Reaction of o-Nitrobenzenesulfonyl Azide/n-Butyl Lithium with Hindered Alcohols

by

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Dr. Salvatore A. Sanders, Associate Dean of Graduate Studies Date

Thesis Abstract

This thesis utilizes the method of "One Pot" synthesis to synthesize a series of alkyl functional groups. These group include… an alkyl azide, alkyl esters, and an alkyl chloride. Results showed that both primary and secondary alcohols were converted into products within the previously mentioned functional groups. The steric environment of each alcohol reagent dictated which product was produced. All of the findings… within this research were supported by high yields, appropriate spectrum data, and confirmed to be consistent with finding within previous literature.

Acknowledgements

I would like to thank my Advisor, Dr. Peter Norris. Dr. Norris you have been so much more than a graduate advisor. You took out the time to nature and develop a mathematician into an organic chemist. In addition to creating a chemist, you've refined a professional. Not only in the classroom and laboratory, but in life. I have become much more than I could have ever imagined. It is through your structure and guidance that I have come thus far. I can't say thank you enough for everything.

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I would like to recognize my fellow Norris group students as well. From the past 2012 to the present 2013, graduate and undergraduate students, I would like to say thank you all for the knowledge and support that you have passed along. You have all become extended family members.

Lastly, and certainly not least I would like to thank… My family and close friends. Without you all, there is no way I could have entertained the thought of even pursing the path that God has set before me. I have been truly blessed to have such a network of encouraging, accommodating, and caring individuals.

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Introduction

Alkyl azides are carbon-nitrogen compounds that consist of an alkyl group and at least one N_3 functional group. These compounds are used as intermediates in a variety of processes. Alkyl azides are useful as High Energy Materials (HEMs) where HEMs are energy stored for use as propellants and/or explosives. There are several practical uses of these types of compounds; often times they are useful in the automotive industry, for example in air bags. Another industry that uses these compounds as intermediates is the pharmaceutical industry. Alkyl azides have been found as intermediates in the synthesis various drugs such as antihistamines, antipsychotics, and acetaminophen? Drugs such as Cymbalta®, Lyrica®, and Adderall®, are a few familiar names that have similar structures to the types of nitrogen containing compounds that are synthesized within this research (Figure 1).

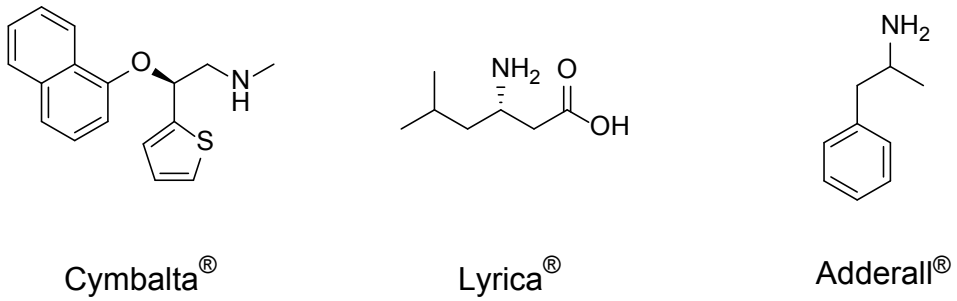


Figure 1: Structures of several *N*-containing pharmaceuticals

The current research is centered on the synthesis of alkyl-azide compounds by new methods. The preparation of the first organic azide, phenyl azide (Figure 2), was accomplished by Peter Grieß in 1864.[1]

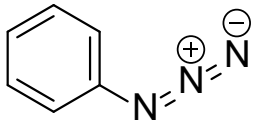


Figure 2: Phenyl azide

For many years organic chemists have studied methods that include multiple steps with highly reactive reagents to create azides. The purpose of this research is to focus on finding a more efficient method of safely producing this particular class of compounds via "one- pot" synthesis. Through exploration of multiple reagents and various solvents, *ortho*-nitro-benzenesulfonylazide has been identified as part of a new route to produce alkyl azides, or their sulfonate ester intermediates safely and in high yields.

Before discussing the proposed approach for the synthesis of alkyl azides it is necessary to review the dangerous nature of azides in general. Much like many other nitrogen-containing compounds alkyl azides have the potential to be highly explosive. The azide (N_3) portion of these compounds is considered a high energy group. Azides tend to explode due to their ability to lose a molecule of nitrogen gas. When a stimulus is applied, such as pressure, impact, or even heat, azides have the ability to explode. Ionic azides such as sodium azide are relatively stable, however covalently bound and heavy-metal azides are thermally decomposable and are considered to be explosive classes of compounds.[1] Sodium azide is a major compound that is used in the production of HEMs and airbags, which in particular have potential dust explosion hazards.[2] There are two general rules to take under consideration for the stability of all nitrogen-containing compounds before synthesizing them.[1]

The number of nitrogen atoms in a compound should not exceed the number of carbon atoms within that compound (Equation 1)

$$Nitrogen\ atoms < Carbon\ atoms \qquad \textbf{(Equation 1)}$$

The sum of the total number of carbon atoms plus the total number of oxygen atoms, when divided by the total number of nitrogen atoms should not exceed 3 (Equation 2)

$$\frac{Carbon\ atoms + Oxygen\ atoms}{Nitrogen\ atoms} < 3 \qquad \textbf{(Equation 2)}$$

In addition to the rules for stability of nitrogen compounds, there are also three safety precautions that are often used once a nitrogen compound has been synthesized. These safety precautions suggest how to handle and store nitrogen compounds upon completion. All three precautions are based on the ratio of carbon atoms to nitrogen atoms of the final product. If the following conditions apply to the ratio of the final product…[3]

$$\frac{Carbon\ atoms}{Nitrogen\ atoms} = 3 \qquad \textbf{(precaution 1)}$$

…then the compound can be isolated and stored in its pure form,

$$\frac{Carbon\ atoms}{Nitrogen\ atoms} > 3 \qquad \textbf{(precaution 2)}$$

…then the compound must be isolated with special storage conditions,

$$\frac{Carbon\ atoms}{Nitrogen\ atoms} < 1 \qquad \textbf{(precaution 3)}$$

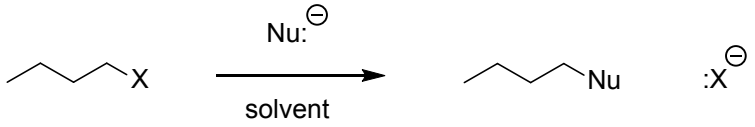
…then the compound should never be isolated and only stored under extreme conditions.

For this research the general nitrogen compound rules and precautions were used before and after each experiment. As previously mentioned one of the primary goals of producing intermediate alkyl azides and their derivatives was to ensure safety.

Another area of review necessary to complete before looking at the details of the proposed synthesis of alkyl azides is bimolecular nucleophilic substitution (S_N2) pathway,[4] since it is believed that the new method that would occur involves the S_N2 mechanism. S_N2 reactions involve an invertion of configuration, a backside attack of a nucleophile onto a substrate. The attack occurs concurrently with the leaving of a functional group when the leaving group is directly attached to the carbon atom of the compound that undergoes attack. The order of the rates in which an S_N2 reaction takes place is just as important as the conversion itself. The pattern of S_N2 reaction rates is known to be as follows:[4]

Methyl > 1˚ > 2˚ > very slow reaction for 3˚

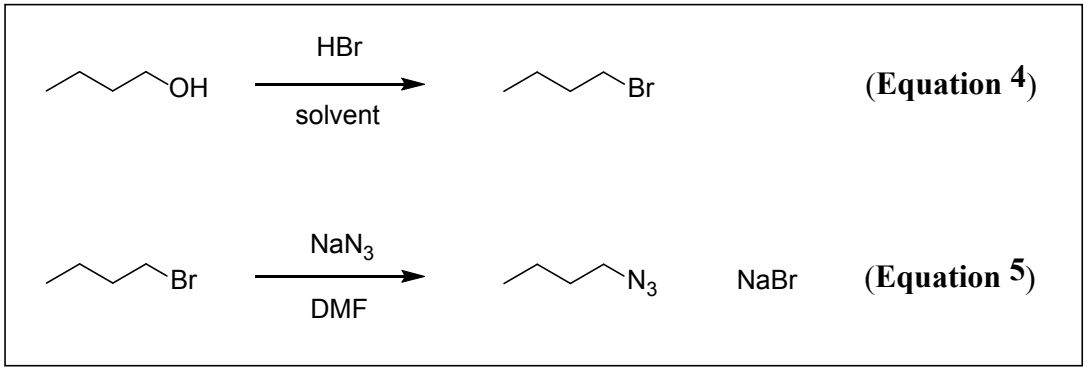
A general S_N2 reaction is shown in Equation 3 where X is the leaving group and Nu is the nucleophile.

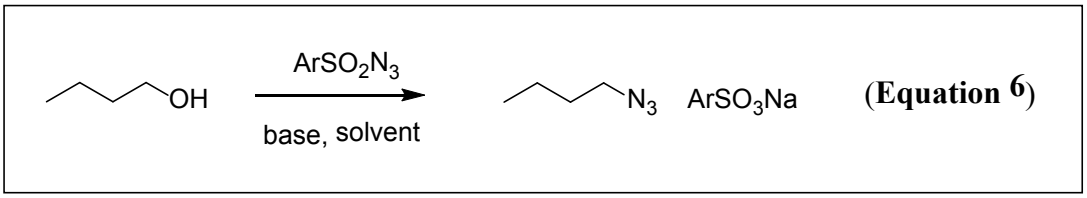


(**Equation 3**)

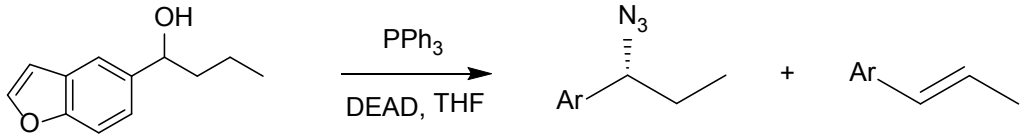
The next sections will expand on the use of the S_N2 pathway as it lays out the proposed mechanism, approach, and design of this research project.

Beginning with the overall approach taken, this research uses the idea of "one-pot" synthesis. A one-pot synthesis approach is simply what it says, a multiple step reaction conducted in a single flask from start to completion without any transfer of the products of intermediates throughout the procedure. Previously a multi-step procedure was used to create alkyl azides. Equation 4 shows how an organic alcohol would be placed into a flask with a solvent and nucleophilic halide to create the halide product, which would next be isolated and purified before being used in a second step. Equation 5**,** the second step, would then involve placing the halide product into a second flask, adding an azide nucleophile to the flask, and left to stir until completion. After completion the azide product would need to undergo isolation and purification as well. Equation 6**,** in comparison, is an example of one-pot synthesis. This equation gives a clear look at what products are produced in a typical S_N2 one-pot approach.



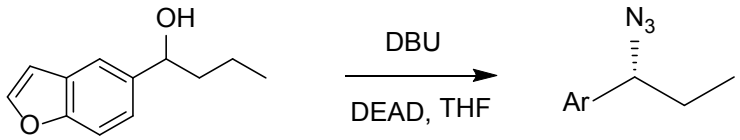


In order to safely produce alkyl azides it was decided to avoid the direct use of sodium azide and organic halides like bromobutane, which tend to be toxic. Sodium azide is explosive, toxic, and mutagenic, hazards have been shown at even low-dose exposures according to several studies.[5, 6] Instead, the proposed plan of action for this research starts by using nontoxic and inexpensive alcohols as reagents. In addition to finding a safe nitrogen source, an alternative method to the well-known Mitsunobu reaction[7] was also considered for the synthesis of the alkyl azides. The Mitsunobu reaction is the substitution of primary or secondary alcohols with nucleophiles mediated by a redox combination of a trialkyl or triarylphosphine and a dialkyl azodicarboxylate.[8] In a previous study conducted by Merck Research Laboratories[7] results from the Mitsunobu reaction versus a direct alternative method were compared. The study took a look at the results from two methods: in method 1, the alcohol and triphenylphosphine were added sequentially to a THF solution of diethyl azodicarboxylate and diphenylphosphorylazide (DPPA) at 0 °C (Equation 7).



(**Equation 7**)

Method 2, the use of a base (DBU) in the presence of DPPA was substituted into the reaction, for the previous use of triphenylphosphine (Equation 8).



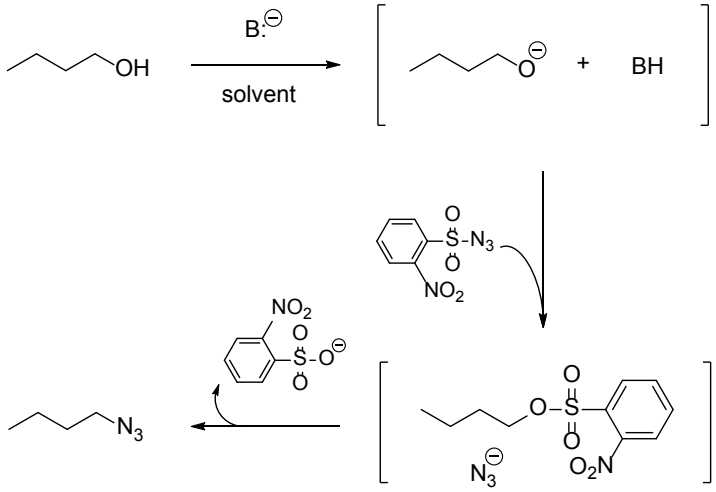
(**Equation 8**)

According to the results observed, method 2 provided a more pure product (91% e.e) and higher yield (91%) for the desired azide product than method 1 (81% ee) and (81% yield), without any byproduct present. Therefore, the concepts behind the procedure and used in method 2 of the previous work was utilized throughout the current research as well.

The first step was to deprotonate an alcohol in solvent with a base to create an alkoxide. The next step is to introduce the nitrogen source to the flask. In this specific research *ortho*-nitrobenzenesulfonylazide (*o*-NBSA, Figure 3) was used as the nitrogen source. The alkoxide then attacks the *o*-NBSA to create a sulfonate ester. During this reaction azide anion is displaced as a leaving group and, since $^{-}N_3$ is a strong nucleophile, it then does an S_N2 attack on the sulfonate ester (Scheme 1). As the N_3 group attacks the

carbon directly attached to the sulfonate group it causes the sulfonate group to be displaced as a leaving group. This action leads to the desired alkyl azide product.

Figure 3: *o*-Nitrobenzenesulfonylazide (*o*-NBSA)



Scheme 1: Proposed one-pot synthesis of alkyl azides

Statement of Problem

The experimental design of this research project involves exploring various bases, alcohols, and solvents in order to produce optimal and efficient combinations for the production of a variety of alkyl azides and intermediates. Starting with the base: *n*-BuLi, pyridine, 2,6-lutidine, 1,8-diazabicycloundecene, triethylamine, dimethylaminopyridine, and imidazole, were the various base explored throughout this study. The sulfonyl azide used within the experiments in this research was *o*-nitrobenzenesulfonylazide (*o*-NBSA). Lastly, the solvents used in the experimental design were tetrahydrofuran (THF), dichloroethane (DCE), and dichloromethane (DCM). Not only will a comparison of the different combinations be evaluated, but also the ratio of each reagent amongst those combinations. Although each base, azide, and solvent was expected to have different results, the proton NMR (HNMR) of each azide product should be identical within each reagent set regardless of the combination used. The peak location range of the final products in comparison to corresponding starting material was expected serve as an important guide to the success of the process. Also, Infrared spectroscopy (IR) would be used for product identification since alkyl azides possess a diagnostic signal at ~2100 cm^{-1}.

Results and Discussion

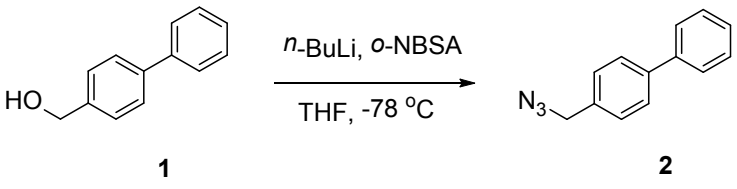
The primary objective of this research was to explore the possibility of converting various alcohols directly to alkyl azides. Reactions with a series of unhindered and hindered primary, along with hindered secondary alcohols were observed and recorded. The ratios listed in Table 1 are based on a mmol scale. The first number of the reaction ratio column refers to the amount of alcohol used in the experiment. The second number represents the amount of *o*-NBSA used, while the third number is the amount of base used in each experiment.

Table 1: Reactions of various alcohols with *n*-BuLi and *o*-NBSA.

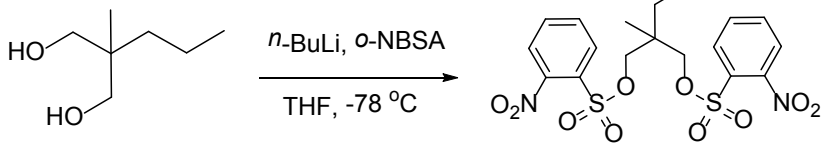
Alcohol	**Product**	**Reaction Ratio**
4-Biphenylmethanol	84% yield	1:1.2:1.2
4-Penten-1-ol	No result	2:2.4:2.4
L(-)-Borneol	73.1% yield	1:2:2
2-Methyl-2-propyl-1,3-propanediol	62.6% yield	3:6.6:6.6
Diacetone-D-Glucose	98.8% yield	1:1.2:1.2

The results showed that both primary and secondary alcohols were converted to the corresponding azide. 4-Biphenylmethanol (**1**), an unhindered primary alcohol, was converted to 4-(azidomethyl)-biphenyl (**2**) (Equation 9), while 2-methyl-2-propyl-1,3-

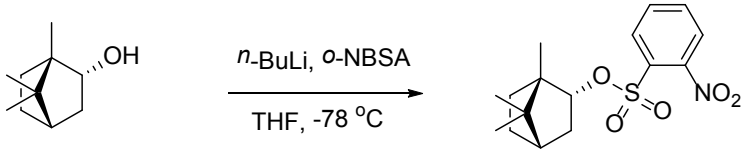
propanediol (**3**), a hindered primary alcohol, was converted to 2-methyl-2-propylpropane-1,3-diyl bis(2-nitrobenzenesulfonate) (**4**) (Equation 10). The two hindered secondary alcohols L-(-)-borneol (**5**) and diacetone-D-glucose (**6**) were converted into sulfonate ester products as well. L-(-)-Borneol was converted into 1,7,7-trimethylbicyclo[2.2.1] heptan-2-yl 2-nitrobenzenesulfonate (**7**) (Equation 11), while diacetone-D-Glucose was converted into the 3-*O*-(2-nitrobenzenesulfonate) ester (**8**) (Equation 12). Only 4-penten-1-ol showed no evidence of producing a characterizable product. The following equations display the conversion of the previously mentioned alcohols used during this study.



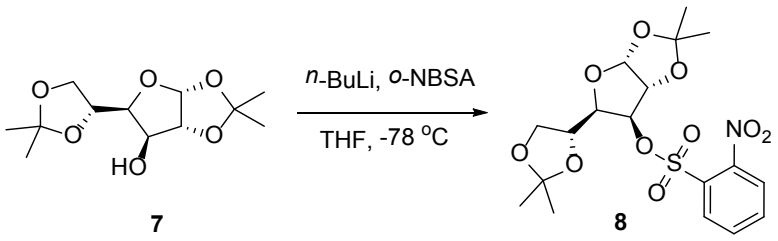
1 **2** (**Equation 9**)



3 **4** (**Equation 10**)



5 **6** (**Equation 11**)



7 **8** (**Equation 12**)

It is notable that the benzylic primary alcohol **1** was completely converted to the azide. Verification of the azide product was confirmed from Infrared spectral data. A sharp signal at 2100 cm^{-1} was visible in the spectrum. This value was compared to other known IR values from a similar study[9] which looked at a series of similar primary alcohols. This indicated that the displaced azide portion of *o*-NBSA had successfully attached itself to the alkyl portion of the intermediate product. However, despite the classification of the alcohol (i.e. 1° or 2°), the remaining three alcohols used stopped at the intermediate sulfonate ester products. The corresponding IR spectra data for each of these compounds lacked a signal in the 2100 cm^{-1} region. Confirmation of the structures of two of these compounds, **4** and **8**, was secured through data obtain from X-Ray crystallography (Figures 4 and 5).

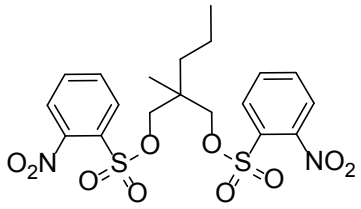
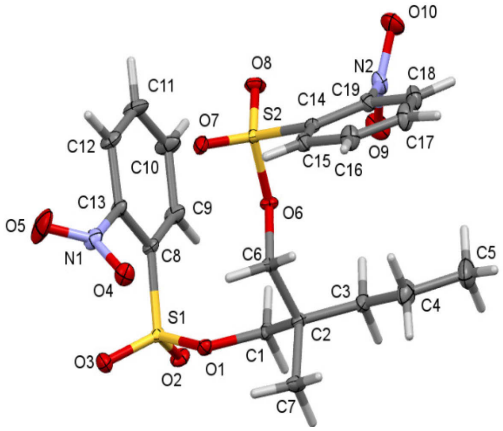
(4)	X-ray crystal structure of bis(sulfonate ester) **4**
	

Figure 4: X-ray crystal structure of sulfonate ester **4**.

