83.0, 79.0, 78.0, 73.8, 72.1, 71.1, 70.5, 70.2, 69.8, 43.5, 41.9, 38.3 (C \times 2), 25.8 (C \times 3),

18.1, 17.6, 15.7, 13.9, 13.7, 12.7, 12.6, -4.4, -4.5; HRMS-ESI (m/z); $[M+Na]^+$ calcd for $C_{48}H_{70}O_{11}SiNa$, 873.4585; found 873.4588.

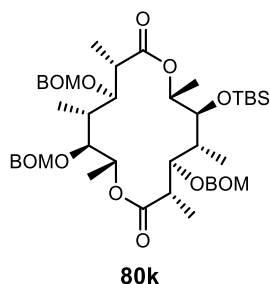


(3*S*,4*R*,5*R*,6*S*,7*R*,10*R*,11*S*,12*S*,13*R*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80i**); According to the procedure of **4.13.**, **79i** (45.6 mg, 52.5 μ mol) was converted to **80i** (12.9 mg, 29%) as a colorless oil; $[\alpha]_D^{27}$ -1.4 (c 0.50, $CHCl_3$); IR; 1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.25 (complex m, 15H), 5.33 (dq, J = 6.3, 2.3 Hz, 1H), 4.87–4.81 (complex m, 3H), 4.79–4.75 (complex m, 4H), 4.72 (d, J = 12.0 Hz, 1H), 4.68 (d, J = 12.0 Hz, 1H), 4.65 (d, J = 12.0 Hz, 1H), 4.61 (d, J = 12.0 Hz, 1H), 4.60 (d, J = 12.0 Hz, 1H), 4.54 (d, J = 12.0 Hz, 1H), 4.11 (dd, J = 6.9, 3.4 Hz, 1H), 3.82 (dd, J = 7.5, 3.4 Hz, 1H), 3.72 (dd, J = 6.9, 2.9 Hz, 1H), 3.57 (dd, J = 8.0, 2.3 Hz, 1H), 2.89 (dq, J = 6.9, 6.9 Hz, 1H), 2.79 (dq, J = 6.9, 6.9 Hz, 1H), 2.15–2.05 (complex m, 2H), 1.39 (d, J = 6.9 Hz, 3H), 1.25 (d, J = 6.9 Hz, 3H), 1.21 (d, J = 6.9 Hz, 3H), 1.16 (d, J = 6.3 Hz, 3H), 1.07 (d, J = 6.9 Hz, 3H), 1.03 (d, J = 7.5 Hz, 3H), 0.85 (s, 9H), 0.04 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 173.9, 137.8, 137.7, 137.6, 128.4 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 5), 127.4 (C \times 2), 96.7, 96.3, 95.9, 82.8, 81.8, 80.7, 76.5, 75.7, 70.5, 70.4, 70.3, 69.9, 45.8, 45.5, 40.9, 37.9, 25.8 (C \times 3), 18.1, 17.8, 16.2, 14.6, 13.5, 11.9, 11.4, -4.4, -4.7; HRMS-ESI (m/z); $[M+Na]^+$ calcd for $C_{48}H_{70}O_{11}SiNa$, 873.4585; found 873.4586.

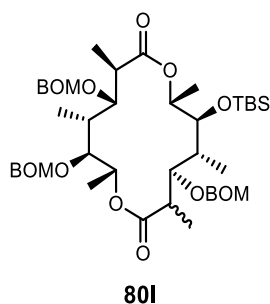


(4*R*,5*R*,6*S*,7*R*,10*S*,11*R*,12*S*,13*R*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80j**); According to the procedure of **4.13.**, **79j** (52.4 mg, 60.3 μ mol) was converted to **80j** (6.1 mg, 12%, diastereo ratio = 2:1) as a colorless oil; IR (neat)/ cm^{-1} ; 3032, 2939, 2885, 2862, 1728, 1458, 1381, 1257, 1188, 1165, 1195, 1026, 841, 741; Shown 1H and ^{13}C NMR peaks of major product as diastereomer; 1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.24 (complex m, 15H), 5.25 (m, 1H), 5.18 (m, 1H), 4.90 (d, J = 6.9 Hz, 1H), 4.78–4.60 (complex m, 7H), 4.57 (d, J = 12.0 Hz, 1H), 4.54 (d, J = 12.6 Hz, 1H), 4.53 (d, J = 11.5 Hz, 1H), 4.47 (d, J = 10.3 Hz, 1H), 4.30 (app brs, 1H), 3.76 (dd, J = 3.4, 3.4 Hz, 1H), 3.53 (dd, J = 9.2, 2.3 Hz, 1H), 3.31 (q, J = 6.9 Hz, 1H), 2.61 (m, 1H), 2.42 (m, 1H), 2.15 (m, 1H), 2.07 (m, 1H), 1.28 (d, J = 6.9 Hz, 3H), 1.22–1.16 (complex m, 12H), 1.13 (d, J = 7.5 Hz, 3H), 0.84 (s, 9H), 0.07 (s, 3H),

0.04 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.4, 174.3, 137.9, 137.7 (C \times 2), 128.4 (C \times 2), 128.4 (C \times 2), 128.2 (C \times 2), 127.9 (C \times 2), 127.8 (C \times 2), 127.8 (C \times 2), 127.6 (C \times 2), 127.5, 95.9, 95.4, 94.5, 82.4, 81.6, 78.5, 77.1, 73.3, 70.2, 70.2, 70.1, 69.8, 42.8, 42.8, 42.0, 38.2, 25.8 (C \times 3), 17.9, 17.6, 17.5, 13.7, 13.1, 12.0, 9.7, -4.8, -5.4; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4578.

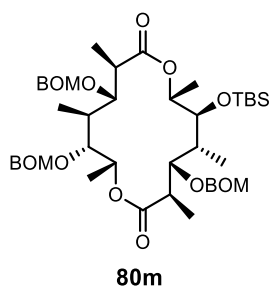


(3*S*,4*R*,5*R*,6*S*,7*R*,10*S*,11*R*,12*R*,13*S*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80k**); According to the procedure of **4.13**, **79k** (93.5 mg, 108 μmol) was converted to **80k** (44.4 mg, 48%) as a colorless oil; $[\alpha]_{\text{D}}^{26} +22.8$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} ; 3062, 3024, 2985, 2947, 2885, 2862, 1728, 1458, 1257, 1196, 1026, 841, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.24 (complex m, 15H), 5.46 (m, 1H), 5.28 (dq, J = 6.9, 4.0 Hz, 1H), 4.77–4.69 (complex m, 6H), 4.66 (d, J = 12.0 Hz, 1H), 4.62–4.56 (complex m, 4H), 4.56 (d, J = 12.0 Hz, 1H), 4.44 (d, J = 9.7 Hz, 1H), 4.40 (d, J = 9.2 Hz, 1H), 3.79 (dd, J = 4.0, 4.0 Hz, 1H), 3.77 (dd, J = 3.4, 3.4 Hz, 1H), 3.27 (q, J = 6.9 Hz, 1H), 3.12 (q, J = 6.9 Hz, 1H), 2.23 (m, 1H), 2.18 (m, 1H), 1.29 (d, J = 6.9 Hz, 3H), 1.25 (d, J = 7.5 Hz, 3H), 1.20 (d, J = 6.9 Hz, 3H), 1.18–1.14 (complex m, 9H), 0.86 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.6, 174.4, 138.0 (C \times 2), 137.7, 128.5 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 128.0 (C \times 4), 127.9 (C \times 2), 127.8, 127.5 (C \times 2), 96.1, 96.0, 92.8, 82.4 (C \times 2), 80.2, 77.4, 72.6, 70.4, 70.2 (C \times 2), 69.8, 43.2, 43.0, 42.6, 40.5, 26.0 (C \times 3), 18.0, 17.5, 17.4, 17.3, 17.0, 10.3, 9.6, -4.8, -5.3; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4591.

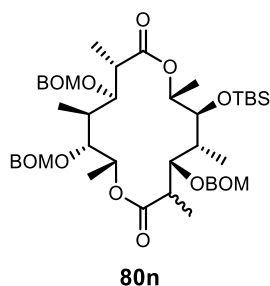


(4*R*,5*R*,6*S*,7*R*,10*R*,11*S*,12*R*,13*S*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80l**); According to the procedure of **4.13**, **79l** (97.5 mg, 112 μmol) was converted to **80l** (36.1 mg, 38%, diastereo ratio = 1:1) as a colorless oil; IR (neat)/ cm^{-1} ; 3062, 2939, 2893, 2862, 1728, 1458, 1381, 1250, 1157, 1026, 833, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.27 (complex m, 15H), 5.03 (dq, J = 6.3, 6.3 Hz, 1/2H), 4.97 (d, J = 6.9 Hz, 1/2H), 4.95 (d, J = 6.9 Hz, 1/2H), 4.90–4.77 (complex m, 13/2H), 4.75–4.58 (complex m, 6H), 3.93 (dd, J = 5.2, 5.2 Hz, 1/2H), 3.86–3.80 (complex m, 3/2H), 3.77 (dd, J = 6.3, 5.7 Hz, 1/2H), 3.73–3.68 (complex m, 1H), 3.52 (app d, J = 8.0 Hz, 1/2H),

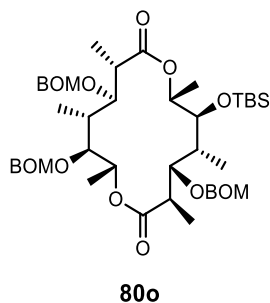
2.87 (m, 1/2H), 2.81–2.72 (complex m, 3/2H), 1.95–1.79 (complex m, 2H), 1.37 (d, $J = 6.3$ Hz, 3/2H), 1.34–1.30 (complex m, 3H), 1.27–1.20 (complex m, 15/2H), 1.09 (d, $J = 6.3$ Hz, 3/2H), 1.03 (d, $J = 6.9$ Hz, 3/2H), 1.00 (d, $J = 6.9$ Hz, 3/2H), 0.95 (d, $J = 6.9$ Hz, 3/2H), 0.92 (s, 9/2H), 0.89 (s, 9/2H), 0.16 (s, 3/2H), 0.14 (s, 3/2H), 0.11 (s, 3/2H), 0.05 (s, 3/2H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.7 (C $\times 1/2$), 174.6 (C $\times 1/2$), 173.3 (C $\times 1/2$), 172.6 (C $\times 1/2$), 137.9 (C $\times 1/2$), 137.9 (C $\times 1/2$), 137.8 (C $\times 1/2$), 137.8 (C $\times 1/2$), 137.8 (C $\times 1/2$), 137.7 (C $\times 1/2$), 128.4 (C $\times 5$), 128.3 (C $\times 1$), 127.8 (C $\times 1$), 127.7 (C $\times 1$), 127.6 (C $\times 2$), 127.6 (C $\times 3/2$), 127.6 (C $\times 1$), 127.6 (C $\times 1$), 127.5 (C $\times 3/2$), 96.6 (C $\times 1/2$), 96.5 (C $\times 1/2$), 96.4 (C $\times 1/2$), 96.0 (C $\times 1/2$), 95.9 (C $\times 1/2$), 95.9 (C $\times 1/2$), 83.7 (C $\times 1/2$), 82.9 (C $\times 1/2$), 82.7 (C $\times 1/2$), 81.5 (C $\times 1/2$), 80.3 (C $\times 1/2$), 78.9 (C $\times 1/2$), 75.9 (C $\times 1/2$), 75.5 (C $\times 1/2$), 74.4 (C $\times 1/2$), 73.3 (C $\times 1/2$), 72.4 (C $\times 1/2$), 70.6 (C $\times 1/2$), 70.5 (C $\times 1/2$), 70.4 (C $\times 1/2$), 70.2 (C $\times 1$), 70.1 (C $\times 1/2$), 70.1 (C $\times 1/2$), 45.4 (C $\times 1/2$), 43.9 (C $\times 1/2$), 43.6 (C $\times 1/2$), 42.0 (C $\times 1/2$), 41.6 (C $\times 1/2$), 40.5 (C $\times 1/2$), 38.9 (C $\times 1/2$), 37.6 (C $\times 1/2$), 26.1 (C $\times 3/2$), 26.0 (C $\times 3/2$), 18.4 (C $\times 1/2$), 18.3 (C $\times 1/2$), 17.9 (C $\times 1$), 17.1 (C $\times 1/2$), 16.9 (C $\times 1/2$), 16.8 (C $\times 1/2$), 15.7 (C $\times 1/2$), 15.7 (C $\times 1/2$), 13.7 (C $\times 1/2$), 12.8 (C $\times 1/2$), 11.7 (C $\times 1/2$), 11.0 (C $\times 1/2$), 10.8 (C $\times 1/2$), –3.3 (C $\times 1/2$), –3.7 (C $\times 1/2$), –3.8 (C $\times 1/2$), –4.2 (C $\times 1/2$); HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.45851; found 873.45958.



(3*R*,4*S*,5*R*,6*S*,7*R*,10*R*,11*S*,12*S*,13*R*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80m**); According to the procedure of **4.13**, **79m** (76.3 mg, 87.7 μmol) was converted to **80m** (25.7 mg, 34%) as a colorless oil; $[\alpha]_{\text{D}}^{28}$ –22.5 (c 1.00, CHCl_3); IR (neat)/ cm^{-1} 3032, 2931, 2885, 2862, 1728, 1458, 1373, 1157, 1026, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.40–7.25 (complex m, 15H), 5.17 (dq, $J = 6.3, 1.7$ Hz, 1H), 4.90 (d, $J = 6.9$ Hz, 1H), 4.84 (d, $J = 6.9$ Hz, 1H), 4.82–4.76 (complex m, 5H), 4.73–4.67 (complex m, 3H), 4.64 (d, $J = 12.0$ Hz, 1H), 4.59 (d, $J = 12.0$ Hz, 1H), 4.54 (d, $J = 12.0$ Hz, 1H), 3.99 (d, $J = 9.2$ Hz, 1H), 3.96 (app d, $J = 6.3$ Hz, 1H), 3.68 (dd, $J = 8.3, 1.7$ Hz, 1H), 3.30 (dd, $J = 10.3, 1.2$ Hz, 1H), 2.74–2.67 (complex m, 2H), 2.11 (m, 1H), 1.84 (m, 1H), 1.24–1.21 (complex m, 12H), 1.11 (d, $J = 6.9$ Hz, 3H), 0.90–0.87 (complex m, 12H), 0.08 (s, 3H), –0.02 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.1, 172.7, 137.9, 137.9, 137.7, 128.4 (C $\times 2$), 128.3 (C $\times 2$), 128.3 (C $\times 2$), 128.0 (C $\times 2$), 127.7, 127.6 (C $\times 4$), 127.6 (C $\times 2$), 97.0, 95.9, 95.7, 85.5, 81.4, 78.4, 72.9, 71.8, 70.8, 70.2, 70.2, 70.2, 44.7, 43.5, 39.9, 39.6, 26.1 (C $\times 3$), 18.5, 18.3, 15.9, 15.5, 13.3, 10.7, 10.4, –2.9, –4.4; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4571.

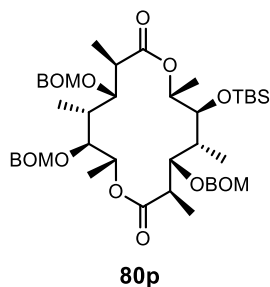


(4*R*,5*R*,6*S*,7*R*,10*S*,11*R*,12*S*,13*R*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80n**); According to the procedure of **4.13.**, **79n** (68.2 mg, 78.5 μ mol) was converted to **80n** (8.7 mg, 13%, diastereo ratio = 2:1) as a colorless oil; IR (neat)/cm⁻¹: 3032, 2931, 2885, 2862, 1728, 1458, 1381, 1250, 1165, 1195, 1026, 833, 741; Shown ¹H and ¹³C NMR peaks of major product as diastereomer; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.26 (complex m, 15H), 4.97 (m, 1H), 4.93 (m, 1H), 4.85–4.76 (complex m, 6H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.69 (d, *J* = 11.5 Hz, 1H), 4.66–4.59 (complex m, 4H), 4.03–3.93 (complex, 2H), 3.85 (m, 1H), 3.47 (dd, *J* = 13.8, 6.9 Hz, 1H), 3.03–2.91 (complex m, 2H), 2.52 (m, 1H), 2.03 (m, 1H), 1.37 (d, *J* = 6.3 Hz, 3H), 1.30–1.25 (complex m, 6H), 1.24 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.3 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 0.87 (s, 9H), 0.08 (s, 3H), 0.01 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 173.7, 173.6, 137.8, 137.8, 137.7, 128.4 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 128.2, 127.8, 127.7 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.5, 96.6, 95.8, 94.9, 83.8, 79.0, 73.8, 73.0, 72.9, 72.5, 70.4, 70.2, 70.0, 44.3, 37.9, 37.2, 35.6, 26.0 (C \times 3), 18.3, 17.8, 16.4, 14.8, 14.7, 14.2, 11.9, -3.5, -4.6; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4568.



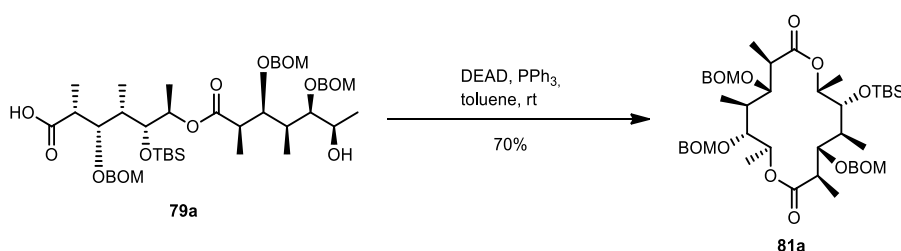
(3*R*,4*S*,5*R*,6*S*,7*R*,10*S*,11*R*,12*R*,13*S*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80o**); According to the procedure of **4.13.**, **79o** (96.8 mg, 111 μ mol) was converted to **80o** (15.2 mg, 16%) as a colorless oil; [α]_D²⁶ -2.0 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 3032, 2939, 2885, 2862, 1728, 1458, 1381, 1250, 1026, 833, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.24 (complex m, 15H), 5.46 (m, 1H), 5.28 (m, 1H), 4.76 (d, *J* = 6.9 Hz, 1H), 4.74–4.69 (complex m, 5H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.62–4.54 (complex m, 5H), 4.44 (d, *J* = 9.7 Hz, 1H), 4.40 (d, *J* = 9.2 Hz, 1H), 3.79 (dd, *J* = 4.0, 3.4 Hz, 1H), 3.77 (dd, *J* = 3.4, 3.4 Hz, 1H), 3.27 (q, *J* = 6.3 Hz, 1H), 3.12 (q, *J* = 6.9 Hz, 1H), 2.23 (m, 1H), 2.18 (m, 1H), 1.29 (d, *J* = 6.9 Hz, 3H), 1.25 (d, *J* = 7.5 Hz, 3H), 1.20 (d, *J* = 6.9 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.16–1.14 (complex m, 6H), 0.86 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 173.1, 172.7, 137.9, 137.7, 137.6, 128.4 (C \times 2), 128.4 (C \times 4), 127.9 (C \times 2), 127.8 (C \times 2), 127.7, 127.6 (C \times 3), 127.6, 97.2, 96.8, 94.8, 85.4, 83.2, 79.5, 73.5, 73.2, 71.4, 70.3, 70.2 (C \times 2), 46.1, 42.6, 39.1, 38.1,

26.1 (C ×3), 18.5, 18.2, 17.9, 16.0, 15.5, 10.4, 9.5, −2.8, −4.2; HRMS-ESI (m/z); $[M+Na]^+$ calcd for $C_{48}H_{70}O_{11}SiNa$, 873.4585; found 873.4573.



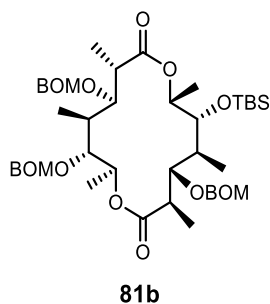
(3*R*,4*S*,5*R*,6*S*,7*R*,10*R*,11*S*,12*R*,13*S*,14*R*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**80p**); According to the procedure of **4.13**, **79p** (68.8 mg, 79.2 μ mol) was converted to **80p** (45.7 mg, 68%) as a colorless oil; $[\alpha]_D^{24}$ −9.4 (c 0.50, $CHCl_3$); IR (neat)/ cm^{-1} : 2939, 2885, 1728, 1458, 1026, 741; 1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.27 (complex m, 15H), 4.91 (d, J = 6.9 Hz, 1H), 4.89–4.77 (complex m, 6H), 4.69 (d, J = 12.0 Hz, 1H), 4.68 (s, 2H), 4.66–4.62 (complex m, 3H), 4.61 (d, J = 12.0 Hz, 1H), 3.82–3.78 (complex m, 2H), 3.76–3.72 (complex m, 2H), 2.89 (m, 1H), 2.84 (m, 1H), 1.90–1.79 (complex m, 2H), 1.26 (d, J = 6.3 Hz, 3H), 1.21 (d, J = 7.5 Hz, 3H), 1.19 (d, J = 7.5 Hz, 3H), 1.16 (d, J = 6.3 Hz, 3H), 1.04 (d, J = 6.9 Hz, 3H), 0.93 (d, J = 6.9 Hz, 3H), 0.92 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.1, 174.9, 137.8, 137.8, 137.8, 128.4 (C ×3), 128.3 (C ×3), 127.6 (C ×7), 127.5 (C ×2), 96.0, 95.9, 95.4, 82.1, 80.7, 79.9, 73.7, 73.2, 71.7, 70.2, 70.0, 69.8, 43.0, 41.8, 41.0, 39.3, 26.1 (C ×3), 18.5, 16.5, 15.7 (C ×2), 15.0, 11.0, 10.8, −3.5, −4.0; HRMS-ESI (m/z); $[M+Na]^+$ calcd for $C_{48}H_{70}O_{11}SiNa$, 873.4585; found 873.4588.

4.14. (3*R*,4*S*,5*S*,6*R*,7*R*,10*R*,11*S*,12*S*,13*R*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81a**);

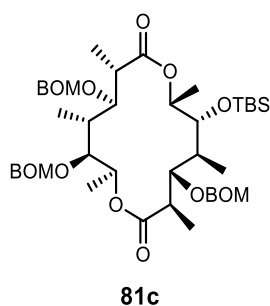


To a solution of PPh_3 (92.3 mg, 352 μ mol) and *seco*-acid **79a** (79.6 mg, 91.6 μ mol) in toluene (18 mL) was added DEAD (40% in toluene, 0.24 ml, 48.0 μ mol) under N_2 at 0 °C. The reaction mixture was stirred for 30 min at 0 °C. After warming to room temperature, the reaction mixture was stirred for 21 h. Silica gel (15 cc) was added to the reaction mixture, which was then concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 9/1 to 6/1) to afford macrodiolide aglycone **81a** (54.3 mg, 70%) as a colorless oil; $[\alpha]_D^{26}$ −2.5 (c 0.50, $CHCl_3$); IR (neat)/ cm^{-1} : 2939, 2885, 2862, 1728, 1458, 1373, 1250, 1026, 841, 733; 1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.26 (complex m, 15H), 5.10 (m, 1H), 4.94 (m, 1H), 4.87–4.76 (complex m, 6H), 4.70–4.67 (complex m, 3H), 4.62 (d, J = 12.0 Hz, 1H), 4.59 (d, J = 12.6 Hz, 2H),

3.97 (d, $J = 9.2$ Hz, 1H), 3.94 (dd, $J = 8.0, 3.4$ Hz, 1H), 3.77 (dd, $J = 9.2, 2.3$ Hz, 1H), 3.65 (dd, $J = 8.6, 2.9$ Hz, 1H), 2.85–2.75 (complex m, 2H), 1.91 (m, 1H), 1.87 (m, 1H), 1.30 (d, $J = 5.7$ Hz, 3H), 1.28 (d, $J = 6.9$ Hz, 3H), 1.23 (d, $J = 6.9$ Hz, 3H), 1.11 (d, $J = 6.3$ Hz, 3H), 1.04 (d, $J = 7.5$ Hz, 3H), 1.02 (d, $J = 7.5$ Hz, 3H), 0.91 (s, 9H), 0.06 (s, 3H), –0.01 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.3, 173.1, 137.9, 137.7, 137.5, 128.4 (C \times 4), 128.3 (C \times 2), 127.6 (C \times 3), 127.6 (C \times 3), 127.5, 127.5 (C \times 2), 96.9, 96.2, 95.7, 82.5, 81.3, 81.2, 74.1, 72.5, 71.2, 70.4, 70.1 (C \times 2), 46.1, 45.9, 39.7, 38.6, 26.0 (C \times 3), 18.3, 18.0, 15.5, 14.9, 14.6, 10.9, 9.4, –3.7, –4.0; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4576.

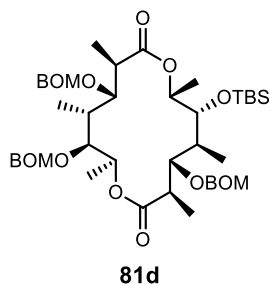


(3*R*,4*S*,5*S*,6*R*,7*R*,10*S*,11*R*,12*S*,13*R*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81b**); According to the procedure of **4.14**, **79b** (72.6 mg, 83.5 μmol) was converted to **81b** (61.0 mg, 86%) as a colorless oil; $[\alpha]_{\text{D}}^{26} -39.0$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} : 3062, 2939, 2885, 1728, 1458, 1250, 1026, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.27 (complex m, 15H), 5.46 (q, $J = 6.3$ Hz, 1H), 5.03–4.97 (complex m, 2H), 4.91 (d, $J = 6.9$ Hz, 1H), 4.84 (d, $J = 6.9$ Hz, 1H), 4.80–4.74 (complex m, 4H), 4.67 (d, $J = 12.0$ Hz, 1H), 4.61 (s, 2H), 4.59 (d, $J = 12.0$ Hz, 1H), 4.55 (d, $J = 12.0$ Hz, 1H), 3.85 (d, $J = 9.7$ Hz, 1H), 3.81 (d, $J = 9.2$ Hz, 1H), 3.62 (dd, $J = 9.7, 2.9$ Hz, 1H), 3.58 (d, $J = 8.6$ Hz, 1H), 2.86 (m, 1H), 2.75 (m, 1H), 1.95 (app dq, $J = 6.9, 2.9$ Hz, 1H), 1.51 (app dq, $J = 7.5, 7.5$ Hz, 1H), 1.31 (d, $J = 6.3$ Hz, 3H), 1.29 (d, $J = 6.9$ Hz, 3H), 1.23 (d, $J = 6.9$ Hz, 3H), 1.07 (d, $J = 7.5$ Hz, 3H), 1.06 (d, $J = 6.9$ Hz, 3H), 0.97 (d, $J = 6.3$ Hz, 3H), 0.91 (s, 9H), 0.09 (s, 3H), –0.02 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 173.4, 172.7, 138.0, 137.6, 137.4, 128.4 (C \times 6), 127.8, 127.6 (C \times 2), 127.6 (C \times 3), 127.6, 127.5 (C \times 2), 97.6, 97.4, 95.6, 85.2, 82.9, 78.2, 76.5, 70.4, 70.2, 70.1, 69.4, 69.2, 46.3, 45.4, 40.2, 36.7, 26.0 (C \times 3), 18.4, 17.8, 17.4, 16.4, 15.6, 11.5, 11.0, –3.2 (C \times 2); HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4589.

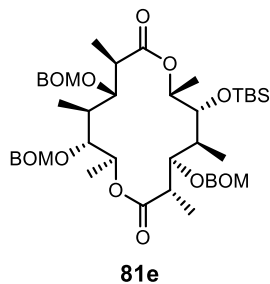


(3*R*,4*S*,5*S*,6*R*,7*R*,10*S*,11*R*,12*R*,13*S*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81c**); According to the procedure of **4.14**, **79c** (94.9 mg, 109 μmol) was converted to **81c** (50.1 mg, 54%) as a colorless oil; $[\alpha]_{\text{D}}^{28} +16.6$ (c 1.00, CHCl_3);

IR (neat)/cm⁻¹; 3062, 2939, 2893, 2862, 1728, 1458, 1381, 1257, 1149, 1026, 841, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.25 (complex m, 15H), 5.18 (dq, *J* = 6.3, 2.3 Hz, 1H), 5.06 (dq, *J* = 6.3, 2.3 Hz, 1H), 4.83–4.72 (complex m, 6H), 4.70–4.60 (complex m, 4H), 4.59 (d, *J* = 11.5 Hz, 1H), 4.54 (d, *J* = 11.5 Hz, 1H), 3.89 (dd, *J* = 6.9, 2.9 Hz, 1H), 3.81 (dd, *J* = 6.6, 3.4 Hz, 1H), 3.70 (dd, *J* = 8.6, 1.7 Hz, 1H), 3.58 (dd, *J* = 8.0, 1.7 Hz, 1H), 2.87 (dq, *J* = 6.9, 6.9 Hz, 1H), 2.80 (dq, *J* = 6.9, 6.9 Hz, 1H), 2.04 (m, 1H), 1.93 (m, 1H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.21–1.18 (complex m, 6H), 1.14 (d, *J* = 7.5 Hz, 3H), 1.14 (d, *J* = 6.3 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 0.09 (s, 3H), 0.02 (s, 3H); ¹³C NMR (125 MHz, CDCl₃, 50 °C) δ 173.4, 173.3, 137.9, 137.7, 137.7, 128.4 (C ×4), 128.4 (C ×2), 127.7 (C ×2), 127.7 (C ×5), 127.5 (C ×2), 96.9, 96.6, 96.4, 82.7, 81.6, 81.2, 75.4, 71.8, 70.7, 70.5, 70.4, 70.3, 45.8, 45.3, 39.3, 38.4, 26.1 (C ×3), 18.4, 16.0, 15.5, 13.0, 12.8, 11.7, 11.4, –3.6, –3.8; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4586.

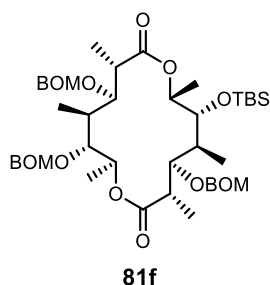


(3*R*,4*S*,5*S*,6*R*,7*R*,10*R*,11*S*,12*R*,13*S*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81d**); According to the procedure of **4.2.14.**, **79d** (165 mg, 190 μmol) was converted to **81d** (79.0 mg, 49%) as a colorless oil; [α]_D²⁷ +15.3 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹; 3008, 2939, 2885, 1720, 1458, 1257, 1157, 1095, 1026, 841, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.39–7.24 (complex m, 15H), 5.27 (m, 1H), 5.11 (q, *J* = 6.3 Hz, 1H), 4.94 (d, *J* = 6.3 Hz, 1H), 4.85 (d, *J* = 6.9 Hz, 1H), 4.81 (d, *J* = 6.3 Hz, 1H), 4.81 (d, *J* = 6.9 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.69 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.65–4.55 (complex m, 4H), 3.85–3.80 (complex m, 2H), 3.78 (m, 1H), 3.70 (d, *J* = 3.4 Hz, 1H), 3.27 (dq, *J* = 6.3, 2.3 Hz, 1H), 2.66 (m, 1H), 2.14 (app q, *J* = 6.9 Hz, 1H), 2.07 (m, 1H), 1.25 (d, *J* = 7.5 Hz, 3H), 1.24 (d, *J* = 6.9 Hz, 3H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.18 (d, *J* = 7.5 Hz, 3H), 1.08 (d, *J* = 7.5 Hz, 3H), 0.97 (s, 9H), 0.16 (s, 3H), 0.11 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.1, 173.7, 138.1, 138.0, 138.0, 128.4 (C ×2), 128.4 (C ×2), 128.3 (C ×2), 128.0 (C ×2), 127.7 (C ×2), 127.6 (C ×3), 127.6, 127.5, 97.0, 96.3, 95.0, 83.7, 82.0, 77.7, 75.7, 71.4, 70.3 (C ×2), 70.1, 68.4, 43.5, 43.3, 41.4, 36.3, 26.0 (C ×3), 18.3, 18.2, 15.9, 15.5, 15.3, 13.3, 10.8, –3.5, –4.7; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4590.

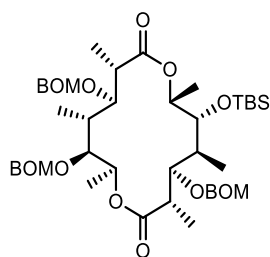


(3*S*,4*R*,5*S*,6*R*,7*R*,10*R*,11*S*,12*S*,13*R*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81e**); According to the procedure of **4.2.14.**,

79e (152 mg, 175 μ mol) was converted to **81e** (108 mg, 73%) as a colorless oil; $[\alpha]_D^{24} +31.6$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹ 3062, 3032, 2939, 2893, 2862, 1728, 1458, 1373, 1180, 1157, 1026, 841, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.25 (complex m, 15H), 4.97–4.86 (complex m, 4H), 4.82 (d, *J* = 6.9 Hz, 1H), 4.75 (d, *J* = 6.9 Hz, 1H), 4.72–4.68 (complex m, 4H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.63–4.55 (complex m, 3H), 4.04 (app br s, 1H), 3.85 (app br s, 1H), 3.81 (app br s, 1H), 3.65 (dd, *J* = 8.6, 2.3 Hz, 1H), 2.67–2.57 (complex m, 2H), 2.24 (app br s, 1H), 1.96 (app br s, 1H), 1.34 (d, *J* = 5.7 Hz, 3H), 1.24–1.19 (complex m, 9H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.94–0.88 (complex m, 12H), 0.13 (s, 3H), 0.09 (s, 3H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 175.1, 174.5, 138.2, 138.1, 137.9, 128.4 (C \times 2), 128.3 (C \times 4), 127.9 (C \times 2), 127.7 (C \times 2), 127.6, 127.6, 127.5, 96.8, 95.0 (C \times 2), 84.5, 80.3, 79.2, 73.2, 71.3, 70.6, 70.5, 70.2, 70.0, 46.5, 41.1, 40.5, 38.5, 25.9 (C \times 3), 18.8, 18.2, 14.5, 12.8, 12.6, 12.0, 9.6, -4.1, -4.7; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4582.

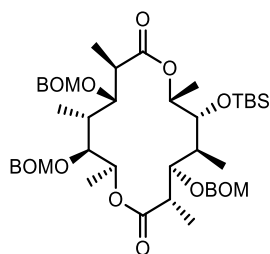


(3*S*,4*R*,5*S*,6*R*,7*R*,10*S*,11*R*,12*S*,13*R*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81f**); According to the procedure of **4.2.14.**, **79f** (98.2 mg, 113 μ mol) was converted to **81f** (36.8 mg, 38%) as a colorless oil; $[\alpha]_D^{26} +16.9$ (*c* 0.20, CHCl₃); IR (neat)/cm⁻¹ 2939, ; ¹H NMR (500 MHz, CDCl₃) δ 7.37–7.27 (complex m, 15H), 5.04 (d, *J* = 6.9 Hz, 1H), 4.93–4.85 (complex m, 2H), 4.84–4.77 (complex m, 4H), 4.76 (d, *J* = 12.0 Hz, 1H), 4.74 (d, *J* = 7.5 Hz, 1H), 4.70–4.55 (complex m, 5H), 3.92 (dd, *J* = 3.4, 3.4 Hz, 1H), 3.75 (d, *J* = 10.3 Hz, 1H), 3.67 (dd, *J* = 9.2, 1.2 Hz, 1H), 3.62 (dd, *J* = 7.7, 1.7 Hz, 1H), 2.82 (dq, *J* = 7.5, 7.5 Hz, 1H), 2.66 (m, 1H), 2.12 (app q, *J* = 6.9 Hz, 1H), 1.74 (app brs, 1H), 1.35 (d, *J* = 5.7 Hz, 3H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.25 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.06 (d, *J* = 7.5 Hz, 3H), 0.90 (s, 9H), 0.11 (s, 3H), 0.08 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 174.6, 174.1, 137.8, 137.8, 137.6, 128.4 (C \times 6), 127.7 (C \times 7), 127.5 (C \times 2), 97.1, 96.7, 95.5, 84.8, 82.4, 78.4, 73.1, 71.0, 70.6, 70.3, 70.3, 70.1, 44.2, 43.4, 39.7, 37.7, 25.9 (C \times 3), 18.2, 17.7, 16.8, 15.8, 14.1, 14.0, 13.0, -4.0, -4.4; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4575.



81g

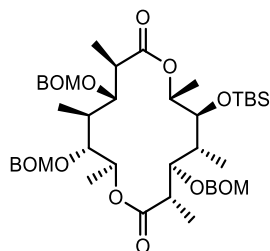
(3*S*,4*R*,5*S*,6*R*,7*R*,10*S*,11*R*,12*R*,13*S*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81g**); According to the procedure of **4.2.14.**, **79g** (66.5 mg, 76.5 μ mol) was converted to **81g** (17.6 mg, 27%) as a colorless oil; $[\alpha]_D^{26} +34.3$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹ 3032, 2939, 2885, 2862, 1728, 1458, 1381, 1250, 1165, 1018, 841, 741; ¹H NMR (500 MHz, CDCl₃, 50 °C) δ 7.36–7.25 (complex m, 15H), 5.31 (q, *J* = 6.3 Hz, 1H), 5.04 (m, 1H), 4.90 (d, *J* = 6.3 Hz, 1H), 4.86 (d, *J* = 7.5 Hz, 1H), 4.82 (d, *J* = 6.9 Hz, 1H), 4.79 (d, *J* = 6.9 Hz, 1H), 4.76 (d, *J* = 12.0 Hz, 1H), 4.70 (s, 2H), 4.68 (d, *J* = 12.0 Hz, 1H), 4.62 (d, *J* = 11.5 Hz, 1H), 4.61 (d, *J* = 11.5 Hz, 1H), 4.59–4.54 (complex m, 2H), 3.92 (d, *J* = 6.9 Hz, 1H), 3.80 (app br s, 1H), 3.79 (dd, *J* = 7.5, 4.0 Hz, 1H), 3.63 (d, *J* = 5.2 Hz, 1H), 3.17 (m, 1H), 2.71 (dq, *J* = 7.5, 7.5 Hz, 1H), 2.17–2.07 (complex m, 2H), 1.31 (d, *J* = 7.5 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.19 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.11 (d, *J* = 6.0 Hz, 3H), 1.10 (d, *J* = 7.2 Hz, 3H), 0.91 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.2, 173.6, 138.1, 137.9, 137.7, 128.5 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 127.8, 127.7 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 2), 127.6 (C \times 2), 96.8, 96.6, 94.9, 82.4, 82.4, 76.9, 72.9, 70.5, 70.4 (C \times 2), 70.3, 67.8, 44.0, 42.3, 38.0, 37.4, 25.9 (C \times 3), 18.2, 18.0, 15.5, 14.6, 14.4, 12.8, 11.4, -4.3, -4.7; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4587.



81h

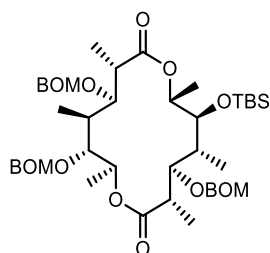
(3*S*,4*R*,5*S*,6*R*,7*R*,10*R*,11*S*,12*R*,13*S*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81h**); According to the procedure of **4.2.14.**, **79h** (149 mg, 171 μ mol) was converted to **81h** (38.7 mg, 27%) as a colorless oil; $[\alpha]_D^{24} +9.6$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹ 2939, 2885, 2862, 1728, 1458, 1381, 1034, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.37–7.24 (complex m, 15H), 5.32 (d, *J* = 6.3 Hz, 1H), 5.24 (d, *J* = 6.3 Hz, 1H), 4.87 (dq, *J* = 6.3, 6.3 Hz, 1H), 4.79 (d, *J* = 7.5 Hz, 1H), 4.76 (d, *J* = 6.9 Hz, 1H), 4.72 (d, *J* = 7.5 Hz, 1H), 4.71 (d, *J* = 6.9 Hz, 1H), 4.66 (s, 2H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.09–4.06 (complex m, 2H), 4.02 (dq, *J* = 6.3, 4.0 Hz, 1H), 3.79 (dd, *J* = 4.0, 2.3 Hz, 1H), 3.66 (dd, *J* = 8.0, 5.7 Hz, 1H), 2.65–2.58 (complex m, 2H), 2.07 (m, 1H), 1.82 (m, 1H), 1.29 (d, *J* = 6.9 Hz, 3H), 1.27 (d, *J* = 6.3 Hz, 3H), 1.18 (d, *J* = 7.5 Hz, 3H), 1.17 (d, *J* = 7.5 Hz, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.87 (d, *J* = 6.9 Hz, 3H),

0.13 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.4, 174.3, 137.7, 137.6, 137.1, 128.4 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 127.9, 127.8 (C \times 4), 127.7 (C \times 3), 127.6, 96.2, 93.1, 89.0, 85.0, 84.3, 82.5, 76.0, 74.1, 71.9, 71.6, 70.2, 69.5, 45.0, 44.2, 41.1, 37.7, 26.0 (C \times 3), 18.4, 17.6, 15.8, 14.7, 13.9, 11.1, 8.3, -4.0, -4.2; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4586.



81i

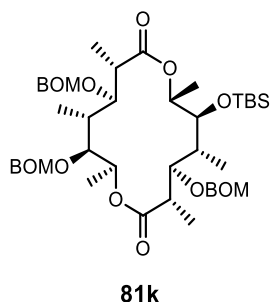
(3*S*,4*R*,5*R*,6*S*,7*R*,10*R*,11*S*,12*S*,13*R*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81i**); According to the procedure of **4.2.14.**, **79i** (76.6 mg, 88.1 μmol) was converted to **81i** (37.8 mg, 50%) as a colorless oil; $[\alpha]_{\text{D}}^{26} +16.9$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} 3062, 2939, 2885, 1728, 1458, 1373, 1257, 1095, 1026, 841, 741; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.25 (complex m, 15H), 4.92 (d, J = 6.3 Hz, 1H), 4.83 (d, J = 6.3 Hz, 1H), 4.82 (d, J = 6.3 Hz, 1H), 4.76 (dq, J = 6.3, 6.3 Hz, 1H), 4.76 (d, J = 6.9 Hz, 1H), 4.71–4.66 (complex m, 5H), 4.64 (d, J = 12.0 Hz, 1H), 4.63 (d, J = 12.0 Hz, 1H), 4.59 (d, J = 12.0 Hz, 1H), 4.58 (d, J = 12.0 Hz, 1H), 4.06 (dd, J = 8.0, 4.0 Hz, 1H), 3.98 (dd, J = 8.6, 5.2 Hz, 1H), 3.77 (dd, J = 9.5, 1.7 Hz, 1H), 3.70 (dd, J = 7.5, 2.9 Hz, 1H), 2.84 (dq, J = 6.9, 3.4 Hz, 1H), 2.65 (dq, J = 6.9, 6.9 Hz, 1H), 2.06 (m, 1H), 2.02 (m, 1H), 1.38 (d, J = 5.7 Hz, 3H), 1.31 (d, J = 5.7 Hz, 3H), 1.28 (d, J = 6.9 Hz, 3H), 1.21 (d, J = 6.9 Hz, 3H), 1.09 (d, J = 7.5 Hz, 3H), 0.96 (d, J = 7.5 Hz, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.6, 174.5, 137.9 (C \times 2), 137.8, 128.3 (C \times 2), 128.3 (C \times 2), 128.3 (C \times 2), 127.7 (C \times 2), 127.6 (C \times 4), 127.6, 127.5, 127.5, 96.4, 95.5, 95.1, 83.9, 80.5, 80.1, 77.4, 74.4, 72.0, 70.4, 70.2, 70.0, 47.2, 44.3, 43.0, 40.7, 25.9 (C \times 3), 18.2, 18.0, 17.8, 15.2, 14.5, 11.7, 9.7, -3.5, -4.6; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4561.



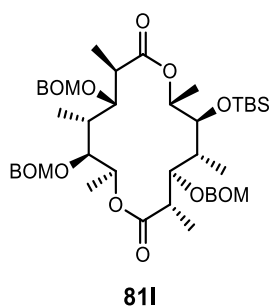
81j

(3*S*,4*R*,5*R*,6*S*,7*R*,10*S*,11*R*,12*S*,13*R*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81j**); According to the procedure of **4.2.14.**, **79j** (258 mg, 297 μmol) was converted to **81j** (149 mg, 59%) as a colorless oil; $[\alpha]_{\text{D}}^{27} +1.4$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} 3062, 2939, 2885, 1728, 1458, 1381, 1157, 1026, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.27 (complex m, 15H), 5.10 (m, 1H), 4.87 (d, J = 6.9 Hz, 1H), 4.83 (d, J = 6.9 Hz, 1H), 4.81–4.71 (complex m, 6H), 4.69 (d, J = 12.0 Hz, 1H), 4.67–4.61 (complex m, 4H), 3.74 (dd, J = 5.2, 4.0 Hz, 1H), 3.70–3.65 (complex m,

2H), 3.56 (d, $J = 5.7$ Hz, 1H), 2.83 (app dd, $J = 6.3, 6.3$ Hz, 1H), 2.58 (app dq, $J = 6.9, 6.9$ Hz, 1H), 2.16–2.05 (complex m, 2H), 1.26 (d, $J = 6.3$ Hz, 3H), 1.25 (d, $J = 6.3$ Hz, 3H), 1.23 (d, $J = 6.3$ Hz, 3H), 1.20 (d, $J = 6.9$ Hz, 3H), 1.07 (d, $J = 6.9$ Hz, 3H), 0.95 (d, $J = 6.9$ Hz, 3H), 0.87 (s, 9H), 0.12 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.0, 173.9, 137.8, 137.7, 137.6, 128.4 (C \times 4), 128.4 (C \times 2), 127.8 (C \times 2), 127.7, 127.6 (C \times 3), 127.6, 127.4 (C \times 2), 95.8, 95.4, 94.8, 81.0, 79.8, 78.9, 77.1, 74.2, 72.2, 70.0, 69.8, 69.8, 45.8, 41.8, 41.5, 39.9, 25.9 (C \times 3), 18.2, 16.3, 15.3, 14.3, 14.1, 10.1, 9.9, –4.2, –4.3; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4581.

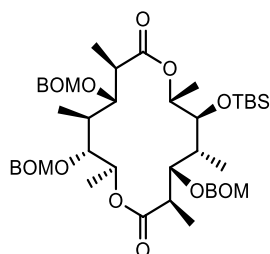


(3*S*,4*R*,5*R*,6*S*,7*R*,10*S*,11*R*,12*R*,13*S*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*t*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81k**); According to the procedure of **4.2.14.**, **79k** (128 mg, 147 μmol) was converted to **81k** (12.2 mg, 10%) as a colorless oil; $[\alpha]_{\text{D}}^{27} +10.5$ (c 1.00, CHCl_3); IR (neat)/ cm^{-1} 3062, 3032, 2939, 2885, 2862, 1720, 1458, 1381, 1250, 1026, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.25 (complex m, 15H), 5.24 (dq, $J = 6.3, 1.7$ Hz, 1H), 4.84–4.72 (complex m, 7H), 4.70 (d, $J = 11.5$ Hz, 1H), 4.69 (d, $J = 12.6$ Hz, 1H), 4.66 (d, $J = 12.0$ Hz, 1H), 4.63 (d, $J = 11.5$ Hz, 1H), 4.62 (d, $J = 12.6$ Hz, 1H), 4.54 (d, $J = 12.0$ Hz, 1H), 3.93 (dd, $J = 6.9, 6.9$ Hz, 1H), 3.86 (dd, $J = 8.0, 2.3$ Hz, 1H), 3.73 (dd, $J = 5.7, 3.4$ Hz, 1H), 3.68 (dd, $J = 8.6, 1.7$ Hz, 1H), 2.86–2.79 (complex m, 2H), 2.01 (m, 1H), 1.88 (m, 1H), 1.25 (d, $J = 6.9$ Hz, 3H), 1.25 (d, $J = 6.3$ Hz, 3H), 1.22 (d, $J = 6.9$ Hz, 3H), 1.18 (d, $J = 6.3$ Hz, 3H), 1.11 (d, $J = 6.9$ Hz, 3H), 1.00 (d, $J = 7.5$ Hz, 3H), 0.89 (s, 9H), 0.18 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.2, 173.3, 138.0, 137.8, 137.5, 128.4 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 127.7 (C \times 3), 127.6 (C \times 3), 127.5 (C \times 2), 127.5, 96.8, 96.5, 95.9, 81.5, 81.3, 80.3, 75.5, 75.1, 70.4, 70.3, 70.1, 70.0, 45.8, 45.2, 42.7, 38.1, 26.0 (C \times 3), 18.2, 17.3, 16.1, 15.0, 13.8, 11.3, 10.6, –3.6, –4.0; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{48}\text{H}_{70}\text{O}_{11}\text{SiNa}$, 873.4585; found 873.4574.



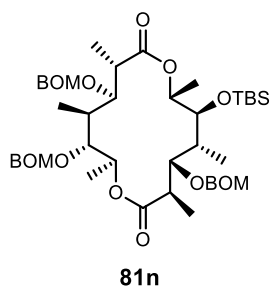
(3*S*,4*R*,5*R*,6*S*,7*R*,10*R*,11*S*,12*R*,13*S*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81l**); According to the procedure of **4.2.14.**, **79l** (143 mg, 164 μmol) was converted to **81l** (30.9 mg, 22%) as a colorless oil; $[\alpha]_{\text{D}}^{26} +20.4$ (c 1.00, CHCl_3);

IR (neat)/cm⁻¹ 3062, 2939, 2885, 1728, 1458, 1381, 1257, 1165, 1095, 1026, 841, 748; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.35–7.23 (complex m, 15H), 5.11 (dq, *J* = 6.3, 3.4 Hz, 1H), 4.89 (dq, *J* = 6.3, 6.3 Hz, 1H), 4.86 (d, *J* = 6.9 Hz, 1H), 4.83 (d, *J* = 6.9 Hz, 1H), 4.81–4.74 (complex m, 4H), 4.69 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 12.6 Hz, 1H), 4.61 (d, *J* = 12.0 Hz, 1H), 4.61 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.25 (dd, *J* = 7.5, 3.4 Hz, 1H), 3.84 (d, *J* = 8.6 Hz, 1H), 3.80 (dd, *J* = 3.7, 3.7 Hz, 1H), 3.74 (dd, *J* = 6.3, 4.0 Hz, 1H), 2.96 (dq, *J* = 6.9, 3.4 Hz, 1H), 2.70 (dq, *J* = 7.5, 7.5 Hz, 1H), 2.18–2.08 (complex m, 2H), 1.31 (d, *J* = 6.9 Hz, 3H), 1.28 (d, *J* = 6.9 Hz, 3H), 1.25 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.05 (d, *J* = 7.5 Hz, 3H), 0.91 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 174.9, 174.5, 138.3, 138.1, 138.0, 128.4 (C ×4), 128.3 (C ×2), 127.8 (C ×4), 127.7 (C ×2), 127.6, 127.6, 127.5, 96.7, 95.6, 95.3, 83.6, 79.3, 77.7, 77.3, 75.0, 72.0, 70.3, 70.2 (C ×2), 44.7, 43.6, 42.5, 36.9, 26.0 (C ×3), 19.0, 18.2, 15.6, 15.0, 14.8, 13.0, 12.2, –3.6, –4.3; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4581.

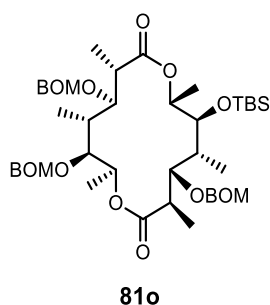


81m

(3*R*,4*S*,5*R*,6*S*,7*R*,10*R*,11*S*,12*S*,13*R*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81m**); According to the procedure of **4.2.14.**, **79m** (160 mg, 184 μmol) was converted to **81m** (124 mg, 79%) as a colorless oil; [α]_D²⁷ +1.6 (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹ 2939, 2885, 1728, 1458, 1157, 1026, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.26 (complex m, 15H), 5.08 (dq, *J* = 6.3, 1.7 Hz, 1H), 5.04 (dq, *J* = 6.9, 2.9 Hz, 1H), 4.85 (d, *J* = 6.9 Hz, 1H), 4.78 (d, *J* = 6.9 Hz, 1H), 4.77 (d, *J* = 7.5 Hz, 1H), 4.77 (d, *J* = 7.5 Hz, 1H), 4.76 (d, *J* = 6.9 Hz, 1H), 4.72 (d, *J* = 6.9 Hz, 1H), 4.69 (d, *J* = 12.0 Hz, 1H), 4.66–4.58 (complex m, 5H), 3.86 (app br s, 1H), 3.78 (dd, *J* = 9.7, 2.9 Hz, 1H), 3.67 (dd, *J* = 5.7, 2.9 Hz, 1H), 3.61 (d, *J* = 8.6 Hz, 1H), 2.80–2.66 (complex m, 2H), 2.27 (m, 1H), 2.00 (m, 1H), 1.28 (d, *J* = 6.9 Hz, 3H), 1.25 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 7.5 Hz, 3H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.08 (d, *J* = 7.5 Hz, 3H), 1.00 (d, *J* = 7.5 Hz, 3H), 0.96 (s, 9H), 0.17 (s, 3H), 0.14 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 175.0, 174.2, 137.8, 137.6, 137.6, 128.4 (C ×2), 128.3 (C ×2), 128.3 (C ×2), 127.8 (C ×2), 127.7 (C ×2), 127.6, 127.6, 127.6 (C ×3), 95.9, 95.3, 94.2, 81.6, 80.3, 78.0, 74.5, 74.1, 73.3, 70.1, 70.1, 69.7, 45.6, 41.5, 40.6, 38.5, 26.1 (C ×3), 18.5, 16.7, 15.1, 13.6, 12.8, 10.6, 9.9, –3.8, –4.2; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4583.

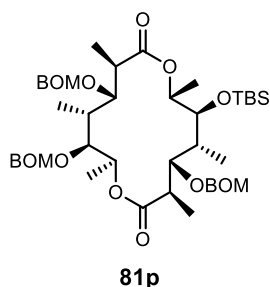


(3*R*,4*S*,5*R*,6*S*,7*R*,10*S*,11*R*,12*S*,13*R*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81n**); According to the procedure of **4.2.14.**, **79n** (136 mg, 156 μ mol) was converted to **81n** (87.6 mg, 66%) as a colorless oil; $[\alpha]_D^{25} +3.6$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹ 3062, 2939, 2885, 1728, 1458, 1250, 1026, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.38–7.25 (complex m, 15H), 4.86–4.78 (complex m, 4H), 4.77–4.69 (complex m, 4H), 4.66–4.62 (complex m, 4H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 3.72 (dd, *J* = 10.3, 2.3 Hz, 1H), 3.70 (app d, *J* = 10.3 Hz, 1H), 3.49–3.45 (complex m, 2H), 2.87 (dq, *J* = 10.3, 10.3 Hz, 1H), 2.72 (dq, *J* = 9.7, 9.7 Hz, 1H), 2.15 (m, 1H), 2.03 (m, 1H), 1.30 (d, *J* = 6.9 Hz, 3H), 1.29 (d, *J* = 6.3 Hz, 3H), 1.21–1.17 (complex m, 9H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 173.8, 173.6, 137.9, 137.5, 137.3, 128.4 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 127.8 (C \times 5), 127.7 (C \times 2), 127.7, 127.5, 95.4, 95.0, 94.9, 79.8 (C \times 2), 78.4, 75.2, 74.0, 73.6, 70.2, 69.9, 69.8, 42.6, 41.7, 40.9, 39.1, 26.1 (C \times 3), 18.4, 15.3, 15.0, 13.1, 12.4, 10.9, 10.4, –3.6, –3.8; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4585.



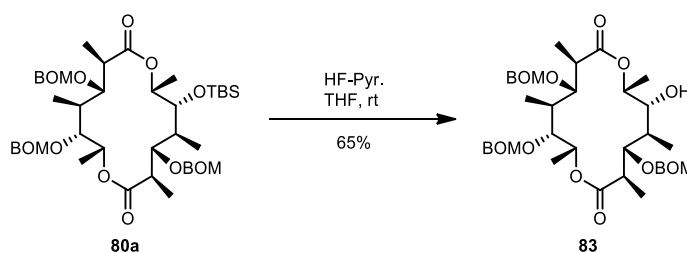
(3*R*,4*S*,5*R*,6*S*,7*R*,10*S*,11*R*,12*R*,13*S*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*t*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81o**); According to the procedure of **4.2.14.**, **79o** (105 mg, 120 μ mol) was converted to **81o** (66.0 mg, 64%) as a colorless oil; $[\alpha]_D^{24} +15.6$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹ 3062, 2939, 2885, 2862, 1728, 1458, 1381, 1250, 1026, 748; ¹H NMR (500 MHz, CDCl₃) δ 7.37–7.27 (complex m, 15H), 5.37 (m, 1H), 4.89 (d, *J* = 6.9 Hz, 1H), 4.85 (m, 1H), 4.82–4.76 (complex m, 5H), 4.71–4.60 (complex m, 5H), 4.54 (d, *J* = 12.0 Hz, 1H), 3.81 (app br s, 1H), 3.73 (d, *J* = 9.7 Hz, 2H), 3.56 (d, *J* = 8.6 Hz, 1H), 2.86 (m, 1H), 2.78 (m, 1H), 1.88 (app br s, 1H), 1.70 (app dd, *J* = 6.9, 6.9 Hz, 1H), 1.31 (d, *J* = 6.9 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.19 (d, *J* = 6.3 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 3H), 1.07 (d, *J* = 6.3 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 0.17 (s, 3H), 0.12 (s, 3H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 173.8, 172.8, 138.1, 138.0, 137.6, 128.4 (C \times 4), 128.4 (C \times 2), 127.8 (C \times 2), 127.7, 127.7 (C \times 4), 127.6, 127.6, 97.6, 96.9, 96.3, 83.0, 82.8, 82.3, 73.5, 72.6, 70.5, 70.5, 70.4, 70.3, 46.0, 43.8, 39.6, 38.3, 26.2 (C \times 3), 18.5, 16.6, 16.1, 15.3, 15.1, 11.0, 9.8, –3.3, –3.3; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found

873.4584.



(3*R*,4*S*,5*R*,6*S*,7*R*,10*R*,11*S*,12*R*,13*S*,14*S*)-4,11,13-Tris[(benzyloxy)methoxy]-6-[(*tert*-butyldimethylsilyl)oxy]-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**81p**); According to the procedure of **4.2.14.**, **79p** (160 mg, 184 μ mol) was converted to **81p** (76.5 mg, 49%) as a colorless oil; $[\alpha]_D^{27} +23.2$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 2939, 2885, 1728, 1458, 1381, 1026, 741; ¹H NMR (500 MHz, CDCl₃) δ 7.37–7.27 (complex m, 15H), 5.13 (dq, *J* = 6.3, 4.0 Hz, 1H), 4.93 (d, *J* = 6.9 Hz, 1H), 4.83 (d, *J* = 6.9 Hz, 1H), 4.81 (d, *J* = 7.5 Hz, 1H), 4.78 (d, *J* = 6.3 Hz, 1H), 4.76 (d, *J* = 5.7 Hz, 1H), 4.74–4.73 (complex m, 3H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 3.87–3.83 (complex m, 2H), 3.74 (d, *J* = 10.3 Hz, 1H), 3.66 (dd, *J* = 8.0, 4.6 Hz, 1H), 2.80 (m, 1H), 2.63 (m, 1H), 2.05 (m, 1H), 1.94 (m, 1H), 1.26–1.23 (complex m, 9H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.17 (d, *J* = 7.5 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 174.5, 174.0, 137.8, 137.7, 137.6, 128.4 (C \times 2), 128.4 (C \times 2), 128.4 (C \times 2), 127.9 (C \times 2), 127.7 (C \times 4), 127.6 (C \times 2), 127.6, 96.8, 95.8, 95.3, 84.7, 80.4, 76.4, 74.2, 73.8, 72.0, 70.2 (C \times 2), 70.0, 44.0, 42.4 (C \times 2), 36.5, 26.1 (C \times 3), 18.4, 17.6, 16.1, 15.6, 14.2, 13.6, 12.5, –3.7, –3.7; HRMS-ESI (*m/z*); [M+Na]⁺ calcd for C₄₈H₇₀O₁₁SiNa, 873.4585; found 873.4560.

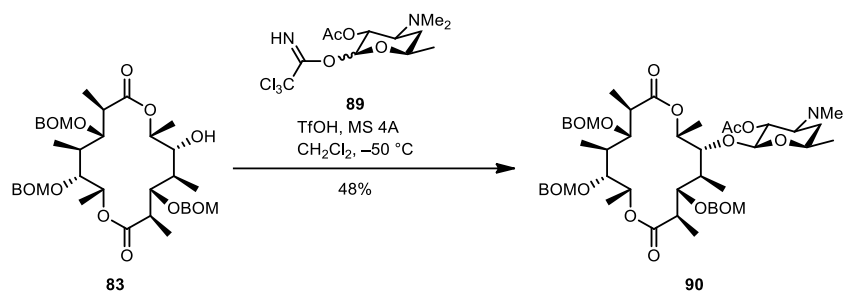
4.15. (3*R*,4*S*,5*S*,6*R*,7*R*,10*R*,11*S*,12*S*,13*R*,14*R*)-3,6,11-Tris[(benzyloxy)methoxy]-13-hydroxy-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,9-dione (**83**);



To a plastic centrifuge tube in THF (1.2 mL) solution of substrate **80a** (35.4 mg, 41.6 μ mol) was added 70% HF·Pyr. (200 μ L) under N₂ at 0 °C. The reaction mixture was stirred for 28 h at room temperature. The reaction mixture was diluted with CH₂Cl₂ (5.0 mL) and quenched by the addition to cold sat. aq. NaHCO₃ (15 mL). The mixture was then poured into water (5 mL) and resulted two layers were separated and the aqueous phase was extracted with CH₂Cl₂ (10 mL \times 3). The combined organic layers were washed with water and brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 4/1 to 2/1) to afford macrodiolide **83** (20.0 mg, 65%) as a colorless oil; $[\alpha]_D^{25} -49.6$ (*c* 1.00, CHCl₃); IR (neat)/cm⁻¹: 3410, 3379, 3062, 3032, 2970, 2939, 2885, 1728, 1450, 1373, 1165, 1088, 1018,

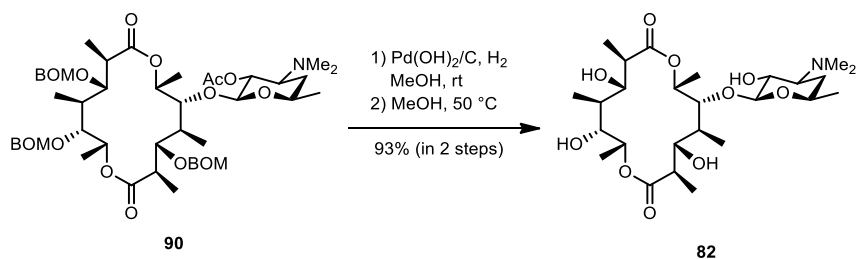
733; ^1H NMR (500 MHz, CDCl_3) δ 7.37–7.24 (complex m, 15H), 5.23–5.15 (complex m, 2H), 4.84 (d, J = 6.9 Hz, 1H), 4.83–4.74 (complex m, 6H), 4.71–4.65 (complex m, 3H), 4.53 (d, J = 11.5 Hz, 2H), 3.73 (d, J = 10.3 Hz, 1H), 3.71 (d, J = 10.3 Hz, 1H), 3.66 (d, J = 9.7 Hz, 1H), 3.51 (m, 1H), 2.81 (m, 1H), 2.75 (m, 1H), 1.62 (m, 1H), 1.44 (m, 1H), 1.19 (d, J = 6.9 Hz, 3H), 1.17 (d, J = 6.9 Hz, 3H), 1.16 (d, J = 6.3 Hz, 3H), 1.13 (d, J = 6.3 Hz, 3H), 1.09 (d, J = 6.9 Hz, 3H), 1.08 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.9, 174.2, 137.9, 137.5, 137.3, 128.5 (C \times 2), 128.3 (C \times 4), 127.8, 127.8 (C \times 2), 127.6, 127.5, 127.5 (C \times 2), 127.5 (C \times 2), 96.9, 96.8, 96.7, 81.3, 81.0, 80.9, 74.4, 70.7, 70.5, 70.2, 70.1, 70.0, 44.4 (C \times 2), 40.2, 39.4, 17.3, 16.8, 14.8, 14.7, 9.9, 9.6; HRMS-ESI (m/z); $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{42}\text{H}_{56}\text{O}_{11}\text{Na}$, 759.3720; found 759.3720.

4.16. Protected macrodiolide (**90**);



To a mixture of trichloroacetimidate **89** (35.3 mg, 97.6 μmol), macrodiolide aglycone **83** (29.5 mg, 40.0 μmol) and molecular sieves 4Å powder (228 mg) were dissolved in CH_2Cl_2 (2.0 mL) and stirred under N_2 at room temperature. After stirring for 1 h, the mixture was cooled to $-50\text{ }^\circ\text{C}$ and then TfOH (13.0 μL , 147 μmol) was added. The resulting mixture was stirred for 26 h at $-50\text{ }^\circ\text{C}$. The reaction was quenched with NaHCO_3 (150 mg) at $0\text{ }^\circ\text{C}$. After filtration through a pad of Celite with $\text{CHCl}_3/\text{MeOH}$ (v/v, 10/1, 10 mL \times 3), the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc/MeOH = 20/1 to 15/1) to afford macrodiolide **90** (18.0 mg, 48%) as a yellow oil; $[\alpha]_{\text{D}}^{24}$ -36.0 (c 0.20, CHCl_3); IR (neat)/ cm^{-1} : 3062, 2978, 2939, 2885, 1728, 1458, 1373, 1165, 1018, 748; ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.24 (complex m, 15H), 5.19 (q, J = 6.3 Hz, 2H), 4.88–4.82 (complex m, 3H), 4.79–4.70 (complex m, 6H), 4.68 (d, J = 12.0 Hz, 1H), 4.63 (d, J = 12.0 Hz, 1H), 4.54 (d, J = 12.6 Hz, 1H), 4.52 (d, J = 12.0 Hz, 1H), 4.31 (d, J = 7.5 Hz, 1H), 3.74 (d, J = 9.7 Hz, 1H), 3.70 (d, J = 10.3 Hz, 1H), 3.67 (dd, J = 9.7, 6.3 Hz, 2H), 3.20 (m, 1H), 2.85–2.72 (complex m, 3H), 2.38 (brs, 6H), 2.11 (s, 3H), 1.73–1.64 (complex m, 2H), 1.36–1.24 (complex m, 2H), 1.22 (d, J = 6.3 Hz, 3H) 1.20–1.16 (complex m, 9H), 1.08–1.04 (complex m, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.5, 174.4, 169.8, 137.9, 137.6, 137.6, 128.5 (C \times 2), 128.4 (C \times 2), 128.3 (C \times 2), 127.7, 127.6, 127.5, 127.5 (C \times 2), 127.5 (C \times 2), 127.3 (C \times 2), 101.9, 97.0, 96.9, 96.5, 81.6, 81.3, 80.9, 79.8, 70.4 (C \times 2), 70.4, 70.1, 70.0, 69.8, 68.6, 63.4, 44.2, 44.1, 40.5 (C \times 2), 39.7, 39.2, 30.6, 21.3, 20.9, 17.3, 17.1, 14.7 (C \times 2), 9.4, 9.3; HRMS-ESI (m/z); $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{52}\text{H}_{74}\text{NO}_{14}$, 936.5109; found 936.5100.

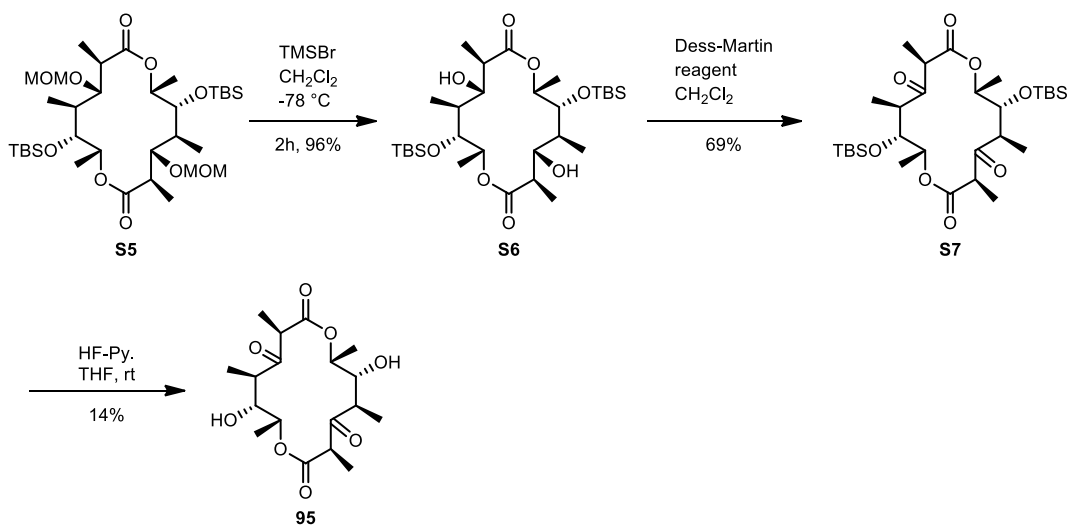
4.17. Macrolide (82)



To a solution of macroide **90** (15.4 mg, 16.5 μmol) in MeOH (1.0 mL) was added Pearlman's catalyst 20% on carbon (wetted with ca. 50% water, 8.0 mg, 5.70 μmol) at 0 °C. The mixture was purged with H₂ under 1 atm at room temperature. After stirring for 22 h, the mixture was filtered through a pad of Celite with CHCl₃/MeOH (v/v, 10/1, 10 mL \times 3) and the filtrate was concentrated *in vacuo*. The resulting crude product was used for subsequent reaction without further purification.

The crude product was dissolved in MeOH (1.5 mL). This mixture was heated to 50 °C and stirred for 4.5 h. The mixture was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (CHCl₃/MeOH = 8/1, 5/1 to 3/1) to afford macrodiolide **82** (8.2 mg, 93%) as a colorless oil; $[\alpha]_{\text{D}}^{23} - 4.4$ (c 0.21, MeOH); IR (neat)/cm⁻¹: 3417, 2978, 2939, 2877, 1728, 1705, 1458, 1373, 1265, 1165, 1026, 756; ¹H NMR (500 MHz, CD₃OD) δ 5.08 (q, J = 6.3 Hz, 1H), 5.05 (m, 1H), 4.32 (d, J = 7.5 Hz, 1H), 3.81 (dd, J = 6.9, 2.9 Hz, 1H), 3.57 (m, 1H), 3.55 (d, J = 10.3 Hz, 1H), 3.52 (d, J = 10.3 Hz, 1H), 3.43 (d, J = 9.7 Hz, 1H), 3.35 (dd, J = 10.3, 7.5 Hz, 1H), 2.74–2.66 (complex m, 2H), 2.61 (dq, J = 9.7, 6.9 Hz, 1H), 2.38 (s, 6H), 1.78 (ddd, J = 12.9, 4.0, 1.7 Hz, 1H), 1.71 (dq, J = 6.9, 6.9 Hz, 1H), 1.63 (m, 1H), 1.31–1.27 (complex m, 7H), 1.22 (d, J = 5.7 Hz, 3H), 1.17 (d, J = 6.9 Hz, 3H), 1.17 (d, J = 6.9 Hz, 3H), 1.09 (d, J = 7.5 Hz, 3H), 1.00 (d, J = 6.9 Hz, 3H); ¹³C NMR (125 MHz, CD₃OD) δ 177.0, 177.0, 106.0, 82.3, 76.0, 75.5, 73.6, 73.3, 71.9, 71.5, 70.3, 65.8, 45.4, 45.1, 40.9 (C \times 2), 40.7, 40.2, 32.1, 21.4, 17.6, 17.3, 15.3, 14.9, 9.4, 8.7; HRMS-ESI (m/z); [M+Na]⁺ calcd for C₂₆H₄₇NO₁₀Na, 556.3098; found 556.3095.

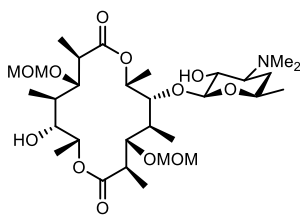
4.18. (3*R*,5*S*,6*R*,7*R*,10*R*,12*S*,13*R*,14*R*)-6,13-hydroxy-3,5,7,10,12,14-hexamethyl-1,8-dioxacyclotetradecane-2,4,9,11-tetraone (**95**)



^1H NMR (500 MHz, CDCl_3) δ 4.96 (q, $J = 6.3$ Hz, 2H), 3.85 (d, $J = 10.3$ Hz, 2H), 3.78 (q, $J = 6.9$ Hz, 1H), 2.77 (m, 2H), 1.37 (d, $J = 6.3$ Hz, 6H), 1.31 (d, $J = 6.9$ Hz, 6H), 1.29 (d, $J = 6.9$ Hz, 6H);

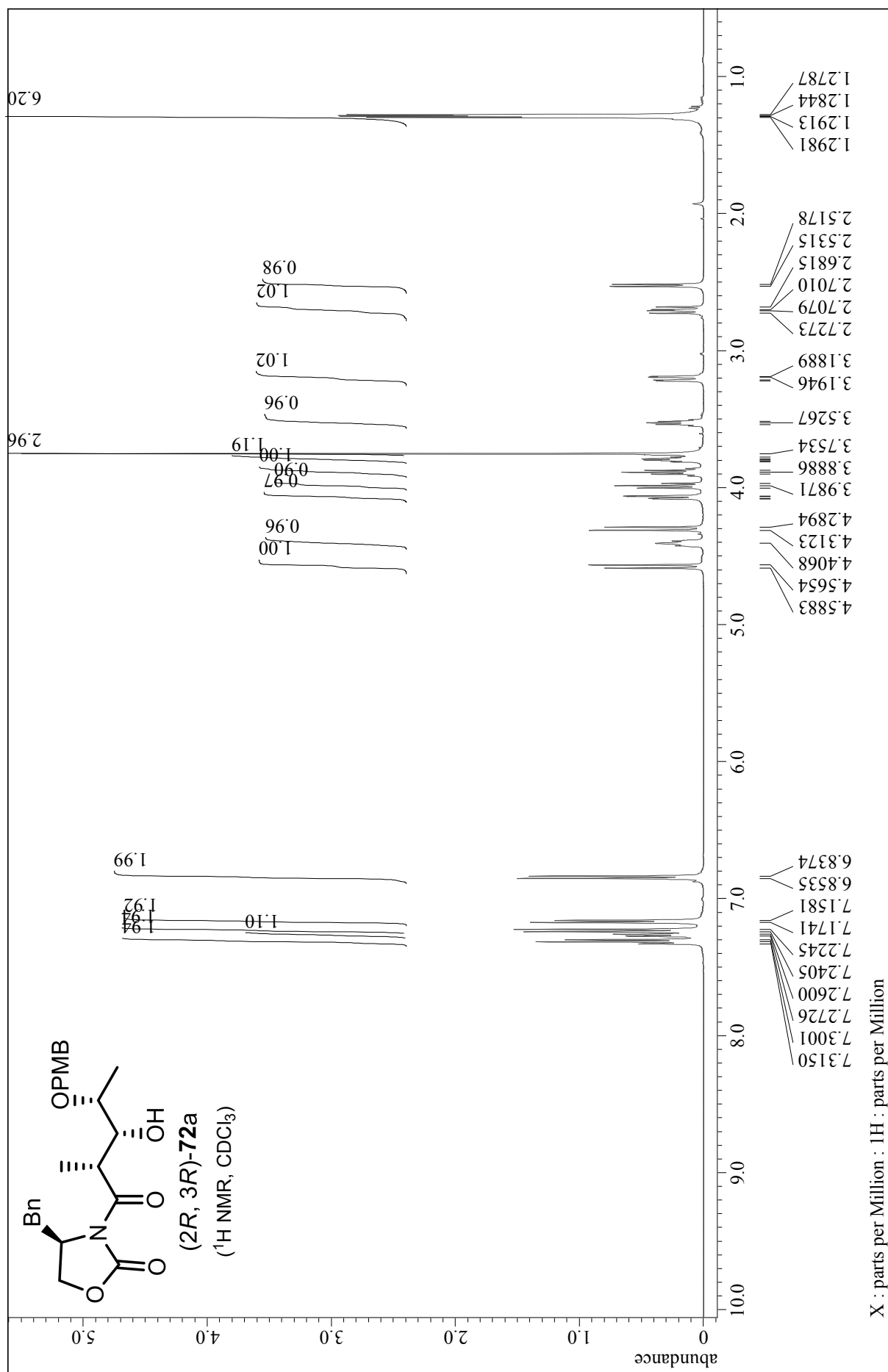
BisTBS 体 (**S7**); ^1H NMR (500 MHz, CDCl_3) δ 5.20 (dq, $J = 6.3, 4.6$ Hz, 2H), 3.93 (dd, $J = 9.2, 4.0$ Hz, 2H), 3.72 (q, $J = 7.5$ Hz, 2H), 3.04 (m, 2H), 1.44 (d, $J = 7.5$ Hz, 6H), 1.26 (d, $J = 6.9$ Hz, 6H), 1.10 (d, $J = 6.9$ Hz, 6H), 0.90 (s, 18H), 0.16 (s, 6H), 0.11 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 206.5 (C \times 2), 169.6 (C \times 2), 72.8 (C \times 2), 71.5 (C \times 2), 53.6 (C \times 2), 43.4 (C \times 2), 25.7 (C \times 6), 18.0 (C \times 2), 15.7 (C \times 2), 13.4 (C \times 2), 12.7 (C \times 2), -4.7 (C \times 2), -4.8 (C \times 2).

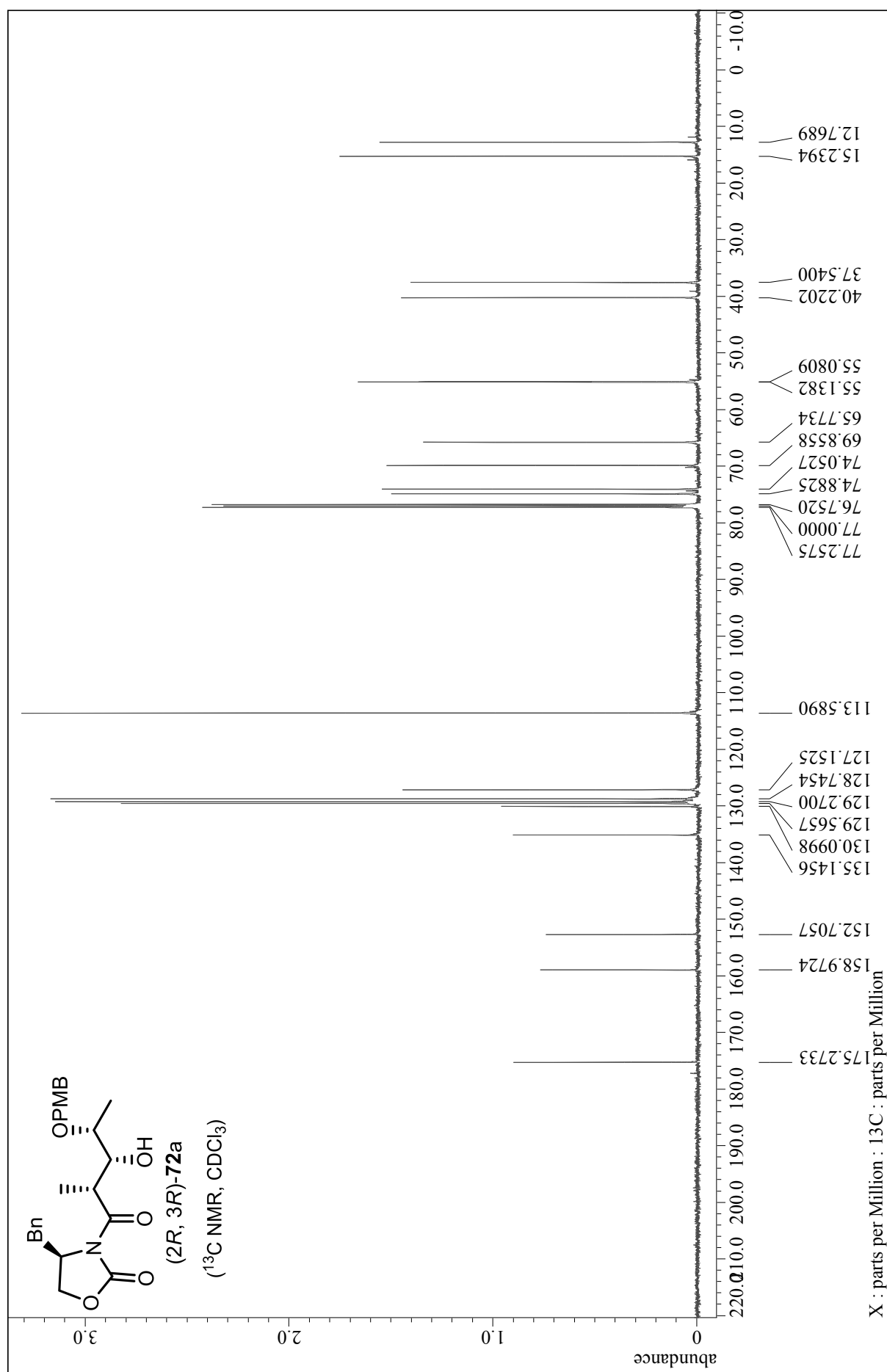
Diol 体 (**S6**); ^1H NMR (500 MHz, CDCl_3) δ 5.09 (q, $J = 6.3$ Hz, 2H), 3.58 (d, $J = 2.9$ Hz, 2H), 3.51 (d, $J = 9.2$ Hz, 2H), 3.38 (q, $J = 6.9$ Hz, 2H), 1.91 (m, 2H), 1.94 (d, $J = 6.9$ Hz, 6H), 1.14 (d, $J = 7.5$ Hz, 6H), 1.05 (d, $J = 6.9$ Hz, 6H), 0.95 (s, 18H), 0.12 (s, 6H), 0.09 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.3 (C \times 2), 77.5 (C \times 2), 72.2 (C \times 2), 67.7 (C \times 2), 41.7 (C \times 2), 40.7 (C \times 2), 25.8 (C \times 6), 18.7 (C \times 2), 18.1 (C \times 2), 14.9 (C \times 2), 11.1 (C \times 2), -3.7 (C \times 2), -5.2 (C \times 2).

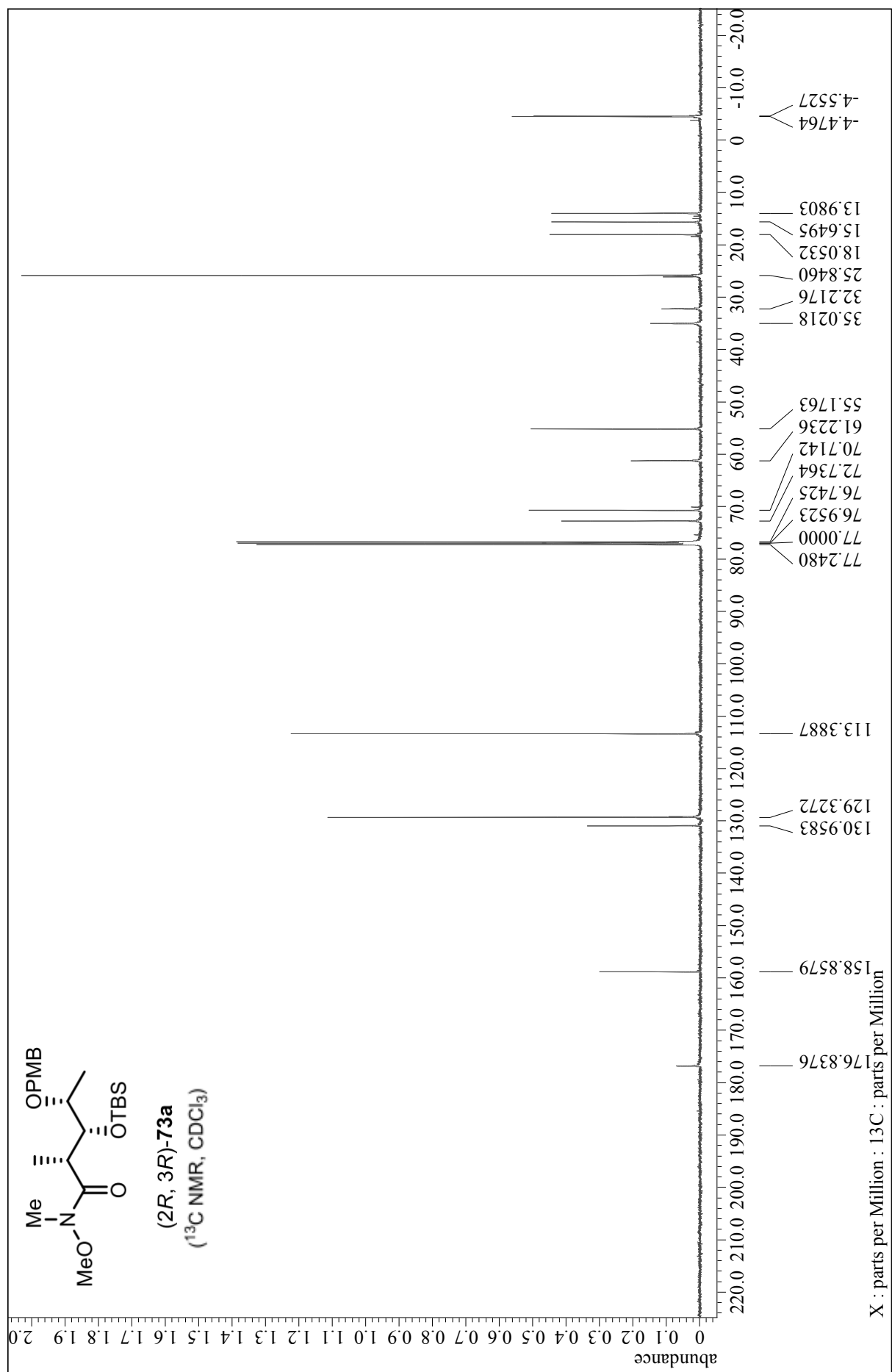


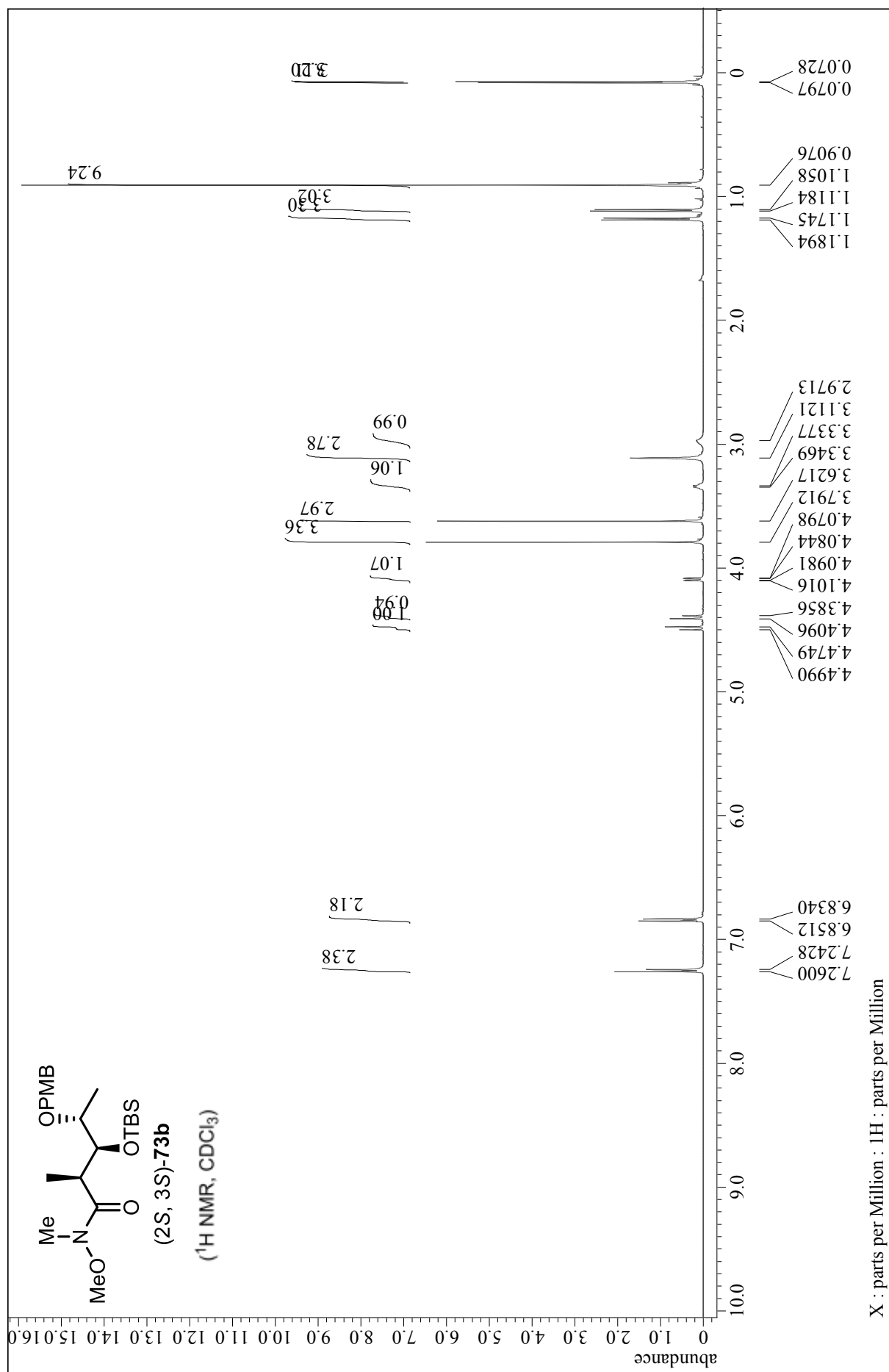
^1H NMR (500 MHz, CDCl_3) δ 5.20 (d

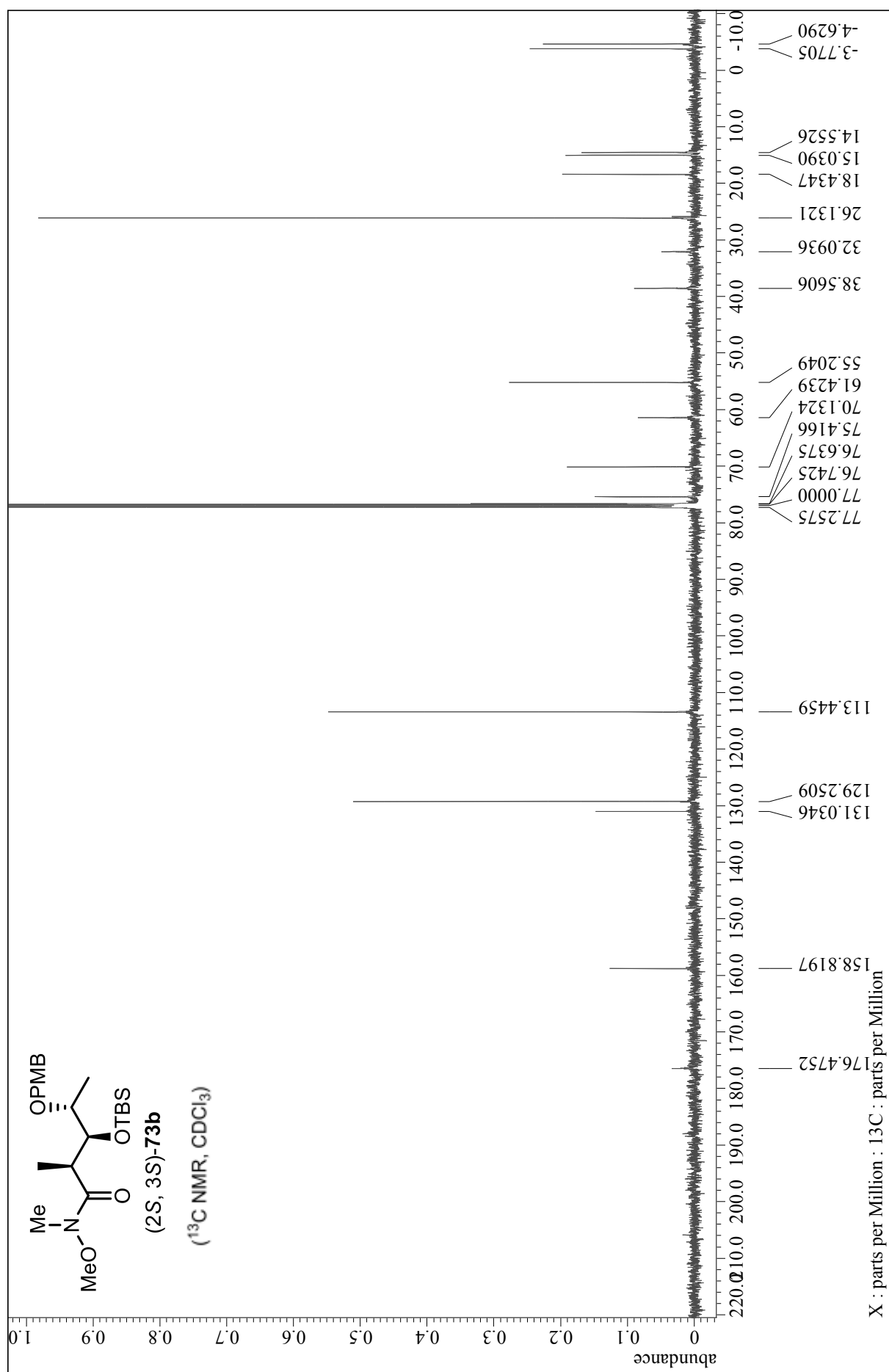
^{13}C NMR (125 MHz, CDCl_3) δ 175.0, 174.1, 103.7, 98.7, 98.6, 80.91, 80.86, 74.7, 70.6, 70.33, 70.28, 69.1, 65.4, 55.9, 55.7, 44.4, 44.3, 40.2, 39.8, 31.9, 29.7 (C \times 2), 21.1, 17.5, 17.1, 14.8, 14.6, 14.51, 9.8, 9.3.

