Synthesis of *C*-Glycosides and *N*-Glycosides

By

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Thesis Abstract

Glucose-derived *C*-glycosides and *N*-glycosides have been studied extensively in the following research. First the formation of a *C*-disaccharide was attempted. In the initial schemes two different glucose-derived dithiane nucleophiles were constructed. They were then treated with *n*-butyl lithium at – 78 °C and added to one of two electrophilic lactones. Although the formation of the desired *C*-disaccharides were not observed it was demonstrated that the dithiane bisphenylthiomethane by itself could be deprotonated at low temperatures and added to the different lactones forming *C*-glycosides. With this accomplished the synthesis of individual glycosyl amides were examined. It was determined that when a previously constructed glycosyl azide was treated with ethylenebis(diphenylphosphine) a phosphinimine ylide was formed. This intermediate readily reacted with a number of different acid chlorides to form various glycosyl amides. These synthetically formed amides were made with the intentions of starting a library of amide compounds. This library could then be referred to in future research.

Acknowledgements

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Introduction

The central role of carbohydrates within the realm of biochemistry has emerged as one of the most important areas of research in the biomedical world today. Originally studies with carbohydrates began with Emil Fischer during the 1890's.[1] Since his era the role that carbohydrates play within cellular activity has been greatly researched. It was discovered that they serve as an energy source for cells in many different biological systems, for example through glycolysis. However, over the past thirty years the importance of carbohydrates in cellular and molecular recognition (*glycobiology*) has emerged as one of the most important areas of research today. Glycobiology has in turn lead to the further investigation of the synthesis of modified carbohydrates. These synthetic carbohydrates could mimic the roles that naturally occurring carbohydrates play in any given biological system. Researchers hope that the synthesis of novel carbohydrate derivatives can help lead to new treatments against diseases such as bacterial infections and various cancers that are presently being studied by the scientific community.

Carbohydrates naturally occur in the form of long chains of sugars referred to as polysaccharides. They can be broken down into smaller parts such as oligosaccharides, disaccharides and monosaccharides. Each monosaccharide is considered to be a polyhydroxylated compound that also contains an aldehyde or ketone functional group when it is in its linear structure. If it forms an aldehyde in solution it is referred to as an aldose. If a ketone is formed in solution then it is referred to as a ketose.

A carbohydrate also receives the label of being either an L or D form of the sugar when it is classified. The L and D labels distinguish whether the hydroxyl group attached

to the stereocenter farthest from the carbonyl group is projected to the right side of the sugar or the left side of the sugar. In a Fischer projection L indicates that the OH projects

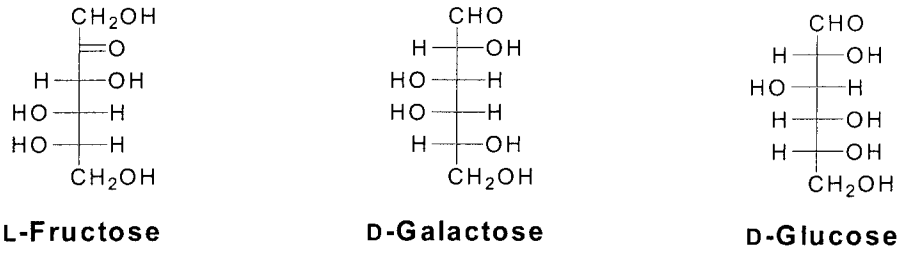


Figure 1. D and L Sugars

outward to the left side of the sugar and D indicates that it is pointed to the right side of the sugar. Examples are shown in Figure 1. A monosaccharide is the simplest form of a sugar because it consists of a single sugar such as glucose, galactose, or fructose. Of these single sugars glucose is one the most important sugars that is consumed on a daily basis. Cells can make use of glucose in a variety of ways and because of this there is a great deal of research on synthetic glucose derivatives. It is hoped that some day one of these newly formed glucose derivatives will be able to bind to an active site on one of the various enzymes being studied. Perhaps synthetic derivatives will act as inhibitors towards such enzymes, which in turn could lead to new treatments for old diseases.

In order to review various techniques that are applicable to constructing synthetic glucose compounds some important themes need to be introduced. For example, there are many different structures that a monosaccharide such as glucose can adopt in solution. In solution glucose exists as a hemiacetal, which allows it to change into different cyclic structures. It can exist in the "alpha" pyranose, "beta" pyranose, "alpha" furanose, "beta" furanose, or the linear, ring-opened, form. In the ring-opened form carbon one has a

double bond to an oxygen atom forming an aldehyde. It is this aldehyde structure that allows a molecule of glucose to form many different structures in solution (Figure 2).

The pyranose structure of the sugar refers to the six-membered ring structure where the hydroxyl group bonded to carbon five has attacked the aldehyde that was at carbon one. As a result the closed ring structure is formed and a hemiacetal exists at carbon one. If the aldehyde was attacked from below the plane and the resulting hydroxyl group is pointed up the hydroxyl group is referred to as being in the beta position. If the aldehyde was attacked from the top and the resulting hydroxyl group is pointed down the hydroxyl group is referred to as being in the alpha position.

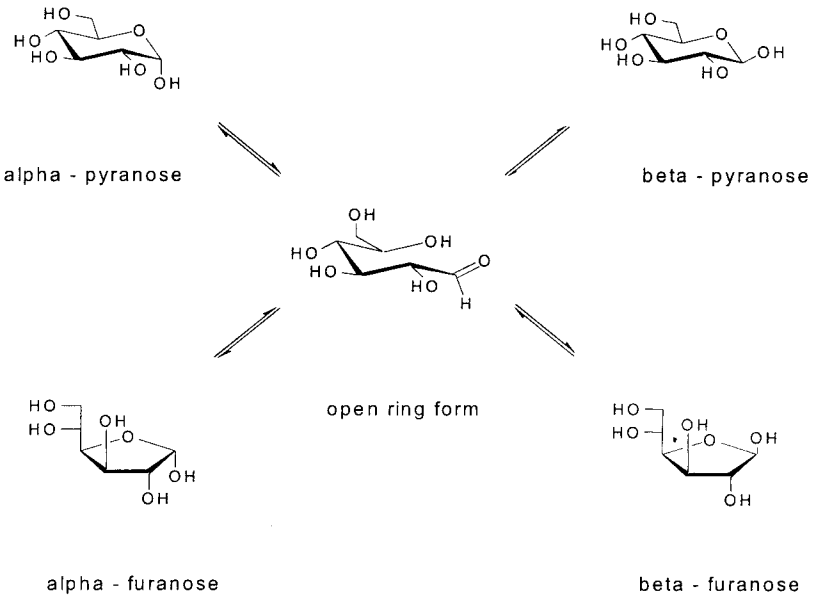


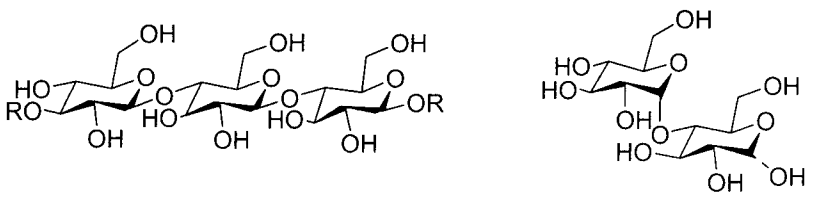
Figure 2. Forms of D-glucose present in solution

Because the hydroxyl group that was formed on carbon one exists in two different configurations that carbon is referred to as the *anomeric carbon*. In the furanose form it is the hydroxyl group that was bonded to carbon four that has attacked the aldehyde on C-1

and as a result produced a five-membered ring structure. Once again the alpha or beta nomenclature depends on the position of the resulting secondary hydroxyl group that has formed off of the anomeric carbon.

The position of the resulting hydroxyl group is very important when research is conducted on any glucose-derived structure. The stereochemistry of the anomeric carbon on a glucose derivative will play an important role in determining whether or not the newly synthesized molecule will be able to interact with the desired active site in a biological system. The stereochemistry of the various glucose derivatives is important when groups other than alcohols are attached at C-1. If the oxygen from the anomeric carbon is bonded to another sugar the position the hydroxyl group maintains, alpha or beta, becomes crucial. This must be understood when different disaccharides are studied and derivatives of them are synthesized, for example derivatives known as *C*-disaccharides. In order to investigate this further the structure of natural disaccharides and synthetic carbon-linked sugars will be discussed.

A disaccharide is formed when two monosaccharides in the cyclic form bond together through a carbon-oxygen-carbon linkage. It is the linkage between these monosaccharides that will play an important role in the following research.



Cellulose **Maltose**

Figure 3. Structures of Cellulose and Maltose

In Figure 3 the disaccharide, known as maltose, is connected by a 1,4-carbon-oxygen-carbon bond. In fact it consists of two molecules of glucose that have been linked together, however if the placement of the hydroxyl group bonded to the anomeric carbon changes from alpha to beta then the identity of the disaccharide also has changed. There is still a 1,4-carbon-oxygen-carbon bond that has formed but now the oxygen bonded to carbon 1 is in the beta position instead of the alpha position. Because of this the sugar maintains a totally different stereochemistry. It is referred to as cellobiose. The fact that maltose can be digested by humans, but cellobiose cannot, demonstrates the importance of a sugar's stereochemistry.

Disaccharides can also vary by having different monosaccharide substituents. For example a molecule of glucose bonded to a molecule of galactose is commonly referred to as lactose. If a glucose molecule is bonded to a fructose molecule the sugar is known as sucrose. There are thousands of other disaccharides that can be formed between simple sugars and the stereochemistry that exists between the two sugars plays an important role. This shows that there is a great amount of complexity present in carbohydrate chemistry and because of the complexity it can prove to be very challenging for researchers to construct certain derivatives of some carbohydrates.

However, with all the diversity that is present within the field of carbohydrate chemistry, many different carbohydrate derivatives can be synthetically produced. If one synthetic compound which should bind to an enzyme cannot be synthesized perhaps a different compound can be made to accomplish the task. It is very important that many new derivatives of a molecule can be synthesized in a short amount of time. Some of these new derivatives hopefully will be active in a biological system. Whether or not a

given synthetic sugar is active in a biological system depends largely on the 3-dimensional structure of the sugar. These structural differences can be examined through the synthesis of *C*-glycosides and *N*-glycosides.

The formation of *C*-glycosides through organic synthesis has recently played an important role in biochemistry research. Many of the *C*-glycosides are actually carbon linked disaccharides, and it has been shown that they may maintain biological activity. These *C*-glycosides are formed from two simple sugars through a carbon-carbon bond commonly referred to as a carbon bridge. Some of these synthetic *C*-glycosides can bind to an enzyme at a specific site, and can then inhibit the active site. This will only occur if the active site allows for the given stereochemistry of the *C*-disaccharide. As mentioned earlier, sugars that are normally found in biological pathways are often linked through an oxygen atom, and these sugars are called *O*-glycosides. *O*-Glycosides may be reduced at the oxygen linkage between the two sugar molecules, however this cannot happen if the oxygen linkage is replaced by a carbon linkage by synthetic means.

The basic concept that is most often practiced to produce a *C*-glycoside synthetically is by adding a nucleophilic species to an electrophile. *C*-Glycosides have been formed by adding carbon nucleophiles to glycals, glycosyl halides, 1,2-anhydrosugars and lactones (Figure 4).

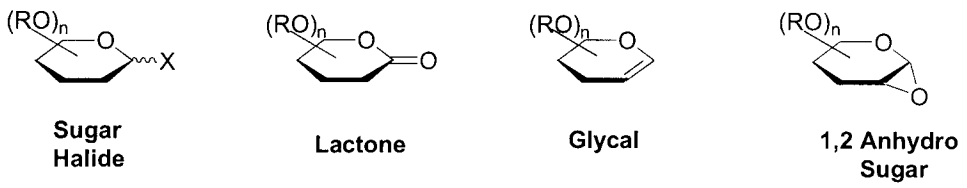
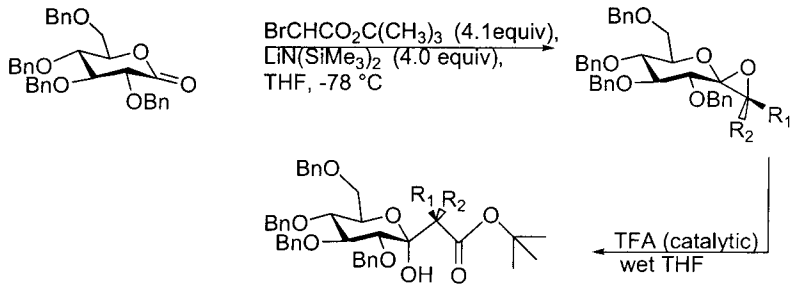


Figure 4. Examples of Sugar Electrophiles

A group lead by Leeuwenburgh demonstrated that when 1,2-anhydro-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside is treated with zinc chloride in the presence of an excess of sodio-di-*tert*-butyl malonate the desired beta *C*-glucoside is produced.[2]

The work of Vogel and coworkers[3] successfully synthesized two *C*-glycosides (α-D-Man-*p*-(1-3)-CH_2-GalNAc and α-D-Man-*p*-(1-3)-CH_2-TalNAc using two proven synthetic techniques. Giese's radical *C*-glucosidation,[4] *C*-galactosidation, and the "naked" sugar methodology were applied to a pre-synthesized enone. After the *C*-glycosides were synthesized, Vogel's group attempted to bind the sugars to an enzyme. They found that the α-D-Man-*p*-(1-3)-CH_2-GalNAc is able to inhibit several glycosidase and fucosyltransferase enzymes. However, the second *C*-glycoside they synthesized was not able to successfully inhibit the same enzymes. The successful inhibition of the various test enzymes by the first *C*-glycoside proved that some *C*-glycosides do in fact act as inhibitors towards enzymes.

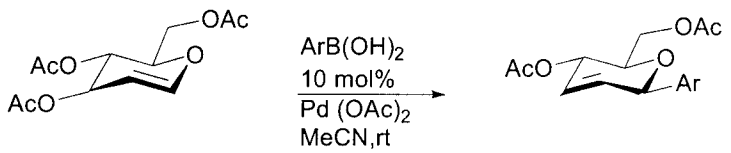
Another study done by Schweizer[5] and colleagues produced various synthetic exocyclic sugar epoxides, which were subject to nucleophilic reagents that produce *C*-glycosides. The initial sugar δ-lactones that had been constructed underwent Claisen condensation with the enolate of *tert*-butyl bromoacetate to produce the different epoxides. These epoxides were then reacted with triethylsilane under TMSOTf-promoted conditions at –78 °C to produce the desired *C*-glycosides. An example of this is demonstrated below in Scheme 1.



Scheme 1

The work of Vogel's group and Schweizer's group demonstrate different methods of synthesizing *C*-glycosides but there are many more that can be used. For example Czernecki and coworkers[6] made use of a Wittig reaction with lactones to form *(Z)- C*-glycosylidenes. They then performed a reduction reaction over Pd/C before completing the synthesis by acetylation of pre-existing *C*-glycosylidenes. They also reported other forms of reduction, which then used Raney nickel reactions to synthesize *C*-glycosides.

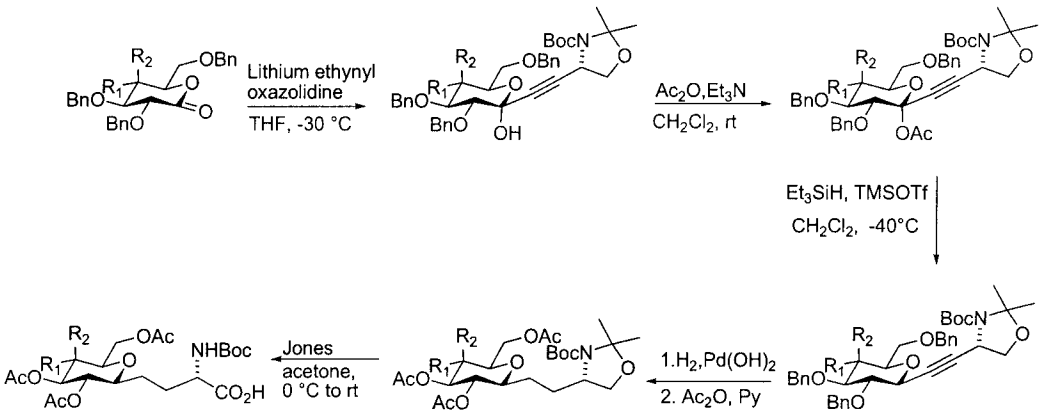
A group lead by Ramnauth[7] also conducted research on *C*-glycosides. They were able to provide a simple stereoselective method for making *C*-arylglycosides. They did so by using arylboronic acids and $Pd(OAc)_2$, which acted as a catalyst. This research had two important results; first it demonstrated a synthetic procedure that would make use of very attainable starting materials to build *C*-glycosides and secondly these starting materials, boronic acid derivatives, are stable in the presence of moisture and air (equation 1).



Equation 1

In another study of *C*-glycoside synthesis a group led by Kovensky[8] synthesized an α-difluoro-*C*-analog of an internal disaccharide. This was accomplished by radical macrocyclization of monosaccharides. The *C*-glycoside was formed in three steps from D-galactono-1,4-lactone.

In work conducted by the Dondoni group a new synthetic means of *C*-glycoside formation was produced.[9] Dondoni and coworkers first provided a detailed synthetic process for producing sugar lactones. In a related project[10] Dondoni developed a synthetic route that produces β-D-linked methylene isosteres of glycosyl serines from simple sugar lactones. The lactones were allowed to react with a lithium derivative of *N*-Boc-4-ethynyl-2,2-dimethyl-1,3-oxazolidine, then the acetoxy group was removed by silane reduction. Finally to complete the C-bridge bond formation the triple bond located on the former nucleophile was reduced using $H_2/Pd(OH)_2$. An oxidative cleavage was applied to the oxazolidine ring using the Jones reagent to give the desired product (Scheme 2).



Scheme 2

Another type of glucose derivative that has been studied extensively in the field of glycomimetics are *N*-glycosides. However there is a major difference in how *N*-glycosides and *C*-glycosides are made synthetically. *C*-Glycosides are most often formed from carbon nucleophiles attacking electrophilic species. However carbon atoms do not exist in a natural nucleophilic state. Instead they must be formed synthetically by use of powerful bases such as *n*-butyl lithium that can deprotonate a carbon atom. However, a nitrogen atom can act as a nucleophile because it has a lone pair of electrons, which allow for it to naturally act as a nucleophile. In many synthetic pathways that produce *N*-glycoside derivatives the nucleophile is in fact a simple amine structure.

These *N*-glycoside derivatives also may maintain the correct overall structure to bind to an active site within a biological system. In fact Spicamycin and Septacidin are two antibiotics that have been isolated and structurally confirmed to be *N*-glycosides. These compounds have adenine nucleosides attached to the nitrogen group, which is bonded to the glucose structure.

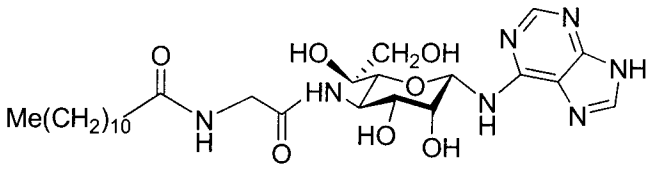
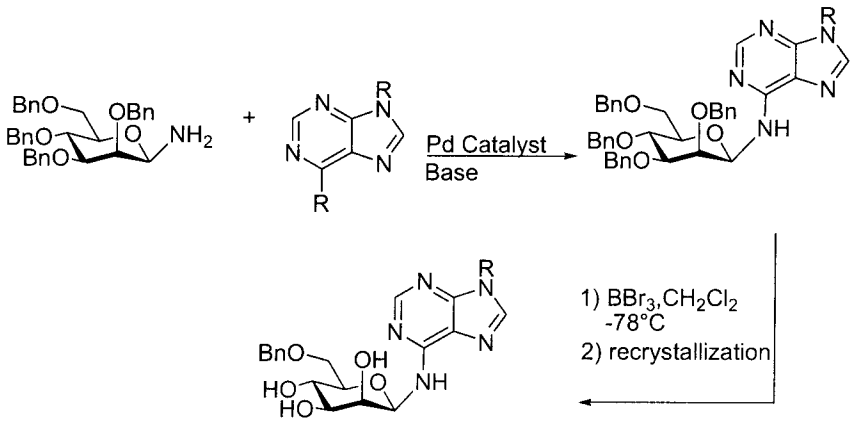


Figure 5. Structure of Spicamycin

In a recent study a group led by Chida[11] tried to synthesize a naturally occurring *N*-glycoside product. The basic backbone of these structures can be formed through a Pd-catalyzed coupling reaction with a mannopyranosylamine and 9-protected-6-chloro-

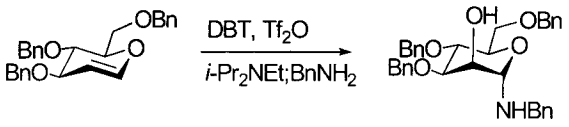
purine. It should also be mentioned that the β-D-glucose derivative of this structure was also produced (Scheme 3).



Scheme 3

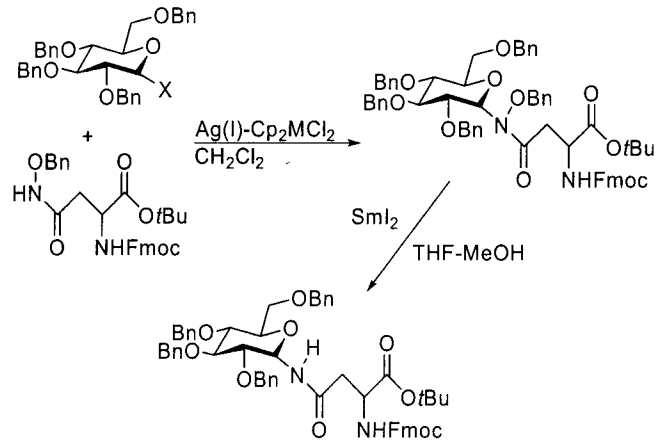
A group lead by Suzuki[12] then completed the synthesis of a Spicamycin congener by using the research completed by Chida's group in order to obtain the backbone structure of the antibiotic. Suzuki's group then took the Spicamycin derivative they had synthesized and did a condensation reaction with dodecanoylglycine to obtain the final structure of their target molecule.

Gin and colleagues[13] produced a *N*-glycoside by means of an oxidative glycolization of benzylamine. This was accomplished using a dibenzothiophene bis-(triflate) and dibenzothiophene-5-oxide-catalyzed reaction, which allows for the stereoselective oxidation of the glucal to take place. The nitrogen group on the benzyl-amine can then act as a nucleophile and attack the anomeric carbon producing the alpha *N*-glycoside (Equation 2).



Equation 2

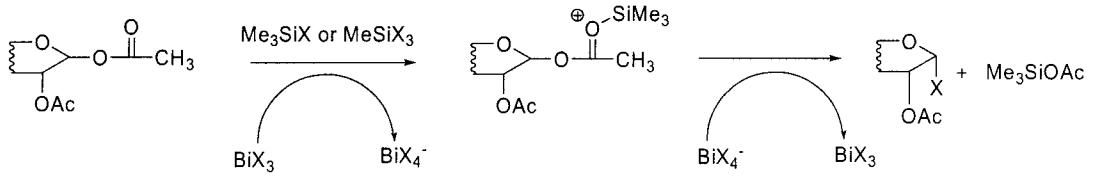
Another synthesis of *N*-glycosides was demonstrated by Ito and coworkers.[14] They employed Asn hydroxamate as a glycosyl acceptor. Then both glycosyl fluoride and glycosyl trichloroacetamide were able to react with the Asn hydroxamate derivative to achieve the desired *N*-glycoside formation. The major improvement of this technique was that the nucleophilic character of the nitrogen atom of the carboxyamide group was greatly enhanced, which allowed the nitrogen to attack the anomeric carbon of both the glycosyflouride and the glycosyl trichloroacetamide with much greater effectiveness. As a result precursors to *N*-glycosides were produced in high yields. The benzyloxy group was then removed by SmI_2 mediated reduction. From this step the final *N*-glycoside was produced (Scheme 4).



