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The Synthesis of Chiral Building Blocks Using Beta-Hydroxy Sulfoxide Dianions

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The Synthesis of Chiral Building Blocks Using Beta-Hydroxy Sulfoxide Dianions

by

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VITA

Carla M. Edwards was born in Green Bay, Wisconsin on August 5, 1960 to Roger Edwards and Helen Parkansky Edwards. After graduating from St. Joseph Academy in 1978, Carla attended UW-Milwaukee and UW-Oshkosh where she received a Bachelor of Science degree in Zoology. Carla then attended UW-Madison where she earned a Bachelor of Science in Biochemistry in 1985. In June of 1985, Carla joined Abbott Laboratories where she is currently employed as an Associate Scientist in Pharmaceutical Discovery. In January of 1988, Carla enrolled as a part-time student in the graduate school of Loyola University of Chicago Department of Chemistry. She expects to receive a Master of Science degree in May 1992.

In September 1985, Carla married Bradley P. Nelson, J.D. On June 7, 1991, Carla and Brad welcomed Andrew Edwards Nelson to the world. The Nelsons make their home in Evanston with their son Andrew, German shorthaired pointer, Sam and domestic shorthaired feline, Chester.

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ABBREVIATIONS

THF: Tetrahydrofuran

DMPU: 1,3-Dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone

RT: Room temperature: 25 ^{o}C

DABCO: 1,4-Diazabicyclo[2.2.2]octane

DMSO: Methyl sulfoxide

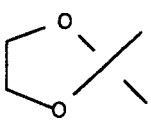
DMS: Dimethyl sulfide

NCS: N-Chlorosuccinimide

N_2: Nitrogen gas

mCPBA: Metachloroperbenzoic acid

DMF: N,N-Dimethyl formamide



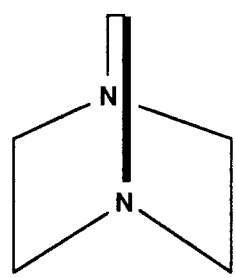
;Isopropylidene

CHAPTER I

INTRODUCTION

The generation of anions from activated carbons has been used extensively by synthetic organic chemists as a means of carbon-carbon bond formation and as a way of introducing unique functional groups into molecules through electrophilic condensation reactions.[1] Depending on the source of activation, the conditions needed for abstraction of a proton from the activated carbon could range from mildly basic to strongly basic with the possible use of co-solvents such a DABCO (1,4-Diazabicyclo[2.2.2]octane) (**Figure 1**) or DMPU (1,3-Dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone) (**Figure 2**) to help stabilize the incipient anion.[2,3]

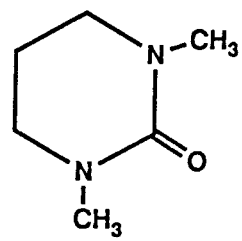
Figure 1



DABCO

Although these reactions generally resulted in minimal side product formation and moderate to good yields, the method was limited to simple molecules that possessed little diverse functionality. From a synthetic standpoint, it was desirable to develop methods that would incorporate the favorable attributes of anion chemistry but be able to extend this to polyfunctional, biologically important precursors.

Figure 2

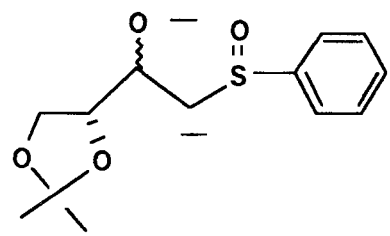


DMPU

Fortuitously, in 1958, Harris et al.[4] published a paper detailing the isolation of a terminally alkylated compound from the dipotassium salt of benzylacetone. Since that publication, the use of dianions as means of carbon-carbon bond formation and regioselective condensation in polyfunctional molecules has become increasingly popular.[5,6,7] In particular, the use of O,C prochiral sulfur dianions (Figure 3) in condensation reactions has been widely cited in the literature as a tool for carbon-carbon bond formation,

stereoselective generation of chiral centers and as a source of building blocks for natural product synthesis.[8,9,10]

Figure 3



Of all the O,C sulfur dianions cited in the literature, the resonance-stabilized, sulfone dianion is one of the most widely investigated. Beta-hydroxy sulfone dianions have been successfully reacted with alkyl halides, aldehydes and ketones.[8,9,10] The stereochemistry of the prochiral chiral centers was established by the degree of chelation of the metal cation with the oxyanion and oxygen sulfonyl group. The stereochemistry of the product also was found to be dependent on the choice of solvent and electrophile. The use of THF as a solvent coupled with a bulky electrophile favored the formation of erythro isomers in the major product.[10,11] Beta-hydroxy sulfone dianions have been successfully utilized to produce natural product building blocks such as 2(5H)-furanones and optically active lactones (1).[8,12] Beta-hydroxy sulfoxide dianions also have been generated and reacted with D_2O, alkyl halides and aldehydes.[9,13] The stereochemical outcomes of

these prochiral additions varied with the reaction time as well as the degree of chelation of metal cation with the sulfinyl group and oxyanion.[13] Finally, a beta-hydroxy sulfide dianion has been postulated as the reactive intermediate in the conversion of 2-hydroxy-1,3-bis-(phenylthio)-propane to the corresponding cyclopropanol (2).[14] The dearth of literature precedent in this area suggests the degree of difficulty associated with the generation of a non-resonance stabilized carbanion beta to an oxyanion.

CHAPTER II

STATEMENT OF PURPOSE

The work presented in this thesis represents the first attempt at combining a chiral building block structure within an O,C sulfur stabilized dianion framework to make a pro-sugar building block. In particular, we investigated the selective coupling of a chiral beta-hydroxy sulfoxide dianion with carbonyl electrophiles in order to generate novel, chain extended building blocks that possess four chiral centers. Synthetic schemes illustrating these reactions are found in Chapter IV. Tables summarizing the results of all experiments are found in Chapter III.

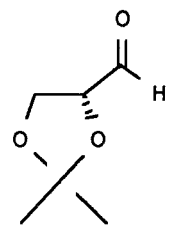
CHAPTER III

RESULTS

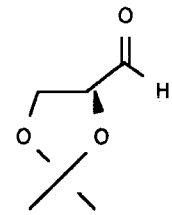
The synthesis of 1,2-O-isopropylidene-2-(R)-glyceraldehyde (**3**) was initiated using D-mannitol as the starting material, protecting this with two isopropylidene groups followed by oxidative cleavage of the protected, chiral, R-glyceraldehyde. The epimer S-glyceraldehyde was prepared using L-ascorbic acid as the starting material. L-Ascorbic acid was then protected similarily and was oxidatively cleaved to form the 1,2-O-isopropylidene-2-(S)-glyceraldehyde (**6**) derivative (**Table 1**).

Thioanisole and methyl phenyl sulfoxide were successfully condensed with 1,2-O-isopropylidene-2-(R)-glyceraldehyde (**3**) to form 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfenyl butane (**9**) and 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfinyl butane (**11**). We were unable to form 1,2-O-isopropylidene-2-(S)-3-(R,S)-trihydroxy-4-phenylsulfenyl butane (**10**) using 1,2-O-isopropylidene-2-(S)-glyceraldehyde (**6**) as the electrophile. Both (**9**) and (**11**) were oxidized to give the sulfone derivative, 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfonyl butane (**12**) (**Table 2**).

Table 1. -- Oxidative cleavage reactions to obtain chiral glyceraldehydes (3) and (6).



(3)

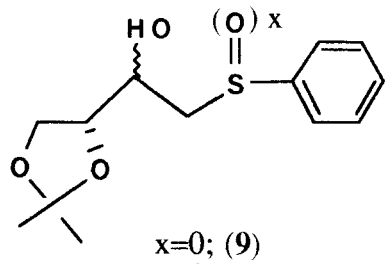


(6)

Scheme	substrate	product	%yield[a, b]
1	(1)	(2)	95[a]
1	(2)	(3)	30-40[a]
2	(4)	(5)	98[a]
2	(5)	(6)	2-3[a,b]
3	(7)	(8)	50[a]
3	(8)	(6)	3-5[a,b]

[a] yields after purification, [b] poor yields, [c] side reactions major products, [d] recovered unreacted starting material

Table 2. -- Formation of sulfur stabilized dianions



x=0; (9)
x=1; (11)
x=2; (12)

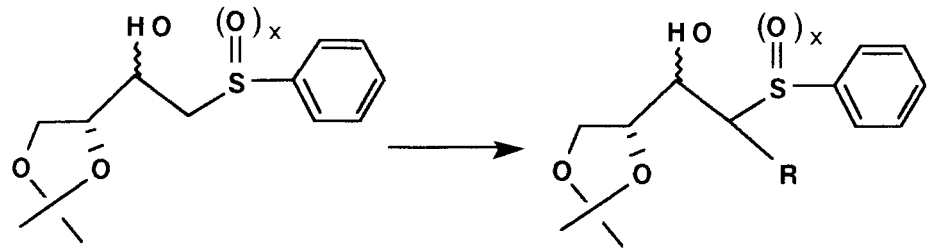
Scheme	substrate	product	%yield[a]
5	(3)	(9)	30-40[a]
6	(3)	(11)	15[a]
7	(3)	(12)	40[a]

[a] yields after purification, [b] poor yields, [c] side reactions major products, [d] recovered unreacted starting material

The dianion of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfonyl butane (**12**) was successfully formed and trapped using methyl iodide and deuterated acetone. Likewise, the dianion of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfinyl butane (**11**) was formed and trapped with allyl bromide, methyl iodide and deuterated acetone. The dianion of (**11**) was successfully condensed with acetaldehyde, butyraldehyde and benzaldehyde. The results from the condensation reactions resulting from the use of acetone and 3-pentanone as the electrophiles were not as sucessful as the reactions using aldehydes as the electrophiles (**Table 3**).