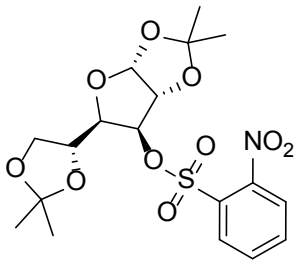
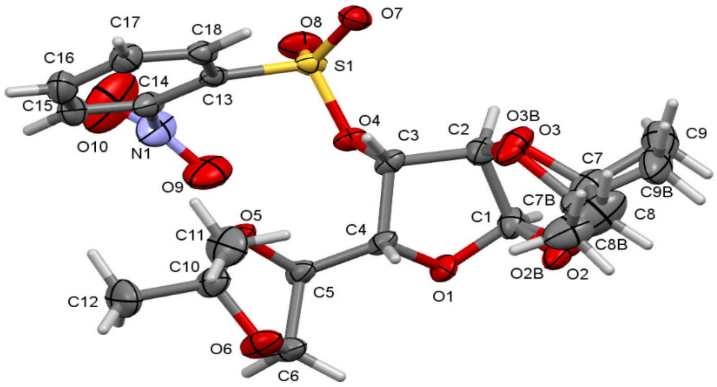
(8)	X-ray crystal structure of sulfonate ester **8**
	

Figure 5: X-ray crystal structure of sulfonate ester **8**.

In these cases the steric environment of each structure prevented the S_N2 attack from occurring and these results confirmed expected outcomes. Previous work done by two former YSU researchers, Charles Hartranft[10] and Brian Dobosh,[11] noted that the attempted formation of similar azide products halted after the initial attack on related sulfonyl azides. In respect to these new sulfonate ester compounds formed here, similar compounds are used in various medications across the analgesic class. One example in particular of this class, which is very similar to compound (**4**), is Carisoprodol also known as Soma® (Figure 6).[12]

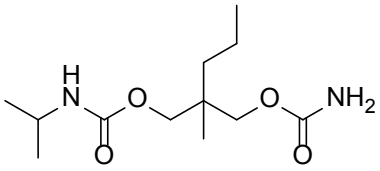
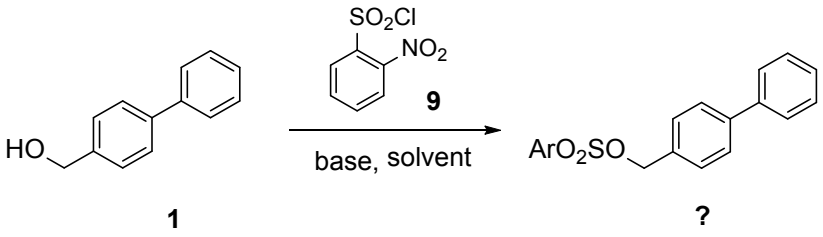


Figure 6: Structure of the analgesic compound *Carisoprodol*.

The secondary objective of this research was to synthesize and isolate intermediate sulfonate ester products that are believed to form during our azidation reactions. In attempts to accomplish this objective the unhindered primary benzylic alcohol (**1**) and the hindered secondary alcohol (**7**) were used for this portion of the study. Initially, 4-biphenylmethanol (**1**) was treated with 2-nitrobenzenesulfonyl chloride (**9**) and several bases to determine which base would provide optimal results (Equation 13).



(**Equation 13**)

Thus, pyridine, 2,6-lutidine, 1,8-diazabicycloundecene (DBU), triethylamine, 4-dimethyl-aminopyridine (4-DMAP), and imidazole were six bases used for optimal base analysis. Seven small scale experiments were run on a carousel reactor to ensure consistency amongst time, temperature, and atmosphere variables. The carousel setup included a mixing of 4-biphenylmethanol (**1**) and 2-nitrobenzenesulfonyl chloride (**9**) with each of the six bases. All of these experiments were performed at room temperature. Dichloromethane was the solvent used in these initial setups and, as a

result, six of the seven reactions showed the formation of product. Table 2 is a display of the results observed from the small scale experiments. The total run time for these experiments was 72 hours and progression of the reactions was monitored daily by TLC. After three days each experiment was worked up separately using an aqueous extraction and the solvent was removed *in vacuo* to provide the crude product mixture.

Table 2: Reactions of 4-biphenylmethanol (**4**) with 2-nitrobenzenesulfonyl chloride (**9**) and various bases: ^{1}H NMR signals for the CH_2 groups in (**4**) and major product.

Carousel	Base	Result	NMR shift	Final shift	Ratio (SM/Prod)
1	Pyridine	No progress	4.66	-	-
2	1 mmol 2,6 Lutidine	Product formed	4.72	4.6214	01:13.4
3	DBU	Product formed	4.74	4.6399	01:01.4
4	Triethylamine	Product formed	4.74	4.6441	01:01.7
5	4-DMAP	Product formed	4.67	4.5726	01:06.0
6	Imidazole	Product formed	4.63	4.5368	01:02.7
7	2 mmol 2,6-Lutidine	Product formed	4.74	4.5701	01:14.1

Figure 7 below is a display of proton NMR data which correlates to the ratio results listed in Table 2. The more downfield signal in each data set represents the starting material left over at the end of the run time. The more upfield signal within each data set represents the final product produced at the end of the same period.

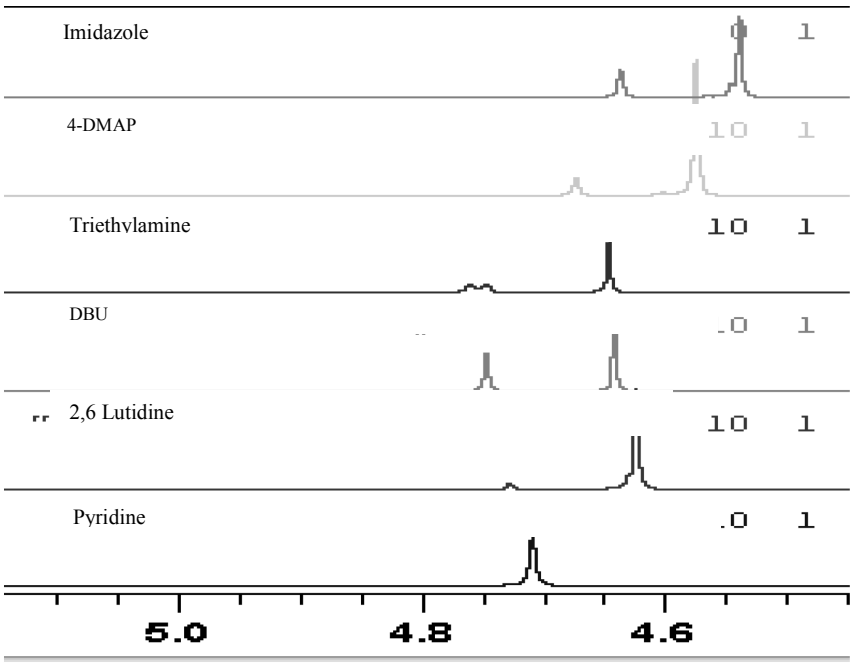
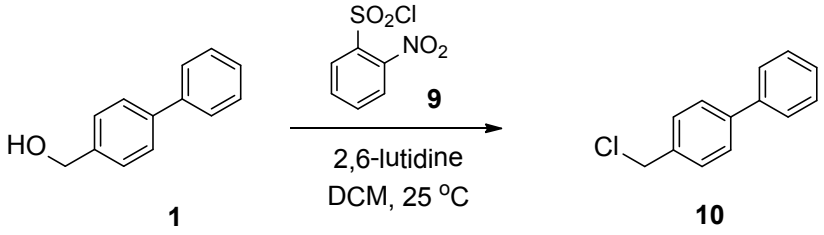


Figure 7: Comparison of Table 1 reaction components by ^{1}H NMR.

In Figure 7, the product signal of each experiment is found between 4.450-4.625 ppm. The starting material signal of each experiment is found between 4.625-4.675 ppm. When comparing the various bases, the reaction ratio for 2,6 lutidine gave the maximum conversion in comparison to its starting material. The ratio for 2,6 lutidine was 1:13.4, and this ratio in comparison to the others implied that using 2,6-lutidine as base left the least amount of starting material at the end of the run period. Therefore, it was

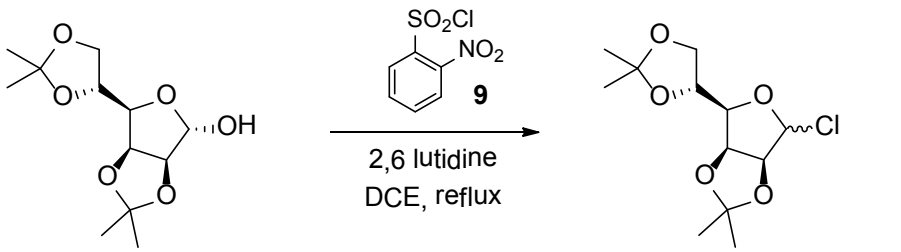
determined to use 2,6 lutidine as the base in the remaining portion of the secondary objective.

The upfield shift of the product signal was of concern since introduction of a sulfonate ester should move the CH_2 signal downfield. Mass spectrometry proved that the actual product observed was the chloride (**10**) and not the expected sulfonate ester. A scale-up of the experiment was carried out in a regular round bottom flask and the chloride (**10**) was isolated in 70% yield (Equation 14).



(**Equation 14**)

A similar experiment was set up using 2,3:5,6-di-O-isopropylidene-α-D-mannofuranose (**11**) as the starting alcohol reagent and this experiment was assembled using a round bottom flask also. However, instead of being conducted at room temperature, the experiment was run under gentle reflux until completion. Equation 15 depicts the glycosyl chlorides (**12**) formed in this experiment, the identity of which were confirmed by ^{1}H NMR spectroscopy.



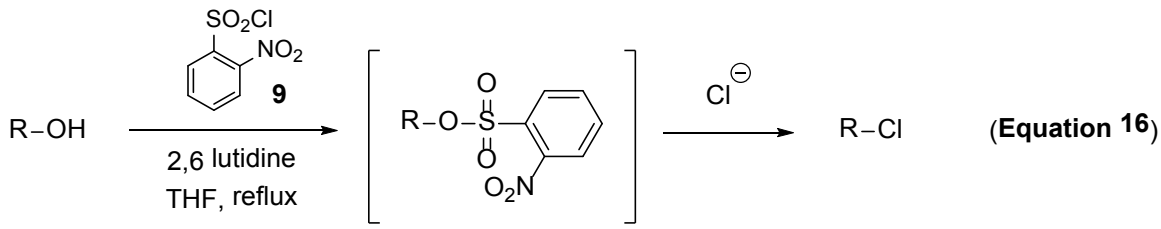
11 **12** (**Equation 15**)

The product yields and reagent ratios used in the experiments can be found in Table 3. The ratios in table 3 are represented as the follow: the amount of (alcohol: sulfonyl chloride: base) used on a mmol scale.

Table 3: Reactions of alcohols (**4**) and (**11**) with 2-nitrobenzenesulfonyl chloride (**9**).

Alcohol	Chloride Product(s)	Reaction ratio
4-Biphenylmethanol (**1**)	**70.3% yield**	4:9:4
2,3:5,6-Di-*O*-isopropylidene-α-D-mannofurnanose (**11**)	**88.7% yield**	1:1.2:1

The formation of chlorides in these experiments suggest that the intermediate sulfonate esters are being formed but that the 2-nitrobenzenesulfonate group is such a good leaving group that chloride anion, which is produced during the sulfonation step, is a strong enough nucleophile to cause S_N2 displacement (Equation 16).



(**Equation 16**)

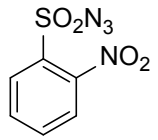
In conclusion, a safe and efficient one-pot synthesis method was confirmed to create either the alkyl azide product or the sulfonate ester intermediates. Specifically the one-pot method used in this research provided complete conversion of an unhindered primary alcohol, similar to previous studies that focused on the direct one-step conversion of alcohols into nitriles.[13] As for hindered systems both primary and secondary, the same method converted the alcohols into their sulfonate ester intermediate forms. Following the same rationale from various other studies, for example one such study that concentrated on the synthesis of amides from esters conducted by a group from the University of York,[14] results suggest that these transformations are sensitive to steric hindrance. In the present work, the reaction of *o*-nitrobenzenesulfonylazide with various alkoxides of different steric nature suggests that the azidation method is following the S_N2 pathway.

Experimental

General Experimental Procedure for Synthesis

All reactions were performed in 100 mL round bottom flasks fitted with pressure sensitive septa caps or in a Radleys carousel reaction system as indicated. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III 400 MHz NMR spectrometer at 400 and 100 MHz, respectively. Chemical Shifts were reported in parts per million (ppm) from a standard of tetramethylsilane in $CDCl_3$ (0.03% v/v TMS). NMR spectra multiplicities are defined as follows: s (singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublets), and all coupling constants, (*J*), are labeled in Hertz. Infrared spectra were taken on a Thermo Electron Corporation IR 200 spectrophotometer and analyzed using EZ-OMNIC software. Thin layer chromatography was performed on Whatman aluminum-backed plates with varying eluent systems. Flash column chromatography was performed using 32-60 Å silica gel with varying eluent systems. COSY spectra were included for completeness as it aided in the assignments of the peaks in the ^{1}H and ^{13}C NMR spectra. All reagent were purchased form Sigma Aldrich and used as received.

Formation of *o*-nitrobenzensulfonyl azide from *o*-nitrobenzensulfonyl chloride.



To a flame-dried, 100 mL round-bottomed flask fitted with magnetic stir-bar, 5.00 g (22.56 mmol) of 2-nitrobenzenesulfonyl chloride was added and then dissolved in 100 mL of anhydrous methanol. Once dissolved, 5.00 g (76.91 mmol) of sodium azide was added. The reaction mixture was then capped and allowed to stir at room temperature for 24 hours. The methanol was them removed with the rotary evaporator with the temperature kept below 40 °C. The resulting slurry was then partitioned between ethyl acetate (50 mL) and water (50 mL), and separated. Ethyl acetate was removed from the organic layer with the rotary evaporator with the temperature kept below 40 °C. Hot anhydrous ethanol was used to dissolve the organic residue and the mixture was covered and allowed to cool to induce crystallization, yielding 4.10 g product for 95.6% final yield of *o*-nitrobenzensulfonyl azide.

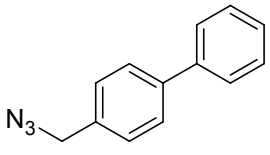
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93-7.80 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.70, 133.01, 131.72, 125.36.

General procedure for the reaction of alcohols with *o*-NBSA

In a clean, flame-dried 100 mL round bottom flask fitted with a magnetic stir-bar, 1.0 equivalent of the alcohol was dissolved in 6.0 mL of dry tetrahydrofuran (THF). The flask was then capped and purged with nitrogen, and placed in a -78 °C dry ice-acetone bath. To this mixture 1.2 equivalents of base was added and the solution was allowed to stir for 30 minutes. Next, 1.3 equivalents of *o*-nitrobenzenesulfonyl azide (*o*-NBSA) dissolved in 10.0 mL THF was added to the reaction mixture which was then allowed to stir until completion. Once completion was confirmed from TLC, with staining by *p*-anisaldehyde or phosphomolybdic acid (PMA), the reaction was poured into ethyl acetate (50 mL) and water (50 mL) in a separatory funnel. After separation the organic layer was neutralized with 5% HCl, washed with water, and then washed with saturated NaCl. The organic layer was dried over $MgSO_4$, filtered, and the solvent removed *in vacuo*. The crude product residue was purified by flash column chromatography, unless otherwise noted.

Formation of 4-biphenyl azide (2) from 4-biphenylmethanol (1).



2

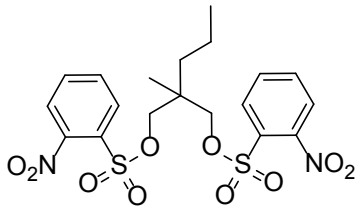
Following the general procedure for azide synthesis, 0.369 g (2.0 mmol, 1.0 eq.) of 4-biphenylmethanol (**1**) was added to THF and reacted with 1.3 mL of the base *n*-BuLi (2.6 mmol, 1.2 eq.) at -78 ˚C for 30 minutes. Then, 0.548 g (2.6 mmol, 1.3 eq.) of *o*-nitrobenzene sulfonyl azide (*o*-NBSA) dissolved in THF, was added to the reaction. During the addition of *o*-NBSA the reaction changed in color from straw yellow to dark brown. The mixture was left overnight to stir until completion. The reaction was determined complete by TLC (1:1 hexane/ethyl acetate) R_f = 0.72. The crude mixture was purified initially with an aqueous workup, the solvent removed *in vacuo*, and separated on a silica gel flash column (75 mL silica, 10:1 hexanes/ethyl acetate), yielding 0.88 g product for 84.2% final yield of azide (**2**).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.41 (m, 9H), 4.73 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.65, 139.91, 135.65, 133.00, 128.78 (double intensity), 127.46 (double intensity), 127.32 (double intensity), 127.09 (double intensity), 65.10.

IR absorption: 2148 cm^{-1} for azide functional group.

Formation of 2-methyl-2-propylpropane-1,3-diyl bis(2-nitrobenzenesulfonate) (4) from 2-methyl-2-propyl-1,3-propanediol.



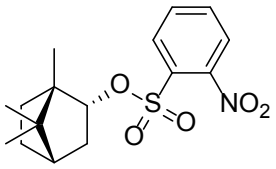
4

Following the general procedure for azide synthesis, 0.397 g (3.0 mmol, 1.0 eq.) of 2-methyl-2-propyl-1,3-propanediol was added to THF and reacted with 3.3 mL of the base *n*-BuLi (6.6 mmol, 2.2 eq.) at -78 ˚C for 30 minutes. After that time, 1.50 g (6.6 mmol, 2.2 eq.) of *o*-nitrobenzenesulfonyl azide (*o*-NBSA) dissolved in THF, was added to the reaction. During the addition of *o*-NBSA the reaction changed in color from pale yellow to dark brown. The mixture was left to stir overnight when the reaction was determined to be complete by TLC (1:1 hexane/ethyl acetate) R_f = 0.38. The crude mixture was initially purified with an aqueous workup, the solvent removed *in vacuo*, and purified using crystallization (hot ethanol), yielding 0.94 g product for a 62.6% final yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12-8.09 (m, 2H), 7.86-7.76 (m, 4H), 0.97 (s, 3H), 0.86 (t, 3H, *J* = 7.02 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.47, 135.03, 132.45, 131.47, 128.81, 125.05, 73.95, 38.37, 35.44, 18.00, 15.97, 14.46.

Formation of 1,7,7-trimethylbicyclo[2.2.1] heptan-2-yl 2-nitrobenzenesulfonate (6) from L-(-)- Borneol.



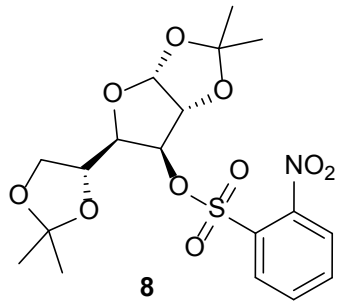
6

Following the general procedures for azide synthesis, 0.309 g (2.0 mmol, 1.0 eq.) of L-borneol was added to THF and reacted with 1.2 mL of the base *n*-BuLi (2.4 mmol, 1.2 eq.) at 0 ˚C for 30 minutes. After that time, 0.548 g (2.4 mmol, 1.2 eq.) of *o*-nitrobenzene sulfonyl azide (*o*-NBSA) dissolved in 6.0 mLTHF, was added to the reaction. During the addition of *o*-NBSA the reaction changed in color from pale yellow to dark gold. After stirring overnight the reaction was determined to be complete by TLC (1:1 hexane/ethyl acetate) $R_f = 0.55$. The crude mixture was worked up with an aqueous extraction, the solvent removed *in vacuo*, and purified on a silica gel flash column (40.0 g silica, 5:1 hexanes/ethyl acetate), yielding 0.26 g of product for a 73.1% final yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15-8.13 (m, 2H), 7.81-7.72 (m, 4H), 4.95-4.91 (m, 2H), 4.71 (s, 1H), 4.49 (s, 2H), 0.87 (s, 3H), 0.83 (s, 6H) (double intensity).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.24, 136.58, 135.93, 132.93, 130.42, 130.10, 125.30, 49.48, 48.01, 45.10, 38.97, 28.26, 25.92, 20.16, 18.65, 13.29.