Scheme 4

There are many other synthetic routes within the literature that describe various ways to construct both *C*-glycosides and *N*-glycosides. Each new compound that is made is a potential drug that could be used to fight a certain illness. This leads researchers to try to develop new and better ways to synthesize glycomimetics.

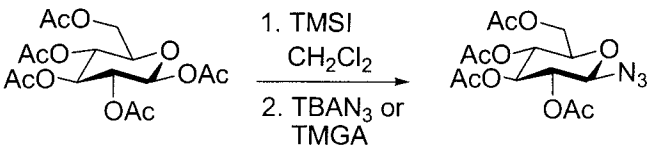
In order to construct these new synthetic *N*-glycosides inexpensive starting materials that are easy to work with must be obtainable in large quantities. For example a group led by Montero[15] reported that the formation of glycosyl halides from peracetylated glycopyranosides using bismuth (III) halides and halogenosilanes is accomplished under mild conditions. In this experimental setup the bismuth (III) halides activate the silicon halogen bond. This leads to a silicenium cation which bonds to the oxygen atom of the carbonyl group of the acetal protecting group located on the anomeric carbon. This allows the protecting group to act as a leaving group. The BiX_4^- complex then induces a nucleophilic attack on the α-carbon atom by the halide. This produces the desired halide (Scheme 5).



Scheme 5

Once the formation of various glycosyl halides is accomplished they can be used to construct glycosyl azides. A group led by Hague[16] demonstrated this by first constructing glycosyl iodides by refluxing the acetylated sugars with iodotrimethylsilane in methylene chloride. Then the glycosyl iodides were reacted with tetrabutylammonium azide or tetramethylguanidinium azide in methylene chloride to produce the per-*O*-acetyl

glycosyl azides. The final product of this two-step synthesis was completed in a single reaction setup. Once the glycosyl iodides were constructed, the azide donors were added to the reaction to complete the synthesis (Equation 3).



Equation 3

Kobe[17] and company also constructed glycosyl azides by making use of phase transfer catalytic conditions. Glycofuranosyl halides were dissolved in a solution of methylene chloride and saturated sodium hydrogencarbonate. Then 5 equivalents of sodium azide and one equivalent of tetrabutylammonium sulfate were added to the solution. The reactions were evaluated and it was determined that they follow the S_N2 mechanism and act in a stereospecific manner while the phase transfer catalyst system is being employed. It was demonstrated when the same reactions are run in polar aprotic solvents the same stereospecific nature is not present.

Kobe's group demonstrates an important point concerning the manipulation of stereochemistry when constructing glycosyl azides. The solvents that are used to run a reaction can be use to manipulate the stereochemistry of the final product. Ultimately the phase transfer catalyst system that was used helped select for the S_N2 reaction mechanism and this resulted in the desired product.

Statement of Problem

The study of carbohydrates has expanded greatly over the past thirty years. This has occurred because of the role that these compounds play in cellular activity. It is hoped that research conducted on various carbohydrates may lead to new treatments for diseases that are prevalent in the world today. The study of synthetically produced *C*-glycosides and *N*-glycosides may provide possible compounds that might be biologically active.

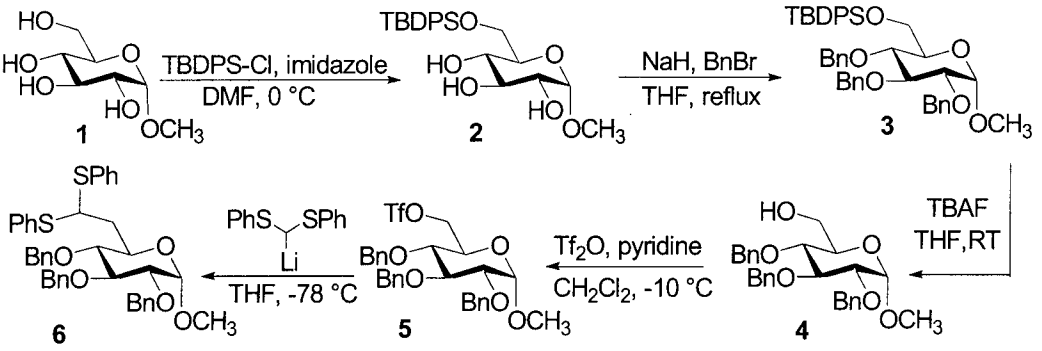
The synthesis of *C*-glycosides will be explored and may lead to the formation *C*-disaccharides. If a dithiane can be added to an electrophilic compound such as a lactone then perhaps the synthesis of a glucose-derived dithiane could be used to form a *C*-disaccharide. Therefore the synthesis of glucose-derived dithianes has been attempted. These compounds will then be used as possible nucleophilic reagents. Different lactones will also be constructed to see if *C*-disaccharides might be formed.

The synthesis of *N*-glycosides can also be explored. The formation of an amide bond from previously constructed glycosyl azides and acid chlorides can be evaluated. The most effect procedure to produce these compounds at high yields and purity may lead to compounds that are very useful in biomedical research. As a result the formation of glucose-derived amides will be studied in order to construct a potentially useful library of compounds.

Results and Discussion

In the following research the construction of different synthetic glucose-derived *C*-glycosides and *N*-glycosides will be discussed. It is hoped that the synthesis of *C*-glycosides through the use of dithane-derived nucleophiles will eventually lead to the construction of a *C*-disaccharide. In order to accomplish this task it had to be proven that a dithiane nucleophile could be constructed from a synthetically altered form of glucose. Previous work done in the Norris group by Jason McCartney had accomplished this.[18]

Methyl-α-D-glucopyranoside was chosen as the starting material for this synthesis. This compound was commercially available and the hydroxyl group bonded to the anomeric carbon had been previously methylated. As a result it was possible to work with only the α-pyranose form of the methylated glucose. A major issue concerning the stereochemistry around the anomeric carbon had been easily dealt with by choosing this synthetically altered form of glucose.



Scheme 6

The first step taken in the designed synthesis was the protection of the primary hydroxyl group at carbon six. This primary alcohol should be accessible when compared

to other secondary alcohols that are located on carbons 2, 3, and 4 of the starting material. Therefore, a large protecting group was selected that would bond selectively to the primary hydroxyl group. *t*-Butyldiphenylchlorosilane was chosen as an appropriate protecting group for the primary alcohol (scheme 6).

The silylation reaction was run at low temperatures under nitrogen atmosphere. After twenty four hours TLC showed that all of the starting material had been consumed and a less polar product had formed. ^{1}H NMR also provided proof of the desired product (**2**) with a 9H signal observed at 1.0 ppm. This singlet was the result of the *t*-butyl group that was present on the TBDPS protecting group. There were also signals present in the region corresponding to aromatic rings (7.0-7.5 ppm), which accounted for the two phenyl groups (signals for 10H) located on the protecting group. A second singlet was observed at 3.4 ppm, which corresponded to 3H and this was assigned to the methoxide group bonded to the anomeric carbon. The remaining peaks for the protons located on the sugar occurred between the 3.5 ppm to 4.7 ppm range.

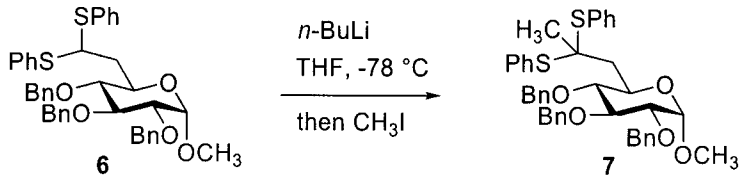
The next step that was completed was the protection of the hydroxyl groups located on carbons 2, 3, and 4 to produce product **3**. Deprotonation of these hydroxyl groups was achieved using NaH and then benzyl bromide was added to the reaction. As a result all of the remaining hydroxyl groups were protected *via* the benzylation reaction. In the ^{1}H spectrum of the product (**3**) a new series of signals appeared in the range of 4.6 ppm to 5.0 ppm. These resulted from the CH_2 groups present on the benzyl protecting groups. When the integration of the aromatic region was calculated it was discovered that three new phenyl groups were present giving a total of 25 hydrogens that were accounted for.

Following the completion of the protection reactions compound **3** was treated with tetra-*N*-butylammonium fluoride in order to remove the TBDPS protecting group. As a result the primary alcohol that was originally present on carbon six was regenerated. This was shown to be successful when the signal for the *t*-butyl group of the large TBDPS protecting group disappeared at 1 ppm in the ^{1}H spectrum of compound **4**. The integration of the aromatic region revealed that there were now only fifteen protons left where originally there were twenty five in the precursor **3**.

In the next reaction the primary hydroxyl group of compound **4** was triflated. The TLC plate showed that complete consumption of **4** had taken place and a new less polar spot had formed. The new triflated compound (**5**) was isolated by a hexanes extraction and used without any additional purification in the next step. In this next reaction bisphenylthiomethane was deprotonated using *n*-butyl lithium at low temperature. Then the triflate **5** was added to the reaction, which led to the formation of the dithiane derivative **6**. The ^{1}H NMR spectrum demonstrated that the new product had been formed by the appearance of two new signals at 1.9 ppm and 2.2 ppm. These signals appeared as a doublet of doublets and they correspond to the protons bonded to carbon six. The integration of the aromatic region revealed that there were now twenty five protons present that correspond to five aromatic rings.

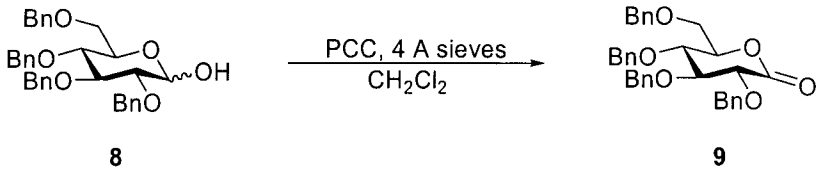
The next step taken was an attempted methylation of product **6** using *n*-butyl lithium at low temperature to deprotonate the glucose dithiane derivative (Equation 4). Methyl iodide was added to the reaction, which was then allowed to run overnight. TLC showed a spot with a very similar R_f value as the starting material. A standard aqueous workup was done and a ^{1}H NMR of the product showed that a reaction had occurred.

Unfortunately it was determined that starting material was still present in the product as well and no means of purification could be found to separate the two compounds because of the similarities of the polarities of the reactant and product (**7**).



Equation 4

At this point the dithiane had been constructed and shown to be reactive. Now it was necessary to synthesize a lactone electrophile to react with the dithiane nucleophile. 2,3,4,6 Tetra-*O*-benzyl-α-D-glucopyranoside (**8**) was oxidized at room temperature using PCC to form the desired lactone **9** (Equation 5). After twenty four hours TLC showed a new less polar spot had formed and the reaction had gone to completion.

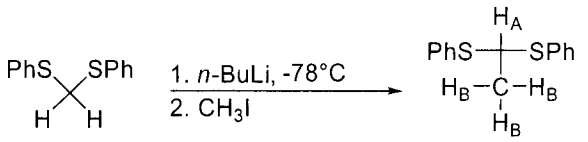


Equation 5

^{1}H NMR showed that there were nine proton signals present between 3.6 ppm and 5.0 ppm. These represented the two distinct types of protons. First there were signals present for the protons bonded to carbons 2, 3, 4, 5, and 6 of the glucose structure. There were also four signals observed for the CH_2 groups of the benzyl protecting groups.

A multiplet located in the region of 7.0 ppm to 7.4 ppm represented the protons located on the four phenyl groups. Upon integration of this region it was revealed that there were twenty protons present from the four phenyl groups. A ^{13}C spectrum revealed

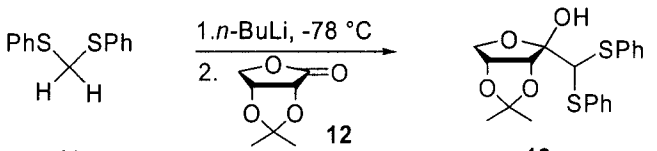
a distinct peak at 170 ppm, which demonstrated that an ester was present in the final product and the lactone had in fact formed.



10 **11**

Equation 6

At this point it was decided to study how effective lithiated bisphenylthiomethane would be when employed as a nucleophilic species. In the first reaction (Equation 6) bisphenylthiomethane (**10**) was deprotonated at –78 °C using *n*-butyl lithium and then methyl iodide was chosen as a simple electrophile. TLC showed the formation of a new less polar spot. A ^{1}H NMR spectrum revealed that a new signal had formed at 4.6 ppm, which was split into a quartet. This signal corresponded to proton H_A (equation 4) which was split by three new neighboring protons. A second signal was observed at 1.7 ppm. This signal resulted from the three protons labeled H_B in **11** and appeared as a doublet because there was one neighboring proton, H_A. Two signals were also observed in the region between 7.2 ppm and 7.6 ppm. These accounted for the two phenyl groups that were present in the product.

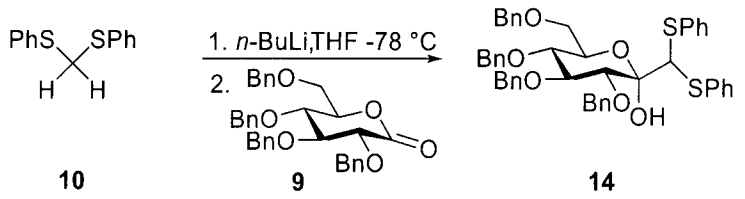


10 **13**

Equation 7

It was then decided to use a commercially available lactone as the electrophilic species (equation 7). Once again bisphenylthiomethane (**10**) was deprotonated at –78 °C

using *n*-butyl lithium. This time 2,3-*O*-isopropylidene-D-erythronolactone (**12**) was added to the reaction (Equation 7). TLC demonstrated that a new less polar spot had formed, which burned after dipping the plate in 5% H_2SO_4/EtOH and heating. The ^1H NMR of the product revealed four new signals between 3.9 ppm and 4.9 ppm. These signals belong to the three protons on the backbone of the furan ring and the single proton located on the exocyclic bisphenylthiomethyl group of **13**. There were also two singlets observed at 1.39 ppm and 2.48 ppm that accounted for the protons on the acetal protecting group. Finally there were signals present in the 7.0 ppm-7.5 ppm range, which accounted for the two phenyl groups of the bisphenylthiomethyl substituent.[18]



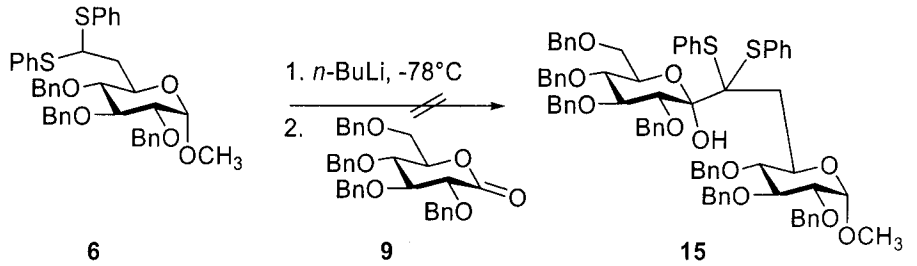
10 **9** **14**

Equation 8

Next an attempt was made to add the bisphenythiomethane nucleophile to lactone **9** (Equation 8). Once again the bisphenylthiomethane was deprotonated using *n*-butyl lithium at low temperature. Lactone **9** was then added to the solution containing the anion. After 55 minutes TLC showed the reaction had gone to completion and a less polar spot had formed. The ^1H NMR spectrum showed several new signals between the region 3.6 ppm and 5.2 ppm. One singlet was distinguishable at 4.37 ppm. This was the result of the proton on the bisphenythiomethyl group. A ^{13}C spectrum of the product **14** revealed that the signal for the carbonyl present on the lactone at 170 ppm had disappeared. This demonstrated the bisphenylthiomethane had added to the lactone forming a hemiacetal. The hemiacetal could form the open or linear form in solution, which could explain all of

the extra signals present in the ^{1}H NMR spectrum from 3.6 ppm to 5.2 ppm. Compound **14** was assumed to be the α-anomer in order to have the large $CH(SPh)_2$ group equatorial and the OH axial, which allows for the anomeric effect.

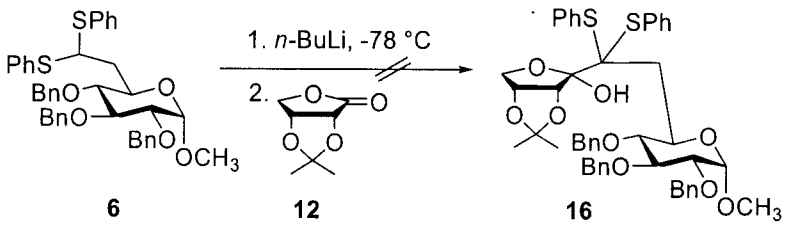
This last reaction provided proof that our bisphenylthiomethane derivatives might be able to add to electrophilic lactones. However, an attempt to use the glucose-derived dithiane **6** to construct a *C*-disaccharide with the lactone **9** was unsuccessful. Standard conditions for deprotonation of the dithiane group using *n*-butyl lithium at low temperature were employed (Equation 9).



6 **9** **15**

Equation 9

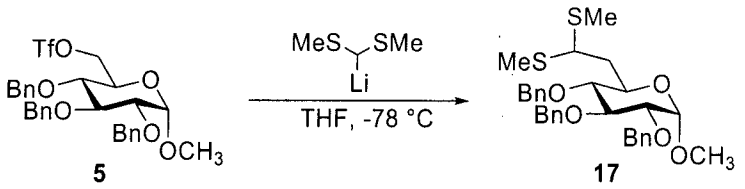
Unfortunately after the addition of the lactone was completed there was no change in the TLC. A second reaction was then set up using the lactone 2,3-*O*-isopropylidene-D-erythronolactone (**12**). Once again *n*-butyl lithium was used to deprotonate the glucose dithiane **6** derivative at low temperature (Equation 10). The lactone was added and the reaction ran overnight. A TLC indicated that a new product had formed but there was still starting material present in the form of the glucose dithiane derivative (**6**). The reaction was then worked up and after purification a ^{1}H NMR was run to work out what had occurred. It showed that the glucose derivative had not reacted but the lactone and *n*-butyl lithium had. There was no evidence that **16** (Equation 10) had formed.



6 12 16

Equation 10

It was thought that maybe the nucleophile derived from glucose was too bulky to add to a lactone. As a result a new derivative of glucose was constructed using bismethylthiomethane. Once again the triflate **5** was reacted with the anion of a dithiane derivative to construct a new dithiane derivative of glucose (Equation 11). TLC revealed the formation of a new less polar spot and complete consumption of the starting material. A ^{1}H spectrum revealed two new signals for the protons on carbon six on the glucose structure. There was a doublet at 2.9 ppm that resulted from the proton still located on the methyl group of the bismethylthiomethane group. Another quartet was present at 2.6 ppm, which was the result of the proton on carbon five being split by the protons present on carbon six and carbon four. The integration of these signals also supported the analysis of this structure as it revealed that the protons were in a 1:1 ratio.

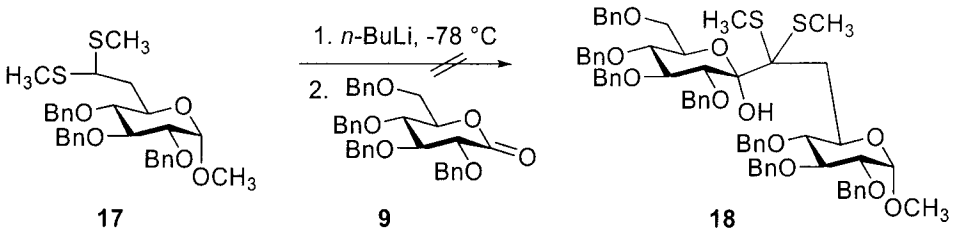


5 17

Equation 11

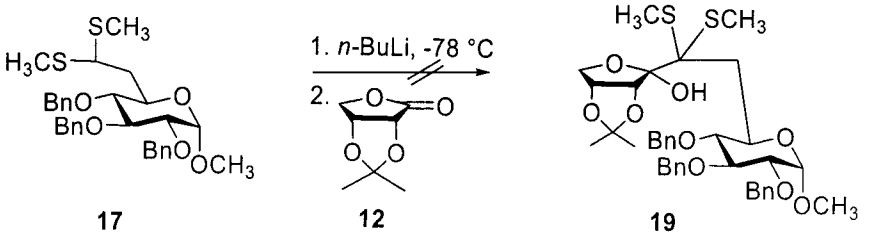
This newly formed glucose derivative **17** was then deprotonated using *n*-butyl lithium at low temperatures. It was attempted to add each of the two previously mentioned lactones (**9** and **12**) to the newly formed glucose derivative in an effort to

make disaccharides **18** and **19** (Equations 12 and 13). However, as before no reaction took place. TLC showed that only starting material was present in both cases. After a work up was completed ^{1}H NMR confirmed that only starting material was present.



17 **9** **18**

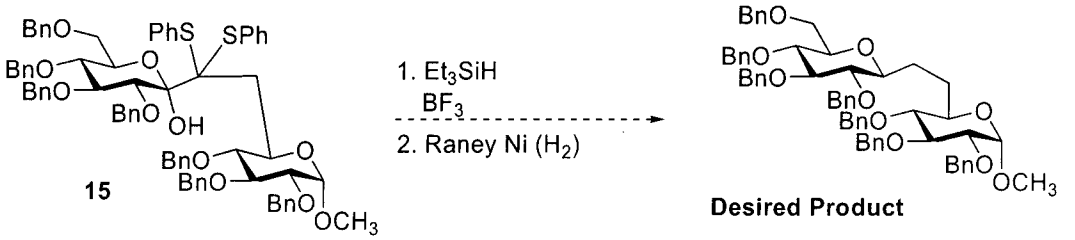
Equation 12



17 **12** **19**

Equation 13

At this point it was determined that problems with the formation of the *C*-disaccharides were going to need further investigation in order to complete the synthesis. Previous research conducted by the Norris group had already determined what steps could be taken in order to complete the reduction and removal of the dithio groups once a related disaccharide was constructed (e.g. **15**, Equation 14).[18]

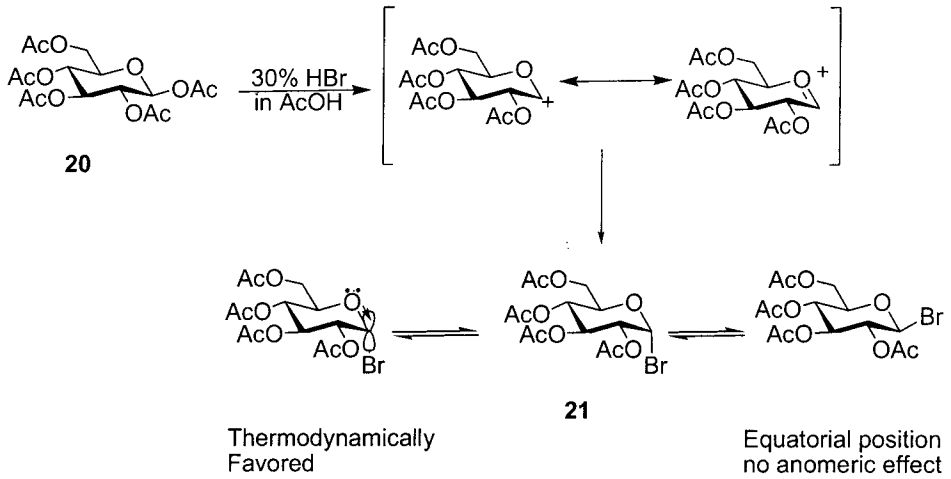


15 **Desired Product**

Equation 14

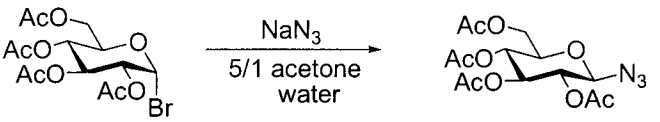
These reactions were not attempted at this time because none of the desired disaccharides were constructed. However the construction of various *N*-glycosides had been accomplished recently in the Norris group and it was decided to investigate whether this synthesis of glucose-derived *N*-glycosides could be improved using different reaction conditions.[19]

In order to form these *N*-glycosides a synthesis using cheap starting materials was employed. β-D-Glucose pentaacetate (**20**, Scheme 7) was treated with 30% HBr in acetic acid, which formed only the α form of the glycosyl bromide (**21**, scheme 7). When the acetyl group of the anomeric carbon on the starting material was protonated it could act as a leaving group, which breaks away because the secondary carbocation that forms is stabilized by the lone electron pairs of the endocyclic oxygen atom. Once this step has occurred the bromine ion can act as a nucleophile by means of a S_N1 reaction. Due to the participation of the lone pair of electrons on the oxygen atom, i.e. the anomeric effect, the thermodynamically favored product is in fact the α-bromide.