The dianion of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfenyl butane (**9**) was not formed and no trapped derivatives were observed. The silyl ether and acetate of (**9**) were formed in an effort to separate the diastereomers as well as to explore resonance versus inductive effects in blocked beta-hydroxy sulfide derivatives. Silica gel chromatographic separations of these ester derivatives were not successful. Preparative hplc was performed on the parent compounds (**9**) and (**12**) in order to separate the diastereomers and determine the absolute configurations at the 2-hydroxy position. The diastereomers of (**9**) and (**12**) were separated and an attempt was made to deprotect the compounds to give the chiral isopropylidene glycerols. The deprotection reaction

Table 3. -- Dianion reactions with (11)

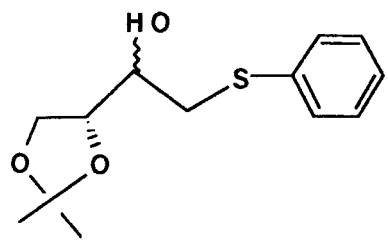


x=1; (**11**) (**14**); R=D (**18**); R=CH(OH)$CH_2CH_2CH_3$
x=2; (**12**) (**15**); R=allyl (**19**); R=CH(OH)Ph
(**16**); R=methyl (**20**); R=CH(OH)$(CH_3)_2$
(**17**); R=$CH(OH)CH_3$ (**21**); R=CH(OH)$(Et)_2$

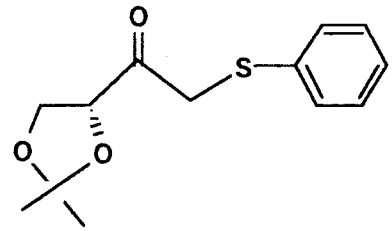
Scheme	substrate	product	%yield[a, b]
8	(12)	(13)	15[a]
9	(11)	(14)	50
9	(11)	(15)	15[a]
9	(11)	(16)	15[a]
9	(11)	(17)	10[a]
9	(11)	(18)	13[a]
9	(11)	(19)	7[a]
9	(11)	(20)	3[a]
10	(11)	(21)	b

[a] yields after purification, [b] poor yields, [c] side reactions major products, [d] recovered unreacted starting material

Table 4. -- Reactions of compound (9) and (26)



(9)



(26)

Scheme	substrate	product	%yield[a, b, d]
10	(9)	(22)	d
11	(9)	(23)	26[a]
12	(9)	(24)	70[a]
13	(9)	(25)	b
14	(9)	(26)	30[a]
15	(26)	(27)	10[a]
16	(26)	(28)	20[a]
17	(26)	(29)	15[a]
18	(26)	(30)	2[a]

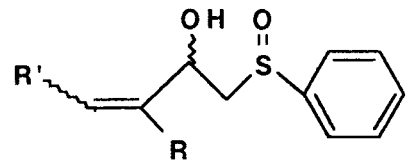
[a] yields after purification, [b] poor yields, [c] side reactions major products, [d] recovered unreacted starting material

went much better with the sulfide derivative than with the sulfone. An optical rotation was performed on the separated, chiral glycerols and was comparable with the literature values. The diastereofacial selectivity was found to be in favor of the syn diastereomer in a ratio of 6:4 (**Table 4**).

The secondary hydroxyl of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-phenylsulfenyl butane (**9**) was oxidized using a standard procedure to give 1,2-O-isopropylidene-2-(R)-3-oxo-4-phenylsulfenyl butanone (**26**). The anion of (**26**) was formed and was trapped using methyl iodide. Acetaldehyde was successfully condensed with the anion of (**26**) to form 1,2-O-isopropylidene-2-(R)-3-oxo-4-phenylsulfenyl-5-(R,S)-hydroxy butanone (**28**). The anion of (**26**) was also condensed with benzaldehyde to give directly the dehydration product rather than the alcohol (**29**). We also attempted to add acetone and 3-pentanone to this anion. However, the desired products were not isolated. With acetone as the electrophile, dehydration products were again directly observed. When the acetone condensation reaction was quenched using acetic anhydride, the 2-acetate ester of the enol ether was formed.

Unprotected prochiral Michael electrophiles acrolein, methacrolein and α-methyl-trans-cinnamaldehyde were reacted with the anion of (**11**) to form the desired unsaturated beta-hydroxy sulfoxide derivatives (**31**), (**32**), and (**33**) (**Table 5**). The condensation reaction was found to occur

Table 5. -- Reactions of Michael acceptors with methyl phenyl sulfoxide



(**31**); R'=H, R=H (**32**); R'=H, R=CH_3

(**33**); R'=Ph, R=CH_3

Scheme	substrate	product	%yield[a]
16	acrolein	(31)	45[a]
17	methacrolein	(32)	70[a]
18	α-methyl-trans-cinnam-aldehyde	(33)	80[a]
19	(31)	(34)	70[a]

Table 6. -- Separation of the diastereomers of (9),(12) and (37),(38)

Scheme	substrate	product	%yield[a]
20	(12)	(35), (36)	50[a]
21	(9)	(37), (38)	46[a]
22	(37), (38)	(39), (40)	20[a]

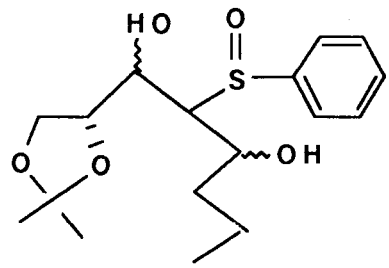
[a] yields after purification, [b] poor yields, [c] side reactions major products, [d] recovered unreacted starting material

in a 1,2 fashion rather than in a 1,4 fashion. The dianion of the methacrolein derivative was formed and trapped with allyl bromide. This experiment showed that dianion chemistry could be extended to non-traditional prochiral building block substrates. These Michael adducts could be stereoselectively functionalized at the olefin to form chiral, polyhydroxylated building blocks

The results of the HPLC separations of the diastereomers of (**9**) and (**12**) are tabulated in **Table 6.**

Finally, pilot experiments were performed on the parent (**11**) and condensation adduct (**18**) to try to establish limits on the degree of required protection prior to oxidation/cyclization steps to form unnatural sugars. An acetonide migration reaction was performed on (**11**) and was found to give mixed products. The adduct (**18**) was treated with acetic anhydride and was found to be highly selective although resistant to acetylation conditions. The adduct (**18**) was also deprotected using Amberlyst 18 and a Corey-Kim oxidation was attemped on this material in the hope of isolating a cyclization product. The results from this experiment were inconclusive (**Table 7**).

Table 7. -- Attempted formation of an unnatural sugar from (18)



(18)

Scheme	substrate	product	%yield[a, b, c, d]
23	(11)	(41)	40[a]
24	(18)	(42)	b,d
25	(42)	(43)	b,d
26	(43)	(44)	c

[a] yields after purification, [b] poor yields, [c] side reactions major products, [d] recovered unreacted starting material

CHAPTER IV

DISCUSSION

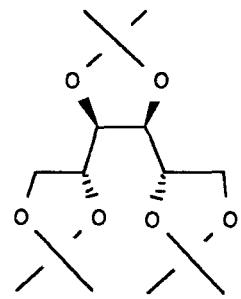
PART 1. Synthesis of 1,2-O-isopropylidene-2-(R)-glyceraldehyde (3) and 1,2-O-isopropylidene-2-(S)-glyceraldehyde (6) (Schemes 1, 2, 3)

A. Synthesis of 1,2,5,6-bis-O-isopropylidene-D-mannitol (2).

The synthesis of 1,2,5,6-bis-O-isopropylidene-D-mannitol (2) was attempted using two literature procedures.[15,16] D-mannitol was dissolved in anhydrous acetone and $ZnCl_2$ was added to the slurry with stirring at RT for 24 hours.[15] The reaction mixture was analyzed by tlc and found to be 85% complete giving two new product spots. When compared with authentic sample (available from Aldrich), the major product co-spotted with authentic sample. However, 25-30% of crude product was found to be the triisopropylidene D-mannitol compound (**Figure 4**). The Baer paper,[15] also noted the production of the triisopropylidene derivative. An alternative method was then sought that would give (2) without this side product. The best method for the exclusive production of (2) was found to be that cited by Kierstead and

co-workers.[16] Here D-mannitol was dissolved in DMSO in the presence of 2,2-dimethoxypropane with a catalytic amount of tosic acid under N_2 at RT for 24 hours.

Figure 4



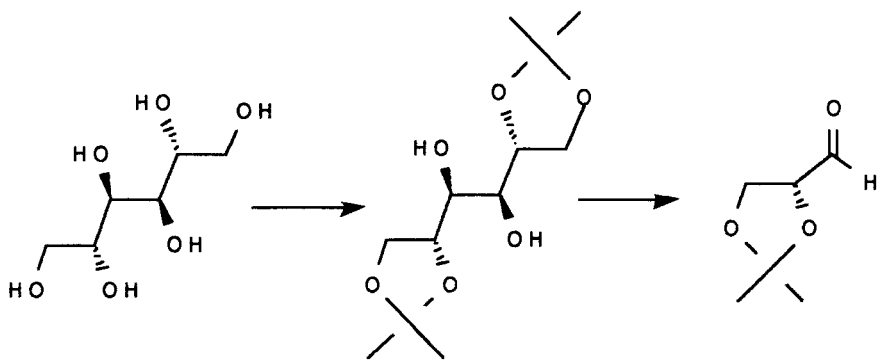
Tlc analysis of the crude reaction mixture showed near complete reaction to the desired compound (**2**). The reaction mixture was easily worked up using successive ethyl acetate washes. The organic phase was evaporated to a white solid that was recrystallized with hot hexane to give 95% yield of white, needle-like crystals. Because of the mild reaction conditions and high yields of crystalline material, this procedure was considered the method of choice for subsequent preparations of (**2**).

B. Synthesis of 2,3-O-isopropylidene-2-(R)-glyceraldehyde (**3**).

The oxidation of (**2**) to (**3**) was first carried out using a modified procedure described by Kierstead and co-

workers.[16] The bis-isopropylidene derivative (2) was dissolved in anhydrous toluene and reacted with $Pb(OAc)_4$ at RT. After 20 minutes, the reaction was shown to be complete via tlc. The white slurry was filtered and the filtrate was neutralized with anhydrous K_2CO_3 and refiltered. However, after evaporation *in vacuo*, it was found that the product co-evaporated with the toluene into the receiving trap.