Formation of 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose-3-*O*-(2-nitrobenzenesulfonate) (8) from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (7).



8

Following the general procedure for azide synthesis, 0.260 g (1.0 mmol, 1.0 eq.) of 1,2,5,6-di-*O*-isopropylidene-α-D-glucofuranose was dissolved in THF and reacted with 0.6 mL of the base *n*-BuLi (1.0 mmol, 1.2 eq.) at 0 ˚C for 30 minutes. Next, 0.274 g (1.2 mmol, 1.2 eq.) of *o*-nitrobenzenesulfonyl azide (*o*-NBSA) dissolved in THF was added to the reaction. During the addition of *o*-NBSA the reaction changed in color from pale yellow to light beige. The reaction was left overnight to stir until completion as determined by TLC (1:1 hexane/ethyl acetate) $R_f = 0.70$. The crude mixture was worked up with an aqueous extraction and the solvent removed *in vacuo* yielding 0.44 g product for a 98.8% final yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90-7.75 (m, 4H), 5.99 (d, 1H, *J* = 3.64 Hz), 5.00 (d, 1H, *J* = 2.88 Hz), 4.88 (d, 1H, *J* = 3.64 Hz), 4.30-4.25 (m, 1H), 4.07 (dd, 1H, J = 8.64, 2.88 Hz), 4.00 (dd, 1H, *J* = 8.86, 6.14), 3.93 (dd, 1H, *J* = 8.90. 4.18), 1.42 (s, 3H), 1.26 (s, 3H), 1.01 (s, 3H), 0.90 (s, 3H).

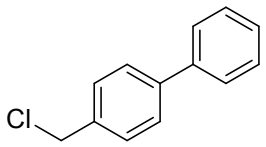
^{13}C NMR (100 MHz, $CDCl_3$) δ 148.52, 134.87, 132.16, 131.87, 129.57, 125.11, 112.74, 108.98, 105.17, 84.19, 83.52, 79.85, 71.86, 67.21, 26.65, 26.63, 26.23, 24.57.

Synthesis of Alkyl chlorides from Alcohols

General procedure for the conversion of alcohols to alkyl chlorides.

In a clean, flame-dried 100 mL round-bottom flask fitted with a magnetic stir-bar, 1.0 equivalent of the alcohol was dissolved in 5.0 mL of dichloromethane (DCM) or dry dichloroethane (DCE). The flask was then capped and purged with nitrogen, and placed in a 0 °C ice bath. To the mixture 1.0 equivalent of base was added and the solution was allowed to stir for 30 minutes. After 30 minutes, 1.2 equivalents of dissolved 2-nitrobenzenesulfonyl chloride in 10.0 mL of DCE were added to the reaction mixture. Total solvent volume for the reaction was 15 mL of DCE. The reaction mixture was allowed to stir until completion, which was confirmed by TLC, with staining by *p*-anisaldehyde or phosphomolybdic acid (PMA). The reaction mixture was then poured into an ethyl acetate (50 mL) and water (50 mL) mixture in a separatory funnel. The organic layer was then neutralized with a weak acid (5% HCl), washed with water, then washed further with aqueous NaCl. The organic layer was dried over $MgSO_4$, filtered, and the solvent removed *in vacuo*. Crude reaction mixtures were purified by flash column chromatography, unless otherwise noted.

Formation of 4-biphenyl chloride (10) from 4-biphenylmethanol (1).



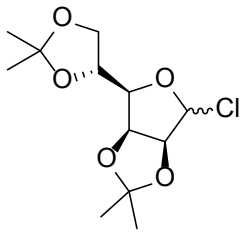
10

Following the general procedures for alkyl chloride synthesis, 0.736 g (4.0 mmol, 1.0 eq.) of 4-biphenylmethanol (**1**) was added to DCM and reacted with 0.90 mL of the base 2,6-lutidine (9.0 mmol, 2.25 eq.) at 0 ˚C temperature for 30 minutes. After which time 0.88 g (4.0 mmol, 1.0 eq.) of 2-nitrobenzenesulfonyl chloride dissolved in DCM was added to the reaction. During the addition of the chloride the reaction changed in color from faint yellow to dark gold and the mixture was then left overnight to stir until completion when the reaction was determined to be over by TLC (1:1 hexane/ethyl acetate) R_f = 0.45, 0.75. The crude mixture was then worked up with an aqueous extraction, the organic solvent removed *in vacuo*, and the residue separated on a silica gel flash column (75 mL silica, 30:1 hexanes/ethyl acetate), yielding 0.57 g of product for 70.3% final yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.18 (m, 9H), 4.52 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.36, 139.47, 135.43, 128.00 (double intensity), 127.78 (double intensity), 126.50, 126.43 (double intensity), 126.08 (double intensity), 44.98.

Formation of 2,3:5,6-di-*O*-isopropylidene-α/β-o-mannofuranosyl chlorides (12) from 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (11).



12

Following the general procedure for alkyl chloride formation, 0.260 g (1.0 mmol, 1.0 eq.) of 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose was added to DCE and reacted with 0.1 mL of the base 2,6-Lutidine (1.0 mmol, 1.0 eq.) under gentle reflux for 30 minutes. After 30 minutes, 0.264 g (1.2 mmol, 1.2 eq.) of 2-nitrobenzenesulfonyl chloride dissolved in DCE was added to the reaction during which the reaction changed in color from pale yellow to dark brown. The mixture was left to stir overnight under gentle reflux until completion. The reaction was determined to be complete by TLC (1:1 hexane/ethyl acetate) R_f = 0.44, 0.52. The crude mixture was worked up with an aqueous extraction, the solvent removed *in vacuo* thereby yielding 0.26 g of product for an 88.7% final yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90-7.75 (m, 4H), 5.99 (d, 1H, *J* = 3.64 Hz), 5.00 (d, 1H, *J* = 2.88 Hz), 4.88 (d, 1H, *J* = 3.64 Hz), 4.30-4.25 (m, 1H), 4.07 (dd, 1H, *J* = 8.64, 2.88 Hz), 4.00 (dd, 1H, *J* = 8.86, 6.14), 3.93 (dd, 1H, *J* = 8.90. 4.18), 1.42 (s, 3H), 1.26 (s, 3H), 1.01 (s, 3H), 0.90 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.52, 134.87, 132.16, 131.87, 129.57, 125.11, 112.74, 108.98, 105.17, 84.19, 83.52, 79.85, 71.86, 67.21, 26.65, 26.63, 26.23, 24.57.

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Appendix A

^{1}H NMR, ^{13}C NMR, IR Spectra, COSY Data

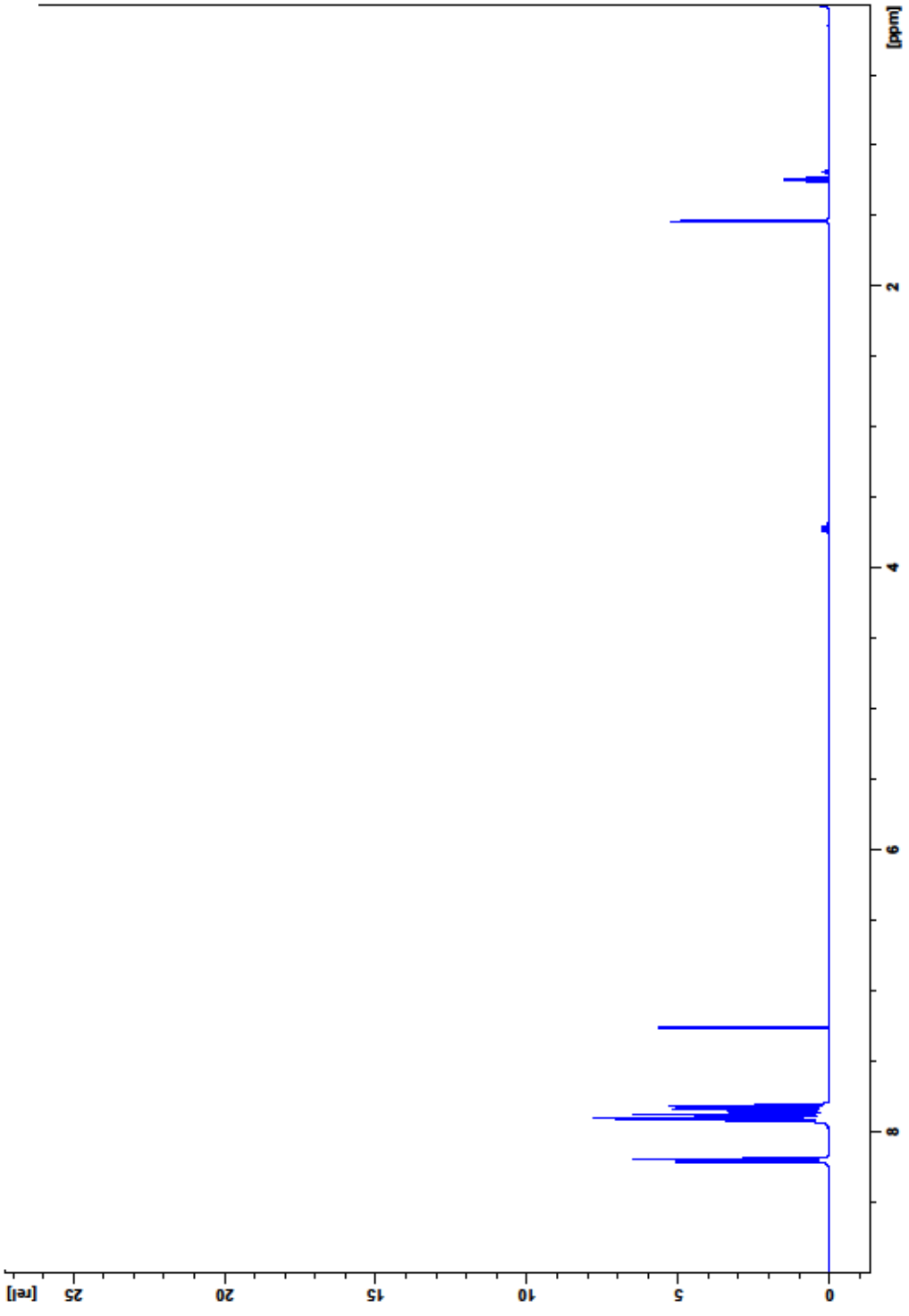


Figure 8: ^{1}H NMR spectrum of *o*-nitrobenzensulfonyl chloride.

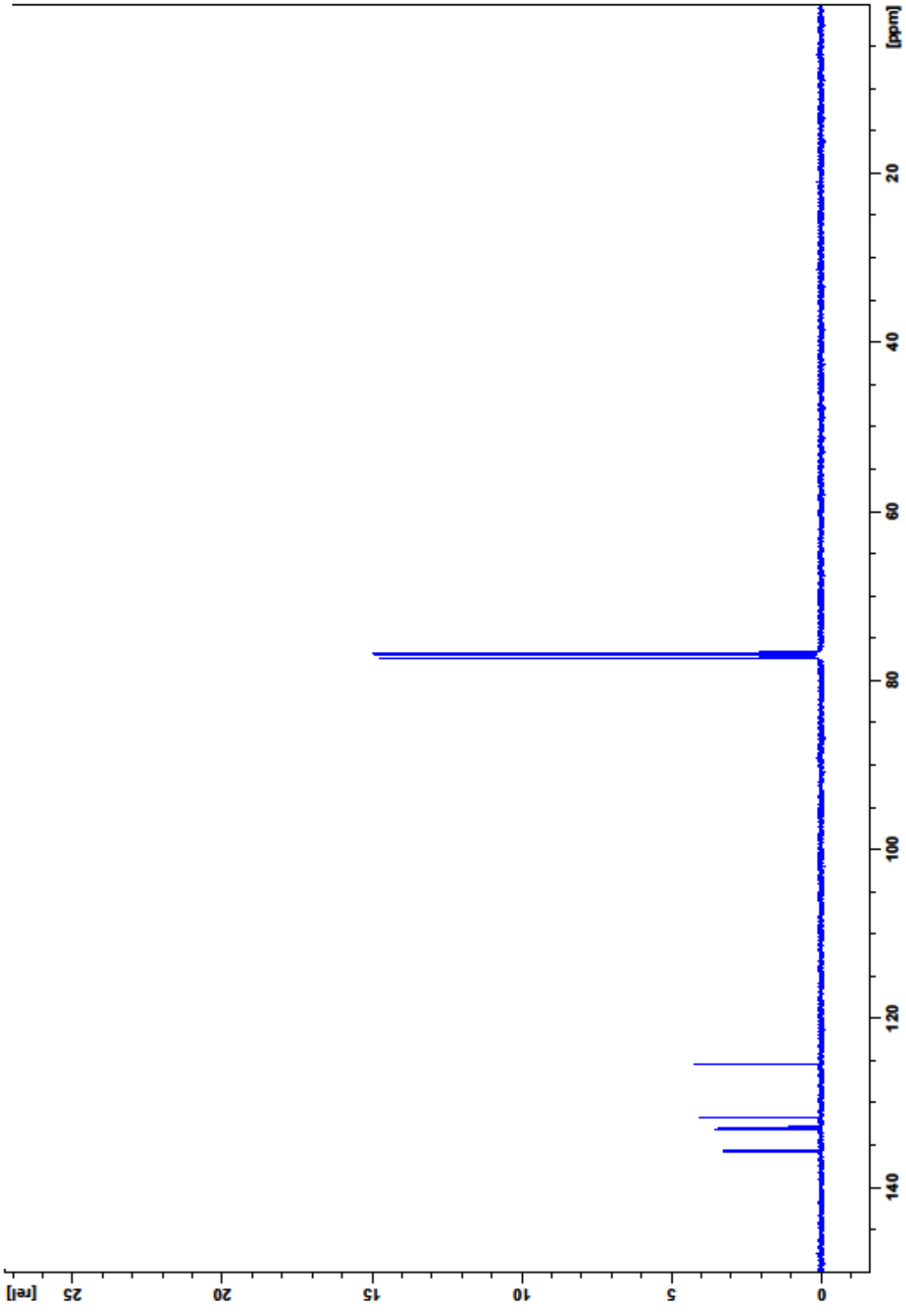


Figure 9: ^{13}C NMR spectrum of *o*-nitrobenzensulfonyl chloride.

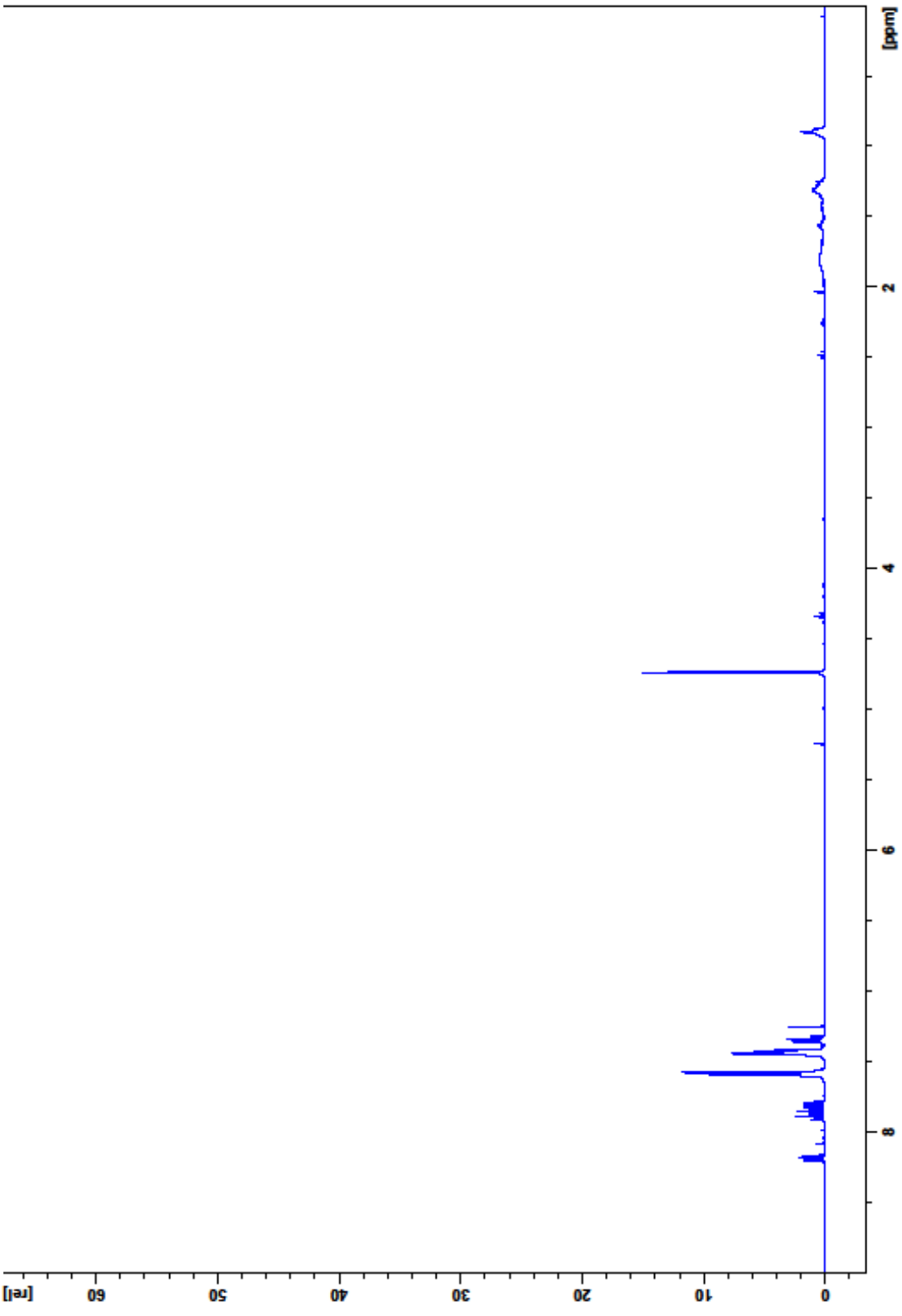


Figure 10: ^{1}H NMR spectrum of 4-biphenyl azide **(2)**

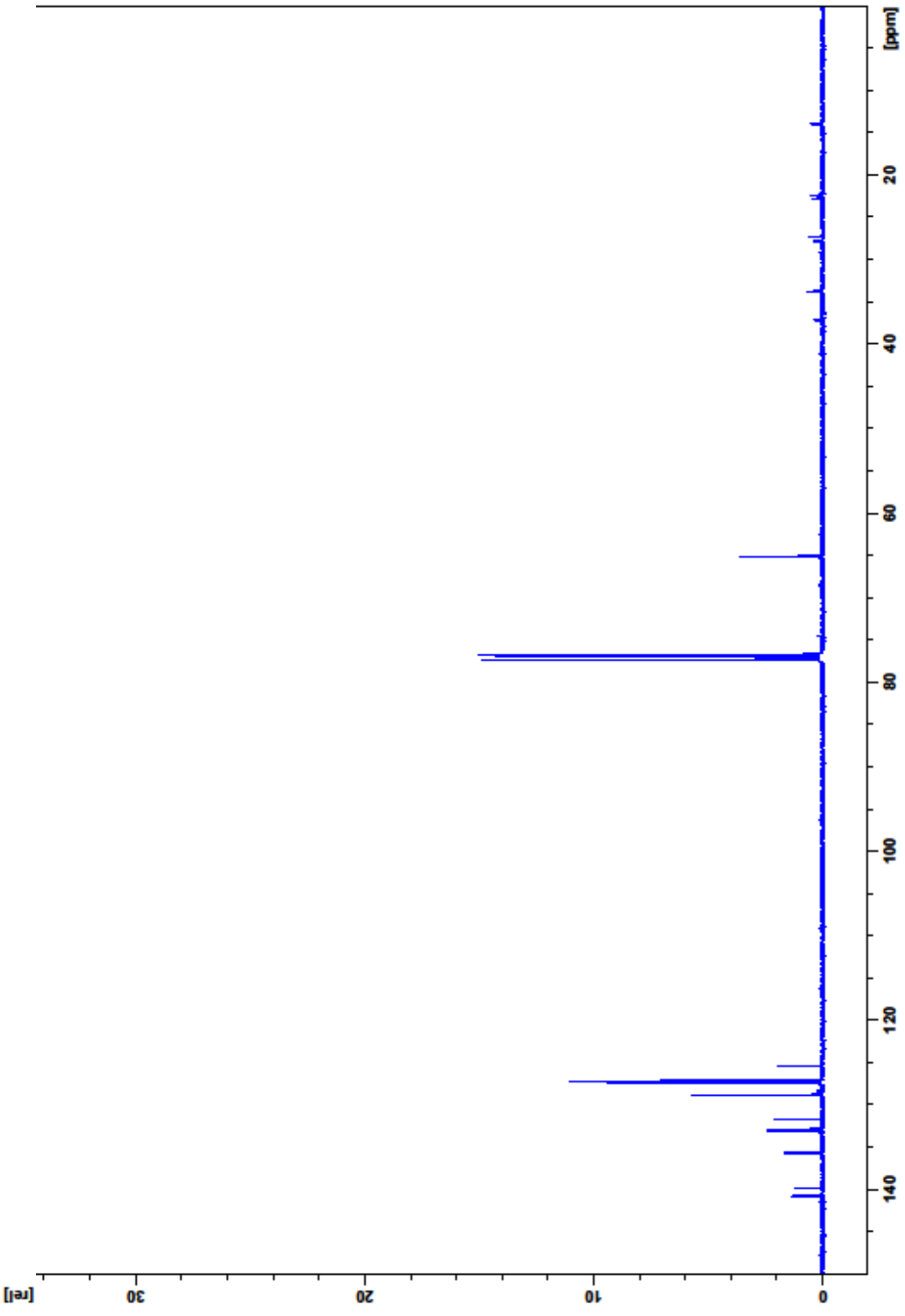


Figure 11: ^{13}C NMR spectrum of 4-biphenyl azide **(2)**.

