Synthesis of *C*-Glycosides as Carbohydrate Mimics

By

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Thesis Abstract

The following work includes methods of synthesizing *C*-disaccharides. Nucleophilic addition of dithiane anions to electrophilic 2,3-*O*-isopropylidene-D-erythronolactone yields *C*-glycosides. The dithiane chemistry includes carbohydrate nucleophiles derived from bis(phenylthio)methane and bis(methylthio)methane. The synthesis of novel 1,2,3-triazole-linked sugars has also been studied in which the "non-reducing" saccharide is linked to the triazole through carbon and not nitrogen. Regiospecificity in the formation of these 1,2,3-triazole compounds will be discussed in detail.

Acknowledgements

I would like to give a special thanks to Dr. Peter Norris for all his help, patience, and guidance. Dr. Norris kept me motivated when I needed that extra kick in the butt. I've learned a lot from him, not just in terms of chemistry, but how to be a professional in the workplace and how hard work pays off. Perhaps most importantly, he taught me that chemistry guys can still get the chicks and where all the bars around campus are located. I will always be his first Amish student.

I would like to thank my parents for giving me the support to become the man I am today. They raised me the best way they knew how and I only hope that one day I will be as good to my kids as they were to me.

I would like to thank Tiffany and Tina for being great sisters. No matter where my path may take me it will always lead back to you two.

I would like to thank Dave for all of our stupid songs and for making my time in the lab a lot more enjoyable (hacky sack calculator). I would also like to thank Dobosh for being my lunch buddy everyday even though he never ate any lunch. I would like to thank Brittany for motivating me to write my thesis in time and being there for me now and in the future. I would like to thank Dana, Kayne, Dunfee, Chad, Hooker, Monica, Matt, Sara, Craig, and Iulia.

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Introduction

Glycosides

Glycosides are a large and very important class of carbohydrate derivatives, due to their roles in biological systems and drug development. They are characterized by the replacement of the anomeric hydroxyl group by some other substituent. Glycosides can be termed *O*-glycoside, *N*-glycoside, *C*-glycoside, etc., according to the atom attached to the anomeric carbon. It is customary to classify glycosides as either α or β according to their configuration at the anomeric carbon. The glycosides pictured in Figure 1 are all in the β conformation because their substituent at the anomeric carbon is in the equatorial position.

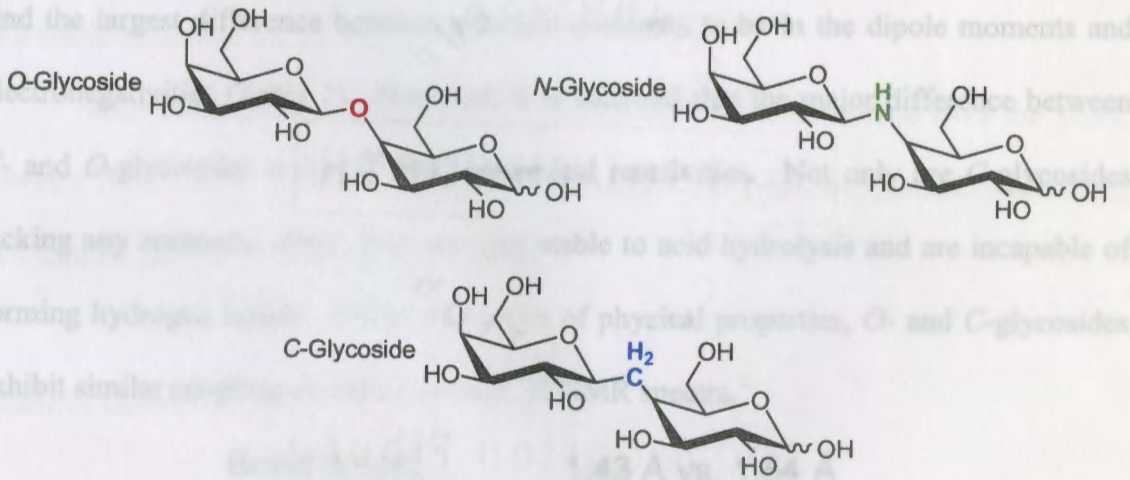


Figure 1. Structures of *O*-, *N*-, and *C*-glycosides

Researchers have been interested in carbohydrates for many years because of their abundance in Nature and the synthetic challenges posed by their polyhydroxylated structures. However, their commercial use has been greatly limited by the hydrolytic lability of the glycosidic bond. In Figure 2, it is shown how the *O*-glycosidic linkage is constructed and hydrolyzed and the ease with which the glycosidic bond can be

hydrolyzed under enzymatic conditions. Because of these *O*-glycosidic linkages and their ability to be hydrolyzed in the body, *C*-glycoside research has become an important component in the pharmaceutical and biotechnology industries as potential pharmacophores[1] for their ability to withstand enzymatic hydrolysis.

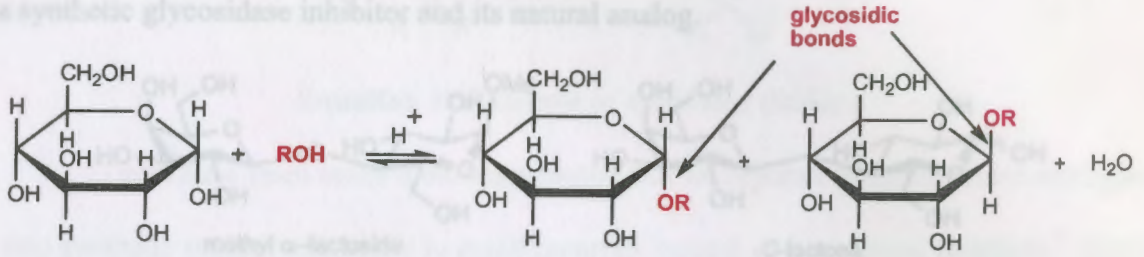


Figure 2. Construction and hydrolysis of glycosidic linkage

Physically, *O*- and *C*-glycosides seem to be quite comparable. In light of the bond lengths and Van der Waal radii being very similar between *O* and *C*-glycosides, we find the largest difference between physical constants to be in the dipole moments and electronegativities (Table 1). However, it is believed that the major difference between *C*- and *O*-glycosides is found within chemical reactivities. Not only are *C*-glycosides lacking any anomeric effect, they are also stable to acid hydrolysis and are incapable of forming hydrogen bonds. Within the realm of physical properties, *O*- and *C*-glycosides exhibit similar coupling constants in their ^{1}H NMR spectra.[1]

Bond length -	1.43 Å vs. 1.54 Å
Van der Waal -	1.52 Å vs. 2.0 Å
Electronegativity -	3.51 vs. 2.35
Dipole moment -	0.74D vs. 0.3D
H-Bonding -	Two vs. None
Anomeric Effect -	Yes vs. No
Stability w/ acid -	Unstable vs. Stable

Table 1. Physical and chemical comparisons of *O*- and *C*-glycosides

Studies have shown that oligosaccharides are involved in a number of recognition events such as cell adhesion, metastasis, and embryonic development, among others.[2] The search for new glycosidase inhibitors has led to a group of oligosaccharides analogues with the glycosidic oxygen substituted by carbon.[3] Figure 3 is an example of a synthetic glycosidase inhibitor and its natural analog.

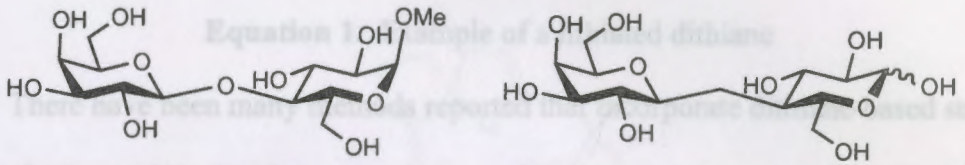


Figure 3. Methyl α-lactoside and *C*-lactose

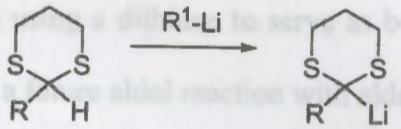
Because of the similarities between *O*- and *C*-glycosides, and the *C*-glycosides ability to withstand enzymatic hydrolysis, the *C*-glycoside is a prime candidate to serve as a stable substitute for the *O*-glycoside.

Many routes to synthesizing *C*-glycosides have been developed over the years, however we are concentrated on making *C*-glycosides using dithiane chemistry and using two distinct pathways for triazole formation.

Dithiane chemistry

Dithioacetals are classified as compounds that have two sulfur atoms attached to a central carbon. Thiols can add to aldehydes and ketones, giving hemimercaptals and dithioacetals. Hemimercaptals are normally unstable, however dithioacetals, like acetals are stable in the presence of bases, with the exception of strong bases that can remove the $(RS)_2CHR$ proton. The removal of the hydrogen adjacent to the sulfur requires a strong

base such as *n*-butyllithium and the product is a lithiated dithiane (Equation 1). The acidity of this hydrogen is largely due to greater polarizability of the sulfur and the greater C-S bond length rather than to the presence of the d orbitals.[4]



Equation 1. Example of a lithiated dithiane

There have been many methods reported that incorporate dithiane-based strategies into synthetic organic chemistry to make complex natural and unnatural products.[5] Quite a few of these methods use a carbonyl as the electrophile (Figure 4).[6] The development of "umpolung" dithiane reactions has increased with the improvement of the removal of the dithiane moiety to restore the carbonyl functionality.[7]

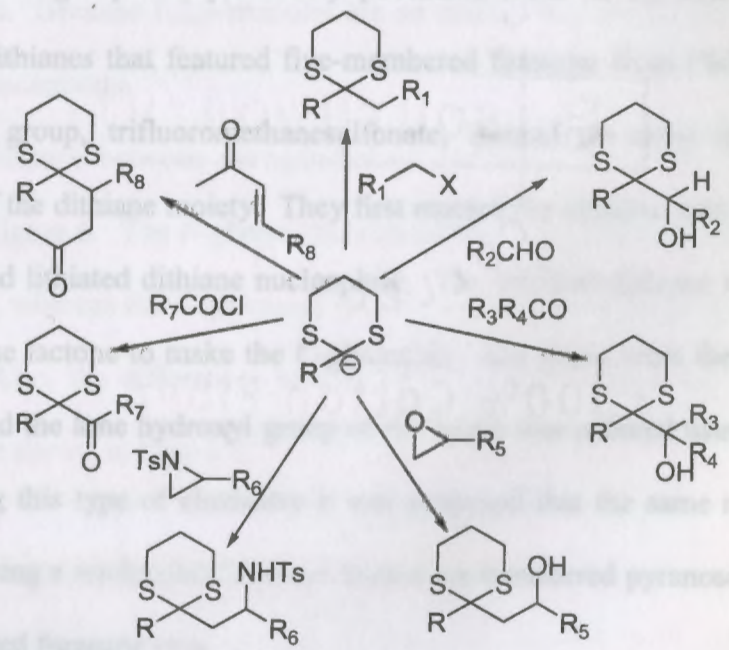
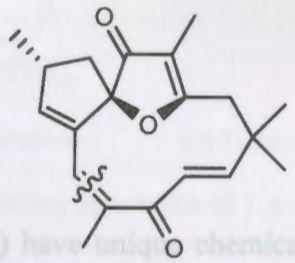


Figure 4. Reaction pathways open to dithiane anions

One example of making a natural product by using dithiane chemistry comes from Smith and Adams from the University of Pennsylvania. They attempted to synthesize

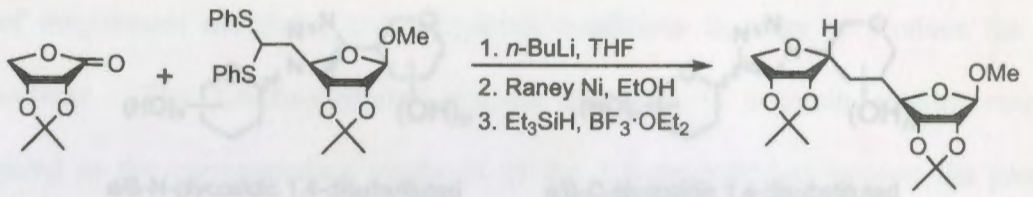
jatrophones (Figure 5), isolated from extracts of the plant *Jatropha gossypiifolia*. It has been suggested that the seeds could be a useful chemotherapeutic agent provided that it is active at a non-lethal dose. This may be because of its reported antihelminthic activity.[8] Their chemistry incorporated using a dithiane to serve as both an acyl anion equivalent and as a masked carbonyl for a future aldol reaction with aldehyde.[6]



(+)-Jatrophone

Figure 5. Stucture of Jatrophone

The Norris group had previously published work in the *Journal of Organic Chemistry* on dithianes that featured five-membered furanose rings (Scheme 1) using a strong leaving group, trifluoromethanesulfonate, instead of using the carbonyl for incorporation of the dithiane moiety. They first reacted the dithiane with *n*-BuLi to make the sugar-derived lithiated dithiane nucleophile. The lithiated dithiane was then reacted with the furanose lactone to make the *C*-glycoside. The thiols were then reduced using Raney nickel and the lone hydroxyl group of the lactol was reduced using $BF_3{\cdot}OEt_2$ and Et_3SiH.[9] Using this type of chemistry it was proposed that the same results would be accomplished using a nucleophile derived from a six-membered pyranose ring instead of the five-membered furanose ring.



Scheme 1. Synthesis of *C*-glycoside using five-membered ring

Triazole Chemistry

1,2,3-Triazoles (Figure 6) have unique chemical properties and structure which should enable their use in organic, organometallic, and medicinal chemistry.[10] They are attractive compounds because of their stability to oxidation, reduction, and both acid and basic hydrolysis. Because 1,2,3-triazoles are so stable, they are quickly becoming very powerful pharmacophores.[11, 12]

The difference between nitrogen-linked triazoles and carbon-linked triazoles is highlighted in Figure 6. The *N*-glycosidic triazoles are linked at the anomeric carbon by a nitrogen atom, whereas the *C*-glycoside triazoles are linked at the anomeric carbon by a carbon atom. Also, the differences between the 1,4-disubstituted and 1,5-disubstituted regioisomers are shown in Figure 6.

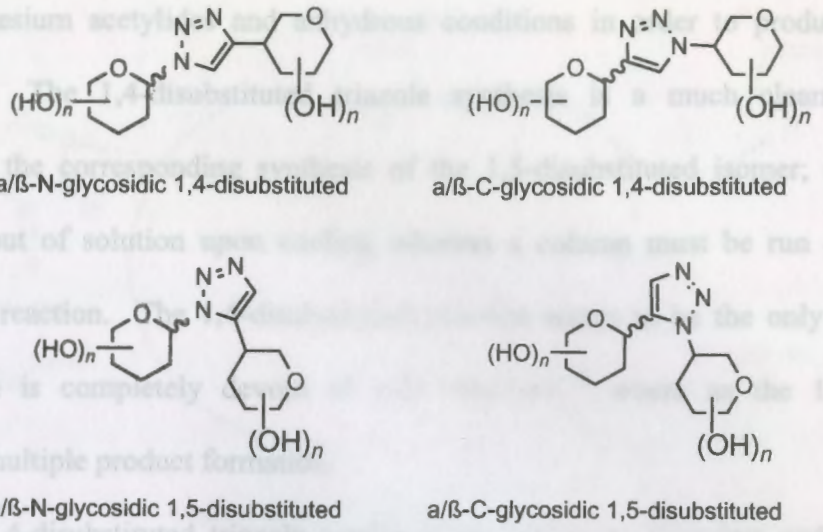
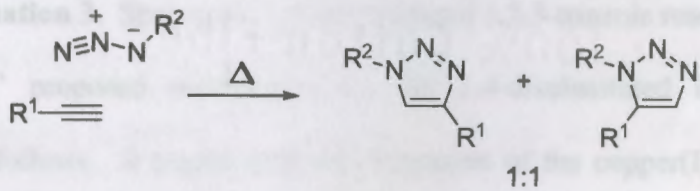


Figure 6. Comparing structures of 1,4- and 1,5-triazoles

The azide's stability toward H_2O, O_2, and most other organic conditions and their spring-loaded nature make azides unique for click chemistry purposes.[13] However, even when an azide is presented with a good dipolarophile, it may require heat for the desired triazole-forming cycloaddition, which usually results in a mixture of 1,4- and 1,5-disubstituted triazoles.[14] An example of this is when a terminal alkyne and azide are dissolved in toluene and refluxed the products are a 1:1 mixture of 1,4- and 1,5- isomers (Equation 2).

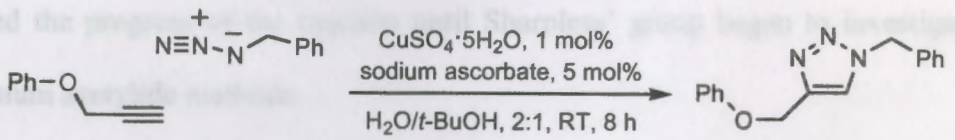


Equation 2. Example of a thermal, non-catalytic triazole reaction

The copper(I)-catalyzed reaction of terminal alkynes and azides to give 1,4-disubstituted 1,2,3-triazoles is very selective[15] and is the best "click" reaction to date.[16] The 1,4-disubstituted reaction is best suited for aqueous conditions, has a very broad temperature range, and is insensitive to pH.[17] The 1,5-disubstituted reaction requires the

use of magnesium acetylides and anhydrous conditions in order to produce the 1,5-regioisomer. The 1,4-disubstituted triazole synthesis is a much cleaner reaction compared to the corresponding synthesis of the 1,5-disubstituted isomer; the product precipitates out of solution upon cooling whereas a column must be run on the 1,5-disubstituted reaction. The 1,4-disubstituted reaction seems to be the only three-atom dipole which is completely devoid of side reactions,[18] where as the 1,5 reaction experiences multiple product formation.

The 1,4-disubstituted triazole synthesis developed by Sharpless and coworkers involves reacting phenyl propargyl ether and benzylazide in the presence of 5 mol % of sodium ascorbate and 1 mol % of copper(II) sulfate in a 2:1 mixture of water and *t*-butyl alcohol (Equation 3). NOE experiments were performed on the product to determine the regiochemistry. This copper-catalyzed reaction entailed little more than mixing the reagents and then filtering off the pure product.



Equation 3. Sharpless' 1,4-disubstituted 1,2,3-triazole reaction

Sharpless' proposed mechanism for the 1,4-disubstituted triazole synthesis (Figure 7) is as follows. It begins with the formation of the copper(I) acetylide which then coordinates with the internal nitrogen of the azide. The formation of the six-membered copper-containing intermediate ring is followed by the copper(I) being expelled out of the ring and reused as a catalyst, consequently forming the 1,4-disubstituted triazole.

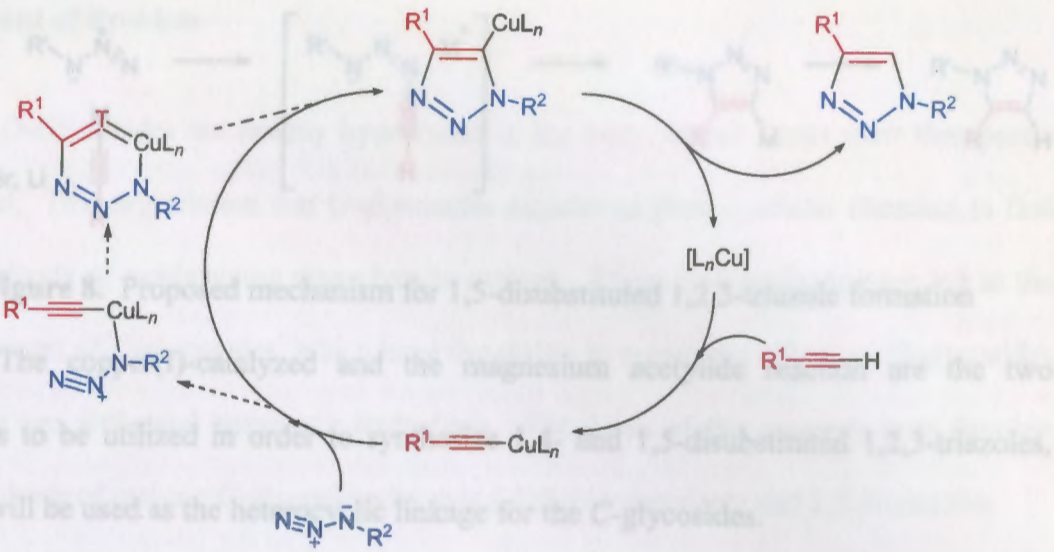


Figure 7. Proposed mechanism for the formation of 1,4-disubstituted 1,2,3-triazole

After discovering an efficient route to synthesize 1,4-disubstituted 1,2,3-triazoles, an equally efficient route needed to be developed that could produce the regioisomeric 1,5-disubstituted 1,2,3-triazole. Akimova et al. investigated using magnesium acetylides with organic azides in the 1960's to produce these 1,5-triazoles[19] However, poor results inhibited the progress of the reaction until Sharpless' group began to investigate these magnesium acetylide methods.

Akimova and coworkers proposed a mechanism for the 1,5-disubstituted 1,2,3-triazole synthesis (Figure 8) as follows. It begins with the nucleophilic attack of the magnesium-containing acetylide on the terminal nitrogen atom of the azide. This is followed by the spontaneous closure of the linear intermediate to a five-membered heterocycle with eventual protonation when the reaction is quenched with aqueous acid.

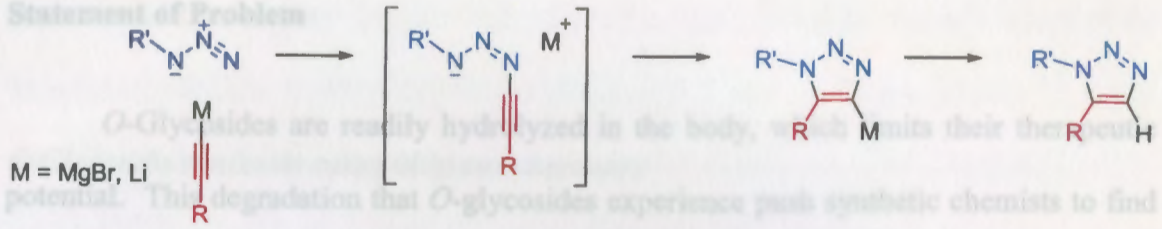


Figure 8. Proposed mechanism for 1,5-disubstituted 1,2,3-triazole formation

The copper(I)-catalyzed and the magnesium acetylide reaction are the two methods to be utilized in order to synthesize 1,4- and 1,5-disubstituted 1,2,3-triazoles, which will be used as the heterocyclic linkage for the *C*-glycosides.

Statement of Problem

O-Glycosides are readily hydrolyzed in the body, which limits their therapeutic potential. This degradation that *O*-glycosides experience push synthetic chemists to find new methods of synthesizing disaccharide analogs. These new methods have led to the development of *C*-glycosides, which have the ability to mimic the effects of *O*-glycosides yet they can withstand enzymatic hydrolysis. The focus of this research is to develop new methods of making *C*-glycosides by using dithiane chemistry and 1,2,3-triazoles.

Results and Discussion

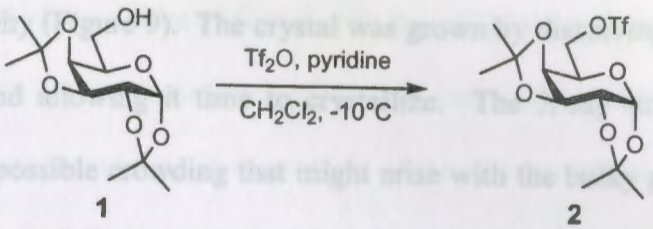
C-Glycoside synthesis using dithiane chemistry

The Norris research group had previously published work in the *Journal of Organic Chemistry* on dithianes that were derived from five-membered furanose rings. A couple of questions arose about dithianes because of this work; could a dithiane be attached at a secondary carbon; could the dithiane chemistry work on a six-membered pyranose ring? How much would the reactivities differ between a phenyl-substituted dithiane ($[PhS]_2CHR$) and a methyl dithiane ($[CH_3S]_2CHR$)? The last two questions were chosen to be answered in this discussion.

The D-galactose derivative, 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (**1**) was the sugar chosen because the hydroxyl groups at C-1, 2, 3, and 4 were already protected with isopropylidene moieties leaving the only reactive free hydroxyl group at C-6. It was thought that if a good leaving group, such as trifluoromethanesulfonate, were added to this free hydroxyl it could be displaced by a lithiated bis(phenylthio)methane nucleophile. Trifluoromethanesulfonate has been shown to be an excellent leaving group, however when formed can be unstable and degrade in a short amount of time. Therefore, it must be used immediately after it is produced.

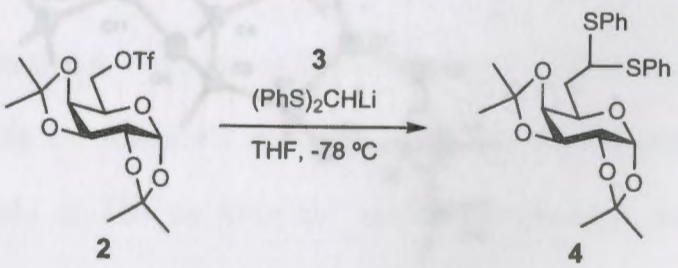
Compound **1** was reacted with trifluoromethanesulfonic anhydride, Tf_2O, in CH_2Cl_2 and pyridine, resulting in the conversion of the free hydroxyl at C-6 to the triflate leaving group to form compound **2** (Equation 4) in good yield (91%). After two hours TLC showed complete consumption of the starting material and formation of a new less

polar spot. After workup the ^{1}H NMR spectrum of the product gave confirmation of the triflated sugar. The position of protons H-6 and H-6' shifted farther downfield, which would be expected with the strongly electronegative CF_3SO_2- group next to C-6.



Equation 4. Synthesis of triflate-derived sugar **2**

Next, bis(phenylthio)methane was reacted with *n*-BuLi in THF to form the lithiated bis(phenylthio)methane nucleophile (**3**). The electrophilic **2** in THF was then added to the lithiated dithiane **3** and the reaction was stirred overnight to form the dithiane sugar **4** (Equation 5) in relatively good yield (68%) after column purification. TLC (10:1 hexane:ethyl acetate) showed formation of a new spot, however, unreacted starting material was observed also.



Equation 5. Synthesis of dithiane-derived sugar **4**

Formation of the dithiane product was confirmed from the analysis of the ^{1}H NMR spectrum, which showed a multiplet in the aromatic region for the new hydrogens of the phenyl rings. Also, the doublet of doublet of doublets signals at 1.84 ppm and 2.37 ppm correspond to H-6 and H-6' of the dithiane sugar, respectively. The H-6 and H-6' protons are now shifted farther upfield and are coupled to one more proton (H-7) than

previously with the triflate sugar. ^{13}C NMR revealed 25 signals and mass spectrometry indicated a mass of 497.2 (474.2 + Na), which agree with the structure assigned to the dithiane. Further confirmation of the structure of the dithiane product was obtained by X-ray crystallography (Figure 9). The crystal was grown by dissolving the purified syrup in hot methanol and allowing it time to crystallize. The X-ray structure allowed for observation of the possible crowding that might arise with the bulky phenyl groups for a future deprotonation at C-7.

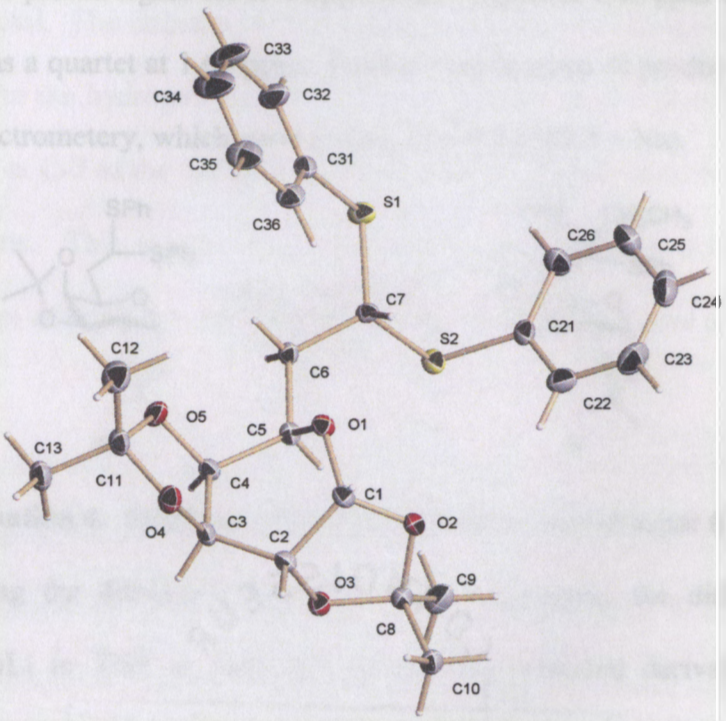
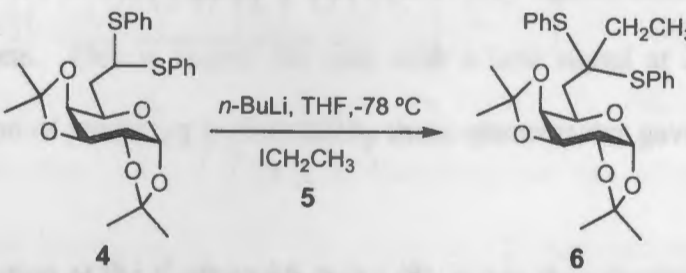


Figure 9. Depiction of the X-ray crystal structure of compound **4**

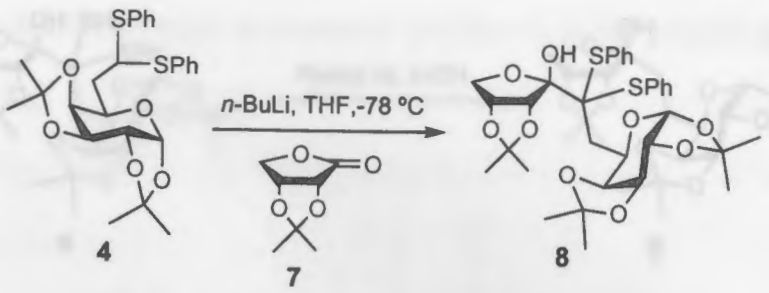
After confirmation of the structure of the dithiane product was complete, compound **4** was deprotonated and reacted with iodoethane to test its reactivity and its potential ability to couple with an electrophilic lactone to make a *C*-glycoside. Thus, compound **4** was reacted with *n*-BuLi in THF for 20 minutes to form the lithiated

dithiane. After lithiation was complete, the nucleophile was reacted with the electrophilic iodoethane (**5**) to form the alkylated product (**6**) (Equation 6) in 40 % yield. TLC showed unreacted starting material and a new UV-active spot that was slightly less polar than the starting material, which would be expected with the addition of a non polar ethyl group. The product structure was confirmed using ^{1}H NMR and mass spectrometry. The doublet of doublet of doublets for protons H-6 and H-6' of the dithiane starting material (**4**) were no longer observed. In their place are doublet of doublet signals at 1.89 and 2.03 ppm for H-6 and H-6'. The proton signal for H-9 appears as a triplet at 1.15 ppm and the protons for H-8 show up as a quartet at 1.69 ppm. Further confirmation of product structure was given by mass spectrometery, which gave a mass of 525.3 (502.3 + Na).



Equation 6. Synthesis of alkylated dithiane-derived sugar **6**

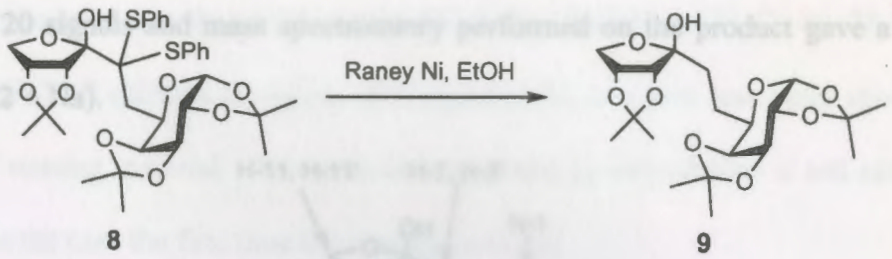
After testing the dithiane's reactivity using iodoethane, the dithiane (**4**) was reacted with *n*-BuLi in THF to form the nucleophilic lithiated derivative. After 20 minutes, the lithiation was complete and the product was then coupled with the electrophilic 2,3-*O*-isopropylidene-D-erythronolactone (**7**) to form the *C*-glycosidic lactol (**8**) in a 40% yield(Equation 7). After 15 hours TLC showed the formation of two more polar, very close-running UV active spots with some unreacted dithiane left over. After column purification, three spots were left over, two of which are believed to be the α- and β-anomers of the *C*-glycoside lactol.



Equation 7. Addition of lactone to the dithiane-derived sugar **8**

Although analysis of the ^{1}H NMR and ^{13}C NMR proved to be difficult, the observation of a new doublet of doublets at 2.49 ppm gave indication of the formation of the *C*-glycoside lactol. The dithiane (**4**) had a doublet of doublet of doublets at 2.37 ppm that corresponded to the hydrogen on C-4 of the six-membered pyranose ring. With the loss of a hydrogen at C-7 of the dithiane, the H-6 and H-6' signals should be observed as doublets of doublets. This is indeed the case with a new signal at 2.49 ppm. Also, further confirmation of product was detected by mass spectrometry gave a mass of 655.2 (632.2 + Na).

After formation of the *C*-glycoside lactol (**8**), it was then decided to try to reduce the thiols first, instead of the hydroxyl group of the *C*-glycoside lactol. The reduction of the thiols was achieved by using Raney nickel to give compound **9** in a 63% yield (Equation 8). Compound **8** was dissolved in ethanol, Raney Ni / water slurry was added *via* pipette, and the reaction was monitored by TLC for formation of product. After 90 minutes the reaction was complete and TLC showed formation of a new more polar spot that was not UV active. This is to be expected with the loss of the -SPh groups from **8**.



8 9

Equation 8. Reduction of dithioacetals **9**

Assignment of the ^{1}H NMR signals for compound **9** was achieved by close examination of integration, expected chemical shifts, and coupling constants. There were five singlets found upfield in the spectrum (1.31, 1.32, 1.34, 1.46, 1.51 ppm) with four having an integration corresponding to three protons each, and the fifth singlet integrating to 6 protons. Each peak corresponds to the methyl groups of the isopropylidene moieties. The loss of the thiols gave a new multiplet splitting pattern for the methylene bridge of C-6 and C-7 in the region between 1.74-2.08 ppm (see Figure 10). This splitting pattern is in agreement with what would be assumed following the loss of the thiols and the addition of two new hydrogens at C-7. The singlet at 3.23 ppm belongs to the hydroxyl group of the lactol. This signal is important to note, because the next step in the synthesis is the reductive removal of this hydroxyl group. There was also a multiplet at 3.86 ppm that integrated to two protons for H-5 and H-11', respectively. A doublet of doublets at 4.01 ppm corresponds to the other proton at C-11 (J = 4.0, 10.3 Hz). The doublet of doublets at 4.17 ppm and 4.30 ppm were found to be for H-4 (J = 1.7, 7.9 Hz) and H-2 (J = 2.2, 5.0 Hz). The proton observed as a doublet at 4.40 ppm for H-9 (J = 6.0 Hz) couples to the doublet of doublets at 4.85 for H-10 (J = 3.9, 6.0 Hz). The doublet of doublets at 4.59 ppm corresponds to H-3 (J = 2.2, 7.9 Hz), which is coupled to the aforementioned H-4. Finally, H-1 (J = 5.1 Hz) shows as a doublet at 5.54 ppm. ^{13}C NMR

resulted in 20 signals and mass spectrometry performed on the product gave a mass of 439.2 (416.2 + Na).

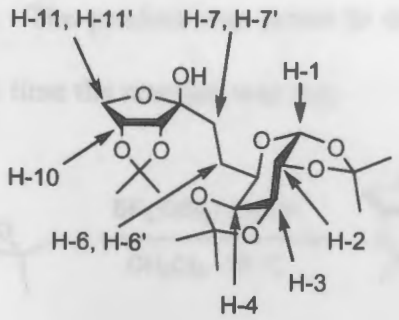


Figure 10. Numbering scheme for compound **9**

It was found that compound **9** would crystallize from methanol with the hydroxyl group pointing above the ring and *trans* to O-2 on the isopropylidene group. The crystal structure gave further confirmation of the coupling of the lactone (**7**) to the nucleophilic dithiane (**4**).

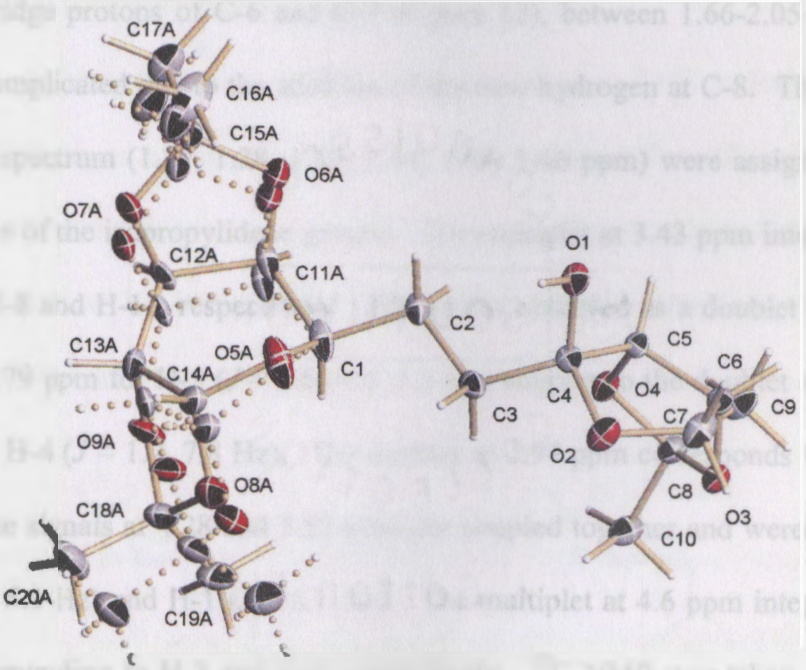
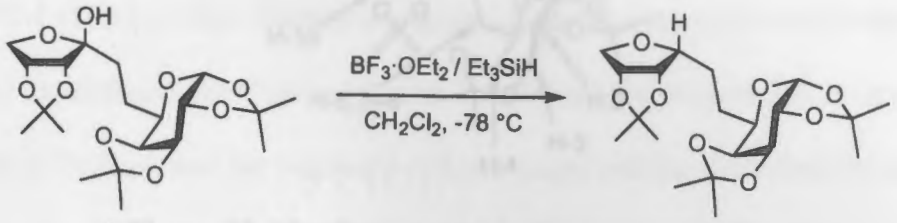


Figure 11. X-ray crystal structure of compound **9**

Compound **9** was then reacted with $BF_3{\cdot}OEt_2$ / Et_3SiH in CH_2Cl_2 at –78 °C for 90 minutes until TLC showed formation of compound **10** as a new less polar spot and the absence of starting material. The product was prone to degradation if left stirring too long, as was the case the first time the reaction was run.



9 **10**

Equation 9. Final reduction to *C*-glycoside **10**

Product confirmation was primarily achieved by examining the ^1H NMR spectrum of **10**. The loss of the singlet at 3.23 ppm that belonged to the hydroxyl group in **9** suggested the successful reduction of compound **9**. Also, the splitting pattern for the methylene bridge protons of C-6 and C-7 (Figure 12), between 1.66-2.05 ppm, is now even more complicated due to the addition of the new hydrogen at C-8. The six singlets found in the spectrum (1.27, 1.28, 1.30, 1.41, 1.43, 1.46 ppm) were assigned to the six methyl groups of the isopropylidene groups. The multiplet at 3.43 ppm integrates to two protons for H-8 and H-11, respectively. The proton observed as a doublet of doublet of doublets at 3.79 ppm for H-5 (J = 1.6, 4.6, 6.2 Hz) couples to the doublet of doublets at 4.17 ppm for H-4 (J = 1.7, 7.8 Hz). The doublet at 3.97 ppm corresponds to H-11' (J = 10.8 Hz). The signals at 4.28 and 5.52 ppm are coupled together and were identified as H-2 (J = 2.2, 5.1 Hz) and H-1 (J = 5.1 Hz). The multiplet at 4.6 ppm integrated to two protons corresponding to H-3 and H-9, respectively. ^{13}C NMR was taken of the totally

reduced *C*-glycoside product and gave 20 carbon signals and mass spectrometry gave a correct mass of 423.2 (400.2 + Na).

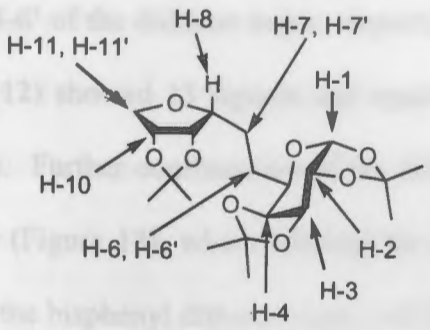
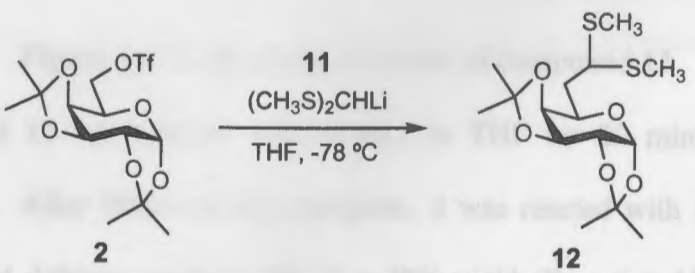


Figure 12. Numbering scheme for compound **10**

With the success of the bis(phenylthio)methane chemistry on furanose and pyranose rings, it was thought that the use of bis(methylthio)methane as the nucleophile precursor would work in a similar fashion to, and possibly better than, the bis(phenylthio)methane-derived nucleophile. To test this hypothesis, similar experiments using bis(methylthio)methane were carried out.