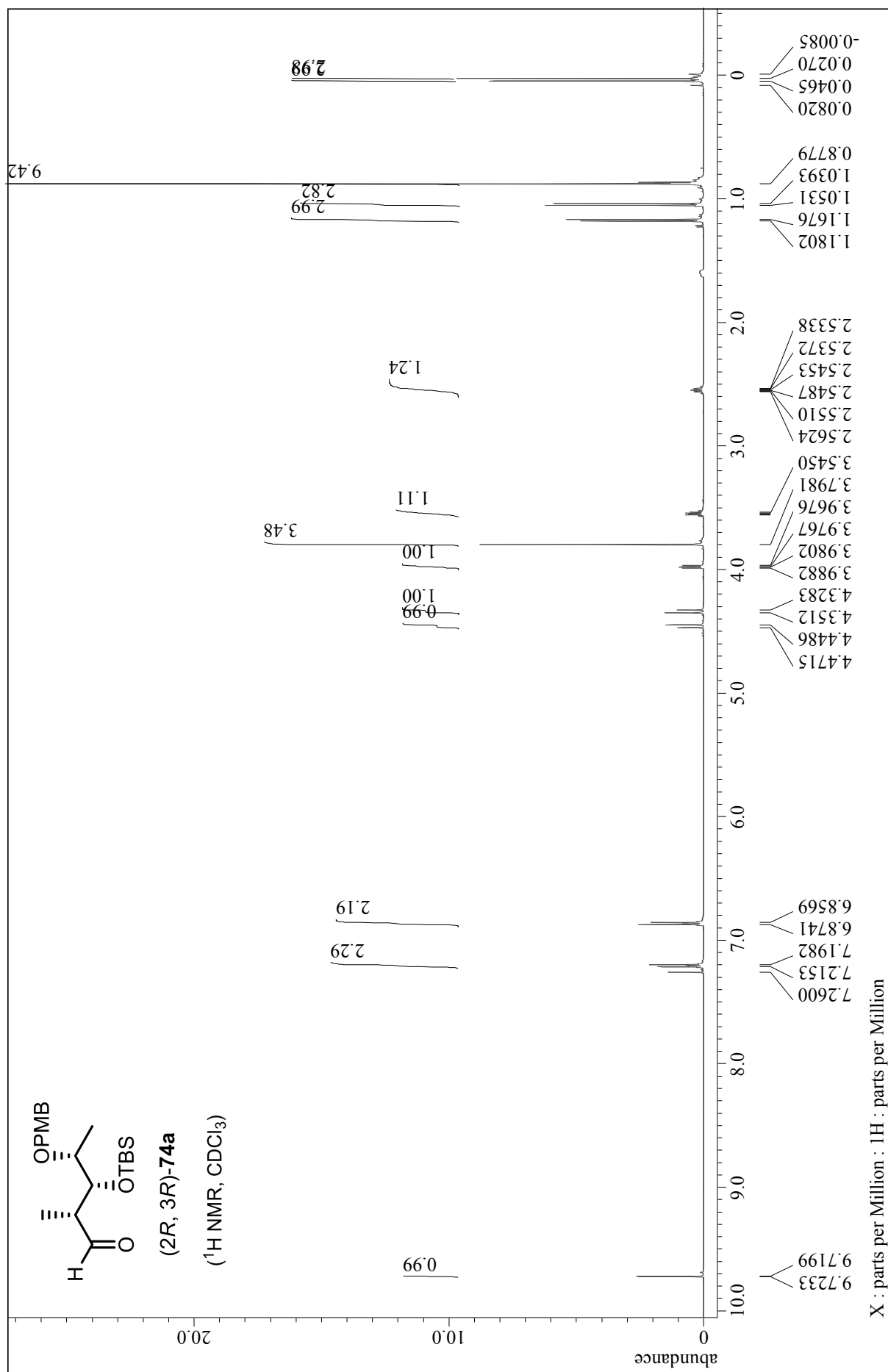


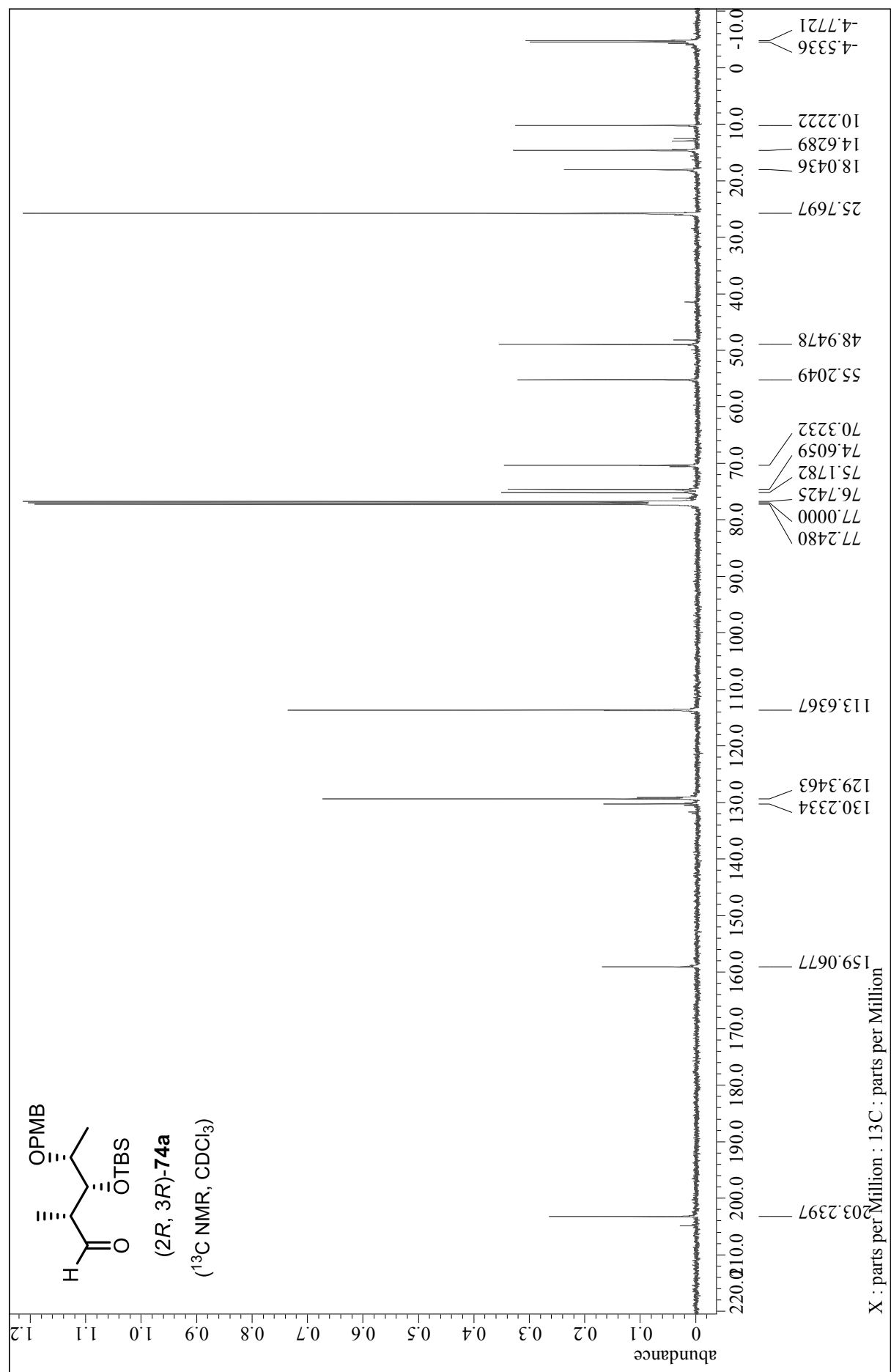


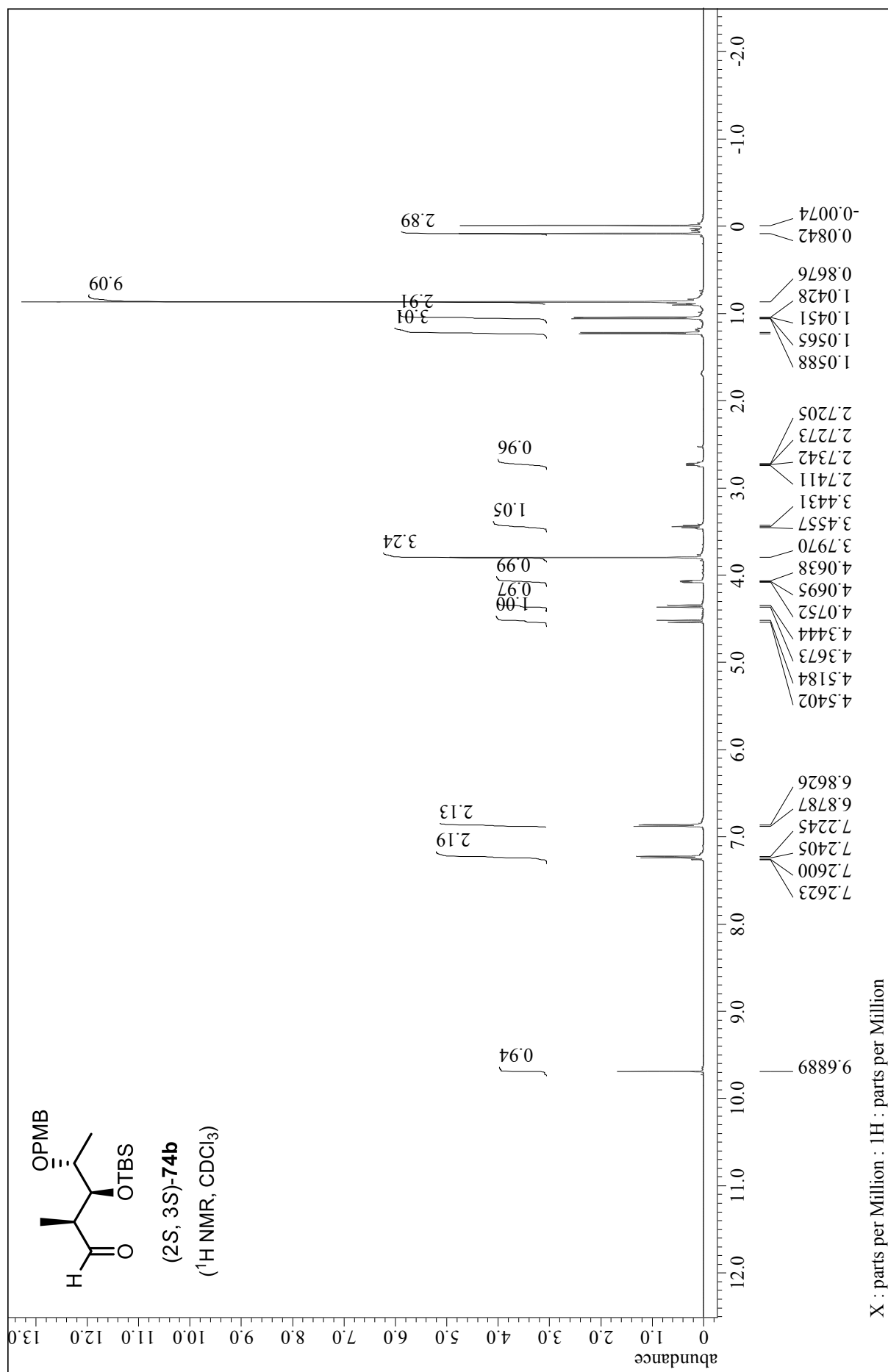


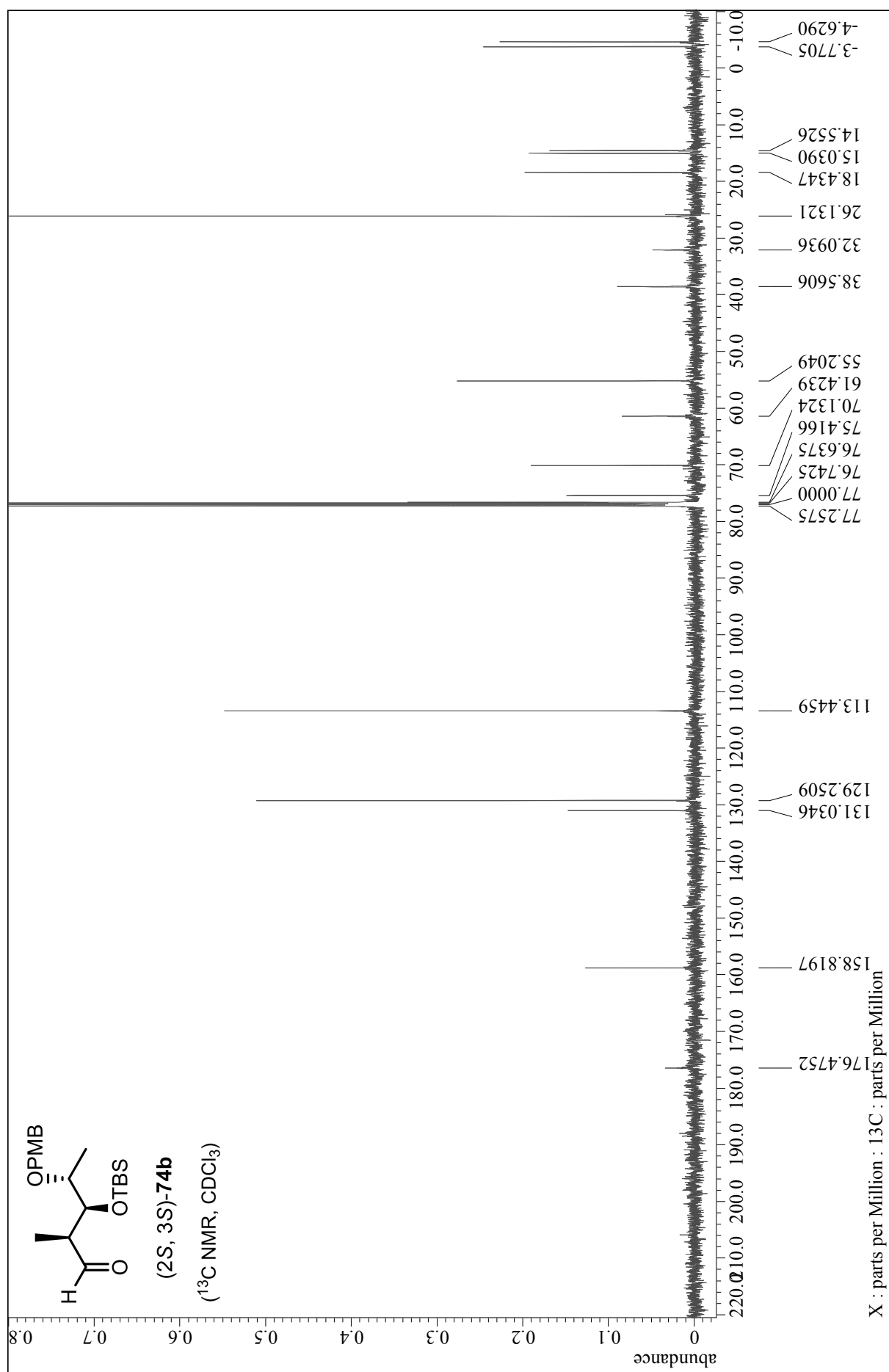


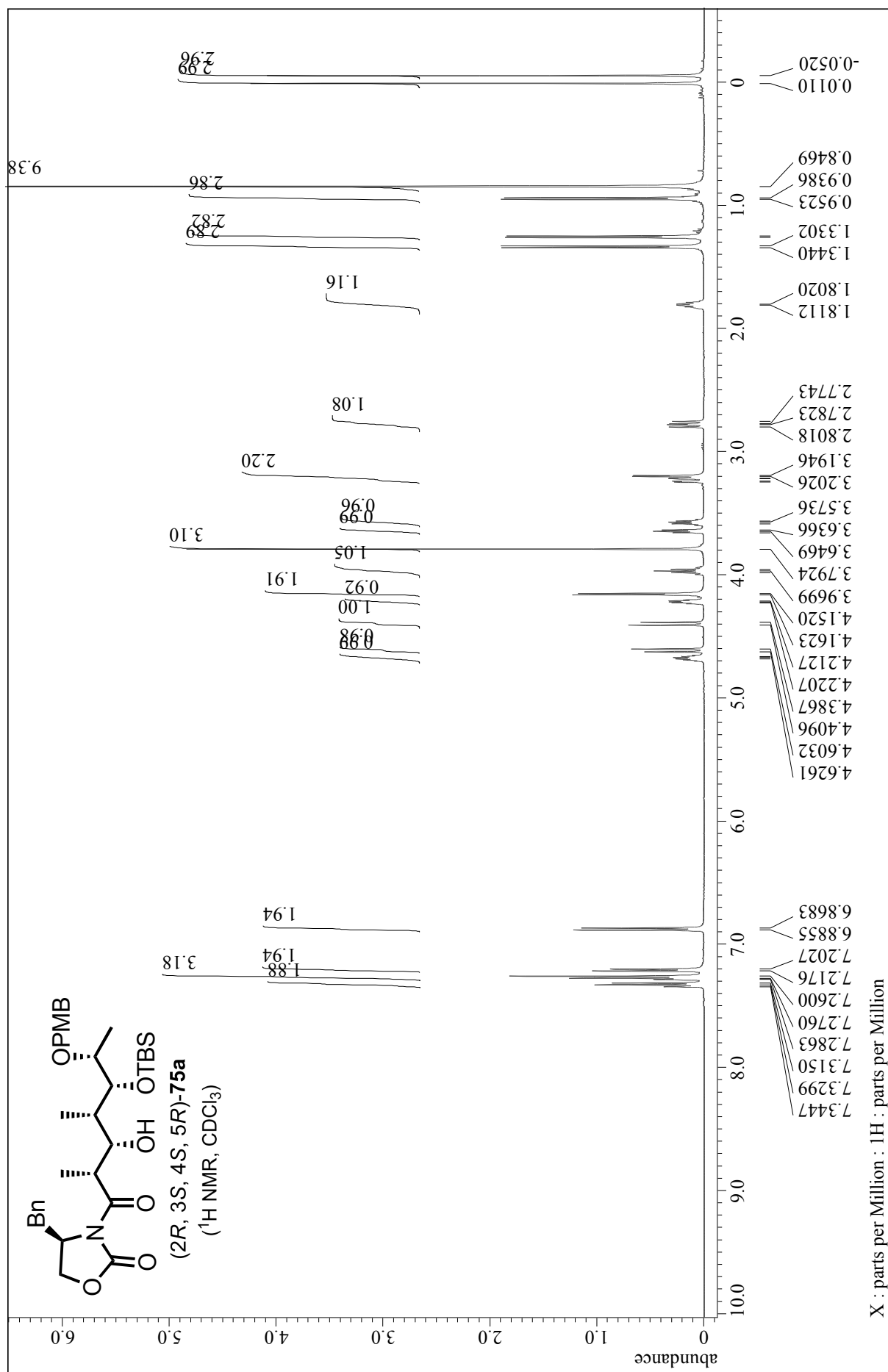


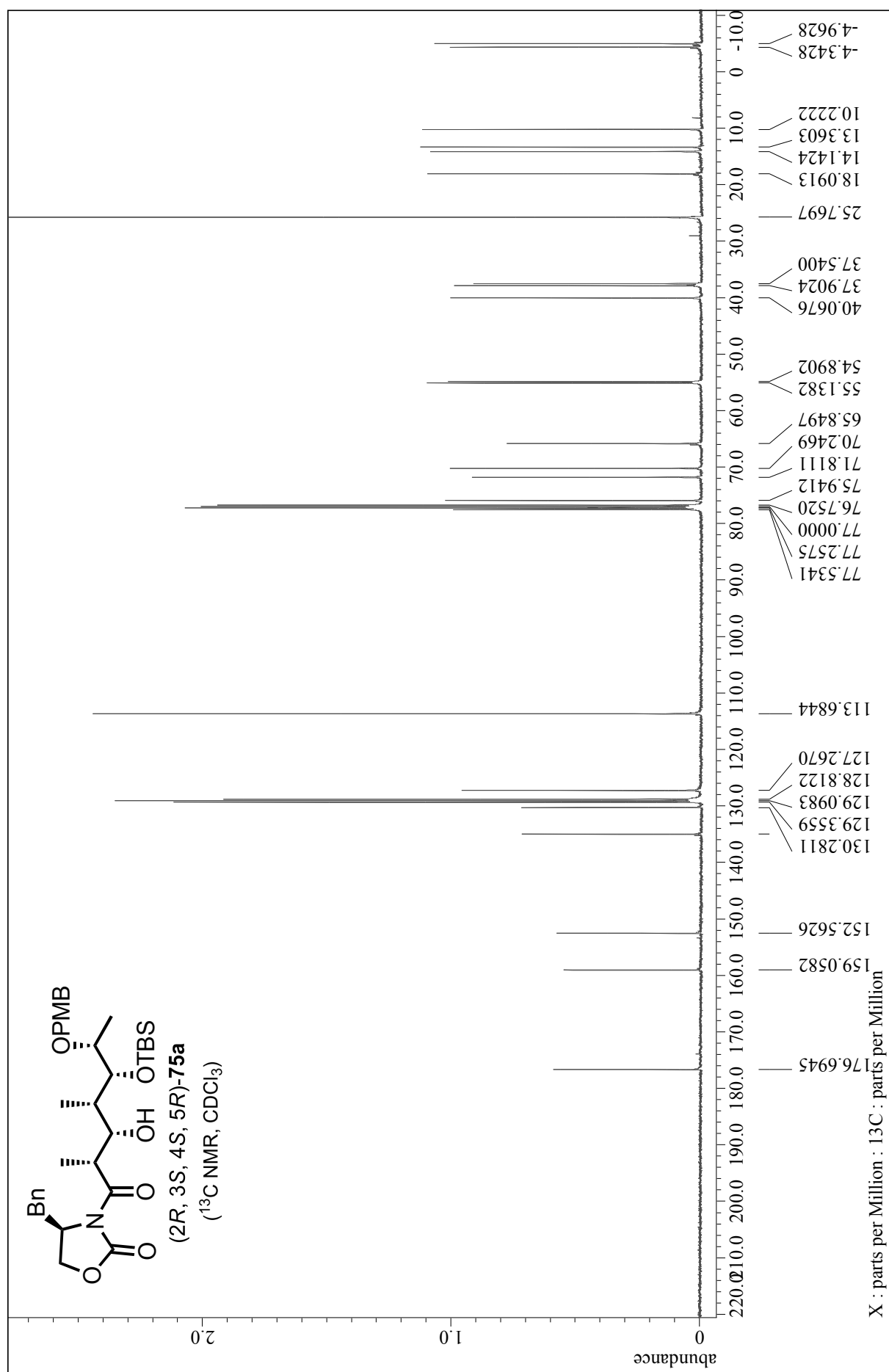


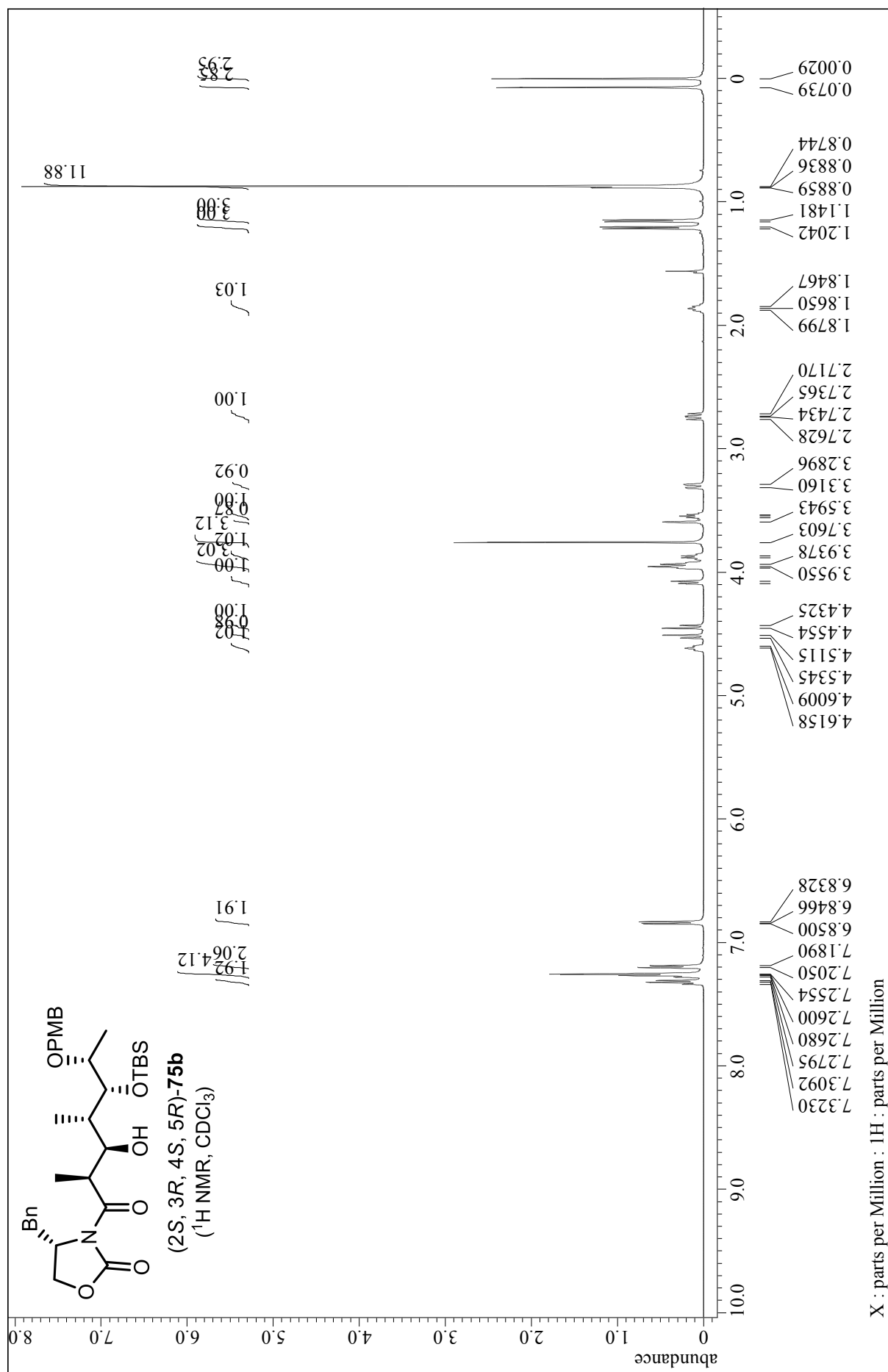


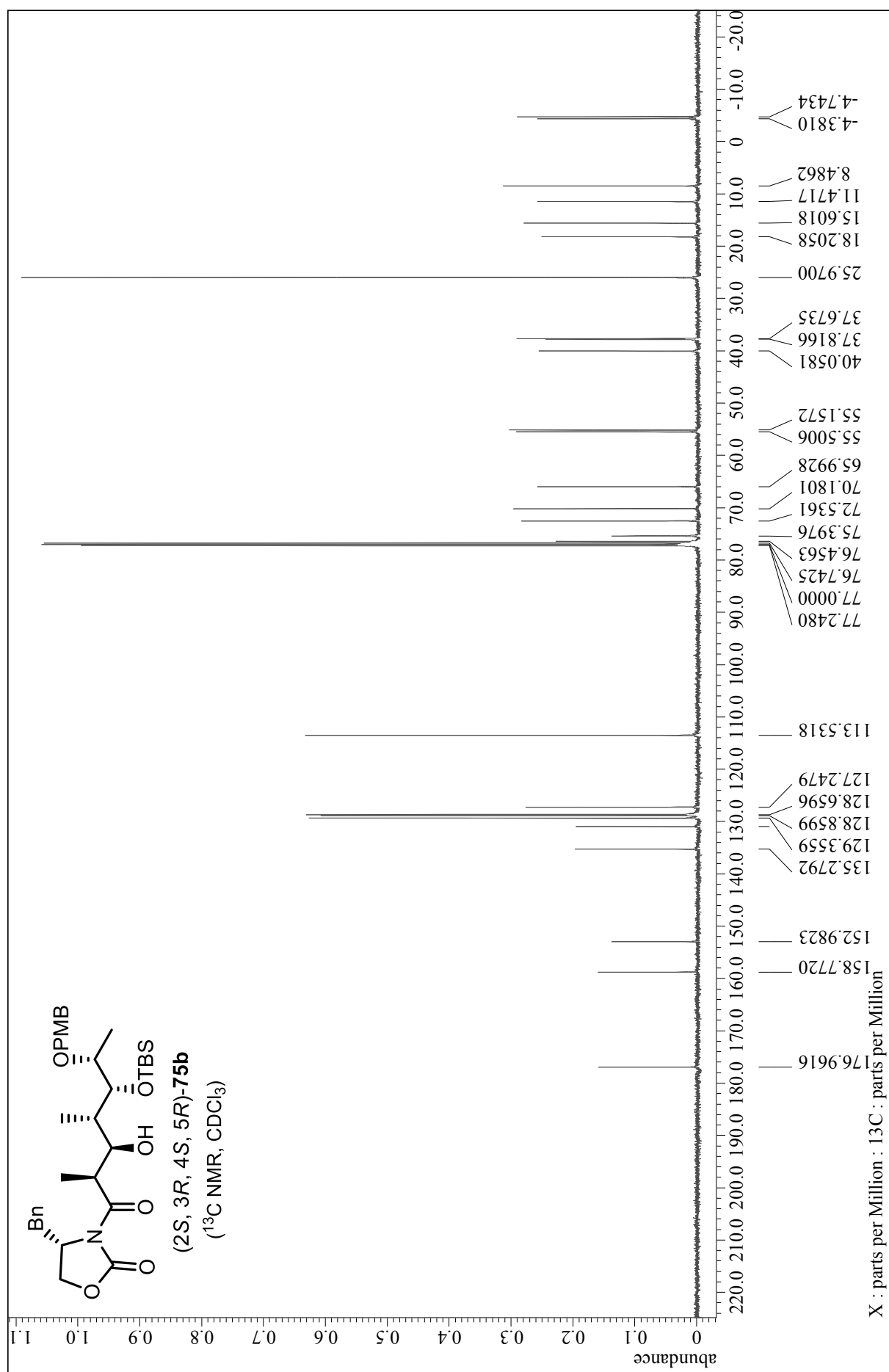


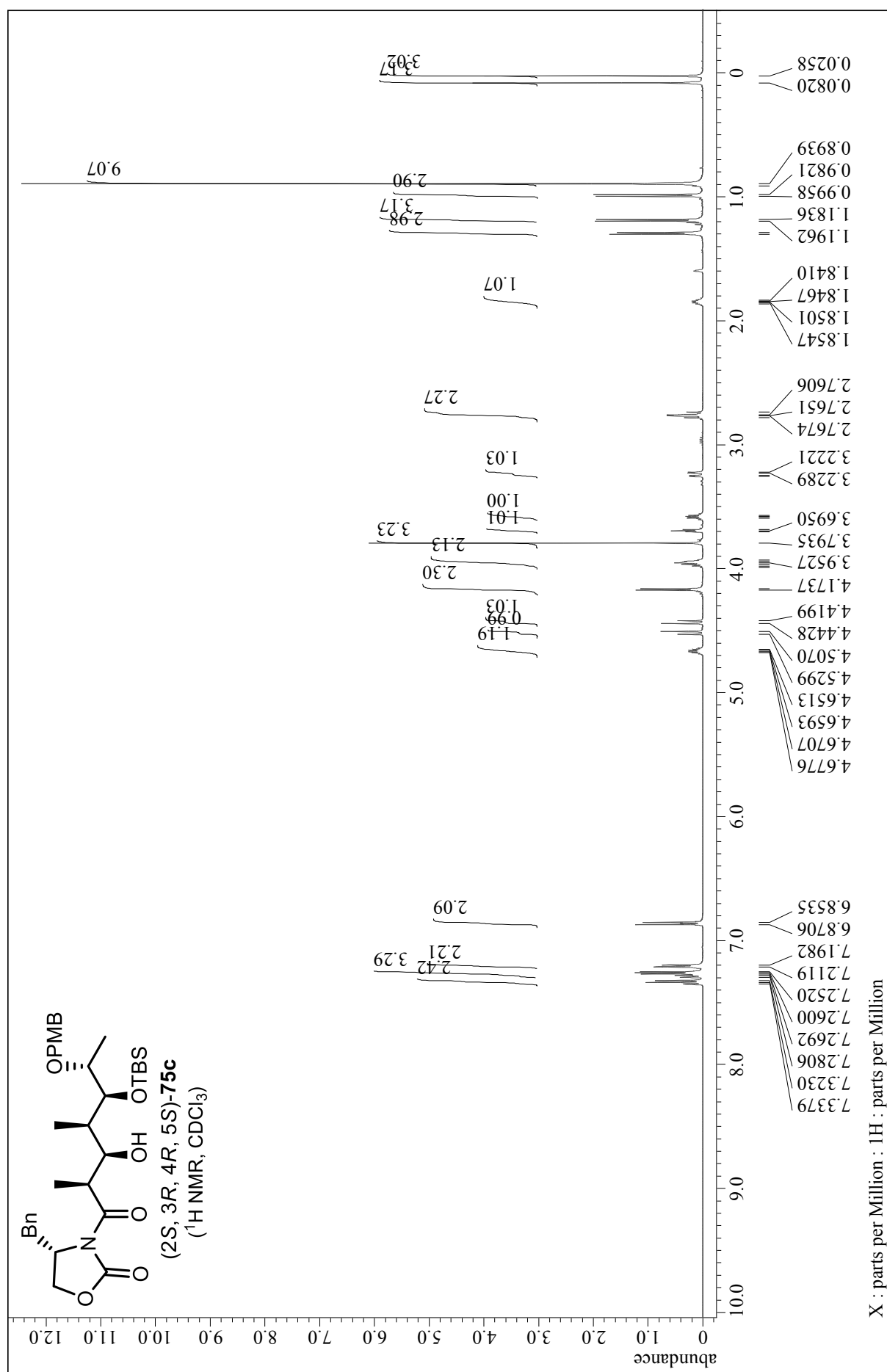


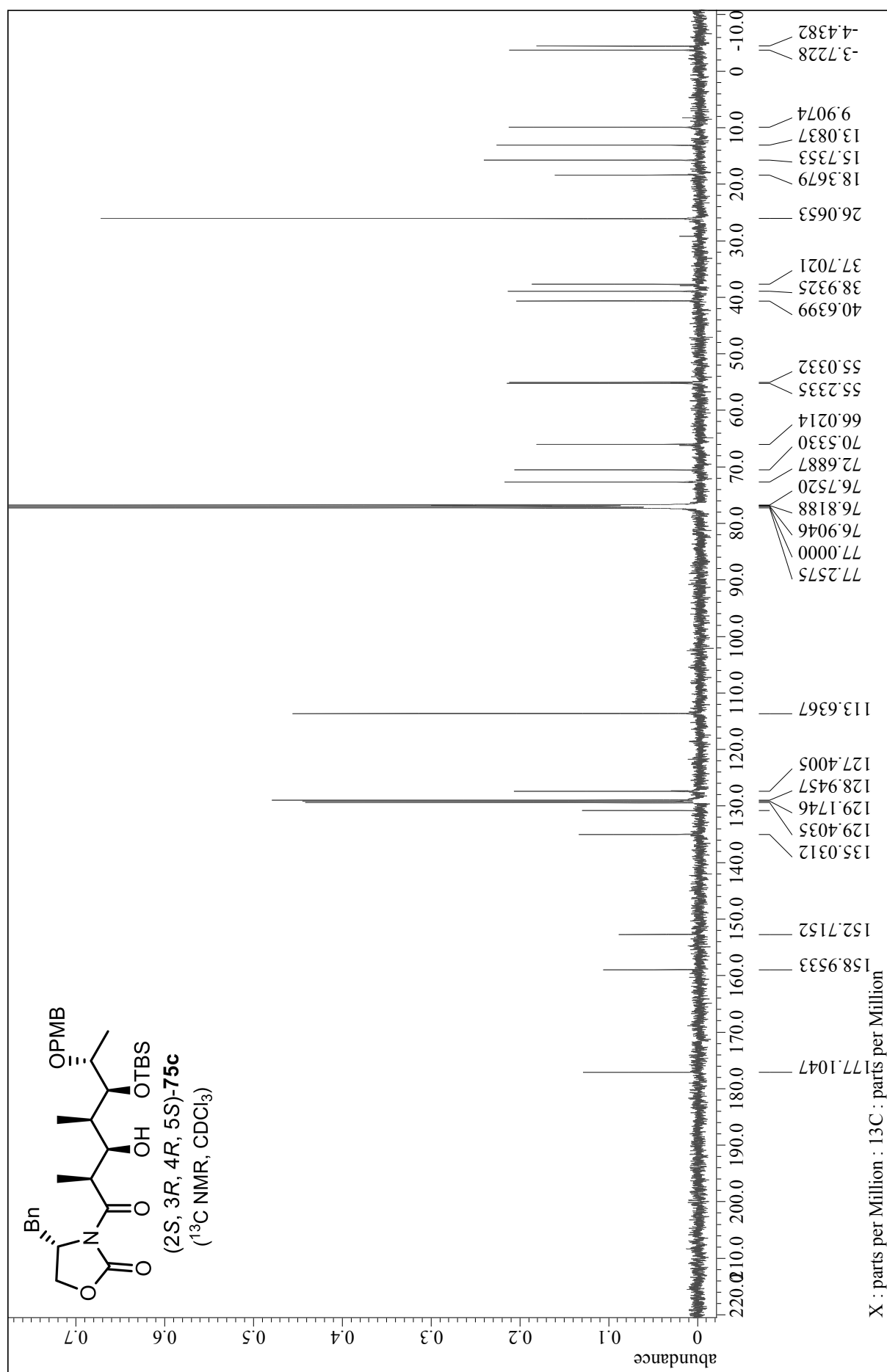


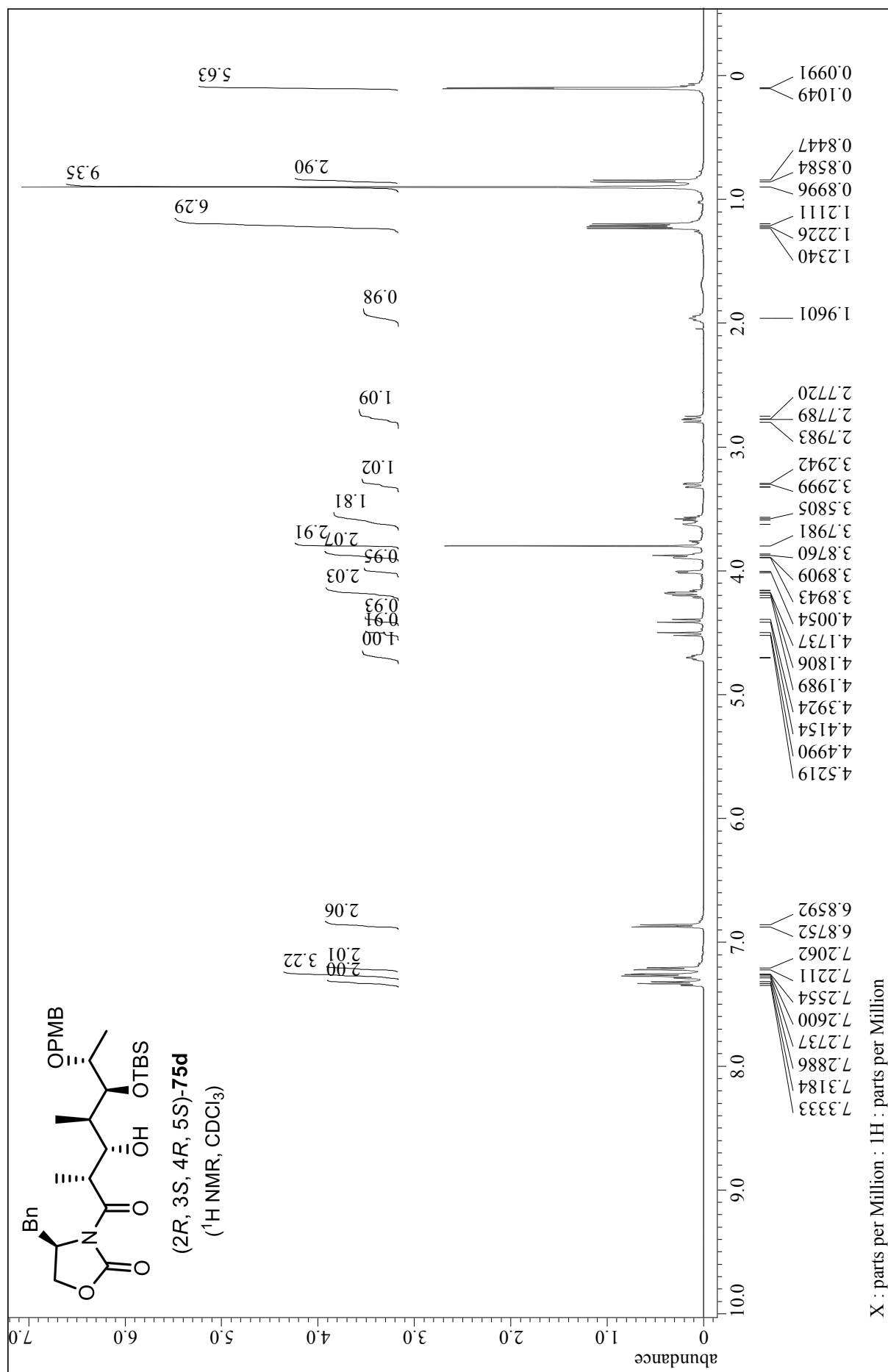


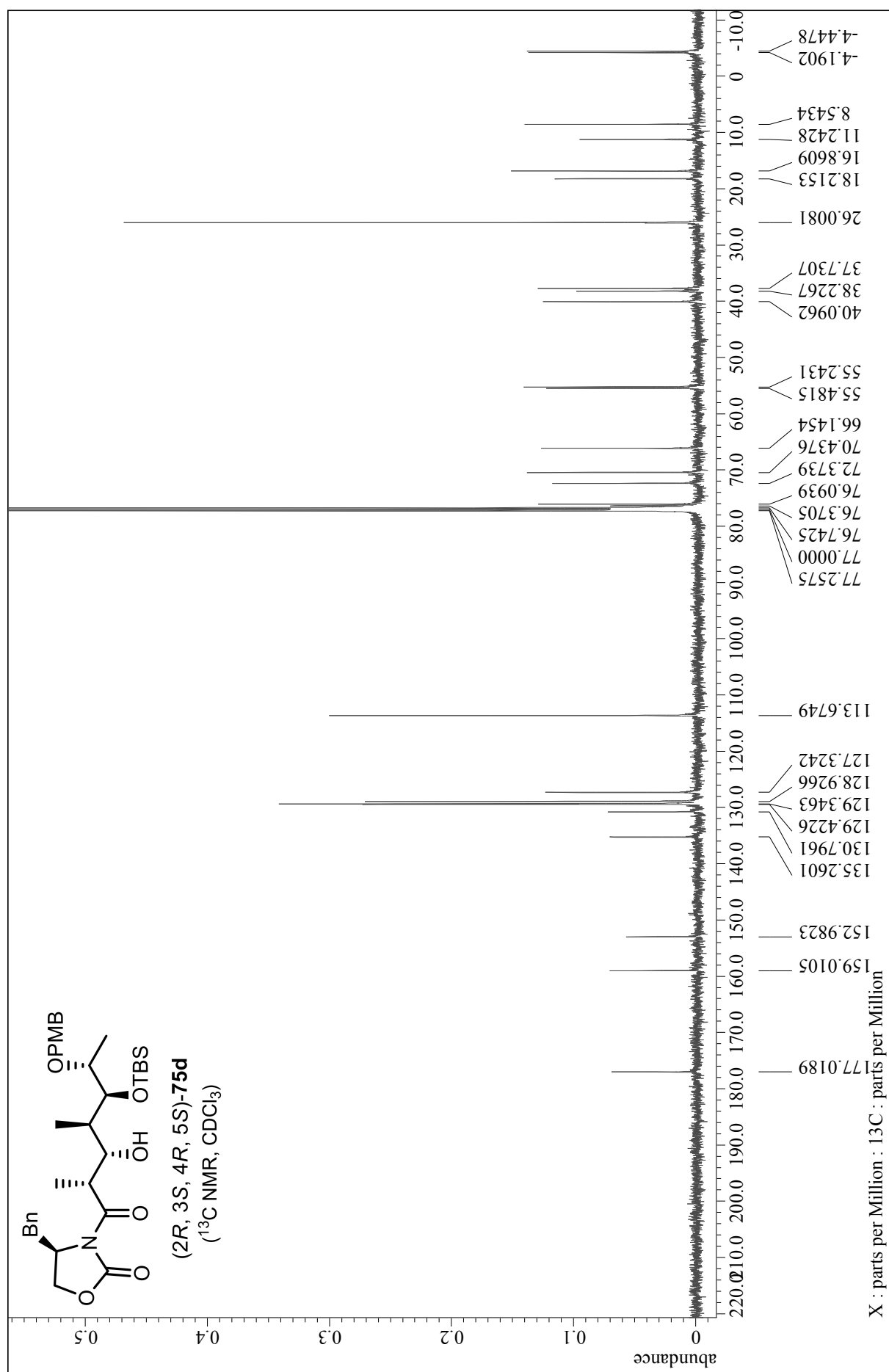


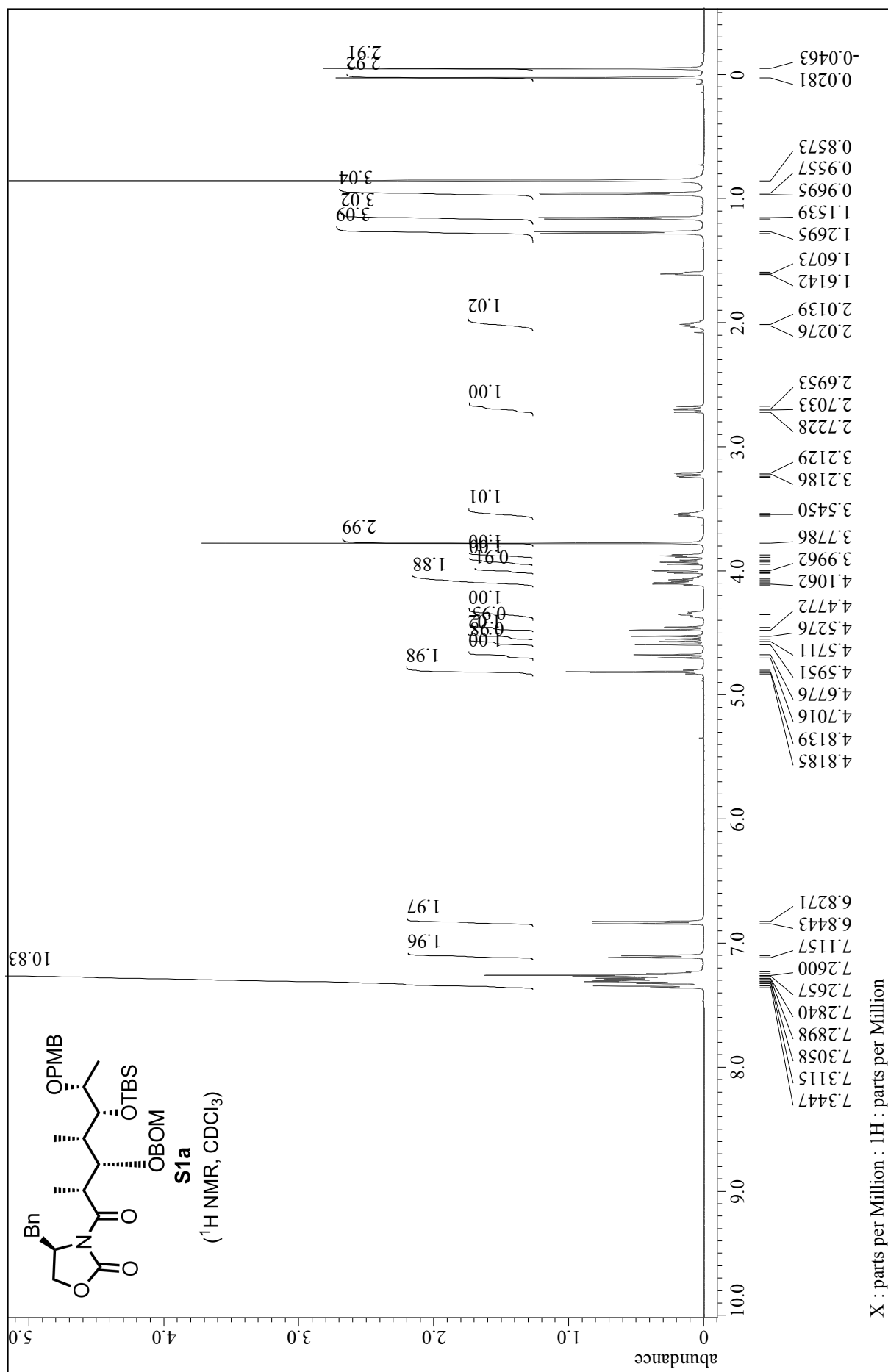


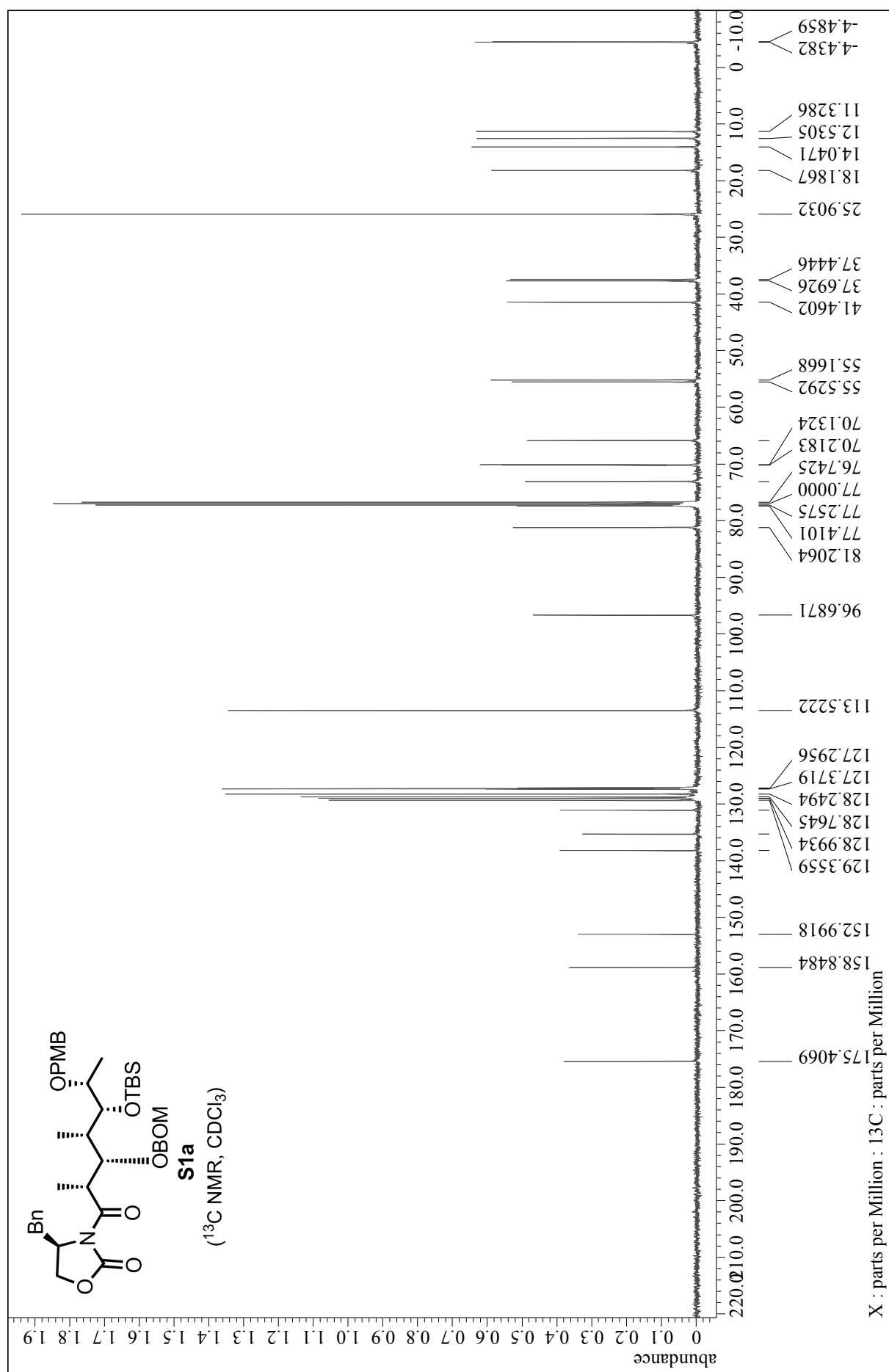


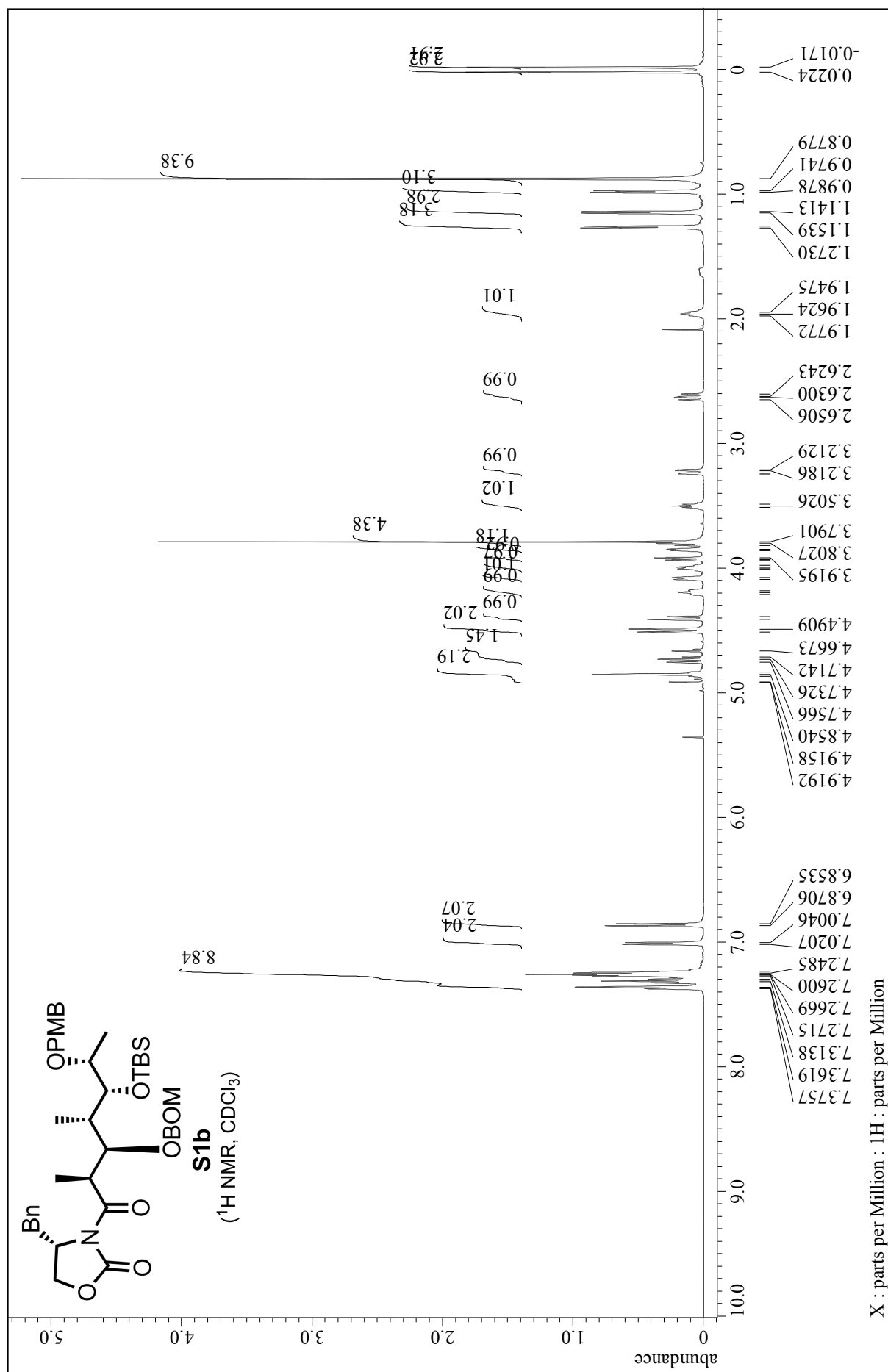


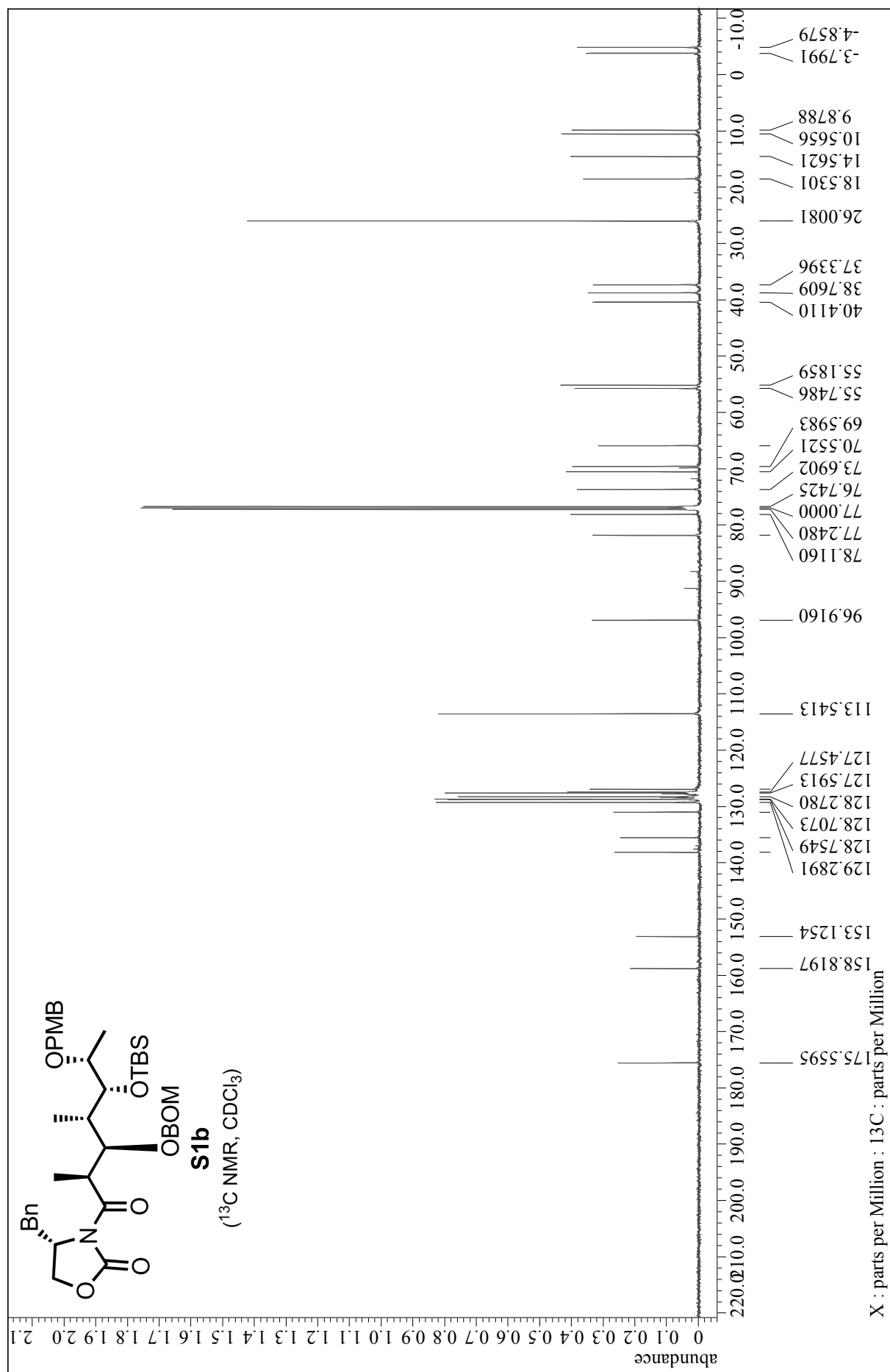


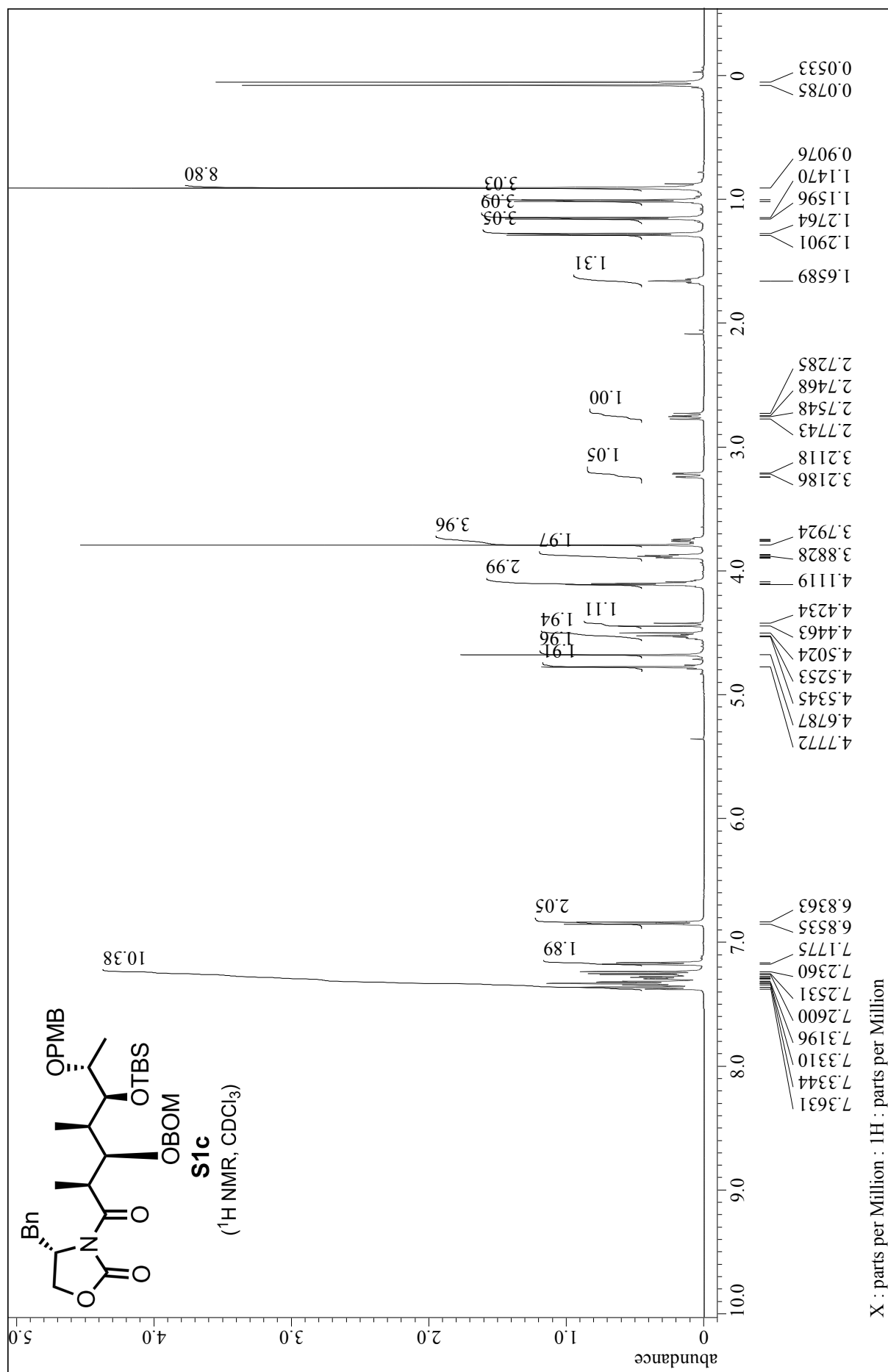


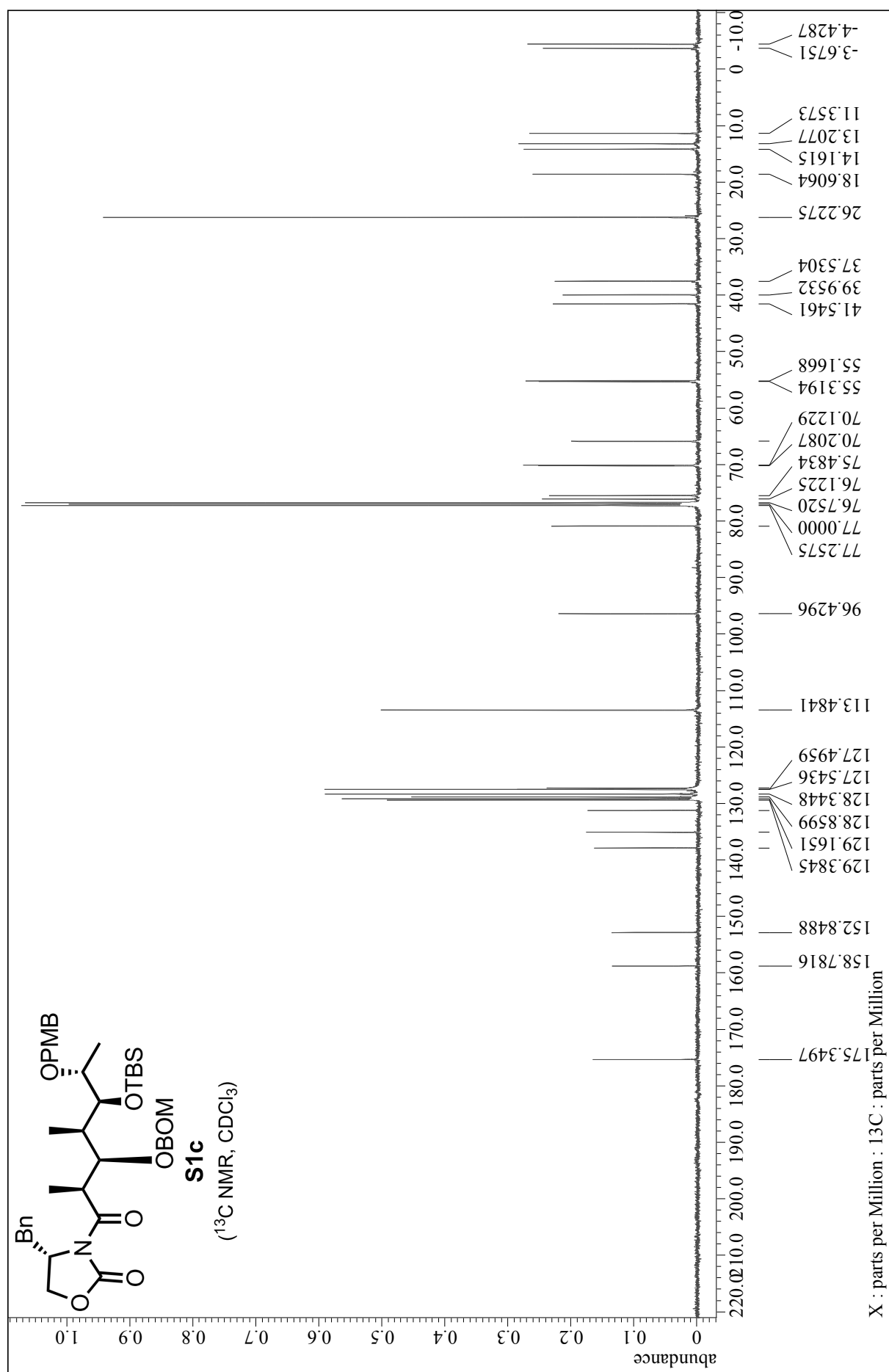


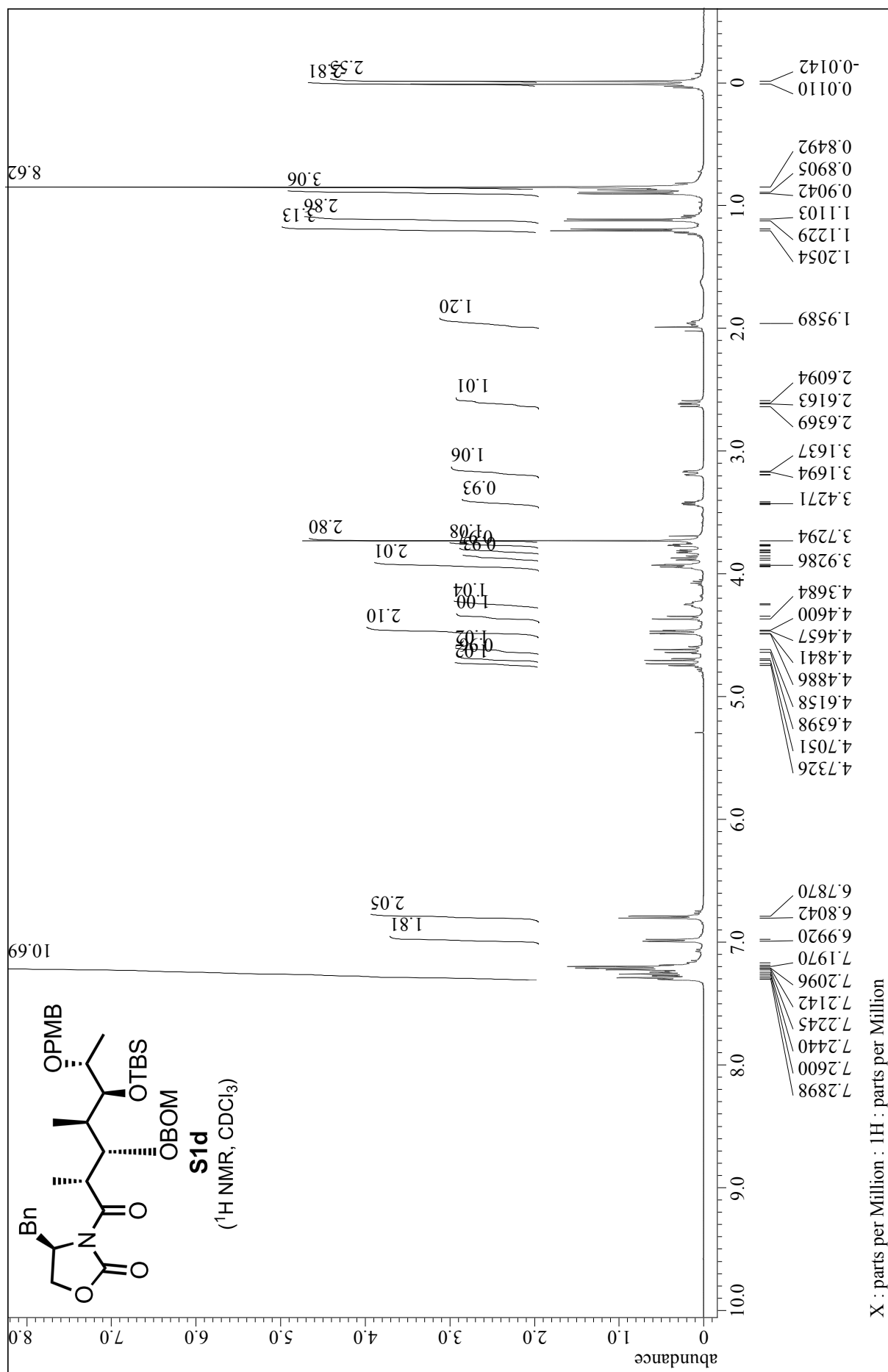


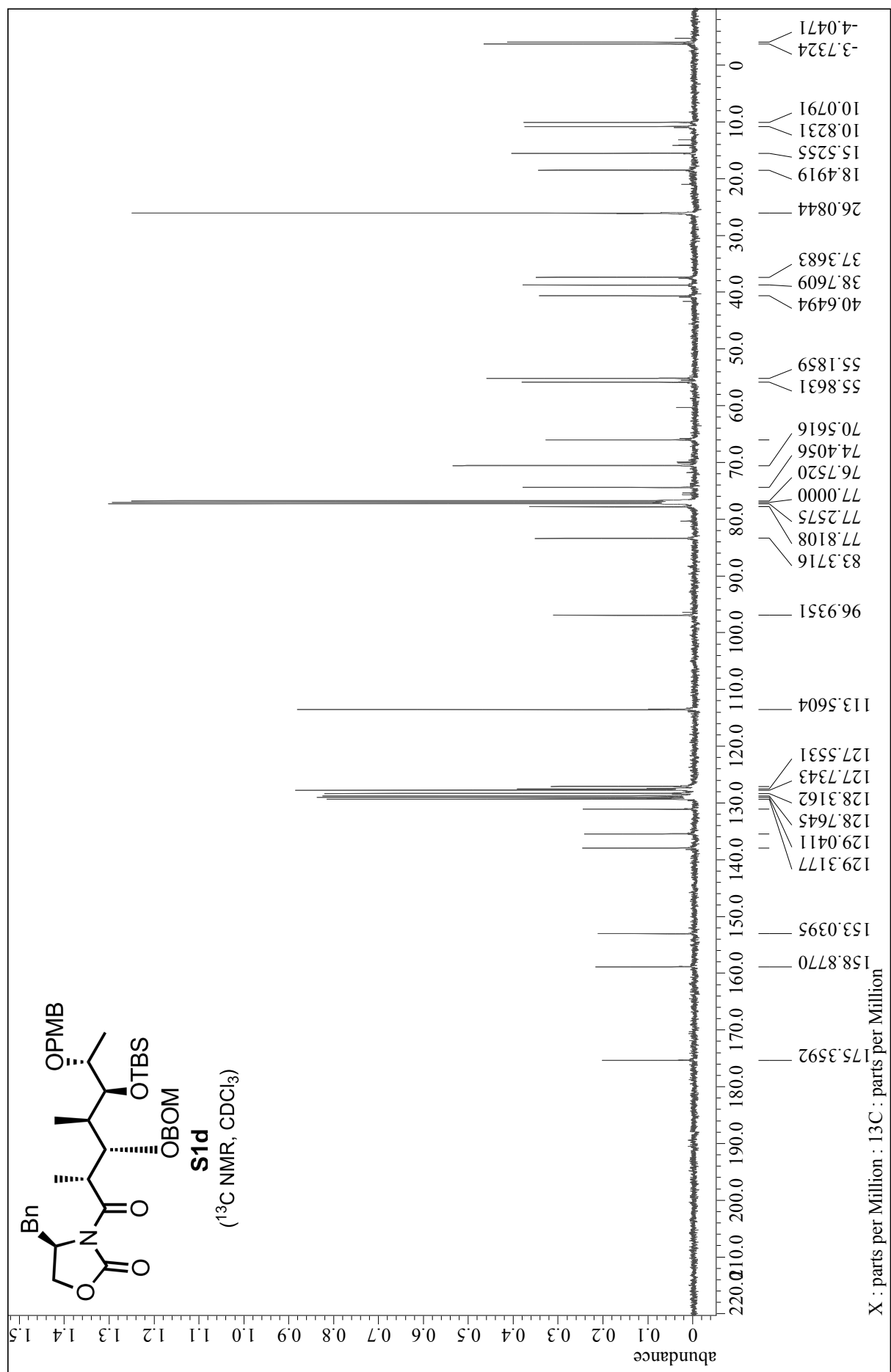


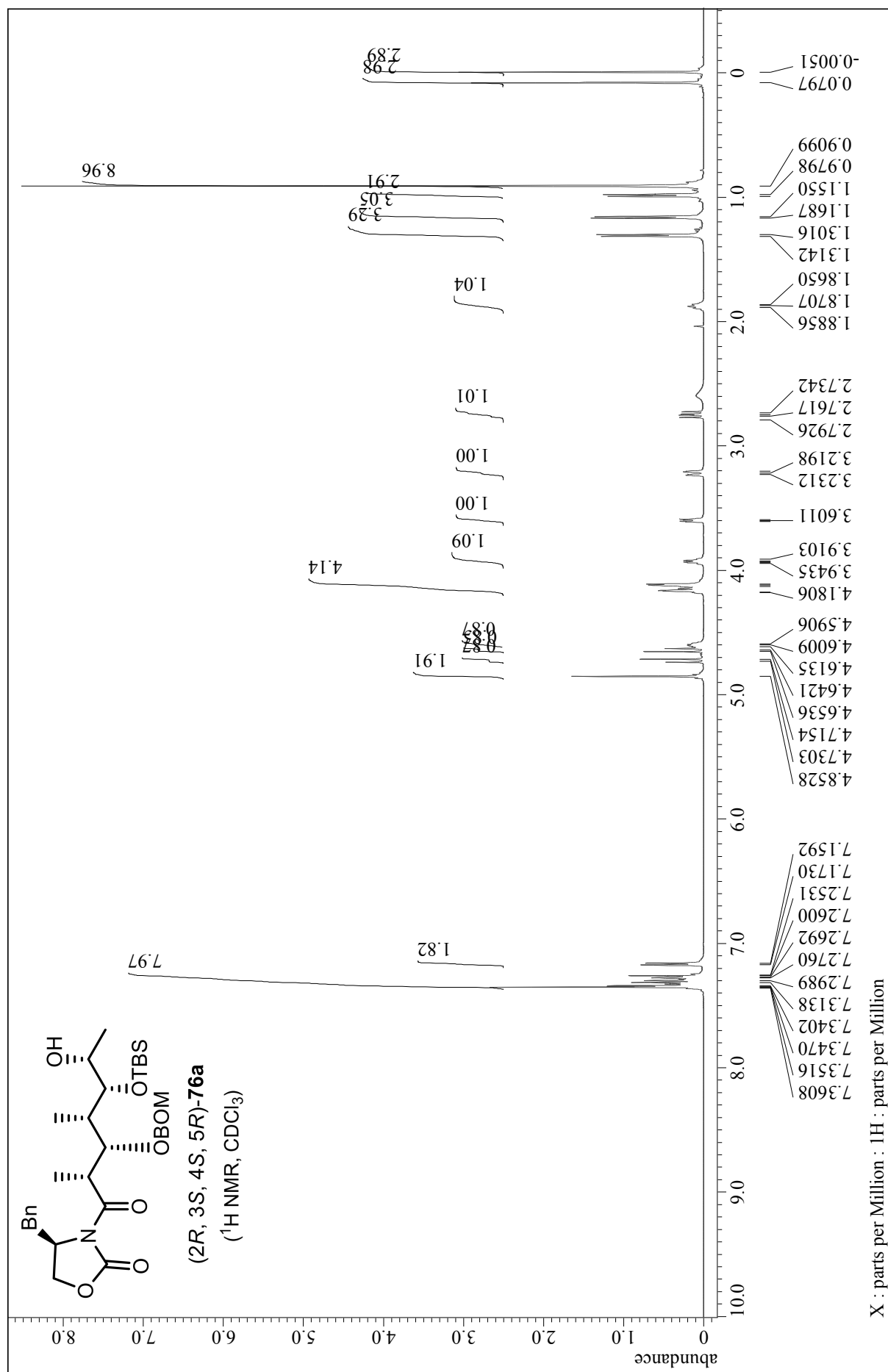


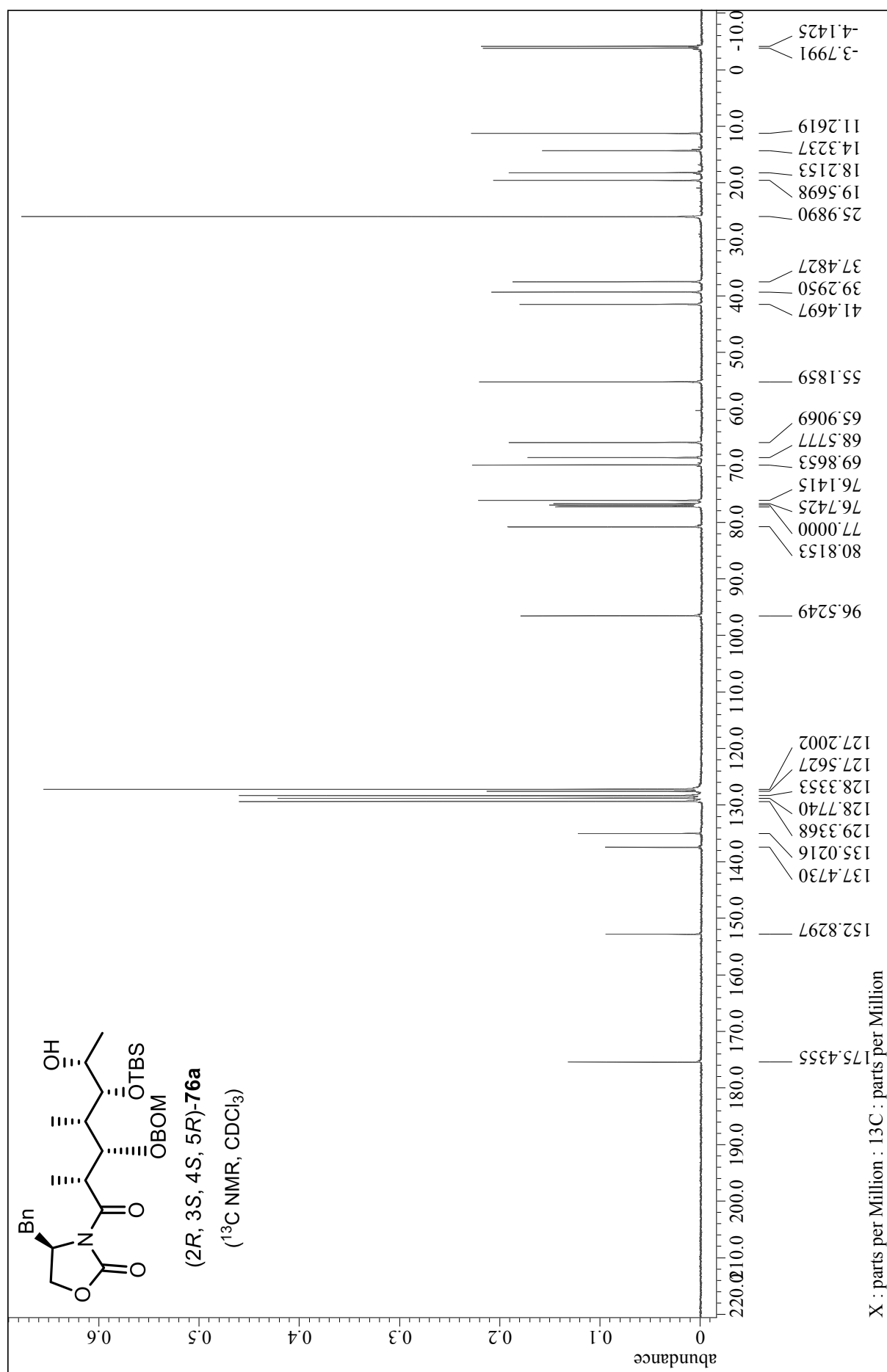


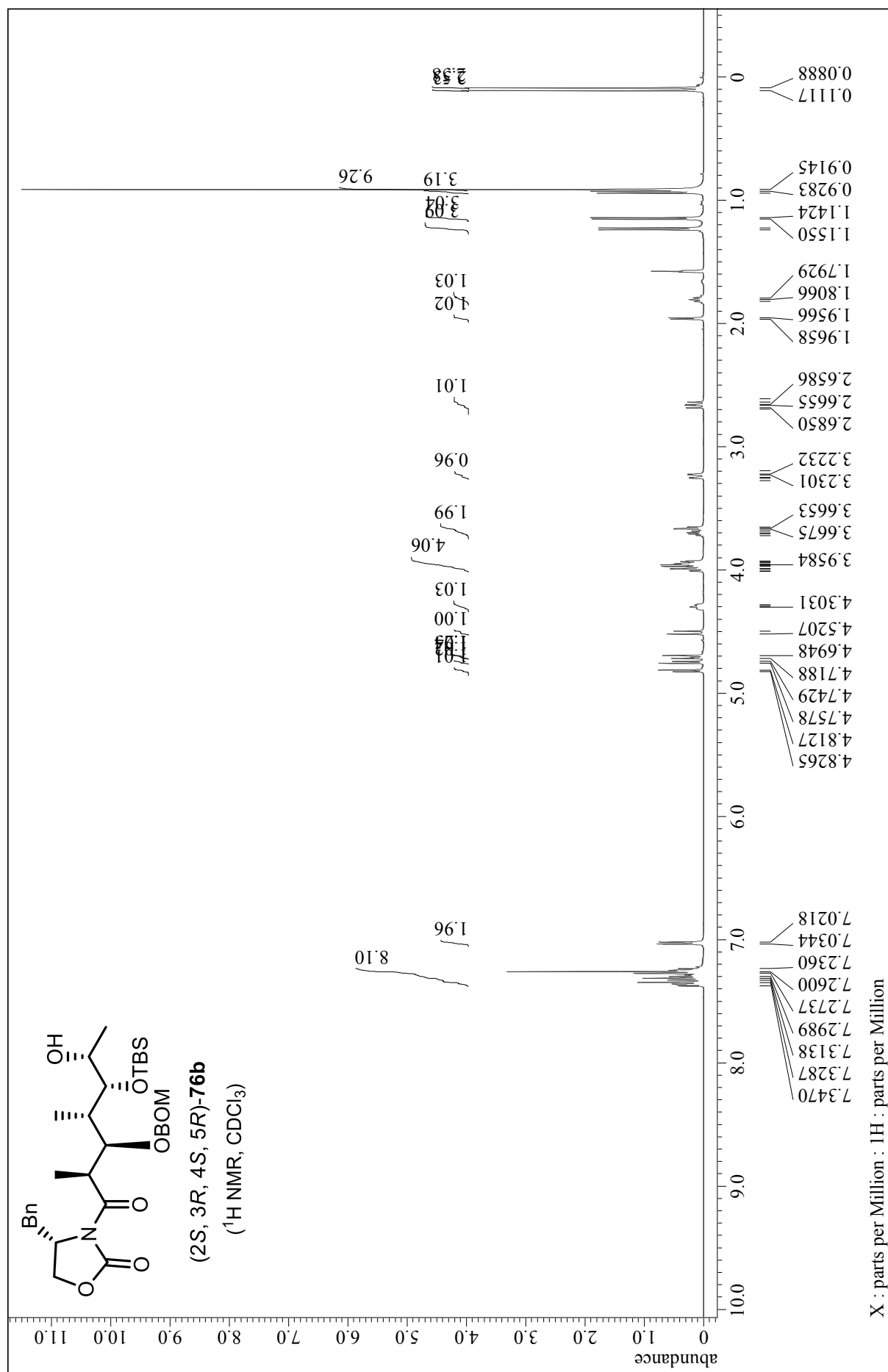


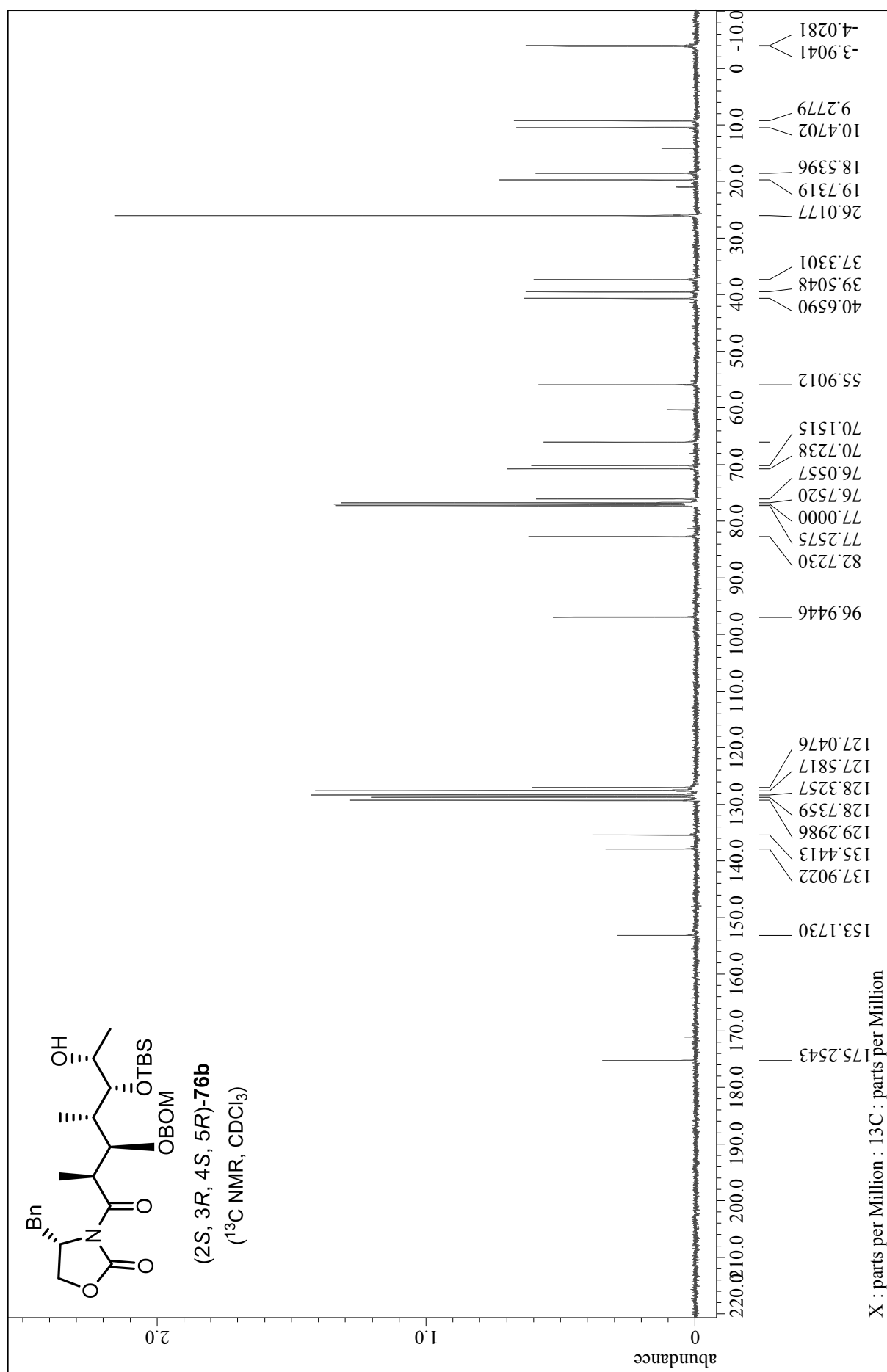


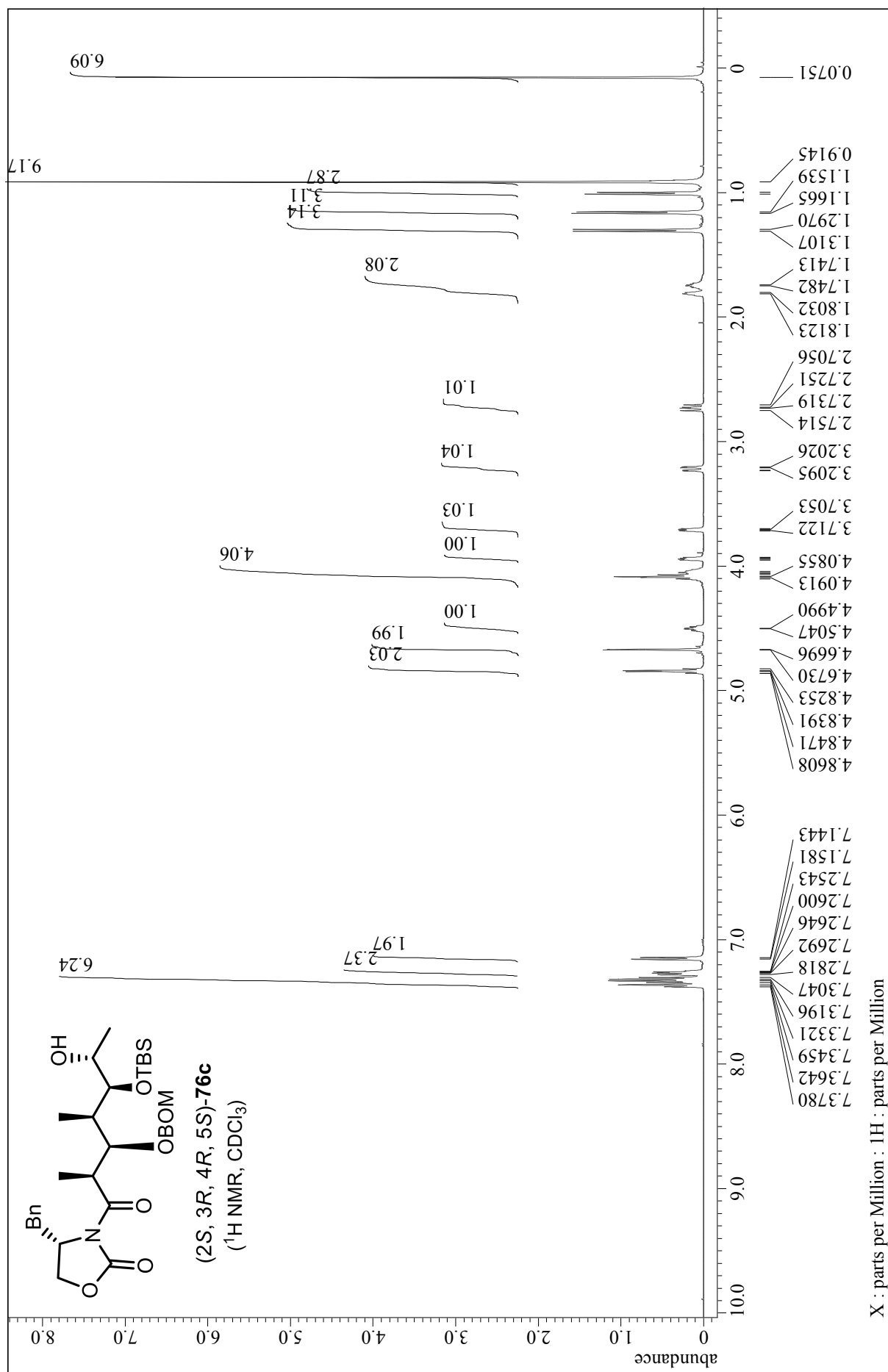


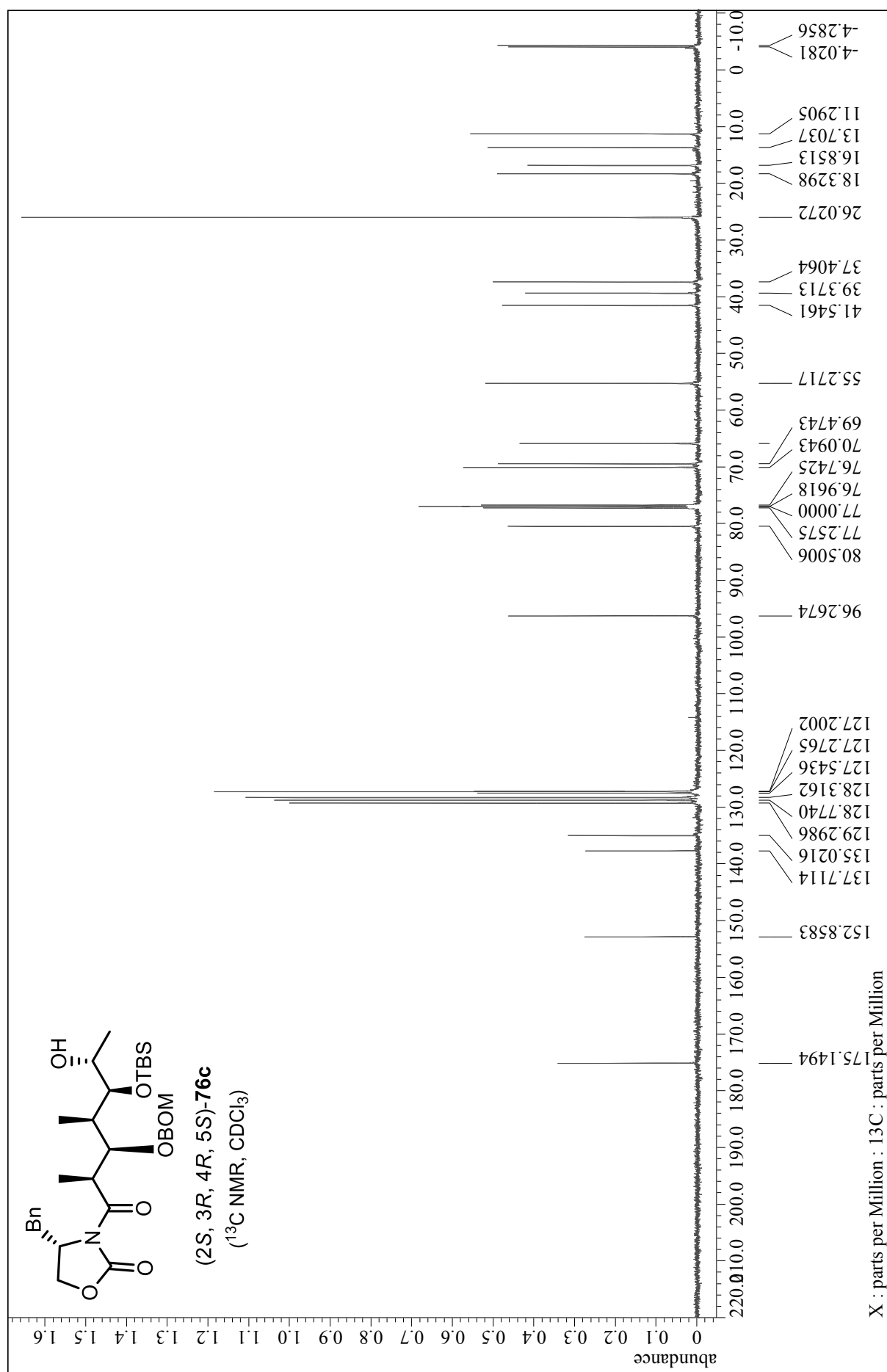


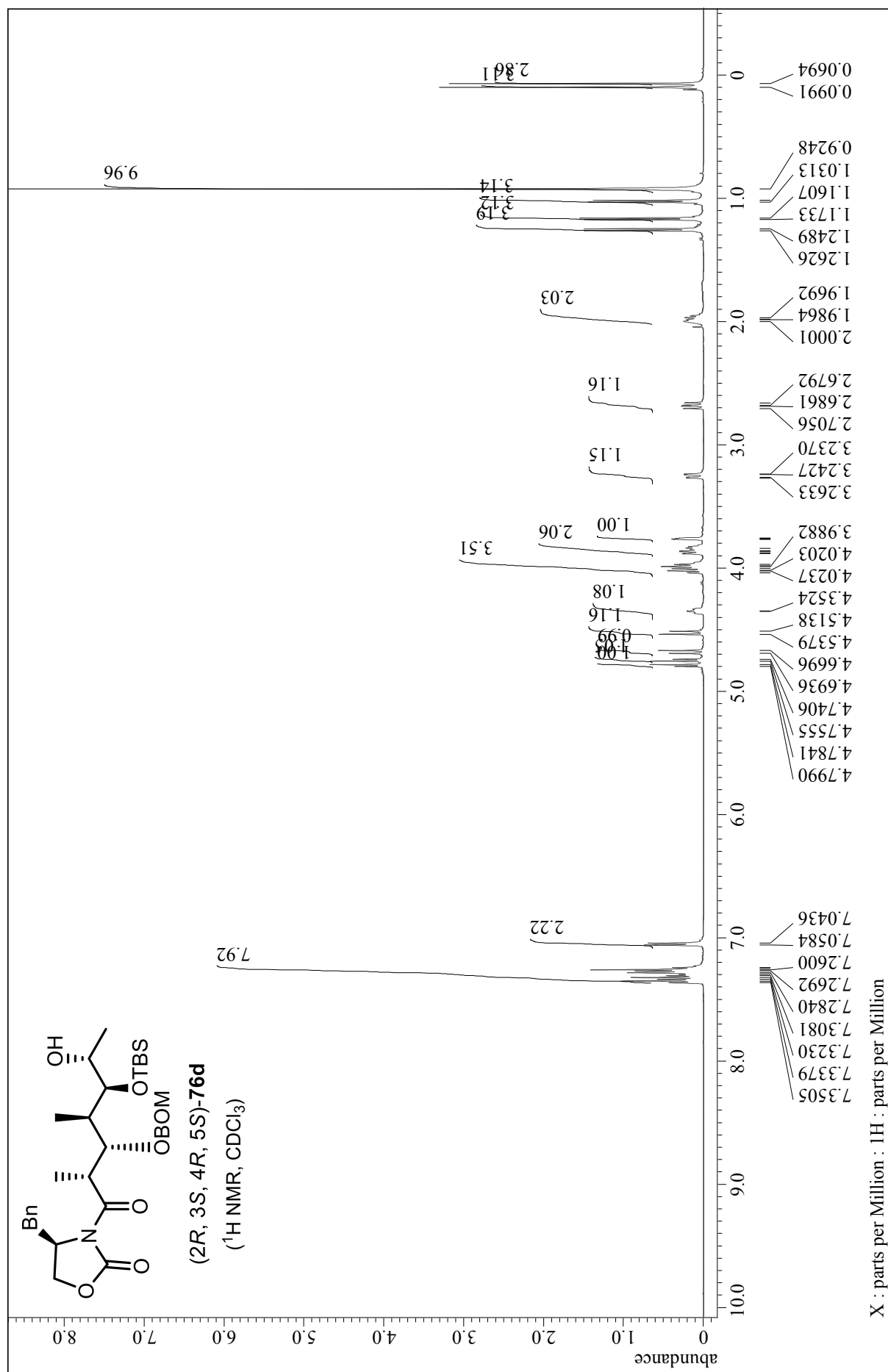


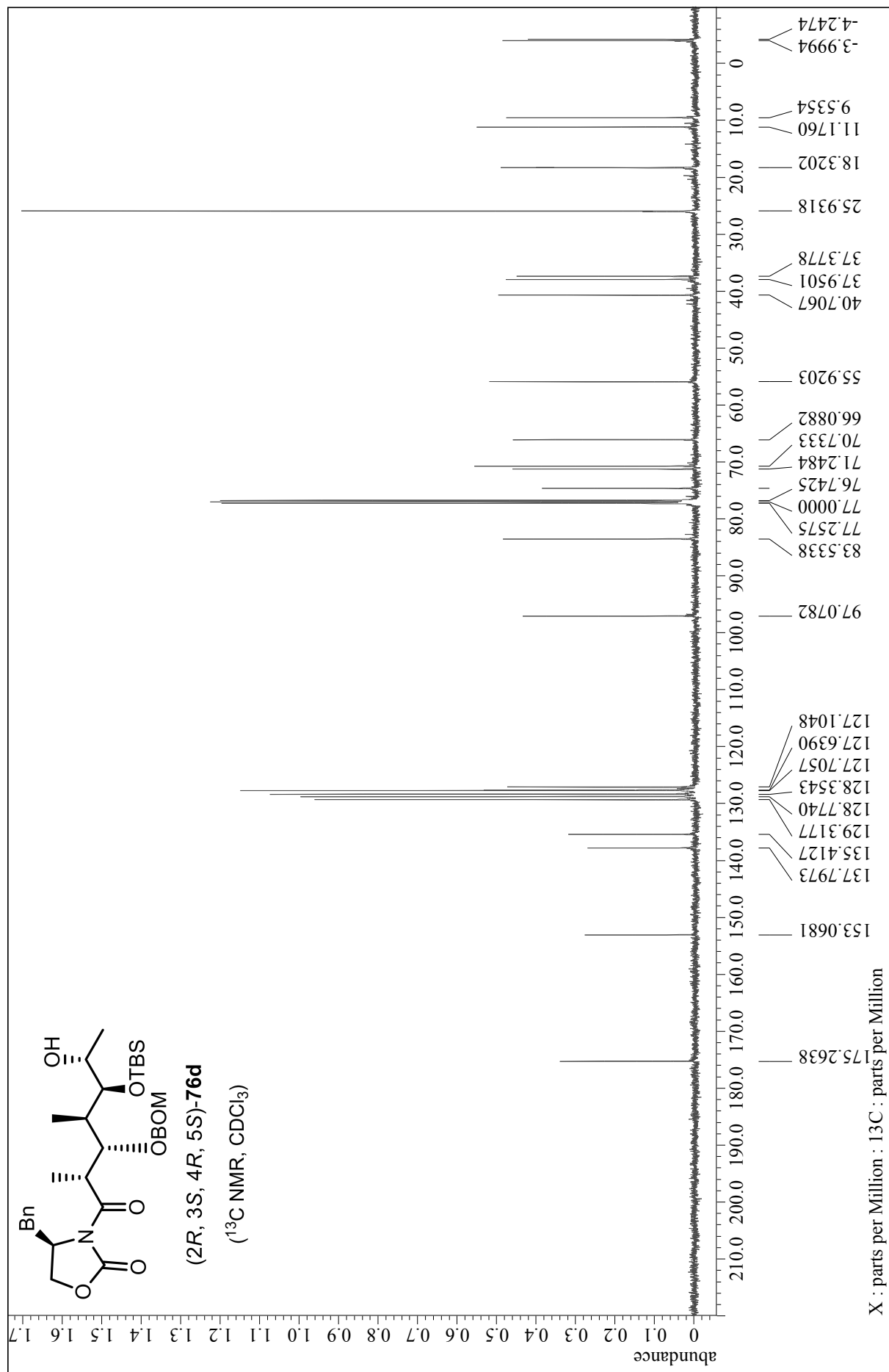


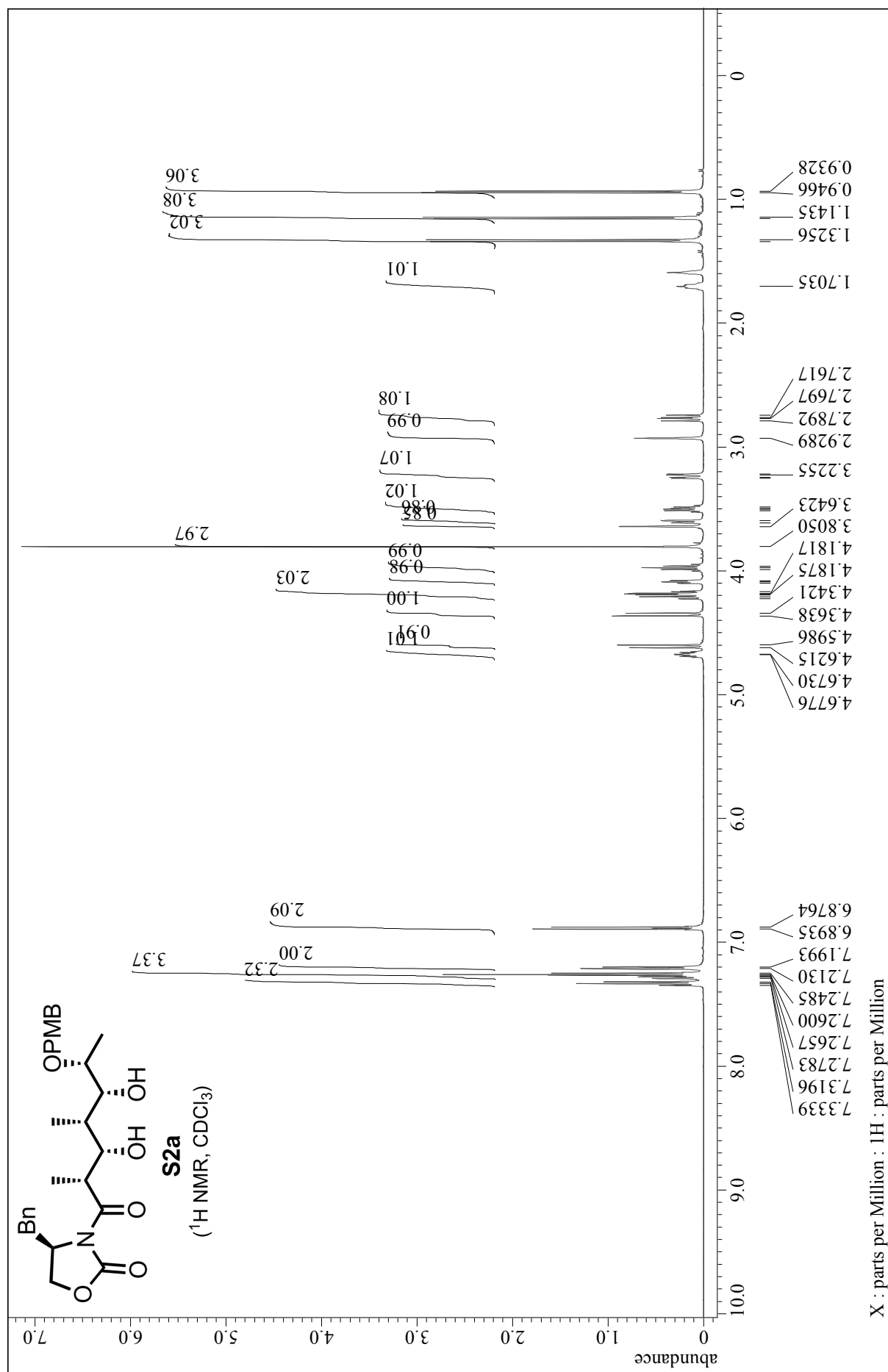


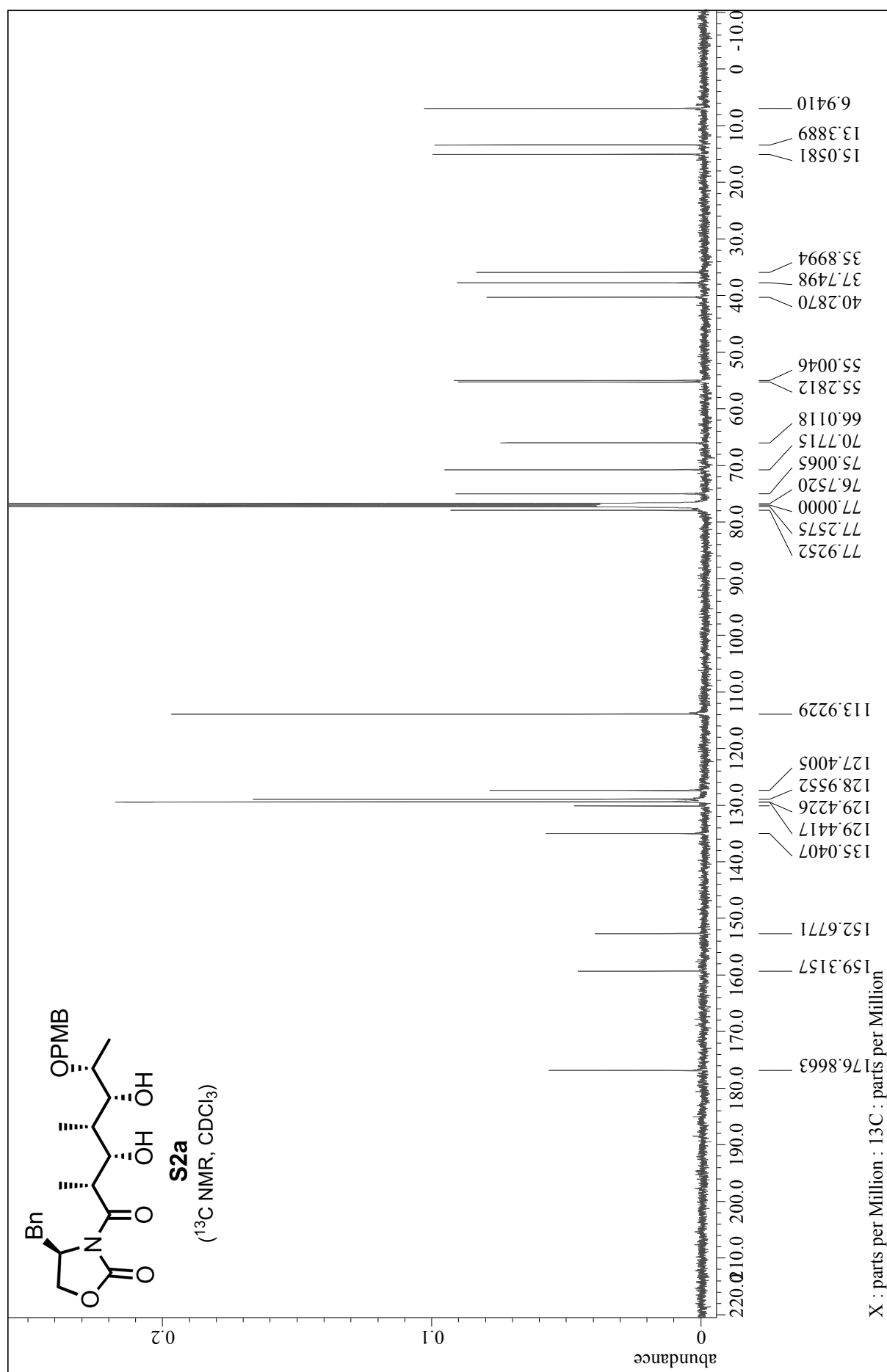