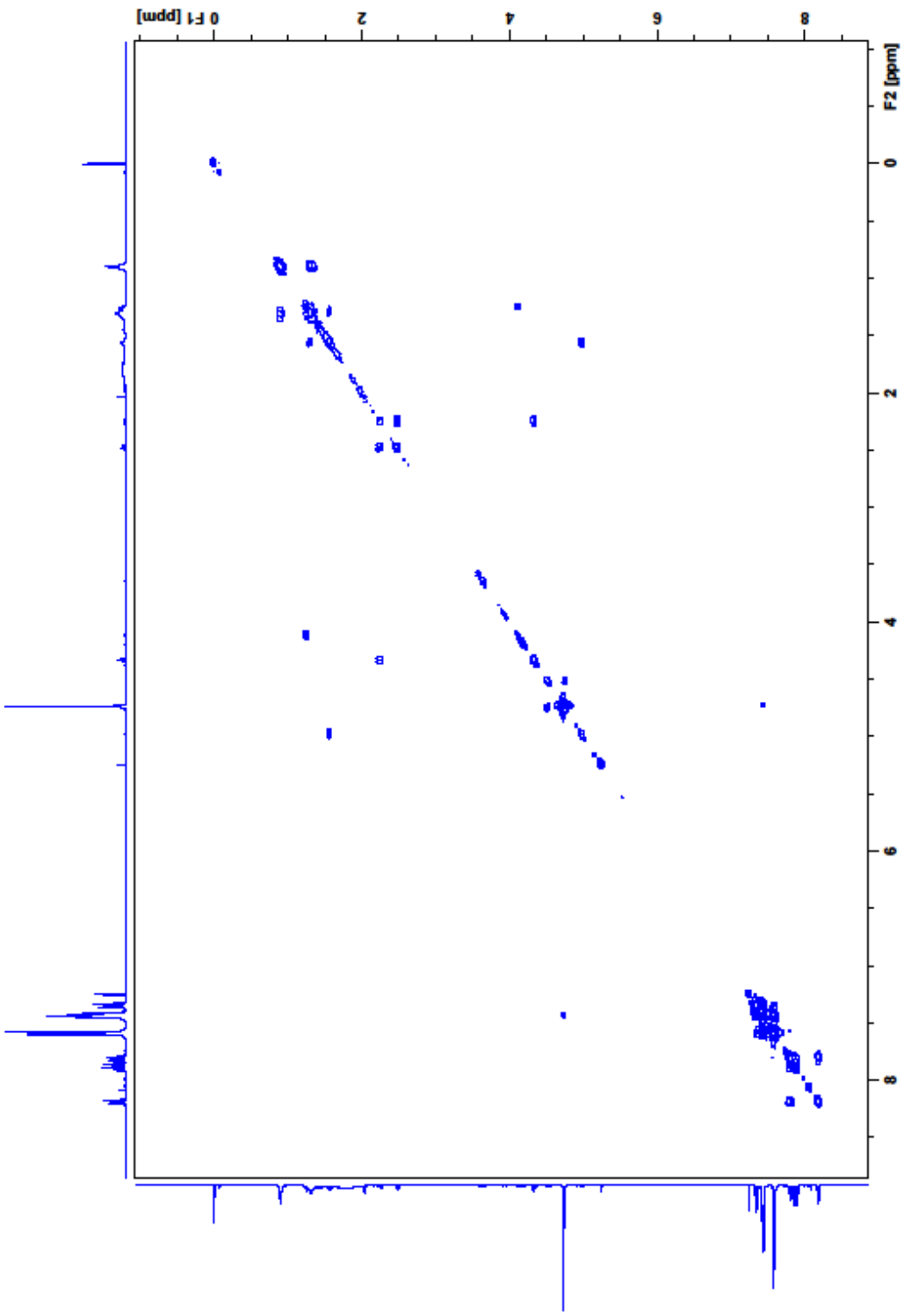


Figure 12: COSY NMR spectrum of 4-biphenyl azide **(2)**.

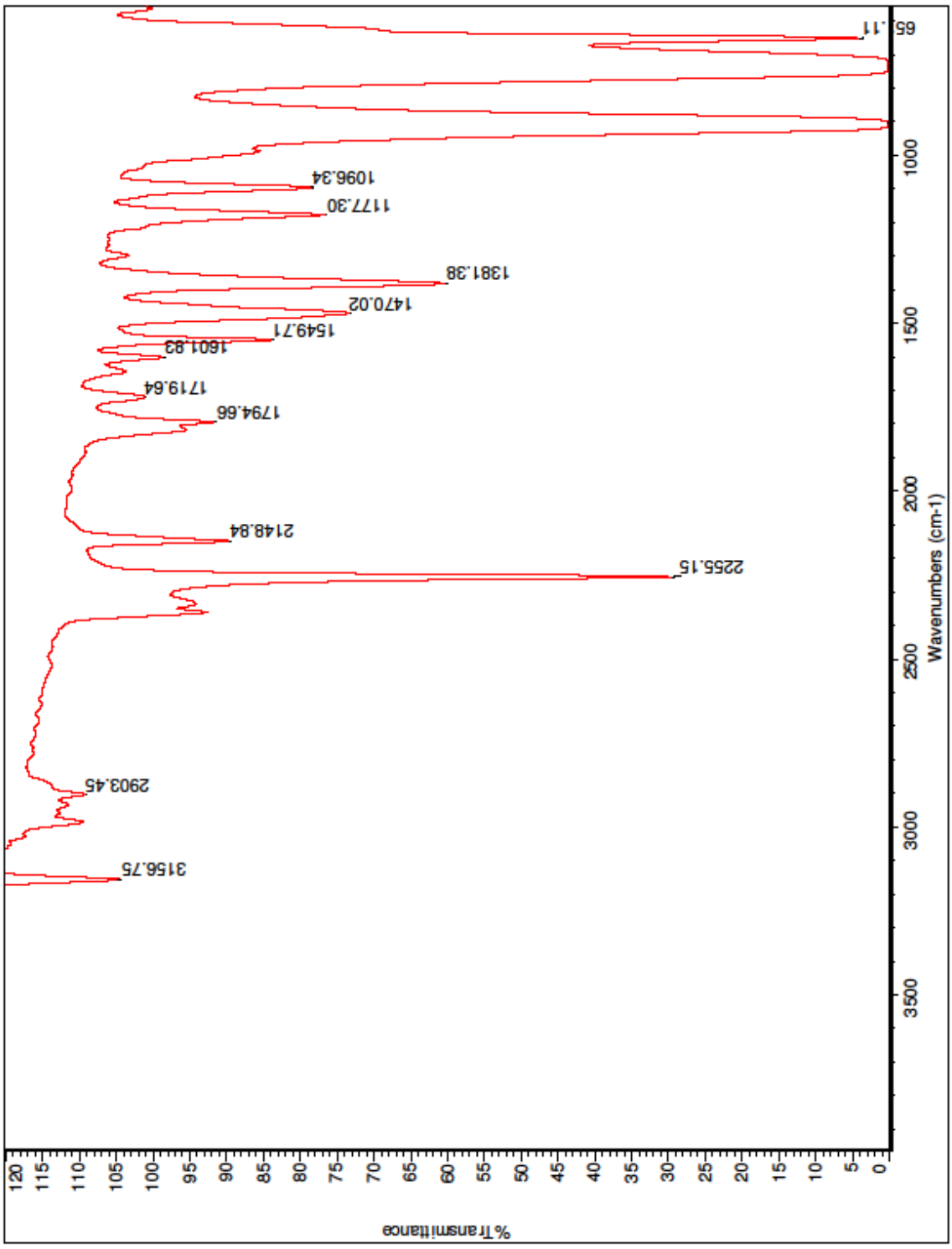


Figure 13: IR spectrum of 4-biphenyl azide **(2)**.

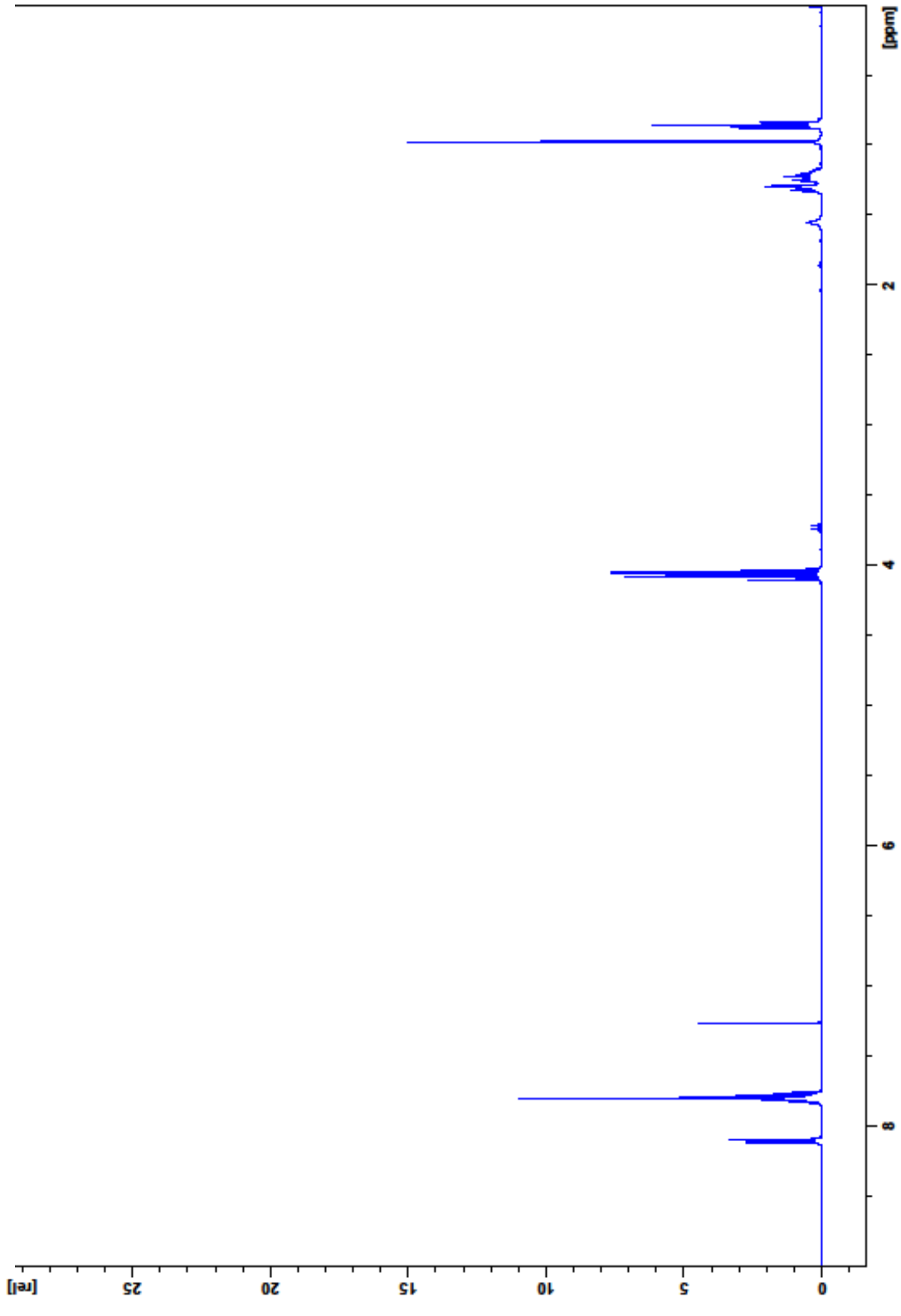


Figure 14: ^{1}H NMR spectrum of 2-methyl-2-propylpropane-1,3-diyl bis(2-nitrobenzenesulfonate) **(4)**.

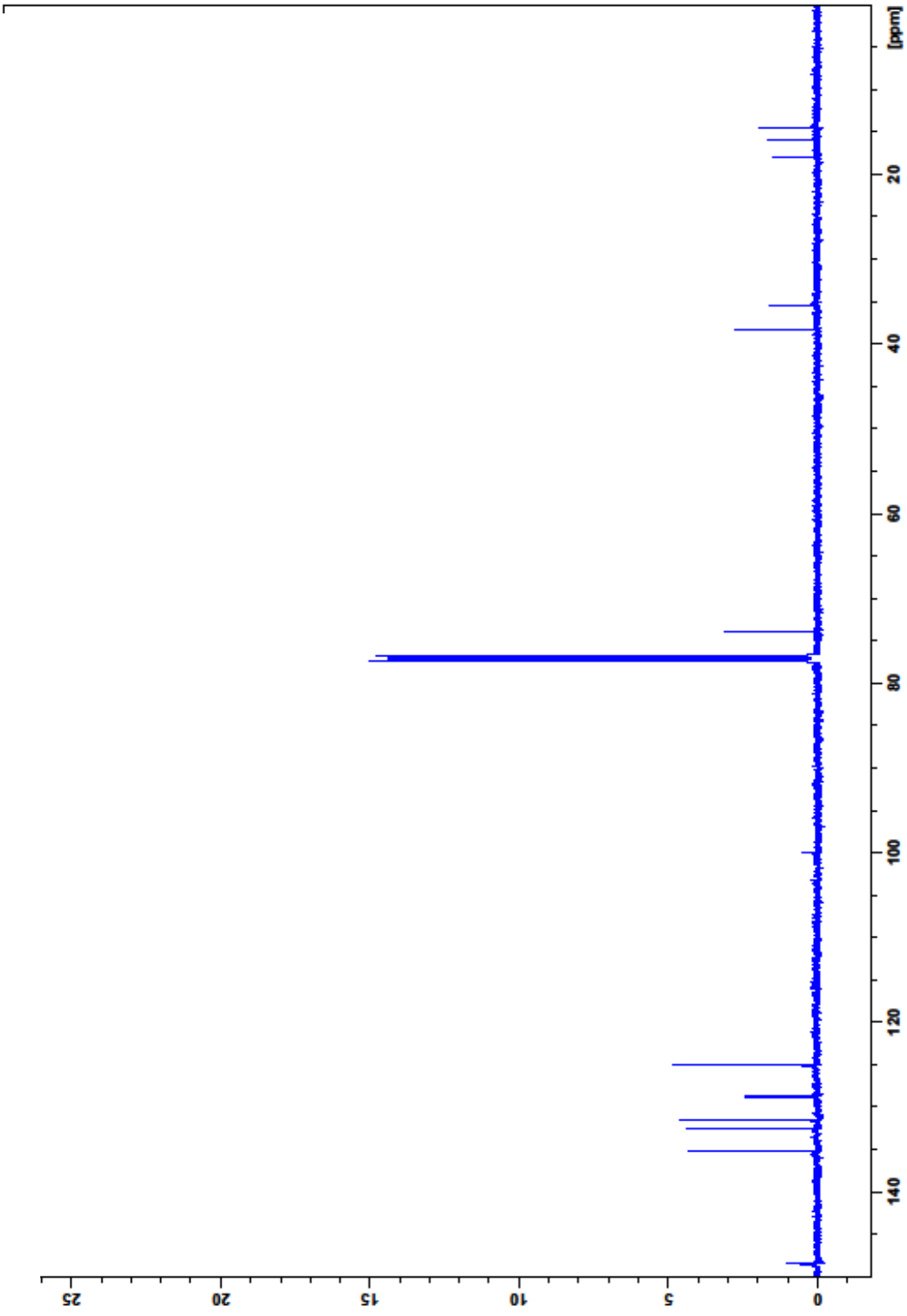


Figure 15: ^{13}C NMR spectrum of 2-methyl-2-propylpropane-1,3-diyl bis(2-nitrobenzenesulfonate) (**4**).

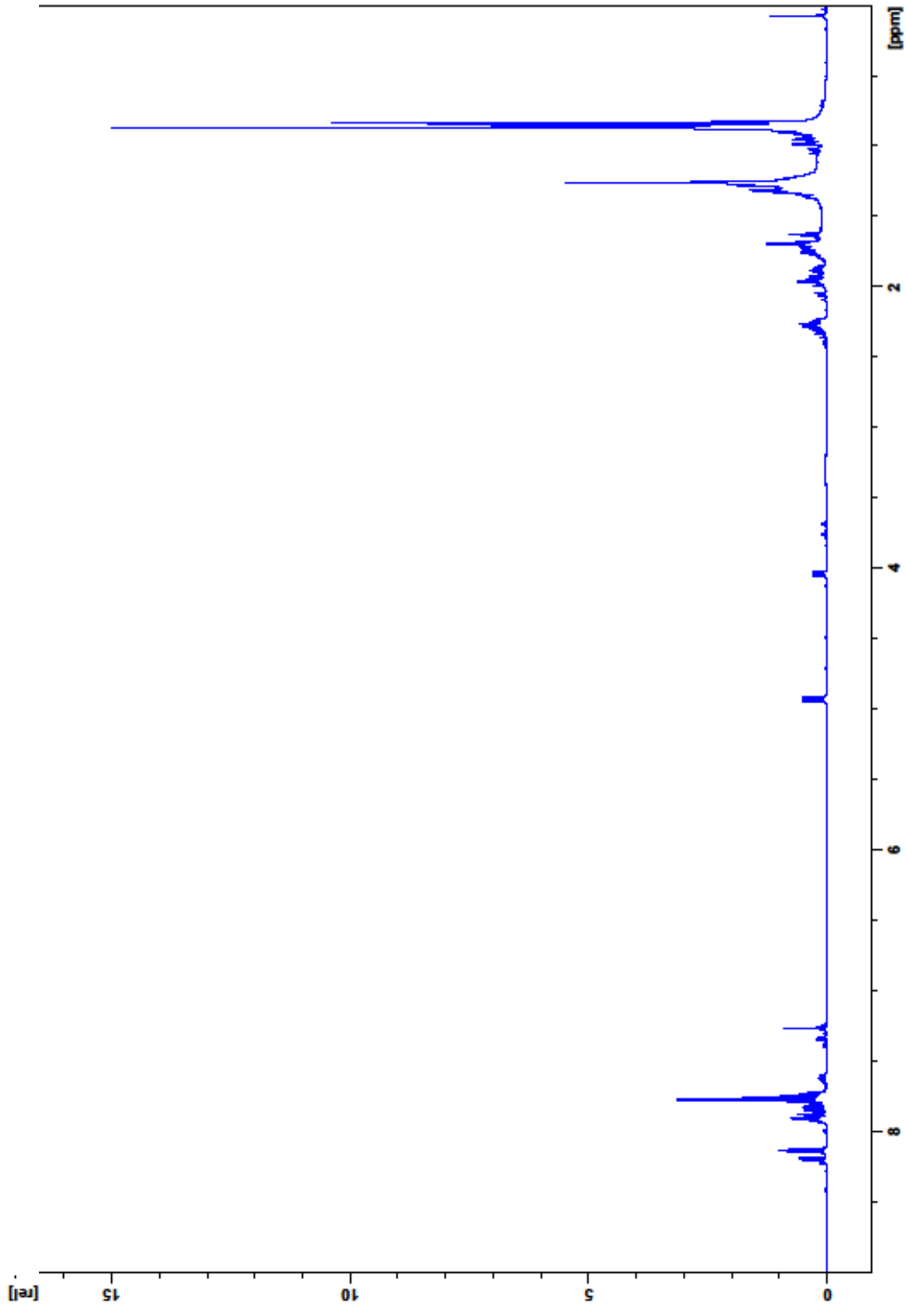


Figure 16: ^{1}H NMR spectrum of 1,7,7-trimethylbicyclo[2.2.1] heptan-2-yl 2-nitrobenzenesulfonate (**6**).