Bis(methylthio)methane was reacted with *n*-BuLi in THF to form the lithiated bis(methylthio)methane nucleophile (**11**). The electrophilic triflate (**2**) in THF was then added to the lithiated dithiane and the mixture was stirred overnight to form the dithiane sugar (**12**) (Equation 10) in a yield of 30%. TLC showed formation of a new spot, however, unreacted starting material was still present.



Equation 10. Synthesis of *S*-methyl dithiane-derived sugar **12**

Confirmation of the dithiane product was obtained from the ^{1}H NMR spectrum, which showed doublet of doublet of doublets signals at 1.84 ppm and 2.18 ppm corresponding to H-6 and H-6' of the dithiane sugar, respectively. ^{13}C NMR performed on the bismethyl dithiane (**12**) showed 15 signals and mass spectrometry resulted in a mass of 373.1 (350.1 + Na). Further confirmation of the dithiane product was obtained from X-ray crystallography (Figure 13), which allowed for observation of the possible crowding at C-7. Now that the bisphenyl dithiane sugar and the bismethyl dithiane sugar had been produced, comparisons between the two sugars' reactivity could be made.

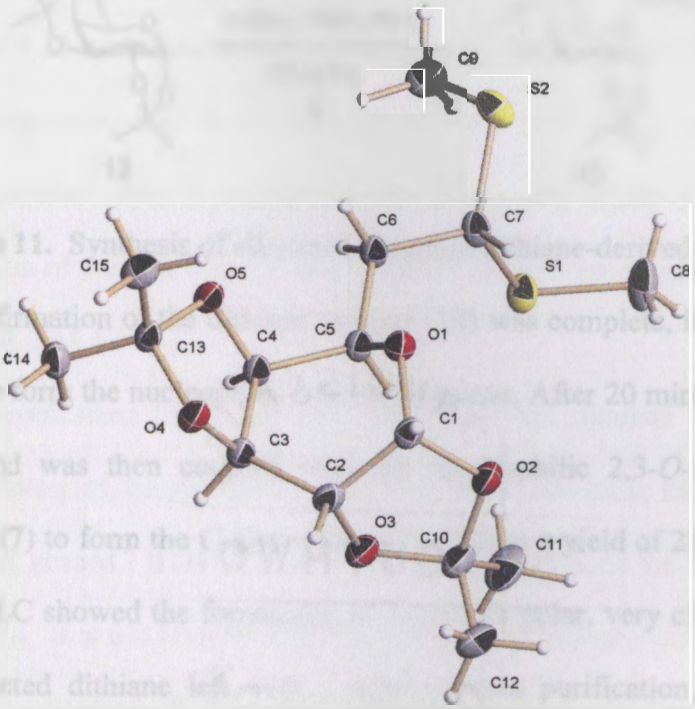
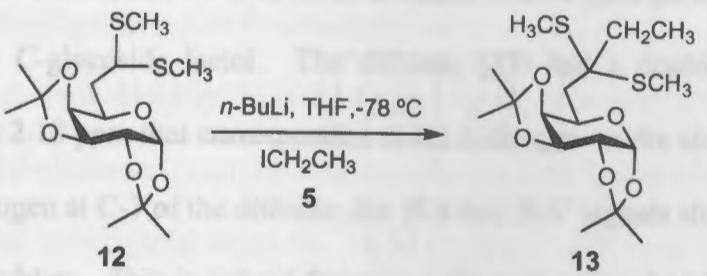


Figure 13. X-ray crystal structure of compound **12**

Compound **12** was reacted with *n*-BuLi in THF for 20 minutes to form the lithiated dithiane. After lithiation was complete, it was reacted with iodoethane (**5**) to form the alkylated dithiane product (**13**) in a 28% yield (Equation 11). TLC showed unreacted starting material and a new spot that was slightly less polar than the starting

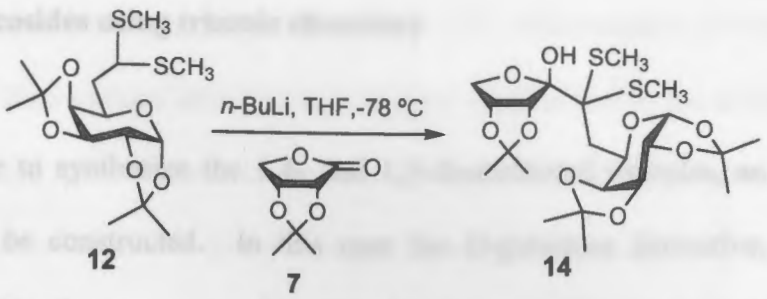
material, which would be expected with the addition of a non-polar ethyl group. The product was confirmed using ^{1}H NMR and mass spectrometry. The protons for H-8 show up as a quartet at 1.69 ppm and the proton signal for H-9 appears as a triplet at 1.05 ppm. The doublet of doublet of doublets for protons H-6 and H-6' of the dithiane starting material (**4**) are now gone. In their place is a multiplet at 1.88-2.07 ppm for H-6 and H-6'. The product was further confirmed by mass spectrometery, which gave a mass of 401.2 (378.2 + Na).



12 **13**

Equation 11. Synthesis of alkylated *S*-methyl dithiane-derived sugar **13**

After confirmation of the dithiane product (**12**) was complete, it was reacted with *n*-BuLi in THF to form the nucleophilic lithiated dithiane. After 20 minutes, the lithiation was complete and was then coupled with the electrophilic 2,3-*O*-isopropylidene-D-erythronolactone (**7**) to form the *C*-glycoside lactol (**14**) in a yield of 28% (Equation 12). After 15 hours TLC showed the formation[of two more polar, very close-running spots with some unreacted dithiane left over. After column purification, two spots were isolated, which are believed to be the α- and β-anomers of the *C*-glycoside lactol.



Equation 12. Addition of lactone to *S*-methyl dithiane-derived sugar **14**

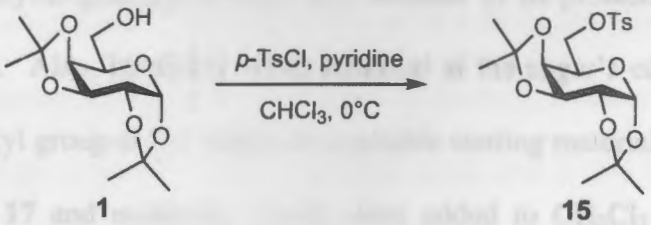
Analysis of the ^{1}H NMR and ^{13}C NMR spectra proved to be very difficult, however, the observation of a new doublet of doublets at 2.49 ppm gave indication of the formation of the *C*-glycoside lactol. The dithiane (**12**) had a doublet of doublet of doublets signal at 2.18 ppm that corresponded to the hydrogen on the sixth carbon. With the loss of a hydrogen at C-7 of the dithiane, the H-6 and H-6' signals should be observed as doublets of doublets. This is indeed the case with a new signal at 2.23 ppm. Also, further confirmation of product identity was detected by mass spectrometry, which gave a mass of 531.2 (508.2 M + Na).

It was hypothesized that addition to the bismethyl dithiane would give better yields than its counterpart, bisphenyl dithiane, because of less steric hindrance caused by the smaller methyl groups. However, that was not the case with the bisphenyl dithiane giving larger yields. It is not known what attributed to the higher yields of the bisphenyl dithiane, but further research on these dithioacetals and others like these, could possibly give the answers in the future.

Dimeric *C*-glycosides using triazole chemistry

In order to synthesize the 1,4- and 1,5-disubstituted triazoles, an azide and an alkyne had to be constructed. In this case the D-galactose derivative, 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (**1**), was the sugar chosen to make the azide from because it was cheap and readily available commercially. Also, the hydroxyl groups at C-1, 2, 3, and 4 were already protected with isopropylidene moieties leaving the only reactive free hydroxyl group at C-6 for manipulation.

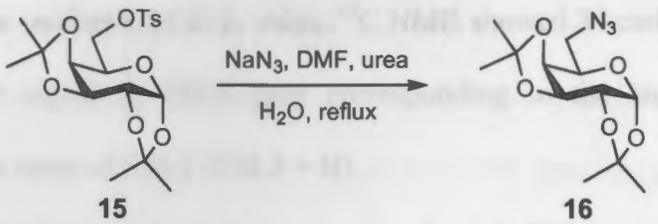
Compound **1** was dissolved in pyridine and the solution cooled to 0 °C, at which time a solution of *p*-toluenesulfonyl chloride dissolved in $CHCl_3$ was added dropwise and the mixture stirred overnight to form the tosylated sugar (**15**) in a 95% yield. TLC showed no starting material and after workup the reaction gave a white solid product (Equation 13). ^1H NMR showed two doublets in the aromatic region at 7.33 and 7.81 ppm for the addition of the phenyl ring. Also, the five singlets (1.28, 1.32, 1.35, 1.51, and 2.45 ppm) correspond to the two isopropylidene groups, with the fifth signal (2.45 ppm) for the methyl group on the phenyl ring. Another change of the product compared to that of the starting material is the chemical shift downfield for the protons H-6 and H-6', to 4.07 and 4.20 ppm respectively.



1 **15**

Equation 13. Synthesis of tosylate-derived sugar **15**.

After formation of the tosylated product (**15**) was complete, it was dissolved in DMF at which time sodium azide, urea, and water were added to the solution and let to stir at reflux until consumption of the starting material had taken place. After TLC showed the absence of the UV-active starting material and formation of a new more polar spot, the reaction was worked up and provided a golden syrup (**16**) for a 95% yield (Equation 14). Examining the ^{1}H NMR spectrum showed the absence of protons in the aromatic region that had previously shown up because of the tosylate group. The protons, H-6 and H-6', that correspond to the doublet of doublets at 3.35 and 3.50 ppm, have shifted farther upfield compared to their previous location, 4.07 and 4.20 ppm for compound **15**. ^{13}C NMR gave 12 signals, which would be expected, and mass spectrometry gave a mass of 308.1 (285.1 + Na).

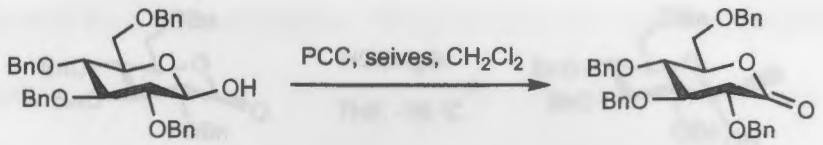


Equation 14. Synthesis of primary azide-derived sugar **16**

After formation of the primary azide was achieved, attention was switched to synthesizing a suitable alkyne. The sugar chosen as the foundation for the alkyne was 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside (**17**) because of its protected hydroxyl groups at C-2, 3, 4, and 6. Also, its ability to be oxidized at the sugar's easily accessible and unprotected hydroxyl group at C-1 makes it a suitable starting material.

Compound **17** and molecular sieves were added to CH_2Cl_2 and stirred for 20 minutes. PCC was then added, turning the solution dark brown, and the mixture was allowed to stir overnight. TLC showed formation of a new UV-active spot that was less

polar than the starting material and the absence of the starting material. Column filtration gave a clear syrup (**18**) in a yield of 92% (Equation 15).



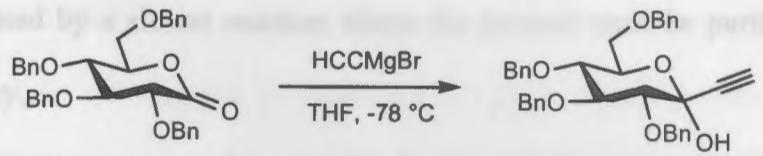
17 **18**

Equation 15. Oxidation to lactone **18**

The structure of the product was confirmed by ^{1}H NMR, ^{13}C NMR, and mass spectrometry. The doublet of doublets at 3.64 ppm and 3.71 ppm were found to be protons H-6 (J = 3.2, 11.1 Hz) and H-6' (J = 2.4, 11.0 Hz). The only other peak that wasn't a multiplet was that of H-4 (J = 6.6 Hz), which showed up as a doublet at 4.11 ppm. The lack of a signal in the 5.5 ppm region, where the anomeric proton would appear, indicates the oxidation of C-1. Also, ^{13}C NMR showed 34 carbon signals and the all important ester signal at 168.9 ppm corresponding to the lactone, while mass spectrometry gave a mass of 539.2 (538.3 + H).

After making the lactone (**18**), it was dissolved in THF and ethynylmagnesium bromide was added while being stirred at -78 °C to form the propargyl alcohol product (**19**) as a brown syrup in 62% yield (Equation 16). TLC showed formation of a more polar spot with a small amount of starting material left over. ^{1}H NMR analysis showed the formation of two anomers. There was a singlet at 2.49 for the terminal alkyne proton. The rest of the spectrum proved to be too difficult to analyze, however after integration of the multiplets between 3.55-4.07 ppm, 4.42-4.60 ppm, and 4.75-5.05 ppm, integration gave 11 protons, 8 protons, and 10 protons, respectively. There was a broad singlet at

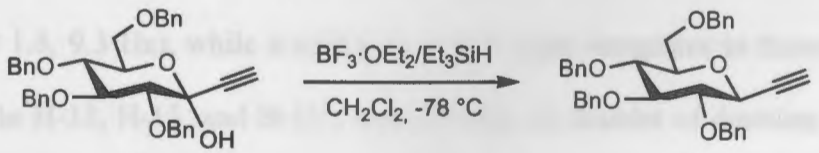
5.19 ppm for the hydroxyl group of the lactol. Finally, a multiplet between 7.10-7.37 ppm corresponded to the protons for the benzyl protecting groups.



18 **19**

Equation 16. Synthesis of propargyl alcohol **19**

Compound **19** was then dissolved in CH_2Cl_2 and cooled to -78 °C. At this time $BF_3{\cdot}OEt_2$ and Et_3SiH were added to the reaction and let to stir for 1 hour and then placed in the freezer overnight to give the alkyne as a clear syrup in a 61% yield after workup (Equation 17). TLC showed complete consumption of the starting material and the formation of a new less polar spot. ^1H NMR gave a doublet at 2.56 ppm for the terminal alkyne proton. The proton at H-5 shows as a multiplet and resides at 3.46 ppm. Further analysis proved to be too difficult to pinpoint each individual proton. A multiplet at 3.70 ppm integrated to 5 protons, while a multiplet at 4.51-5.05 ppm integrated to 9 protons. Finally, the multiplet between 7.14-7.40 ppm corresponds to the 20 protons of the benzyl protecting groups. Mass spectrometry taken on the product gave a mass of 571.3 (548.3 M + Na).



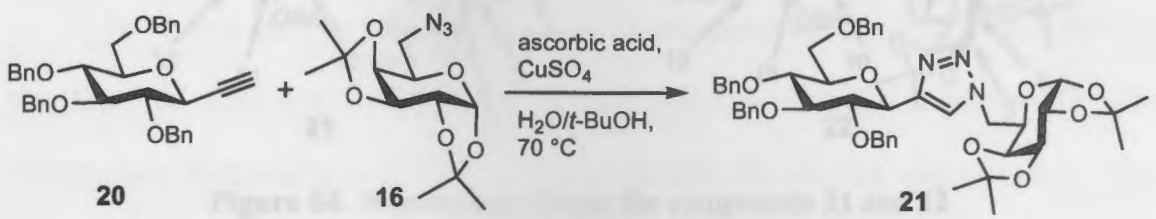
19 **20**

Equation 17. Synthesis of alkyne-derived sugar **20**

After the alkyne and the azide had been synthesized, it was decided to study the formation of 1,4-disubstituted and 1,5-disubstituted triazoles from the newly made

products. The synthesis of the 1,4-disubstituted triazole is a much faster and cleaner reaction where the product precipitates out of solution, whereas the 1,5-disubstituted product is formed by a slower reaction where the product must be purified by column chromatography.

The first attempts at making a triazole were performed under Sharpless' Cu(I) conditions. Compound **20** was dissolved in *t*-BuOH/H_2O, then **16** was dissolved in the solution along with the $CuSO_4$ and ascorbic acid (Equation 18). The solution was then heated at 70 °C for two hours until the reaction was complete. The reaction was then cooled and the product (**21**) precipitated out of solution for a yield of 86%.



Equation 18. Synthesis of 1,4-disubstituted triazole **21**

Analysis of the ^{1}H NMR spectrum showed there were three singlets found upfield in the spectrum (1.20, 1.31, 1.49 ppm) with two having an integration corresponding to three protons each, and the third singlet integrating to 6 protons. Each peak corresponds to the methyl groups of the isopropylidene moieties. A doublet at 3.62 ppm corresponds to H-14 (J = 1.8, 9.3 Hz), while a multiplet at 3.71 ppm integrates to three protons and corresponds to H-13, H-15, and H-15', respectively. A doublet of doublets at 3.80 ppm corresponds to H-11 (J = 8.9 Hz), while a doublet of doublets at 3.99 ppm belongs to H-12 (J = 9.3 Hz). The doublet of doublets at 4.10 ppm corresponds to H-4 (J = 1.8, 7.8 Hz), while the doublet of doublet of doublets at 4.21 ppm belongs to H-5 (J = 1.8, 4.8, 8.1 Hz). The multiplet at 4.29 ppm corresponds to H-2 and H-6, respectively (see Figure

14 for numbering scheme). The doublet of doublet at 4.43 ppm integrates to one proton and belongs to H-6' (J = 8.2 Hz). The multiplet at 4.50-4.86 ppm integrates to 10 protons and belongs to H-3, H-9, and the CH_2 of the protecting groups. The doublet at 5.44 ppm belongs to H-1 (J = 4.9 Hz) and the multiplet at 7.04-7.32 ppm corresponds to the 20 protons on the benzyl protecting groups. Finally, the singlet at 7.68 ppm belongs to the triazole proton on the heterocycle. Mass spectrometry taken on the product gave a mass of 834.6 (833.6 M + H),

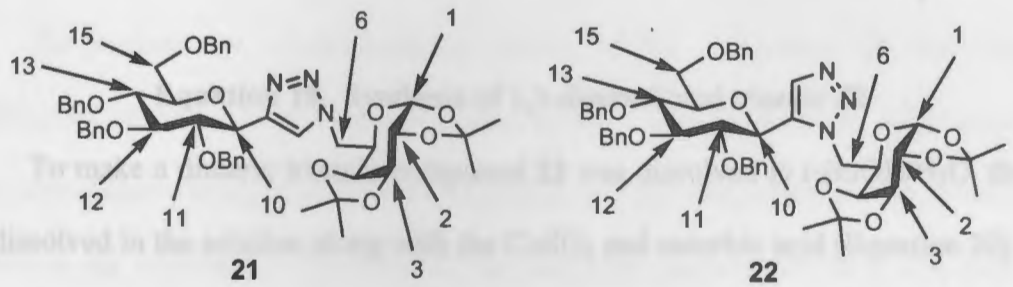
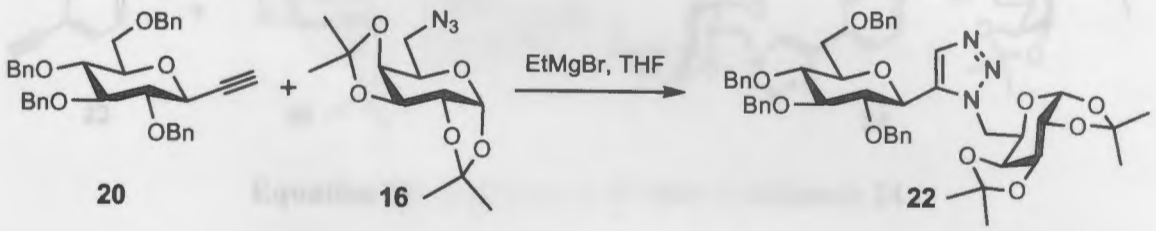


Figure 14. Numbering scheme for compounds **21** and **22**

Compound **20** was added to ethylmagnesium bromide in THF and heated to 50 °C for 20 minutes. After cooling to room temperature, compound **16** was dissolved in THF and added to the reaction, which was then allowed to stir overnight to form the 1,5-disubstituted product **22** in a 30% yield as a white solid (Equation 19). TLC of the reaction mixture showed formation of a more polar spot with unreacted starting materials left over. ^{1}H NMR showed four singlets that were found upfield in the spectrum (1.25, 1.29, 1.47, and 1.51 ppm) which integrated to three protons each. These protons corresponded to the methyl groups on the isopropylidene moieties. A multiplet at 3.55 ppm integrated to one proton and belonged to H-5. A multiplet at 3.72-4.14 ppm integrated to 8 protons, while a doublet of doublets at 4.29 corresponded to H-2 (J = 2.3, 4.9 Hz). A multiplet at 4.42-4.92 ppm integrated to eleven protons. A doublet of

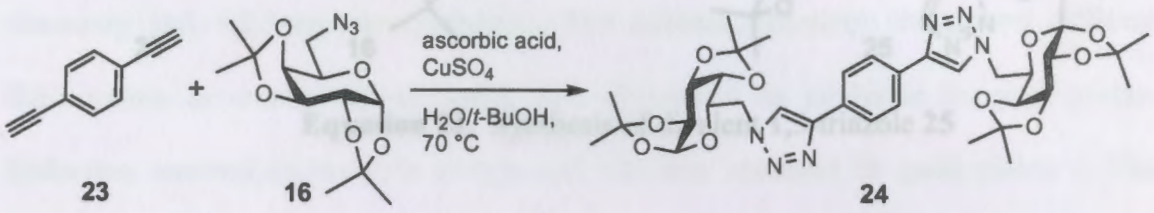
doublets at 5.48 corresponded to H-1 (J = 4.9 Hz). A multiplet at 6.97-7.39 corresponded to the protons on the benzyl protecting groups. Finally, a singlet at 7.67 ppm belonged to the triazole proton on the heterocycle. Mass spectrometry taken of the product gave a mass of 833.7 (834.7 M + H).



Equation 19. Synthesis of 1,5-disubstituted triazole **22**

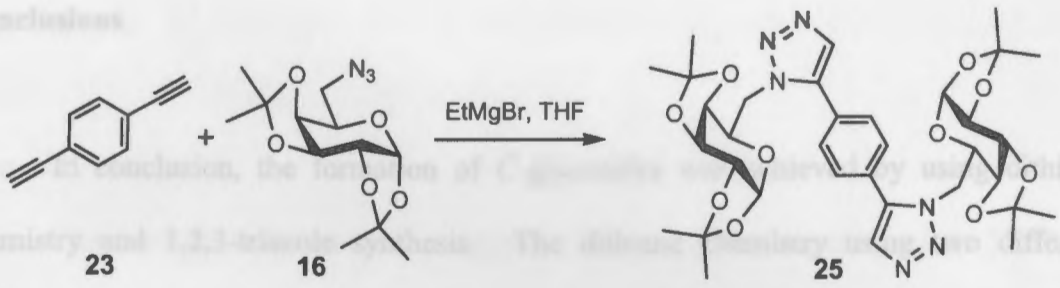
To make a dimeric triazole compound **23** was dissolved in *t*-BuOH/H_2O, then **16** was dissolved in the solution along with the $CuSO_4$ and ascorbic acid (Equation 20). The solution was then heated at 70 °C for two hours until the reaction was complete. The reaction was cooled and the product (**24**) precipitated out of solution for a yield of 90%. Confirmation of the product structure was achieved by analysis of ^{1}H NMR and mass spectrometry. ^{1}H NMR showed four singlets that were found upfield in the spectrum (1.30, 1.38, 1.42, and 1.52 ppm) which integrated to six protons each. These protons corresponded to the methyl groups on the isopropylidene moieties. There was a multiplet at 4.25 ppm that integrated to four protons and corresponded to H-4 and H-5. A doublet of doublets at 4.35 and 4.51 ppm which belonged to H-2 (J = 2.6, 4.9 Hz) and H-6 (J = 8.2 Hz). A multiplet at 4.69 ppm integrates to four protons corresponding to H-3 and H-6'. A doublet of doublets at 5.56 ppm belongs to H-1 (J = 4.9 Hz), while the singlet at 7.91 ppm corresponds to the four protons on the middle benzene ring. The singlet at 8.01

ppm integrates to two protons corresponding to the triazole protons on each heterocycle. Mass spectrometry taken of the product gave a mass of 697.5 (696.5 M + H).



Equation 20. Synthesis of divalent 1,4-triazole **24**

To produce the 1,5-disubstituted analog of **22**, compound **23** was added to ethylmagnesium bromide in THF and heated to 50 °C for 20 minutes. After cooling to room temperature, compound **16** was dissolved in THF and added to the reaction and allowed to stir overnight to form the 1,5-disubstituted product (**25**) in a 52% yield as a white solid (Equation 21). TLC showed formation of a more polar spot with unreacted starting materials left over. ^{1}H NMR showed four singlets that were found upfield in the spectrum (1.29, 1.32, 1.39, and 1.49 ppm) which integrated to six protons each. These protons corresponded to the methyl groups on the isopropylidene moieties. A doublet at 4.26 ppm corresponded to H-4 (J =7.9 Hz), while a doublet of doublets at 4.33 ppm corresponds to H-2 (J = 2.5, 5.0 Hz). A multiplet at 4.51 ppm integrates to six protons for H-5, H-6, and H-6', respectively. A doublet of doublets at 4.66 ppm corresponds to H-3 (J = 2.5, 7.9 Hz). A doublet at 5.44 ppm belonged to H-1 (J = 5.0 Hz). A singlet at 7.69 ppm integrated to four protons corresponding to the protons on the middle benzene ring. A singlet at 7.74 ppm corresponds to the triazole proton on the heterocycles. Mass spectrometry taken of the product gave a mass of 697.5 (696.5 M + H).



Equation 21. Synthesis of divalent 1,5-triazole **25**

Conclusions

In conclusion, the formation of *C*-glycosides was achieved by using dithiane chemistry and 1,2,3-triazole synthesis. The dithiane chemistry using two different dithioacetals to create a *C*-glycoside was successful in moderate to good yields. Reductive removal of the SPh groups and OH was achieved in good yields. The synthesis of 1,4-disubstituted 1,2,3-triazoles was achieved in high yields and was quick and efficient. Synthesis of 1,5-disubstituted 1,2,3-triazoles was achieved in much lower yields and was slow and inefficient when compared to the 1,4-disubstituted 1,2,3-triazoles.

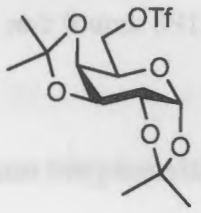
Future work in this field could involve more testing of different dithioacetals and their reactivities. Also, a larger library of 1,2,3-triazoles could be made by experimenting with other alkynes and sugar-derived azides.

Experimental

General Procedures

The reaction rates were investigated by thin layer chromatography (TLC) on Whatman aluminum-backed plates coated with silica gel. UV light was used to detect the UV-active spots. TLC plates were treated with 5% sulfuric acid/ 95% ethanol solution to burn the reaction spots to indicate the carbohydrate product. The products from the reaction were purified *via* flash column chromatography using 60-Å silica gel with hexane/ethyl acetate solvent mixtures. The products obtained were identified by Nuclear Magnetic Resonance spectroscopy on samples dissolved in $CDCl_3$, using a Varian Gemini 2000 system, at a frequency of 400 MHz for ^{1}H spectra and 100 MHz for ^{13}C spectra. All chemical shifts were 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), q (quartet), m (multiplet) and coupling constants (*J*) are measured in Hertz. A Bruker Esquire-HP 1100 mass spectrometer was used for low-resolution MS. A Perkin-Elmer polarimeter was used to obtain optical rotation data.

Reaction of 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (1) with trifluoromethanesulfonic anhydride to form the triflate (2)



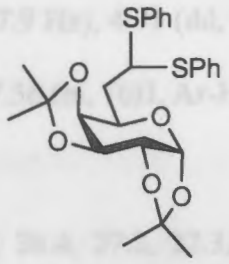
To a flame-dried 250 mL 3 neck round bottom flask, under nitrogen atmosphere, was added CH_2Cl_2 (40 mL) and anhydrous pyridine (2.0 mL, 24.7 mmol) and the resulting solution was cooled to –10 °C. Trifluoromethanesulfonic anhydride, Tf_2O, (2.6 mL, 15.5 mmol) in CH_2Cl_2 (10 mL) was added dropwise and let stir for 10 minutes resulting in a thick white precipitate. At this point a solution of 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (2.0 g, 7.7 mmol) in CH_2Cl_2 (10 mL) was added dropwise, turning the mixture light brown, and the reaction mixture was allowed to stir for 2 hours while warming to room temperature. TLC (5:1 hexane:ethyl acetate) showed complete consumption of starting material and formation of a new compound. The reaction was poured over ice water (30 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were collected and then washed with 5% H_2SO_4 and extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated down to a light brown syrup to afford **2** in an overall yield of 2.74 g (91%).

^{1}H NMR ($CDCl_3$): δ 1.33 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 4.10 (ddd, 1H, H-5, J = 1.9, 4.8, 7.0 Hz), 4.24 (dd, 1H, H-4, J = 2.0,

7.9 Hz), 4.36 (dd, 1H, H-2, J = 2.6, 4.9 Hz), 4.5-4.6 (m, 3H, H-3, H-6, H-6'), 5.54 (d, 1H, H-1, J = 4.9 Hz).

m/z calculated: 392.3 *m/z* found: 391.3 (M - H)

Formation of 4 by addition of lithium bis(phenylthio)methane (3) to triflate 2



In a flame-dried 100 mL round bottom flask under nitrogen atmosphere, bis(phenylthio)methane (4.0 g, 17.5 mmol) was dissolved in dry THF (30 mL) and the solution was cooled to –78 °C. A solution of 1.6 M *n*-BuLi in hexane (9.0 mL, 14.4 mmol) was added *via* syringe and the mixture was allowed to stir for 30 minutes resulting in a thick semi-solid yellow solution. At this time a solution of **2** (2.74 g, 7.0 mmol) in THF (10 mL) was added dropwise *via* syringe. After addition of **2**, the reaction mixture turned dark red and then changed into a black solution, at which time the reaction was allowed to stir overnight while warming to room temperature. TLC (10:1 hexane:ethyl acetate) showed the formation of a new compound with some of the starting material left unreacted. The reaction mixture was quenched with saturated NH_4Cl (40 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined, dried over

$MgSO_4$, and evaporated to a dark brown syrup. The syrup was purified *via* flash column chromatography using an eluent of 15:1 hexane:ethyl acetate to afford 2.25 g (68%) of **4** as crystalline product.

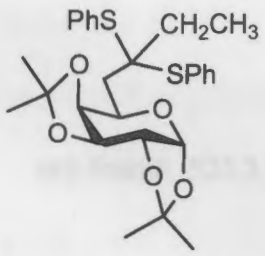
^{1}H NMR ($CDCl_3$): δ 1.31 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.60 (s, 3H, CH_3), 1.84 (ddd, 1H, H-6, J = 2.9, 10.0, 10.8 Hz), 2.37 (ddd, 1H, H-6', J = 3.8, 10.0, 10.9 Hz), 4.09 (dd, 1H, H-4, J = 1.8, 7.7 Hz), 4.32 (m, 2H, H-2, H-5), 4.62 (dd, 1H, H-3, J = 2.6, 7.9 Hz), 4.71 (dd, 1H, H-7, J = 3.7, 10.6 Hz), 5.54 (d, 1H, H-1, J = 5.1 Hz), 7.20-7.56 (m, 10H, Ar-H).

^{13}C NMR ($CDCl_3$): δ 25.9, 26.4, 27.2, 27.3, 37.4, 55.7, 66.3, 71.7, 72.2, 74.2, 97.6, 109.9, 110.4, 128.2, 128.8, 129.7 (2 x C), 129.8 (2 x C), 133.0 (2 x C), 134.3, 134.5 (2 x C), 135.3

m/z calculated: 474.2 *m/z* found: 497.2 (M + Na)

melting point: 84-86 °C

Reaction of lithiated dithiane derivative with iodoethane (5) to form the alkylated dithiane (6)



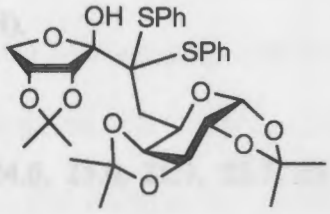
In a flame-dried 100 mL round bottom flask under nitrogen atmosphere, the dithiane product (**4**) (0.23 g, 0.5 mmol) was dissolved in dry THF (10 mL) and the solution cooled to –78 °C. A solution of 1.6 M *n*-BuLi in hexane (0.35 mL, 0.6 mmol) was added *via* syringe and allowed to stir for 30 minutes resulting in a yellow solution. At this time iodoethane (**5**) (0.15 mL, 1.8 mmol) was added dropwise *via* syringe, turning the reaction mixture into a brown color, and the mixture was allowed to stir overnight. TLC (10:1 hexane:ethyl acetate) showed the formation of a new UV-active compound with a slightly less polar spot compared to the dithiane starting material. The reaction mixture was quenched with saturated NH_4Cl (40 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to a light yellow syrup. The syrup was purified *via* flash column chromatography using an eluent of 12:1 hexane:ethyl acetate afford **6** as a yellow syrup in a yield of 0.1 g (40%).

^{1}H NMR ($CDCl_3$): δ 1.15 (t, 3H, H-9, J = 7.3 Hz) 1.26 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.70 (q, 2H, H-8, J = 7.3 Hz), 1.77 (s, 3H, CH_3), 1.89 (dd, 1H, H-6, J = 2.0, 15.7 Hz), 2.03 (dd, 1H, H-6', J = 7.3, 15.7 Hz), 3.77 (dd,

1H, H-4, J = 1.8, 7.9 Hz), 4.27 (dd, 1H, H-2, J = 2.5, 5.1 Hz), 4.46 (m, 1H, H-5), 4.54 (dd, 1H, H-3, J = 2.4, 7.9 Hz), 5.48 (d, 1H, H-1, J = 5.1 Hz), 7.30-7.76 (m, 10H, Ar-H).

m/z calculated: 502.2 *m/z* found: 525.3 (M + Na)

Addition of lithiated dithiane derivative to 2,3-*O*-isopropylidene-D-erythronolactone (7) to form the *C*-glycoside lactol (8)



In a flame-dried 100 mL round bottom flask under nitrogen atmosphere, the dithiane product (**4**) (1.0 g, 2.1 mmol) was dissolved in dry THF (10 mL) and the solution cooled to –78 °C. A solution of 1.6 M *n*-BuLi in hexane (1.5 mL, 2.4 mmol) was added *via* syringe and the mixture was allowed to stir for 30 minutes resulting in a yellow solution. At this time a solution of 2,3-*O*-isopropylidene-D-erythronolactone (**7**) (1.0 g, 6.3 mmol) in THF (10 mL) was added dropwise *via* syringe, turning the reaction mixture into a dark brown color, and the mixture was allowed to stir overnight. TLC (4:1 hexane:ethyl acetate) showed the formation of a new compound that was more polar compared to the dithiane starting material. The reaction mixture was quenched with saturated NH_4Cl (40 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The organic layers

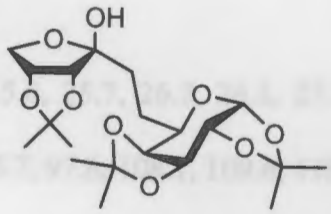
were combined, dried over $MgSO_4$, and evaporated to a light yellow syrup. The syrup was purified *via* flash column chromatography using an eluent of 5:1 hexane:ethyl acetate to give three very close-running spots, two of which are believed to be the α- and β-anomers of the *C*-glycoside lactol, to afford **8** as a clear syrup in a yield of 0.59 g (45%).

^{1}H NMR ($CDCl_3$): δ 1.27 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.65 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 1.73-1.78 (m, 1H, H-6), 2.49 (d, 1H, H-6', J = 5.3 Hz), 3.88-4.22 (m, 3H), 4.13 (m, 1H), 4.26 (m, 3H), 4.38-4.53 (m, 4H), 4.72 (m, 1H), 4.85-4.98 (m, 2H), 5.54 (d, 1H, H-1, J = 5.1 Hz), 7.17-7.78 (m, 10H, Ar-H).

^{13}C NMR ($CDCl_3$): δ 24.6, 25.0, 25.1, 25.7, 25.8, 26.2, 65.3, 70.3, 70.6, 71.0, 72.4, 73.0, 79.2, 82.2, 96.5, 106.8, 108.3, 108.5, 108.6, 114.9, 127.7, 127.8 (2 x C), 127.9, 128.0 (2 x C), 128.6, 128.8, 137.2 (2 x C), 138.2 (2 x C).

m/z calculated: 632.2 *m/z* found: 655.2 (M + Na)

Reduction of 8 with Raney nickel to form 9



To a solution of **8** (1.2 g, 1.9 mmol) in 95% EtOH (15 mL) at room temperature was added excess Raney Ni / H_2O slurry (6 mL) and the mixture was stirred for 2 hours. TLC (2:1 hexane:ethyl acetate) showed complete consumption of starting material and formation of a new compound that was less polar than the starting material. The reaction mixture was gravity filtered and rinsed with EtOH to remove the Raney Ni and the EtOH was evaporated under vacuum. The solution was extracted with CH_2Cl_2 (3 x 10 mL). The organic layers were then combined, dried over $MgSO_4$, and evaporated under vacuum to give a clear syrup. The syrup was purified *via* flash column chromatography using an eluent of 5:2 hexane:ethyl acetate to give two inseparable spots believed to be the α- and β-anomers of the reduced *C*-glycoside. Compound **9** was isolated as a white crystalline product in an overall yield of 0.49 g (63%).

^{1}H NMR ($CDCl_3$): δ 1.31 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.46 (s, 6H, 2 x CH_3), 1.52 (s, 3H, CH_3), 1.74-2.08 (m, 4H, H-6, H-6', H-7, H-7'), 3.23 (s, 1H, OH), 3.86 (m, 2H, H-5, H-11'), 4.01 (dd, 1H, H-11, J = 4.0, 10.3), 4.17 (dd, 1H, H-4, J = 1.7, 7.9 Hz), 4.30 (dd, 1H, H-2, J = 2.2, 5.0 Hz), 4.40 (d, 1H, H-

9, J = 6.0 Hz), 4.59 (dd, 1H, H-3, J = 2.2, 7.9 Hz), 4.85 (dd, 1H, H-10, J = 3.9, 6.0 Hz), 5.54 (d, 1H, H-1, J = 5.1 Hz).

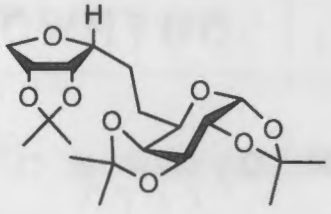
^{13}C NMR ($CDCl_3$): δ 25.6, 25.7, 26.2, 26.2, 27.1, 27.2, 27.6, 32.3, 68.6, 71.7, 71.9, 72.1, 74.1, 81.7, 85.7, 97.6, 108.1, 109.6, 110.1, 113.2.

m/z calculated: 417.2 *m/z* found: 439.2 (M + Na)

melting point: 118-121 °C

$[\alpha]_D$ -71.0 (*c*, 1.0, CH_2Cl_2)

Reduction of 9 with $BF_3 \cdot OEt_2$ / Et_3SiH to form 10



To a solution of **9** (0.28 g, 0.67 mmol) in dry CH_2Cl_2 (4 mL) at –78 °C, $BF_3 \cdot OEt_2$ (0.21 mL, 2.0 mmol) and Et_3SiH (0.32 mL, 2.0 mmol) were added *via* syringe, resulting in a light brown solution, and the reaction mixture stirred for 1.5 hours. TLC (4:1 hexane:ethyl acetate) showed complete consumption of starting material and the formation of a new spot that was less polar than the starting material. The reaction mixture was poured over ice water (5 mL) and extracted with CH_2Cl_2 (2 x 5 mL). The organic layers were combined, dried over anhydrous $MgSO_4$, and evaporated down to a

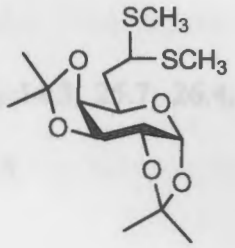
light brown syrup. The product was then purified *via* flash column chromatography using an eluent of 5:1 hexane:ethyl acetate to afford **10** as a clear syrup in an overall yield of 0.17 g (64%).

^{1}H NMR ($CDCl_3$): δ 1.27 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.66-2.05 (m, 4H, H-6, H-6', H-7, H-7'), 3.43 (m, 2H, H-8, H-11), 3.79 (ddd, 1H, H-5, J = 1.6, 4.6, 6.2 Hz), 3.97 (d, 1H, H-11', J = 10.8 Hz), 4.17 (dd, 1H, H-4, J = 1.7, 7.8 Hz), 4.28 (dd, 1H, H-2, J = 2.2, 5.1 Hz), 4.6 (m, 2H, H-3, H-9), 4.74 (dd, 1H, H-10, J = 3.7, 6.0 Hz), 5.52 (d, 1H, H-1, J = 5.1 Hz).

^{13}C NMR ($CDCl_3$): δ 25.6, 25.6, 26.1, 26.2, 27.2, 27.3, 27.7, 68.1, 71.6, 72.0, 73.7, 82.2, 83.1, 97.6, 109.2, 109.9, 112.8.

m/z calculated: 400.2 *m/z* found: 423.2 (M + Na)

Formation of 12 by addition of lithium bis(methylthio)methane (11) to triflate 2



In a flame-dried 100 mL round bottom flask under nitrogen atmosphere, bis(methylthio)methane (1.0 mL, 9.3 mmol) was dissolved in dry THF (10 mL) and cooled to –78 °C. A solution of 1.6 M *n*-BuLi in hexane (5.0 mL, 8.0 mmol) was added *via* syringe and the mixture was allowed to stir for 30 minutes resulting in a yellow solution (**11**). At this time a solution of **2** (1.74 g, 4.5 mmol) in THF (5mL) was added dropwise *via* syringe and the reaction was allowed to stir overnight. TLC (10:1 hexane:ethyl acetate) showed the formation of a new compound with some of the starting material left unreacted. The reaction mixture was quenched with saturated NH_4Cl (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to a dark brown syrup. The syrup was purified *via* flash column chromatography using an eluent of 10:1 hexane:ethyl acetate to afford 0.44 g (28%) of **12** as an off-white crystalline product.