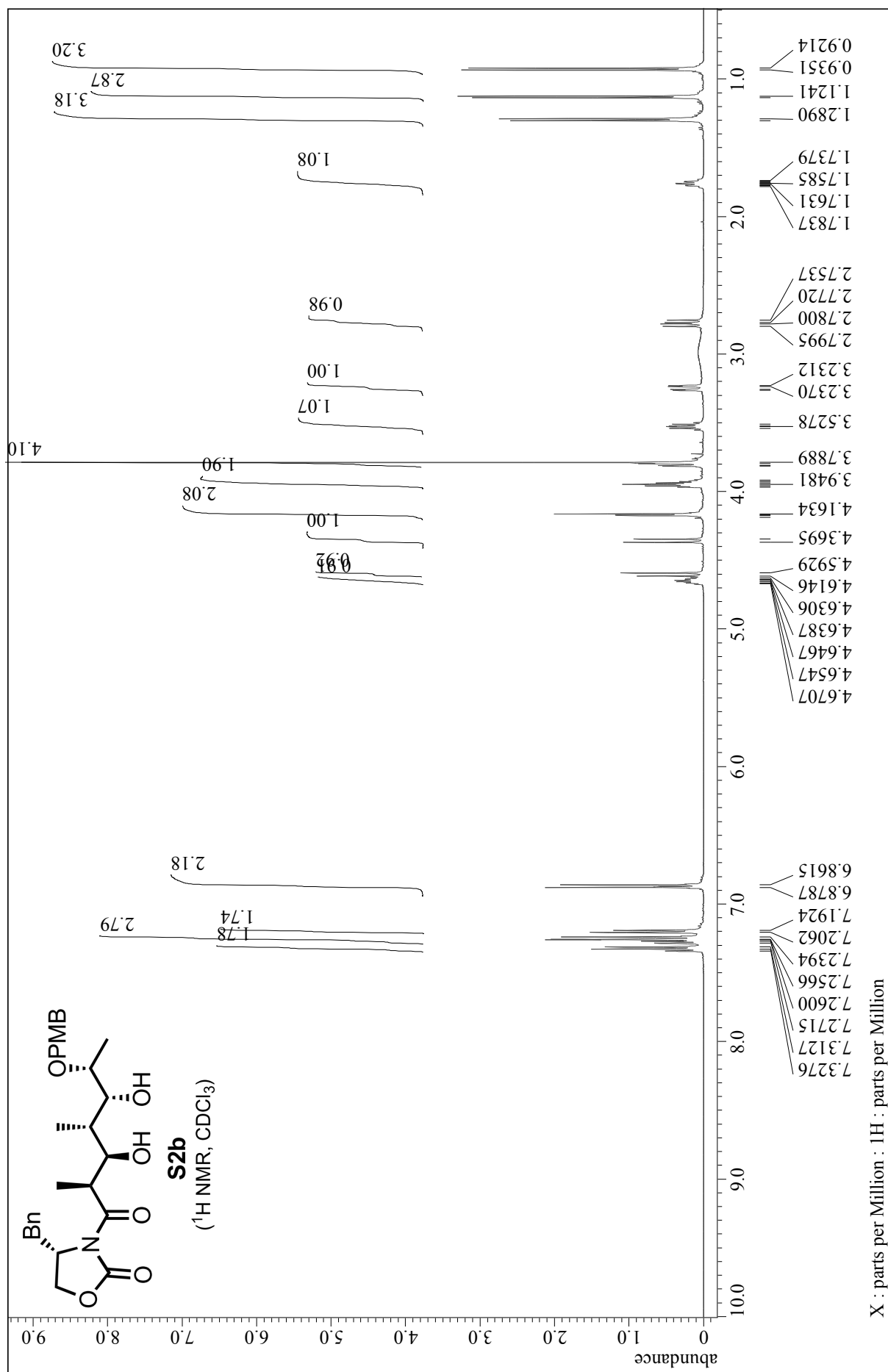


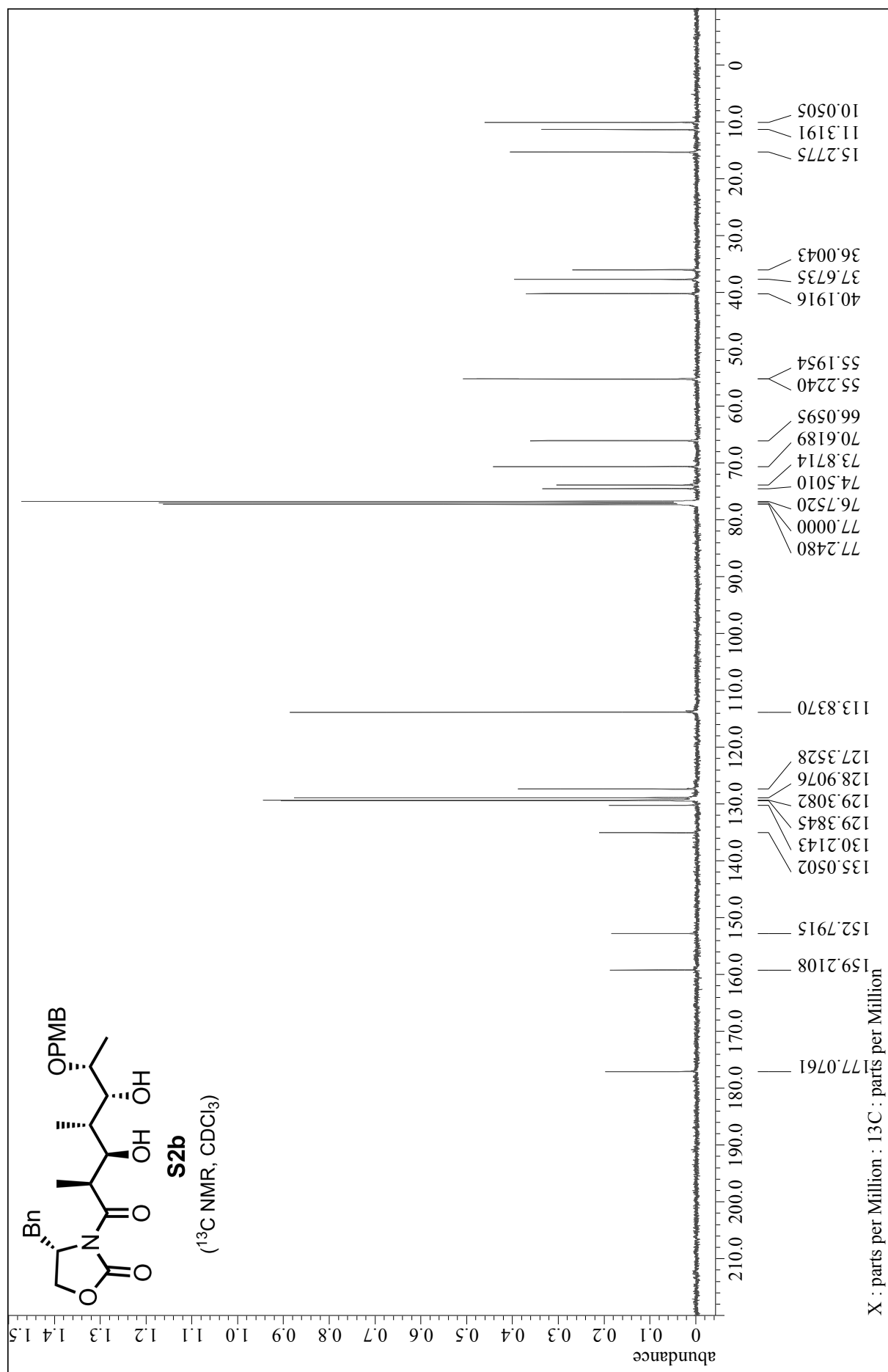


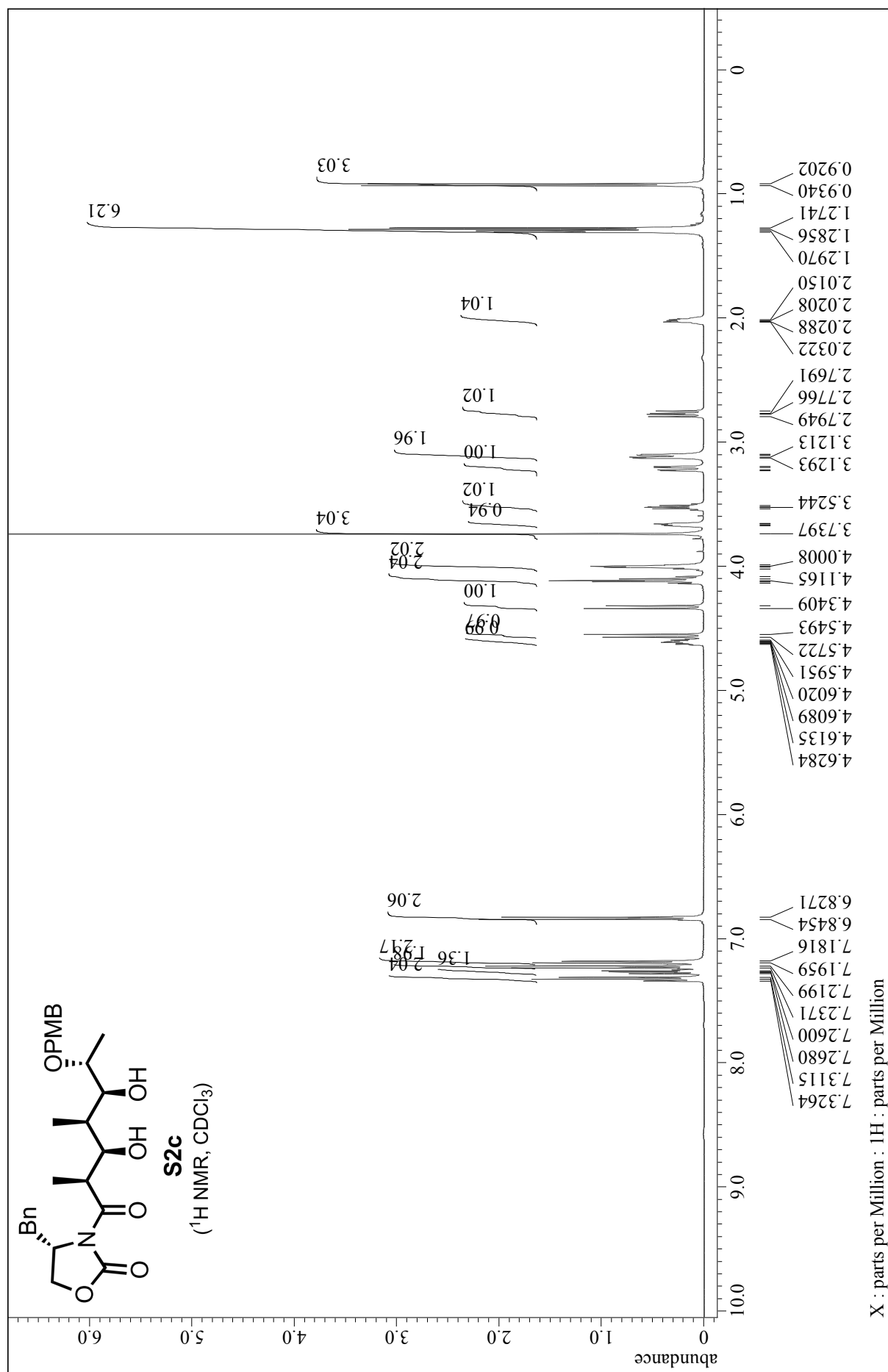


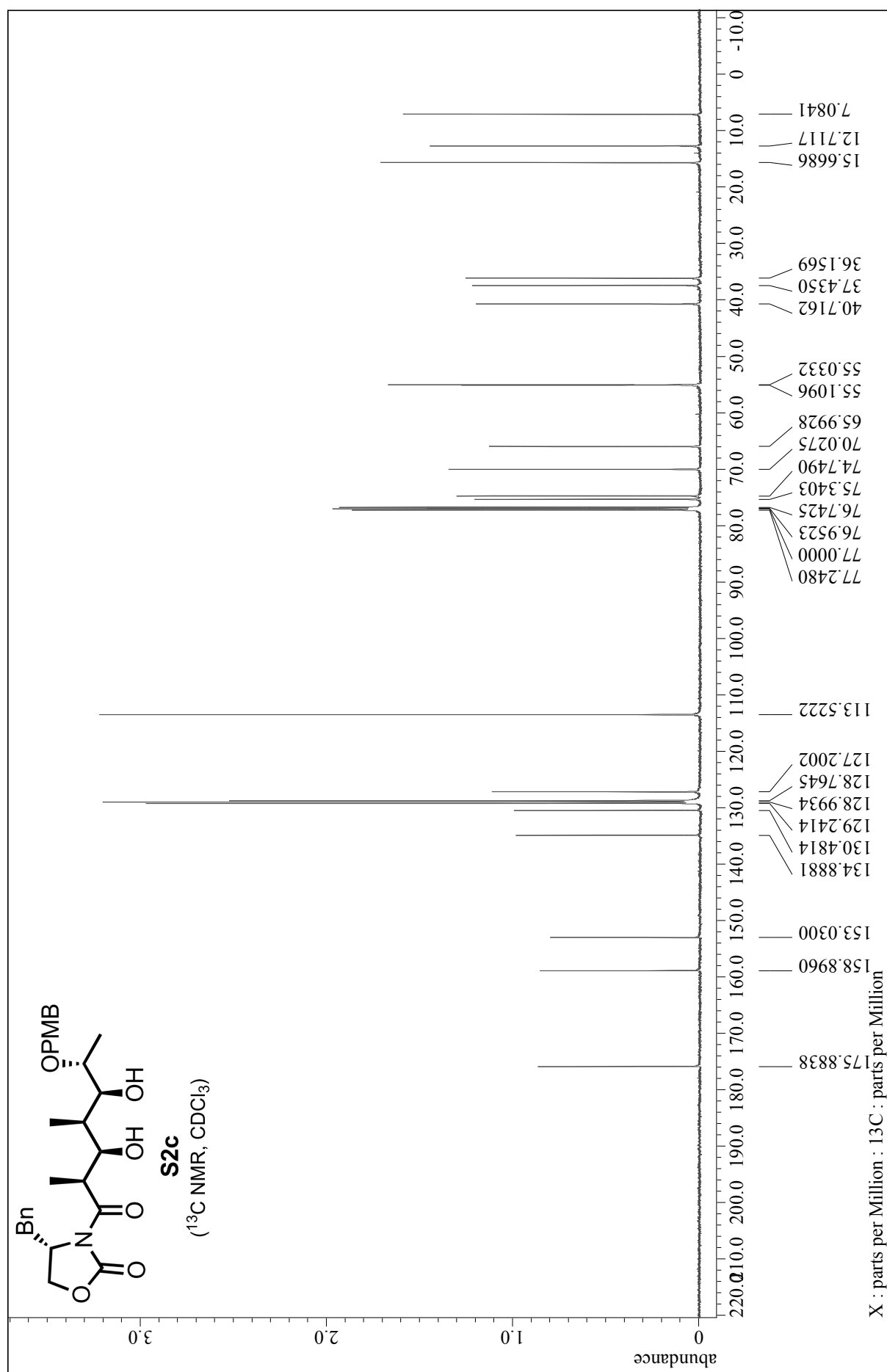


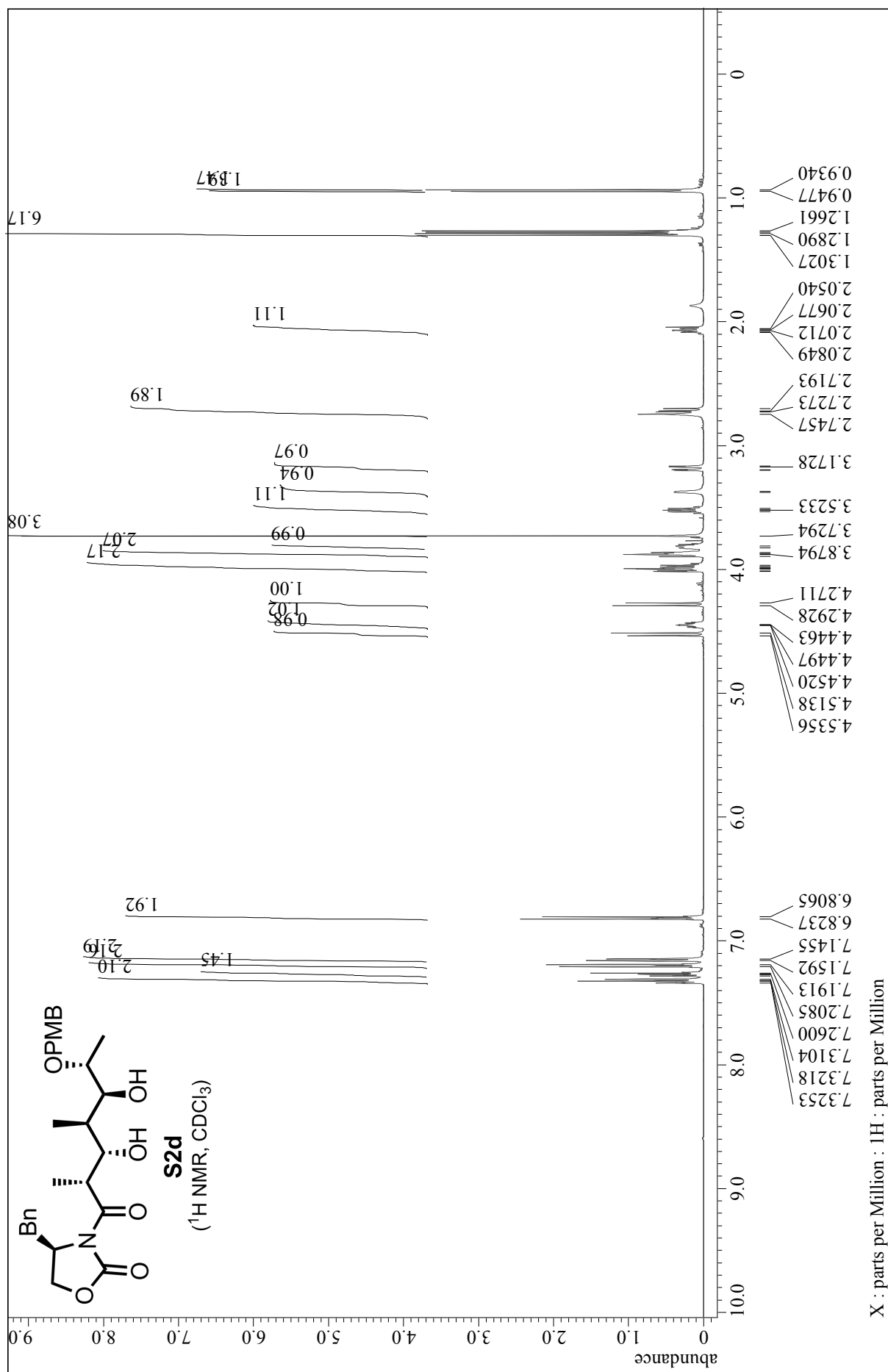


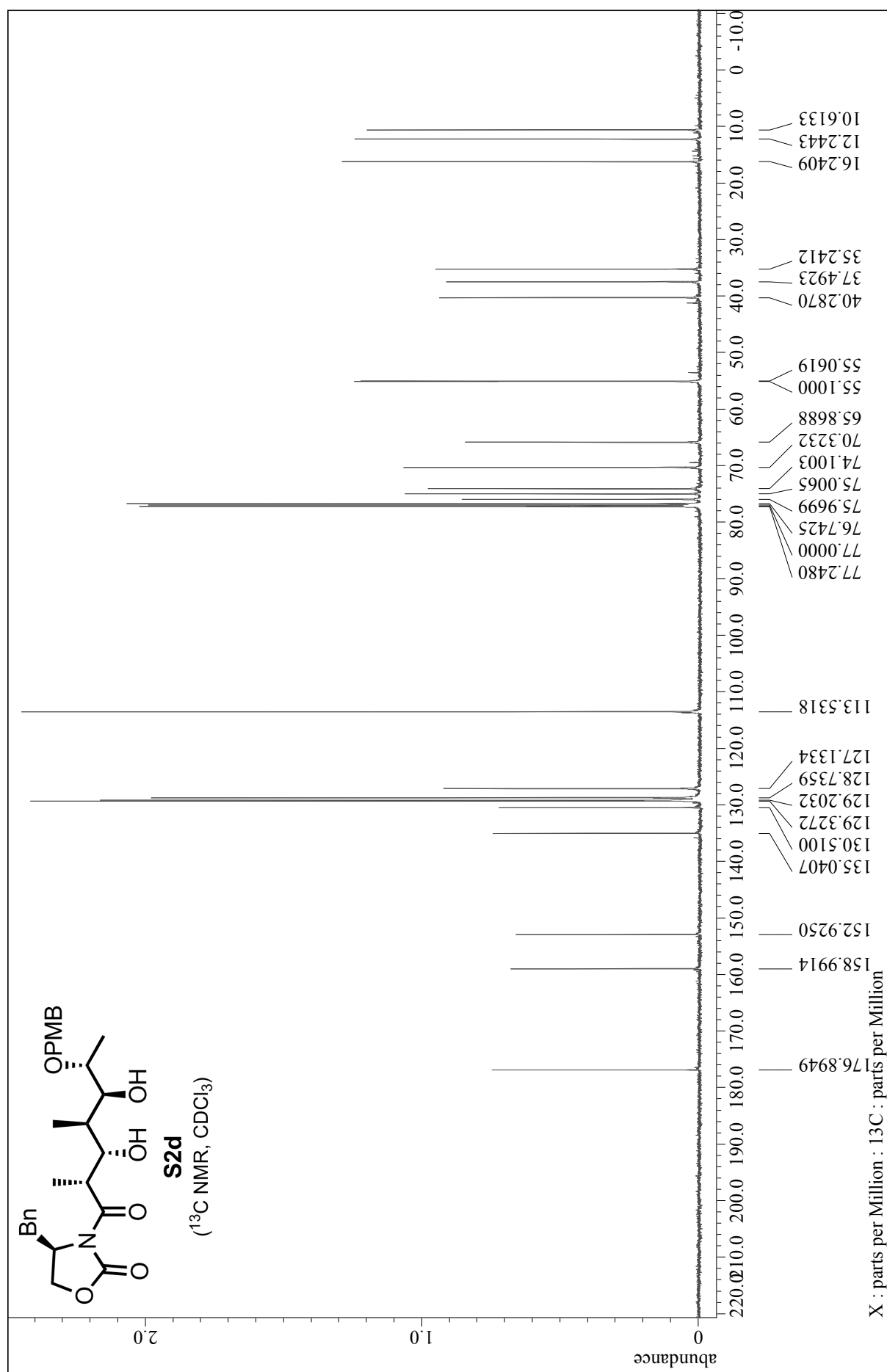


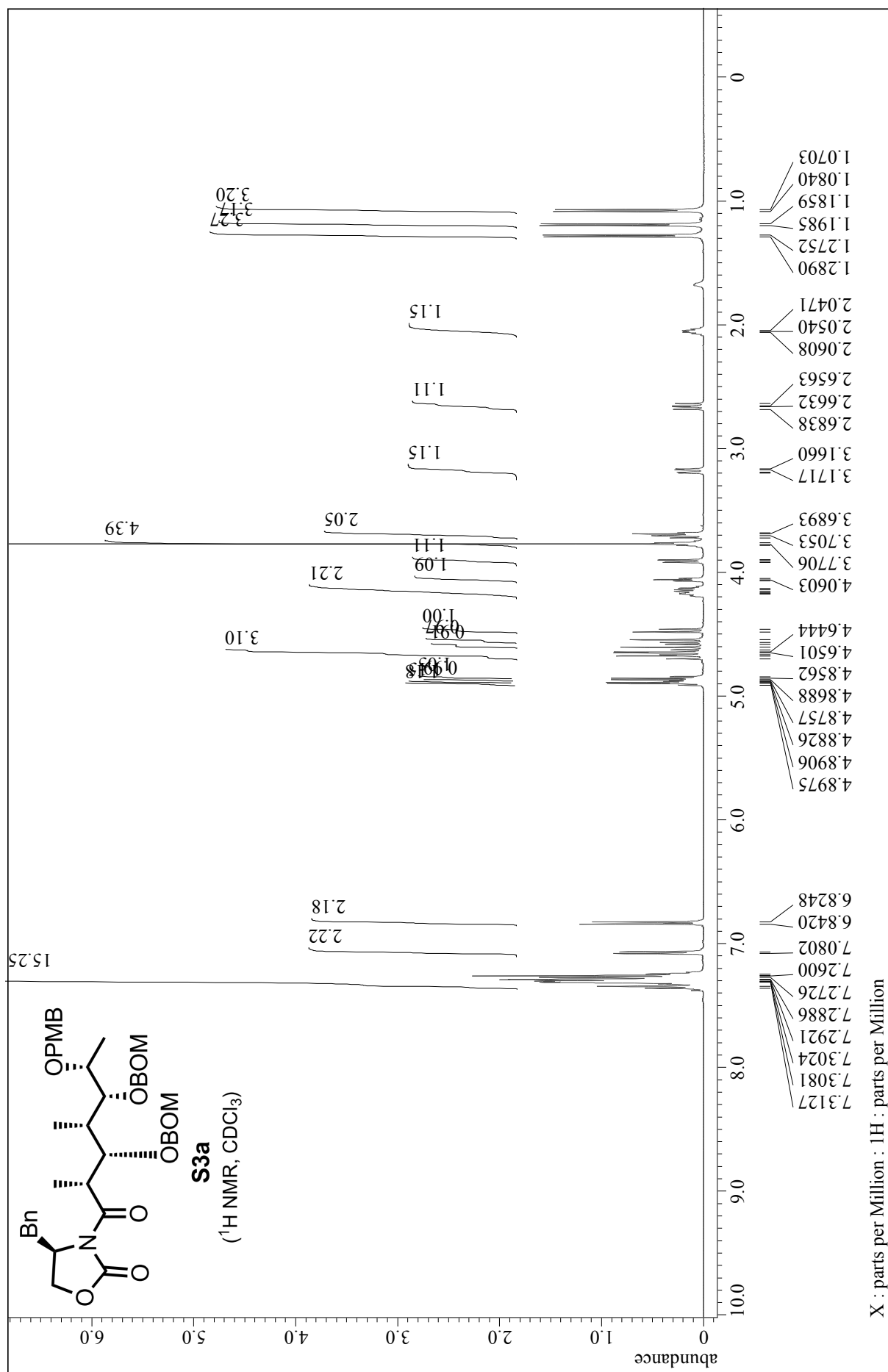


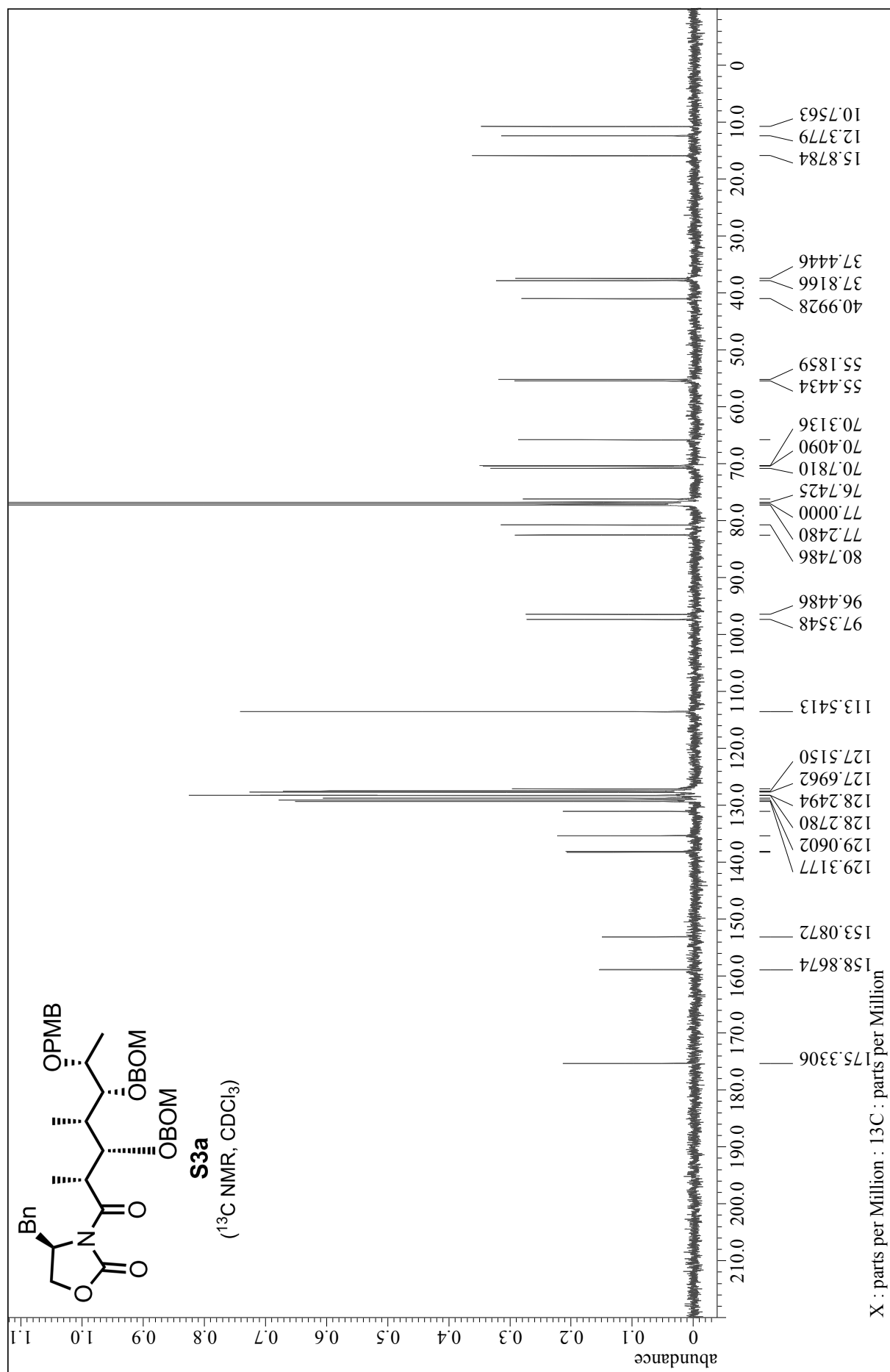


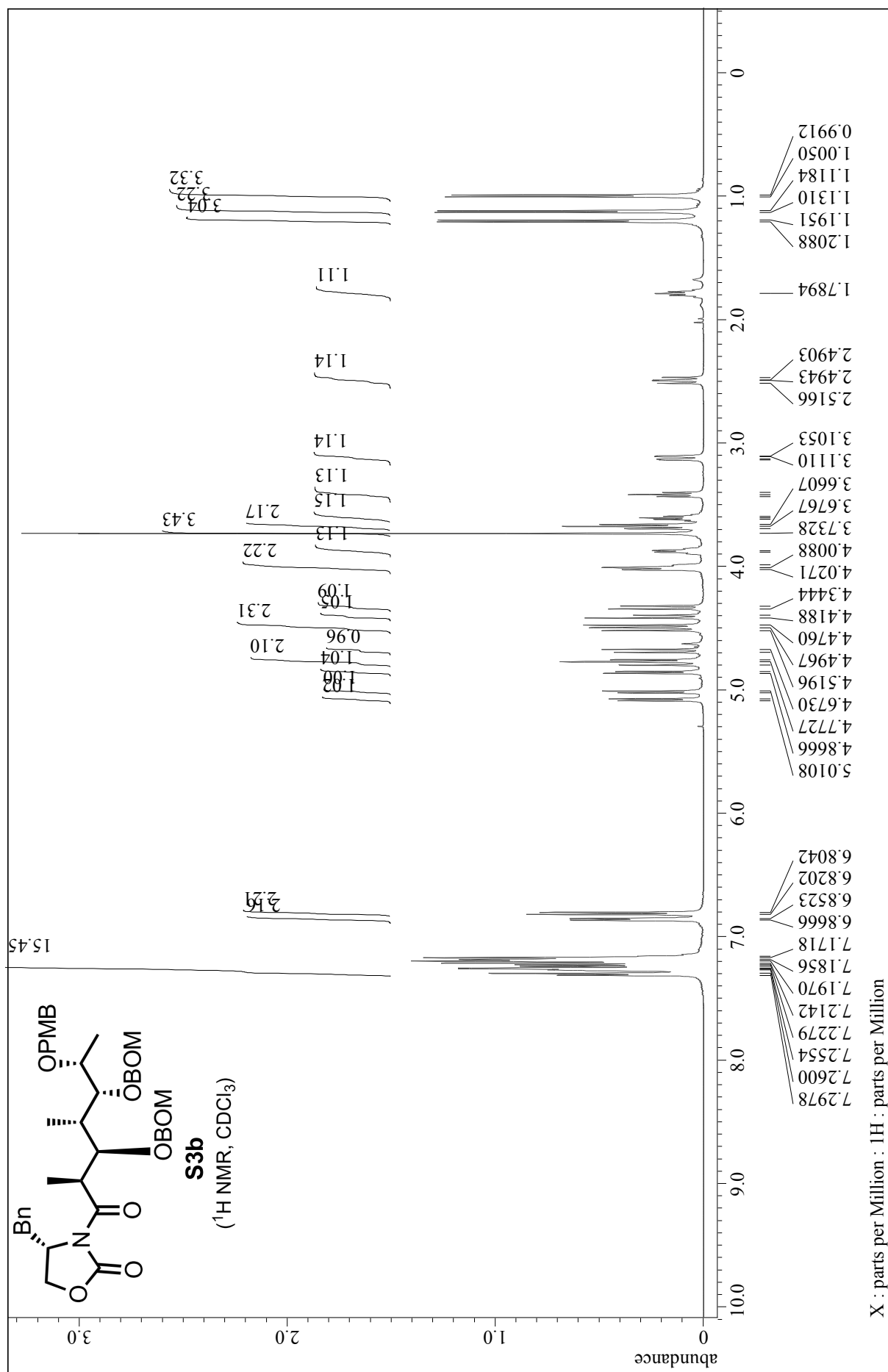


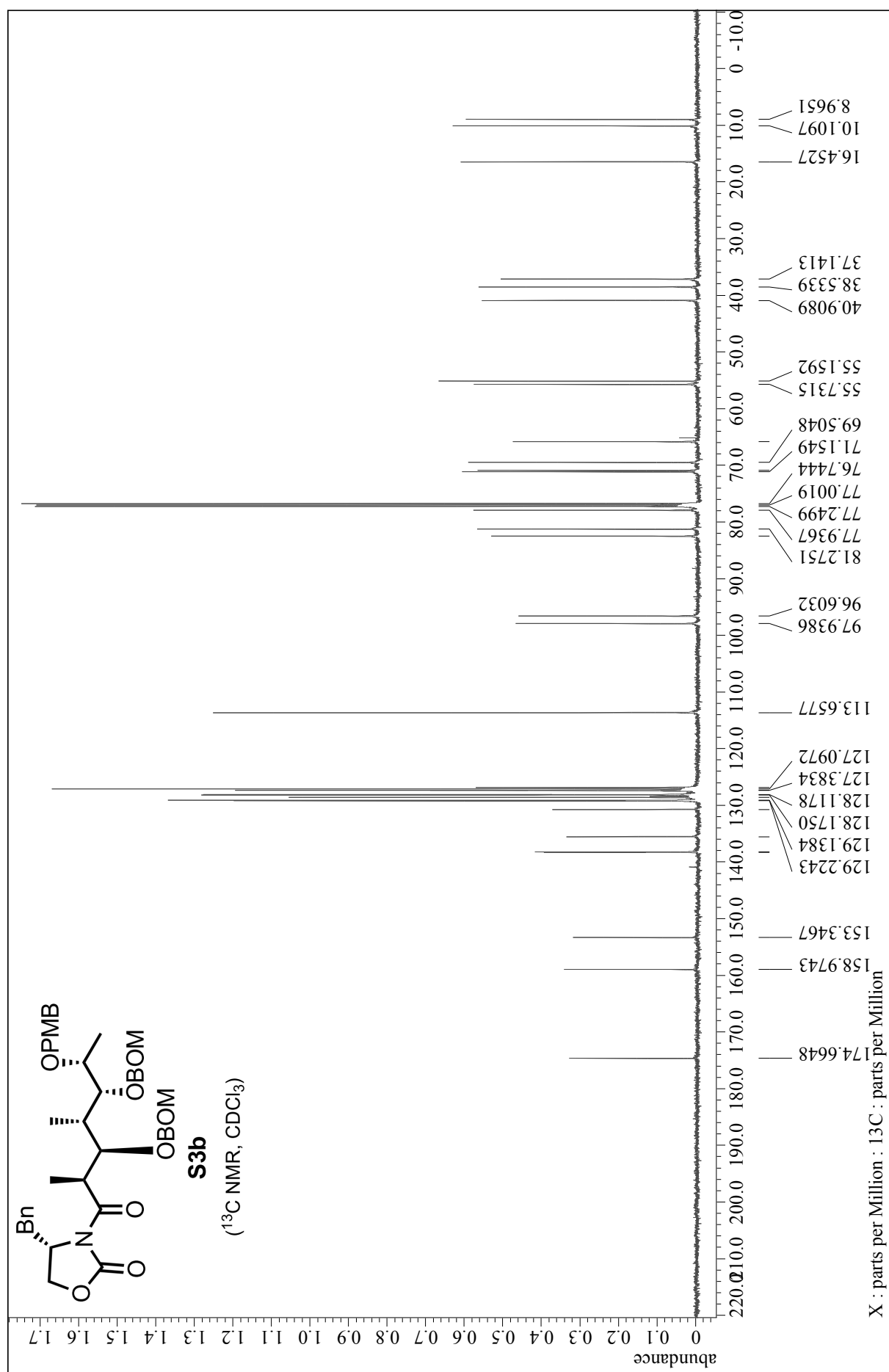


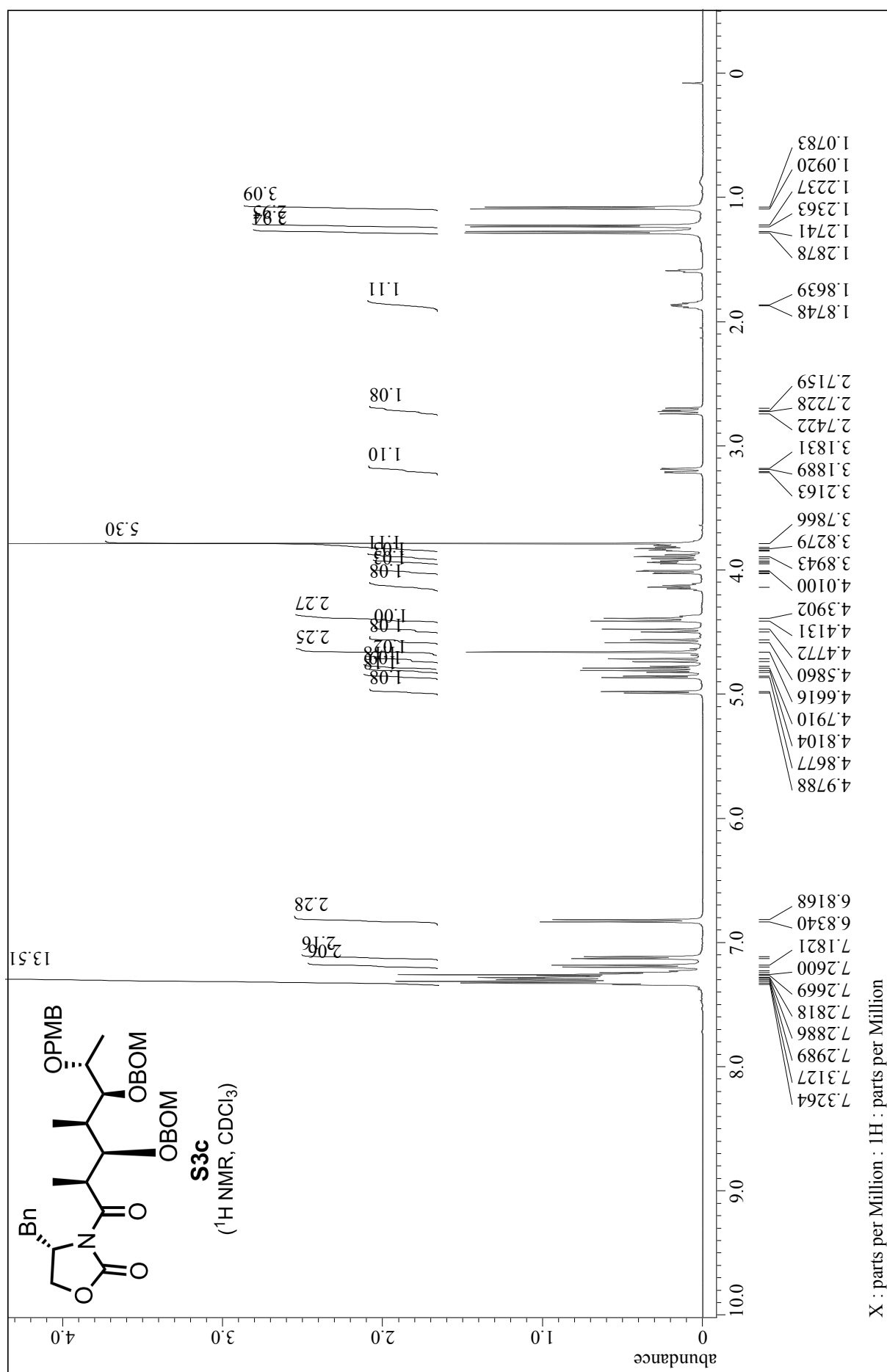


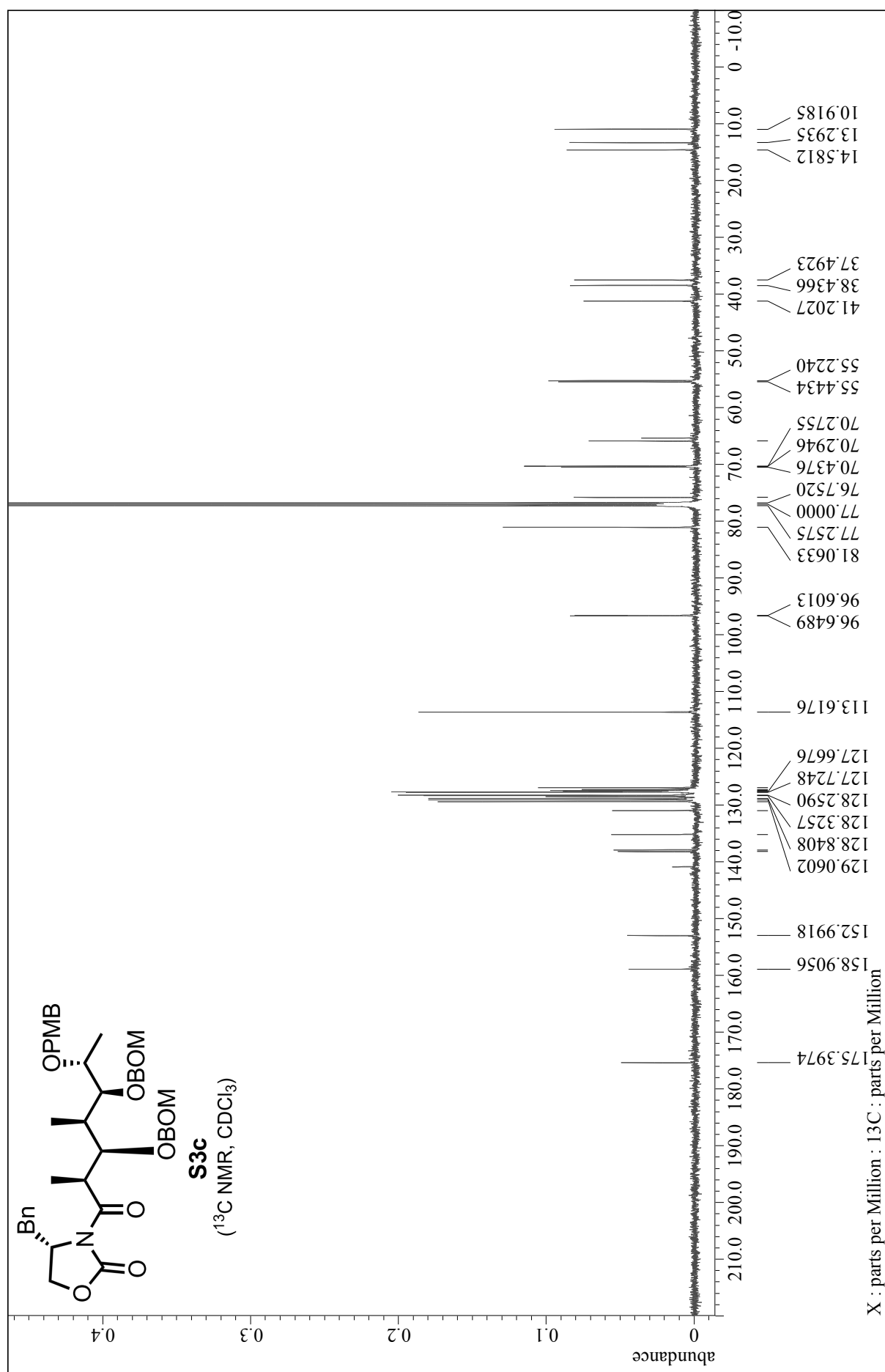


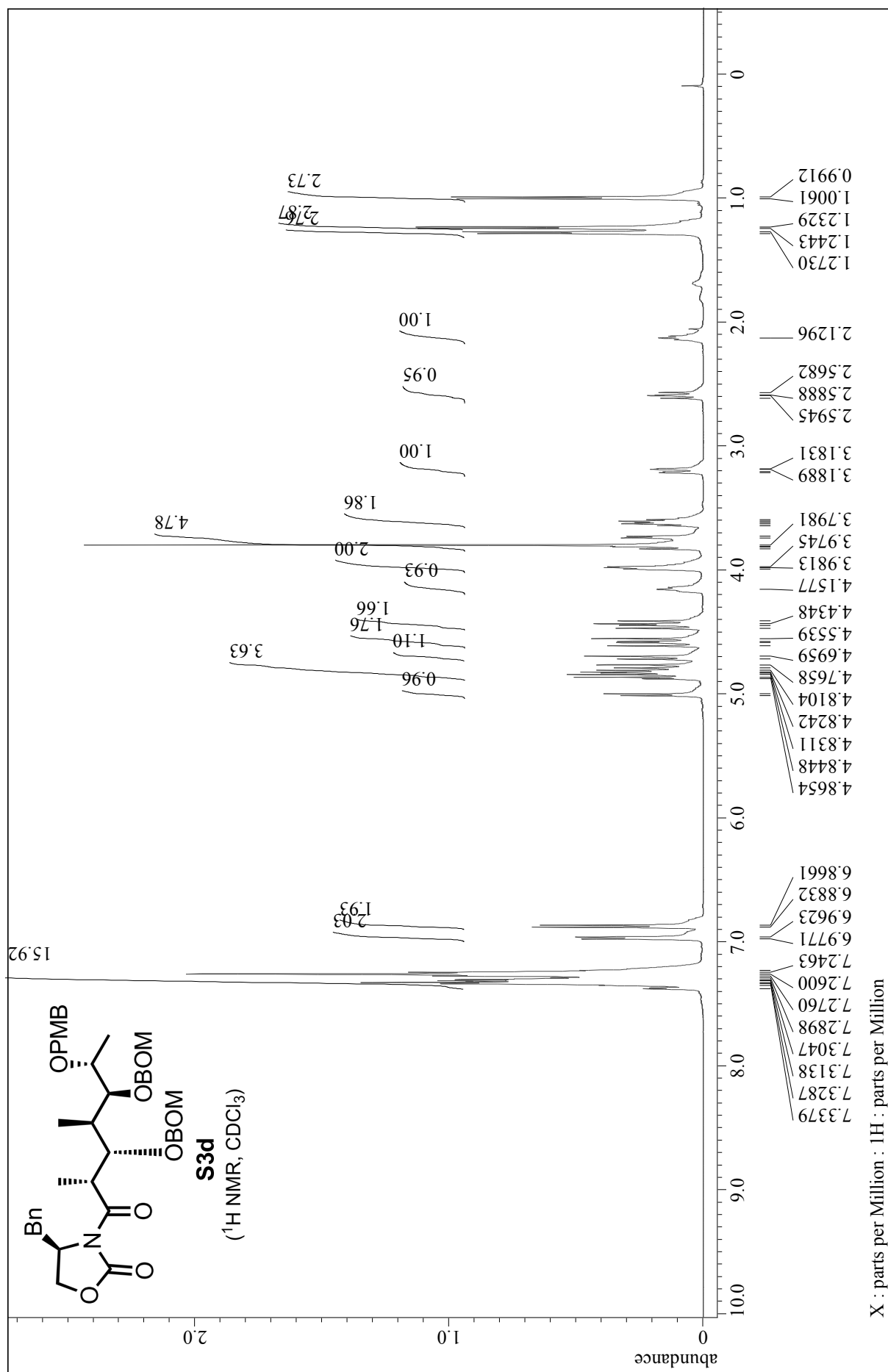


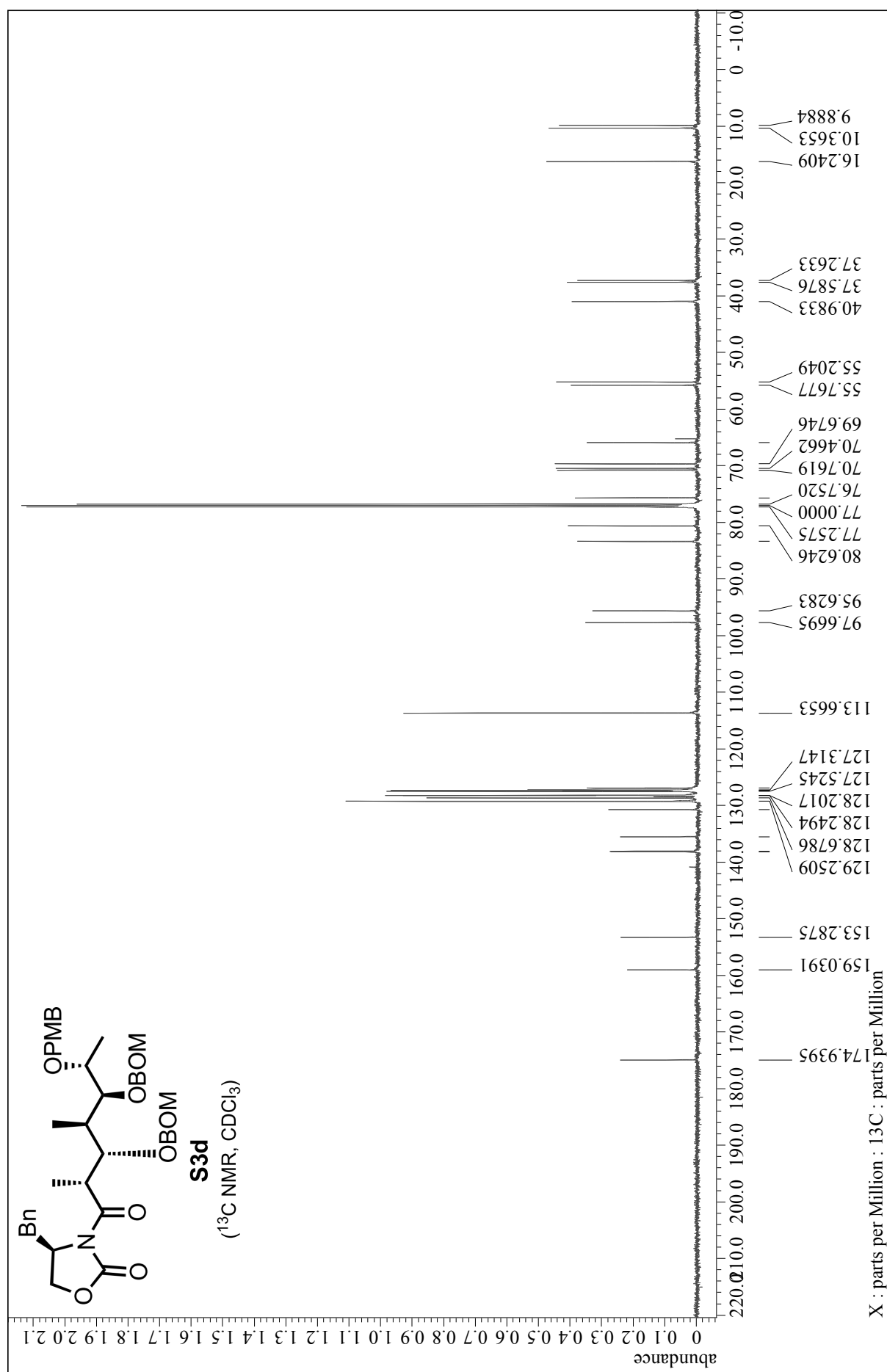


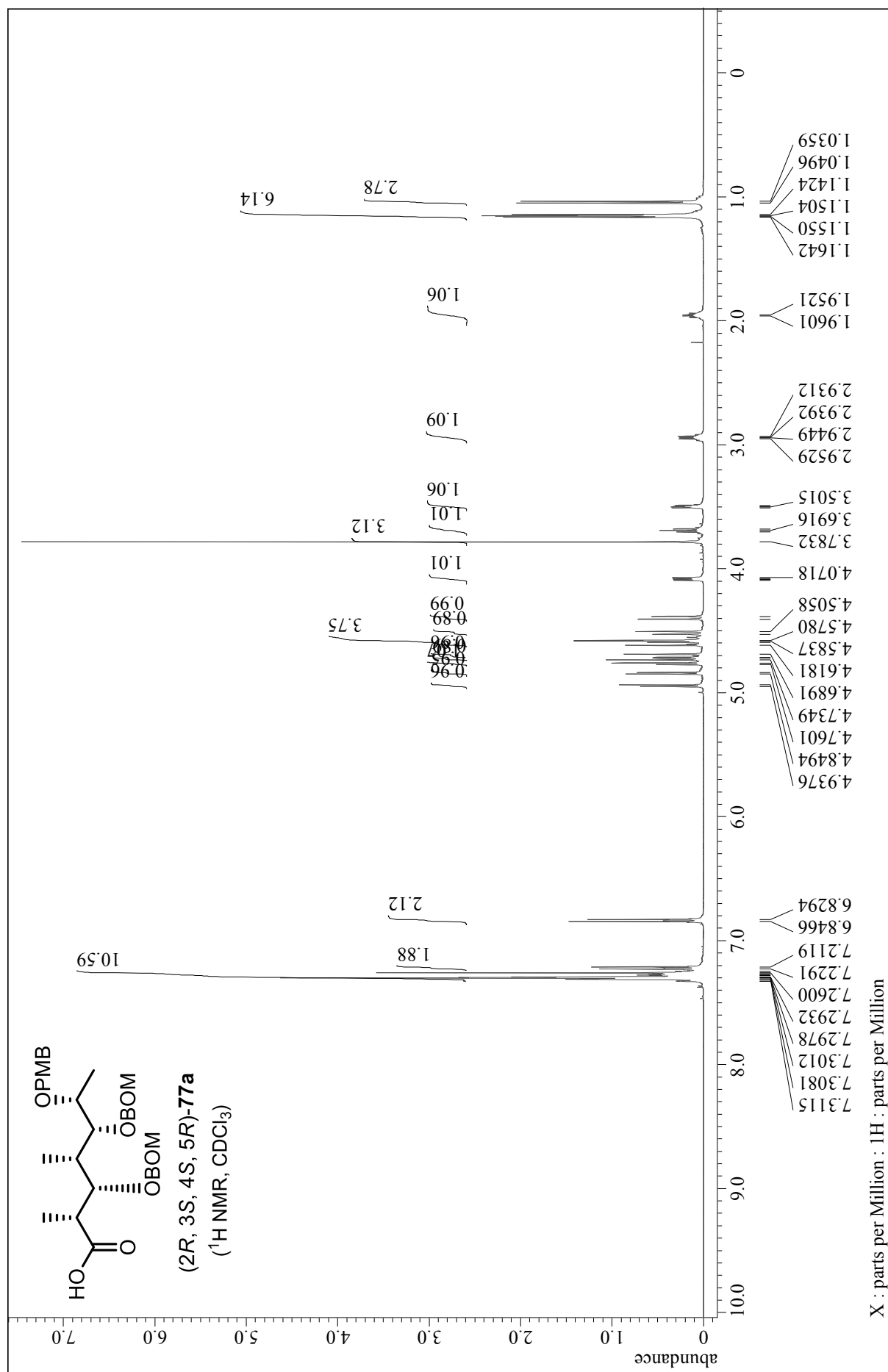


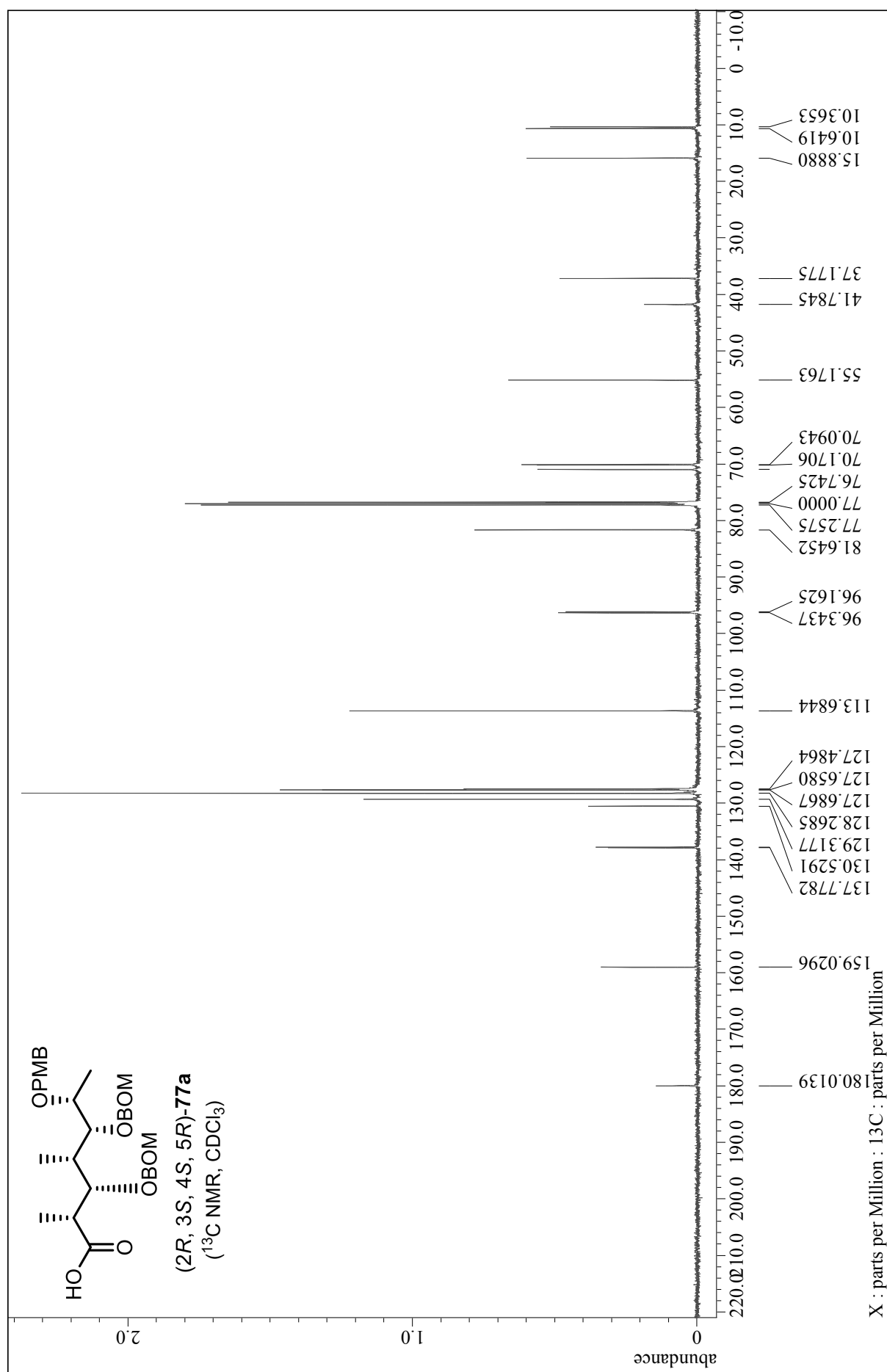


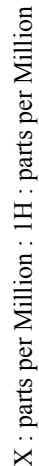
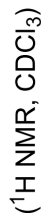


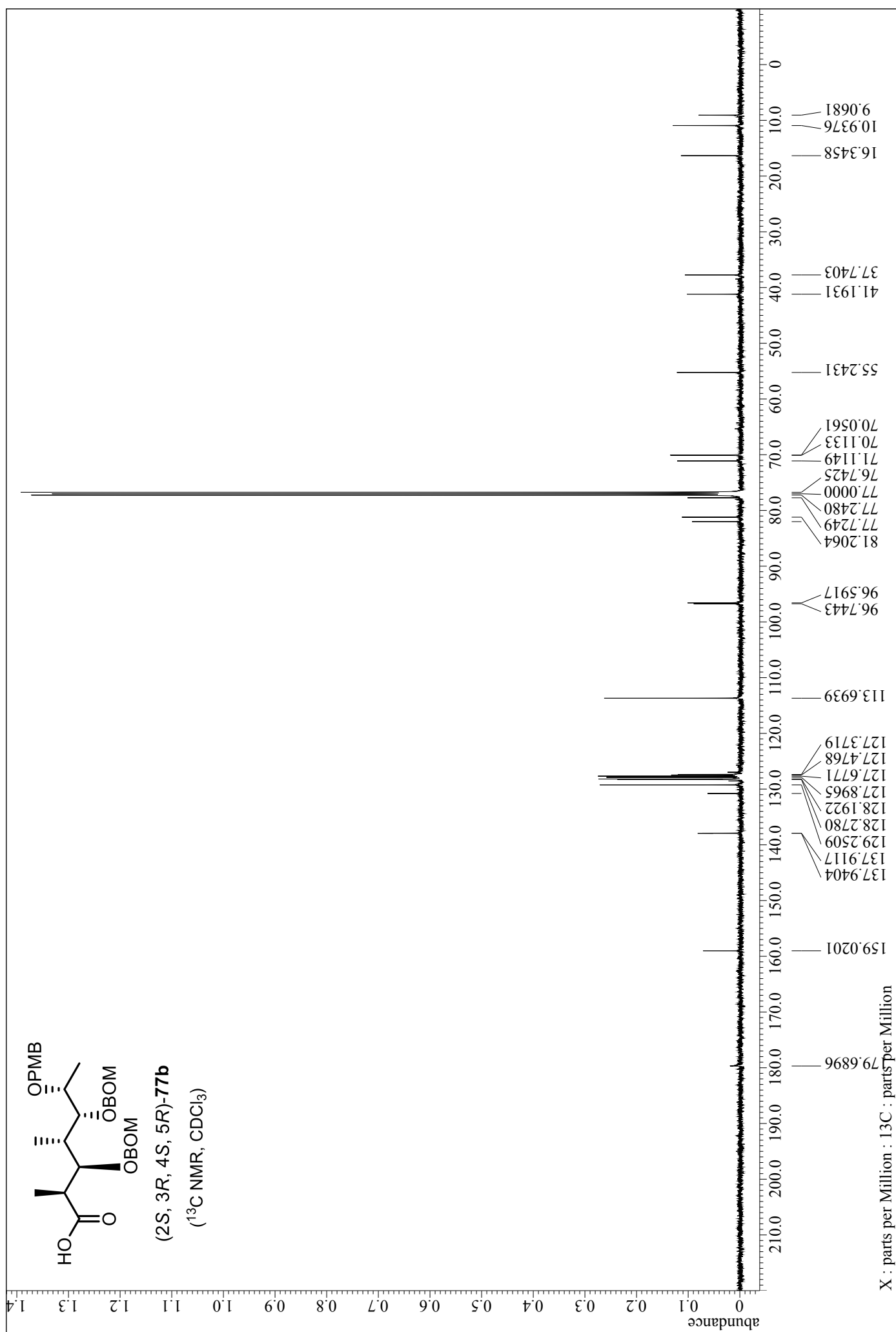


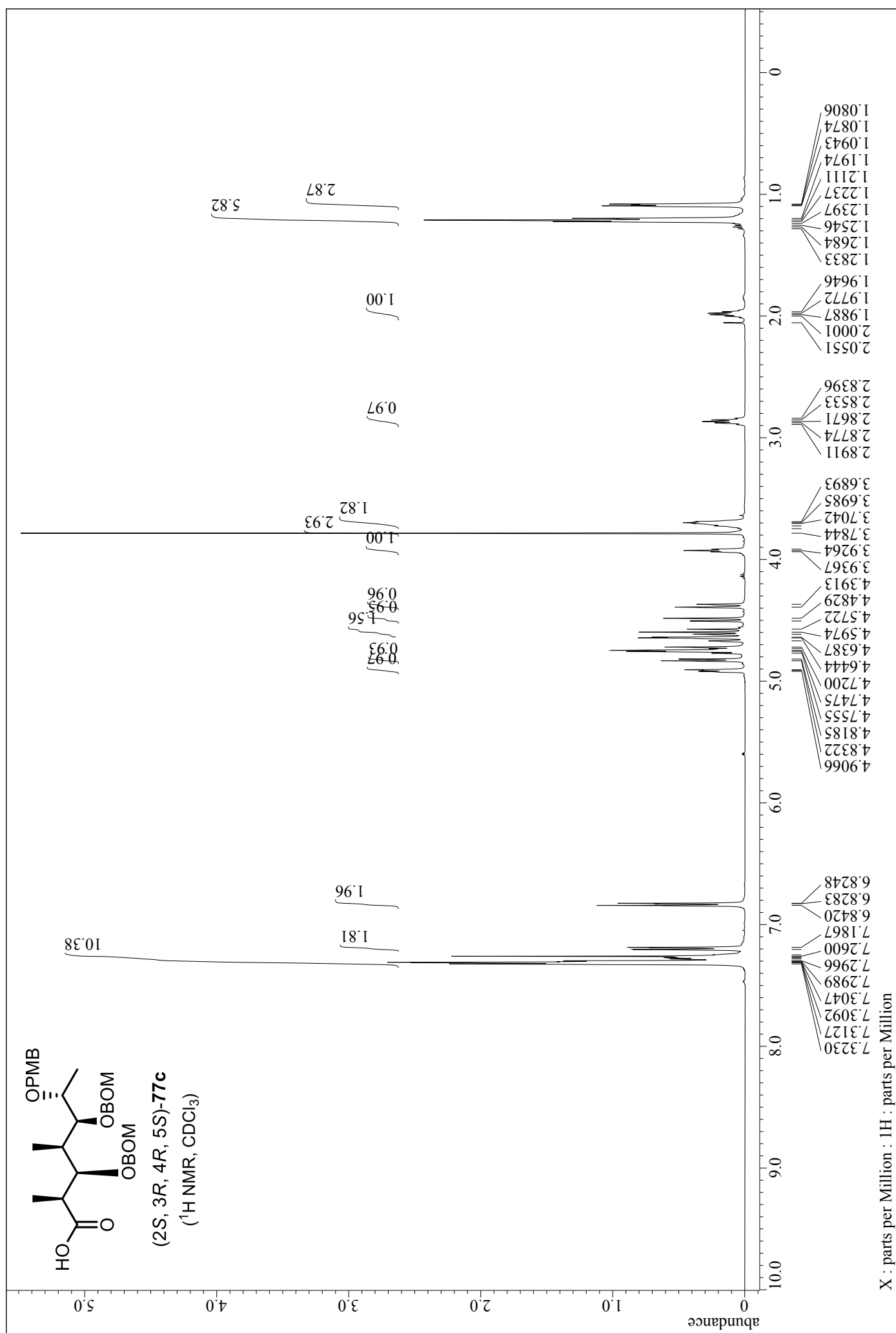


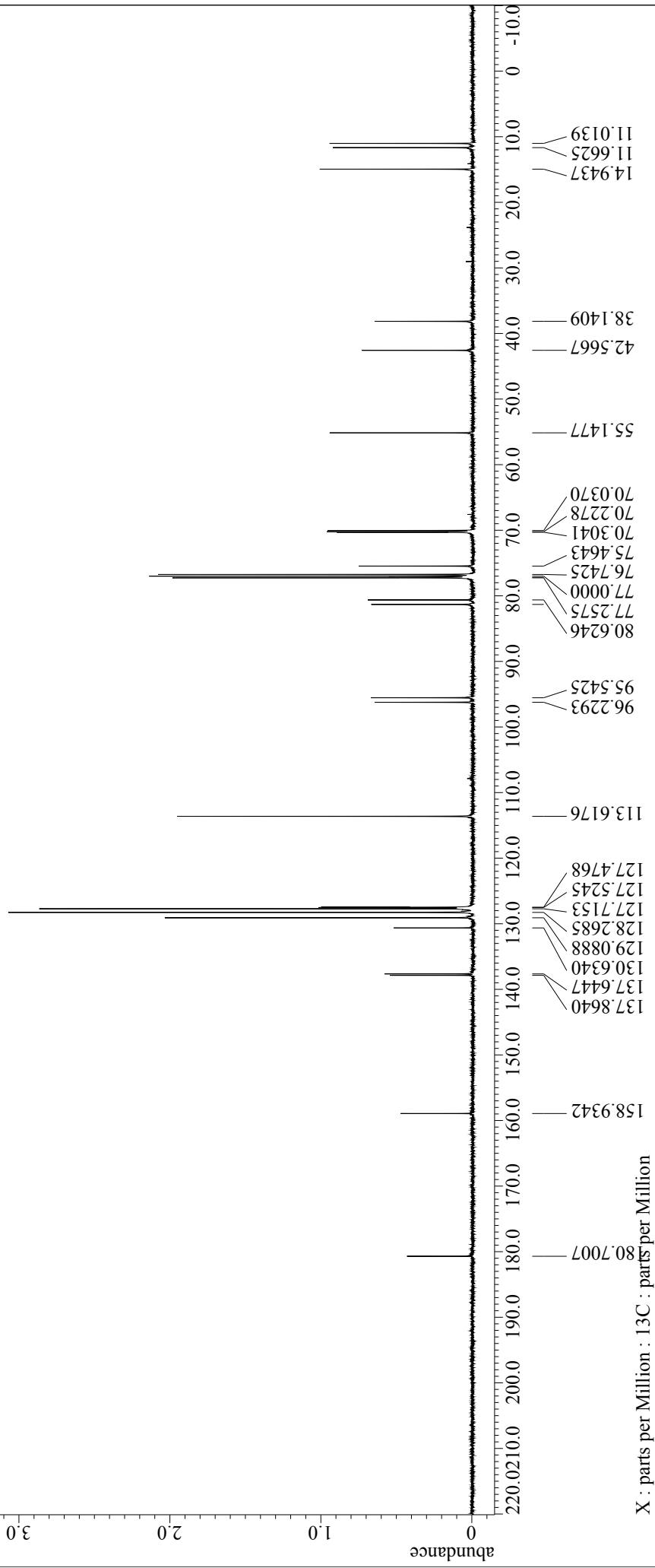
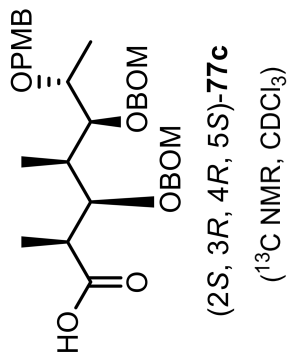


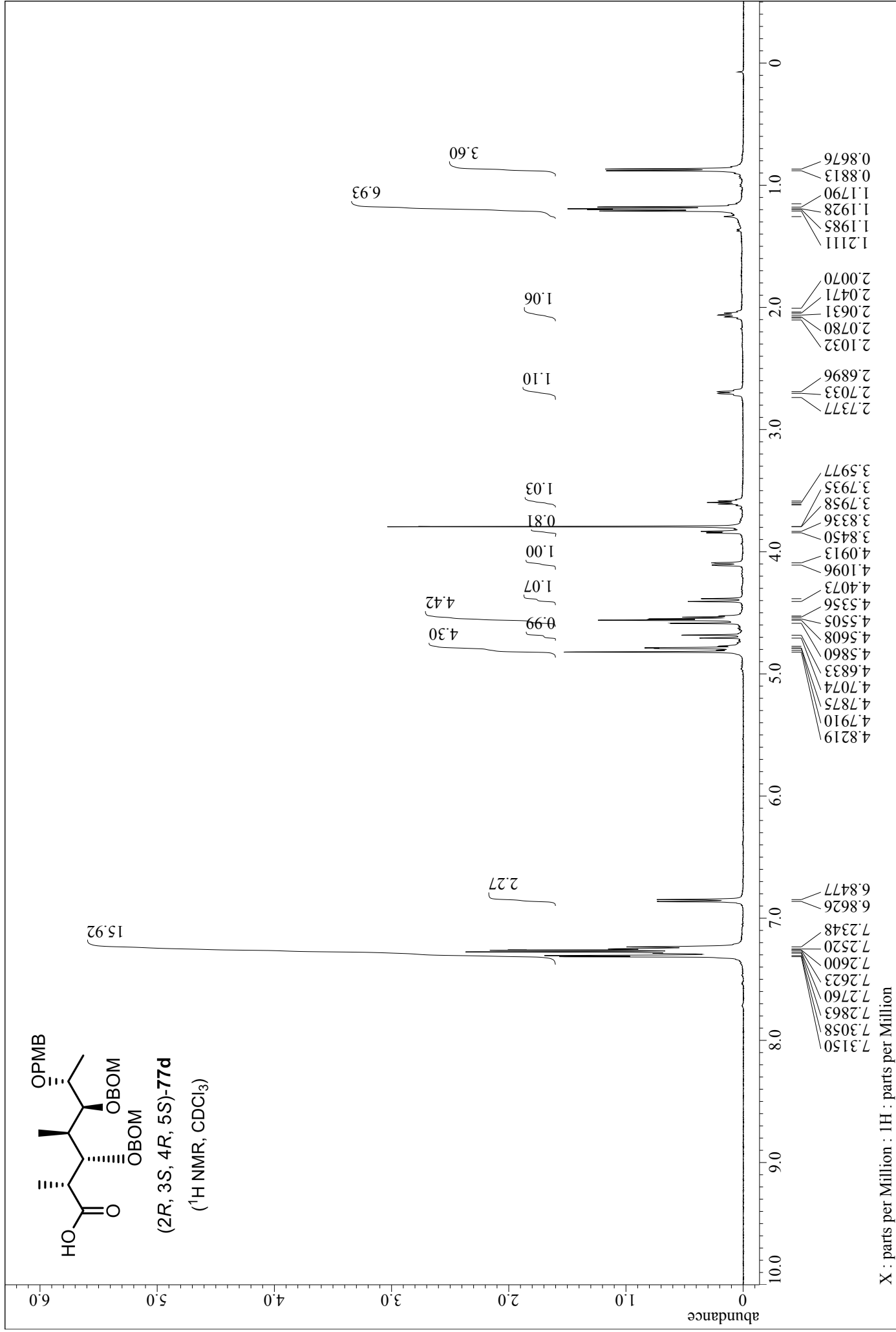




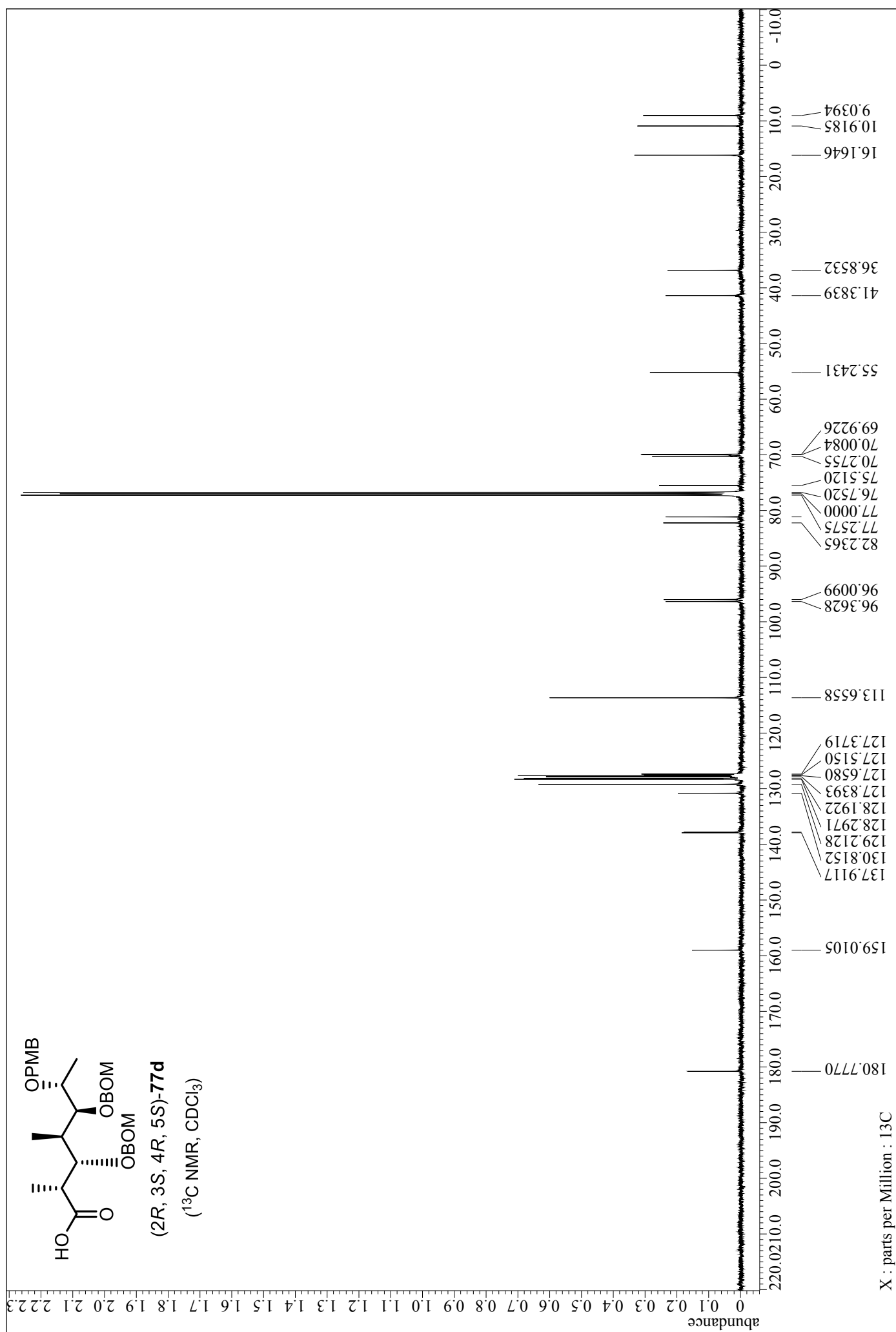


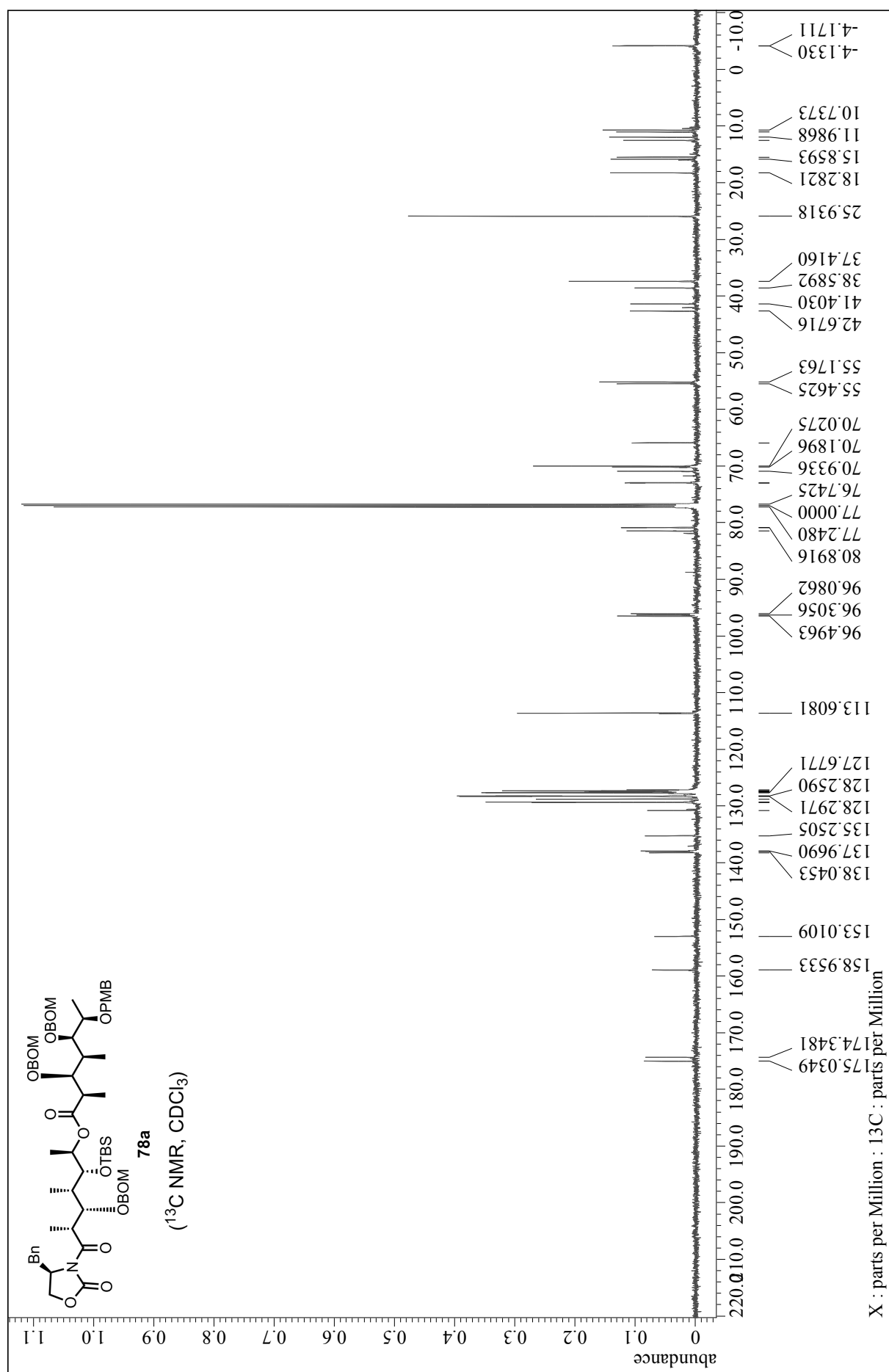


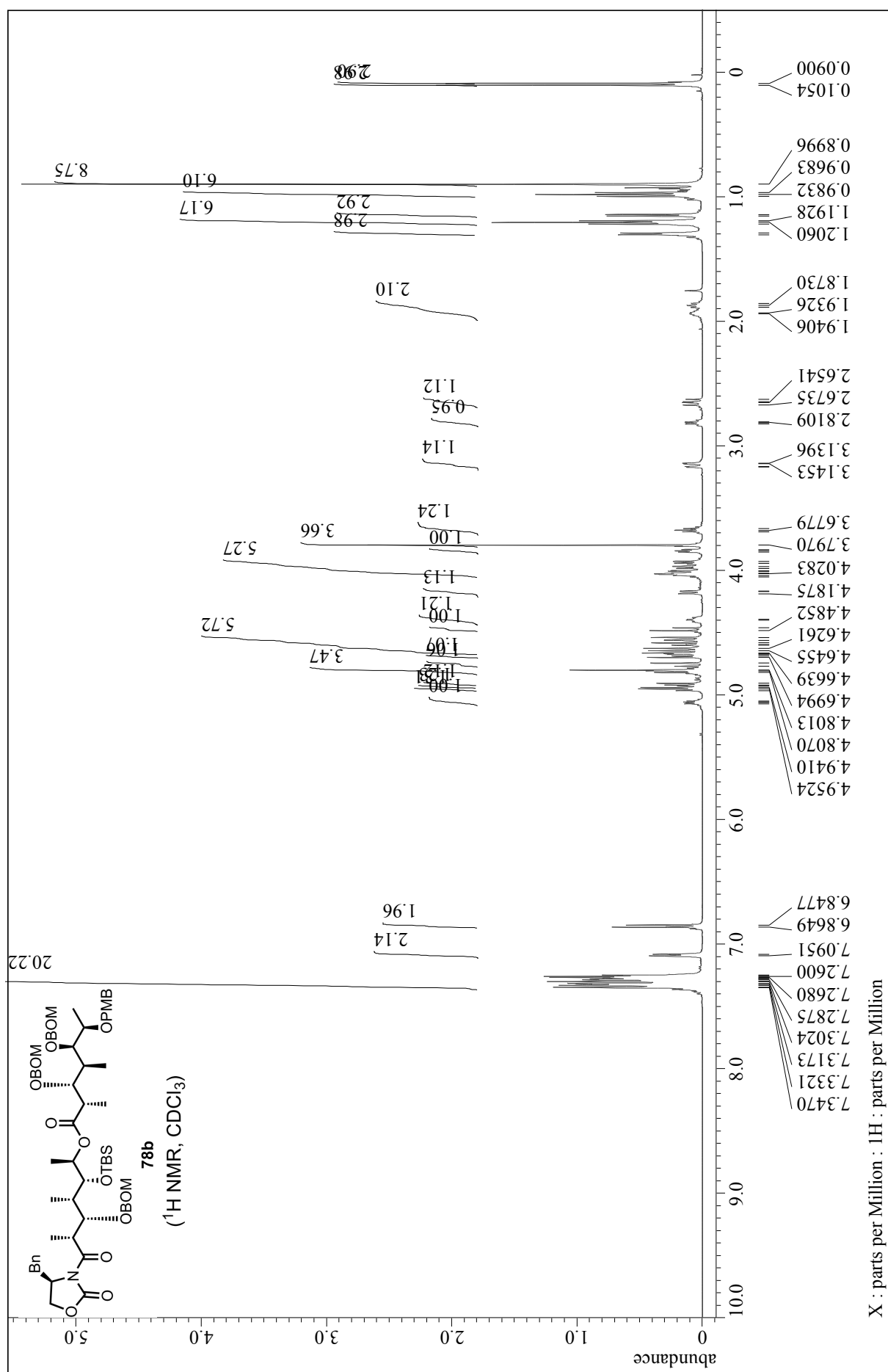


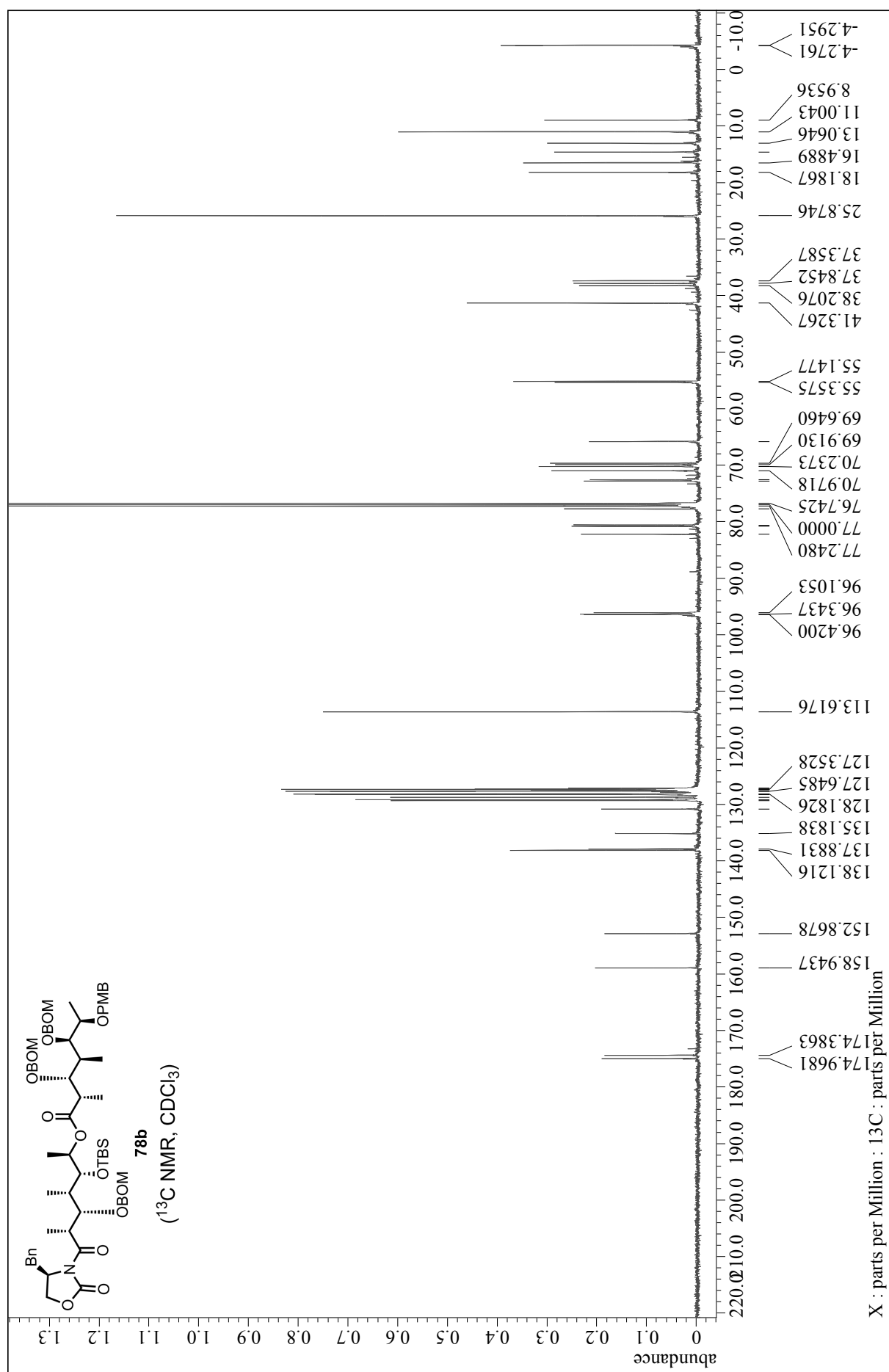


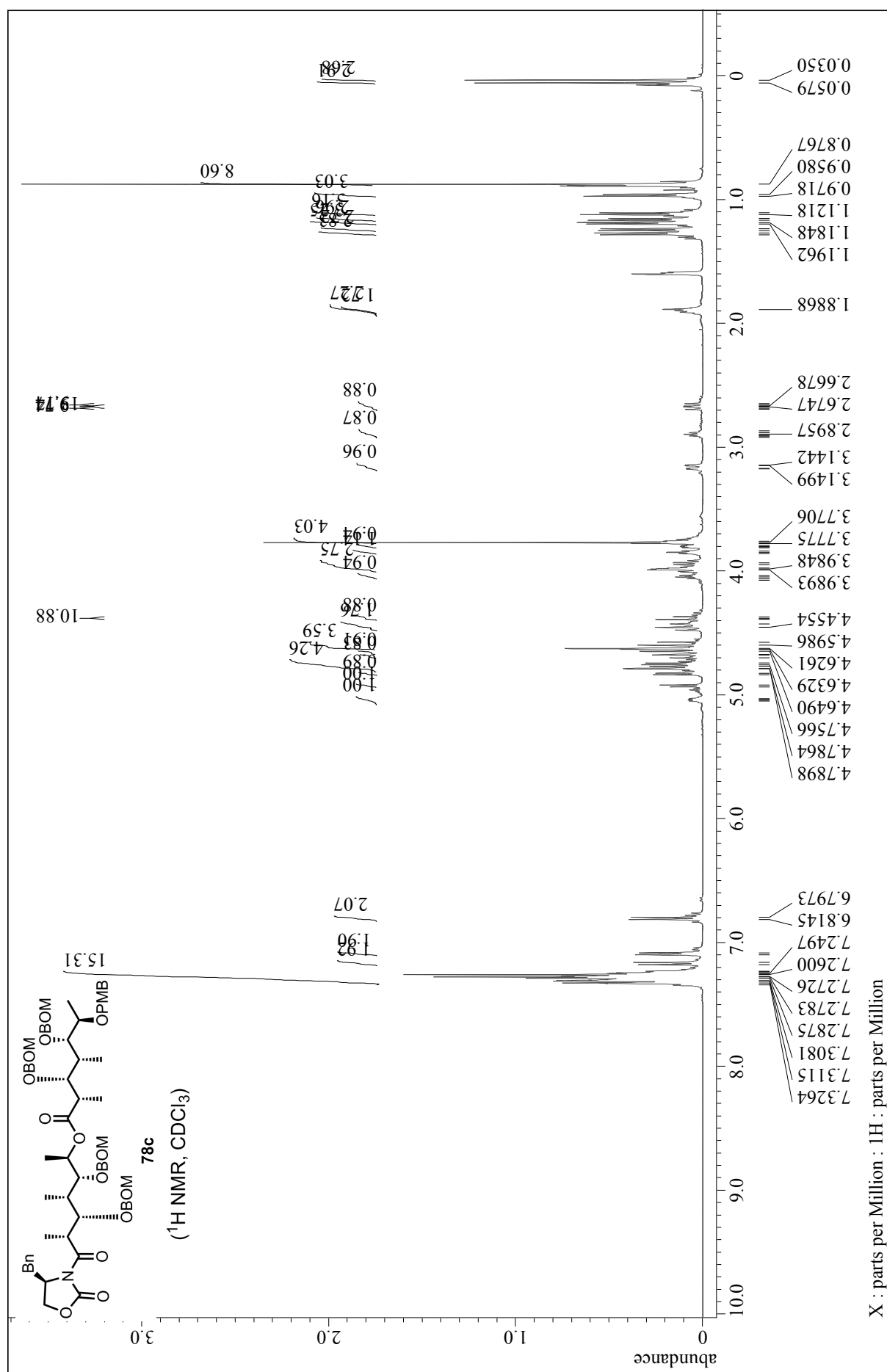
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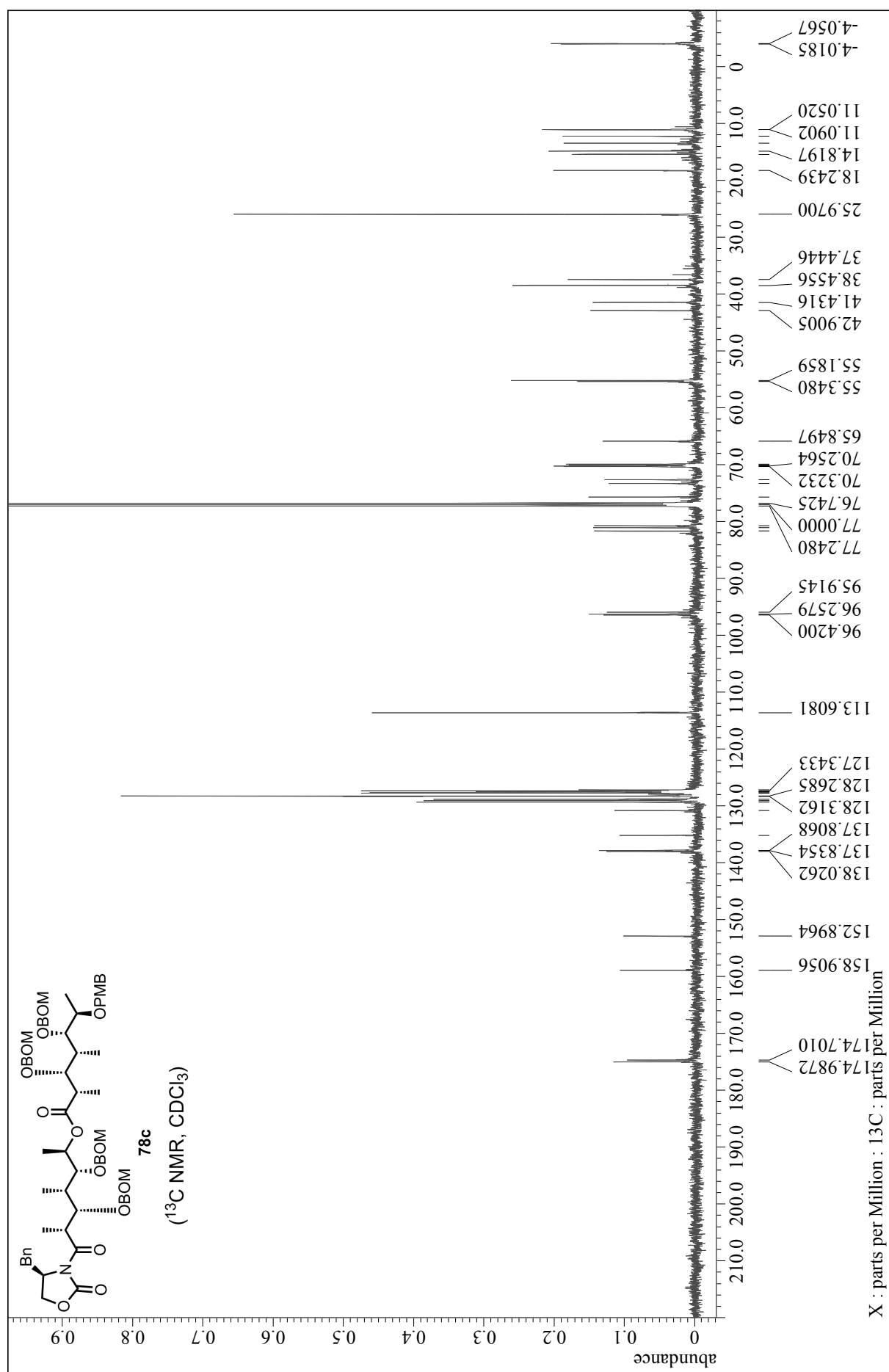