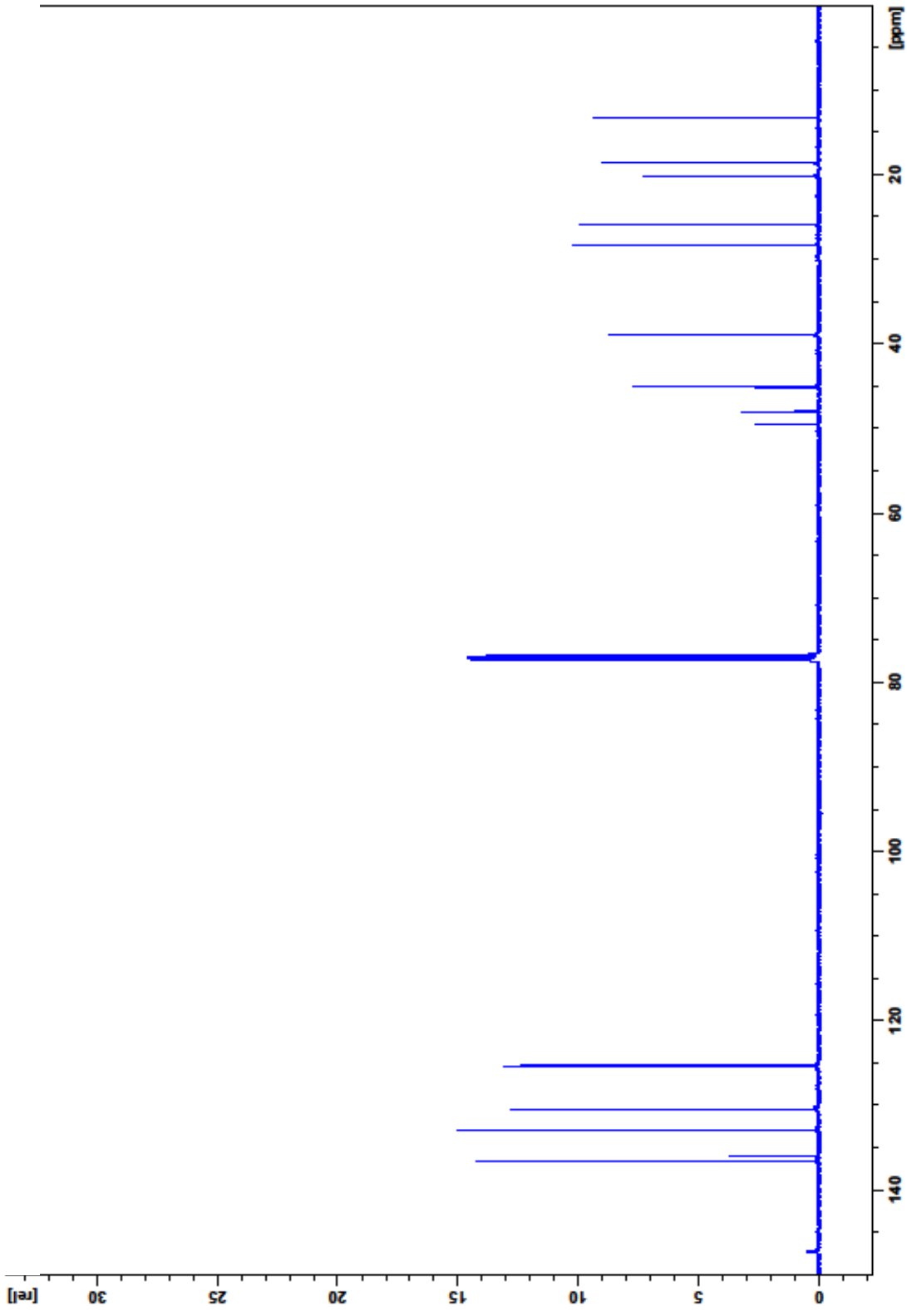


Figure 17: ^{13}C NMR spectrum of 1,7,7-trimethylbicyclo[2.2.1] heptan-2-yl 2-nitrobenzenesulfonate **(6)**.

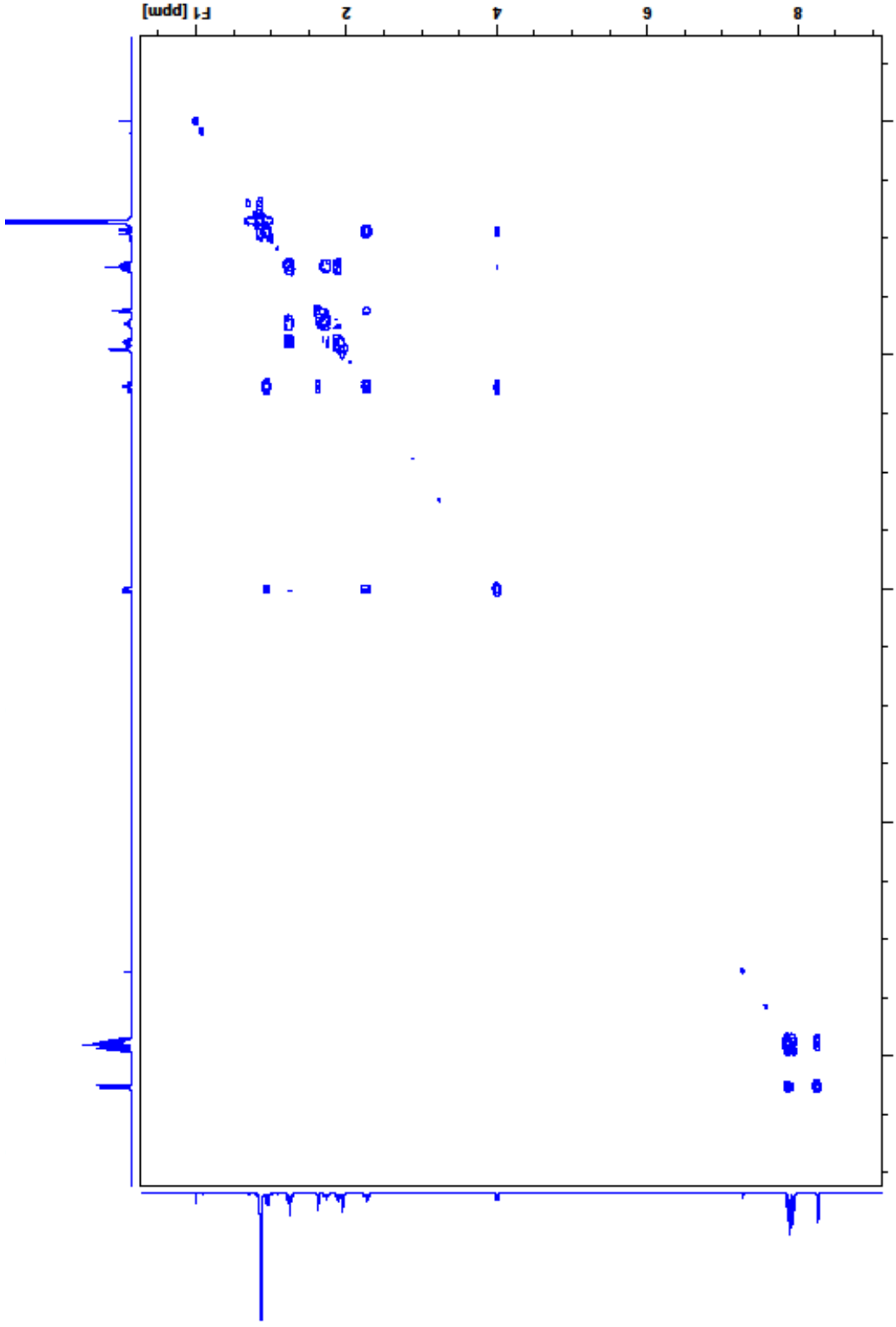


Figure 18: COSY NMR spectrum of 1,7,7-trimethylbicyclo[2.2.1] heptan-2-yl 2-nitrobenzenesulfonate (**6**).

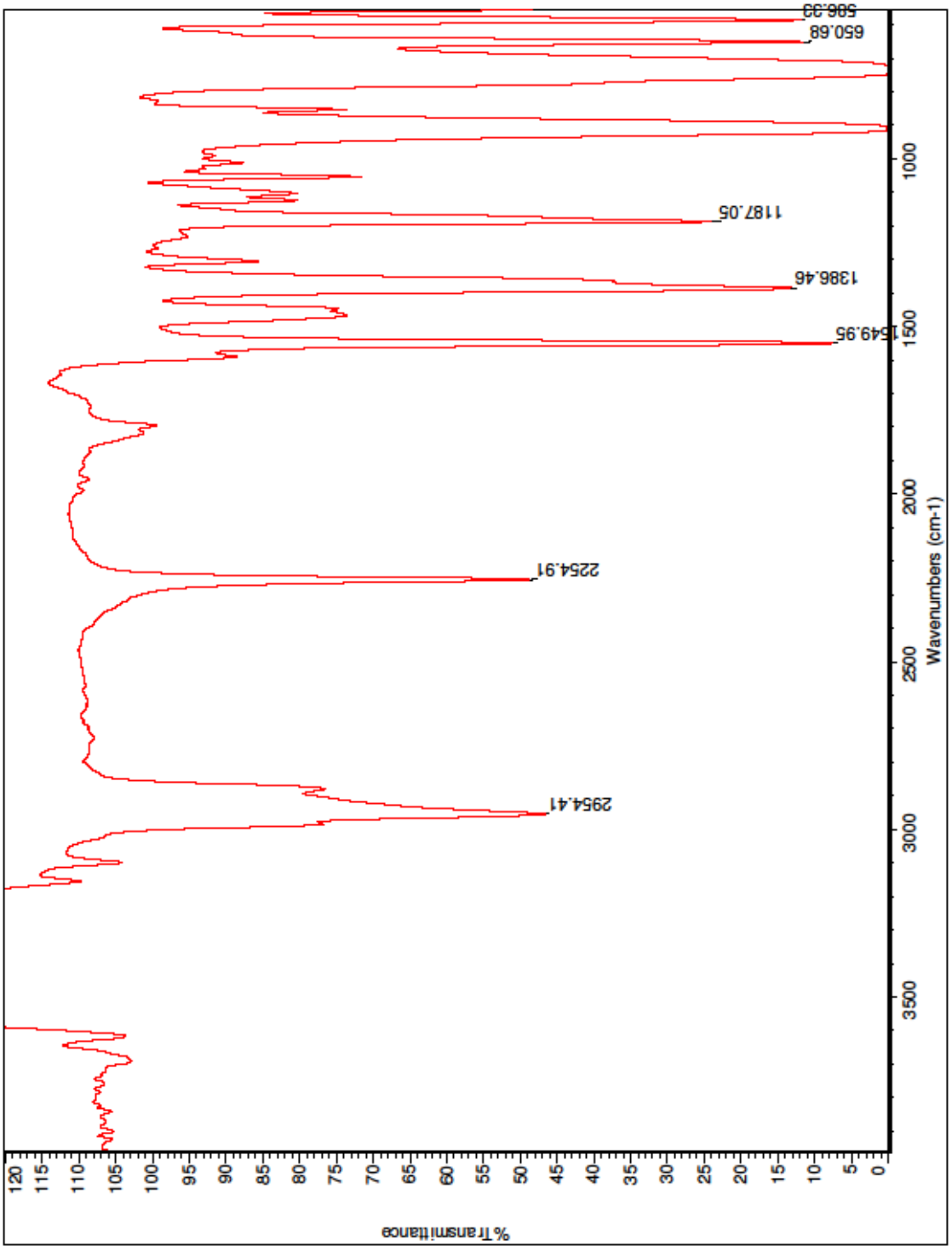


Figure 19: IR spectrum of 1,7,7-trimethylbicyclo[2.2.1] heptan-2-yl 2-nitrobenzenesulfonate **(6)**.

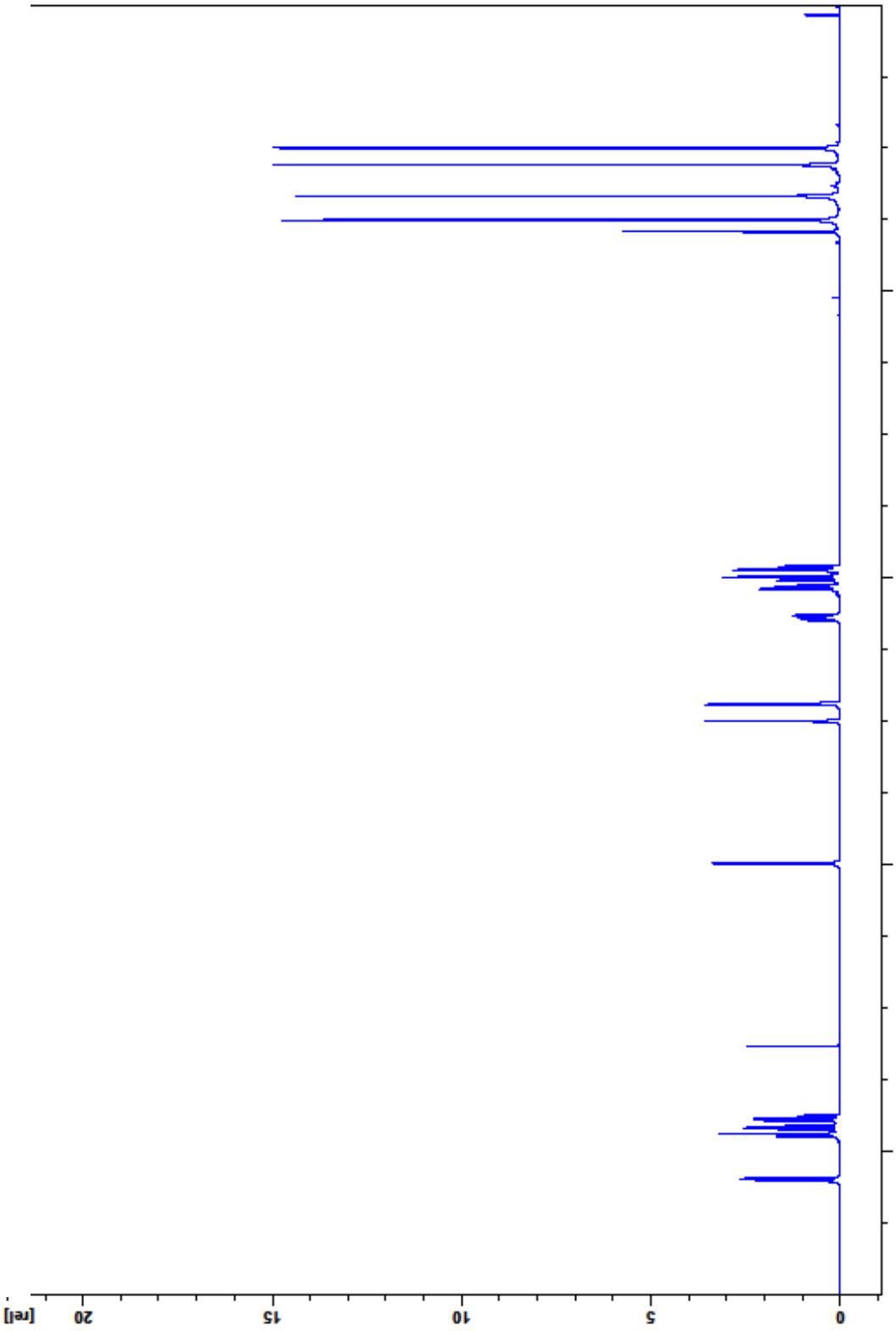


Figure 20: ^{1}H NMR spectrum of 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose-3-*O*-(2-nitrobenzenesulfonate) **(8)**.

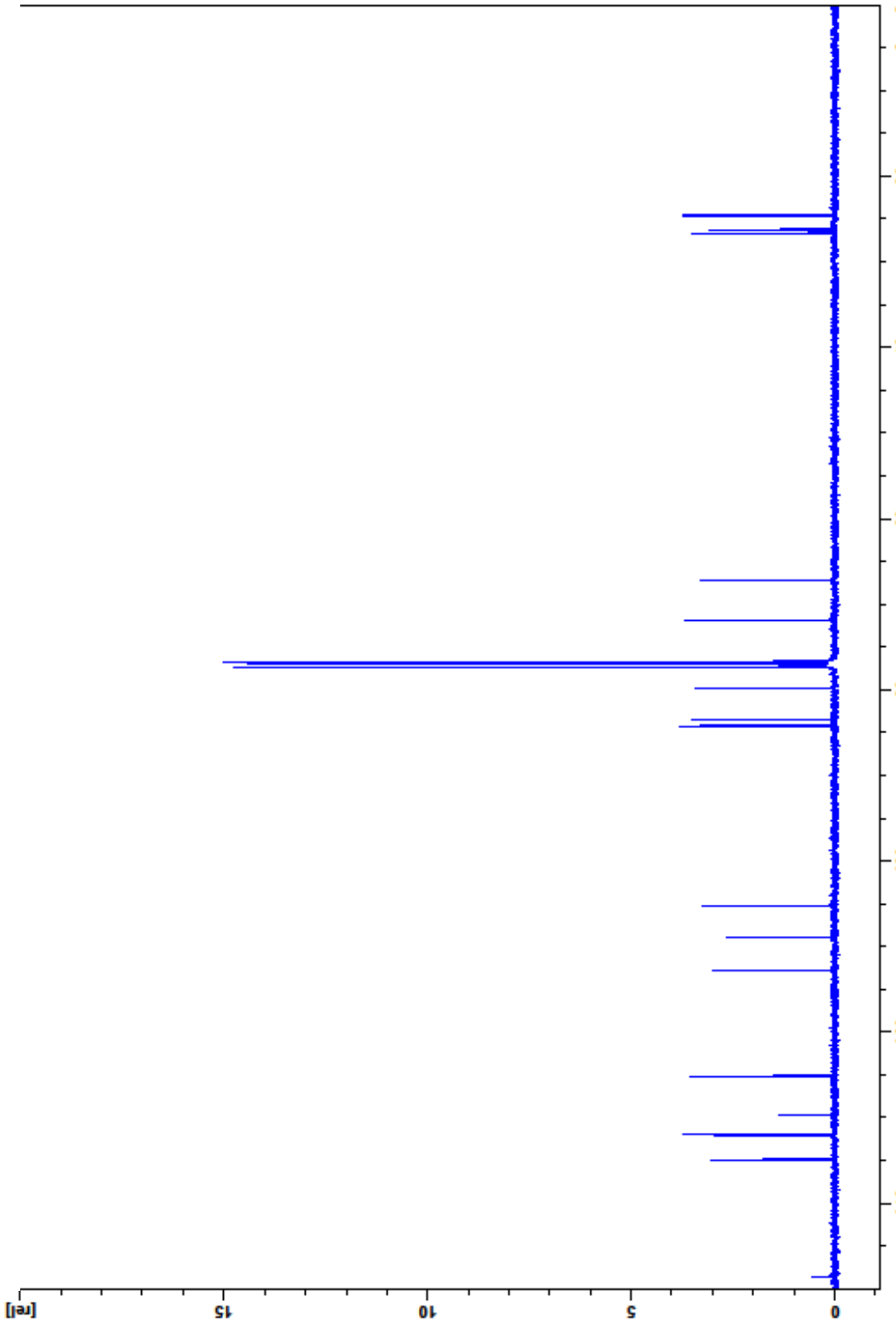


Figure 21: ^{13}C NMR spectrum of 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose-3-*O*-(2-nitrobenzenesulfonate) **(8)**.