^{1}H NMR ($CDCl_3$): δ 1.33 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.61 (s, 3H, CH_3), 1.84 (ddd, 1H, H-6, J = 3.1, 10.4, 14.8 Hz), 2.08 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 2.18 (ddd, 1H, H-6', J = 4.2, 9.5, 14.3 Hz), 3.89 (dd, 1H, H-4, J =

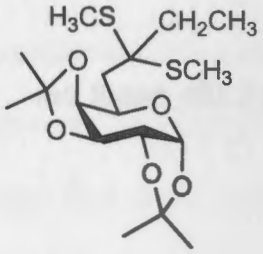
4.2, 10.4 Hz), 4.16 (m, 2H, H-2, H-5), 4.31 (dd, 1H, H-3, J = 2.5, 4.9 Hz), 4.62 (dd, 1H, H-7, J = 2.5, 7.7 Hz), 5.51 (d, 1H, H-1, J = 4.9 Hz).

^{13}C NMR ($CDCl_3$): δ 13.2, 14.3, 25.7, 26.4, 27.2, 27.3, 36.8, 51.9, 66.3, 71.7, 72.1, 74.1, 97.5, 109.8, 110.3.

m/z calculated: 350.1 *m/z* found: 373.1 (M + Na)

melting point: 59-61 °C

Reaction of lithiated dithiane derivative of 12 with iodoethane (5) to form the alkylated dithiane (13)



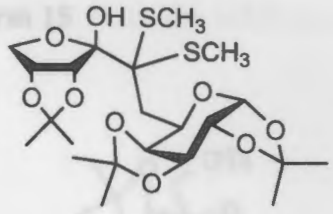
In a flame-dried 100 mL round bottom flask under nitrogen atmosphere, the dithiane (**12**) (0.20 g, 0.57 mmol) was dissolved in dry THF (2 mL) and the solution was cooled to –78 °C. A solution of 1.6 M *n*-BuLi in hexane (0.4 mL, 0.7 mmol) was added *via* syringe and the mixture was allowed to stir for 30 minutes resulting in a clear solution. At this time iodoethane (**5**) (0.15 mL, 1.8 mmol) was added dropwise *via* syringe and the reaction was allowed to stir overnight. TLC (10:1 hexane:ethyl acetate)

showed the formation of a new compound with some unreacted starting material remaining. The reaction mixture was quenched with saturated NH_4Cl (40 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to a clear syrup. The syrup was purified *via* flash column chromatography using an eluent of 12:1 hexane:ethyl acetate to afford **13** in 30% yield (0.06 g).

^{1}H NMR ($CDCl_3$): δ 1.05 (t, 1H, H-9, J = 7.1 Hz), 1.33 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.61 (s, 3H, CH_3), 1.76-2.07 (m, 4H, H-6, H-8), 1.98 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 4.14 (dd, 1H, H-4, J = 1.8, 7.9 Hz), 4.22 (ddd, 1H, H-5, J = 2.3, 4.6, 7.0 Hz), 4.28 (dd, 1H, H-2, J = 2.5, 5.1 Hz), 4.59 (dd, 1H, H-3, J = 2.4, 7.9 Hz), 5.49 (d, 1H, H-1, J = 5.1 Hz).

m/z calculated: 378.2 *m/z* found: 401.2 (M + Na)

Addition of lithiated derivative of dithiane product 12 to 2,3-*O*-isopropylidene-D-erythronolactone (7) to form the *C*-glycoside lactol 14



In a flame-dried 100 mL round bottom flask under nitrogen atmosphere, the dithiane product (**12**) (0.32 g, 0.9 mmol) was dissolved in dry THF (3 mL) and cooled to –78 °C. A solution of 1.6 M *n*-BuLi in hexane (0.6 mL, 1 mmol) was added *via* syringe and the mixture was allowed to stir for 30 minutes resulting in a clear solution. At this time a solution of 2,3-*O*-isopropylidene-D-erythronolactone (**7**) (0.5 g, 3.5 mmol) in THF (10 mL) was added dropwise *via* syringe and the reaction was allowed to stir overnight. TLC (4:1 hexane:ethyl acetate) showed the formation of a new compound with some unreacted starting material remaining. The reaction mixture was quenched with saturated NH_4Cl (40 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to a light yellow syrup. The syrup was purified *via* flash column chromatography using an eluent of 3:1 hexane:ethyl acetate to afford **14** in 28% yield (0.13 g).

^{1}H NMR ($CDCl_3$): δ 1.25-1.63 (m, 25H, 8 x CH_3, H-6'), 2.22 (m, 1H, H-6), 3.91-4.04 (m, 3H), 4.27 (m, 2H), 4.39 (m, 2H), 4.71-4.87 (m, 2H).

m/z calculated: 508 .2 *m/z* found: 531.2 (M + Na)

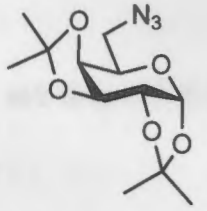
Reaction of 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (1) with *p*-toluenesulfonyl chloride to form 15

To a flame-dried 100 mL round bottom flask 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (**1**) (4.1 g, 15.8 mmol) was dissolved in 40 mL of pyridine and the solution was cooled to 0 °C. A solution of *p*-toluenesulfonyl chloride (4.5 g, 23.8 mmol) dissolved in 20 mL of $CHCl_3$ was added dropwise and the solution was stirred overnight. TLC (4:1 hexane:ethyl acetate) showed no starting material. Water (15 mL) was added and the mixture was stirred for 20 minutes. The reaction was then extracted with CH_2Cl_2 (3 x 25 mL) and the organic extracts washed with 5% sulfuric acid (3 x 25 mL). The organic layer was dried over anhydrous $MgSO_4$ and evaporated down to yield the white solid tosylate product **15** in 95% yield (6.2 g).

^{1}H NMR ($CDCl_3$): δ 1.28 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 4.07 (m, 2H, H-5, H-6'), 4.20 (m, 2H, H-4, H-6), 4.29 (dd, 1H, H-2, J = 2.5, 5.0 Hz), 4.59 (dd, 1H, H-3, J = 2.6, 8.0 Hz), 5.46 (d,

1H, H-1, J = 5.1 Hz), 7.27 (d, 2H, Ar-H, J = 6.7 Hz), 7.82 (d, 2H, Ar-H, J = 6.7 Hz).

Reaction of 15 with sodium azide to form the azide product (16)



In a 250 mL round bottom flask, the tosylate (**15**) (6.2 g, 15 mmol) was dissolved in DMF (100 mL). Sodium azide (4.0 g, 61.7 mmol), urea (0.2 g), and water (6 mL) were added to the solution and then the mixture was allowed to reflux for 5 days until complete consumption of the starting material was observed by TLC (4:1 hexane:ethyl acetate). The reaction was evaporated down, with the syrup then dissolved in 50 mL of CH_2Cl_2 and washed with water (3 x 500 mL) to remove the residual DMF. The organic layer was then dried over anhydrous $MgSO_4$ and evaporated down to a golden syrup. The syrup was then purified *via* flash column chromatography using an eluent of 5:1 hexane:ethyl acetate to afford **16** as a golden syrup in a yield of 4.0 g (92%).

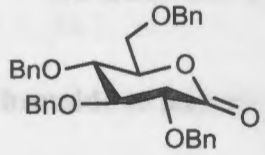
^{1}H NMR ($CDCl_3$): δ 1.33 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 3.35 (dd, 1H, H-6', J = 5.2, 12.8 Hz), 3.50 (dd, 1H, H-6, J = 7.9, 12.8 Hz), 3.91 (ddd, 1H, H-5, J = 1.9, 5.2, 7.7 Hz), 4.19 (dd, 1H, H-4, J = 2.0,

7.9), 4.33 (dd, 1H, H-2, J = 2.5, 5.1 Hz), 4.63 (dd, 1H, H-3, J = 2.6, 7.9 Hz), 5.44 (d, 1H, H-1, J = 5.1 Hz).

^{13}C NMR ($CDCl_3$): δ 24.3, 24.8, 25.8, 25.9, 50.5, 66.8, 70.2, 70.6, 70.9, 96.1, 108.5, 109.3.

m/z calculated: 285.1 *m/z* found: 308.1 (M + Na)

Oxidation of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside (17) with PCC to form lactone 18



In a flame-dried 250 mL round bottom flask 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**17**) (2.5 g, 4.6 mmol) and 4 g of 4 Å molecular sieves were mixed in CH_2Cl_2 (50 mL) under nitrogen atmosphere and the mixture was stirred for 20 minutes. PCC (4.0 g, 18.4 mmol) was then added, with the reaction turning dark brown, and stirring was continued overnight. TLC (6:1 hexanes:ethyl acetate) showed the formation of a less polar spot and complete consumption of the starting material. Next, 250 mL of hexanes and 250 mL of ether were added to the reaction mixture, which was then filtered using a dry silica column to remove the chromium salts from the reaction mixture. The

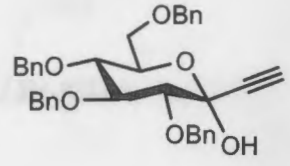
fractions were collected and evaporated down to a clear syrup of product (**18**) for a yield of 2.3 g (92%).

^{1}H NMR ($CDCl_3$): δ 3.64 (dd, 1H, H-6, J = 3.2, 11.1 Hz), 3.71 (dd, 1H, H-6', J = 2.4, 11.0 Hz), 3.92 (m, 2H, H-3, H-5), 4.11 (d, 1H, H-4, J = 6.6 Hz), 4.43-4.73 (m, 8H, 4 x CH_2), 4.97 (d, 1H, H-2, J = 11.3 Hz), 7.15-7.38 (m, 20H, Ar-H).

^{13}C NMR ($CDCl_3$): δ 68.0, 73.3, 73.5, 73.7, 75.8, 76.6, 76.9, 80.6, 127.5 (3 x C), 127.6, 127.6 (3 x C), 127.6 (3 x C), 127.7, 128.0 (3 x C), 128.1 (4 x C), 128.1 (3 x C), 136.5, 137.1, 137.1, 137.2, 168.9.

m/z calculated: 538.2 *m/z* found: 539.1 (M + H)

Addition of ethynyl magnesium bromide to lactone 18 to form the propargyl alcohol (19)



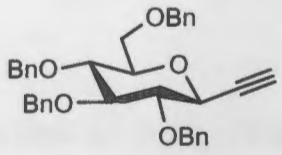
In a flame-dried 100 mL round bottom flask lactone **18** (1.0 g, 1.8 mmol) was dissolved in 10 mL of dry THF under nitrogen atmosphere and the solution was cooled to –78 °C. At this time, ethynyl magnesium bromide (5.7 mL, 2.8 mmol) was added to the solution, which was then allowed to stir overnight. TLC (3:1 hexanes:ethyl acetate) showed formation of a more polar spot with a small amount of starting material left over. The reaction mixture was quenched with saturated NH_4Cl (20 mL) and extracted with

CH_2Cl_2 (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to down a brown syrup. The syrup was purified *via* flash column chromatography using an eluent of 3:1 hexane:ethyl acetate to give two very close-running spots, which are believed to be α- and β- anomers of the propargyl alcohol, to afford **19** as a colorless syrup in a yield of 0.65 g (62%).

^{1}H NMR ($CDCl_3$): δ 2.49 (s, 1H, CH), 2.67 (s, 1H, CH), 3.55-4.07 (m, 11H), 4.42-4.60 (m, 8H), 4.75-5.05 (m, 10H), 5.19 (s, 1H, OH), 7.10-7.37 (m, 40H, Ar-H).

^{13}C NMR ($CDCl_3$): δ 69.6, 69.7, 72.9, 73.7, 74.5, 74.6, 75.1, 76.1, 76.3, 76.4, 77.1, 77.8, 79.1, 80.1, 83.6, 84.3, 84.9, 85.1, 85.4, 92.6, 96.7, 128.7 (2 x C), 128.8, 128.9, 129.0 (7 x C), 129.1 (3 x C), 129.2 (8 x C), 129.3, 129.4 (6 x C), 129.5 (6 x C), 129.6 (9 x C), 129.7, 138.9, 139.0, 139.2, 139.3, 139.6, 139.7.

Reduction of 19 with $BF_3{\cdot}OEt_2$ / Et_3SiH to form 20



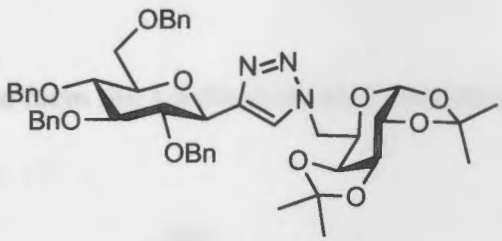
To a solution of **19** (0.53 g, 0.94 mmol) in dry CH_2Cl_2 (5 mL) at –78 °C, $BF_3{\cdot}OEt_2$ (0.32 mL, 3.0 mmol) and Et_3SiH (0.48 mL, 3.0 mmol) were added *via* syringe and the mixture stirred for 1 hour and then placed in the freezer overnight. TLC (5:1

hexane:ethyl acetate) showed complete consumption of starting material and the formation of two new spots. The reaction mixture was poured over ice water (5 mL) and extracted with CH_2Cl_2 (2 x 5 mL). The organic layers were combined and dried over anhydrous $MgSO_4$ and evaporated down. The product was then purified *via* flash column chromatography using an eluent of 5:1 hexane:ethyl acetate to afford **20** as a colorless syrup in an overall yield of 0.31 g (61%).

^{1}H NMR ($CDCl_3$): δ 2.56 (d, 1H, CH), 3.46 (m, 1H, H-5), 3.70 (m, 5H), 4.51-5.05 (m, 9H), 7.14-7.40 (m, 20H, Ar-H).

m/z calculated: 548.3 *m/z* found: 571.3 (M + Na)

Reaction of 20 with 16 to form the 1,4-disubstituted triazole (21)



In a 100 mL round bottom flask **16** (0.4 g, 1.4 mmol) was dissolved in 6 mL of a 50:50 mixture of *t*-BuOH/H_2O, then **20** (0.78 g, 1.4 mmol) was added to the solution. $CuSO_4$ (4% solution in water) and ascorbic acid (40% solution in water) was added to generate the Cu(I) catalyst, the round bottom was fitted with a reflux condenser and stir bar, and heated to 70 °C for 15 hours turning the solution light green. TLC (2:1

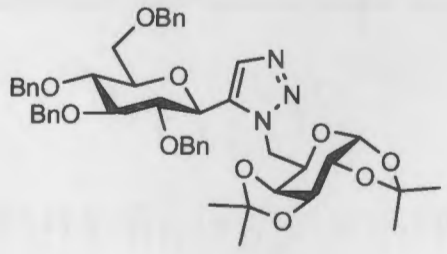
hexane:ethyl acetate) showed formation of a new product with no alkyne starting material left over. The reaction was cooled and a precipitate formed. The solution was cooled further in the freezer for 20 minutes at which time the precipitate was vacuum filtered to afford **21** in 1.0 g (86%) as a white solid product.

^{1}H NMR ($CDCl_3$): δ 1.20 (s, 3H, CH_3), 1.31 (s, 6H, 2 x CH_3), 1.49 (s, 3H, CH_3), 3.62 (dd, 1H, H-14, J = 1.8, 9.3 Hz), 3.71 (m, 3H, H-13, H-15, H-15'), 3.80 (dd, 1H, H-11, J = 8.9 Hz), 3.99 (dd, 1H, H-12, J = 9.3 Hz), 4.10 (dd, 1H, H-4, J = 1.8, 7.8 Hz), 4.21 (ddd, 1H, H-5, J = 1.8, 4.8, 8.1 Hz), 4.29 (m, 2H, H-2, H-6), 4.43 (dd, 1H, H-6', J = 8.2 Hz), 4.50-4.86 (m, 10H, H-3, H-10, CH_2), 5.44 (d, 1H, H-1, J = 4.9 Hz), 7.04-7.32 (m, 20H, Ar-H), 7.68 (s, 1H, triazole-H).

m/z calculated: 833.4 *m/z* found: 834.6 (M + H)

melting point: 140-142 °C

Reaction of 20 with 16 to form the 1,5-disubstituted triazole (22)



In a flame-dried 50 mL round bottom flask **20** (0.27 g, 0.5 mmol) was added and then a solution of ethylmagnesium bromide in tetrahydrofuran (0.75 mL, 0.75 mmol) was

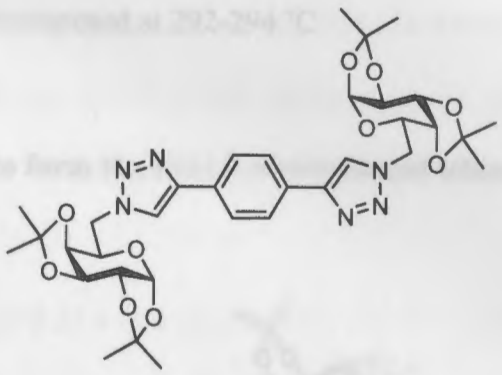
added dropwise. The solution was gently heated to 50 °C for 20 minutes and then allowed to cool to room temperature. After cooling was completed a solution of **16** (0.32 g, 1.1 mmol) dissolved in 0.2 mL of THF was added to the reaction and the mixture was allowed to stir overnight. TLC (2:1 hexane:ethyl acetate) showed new product formation with some unreacted alkyne and azide left over. The reaction mixture was quenched with saturated NH_4Cl (20 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to a brown syrup. The syrup was purified *via* flash column chromatography using an eluent of 2:1 hexane:ethyl acetate to afford 0.18 g (30%) of **22** as a white solid.

^{1}H NMR ($CDCl_3$): δ 1.25 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 3.55 (m, 1H, H-5), 3.72-4.14 (m, 8H), 4.29 (dd, 1H, H-2, J = 2.3, 4.9 Hz), 4.42-4.92 (m, 11H), 5.48 (d, 1H, H-1, J = 4.9 Hz), 6.97-7.39 (m, 20H, Ar-H), 7.67 (s, 1H, triazole-H)

m/z calculated: 833.4 (M + H) *m/z* found: 834.7 (M + H)

melting point: 176-179 °C

Reaction of 23 with 16 to form the bis(1,4-disubstituted triazole) (24)



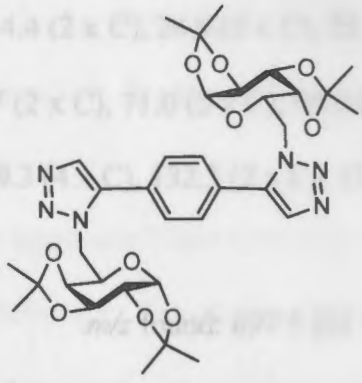
In a 100 mL round bottom flask **16** (0.4 g, 1.4 mmol) was dissolved in 6 mL of a 50:50 mixture of *t*-BuOH/H_2O, then 1,4-diethynylbenzene (**23**) (0.07 g, 0.6 mmol) was added to the solution. $CuSO_4$ (4% solution in water) and ascorbic acid (40% solution in water) was added to generate the catalyst and the flask was fitted with a reflux condenser and stir bar, and heated to 70 °C for 2 hours. TLC (3:1 hexane:ethyl acetate) showed formation of a new product with no alkyne starting material left over. The reaction was taken off the heat, at which time a precipitate began to form as the solution cooled to room temperature. The solution was placed in the freezer for 30 minutes at which time the precipitate was vacuum filtered to afford **24** in 0.37 g (90%) as a yellowish solid product.

^{1}H NMR ($CDCl_3$): δ 1.30 (s, 6H, 2 x CH_3), 1.38 (s, 6H, 2 x CH_3), 1.42 (s, 6H, 2 x CH_3), 1.52 (s, 6H, 2 x CH_3), 4.25 (m, 4H, H-4, H-5), 4.35 (dd, 2H, H-2, J = 2.6, 4.9 Hz), 4.51 (dd, 2H, H-6, J = 8.2 Hz), 4.69 (m, 4H, H-3, H-6'), 5.56 (d, 2H, H-1, J = 4.9 Hz), 7.91 (s, 4H, Ar-H), 8.01 (s, 2H, triazole-H).

m/z calculated: 696.3 *m/z* found: 697.5 (M + H)

melting point: Decomposed at 292-294 °C

Reaction of 23 with 16 to form the bis(1,5-disubstituted triazole) (25)



In a flame-dried 50 mL round bottom flask 1,4-diethynylbenzene (**23**) (0.06 g, 0.5 mmol) was added, and then a solution of ethylmagnesium bromide in tetrahydrofuran (1.5 mL, 1.5 mmol) was added dropwise. The solution was gently heated to 50 °C for 20 minutes and then allowed to cool to room temperature. After cooling a solution of **16** (0.4 g, 1.4 mmol) dissolved in 0.3 mL of THF was added to the reaction, which was then allowed to stir overnight. TLC (2:1 hexane:ethyl acetate) showed new product formation that was much more polar than both starting materials. The reaction mixture was quenched with saturated NH_4Cl (40 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to a brown syrup. The syrup was purified *via* flash column chromatography using an eluent of 2:1 hexane:ethyl acetate to afford 0.1 g of **25** (30%) as a white solid product.

^{1}H NMR ($CDCl_3$): δ 1.29 (s, 6H, 2 x CH_3), 1.32 (s, 6H, 2 x CH_3), 1.39 (s, 6H, 2 x CH_3), 1.49 (s, 6H, 2 x CH_3), 4.26 (d, 2H, H-4, J = 7.9 Hz), 4.33 (dd, 2H, H-2, J = 2.5, 5.0 Hz), 4.51 (m, 6H, H-5, H-6, H-6'), 4.66 (dd, 2H, H-3, J = 2.5, 7.9 Hz), 5.44 (d, 2H, H-1, J = 5.0 Hz), 7.69 (s, 4H, Ar-H), 7.74 (s, 2H, triazole-H).

^{13}C NMR ($CDCl_3$): δ 24.4 (2 x C), 24.9 (2 x C), 25.9 (4 x C), 47.8 (2 x C), 67.4 (2 x C), 70.2 (2 x C), 70.7 (2 x C), 71.0 (2 x C), 95.9 (2 x C), 109.0 (2 x C), 109.5 (2 x C), 127.8 (2 x C), 129.3 (4 x C), 132.5 (2 x C), 137.9 (2 x C).

m/z calculated: 696.3 *m/z* found: 697.5 (M + H)

melting point: 179-182 °C

References

1. Levy, D. E.; Tang, C.; "The Chemistry of *C*-Glycosides." Pergamon: Tarrytown, New York, **1995**.
2. Phillips, M. L.; Nudelman, E.; Gaeta, F. C. A.; Perez, M., Shingal, A. K.; Hakomori, S.; Paulson, J. C. *Science* **1990**, *250*, 1130-1133.
3. Espinosa, J.; Canada, F. J.; Aseniso, J. L.; Martin-Pastor, M.; Dietrich, H.; Martin-Lomas, M.; Schmidt, R. R.; Jimenez-Barbero, J. *J. Am. Chem. Soc.* **1996**, *118*, 10862-10871.
4. Smith, M. B.; "Organic Synthesis," McGraw-Hill: New York, New York, **2002**.
5. Yus, M.; Najera, C.; Foubelo, F. *Tetrahedron* **2003**, *59*, 6147-6212.
6. Smith, A.; Adams, C. *Acc. Chem. Res.* **2004**, *37*, 365-377.
7. Greene, T. W.; Wuts, P. G. M. "Protective Groups in Organic Synthesis, 3rd ed.," John Wiley & Sons: New York, **1995**, 329-344.
8. http://www.hear.org/species/jatropha%5Fgossypiifolia/
9. McCartney, J. L.; Meta, C. T.; Cicchillo, R. M.; Bernardina, M.; Wagner, T. R.; Norris, P. *J. Org. Chem.* **2003**, *68*, 10152-10155.
10. Bourne, Y.; Kolb, H. C.; Radic, Z.; Sharpless, K. B; Taylor, P.; Marchot, P. *Proc. Natl. Acad. Aci. U.S.A.* **2004**, *101*, 1449-1452.
11. Lewis, W. G.; Green, L. G.; Grynszpan, F.; Radic, Z.; Carlier, P. R.; Taylor, P.; Finn. M. G.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 1053-1059.
12. Krasinski, A.; Fokin, V. V.; Sharpless, K. B.; *Org. Lett.* **2004**, *6*, 1237-1240.

13. Kiick, K. L., Saxon, E., Bertozzi, C. R. *Proc. Natl. Acad. Sci. U.S.A* **2002**, *99*, 19-24.

14. Clarke, D.; Mares, R. W.; McNab, H. *J. Chem. Soc. Perkin. Trans. 1* **1997**, 1799-1804.

15. Tornoe, C. W.; Christiansen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057.

16. Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004.

17. Himo, F.; Lovell, T.; Hilgraf, R.; Rostovstev, V. V.; Noodleman, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **2005**, *127*, 210-216.