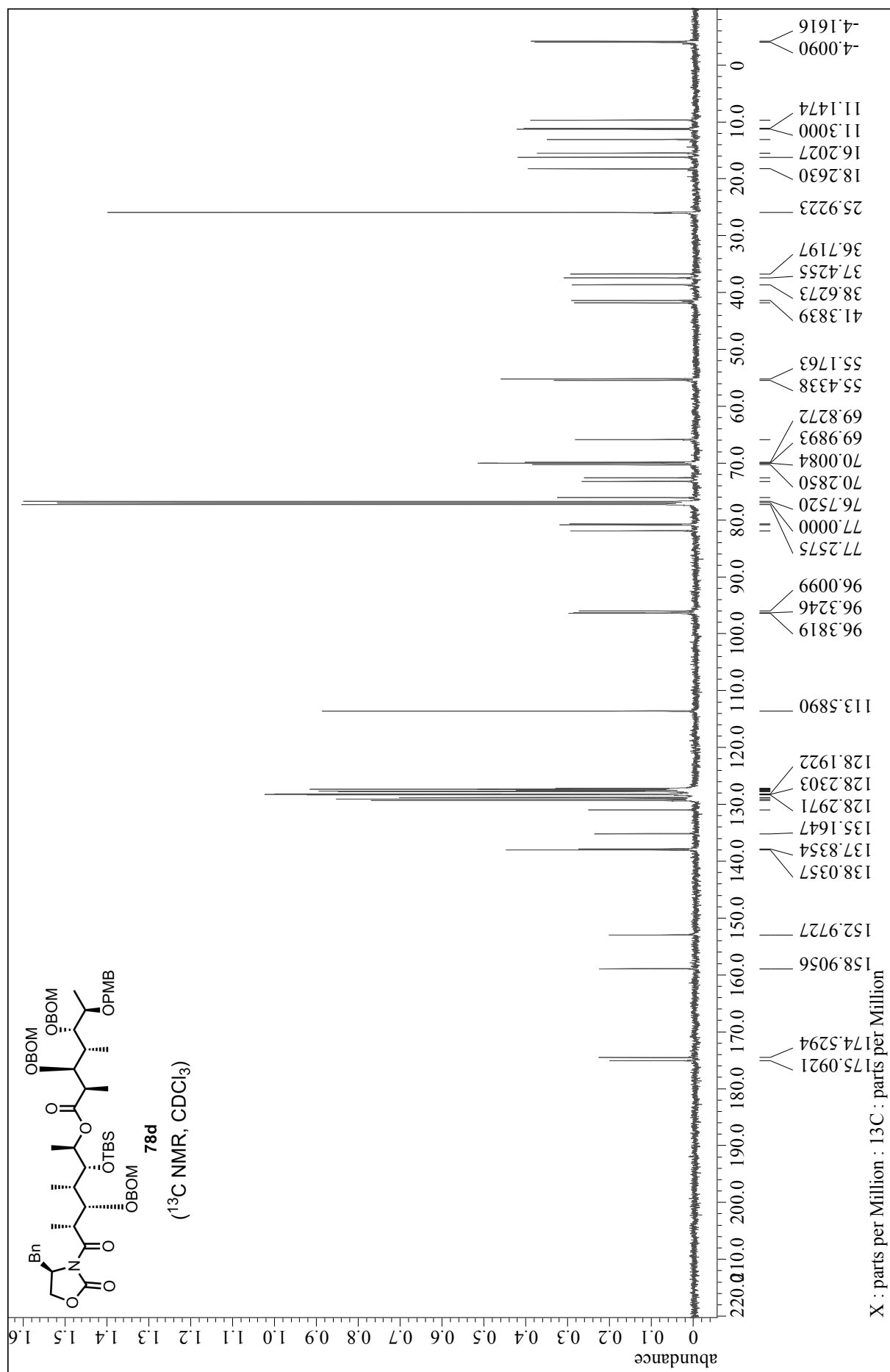


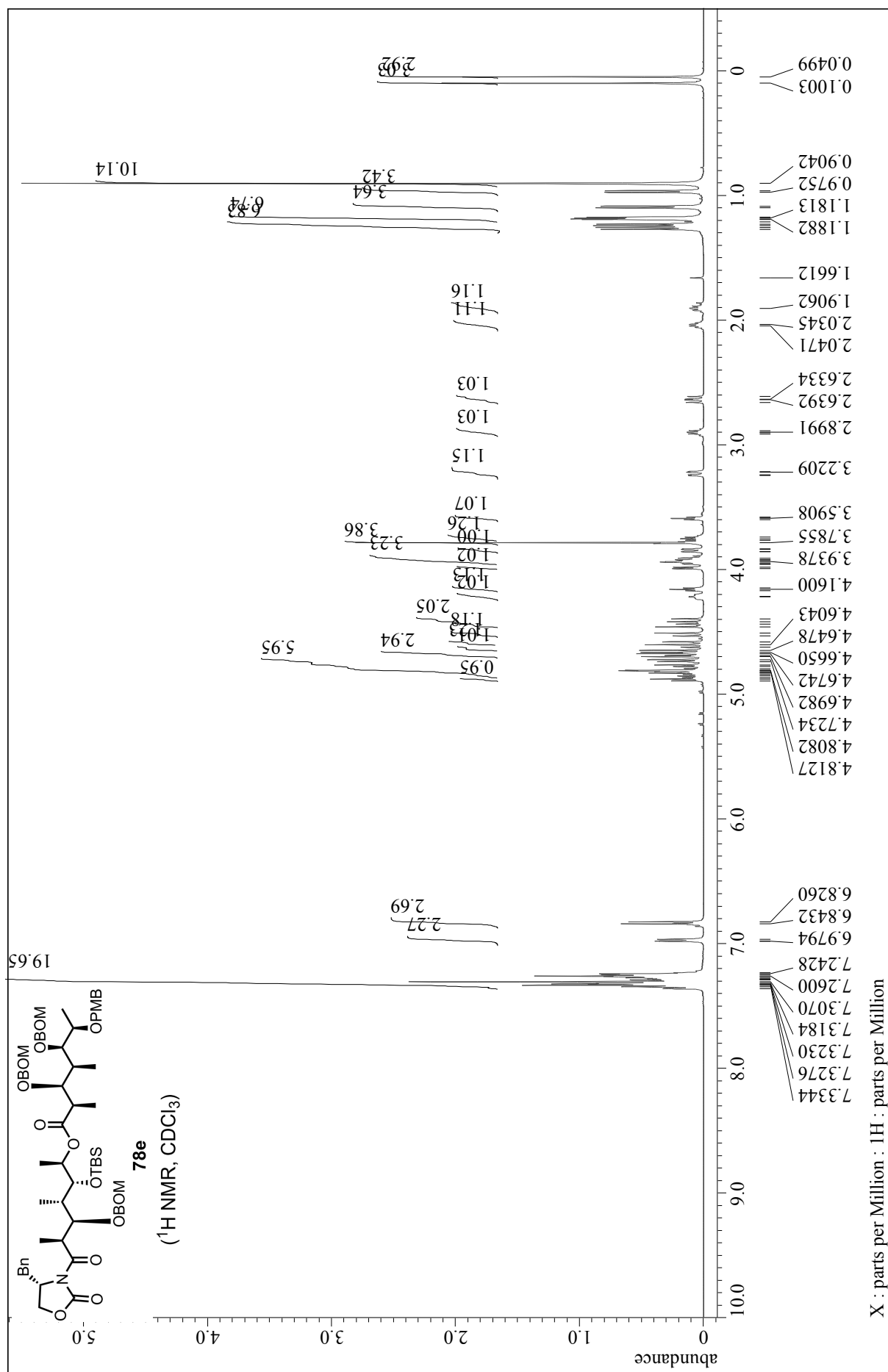


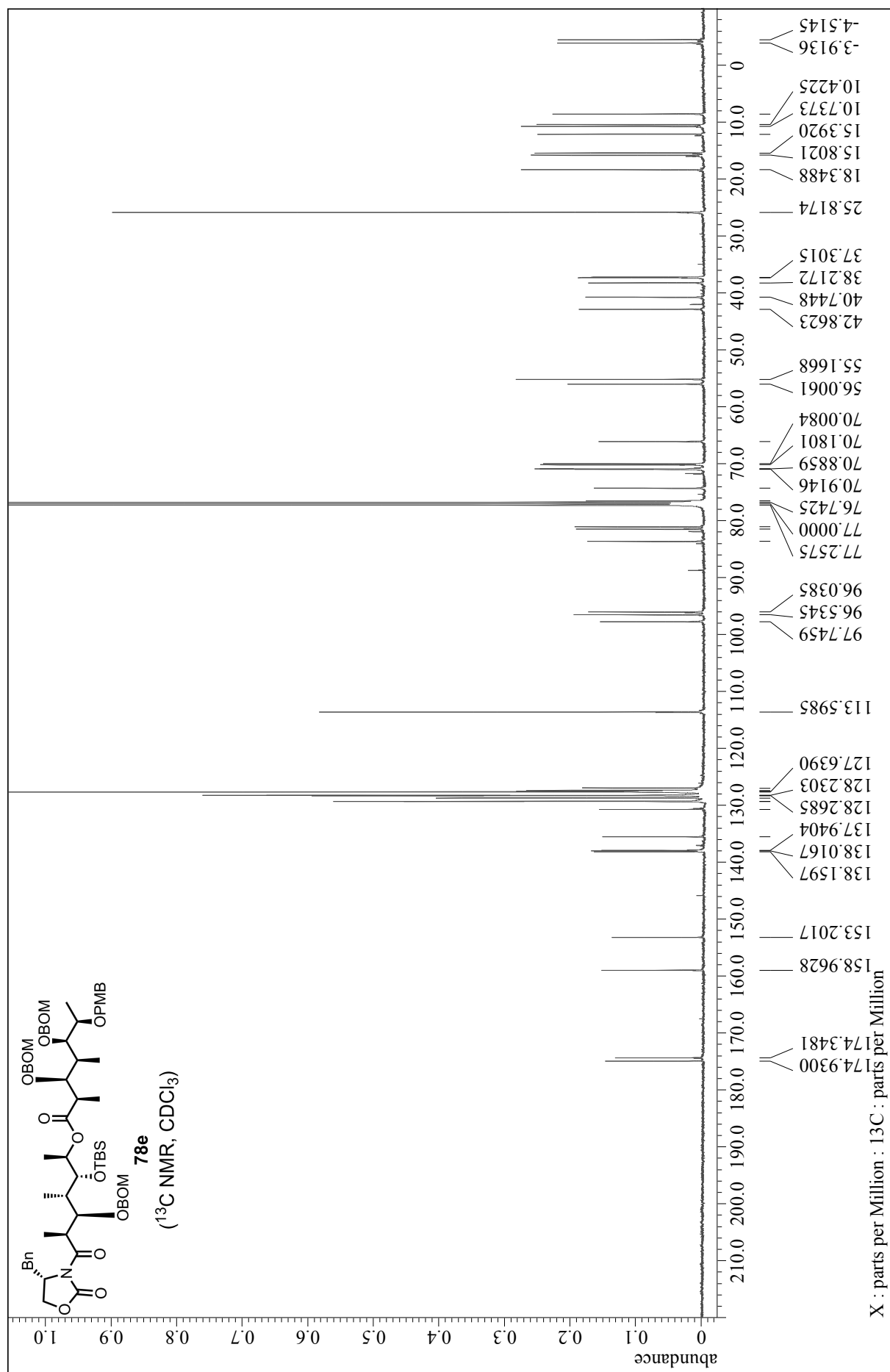


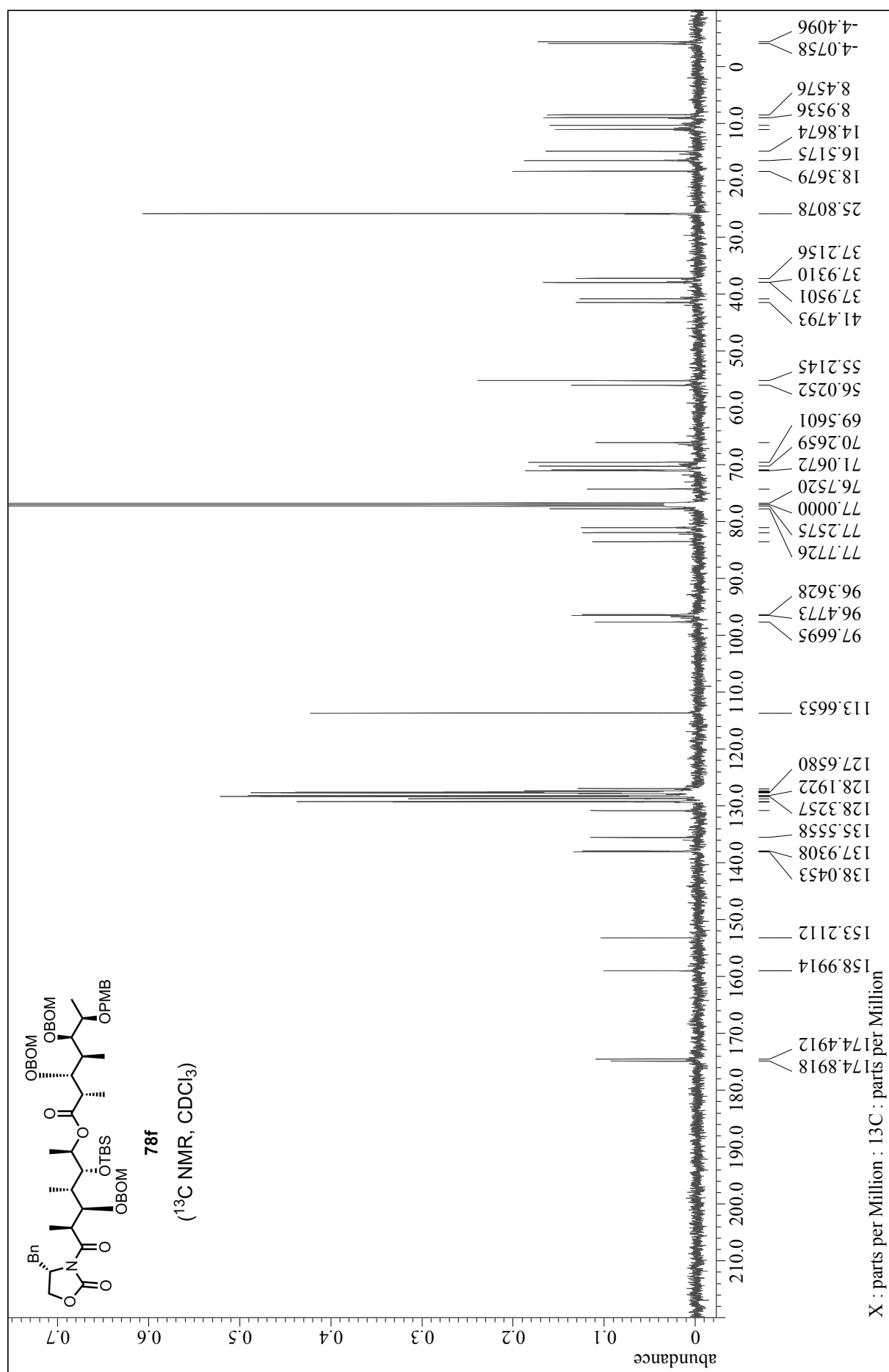


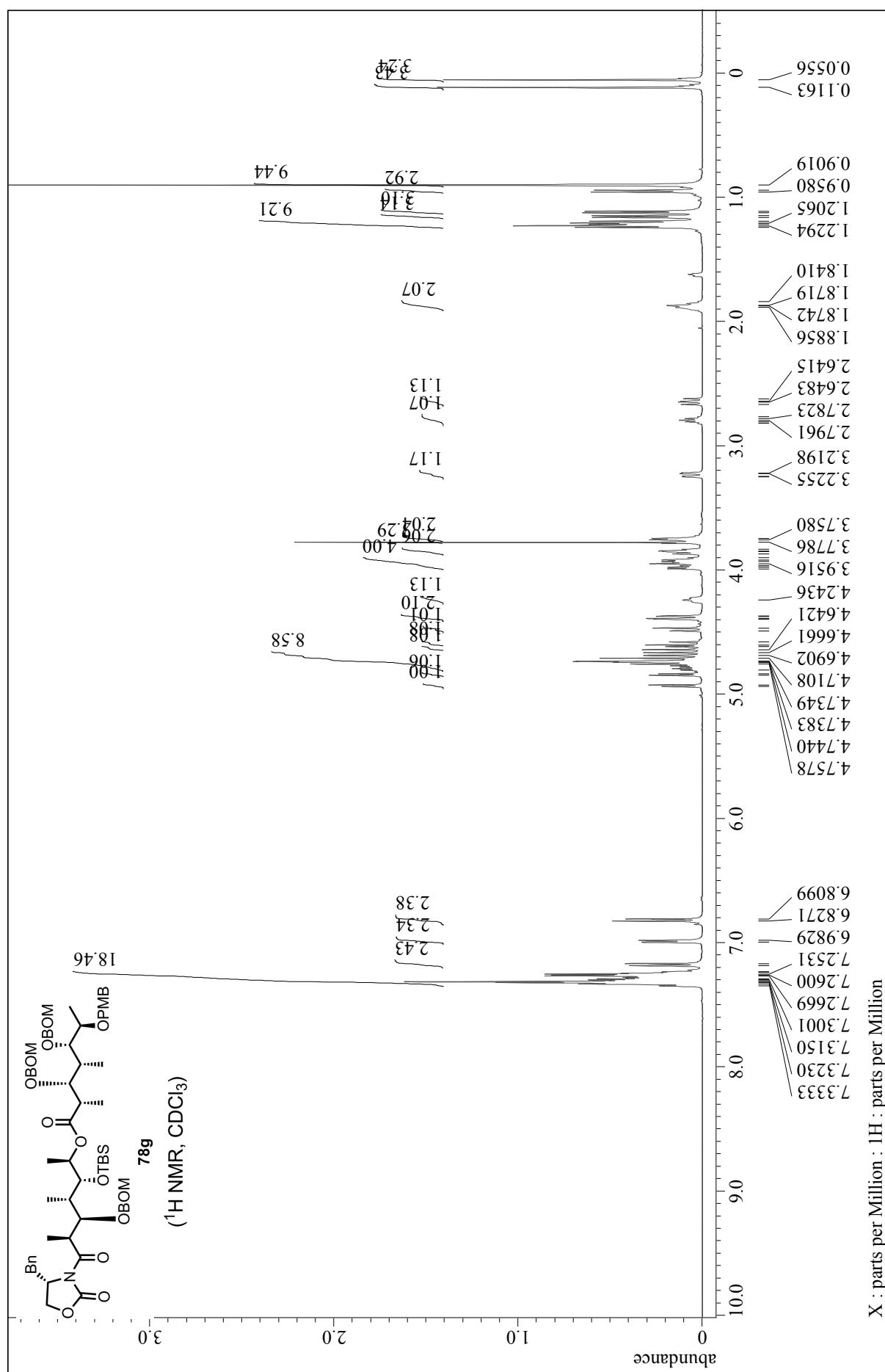


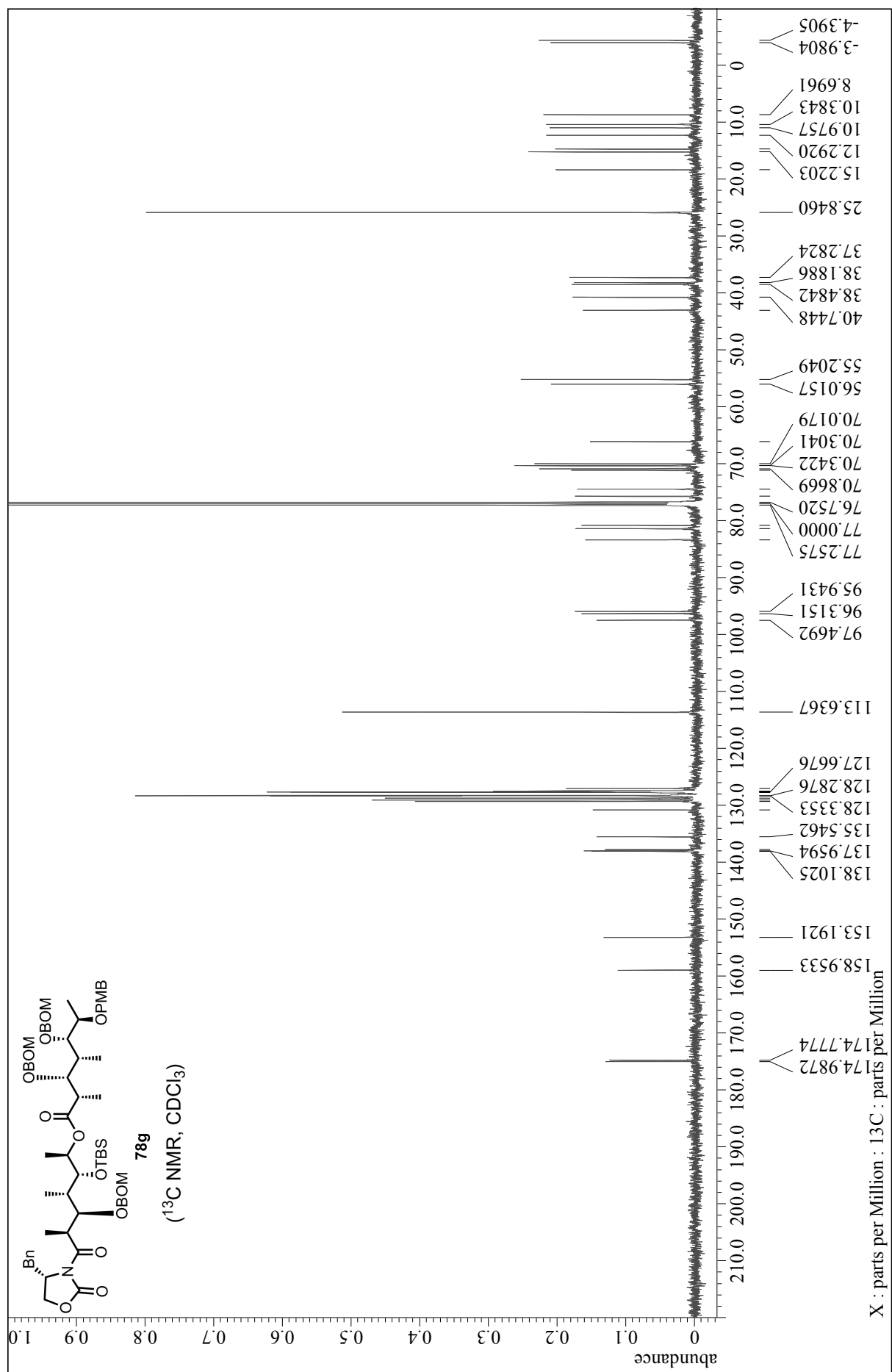


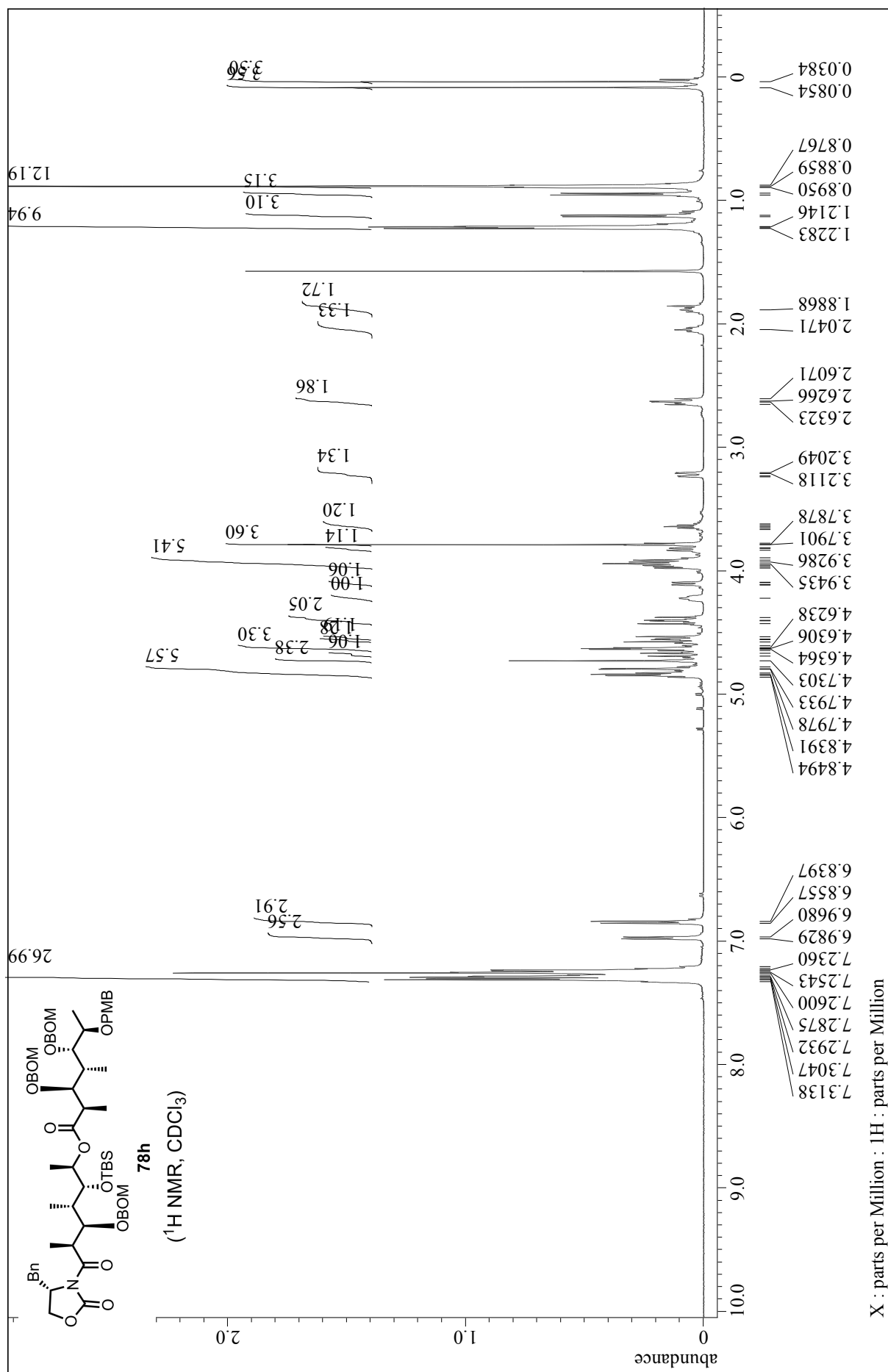


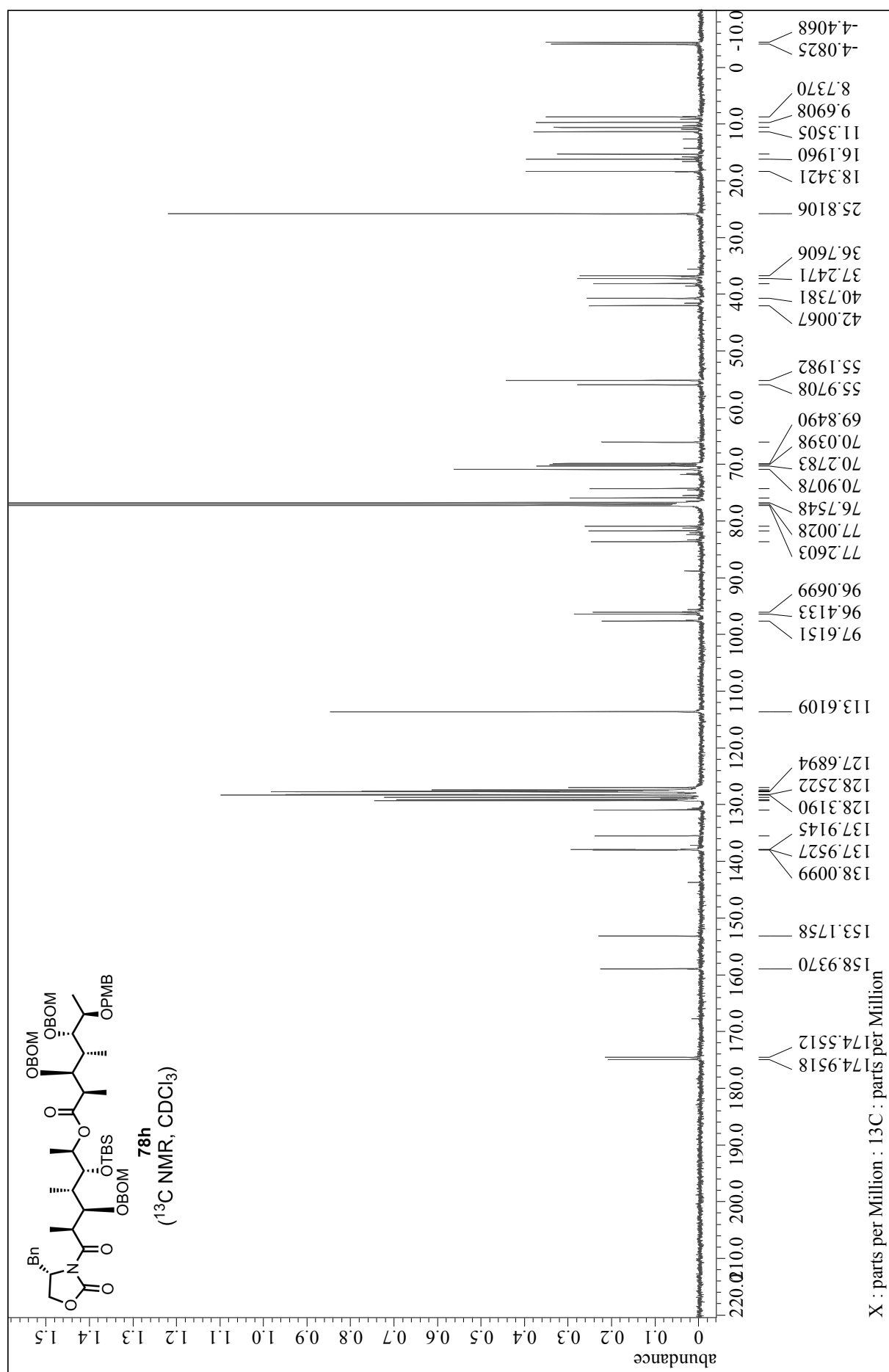


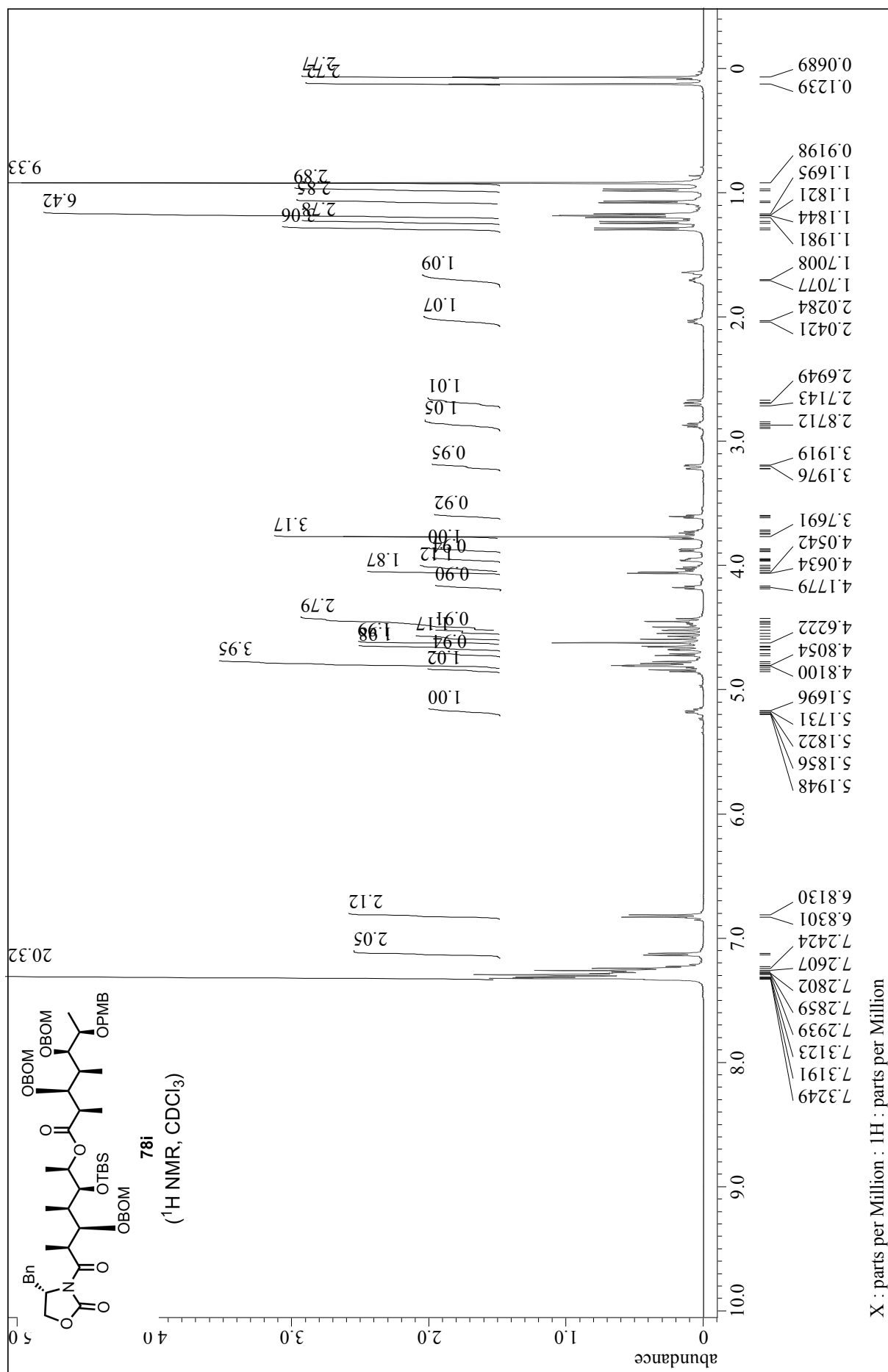


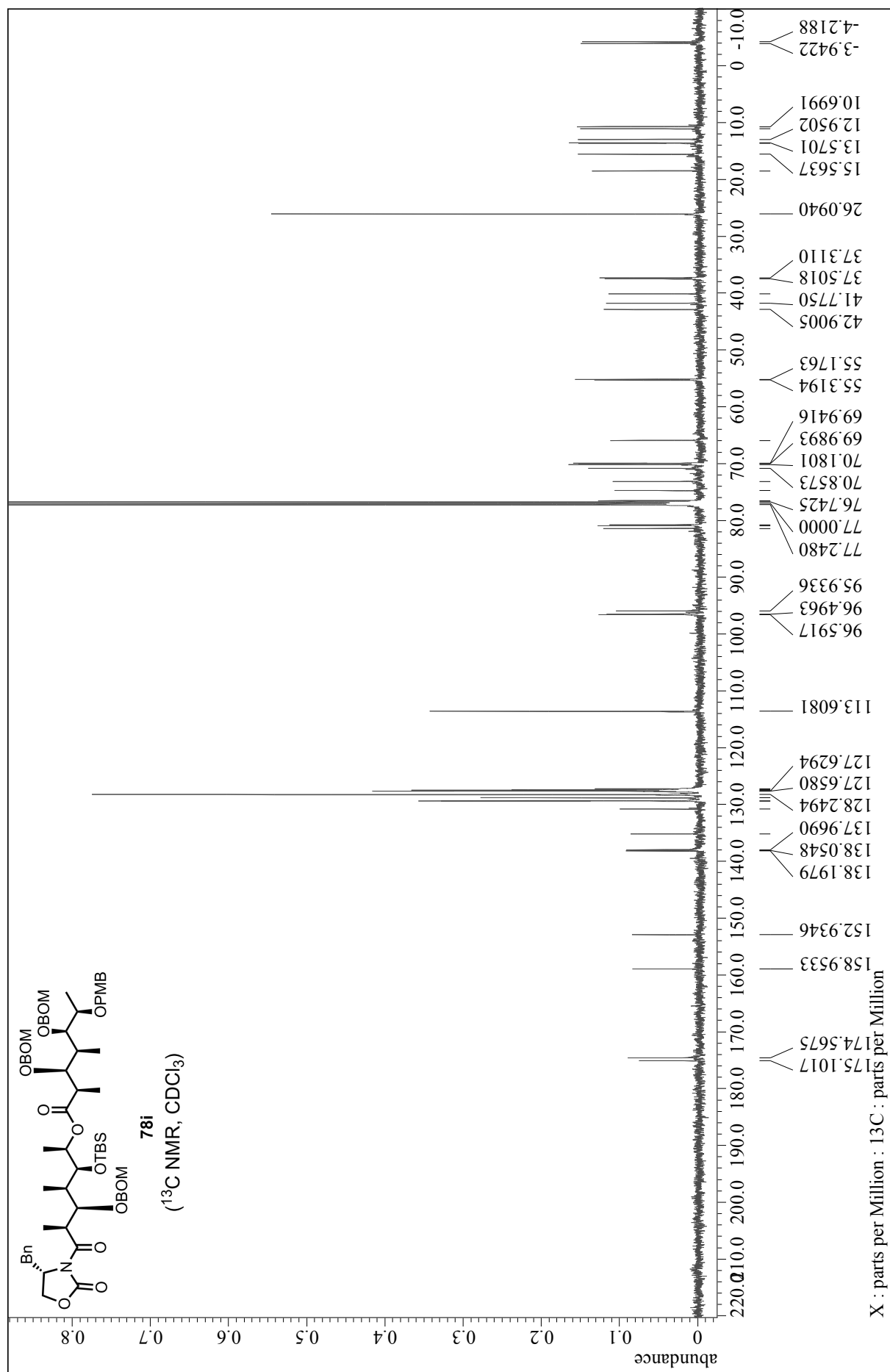


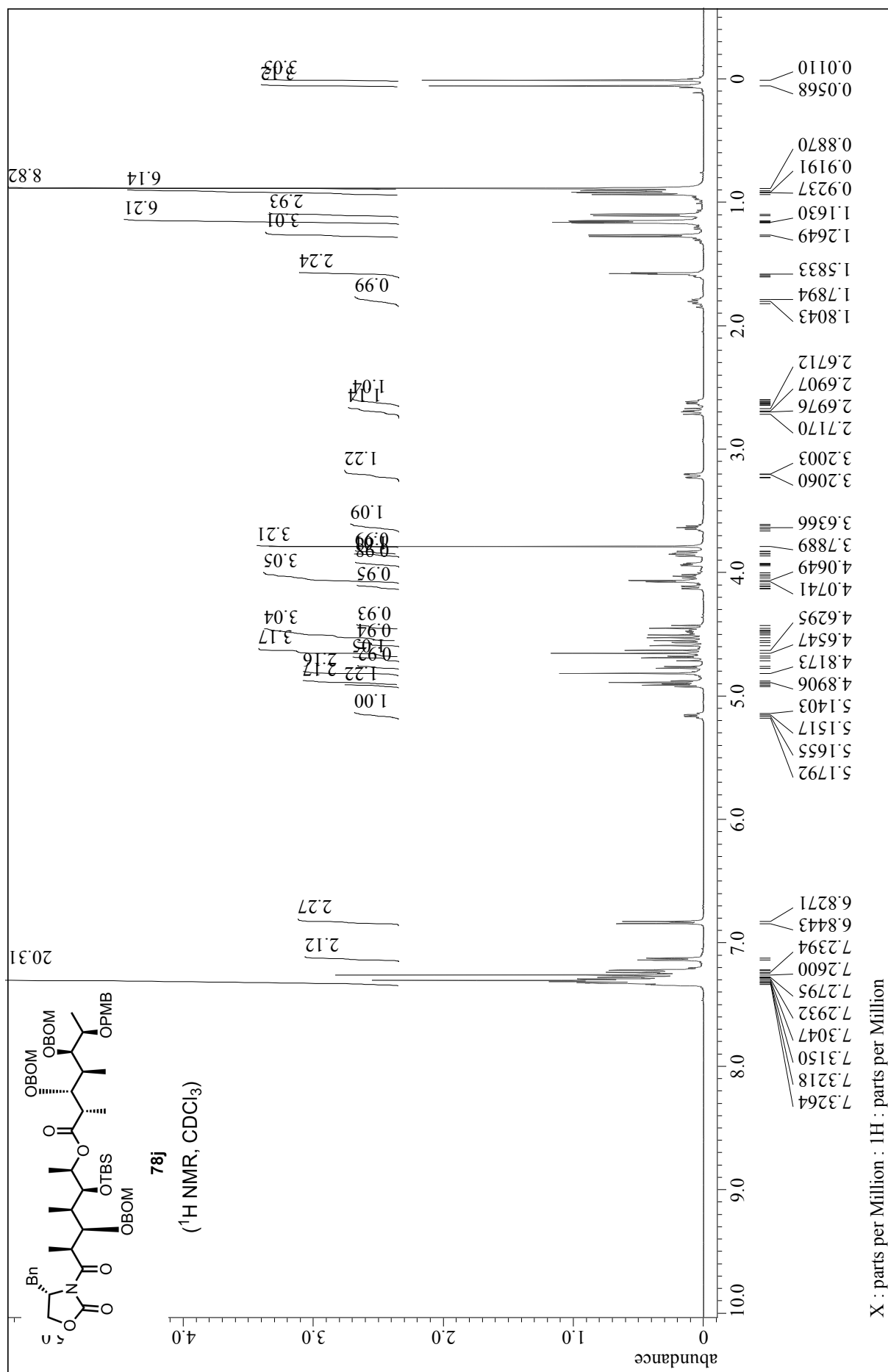


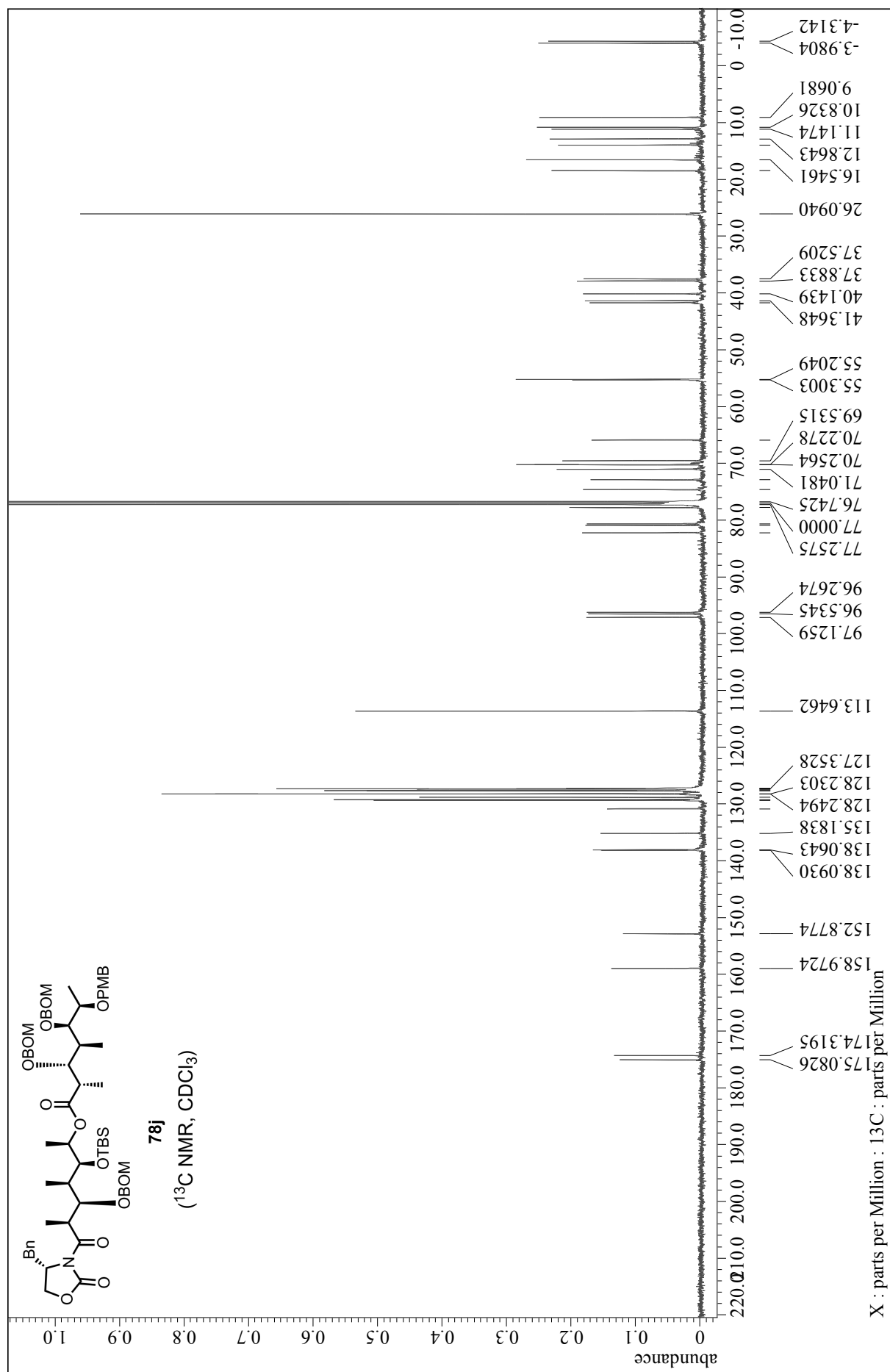


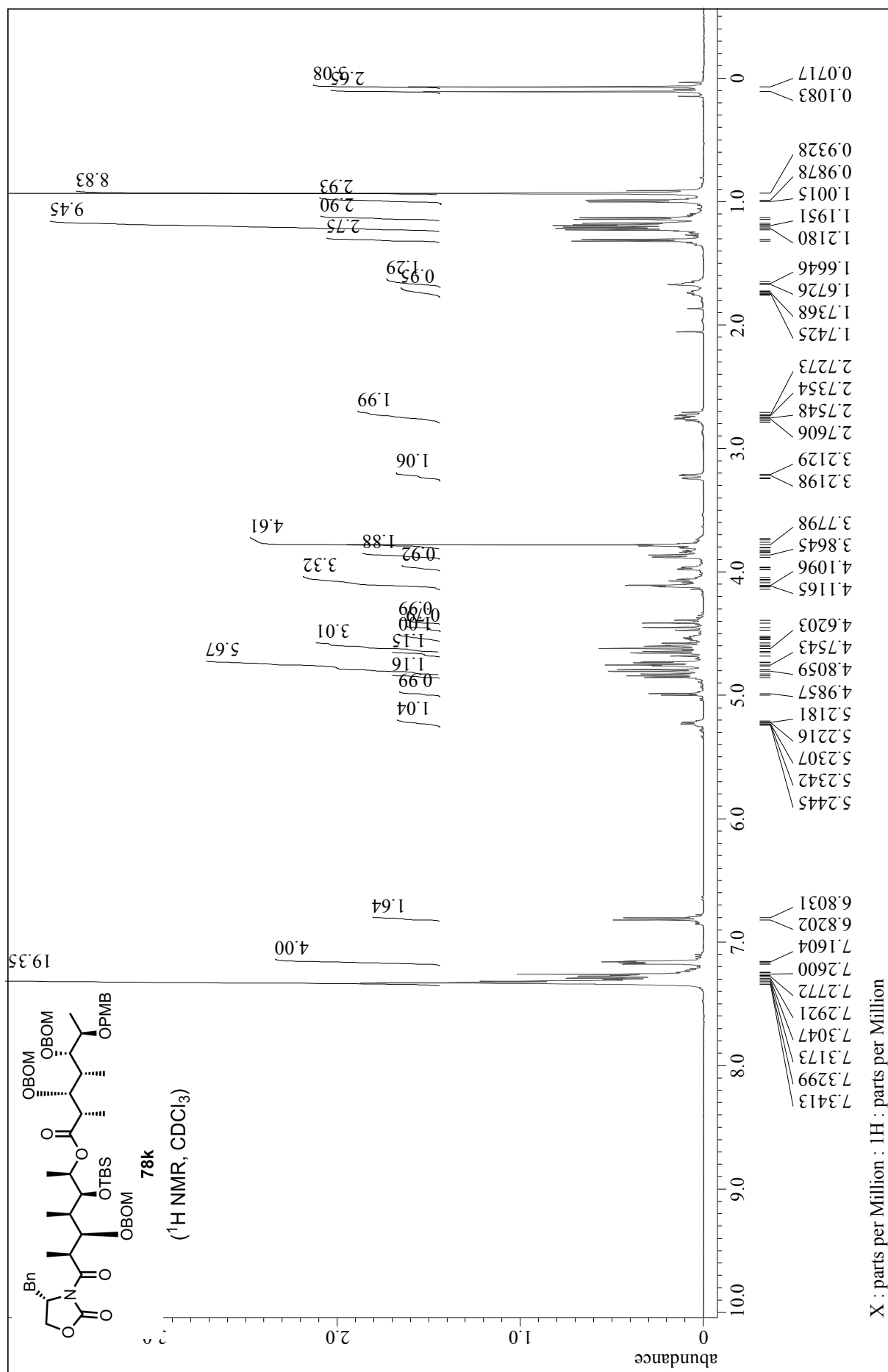


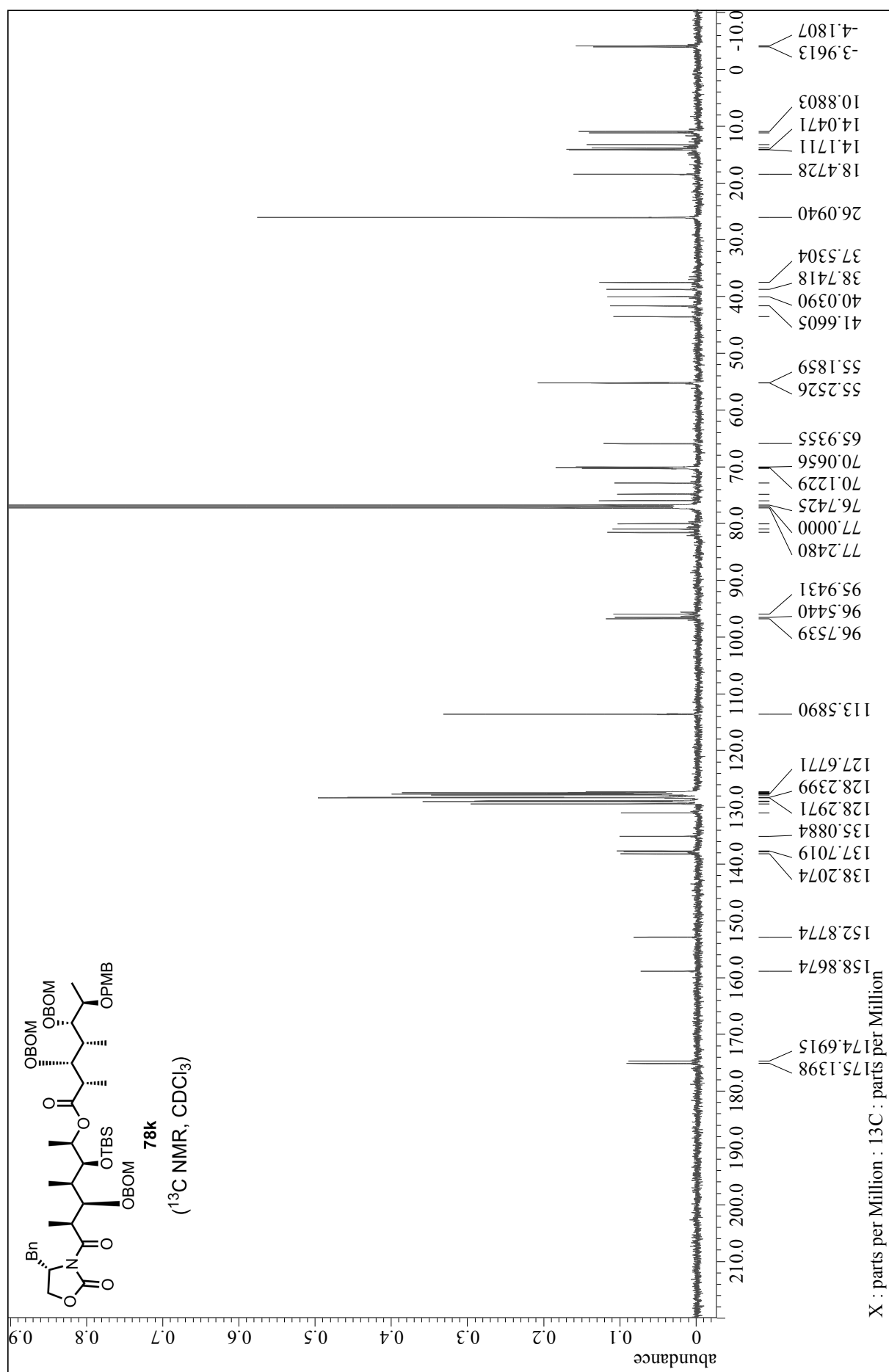


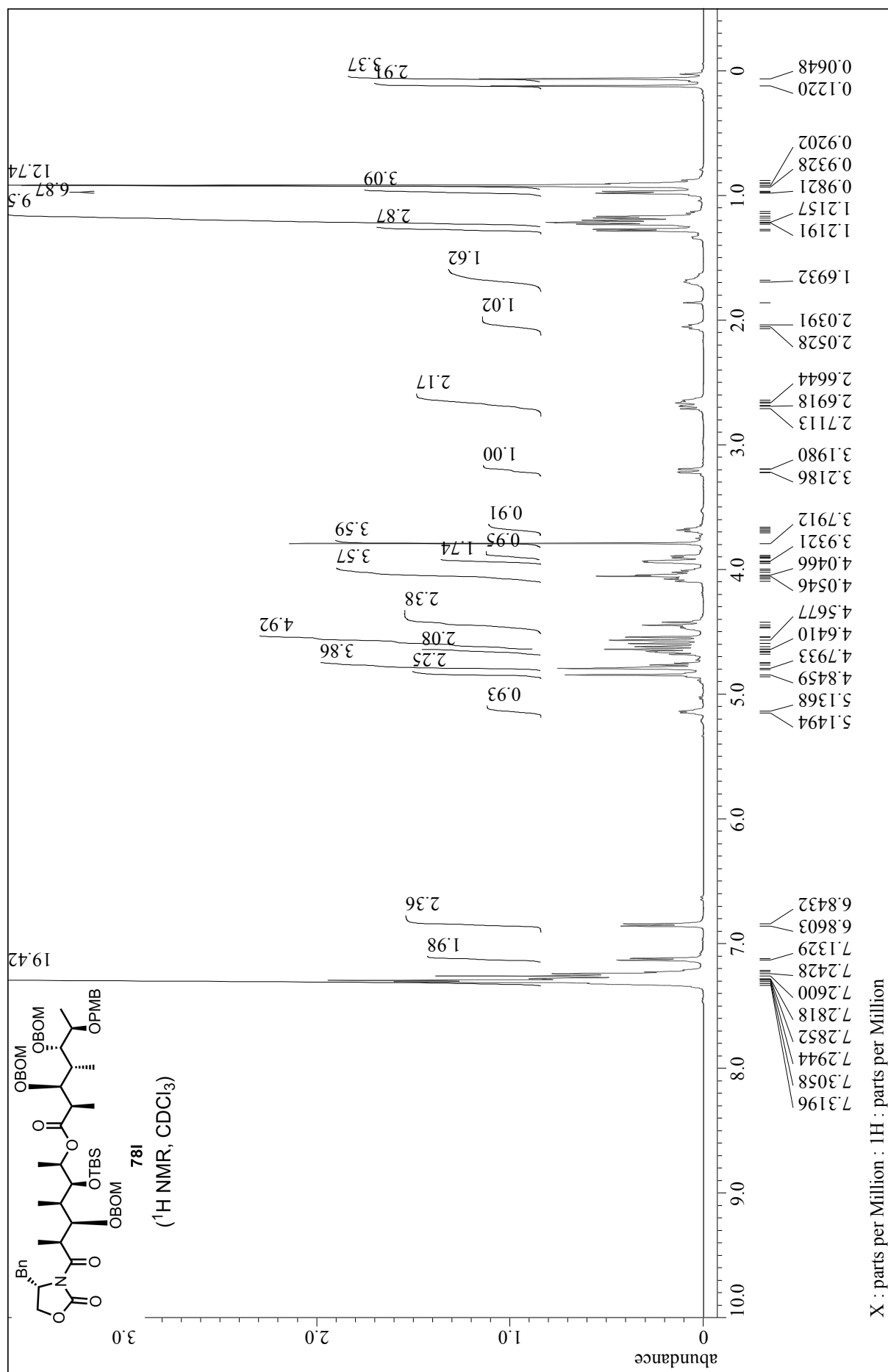


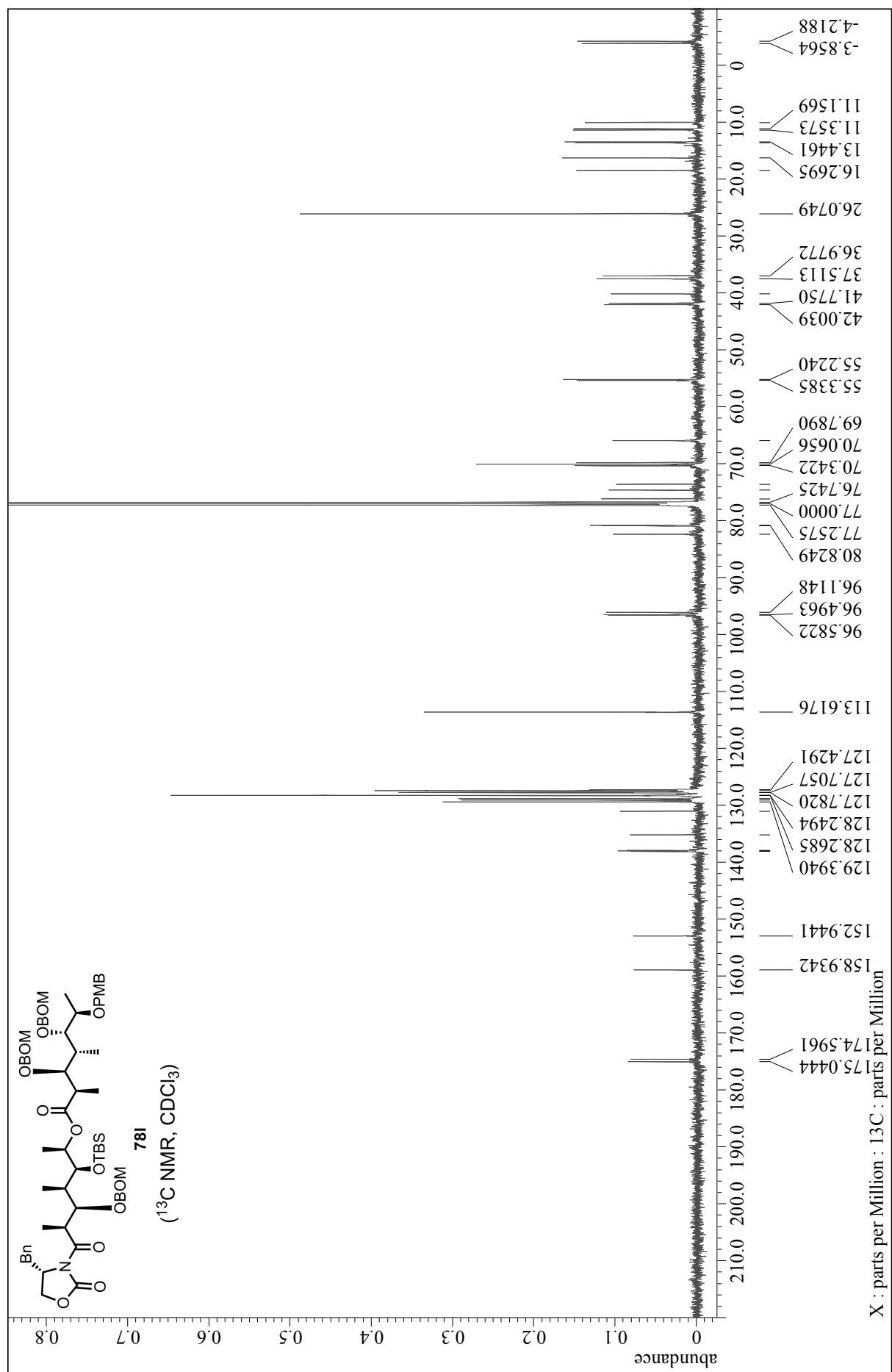


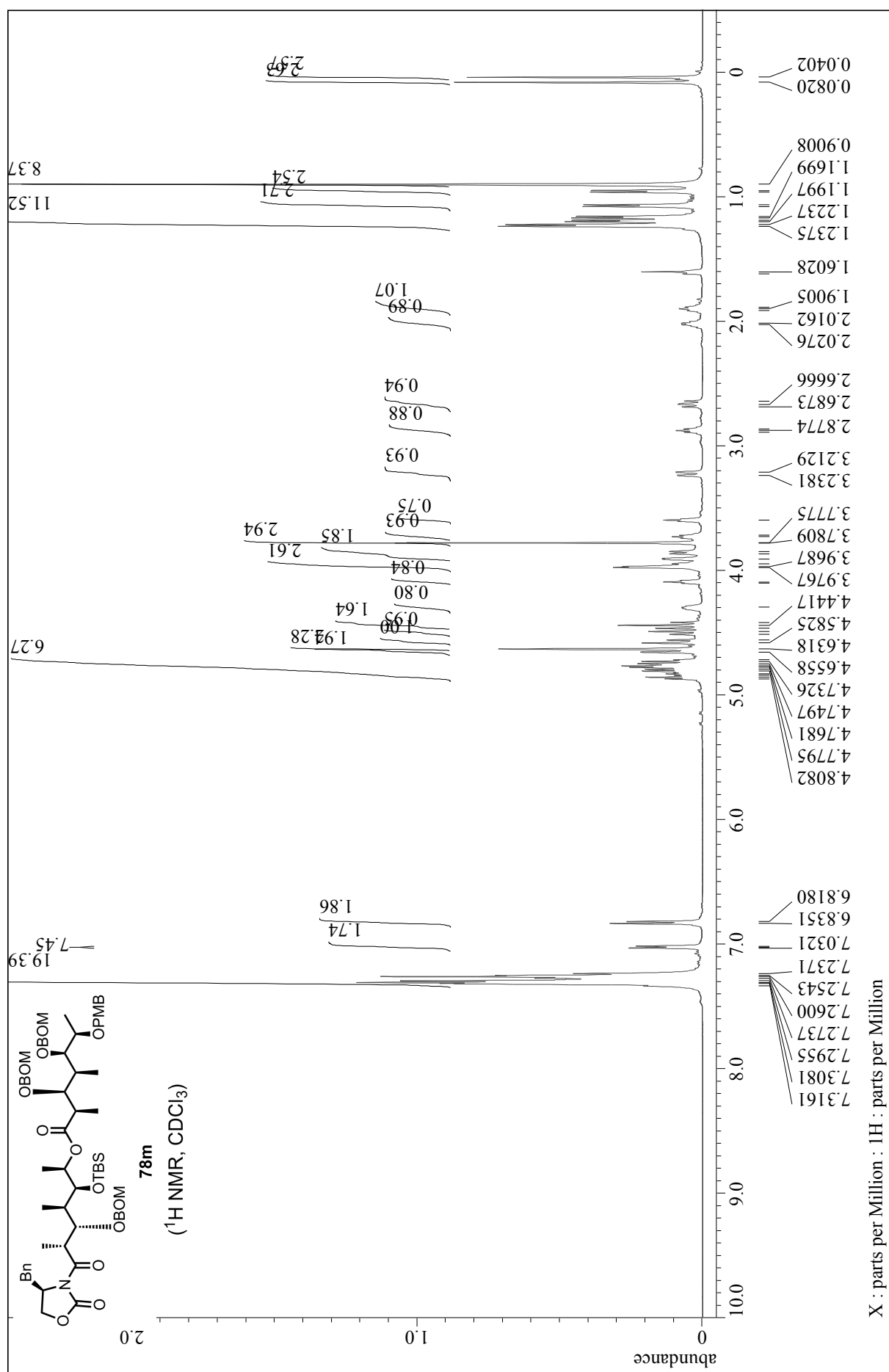


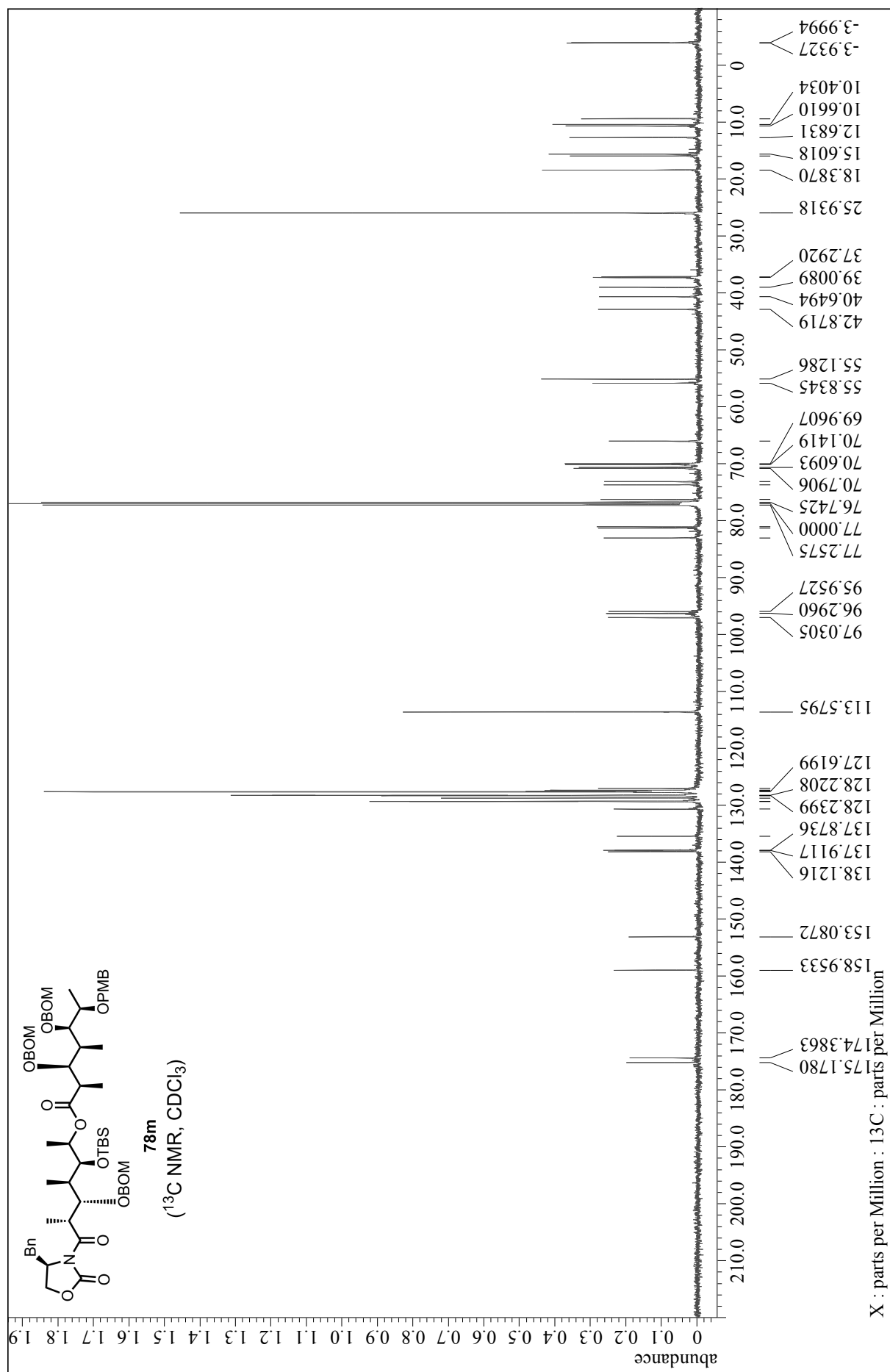


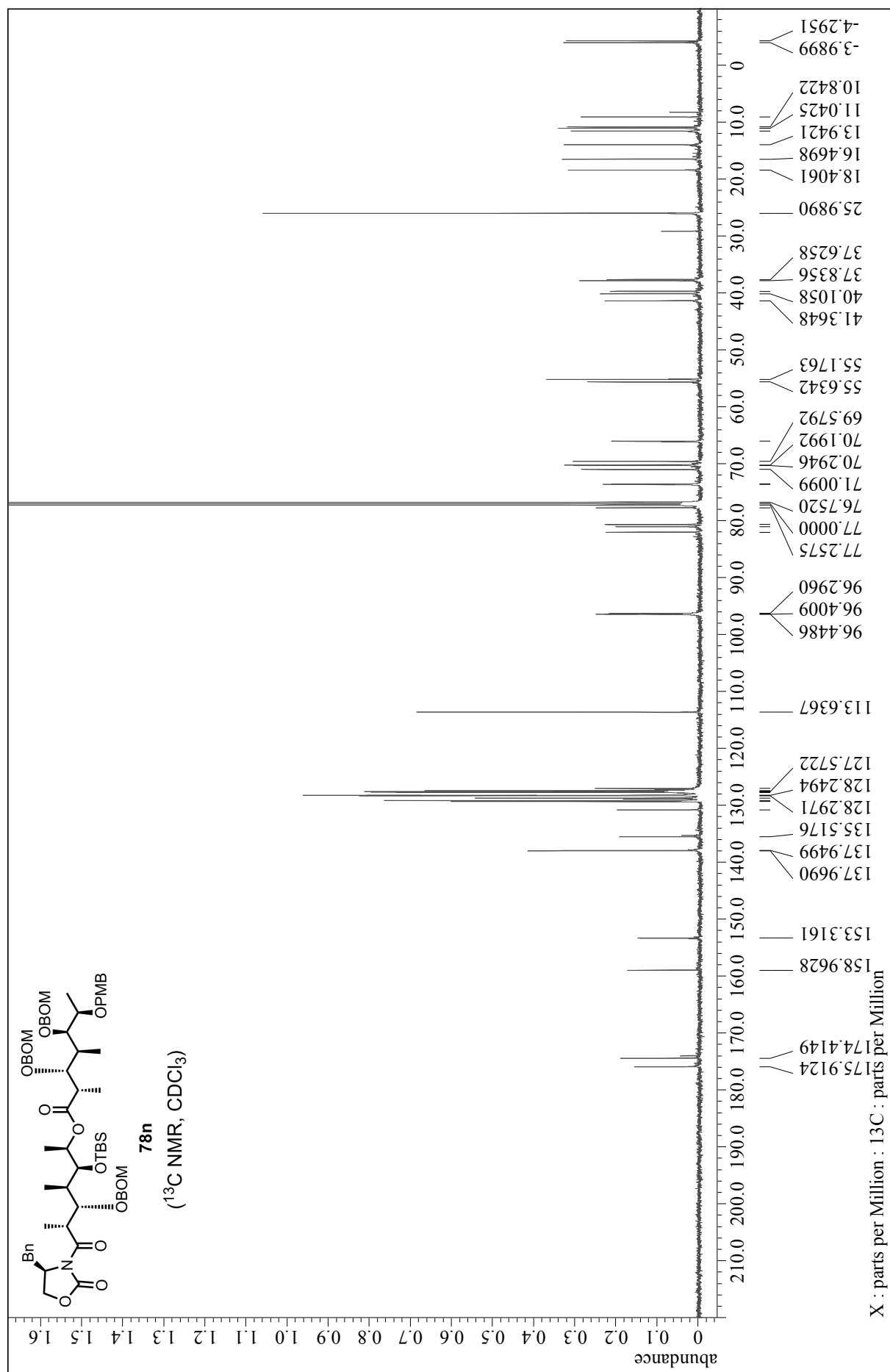


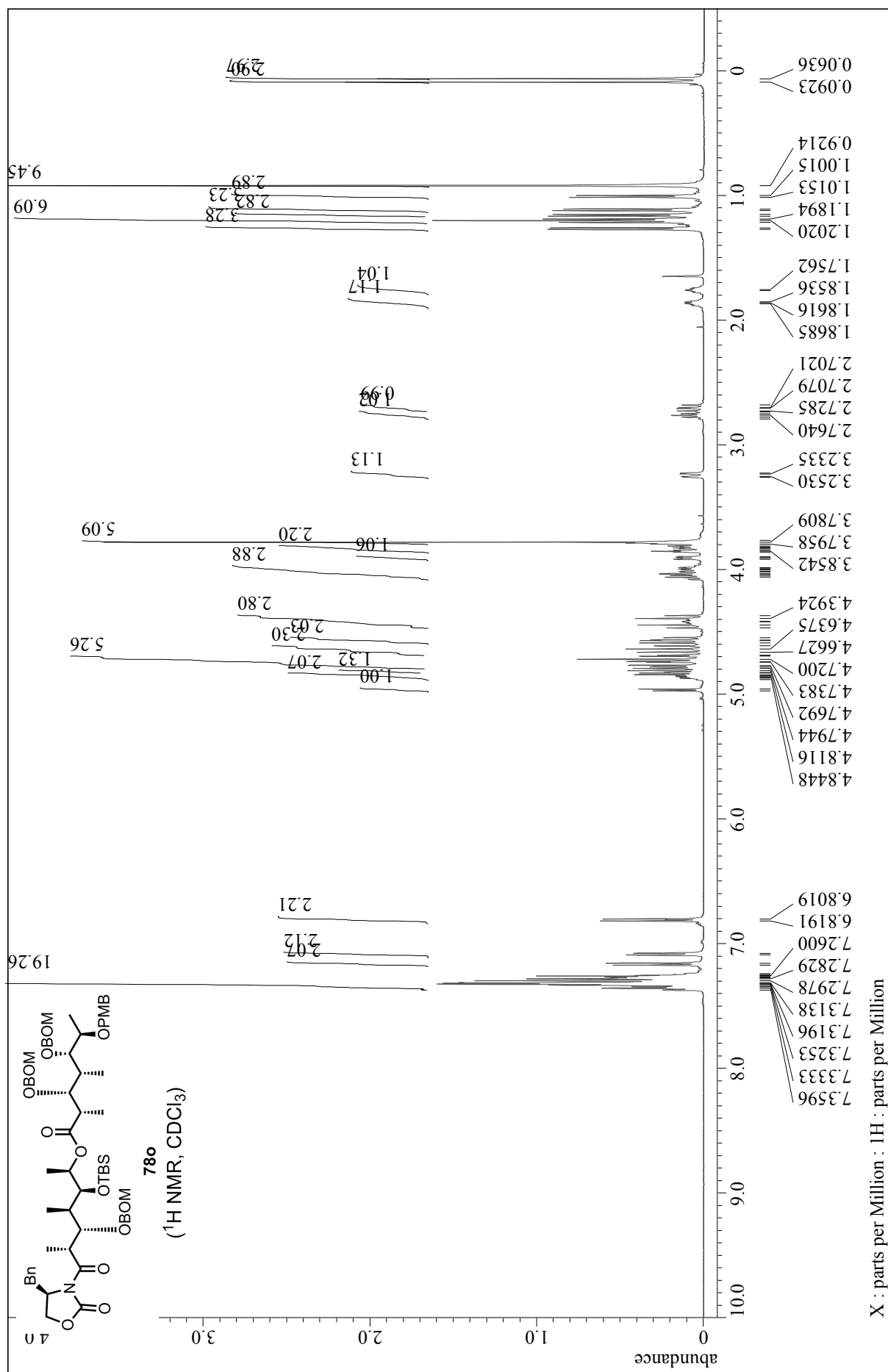


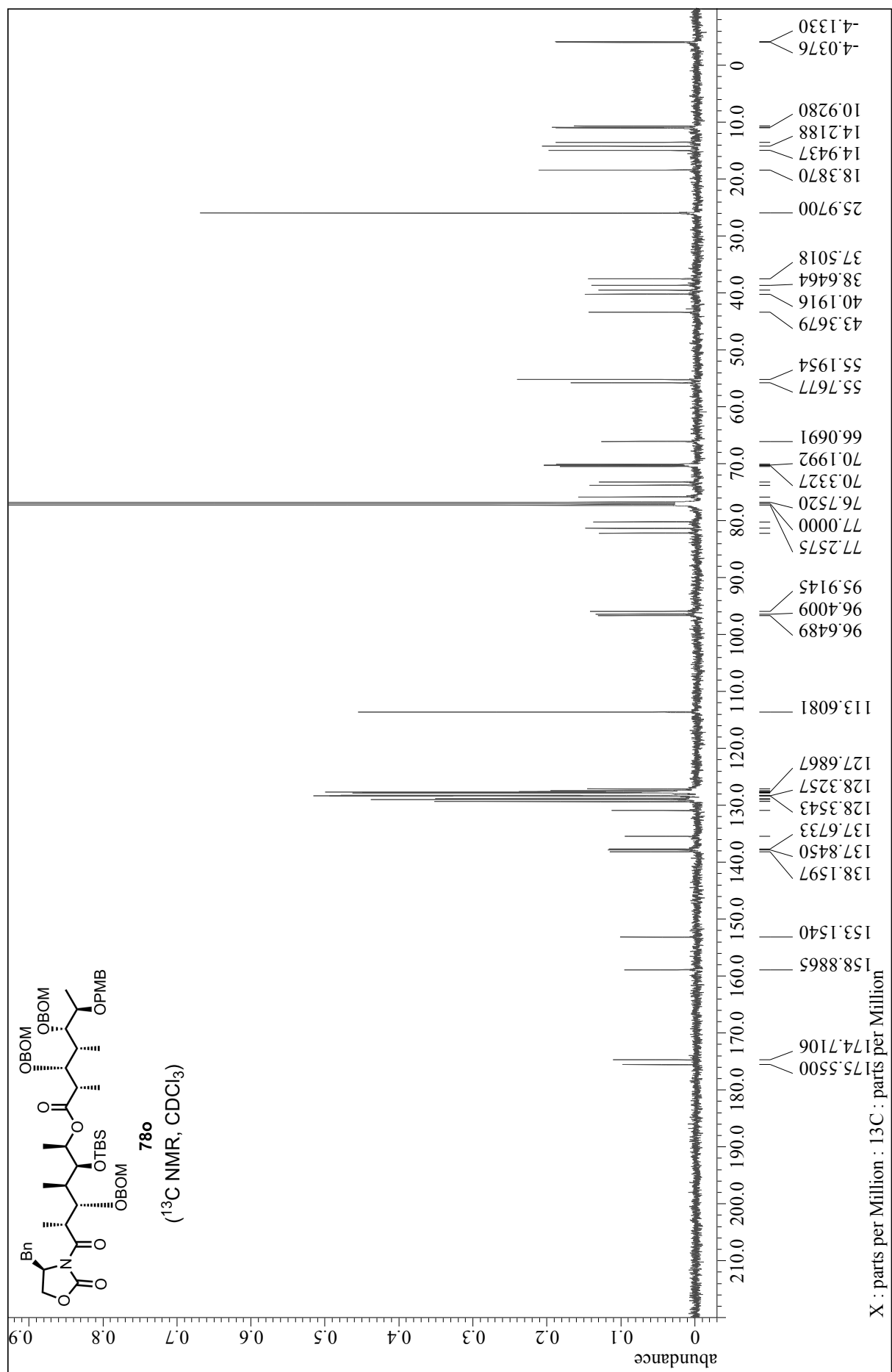


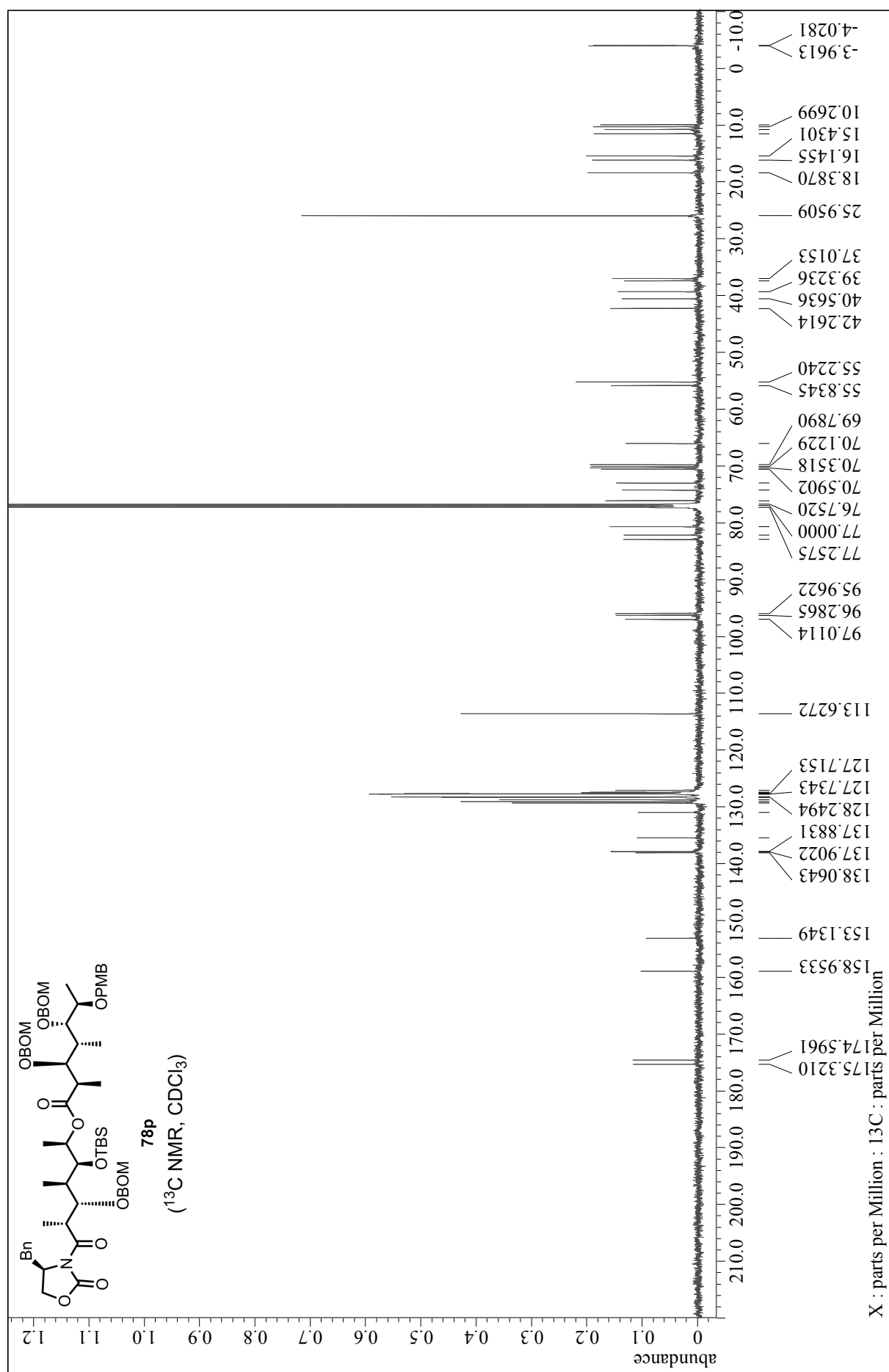


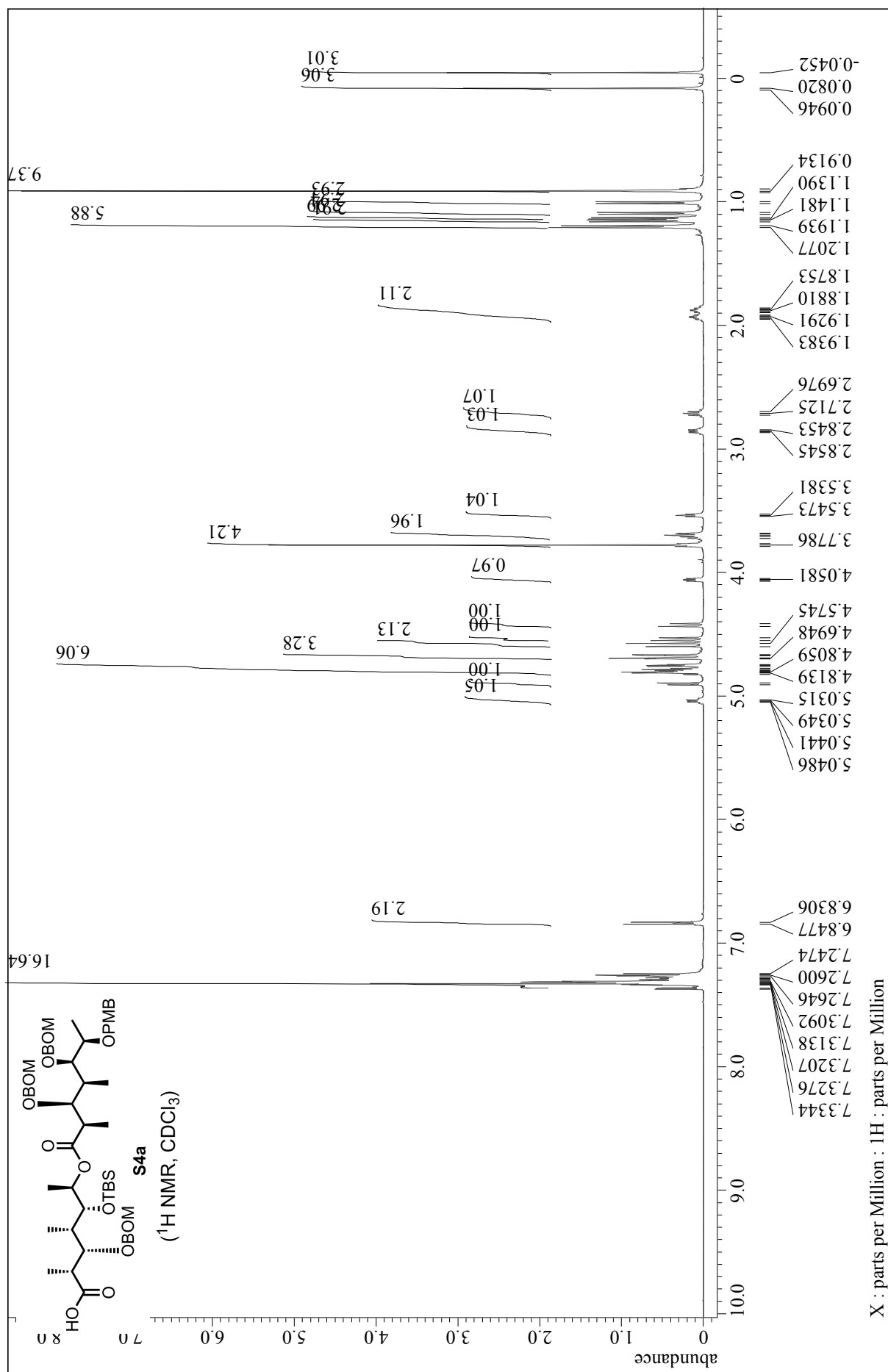


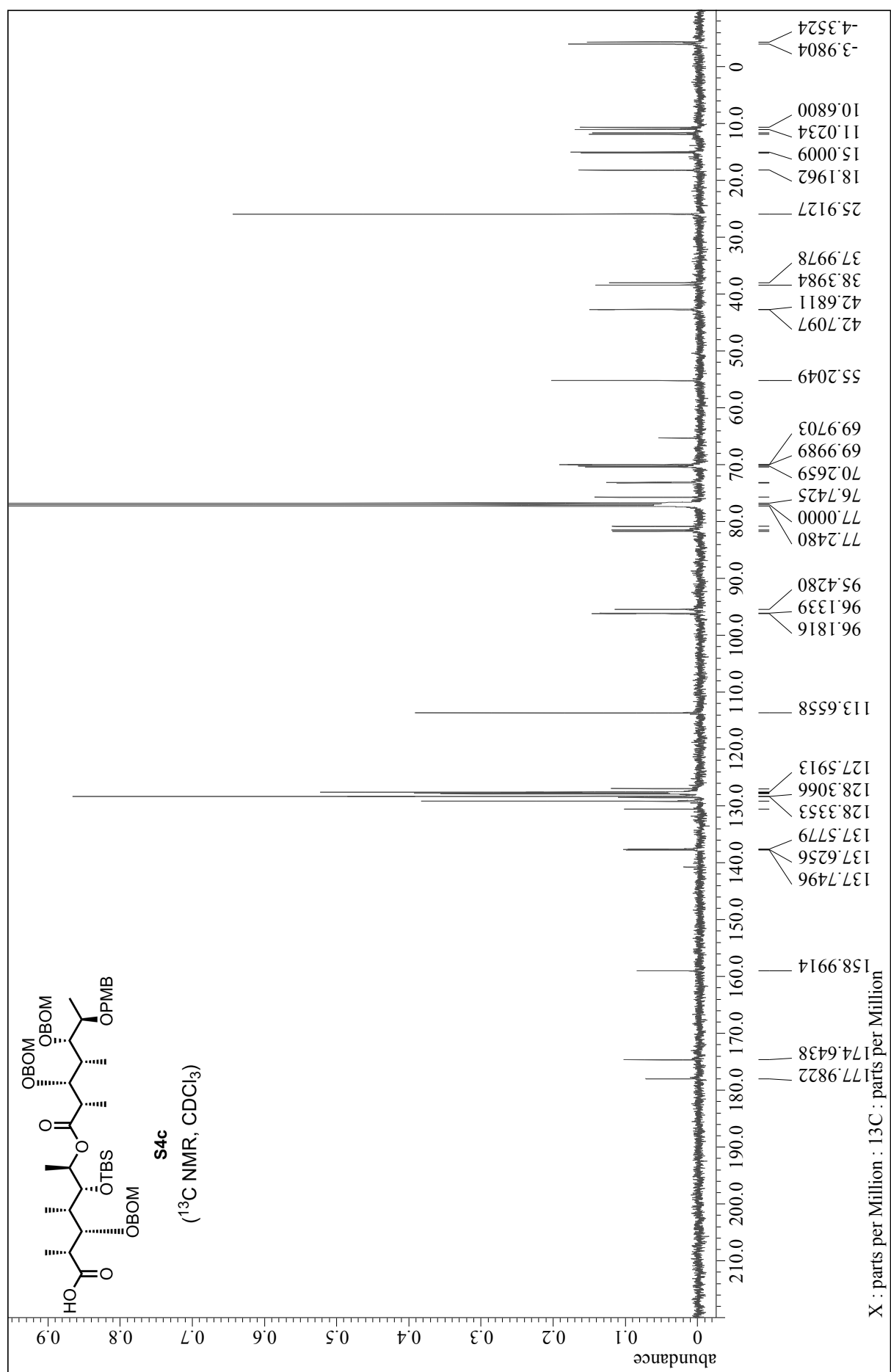


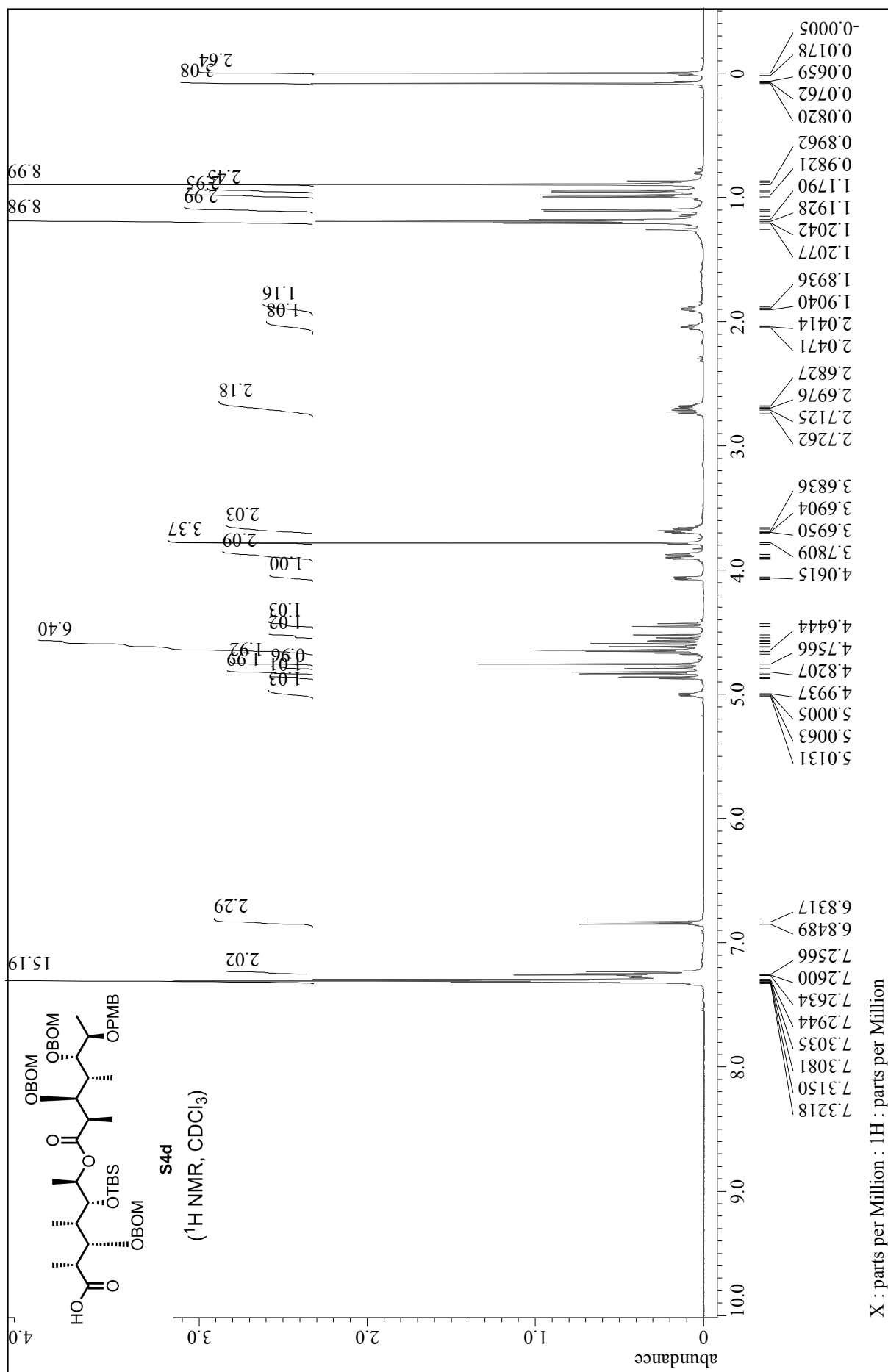


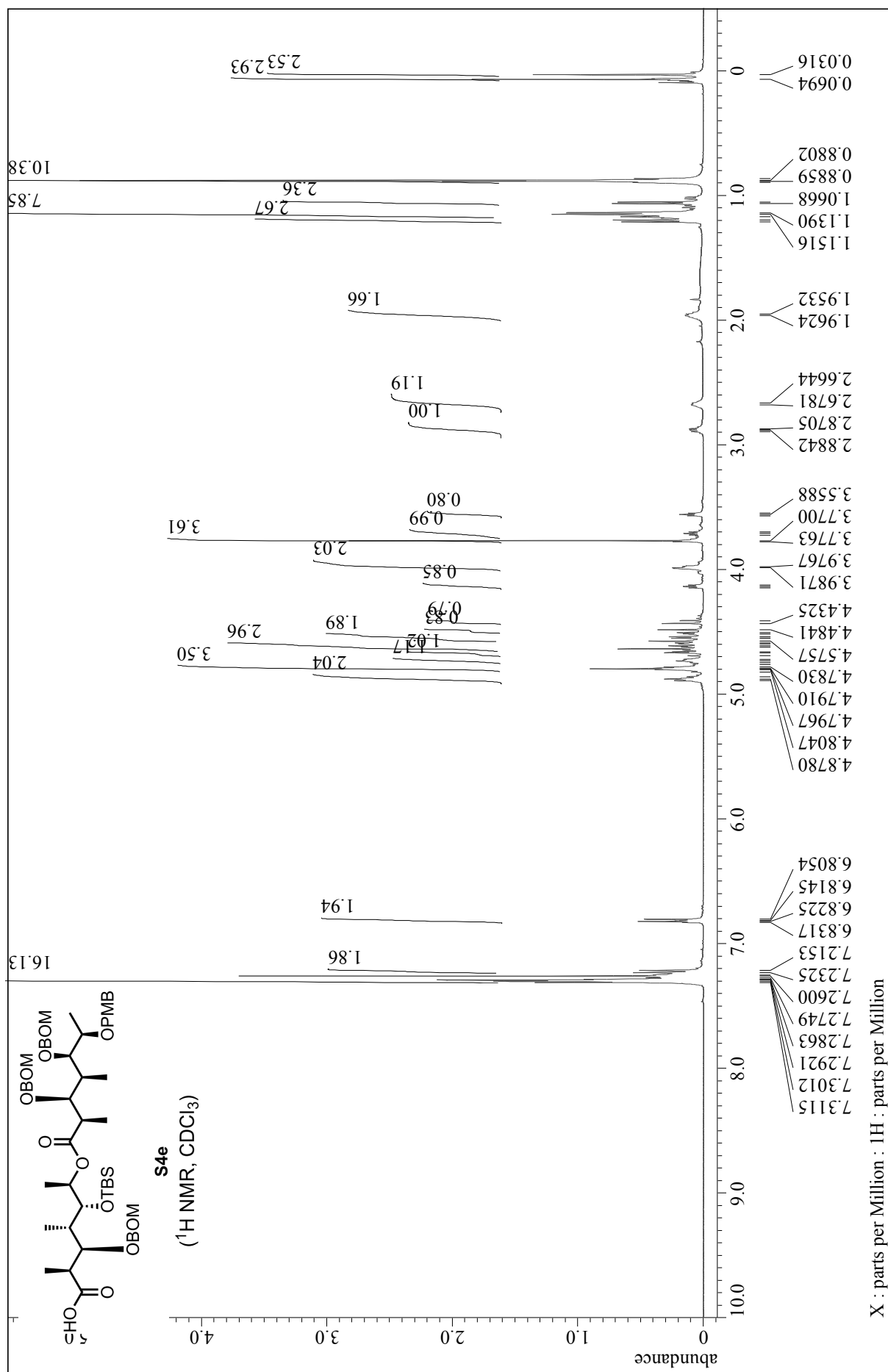


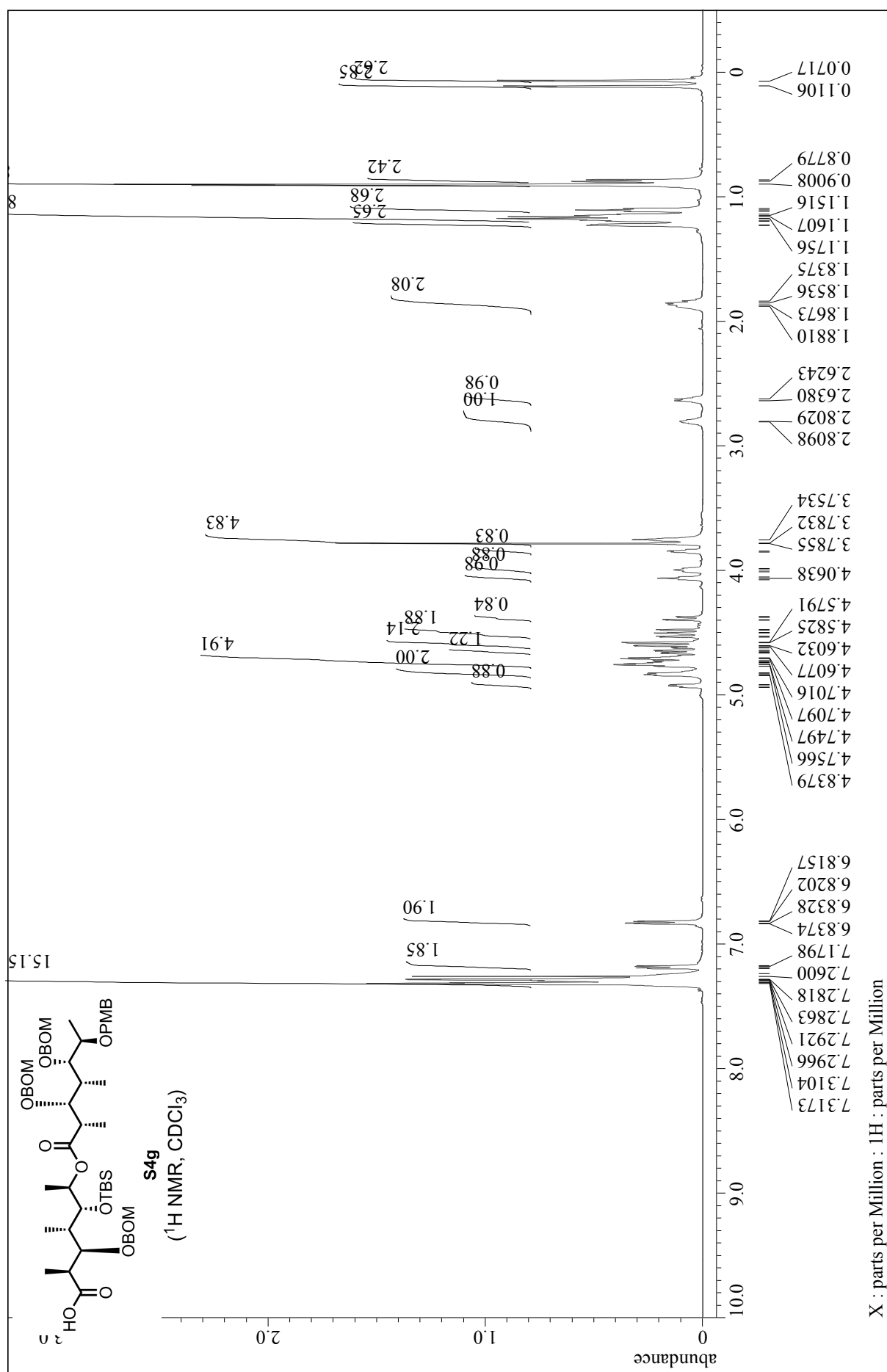


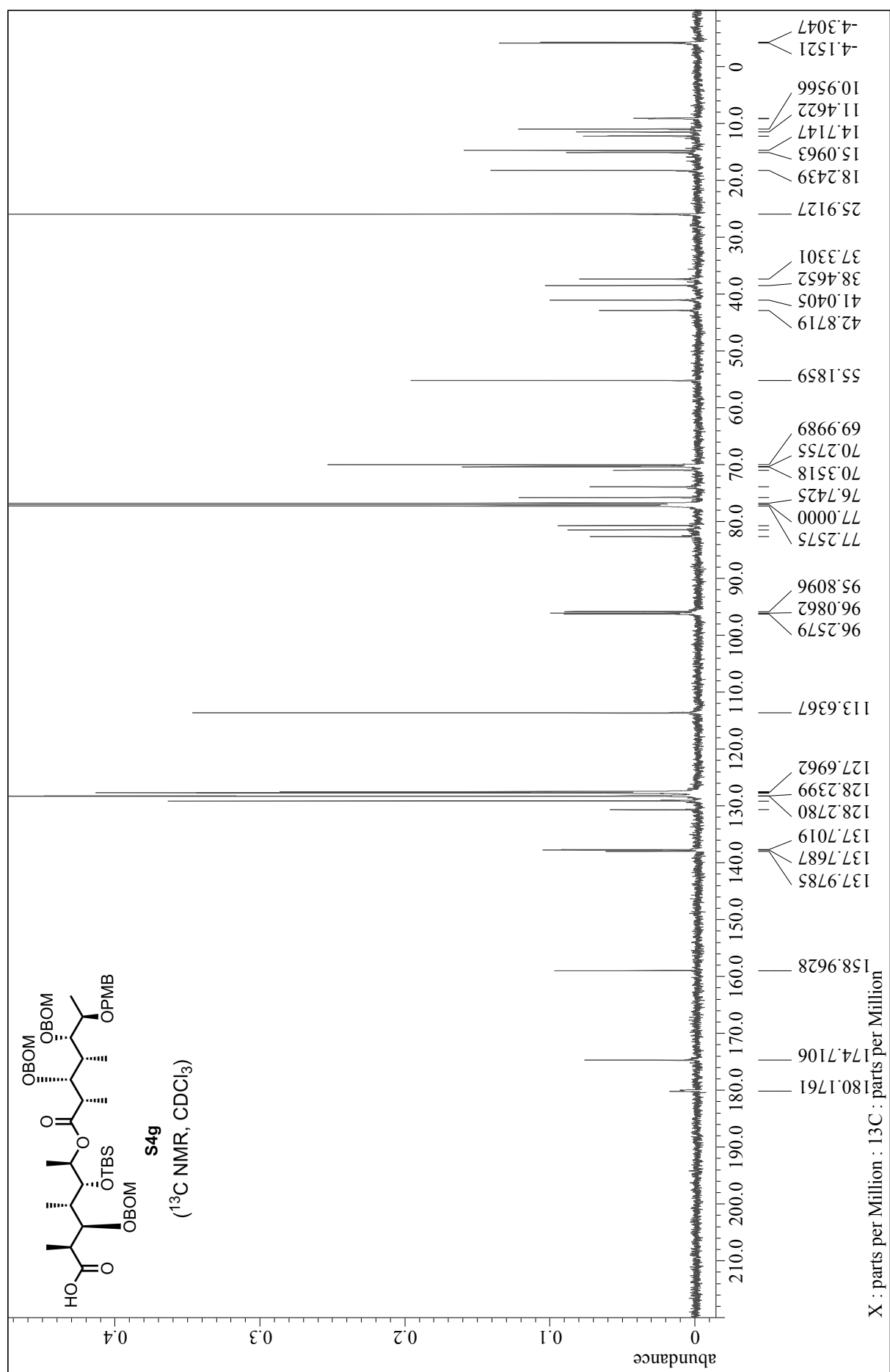


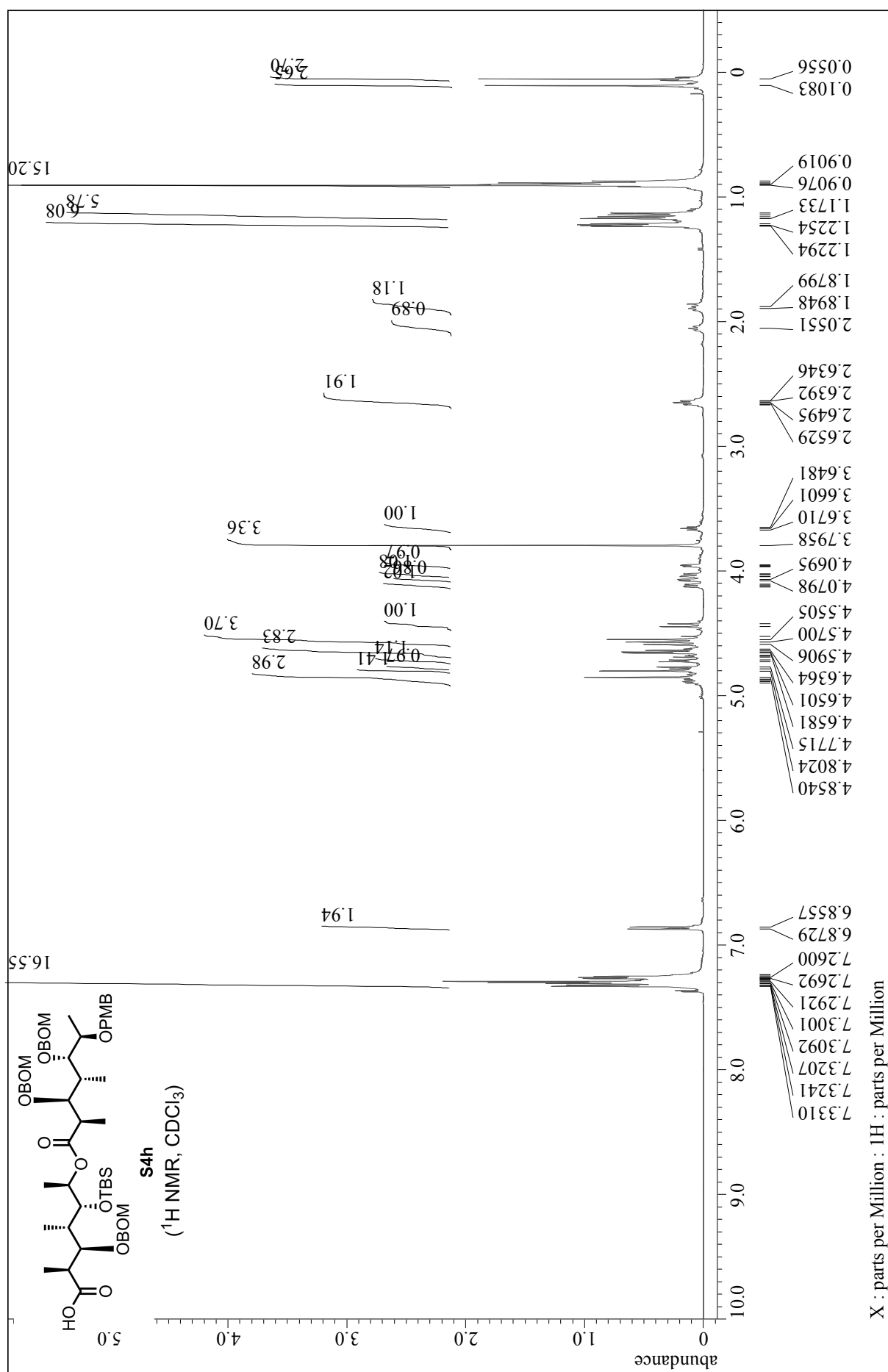


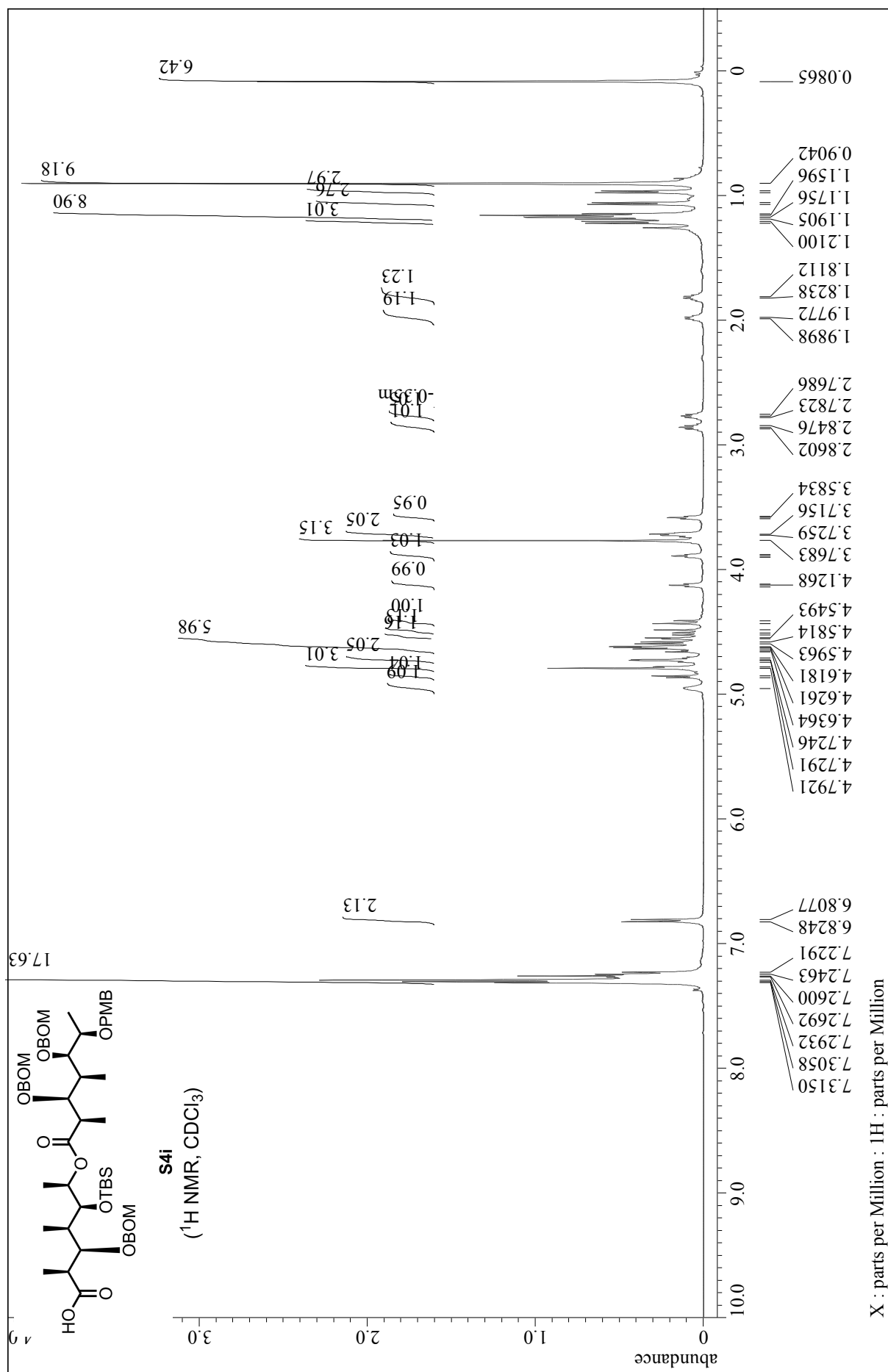


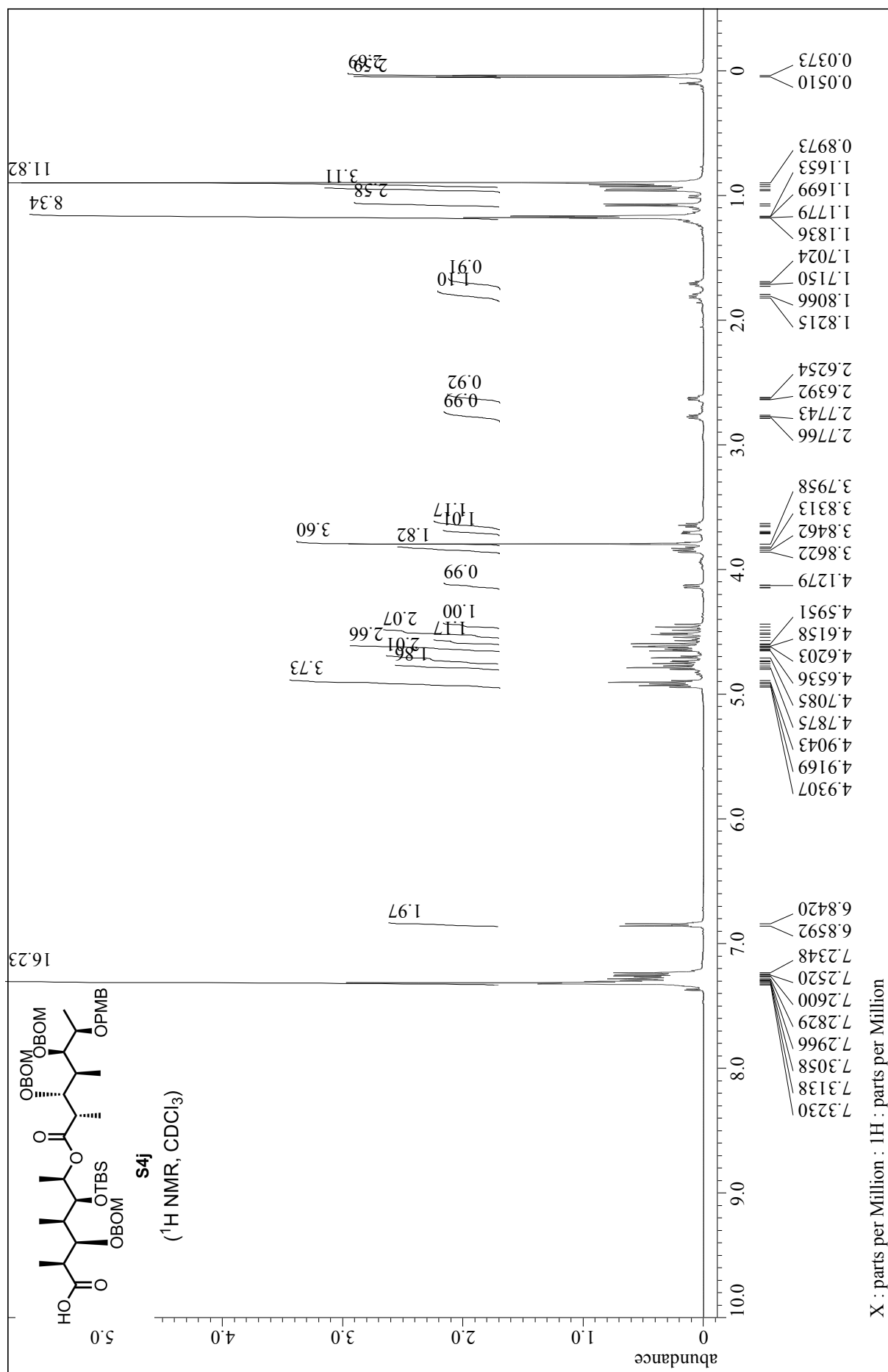




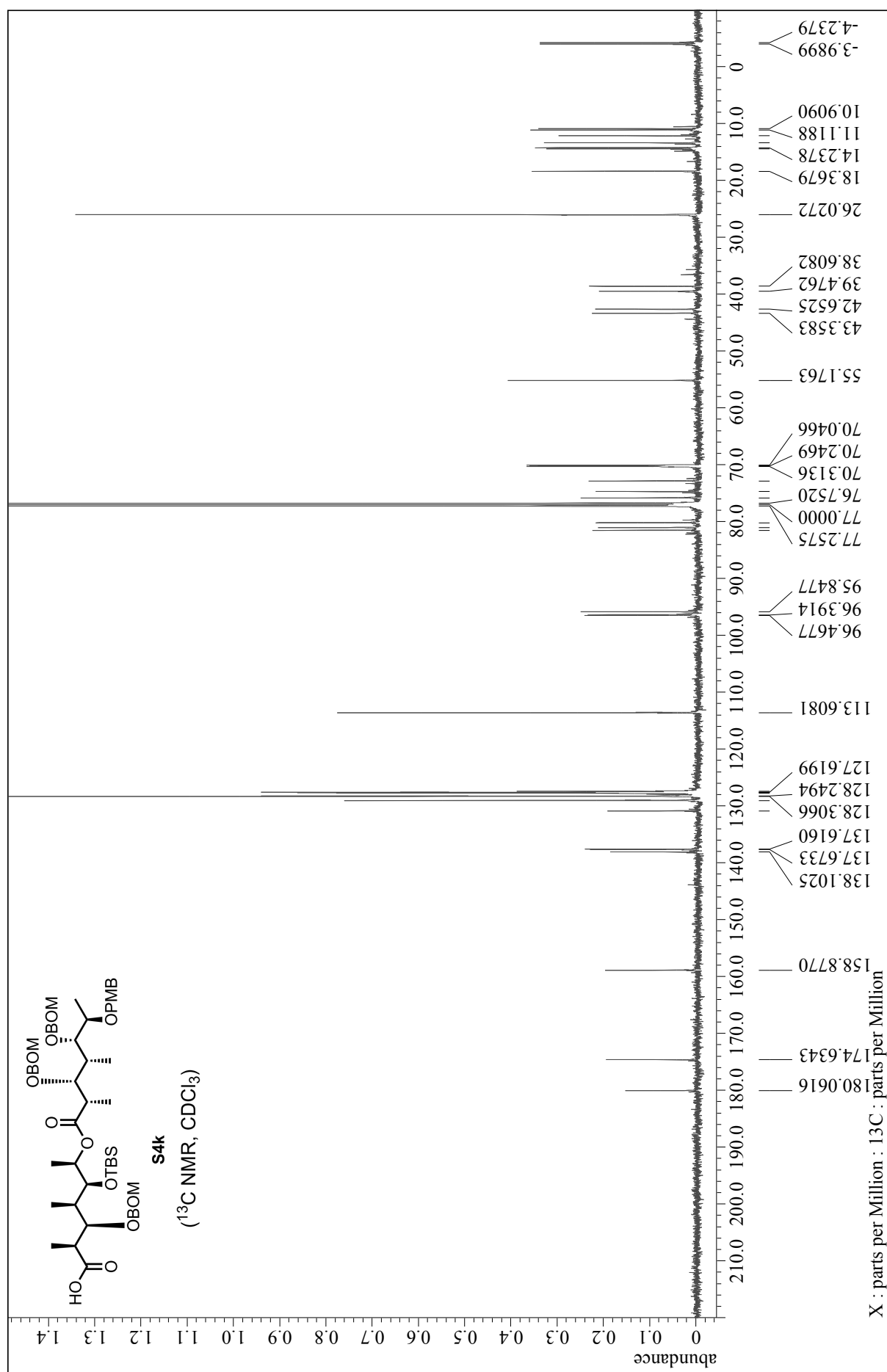


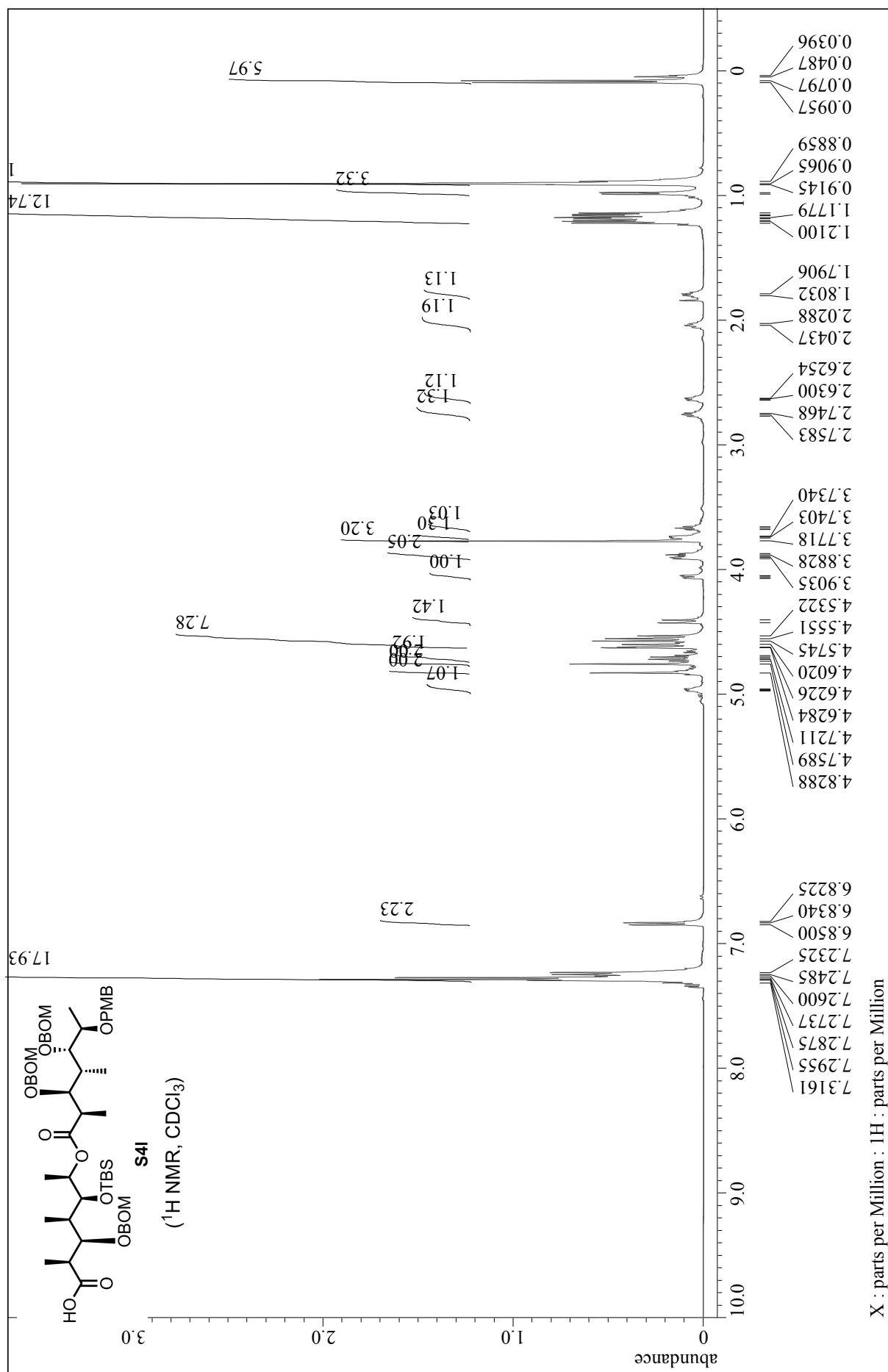


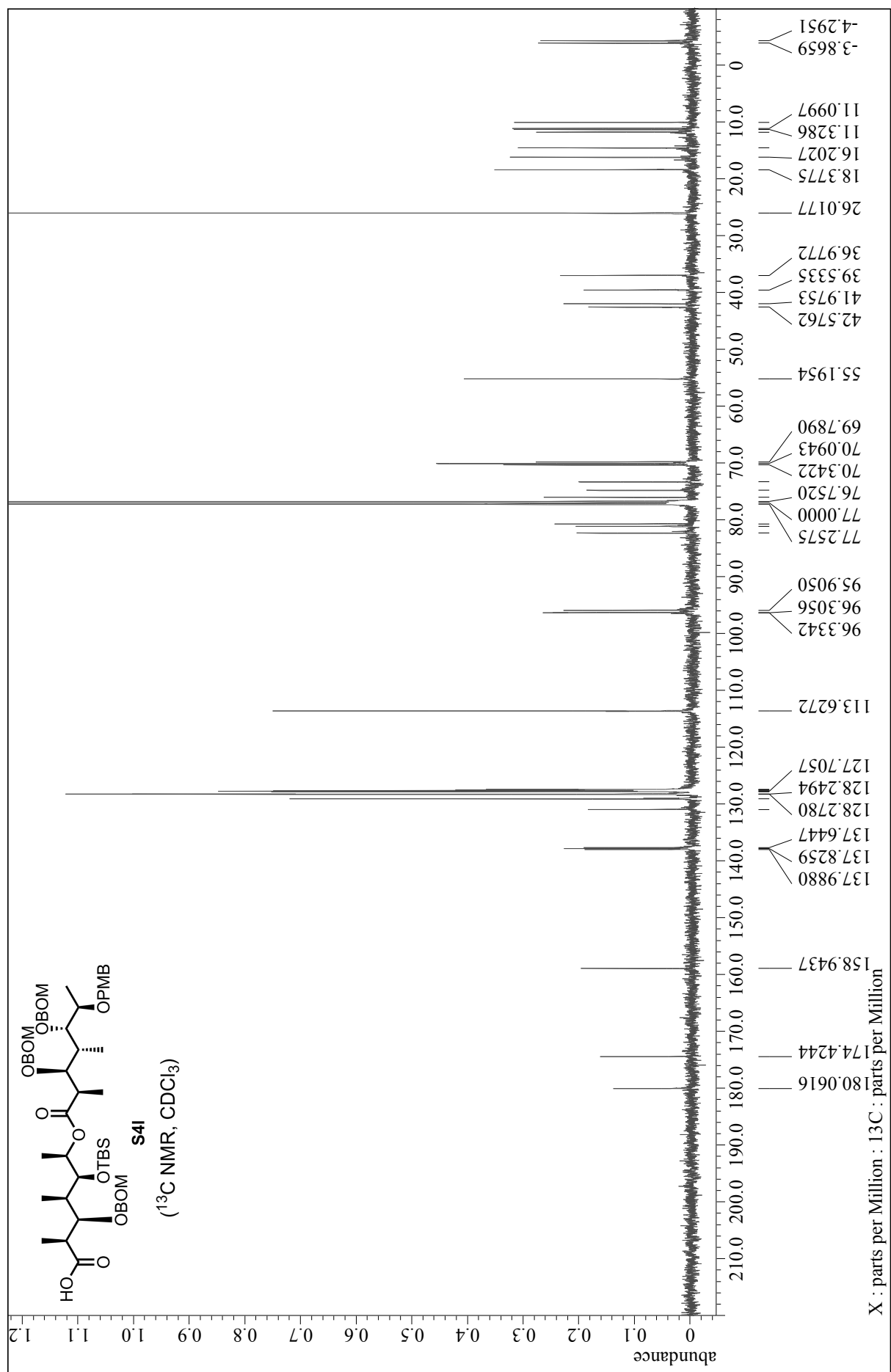


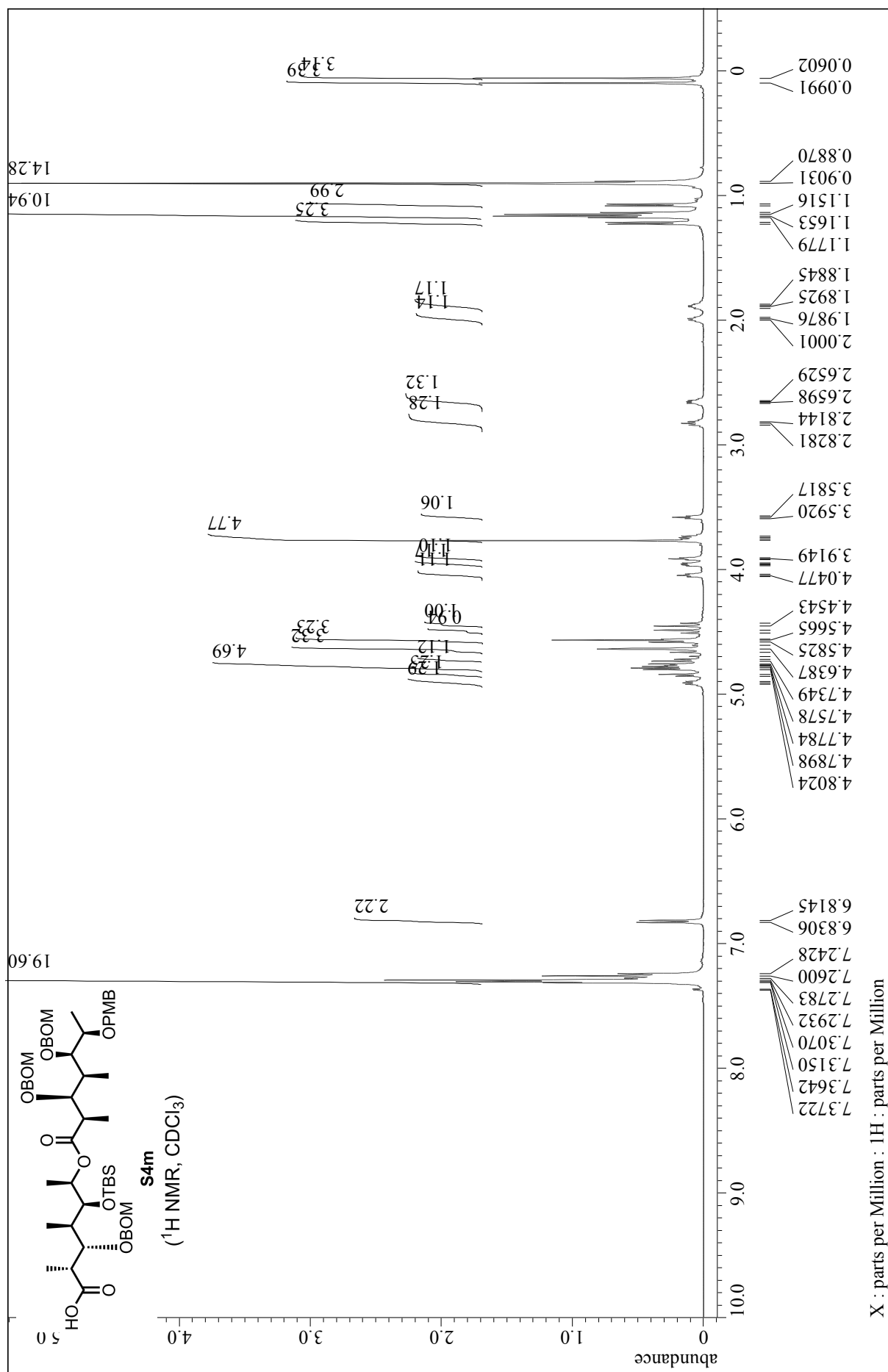


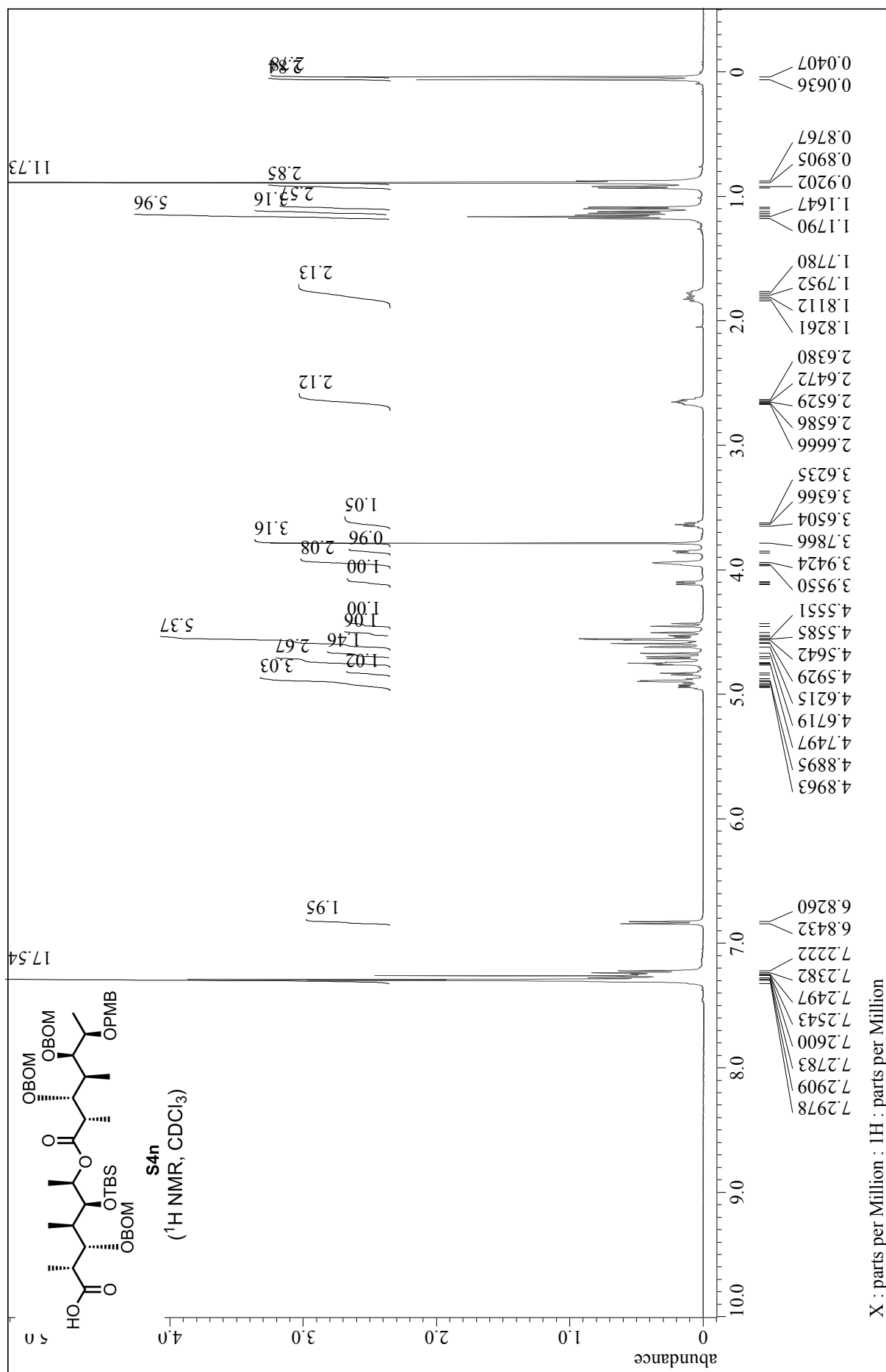