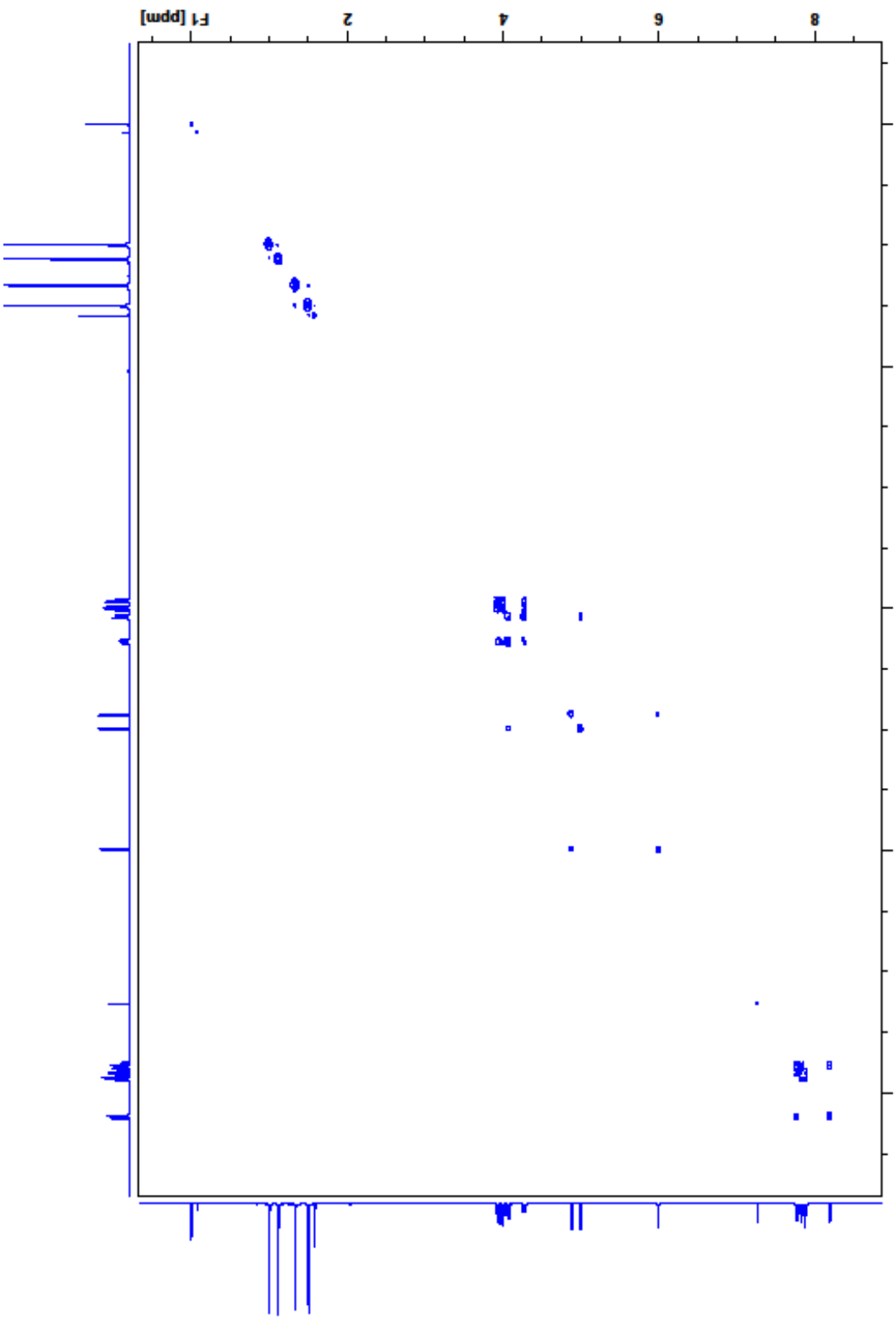


Figure 22: COSY NMR spectrum of 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose-3-*O*-(2-nitrobenzenesulfonate) **(8)**.

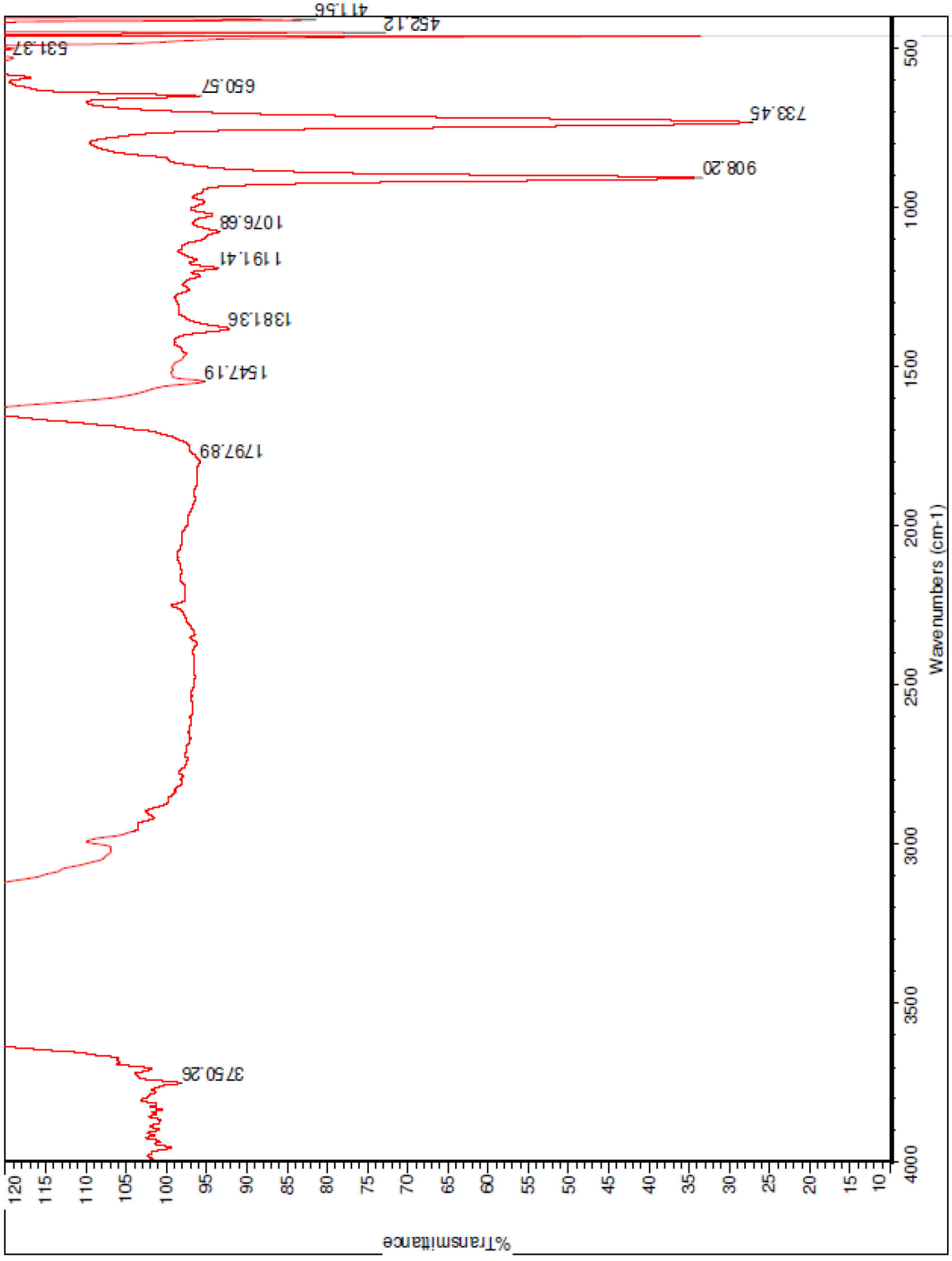


Figure 23: IR spectrum of 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose-3-*O*-(2-nitrobenzenesulfonate) **(8)**.

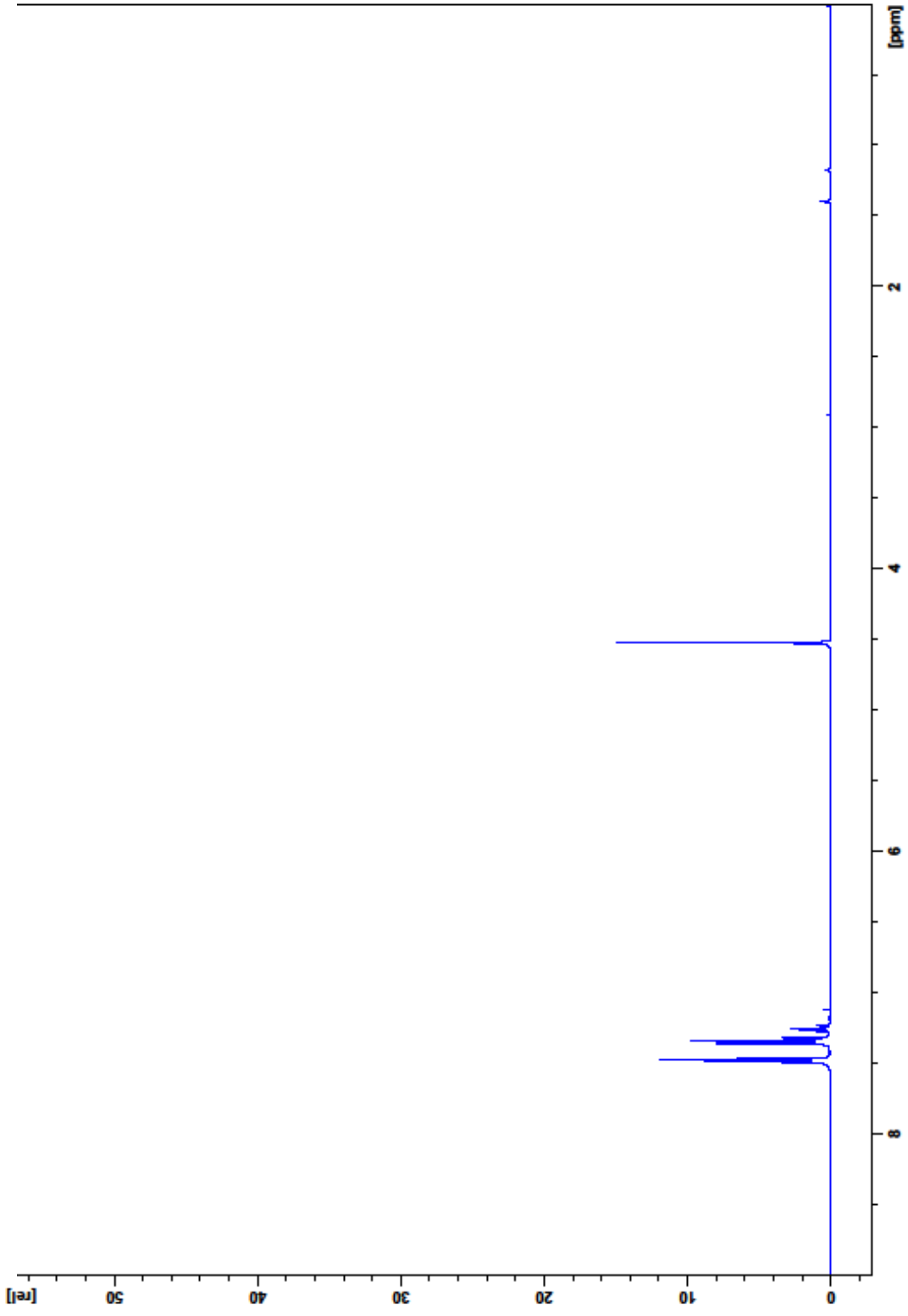


Figure 24: ^{1}H NMR spectrum of 4-biphenyl chloride (**10**).

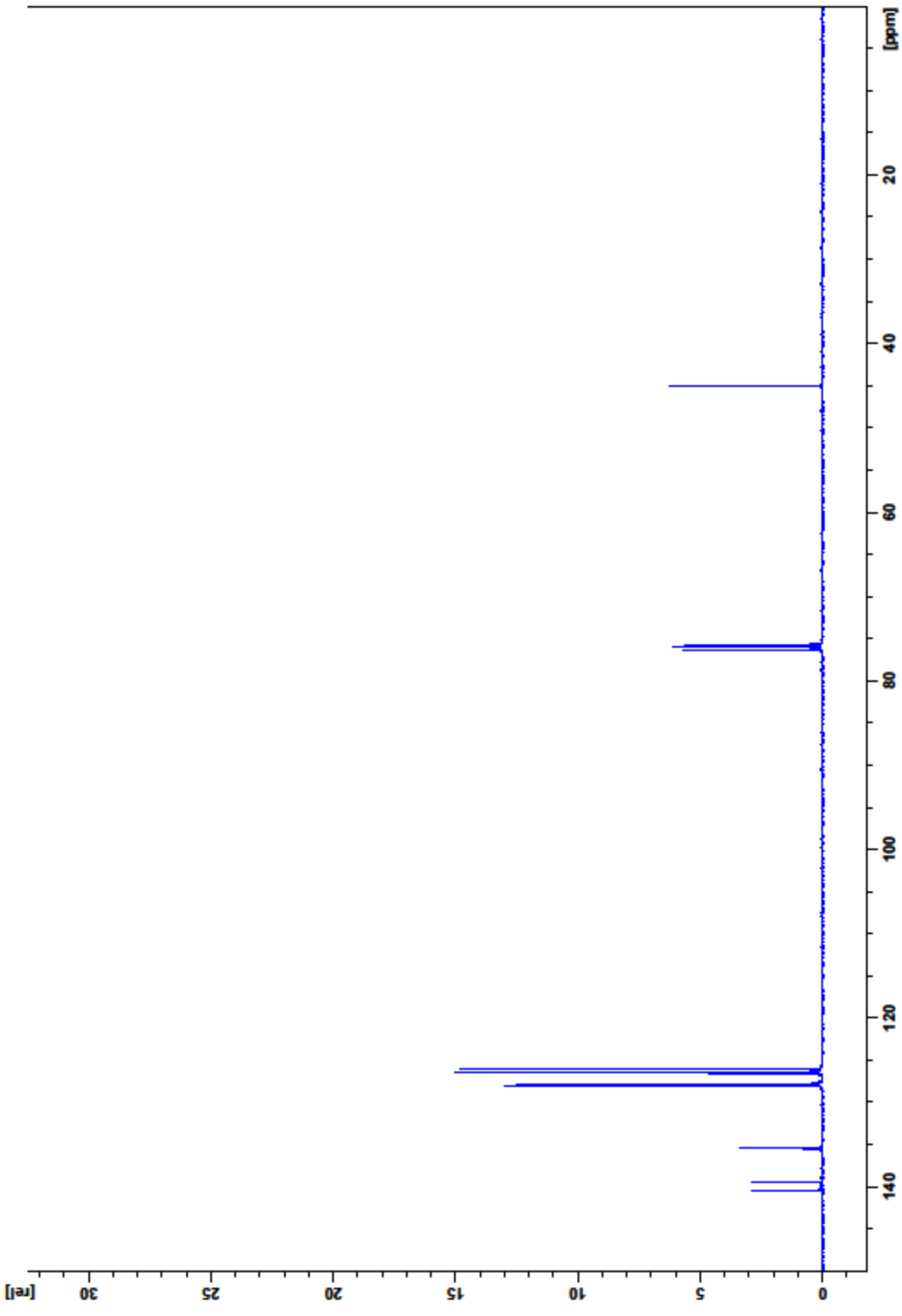


Figure 25: ^{13}C NMR spectrum of 4-biphenyl chloride **(10)**.

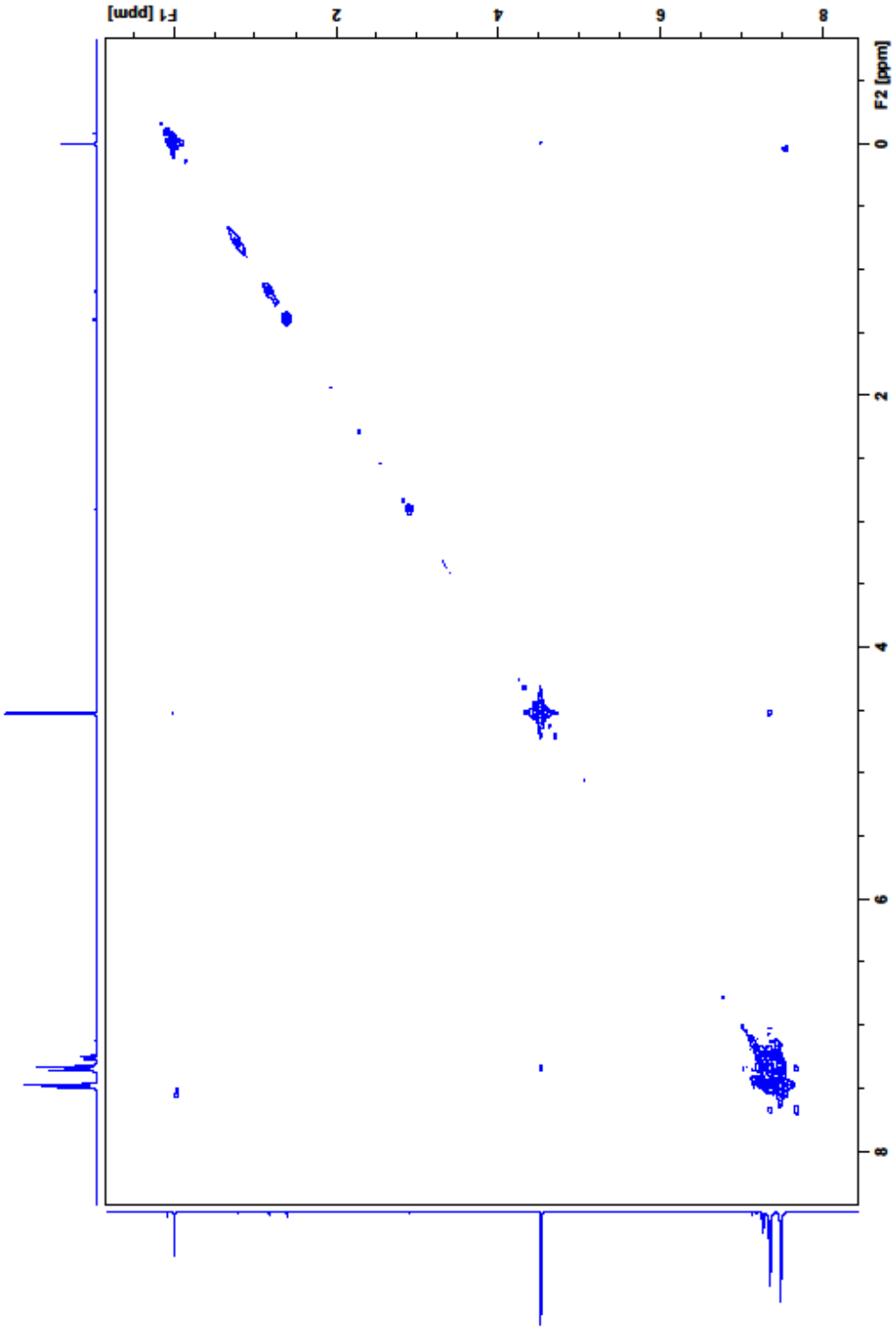


Figure 26: COSY NMR spectrum of 4-biphenyl chloride **(10)**.

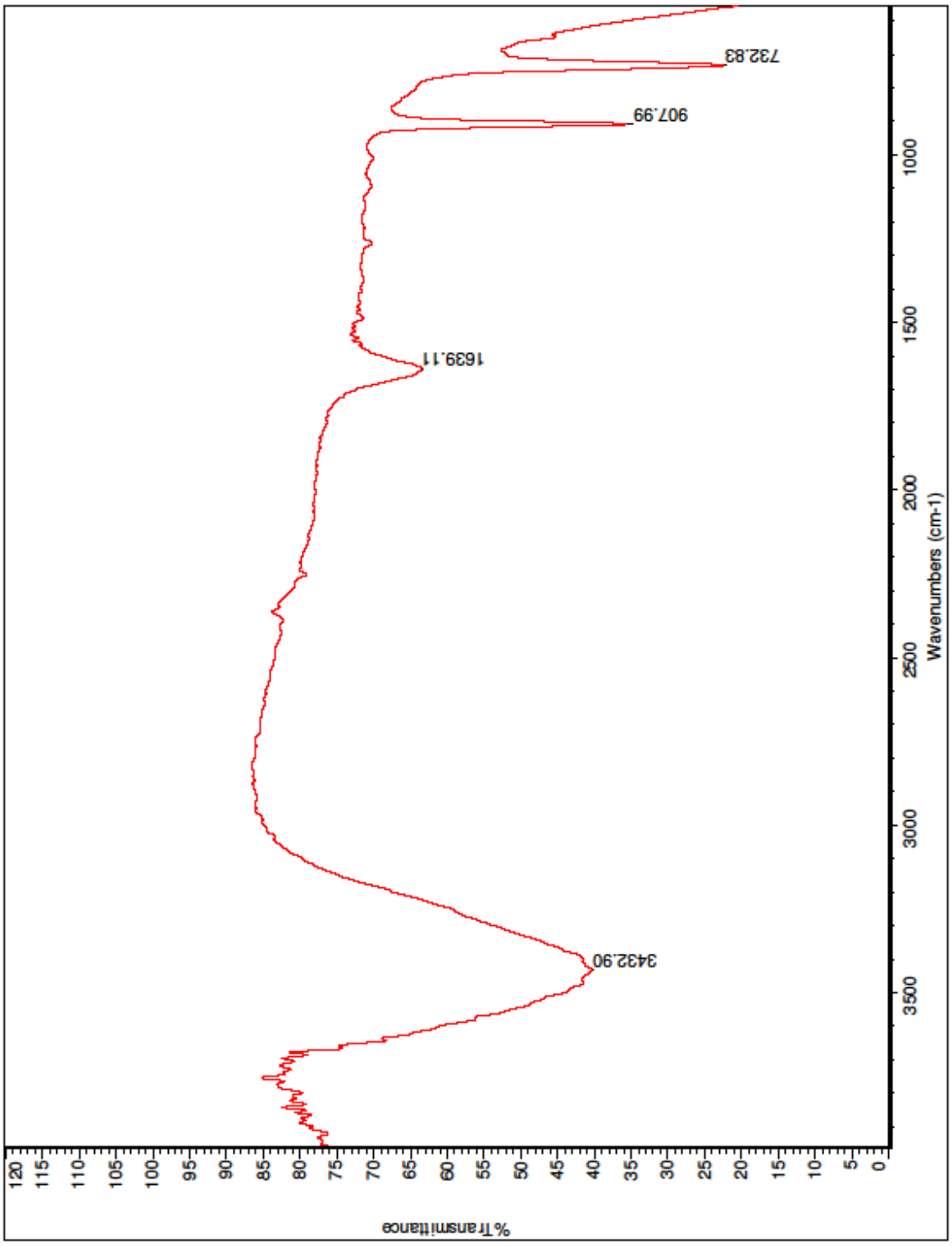


Figure 27: IR spectrum of 4-biphenyl chloride **(10)**.