18. Rostovtsev, V. V., Green. L. G., Fokin, V. V., Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2596-2599.

19. Akimova, G. S.; Chisttokletov, V. N.; Petrov, A. A. *Org. Khim.* **1967**, *3*, 968.

Appendix A

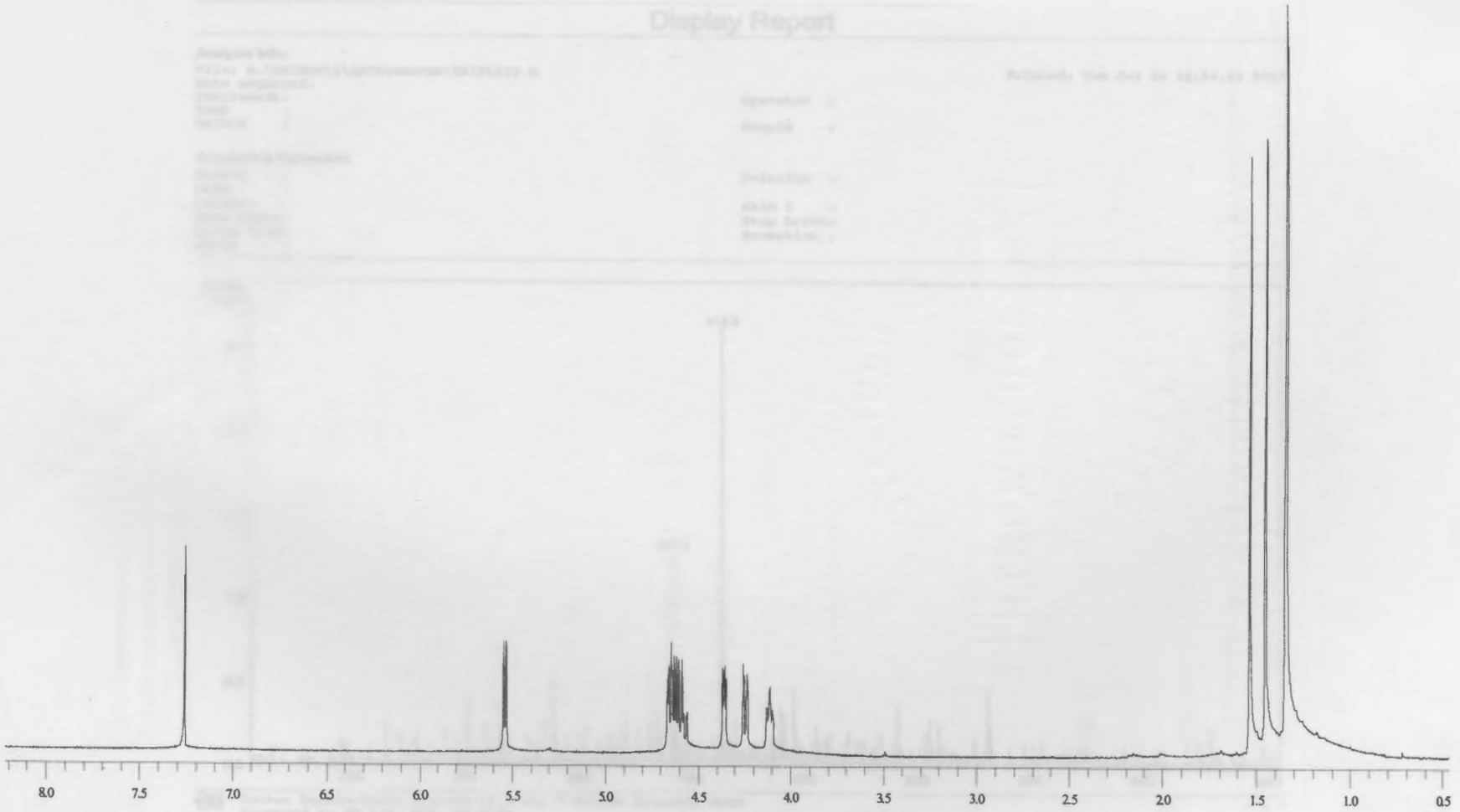


Figure 15. 400 MHz ^{1}H NMR spectrum of compound **2**

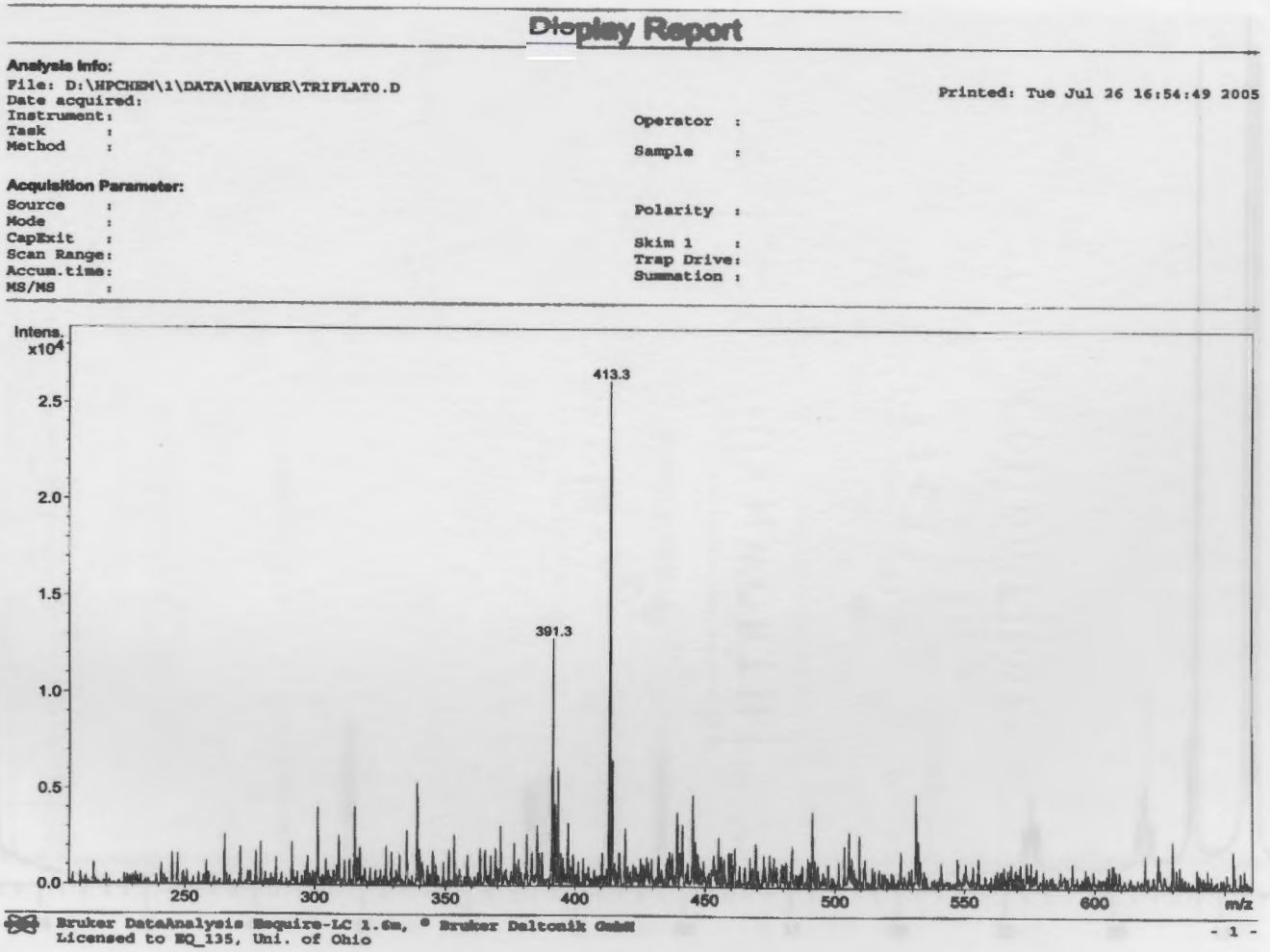


Figure 16. Mass spectrum of compound **2**

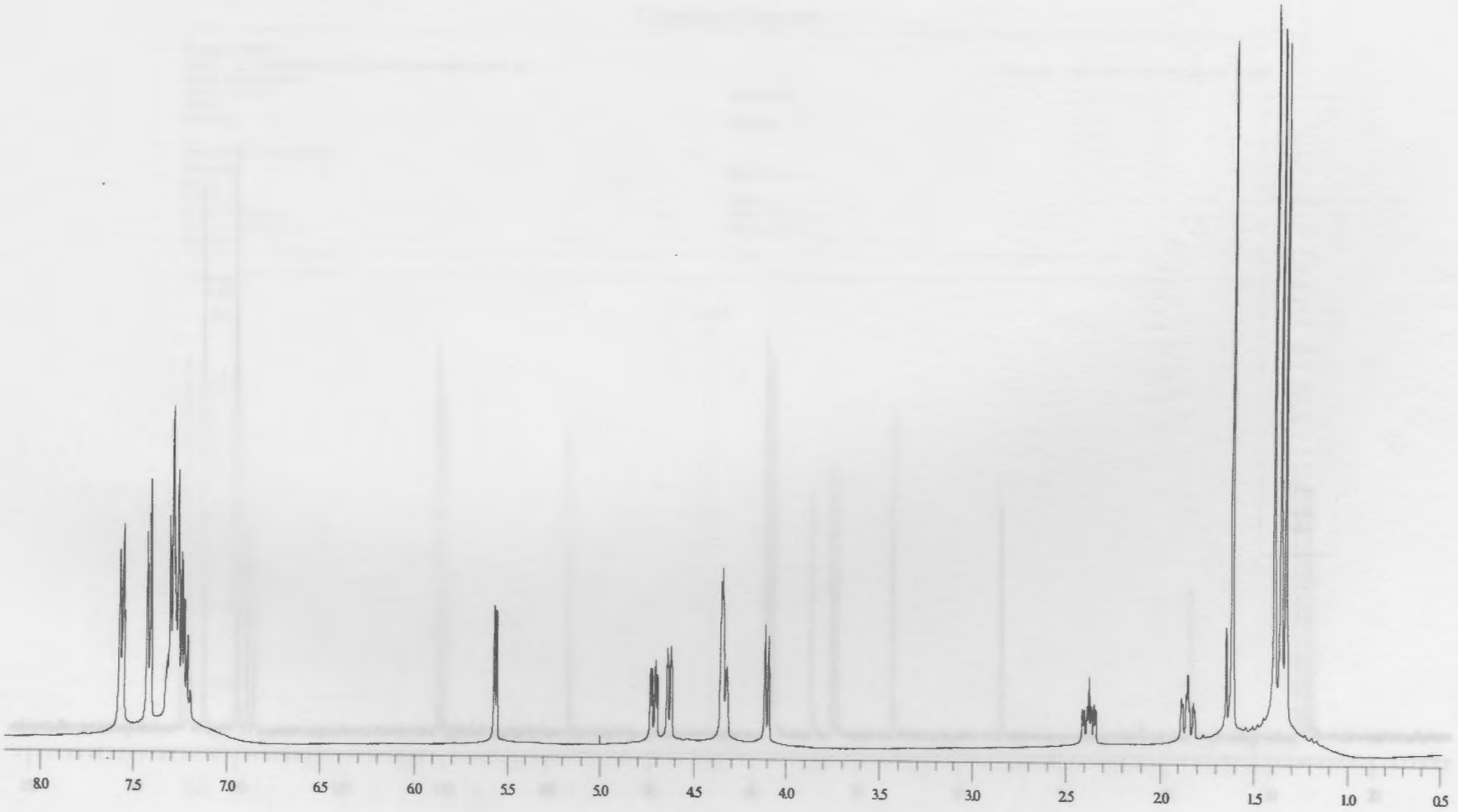


Figure 17. 400 MHz ^{1}H NMR spectrum of compound **4**

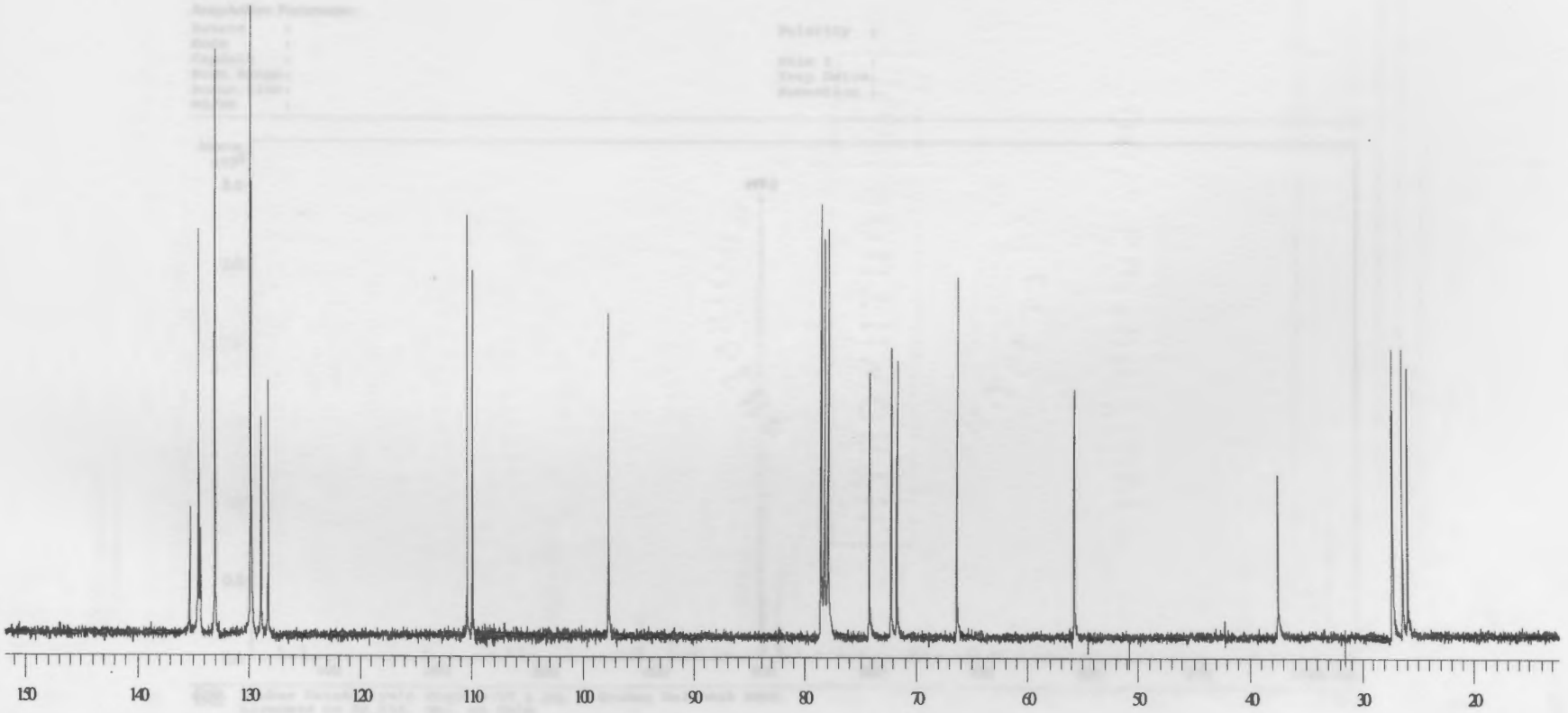


Figure 18. 100 MHz ^{13}C NMR spectrum of compound **4**

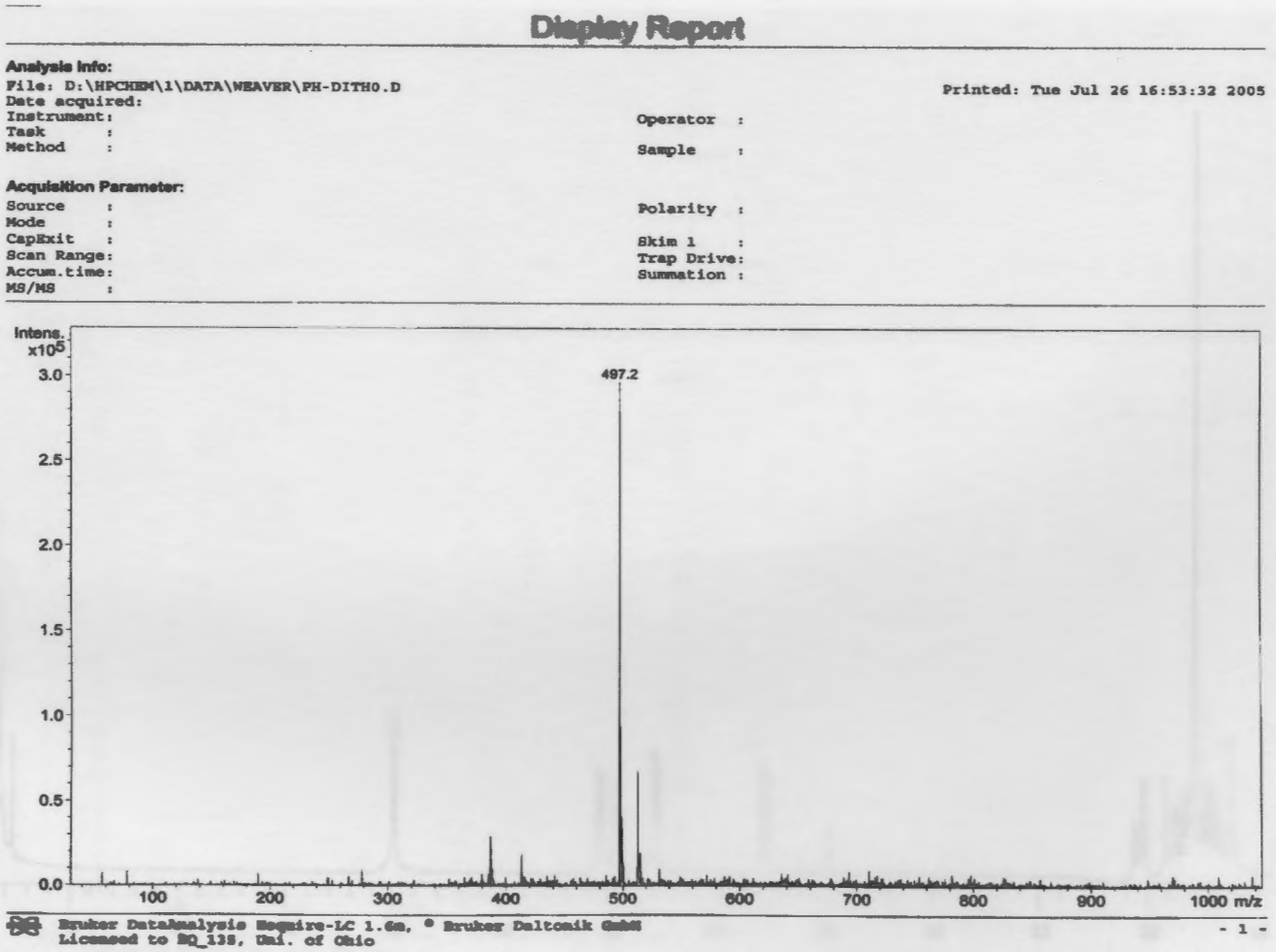


Figure 19. Mass spectrum of compound 4

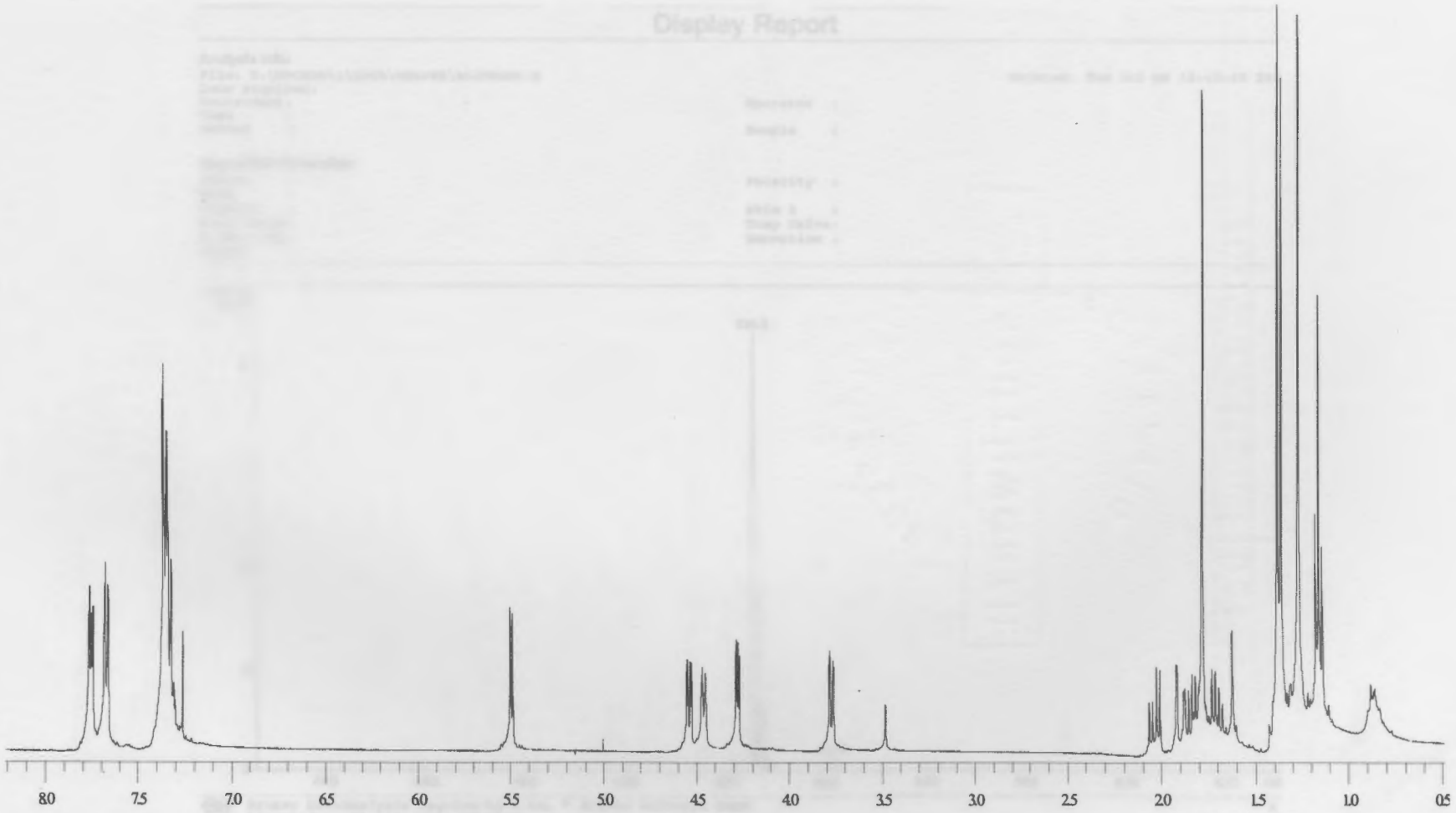


Figure 20. 400 MHz ^{1}H NMR spectrum of compound **6**

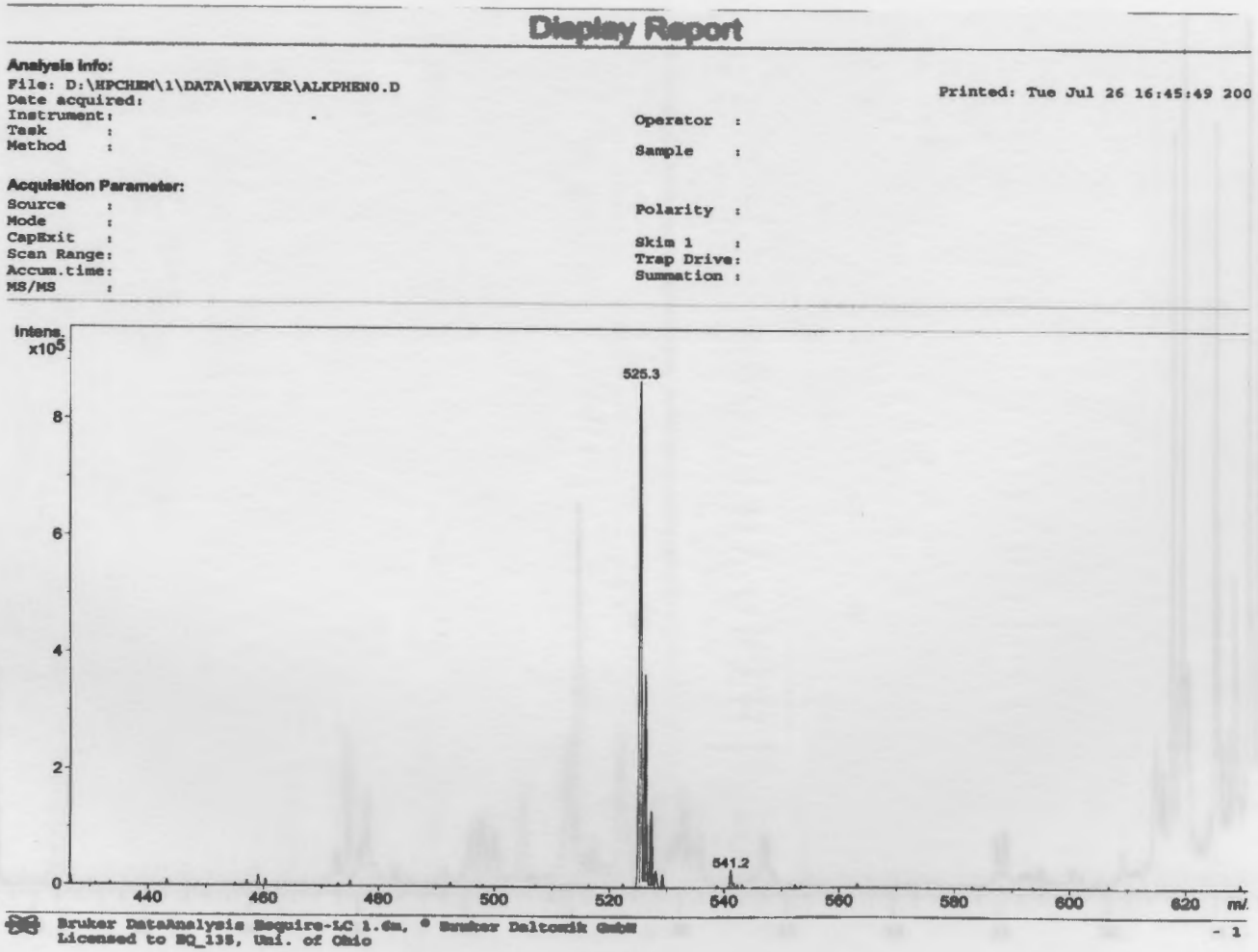


Figure 21. Mass spectrum of compound **6**

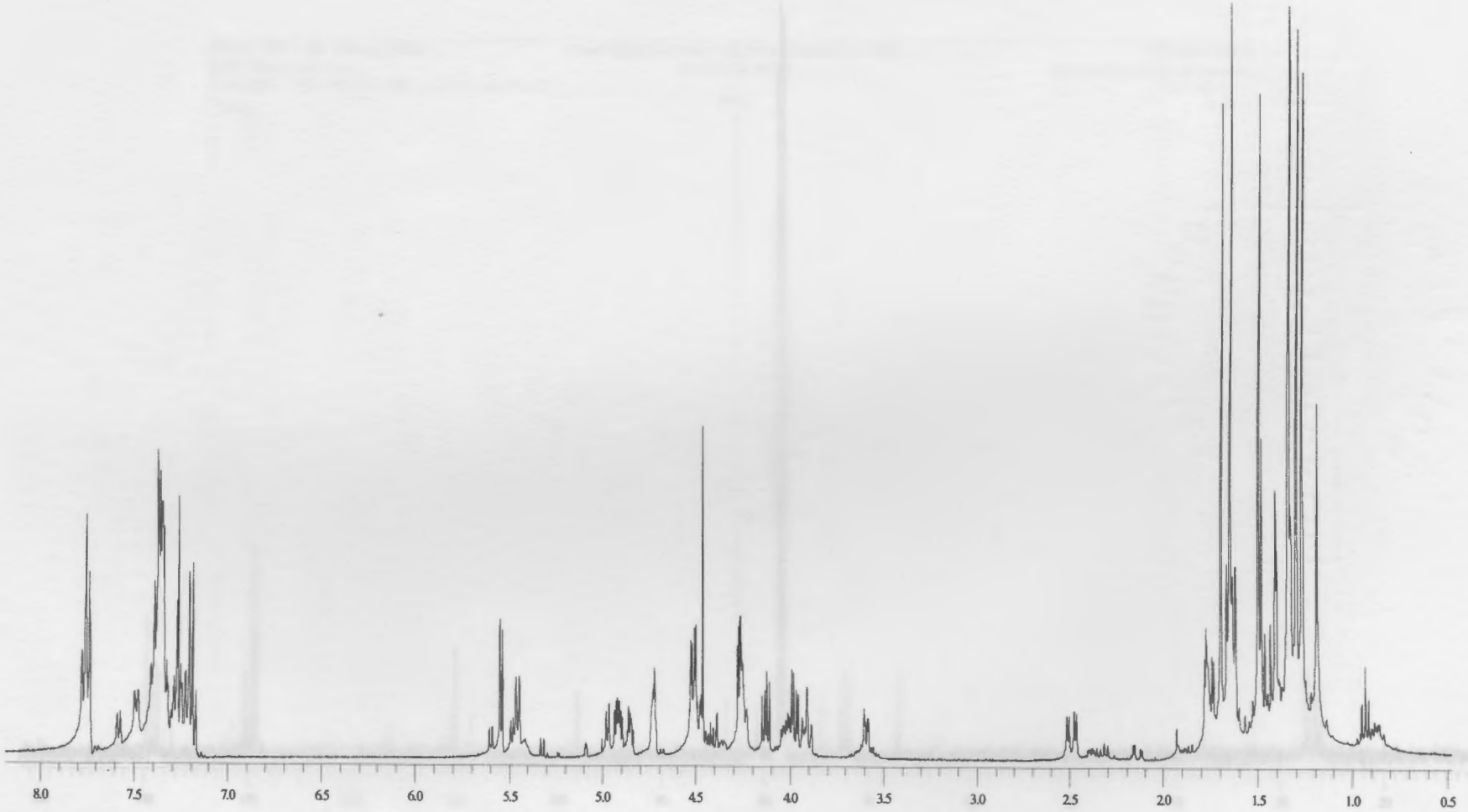


Figure 22. 400 MHz ^{1}H NMR spectrum of compound **8**

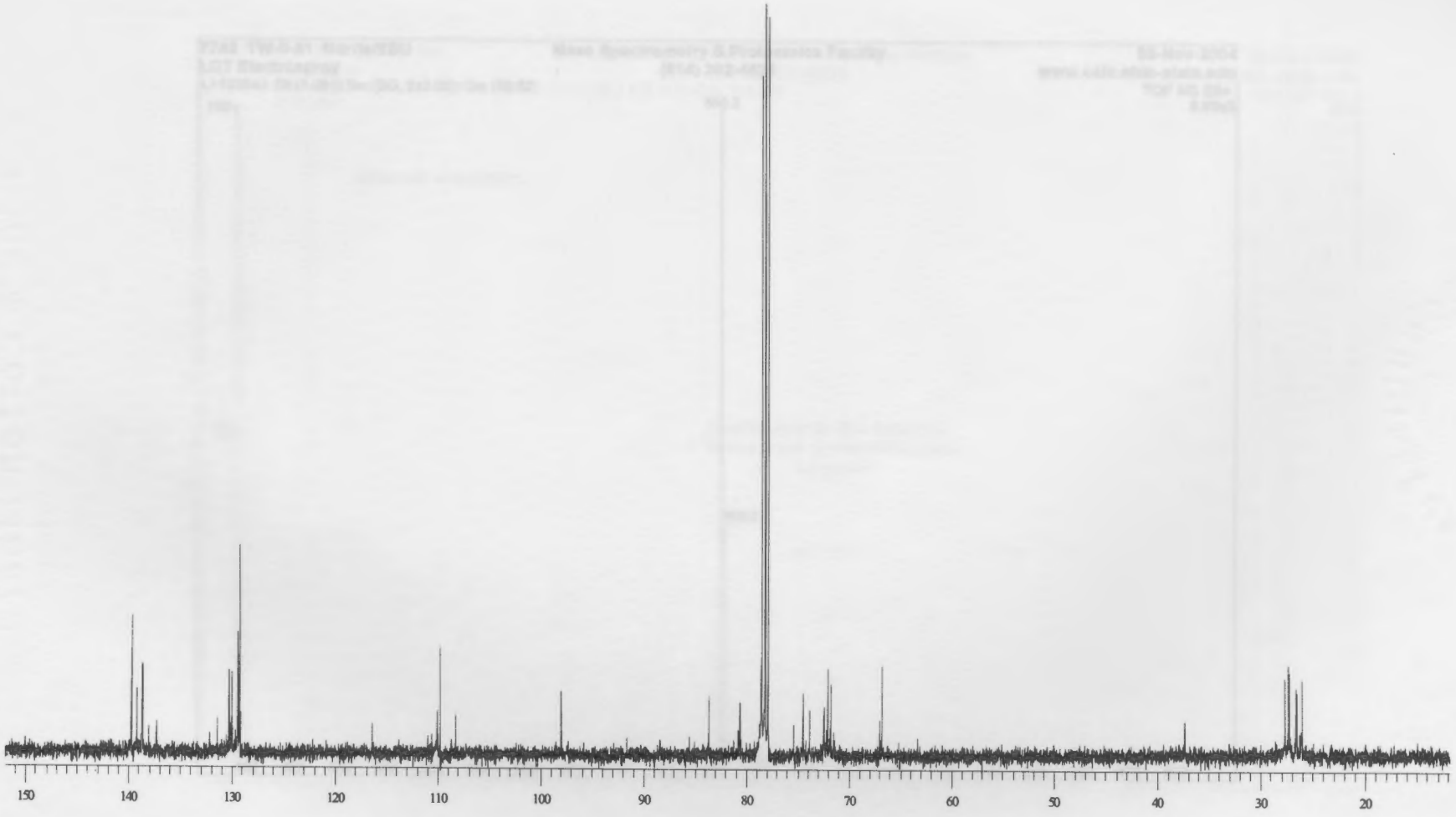


Figure 23. 100 MHz ^{13}C NMR spectrum of compound **8**

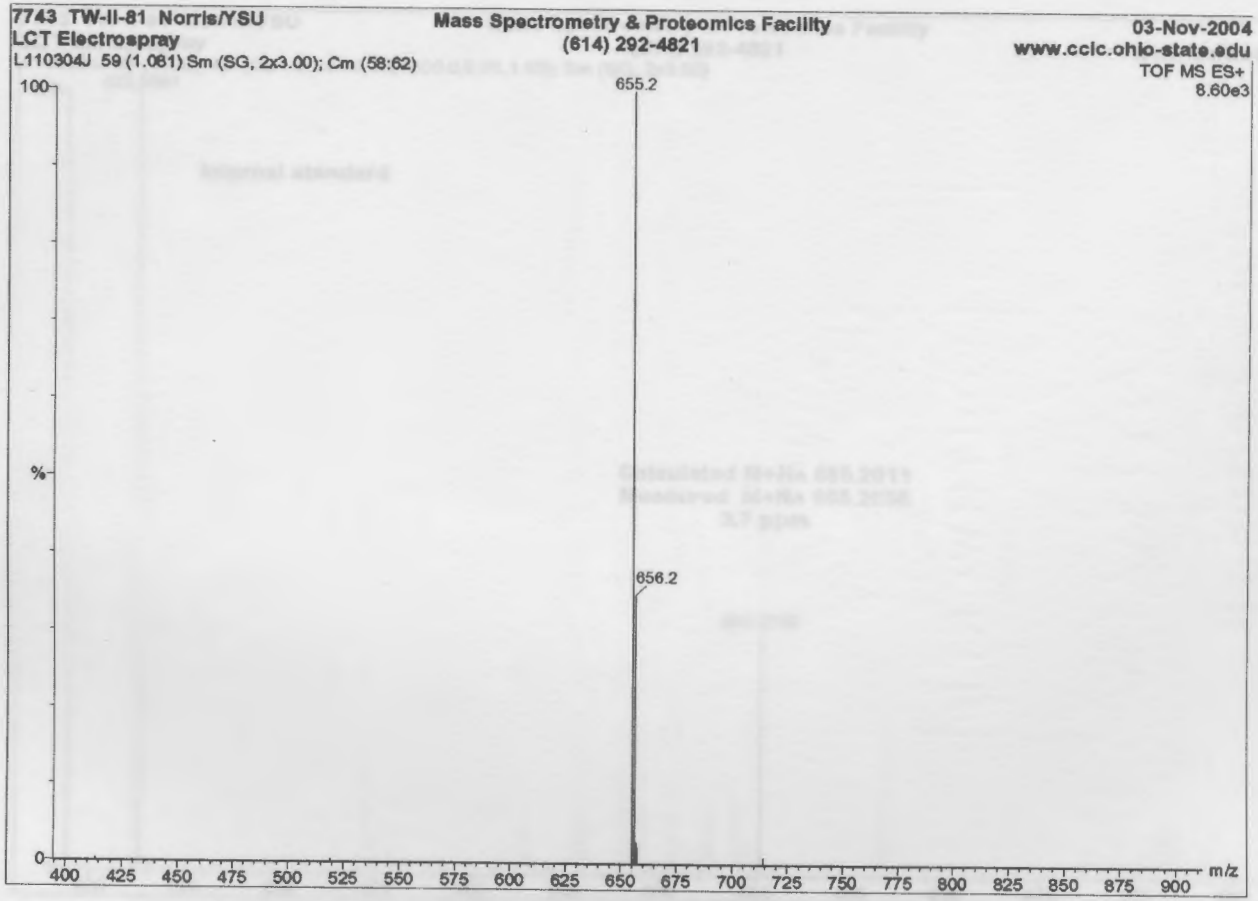


Figure 24. Mass spectrum of compound **8**

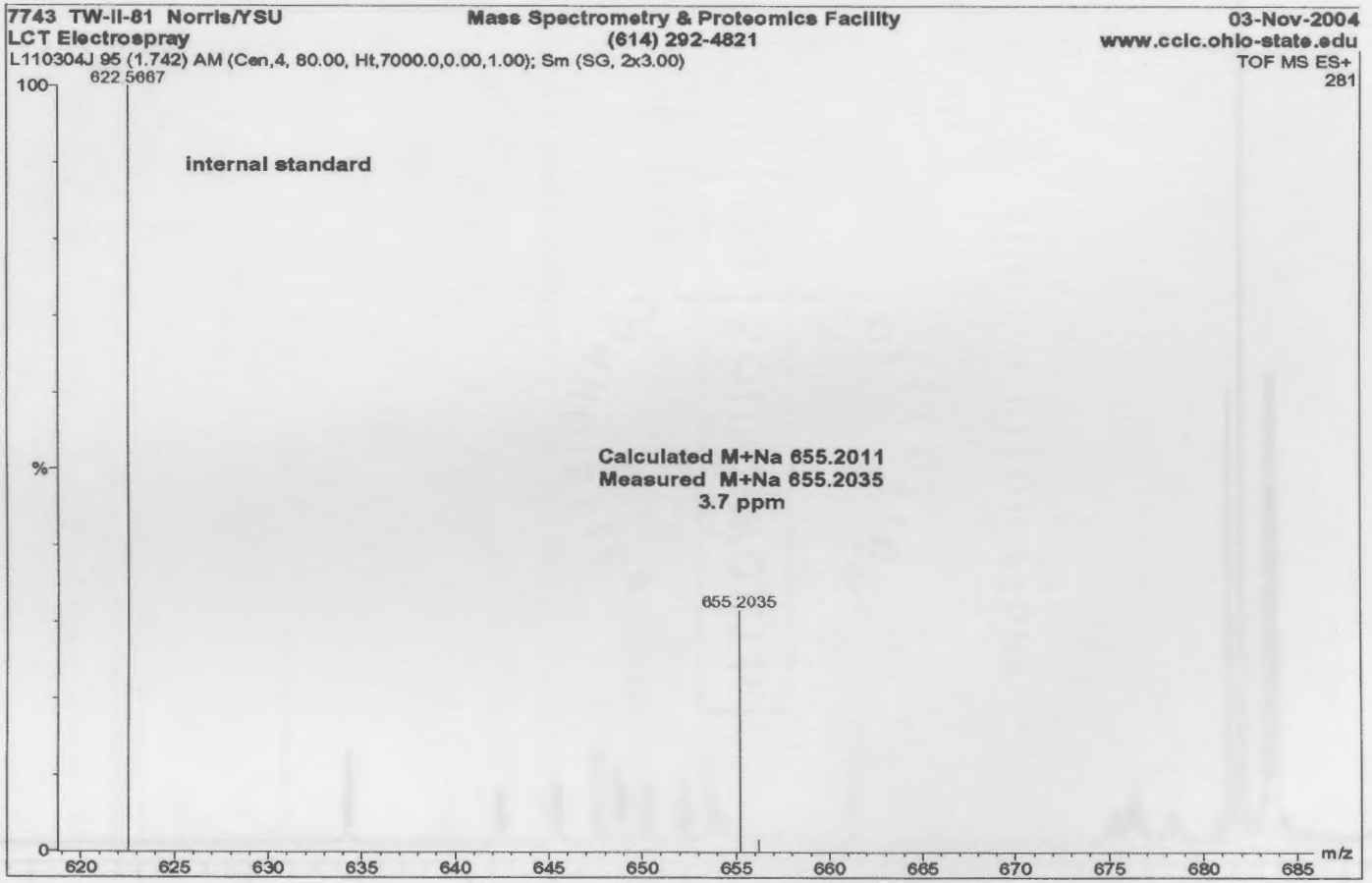


Figure 25. High resolution mass spectrum of compound **8**

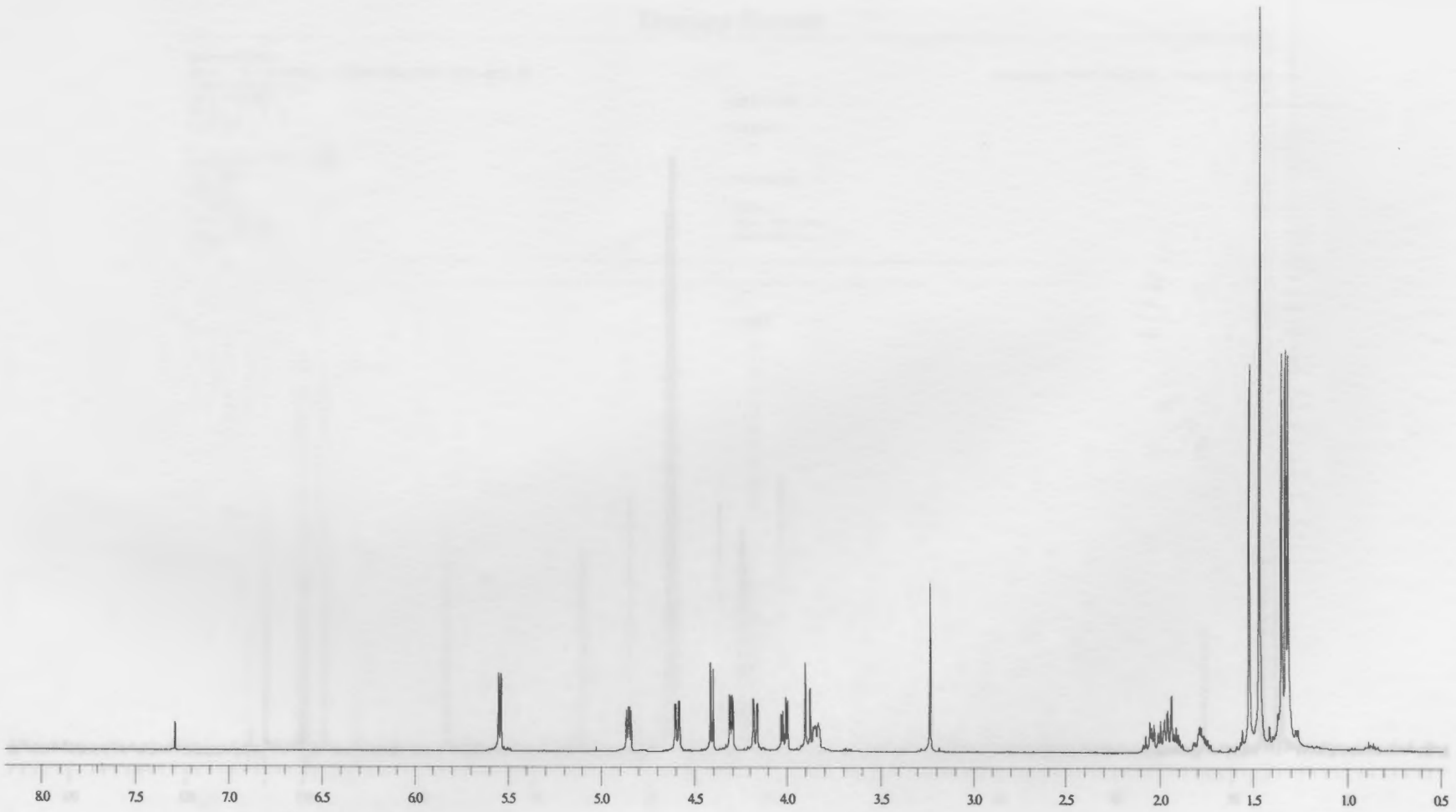


Figure 26. 400 MHz ^{1}H NMR spectrum of compound **9**

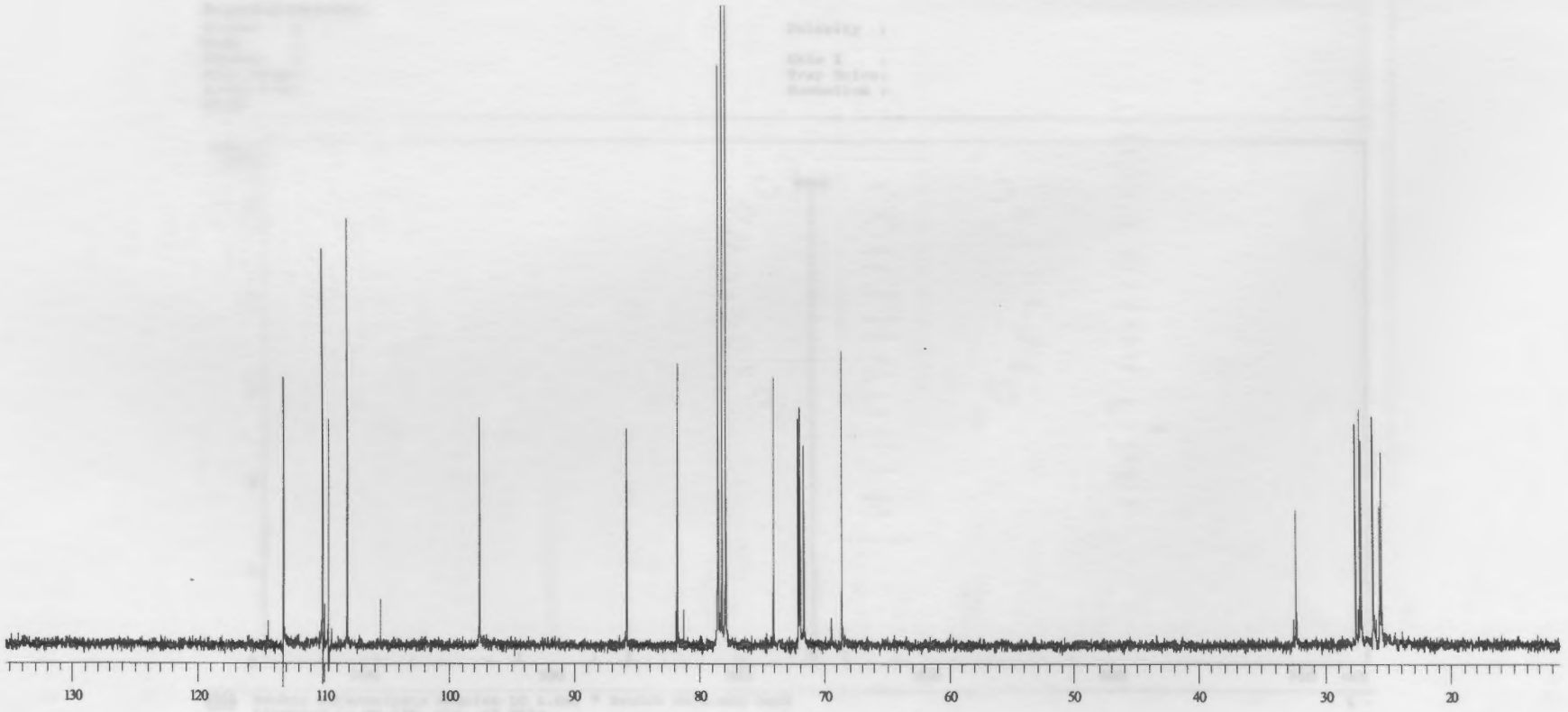


Figure 27. 100 MHz ^{13}C NMR spectrum of compound **9**

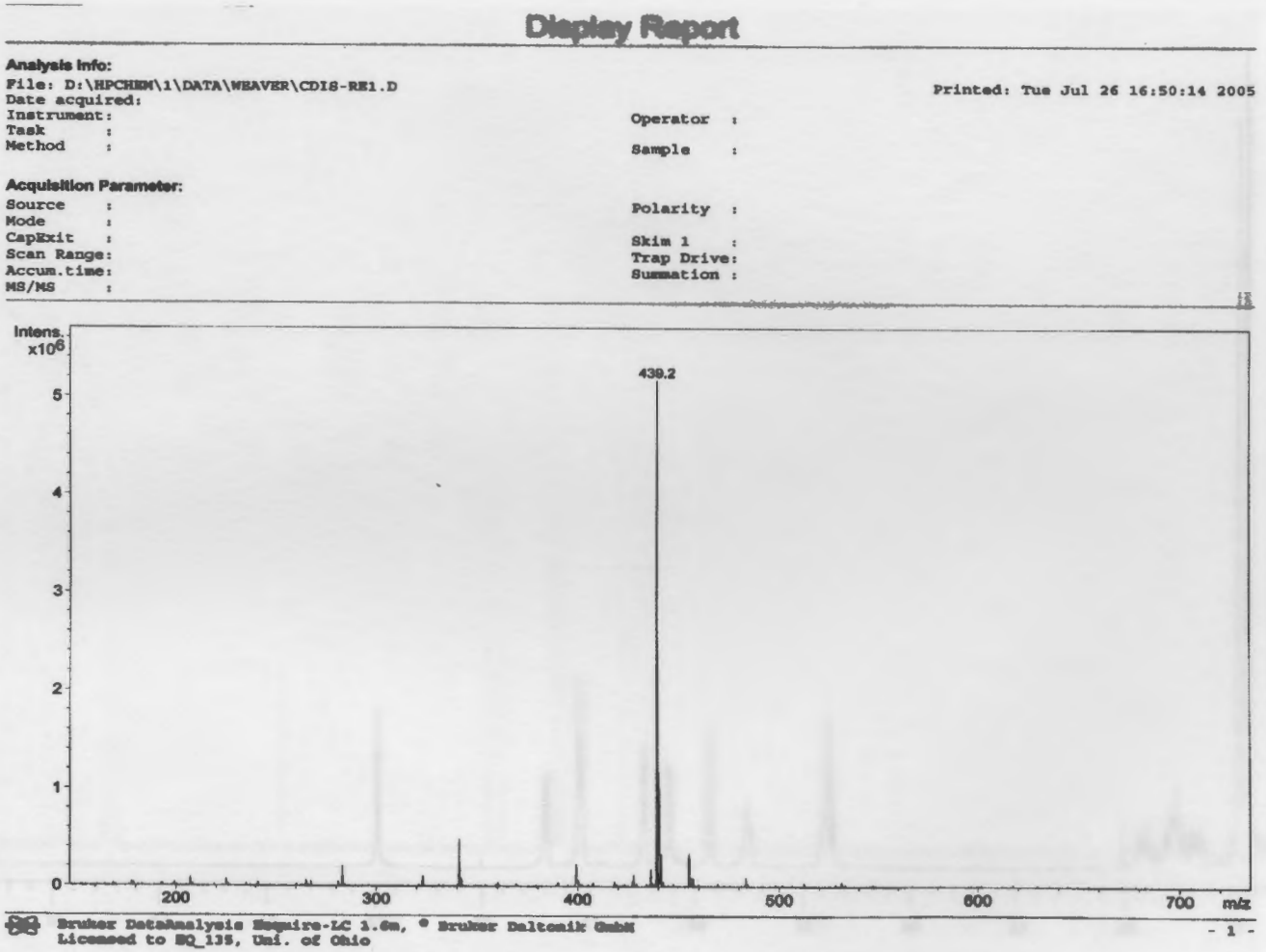


Figure 28. Mass spectrum of compound **9**

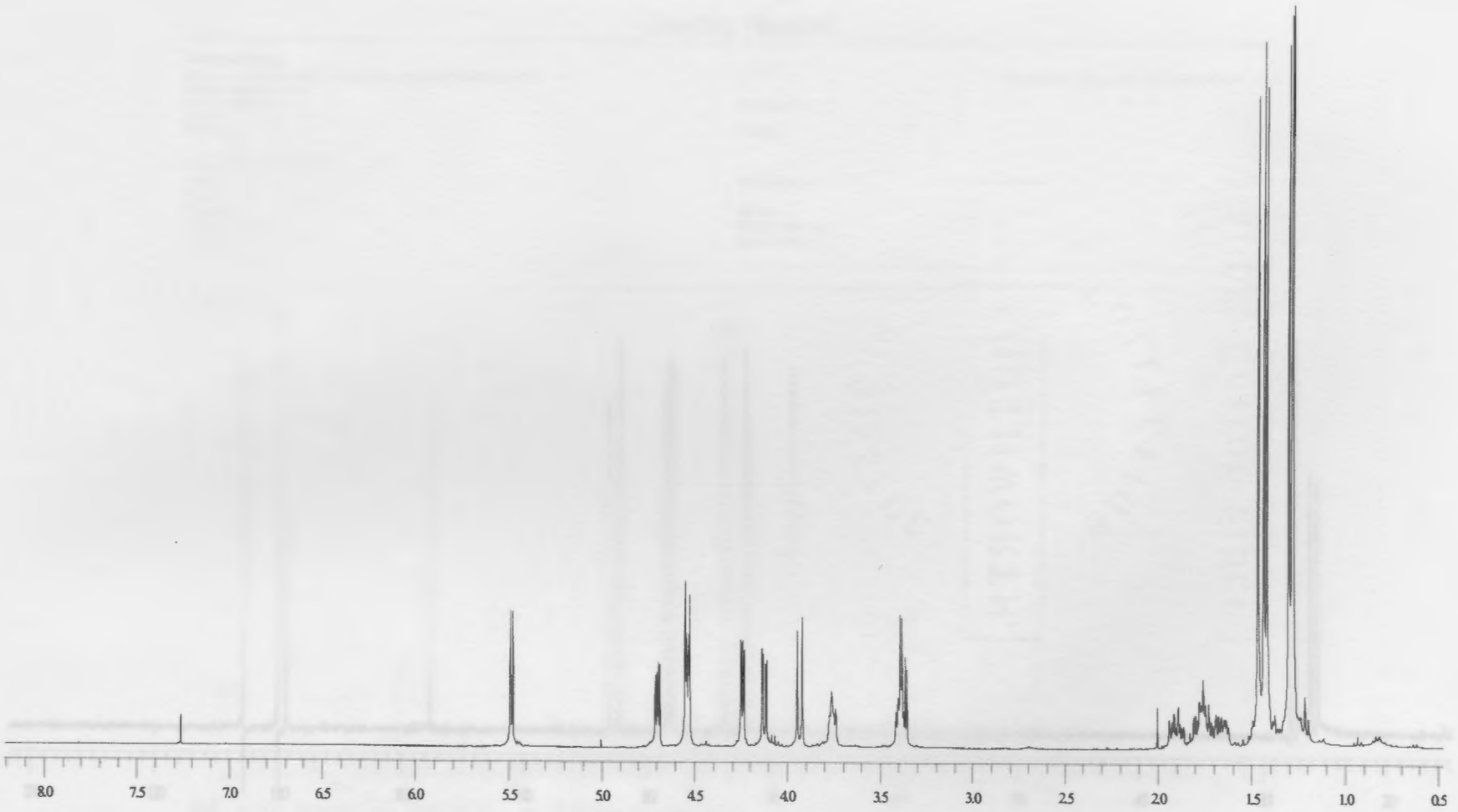


Figure 29. 400 MHz ^{1}H NMR spectrum of compound **10**

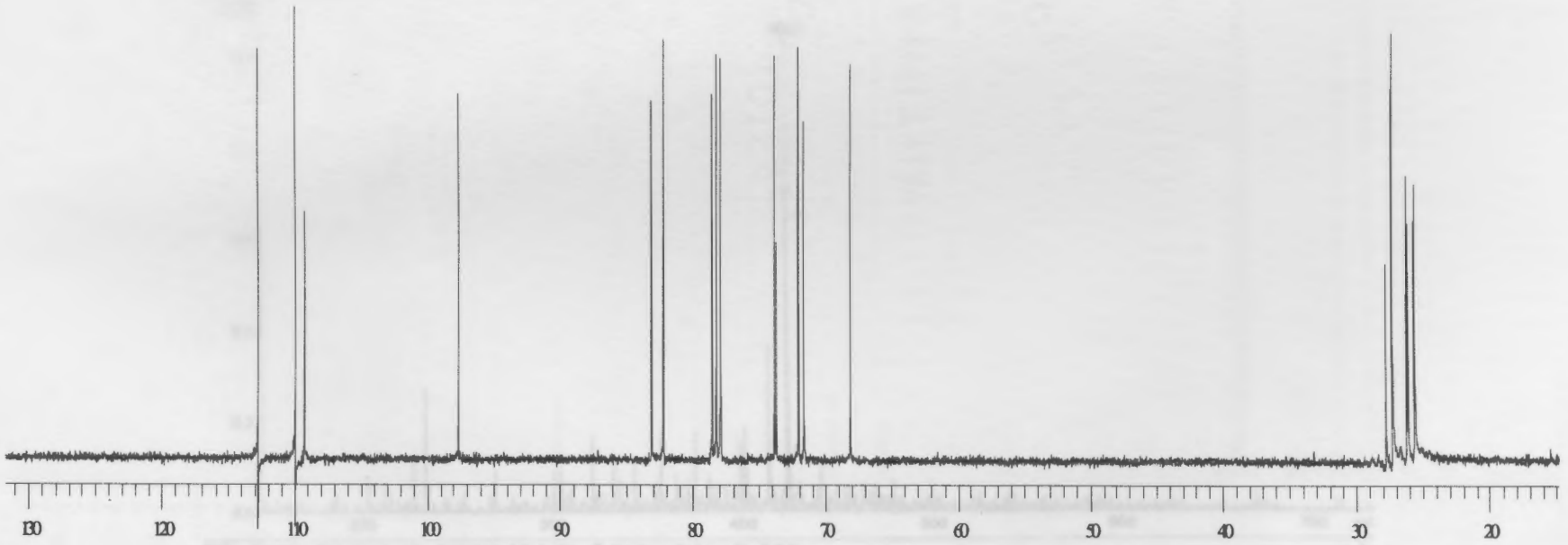


Figure 30. 100 MHz ^{13}C NMR spectrum of compound **10**

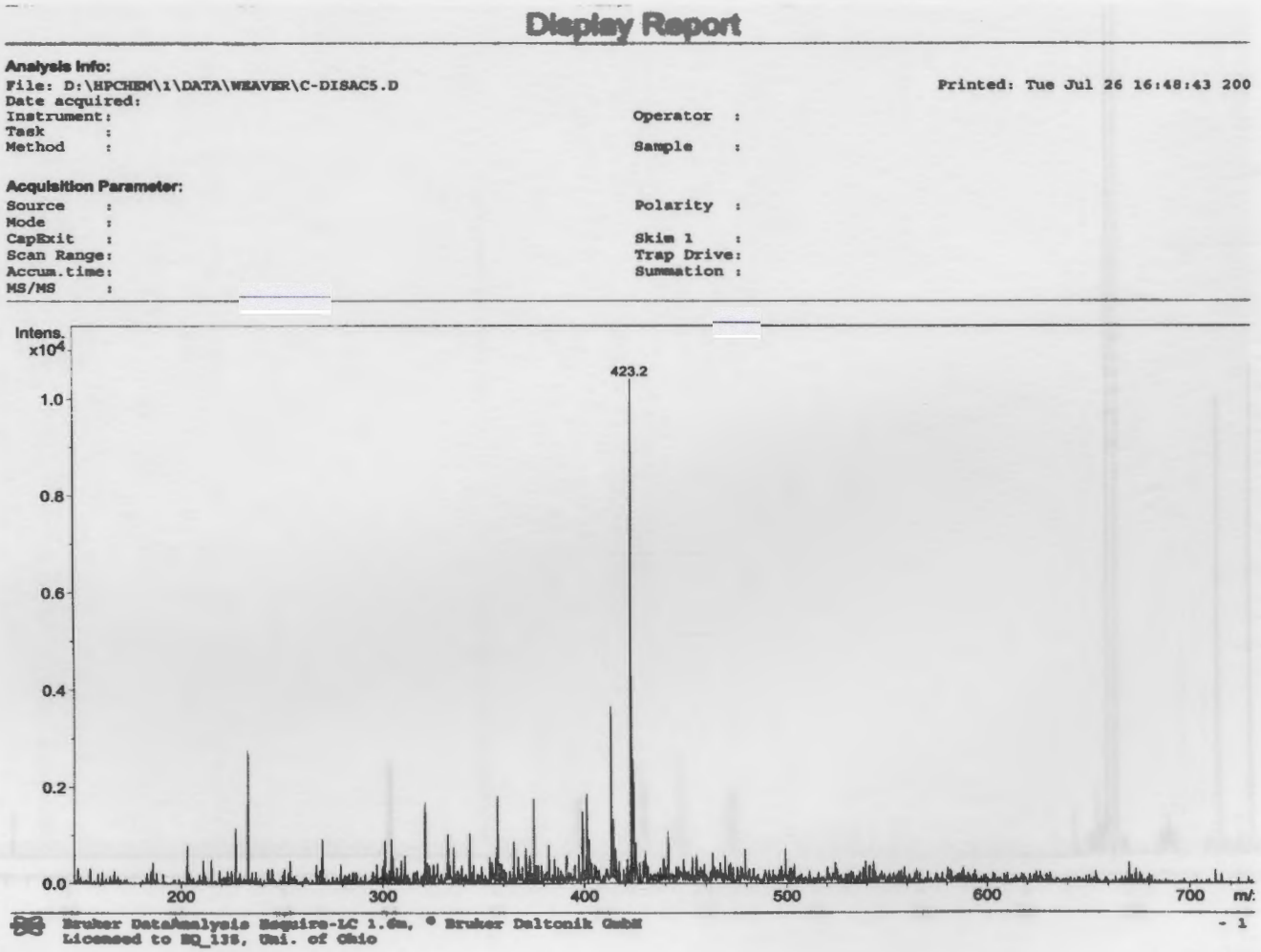


Figure 31. Mass spectrum of compound **10**

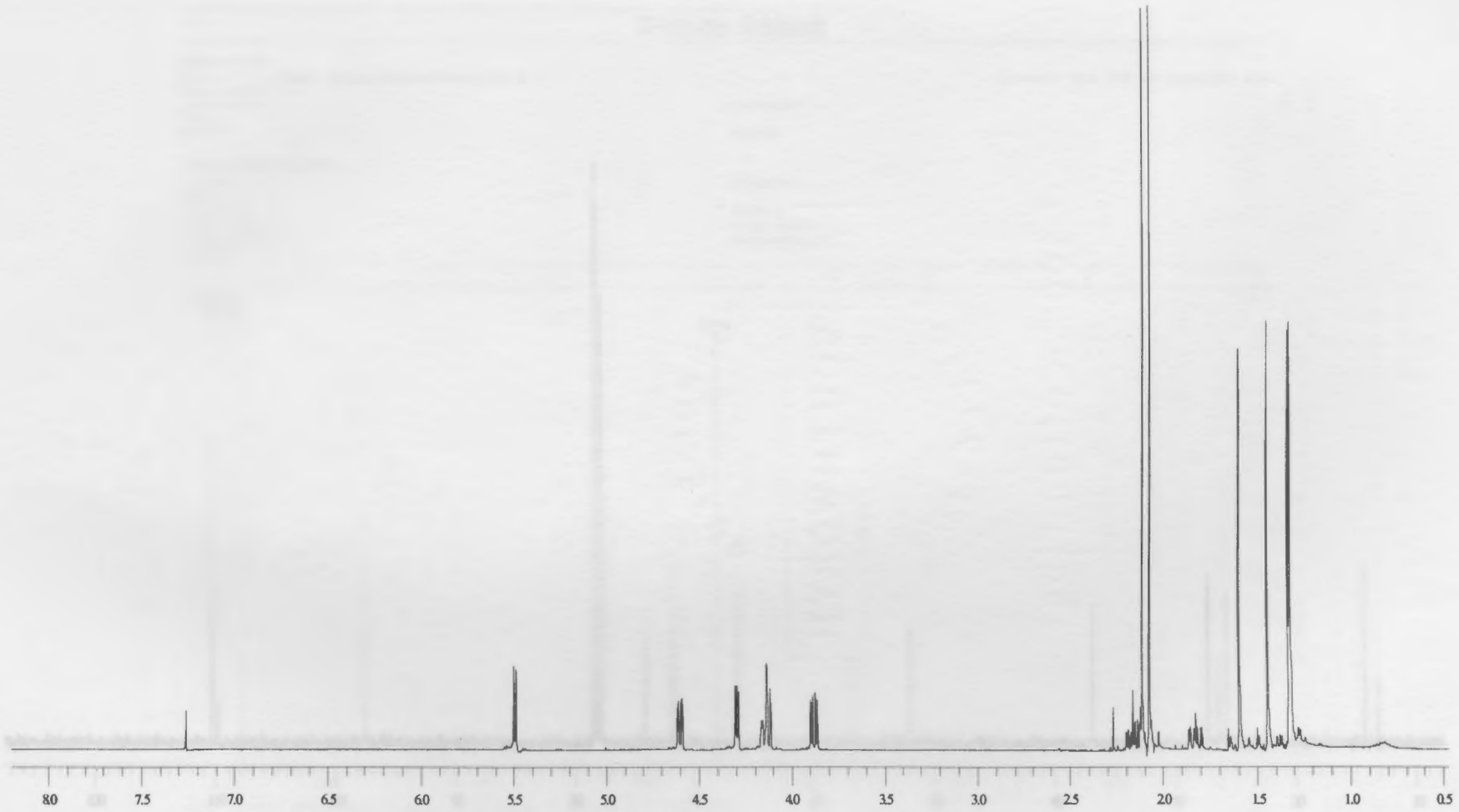


Figure 32. 400 MHz ^{1}H NMR spectrum of compound **12**

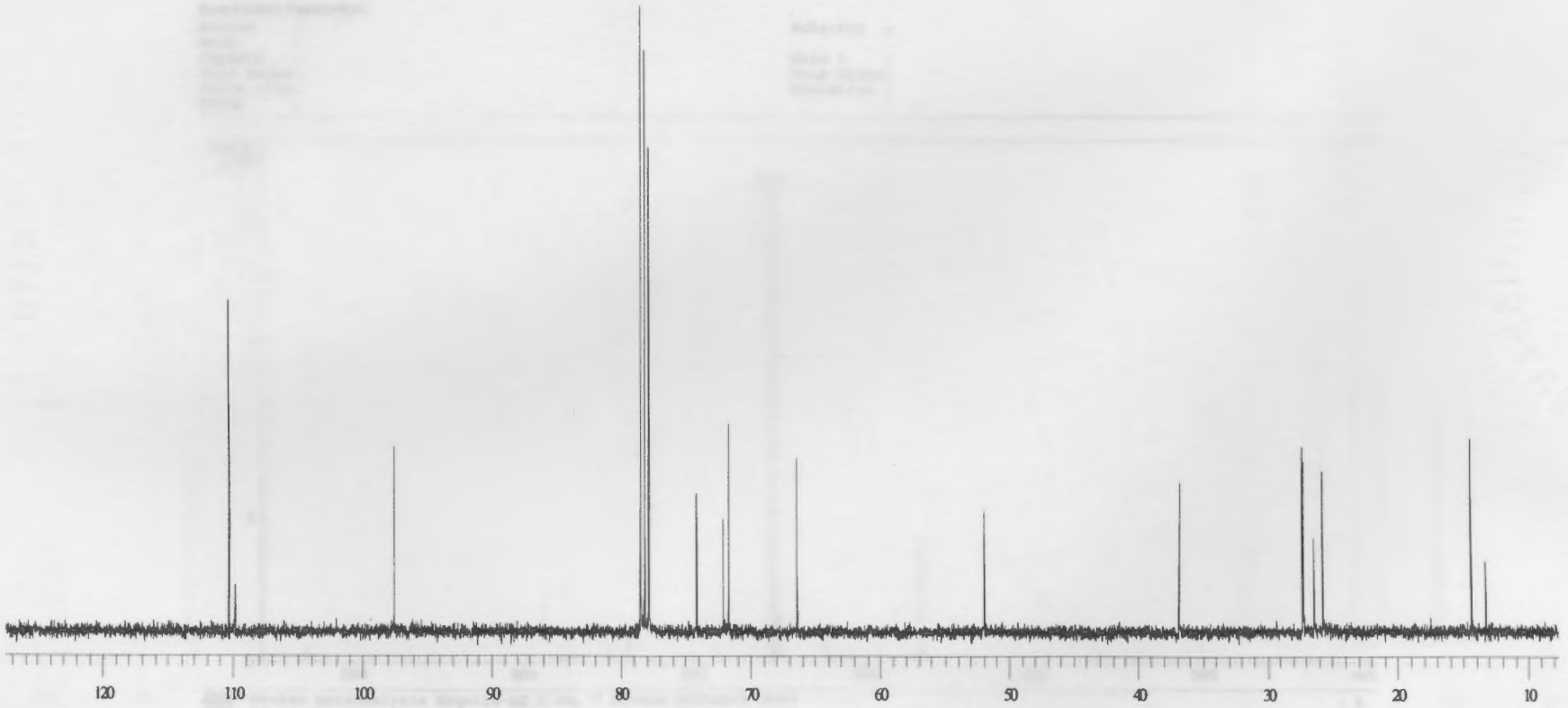


Figure 33. 100 MHz ^{13}C NMR spectrum of compound **12**

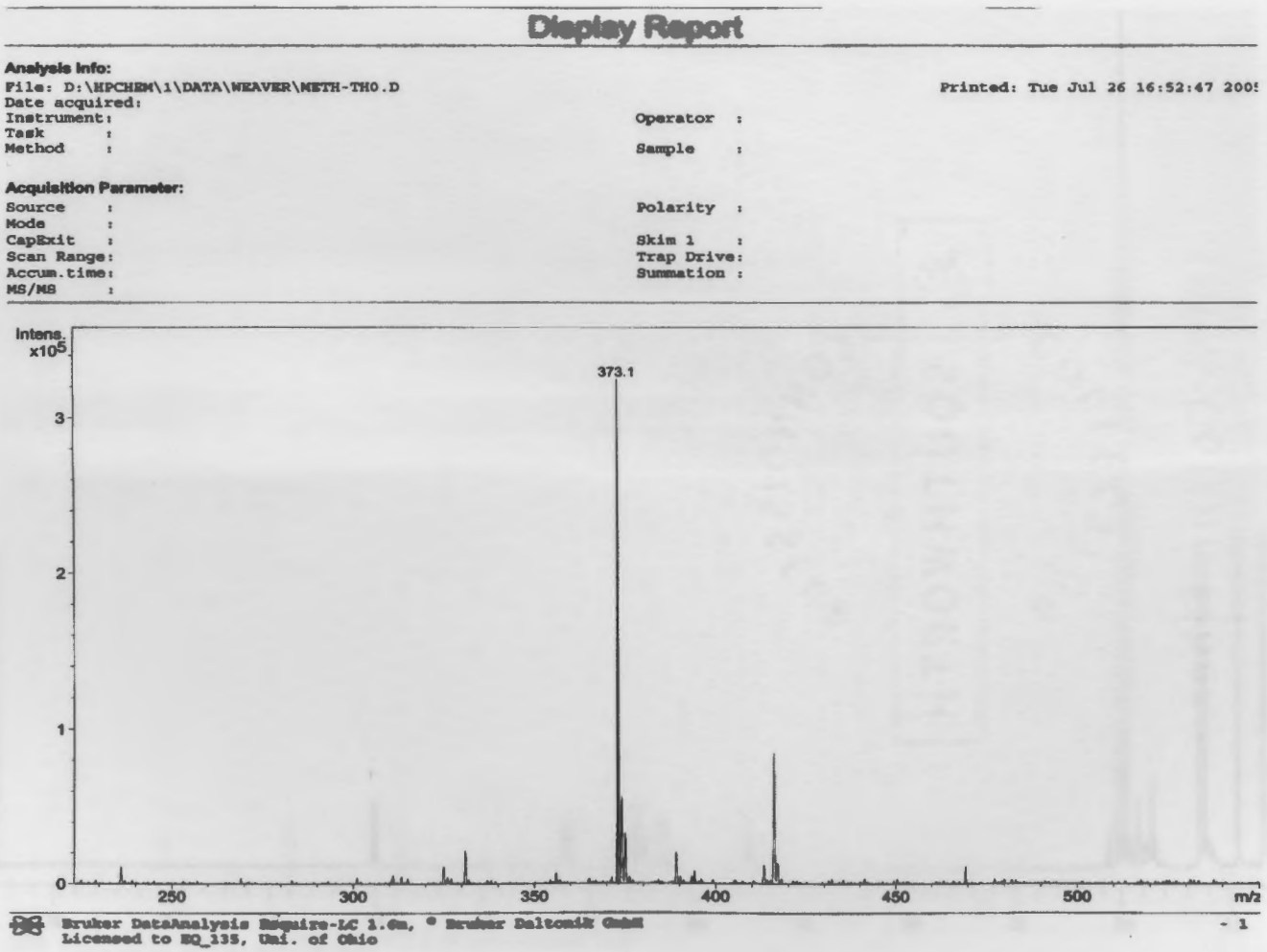


Figure 34. Mass spectrum of compound **12**

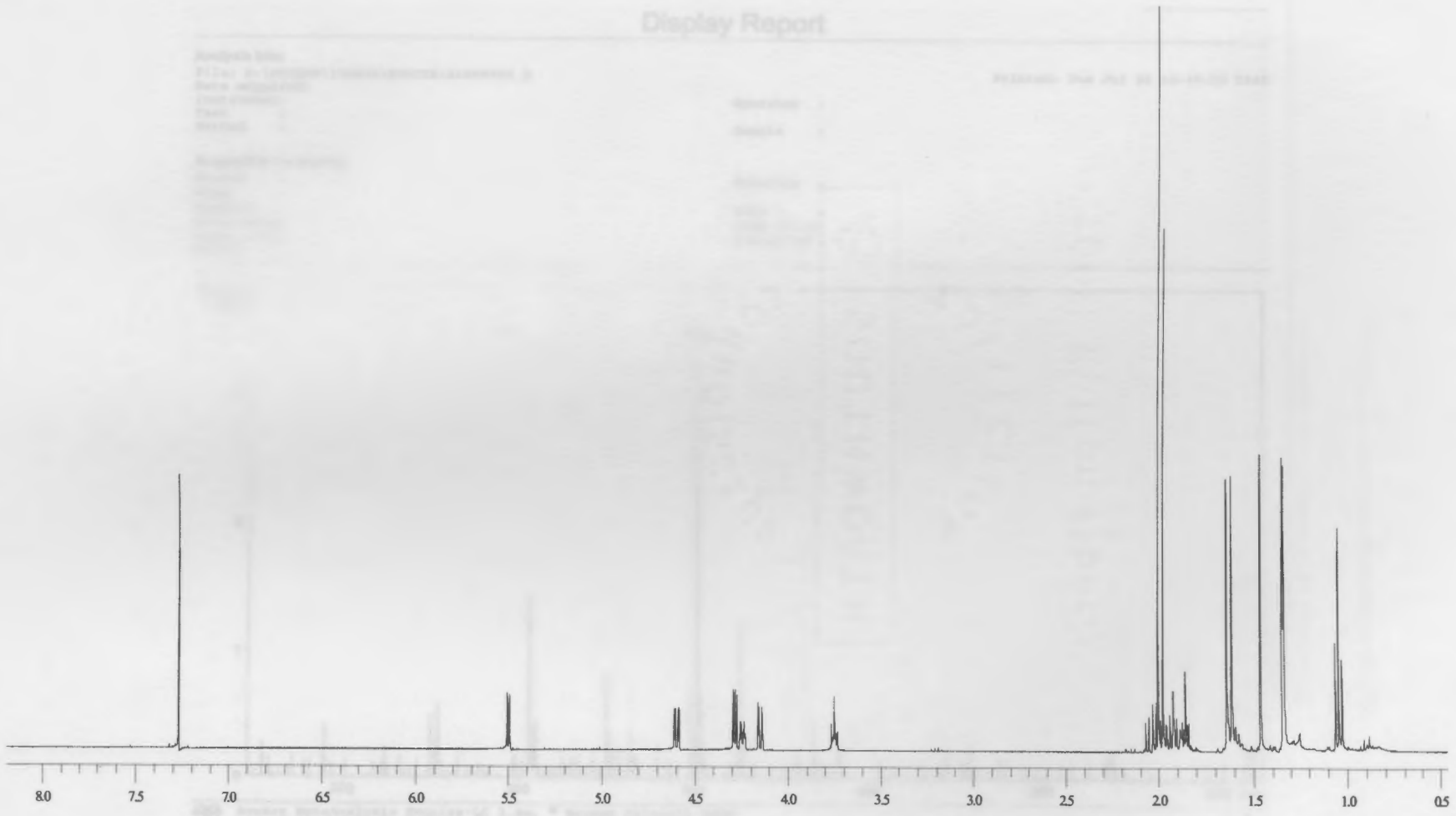


Figure 35. 400 MHz ^{1}H NMR spectrum of compound **13**

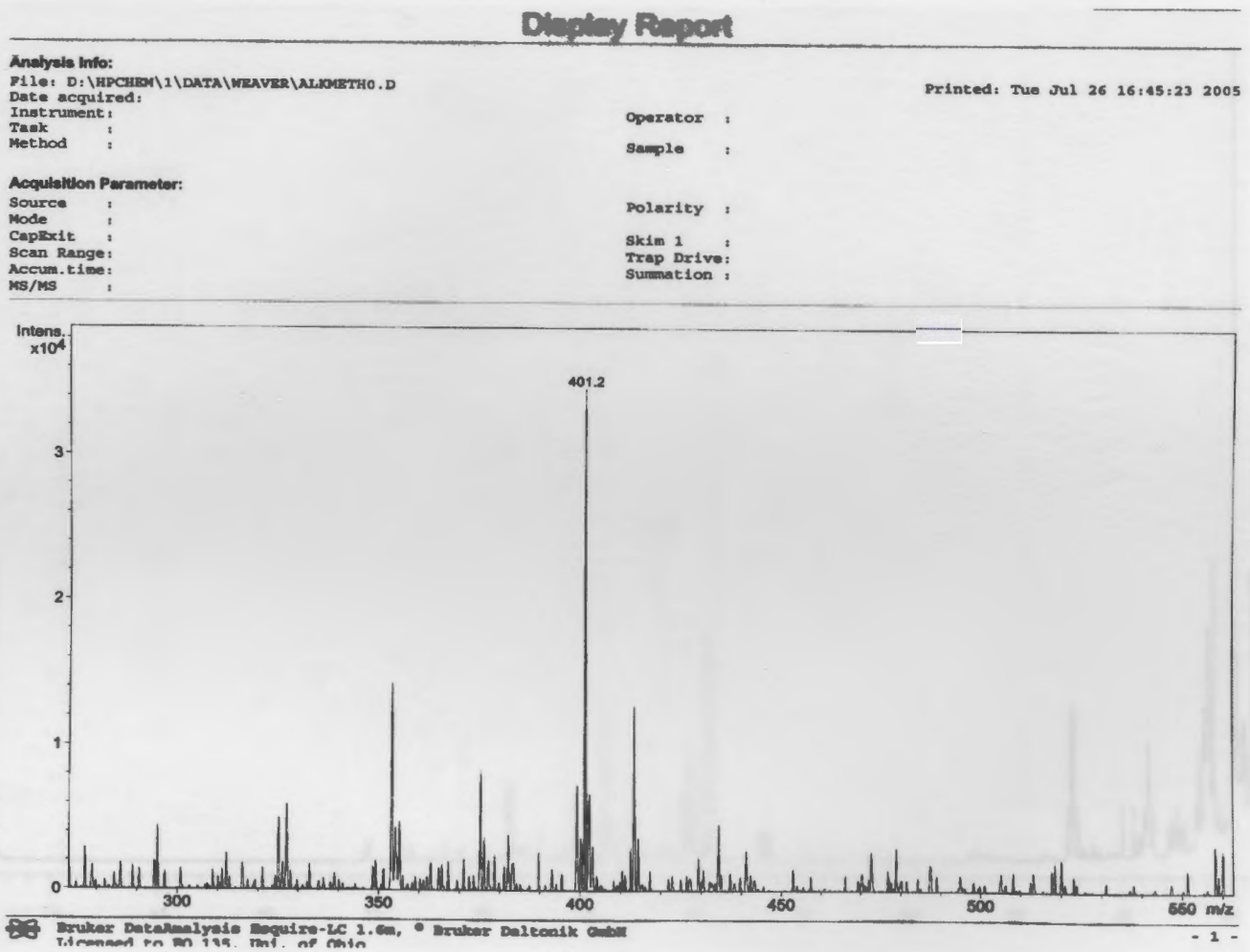


Figure 36. Mass spectrum of compound **13**

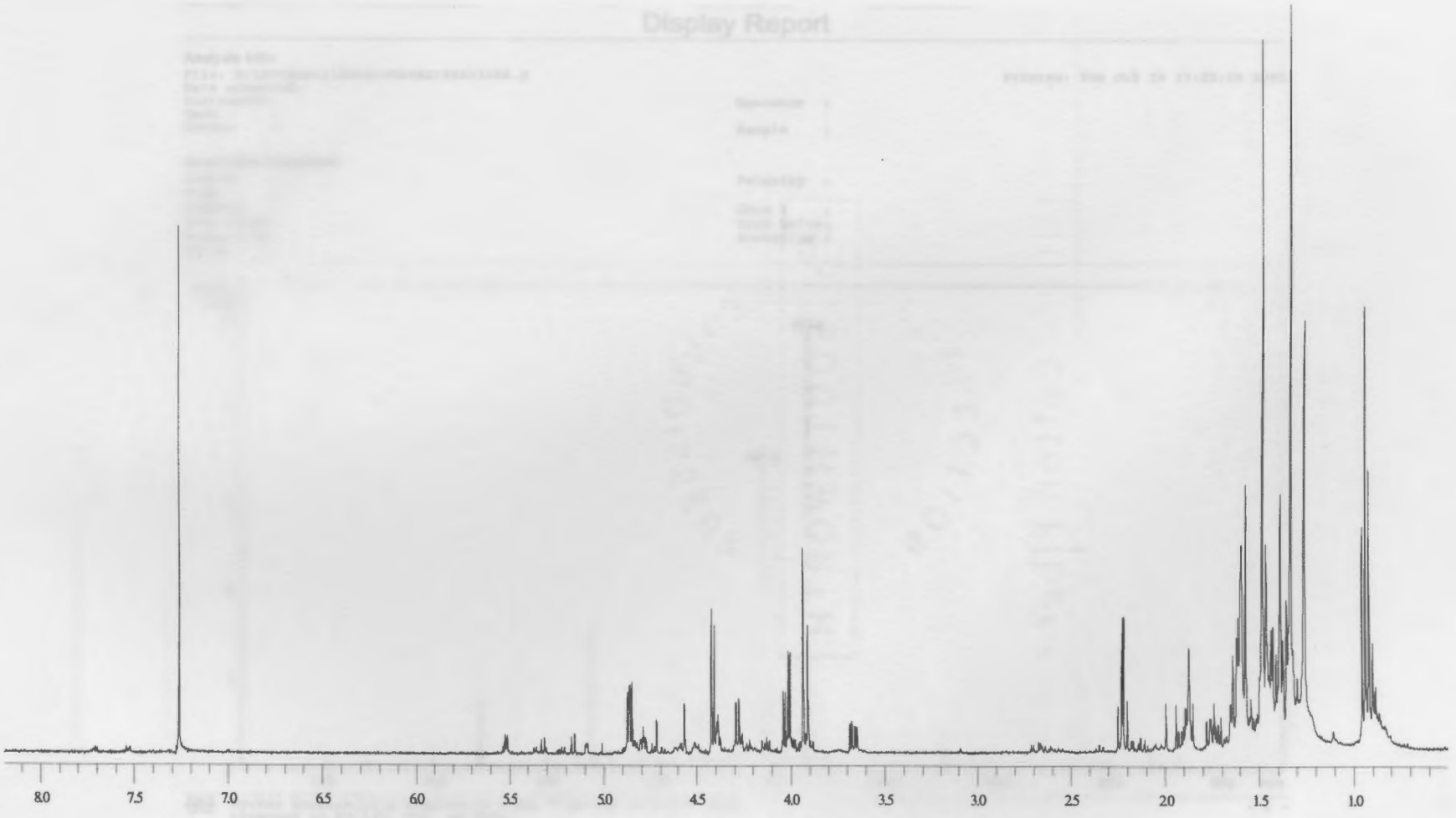


Figure 37. 400 MHz ^{1}H NMR spectrum of compound **14**

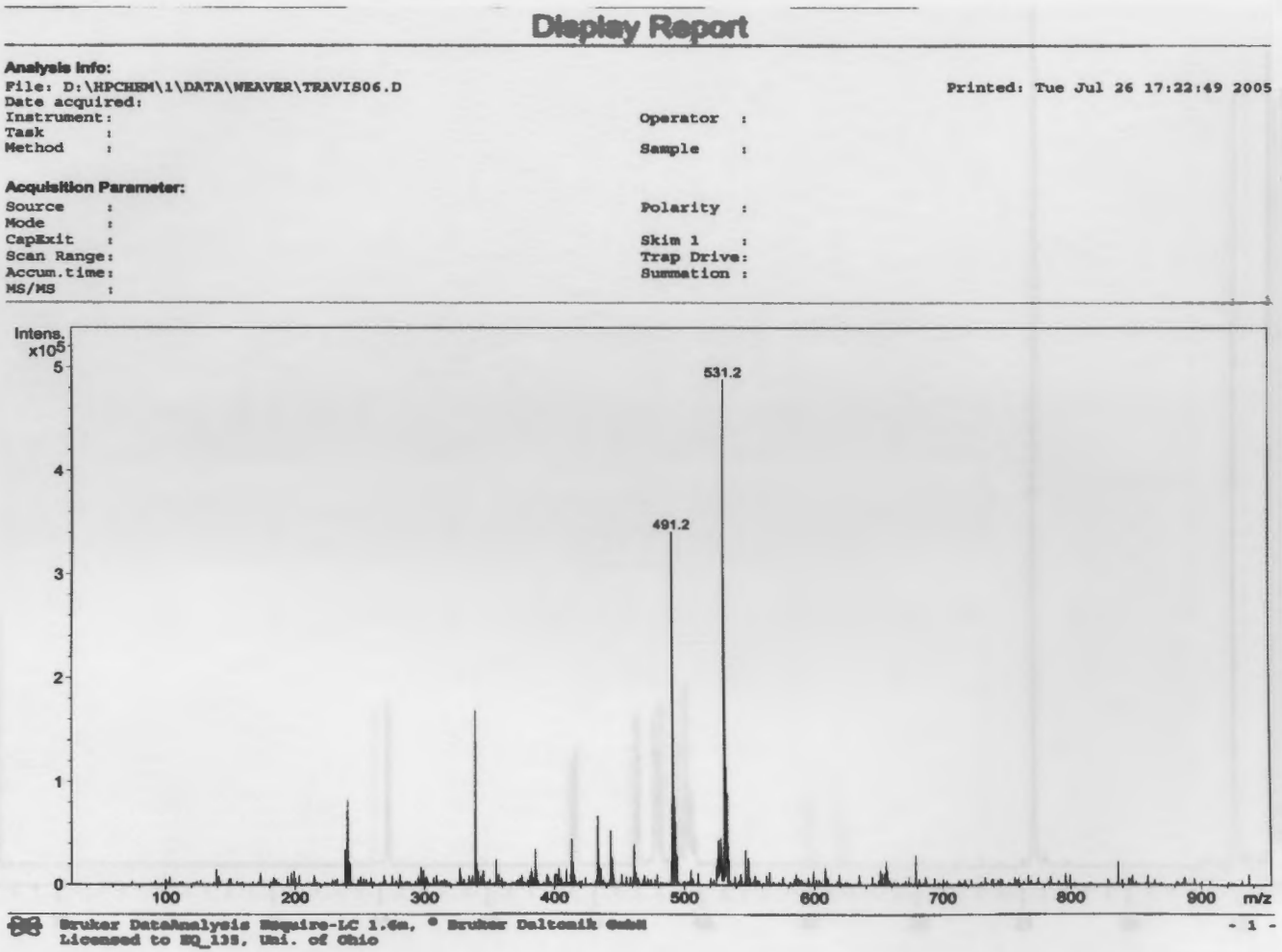


Figure 38. Mass spectrum of compound **14**

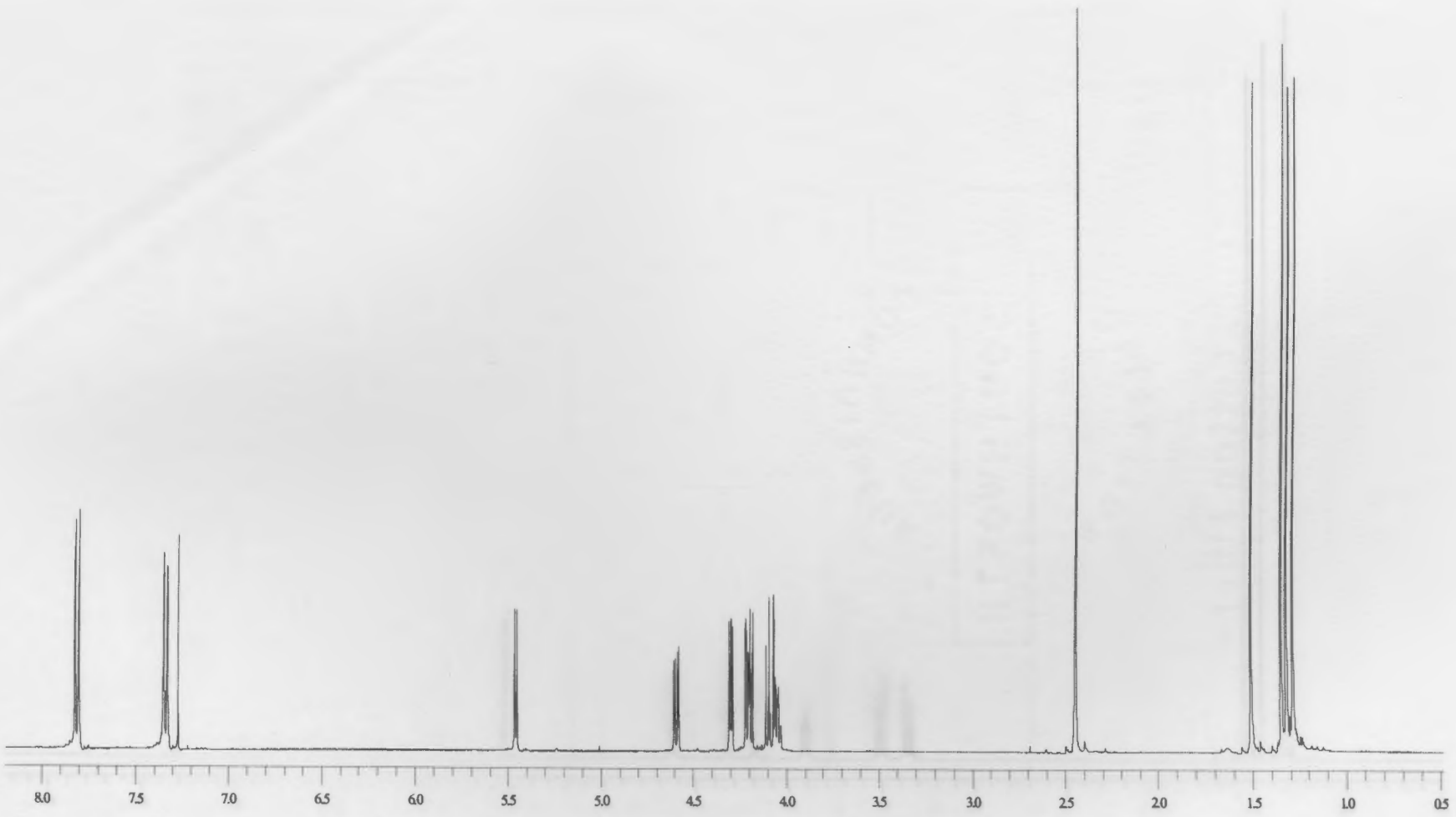


Figure 39. 400 MHz ^{1}H NMR spectrum of compound **15**

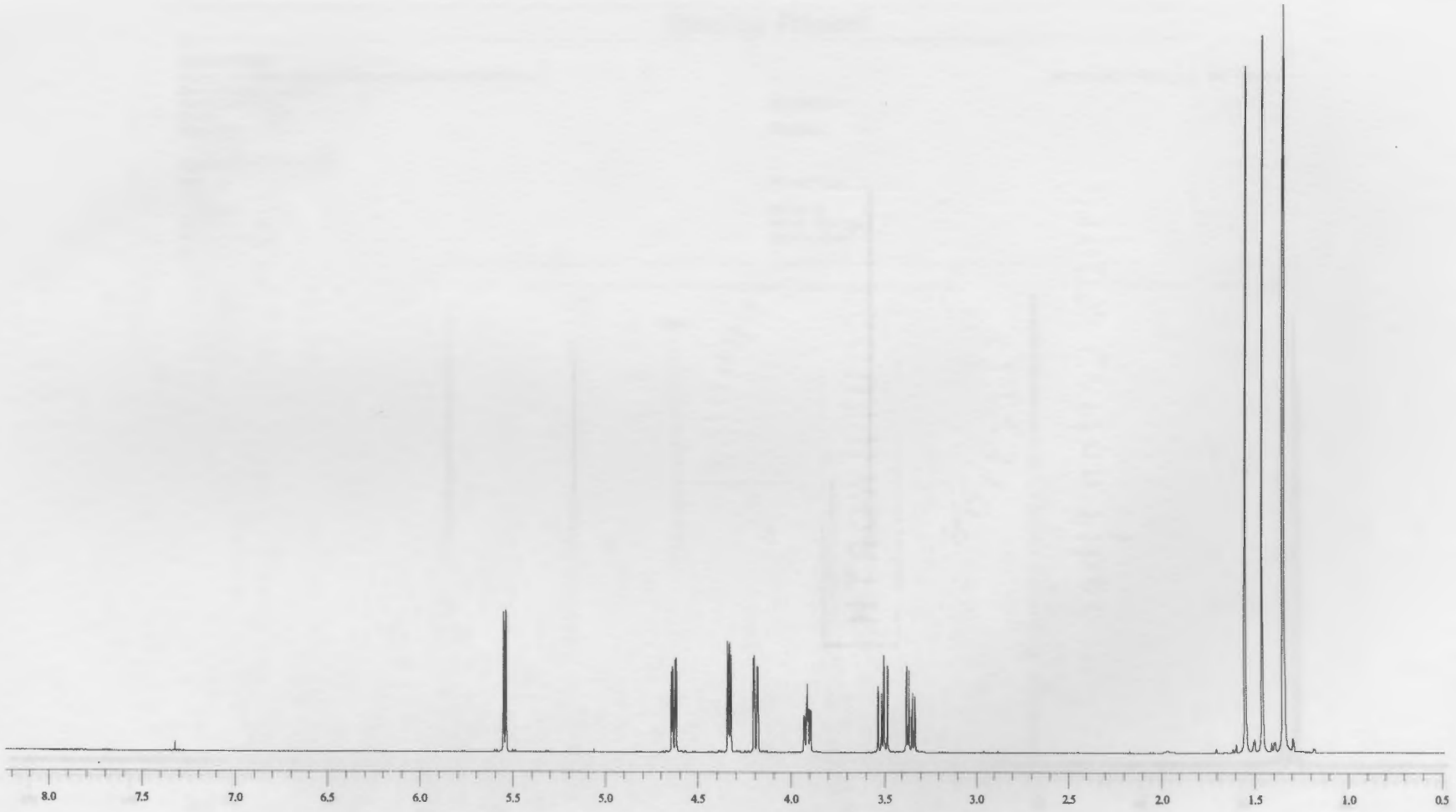


Figure 40. 400 MHz ^{1}H NMR spectrum of compound **16**

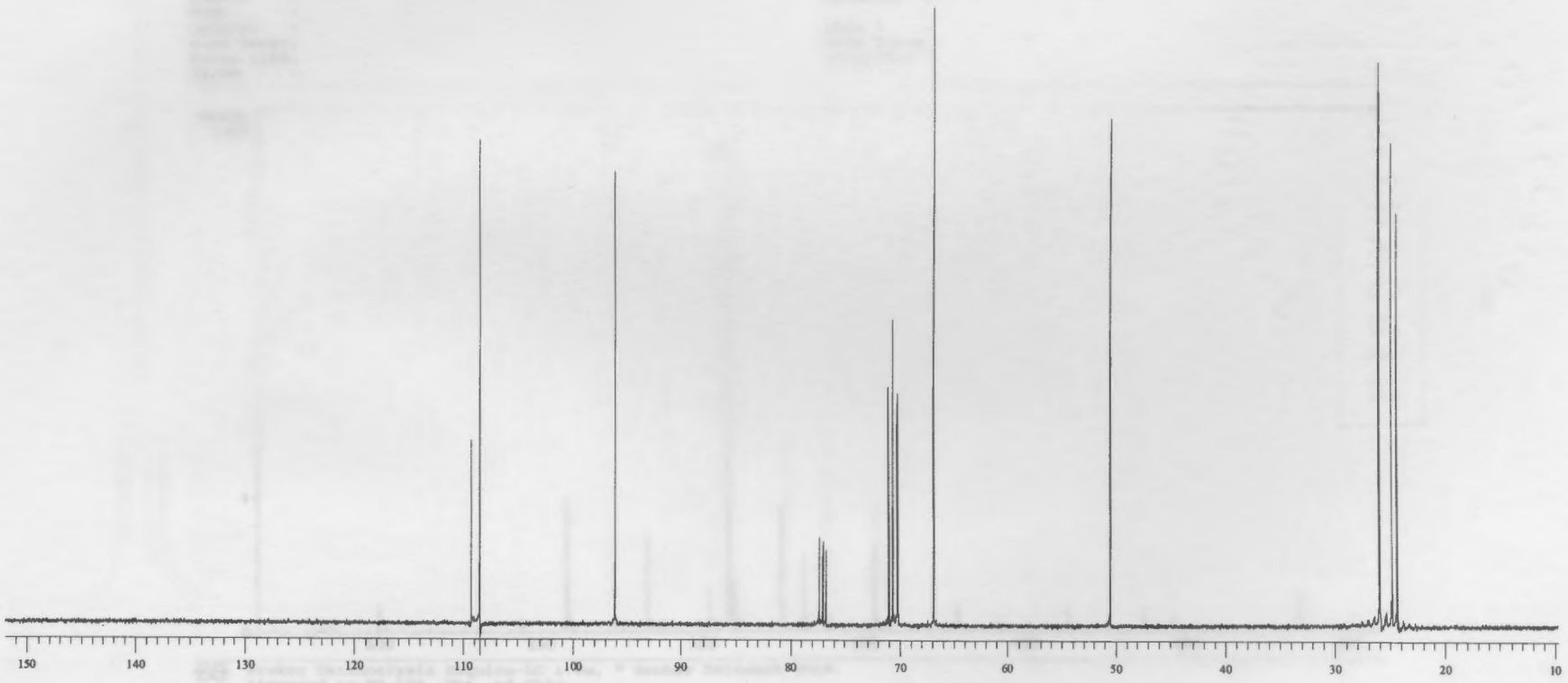


Figure 41. 100 MHz ^{13}C NMR spectrum of compound **16**

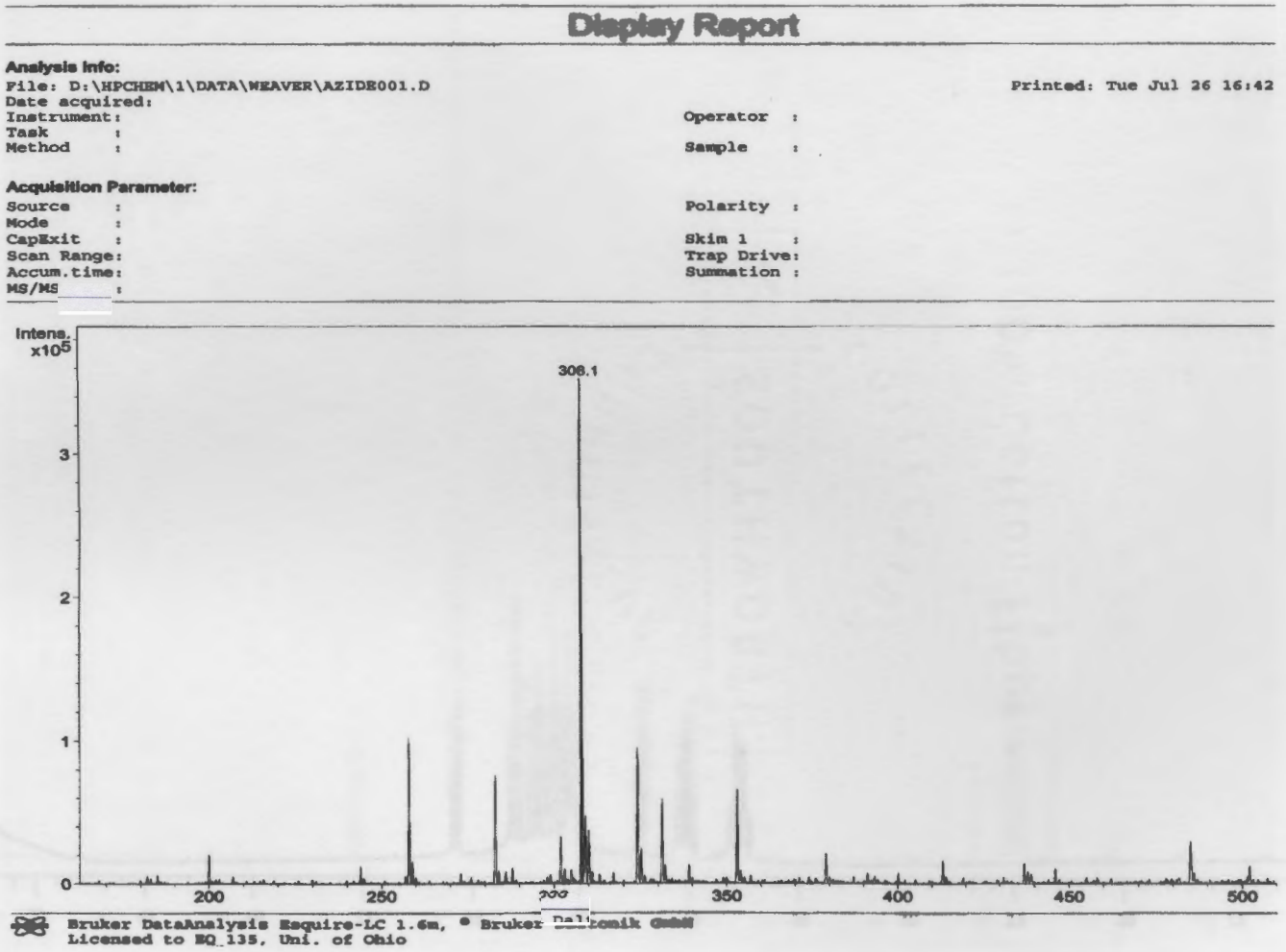


Figure 42. Mass spectrum of compound **16**

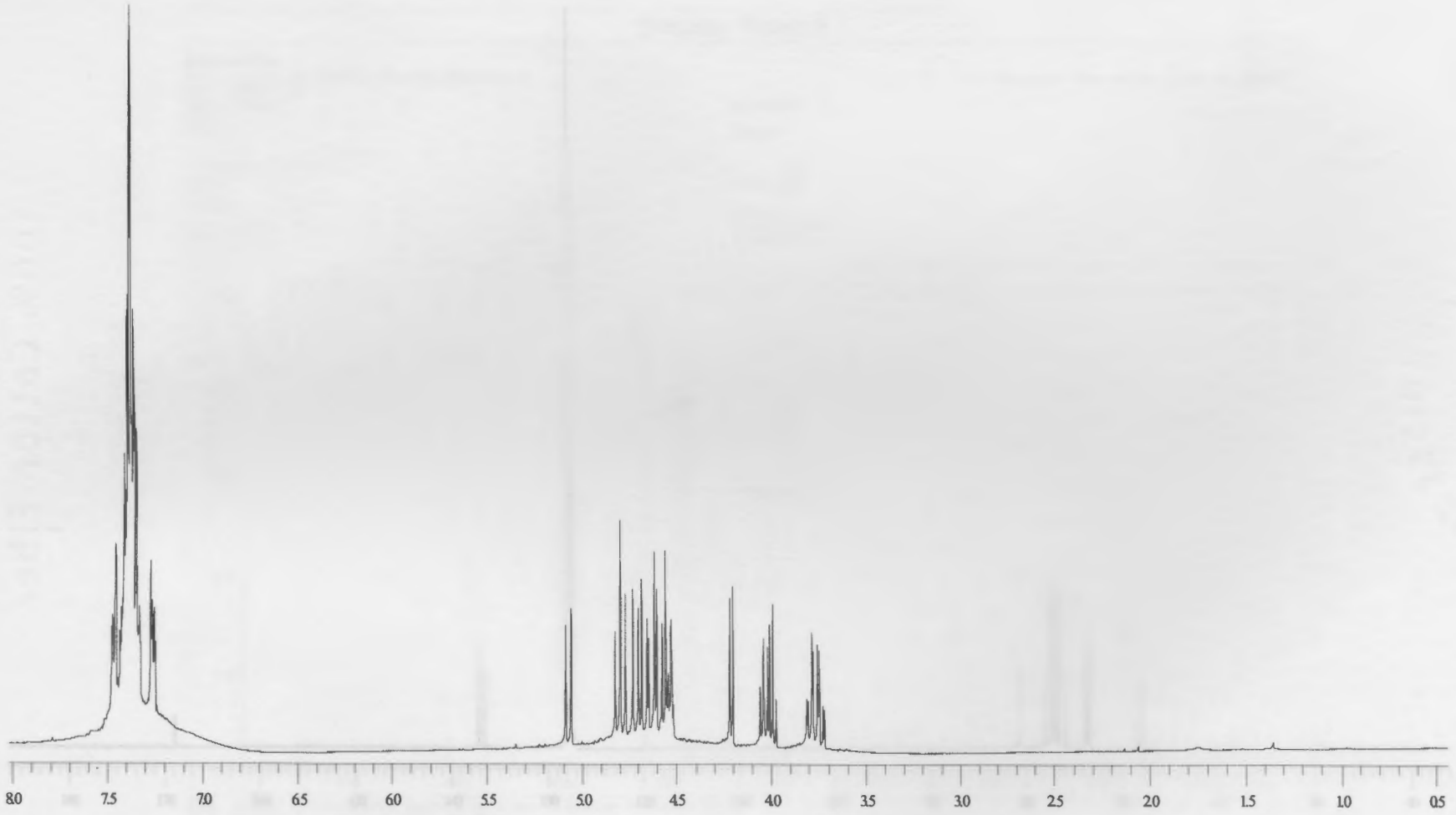


Figure 43. 400 MHz ^{1}H NMR spectrum of compound **18**

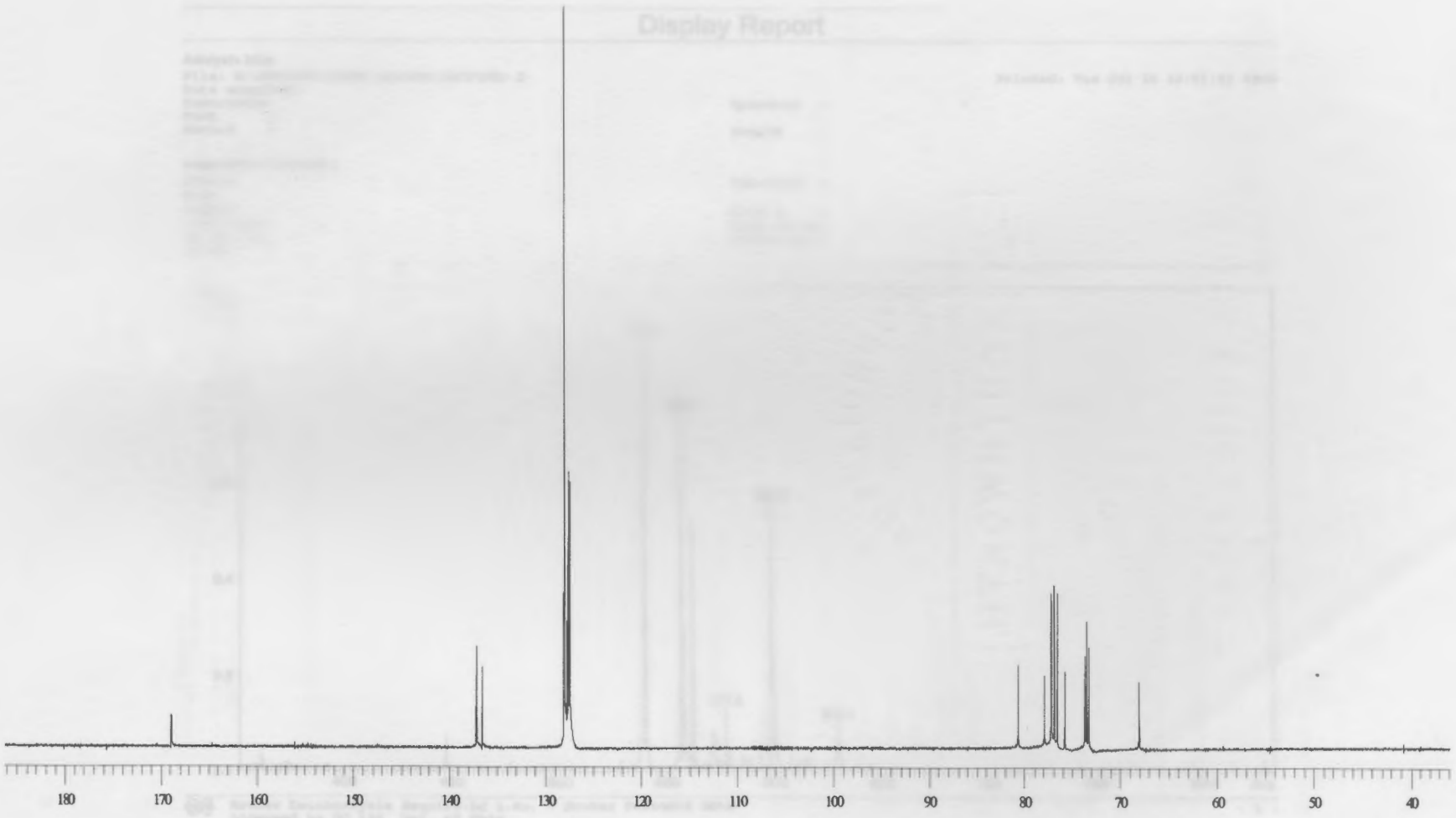


Figure 44. 100 MHz ^{13}C NMR spectrum of compound **18**

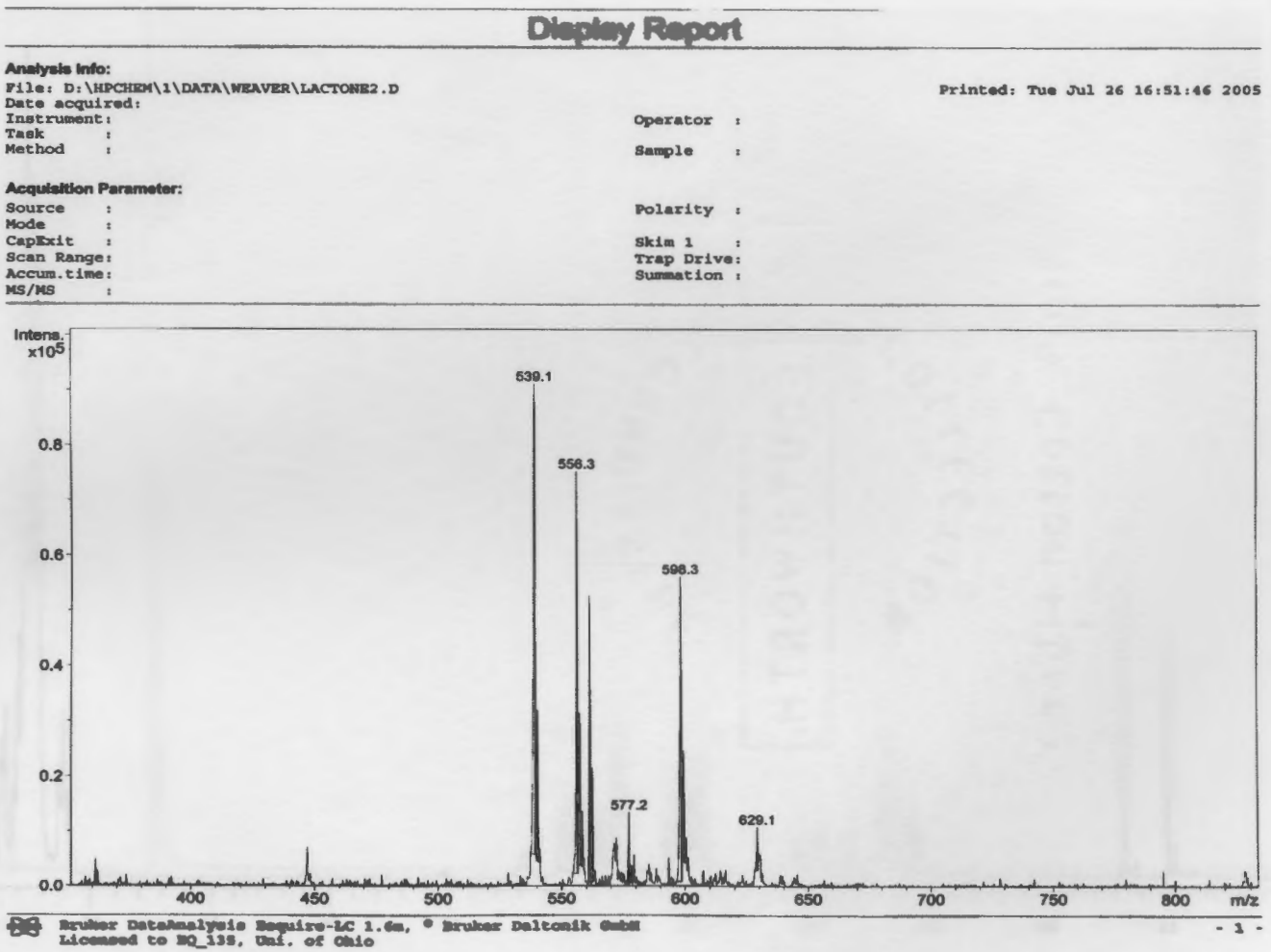


Figure 45. Mass spectrum of compound **18**

Figure 46. 400 MHz ^{1}H NMR spectrum of compound **19**

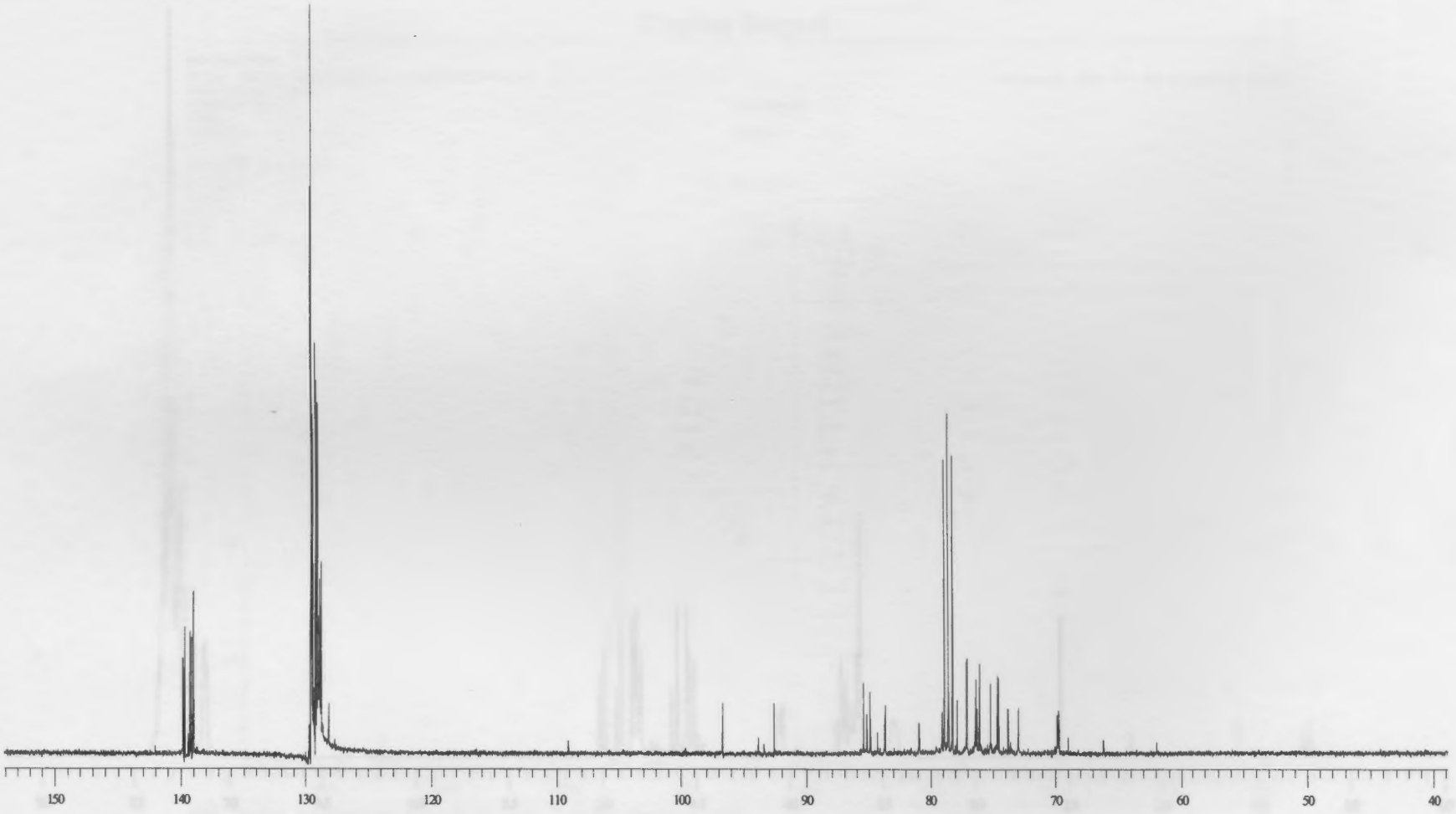


Figure 47. 100 MHz ^{13}C NMR spectrum of compound **19**

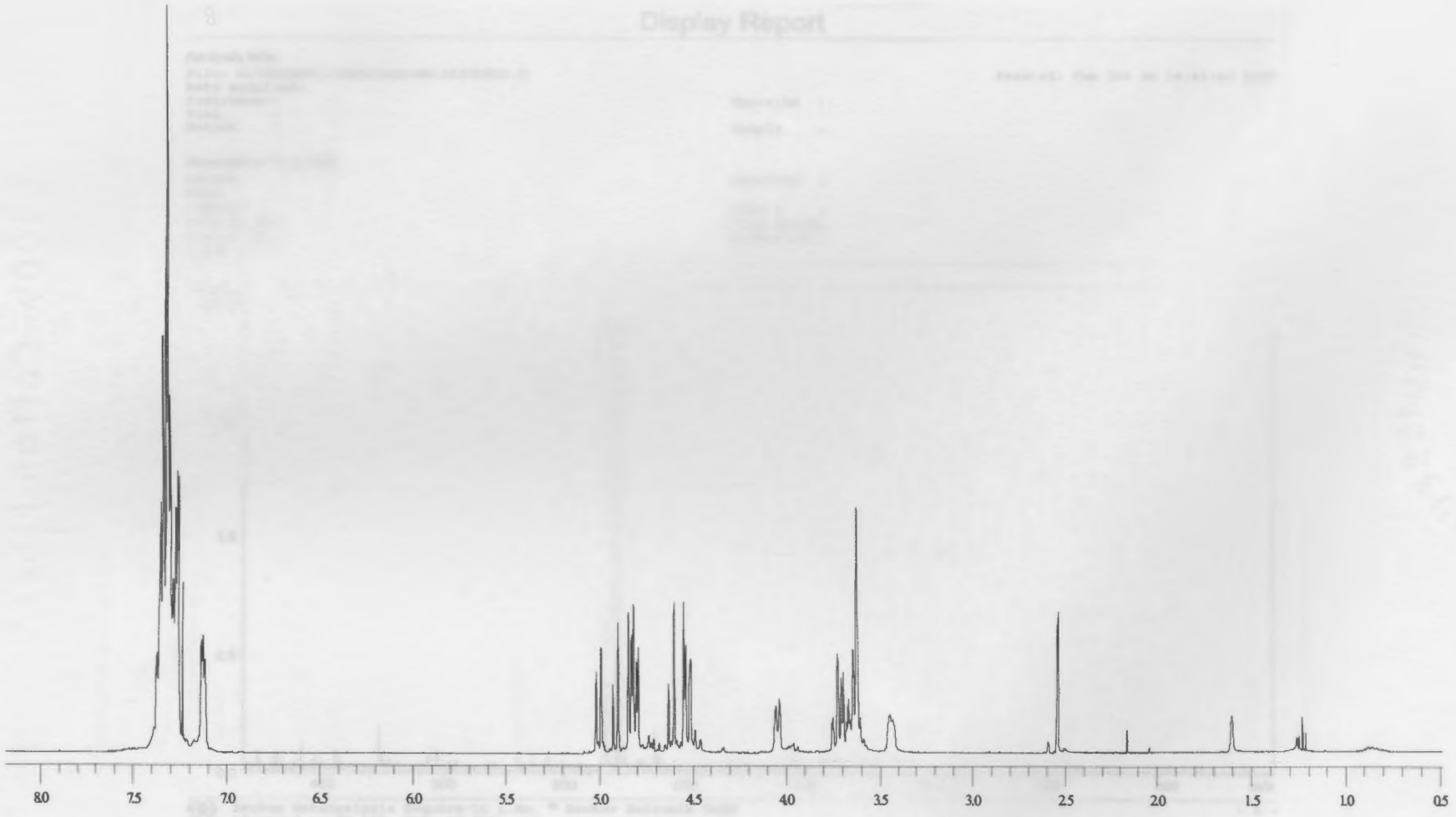


Figure 48. 400 MHz ^{1}H NMR spectrum of compound **20**

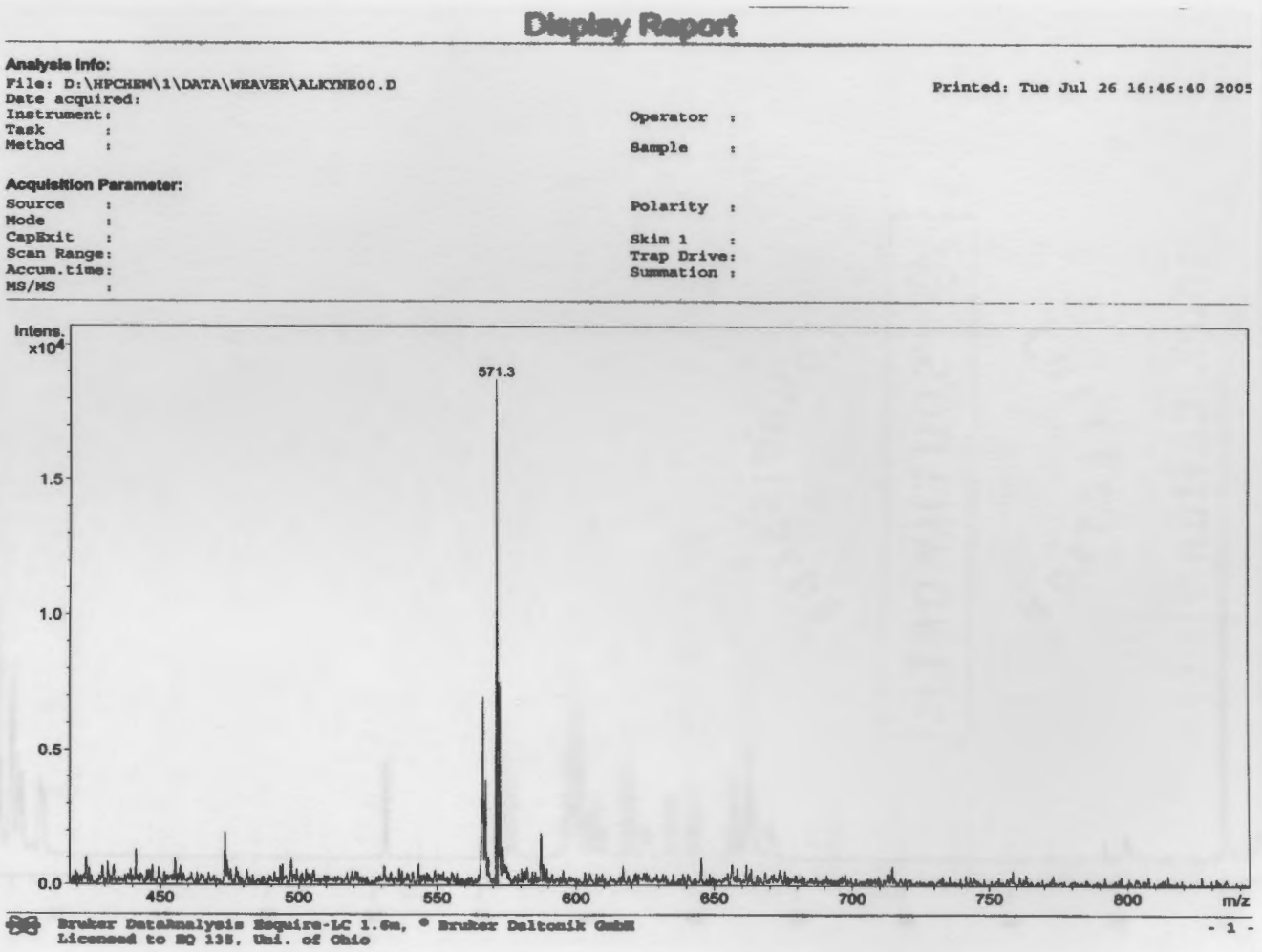


Figure 49. Mass spectrum of compound **20**

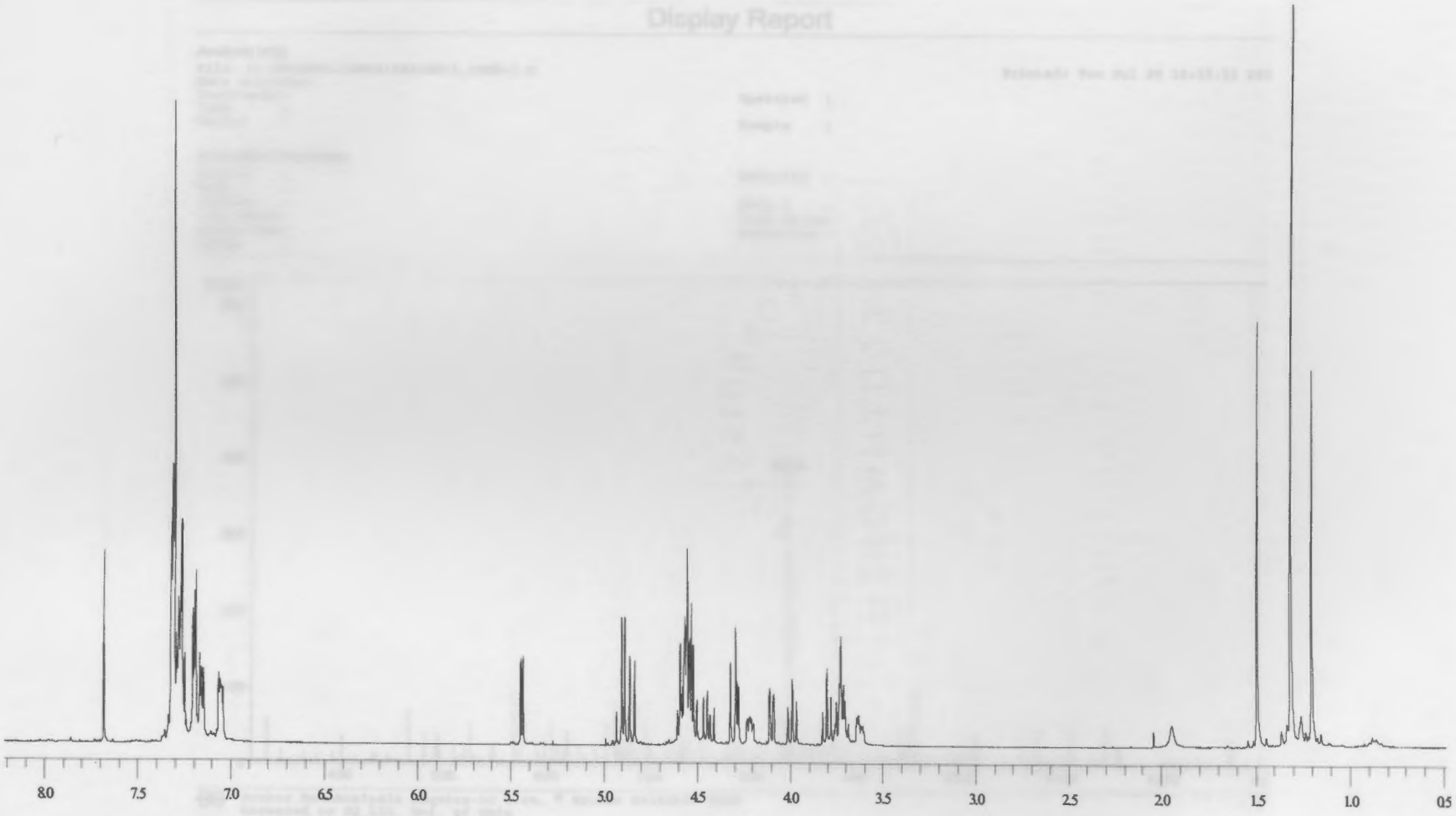


Figure 50. 400 MHz ^{1}H NMR spectrum of compound **21**

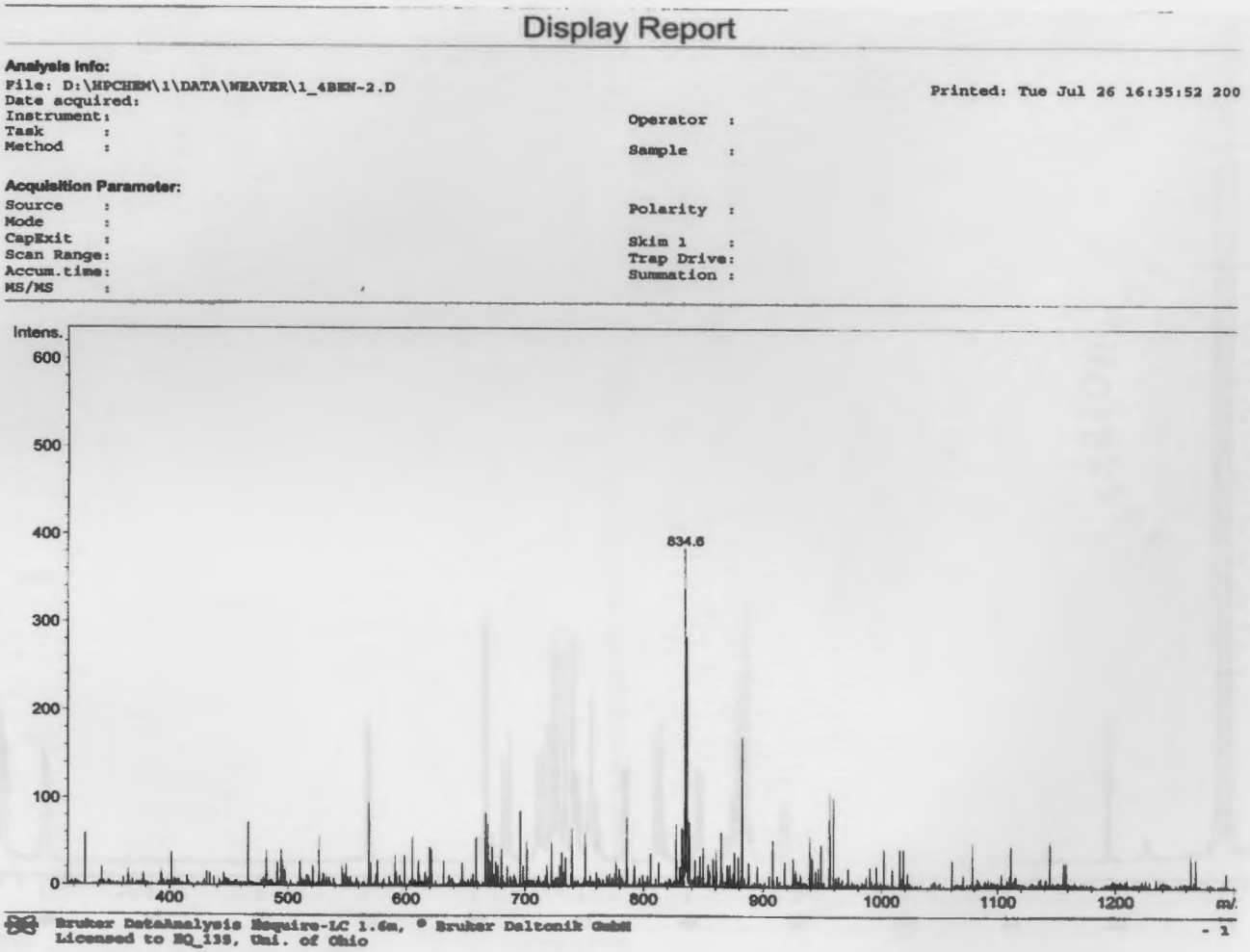


Figure 51. Mass spectrum of compound **21**

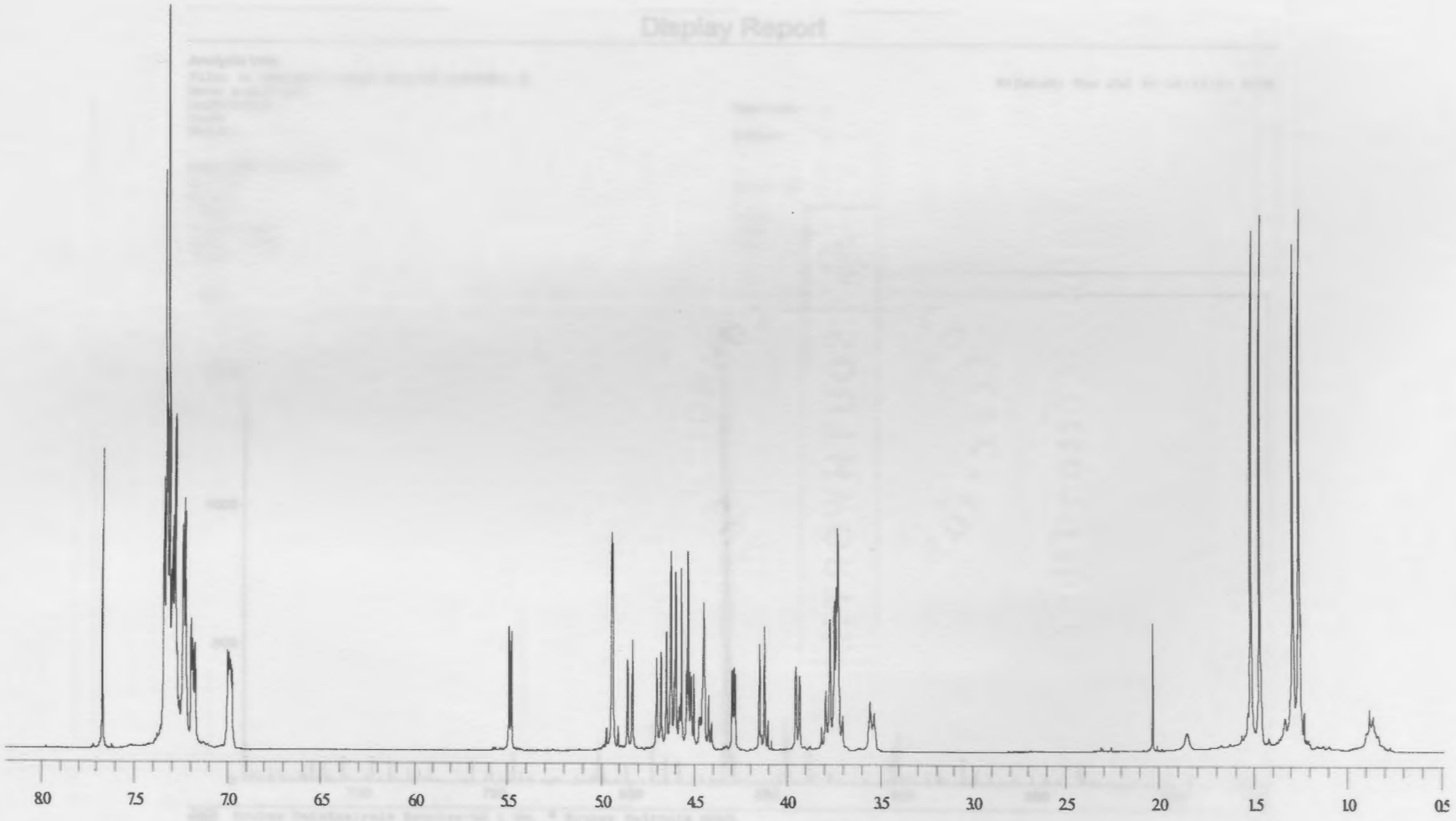


Figure 52. 400 MHz ^{1}H NMR spectrum of compound **22**

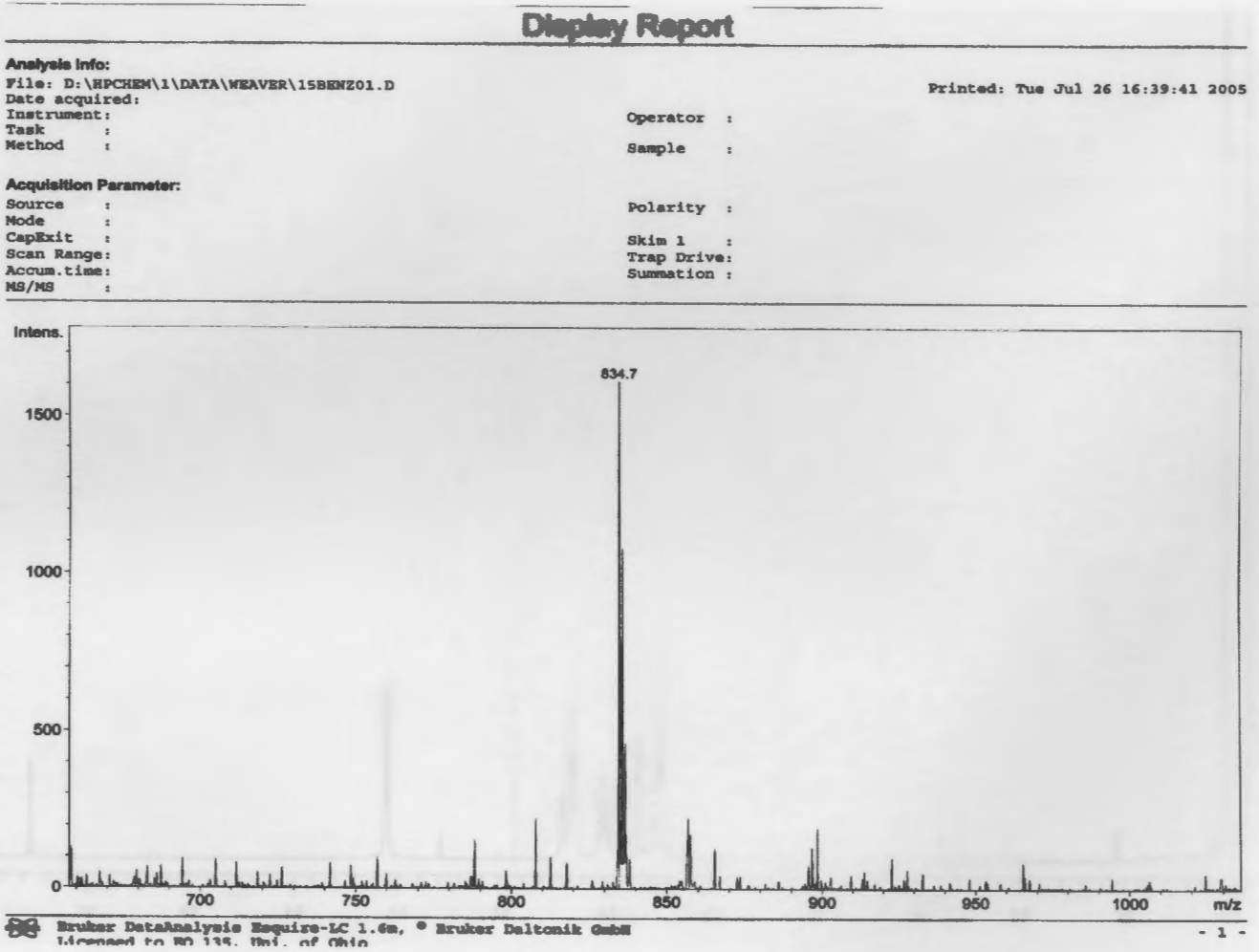


Figure 53. Mass spectrum of compound **22**

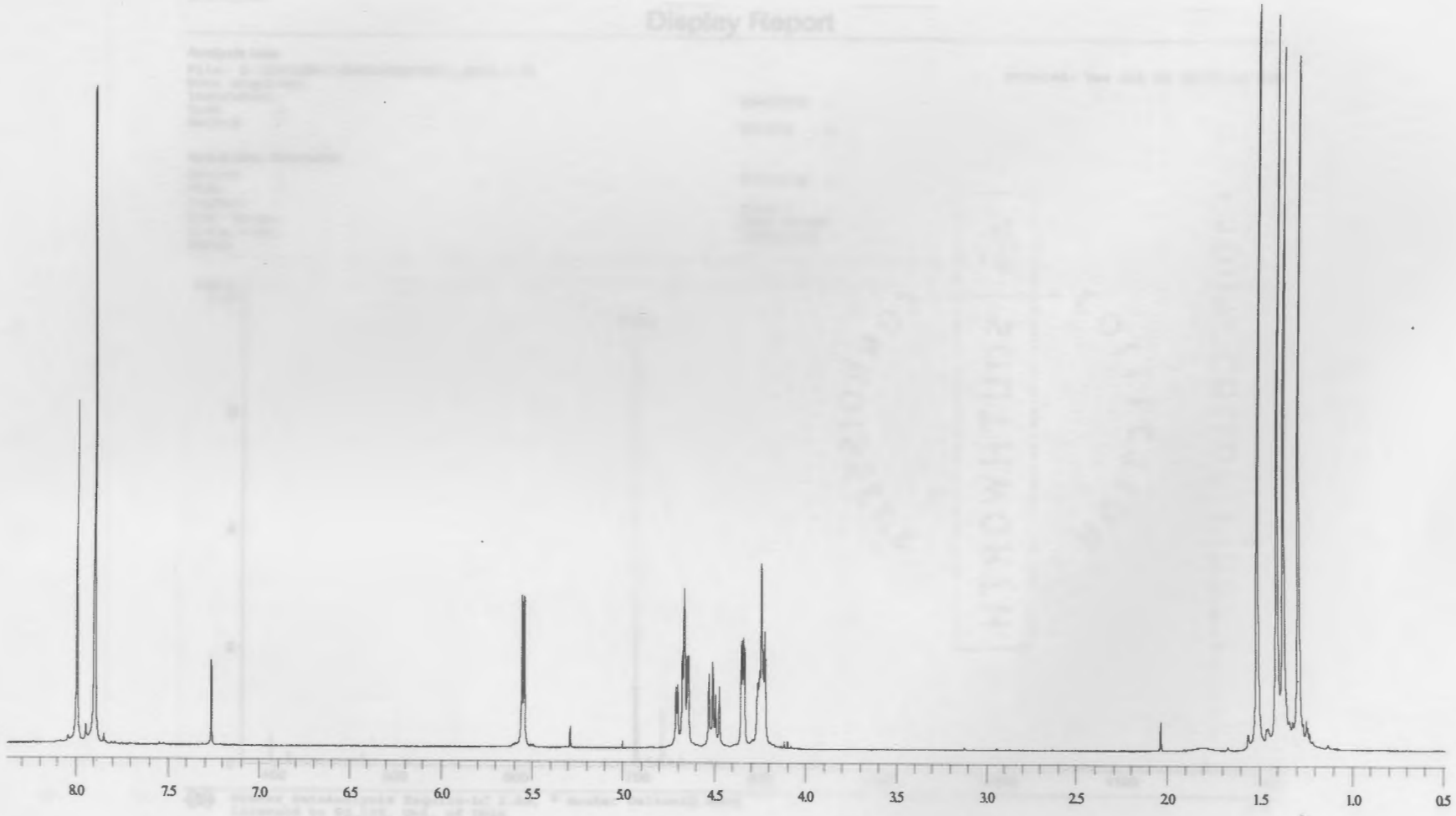