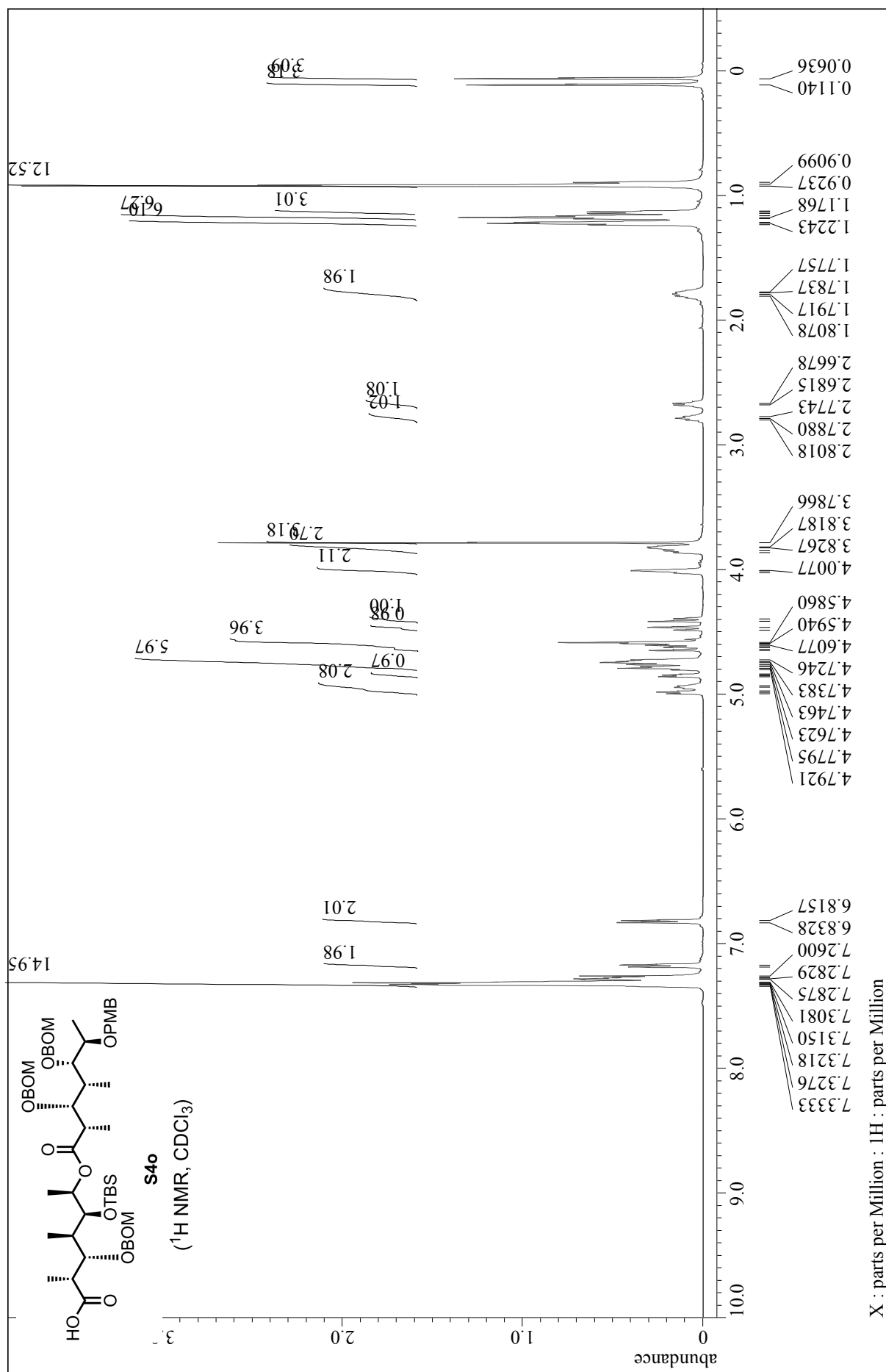


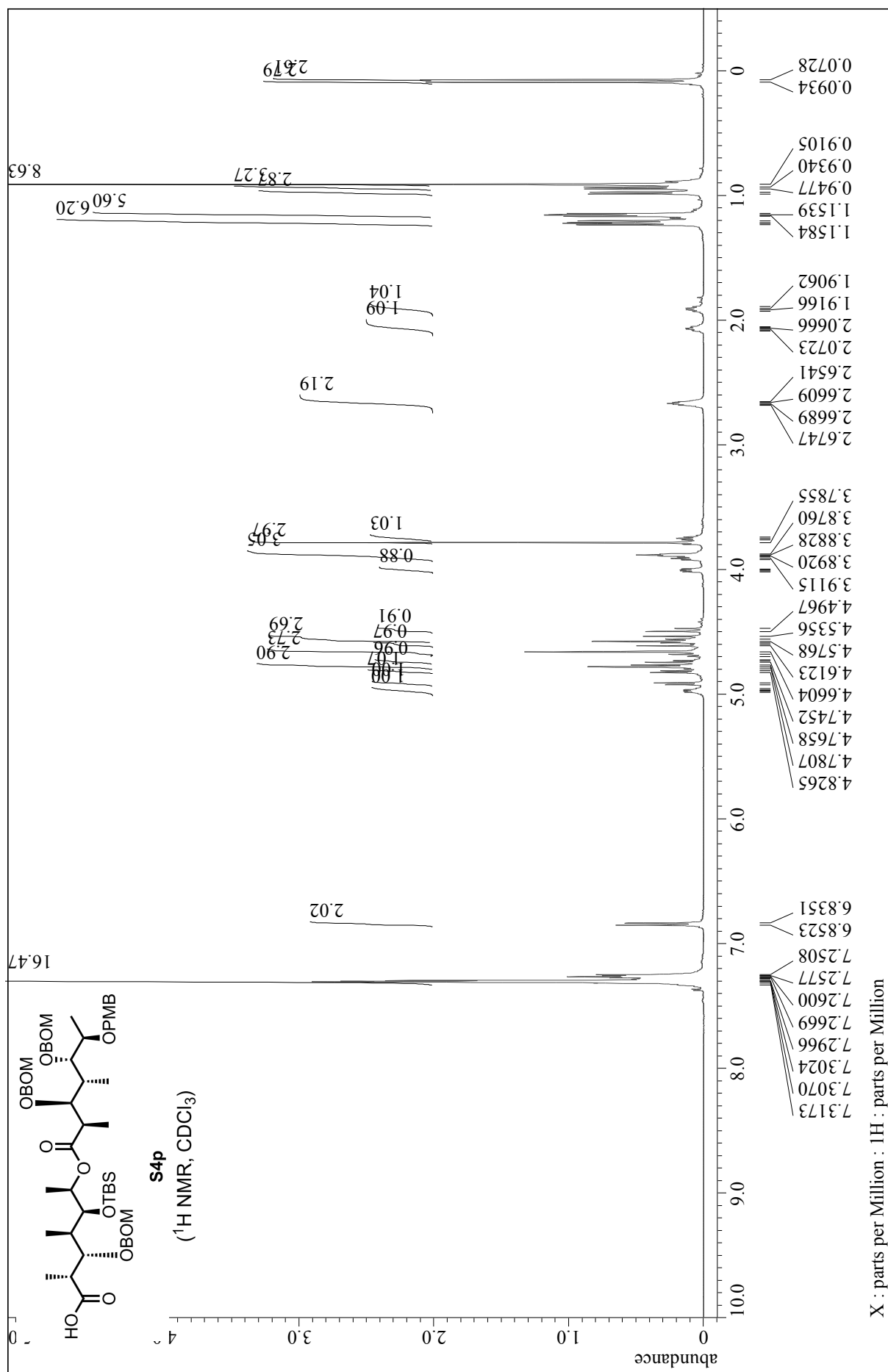


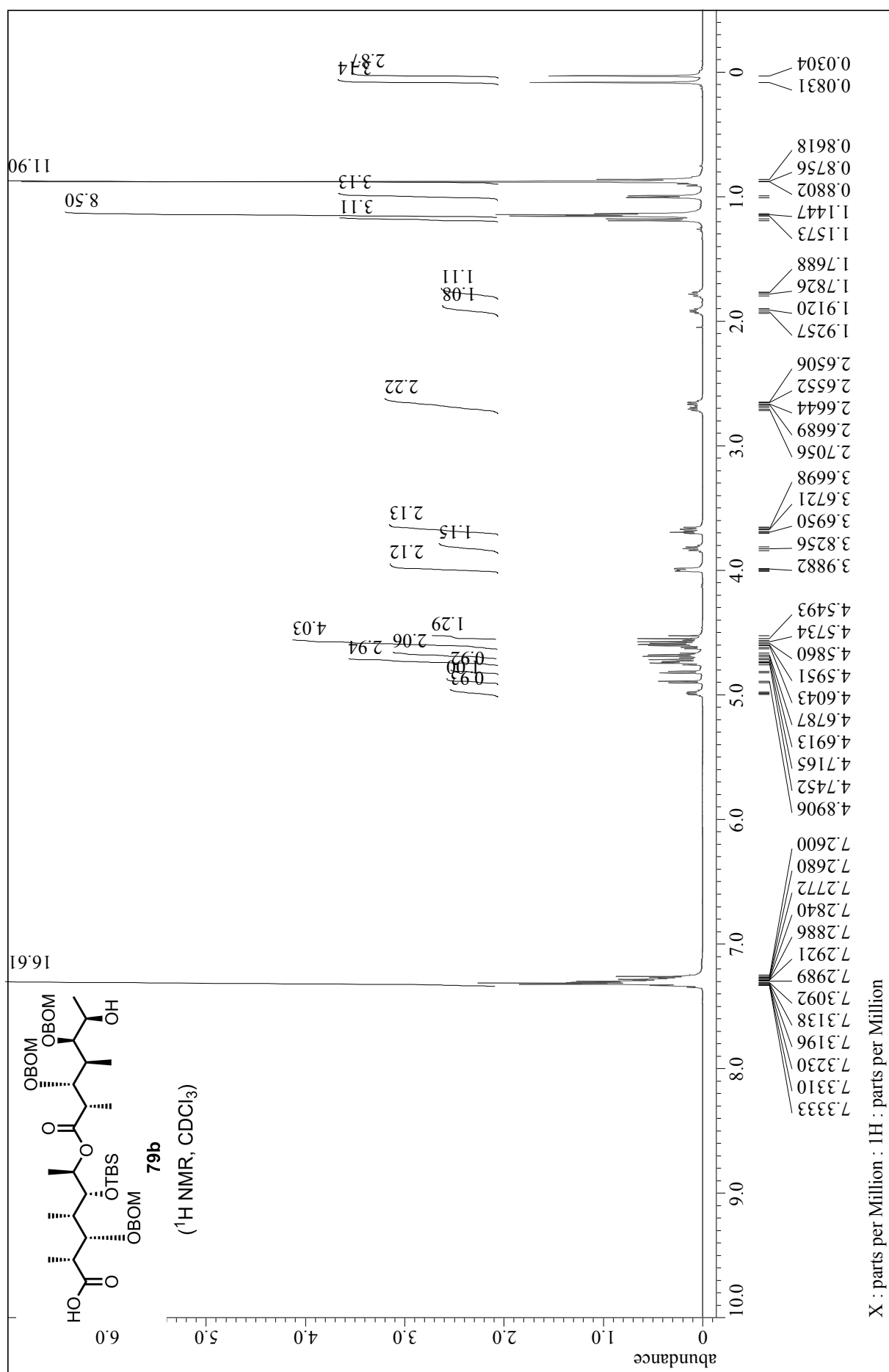


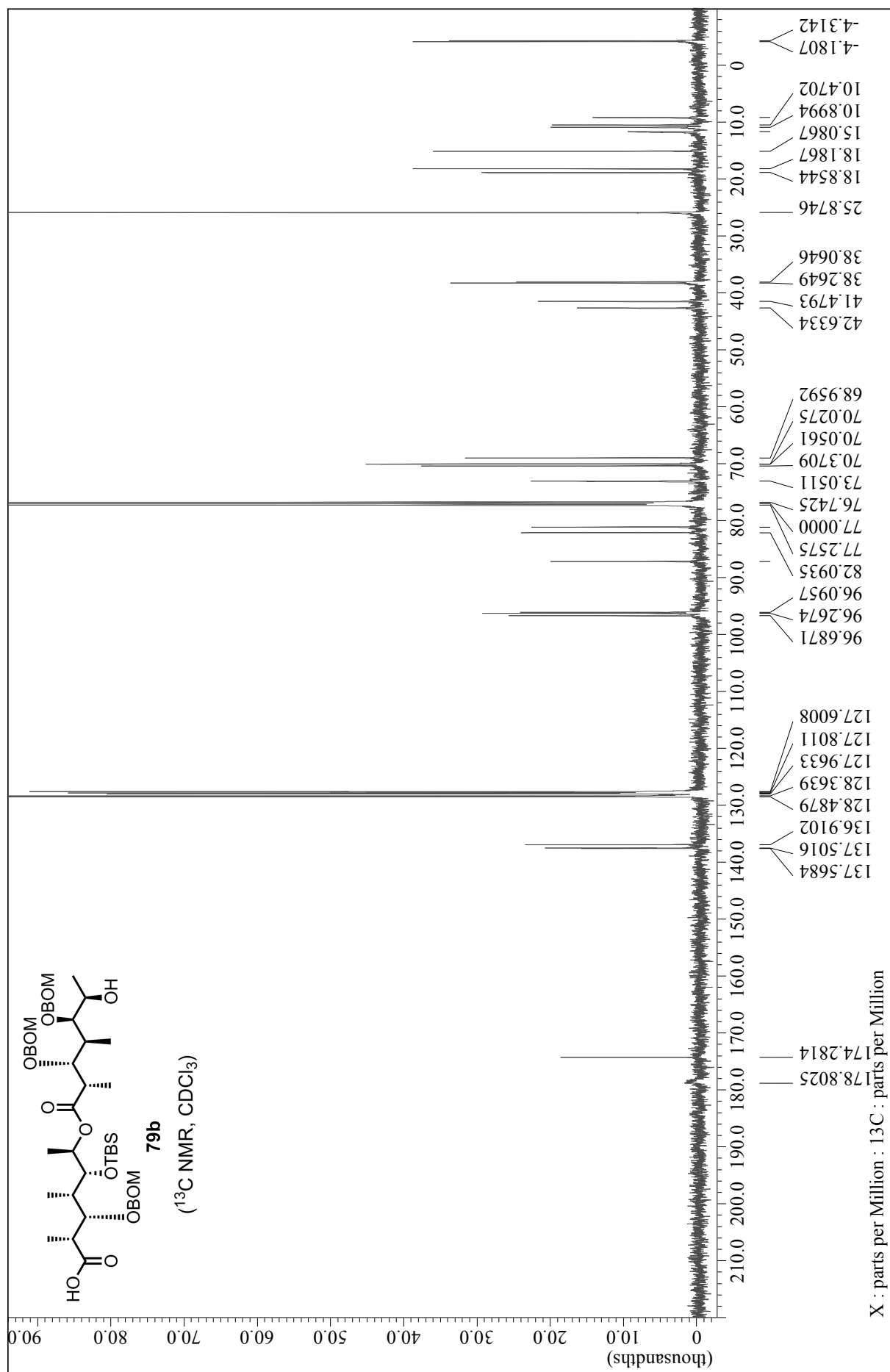


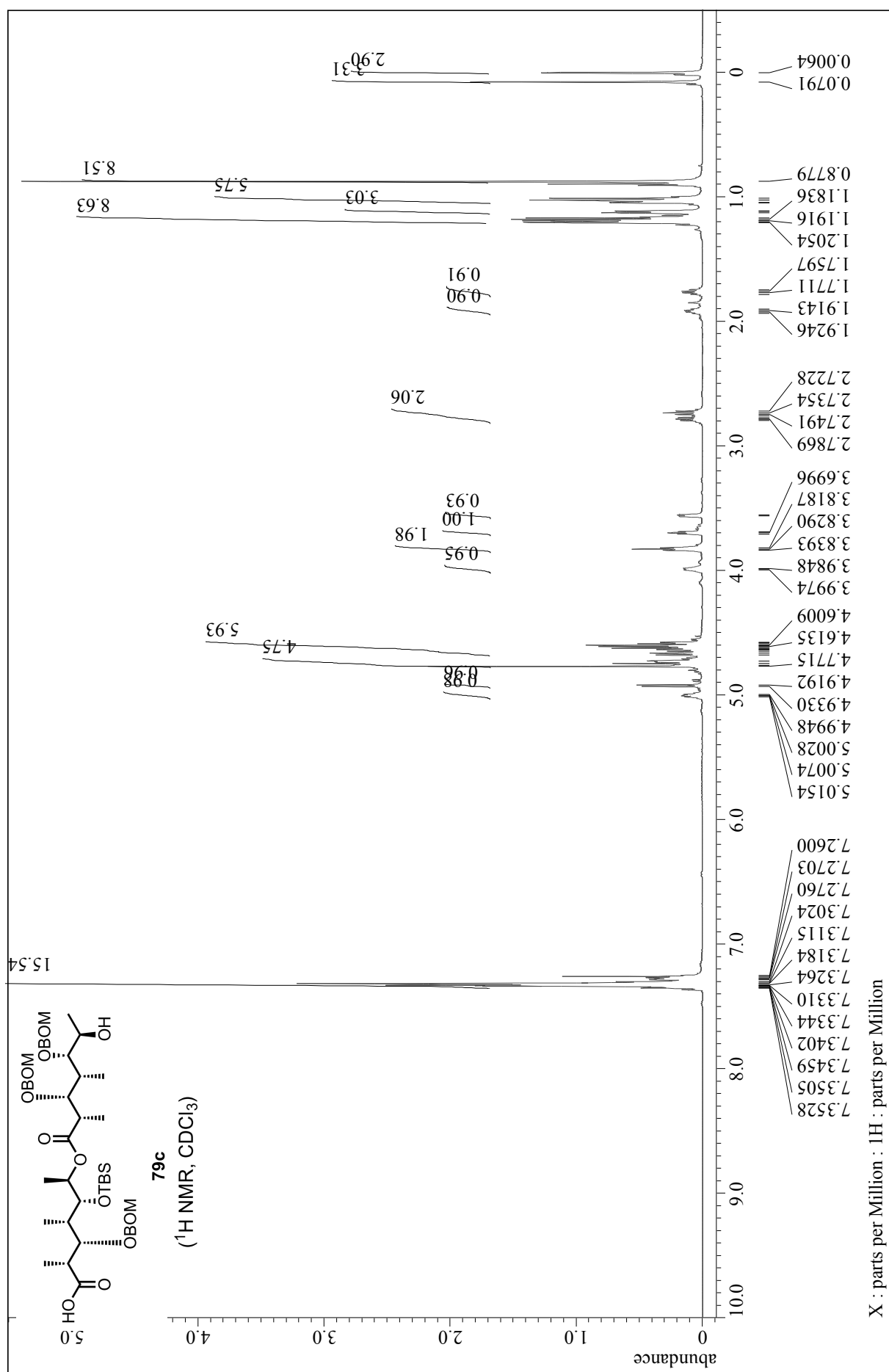


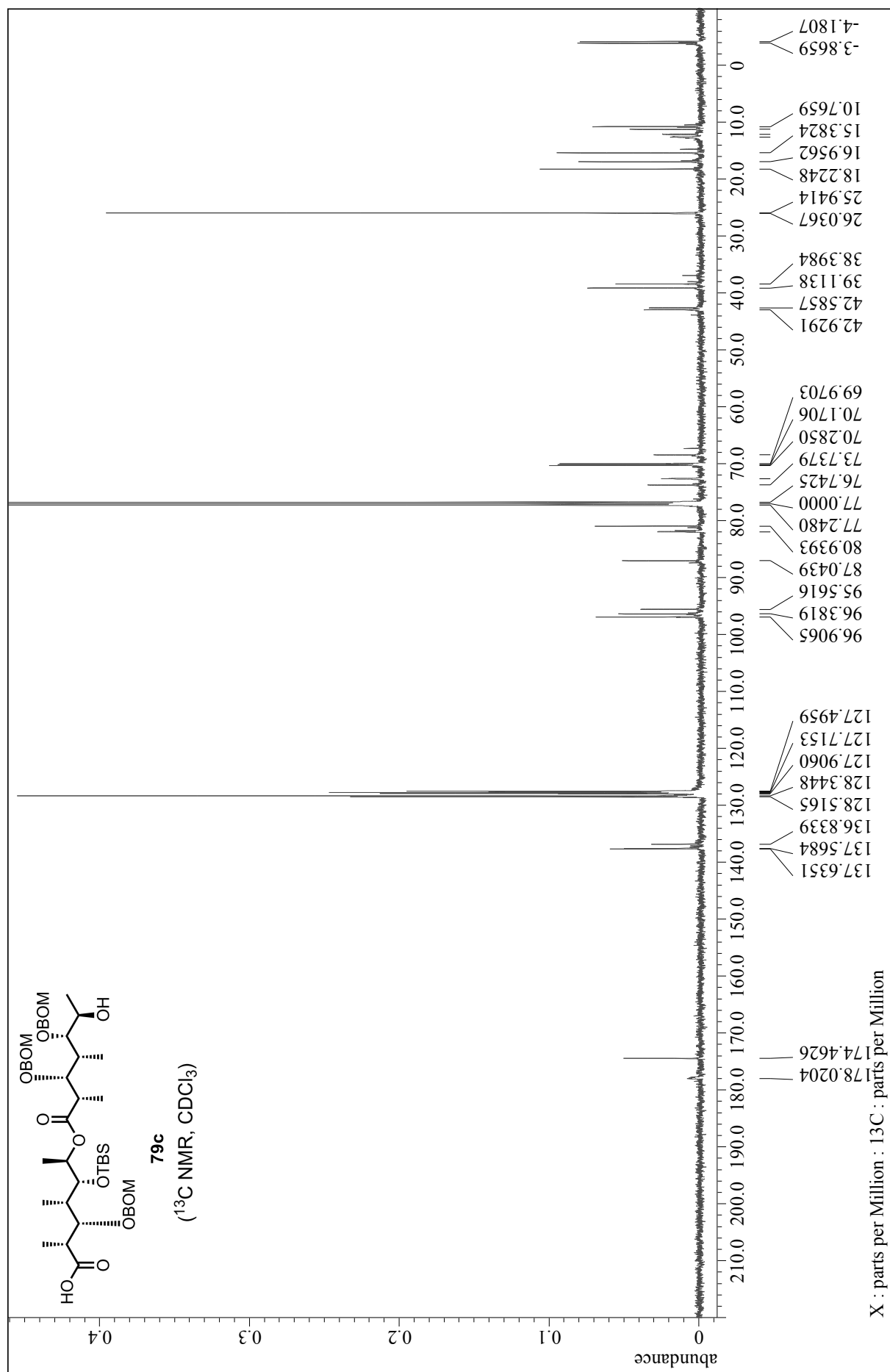


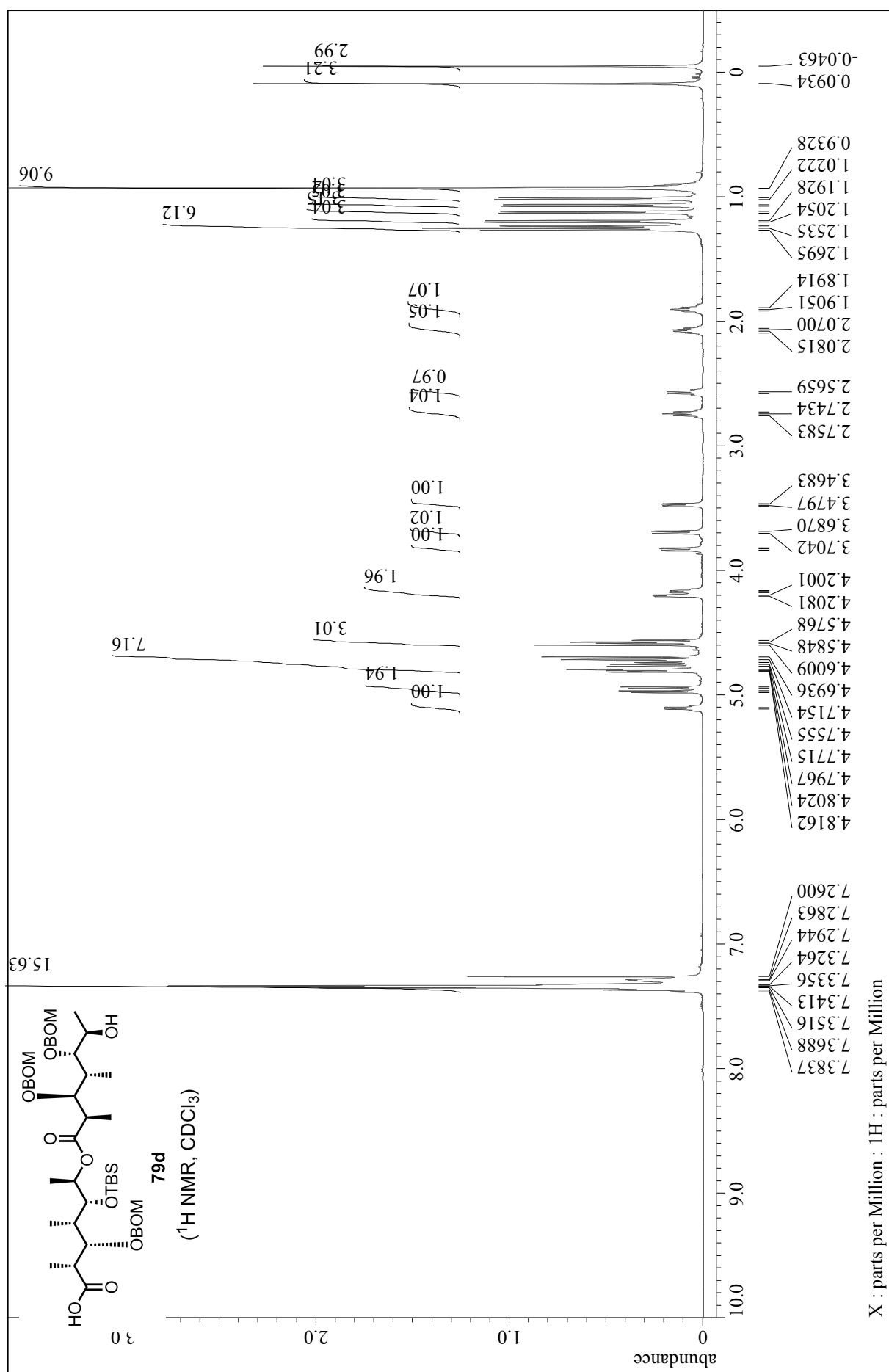


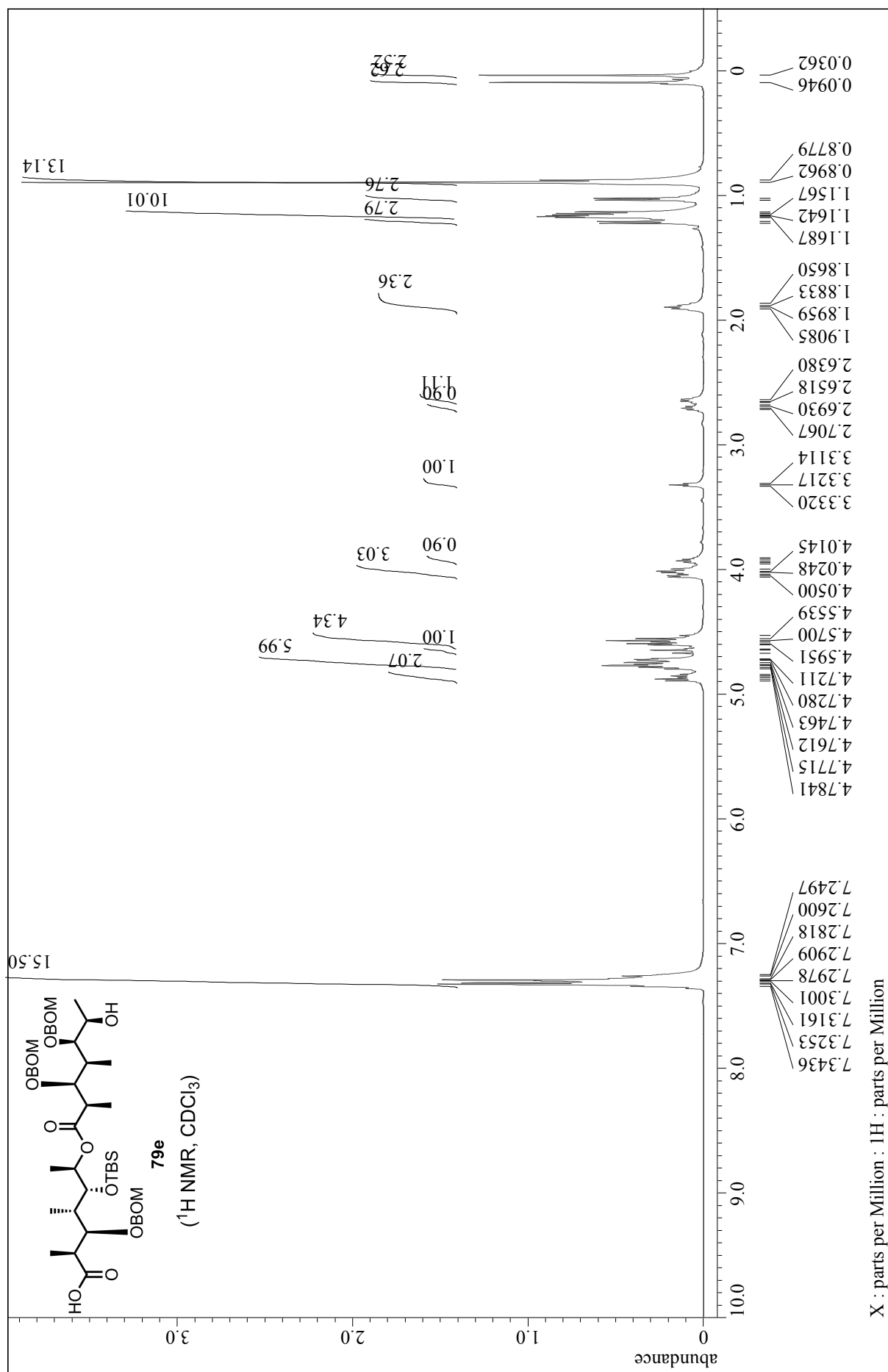


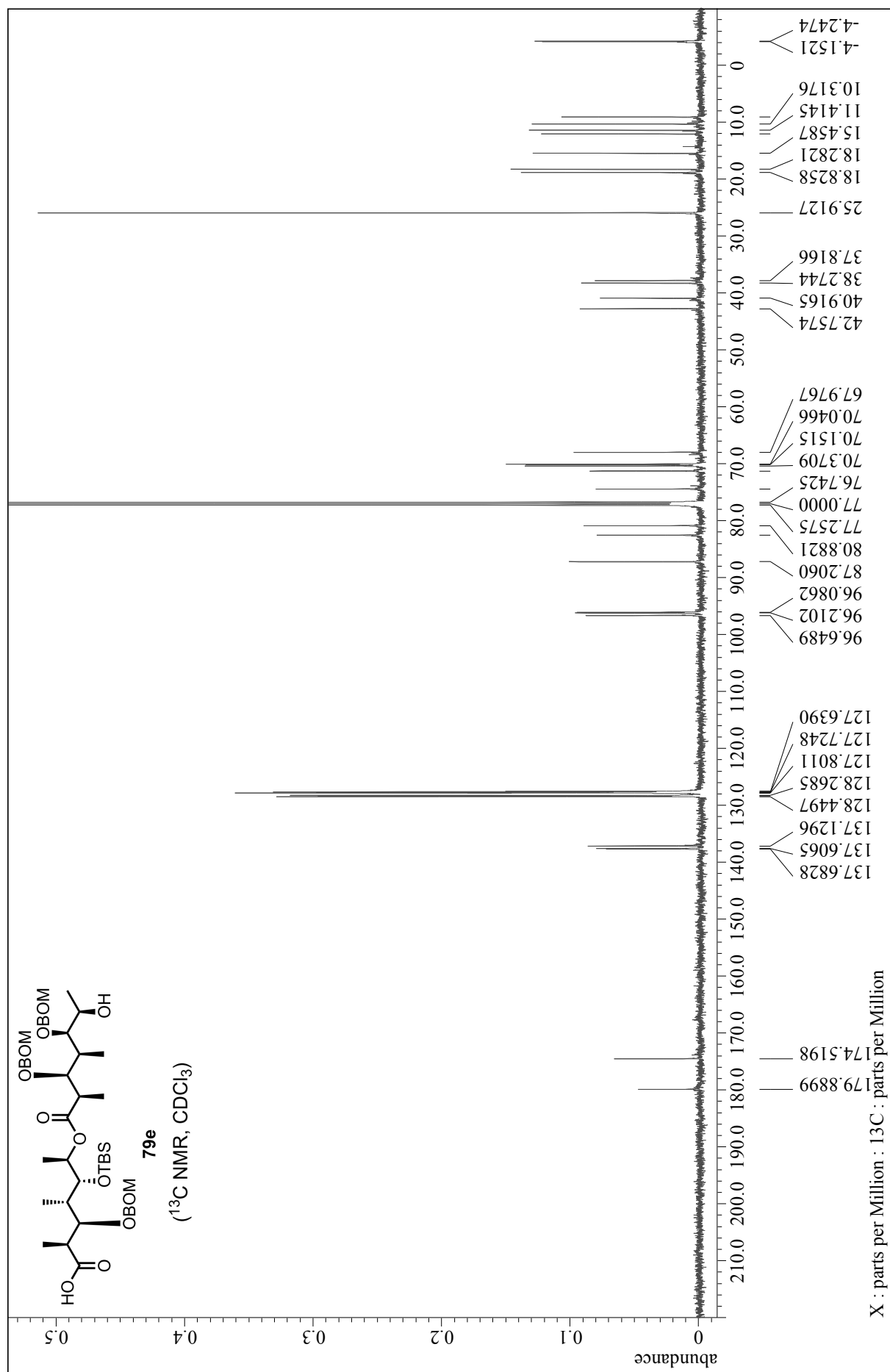


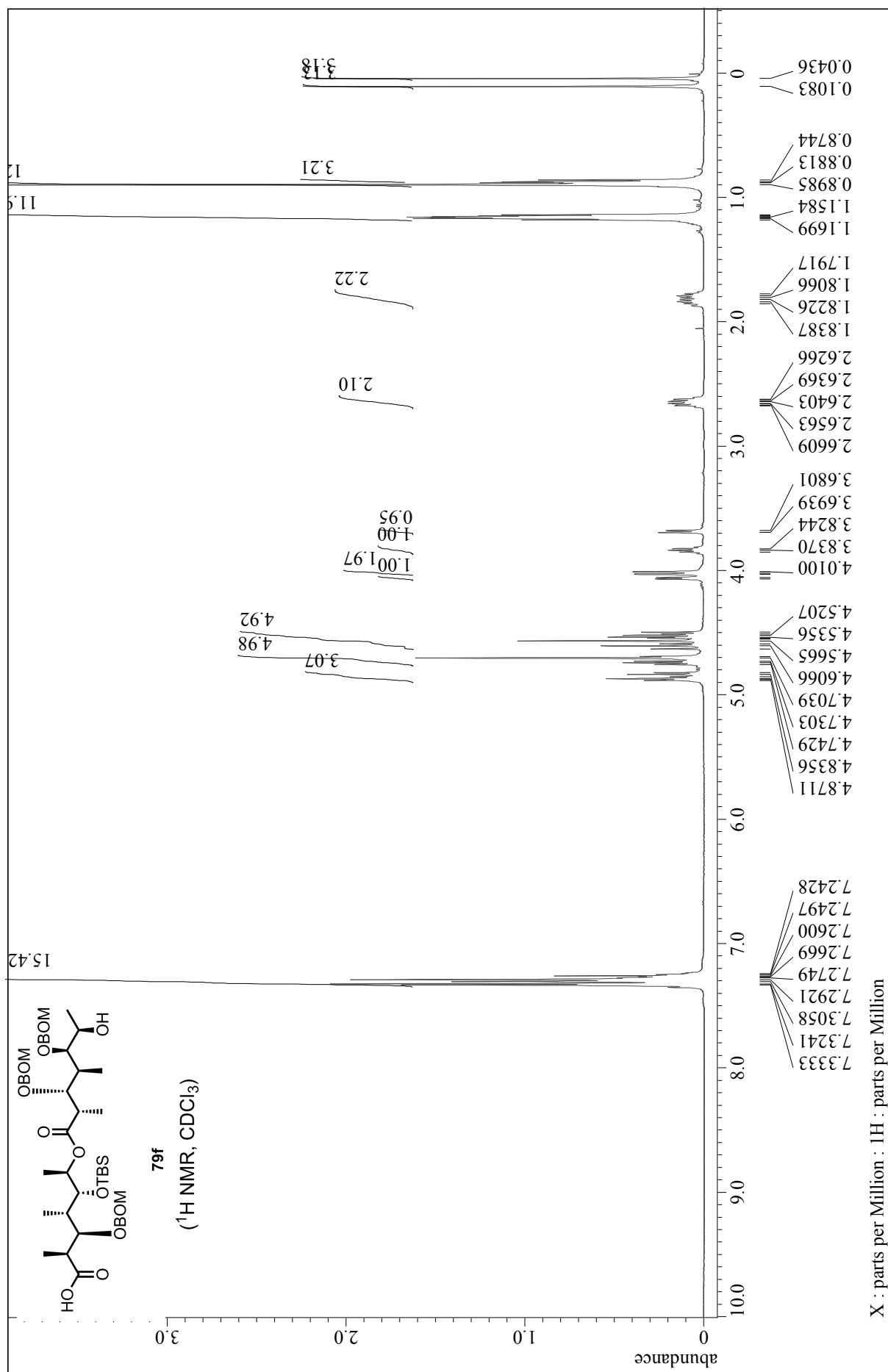


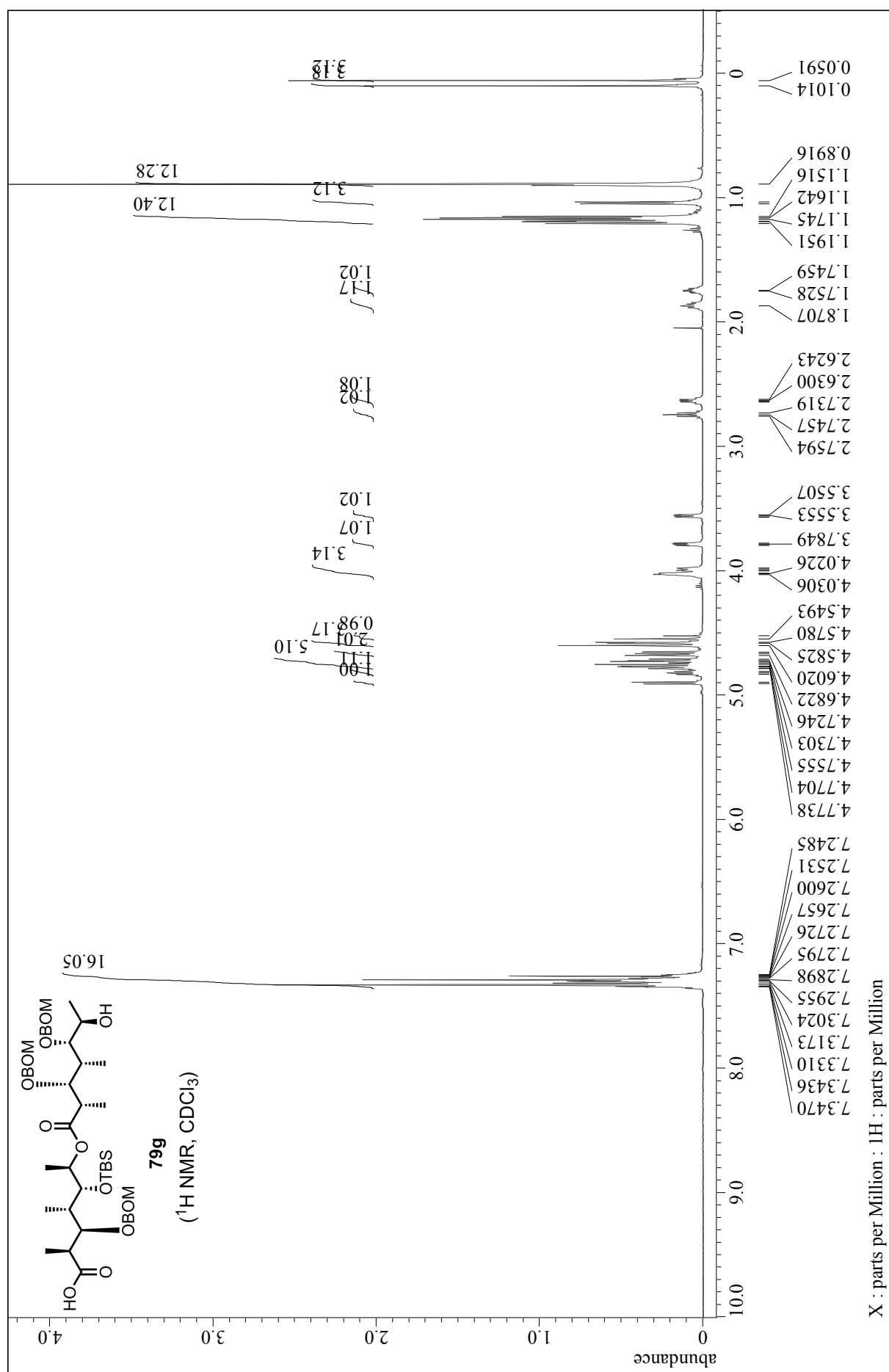


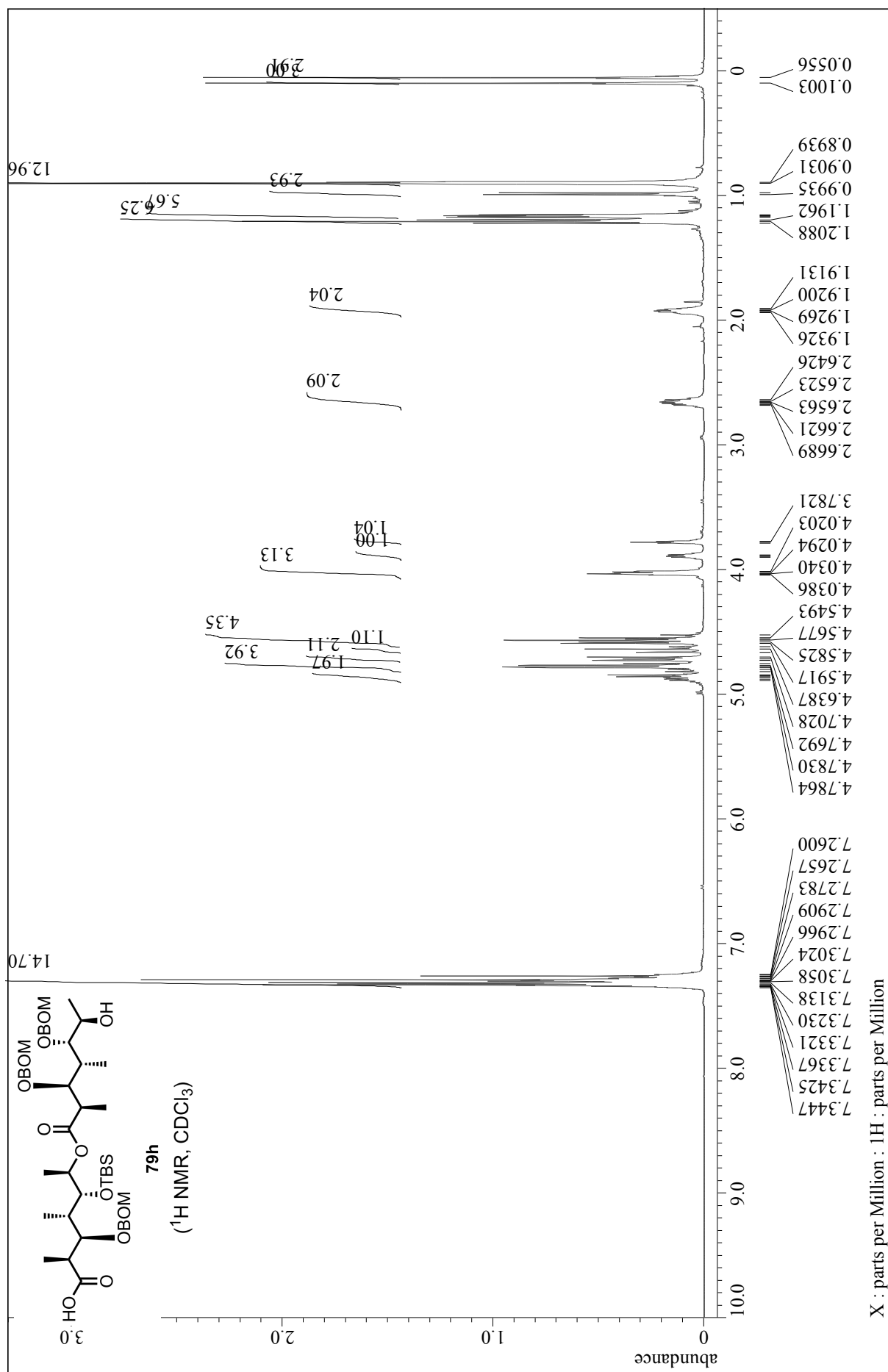


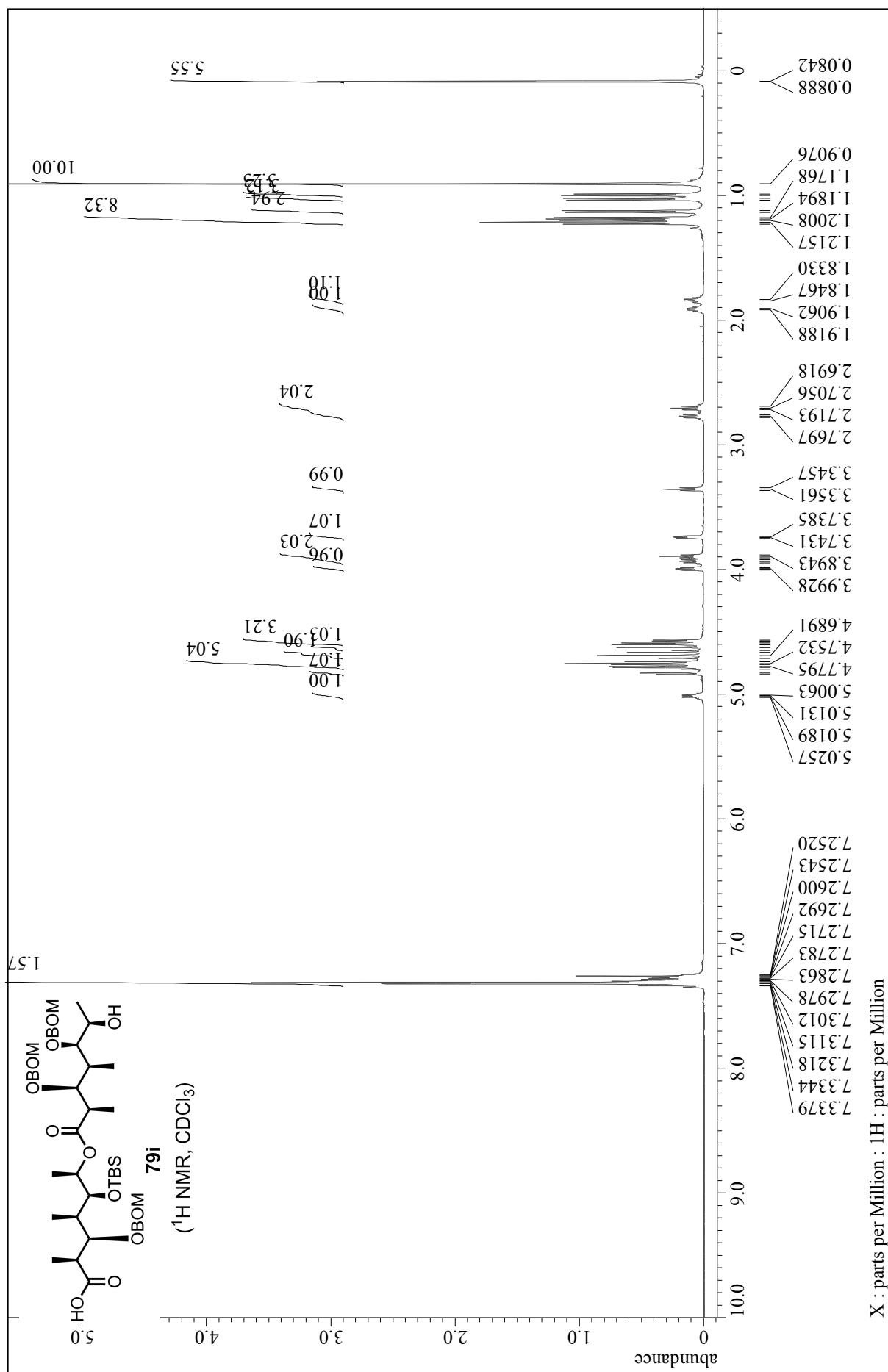


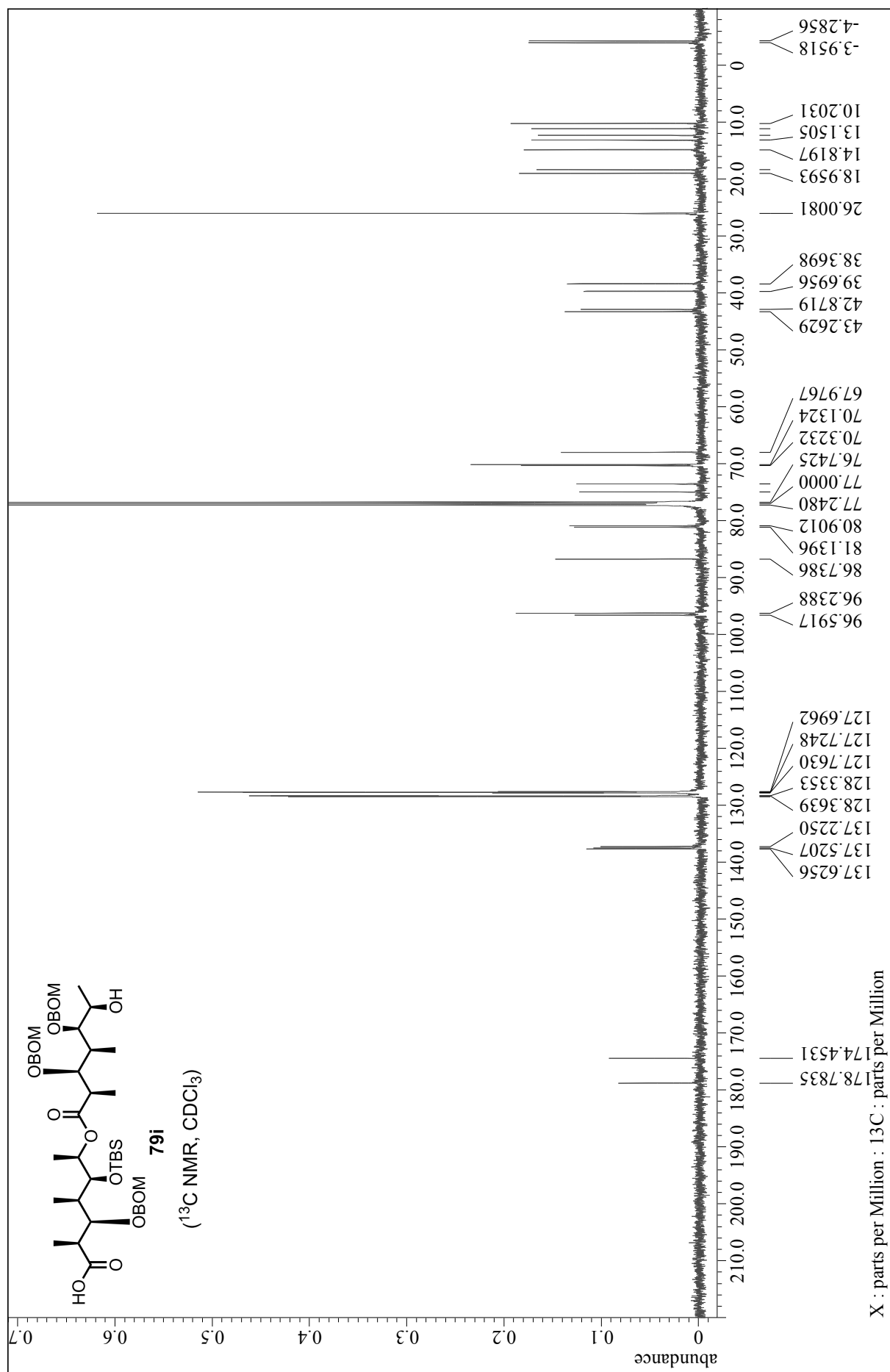


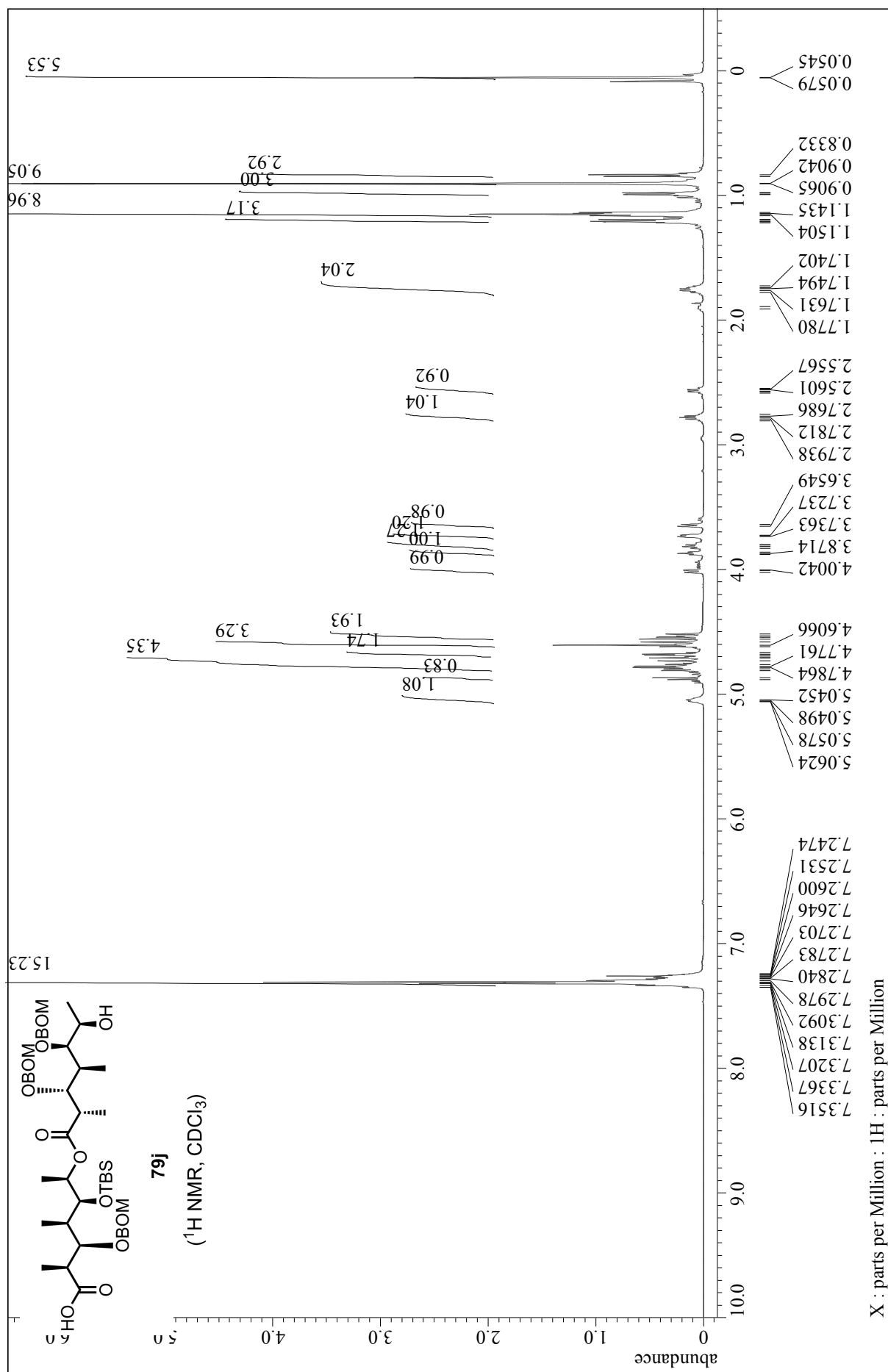


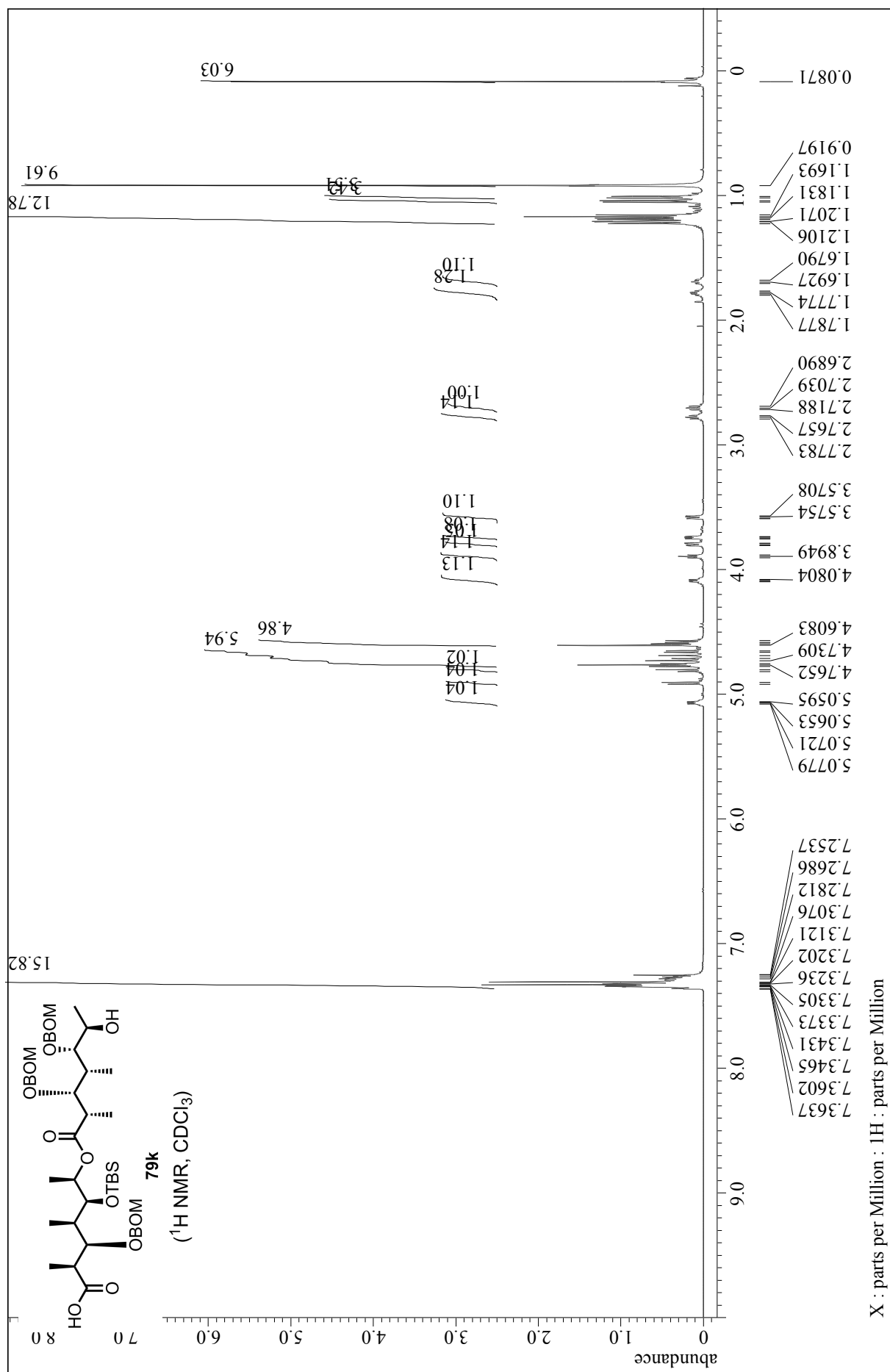


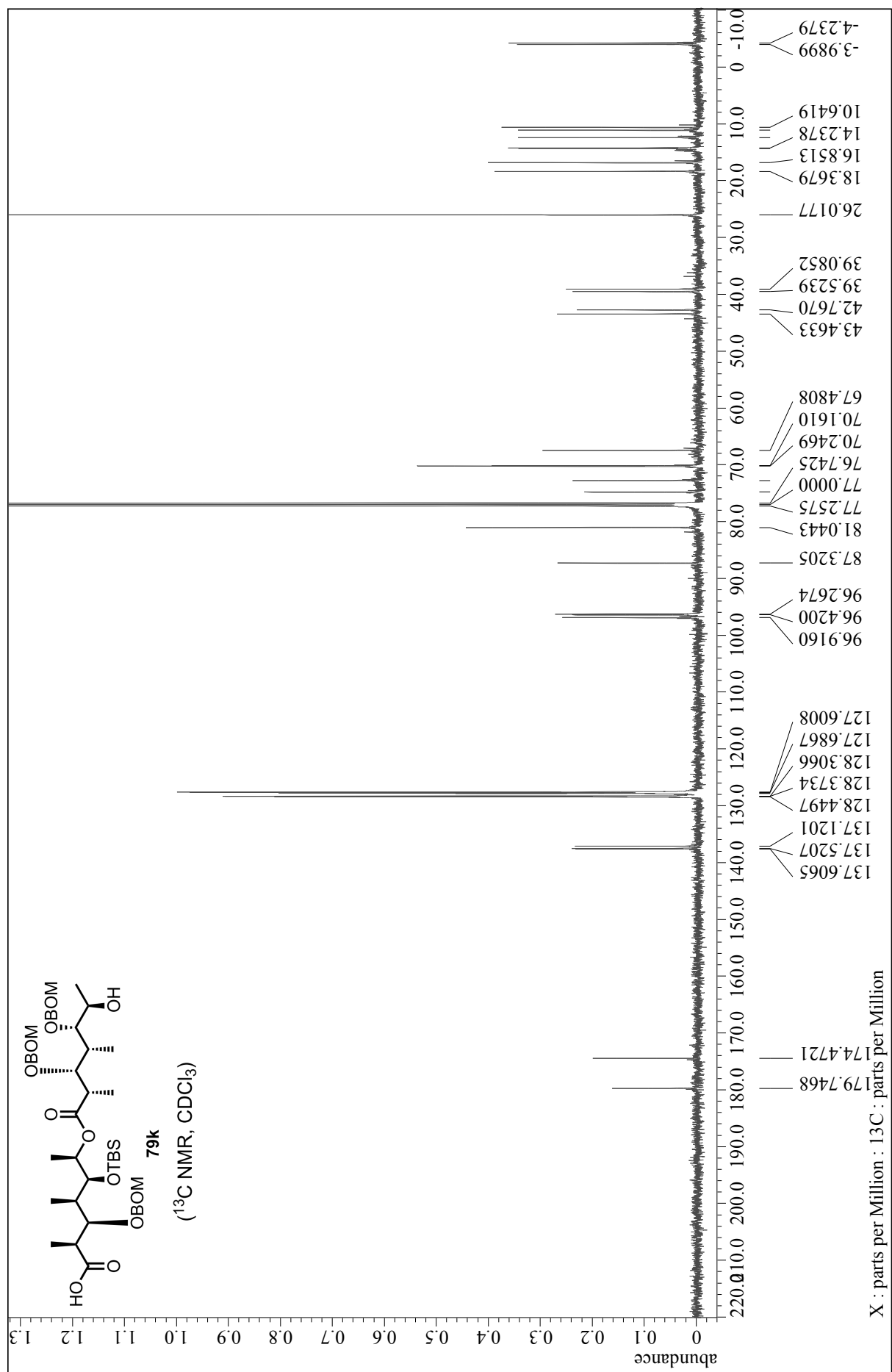


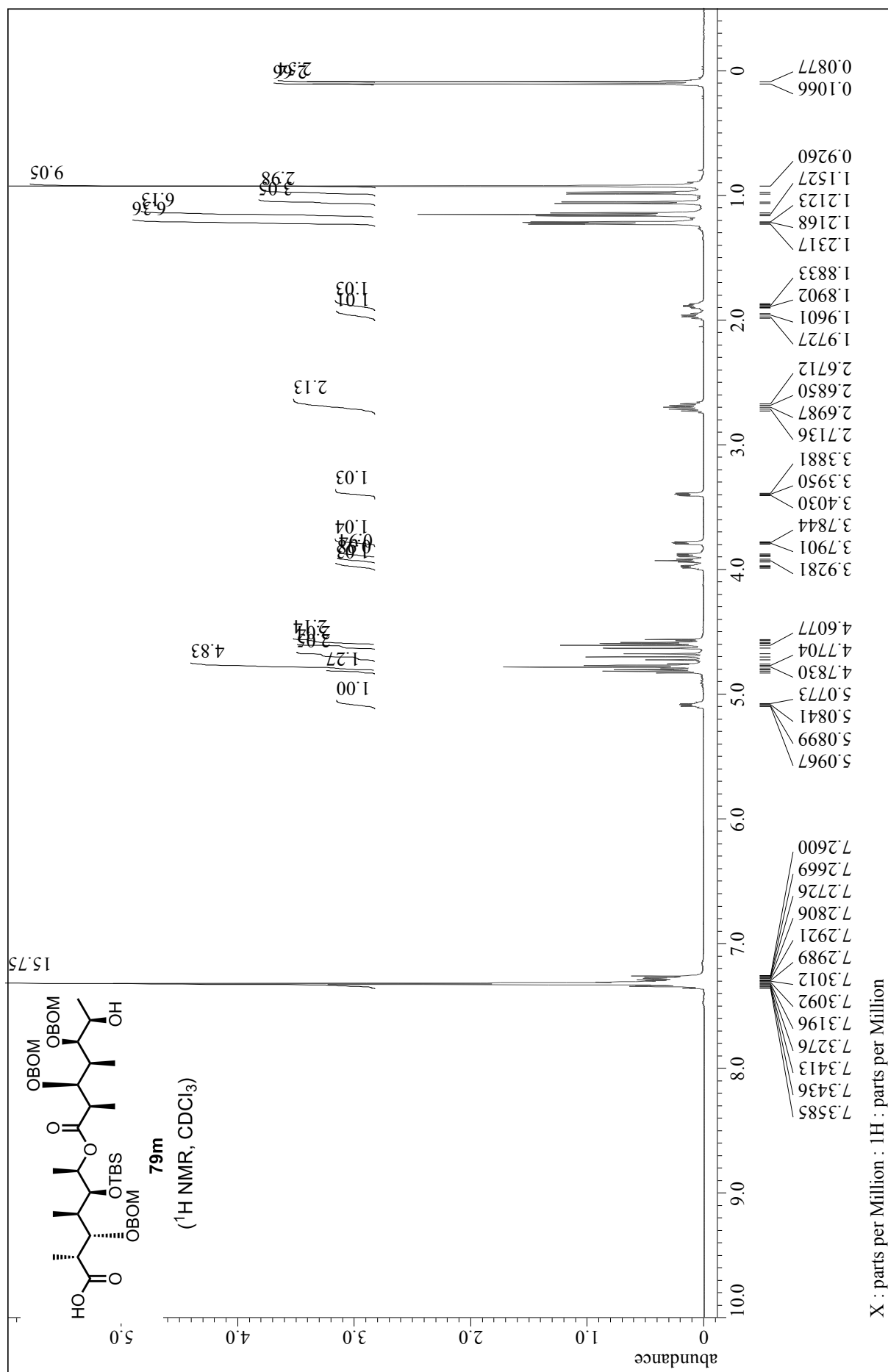


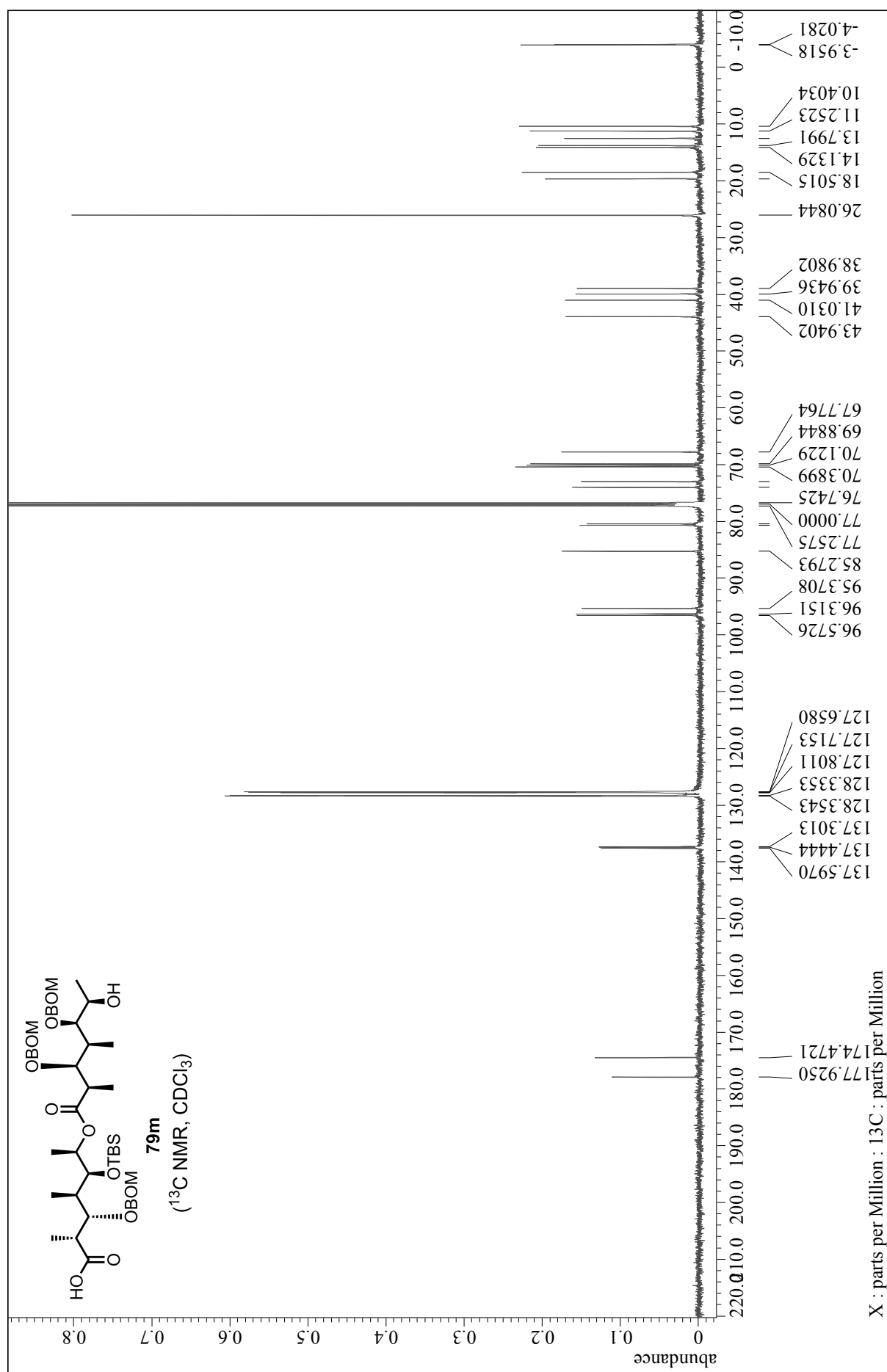


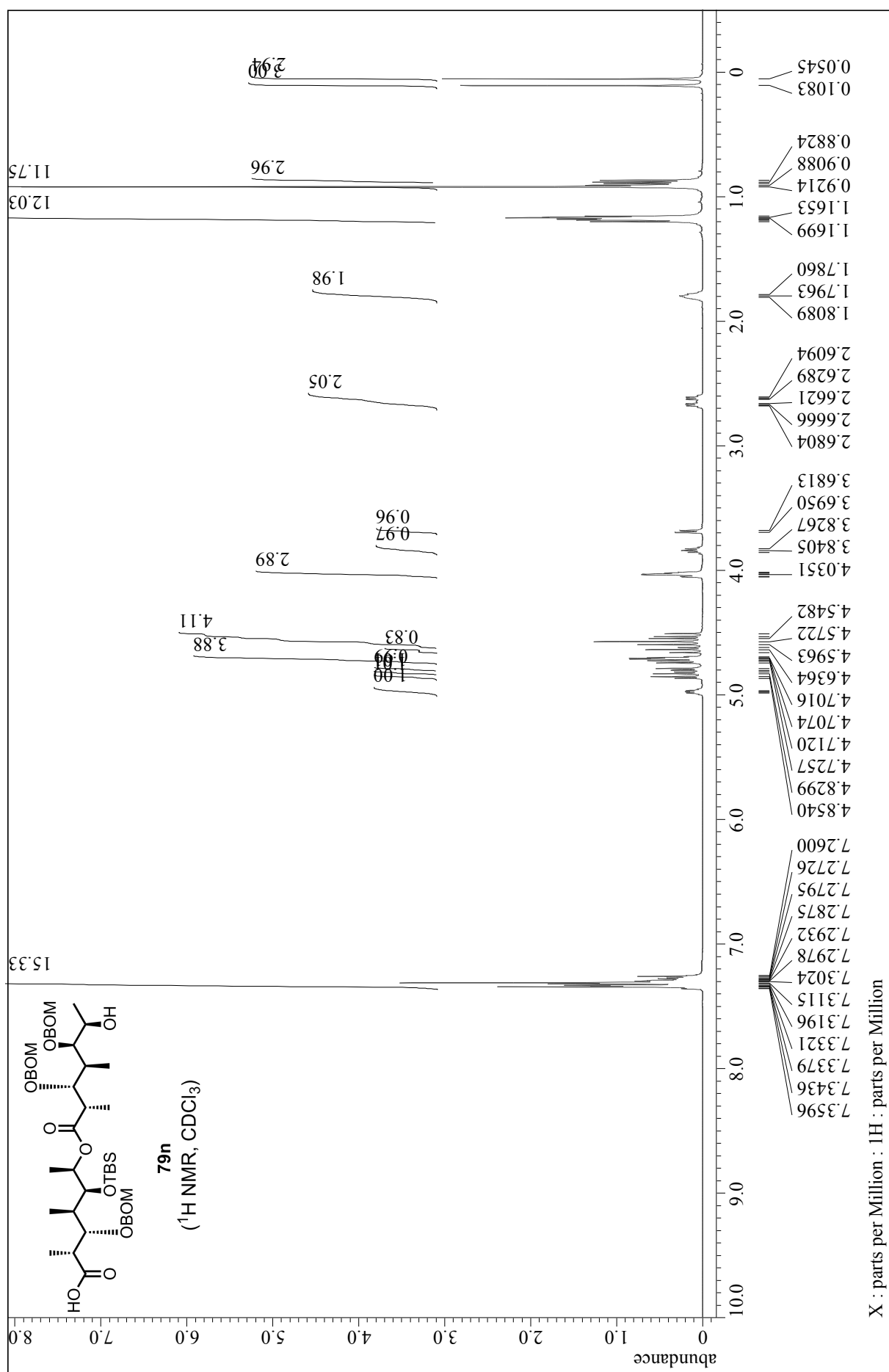


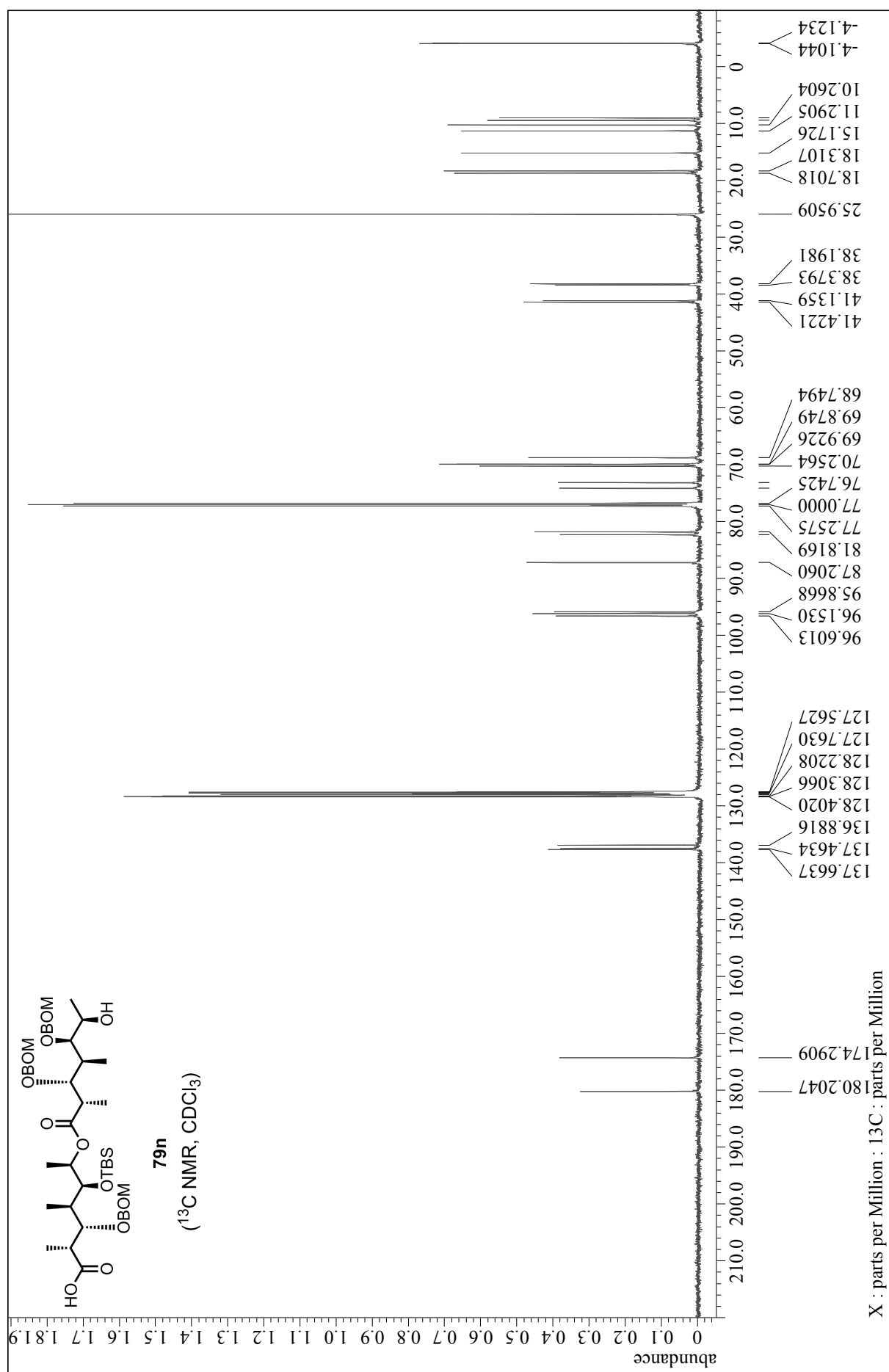


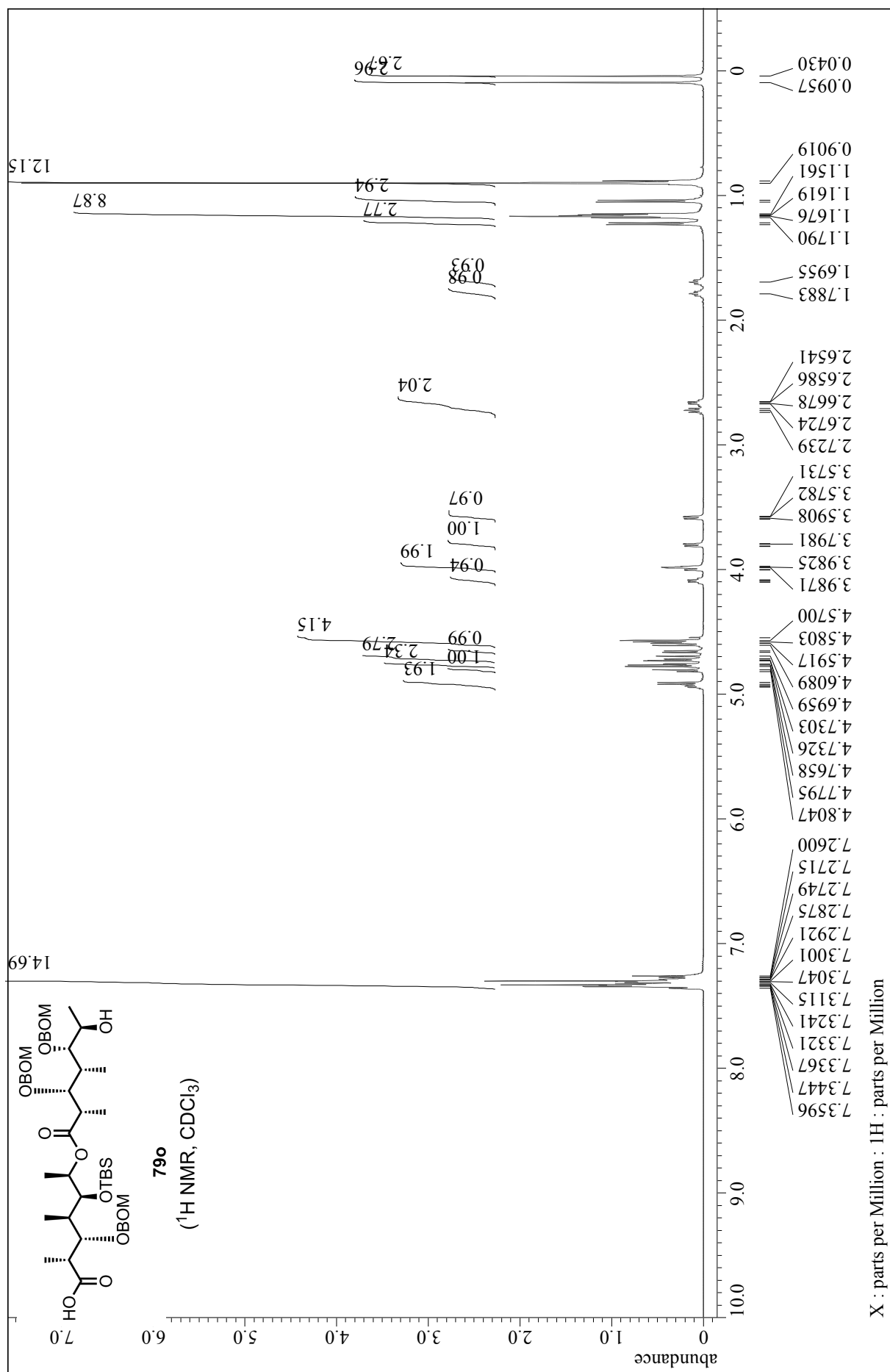


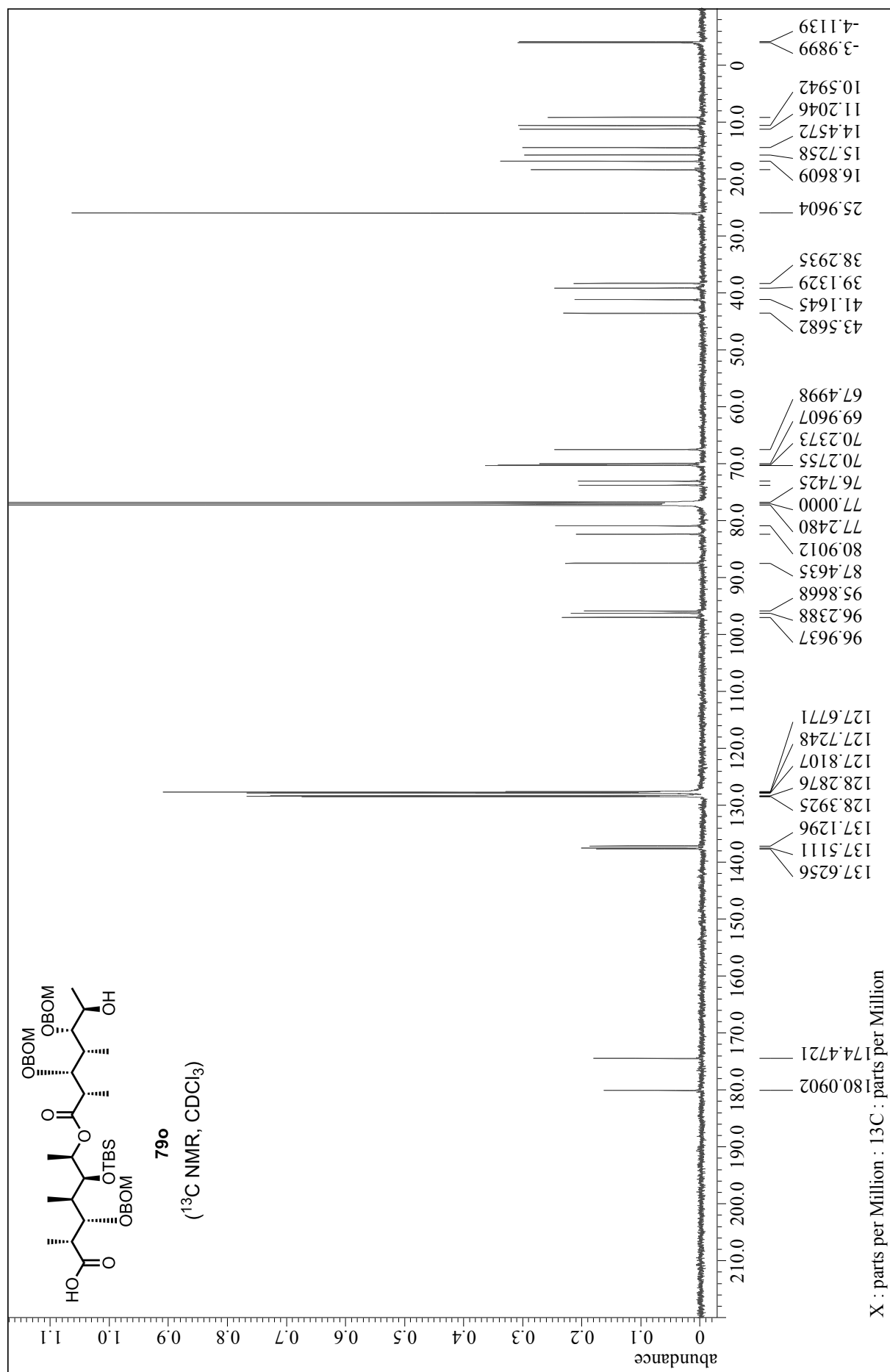


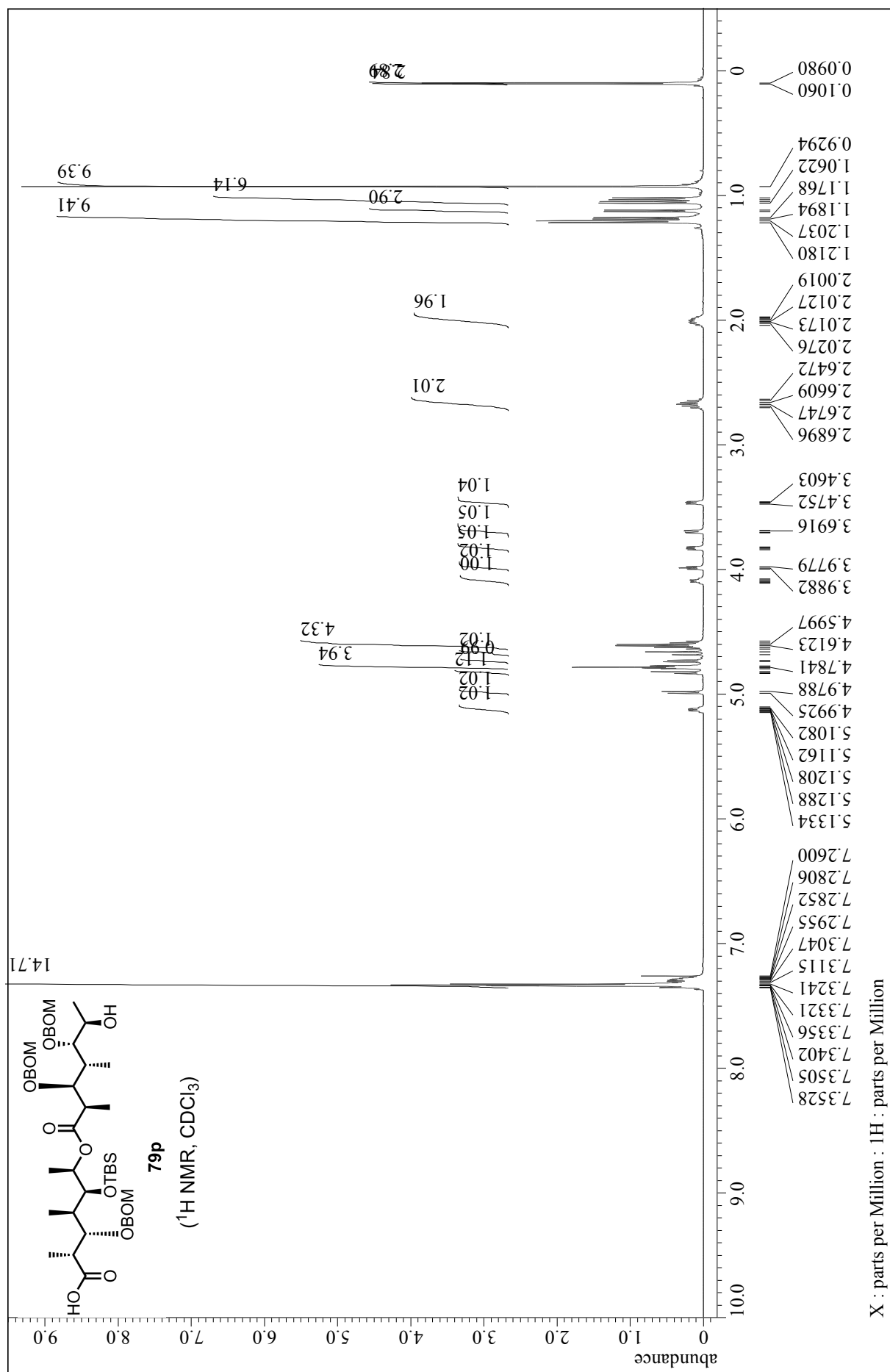


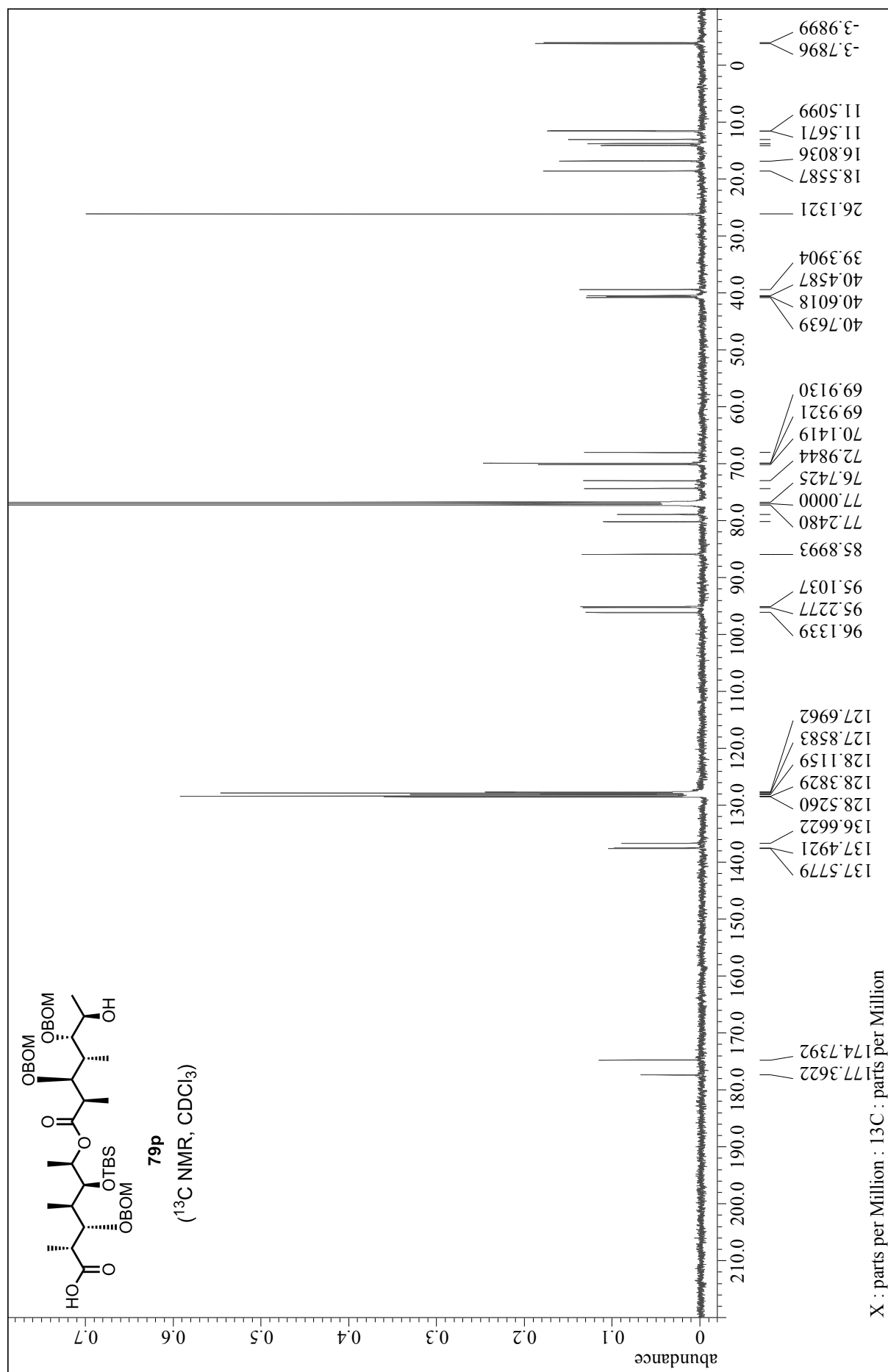


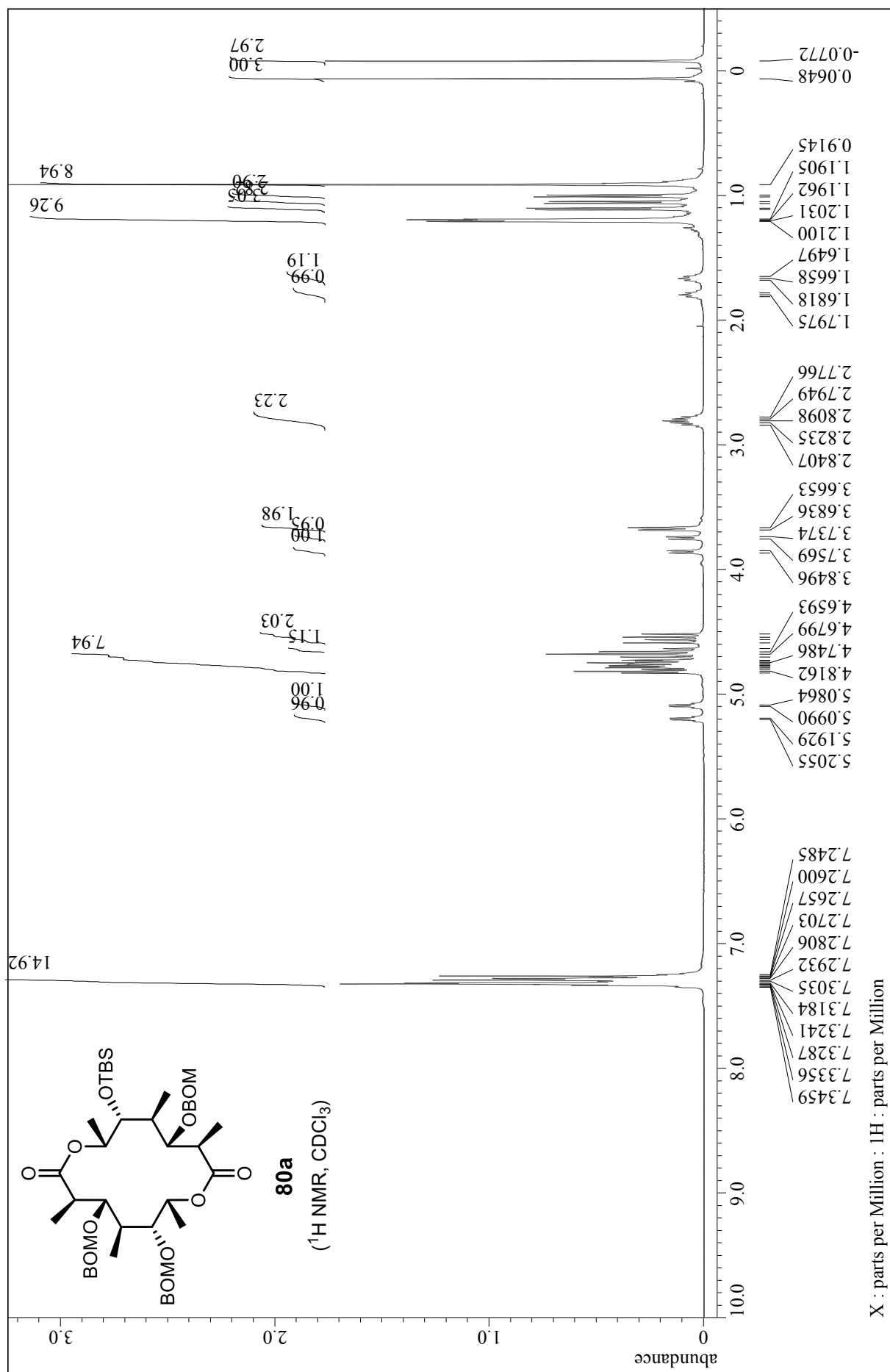


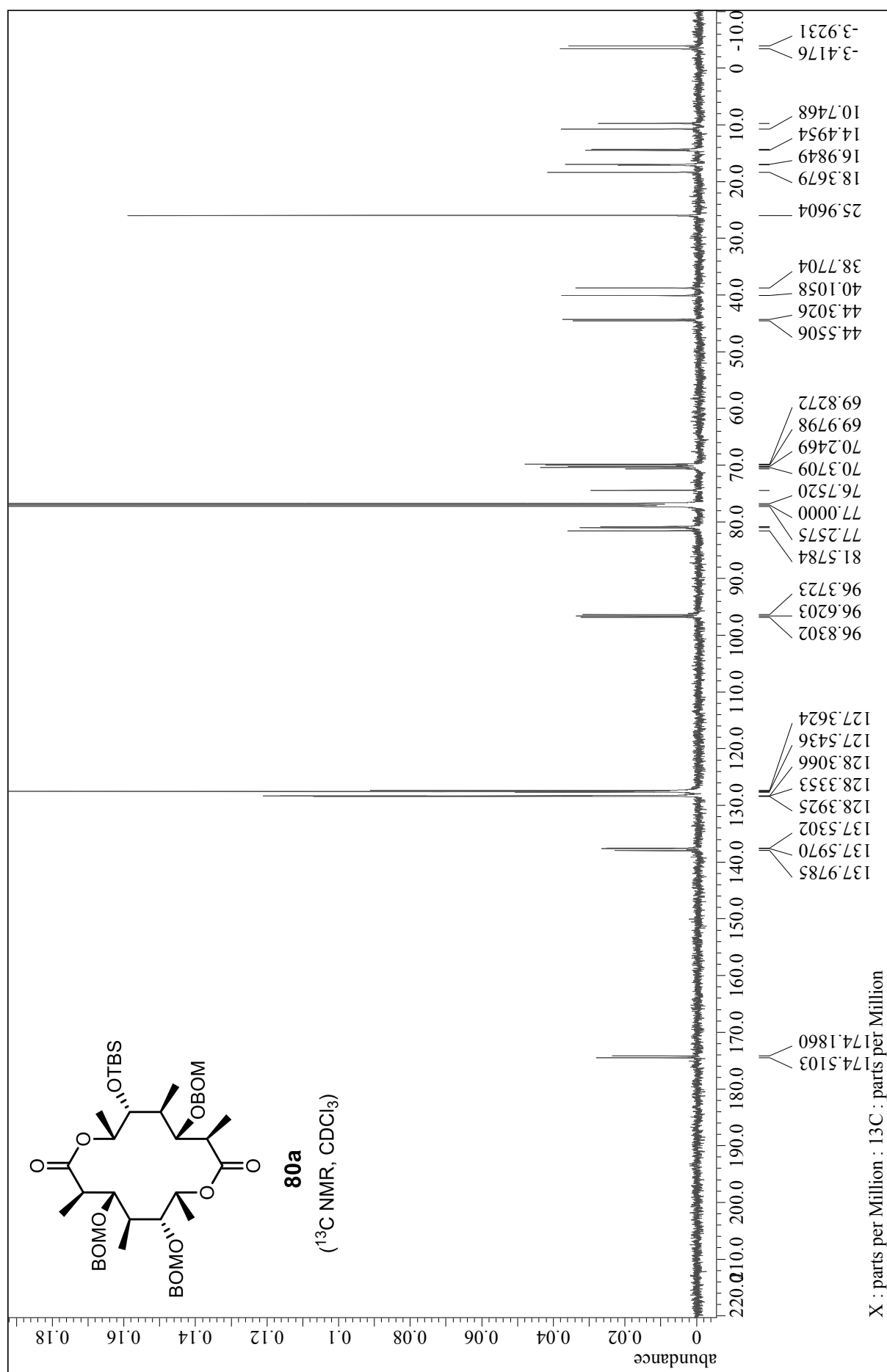


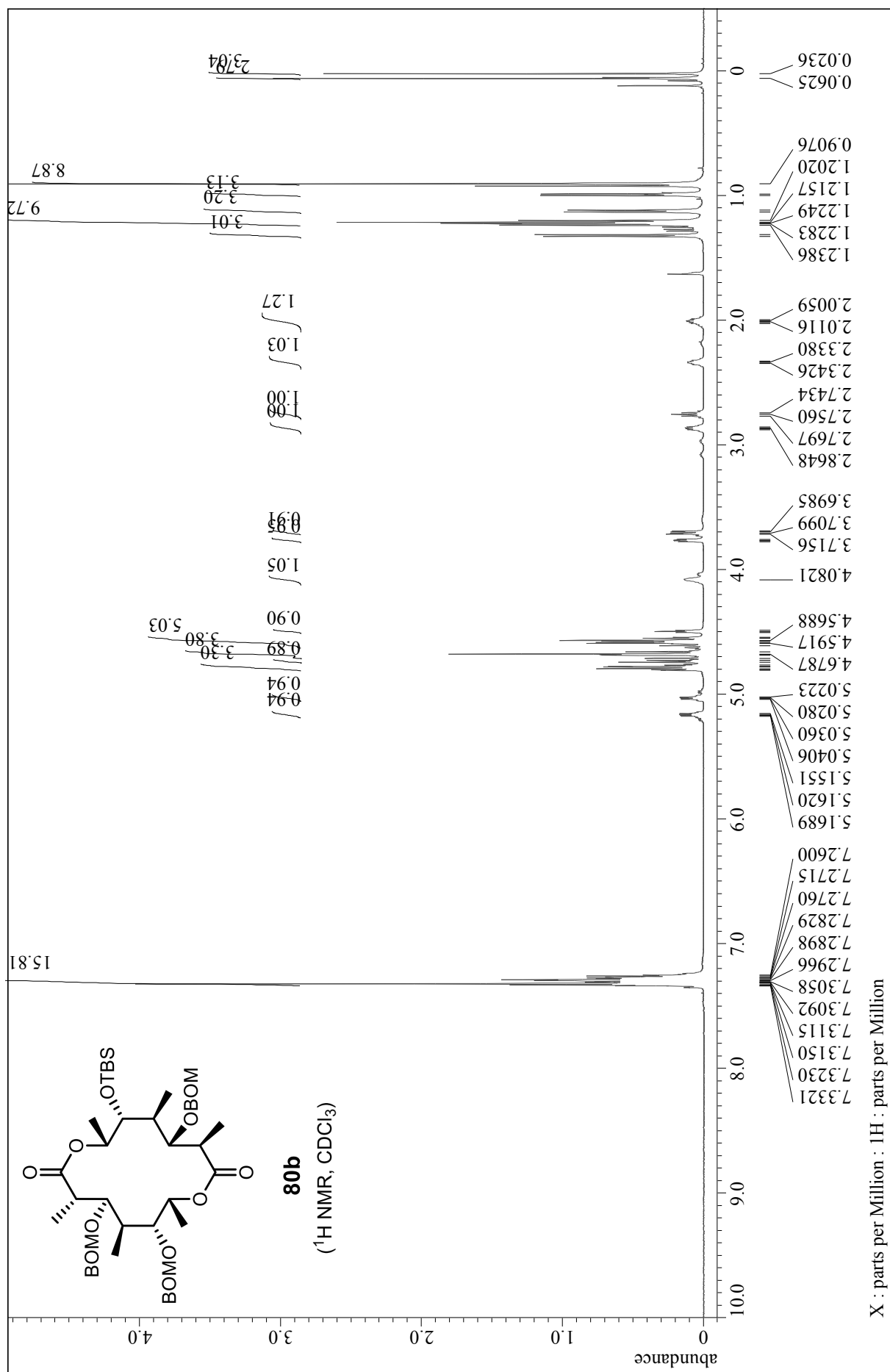


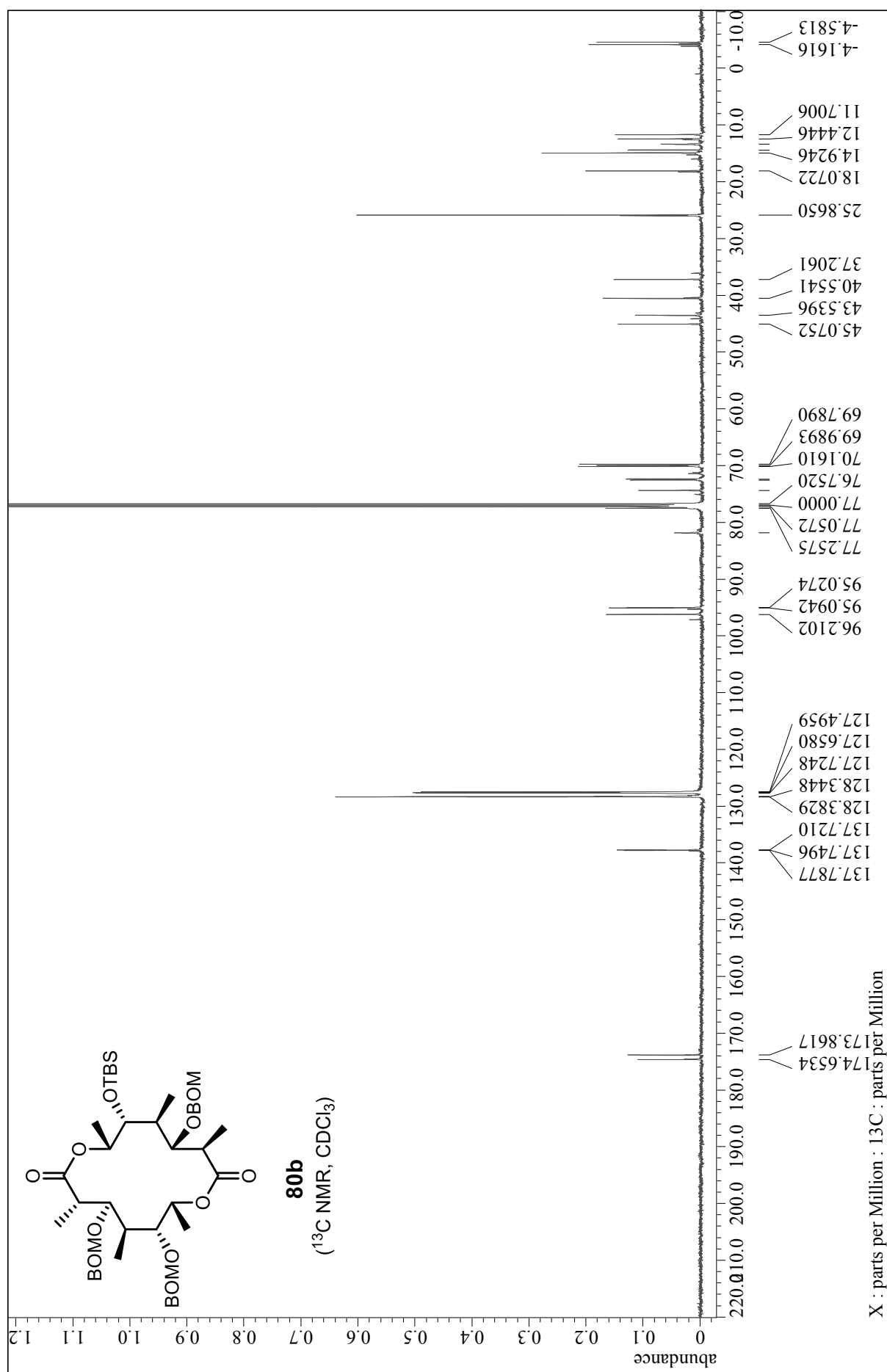


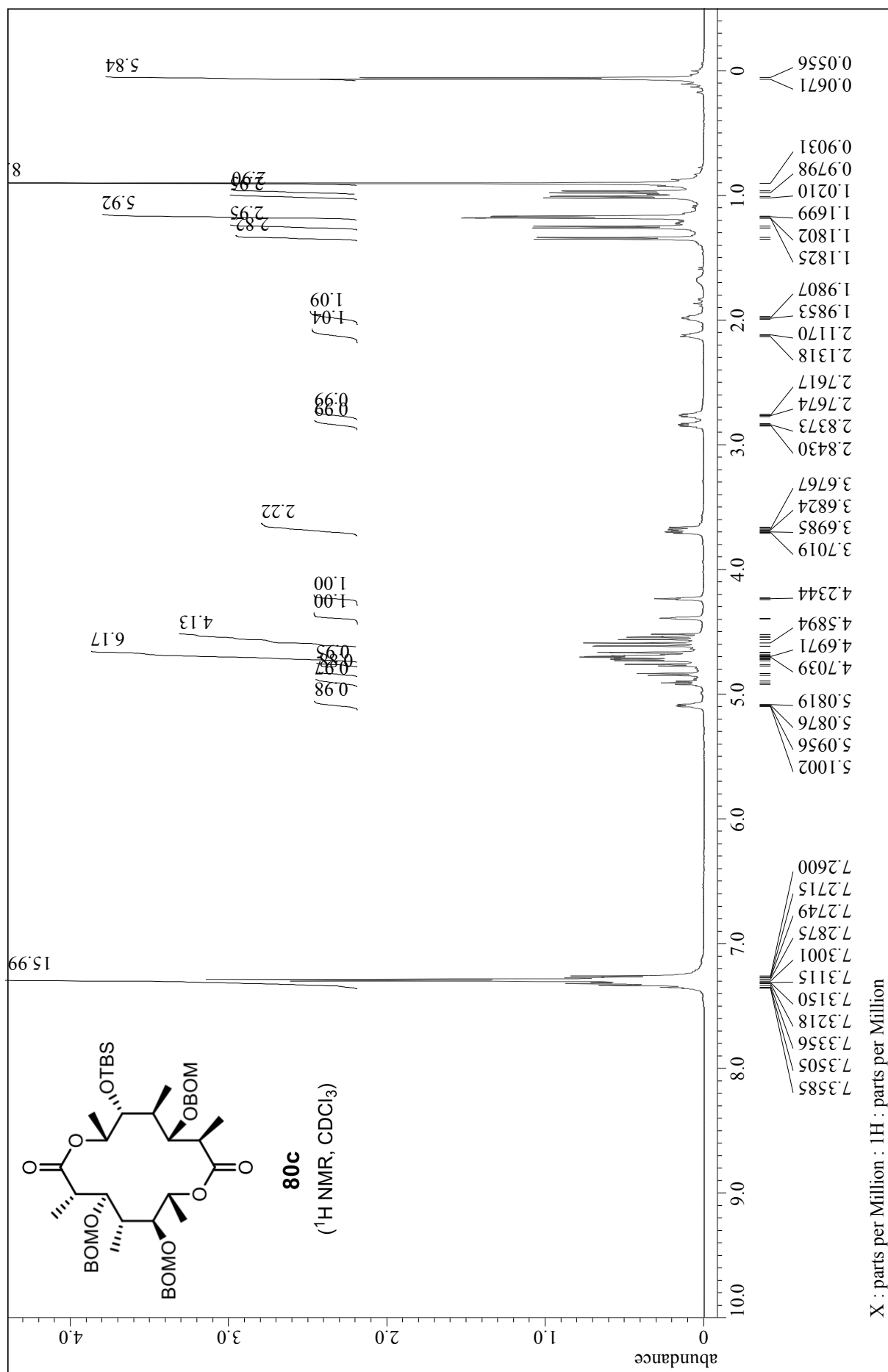


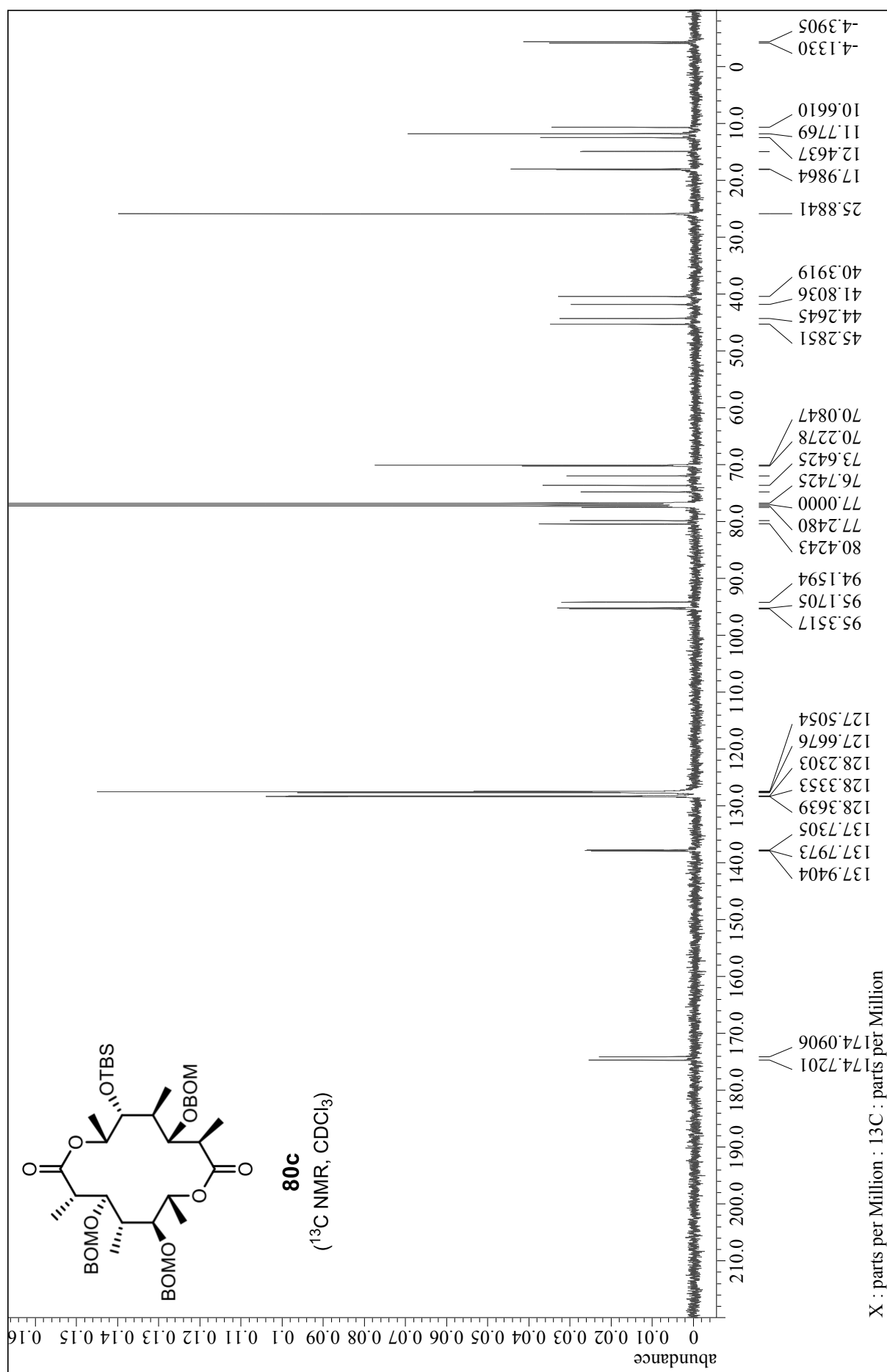


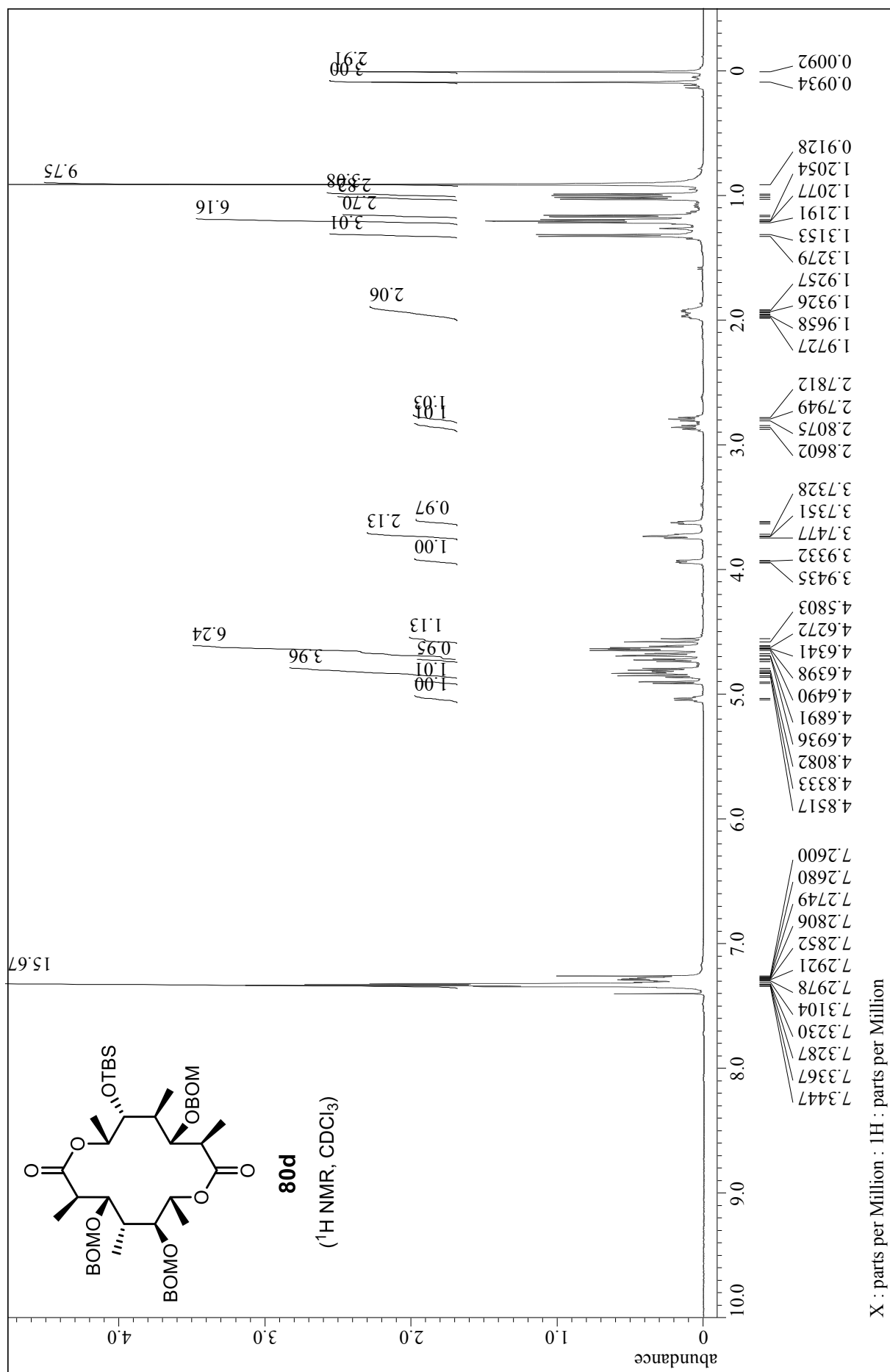


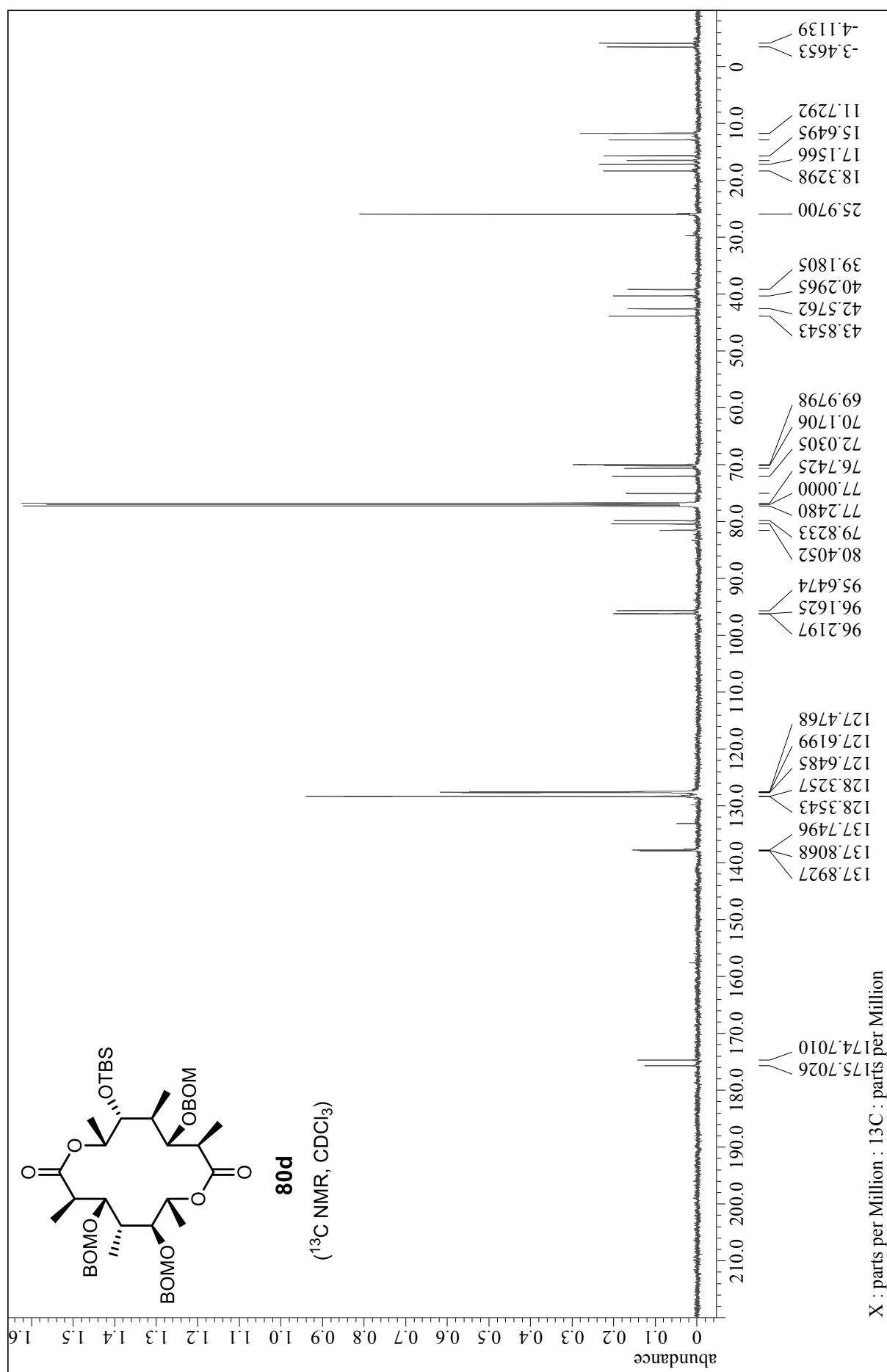


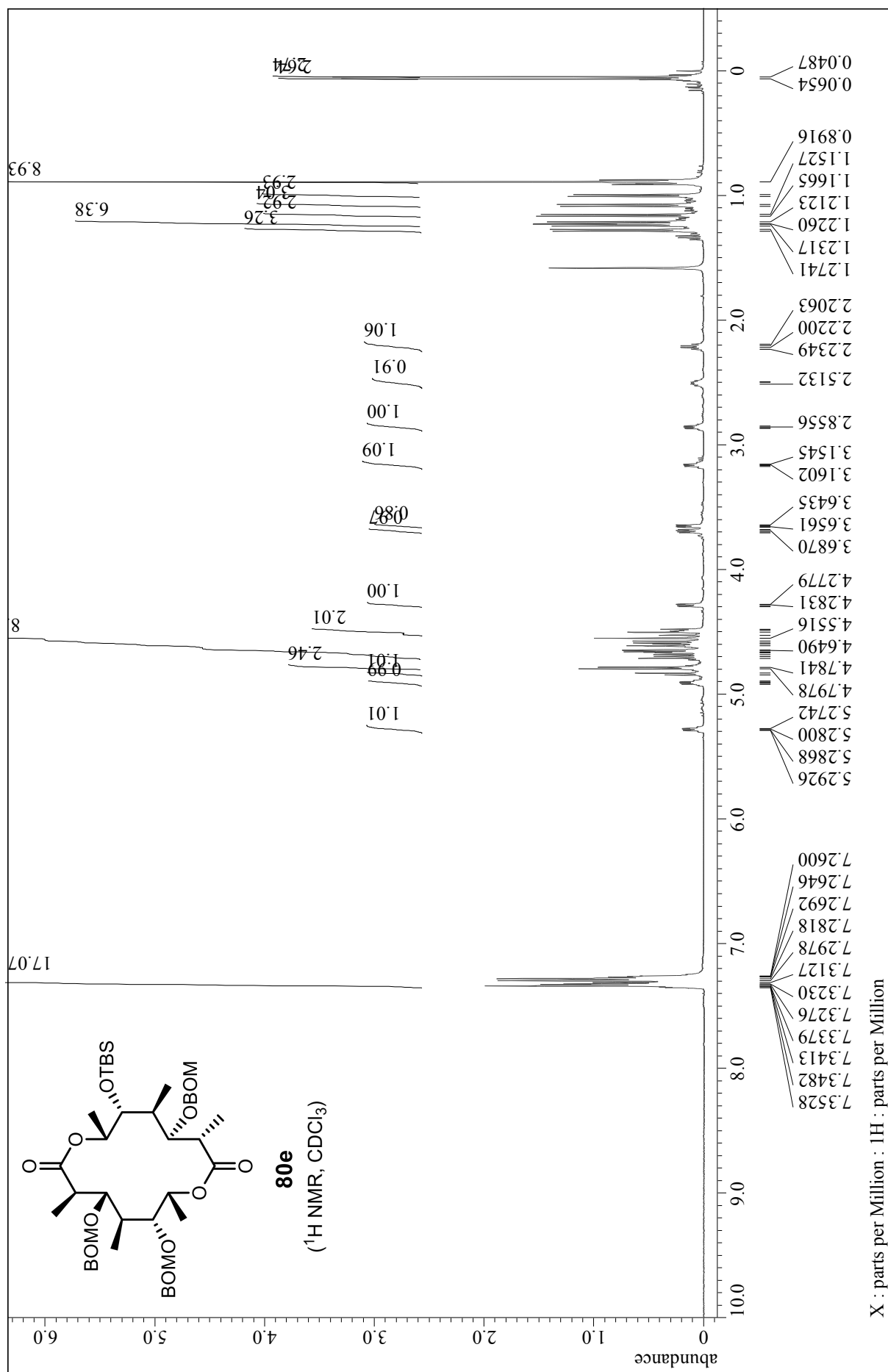


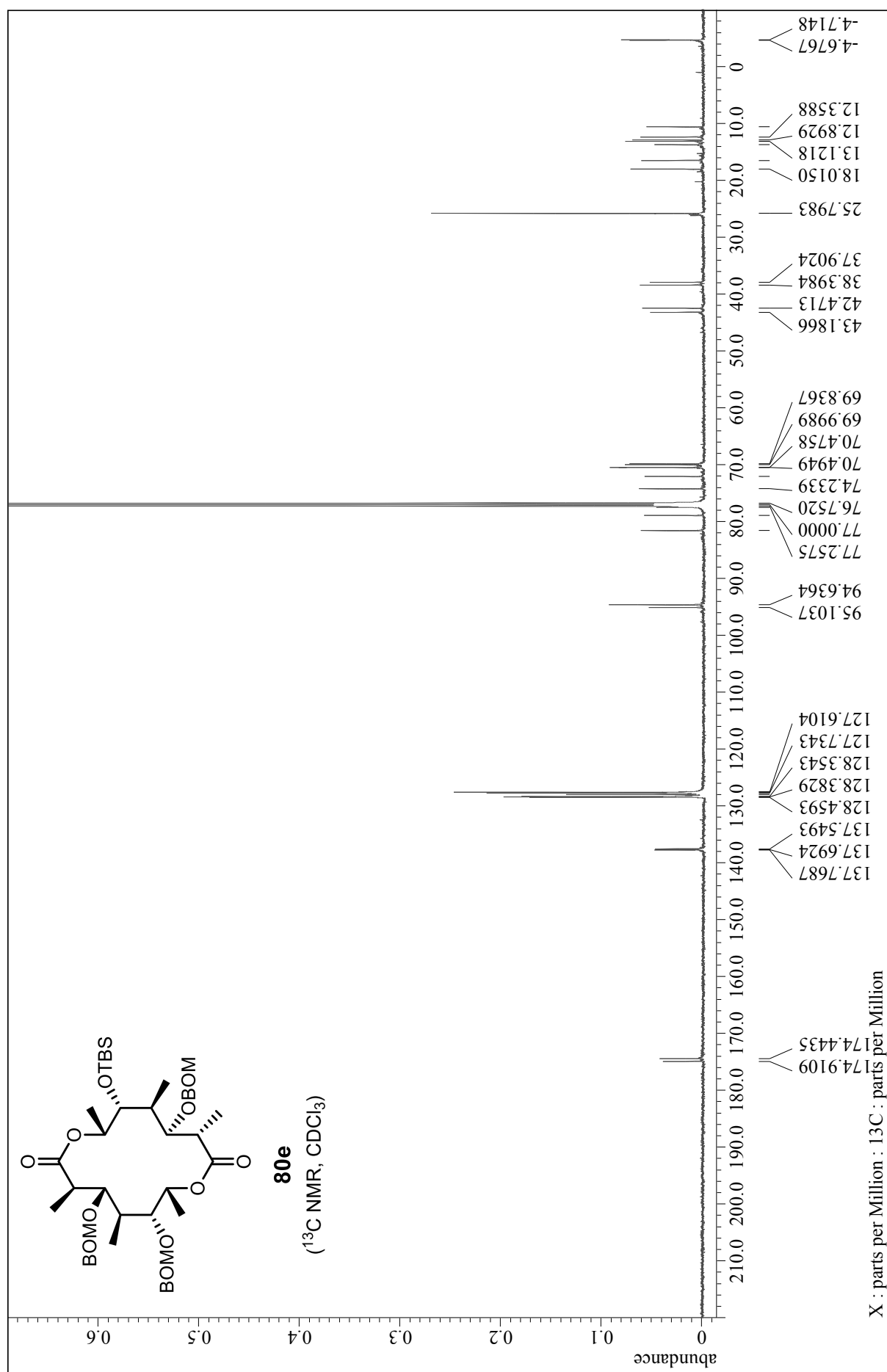