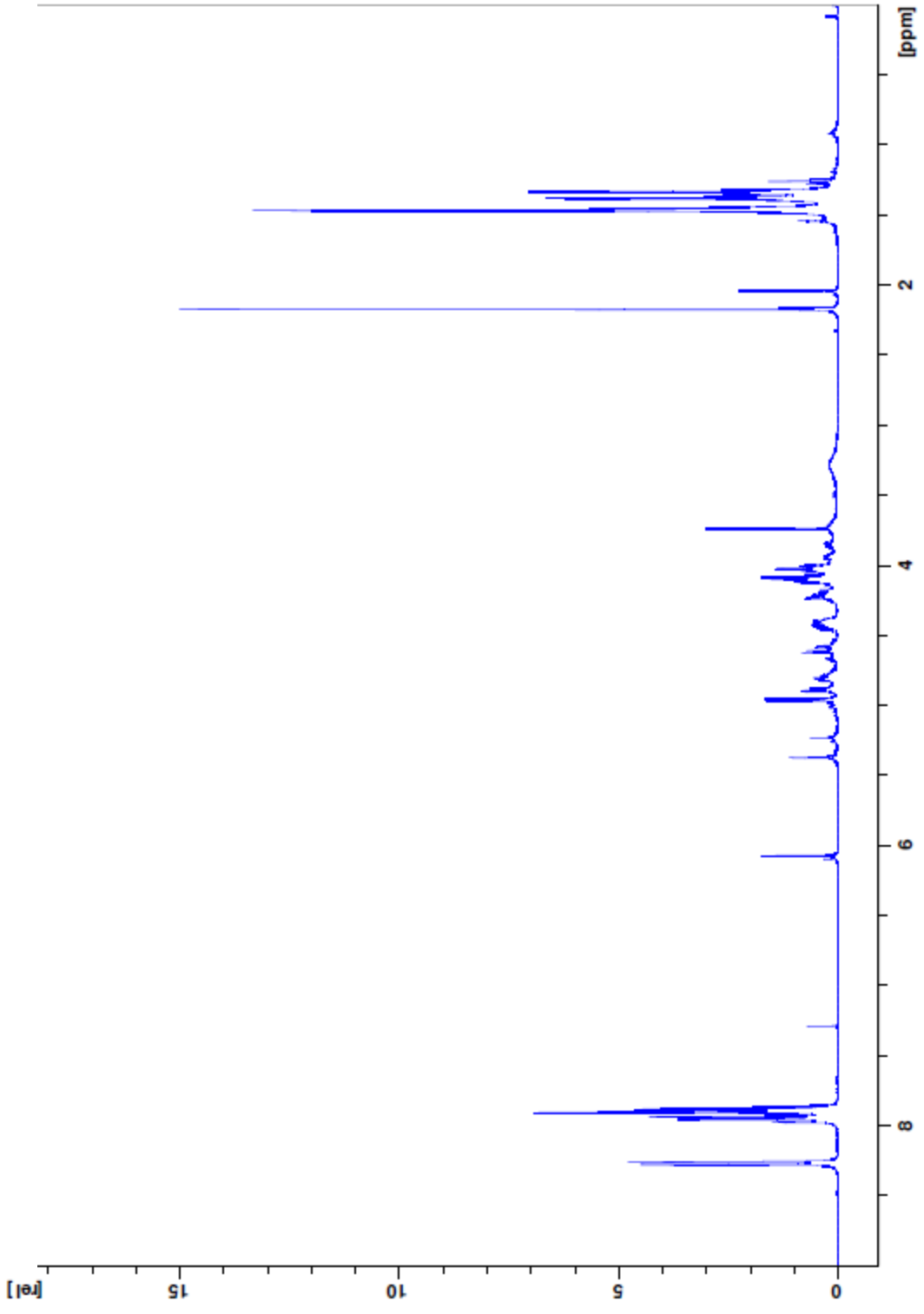


Figure 28: ^{1}H NMR spectrum of 2,3:5,6-di-*O*-isopropylidene-α/β-o-mannofuranosyl chloride **(12)**.

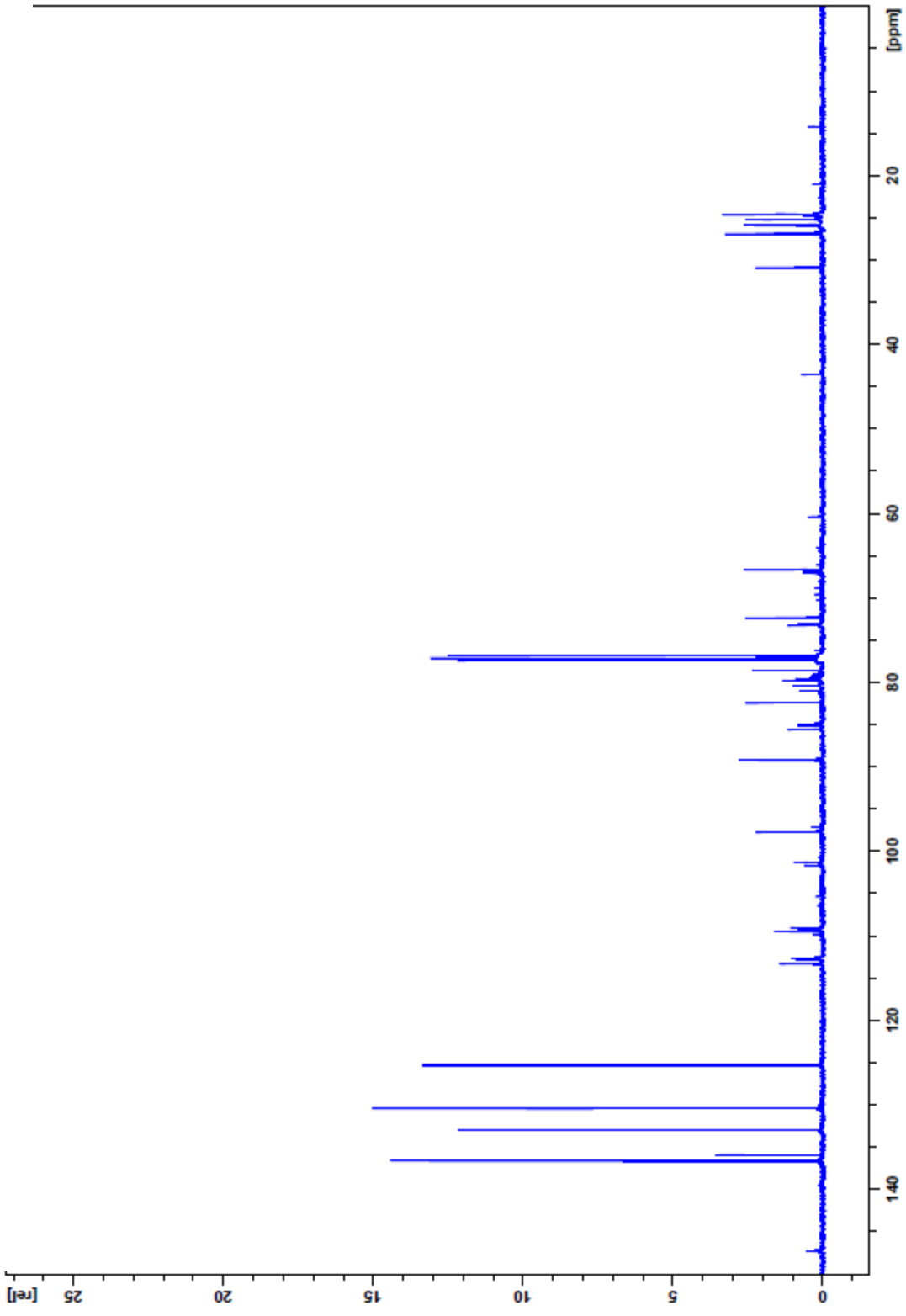


Figure 29: ^{13}C NMR spectrum of 2,3:5,6-di-*O*-isopropylidene-α/β-o-mannofuranosyl chloride **(12)**.

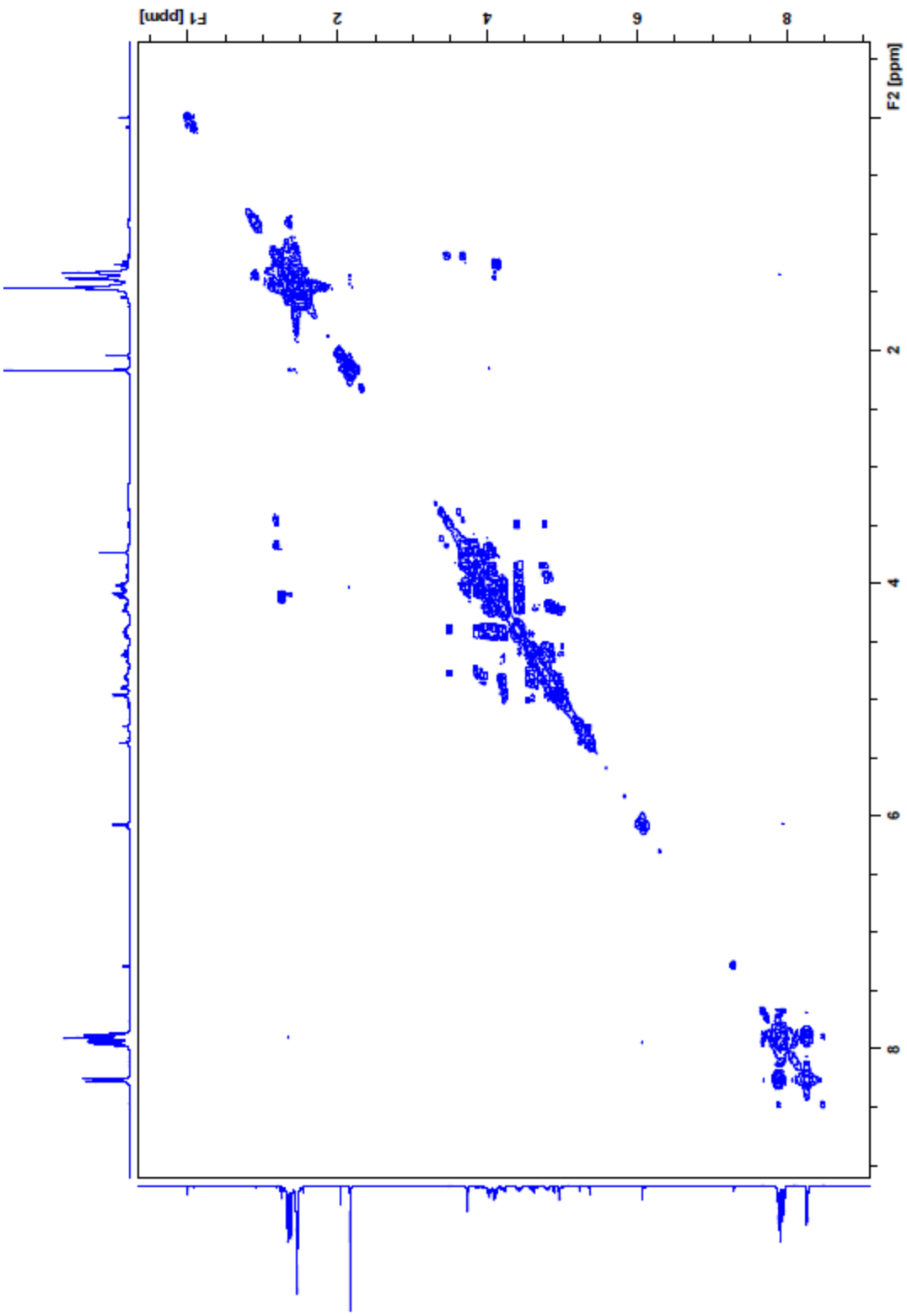


Figure 30: COSY NMR spectrum of 2,3:5,6-di-*O*-isopropylidene-α/β-o-mannofuranosyl chloride **(12)**.

Appendix B

X-Ray Crystallography

Diffraction data were collected on a Bruker AXS SMART APEX CCD diffractometer equipped with an ApexII area detector upgrade at room temperature or 100 K using monochromatic Mo Kα radiation with the omega scan technique. An Oxford Cryosystems series 600 variable temperature unit has been used. Data for the structures were collected and their unit cells determined using the Apex2 suite of programs (v2013.4-1, Bruker, 2012). Data were integrated using SAINT (V8.30C, Bruker, 2012) and corrected for absorption and other systematic errors using SADABS (2008/1, Bruker, 2008). Space groups were assigned using XPREP, and the structures were solved by direct methods using ShelXS (SHELXS-97, Sheldrick, 2008) and refined by full matrix least squares against F^2 with all reflections using SHELXL-2013 (Sheldrick, 2013). The graphical interface used was Shelxle Rev609 (Hübschle et al., 2011). H-atoms were treated using a riding model with $U_{iso}(H) = 1.2\ U_{eq}(C)$ for methylene and methyne C atoms, and $1.5\ U_{eq}(C)$ for methyl C atoms. For C-H distances and angles used, see the bond distance tables, below. Methyl H atoms were allowed to rotate at a fixed angle to best fit the experimental electron density.

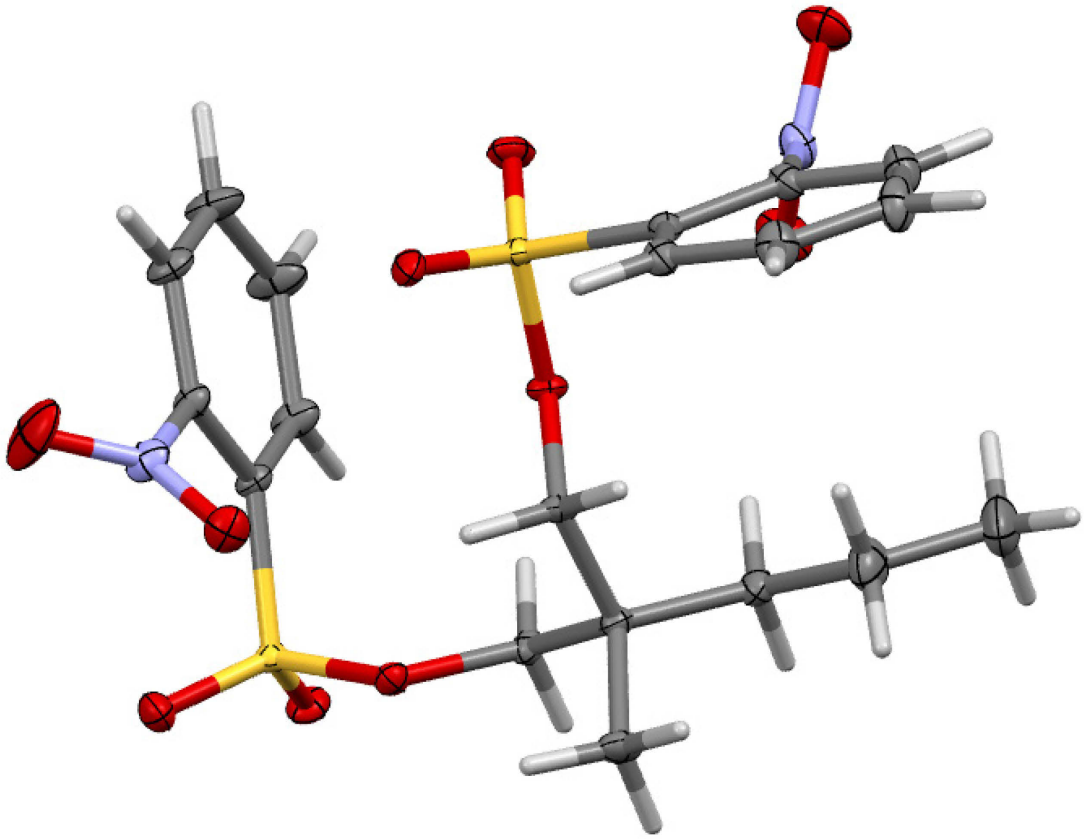
References:

Bruker (2012). APEX2, SAINT. Bruker AXS Inc., Madison, Wisconsin, USA.

Hübschle, C. B., Sheldrick, G. M. and Dittrich, B. (2011). ShelXle: a Qt graphical user interface for SHELXL, J. Appl. Cryst., 44, 1281-1284.

Sheldrick, G. M. (2008). Acta Cryst. A64, 112-122.

Sheldrick, G. M. (2013). SHELXL2013. University of Göttingen, Germany.



X-ray crystal structure of bis(sulfonate ester) **4**. Thermal ellipsoids are at the 50% probability level.

Table 1. Experimental details

2-methyl-2-propylpropane-1,3-diyl bis(2-nitrobenzenesulfonate) **(4)**

Crystal data	
Chemical formula	$C_{19}H_{22}N_2O_{10}S_2$
M_r	502.50
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	100
a, b, c (Å)	16.2486 (17), 8.2565 (9), 17.1666 (18)
β (°)	95.1414 (14)
V (Å^3)	2293.7 (4)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.29
Crystal size (mm)	0.55 × 0.48 × 0.18
Data collection	
Diffractometer	Bruker AXS *SMART APEX* CCD diffractometer
Absorption correction	Multi-scan Apex2 v2012.4-3 (Bruker, 2012)
T_{min}, T_{max}	0.621, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	22699, 7157, 6418
R_{int}	0.025
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.737
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.036, 0.100, 1.03
No. of reflections	7157
No. of parameters	300
No. of restraints	0
H-atom treatment	H-atom parameters constrained
P⟩$_{max}$, P⟩$_{min}$ (e Å^{-3})	0.64, -0.31

Table 2. Bond Lengths (Å)

C1—O1	1.4688 (13)	C10—H10	0.9500
C1—C2	1.5285 (15)	C11—C12	1.3893 (18)
C1—H1A	0.9900	C11—H11	0.9500
C1—H1B	0.9900	C12—C13	1.3805 (16)
C2—C6	1.5237 (15)	C12—H12	0.9500
C2—C7	1.5379 (15)	C13—N1	1.4748 (15)
C2—C3	1.5420 (16)	C14—C15	1.3943 (15)
C3—C4	1.5298 (18)	C14—C19	1.4003 (15)
C3—H3A	0.9900	C14—S2	1.7664 (11)
C3—H3B	0.9900	C15—C16	1.3939 (16)
C4—C5	1.524 (2)	C15—H15	0.9500
C4—H4A	0.9900	C16—C17	1.3875 (18)
C4—H4B	0.9900	C16—H16	0.9500
C5—H5A	0.9800	C17—C18	1.3922 (18)
C5—H5B	0.9800	C17—H17	0.9500
C5—H5C	0.9800	C18—C19	1.3811 (16)
C6—O6	1.4766 (12)	C18—H18	0.9500
C6—H6A	0.9900	C19—N2	1.4780 (15)
C6—H6B	0.9900	N1—O4	1.2156 (14)
C7—H7A	0.9800	N1—O5	1.2255 (14)
C7—H7B	0.9800	N2—O9	1.2207 (14)
C7—H7C	0.9800	N2—O10	1.2254 (14)
C8—C9	1.3919 (15)	O1—S1	1.5634 (8)
C8—C13	1.3994 (15)	O2—S1	1.4310 (9)
C8—S1	1.7701 (11)	O3—S1	1.4285 (9)
C9—C10	1.3950 (17)	O6—S2	1.5663 (8)
C9—H9	0.9500	O7—S2	1.4298 (9)
C10—C11	1.3879 (19)	O8—S2	1.4264 (9)

Table 3. Angles (º)