Scheme 7

The ^{1}H NMR spectrum of this product revealed a signal at 6.6 ppm that was the result of the bromide being added to the anomeric carbon. There were also signals present at 5.58, 5.18, 4.8, 4.3, and 4.15 ppm, which corresponded to other protons on the ring of the sugar. There were also four signals found at 2.0 ppm that resulted from the acetyl protecting groups that were located at carbons 2, 3, 4, and 6.



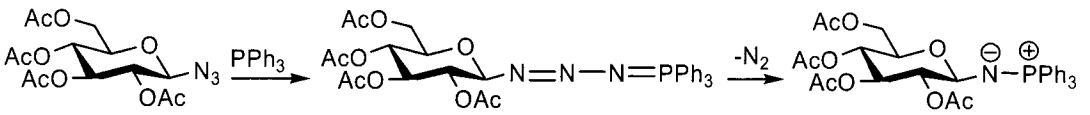
21 **22**

Equation 15

At this point the product glycosyl bromide was treated with sodium azide in a solution of 5/1 acetone to water. The stereospecificity of this S_N2 reaction resulted in only the beta product being produced (**22,** equation 15). The ^{1}H NMR of this product showed that the proton signal of the anomeric carbon, which was formerly found at 6.6 ppm in the bromide had now moved upfield to 4.62 ppm. This could be accounted for by the observation that a less electronegative azide group that allowed the H-1 to be shielded had replaced the electronegative bromine atom. The rest of the signals for the protons on the glucose ring structure were located in two different regions. There were three triplets found downfield from the anomeric proton's signal in the range between 4.9 ppm and 5.29 ppm. There were also two more signals found farther upfield at 4.19 ppm and 4.3 ppm. The signals for the acetate protecting groups remained unchanged at 2.0 ppm.

With the construction of the glycosyl azide complete the synthesis of different *N*-glycosides could now be investigated. It was decided to employ the use of polymer supported triphenylphosphine and various acid chlorides in an attempt to construct amide

bonds *via* the Staudinger reaction.[20] In the sequence below the intermediates are shown as phenyltriphosphine reacts with the glycosyl azide (Scheme 8).

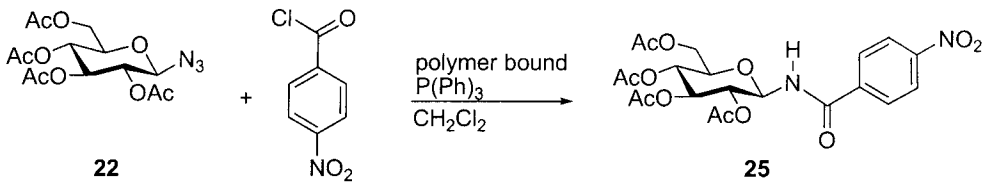


22 **23** **24**

Scheme 8

First the triazaphospadiene intermediate (**23**) forms. Then nitrogen gas is lost as the phosphinimine ylide (**24**) forms. Next one of a number of acid chlorides was added and the progress of the reaction was monitored by TLC. At this point the most effective reaction conditions had to be worked out.

The first acid chloride to be examined was *p*-nitrobenzoyl chloride. The nitrogen located in the phosphinimine ylide was able to act as a nucleophile and attack the highly electrophilic carbonyl group of the acid chloride. The resulting chloroimine intermediate was then attacked by a molecule of water. The chlorine acted as a leaving group and this sequence resulted in the formation of the final amide bond in **25** (equation 16).



22 **25**

Equation 16

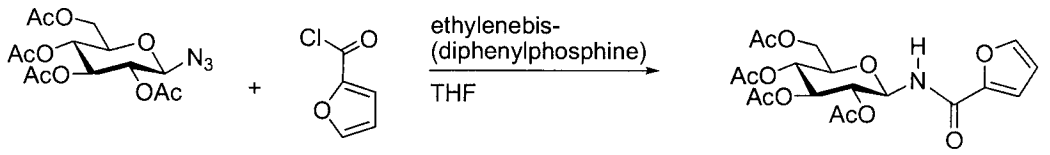
It was determined that if one equivalent of the acid chloride was added to the reaction mixture and the reaction refluxed for three hours the desired amide could be produced in yields ranging from 50-65%. However if two equivalents of acid chloride

were added to the reaction mixture the yield increased to greater then 85%. After complete reaction 1.3 equivalents of polymer-bound tris-(2-aminoethyl)-amine was added to the reaction mixture in order to remove the excess acid chloride. The acylated polymer was then removed *via* gravity filtration during the work up.

This reaction was then run with the cheaper tri(*n*-butyl)phosphine in order to obtain the desired amides. The solvent was also changed from methylene chloride to $CDCl_3$. The reaction was then monitored by ^1H NMR over a selected time period to see if the formation of any of the desired intermediates could be observed. Unfortunately the 1H spectra of the unpurified products were not clean. ^1H NMR of the final product revealed a singlet at 7.3 ppm. This corresponded to the N-H bonding to the anomeric carbon. The former signal at 4.62 ppm of the glycosyl azide had also disappeared. A new set of signals also appeared in the region between 8.2 ppm and 8.4 ppm, which accounted for the protons located on the phenyl group. The electron-withdrawing nitro group would have further deshielded these signals leading to the shift downfield from the normal aromatic region.

The method that had been employed for the reaction between the glycosyl azide **22** and *p*-nitrobenzoylchloride had produced the desired product; however it was found that a second method using a different phosphine derivative could produce the desired products in greater purity. It was discovered that the use of ethylenebis-(diphenylphosphine) (DPPE) in THF could be used in a quick and simple manner producing cleaner products. The reactions were still refluxed for various amounts of time and polymer-bound tris-(2-aminoethyl)-amine was still used to remove excess amounts of the acid chloride but the reaction mixtures were now washed over celite with cold THF as

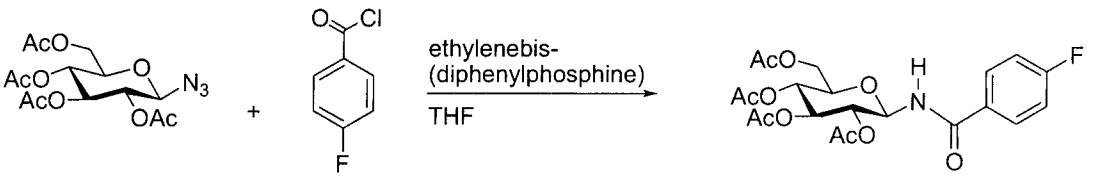
the organic layers were collected through a gravity filtration. Some of the amide products still were placed on wet silica columns and washed with the proper eluent system in order to produce clean material. The end result of this method was cleaner ^{1}H and ^{13}C spectra for amide **25** that were easy to interpret and purer products with accurate yields.



22 **26**

Equation 17

One of the first acid chlorides to be reacted with the azide was 2-furyl chloride (Equation 17). This reaction was refluxed for twenty four hours, and the formation of a new more polar spot on the TLC plate demonstrated that a reaction had taken place. After the work up the reaction yield was found to be 70%. A ^{1}H spectrum of the product (**26**) revealed that new signals were present in the range of 6.58 ppm to 7.75 ppm. These were the result of the protons on the aromatic ring of **26**. A new doublet also appeared at 7.2 ppm that resulted from the downfield shift of the proton bonded to the amide functional group.

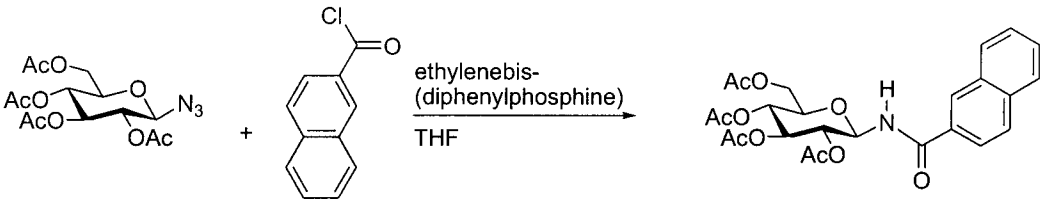


22 **27**

Equation 18

The next acid chloride that was reacted with the azide was 4-fluorobenzoyl chloride. TLC indicated that this reaction had gone to completion after 4.5 hours. A more polar spot had formed that was UV active, and this material was collected off of a wet

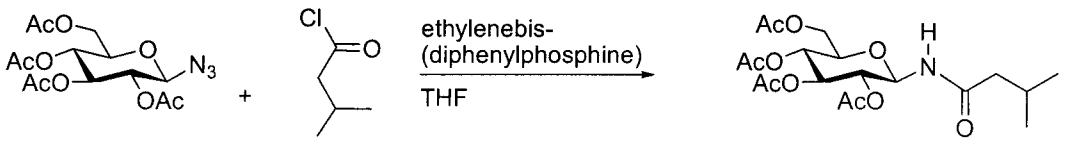
silica column after the workup was completed. The yield of this product was found to be 87.6%. A ^{1}H spectrum of this product (**27**, Equation 18) revealed a new set of signals in the range of 7.0 ppm to 8.15 ppm, which accounted for the protons in the aromatic system. The signal farthest downfield at 8.08 ppm could be accounted for by the deshielding effect of the fluorine atom attached to the aromatic ring. At 7.11 ppm a doublet was observed that resulted from the N-H of the amide functional group.



22 **28**

Equation 19

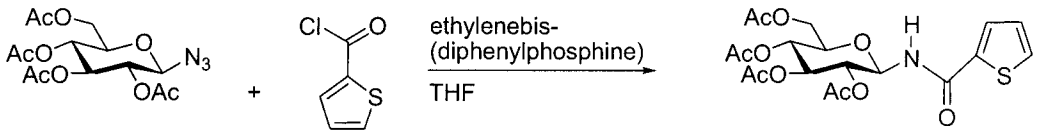
Another acid chloride that was reacted with the glycosyl azide **21** was 2-naphthoylchloride to give amide **28** (Equation 19). This reaction was refluxed overnight. TLC showed the formation of a less polar spot, which was isolated in 92.6% yield. The ^{1}H spectrum revealed two sets of multiplets in the region of 7.2 ppm – 7.4 ppm and 7.78 ppm – 7.84 ppm. These signals demonstrated that there were two types of aromatic protons located on the final product. A signal at 7.29 ppm revealed that the N-H bond had in fact formed and the amide functional group was present.



22 **29**

Equation 20

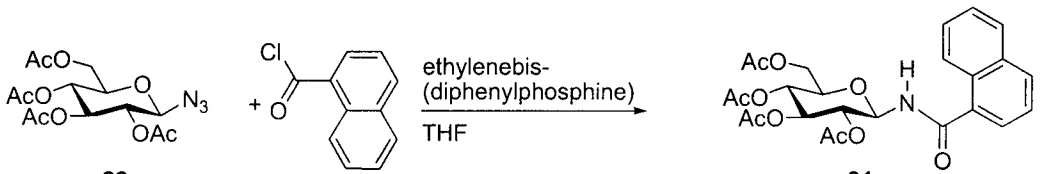
Next isovaleroyl chloride was reacted with the glycosyl azide to give amide **29** (Equation 20). After twenty four hours of refluxing TLC showed complete consumption of the starting material and the formation of a new more polar product. ^{1}H NMR showed a doublet at 6.29 ppm, which accounted for the N-H bond. There were also new signals present at 0.9 ppm and 1.2 ppm that accounted for the alpha and beta carbons on the isovaleroyl side chain bonded to the amide functional group.



22 **30**

Equation 21

2-Thiophenecarbonyl chloride was then reacted with the glycosyl azide **22**. After forty eight hours of refluxing the reaction TLC showed the formation of several spots. It was determined that a more polar spot that was forming represented the desired product (**30**, Equation 21). Polymer-bound tris-(2-aminoethyl)-amine was then added to the reaction as it was stirring to remove the excess acid chloride. Then the reaction was washed over celite and the organic layers were collected and concentrated under reduced pressure. A ^{1}H NMR spectrum was then taken of the product, in which the signals in the range of 7.0 ppm to 8.0 ppm demonstrated that an aromatic group was present on the new product. A doublet located at 7.38 ppm revealed that the N-H bond had in fact formed.



22 **31**

Equation 22

Finally 1-naphthoylchloride was added to the glycosyl azide **22** (Equation 22). After eight hours TLC showed the formation of a more polar spot, and after the reaction was worked up a ^{1}H NMR showed a series of signals located in the region between 7.4 ppm and 8.0 ppm. These were the result of the aromatic protons present in the aromatic system of amide **31**. A doublet at 6.9 ppm showed the N-H bond had formed.

In conclusion it can be demonstrated that new synthetic methods were investigated in order to improve the overall purity and yield of several previously constructed compounds. With the completion of the glycosyl amide compounds the construction of a library of synthetic sugars has begun. In the future this library may be expanded due to the research that has presently been completed.

Progress has also been made with the different dithiane derivatives that were synthesized. Hopefully one of these derivatives will be used in the final formation of a *C*-disaccharide. Perhaps future work will lead to other dithiane derivatives that may be successfully employed in the desired synthesis. If this occurs the research that was recently completed should provide useful insights for different problems that might arise.

Experimental

General Procedures

The reaction progress was monitored by thin layer chromatography (TLC) with UV light detection since most of the reaction materials are UV active. The TLC plate was treated with a 5% sulfuric acid/ethanol solution to burn the reaction material to provide the indication of carbohydrate product. Isolation of products was done by recrystallization and flash chromatography performed with 32-63 μm, 60-Å silica gel. A Varian Gemini 2000 NMR system was used for ^{1}H and ^{13}C NMR spectroscopy at 400 MHz and 100 MHz respectively, using $CDCl_3$. Proton and carbon chemical shifts (δ) are recorded in parts per million (ppm). Splitting patterns of multiplets are labeled as follows: s (singlet), d (doublet), dd (doublet of doublets), ddd (doublet of doublet of doublets), t (triplet), q (quartet), and m (multiplet) with coupling constants (*J*) measured in Hz.

Formation of 2 by reaction of *tert*-butylchlorodiphenylsilane (TBDPSCl) with methyl α-D-glucopyranoside.

4.2 grams (20.16 mmol) of methyl α-D-glucopyranoside and 2.9 grams of imidazole were placed in an oven-dried round bottom flask. A septum was added. The reagents were then dissolved in anhydrous DMF (50 mL) by use of a needle and syringe. The reaction mixture was placed under inert atmosphere (N_2) by use of a balloon. A mixture of acetone and ice was used to cool the reaction mixture to –10 °C. The mixture was then magnetically stirred for ten minutes, and then 5 mL of TBDPSCl was added dropwise by syringe. The reaction then stirred for 42 hours. TLC (ethyl acetate) showed complete consumption of the starting material and that a new less polar spot had formed. The

reaction was then poured over 30 mL of distilled water in a separatory funnel. It was then washed with CH_2Cl_2 (2 x 30mL). The organic layers were collected and dried over magnesium sulfate. The drying agent was removed by gravity filtration. The organic layers were then concentrated under vacuum to produce a white syrup (8.7 grams, 20.12 mmol) that revealed a yield of 99.8 %.

^{1}H NMR ($CDCl_3$): δ 1.04 (s, 9H, *t*-butyl), 3.37 (s, 3H, OCH_3), 3.51 (m, 2H, H6, H6'), 3.64 (m, 1H, H5), 3.73 (t, 1H, J = 9.15 Hz, H4), 3.90 (m, 2H, H2, H3), 4.73 (d, 1H, J = 3.66 Hz, H1), 7.35 - 7.72 (m, 10H, Ar-H).

The signals in this ^{1}H NMR spectrum agreed with a known compound reported by Jason L. McCartney in his thesis completed at Youngstown State University in August, 2001.[18]

Protection of hydroxyl groups of 2 as benzyl ethers to form 3.

A three neck round bottom flask was oven-dried and fitted with a reflux condenser. Then 4.0 grams (9.26 mmol) of compound **2** was placed inside and septa were added to the flask. Compound **2** was dissolved in dry THF (50 mL) and an inert atmosphere was established using a balloon and nitrogen gas. Next 1.47 grams (37.98 mmol) of sodium hydride was added slowly *via* spatula. The reaction mixture was stirred for twenty minutes and turned a milky white. The reaction was then gently warmed as 4.5 mL (37.98 mmol) of benzyl bromide was added dropwise by syringe over a five-minute span. After twenty four hours TLC (6/1 hexanes to ethyl acetate) showed the formation of several less polar spots. The reaction mixture was poured over distilled water in a separatory funnel and then washed with methylene chloride (2 x 20 mL). The organic layers were

collected and dried over magnesium sulfate. The drying agent was removed by gravity filtration and the organic layers were then removed under vacuum. A thick yellow syrup was collected and placed on a silica column (65 grams). The product was eluted with hexanes to remove excess benzyl bromide and then 20/1 hexanes to ethyl acetate to collect the 3.6 grams of the desired product for a yield of 55%. Thin white crystals were collected from the eluent under reduced pressure and a ^{1}H spectrum was taken.

^{1}H NMR ($CDCl_3$): δ 1.03 (s, 9H, *t*-butyl), 3.36 (s, 3H, OCH_3), 3.53 - 3.70 (m, overlapping, 3H, H5, H6, H6'), 3.86 (m, 2H, H2, H3), 3.98 (t, 1H, J = 8.79 Hz, H4), 4.58 (d, 1H, J = 3.67 Hz, H1), 4.65 - 4.98 (m, overlapping, 6H, CH_2Ph), 7.24 - 7.70 (m, 25H, Ar-H).

The signals in this ^{1}H spectrum agree with the previously known compound reported by Jason L. McCartney in his thesis completed in August, 2001.[18]

Desilylation of 3 to form primary alcohol 4.

In a round bottom flask 1.3 grams (1.8 mmol) of compound **3** was dissolved in 35 mL of dry THF. A septum was added to enclose the solution and 1.84 mL of TBAF was then added dropwise to the reaction mixture. After eight hours TLC (4/1 hexanes to ethyl acetate) showed complete consumption of the starting material and a more polar spot had formed. The reaction was poured over distilled water in a separatory funnel and then washed with methylene chloride (2 x 20 mL). The organic layers were collected and dried over magnesium sulfate. The drying agent was removed by gravity filtration and the organic layers were concentrated under reduced atmosphere. A dark yellow-orange syrup was collected and placed on a wet column of silica gel (28 grams). The product was then

washed with 5/1 hexanes to ethyl acetate followed by 1/1 hexanes to ethyl acetate. After the desired product was collected from the fractions the eluent was removed under reduced pressure. A yellow syrup (0.6 grams, 1.29 mmol) of was then collected for an overall yield of 69%.

^{1}H NMR ($CDCl_3$): δ 3.37 (s, 3H, *t*-butyl), 3.52 (m, 2H, H6, H6'), 3.63 - 3.77 (m, overlapping, 3H, H2, H3, H5), 4.02 (t, 1H, J = 9.15 Hz, H4), 4.56 (d, 1H, J = 3.66 Hz, H1), 4.62 - 5.01 (m, overlapping, 6H, CH_2Ph), 7.27 - 7.40 (m, 15H, Ar-H).

The signals in this ^{1}H spectrum agreed with the known compound reported by Jason L. McCartney in his thesis completed in August, 2001.[18]

Formation of triflate 5.

A round bottom flask was flame dried and then fitted with a septum after it had cooled to room temperature. Pyridine (0.47 mL) was then added by syringe. Then distilled methylene chloride (40 mL) was added by syringe. The reaction mixture was then cooled to –10 °C by placing the round bottom flask in an acetone and ice mixture. An inert atmosphere (N_2) was then established by use of a balloon. Next 0.65 mL of Tf_2O was added to the solution dropwise by syringe. The reaction stirred for twenty minutes as a cloudy white precipitate formed. Then 0.7 grams (1.5 mmol) of compound **4** was dissolved in 5mL of dry methylene chloride and added to the reaction mixture dropwise *via* syringe. The reaction stirred for three hours when TLC (4/1 hexanes to ethyl acetate) showed complete consumption of the starting material and the formation of a less polar product. The mixture was then poured over distilled water in a separatory funnel and the solution was then washed with methylene chloride (2 x 20mL). The organic layers were

collected and dried over magnesium sulfate. The drying agent was removed by gravity filtration and the organic layers were then condensed under reduced pressure. A brown syrup was collected, which was then extracted using hot hexanes (2 x 15 mL). The extracted layers were then condensed under reduced pressure to produce 0.7 grams (1.1 mmol) of a yellow syrup for a yield of 78%.

This compound was reported by Jason L. McCartney in his thesis completed in August, 2001.[18]

Formation of bisphenylthiomethane derivative 6.

1.76 g of bisphenylthiomethane was placed in a flame-dried round bottom flask. The flask was sealed with a septum and the solid was dissolved in dry THF (40 mL) by use of a syringe. Inert atmosphere was then established using a balloon and needle (N_2). The reaction mixture was then cooled to – 78 °C by lowering the round bottom flask into a mixture of dry ice and acetone. Then 4.7 mL (7.5 mmol) of *n*-butyl lithium was added dropwise *via* syringe and the solution turned a light yellow. The reaction was then stirred magnetically for twenty minutes after which 1.24 g (2.0 mmol) of triflate **5** was dissolved in 5mL of dry THF and added dropwise to the solution. The reaction ran overnight as it warmed to room temperature. TLC (6/1 hexanes to ethyl acetate) then revealed the formation of a less polar spot. The reaction was poured over distilled water in a separatory funnel. It was then washed with methylene chloride (2 x 25 mL) and the organic layers were collected. The organic layers were then dried over magnesium sulfate. Then the drying agent was removed by gravity and the organic layers were collected and concentrated to a red syrup under reduced pressure. The residue was then

placed on a wet silica column and flushed with hexanes, to remove excess bisphenyl-thiomethane, and then 18/1 hexanes to ethyl acetate to collect the desired product. The eluent was removed from the identified fractions by concentration under reduced pressure to afford 0.9 grams (1.32 mmol) of a reddish-brown syrup as a product for an overall yield of 64%.