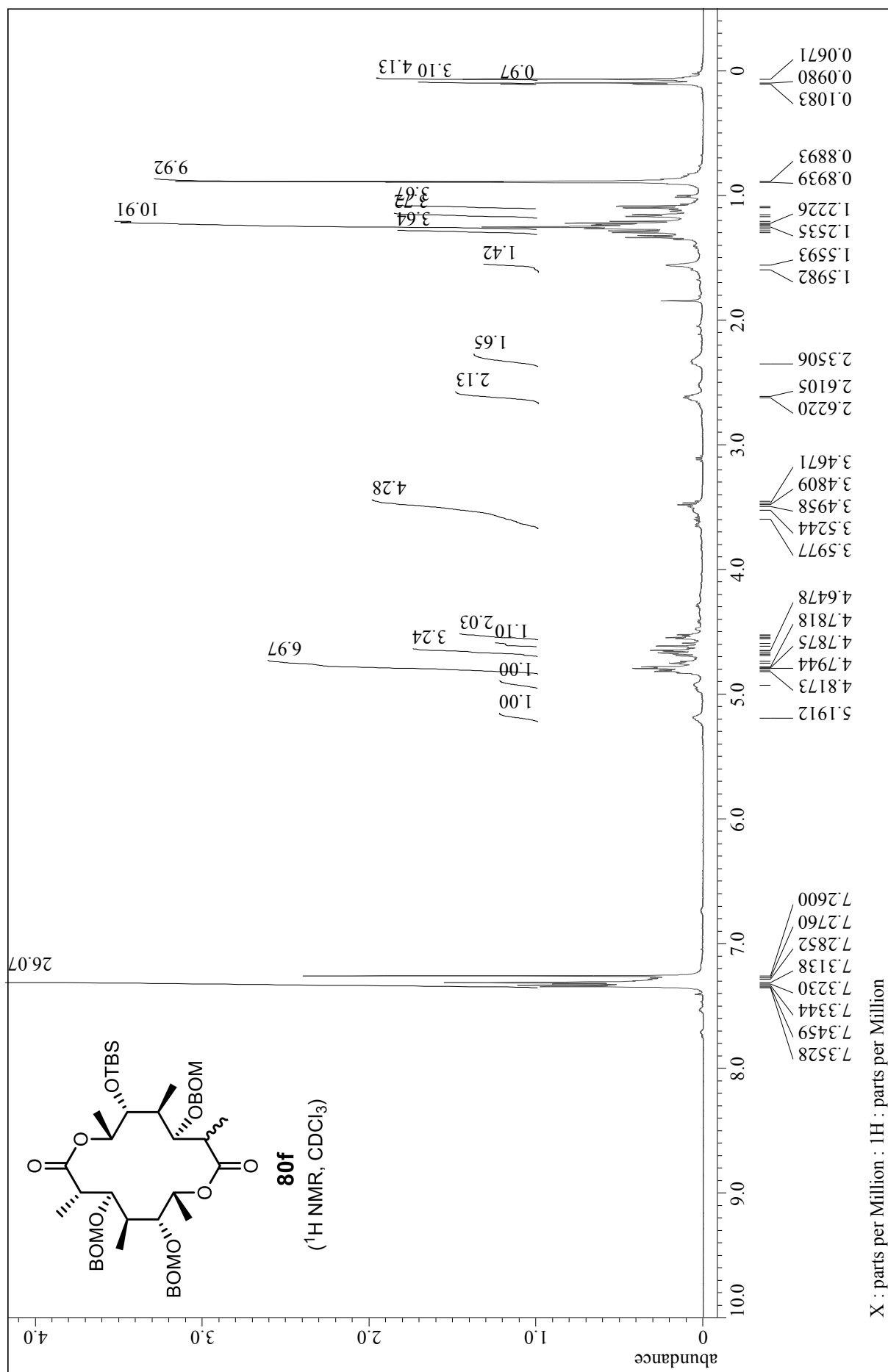


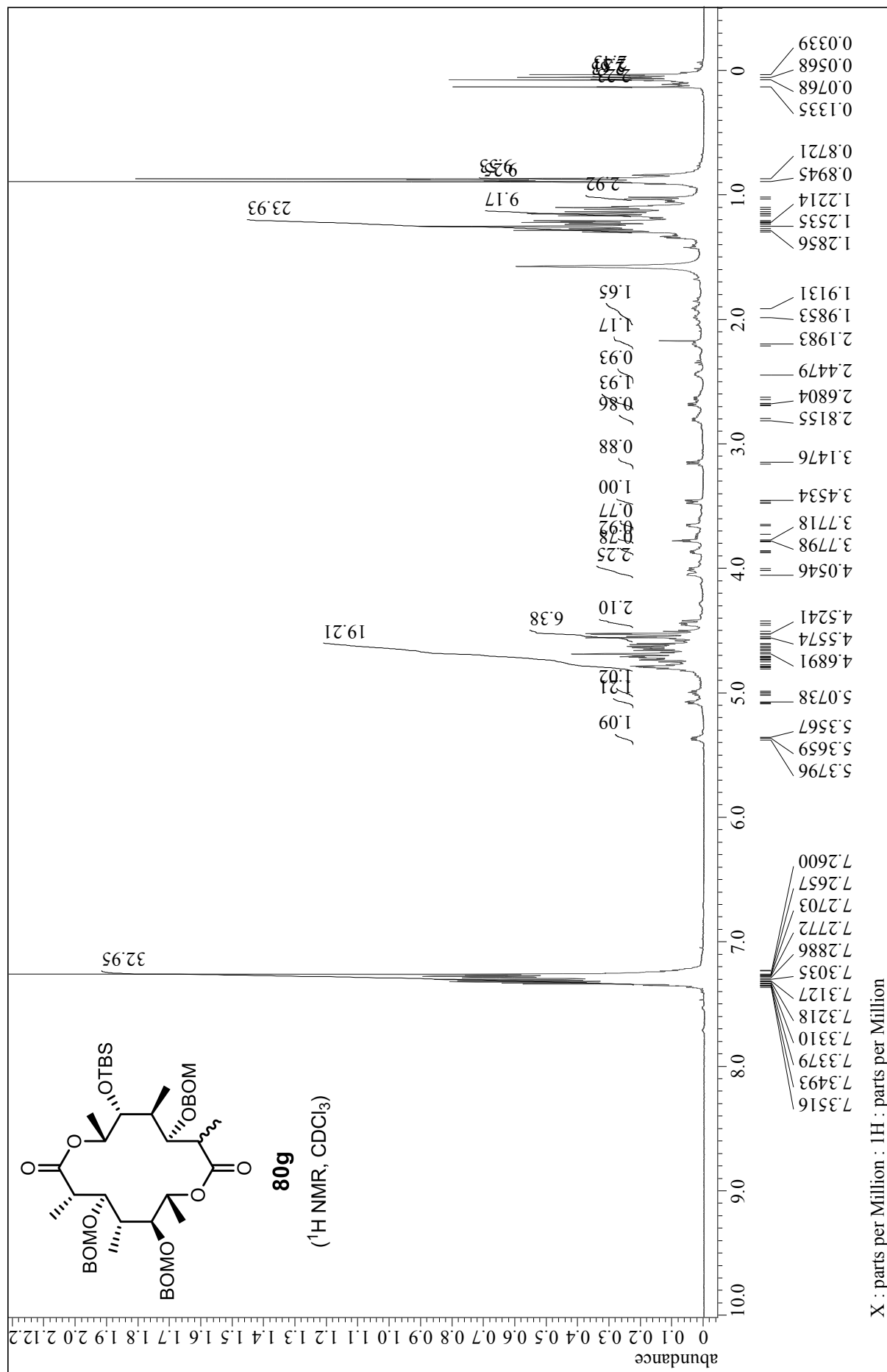


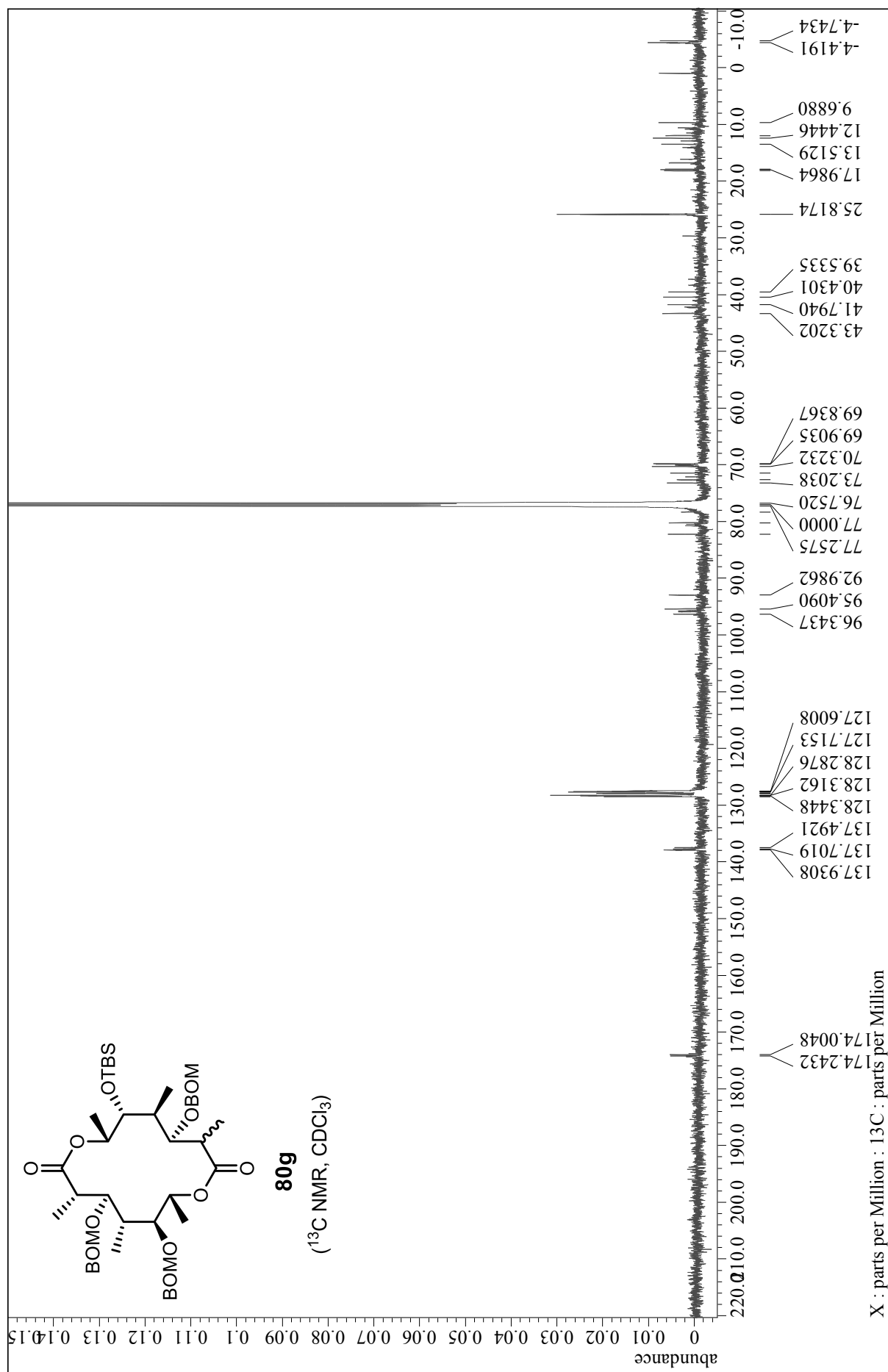


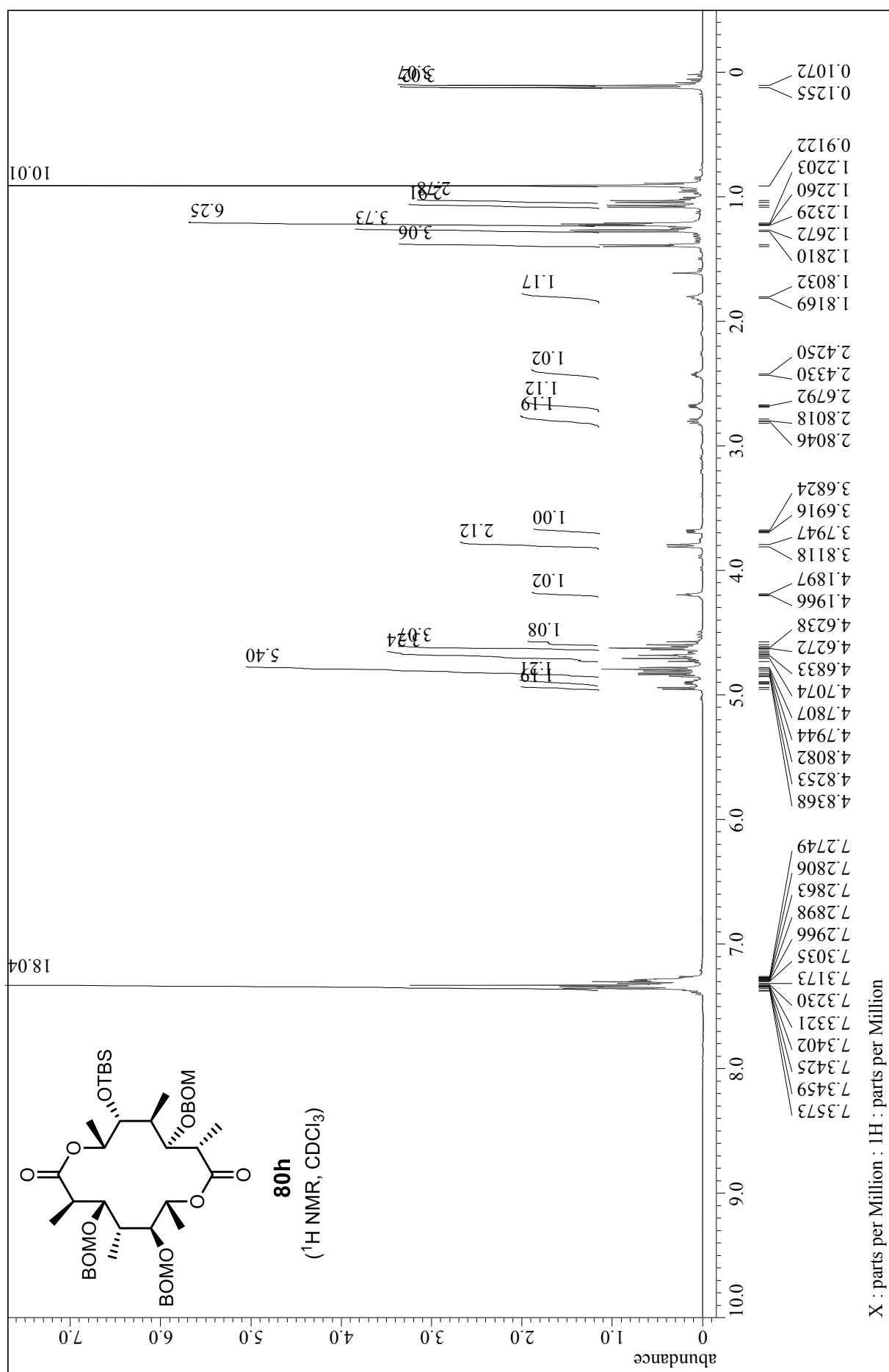


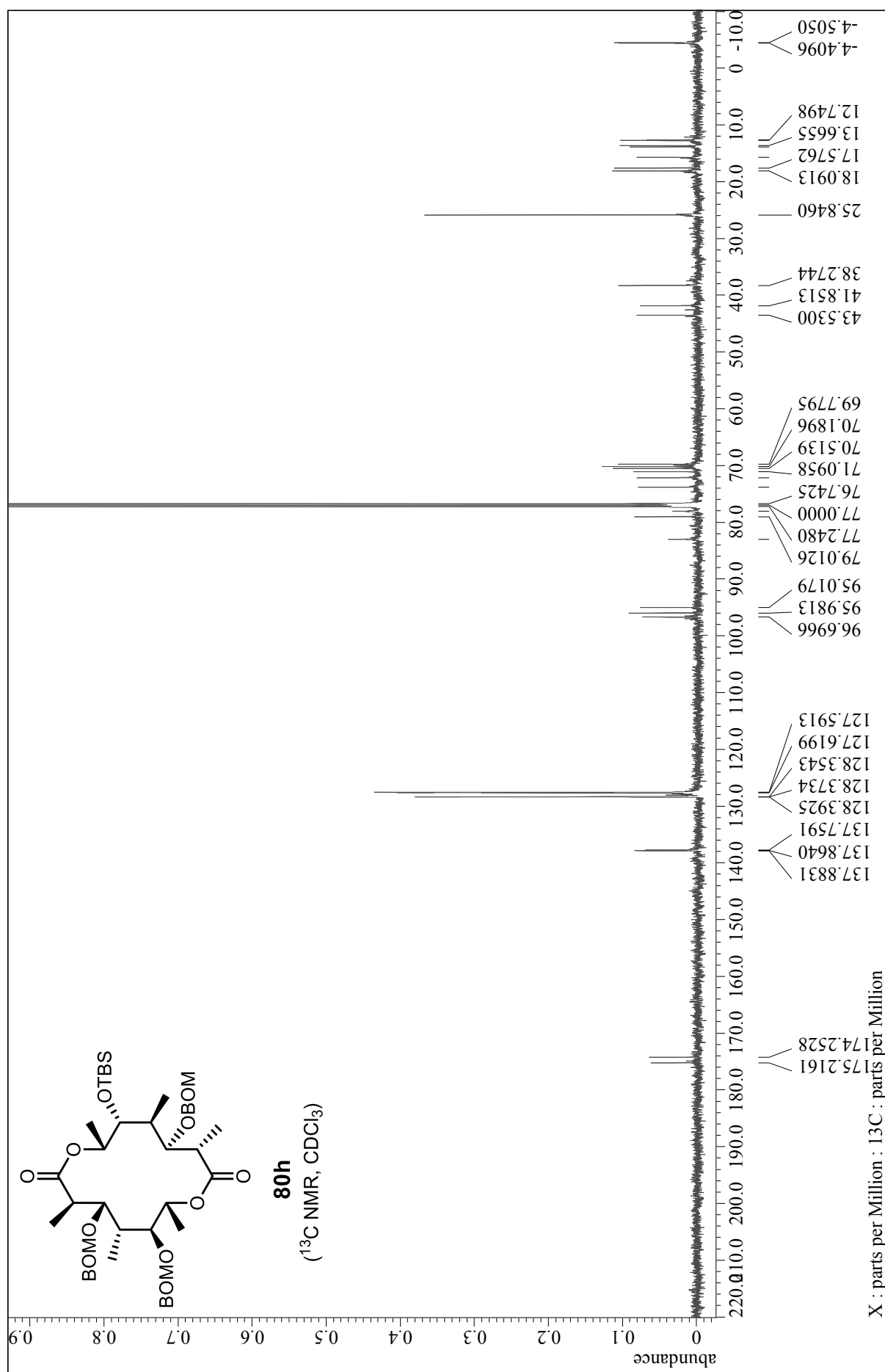


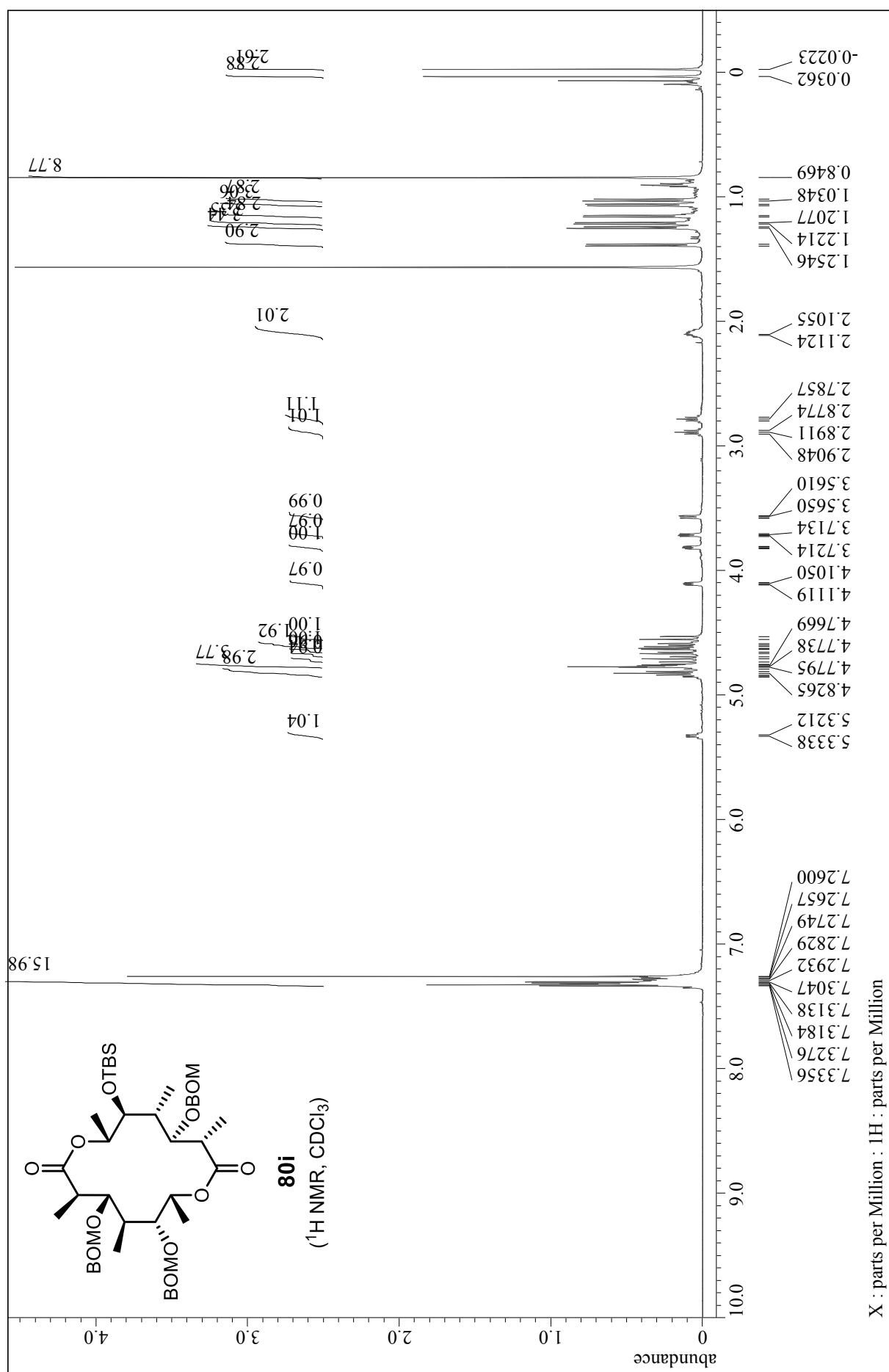


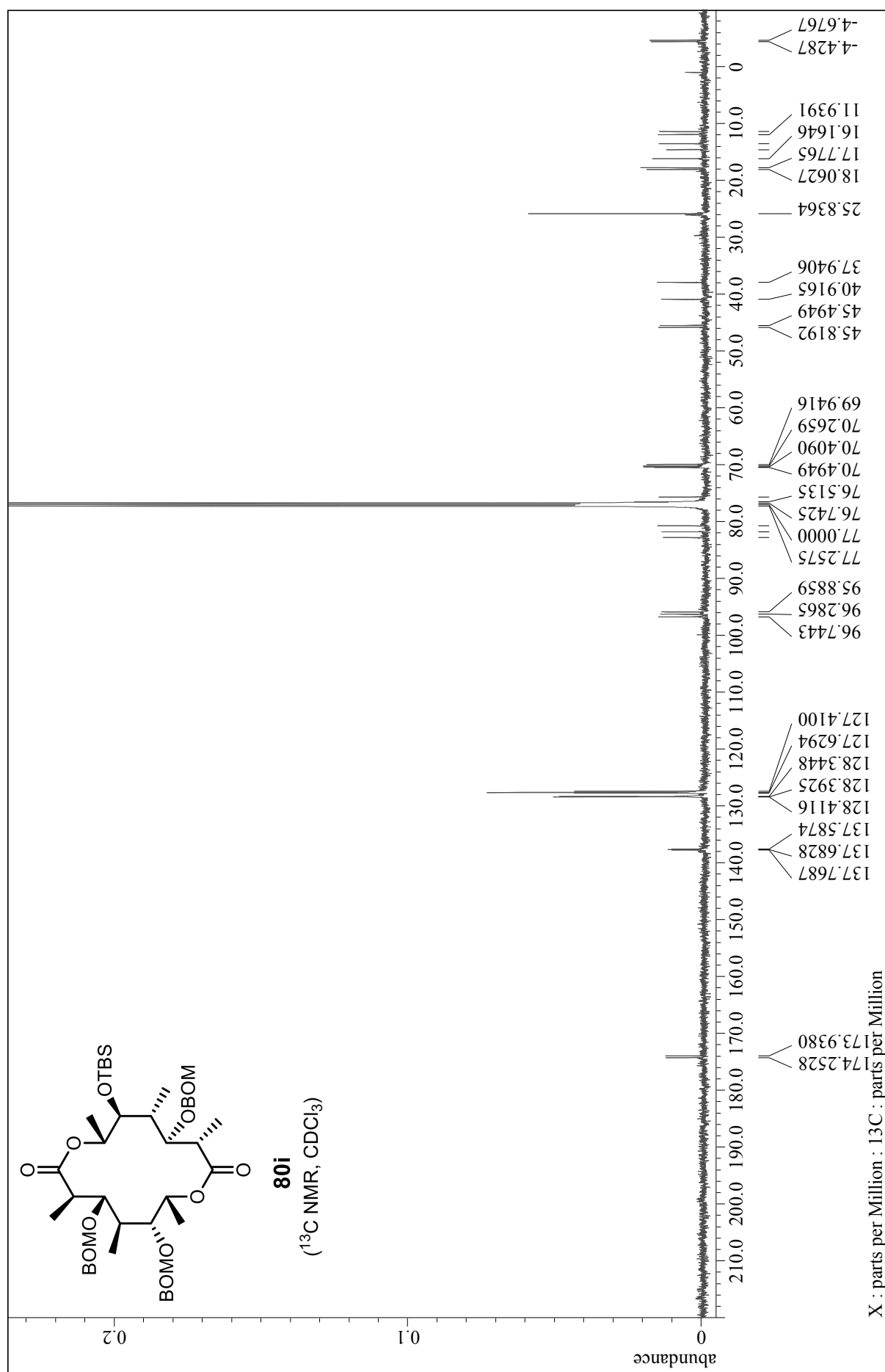


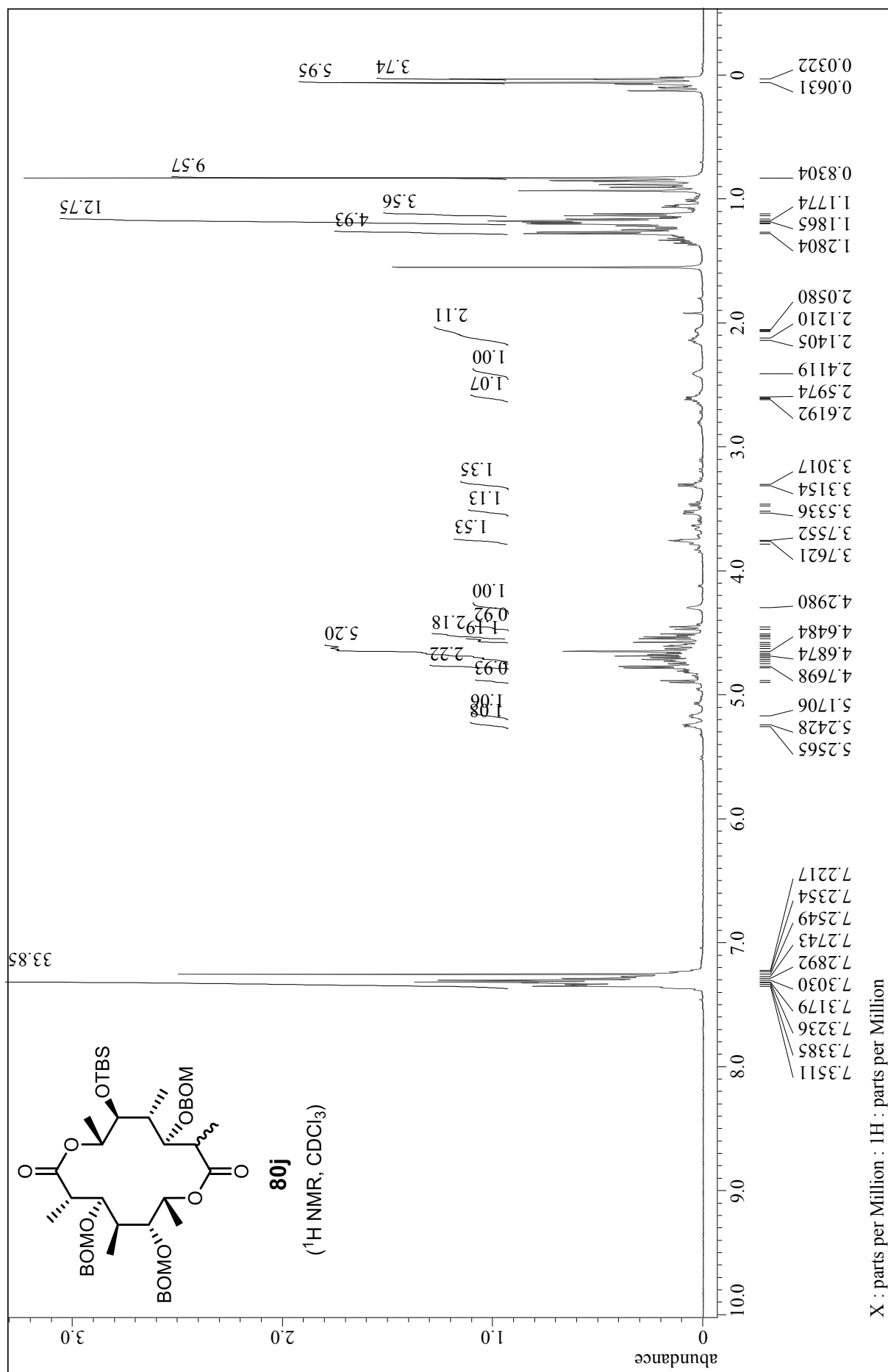


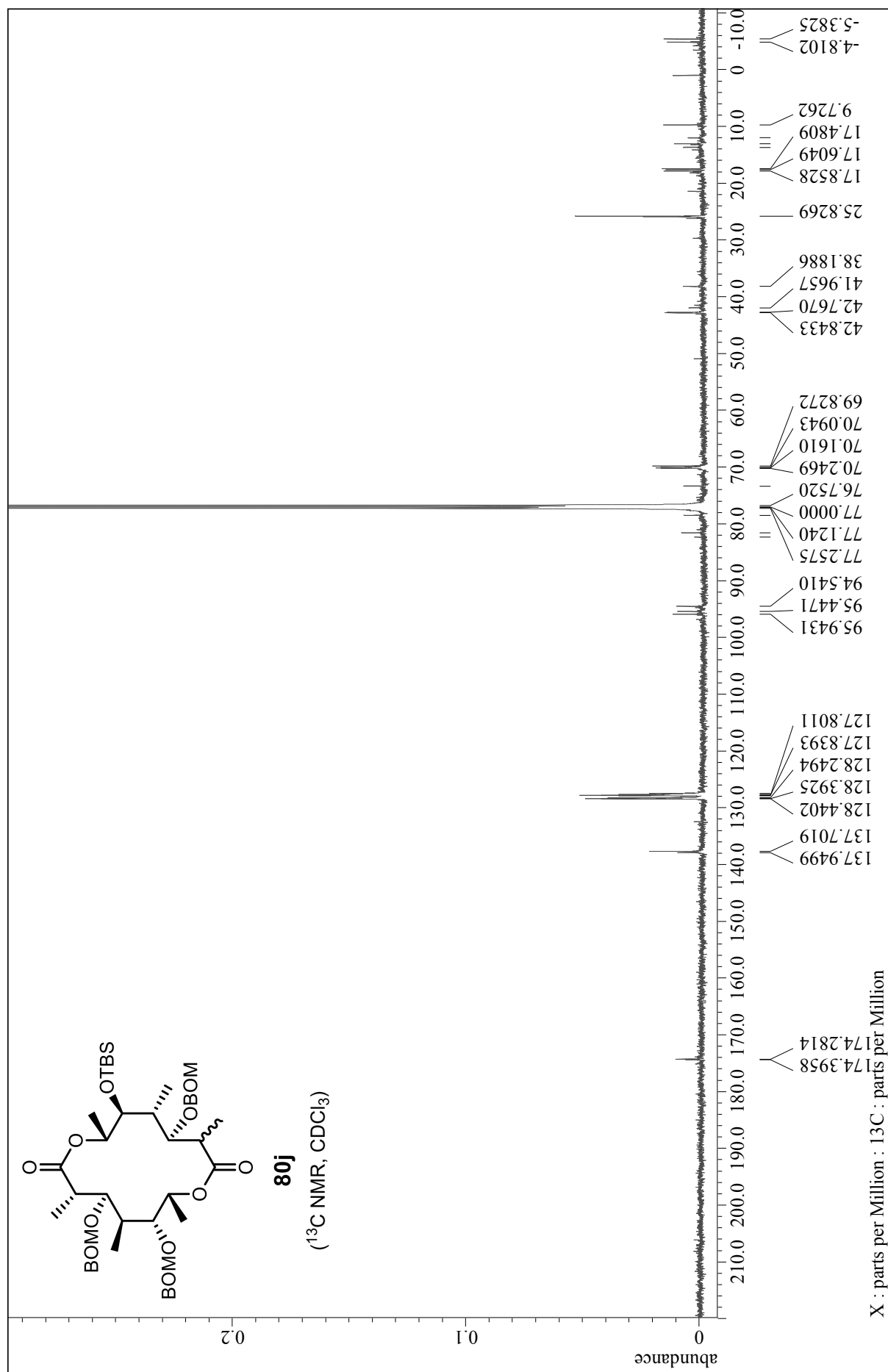


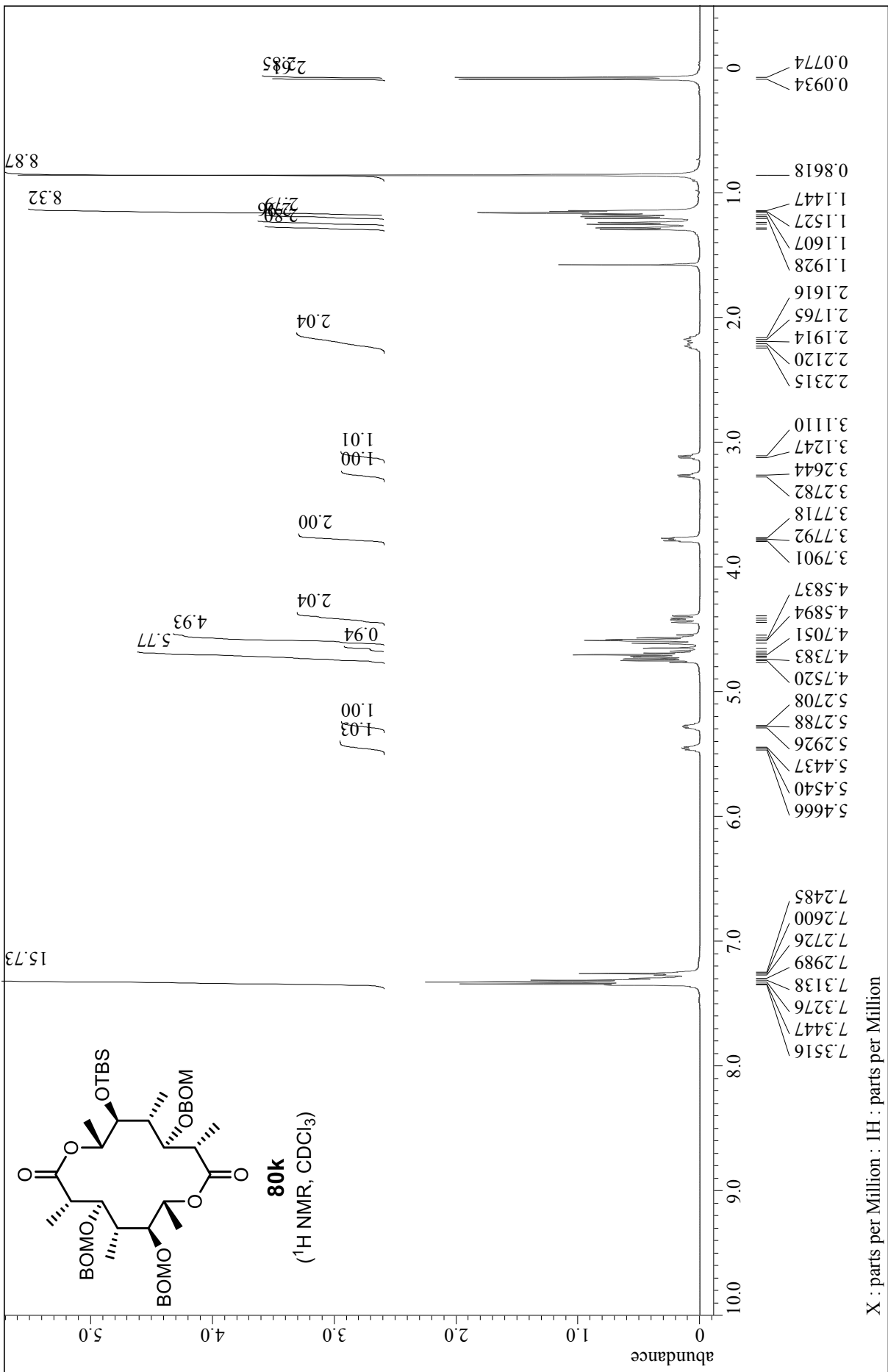


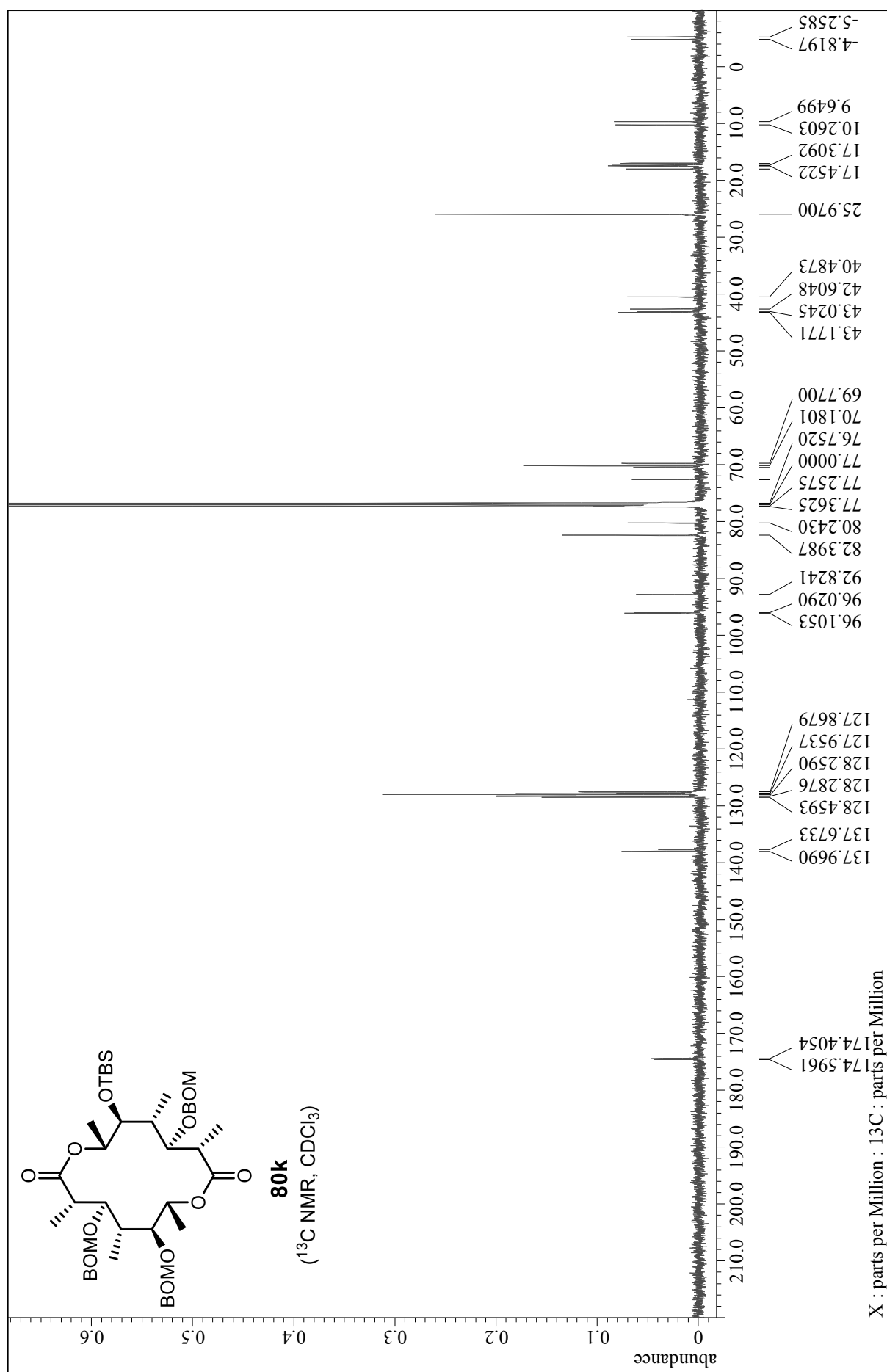


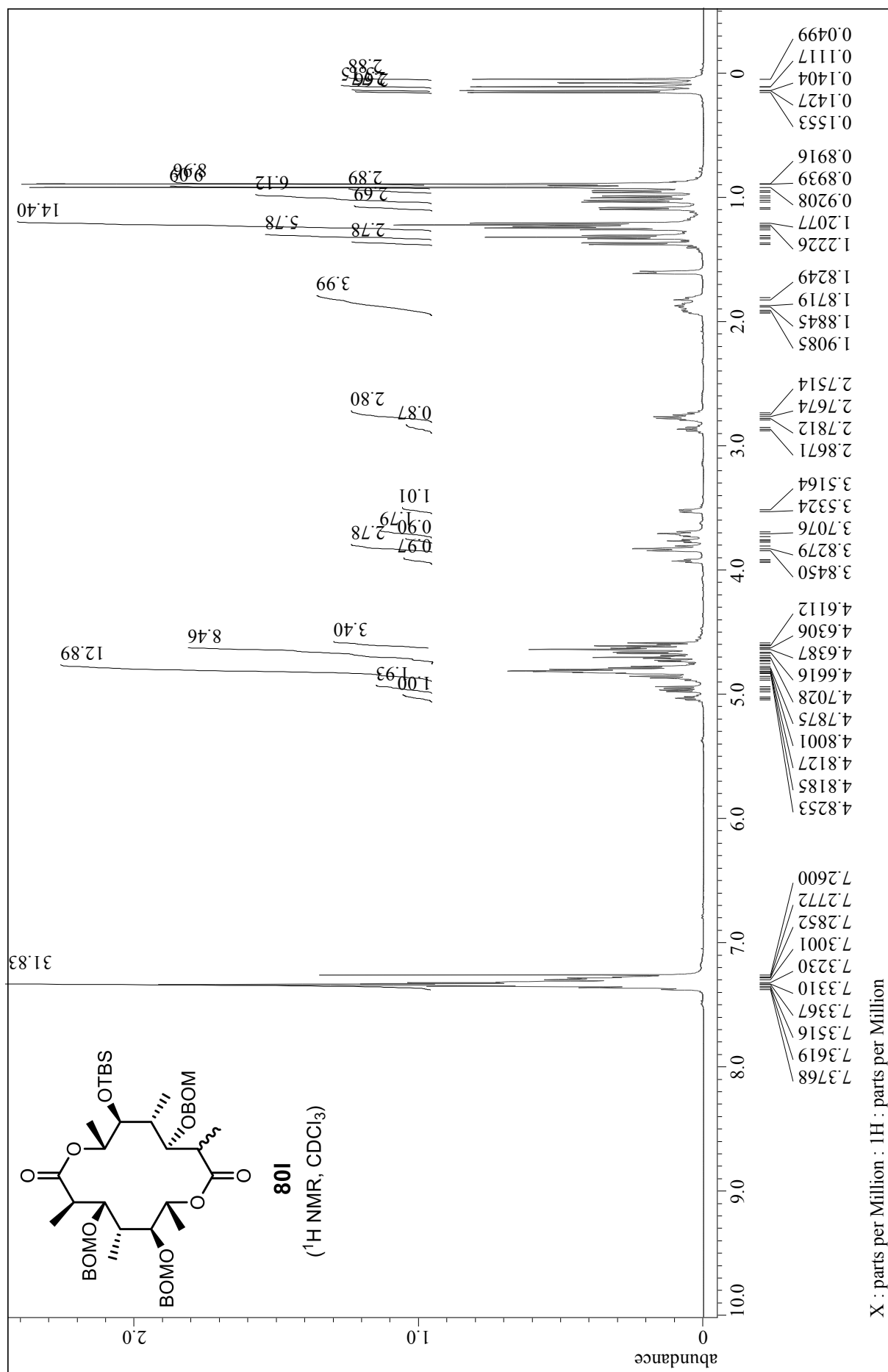


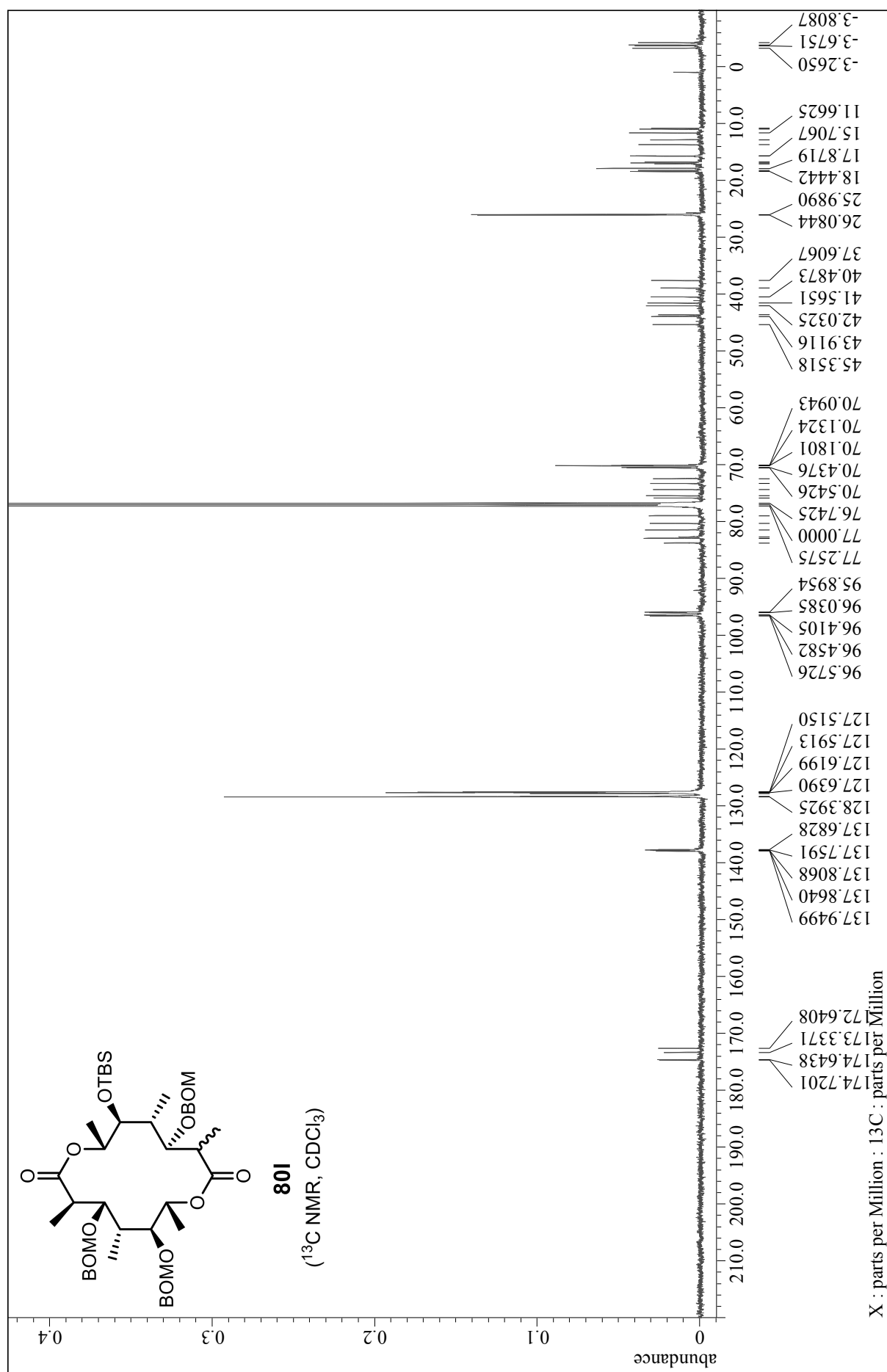


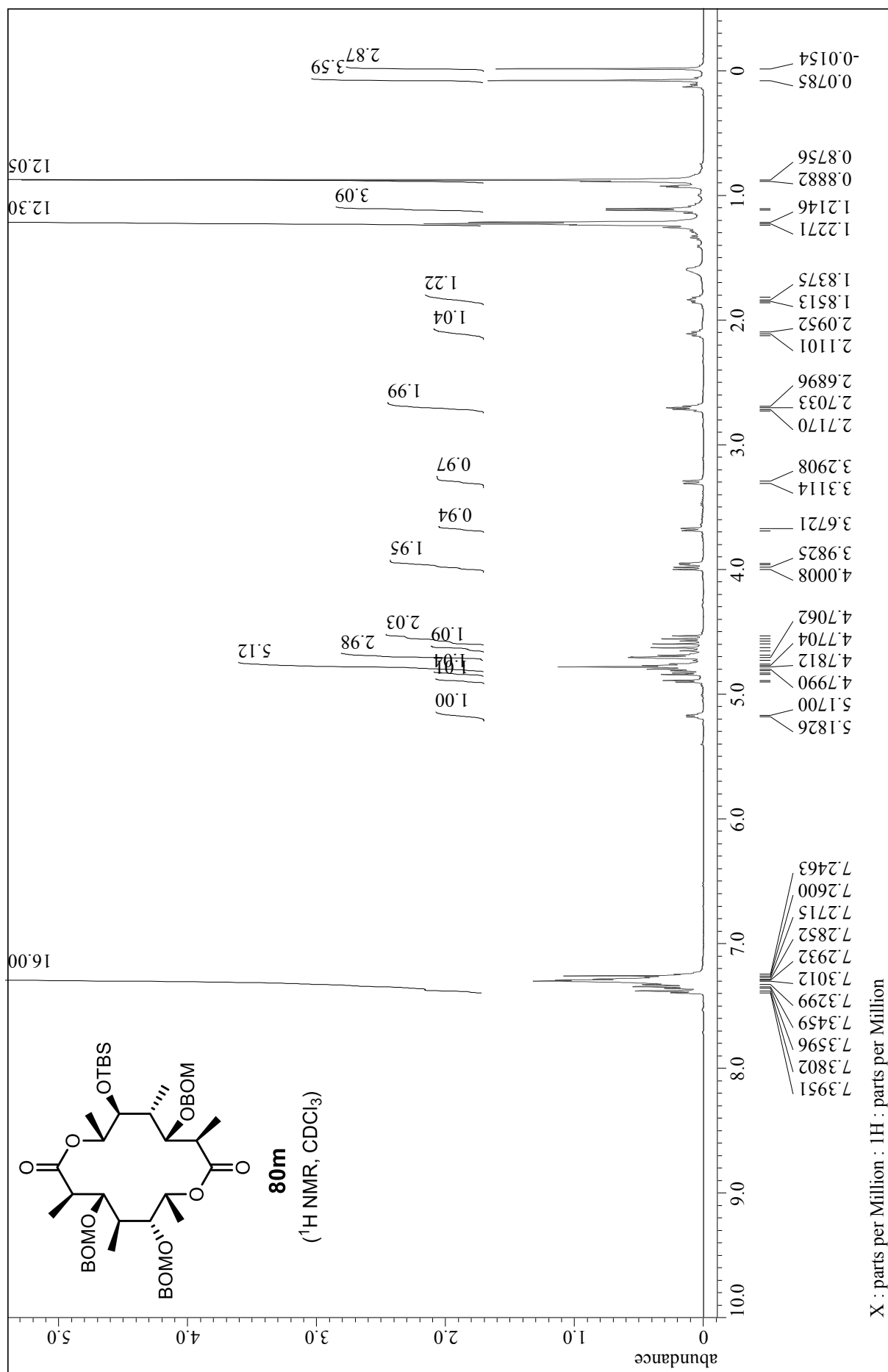


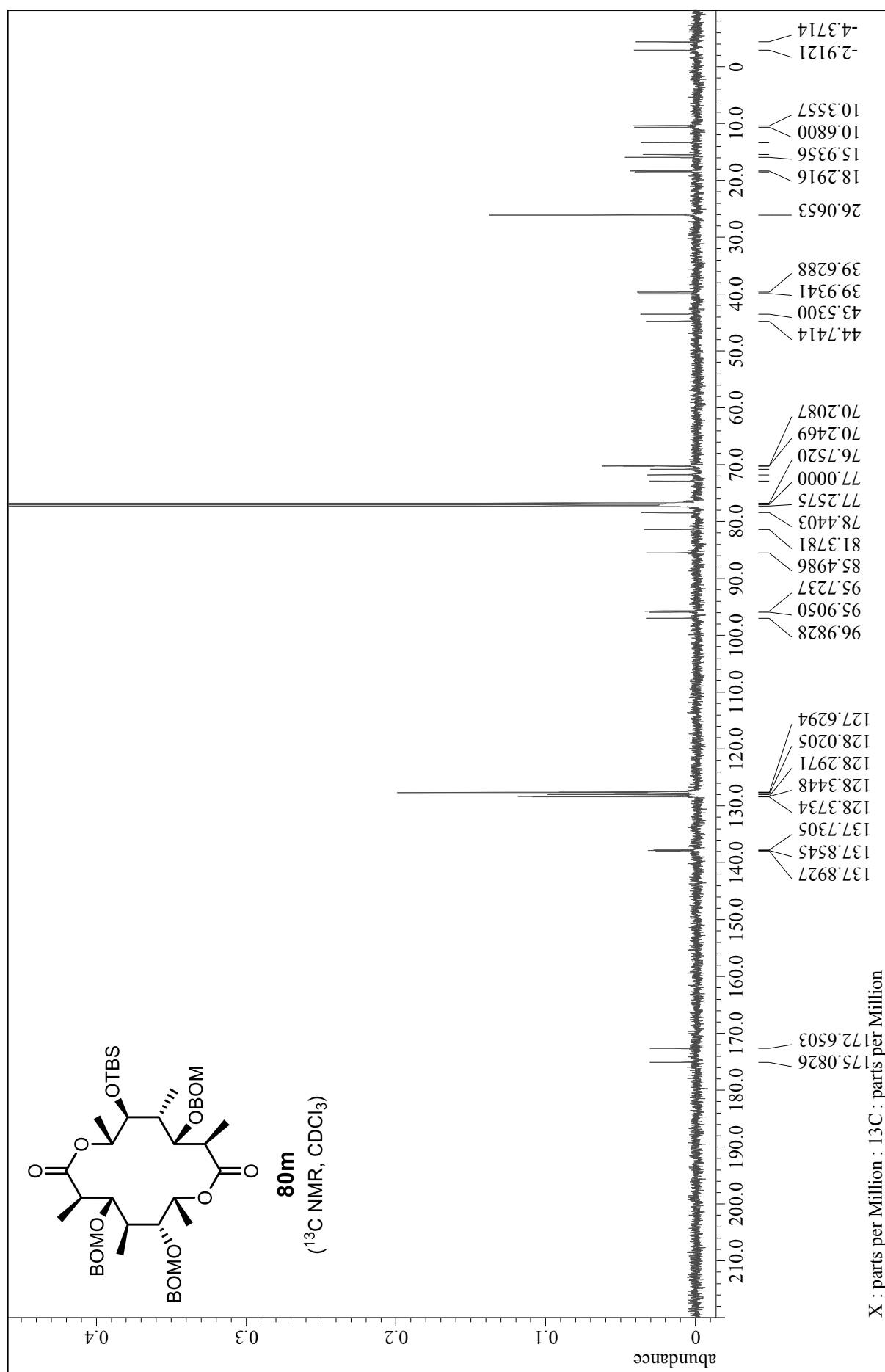


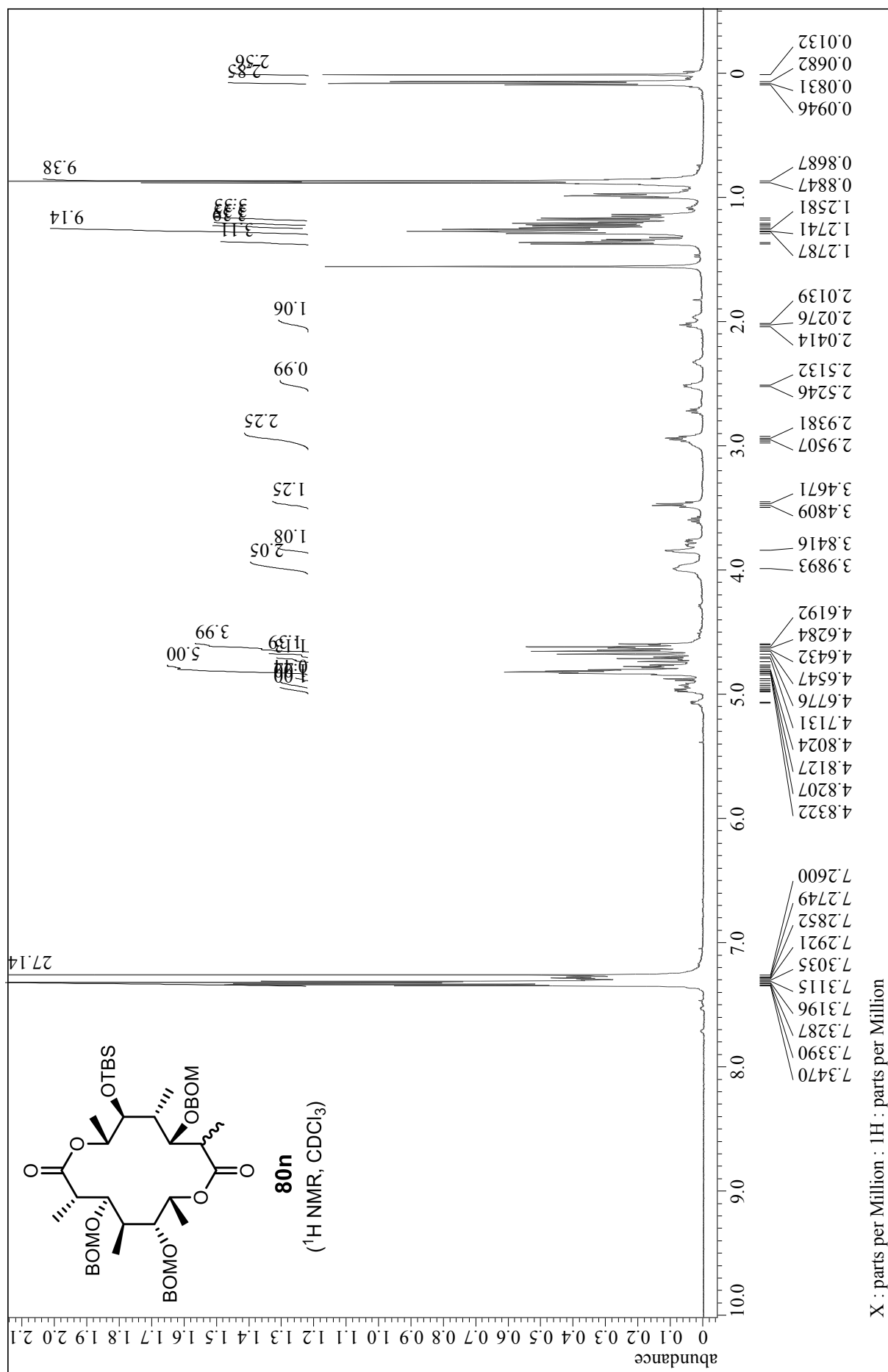


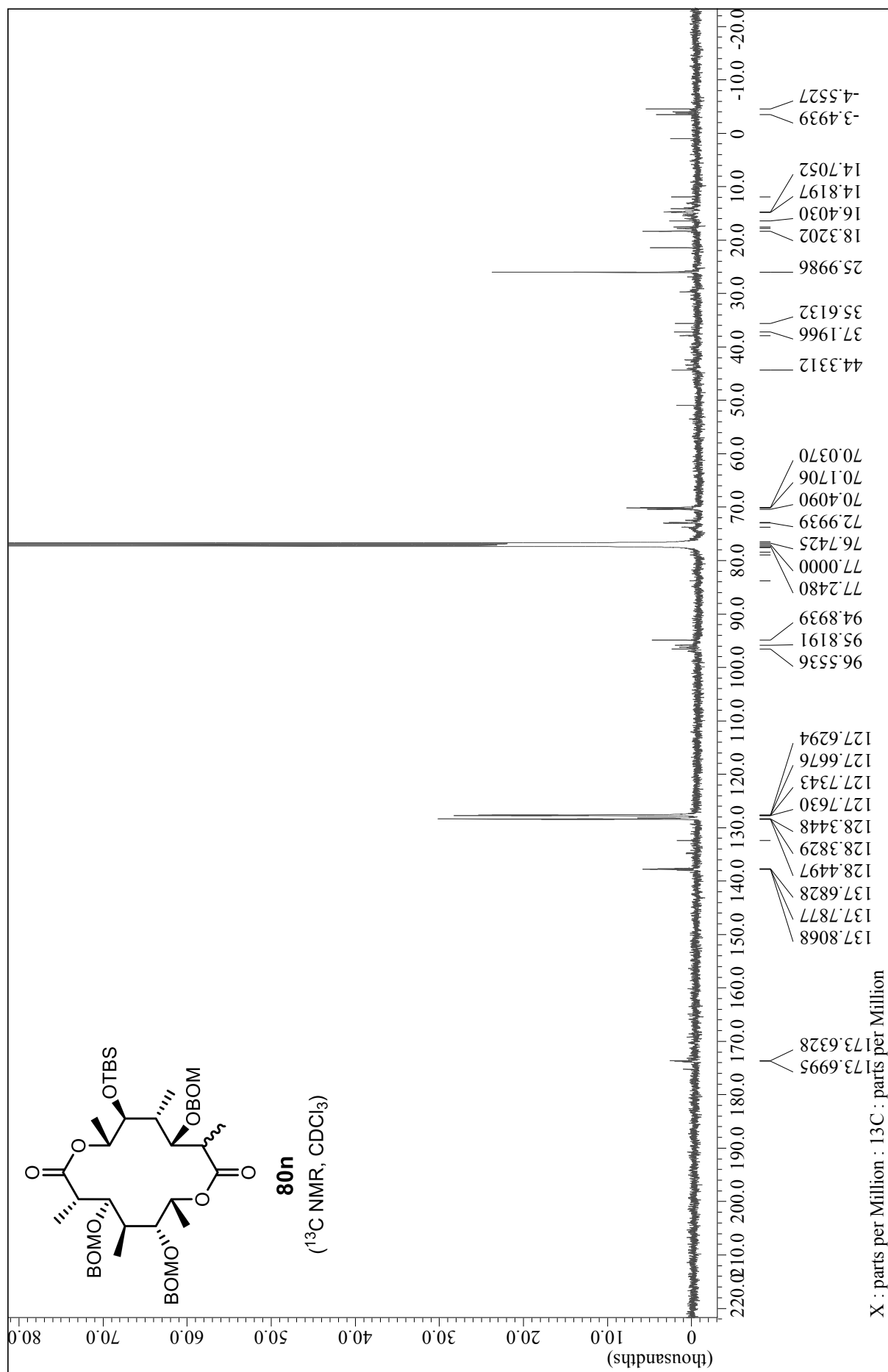


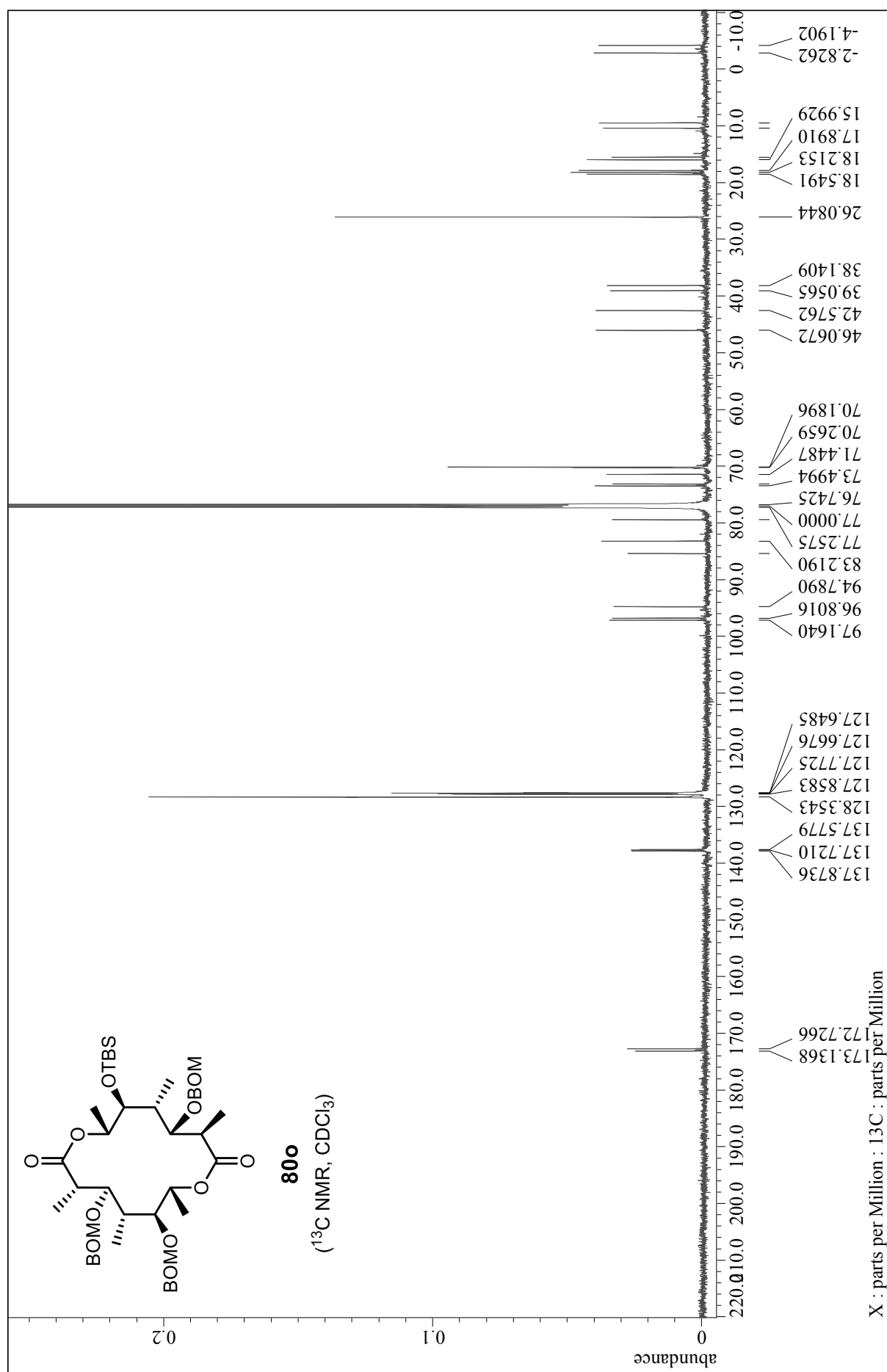


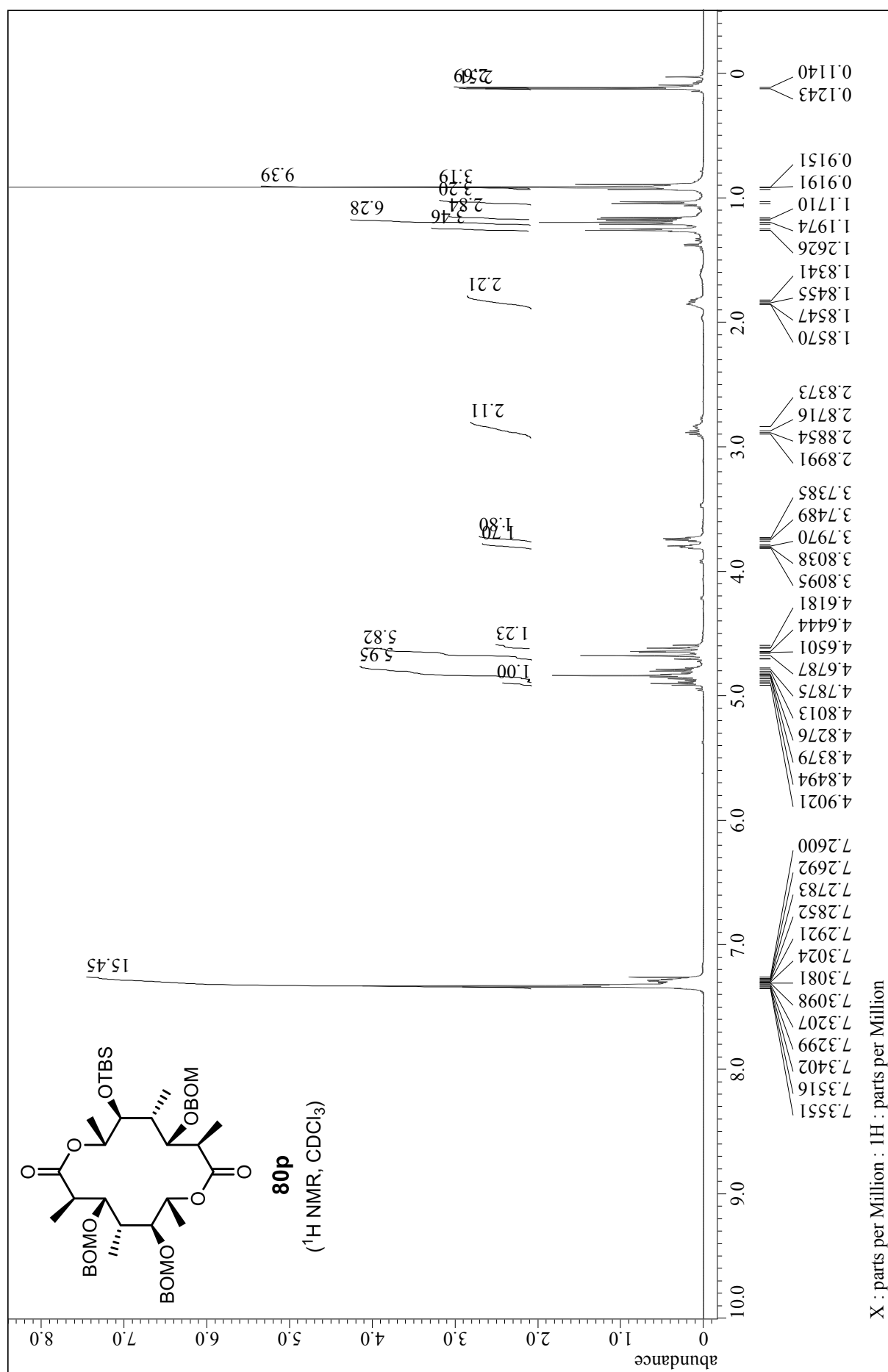


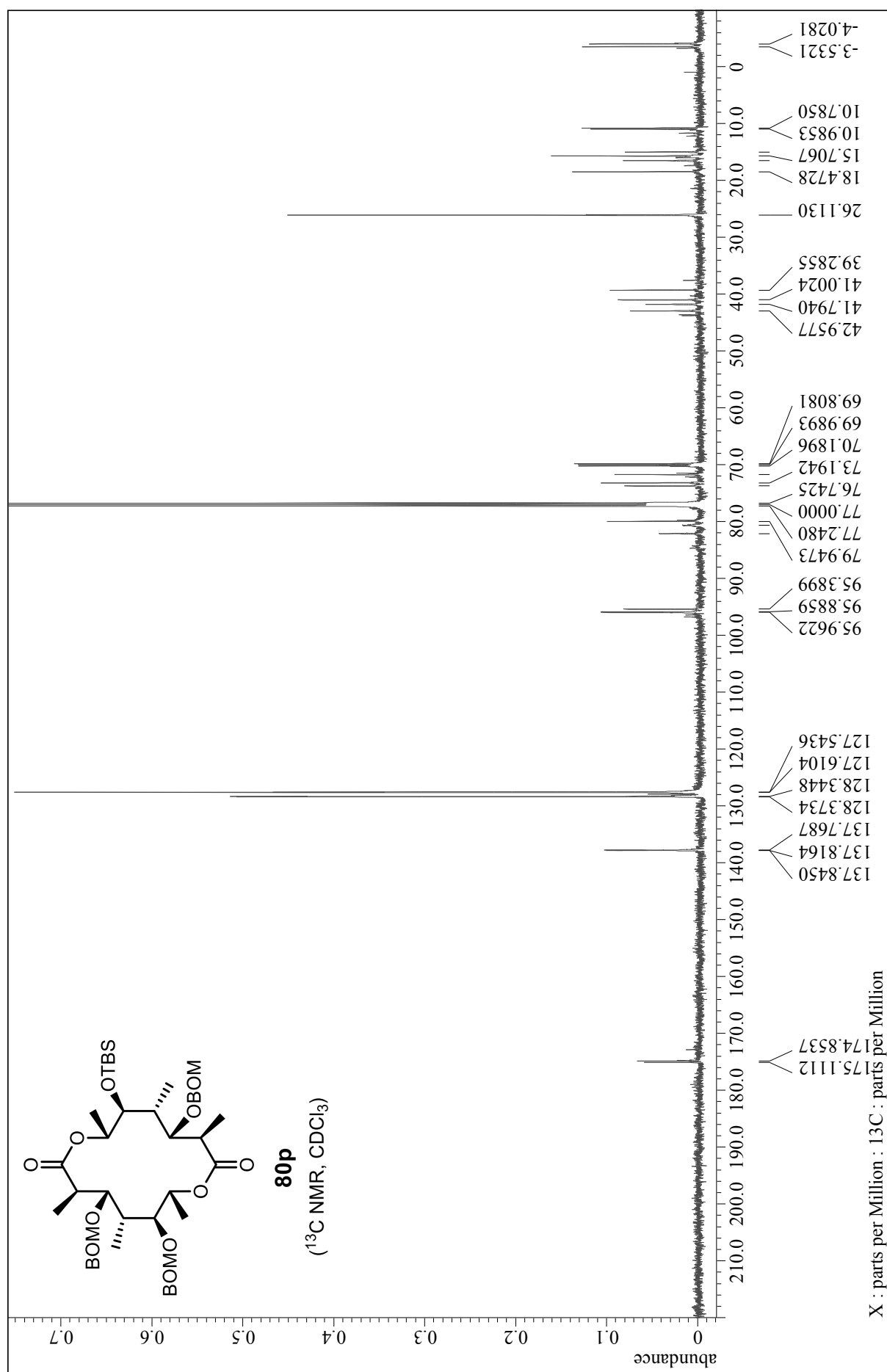


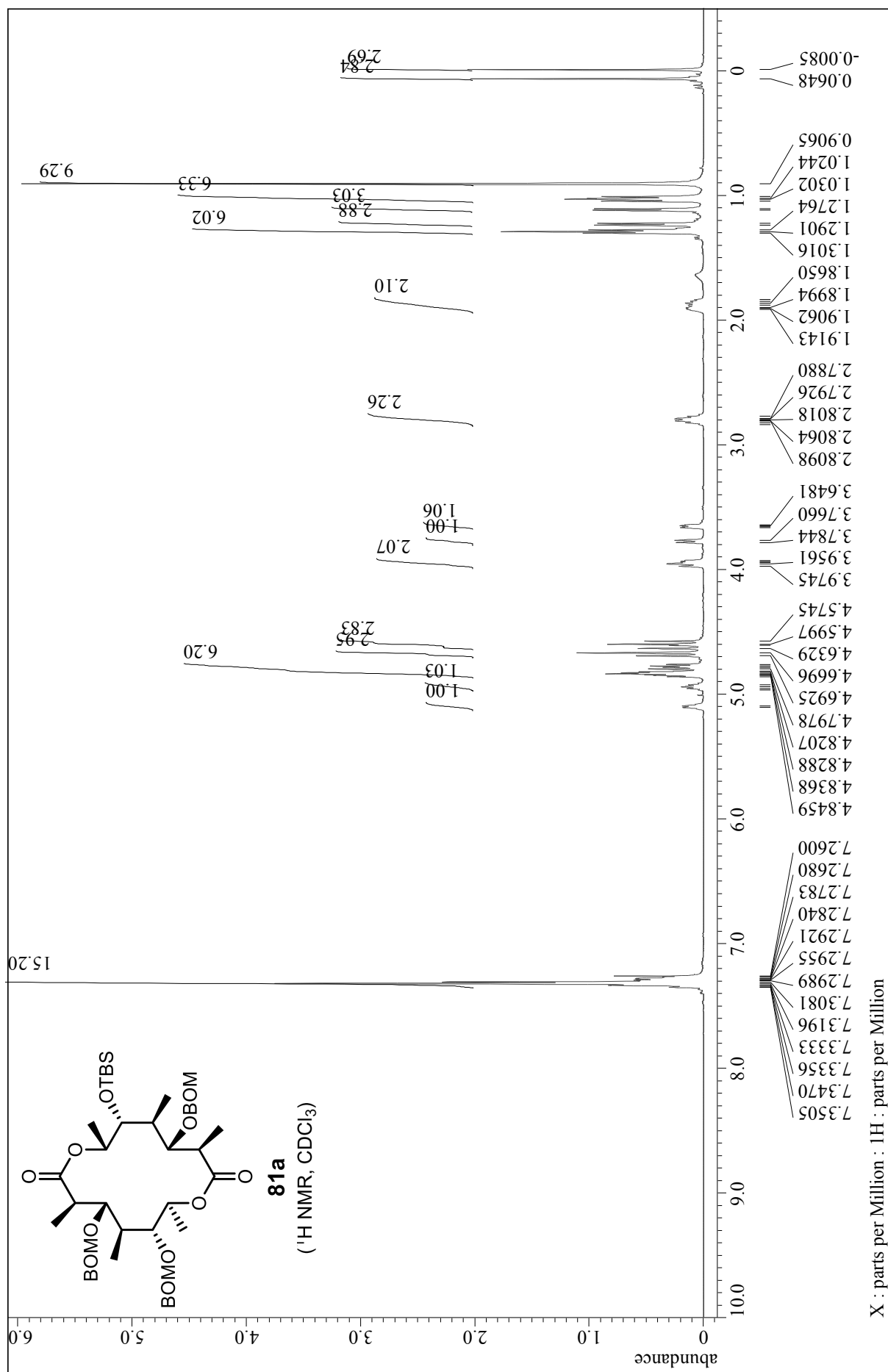


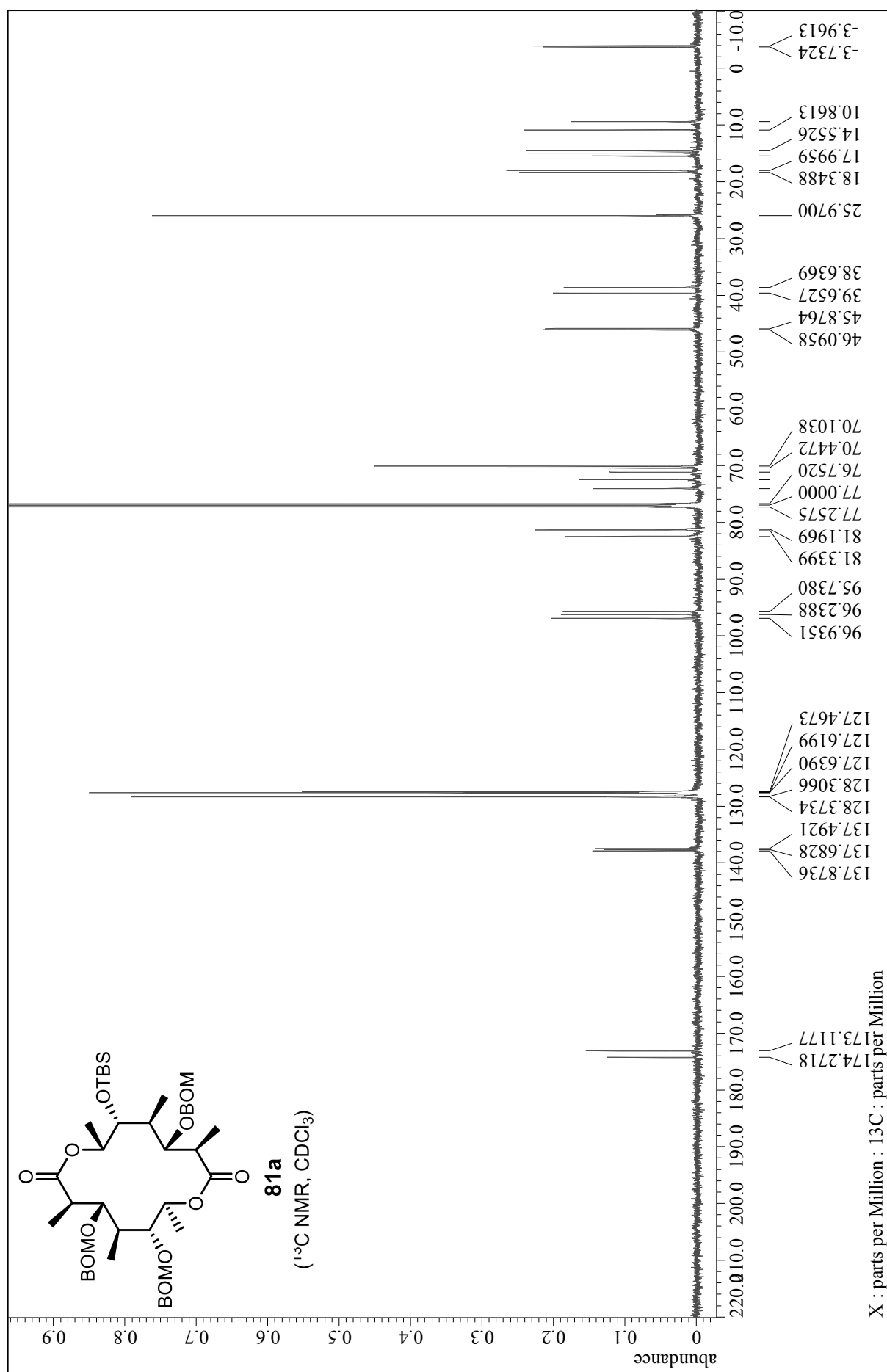


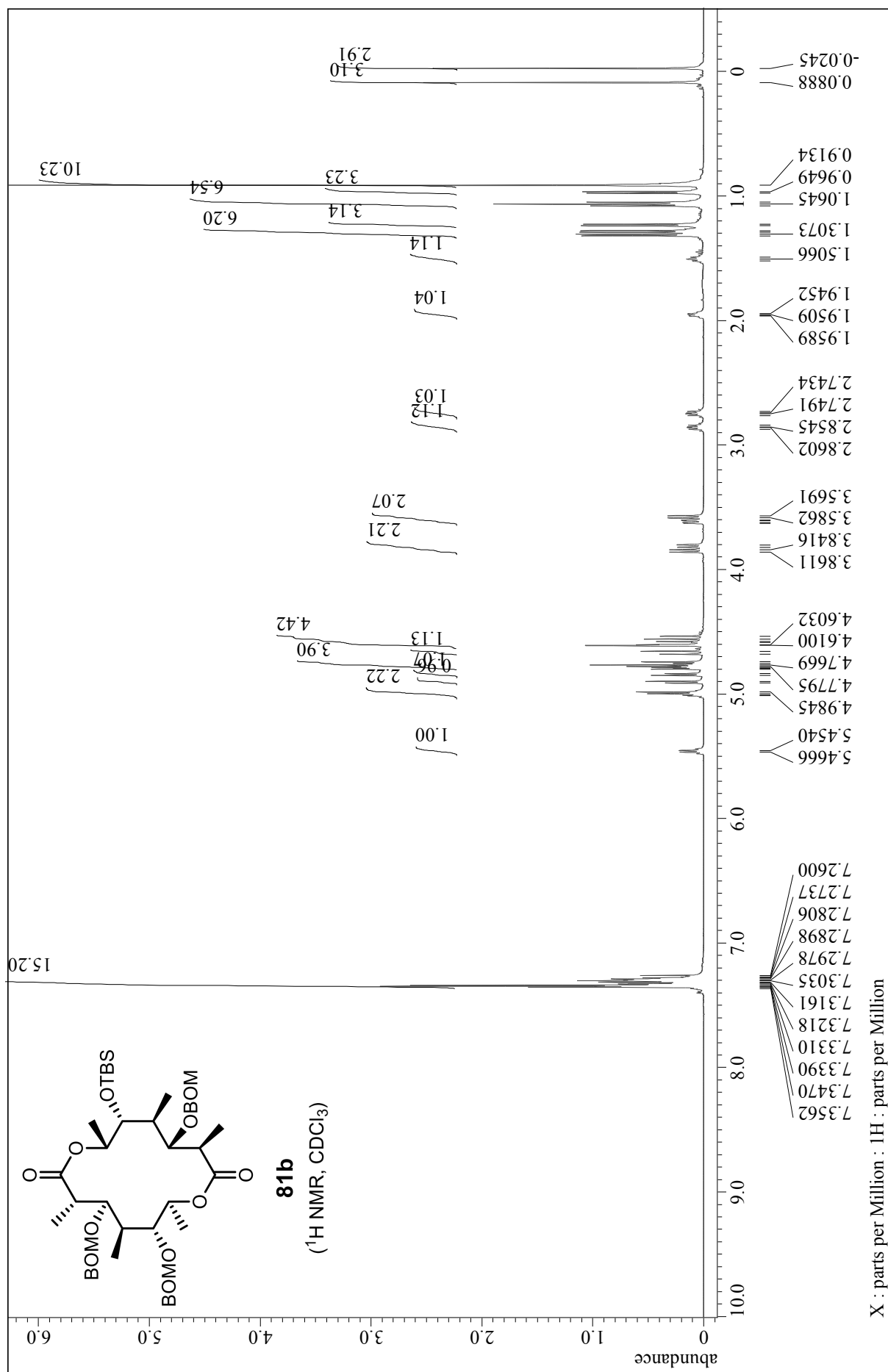


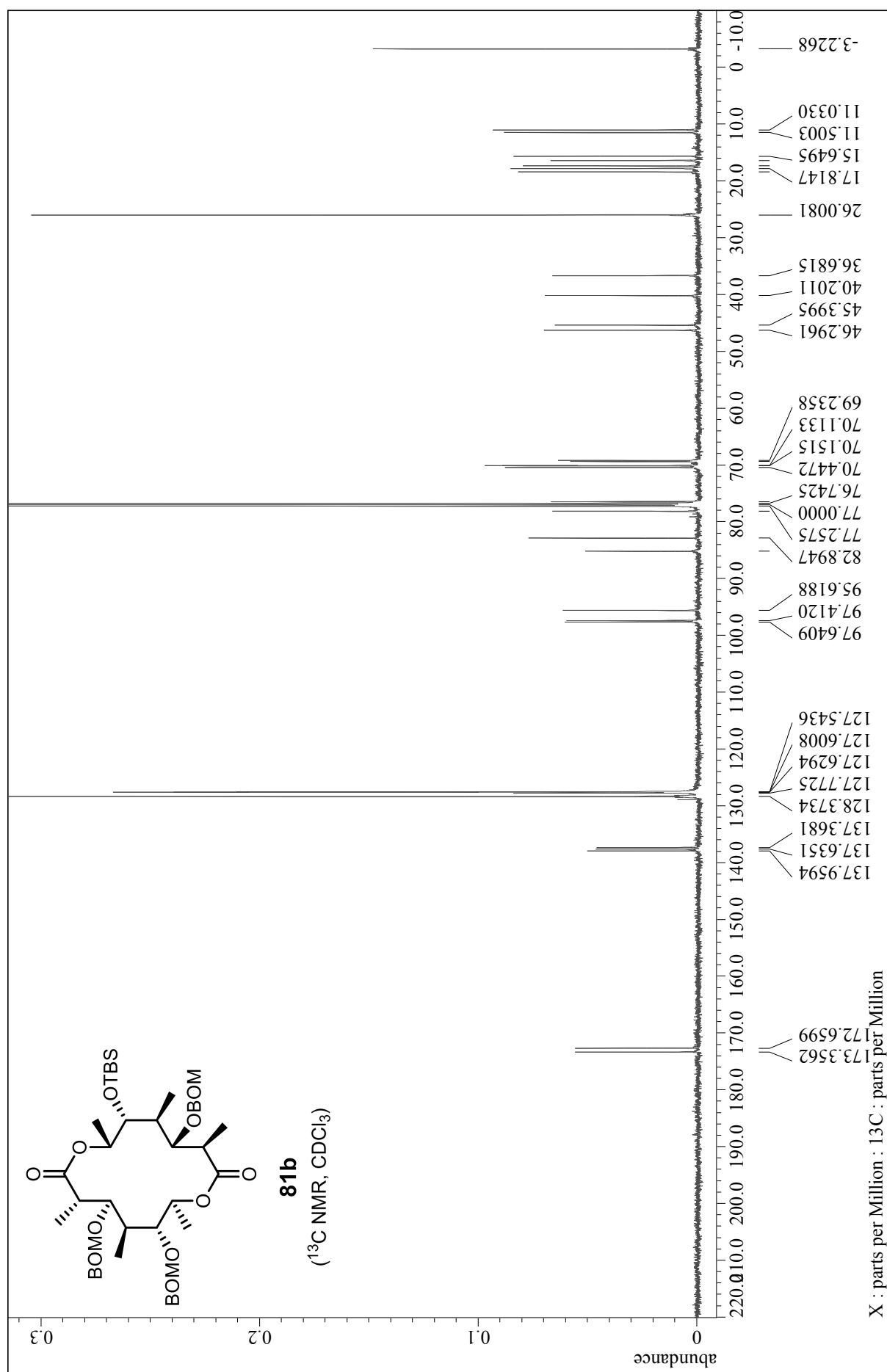


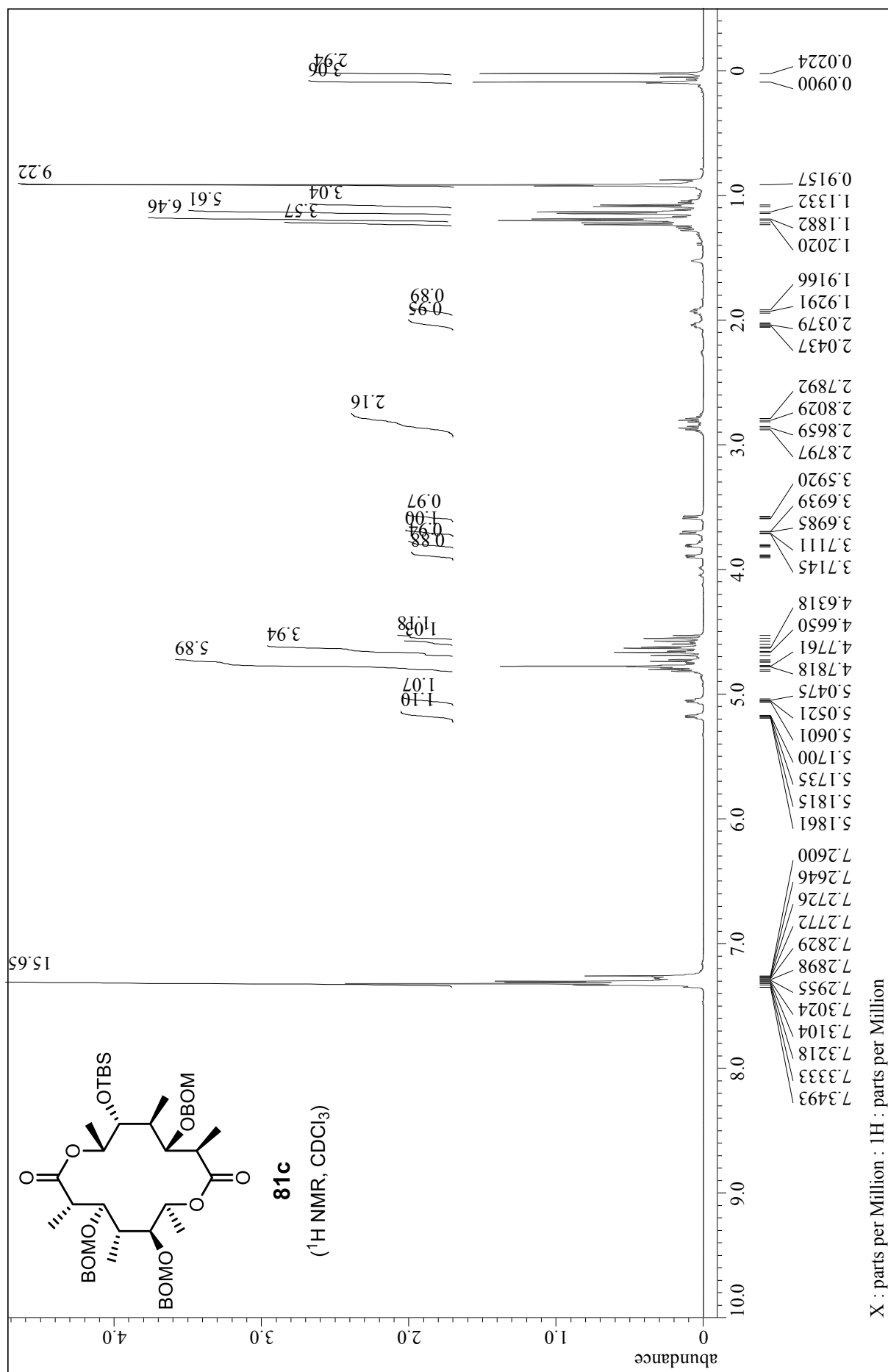


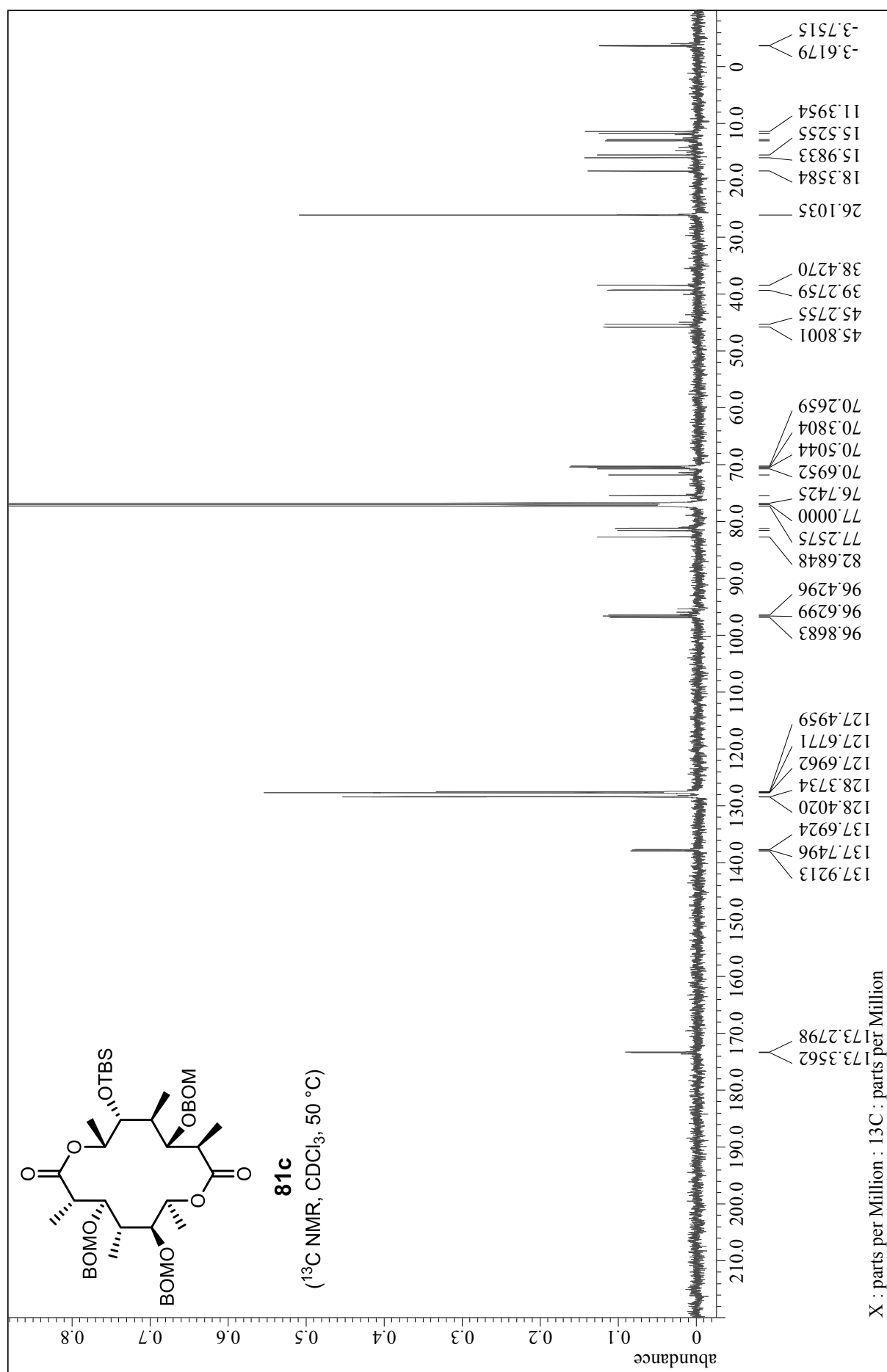


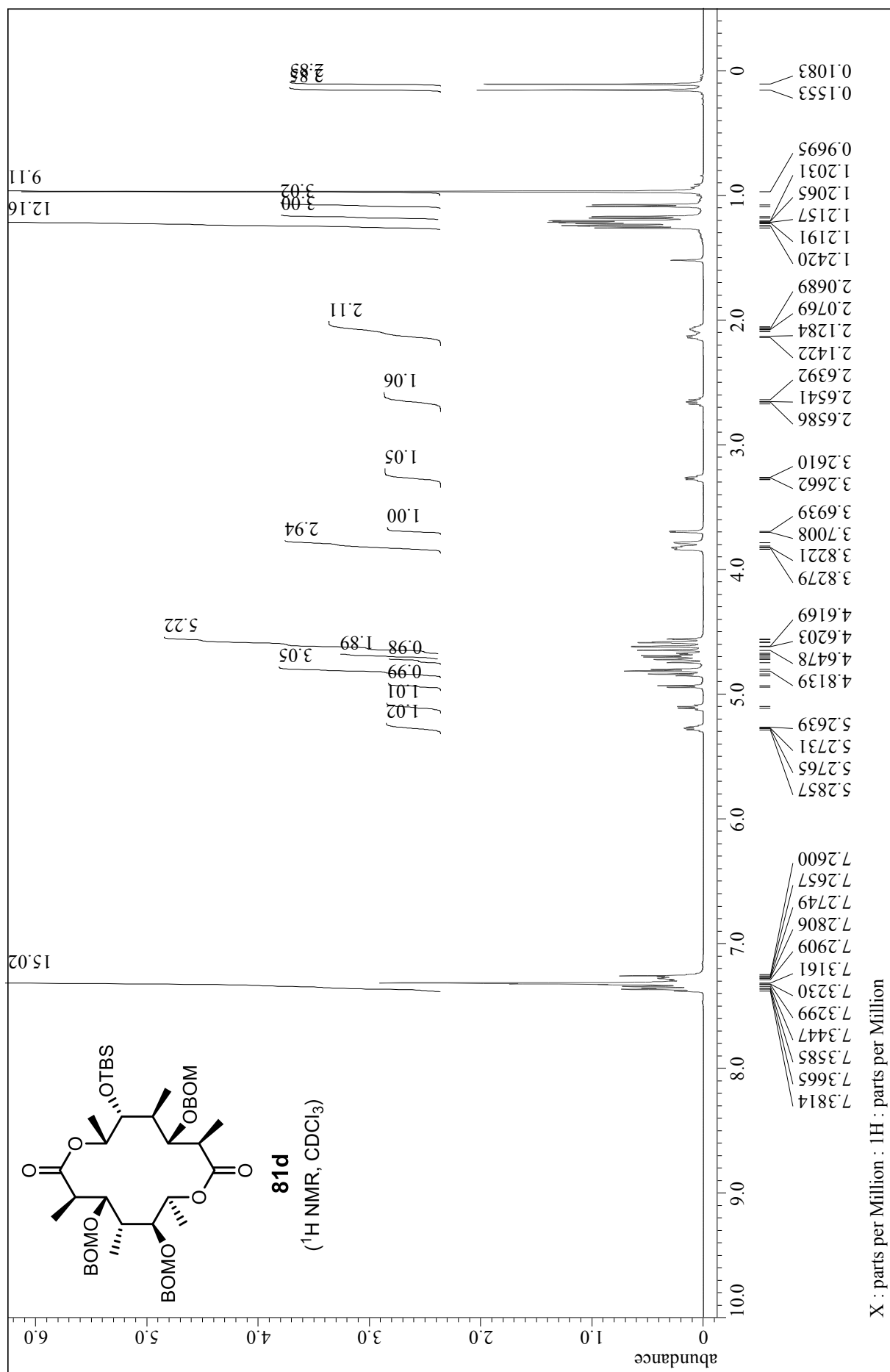


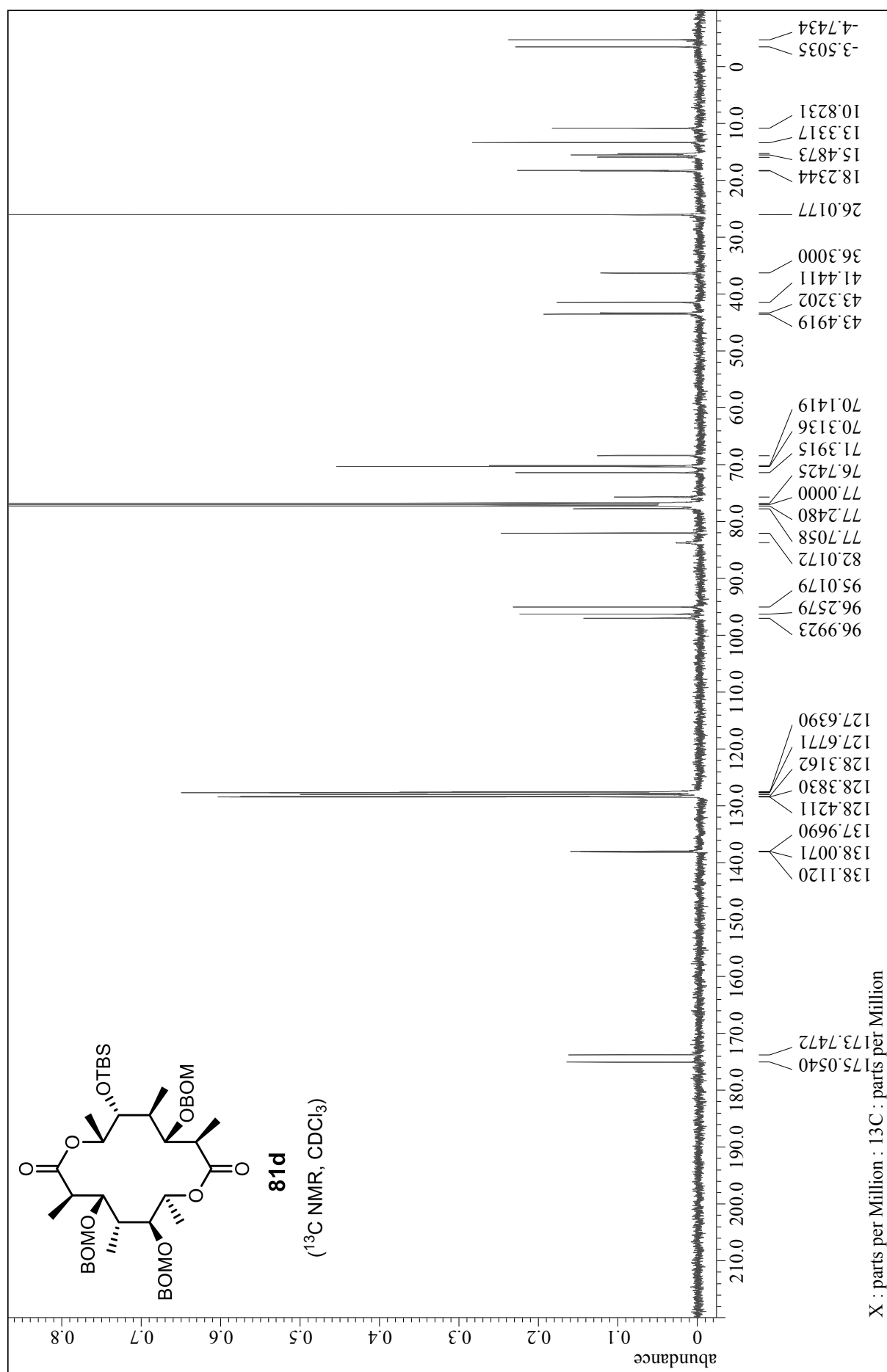


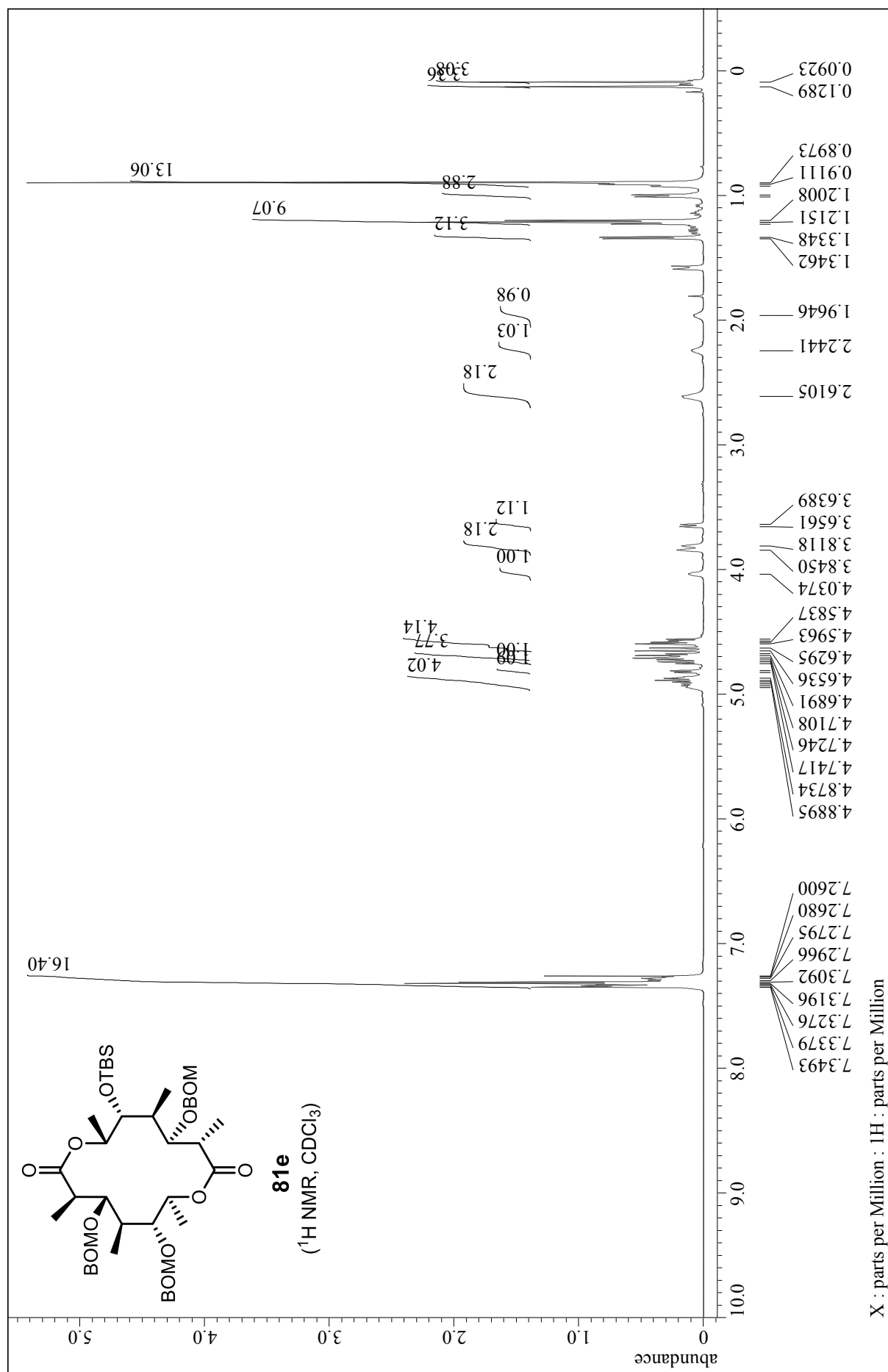


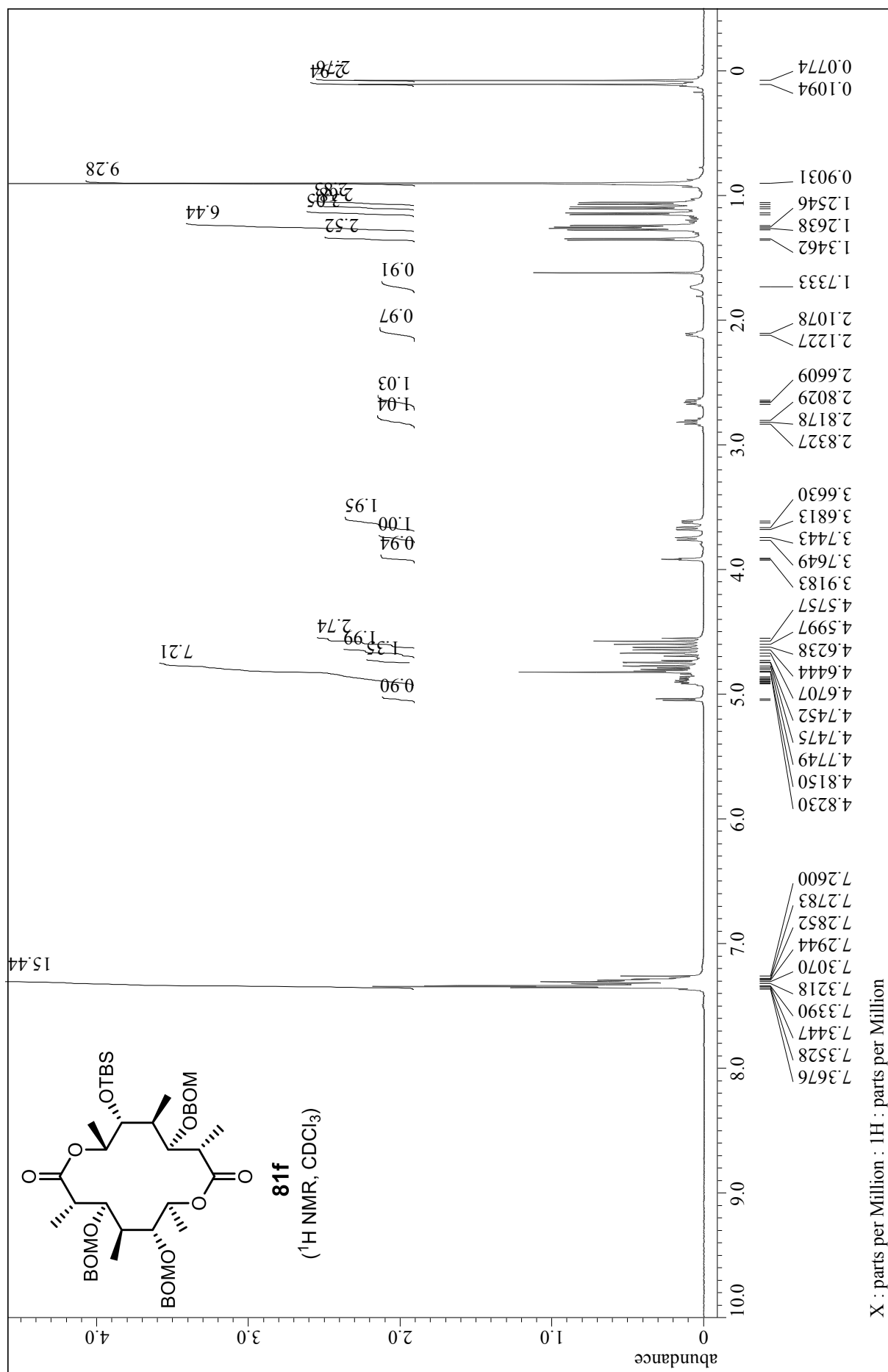


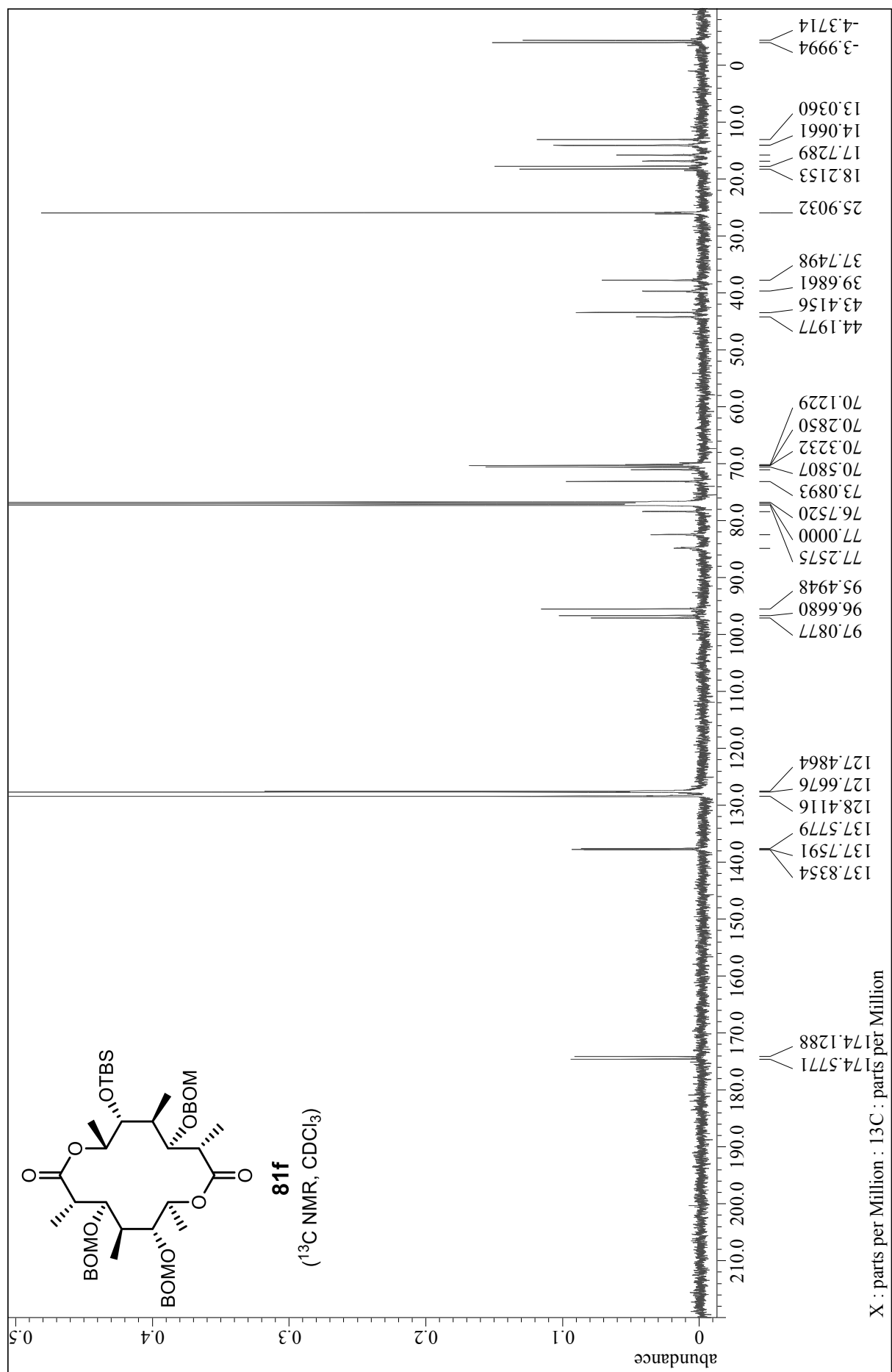


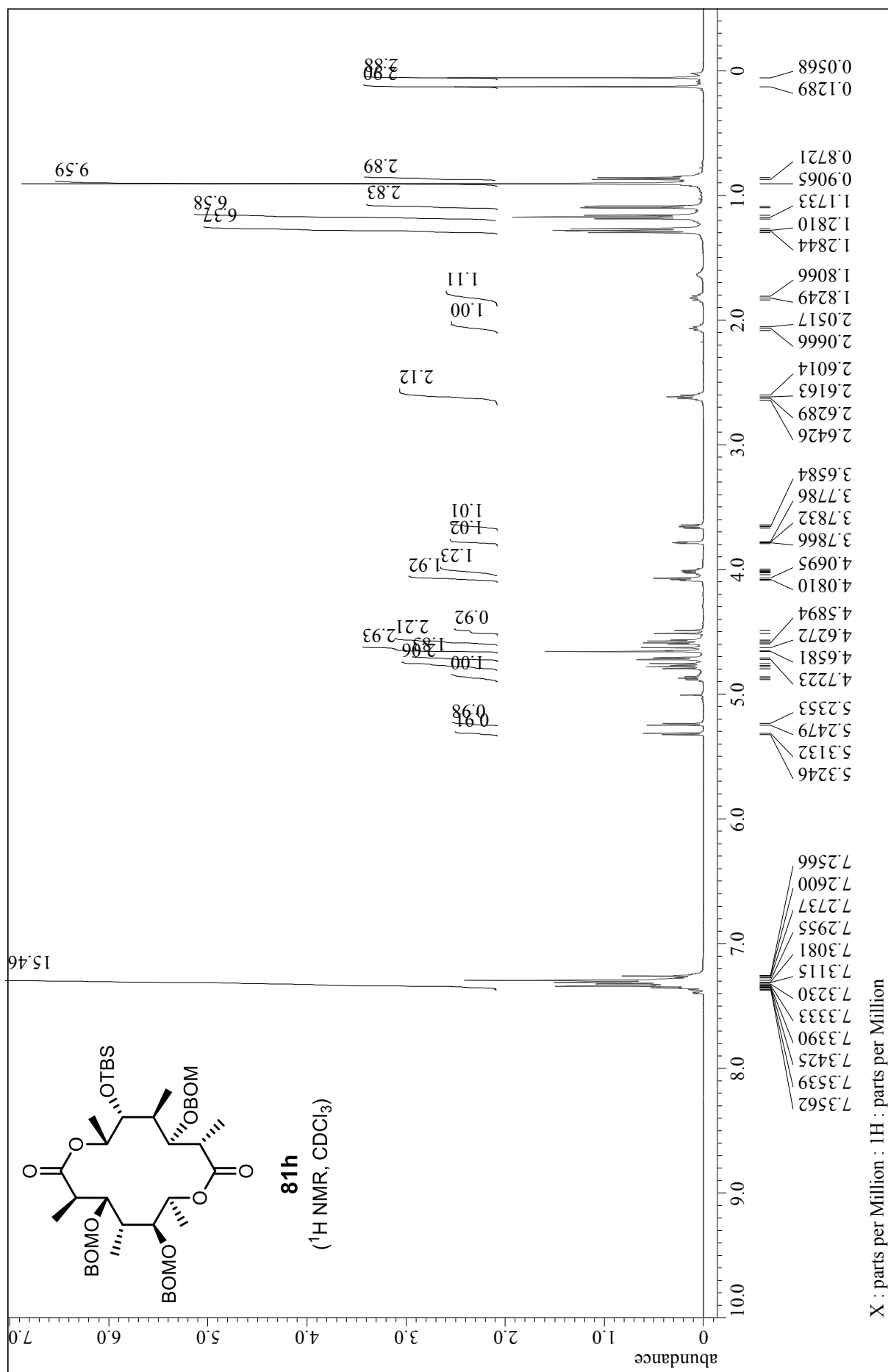


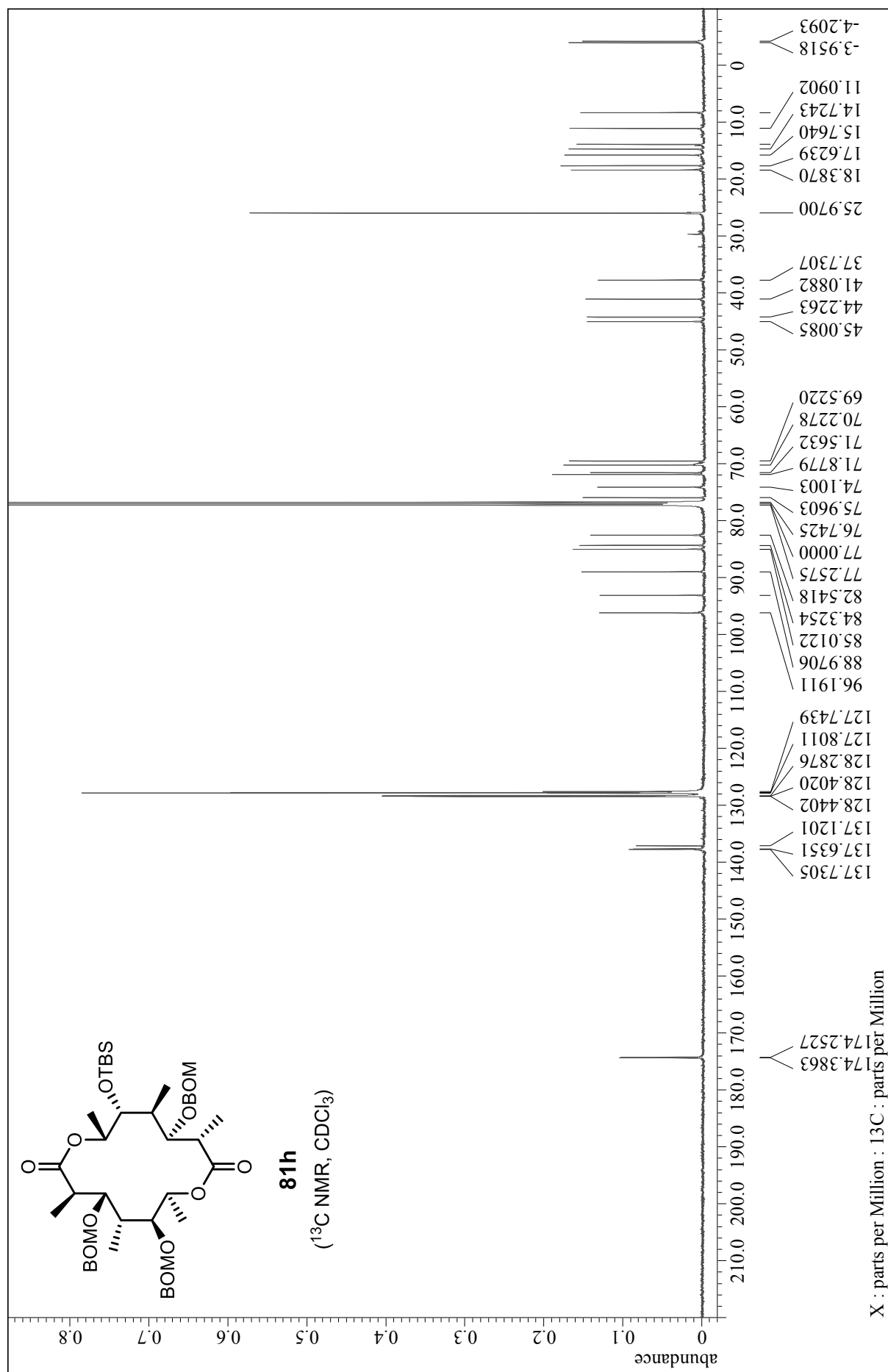


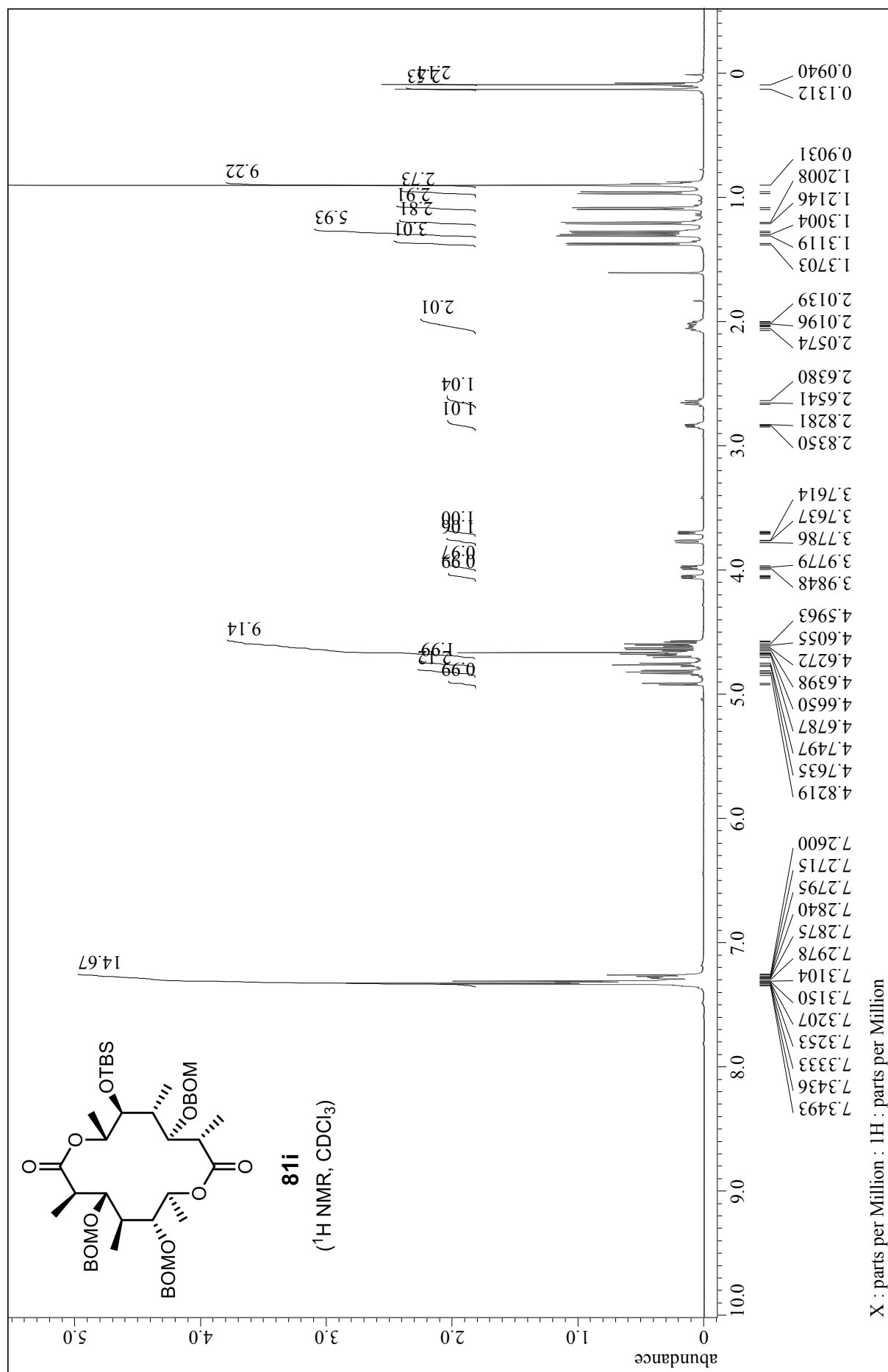


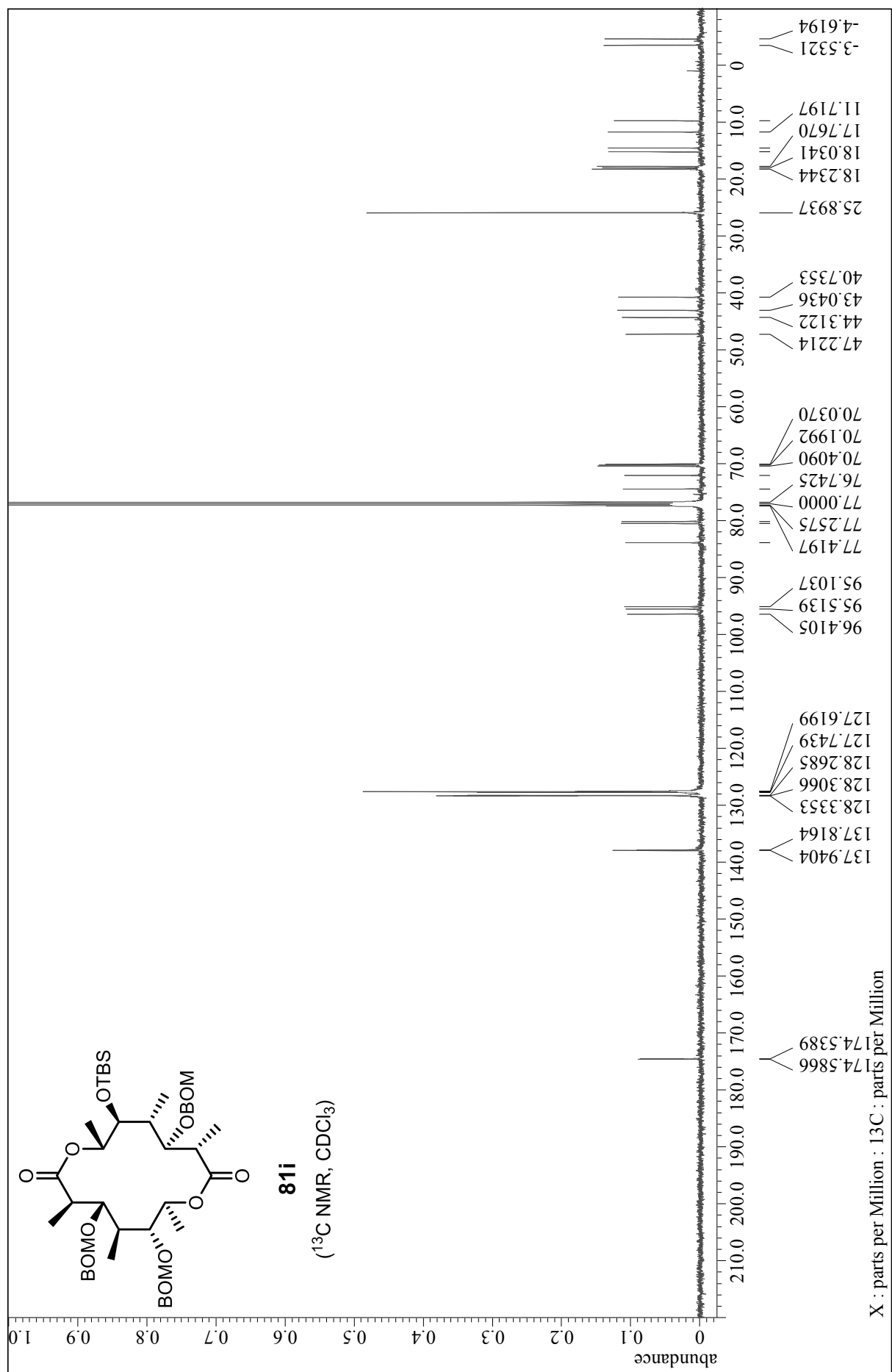


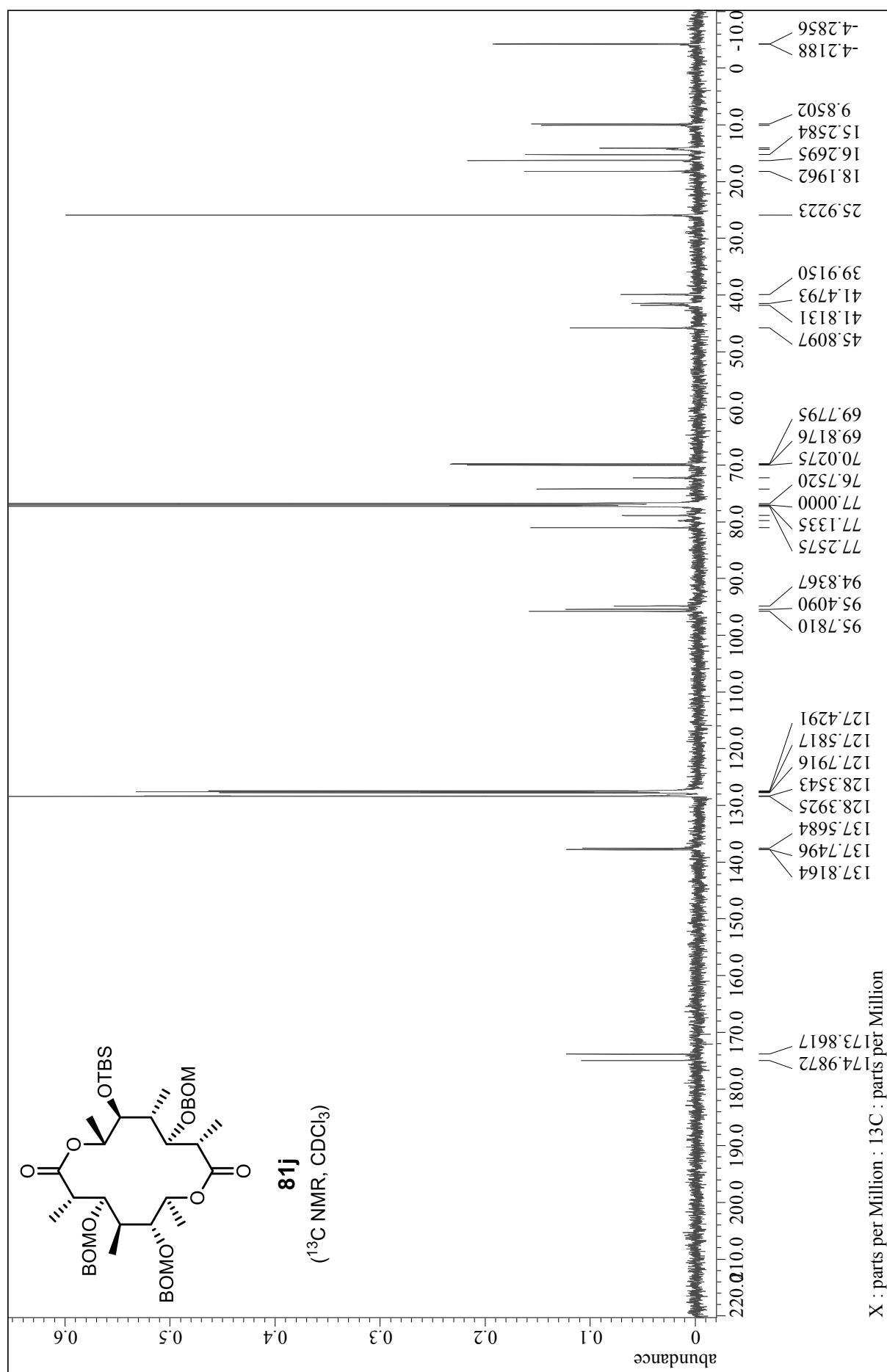