Scheme 1



(1) **(2)** **(3)**

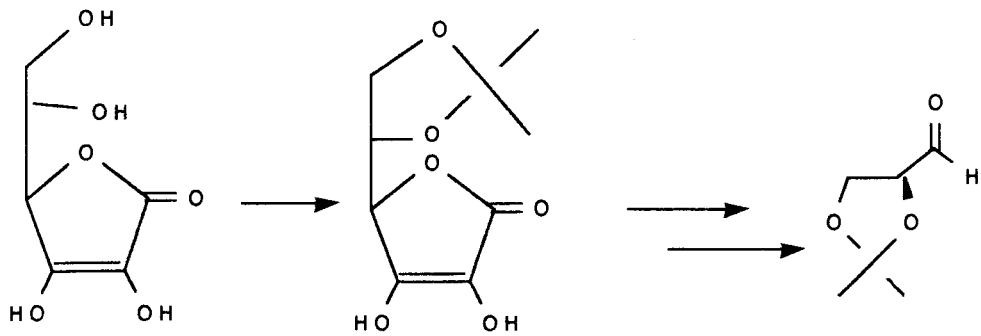
In order to avoid this problem, anhydrous methylene chloride was used as a lower boiling reaction solvent.[17] The use of methylene chloride was found to give minimal co-evaporation and distillation of the resulting solution gave 35-40% yield of the desired aldehyde (3). Although this method gave the desired aldehyde in fair yields, the toxicity of $Pb(OAc)_4$ coupled with the carcinogenic properties of alkyl halides made

this method very undesirable as a preparative method of obtaining (3). An alternative method was reported by Kuszmann[18] where $NaIO_4$ was used as the oxidizing agent resulting in an aqueous solution of (3). For our purposes, however, it was necessary to maintain anhydrous conditions to ensure successful reactions. Even though this method was mild and relatively free from toxicants, the aqueous aldehyde solution would not be useful to us from a synthetic standpoint. Recently, Schmid and collegues[19] reported a new preparative method for the synthesis of both (2) and (3).

C. Synthesis of 1,2-isopropylidene L-ascorbic acid (5).

Since the series of reactions described in this thesis required the production of chiral building blocks of glyceraldehyde, it was of interest to prepare the optical antipode of (3). This goal was initiated using L-ascorbic acid as the chiral building block starting material. Using a procedure described by Jackson and Jones,[20] L-ascorbic acid was dissolved in acetone and acetyl chloride was gradually added to the slurry. After stirring this slurry at RT for 24 hours, the reaction was found to be complete. Simple suction filtration furnished the product (5) as white crystalline needles. The procedure was free from side reactions and was readily amenable to scale-up synthesis giving 98% yield.

Scheme 2



(4) (5) (6)

D. The synthesis of 2,3-O-isopropylidene-2-(S)-glyceraldehyde (**6**) from (**5**).

The synthesis of 1,2-O-isopropylidene-2-(S)-glyceraldehyde (**6**) followed a literature procedure described by Jung and Shaw.[21] The small scale synthesis of (**6**) involved first reducing the double bond of (**5**) followed by oxidative cleavage of this protected lactone with $Pb(OAc)_4$ in ethyl acetate. The first step was pH dependent and had to be followed for four hours. The slurry was then stirred overnight and azeotroped to a white powder with absolute ethanol. The spectral data obtained for this intermediate suggested a great deal of salt formation. The oxidative cleavage was performed using the powder in ethyl acetate and $Pb(OAc)_4$ as the oxidizing

agent. The reaction was found to be complete via tlc analysis within 2 hours. After neutralization and several suction filtrations and rinses, the filtrate was evaporated, *in vacuo*, to a clear, oily solution. The oil was fractionally distilled at room pressure giving a major fraction at 139-143 ^{o}C. The oil was stored at -25 ^{o}C under N_2. The analytical data obtained on this oil suggested the desired aldehyde had formed, however, the yields were poor (10-15%).

Scale up experiments were attempted using 40 g of substrate (**5**). The results were even more discouraging than that found at the 4 g scale. Besides the hazards of this experiment (120 g $Pb(OAc)_4$), the product yield was estimated to be around 5% yield via tlc. It was suggested in several publications[22] that the desired aldehyde (**6**) was not only unstable in organic solvents and subject to racemization but that the procedure as proposed by Jung and Shaw[21] was not amenable to scale up because of the tendency of the aldehyde to undergo overreaction in the reduction step.

An alternate procedure also was attempted using $LiAlH_4$ as the reducing agent and $NaIO_4$ as the oxidant.[23] The procedure called for dissolving substrate in THF over N_2 and cooling this mixture to 0 ^{o}C. The $LiAlH_4$/THF solution was added to substrate and the mixture was stirred at 0 ^{o}C for 1 hour followed by heating to reflux temperature for 0.5 hour. After 10 minutes of heating, the solution turned to an

preparative scale. Alternate literature methods using other prochiral starting materials would perhaps help solve some of the problems associated with working on a preparative scale.[24, 25, 26] Aldehyde instability could perhaps be reconciled by trapping the aldehyde *in situ* [27] with the subsequent use of the derivitized aldehyde as a prochiral substrate.

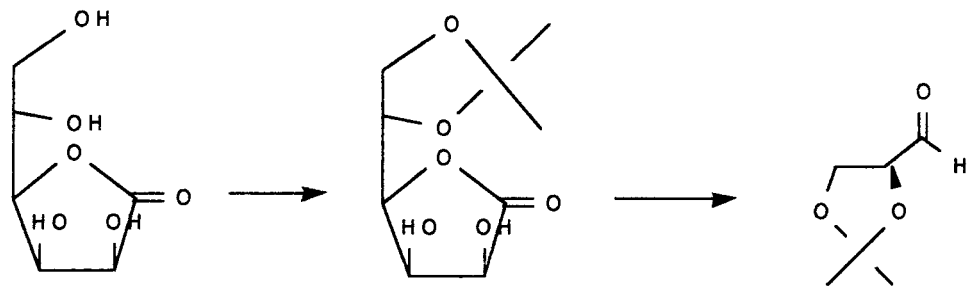
E. Synthesis of 1,2-isopropylidene-L-gulonic-γ-lactone (**8**).

One of the possible factors cited for the poorer than expected yields of (**6**) from the Jung and Shaw procedure could be overreaction in the reduction of the double bond of 1,2-isopropylidene L-ascorbic acid (**5**).[22] Since this was a possible source of the synthetic problems we had been having in the synthesis of (**6**), we decided it was of interest to find a procedure that used both a reduced and protected derivative of L-ascorbic acid as the substrate.

A procedure that involved the protection of the reduced form of L-ascorbic acid (**7**) was found in the literature and the synthesis was attempted.[22] The protection of the substrate was conducted with 2-methoxy propene, tosic acid and DMF at 10-25 ^{o}C. After 24 hours, the reaction was judged complete via tlc and was worked up. The remaining DMF was removed either by repeated ethyl acetate washes or concentrating the solution under reduced pressure at RT. The

resulting yellow-orange solid was repeatedly washed with a hexane/ethanol mixture and was suction filtered. The resulting residue resembled off-white, plate-like crystals. The procedure gave 50% yield of >98% pure (**8**).

Scheme 3



(**7**) (**8**) (**6**)

F. The synthesis of 1,2-O-isopropylidene-2-(S)-glyceraldehyde (**6**) from (**8**).

The substrate (**8**) was suspended in water and cooled to 5 ^{o}C. The oxidant, $NaIO_4$, was added portion-wise to the substrate solution while the pH was kept at 5.5 with 2N NaOH. The reaction was judged complete via tlc in 3.5-4 hours. Although the literature synthesis proposed to isolate the aldehyde in aqueous solution, we needed to isolate the aldehyde in as near as anhydrous conditions as we could in the synthesis for subsequent anion additions. The work-up procedure was modified so that the aqueous aldehyde solution was rinsed 3 times with 10 mL portions of ethyl acetate. The ethyl acetate

solution was fractionally distilled at room pressure to give an aldehyde enriched ethyl acetate solution. The solution of (**6**) was stored at -25 ^{o}C under N_2. The product yields using this modified method were comparable to the Jung and Shaw procedure. Overall for the two steps, the yields of (**6**) from the Hubschwelen[22] procedure ranged from 3-5% yield. The only apparent advantage of this method over the Jung and Shaw method was the use of relatively non-hazardous $NaIO_4$ as the oxidant.

PART 2. Synthesis of 1,2-O-isopropylidene-2-(R,S)-3-(R,S)-trihydroxy-4-phenylsulfenyl butane (**9**) (**10**) 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfinyl butane (**11**) and phenyl sulfonyl butane (**12**) (**Schemes 4, 5, 6, 7**).

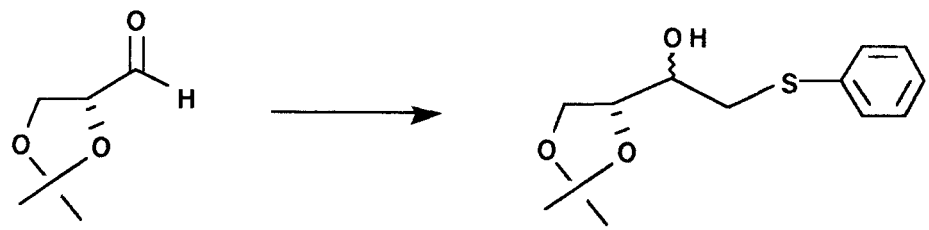
A. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfenyl butane (**9**).

The reaction of the anion of thioanisole with (**3**) was first attempted according to a modified procedure by Corey and Seebach.[28] Nmr analysis of the crude oil suggested a diastereomeric mixture of desired (**9**) had formed in the reaction as well as other products from side reactions and unreacted thioanisole. Because the crude oil was a complex mixture of products and starting material, it was difficult to

determine if any diastereofacial selectively had occurred in the reaction. The crude oil was chromatographed on a silica gel gravity column, to give an odorless, clear oil. The analytical data of the purified oil suggested the desired compound had formed in a 60/40 mixture of diastereomers. After repeated attempts at separating these isomers by conventional means, the mixture was ultimately separated by the use of preparative hplc.

Apart from the noxious odor of this reaction and difficulty in separating the diastereomers, this procedure was found to be satisfactory on a preparative scale giving 30-40% yield of (**9**). In our hands, the use of cosolvent[28] (DMPU), was not found to greatly enhance the yields of desired product. The unresponsiveness of the reaction to the addition of DMPU could have been due to the nature of the anion generated as well as subsequent stabilization of the anion by chelation with the spectator metal.[29] The impure and unstable nature of the aldehyde electrophile[30, 31] could have also contributed to the apparent ineffectiveness of co-solvent as well as add to the side product formation in the reaction.