^{1}H NMR ($CDCl_3$): δ 1.96 (m, 1H, H6), 2.28 (m, 1H, H6'), 3.21 (t, 1H, J = 9.52 Hz, H3), 3.48 (s, 3H, OCH_3) 3.55 (dd, 1H, J = 3.30, 9.20 Hz, H2), 4.01 (dd, 1H, J = 9.20, 9.52 Hz, H4), 4.24 (m, 1H, H5), 4.54 (m, 1H, H7), 4.63 (d, 1H, J = 3.30 Hz, H1), 4.72 - 5.09 (m, overlapping, 6H, CH_2Ph), 7.23 - 7.58 (m, 25H, Ar-H).

The signals in this ^{1}H spectrum agree with those of a known compound reported by Jason L. McCartney in his thesis completed in August, 2001.[18]

Methylation of dithiane 6.

0.1 grams (0.147 mmol) of **5** was dissolved in anhydrous THF (15 mL) in a flame dried round bottom flask. The reaction flask was fitted with a septum and N_2 atmosphere was established. The reaction was cooled to –78 °C and 0.11 mL (0.68 mmols) of *n*-butyl lithium was added dropwise to the solution. The reaction then stirred for twenty minutes, after which 0.1 mL of methyl iodide was added dropwise. The reaction then stirred overnight. TLC (6/1 hexanes to ethyl acetate) showed the formation of a new slightly less polar spot. The reaction was poured over saturated ammonium chloride and placed in a separatory funnel. The mixture was then washed with methylene chloride (2 x 20 mL). The organic layers were collected and dried over magnesium sulfate. Gravity filtration was used to remove the drying agent and the organic layers were collected and then

condensed under reduced pressure. 0.08 grams (0.115 mmol) of crude product were collected for a 78 % yield. A ^{1}H NMR spectrum was then taken of the crude product.

^{1}H NMR ($CDCl_3$): δ 1.86 (q, 1H, H6'), 2.34 (d, 1H, H6), 3.14 (q, 1H, H3), 3.42 (s, 3H, OCH_3), 3.52 (m, 1H, H2), 3.63 (s, 3H, H7), 4.02 (m, 1H, H4), 4.18 (t, 1H, H5), 4.40 - 5.04 (m, 6H, CH_2Ph), 7.14 - 7.74 (m, 25H, Ar-H).

Oxidation of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (8) to form lactone 9.

In an oven dried round bottom flask 2.0 grams (3.7 mmol) of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose and 3.7 grams of 4 Å molecular sieves were added to 50 mL of dry methylene chloride. The flask was sealed with a septum and magnetically stirred for twenty minutes. 3.7 grams (17.1 mmol) of PCC was then added to the reaction and it turned dark brown. The reaction was allowed to stir overnight. After twenty four hours TLC 6/1 hexanes to ethyl acetate showed the formation of a less polar spot and complete consumption of the starting material. The reaction was then poured over thirty grams of wet silica in a flash column. The column was then run using an eluent of 6/1 hexanes to ethyl acetate. The product was then collected and concentrated under reduced pressure. 1.96 grams (3.6 mmol) of product was collected as a clear syrup for an overall yield of 97.3%. A ^{1}H spectrum was then taken of the final product.

^{1}H NMR: δ 3.70 (m, 1H, H6), 3.95 (m, 1H, H6'), 4.17 (m, 2H, H3, H5), 4.50 - 5.01 (m, 9H, 4 x CH_2Ph, H2), 7.24 - 7.42 (m, 20 H, Ar-H).

^{13}C NMR ($CDCl_3$): δ 69.4, 74.7, 74.9, 75.2, 79.3, 128.9, 129.0, 129.4, 129.5, 138.5, 170.3.

Addition of methyl iodide to bisphenylthiomethane to produce 11.

In a flame-dried round bottom flask 0.55 grams (2.36 mmol) of bisphenylthiomethane was dissolved in 15 mL of anhydrous THF. A septum was added and N_2 atmosphere was established. The reaction was cooled to –78 °C and 1.55 mL of *n*-butyl lithium (2.5 mmol) was added dropwise to the reaction mixture. The reaction then stirred for twenty minutes, after which 0.2 mL of methyl iodide (3.2 mmol) was then added to the reaction by syringe. The reaction then stirred overnight and (TLC 6/1 hexanes to ethyl acetate) showed little change. The reaction was poured over water and placed in a separatory funnel. It was washed with methylene chloride (2 x 10 mL) and the organic layers were collected. The organic layers were dried over magnesium sulfate and the drying agent was then removed by gravity filtration. The organic layers were condensed under reduced pressure to give 0.41 g (1.6 mmol) of crude product for a yield of 67 %.

^{1}H NMR ($CDCl_3$): δ 1.66 (d, 3H, J = 6.67 Hz, H_b), 4.60 (q, 1H, J = 6.95 Hz, H_a), 7.31 - 7.55 (m, 10H, Ar-H).

Addition of lithiated bisphenylthiomethane to lactone 12 to form 13.

0.5 grams of bisphenylthiomethane was placed in an oven-dried round bottom flask. It was then dissolved in dry THF (15 mL) and the flask was fitted with a septum. A needle and balloon were then employed to establish an inert atmosphere using N_2 gas. The solution was then cooled to – 78 °C using a mixture of dry ice and acetone. Then 3.0 mL (4.7 mmoL) of *n*-butyl lithium was added dropwise to the solution. The solution stirred for twenty minutes. Then 0.5 grams (3.16 mmol) of the lactone 2-3-*O*-isopropyldene-D-erythronolactone was dissolved in THF and added dropwise to the solution. The reaction

stirred for two days. TLC (6/1 hexanes to ethyl acetate) showed the formation of a new less polar spot. The reaction was then quenched in a separatory funnel using saturated NH_4Cl. The reaction was washed with methylene chloride 2 x 20 mL in the separatory funnel and the organic layers were then collected. Magnesium sulfate was then used to dry the organic layers and it was removed by gravity filtration. The organic layers were then concentrated under reduced pressure to produce 0.62 grams of a clear syrup for a yield of 50%. A ^1H NMR spectrum was then taken of the product.

^1H NMR: δ 1.38 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 3.95 (d, 1H, J = 10.61 Hz, H-5), 4.20 (dd, 1H, J = 3.75, 10.25 Hz, H5'), 4.79 (d, 1H, J = 5.92 Hz, H1), 4.91 (m, 2H, H4, H-3), 7.19 - 7.53 (m, 10H, Ar-H).

The signals in this ^1H spectrum agree with those of a known compound reported by Jason L. McCartney in his thesis completed in August, 2001.[18]

Addition of bisphenylthiomethane to lactone 9 to form 14.

In an oven-dried round bottom flask 0.464 grams (2.0 mmol) of bisphenylthiomethane was dissolved in dry THF (15 mL). An inert atmosphere was then established using a septum, N_2 gas, and a balloon. The reaction was cooled to –78 °C using an acetone and dry ice bath. Then 1.25 mL (2 mmol) of *n*-butyl lithium was added to the reaction dropwise. The reaction stirred for twenty minutes and then 0.86 grams of the 2,3,4,6 - tetra-*O*-benzyl-D-gluconolactone was dissolved in THF and added dropwise to the solution. The reaction stirred for fifty five minutes after which (TLC 6/1 hexanes to ethyl acetate) showed the formation of a non polar spot. The reaction was quenched in a separatory funnel over saturated NH_4Cl, and then the mixture was washed with

methylene chloride (2 x 20 mL). The organic layers were collected and dried over magnesium sulfate. The drying agent was removed by gravity filtration and the organic layers were then concentrated under reduced pressure. A thick white syrup was collected and placed on a wet silica column (20 grams of silica). The column was then eluted with 6/1 hexanes to ethyl acetate and the relevant fractions were collected and concentrated under reduced pressure producing 0.58 grams (0.75 mmol) of product for an overall yield of 46.5%. A ^{1}H NMR spectrum of the product was then taken.

^{1}H NMR ($CDCl_3$): δ 3.68 - 4.07 (m, overlapping, H3, H4, H5), 4.37 - 4.83 (m, overlapping, 8H, CH_2Ph), 4.91 - 5.15 (m, overlapping, 2H, H2, H7), 7.15 - 7.50 (m, 30H, Ar-H).

^{13}C NMR ($CDCl_3$): δ 41.78, 54.89, 68.94, 69.50, 69.80, 73.95, 74.39, 74.81, 76.18, 77.42, 77.79, 79.74, 80.82, 82.19, 85.22, 85.71, 99.58, 170.31.

Formation of bismethylthiomethane derivative 17.

In a flame-dried round bottom flask 0.37 mL of bismethylthiomethane (3.7 mmols) was dissolved in anhydrous THF. A septum was added and N_2 atmosphere was established. The reaction was cooled to –78 °C and 2.3 mL of *n*-butyl lithium (3.7 mmols) was added dropwise turning the reaction mixture light yellow. The reaction stirred for twenty minutes and then 1.48 grams of triflate **5** (2.4 mmols) was added by syringe to the reaction. The reaction stirred overnight. TLC 6/1 (hexanes to ethyl acetate) showed the formation of a less polar spot. The reaction was then poured over ammonium chloride and placed in a separatory funnel. It was then washed with methylene chloride (2 x 20 mL). The organic layers were collected and dried over magnesium sulfate. The drying

agent was removed by gravity filtration and the organic layers were condensed under reduced pressure to produce 0.9 grams of a yellow syrup for an overall yield of 66%. A ^{1}H NMR spectrum was then taken of the final product.

^{1}H NMR ($CDCl_3$): δ 2.16 (s, 6H, SCH_3) 2.62 (m, 1H, H6) 2.88 (m, 1H, H6'), 3.44 (m, overlapping, 4H, OCH_3, H7), 3.57 (dd, 1H, J = 3.70, 5.92 Hz, H2), 3.87 (m, 1H, H3), 4.04 (m, 1H, H4), 4.60 - 5.01 (m, overlapping, 7H, H1, CH_2Ph), 7.29 - 7.42 (m, 15H, Ar-H).

^{13}C NMR ($CDCl_3$): δ 20.24, 27.75, 28.07, 30.02, 56.12, 56.33, 71.76, 81.23, 83.07, 98.72, 99.48, 128.45, 128.72, 129.25, 129.80, 130.16, 135.49, 136.14, 136.28, 139.00, 139.63.

Formation of glycosyl bromide 21.

10.0 g (25 mmol) of β-D-glucose pentaacetate was placed in a round bottom flask. A septum was used to seal the flask and then 40 mL of 30 % HBr in acetic acid was added by syringe. The reaction stirred overnight. TLC (1/1 hexanes to ethyl acetate) showed the starting material was completely consumed and a less polar spot had formed. The reaction mixture was poured over saturated sodium bicarbonate solution in a separatory funnel and washed with methylene chloride (2 x 30 mL). The organic layers were collected and dried over magnesium sulfate. The drying agent was removed by gravity filtration. The organic layers were then concentrated under reduced pressure to give 9.7 grams (23 mmol) of product as an orange syrup for an overall yield of 94 %. A ^{1}H NMR spectrum was then taken of the product.

^{1}H NMR ($CDCl_3$): δ 2.03 - 2.10 (4s, 12H, $COCH_3$), 4.13 (d, 1H, J = 10.6 Hz, H6), 4.31 (m, 2H, H5, H6'), 4.83 (dd, 1H, J = 4.02, 9.93 Hz, H2), 5.16 (t, 1H, J = 9.51 Hz, H3), 5.56 (t, 1H, J = 9.53 Hz, H4), 6.61 (d, 1H, J = 4.02 Hz, H1).

The signals in this ^{1}H spectrum agree with those of the known compound reported by Yuriko Root in her thesis completed in May, 2003.[19]

Formation of the glycosyl azide 22.

In a round bottom flask 8.4 g (20.0 mmol) of the bromo sugar (**21**) was dissolved in a 5/1 acetone to water mixture. 4.0 g of sodium azide was added to the solution and it stirred magnetically overnight. TLC (1/1 hexanes to ethyl acetate) showed a more polar spot had formed. The reaction was poured over a saturated sodium bicarbonate solution in a separatory funnel and washed with methylene chloride (2 x 25 mL). The organic layers were collected and dried over magnesium sulfate. The drying agent was removed by gravity filtration. The product was then concentrated under reduced pressure yielding a thick brown syrup. This syrup was recrystallized using methanol to give 7.83 grams (20.0 mmol) of a white powder for a yield of 100%. A ^{1}H NMR spectrum was then taken of the final product.

^{1}H NMR ($CDCl_3$): δ 2.00 - 2.09 (4s, 12H, $COCH_3$), 3.79 (m, 1H, H5), 4.16 (dd, 1H, J = 2.21, 12.40 Hz, H6) 4.26 (dd, 1H, J = 4.81, 12.40 Hz, H6'), 4.64 (d, 1H, J = 8.72 Hz, H1), 4.95 (t, 1H, J = 9.54 Hz, H2), 5.09 (t, 1H, J = 9.53 Hz, H3), 5.21 (t, 1H, J = 9.51 Hz, H4).

The signals in this ^{1}H spectrum agree with those of the known compound reported by Yuriko Root in her thesis completed in May, 2003.[19]

Addition of *p*-nitrobenzoyl chloride to glycosyl azide 22 to form amide 25.

0.1 g (0.26 mmol) of glycosyl azide **22** and 0.09 g (~0.5 mmol) of *p*-nitrobenzoyl chloride were placed in a two neck round bottom flask and then dissolved with 7 mL of methylene chloride. The flask was fitted with a reflux condenser and a septum. Polymer-supported triphenylphosphine (1.0 g) was then added to the reaction and it was stirred magnetically for thirty minutes. The reaction was then refluxed for three hours. TLC (3/1 hexanes to ethyl acetate) showed the formation of a new more polar spot with some starting material left over. The reaction was gravity filtered and the solids washed with methylene chloride (3 x 15 mL). The organic layers were collected and were concentrated under reduced pressure. A ^{1}H NMR spectrum was then taken of the product.

^{1}H NMR ($CDCl_3$): δ 2.01 - 2.08 (3s, 12H, 4 x $COCH_3$), 3.91 (m, 1H, H5), 4.10 (m, 1H, H6), 4.34 (dd, 1H, J = 4.33, 12.80 Hz, H6'), 5.01 - 5.13 (m, 2H, H3, H4), 5.40 (m, 1H, H2), 7.26 (d, 1H, N-H), 7.93 - 8.30 (m, 4H, Ar-H).

The signals in this ^{1}H spectrum agree with the same compound reported by Yuriko Root in her thesis completed in May, 2003.[19]

Addition of 2-furoyl chloride to the glycosyl azide 22 to form amide 26.

In an oven-dried round bottom flask 0.37g (1 mmol) of the glycosyl azide was dissolved in dry THF. 0.194 mL of 2-furoyl chloride (2.0 mmol) was then added dropwise to the reaction mixture. DPPE (0.5 mmol) in THF was then added dropwise to the solution and it was stirred for thirty minutes. The round bottom flask was then fitted with a reflux condenser and the reaction was refluxed for twenty four hours. TLC (1/1 hexanes to ethyl acetate) showed the formation of a more polar spot. The reaction was cooled to room

temperature and 0.6 grams of polymer-bound tris-(2-aminoethyl)-amine was added and the reaction stirred. The reaction was then filtered through celite and washed with cold THF. The filtrate was then condensed under reduced pressure and a ^{1}H spectrum of the crude material was taken. The crude product was then placed on a wet silica column (15 grams) and washed through by an eluent system of 1/1 hexanes to ethyl acetate. A ^{1}H NMR spectrum was taken of the purified product. 0.31 g of product was collected to afford a yield of 70%.

^{1}H NMR ($CDCl_3$): δ 2.01 - 2.06 (4s, 12H, 4 x $COCH_3$), 3.88 (m, 1H, H5), 4.08 (dd, 1H, J = 1.85, 12.40 Hz, H6), 4.31 (dd, 1H, J = 4.40, 12.41 Hz, H6') 5.08 (m, 2H, H3, H4), 5.37 (m, 2H, H1, H2), 7.17 (d, 1H, NH), 7.41 - 7.70 (m, 3H, Ar-H). The signals in this ^{1}H spectrum agree with those of the previously known compound reported by Yuriko Root in her thesis completed in May, 2003.[19]

Addition of 4-fluorobenzoyl chloride to the glycosyl azide 22 to form amide 27.

In an oven-dried round bottom flask 0.37g (1 mmol) of the glycosyl azide was dissolved in dry THF. 0.24 mL (2.0 mmol) of 4-fluorobenzoyl chloride was then added dropwise to the reaction mixture. DPPE (0.5 mmol) in THF was then added dropwise to the solution and it was stirred for thirty minutes. The round bottom flask was then fitted with a reflux condenser and the reaction was refluxed for four and a half hours. TLC (1/1 hexanes to ethyl acetate) showed the formation of a more polar spot. The reaction was cooled to room temperature. 1.0 g of polymer-supported tris-(2-aminoethyl)-amine was added and the reaction stirred for thirty minutes. The reaction was then filtered through celite and washed with cold THF. The mixture was then condensed under reduced pressure to

collect the crude product, which was then placed on a wet silica column (30 grams) and washed through by an eluent system of 1/1 hexanes to ethyl acetate. 0.41 g of product was collected to afford a yield of 87.6%.

^{1}H NMR ($CDCl_3$): δ 2.03 - 2.08 (4s, 12H, 4 x $COCH_3$), 3.89 (m, 1H, H5), 4.08 (dd, 1H, J = 1.82, 12.40 Hz, H6), 4.33 (dd, 1H, J = 4.31, 12.80 Hz, H6'), 5.04 - 5.46 (m, 4H, H1, H2, H3, H4), 7.10 (d, 1H, NH), 7.11 - 8.12 (m, 4H, Ar-H).

^{13}C NMR ($CDCl_3$): δ 21.76, 21.98, 22.12, 22.30, 68.93, 69.64, 71.64, 72.34, 73.56, 74.60, 116.78, 116.83, 129.83, 129.86, 167.20, 170.62.

The signals in these spectra agree with those of the known compound reported by Yuriko Root in her thesis completed in May, 2003.[19]

Addition of 2-naphthoyl chloride to glycosyl azide 22 to form amide 28.

In an oven-dried round bottom flask 0.37 g (1 mmol) of the glycosyl azide was dissolved in dry THF. 0.38 g of 2 naphthoyl chloride (2 mmol) was then added dropwise to the reaction mixture. DPPE (0.5 mmol) in THF was then added dropwise to the solution and it was stirred for thirty minutes. The round bottom flask was then fitted with a reflux condenser and the reaction refluxed overnight. TLC (1/1 hexanes to ethyl acetate) showed the formation of a more polar spot. The reaction was cooled to room temperature and 1.0 g of polymer-bound tris-(2-aminoethyl)-amine was added and the reaction stirred for one and a half hours. The reaction was then filtered through celite and washed with cold THF. The solution was then condensed under reduced pressure and the crude product was placed on a wet silica column (30 grams) and washed through by an eluent

system of 1/1 hexanes to ethyl acetate. A ^{1}H NMR spectrum was taken of the purified product. 0.436 g of product was collected to afford a yield of 92.6%.

^{1}H NMR ($CDCl_3$): δ 2.03 -2.06 (4s, 12H, $COCH_3$), 3.92 (m, 1H, H5), 4.11 (dd, 1H, J = 1.82, 12.40 Hz, H6), 4.36 (dd, 1H, J = 4.32, 12.81 Hz, H6'), 5.12 (m, 2H, H3, H4), 5.41 (t, 1H, J = 9.51 Hz, H2), 5.51 (t, 1H, J = 9.52 Hz, H1), 7.31 (d, 1H, J = 9.20 Hz, NH), 7.52 - 7.94 (m, 7H, Ar-H).

^{13}C NMR ($CDCl_3$): δ 20.0, 63.0, 69.0, 72.0, 74.0, 75.0, 80.0, 129.0, 169.5, 170, 171.0, 172.0, 173.0.

The signals in these spectra agree with those of the known compound reported by Yuriko Root in her thesis completed in May, 2003.[19]

Addition of isovaleroyl chloride to the glycosyl azide 22 to form amide 29.

In an oven-dried round bottom flask 0.37g (1 mmol) of the glycosyl azide was dissolved in dry THF. 0.24 mL of isovaleroyl chloride was added dropwise to the solution as it was magnetically stirred. DPPE (0.5 mmol) in THF was then added dropwise to the solution and it was stirred for thirty minutes. Then the reaction was refluxed for twenty four hours. As it refluxed the reaction turned brown and a white precipitate formed. TLC (1/1hexanes to ethyl acetate) showed a more polar spot had formed. The reaction mixture was poured over celite and washed with cold THF. The organic layer was collected and concentrated under reduced pressure. 0.53 grams of the crude product was placed on a wet silica column and washed through with a 1/1 hexanes to ethyl acetate eluent system. The relevant fractions were collected and concentrated under reduced pressure. A ^{1}H

NMR spectrum of the pure product was taken. 0.421 grams of the final product was collected to produce a yield of 97.6 %.

^{1}H NMR ($CDCl_3$): δ 0.83 - 0.90 (m, 7H, 2 x CH_3, CH), 1.95 - 2.00 (4s, 12H, 4 x $COCH_3$), 2.13 (t, 2H, CH_2), 3.77 (m, 1H, H5), 4.02 (m, 1H, H6), 4.26 (dd, 1H, J = 4.30, 12.41 Hz, H6'), 4.87 (t, 1H, J = 9.80 Hz, H2), 5.00 (t, 1H, J = 9.80 Hz, H4), 5.24 (m, 1H, H3), 6.53 (d, 1H, J = 9.50 Hz, N-H).

The signals in this ^{1}H NMR spectrum correspond to those of the known compound reported by Yuriko Root in her thesis completed in May, 2003.[19]

Addition of 2-thiophenecarbonyl chloride to the glycosyl azide 22 to form amide 30.

In an oven-dried round bottom flask 0.37g (1 mmol) of the glycosyl azide was dissolved in dry THF. 0.216 mL (2 mmol) of 2-thiophenecarbonyl chloride was added dropwise to the solution. DPPE (0.5 mmol) in THF was then added dropwise to the solution and it began to fizz slightly. The reaction stirred for twenty minutes. Then the reaction was allowed to reflux for forty eight hours. TLC showed the formation of several new U.V. active spots with the complete consumption of the starting material. 1 g of polymer-supported tris-(2-aminoethyl)-amine was added to the reaction and it was allowed to stir for twenty minutes. The reaction was then poured over celite and washed with cool THF. The organic layer was collected and concentrated under reduced pressure. A ^{1}H NMR spectrum was taken of the product. 0.35 g of product corresponded to a yield of 76.9%.

^{1}H NMR ($CDCl_3$): δ 2.02 - 2.08 (4s, 12H, 4 x $COCH_3$), 3.90 (m, 1H, H5), 4.09 (m, 1H, H6), 4.34 (dd, 1H, J = 4.30, 12.82 Hz, H6'), 5.01 - 5.13 (m, 2H, H2, H4),

5.37 (m, 2H, H1, H3), 7.00 (d, 1H, J = 8.40 Hz, N-H), 7.08 (t, 1H, H9), 7.51 (dd, 2H, H7, H8).

The signals in this ^{1}H NMR spectrum agree with those of the known compound reported by Yuriko Root in her thesis completed in May, 2003.[19]

Addition of 1-naphthoyl chloride to the glycosyl azide 22 to form amide 31.