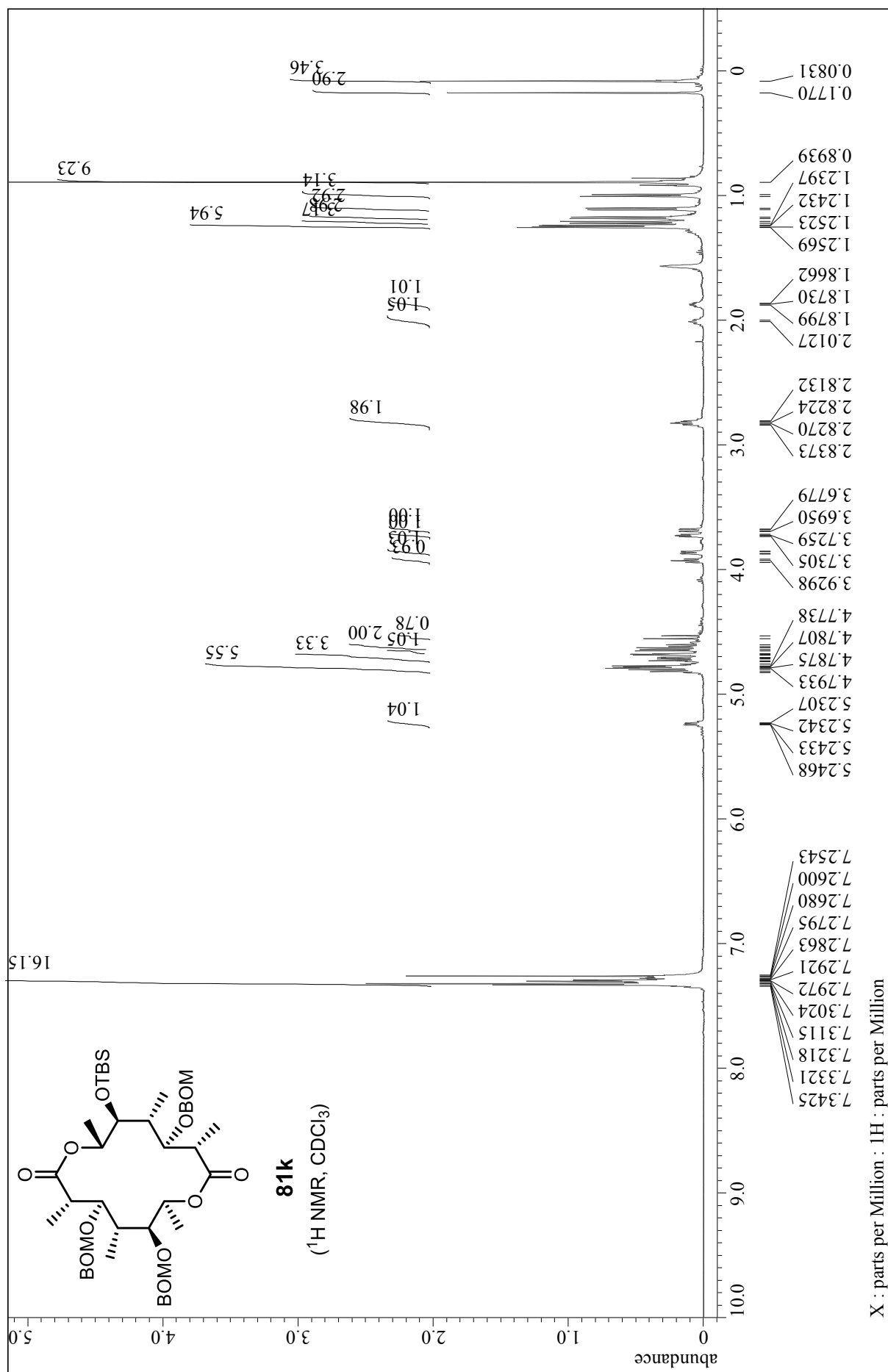


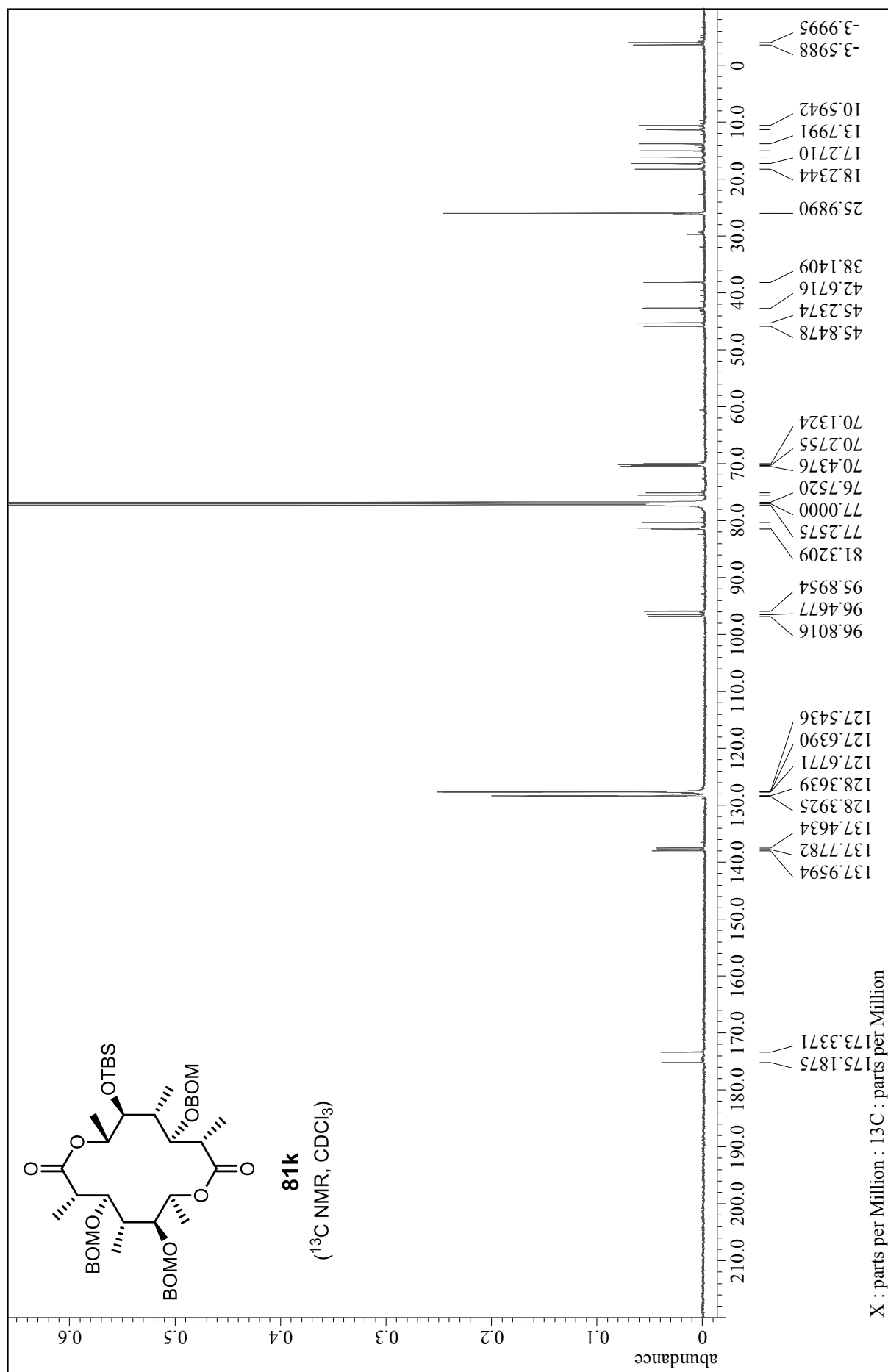


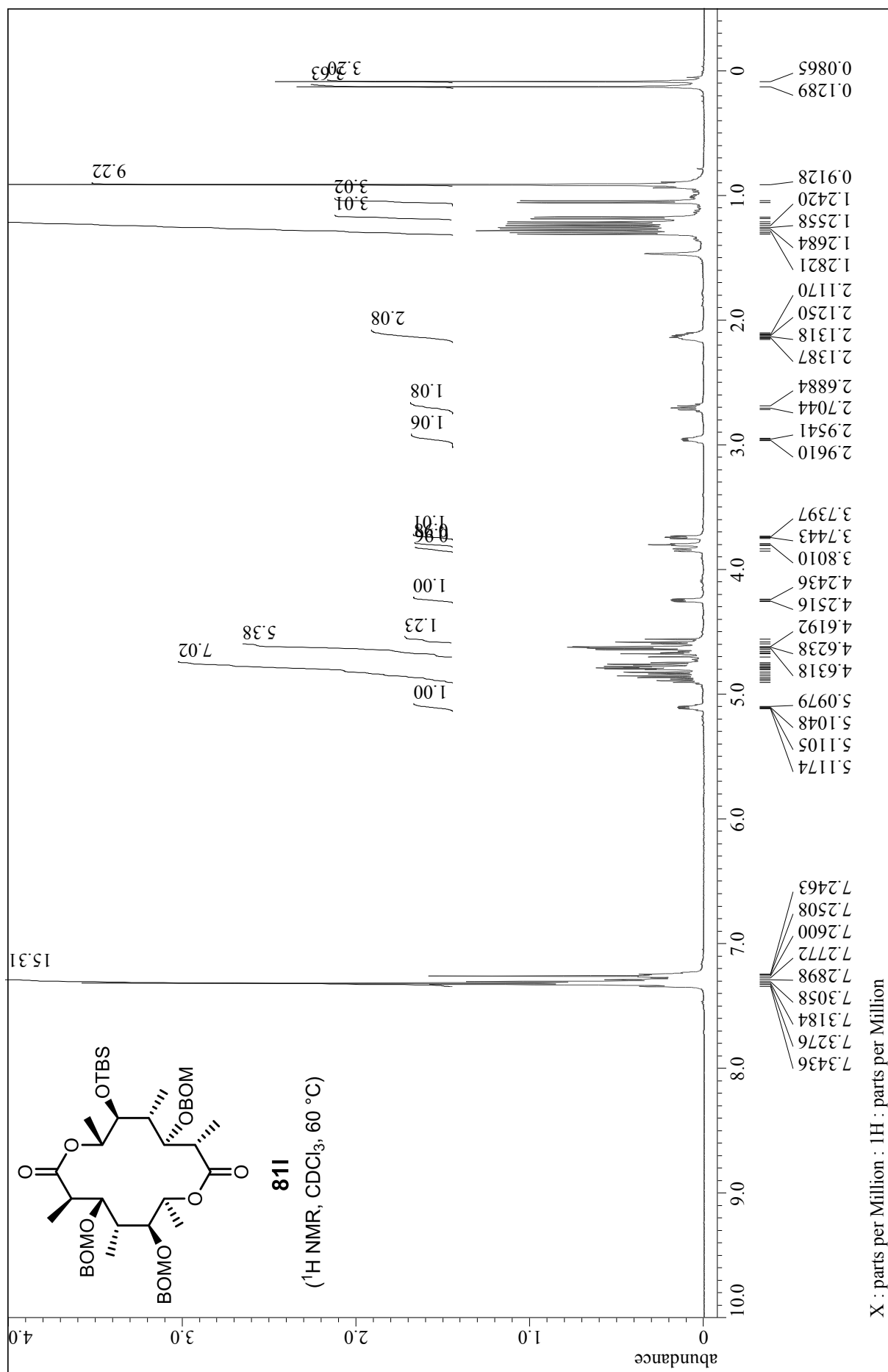


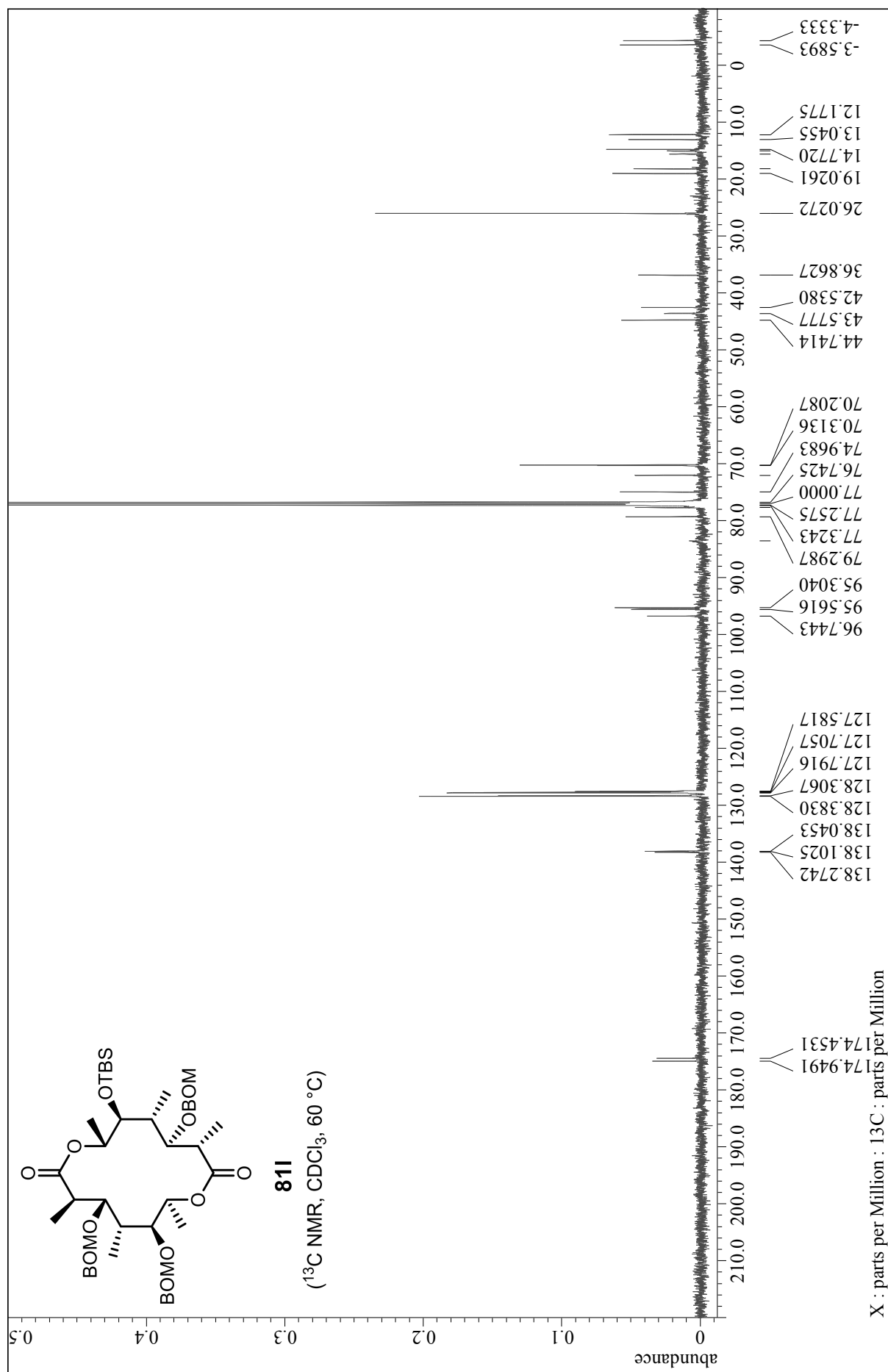


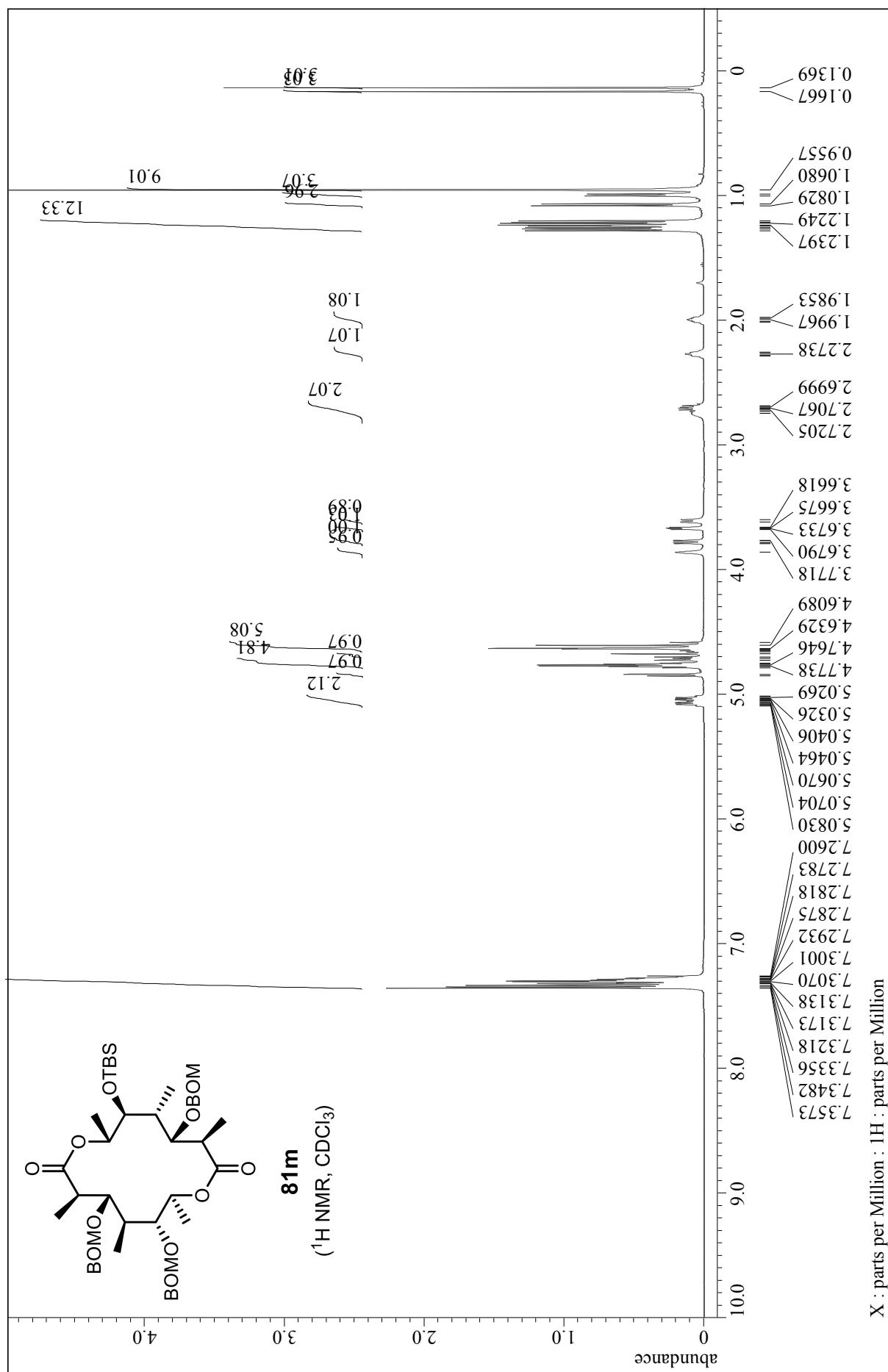


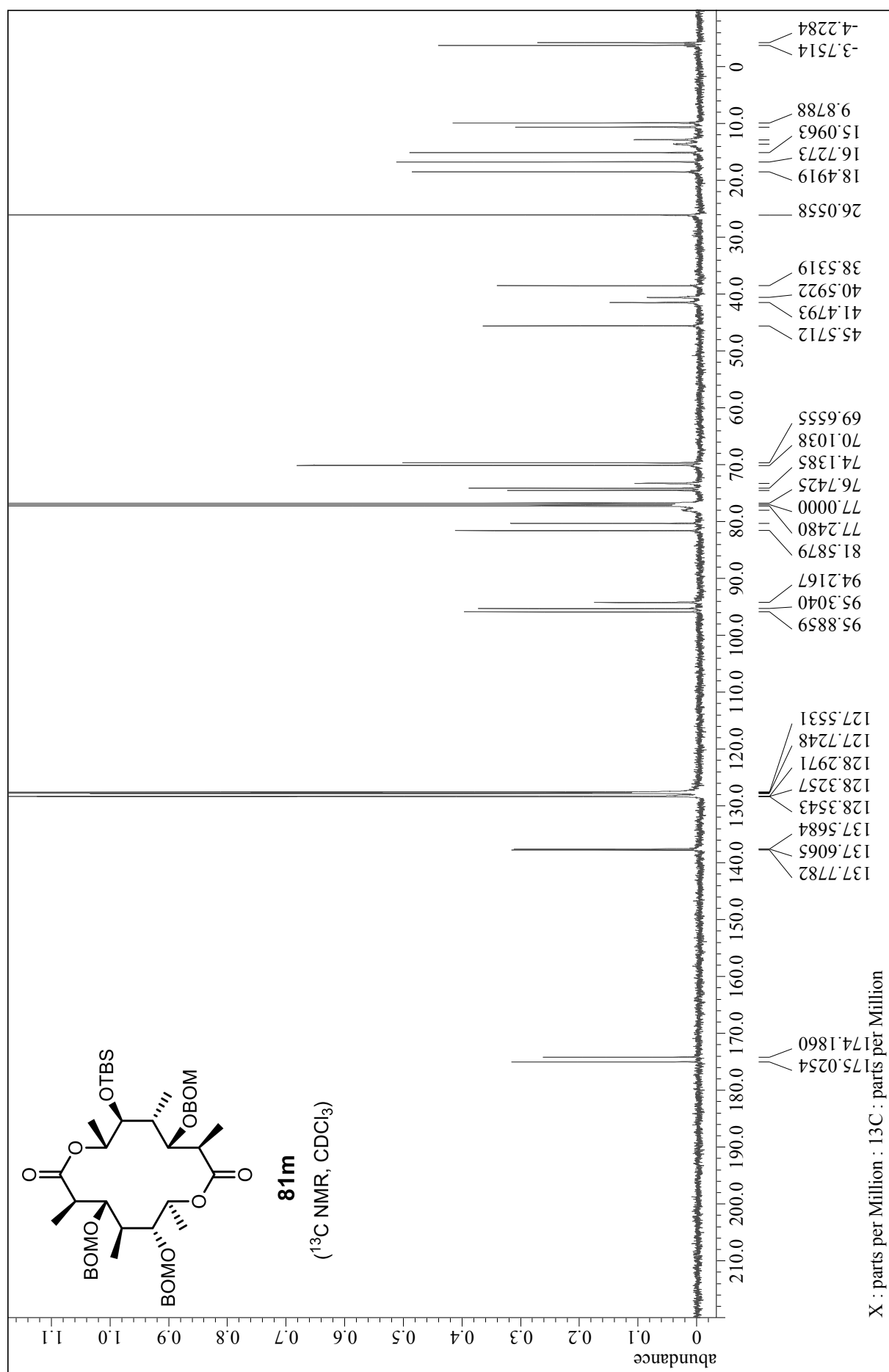


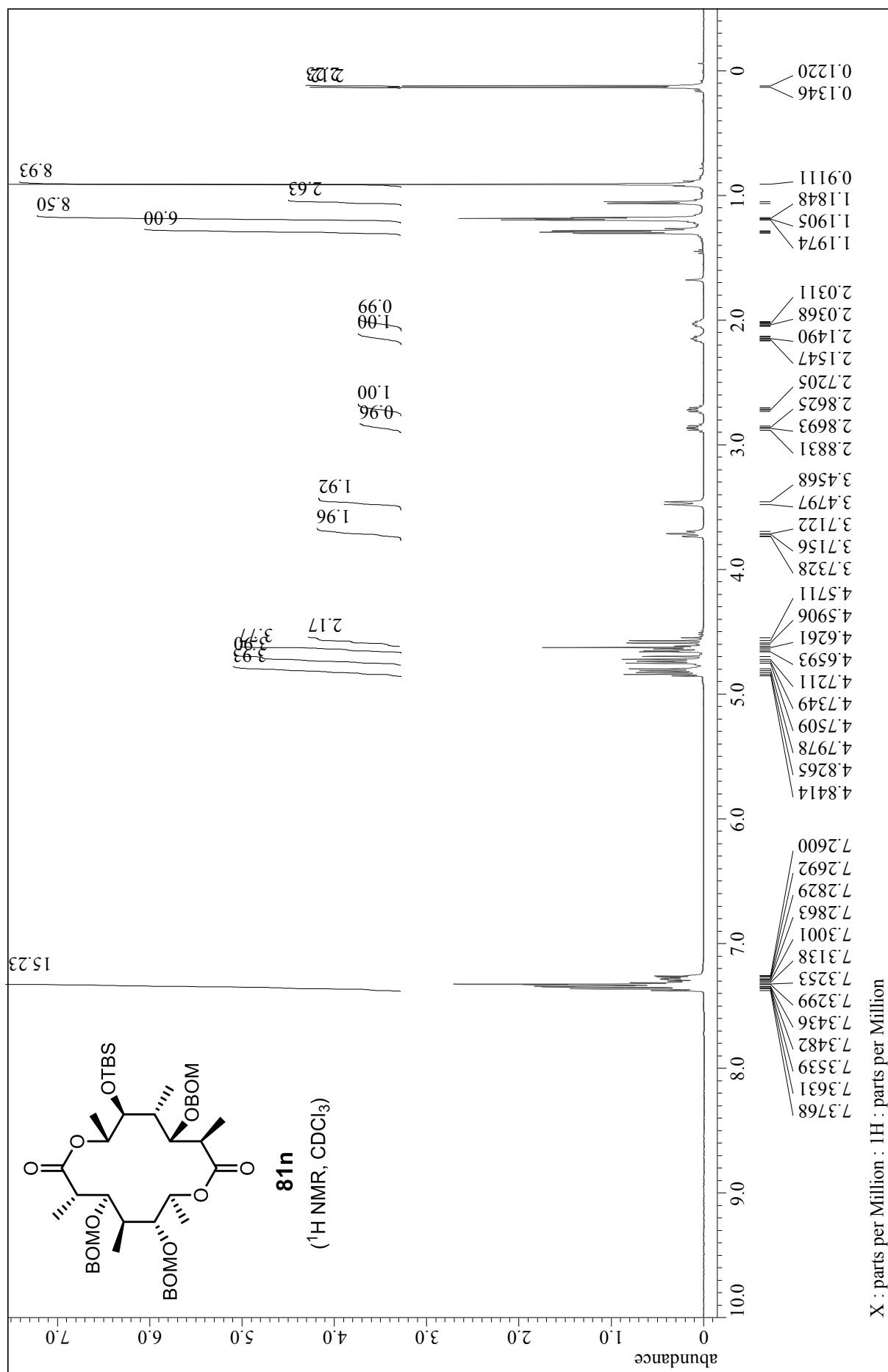


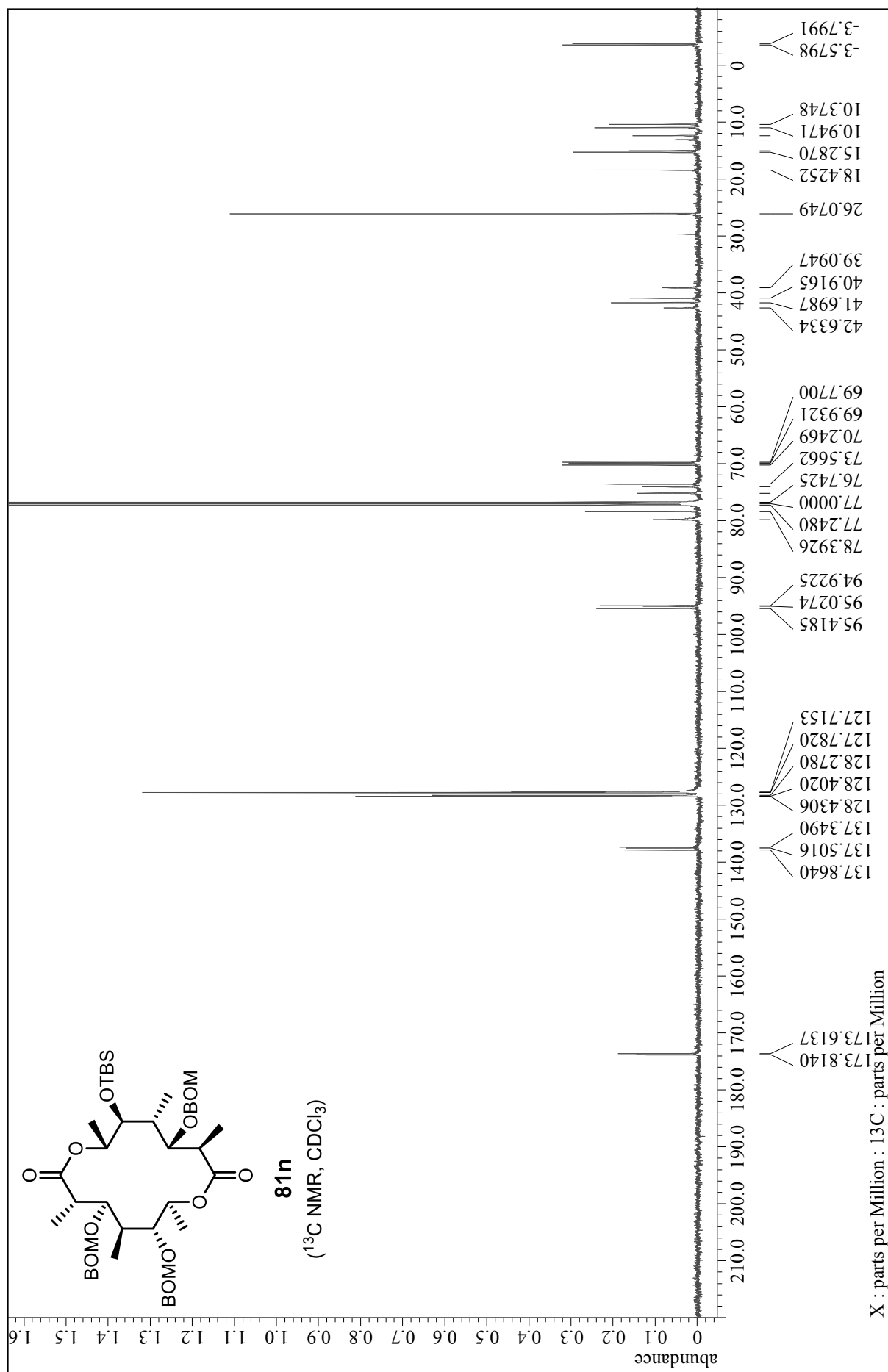


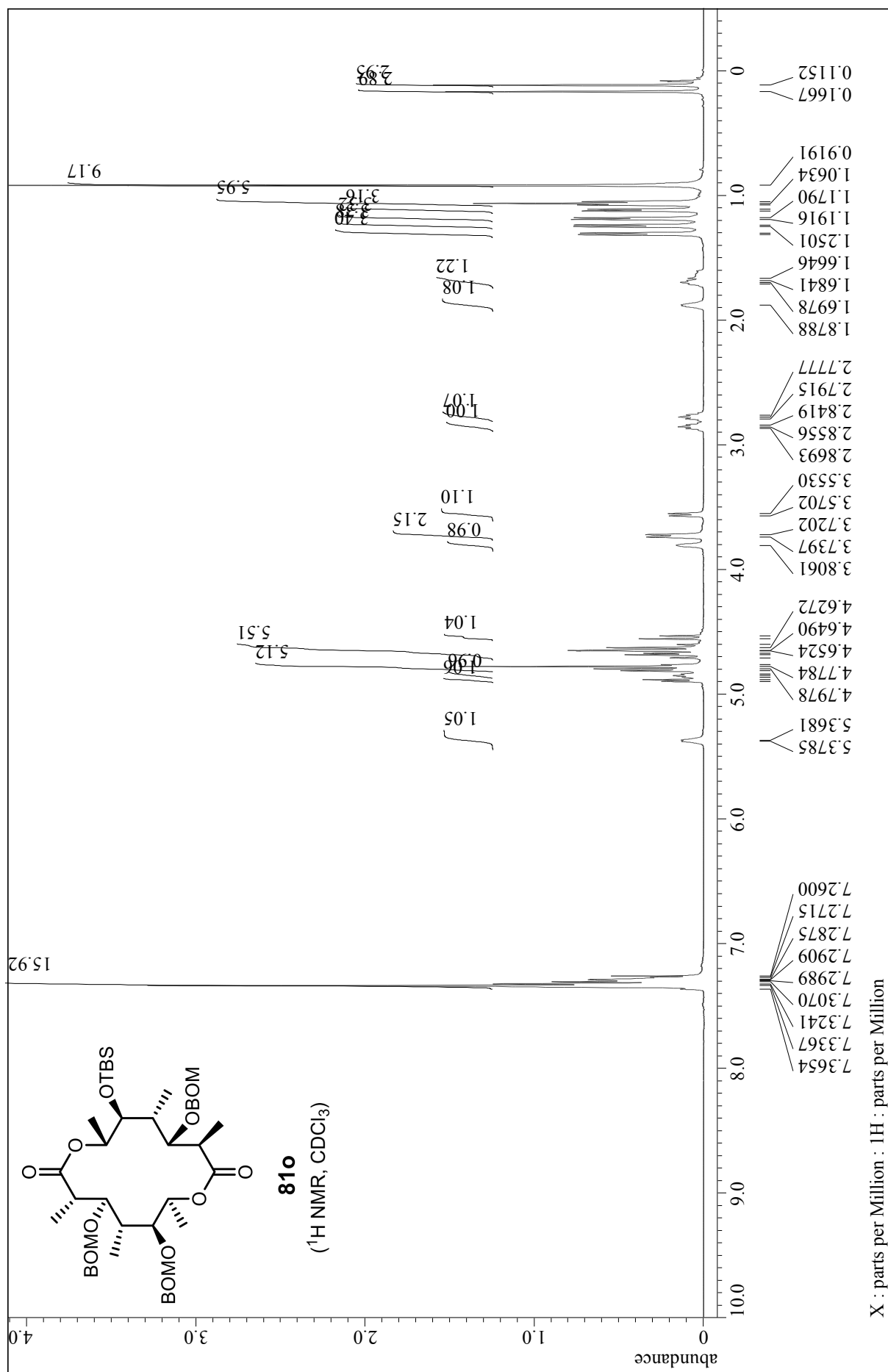


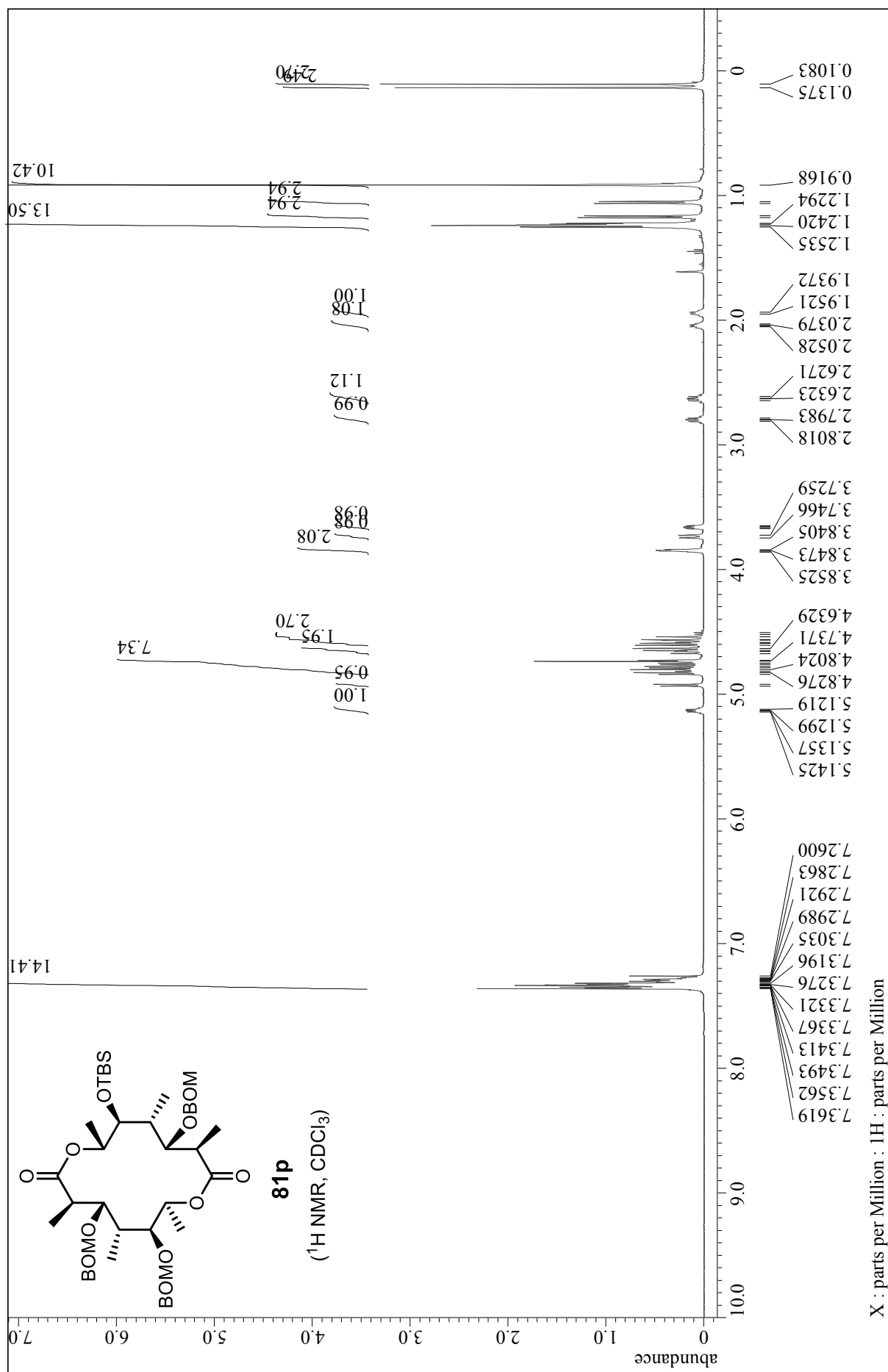


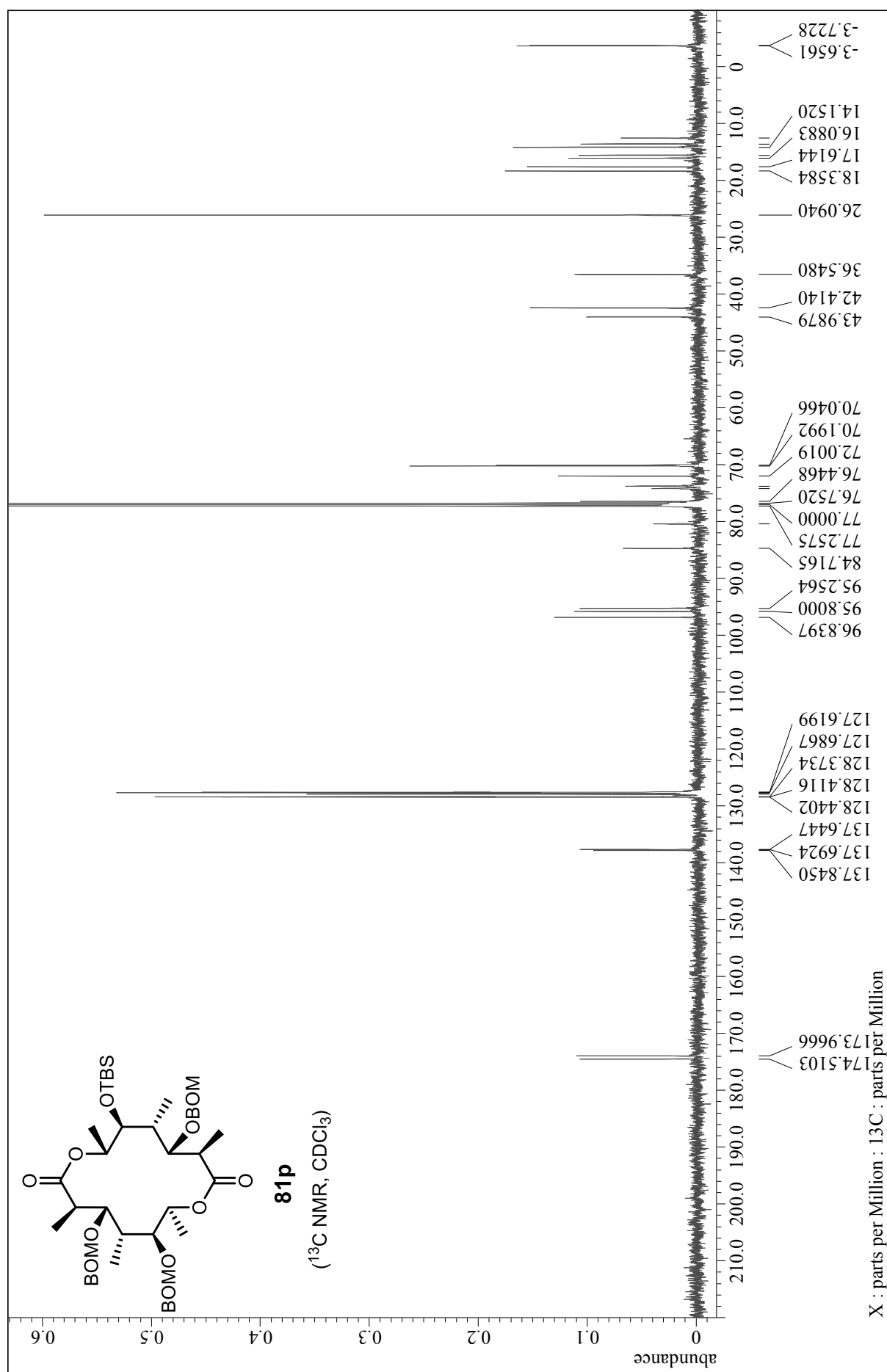


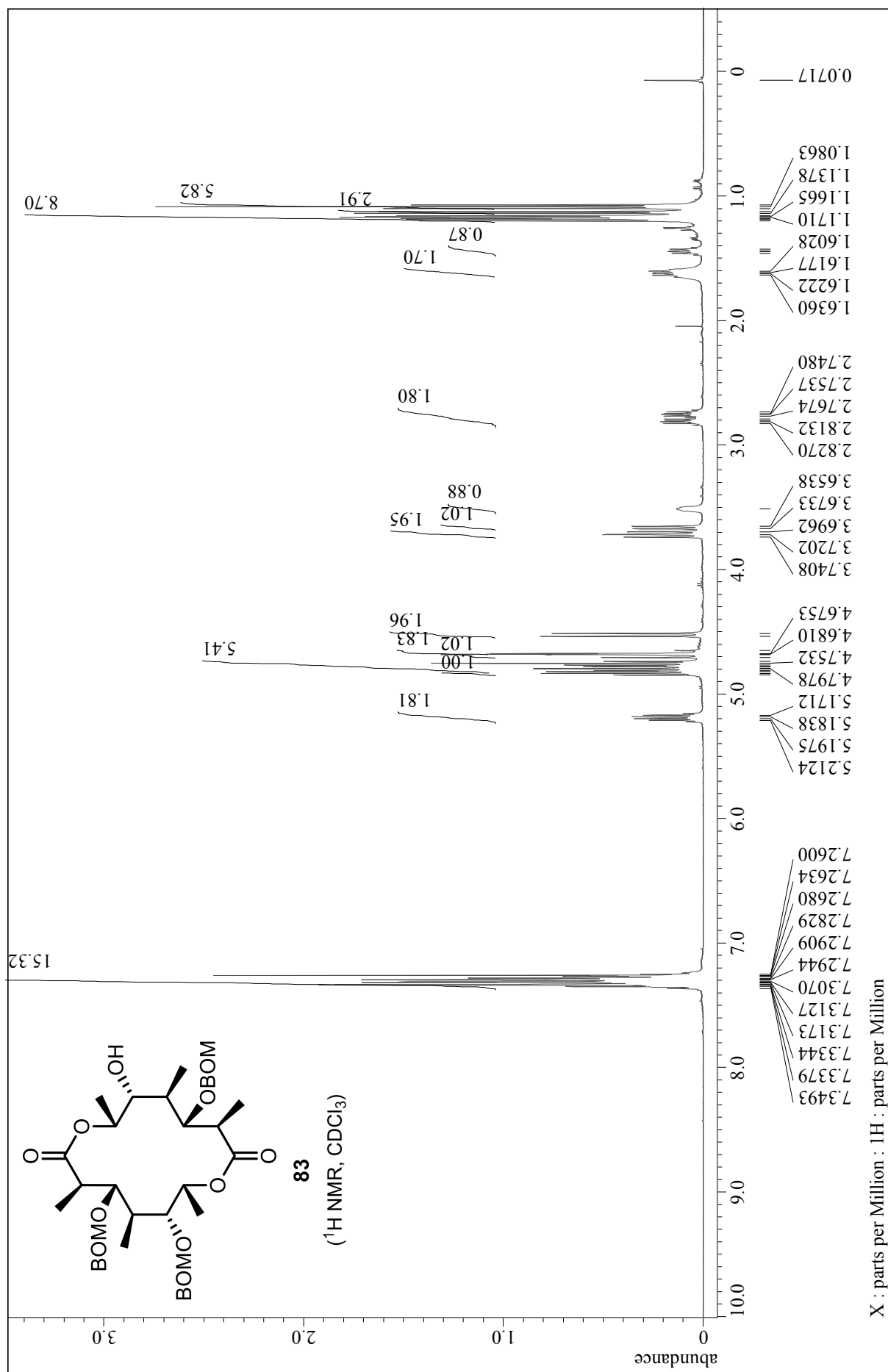


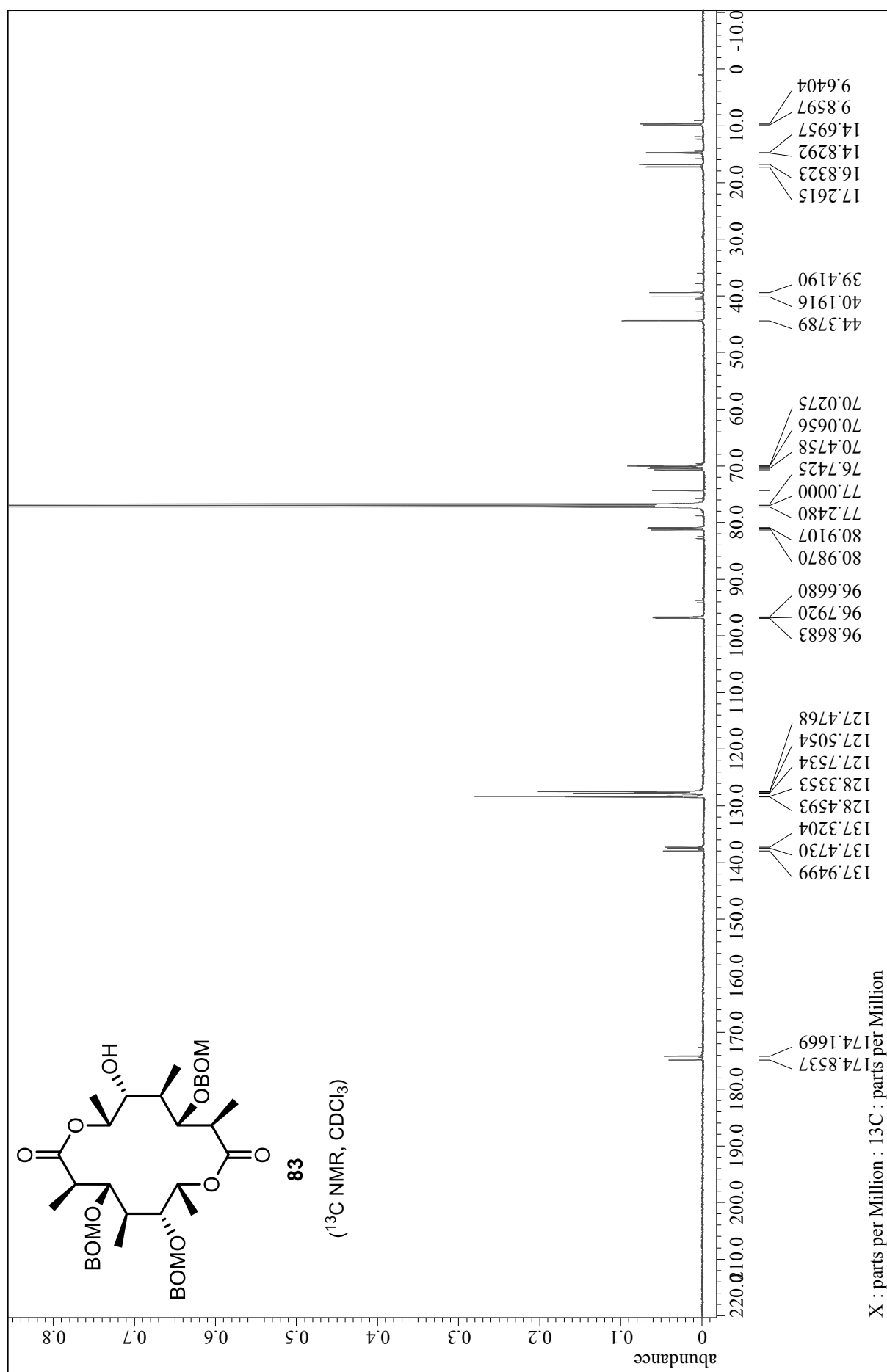


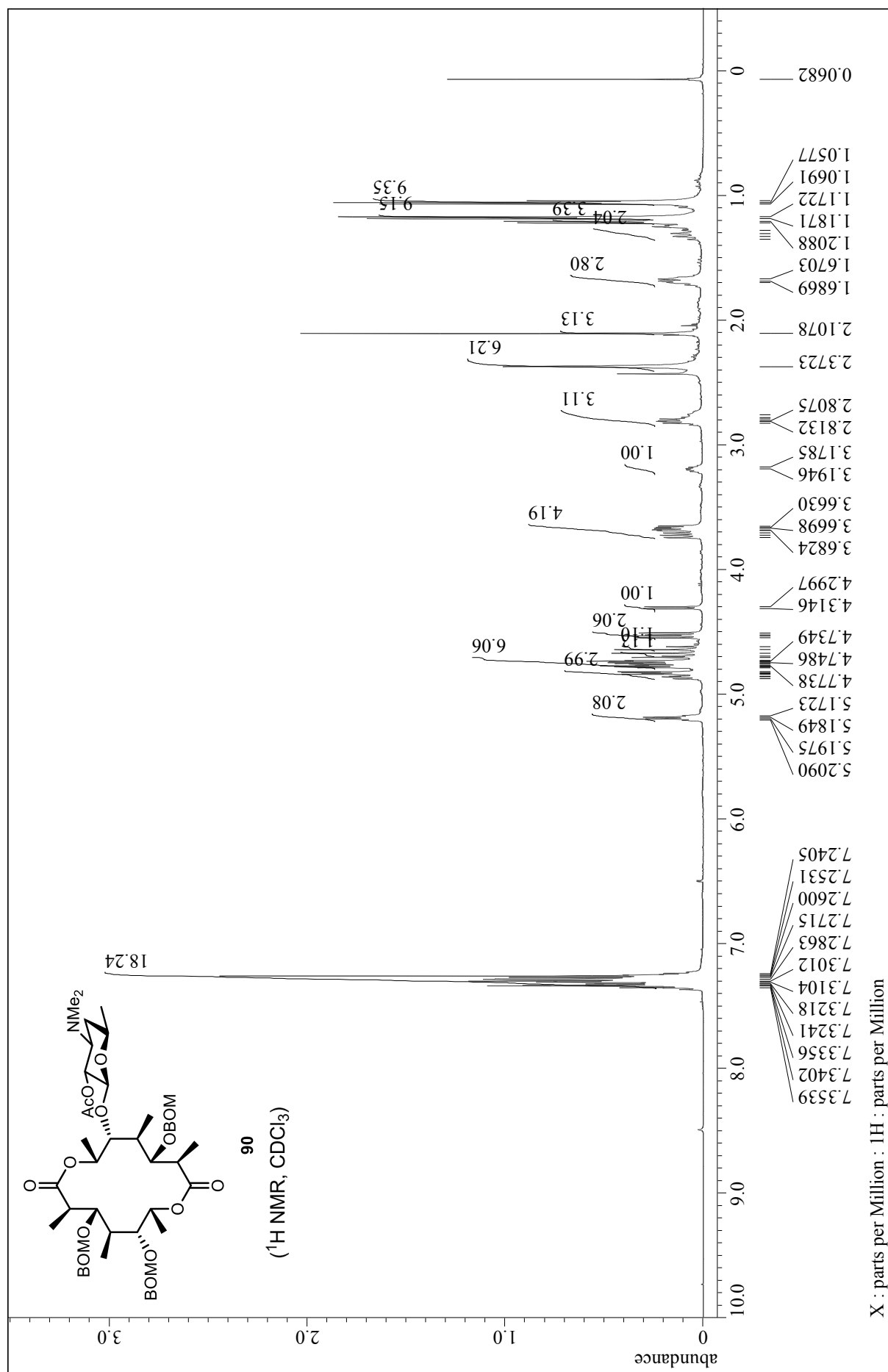


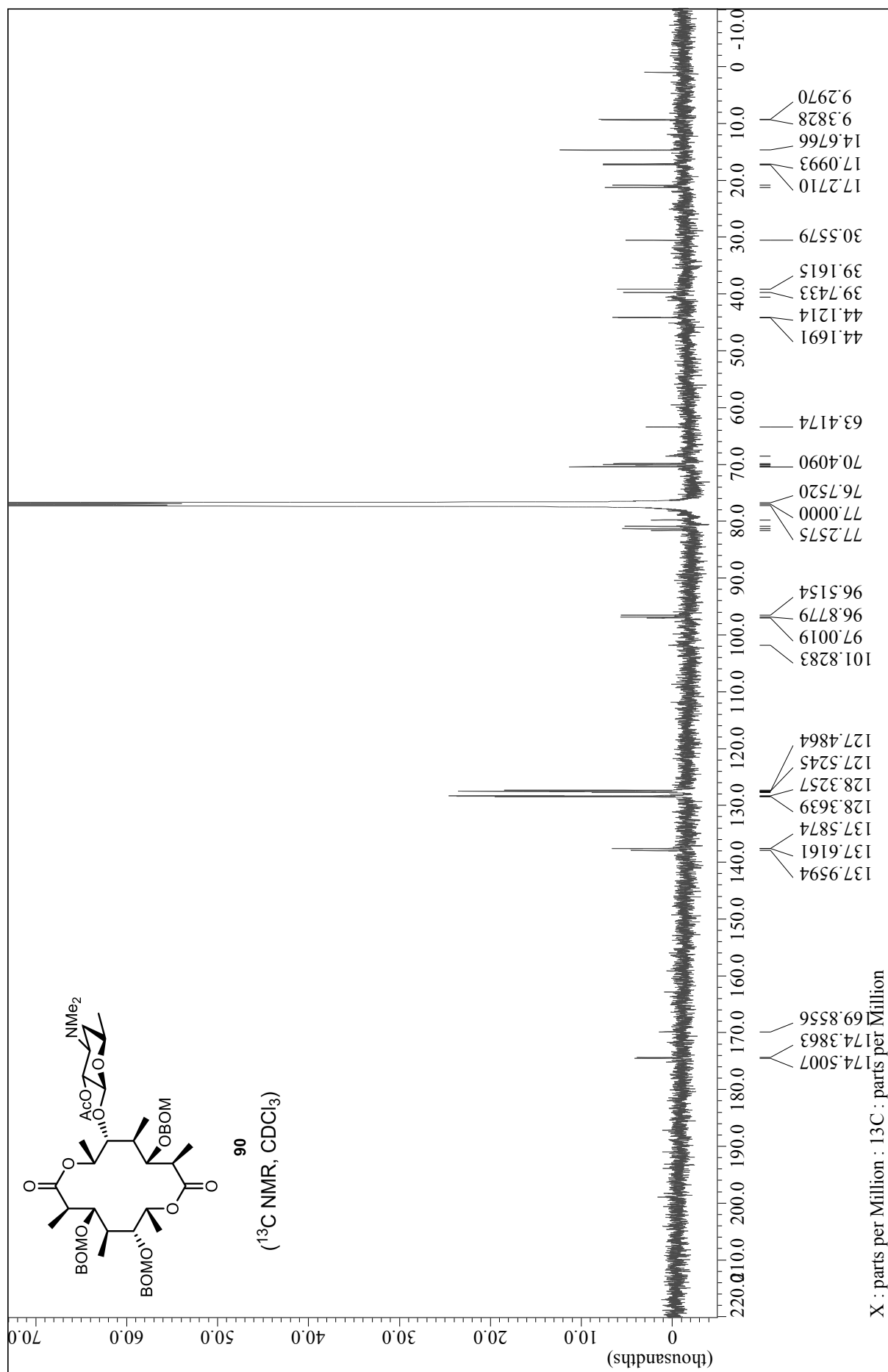


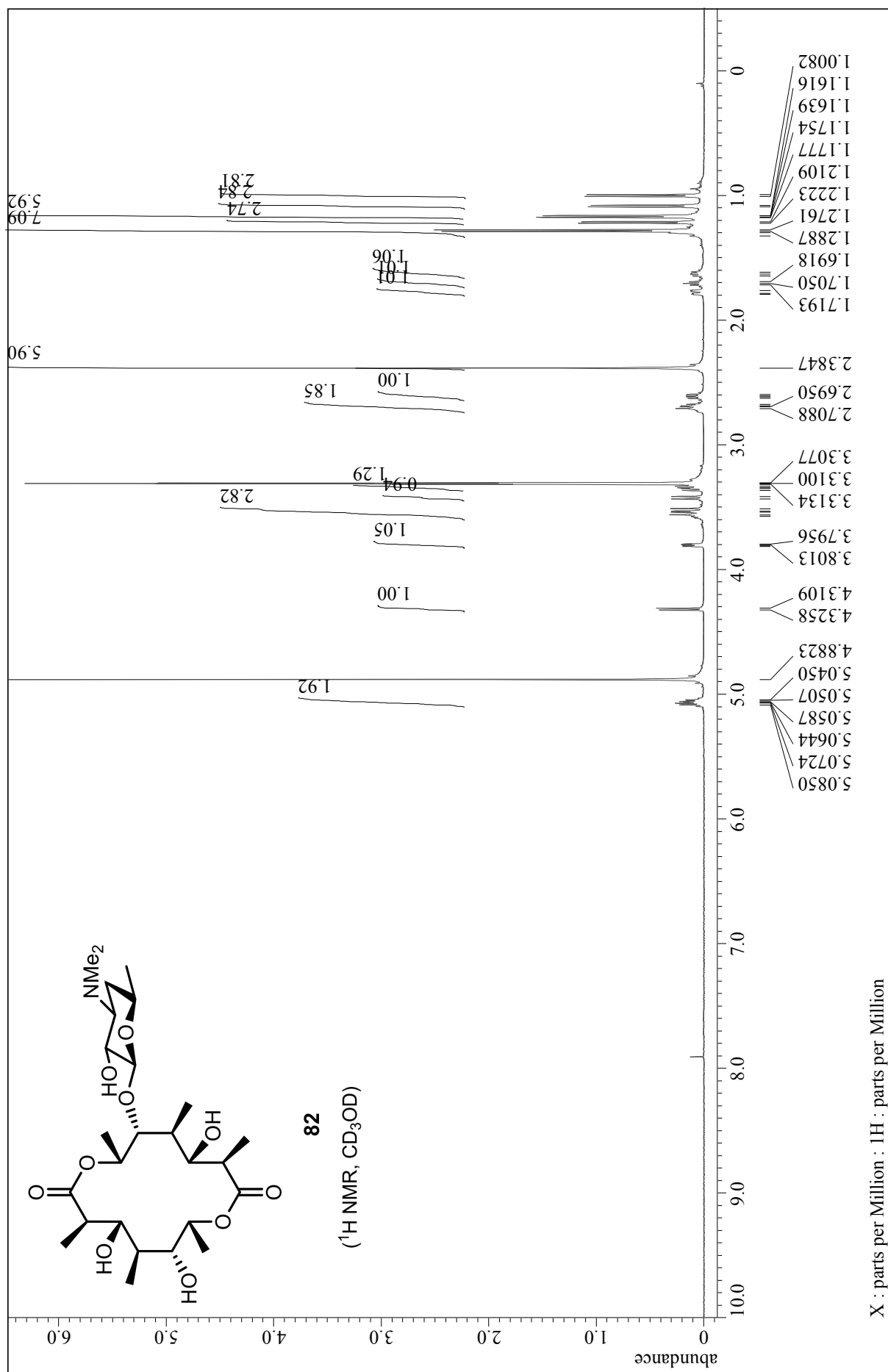








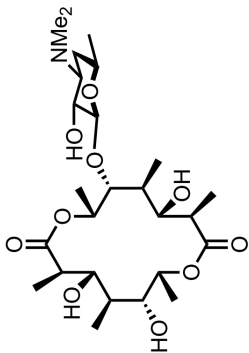




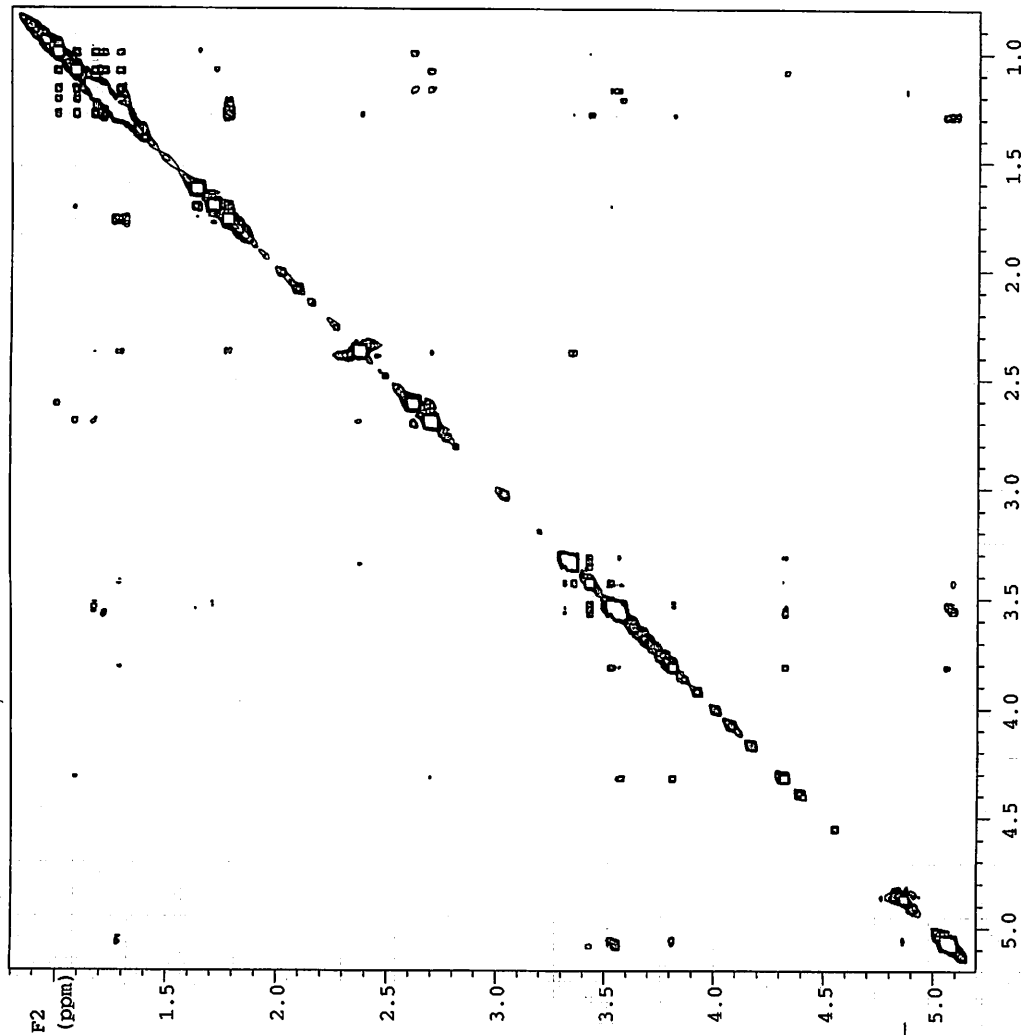
HNS32

exp531 ROESY

SAMPLE
 date Sep 8 2014
 solvent CD3OD
 sample undefined
 ACQUISITION
 sw 3058.3
 at 0.167 temp not used
 np 1024 gain 46
 fb 2000 spin 16
 ss 64 F2 PROCESSING
 d1 1.000 gf 0.078
 nt 16 gfs not used
 2D ACQUISITION
 sw1 3058.3 F1 PROCESSING
 n1 120 gf1 0.018
 TRANSMITTER H1 procl ip
 tn 599.798 fml 2048
 af1q -1198.4 DISPLAY
 tpr 56 sp 478.5
 pw 7.800 wp 2636.8
 ROESY
 mix 0.300 wpl 479.9
 slpw 45.7761 rfl 2636.8
 slpwr 41.000 rfp 2001.1
 PRESATURATION
 rf11 1999.7
 rf1 2285.2
 satmode n rfp1 2285.2
 satpwr 0 PLOT
 satdly 0 wc 180.0
 satf1q 0 sc 10.0
 DECOUPLER
 H1 sc2 180.0
 H1 sc2 0
 nnn vs 1026
 th al 2
 ph



82
(2D ROESY NMR, CD₃OD)



Nucleus _____ Freq _____ MHz
 Spec. Width _____ Hz
 Acq. Time _____ sec
 Pules Width _____ μsec