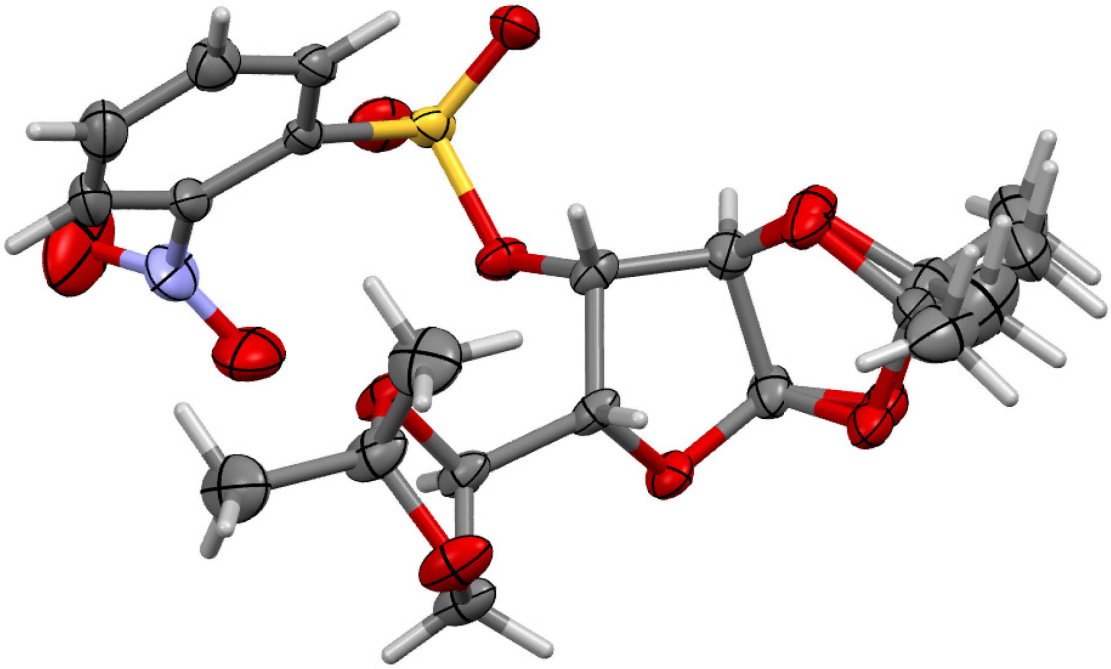
O1—C1—C2	107.62 (8)	C11—C10—H10	119.8
O1—C1—H1A	110.2	C9—C10—H10	119.8
C2—C1—H1A	110.2	C10—C11—C12	120.01 (12)
O1—C1—H1B	110.2	C10—C11—H11	120.0
C2—C1—H1B	110.2	C12—C11—H11	120.0
H1A—C1—H1B	108.5	C13—C12—C11	119.22 (11)
C6—C2—C1	110.12 (9)	C13—C12—H12	120.4
C6—C2—C7	106.33 (9)	C11—C12—H12	120.4
C1—C2—C7	110.36 (9)	C12—C13—C8	121.78 (10)
C6—C2—C3	112.24 (9)	C12—C13—N1	116.90 (10)
C1—C2—C3	105.89 (9)	C8—C13—N1	121.32 (10)
C7—C2—C3	111.95 (9)	C15—C14—C19	118.72 (10)
C4—C3—C2	116.53 (10)	C15—C14—S2	118.18 (8)
C4—C3—H3A	108.2	C19—C14—S2	123.09 (9)
C2—C3—H3A	108.2	C16—C15—C14	119.89 (11)
C4—C3—H3B	108.2	C16—C15—H15	120.1
C2—C3—H3B	108.2	C14—C15—H15	120.1
H3A—C3—H3B	107.3	C17—C16—C15	120.21 (11)
C5—C4—C3	111.50 (13)	C17—C16—H16	119.9
C5—C4—H4A	109.3	C15—C16—H16	119.9
C3—C4—H4A	109.3	C16—C17—C18	120.64 (11)
C5—C4—H4B	109.3	C16—C17—H17	119.7
C3—C4—H4B	109.3	C18—C17—H17	119.7
H4A—C4—H4B	108.0	C19—C18—C17	118.67 (11)
C4—C5—H5A	109.5	C19—C18—H18	120.7
C4—C5—H5B	109.5	C17—C18—H18	120.7
H5A—C5—H5B	109.5	C18—C19—C14	121.80 (11)
C4—C5—H5C	109.5	C18—C19—N2	116.67 (10)
H5A—C5—H5C	109.5	C14—C19—N2	121.53 (10)
H5B—C5—H5C	109.5	O4—N1—O5	124.25 (11)
O6—C6—C2	108.35 (8)	O4—N1—C13	118.24 (10)
O6—C6—H6A	110.0	O5—N1—C13	117.50 (10)
C2—C6—H6A	110.0	O9—N2—O10	125.33 (11)
O6—C6—H6B	110.0	O9—N2—C19	117.89 (10)
C2—C6—H6B	110.0	O10—N2—C19	116.73 (10)
H6A—C6—H6B	108.4	C1—O1—S1	117.87 (7)
C2—C7—H7A	109.5	C6—O6—S2	116.50 (6)

C2—C7—H7B	109.5	O3—S1—O2	119.85 (5)
H7A—C7—H7B	109.5	O3—S1—O1	105.77 (5)
C2—C7—H7C	109.5	O2—S1—O1	109.15 (5)
H7A—C7—H7C	109.5	O3—S1—C8	109.09 (5)
H7B—C7—H7C	109.5	O2—S1—C8	107.38 (5)
C9—C8—C13	118.44 (10)	O1—S1—C8	104.60 (5)
C9—C8—S1	117.64 (8)	O8—S2—O7	119.62 (5)
C13—C8—S1	123.74 (8)	O8—S2—O6	105.62 (5)
C8—C9—C10	120.07 (11)	O7—S2—O6	110.10 (5)
C8—C9—H9	120.0	O8—S2—C14	109.56 (5)
C10—C9—H9	120.0	O7—S2—C14	107.76 (5)
C11—C10—C9	120.45 (12)	O6—S2—C14	102.92 (5)

Table 4. Torsion Angles (º)

O1—C1—C2—C6	-57.72 (11)	C15—C14—C19—N2	-178.78 (10)
O1—C1—C2—C7	59.38 (11)	S2—C14—C19—N2	2.55 (16)
O1—C1—C2—C3	-179.28 (8)	C12—C13—N1—O4	-129.59 (12)
C6—C2—C3—C4	62.91 (13)	C8—C13—N1—O4	49.51 (16)
C1—C2—C3—C4	-176.90 (10)	C12—C13—N1—O5	49.10 (17)
C7—C2—C3—C4	-56.59 (14)	C8—C13—N1—O5	-131.80 (13)
C2—C3—C4—C5	-177.60 (12)	C18—C19—N2—O9	113.75 (13)
C1—C2—C6—O6	-57.47 (11)	C14—C19—N2—O9	-65.80 (15)
C7—C2—C6—O6	-177.03 (8)	C18—C19—N2—O10	-63.84 (15)
C3—C2—C6—O6	60.24 (11)	C14—C19—N2—O10	116.61 (13)
C13—C8—C9—C10	1.33 (18)	C2—C1—O1—S1	157.94 (7)
S1—C8—C9—C10	176.57 (10)	C2—C6—O6—S2	-167.49 (7)
C8—C9—C10—C11	-1.7 (2)	C1—O1—S1—O3	172.52 (7)
C9—C10—C11—C12	0.5 (2)	C1—O1—S1—O2	42.31 (9)
C10—C11—C12—C13	1.0 (2)	C1—O1—S1—C8	-72.35 (8)
C11—C12—C13—C8	-1.40 (19)	C9—C8—S1—O3	-140.47 (9)
C11—C12—C13—N1	177.70 (12)	C13—C8—S1—O3	34.49 (11)
C9—C8—C13—C12	0.23 (17)	C9—C8—S1—O2	-9.15 (11)
S1—C8—C13—C12	-174.70 (9)	C13—C8—S1—O2	165.81 (9)
C9—C8—C13—N1	-178.83 (10)	C9—C8—S1—O1	106.74 (9)
S1—C8—C13—N1	6.25 (15)	C13—C8—S1—O1	-78.30 (10)

C19—C14—C15—C16	-2.08 (17)	C6—O6—S2—O8	-179.73 (7)
S2—C14—C15—C16	176.66 (9)	C6—O6—S2—O7	-49.27 (8)
C14—C15—C16—C17	0.19 (19)	C6—O6—S2—C14	65.39 (8)
C15—C16—C17—C18	2.2 (2)	C15—C14—S2—O8	146.25 (9)
C16—C17—C18—C19	-2.6 (2)	C19—C14—S2—O8	-35.07 (11)
C17—C18—C19—C14	0.61 (19)	C15—C14—S2—O7	14.60 (10)
C17—C18—C19—N2	-178.94 (12)	C19—C14—S2—O7	-166.72 (9)
C15—C14—C19—C18	1.70 (17)	C15—C14—S2—O6	-101.75 (9)
S2—C14—C19—C18	-176.98 (9)	C19—C14—S2—O6	76.94 (10)



X-ray crystal structure of sulfonate ester **8**.

Table 1. Experimental details

1,2:5,6-di-*O*-isopropylidene-D-glucofuranose-3-*O*-(2-nitrobenzenesulfonate) **(8)**

Crystal data	
Chemical formula	$C_{18}H_{23}NO_{10}S$
M_r	445.43
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	150
a, b, c (Å)	12.6123 (8), 12.8792 (8), 13.6154 (8)
V (Å^3)	2211.6 (2)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.20
Crystal size (mm)	0.55 × 0.45 × 0.39
Data collection	
Diffractometer	Bruker AXS *SMART APEX* CCD diffractometer
Absorption correction	Multi-scan Apex2 v2013.4-1 (Bruker, 2012)
T_{min}, T_{max}	0.651, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	29258, 6860, 6614
R_{int}	0.022
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.732
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.033, 0.091, 1.04
No. of reflections	6860
No. of parameters	311
No. of restraints	16
H-atom treatment	H-atom parameters constrained
P⟩$_{max}$, P⟩$_{min}$ (e Å^{-3})	0.44, -0.23
Absolute structure	Flack x determined using 2837 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons and Flack (2004), Acta Cryst. A60, s61).
Absolute structure parameter	0.003 (12)

Table 2. Bond Lengths (Å)

O2—C1	1.397 (10)	O6—C6	1.432 (2)
O2—C7	1.444 (9)	O9—N1	1.211 (2)
O3—C2	1.415 (12)	O10—N1	1.227 (2)
O3—C7	1.432 (12)	N1—C14	1.473 (2)
C7—C8	1.479 (9)	C1—C2	1.547 (2)
C7—C9	1.526 (9)	C1—H1	1.0000
C8—H8A	0.9800	C2—C3	1.524 (2)
C8—H8B	0.9800	C2—H2	1.0000
C8—H8C	0.9800	C3—C4	1.5259 (19)
C9—H9A	0.9800	C3—H3	1.0000
C9—H9B	0.9800	C4—C5	1.518 (2)
C9—H9C	0.9800	C4—H4	1.0000
O2B—C7B	1.428 (11)	C5—C6	1.520 (2)
O2B—C1	1.445 (11)	C5—H5	1.0000
O3B—C2	1.423 (14)	C6—H6A	0.9900
O3B—C7B	1.444 (13)	C6—H6B	0.9900
C7B—C8B	1.503 (10)	C10—C11	1.505 (3)
C7B—C9B	1.518 (10)	C10—C12	1.520 (3)
C8B—H8D	0.9800	C11—H11A	0.9800
C8B—H8E	0.9800	C11—H11B	0.9800
C8B—H8F	0.9800	C11—H11C	0.9800
C9B—H9D	0.9800	C12—H12A	0.9800
C9B—H9E	0.9800	C12—H12B	0.9800
C9B—H9F	0.9800	C12—H12C	0.9800
S1—O8	1.4232 (12)	C13—C14	1.3961 (18)
S1—O7	1.4277 (11)	C13—C18	1.396 (2)
S1—O4	1.5727 (10)	C14—C15	1.378 (3)
S1—C13	1.7614 (15)	C15—C16	1.389 (3)
O1—C1	1.4121 (18)	C15—H15	0.9500
O1—C4	1.4355 (15)	C16—C17	1.385 (2)
O4—C3	1.4628 (16)	C16—H16	0.9500
O5—C5	1.4287 (16)	C17—C18	1.391 (2)
O5—C10	1.4392 (19)	C17—H17	0.9500
O6—C10	1.426 (2)	C18—H18	0.9500

Table 3. Angles (º)

C1—O2—C7	111.3 (8)	C3—C2—C1	103.73 (12)
C2—O3—C7	106.6 (10)	O3—C2—H2	112.3
O3—C7—O2	104.1 (10)	C3—C2—H2	112.3
O3—C7—C8	108.7 (10)	C1—C2—H2	112.3
O2—C7—C8	108.5 (7)	O4—C3—C2	108.53 (11)
O3—C7—C9	111.2 (13)	O4—C3—C4	107.71 (11)
O2—C7—C9	109.4 (7)	C2—C3—C4	102.77 (11)
C8—C7—C9	114.4 (7)	O4—C3—H3	112.4
C7—C8—H8A	109.5	C2—C3—H3	112.4
C7—C8—H8B	109.5	C4—C3—H3	112.4
H8A—C8—H8B	109.5	O1—C4—C5	109.61 (12)
C7—C8—H8C	109.5	O1—C4—C3	104.03 (10)
H8A—C8—H8C	109.5	C5—C4—C3	115.13 (11)
H8B—C8—H8C	109.5	O1—C4—H4	109.3
C7—C9—H9A	109.5	C5—C4—H4	109.3
C7—C9—H9B	109.5	C3—C4—H4	109.3
H9A—C9—H9B	109.5	O5—C5—C4	107.62 (12)
C7—C9—H9C	109.5	O5—C5—C6	103.23 (11)
H9A—C9—H9C	109.5	C4—C5—C6	113.57 (12)
H9B—C9—H9C	109.5	O5—C5—H5	110.7
C7B—O2B—C1	108.5 (8)	C4—C5—H5	110.7
C2—O3B—C7B	110.9 (11)	C6—C5—H5	110.7
O2B—C7B—O3B	104.4 (11)	O6—C6—C5	102.28 (12)
O2B—C7B—C8B	109.6 (7)	O6—C6—H6A	111.3
O3B—C7B—C8B	108.2 (12)	C5—C6—H6A	111.3
O2B—C7B—C9B	111.7 (8)	O6—C6—H6B	111.3
O3B—C7B—C9B	108.2 (14)	C5—C6—H6B	111.3
C8B—C7B—C9B	114.2 (7)	H6A—C6—H6B	109.2
C7B—C8B—H8D	109.5	O6—C10—O5	105.90 (11)
C7B—C8B—H8E	109.5	O6—C10—C11	108.78 (18)
H8D—C8B—H8E	109.5	O5—C10—C11	109.07 (16)
C7B—C8B—H8F	109.5	O6—C10—C12	112.13 (16)
H8D—C8B—H8F	109.5	O5—C10—C12	107.48 (17)
H8E—C8B—H8F	109.5	C11—C10—C12	113.18 (16)
C7B—C9B—H9D	109.5	C10—C11—H11A	109.5
C7B—C9B—H9E	109.5	C10—C11—H11B	109.5
H9D—C9B—H9E	109.5	H11A—C11—H11B	109.5

C7B—C9B—H9F	109.5	C10—C11—H11C	109.5
H9D—C9B—H9F	109.5	H11A—C11—H11C	109.5
H9E—C9B—H9F	109.5	H11B—C11—H11C	109.5
O8—S1—O7	119.63 (7)	C10—C12—H12A	109.5
O8—S1—O4	105.64 (7)	C10—C12—H12B	109.5
O7—S1—O4	109.07 (6)	H12A—C12—H12B	109.5
O8—S1—C13	108.98 (7)	C10—C12—H12C	109.5
O7—S1—C13	107.77 (7)	H12A—C12—H12C	109.5
O4—S1—C13	104.80 (6)	H12B—C12—H12C	109.5
C1—O1—C4	107.69 (11)	C14—C13—C18	118.44 (14)
C3—O4—S1	117.36 (9)	C14—C13—S1	123.65 (12)
C5—O5—C10	109.08 (11)	C18—C13—S1	117.75 (10)
C10—O6—C6	106.59 (12)	C15—C14—C13	121.76 (16)
O9—N1—O10	124.3 (2)	C15—C14—N1	117.20 (14)
O9—N1—C14	118.50 (15)	C13—C14—N1	121.05 (16)
O10—N1—C14	117.15 (18)	C14—C15—C16	119.16 (15)
O2—C1—O1	117.1 (5)	C14—C15—H15	120.4
O1—C1—O2B	103.6 (4)	C16—C15—H15	120.4
O2—C1—C2	102.8 (5)	C17—C16—C15	120.27 (17)
O1—C1—C2	107.38 (11)	C17—C16—H16	119.9
O2B—C1—C2	106.0 (5)	C15—C16—H16	119.9
O2—C1—H1	109.7	C16—C17—C18	120.30 (17)
O1—C1—H1	109.7	C16—C17—H17	119.9
C2—C1—H1	109.7	C18—C17—H17	119.9
O3—C2—C3	109.4 (10)	C17—C18—C13	120.05 (14)
O3B—C2—C3	105.7 (12)	C17—C18—H18	120.0
O3—C2—C1	106.5 (7)	C13—C18—H18	120.0
O3B—C2—C1	103.1 (8)		

Table 4. Torsion Angles (º)

C2—O3—C7—O2	-30 (2)	O3B—C2—C3—C4	-86.4 (11)
C2—O3—C7—C8	-145.7 (14)	C1—C2—C3—C4	21.73 (14)
C2—O3—C7—C9	87.5 (18)	C1—O1—C4—C5	161.19 (11)
C1—O2—C7—O3	25.2 (13)	C1—O1—C4—C3	37.57 (14)
C1—O2—C7—C8	140.9 (7)	O4—C3—C4—O1	78.36 (12)
C1—O2—C7—C9	-93.7 (8)	C2—C3—C4—O1	-36.13 (13)
C1—O2B—C7B—O3B	25.8 (15)	O4—C3—C4—C5	-41.60 (14)
C1—O2B—C7B—C8B	141.5 (7)	C2—C3—C4—C5	-156.09 (12)
C1—O2B—C7B—C9B	-90.9 (9)	C10—O5—C5—C4	-103.01 (15)
C2—O3B—C7B—O2B	-27 (2)	C10—O5—C5—C6	17.37 (18)
C2—O3B—C7B—C8B	-143.6 (18)	O1—C4—C5—O5	-170.07 (10)
C2—O3B—C7B—C9B	92 (2)	C3—C4—C5—O5	-53.23 (15)
O8—S1—O4—C3	161.79 (10)	O1—C4—C5—C6	76.31 (14)
O7—S1—O4—C3	32.01 (11)	C3—C4—C5—C6	-166.85 (12)
C13—S1—O4—C3	-83.16 (10)	C10—O6—C6—C5	35.84 (18)
C7—O2—C1—O1	-127.4 (5)	O5—C5—C6—O6	-32.20 (17)
C7—O2—C1—O2B	-115 (4)	C4—C5—C6—O6	84.02 (15)
C7—O2—C1—C2	-10.0 (7)	C6—O6—C10—O5	-25.8 (2)
C4—O1—C1—O2	91.5 (5)	C6—O6—C10—C11	-142.92 (16)
C4—O1—C1—O2B	88.5 (5)	C6—O6—C10—C12	91.13 (18)
C4—O1—C1—C2	-23.32 (15)	C5—O5—C10—O6	4.2 (2)
C7B—O2B—C1—O2	62 (4)	C5—O5—C10—C11	121.11 (16)
C7B—O2B—C1—O1	-128.9 (6)	C5—O5—C10—C12	-115.83 (16)
C7B—O2B—C1—C2	-16.0 (8)	O8—S1—C13—C14	33.57 (13)
C7—O3—C2—O3B	82 (11)	O7—S1—C13—C14	164.82 (11)
C7—O3—C2—C3	136.1 (14)	O4—S1—C13—C14	-79.12 (12)
C7—O3—C2—C1	25 (2)	O8—S1—C13—C18	-141.82 (11)
C7B—O3B—C2—O3	-107 (13)	O7—S1—C13—C18	-10.58 (12)
C7B—O3B—C2—C3	125.3 (18)	O4—S1—C13—C18	105.49 (10)
C7B—O3B—C2—C1	17 (2)	C18—C13—C14—C15	-1.7 (2)
O2—C1—C2—O3	-9.0 (13)	S1—C13—C14—C15	-177.05 (12)
O1—C1—C2—O3	115.1 (12)	C18—C13—C14—N1	178.43 (14)
O2B—C1—C2—O3	4.9 (13)	S1—C13—C14—N1	3.1 (2)

O2—C1—C2—O3B	-14.3 (14)	O9—N1—C14—C15	-124.9 (2)
O1—C1—C2—O3B	109.8 (14)	O10—N1—C14—C15	55.8 (3)
O2B—C1—C2—O3B	-0.4 (14)	O9—N1—C14—C13	55.0 (3)
O2—C1—C2—C3	-124.4 (5)	O10—N1—C14—C13	-124.3 (2)
O1—C1—C2—C3	-0.26 (16)	C13—C14—C15—C16	0.8 (2)
O2B—C1—C2—C3	-110.5 (5)	N1—C14—C15—C16	-179.29 (16)
S1—O4—C3—C2	-99.99 (12)	C14—C15—C16—C17	0.7 (3)
S1—O4—C3—C4	149.42 (9)	C15—C16—C17—C18	-1.4 (3)
O3—C2—C3—O4	154.5 (10)	C16—C17—C18—C13	0.5 (2)
O3B—C2—C3—O4	159.7 (11)	C14—C13—C18—C17	1.01 (19)
C1—C2—C3—O4	-92.16 (13)	S1—C13—C18—C17	176.65 (11)
O3—C2—C3—C4	-91.6 (10)		