In an oven-dried round bottom flask 0.37g (1 mmol) of the glycosyl azide was dissolved in dry THF. 0.3 mL (2 mmol) of 1-naphthoyl chloride (2 mmol) was then added dropwise to the reaction mixture. DPPE (0.5 mmol) in THF was then added dropwise to the solution and it was stirred. The round bottom flask was then fitted with a reflux condenser and the reaction was refluxed for eighteen and a half hours. TLC (1/1 hexanes to ethyl acetate) showed the formation of a U.V. active spot that was more polar than the starting material. 1.0 g of polymer-bound tris-(2-aminoethyl)-amine was added to the reaction mixture and it was allowed to stir for ten minutes. The reaction was poured over celite and washed with cold THF. The organic layer was collected and concentrated under reduced pressure. A ^{1}H NMR spectrum was then taken of the product. 0.45 g (0.89 mmol) of product was collected to produce a percent yield of 89 %.

^{1}H NMR ($CDCl_3$): δ 2.04 - 2.09 (3s, 3H, $COCH_3$), 3.95 (m, 1H, H5), 4.15 (d, 1H, J = 12.40 Hz, H6) 4.37 (dd, 1H, J = 4.42, 12.44 Hz, H6'), 5.04 (m, 2H, H3, H4), 5.40 (t, 1H, J = 9.86 Hz, H2), 5.58 (t, 1H, J = 9.52 Hz, H1), 6.81 (d, 1H, NH), 7.45 - 7.95 (m, 7H, Ar-H).

^{13}C NMR ($CDCl_3$): δ 22.0, 63.0, 69.0, 72.0, 74.0, 75.0, 79.0, 125.0 - 135.0, 170. 171.0 - 172.0.

The signals in these spectra are in agreement with those of the known compound reported by Yuriko Root in her thesis completed in May, 2003.[19]

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Appendix

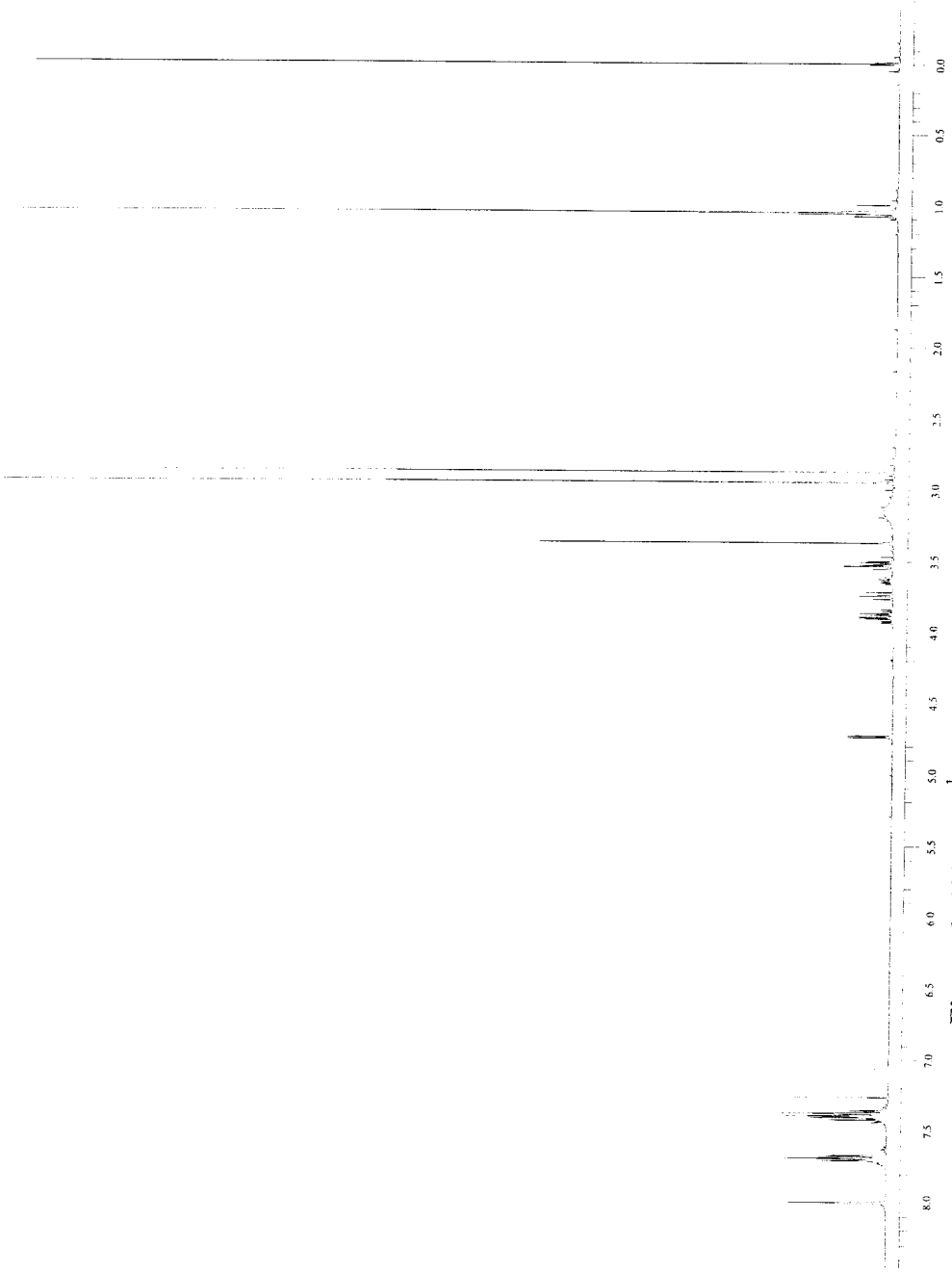

Figure 6: 400 MHz ^{1}H NMR spectrum of TBDPS derivative **2**.

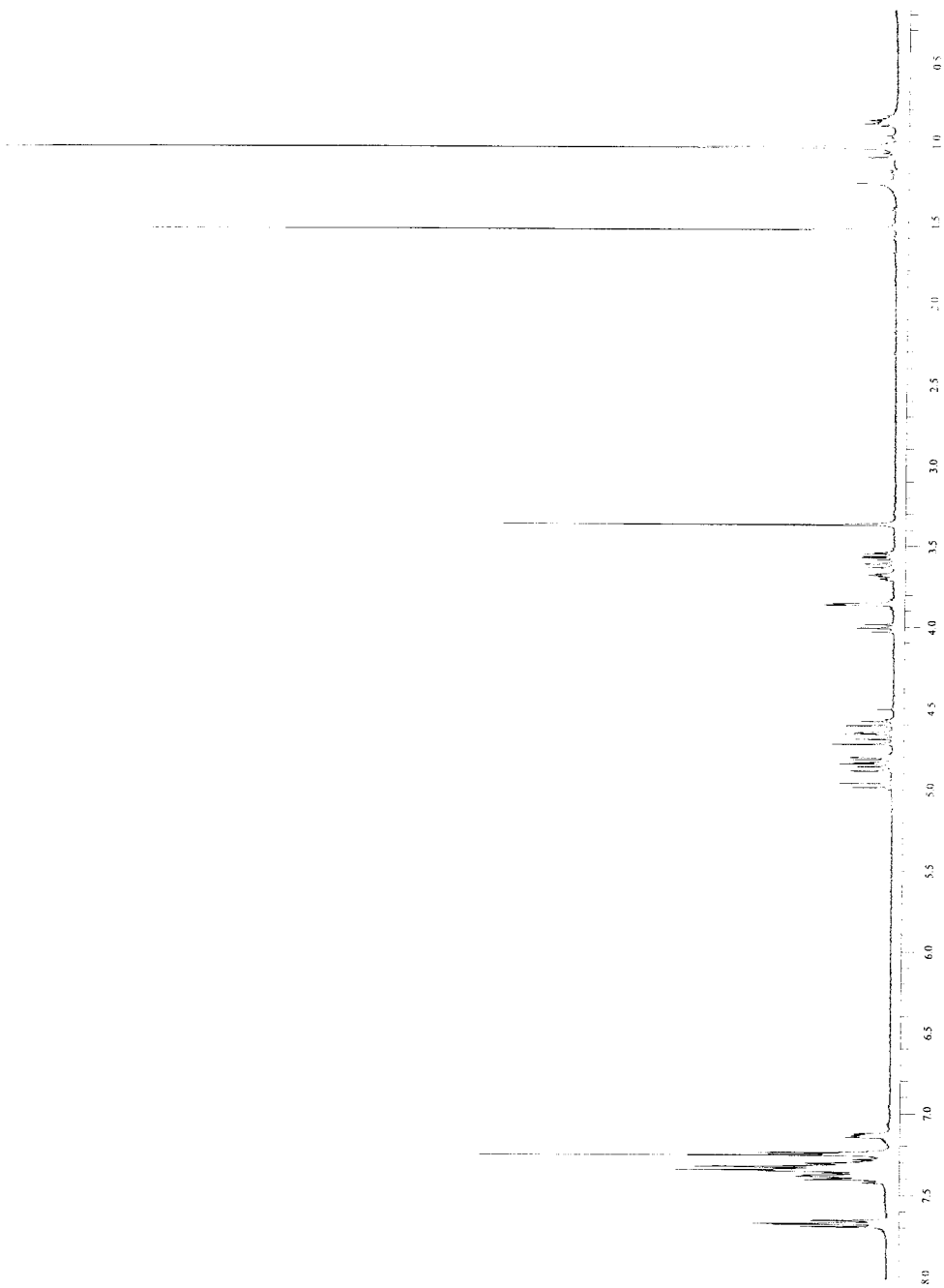

Figure 7: 400 MHz ^{1}H NMR spectrum of benzylated TBDPS derivative **3**.

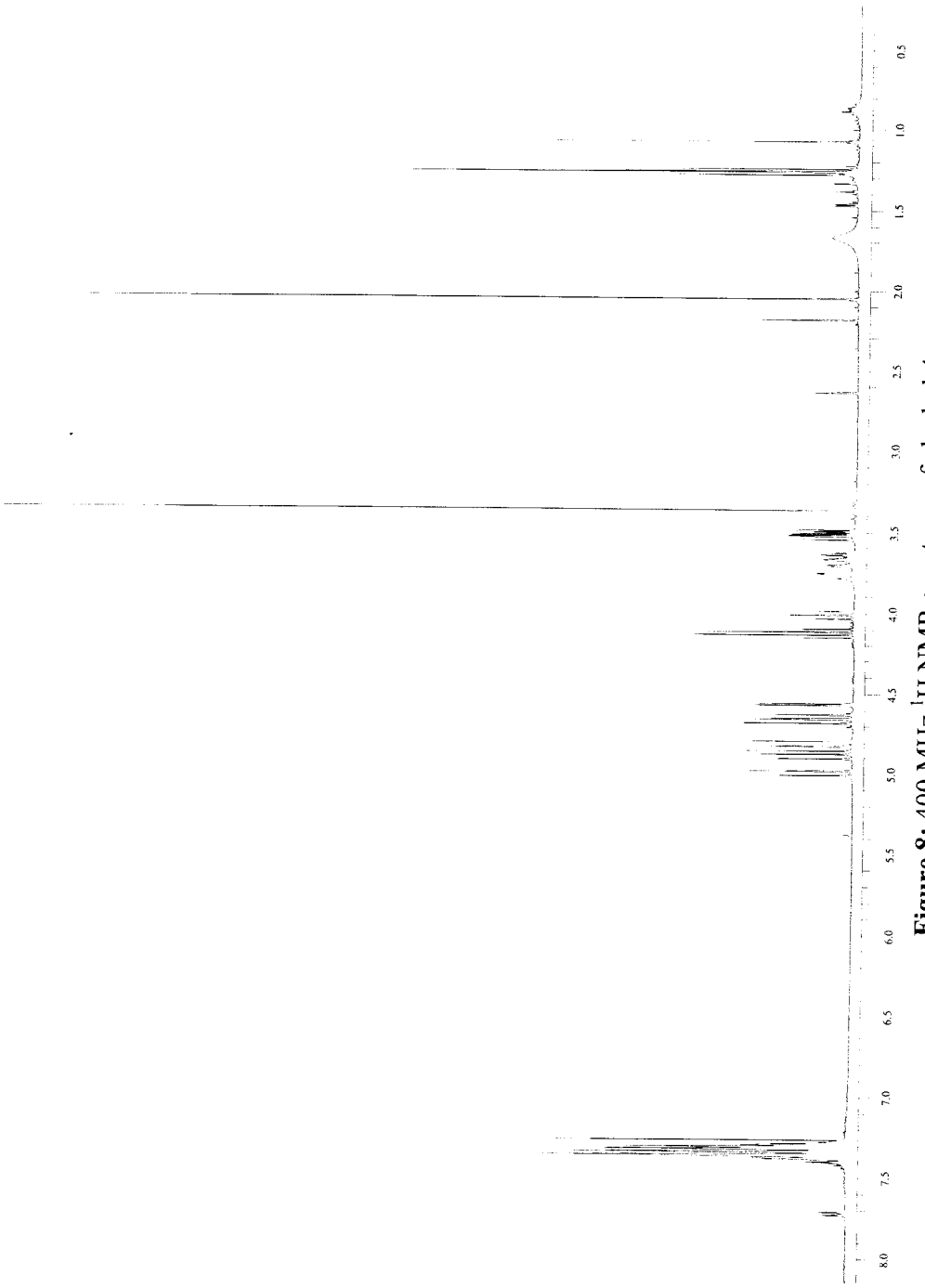

Figure 8: 400 MHz ^{1}H NMR spectrum of alcohol **4**.

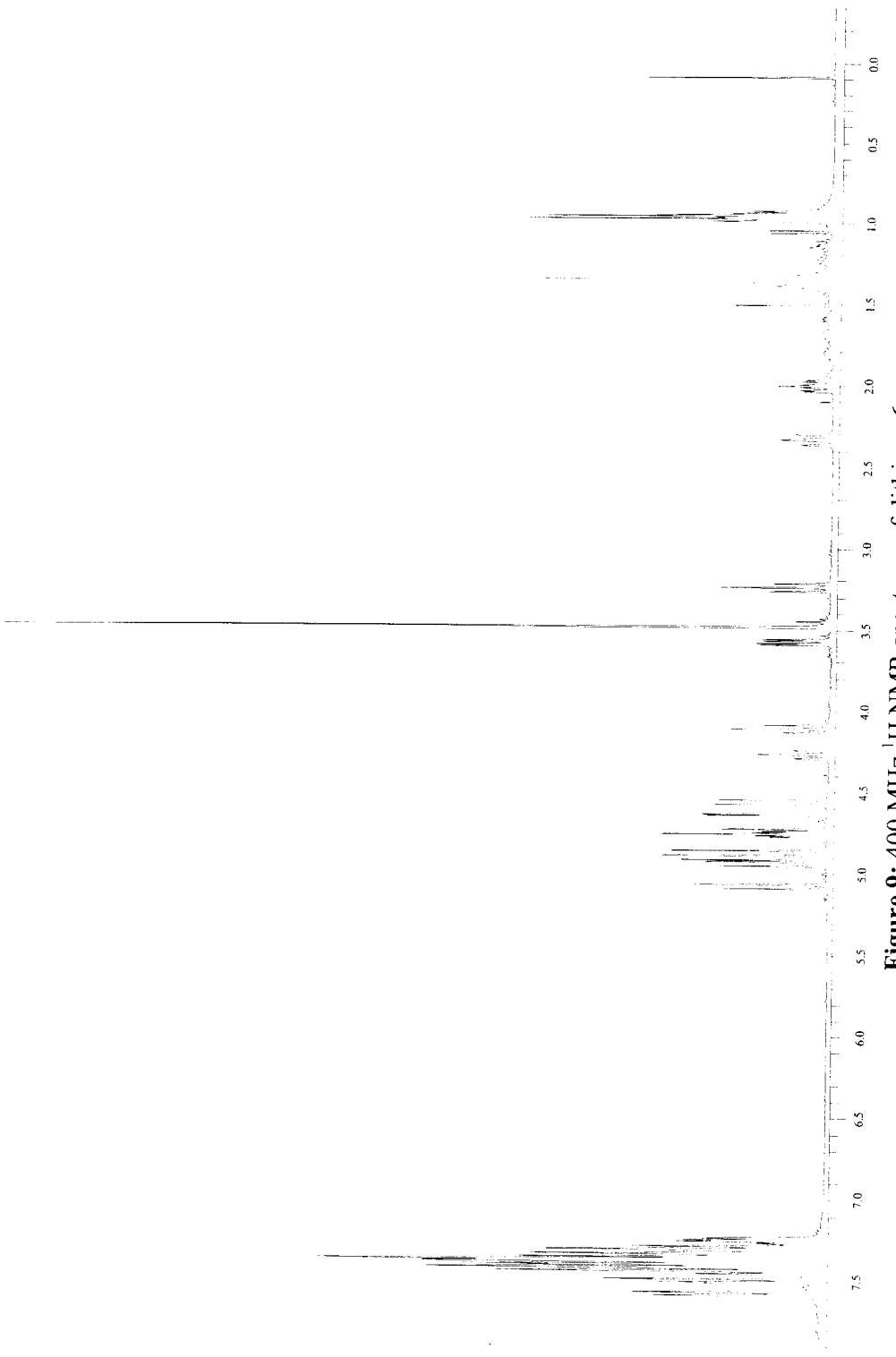

Figure 9: 400 MHz ^{1}H NMR spectrum of dithiane **6**.

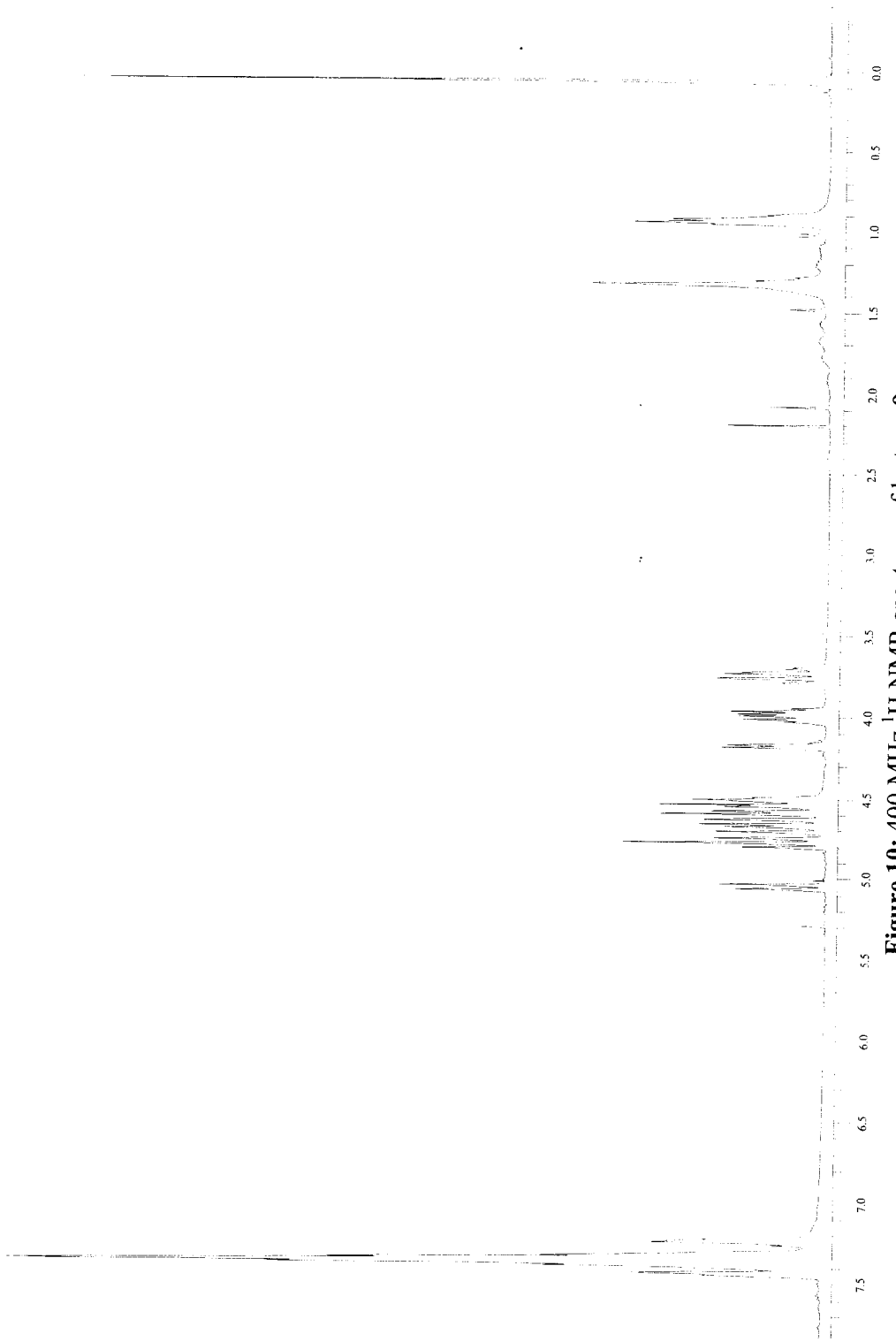

Figure 10: 400 MHz ^{1}H NMR spectrum of lactone **9**.

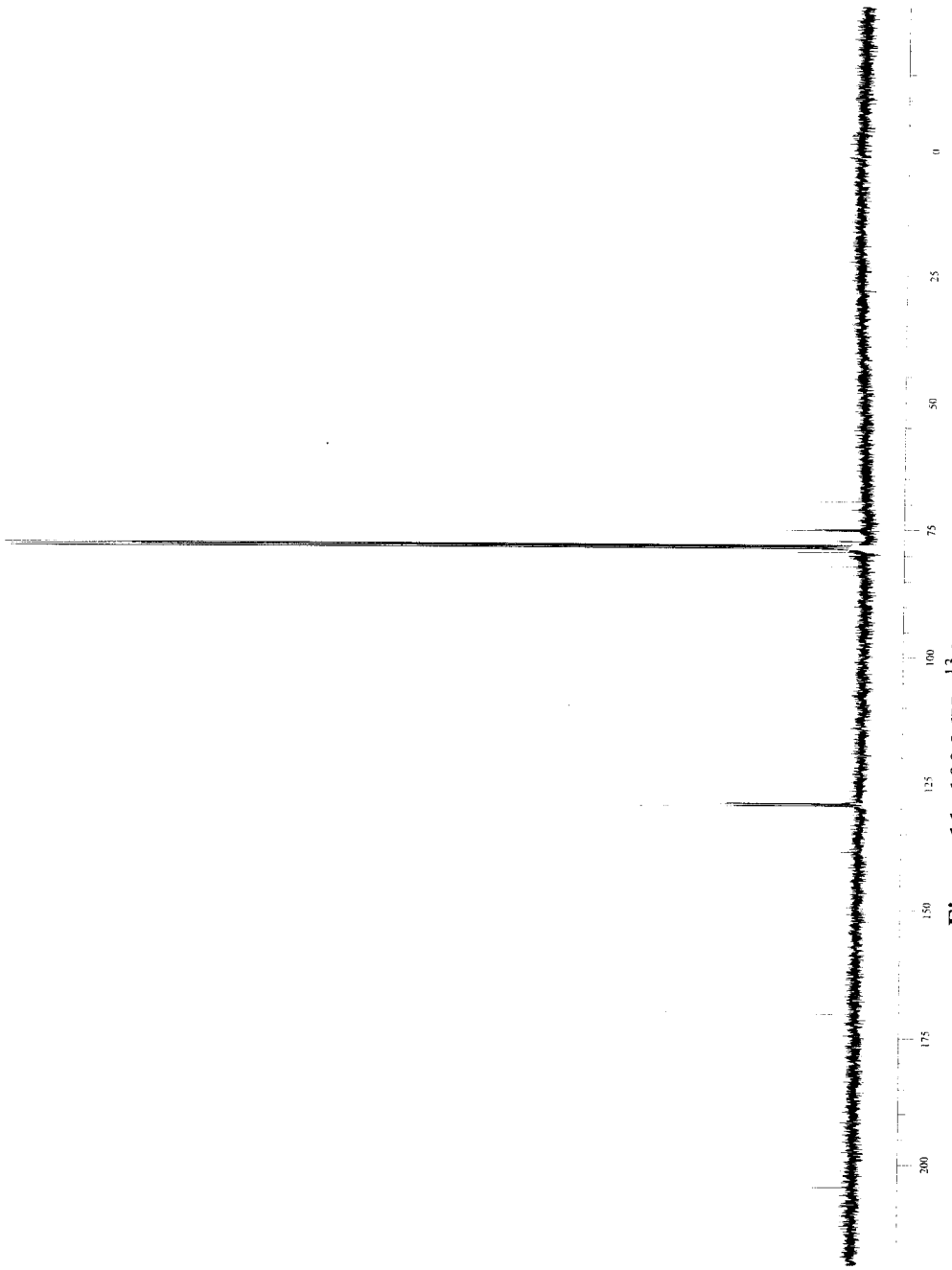

Figure 11: 100 MHz ^{13}C NMR spectrum of lactone **9**.