Figure 54. 400 MHz ^{1}H NMR spectrum of compound **24**

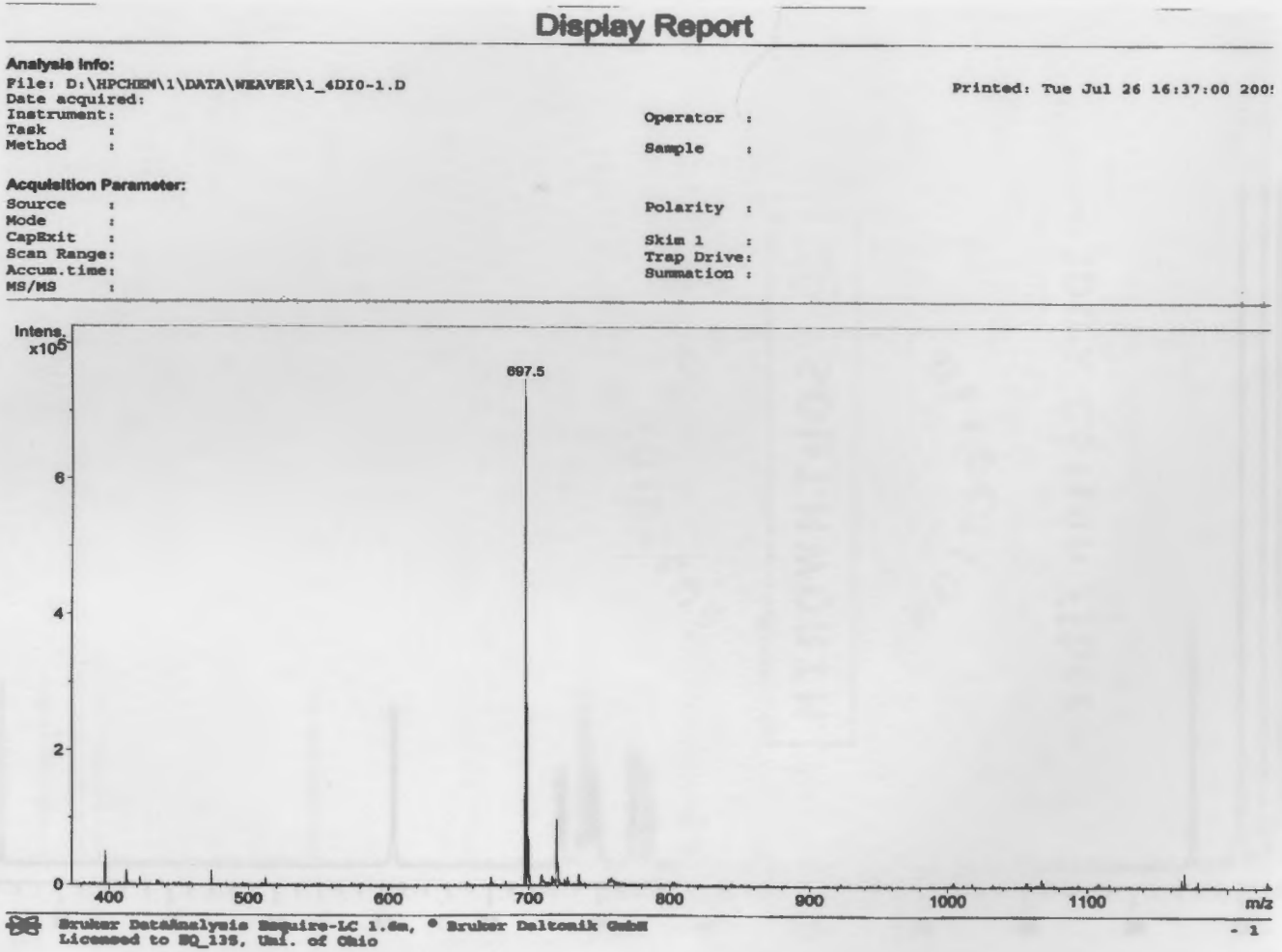


Figure 55. Mass spectrum of compound **24**

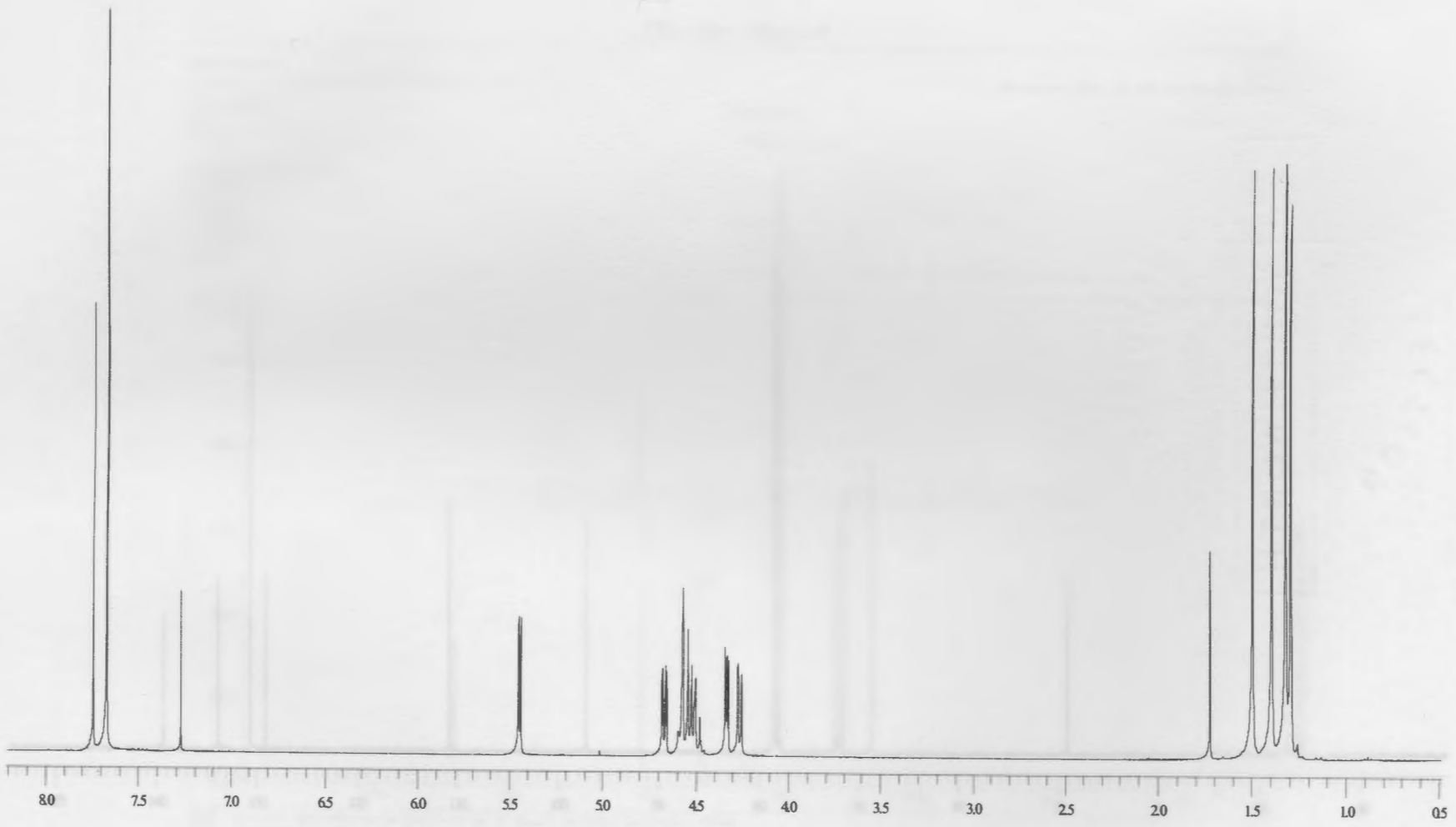


Figure 56. 400 MHz ^{1}H NMR spectrum of compound **25**

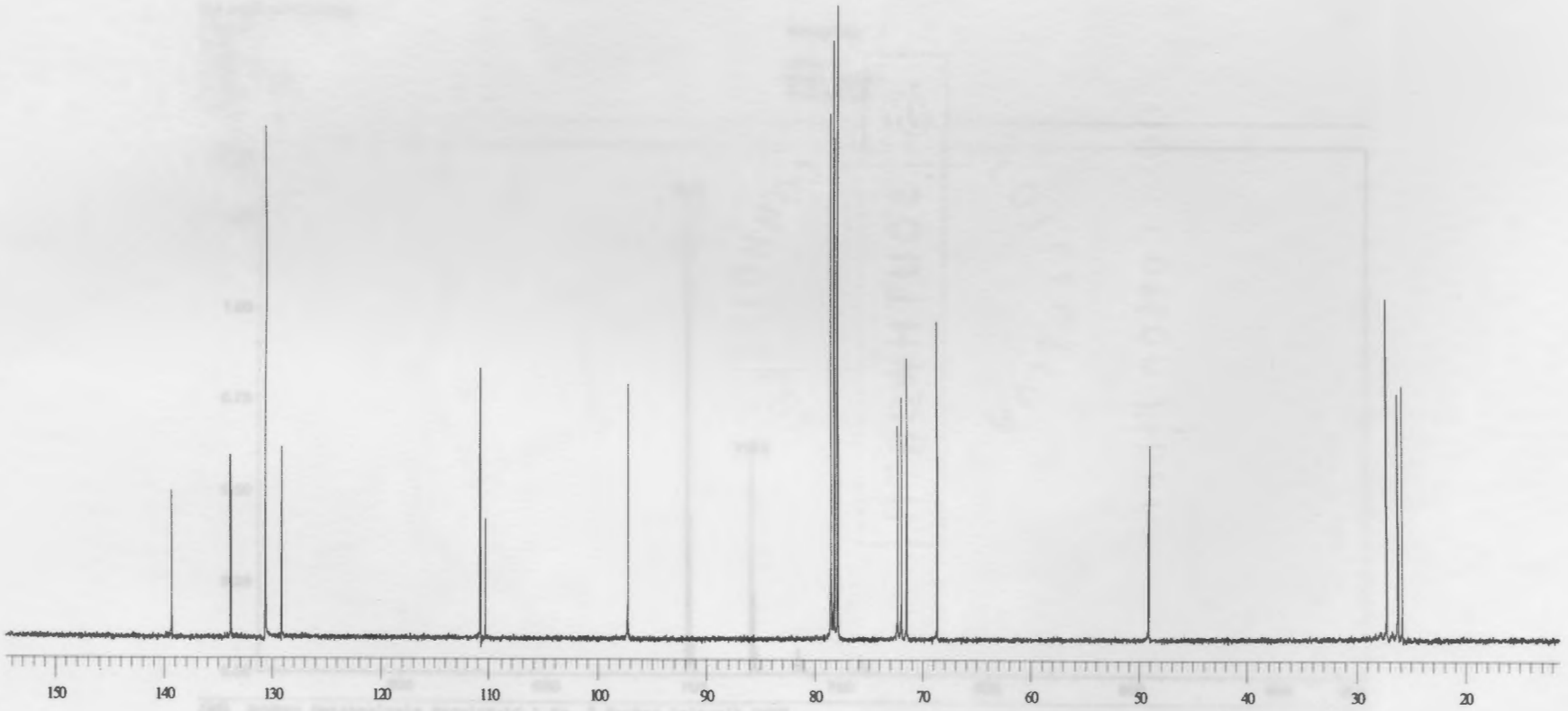


Figure 57. 100 MHz ^{13}C NMR spectrum of compound **25**

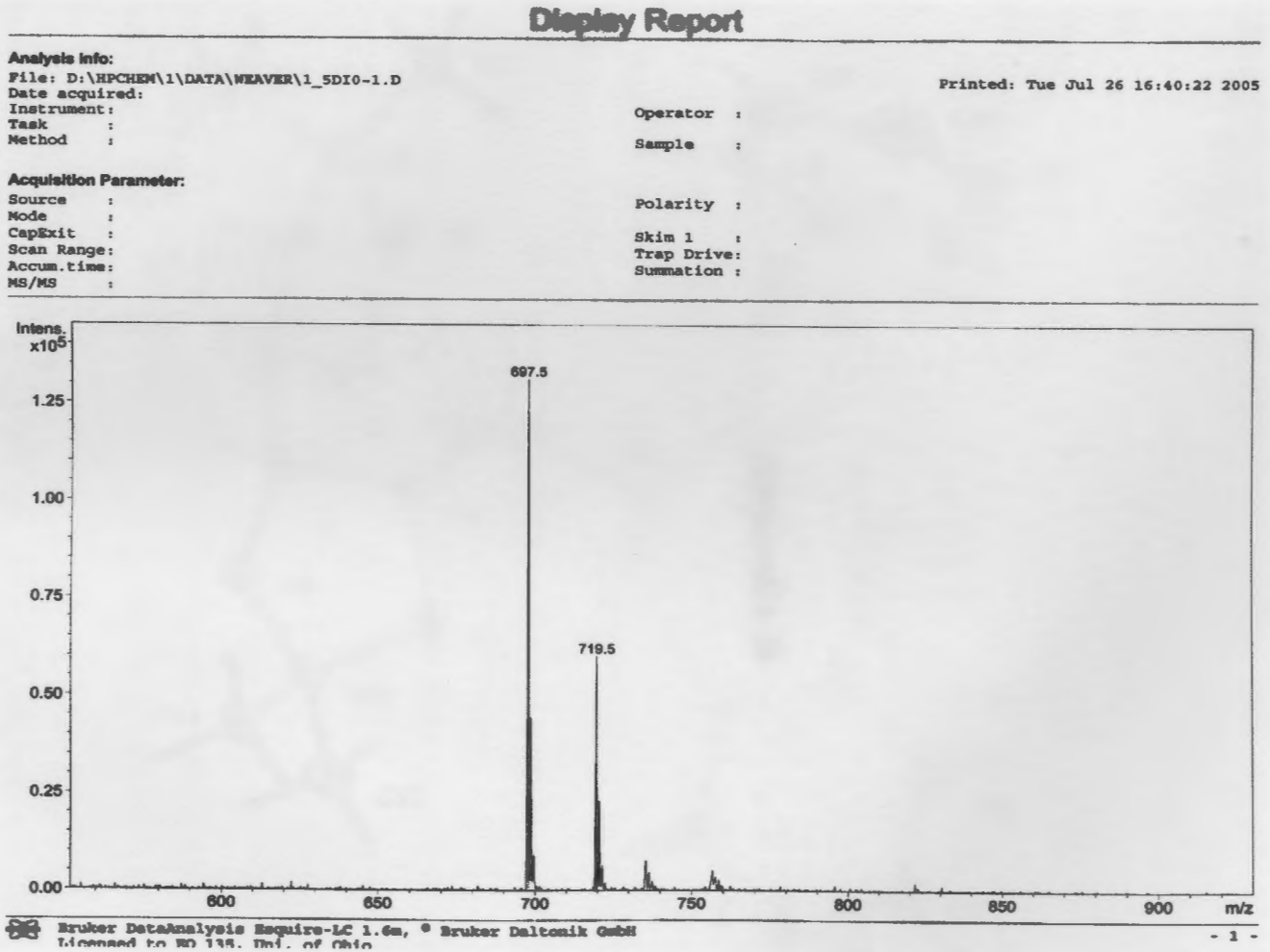


Figure 58. Mass spectrum of compound **25**

Appendix B

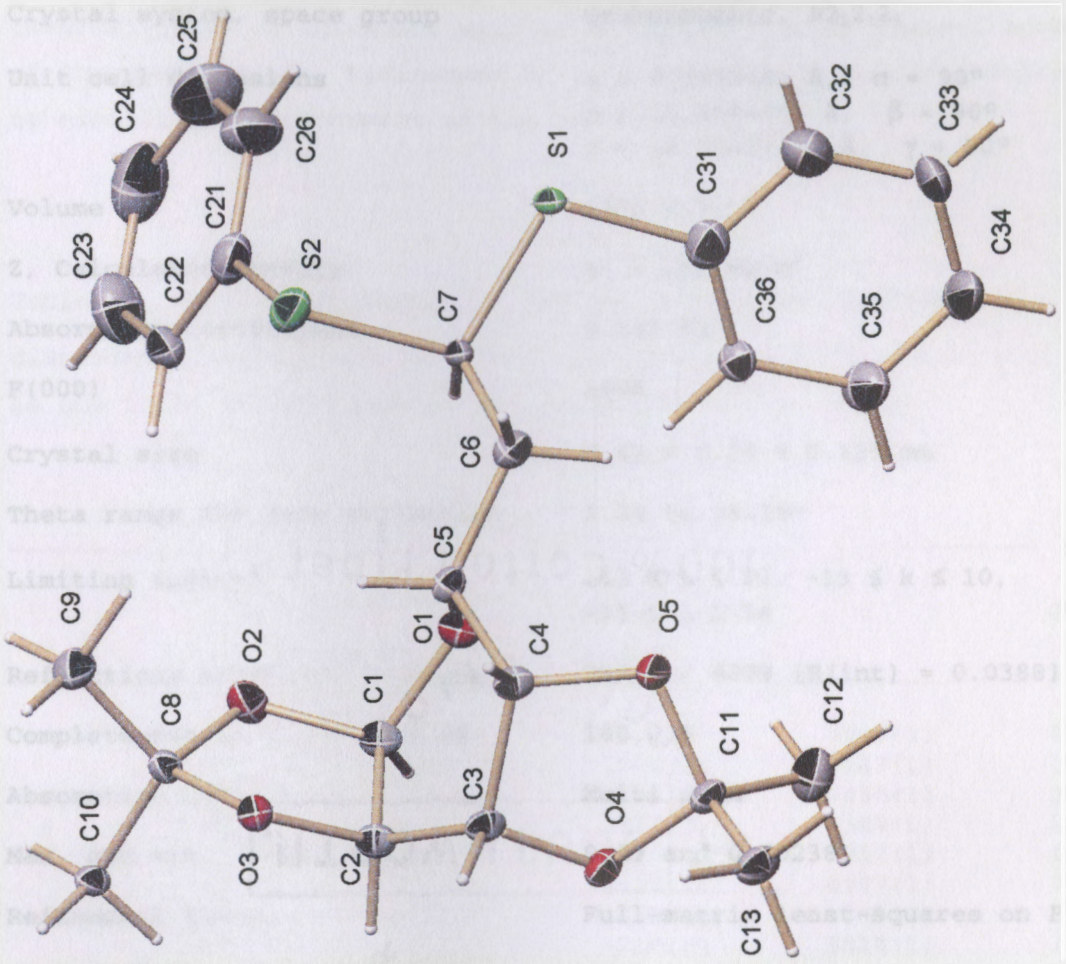


Figure 59. X-ray depiction of compound **8**

Table 1. Crystal data and structure refinement for 04mz41am.

Identification code	04mz41am
Empirical formula	C25 H30 O5 S2
Formula weight	474.61
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Unit cell dimensions	a = 9.0880(4) Å, α = 90° b = 10.2194(5) Å, β = 90° c = 26.5100(13) Å, γ = 90°
Volume	2462.1(2) $Å^3$
Z, Calculated density	4, 1.280 Mg/m^3
Absorption coefficient	0.249 mm^{-1}
F(000)	1008
Crystal size	0.43 × 0.25 × 0.125 mm
Theta range for data collection	1.54 to 28.28°
Limiting indices	$-12 \le h \le 12$, $-13 \le k \le 10$, $-35 \le l \le 34$
Reflections collected / unique	29848 / 6099 [R(int) = 0.0388]
Completeness to theta = 28.28	100.0 %
Absorption correction	Multi scan
Max. and min. transmission	0.97 and 0.70238
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6099 / 0 / 347
Goodness-of-fit on F^2	1.367
Final R indices [$I>2\sigma(I)$]	R1 = 0.0452, wR2 = 0.1065
R indices (all data)	R1 = 0.0455, wR2 = 0.1066
Absolute structure parameter	0.04(7)
Largest diff. peak and hole	0.404 and -0.238 e × $Å^{-3}$

Comments:

Treatment of hydrogen atoms: Methyl hydrogen atoms have been added in calculated positions with isotropic displacement parameters 1.5 times that of the adjacent carbon atom. The coordinates of all other hydrogen atoms have been fully refined with isotropic displacement parameters 1.2 times that of the adjacent carbon atom. Phenyl groups: Both phenyl groups, but especially C31 to C36, show much larger thermal ellipsoids than the other atoms of the molecule. The thermal libration is growing with a growing distance to the respective sulfur atom, and thus the observation is in agreement with an altogether larger thermal movement of the phenyl rings. Refinement of disorder for C31 to C36 results in no significant improvement of the refinement.

Table 2. Atomic coordinates [$\times 10^4$] and equivalent isotropic displacement parameters [$Å^2 \times 10^3$] for 04mz41am. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	2855(2)	913(2)	9042(1)	16(1)
C(2)	3619(2)	1739(2)	9447(1)	16(1)
C(3)	3155(2)	3162(2)	9450(1)	17(1)
C(4)	1481(2)	3371(2)	9389(1)	16(1)
C(5)	691(2)	2135(2)	9212(1)	16(1)
C(6)	-801(2)	2428(2)	8977(1)	15(1)
C(7)	-1529(2)	1220(2)	8745(1)	15(1)
C(8)	2935(3)	-212(2)	9814(1)	18(1)
C(9)	1698(3)	-708(3)	10140(1)	27(1)
C(10)	4364(3)	-950(2)	9896(1)	20(1)
C(11)	2817(3)	4792(2)	8871(1)	20(1)
C(12)	2881(3)	4923(3)	8304(1)	32(1)
C(13)	3182(3)	6051(2)	9153(1)	25(1)
C(21)	-2175(3)	-1405(2)	8902(1)	19(1)
C(22)	-970(3)	-2232(3)	8909(1)	26(1)
C(23)	-1023(3)	-3406(3)	8647(1)	34(1)
C(24)	-2251(4)	-3737(3)	8371(1)	35(1)
C(25)	-3448(3)	-2901(3)	8361(1)	34(1)
C(26)	-3426(3)	-1743(3)	8632(1)	27(1)
C(31)	-2557(3)	2568(2)	7883(1)	20(1)

C(32)	-3627(3)	3295(3)	7630(1)	31(1)
C(33)	-3231(4)	4058(4)	7223(1)	46(1)
C(34)	-1784(4)	4126(4)	7064(1)	48(1)
C(35)	-713(3)	3412(3)	7311(1)	34(1)
C(36)	-1101(3)	2621(3)	7719(1)	23(1)
O(1)	1578(2)	1487(2)	8840(1)	16(1)
O(2)	2520(2)	-279(2)	9290(1)	21(1)
O(3)	3134(2)	1164(2)	9910(1)	18(1)
O(4)	3777(2)	3761(2)	9017(1)	21(1)
O(5)	1375(2)	4363(2)	9011(1)	22(1)
S(1)	-3189(1)	1621(1)	8397(1)	21(1)
S(2)	-2097(1)	97(1)	9243(1)	19(1)

Table 3. Bond lengths [A] and angles [deg] for 04mz41am.

C(1)-O(1)	1.406(3)
C(1)-O(2)	1.417(3)
C(1)-C(2)	1.533(3)
C(1)-H(1)	0.89(3)
C(2)-O(3)	1.429(3)
C(2)-C(3)	1.515(3)
C(2)-H(2)	0.97(3)
C(3)-O(4)	1.417(3)
C(3)-C(4)	1.545(3)
C(3)-H(3)	0.96(3)
C(4)-O(5)	1.428(3)
C(4)-C(5)	1.526(3)
C(4)-H(4)	0.96(3)