Scheme 4



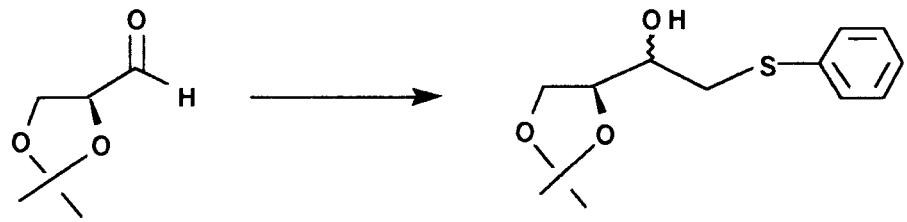
(3) (9)

B. The attempted synthesis of 1,2-O-isopropylidene-2-(S)-3-(R,S)-trihydroxy-4-phenylsulfenyl butane (**10**).

The initial conditions used for the synthesis of (**10**) were identical to those used for the production of (**9**). The worked up sample was chromatographed and the product isolated as an oil, was analyzed. The product was found to be a thioanisole adduct but a more precise analysis suggested that elimination had occurred. The procedure was once again tried generating the thioanisole anion at -10 ^{o}C but by adding the aldehyde at -78 ^{o}C and quenching at 1 minute, 5 minute and 10 minute time intervals. The yellow color was found not to be as pronounced in these runs as they were in the first experiment. However, the aldehyde was not entirely consumed in any of these reactions. Two products were formed in these reactions; one identical to the elimination product isolated in the first experiment and the other was isolated in a small amount and was not identified. The problem with this reaction could have originated from several sources. The unstable nature of the

aldehyde coupled to the resulting stereochemistry of the adduct might have led to decomposition or elimination products as the major components of the reaction.

Scheme 5



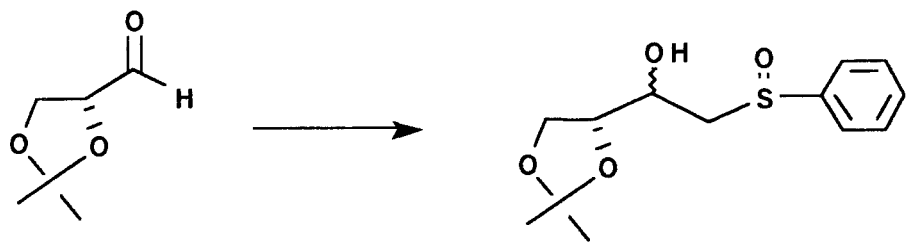
(**6**) (**10**)

C. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfinyl butane (**11**).

The synthesis of this compound was conducted in a similar fashion as in the phenyl sulfide (**9**) case. The procedure leading to the formation of (**11**) was found to be readily extended to preparative scale. The only disadvantage of the procedure was that the methyl phenyl sulfoxide was sold as a very hard, white crystalline, moisture and heat sensitive solid that came in a small brown, glass bottle. Placing the sample at RT for 5-10 minutes under N_2, prior to weighing out, expedites the procurement of the compound from the bottle. The nmr data obtained for the pure sulfoxide (**11**) was very complex due to the introduction of another chiral center at the sulfoxide moiety. As a result, it is not known whether or not

diastereofacial selectivity occurred in this reaction. The separation of the various sulfoxide isomers via silica gel chromatography was attempted and was only partially successful.

Scheme 6



(**3**) (**11**)

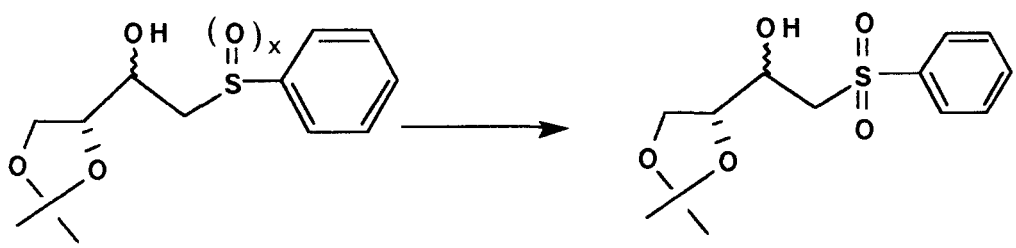
D. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenyl sulfonyl butane (**12**).

The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-hydroxy-phenyl sulfonyl butane (**12**) was of interest because the phenyl sulfonyl moiety was used as a resonance stabilized chromophore in many literature examples of dianion[32, 33] and anion generation.[34, 35] It was of interest to see whether or not our adduct would perform in accordance with literature precedent and serve as a model for sulfinyl dianion additions.

The substrate for the reaction was either (**9**) or (**11**), differing in the number of equivalents of oxidizing agent, (mCPBA) that was used. In the former case, 2-3 equivalents of

mCPBA were necessary to complete the oxidation of the sulfide to the sulfone while in the latter case, 1.5-2.5 equivalents of mCPBA were needed to complete the oxidation of the sulfoxide to the sulfone. The reactions were carried out at RT with dry methylene chloride as the solvent. In both cases, it was found that the isopropylidene protecting group was cleaved if the system was not buffered. As a result, 1.5 equivalents of K_2CO_3 was added to the reaction mixture to prevent protecting group cleavage. The addition of K_2CO_3 probably slowed the reaction down and contributed to the use of excess mCPBA. The end result was the clean formation desired sulfone in 40% yield after chromatography for both reactions.

Scheme 7



x=0 (**9**)
x=1 (**11**)

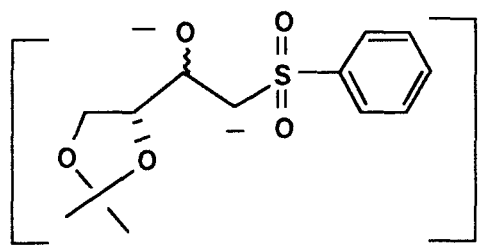
(**12**)

PART 3. The attempted generation and reaction of C-O sulfur stabilized dianion. **(Scheme 8, 9).**

A. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfonyl-6-heptene (**13**).

As a first approximation to the character of this novel, pro-sugar building block series, the trapping of the sulfone stabilized dianion (**Figure 5**) was attempted using allyl bromide as the alkylating agent.[36, 37, 38]

Figure 5



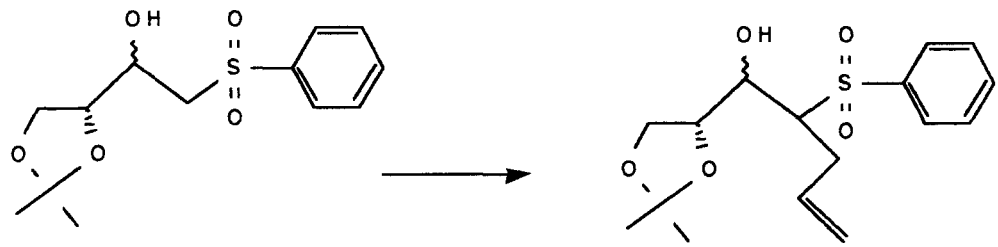
The use of co-solvent (DMPU) was found to be necessary for the solubilization of the incipient dianion. Nmr analysis of the oil suggested the formation of the desired allyl adduct (**13**).

B. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-deutero-4-phenylsulfinyl butane (**14**).

The beta-hydroxy sulfoxyl stabilized dianion was formed using a literature procedure designed for use on another beta-hydroxy sulfonyl compound.[39, 40] The reaction was quenched with deuterated methanol and the crude oil was analyzed for deuterium incorporation via comparison of the proton spectrum of the product and the substrate (**11**). The proton spectrum of the quenched reaction showed a

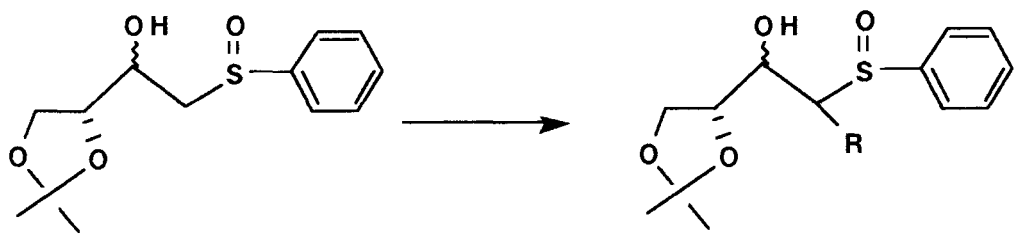
disappearance of certain peaks suggesting dianion formation and trapping with deuterium had occurred. There was about a 50% recovery of mass after work-up. This fair recovery could be a indicator as to the nature and reactivity of this particular dianion to these conditions.

Scheme 8



(12) (13)

Scheme 9



(11)

(14); R=D
(15); R=allyl
(16); R=methyl
(17); R=CH(OH)CH_3
(18); R=CH(OH)$(CH_2)_2CH_3$
(19); R=CH(OH)Ph
(20); R=CH(OH)$(CH_3)_2$
(21); R=CH(OH)$(Et)_2$

C. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfinyl-6-heptene (**15**).

Alkylation with allyl bromide of (**11**) was conducted using a modified literature procedure [10, 11, 12] followed for the sulfonyl butane (**13**). The yield of product (**15**) was found to be around 30%. The low yield of the reaction could be due to moisture in the system, impurities in the allyl bromide or the sulfoxide causing side reactions. The congested nature of the dianion transition state could also result in a lower than expected yield for the reaction, leading to a lower incorporation of the allyl bromide electrophile with respect to deuterium.

D. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfinyl pentane (**16**).

The alkylation of (**11**) was performed using the conditions cited for the synthesis of the allyl derivative (**15**). In this case the alkylating agent was methyl iodide. There was a 70% recovery of crude product after work-up. The crude oil was chromatographed on a silica gel gravity column, resulting in two sets of fractions with an overall yield of 50% of desired product (**16**). Nmr analysis of the oil suggested the formation of the desired methyl adduct.

E. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-tetrahydroxy-4-phenylsulfinyl-hexane (**17**).

Since the experiments to trap an incipient dianion were moderately successful, an attempt was then made to add a series of carbonyl electrophiles to the transiently generated

dianion. The first carbonyl electrophile that was condensed with (**11**) was the sterically unincumbered and reactive acetaldehyde. As with the formation of (**14**), (**15**), (**16**), a modified literature procedure was used in an attempt to form (**17**).

Acetaldehyde is a relatively reactive carbonyl electrophile, because of its small size. Although reactive, acetaldehyde may not add to the dianion as readily as deuterated acetone or alkyl halides. This may account for the lower yields of this reaction in comparison to the former two anion additions. Additionally, the acetaldehyde used for the synthesis was not distilled prior to use. This also may account for the low yields of desired (**17**) through the introduction of impurities and moisture.

F. The attempted synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-tetrahydroxy-4-phenylsulfinyl octane (**18**).

The next aldehyde that was added to the sulfoxide dianion was butyraldehyde. Butyraldehyde was chosen as an electrophile because of its long carbon chain. Although butyraldehyde was distilled and presumed to be anhydrous, impurities and/or moisture in the butyraldehyde or the starting sulfoxide could have played a role in a low yield for this experiment.

G. The attempted synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-tetrahydroxy-4-phenylsulfinyl-5-phenyl hexane (**19**).

Benzaldehyde was chosen as the next carbonyl electrophile because of its availability, and its conjugated system. Mechanistically, it is also of interest to observe whether elimination or addition will predominate in this reaction. The isolated product was found to be the desired addition product (**19**).

H. The attempted synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-hydroxy-4-phenylsulfinyl-5-hydroxy-5-methyl-hexane (**20**).

The next series of experiments used ketones as the electrophile in the reaction. Although carbonyl electrophiles in the form of symmetric ketones would not result in the generation of a new chiral center, it was of interest to see whether or not ketones of this type were active enough to add to the generated dianion and at what level desired product formation would occur. Acetone was chosen as the first ketone carbonyl electrophile because of its small size, and availability. The reaction gave a mixture of the desired acetone adduct and other UV(+) side-products.

I. The attempted synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-hydroxy-4-phenylsulfinyl-5-hydroxy-5-ethyl-heptane (**21**).

The next ketone used as an electrophile in the dianion reaction was 3-pentanone. 3-Pentanone was chosen as an electrophile because of its long, aliphatic chain. In general, the two ketones used as electrophile candidates for addition to the sulfoxide dianion, gave many side products, similar crude product yields and poor desired product formation. Perhaps the additional R group present in ketones as opposed to aldehydes increases steric congestion and creates a softer carbonyl carbon making it more incompatible with the dianion resulting in less desired product formation.

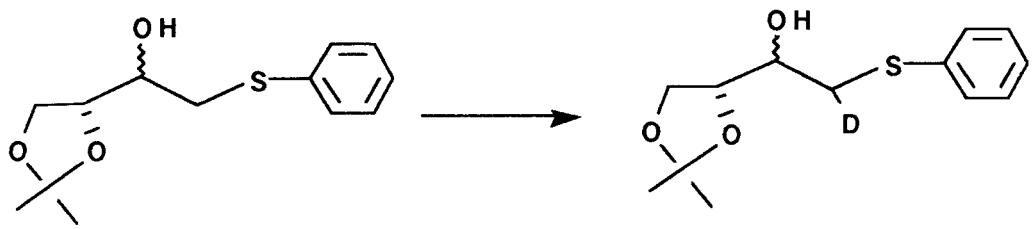
PART 4 The attempted generation of the dianion of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfenyl butane (**9**) and investigational chemistry of derivatives of (**26**) (**Schemes 10, 11, 12, 13, 14, 15**)

A. The attempted synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-deutero-4-phenylsulfenyl butane (**22**).

Since there is little or no precedent for the generation of dianions from beta-hydroxy methyl phenyl

sulfides, an attempt was made to generate a dianion with our substrate (**9**), and trap this dianion with deuterated methanol.

Scheme 10

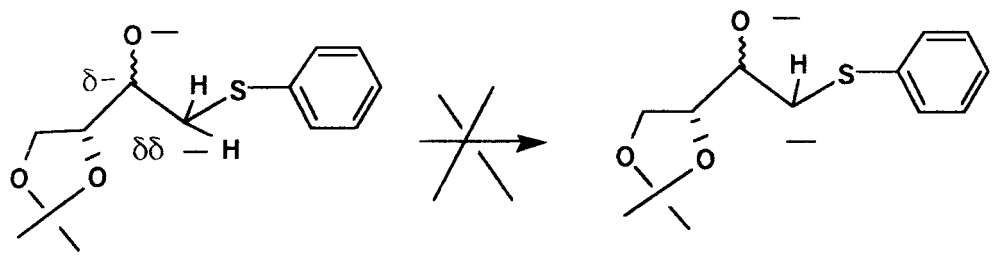


(**9**) (**22**)

The generation of the dianion was attemped as noted in part 3. Deuterated methanol (2 eq) was added to individual reactions at varying time intervals; 30 minutes, 1 hour, 1.5 hour, 2 hours, 3 hours, and 5 hours. In nearly each case, (3 hour and 5 hour quenches were exceptions), the addition of deuterated methanol turned each solution from pale yellow to near colorless. In each case, however, no deuterium incorporation was evident via nmr analysis of the alpha methylene proton resonances. This result suggests that no dianion of (**9**) formed in the reaction. In fact at the 3 hour and 5 hour time points, there was evidence via nmr, that the solvent or the oxy-anion of substrate had started to react with n-BuLi to form side products. Perhaps this would explain the presence of color in these reaction after deuterated acetone was added to the reaction as compared with the other reactions. Several reaction temperatures were also

tried while varying the times of deuterated acetone additions; 30 minutes/0 °C, 1 hour/0 °C, 30 minutes/-40 °C, 1 hour/-40 °C. All of the reactions resulted in no deuterium incorporation and each showed evidence of degradation reactions. Anhydrous diethyl ether was also tried as a solvent for these reaction using the same criteria and time points as already cited for the runs using THF. Similarly, no deuterium incorporation was observed for these reactions. Solvent degradation products were observed to form at the 2 hour time points for this series of reactions. Alternate bases were tried to see if the dianion of (**9**) could be generated using these as opposed to n-BuLi as the base. Reactions using NaH, LDA, sec-BuLi, and t-BuLi all resulted in no deuterium incorporation in the product. Finally, a combination of literature procedures from other classes of compounds were used in an attempt to generate the dianion of (**9**). The conclusion reached as a result of these experiments was that no dianion was generated from (**9**) possibly because of destabilizing inductive effects and lack of a resonance stabilized sulfur moiety alpha to the second generated anion leading to low acidity of this proton (**Figure 6**).

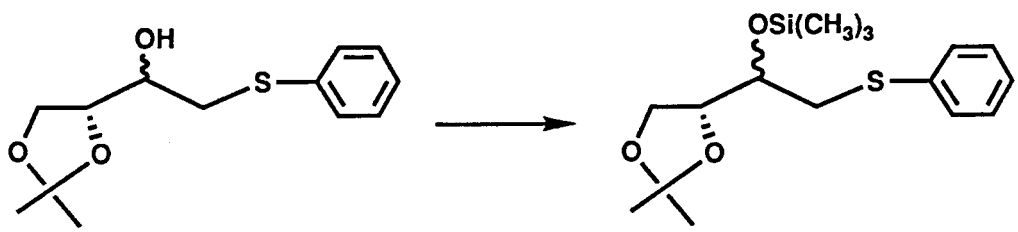
Figure 6



B. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trimethylsiloxy-4-phenylsulfenyl butane (**23**).

Since the desired dianion of (**9**) was not generated by conventional or by following extensions of literature procedure, it was of interest to observe whether an anion could be generated alpha to the sulfur moiety when the hydroxide group at position 2 was blocked with a protecting group.

Scheme 11



(**9**) (**23**)

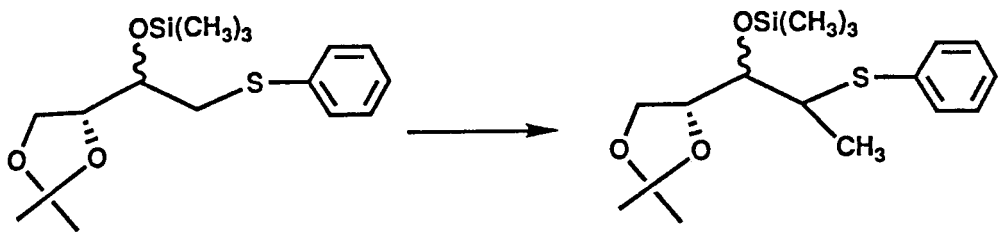
The TMS (trimethylsilyl) group was chosen as a potential protecting group because of its relative ease of removal (using fluoride ion), and its stability in the presence of

mild to strong bases. Since the 2-hydroxy position was diastereomeric, it was also of interest to see whether or not derivitization at this position with TMS would result in a favorable separation of the isomers via tlc and ultimately via chromatography. Several attempts were made to separate the isomers via tlc, however, all were unsuccessful.

C. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trimethylsiloxy-4-methyl-4-phenylsulfenyl butane (**24**).

The attempted generation of an anion alpha to the sulfide group of (**23**) was conducted using anhydrous THF as the solvent 2.2 equivalents of DMPU as co-solvent, and 1.8 equivalents of base (NaH, LDA, sec-BuLi, n-BuLi and t-BuLi) in successive experiments. After 3 hours at -78 $^{o}C/N_2$, 2 equivalents of methyl iodide was added to the solutions and stirred at -78 $^{o}C/N_2$ for 15 minutes. In each case, mini work-up and tlc showed little or no reaction. This resulted in 80-90% recovery of unreacted starting material (**23**) after work-up. These experiments demonstrated that even with the inductive factor eliminated by blocking the 2-hydroxy position, the inherent low acidity of the alpha sulfide proton was still a formidable barrier to the generation of an anion of (**23**). Alternatively, the sterically congested protecting group did not permit approach of the RLi reagent.