DECOUPLE
 Nucleus _____ Offset _____ Hz
 Mode _____ Power _____ db
 Modulation Mode _____ Freq _____ Hz
 Pules Width _____ μsec

PLOT/PROCESSING
 FN _____ K RE _____ sec CD _____ sec
 LB _____ Hz AF _____ sec CD _____ sec
 Width _____ Hz/ppm Start _____ Hz/ppm
 Reference _____

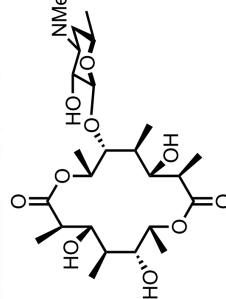
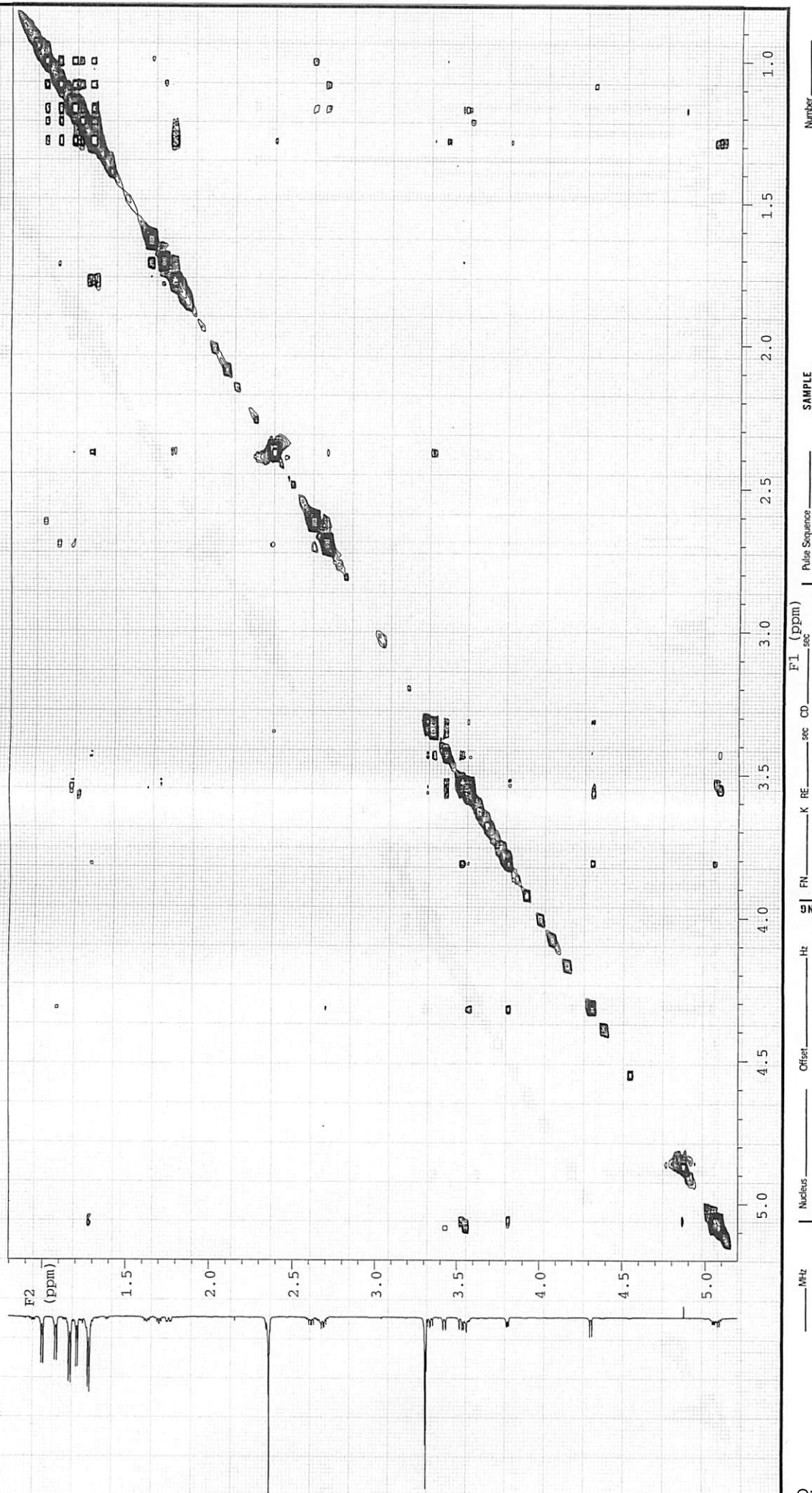
EXPERIMENT
 Pulse Sequence _____
 Tube O.D. _____ mm
 Temp. _____ °C
 Solvent _____

F1 (ppm) SAMPLE
 F2 (ppm)
 Number _____
 File _____
 Date _____
 XL _____

NO 997259J

HN532

Pulse Sequence: ROESY



Decouple
Nucleus _____ MHz
Mode _____
Modulation: Mode _____
Pulse Width _____ μ sec

Offset _____ Hz
Power _____ db
Freq _____ Hz
Power Mode _____

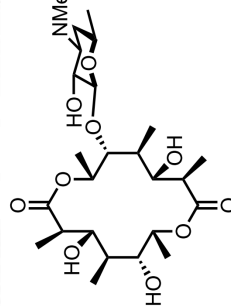
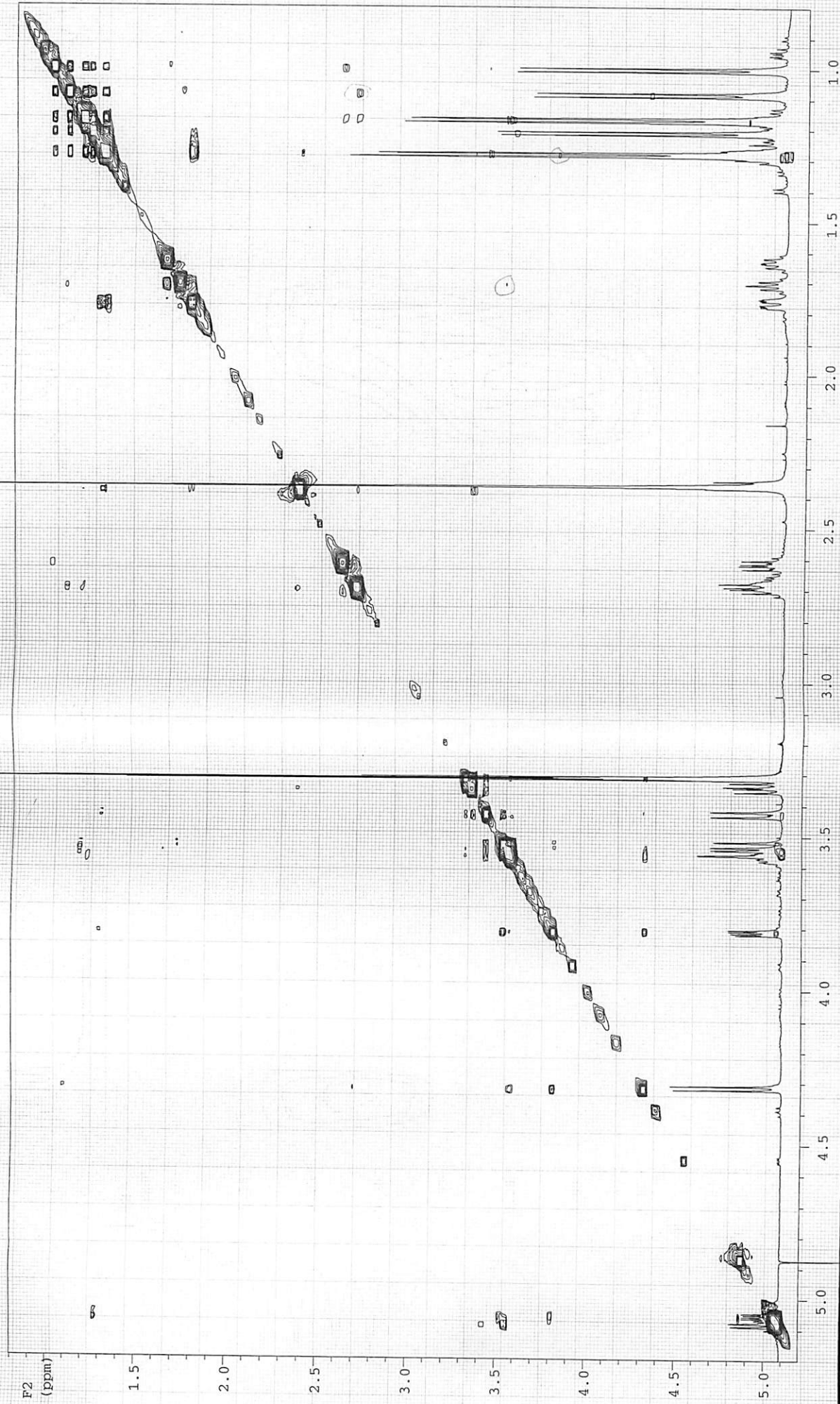
PLT/PROCESSING
FN _____ K RE _____ sec CD _____
LB _____ Hz AF _____ sec CCD _____
Width _____ Hz/ppm Start _____ Hz/ppm
Reference _____

EXPERIMENT
Pulse Sequence _____
Tube O.D. _____ mm
Temp _____ $^{\circ}$ C
Solvent _____

SAMPLE

Number _____
File _____
Date _____
XL _____

NO 997259J



____ MHz
Nucleus
____ Hz
Mode
____ Hz
Modulation: Mode
____ sec
Pulse Width: ____ μ sec

DECOUPLE

____ Hz
Offset
____ db
Power
____ Hz
Freq
____ μ sec
Power Mode

PLOT/PROCESSING

____ sec
FN
____ K
____ Hz
LB
____ Hz
Width
____ Hz/ppm
Start
____ Hz/ppm
Reference

EXPERIMENT

Pulse Sequence
____ mm
Tube O.D.
____ $^{\circ}$ C
Temp

Solvent

SAMPLE

Number

File

Date

XL

NO 997259J

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印