C(5)-O(1)	1.436(3)
C(5)-C(6)	1.522(3)
C(5)-H(5)	0.90(3)
C(6)-C(7)	1.530(3)
C(6)-H(6A)	0.98(3)
C(6)-H(6B)	0.95(3)
C(7)-S(1)	1.816(2)
C(7)-S(2)	1.823(2)
C(7)-H(7)	0.96(3)
C(8)-O(2)	1.439(3)
C(8)-O(3)	1.441(3)
C(8)-C(9)	1.506(3)
C(8)-C(10)	1.517(3)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-O(4)	1.423(3)

C(11)-O(5)	1.431(3)
C(11)-C(12)	1.510(3)
C(11)-C(13)	1.524(3)
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(21)-C(22)	1.383(4)
C(21)-C(26)	1.387(3)
C(21)-S(2)	1.782(2)
C(22)-C(23)	1.387(4)
C(22)-H(22)	0.91(3)
C(23)-C(24)	1.376(4)
C(23)-H(23)	0.91(3)
C(24)-C(25)	1.383(5)
C(24)-H(24)	0.87(3)
C(25)-C(26)	1.385(4)
C(25)-H(25)	0.87(3)
C(26)-H(26)	0.94(3)
C(31)-C(36)	1.394(4)
C(31)-C(32)	1.396(3)
C(31)-S(1)	1.767(2)
C(32)-C(33)	1.378(4)
C(32)-H(32)	0.87(4)
C(33)-C(34)	1.383(5)
C(33)-H(33)	0.91(4)
C(34)-C(35)	1.382(5)
C(34)-H(34)	0.93(4)
C(35)-C(36)	1.394(4)
C(35)-H(35)	0.96(4)
C(36)-H(36)	0.97(3)

O(1)-C(1)-O(2)	110.96(18)
O(1)-C(1)-C(2)	114.27(18)
O(2)-C(1)-C(2)	104.20(17)
O(1)-C(1)-H(1)	107(2)
O(2)-C(1)-H(1)	107(2)
C(2)-C(1)-H(1)	113(2)
O(3)-C(2)-C(3)	107.78(18)
O(3)-C(2)-C(1)	103.57(17)
C(3)-C(2)-C(1)	113.92(18)
O(3)-C(2)-H(2)	108.7(19)
C(3)-C(2)-H(2)	112(2)
C(1)-C(2)-H(2)	110.1(19)
O(4)-C(3)-C(2)	107.45(18)
O(4)-C(3)-C(4)	104.37(18)
C(2)-C(3)-C(4)	114.01(18)
O(4)-C(3)-H(3)	112.3(19)
C(2)-C(3)-H(3)	107.2(19)
C(4)-C(3)-H(3)	111.6(19)
O(5)-C(4)-C(5)	109.96(18)
O(5)-C(4)-C(3)	103.77(17)
C(5)-C(4)-C(3)	112.36(19)
O(5)-C(4)-H(4)	108.4(19)
C(5)-C(4)-H(4)	111(2)

C(3)-C(4)-H(4)	111.2(18)
O(1)-C(5)-C(6)	108.02(18)
O(1)-C(5)-C(4)	109.17(18)
C(6)-C(5)-C(4)	112.42(19)
O(1)-C(5)-H(5)	107(2)
C(6)-C(5)-H(5)	112(2)
C(4)-C(5)-H(5)	108(2)
C(5)-C(6)-C(7)	113.05(19)
C(5)-C(6)-H(6A)	108.4(19)
C(7)-C(6)-H(6A)	104.3(19)
C(5)-C(6)-H(6B)	108.7(19)
C(7)-C(6)-H(6B)	112(2)
H(6A)-C(6)-H(6B)	111(3)
C(6)-C(7)-S(1)	112.44(16)
C(6)-C(7)-S(2)	109.84(15)
S(1)-C(7)-S(2)	105.94(11)
C(6)-C(7)-H(7)	110.6(19)
S(1)-C(7)-H(7)	112.0(18)
S(2)-C(7)-H(7)	105.6(19)
O(2)-C(8)-O(3)	104.41(16)
O(2)-C(8)-C(9)	109.96(19)
O(3)-C(8)-C(9)	108.70(19)
O(2)-C(8)-C(10)	109.90(19)
O(3)-C(8)-C(10)	110.61(18)
C(9)-C(8)-C(10)	112.90(19)
C(8)-C(9)-H(9A)	109.5
C(8)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(8)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(8)-C(10)-H(10A)	109.5
C(8)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
C(8)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
O(4)-C(11)-O(5)	105.29(17)
O(4)-C(11)-C(12)	108.3(2)
O(5)-C(11)-C(12)	108.7(2)
O(4)-C(11)-C(13)	110.99(19)
O(5)-C(11)-C(13)	109.3(2)
C(12)-C(11)-C(13)	113.9(2)
C(11)-C(12)-H(12A)	109.5
C(11)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(11)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(11)-C(13)-H(13A)	109.5
C(11)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(11)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(22)-C(21)-C(26)	120.2(2)

C(22)-C(21)-S(2)	119.26(19)
C(26)-C(21)-S(2)	120.6(2)
C(21)-C(22)-C(23)	119.7(3)
C(21)-C(22)-H(22)	120(2)
C(23)-C(22)-H(22)	120(2)
C(24)-C(23)-C(22)	120.4(3)
C(24)-C(23)-H(23)	118(2)
C(22)-C(23)-H(23)	122(2)
C(23)-C(24)-C(25)	119.7(3)
C(23)-C(24)-H(24)	122(2)
C(25)-C(24)-H(24)	118(2)
C(24)-C(25)-C(26)	120.4(3)
C(24)-C(25)-H(25)	120(2)
C(26)-C(25)-H(25)	119(2)
C(25)-C(26)-C(21)	119.5(3)
C(25)-C(26)-H(26)	120(2)
C(21)-C(26)-H(26)	120(2)
C(36)-C(31)-C(32)	119.3(2)
C(36)-C(31)-S(1)	124.82(19)
C(32)-C(31)-S(1)	115.8(2)
C(33)-C(32)-C(31)	119.7(3)
C(33)-C(32)-H(32)	123(2)
C(31)-C(32)-H(32)	117(2)
C(32)-C(33)-C(34)	121.0(3)
C(32)-C(33)-H(33)	118(3)
C(34)-C(33)-H(33)	120(3)
C(35)-C(34)-C(33)	119.9(3)
C(35)-C(34)-H(34)	122(3)
C(33)-C(34)-H(34)	119(3)
C(34)-C(35)-C(36)	119.7(3)
C(34)-C(35)-H(35)	118(2)
C(36)-C(35)-H(35)	122(2)
C(31)-C(36)-C(35)	120.3(3)
C(31)-C(36)-H(36)	120.8(19)
C(35)-C(36)-H(36)	119(2)
C(1)-O(1)-C(5)	113.20(16)
C(1)-O(2)-C(8)	110.53(16)
C(2)-O(3)-C(8)	106.79(16)
C(3)-O(4)-C(11)	107.20(17)
C(4)-O(5)-C(11)	109.75(16)
C(31)-S(1)-C(7)	104.20(11)