Scheme 12

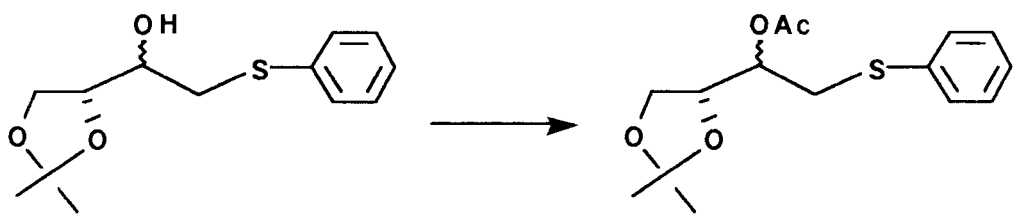


(23) (24)

D. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-acetoxy-4-phenylsulfenyl butane (**25**).

As cited in part 4 example B, the attempt at separating the silyl sulfide derivative epimers (**23**) by tlc analysis and column chromatography failed. An attempt was then made to form the acetate ester at the 3-hydroxyl in order to separate the epimers.

Scheme 13



(9) (25)

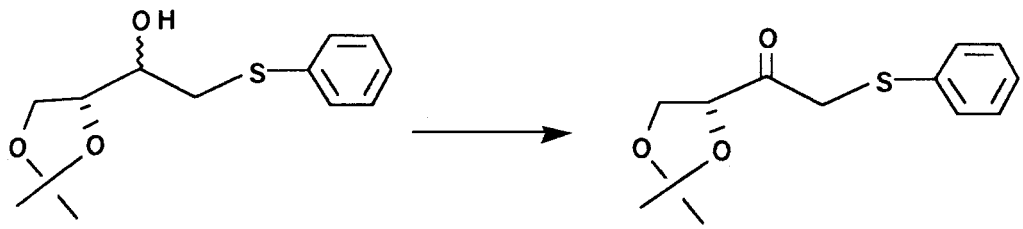
The acetylation of (**9**) was conducted in accordance with a conventional procedure[49] using dry pyridine as the solvent with 1.5 equivalents of acetic anhydride as the acetylating

agent. Chromatography enriched the mixtures to not greater than 70%.

E. The synthesis of 1,2-O-isopropylidene-2-(R)-3-oxo-4-phenylsulfenyl butanone (**26**).

Since the elimination of the inductive factor did not appear to raise the acidity of the alpha sulfide proton substantially, it was of interest to see if one activated the beta position, whether or not anion generation in the alpha position would be observed. The oxidation of the 2-hydroxy to the ketone would serve as a activator to the alpha position via resonance stabilization of the incipient anion. The oxidation of the 2 hydroxyl group was accomplished using the Corey-Kim modification of Swern oxidation conditions (**Scheme 14**).[40,41] It was observed that if the reaction temperature deviated much higher than -10 ^{o}C, unidentified, more non-polar, elimination products were formed in the reaction as well as the desired ketone (**26**). Chromatography was immediately performed on the crude yellow, smelly oil product resulting in 30% yield of desired beta-keto sulfide (**26**). This oil was stored at -25 ^{o}C under nitrogen when it was observed that the product decomposed after sitting under nitrogen at room temperature for several days. Because of its instability at room temperature, data procurement was a problem for this compound especially for micro analysis.

Scheme 14

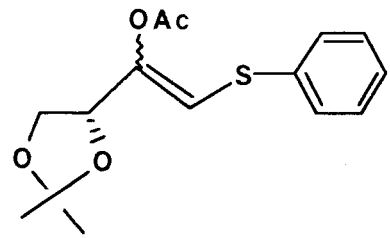


(9) (26)

F. The synthesis of 1,2-O-isopropylidene-2-(R)-3-oxo-4-methyl-4-phenylsulfenyl butanone (**27**).

The attempted generation of the anion of (**26**) was performed using the same procedure as cited for part 4, example C. This result seemed peculiar because in other similar substrates, NaH seemed to able a strong enough base to abstract a proton from a carbon alpha to a ketone.[43] An example of this reaction can be illustrated by the aldol condensation reaction. With the reaction of NaH and compound (**26**), we were able to trap the oxy-acetate of the enol ether using acetic anhydride (**Figure 7**). This result suggested that the anion of (**26**) was indeed generated. However, some other factors must have been operating in the system to prevent reaction with an electrophile.

Figure 7



G. The synthesis of 1,2-O-isopropylidene-2-(R)-3-oxo-4-phenylsulfonyl-5-(R,S)-hydroxy hexanone (**28**).

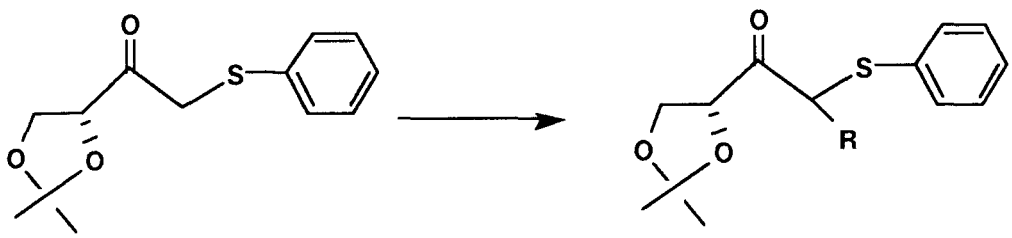
Carbonyl additions also were attempted on the beta-keto sulfide (**26**) derivative with the intent of gaining a better understanding as to the character of the anion in solution with the ultimate hope of determining what conditions would be suitable for the generation of a dianion from (**11**).

The first attempted carbonyl electrophile addition was acetaldehyde. Hplc analysis of the purified mixture showed the isomers to be present in a 60/40 ratio suggesting some diastereofacial selectivity occurred in this reaction. The presence of unreacted starting material in this product could suggest that the system was not anhydrous or the titer of the t-BuLi was lower than anticipated. There was no observed trapping of the enol form of the beta-keto sulfide using acetaldehyde. Another experiment was attempted using 1.3 equivalents of acetic anhydride, as a quencher, in hopes of trapping the enol as the acetate. No acetylated ene sulfide was isolated from this experiment.

H. The synthesis of 1,2-O-isopropylidene-2-(R)-3-oxo-4-phenylsulfonyl-5-(R,S)-hydroxy-5-phenyl pentanone (**29**).

The next electrophile that was added to (**26**) was benzaldehyde. The reaction was quenched in two fashions, one-half with 10%NH_4Cl/ether followed by washes with 5% $NaHCO_3$ and brine and the other half with 1.3 equivalents of acetic anhydride.

Scheme 15

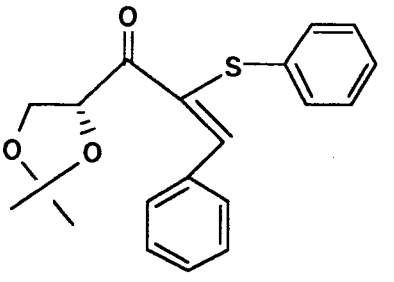


(**26**)

(**27**);R=methyl
(**28**);R=$CH(OH)CH_3$
(**29**);R=CH(OH)Ph
(**30**);R=$CH(OH)(CH_3)_2$

From the aqueous quench the resulting oil was purified to afford eliminated benzaldehyde adduct (**29a**) (**Figure 8**) as product in a product yield of 15%. This result suggested that extended conjugation was a stabilizing factor for the benzaldehyde adduct.

Figure 8



(29a)

Trapped acetoxy enol of beta-keto sulfide (**26**) (**Figure 7**) was observed in the acetic anhydride quenched experiment.

I. The attempted synthesis of 1,2-O-isopropylidene-2-(R)-3-oxo-4-phenylsulfonyl-5-hydroxy-5-methyl hexanone (**30**).

Acetone was chosen as the ketone carbonyl candidate because of its small size. The reaction was quenched in two ways, one-half with 10% NH_4Cl/ether followed by washes with 5% $NaHCO_3$ and brine and the other half with 1.3 equivalents of acetic anhydride. After evaporation to a near colorless oil, the crude product yield was found to contain 50% of starting material. From both quenches the resulting oils were purified giving eliminated acetone adduct from the 10% NH_4Cl/ether quench and trapped enol beta-keto sulfide from the acetic anhydride quench. These findings suggest that a substantial amount of the enol form of the beta-keto sulfide is present in solution and is available for condensation with the

electrophile, acetone. However a large amount of unreacted starting material was recovered with little or no desired (**30**) found in the reaction. This also suggests that resonance stabilization and extended conjugation are powerful driving forces in reaction dealing with the formation of anions alpha to a beta-keto sulfide. In terms of addressing the dianion formation problem of (**9**), these reactions show that the inductive effect plays a role in destabilizing the generation of a second anion alpha to an oxy-anion and methyl phenyl sulfide. Most importantly, these reactions show that resonance stabilization of the second generated anion is a powerful and necessary requirement for dianion formation in the series of compounds where (**9**) is the parent.

Part 5 The condensation reactions of prochiral Michael acceptors with methyl phenylsulfinyl anion and attempted generation of a dianion from 2-methyl-3-(R,S)-hydroxy-4-phenylsulfinyl-1-butene (**32**) **(Schemes 16, 17, 18, 19)**

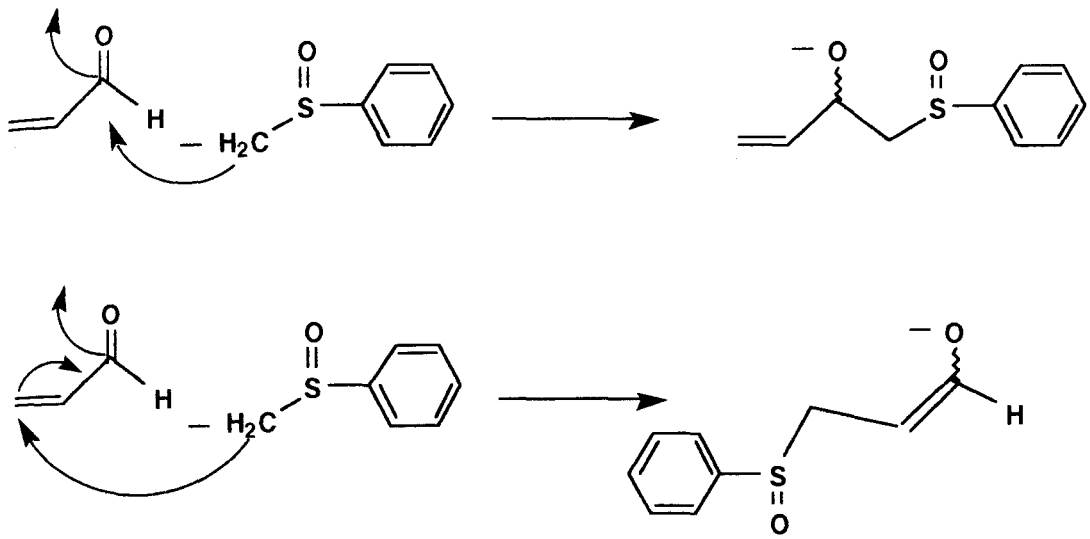
A. The synthesis of 3-ene-3-(R,S)-hydroxy-4-phenylsulfinyl-1-butene (**31**).