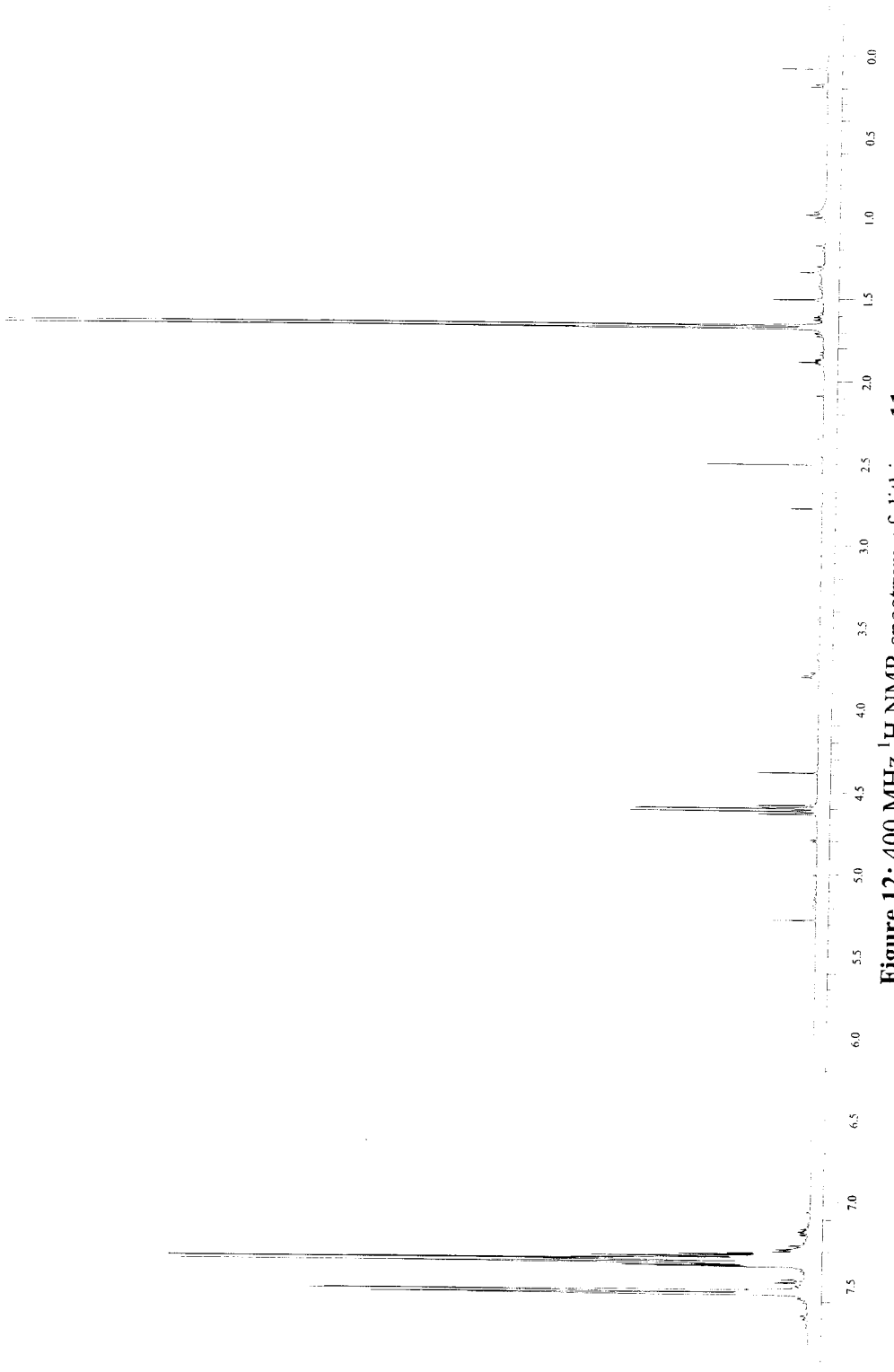

Figure 12: 400 MHz ^{1}H NMR spectrum of dithiane **11**.

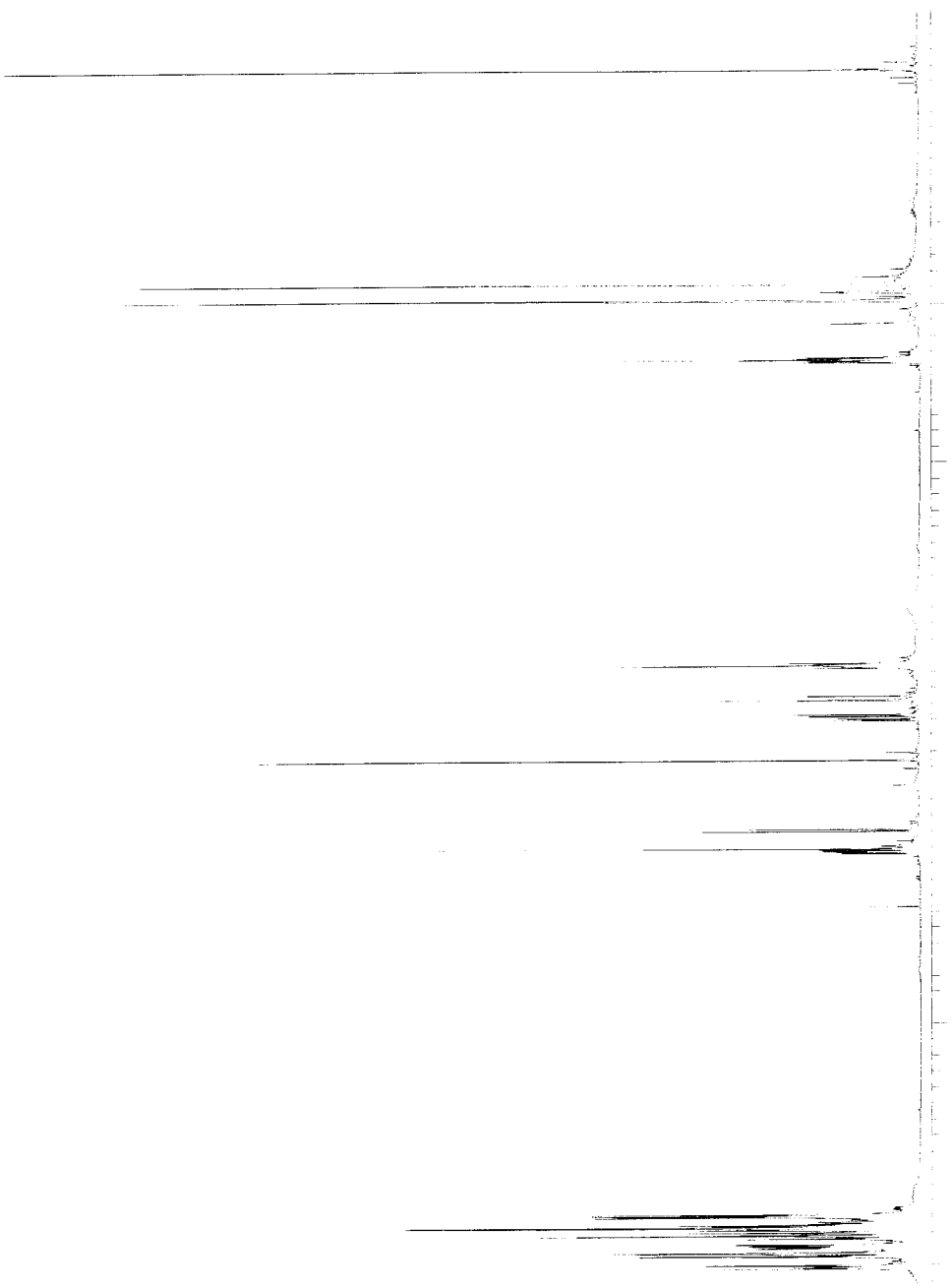

Figure 13: 400 MHz ^{1}H NMR spectrum of lactol **13**.

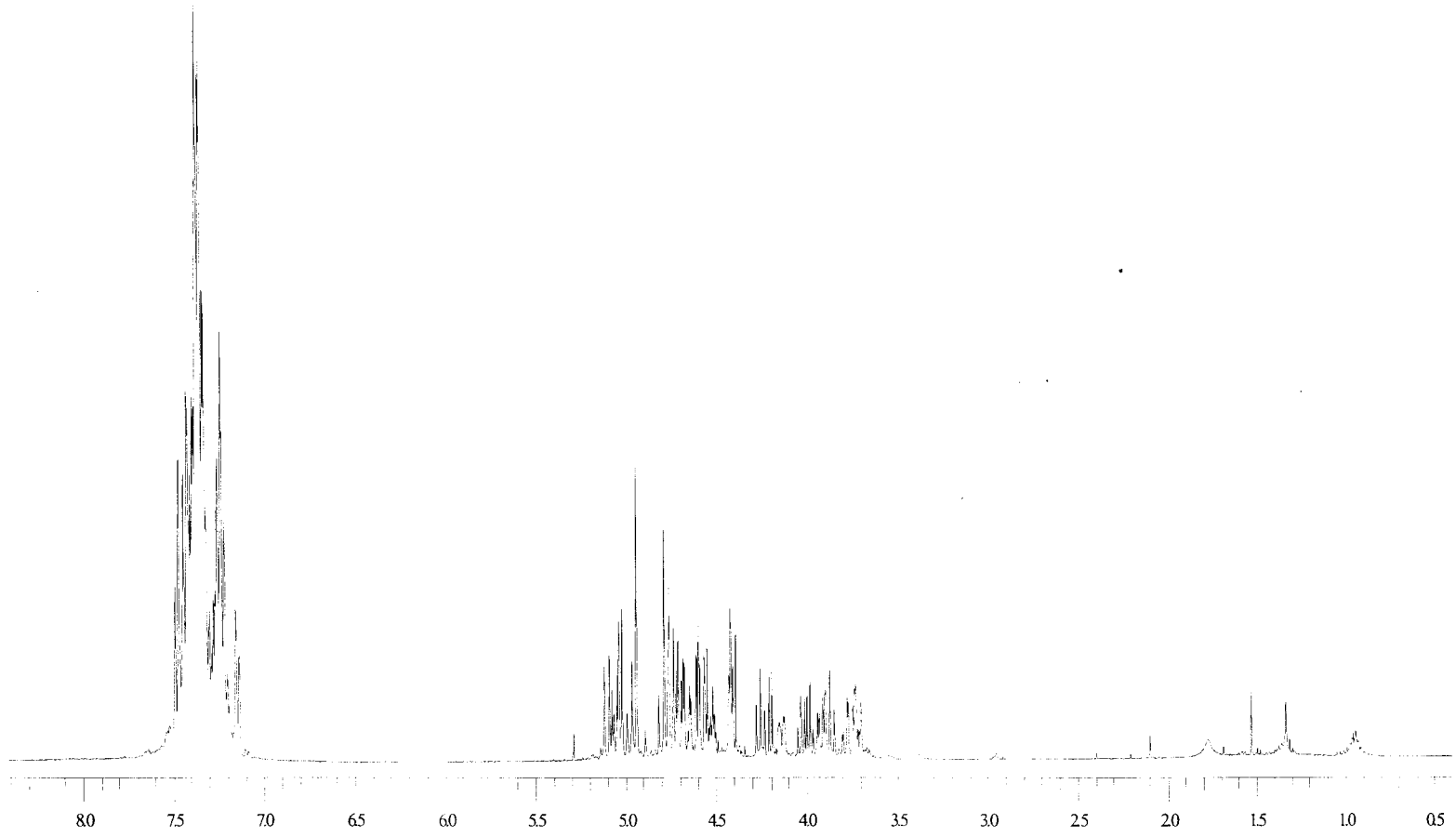

Figure 14: 400 MHz ^{1}H NMR spectrum of lactol **14**.

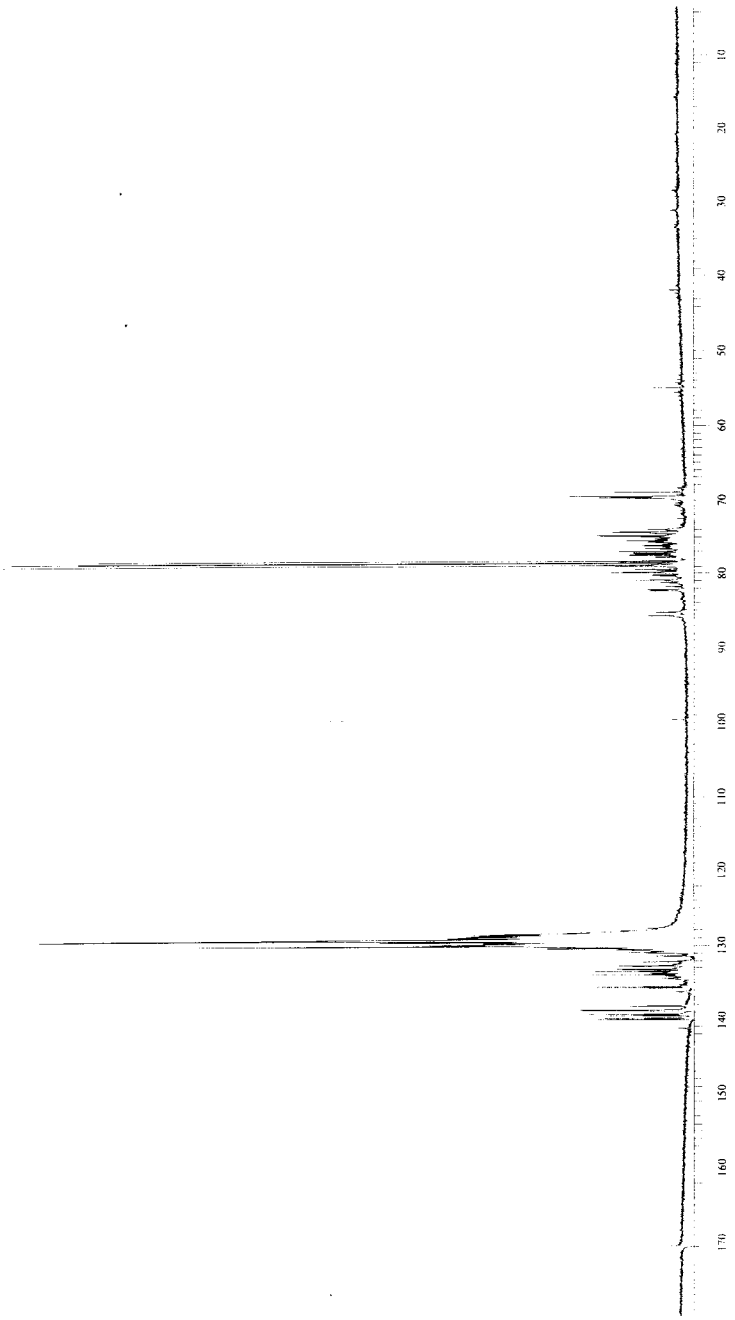

Figure 15: 100 MHz ^{13}C NMR spectrum of lactol **14**.

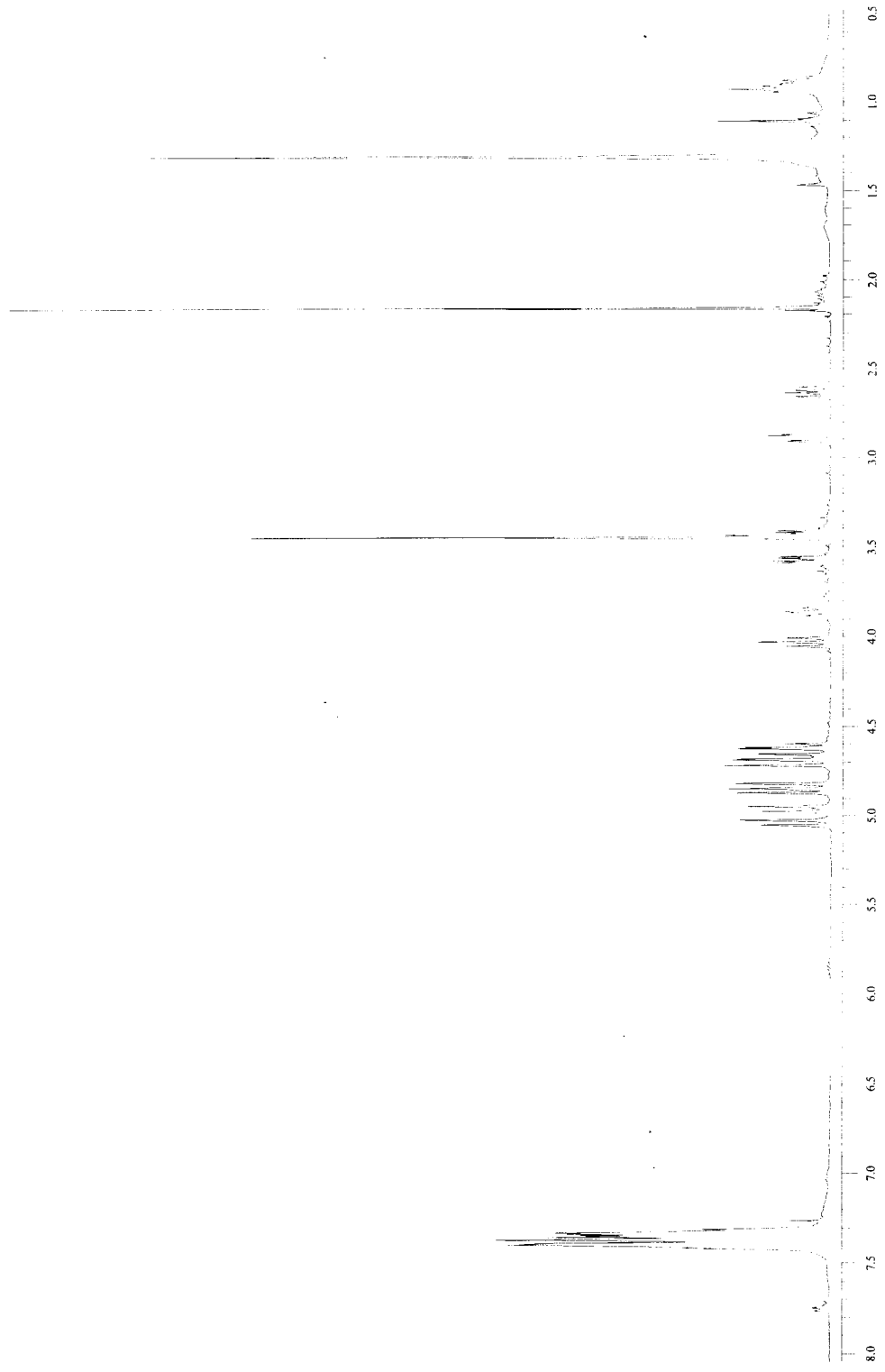

Figure 16: 400 MHz ^{1}H NMR spectrum of dithiane **17**.

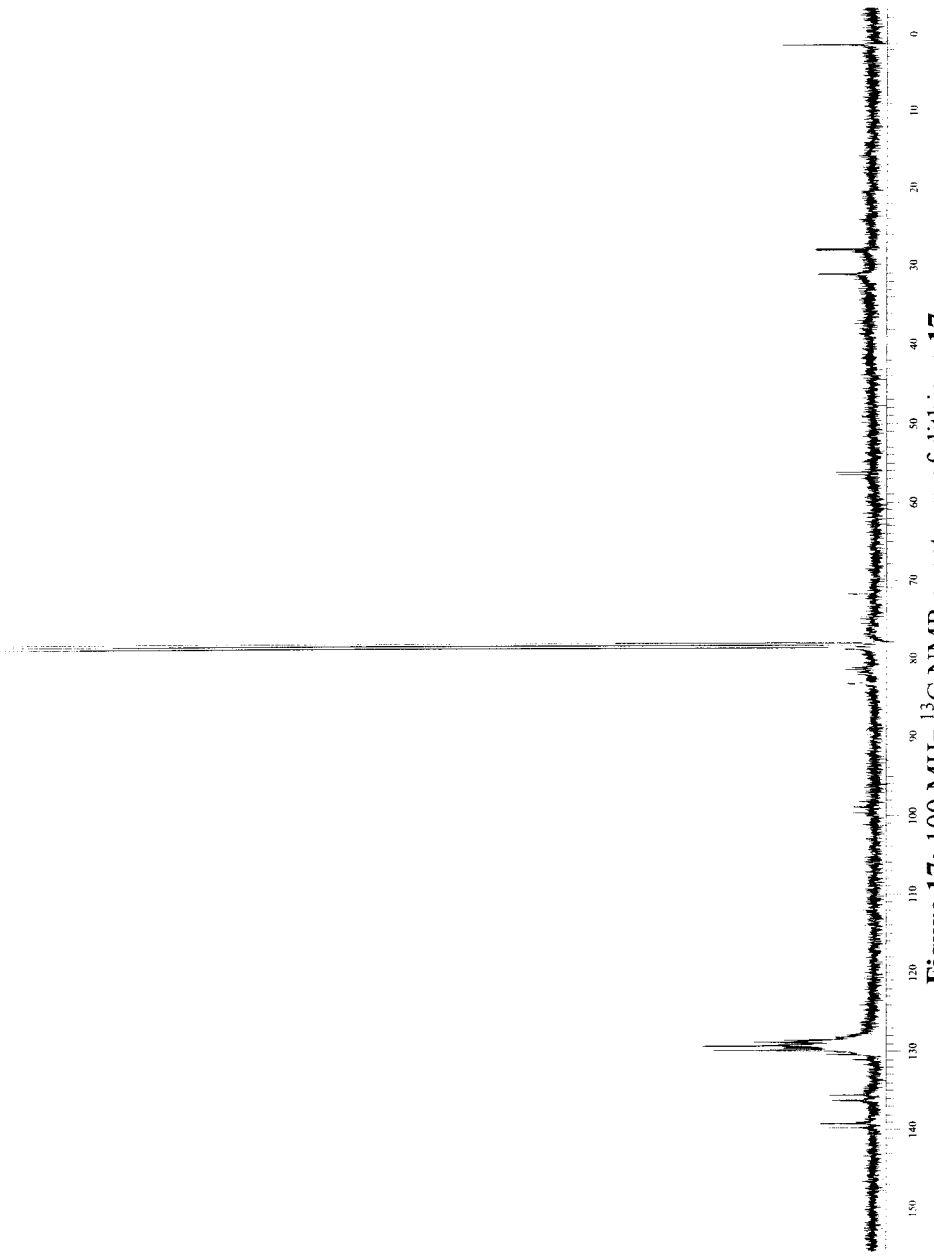

Figure 17: 100 MHz ^{13}C NMR spectrum of dithiane **17**.