C(21)-S(2)-C(7)	100.79(10)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters [$Å^2 \times 10^3$] for 04mz41am. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [(h a^*)^2 U11 + ... + 2 h k a^* b^* U12]$

	U11	U22	U33	U23	U13	U12

C(1)	15(1)	17(1)	17(1)	-3(1)	0(1)	0(1)
C(2)	14(1)	17(1)	16(1)	-3(1)	-1(1)	-1(1)
C(3)	15(1)	14(1)	23(1)	-3(1)	-1(1)	-2(1)
C(4)	14(1)	16(1)	19(1)	-3(1)	-1(1)	0(1)
C(5)	19(1)	15(1)	13(1)	-1(1)	2(1)	-2(1)
C(6)	15(1)	14(1)	17(1)	1(1)	1(1)	-3(1)
C(7)	12(1)	18(1)	16(1)	4(1)	-1(1)	-2(1)
C(8)	19(1)	16(1)	20(1)	1(1)	-3(1)	0(1)
C(9)	18(1)	28(1)	36(1)	9(1)	2(1)	0(1)
C(10)	17(1)	18(1)	26(1)	1(1)	-2(1)	1(1)
C(11)	20(1)	16(1)	25(1)	1(1)	0(1)	-6(1)
C(12)	40(2)	28(1)	28(1)	4(1)	1(1)	-4(1)
C(13)	23(1)	17(1)	36(1)	-1(1)	-2(1)	-4(1)
C(21)	24(1)	15(1)	19(1)	4(1)	0(1)	-4(1)
C(22)	25(1)	29(1)	24(1)	6(1)	-4(1)	1(1)
C(23)	40(2)	28(1)	35(2)	3(1)	0(1)	12(1)
C(24)	54(2)	21(1)	31(1)	0(1)	2(1)	-6(1)
C(25)	34(2)	28(1)	39(2)	-3(1)	-9(1)	-11(1)
C(26)	20(1)	25(1)	35(1)	-1(1)	-5(1)	-4(1)
C(31)	23(1)	18(1)	18(1)	2(1)	-3(1)	-4(1)
C(32)	22(1)	31(1)	39(2)	14(1)	-10(1)	-5(1)
C(33)	39(2)	52(2)	47(2)	31(2)	-19(2)	-7(2)
C(34)	44(2)	60(2)	39(2)	31(2)	-14(2)	-20(2)
C(35)	34(1)	46(2)	23(1)	9(1)	0(1)	-8(1)
C(36)	27(1)	27(1)	17(1)	3(1)	0(1)	-1(1)
O(1)	15(1)	17(1)	15(1)	-4(1)	-1(1)	1(1)
O(2)	24(1)	15(1)	23(1)	-2(1)	-8(1)	-1(1)
O(3)	20(1)	16(1)	17(1)	-2(1)	0(1)	1(1)
O(4)	19(1)	17(1)	28(1)	2(1)	2(1)	-2(1)
O(5)	17(1)	17(1)	31(1)	8(1)	-4(1)	-2(1)
S(1)	14(1)	27(1)	22(1)	6(1)	-2(1)	-3(1)
S(2)	22(1)	20(1)	17(1)	3(1)	1(1)	-6(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for 04mz41am.

	x	y	z	U(eq)
H(9A)	787	-250	10051	41
H(9B)	1932	-547	10495	41
H(9C)	1571	-1650	10085	41
H(10A)	4686	-836	10246	30
H(10B)	5120	-608	9668	30
H(10C)	4209	-1882	9828	30

H(12A)	2233	5637	8196	48
H(12B)	2557	4103	8148	48
H(12C)	3893	5114	8200	48
H(13A)	3118	5895	9517	38
H(13B)	2480	6735	9057	38
H(13C)	4182	6331	9066	38
H(32)	-4520(40)	3250(40)	7744(13)	37
H(33)	-3930(40)	4580(40)	7080(16)	55
H(34)	-1560(50)	4660(40)	6792(15)	57
H(35)	270(40)	3450(40)	7183(13)	41
H(36)	-350(40)	2090(30)	7876(12)	28
H(1)	3440(40)	720(30)	8784(12)	28
H(2)	4680(30)	1640(30)	9422(12)	28
H(3)	3510(30)	3540(30)	9757(12)	28
H(4)	1050(30)	3700(30)	9693(12)	28
H(5)	620(30)	1590(30)	9477(12)	28
H(7)	-840(30)	740(30)	8543(11)	28
H(22)	-150(40)	-2010(30)	9084(12)	28
H(23)	-250(40)	-3980(30)	8649(11)	28
H(24)	-2270(40)	-4430(30)	8178(11)	28
H(25)	-4220(40)	-3090(30)	8179(12)	28
H(26)	-4250(40)	-1190(30)	8636(11)	28
H(6A)	-650(30)	3020(30)	8692(12)	28
H(6B)	-1410(30)	2830(30)	9224(12)	28

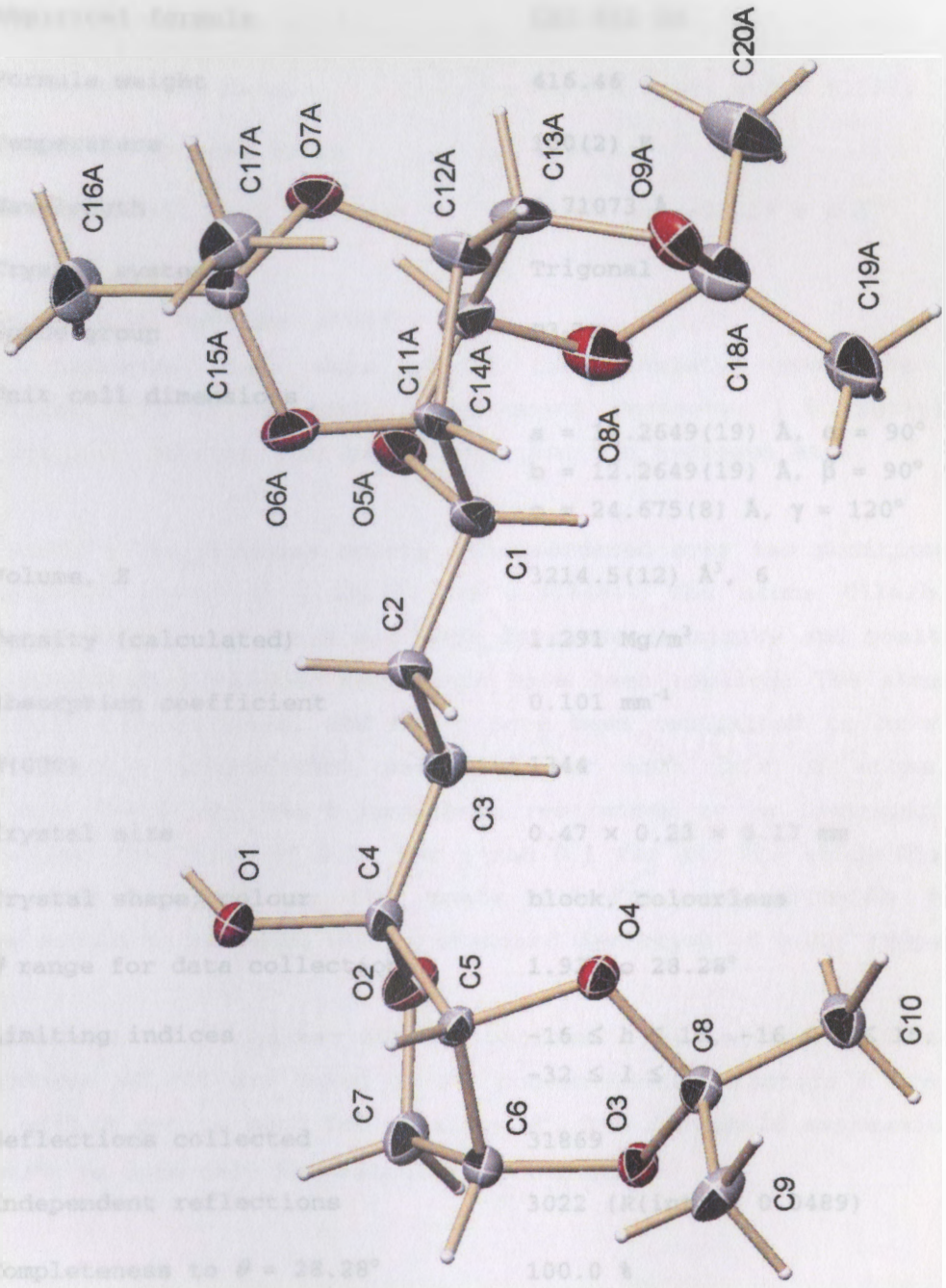


Figure 60. X-ray depiction of compound **9**

Table 1. Crystal data and structure refinement for 04mz146m:

Identification code	04mz146m
Empirical formula	C20 H32 O9
Formula weight	416.46
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Trigonal
Space group	$P3_221$
Unit cell dimensions	a = 12.2649(19) Å, α = 90° b = 12.2649(19) Å, β = 90° c = 24.675(8) Å, γ = 120°
Volume, *Z*	3214.5(12) $Å^3$, 6
Density (calculated)	1.291 Mg/m^3
Absorption coefficient	0.101 mm^{-1}
F(000)	1344
Crystal size	0.47 × 0.23 × 0.17 mm
Crystal shape, colour	block, colourless
θ range for data collection	1.92 to 28.28°
Limiting indices	$-16 \le h \le 16$, $-16 \le k \le 16$, $-32 \le l \le 32$
Reflections collected	31869
Independent reflections	3022 (*R*(int) = 0.0489)
Completeness to θ = 28.28°	100.0 %
Absorption correction	multi-scan
Max. and min. transmission	0.98 and 0.7517

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3022 / 50 / 379
Goodness-of-fit on F^2	1.314
Final R indices [$I>2\sigma(I)$]	R1 = 0.0524, wR2 = 0.1222
R indices (all data)	R1 = 0.0526, wR2 = 0.1223
Number of Friedel Pairs	2964
Largest diff. peak and hole	0.366 and -0.229 e × $Å^{-3}$

Treatment of hydrogen atoms:

All hydrogen atoms were placed in calculated positions and were refined with an isotropic displacement parameter 1.5 (methyl) or 1.2 times (all others) that of the adjacent non hydrogen atom.