The stereoselective generation of chiral centers has been used extensively in literature[44,45] as a strategy for designing a chiral molecule without having to rely on using

expensive chiral building blocks and dealing with unstable reactive intermediates such as 1,2-O-isopropylidene-2-(R)-glyceraldehyde (**3**). Besides the former two problems associated with starting from a chiral building block framework, we found that protecting groups can sometimes be lost during synthetic manipulations exposing the chiral centers to attack by bases and other reactants. The other problem we encountered was the toxicity issue. We had to use large amounts of lead tetracetate to generate required amounts of 1,2-O-isopropylidene-2-(R)-glyceraldehyde (**3**) due to the instability of (**3**) and the poor yields from the synthesis. As a result of these problems, it was of interest to investigate if other prochiral derivatives of the beta-hydroxy sulfoxide (**11**), could be formed without having to deal with the isopropylidene protecting group and conventional prochiral building blocks.

The first attempt at the construction of prochiral methyl phenyl sulfoxide was performed using a traditional Michael acceptor, acrolein, with the hope that 1,2 addition would occur predominantly over 1,4 addition (**Figure 9**).

Figure 9



As **Scheme 16** illustrates, the reaction occurred in a 1,2 fashion to give (**31**) in 45% yield.

Scheme 16

(**31**)

B. The synthesis of 2-methyl-3-(R,S)-hydroxy-4-phenylsulfinyl-1-butene (**32**).

Since the first reaction with acrolein was successful in giving the desired 1,2 adduct, it was of interest

to extend this synthesis to other Michael acceptors to create adducts with varying degrees of substitution at the vinyl bond. Methacrolein was tried as the next Michael electrophile because of its substitution pattern. The reaction is illustrated in **Figure 17**.

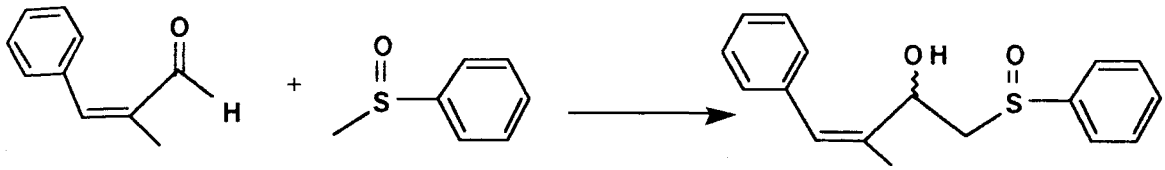
Scheme 17

(32)

C. The synthesis of 1-phenyl-trans-2-methyl-(R,S)-3-hydroxy-4-phenylsulfinyl-1-butene (**33**).

The next Michael acceptor adduct that was prepared was 1-benzyl-trans-2-methyl-(R,S)-3-hydroxy-4-phenylsulfinyl-1-butene (**33**) using α-methyl-trans-cinnamaldehyde (**Scheme 18**). In general, all three of the preparations of prochiral Michael adducts gave purer compounds, higher yields of products with shorter reaction times than their chiral building block brothers (**11**) and (**12**).

Scheme 18



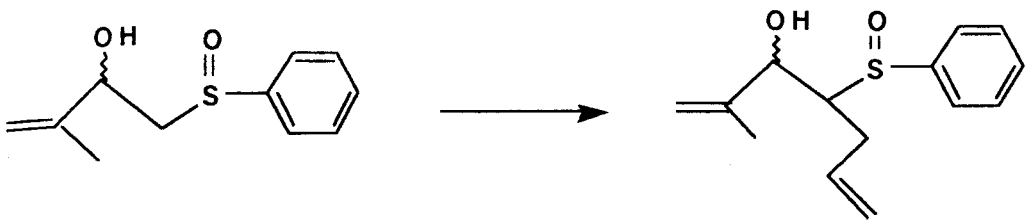
(33)

The compounds were stable at room temperature *in vacuo* for several weeks without observing evidence of decomposition or oxidation.

D. The synthesis of 2-methyl-3-(R,S)-hydroxy-4-phenylsulfinyl-1,6-hexadiene (**34**).

Finally, since we wished to extend the use of these adducts to dianion chemistry, the preparation of the dianion of (**32**) was attempted using the same procedure used for the trapping of the dianion of (**11**) with allyl bromide. The low yield of the reaction could be due to moisture in the system, impurities in the allyl bromide or the sulfoxide causing side reactions. However, this experiment does demonstrate that dianion chemistry can be successfully extended to this achiral system. One can then propose to stereoselectively hydroxylate the double bond[44,45,46] in order to form the structure necessary to make unnatural sugars (**Scheme 19**).

Scheme 19



(32) (34)

Part 6. The assignment of stereochemistry about the hydroxyl group in 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfonyl butane (**12**) and 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfenyl butane (**9**) **(Schemes 20, 21, 22)**

The preparation of intermediates (**9**) and (**12**) generated a chiral center at position 2 while a similar preparation of (**11**) gave 2 chiral centers at position 1, 2 and at the sulfoxide. Of these three compounds, (**9**) or (**12**) seemed better candidates for the assignment of stereochemistry at position 2 because the absence of the additional chiral center of the sulfoxide simplifies the proton spectrum and enhances the possibility of the separation of the epimers using conventional means. In order to resolve the epimers, several strategies were attempted:

(1) the formation of derivatives at position 2 and the separation of diastereomers using chromatography,

(2) preparative hplc of the parent molecules (**9**) and (**12**).

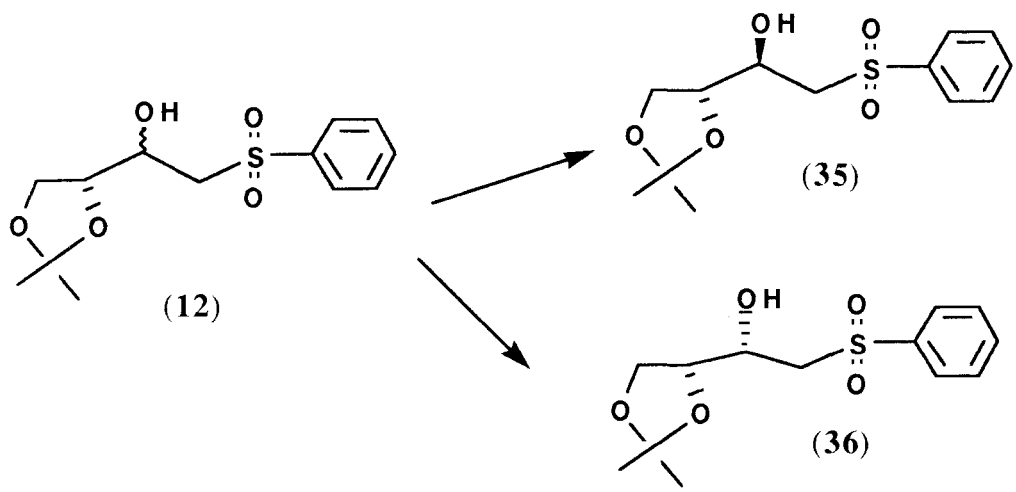
The preparative hplc was used to follow the cleavage of the sulfur moieties to form the protected aliphatic alcohols (**39**) and (**40**). The optical rotations of the alcohols were then compared with with those cited in the literature[47] values. Out of the intermediates (**9**) and (**12**), the sulfide (**9**) cleaved the most cleanly to liberate the protected alcohol.

A. The separation of 1,2-O-isopropylidene-2-(R)-3-(S)-trihydroxy-4-phenyl sulfonyl butane (**35**) from 1,2-O-isopropylidene-2-(R)-3-(R)-trihydroxy-4-phenyl sulfonyl butane (**36**) using preparative HPLC.

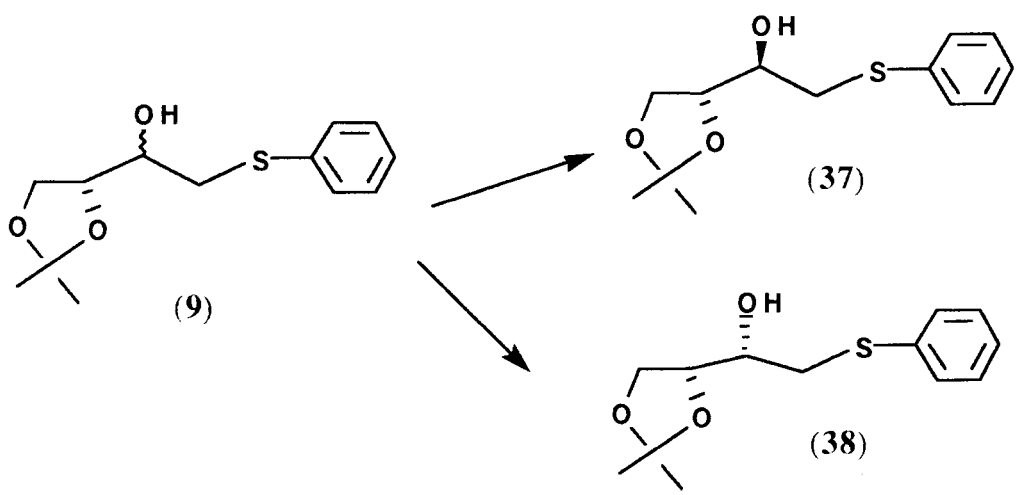
The yields of purified compound from a supposedly pure mixture were suprizingly low. This result could have been due to non-organic salts being present in the sample or compound (desired compound or salts) being retained on the column. Upon standing at room temperature, both samples solidified to give white crystalline solids. The nmr spectra showed the samples to be 97% pure. Stereochemistry was determined by oxidizing (**37**) using the conditions cited in the experimental section, example 7. The proton spectra obtained from this sample was identical to that of (**35**). One of the sulfonyl epimers, (**35**), was found to have an optical rotation of $[\alpha]^{25}_{D}$ -5.04° (c=1.3, MeOH). An optical rotation was not run on

epimer (**36**) due to the small quantity of material obtained after work-up.