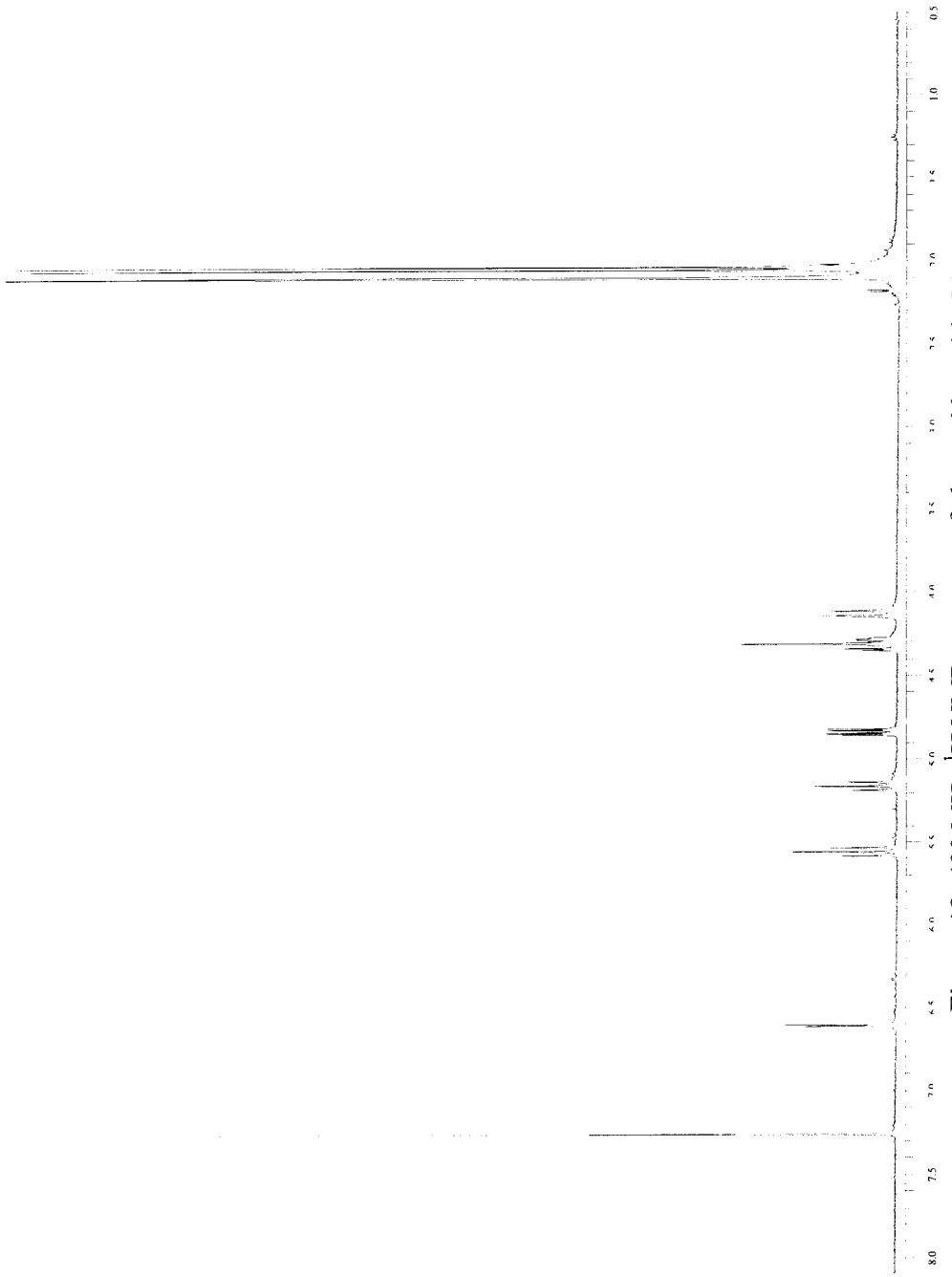

Figure 18: 400 MHz ^{1}H NMR spectrum of glycosyl bromide **21**.

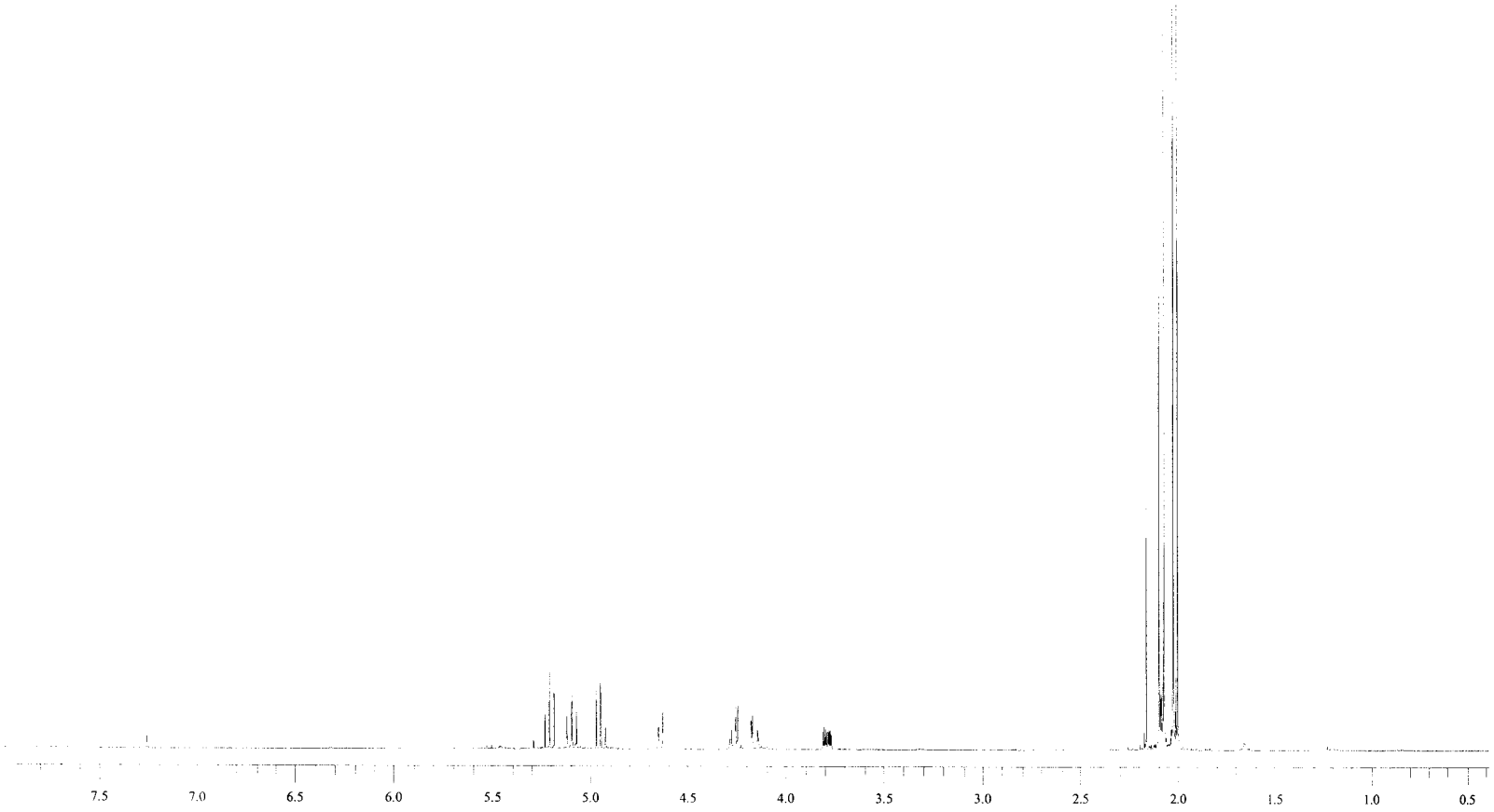

Figure 19: 400 MHz ^{1}H NMR spectrum glycosyl azide **22**.

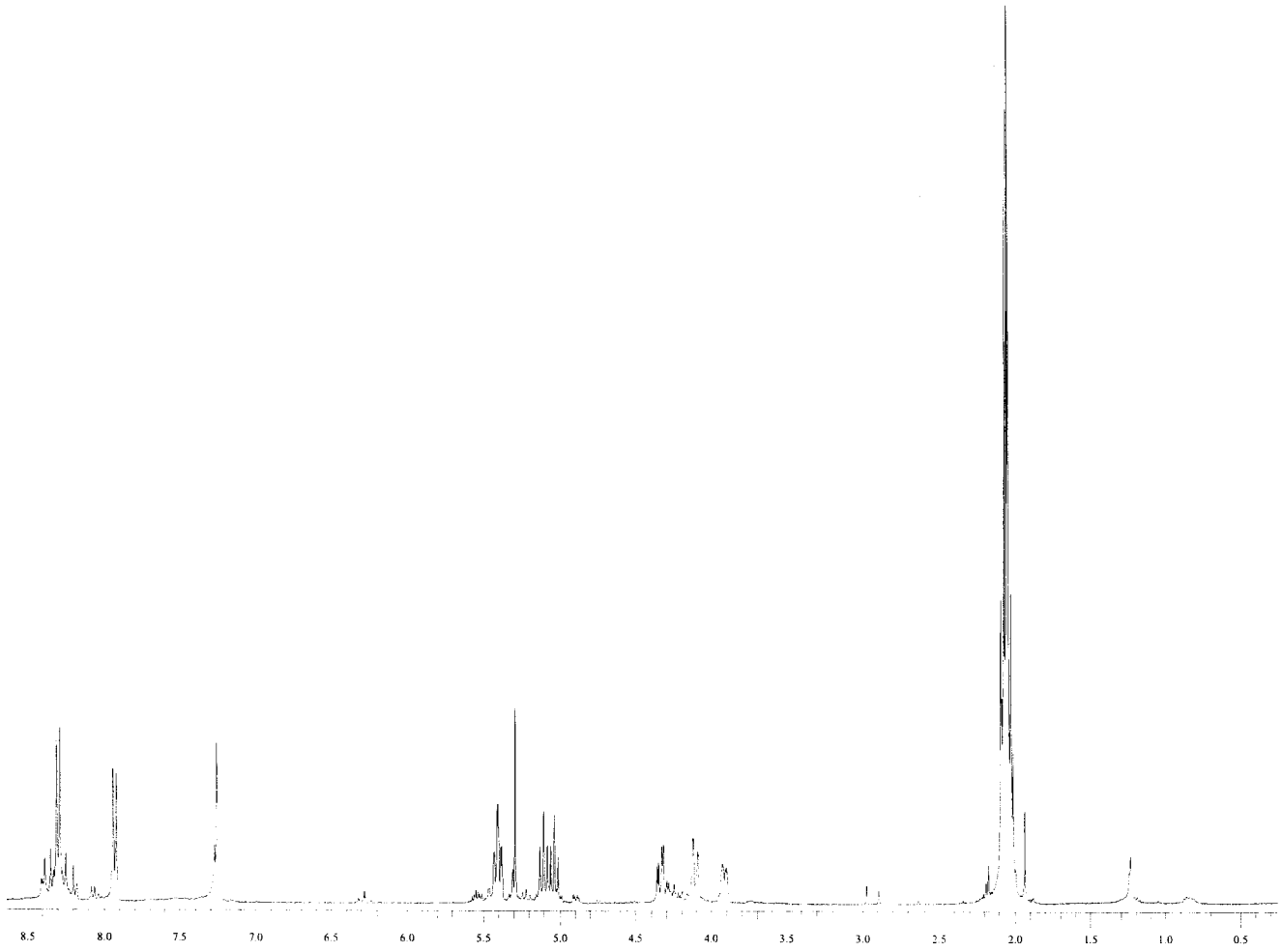

Figure 20: 400 MHz ^{1}H NMR spectrum of *p*-nitrobenzoic acid-β-D-glucopyranosyl amide **25**.

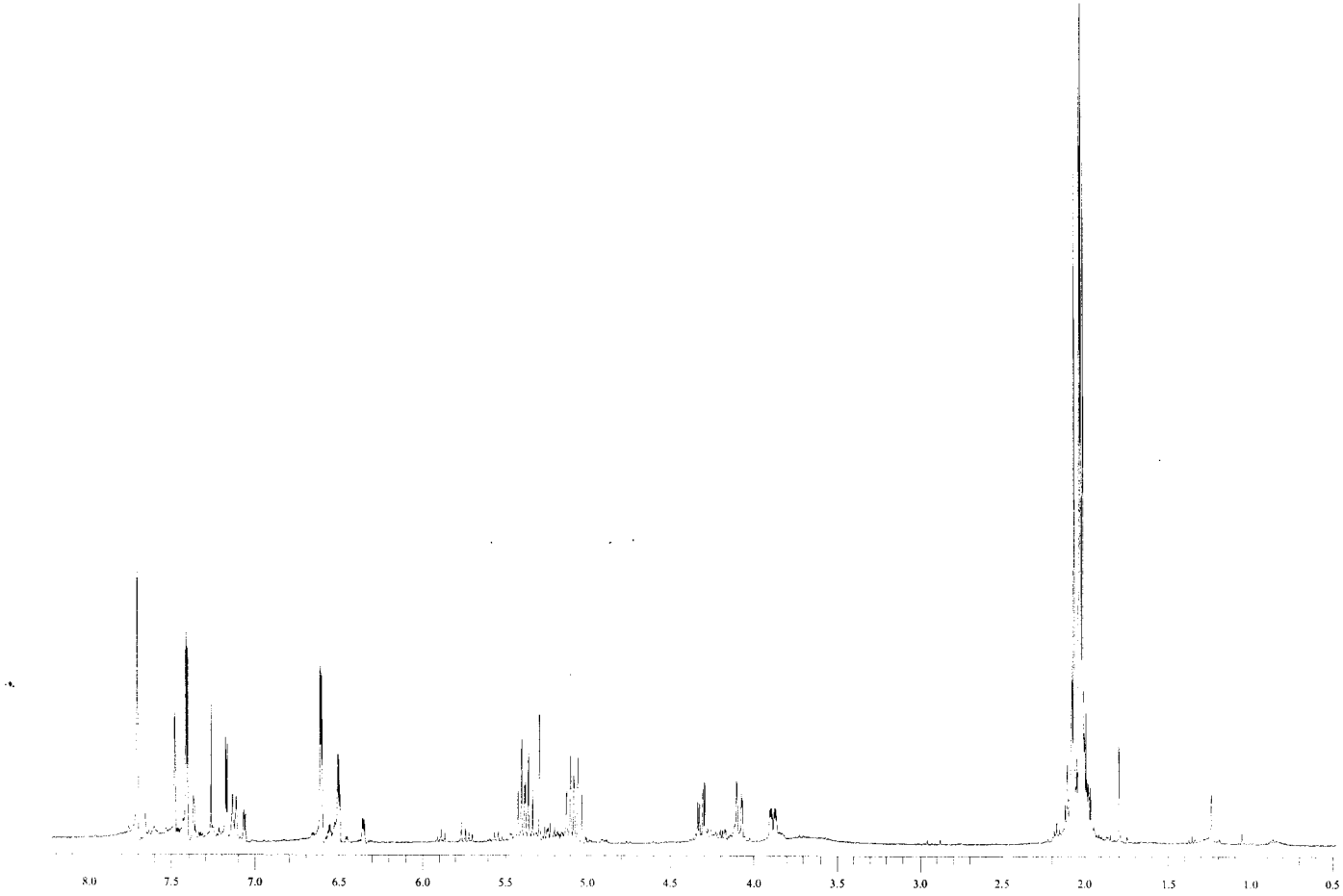

Figure 21: 400 MHz ^{1}H NMR spectrum of furan-2-carboxylic acid-β-D-glucopyranosyl amide **26**.

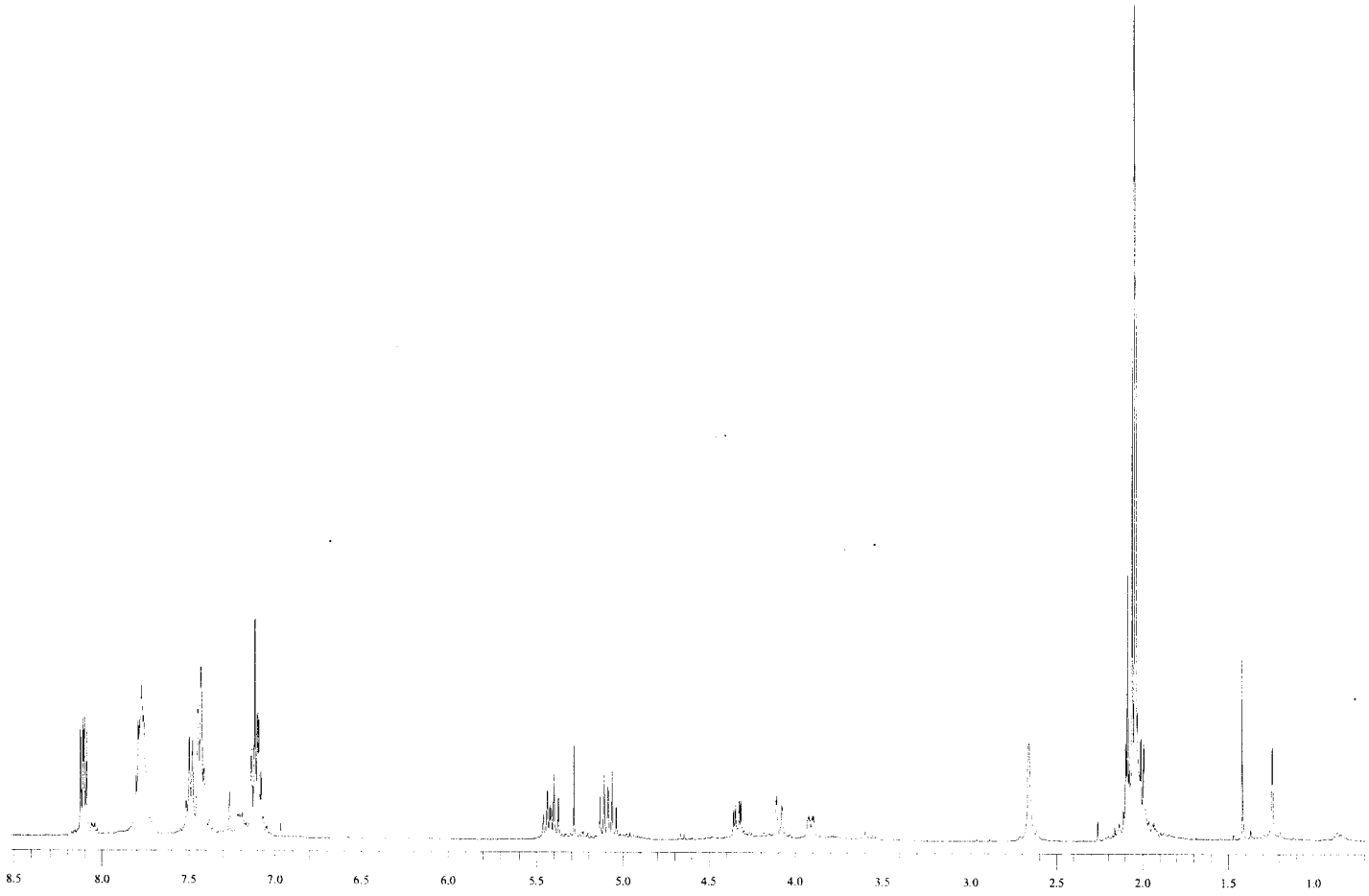

Figure 22: 400 MHz ^{1}H NMR spectrum of 4-flourobenzoic acid-β-D-glucopyranosyl amide **27**.

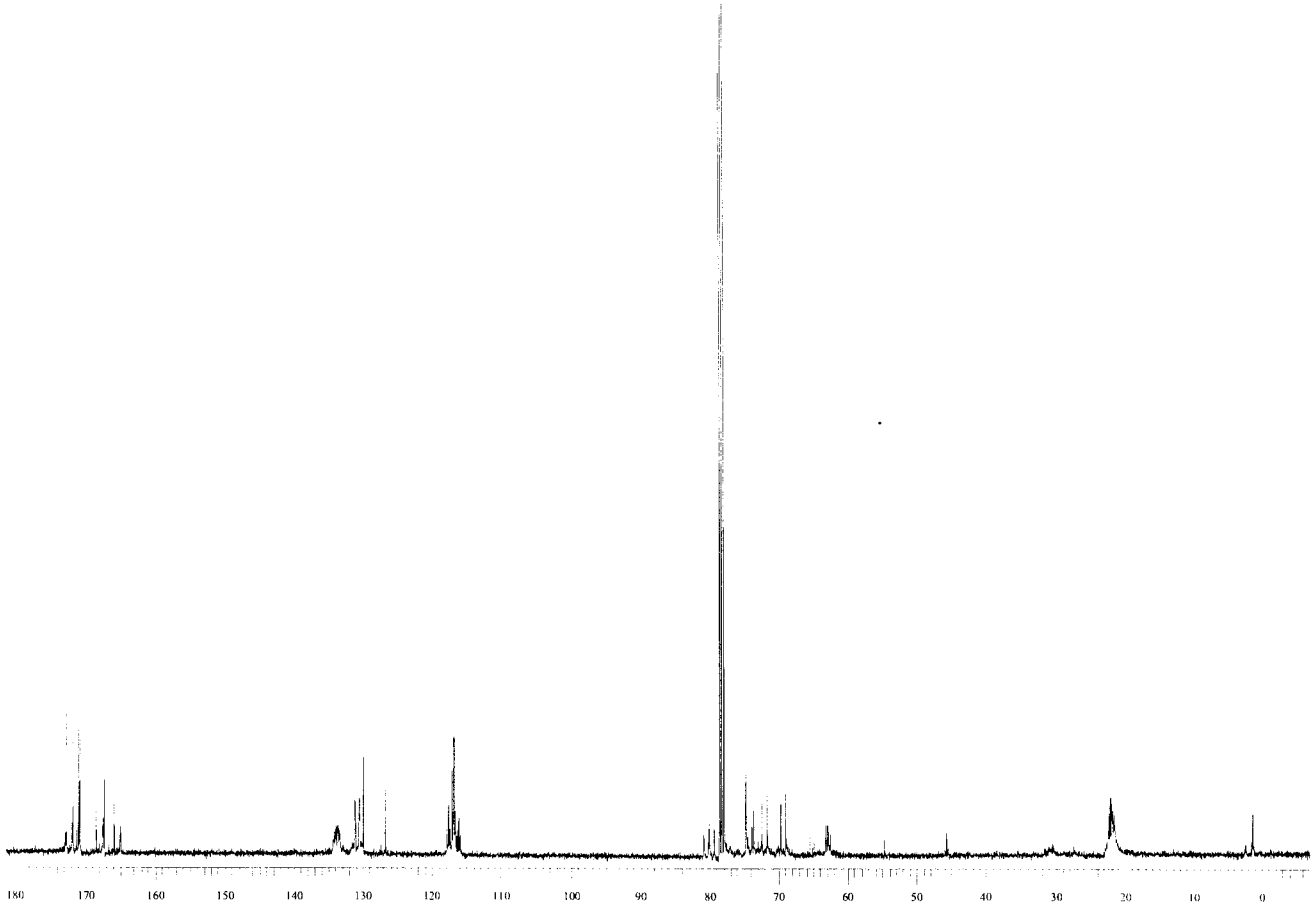

Figure 23: 100 MHz ^{13}C NMR spectrum of 4-flourobenzoic acid-ß-D-gluconyranosyl amide **27**.