Disorder: The pyranose moiety is disordered over two positions with an occupancy ratio of 0.492(8) to 0.508(8). The atoms C11a/b, C14a/b, C15a/b O5a/b, and O6a/b are each in close proximity and positional and displacement parameter restraints have been applied: The atoms C11a/b, C14a/b, C15a/b O5a/b, and O6a/b have been restrained to have the same anisotropic displacement parameter for each pair of atoms. C11a/b, C15a/b O5a/b, and O6a/b have been restrained to be isotropic within a standard deviation of 0.05 for s and 0.1 for st. The bonds O5a-C14a and O5b-C14b as well as the bonds C11a-O6a and C11b-O6b have been restrained to be equal with a standard deviation of 0.02, respectively.

Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors.

Table 2. Atomic coordinates [$\times 10^4$] and equivalent isotropic displacement parameters [$Å^2 \times 10^3$] for 04mz146m. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	8341(2)	4961(3)	9973(1)	25(1)
C(2)	7538(2)	4189(3)	10450(1)	19(1)
C(3)	7401(2)	5037(2)	10866(1)	19(1)
C(4)	6628(2)	4351(2)	11362(1)	16(1)
C(5)	5185(2)	3497(2)	11286(1)	15(1)
C(6)	4614(2)	3886(2)	11755(1)	18(1)
C(7)	5736(3)	4768(3)	12100(1)	24(1)
C(8)	3808(3)	4104(2)	10949(1)	18(1)
C(9)	2508(3)	2928(3)	10944(1)	24(1)
C(10)	3921(3)	5138(3)	10582(1)	24(1)
O(1)	7016(2)	3567(2)	11611(1)	21(1)
O(2)	6767(2)	5321(2)	11731(1)	24(1)
O(3)	4134(2)	4593(2)	11485(1)	17(1)
O(4)	4752(2)	3798(2)	10803(1)	18(1)
C(11A)	8440(40)	4050(30)	9544(18)	24(3)
C(12A)	9514(11)	4752(9)	9120(4)	21(2)
C(13A)	10183(8)	6148(9)	9172(3)	24(2)
C(14A)	10338(14)	6640(12)	9765(6)	23(2)
C(15A)	9782(12)	3192(9)	9503(5)	19(2)
C(16A)	10636(19)	3135(16)	9922(7)	35(3)
C(17A)	9331(8)	2121(9)	9077(4)	28(2)
C(18A)	9716(8)	7740(9)	9183(4)	30(2)
C(19A)	8609(9)	7933(7)	9151(4)	40(2)
C(20A)	10936(8)	8862(7)	8946(3)	42(2)
O(5A)	9580(110)	5760(80)	10160(40)	28(7)
O(6A)	8720(30)	3150(18)	9765(13)	29(2)
O(7A)	10411(7)	4365(7)	9246(3)	25(1)
O(8A)	9955(8)	7565(8)	9746(3)	31(2)
O(9A)	9433(5)	6603(6)	8925(2)	27(1)
C(11B)	8450(40)	4300(30)	9503(17)	24(3)
C(12B)	9582(9)	5206(8)	9139(4)	20(2)
C(13B)	10133(7)	6572(8)	9247(3)	21(2)
C(14B)	10273(13)	6941(11)	9849(6)	23(2)
C(15B)	9890(11)	3617(9)	9436(4)	19(2)
C(16B)	10750(20)	3478(16)	9832(7)	33(3)
C(17B)	9473(9)	2660(9)	8995(4)	33(2)
C(18B)	9492(7)	8031(7)	9363(3)	29(2)
C(19B)	8257(8)	8029(8)	9406(3)	37(2)
C(20B)	10564(8)	9275(7)	9132(3)	42(2)
O(5B)	9590(100)	5880(80)	10180(30)	28(7)
O(6B)	8800(30)	3449(17)	9731(13)	29(2)
O(7B)	10506(6)	4856(7)	9238(3)	21(1)
O(8B)	9889(7)	7856(7)	9886(3)	26(1)
O(9B)	9302(6)	6988(7)	9049(2)	27(1)

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Table 3. Bond lengths [Å] and angles [deg] for 04mz146m.

C(1)-O(5A)	1.42(11)	C(12A)-C(13A)	1.488(10)
C(1)-C(11B)	1.46(5)	C(12A)-H(12A)	1.0000
C(1)-O(5B)	1.47(11)	C(13A)-O(9A)	1.429(10)
C(1)-C(2)	1.524(3)	C(13A)-C(14A)	1.559(14)
C(1)-C(11A)	1.58(5)	C(13A)-H(13A)	1.0000
C(1)-H(1)	1.0000	C(14A)-O(5A)	1.41(2)
C(2)-C(3)	1.529(4)	C(14A)-O(8A)	1.430(11)
C(2)-H(2A)	0.9900	C(14A)-H(14A)	1.0000
C(2)-H(2B)	0.9900	C(15A)-O(7A)	1.398(8)
C(3)-C(4)	1.518(3)	C(15A)-O(6A)	1.43(3)
C(3)-H(3A)	0.9900	C(15A)-C(16A)	1.499(19)
C(3)-H(3B)	0.9900	C(15A)-C(17A)	1.552(13)
C(4)-O(1)	1.409(3)	C(16A)-H(16A)	0.9800
C(4)-O(2)	1.439(3)	C(16A)-H(16B)	0.9800
C(4)-C(5)	1.553(3)	C(16A)-H(16C)	0.9800
C(5)-O(4)	1.427(3)	C(17A)-H(17A)	0.9800
C(5)-C(6)	1.545(3)	C(17A)-H(17B)	0.9800
C(5)-H(5)	1.0000	C(17A)-H(17C)	0.9800
C(6)-O(3)	1.433(3)	C(18A)-O(9A)	1.410(9)
C(6)-C(7)	1.517(4)	C(18A)-O(8A)	1.456(11)
C(6)-H(6)	1.0000	C(18A)-C(19A)	1.493(12)
C(7)-O(2)	1.426(3)	C(18A)-C(20A)	1.554(10)
C(7)-H(7A)	0.9900	C(19A)-H(19A)	0.9800
C(7)-H(7B)	0.9900	C(19A)-H(19B)	0.9800
C(8)-O(3)	1.425(3)	C(19A)-H(19C)	0.9800
C(8)-O(4)	1.430(3)	C(20A)-H(20A)	0.9800
C(8)-C(10)	1.506(4)	C(20A)-H(20B)	0.9800
C(8)-C(9)	1.524(4)	C(20A)-H(20C)	0.9800
C(9)-H(9A)	0.9800	C(11B)-O(6B)	1.430(11)
C(9)-H(9B)	0.9800	C(11B)-C(12B)	1.56(4)
C(9)-H(9C)	0.9800	C(11B)-H(11B)	1.0000
C(10)-H(10A)	0.9800	C(12B)-O(7B)	1.420(12)
C(10)-H(10B)	0.9800	C(12B)-C(13B)	1.484(10)
C(10)-H(10C)	0.9800	C(12B)-H(12B)	1.0000
O(1)-H(1A)	0.8400	C(13B)-O(9B)	1.434(9)
C(11A)-O(6A)	1.425(11)	C(13B)-C(14B)	1.536(14)
C(11A)-C(12A)	1.56(4)	C(13B)-H(13B)	1.0000
C(11A)-H(11A)	1.0000	C(14B)-O(5B)	1.41(2)
C(12A)-O(7A)	1.435(12)	C(14B)-O(8B)	1.420(10)
C(14B)-H(14B)	1.0000	O(4)-C(5)-C(4)	111.87(19)
C(15B)-O(7B)	1.403(8)	C(6)-C(5)-C(4)	104.02(19)
C(15B)-O(6B)	1.45(3)	O(4)-C(5)-H(5)	111.8

C(15B)-C(17B)	1.491(13)
C(15B)-C(16B)	1.506(19)
C(16B)-H(16D)	0.9800
C(16B)-H(16E)	0.9800
C(16B)-H(16F)	0.9800
C(17B)-H(17D)	0.9800
C(17B)-H(17E)	0.9800
C(17B)-H(17F)	0.9800
C(18B)-O(9B)	1.411(9)
C(18B)-O(8B)	1.433(10)
C(18B)-C(19B)	1.517(11)
C(18B)-C(20B)	1.541(9)
C(19B)-H(19D)	0.9800
C(19B)-H(19E)	0.9800
C(19B)-H(19F)	0.9800
C(20B)-H(20D)	0.9800
C(20B)-H(20E)	0.9800
C(20B)-H(20F)	0.9800

O(5A)-C(1)-C(11B)	107(6)
C(11B)-C(1)-O(5B)	111(6)
O(5A)-C(1)-C(2)	108(2)
C(11B)-C(1)-C(2)	118.6(13)
O(5B)-C(1)-C(2)	108(2)
O(5A)-C(1)-C(11A)	106(6)
C(11B)-C(1)-C(11A)	11.1(17)
C(2)-C(1)-C(11A)	109.3(13)
O(5A)-C(1)-H(1)	111.1
C(11B)-C(1)-H(1)	101.0
O(5B)-C(1)-H(1)	106.7
C(2)-C(1)-H(1)	111.1
C(11A)-C(1)-H(1)	111.1
C(1)-C(2)-C(3)	110.7(2)
C(1)-C(2)-H(2A)	109.5
C(3)-C(2)-H(2A)	109.5
C(1)-C(2)-H(2B)	109.5
C(3)-C(2)-H(2B)	109.5
H(2A)-C(2)-H(2B)	108.1
C(4)-C(3)-C(2)	114.5(2)
C(4)-C(3)-H(3A)	108.6
C(2)-C(3)-H(3A)	108.6
C(4)-C(3)-H(3B)	108.6
C(2)-C(3)-H(3B)	108.6
H(3A)-C(3)-H(3B)	107.6
O(1)-C(4)-O(2)	110.34(18)
O(1)-C(4)-C(3)	113.5(2)
O(2)-C(4)-C(3)	105.6(2)
O(1)-C(4)-C(5)	104.6(2)
O(2)-C(4)-C(5)	104.89(19)
C(3)-C(4)-C(5)	117.54(19)
O(4)-C(5)-C(6)	105.12(19)
C(12A)-C(13A)-C(14A)	114.7(8)
O(9A)-C(13A)-H(13A)	110.1
C(12A)-C(13A)-H(13A)	110.1
C(14A)-C(13A)-H(13A)	110.1
O(5A)-C(14A)-O(8A)	106(7)
O(5A)-C(14A)-C(13A)	117(5)

C(6)-C(5)-H(5)	111.8
C(4)-C(5)-H(5)	111.8
O(3)-C(6)-C(7)	109.3(2)
O(3)-C(6)-C(5)	103.07(18)
C(7)-C(6)-C(5)	104.5(2)
O(3)-C(6)-H(6)	113.1
C(7)-C(6)-H(6)	113.1
C(5)-C(6)-H(6)	113.1
O(2)-C(7)-C(6)	104.62(19)
O(2)-C(7)-H(7A)	110.8
C(6)-C(7)-H(7A)	110.8
O(2)-C(7)-H(7B)	110.8
C(6)-C(7)-H(7B)	110.8
H(7A)-C(7)-H(7B)	108.9
O(3)-C(8)-O(4)	104.50(19)
O(3)-C(8)-C(10)	108.4(2)
O(4)-C(8)-C(10)	108.9(2)
O(3)-C(8)-C(9)	110.2(2)
O(4)-C(8)-C(9)	110.5(2)
C(10)-C(8)-C(9)	113.9(2)
C(8)-C(9)-H(9A)	109.5
C(8)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(8)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(8)-C(10)-H(10A)	109.5
C(8)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
C(8)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(4)-O(1)-H(1A)	109.5
C(7)-O(2)-C(4)	107.5(2)
C(8)-O(3)-C(6)	106.87(18)
C(5)-O(4)-C(8)	108.23(17)
O(6A)-C(11A)-C(12A)	102(2)
O(6A)-C(11A)-C(1)	115(3)
C(12A)-C(11A)-C(1)	114(2)
O(6A)-C(11A)-H(11A)	108.4
C(12A)-C(11A)-H(11A)	108.4
C(1)-C(11A)-H(11A)	108.4
O(7A)-C(12A)-C(13A)	106.8(9)
O(7A)-C(12A)-C(11A)	104.3(11)
C(13A)-C(12A)-C(11A)	113.8(16)
O(7A)-C(12A)-H(12A)	110.6
C(13A)-C(12A)-H(12A)	110.6
C(11A)-C(12A)-H(12A)	110.6
O(9A)-C(13A)-C(12A)	108.7(7)
O(9A)-C(13A)-C(14A)	103.1(7)
O(8B)-C(14B)-C(13B)	105.2(10)
O(5B)-C(14B)-H(14B)	108.5
O(8B)-C(14B)-H(14B)	108.5
C(13B)-C(14B)-H(14B)	108.5
O(7B)-C(15B)-O(6B)	106.8(9)
O(7B)-C(15B)-C(17B)	112.7(8)

O(8A)-C(14A)-C(13A)	104.5(11)	O(6B)-C(15B)-C(17B)	109.1(14)
O(5A)-C(14A)-H(14A)	109.7	O(7B)-C(15B)-C(16B)	108.6(10)
O(8A)-C(14A)-H(14A)	109.7	O(6B)-C(15B)-C(16B)	107.9(15)
C(13A)-C(14A)-H(14A)	109.7	C(17B)-C(15B)-C(16B)	111.6(11)
O(7A)-C(15A)-O(6A)	105.5(9)	C(15B)-C(16B)-H(16D)	109.5
O(7A)-C(15A)-C(16A)	108.7(10)	C(15B)-C(16B)-H(16E)	109.5
O(6A)-C(15A)-C(16A)	109.2(17)	H(16D)-C(16B)-H(16E)	109.5
O(7A)-C(15A)-C(17A)	110.2(8)	C(15B)-C(16B)-H(16F)	109.5
O(6A)-C(15A)-C(17A)	110.1(15)	H(16D)-C(16B)-H(16F)	109.5
C(16A)-C(15A)-C(17A)	112.9(10)	H(16E)-C(16B)-H(16F)	109.5
O(9A)-C(18A)-O(8A)	104.6(6)	C(15B)-C(17B)-H(17D)	109.5
O(9A)-C(18A)-C(19A)	109.8(7)	C(15B)-C(17B)-H(17E)	109.5
O(8A)-C(18A)-C(19A)	109.9(8)	H(17D)-C(17B)-H(17E)	109.5
O(9A)-C(18A)-C(20A)	111.0(7)	C(15B)-C(17B)-H(17F)	109.5
O(8A)-C(18A)-C(20A)	108.3(7)	H(17D)-C(17B)-H(17F)	109.5
C(19A)-C(18A)-C(20A)	112.9(7)	H(17E)-C(17B)-H(17F)	109.5
C(14A)-O(5A)-C(1)	111(7)	O(9B)-C(18B)-O(8B)	105.8(6)
C(11A)-O(6A)-C(15A)	112(2)	O(9B)-C(18B)-C(19B)	108.9(6)
C(15A)-O(7A)-C(12A)	108.6(7)	O(8B)-C(18B)-C(19B)	110.6(6)
C(14A)-O(8A)-C(18A)	108.7(8)	O(9B)-C(18B)-C(20B)	111.5(6)
C(18A)-O(9A)-C(13A)	107.8(6)	O(8B)-C(18B)-C(20B)	107.2(6)
O(6B)-C(11B)-C(1)	104(2)	C(19B)-C(18B)-C(20B)	112.6(7)
O(6B)-C(11B)-C(12B)	105(2)	C(18B)-C(19B)-H(19D)	109.5
C(1)-C(11B)-C(12B)	111(2)	C(18B)-C(19B)-H(19E)	109.5
O(6B)-C(11B)-H(11B)	112.3	H(19D)-C(19B)-H(19E)	109.5
C(1)-C(11B)-H(11B)	112.3	C(18B)-C(19B)-H(19F)	109.5
C(12B)-C(11B)-H(11B)	112.3	H(19D)-C(19B)-H(19F)	109.5
O(7B)-C(12B)-C(13B)	109.2(7)	H(19E)-C(19B)-H(19F)	109.5
O(7B)-C(12B)-C(11B)	104.5(11)	C(18B)-C(20B)-H(20D)	109.5
C(13B)-C(12B)-C(11B)	116.1(16)	C(18B)-C(20B)-H(20E)	109.5
O(7B)-C(12B)-H(12B)	108.9	H(20D)-C(20B)-H(20E)	109.5
C(13B)-C(12B)-H(12B)	108.9	C(18B)-C(20B)-H(20F)	109.5
C(11B)-C(12B)-H(12B)	108.9	H(20D)-C(20B)-H(20F)	109.5
O(9B)-C(13B)-C(12B)	109.7(8)	H(20E)-C(20B)-H(20F)	109.5
O(9B)-C(13B)-C(14B)	102.7(7)	C(14B)-O(5B)-C(1)	114(7)
C(12B)-C(13B)-C(14B)	115.3(8)	C(11B)-O(6B)-C(15B)	107(2)
O(9B)-C(13B)-H(13B)	109.6	C(15B)-O(7B)-C(12B)	107.9(7)
C(12B)-C(13B)-H(13B)	109.6	C(14B)-O(8B)-C(18B)	109.4(8)
C(14B)-C(13B)-H(13B)	109.6	C(18B)-O(9B)-C(13B)	108.1(6)
O(5B)-C(14B)-O(8B)	114(6)		
O(5B)-C(14B)-C(13B)	111(5)	H(17B)-C(17)-H(17C)	109.5

Table 4. Anisotropic displacement parameters [$Å^2 \times 10^3$] for 04mz146m. The anisotropic displacement factor exponent takes the form: $-2\pi^2$ [(h ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	12(1)	37(2)	21(1)	11(1)	1(1)	8(1)
C(2)	15(1)	25(1)	17(1)	4(1)	2(1)	9(1)
C(3)	15(1)	18(1)	24(1)	5(1)	2(1)	8(1)
C(4)	12(1)	18(1)	17(1)	1(1)	-3(1)	8(1)
C(5)	12(1)	17(1)	18(1)	1(1)	0(1)	8(1)
C(6)	18(1)	22(1)	17(1)	3(1)	1(1)	13(1)
C(7)	24(1)	37(2)	18(1)	-6(1)	-6(1)	21(1)
C(8)	20(1)	21(1)	16(1)	-3(1)	-3(1)	12(1)
C(9)	16(1)	26(1)	33(1)	-10(1)	-5(1)	12(1)
C(10)	36(2)	29(1)	16(1)	-2(1)	-2(1)	23(1)
O(1)	15(1)	28(1)	21(1)	3(1)	0(1)	13(1)
O(2)	18(1)	27(1)	27(1)	-10(1)	-5(1)	12(1)
O(3)	19(1)	22(1)	14(1)	-2(1)	-2(1)	13(1)
O(4)	18(1)	26(1)	15(1)	-2(1)	-2(1)	14(1)
C(11A)	15(1)	35(11)	19(5)	13(6)	5(3)	9(6)
C(12A)	19(3)	9(4)	22(3)	2(4)	5(2)	-2(4)
C(13A)	24(4)	24(6)	21(3)	0(3)	10(2)	11(4)
C(14A)	20(2)	19(5)	30(4)	1(3)	6(2)	9(3)
C(15A)	19(2)	24(5)	17(3)	5(3)	4(2)	13(4)
C(16A)	33(7)	63(10)	17(5)	-8(6)	-14(5)	30(7)
C(17A)	21(3)	32(4)	28(3)	-14(3)	-7(3)	12(4)
C(18A)	43(5)	18(4)	31(4)	2(3)	8(3)	17(4)
C(19A)	61(5)	32(4)	41(4)	13(3)	13(4)	34(4)
C(20A)	52(5)	23(3)	38(4)	8(3)	13(3)	8(3)
O(5A)	14(2)	33(11)	25(4)	10(7)	-1(3)	4(7)
O(6A)	28(3)	30(8)	35(3)	9(6)	15(2)	19(6)
O(7A)	17(3)	17(3)	36(3)	8(3)	10(2)	5(3)
O(8A)	37(3)	20(4)	32(4)	-1(3)	8(3)	11(3)
O(9A)	34(3)	12(3)	30(3)	5(2)	1(2)	9(2)
C(11B)	15(1)	35(11)	19(5)	13(6)	5(3)	9(6)
C(12B)	15(3)	16(6)	21(3)	6(4)	8(2)	1(5)
C(13B)	17(3)	17(4)	26(3)	7(3)	12(2)	5(3)
C(14B)	20(2)	19(5)	30(4)	1(3)	6(2)	9(3)
C(15B)	19(2)	24(5)	17(3)	5(3)	4(2)	13(4)
C(16B)	37(5)	46(7)	23(6)	2(4)	5(4)	25(5)
C(17B)	29(4)	36(5)	36(4)	-14(4)	0(3)	18(4)
C(18B)	40(4)	16(3)	29(3)	7(3)	9(3)	13(3)
C(19B)	45(4)	36(4)	40(4)	2(3)	4(3)	27(3)
C(20B)	55(5)	25(3)	42(4)	13(3)	18(3)	17(3)
O(5B)	14(2)	33(11)	25(4)	10(7)	-1(3)	4(7)
O(6B)	28(3)	30(8)	35(3)	9(6)	15(2)	19(6)
O(7B)	14(2)	17(3)	28(2)	5(3)	8(2)	4(3)
O(8B)	29(3)	19(3)	29(3)	5(2)	2(2)	11(2)
O(9B)	44(3)	20(3)	23(2)	2(2)	2(2)	21(3)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for 04mz146m.

	x	y	z	U(eq)
H(1)	7987	5458	9803	30
H(2A)	7934	3746	10624	23
H(2B)	6695	3548	10318	23
H(3A)	8251	5688	10986	23
H(3B)	7004	5474	10687	23
H(5)	4922	2584	11304	18
H(6)	3954	3150	11962	22
H(7A)	5599	5420	12271	29
H(7B)	5888	4297	12388	29
H(9A)	2500	2302	11193	36
H(9B)	2312	2578	10577	36
H(9C)	1878	3148	11059	36
H(10A)	3279	5355	10679	36
H(10B)	3799	4849	10205	36
H(10C)	4759	5881	10623	36
H(1A)	7791	3986	11678	31
H(11A)	7620	3590	9346	29
H(12A)	9183	4491	8743	25
H(13A)	11023	6526	8990	28
H(14A)	11243	7047	9875	28
H(16A)	11430	3313	9752	53
H(16B)	10231	2294	10085	53
H(16C)	10806	3763	10205	53
H(17A)	8769	2196	8817	41
H(17B)	8878	1304	9261	41
H(17C)	10061	2186	8886	41
H(19A)	8447	8041	8771	60
H(19B)	8784	8687	9357	60
H(19C)	7867	7199	9303	60
H(20A)	11654	8746	9026	63
H(20B)	11076	9649	9111	63
H(20C)	10847	8899	8553	63
H(11B)	7641	3855	9293	29
H(12B)	9321	5036	8750	24
H(13B)	10968	7051	9062	26
H(14B)	11184	7349	9948	28
H(16D)	11519	3637	9646	50
H(16E)	10320	2621	9980	50
H(16F)	10960	4084	10128	50
H(17D)	9020	2850	8718	50
H(17E)	8915	1822	9146	50
H(17F)	10211	2679	8832	50
H(19D)	7991	8132	9044	56
H(19E)	8370	8724	9639	56
H(19F)	7613	7228	9562	56
H(20D)	11324	9210	9090	63
H(20E)	10737	9967	9380	63
H(20F)	10313	9440	8778	63

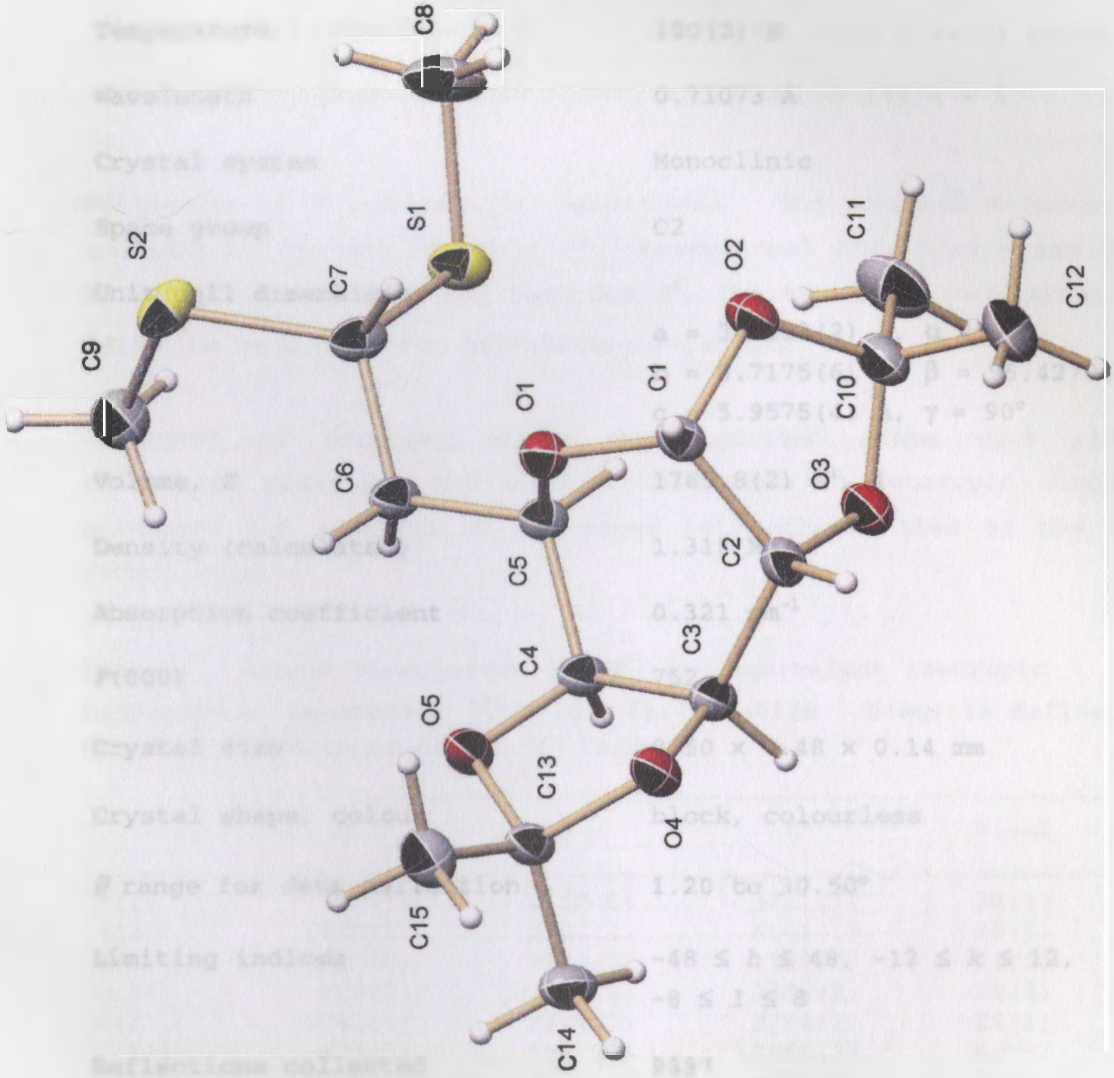


Figure 61. X-ray depiction of compound **12**

Table 1. Crystal data and structure refinement for 05mz062m:

Identification code	05mz062m
Empirical formula	C15 H26 O5 S2
Formula weight	350.48
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C2
Unit cell dimensions	a = 34.153(2) Å, α = 90° b = 8.7175(6) Å, β = 95.4270(10)° c = 5.9575(4) Å, γ = 90°
Volume, *Z*	1765.8(2) Å^3, 4
Density (calculated)	1.318 Mg/m^3
Absorption coefficient	0.321 mm^{-1}
F(000)	752
Crystal size	0.50 × 0.48 × 0.14 mm
Crystal shape, colour	block, colourless
θ range for data collection	1.20 to 30.50°
Limiting indices	$-48 \le h \le 48$, $-12 \le k \le 12$, $-8 \le l \le 8$
Reflections collected	9887
Independent reflections	5255 (*R*(int) = 0.0194)
Completeness to θ = 30.50°	99.7 %
Absorption correction	multi-scan
Max. and min. transmission	0.96 and 0.6486

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5255 / 1 / 205
Goodness-of-fit on F^2	1.039
Final R indices [$I>2\sigma(I)$]	R1 = 0.0347, wR2 = 0.0931
R indices (all data)	R1 = 0.0366, wR2 = 0.0946
Absolute structure parameter	-0.04(5), 2403 Friedel pairs
Largest diff. peak and hole	0.583 and -0.186 e × Å^{-3}

Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors.

Treatment of hydrogen atoms: All hydrogen atoms were placed in calculated positions and were refined with an isotropic displacement parameter 1.5 (methyl) or 1.2 times (all others) that of the adjacent carbon atom.

Table 2. Atomic coordinates [× 10^4] and equivalent isotropic displacement parameters [Å^2 × 10^3] for 05mz062m. U(eq) is defined as trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
S(1)	852(1)	2632(1)	2011(1)	28(1)
S(2)	1339(1)	2627(1)	6561(1)	30(1)
O(2)	643(1)	7597(1)	797(2)	26(1)
O(3)	958(1)	7671(2)	-2396(2)	29(1)
O(1)	1243(1)	6892(1)	2714(2)	21(1)
C(11)	371(1)	6191(3)	-2460(3)	42(1)
C(7)	1172(1)	3716(1)	4051(2)	23(1)
C(10)	576(1)	7650(2)	-1620(2)	30(1)
C(5)	1384(1)	5710(1)	1322(2)	19(1)
C(6)	1514(1)	4387(1)	2870(2)	22(1)
C(9)	1651(1)	1227(2)	5423(3)	30(1)
C(8)	417(1)	2547(2)	3486(3)	42(1)
C(12)	354(1)	9098(2)	-2354(3)	43(1)
O(5)	2057(1)	6606(1)	1651(2)	24(1)
O(4)	1885(1)	8956(1)	295(2)	23(1)
C(4)	1720(1)	6337(1)	80(2)	21(1)
C(3)	1621(1)	7937(1)	-958(2)	22(1)

C(2)	1205(1)	8480(2)	-730(2)	23(1)
C(1)	1037(1)	8058(1)	1493(2)	21(1)
C(14)	2510(1)	7911(2)	-605(2)	28(1)
C(13)	2216(1)	8064(1)	1153(2)	22(1)
C(15)	2390(1)	8779(2)	3320(3)	32(1)

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. plan

Table 3. Bond lengths [Å] and angles [deg] for 05mz062m.

S(1)-C(8)	1.7976(15)	S(2)-C(9)	1.7938(15)
S(1)-C(7)	1.8195(14)	S(2)-C(7)	1.8173(13)
O(2)-C(1)	1.4258(14)	H(11A)-C(11)-H(11B)	109.5
O(2)-C(10)	1.4371(16)	C(10)-C(11)-H(11C)	109.5
O(3)-C(10)	1.4242(15)	H(11A)-C(11)-H(11C)	109.5
O(3)-C(2)	1.4256(16)	H(11B)-C(11)-H(11C)	109.5
O(1)-C(1)	1.4007(15)	C(6)-C(7)-S(2)	112.39(9)
O(1)-C(5)	1.4356(14)	C(6)-C(7)-S(1)	109.07(9)
C(11)-C(10)	1.515(3)	S(2)-C(7)-S(1)	113.62(7)
C(11)-H(11A)	0.9800	C(6)-C(7)-H(7)	107.1
C(11)-H(11B)	0.9800	S(2)-C(7)-H(7)	107.1
C(11)-H(11C)	0.9800	S(1)-C(7)-H(7)	107.1
C(7)-C(6)	1.5368(17)	O(3)-C(10)-O(2)	105.20(9)
C(7)-H(7)	1.0000	O(3)-C(10)-C(11)	108.19(14)
C(10)-C(12)	1.516(2)	O(2)-C(10)-C(11)	109.16(14)
C(5)-C(6)	1.5162(16)	O(3)-C(10)-C(12)	110.22(14)
C(5)-C(4)	1.5221(16)	O(2)-C(10)-C(12)	110.10(14)
C(5)-H(5)	1.0000	C(11)-C(10)-C(12)	113.61(12)
C(6)-H(6A)	0.9900	O(1)-C(5)-C(6)	106.82(10)
C(6)-H(6B)	0.9900	O(1)-C(5)-C(4)	109.46(10)
C(9)-H(9A)	0.9800	C(6)-C(5)-C(4)	112.25(10)
C(9)-H(9B)	0.9800	O(1)-C(5)-H(5)	109.4
C(9)-H(9C)	0.9800	C(6)-C(5)-H(5)	109.4
C(8)-H(8A)	0.9800	C(4)-C(5)-H(5)	109.4
C(8)-H(8B)	0.9800	C(5)-C(6)-C(7)	112.13(10)
C(8)-H(8C)	0.9800	C(5)-C(6)-H(6A)	109.2
C(12)-H(12A)	0.9800	C(7)-C(6)-H(6A)	109.2
C(12)-H(12B)	0.9800	C(5)-C(6)-H(6B)	109.2
C(12)-H(12C)	0.9800	C(7)-C(6)-H(6B)	109.2
O(5)-C(13)	1.4242(15)	H(6A)-C(6)-H(6B)	107.9
O(5)-C(4)	1.4329(16)	S(2)-C(9)-H(9A)	109.5

O(4)-C(3)	1.4249(15)	S(2)-C(9)-H(9B)	109.5
O(4)-C(13)	1.4258(15)	H(9A)-C(9)-H(9B)	109.5
C(4)-C(3)	1.5504(17)	S(2)-C(9)-H(9C)	109.5
C(4)-H(4)	1.0000	H(9A)-C(9)-H(9C)	109.5
C(3)-C(2)	1.5170(17)	H(9B)-C(9)-H(9C)	109.5
C(3)-H(3)	1.0000	S(1)-C(8)-H(8A)	109.5
C(2)-C(1)	1.5370(18)	S(1)-C(8)-H(8B)	109.5
C(2)-H(2)	1.0000	H(8A)-C(8)-H(8B)	109.5
C(1)-H(1)	1.0000	S(1)-C(8)-H(8C)	109.5
C(14)-C(13)	1.5239(18)	H(8A)-C(8)-H(8C)	109.5
C(14)-H(14A)	0.9800	H(8B)-C(8)-H(8C)	109.5
C(14)-H(14B)	0.9800	C(10)-C(12)-H(12A)	109.5
C(14)-H(14C)	0.9800	C(10)-C(12)-H(12B)	109.5
C(13)-C(15)	1.505(2)	H(12A)-C(12)-H(12B)	109.5
C(15)-H(15A)	0.9800	C(10)-C(12)-H(12C)	109.5
C(15)-H(15B)	0.9800	H(12A)-C(12)-H(12C)	109.5
C(15)-H(15C)	0.9800	H(12B)-C(12)-H(12C)	109.5
		C(13)-O(5)-C(4)	107.96(9)
C(8)-S(1)-C(7)	99.58(8)	C(3)-O(4)-C(13)	106.76(9)
C(9)-S(2)-C(7)	101.35(7)	O(5)-C(4)-C(5)	109.68(10)
C(1)-O(2)-C(10)	109.77(10)	O(5)-C(4)-C(3)	104.14(10)
C(10)-O(3)-C(2)	106.16(10)	C(5)-C(4)-C(3)	111.83(10)
C(1)-O(1)-C(5)	113.67(10)	O(5)-C(4)-H(4)	110.3
C(10)-C(11)-H(11A)	109.5	C(5)-C(4)-H(4)	110.3
C(10)-C(11)-H(11B)	109.5	C(3)-C(4)-H(4)	110.3
O(4)-C(3)-C(2)	108.09(10)	C(13)-C(14)-H(14A)	109.5
O(4)-C(3)-C(4)	104.41(10)	C(13)-C(14)-H(14B)	109.5
C(2)-C(3)-C(4)	114.53(10)	H(14A)-C(14)-H(14B)	109.5
O(4)-C(3)-H(3)	109.9	C(13)-C(14)-H(14C)	109.5
C(2)-C(3)-H(3)	109.9	H(14A)-C(14)-H(14C)	109.5
C(4)-C(3)-H(3)	109.9	H(14B)-C(14)-H(14C)	109.5
O(3)-C(2)-C(3)	106.26(11)	O(5)-C(13)-O(4)	104.91(9)
O(3)-C(2)-C(1)	103.76(10)	O(5)-C(13)-C(15)	108.60(11)
C(3)-C(2)-C(1)	115.61(10)	O(4)-C(13)-C(15)	108.52(11)
O(3)-C(2)-H(2)	110.3	O(5)-C(13)-C(14)	110.68(10)
C(3)-C(2)-H(2)	110.3	O(4)-C(13)-C(14)	110.66(11)
C(1)-C(2)-H(2)	110.3	C(15)-C(13)-C(14)	113.12(12)
O(1)-C(1)-O(2)	111.10(11)	C(13)-C(15)-H(15A)	109.5
O(1)-C(1)-C(2)	114.25(10)	C(13)-C(15)-H(15B)	109.5
O(2)-C(1)-C(2)	103.59(10)	H(15A)-C(15)-H(15B)	109.5
O(1)-C(1)-H(1)	109.2	C(13)-C(15)-H(15C)	109.5
O(2)-C(1)-H(1)	109.2	H(15A)-C(15)-H(15C)	109.5
C(2)-C(1)-H(1)	109.2	H(15B)-C(15)-H(15C)	109.5

Table 4. Anisotropic displacement parameters [$Å^2 \times 10^3$] for 05mz062m. The anisotropic displacement factor exponent takes the form: $-2\pi^2$ [(h a*)^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
S(1)	24(1)	21(1)	39(1)	-1(1)	7(1)	-4(1)
S(2)	42(1)	20(1)	29(1)	3(1)	10(1)	-3(1)
O(2)	17(1)	30(1)	30(1)	1(1)	1(1)	-1(1)
O(3)	21(1)	38(1)	27(1)	0(1)	-1(1)	1(1)
O(1)	21(1)	16(1)	25(1)	1(1)	3(1)	2(1)
C(11)	27(1)	55(1)	44(1)	-15(1)	-5(1)	-7(1)
C(7)	24(1)	15(1)	32(1)	1(1)	9(1)	-2(1)
C(10)	20(1)	37(1)	31(1)	0(1)	-1(1)	2(1)
C(5)	18(1)	14(1)	26(1)	1(1)	4(1)	-1(1)
C(6)	21(1)	15(1)	31(1)	5(1)	6(1)	0(1)
C(9)	33(1)	18(1)	39(1)	2(1)	1(1)	-1(1)
C(8)	27(1)	33(1)	68(1)	-1(1)	17(1)	-8(1)
C(12)	27(1)	56(1)	46(1)	12(1)	-2(1)	13(1)
O(5)	18(1)	18(1)	37(1)	9(1)	1(1)	-2(1)
O(4)	20(1)	15(1)	35(1)	4(1)	0(1)	1(1)
C(4)	18(1)	15(1)	29(1)	4(1)	5(1)	0(1)
C(3)	19(1)	17(1)	29(1)	5(1)	3(1)	0(1)
C(2)	21(1)	21(1)	28(1)	5(1)	0(1)	3(1)
C(1)	18(1)	17(1)	29(1)	1(1)	1(1)	1(1)
C(14)	23(1)	26(1)	37(1)	6(1)	9(1)	0(1)
C(13)	17(1)	17(1)	32(1)	5(1)	3(1)	-1(1)
C(15)	29(1)	28(1)	36(1)	0(1)	-3(1)	0(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for 05mz062m.

	x	y	z	U(eq)
H(11A)	371	6127	-4102	64
H(11B)	100	6198	-2059	64
H(11C)	510	5302	-1762	64
H(7)	1015	4601	4549	28
H(5)	1166	5362	201	23
H(6A)	1721	4749	4023	26
H(6B)	1629	3571	1981	26
H(9A)	1491	546	4397	45
H(9B)	1784	623	6655	45
H(9C)	1847	1747	4597	45
H(8A)	484	2125	4998	63
H(8B)	221	1888	2654	63
H(8C)	309	3582	3608	63
H(12A)	496	9994	-1705	65
H(12B)	91	9065	-1828	65
H(12C)	331	9171	-4003	65
H(4)	1786	5602	-1116	25
H(3)	1674	7945	-2581	26
H(2)	1183	9610	-1000	28
H(1)	1031	8995	2459	25
H(14A)	2730	7265	-6	42
H(14B)	2608	8929	-966	42
H(14C)	2380	7441	-1974	42
H(15A)	2187	8862	4373	47
H(15B)	2490	9804	3011	47
H(15C)	2606	8138	3987	47