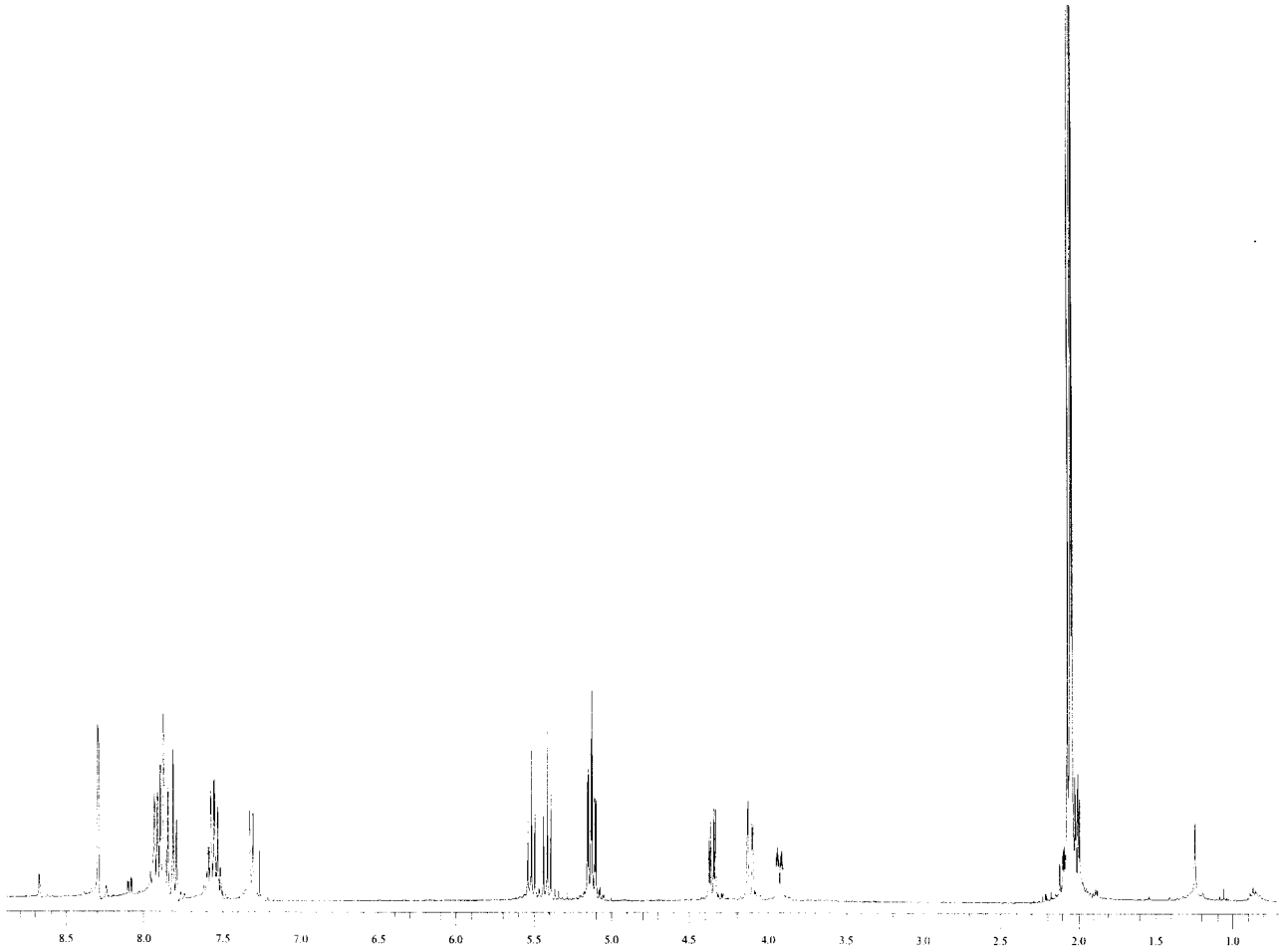

Figure 24: 400 MHz ^{1}H NMR spectrum of 2-napthoic acid-β-D-glucopyranosyl amide **28**.

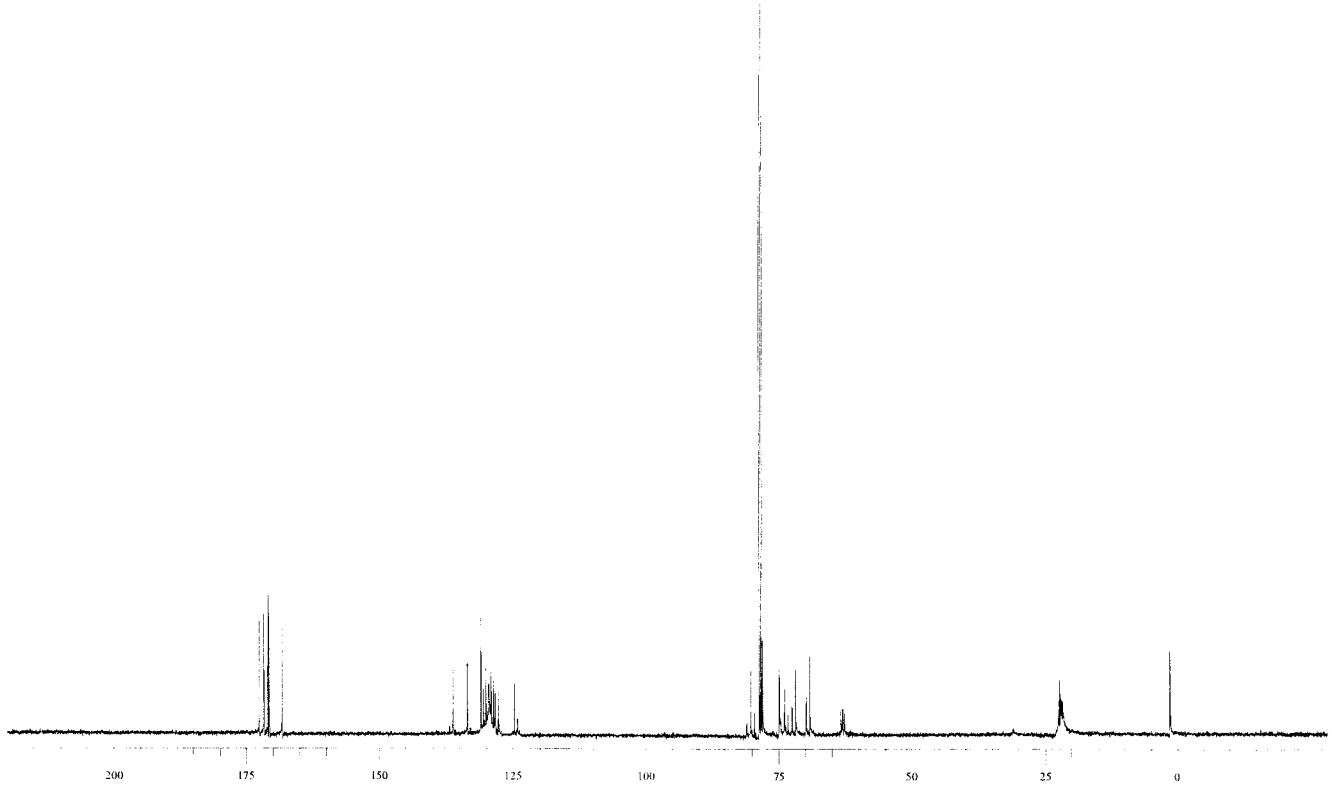

Figure 25: 100 MHz ^{13}C NMR spectrum of 2-napthoic acid-β-D-glucopyranosyl amide **28**.

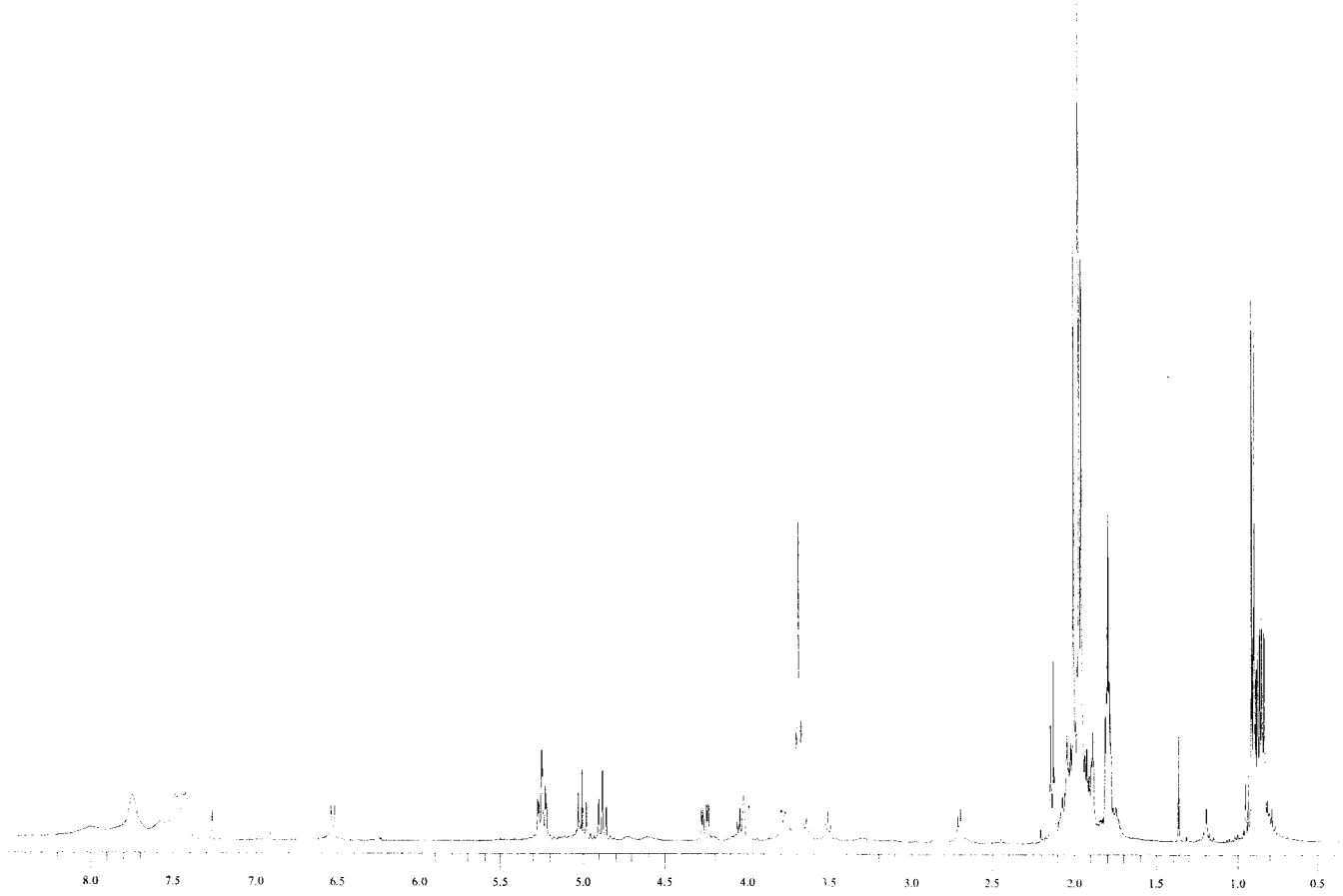

Figure 26: 400 MHz ^{1}H NMR spectrum of isovaleroic acid-β-D-glucopyranosyl amide **29**.

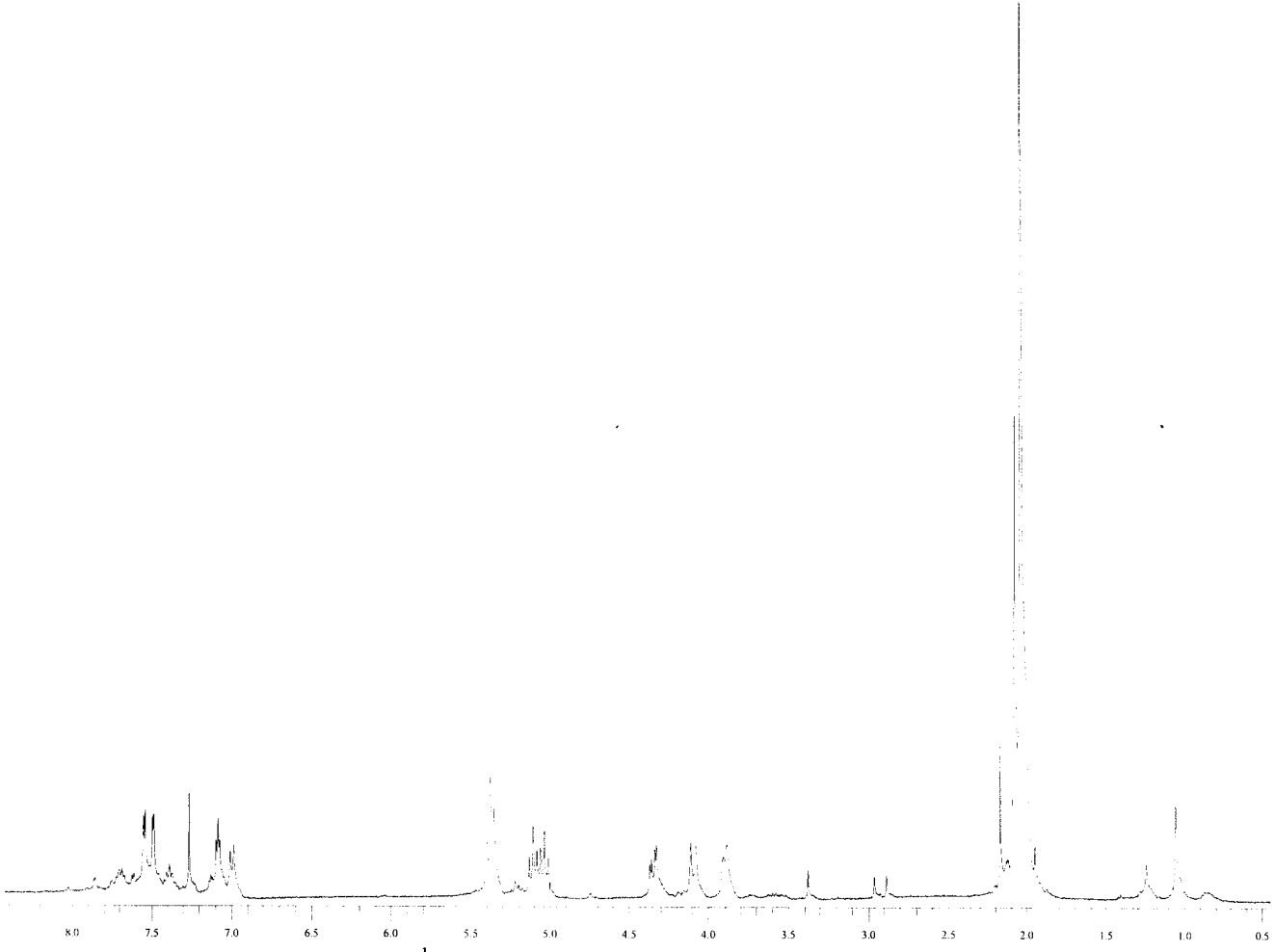

Figure 27: 400 MHz ^{1}H NMR spectrum of thiophene-2-β-D-glucopyranosyl amide **30**.

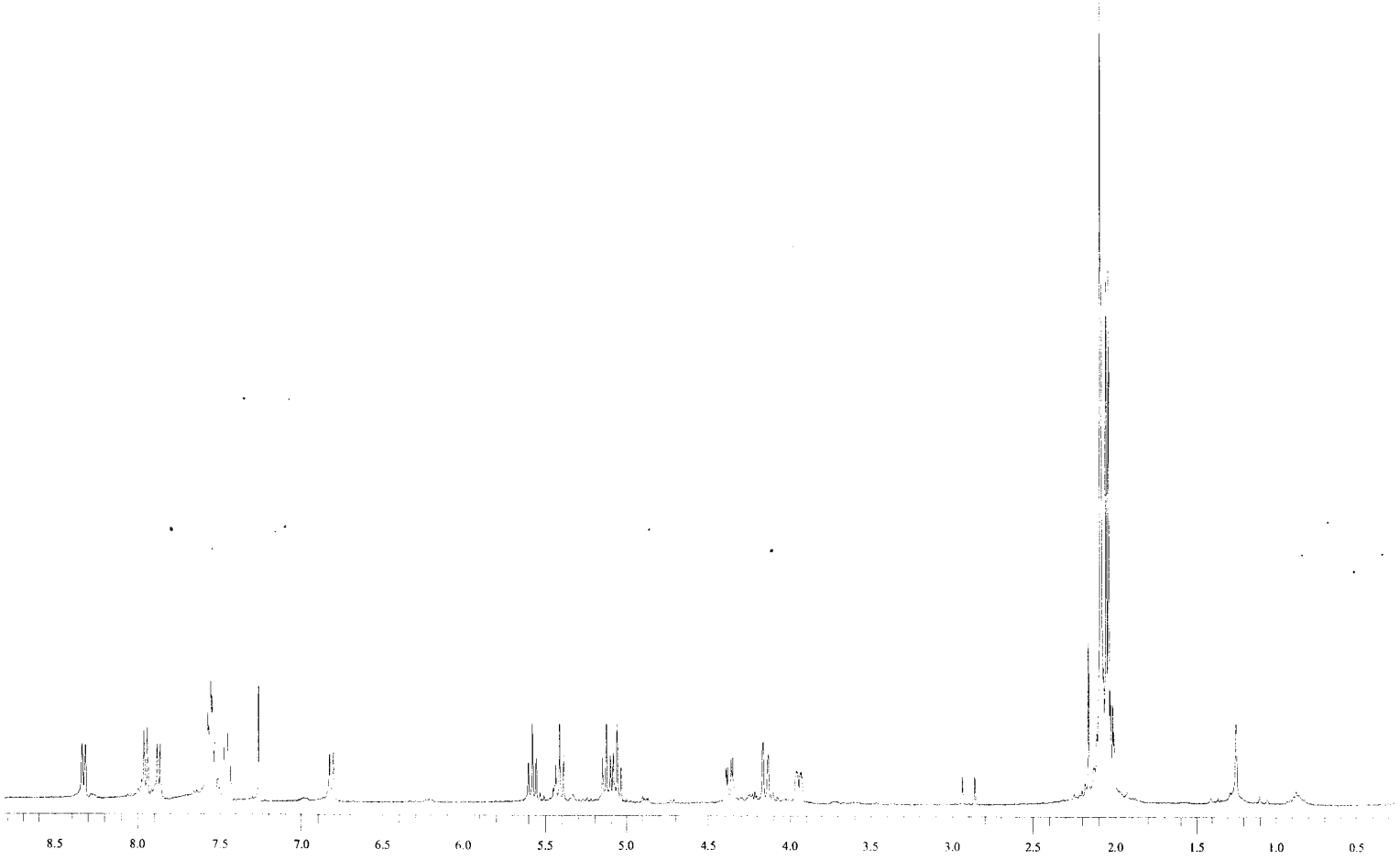

Figure 28: 400 MHz ^{1}H NMR spectrum of 1-napthoic acid-β-D-glucopyranosyl amide **31**.

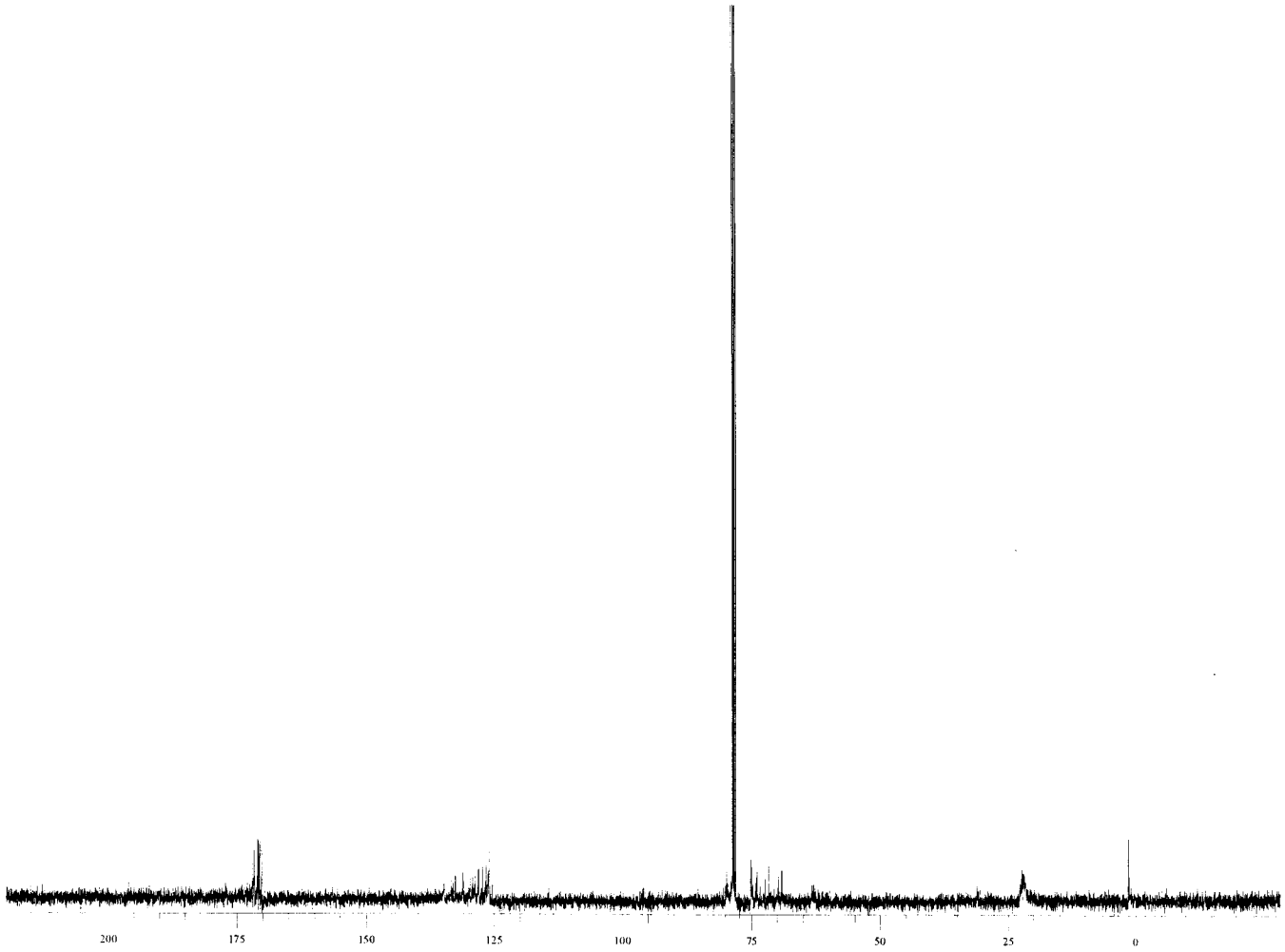

Figure 29: 100 MHz ^{13}C NMR spectrum of 1-napthoic acid-β-D-glucopyranosyl amide **31.**