Scheme 20



Scheme 21



B. The separation of 1,2-O-isopropylidene-2-(R)-3-(R)-trihydroxy-4-phenylsulfenyl butane (**37**) from 1,2-O-isopropylidene-2-(R)-3-(S)-trihydroxy-4-phenylsulfenyl butane (**38**) using preparative HPLC.

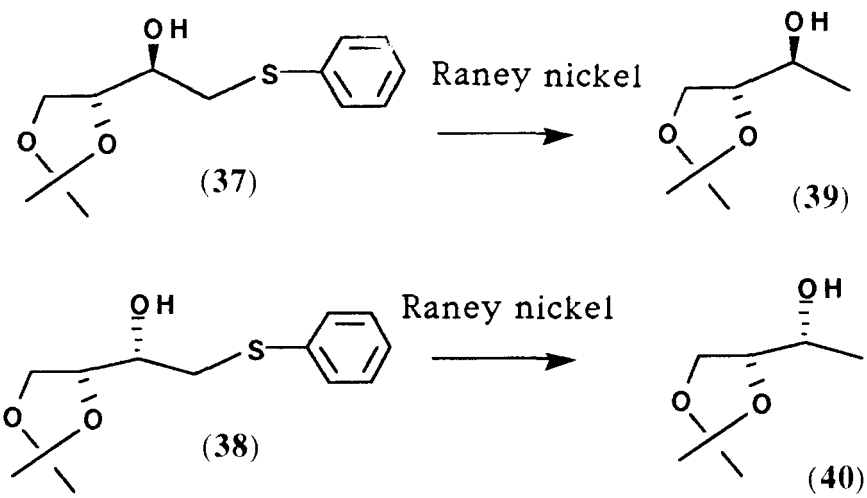
Optical rotations were performed using methanol as the solvent. Epimer (**37**) was found to have an optical rotation of $[\alpha]^{25}_{D}$-46.8° (c=1.19,MeOH) (**Scheme 21**).

C. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(S)-trihydroxy butane (**39**) and 1,2-O-isopropylidene-2-(R)-3-(R)-trihydroxy butane (**40**).

The respective sulfide epimers (**37**) and (**38**) were cleaved to the protected aliphatic compounds (**39**) and (**40**) (**Scheme 22**). Optical rotations were performed on both samples and compared with the literature values. For the derivative from (**37**), the rotation was $[\alpha]^{25}_{D}$ =33.9° (c=0.73, C_6H_6), $[\alpha]^{25}_{D}$=33.8° (c=1.6, C_6H_6) (lit)[47]; the derivative from (**38**) was found to be $[\alpha]^{25}_{D}$ =2.9° (c=1.14, C_6H_6), $[\alpha]^{25}_{D}$ =5.9° (c=1.4,C_6H_6) (lit).[47] The rotation for (**39**) probably does not match up perfectly because of trace amounts of Raney nickel residue of other benzyl impurities in the system that were difficult to remove due to the water soluble nature of the cleavage products of (**37**) and (**38**). Although the rotations of the cleavage products of (**37**) and (**38**) do not precisely match up with the literature values, the order of magnitude of the

values suggest the following structure assignments; (37) gives (39) and (38) gives (40).

Scheme 22



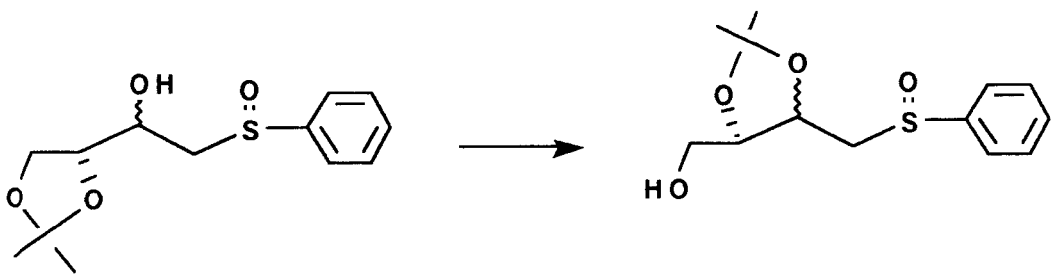
PART 7. Isopropylidene migration studies of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfinyl butane (**11**) and attempted sugar formation usingdeprotected and derivitised 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S) tetrahydroxy-4-phenylsulfinyl-octane (**18**) **(Schemes 23, 24, 25)**

A. The attempted formation of 2,3-O-isopropylidene-2-(R)-3-(R,S)-4-phenylsulfinyl butan-1-ol (**41**)

Since we were successful in preparing the necessary building blocks required for the synthesis of unnatural sugars, it was of interest to see whether or not protection or deprotection steps would be necessary prior to

the final oxidation/cyclization steps. One strategy utilized was that of acetonide migration.[50, 51,52] As a pilot attempt, (**11**) was used as the substrate for the reaction (**Scheme 23**). There were several literature procedures to chose from but the most reasonable for our purposes was that described by Williams[52] where the substrate was dissolved in methanol in the presence of a catalytic amount of sulfuric acid. After subjecting (**11**) to these conditions, hplc analysis of the resulting product mixture clearly showed new peaks had formed at the expense of substrate peaks.

Scheme 23



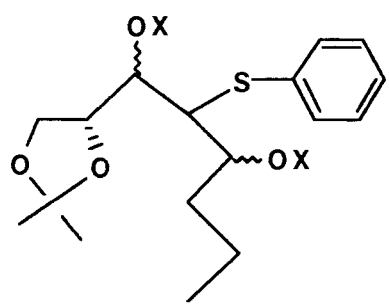
(**11**) (**41**)

The nmr spectra of the crude product clearly showed shifts in the isopropylidene methyl peaks. However, the reaction appeared to be incomplete leading to the conclusion that the 1,2 isopropylidene must be the more thermodynamically stable product[53] or the barrier to migration was too high.

B. The attempted synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-diacetoxy-4-phenylsulfinyl-octane (**42**).

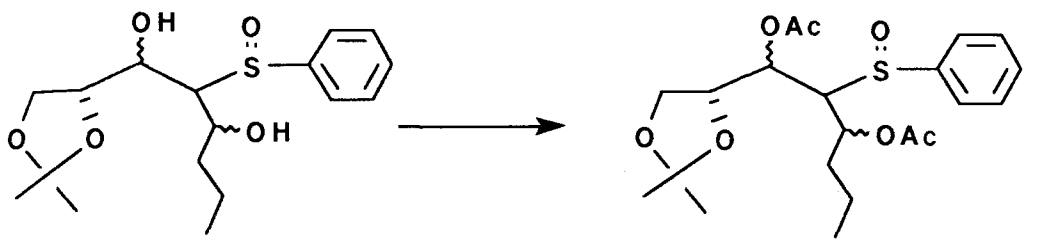
An acetylation reaction of the buytraldehyde sulfoxide adduct (**18**) was conducted using dry pyridine as the solvent and using 2.1 equivalents of acetic anhydride as the acetylating agent. After purification and analysis by nmr and ms, it was revealed that only 1 hydroxyl was converted to the acetate **(Figure 11, Scheme 24).** The results of the experiment show that some acetylation proceeded selectively but to derivitise both hydroxyls would require more forceful conditions.

Figure 10



X= Acetate or H

Scheme 24



(18) (42)

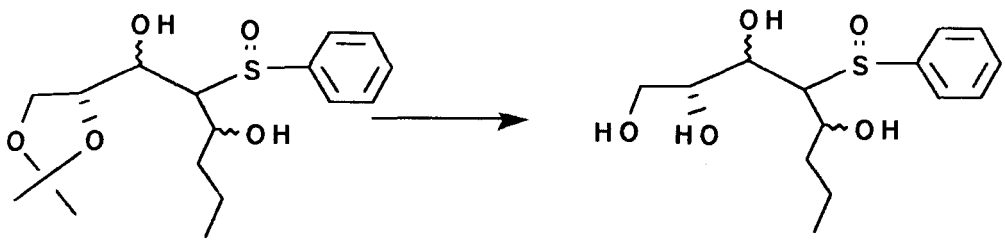
C. The attempted synthesis of 1-hydroxy-2-(R)-hydroxy-3-(R,S)-5-(R,S)-tetrahydroxy-4-phenylsulfinyl-octane (**43**).

The deprotection of (**18**) was conducted using a common literature procedure[48] for the deacetonidation of alcohols (**Scheme 25**). Nmr analysis revealed that the desired (**43**) liberated pro-sugar adduct had formed in the reaction.

D. The attempted synthesis of 1-oxo-2-(R)-hydroxy-3-(R,S)-5-(R,S)-trihydroxy-4-phenylsulfinyl-octanal (**44**).

The substrate used for this reaction possessed 4 hydroxyls; 2 primary and 2 secondary. The oxidation of (**43**) was performed on a small scale (15mg) in the hopes that some determination could be made as to oxidation selectively and propensity to form cyclization products.

Scheme 25



(18) (43)

The oxidation was carried out using the Corey-Kim modifiation of Swern oxidation conditions.[40] After work-up, the analysis of the 10 mg of isolated product oil proved to be inconclusive. Further experimentation to produce larger and purer quanities of intermediate (3), in particular, could lead to success in producing the desired chiral, pro-sugar analogs.

CHAPTER V

EXPERIMENTAL

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Melting points were taken in a Thomas-Hoover capillary apparatus and were uncorrected. Elemental analyses were obtained for some of the new compounds reported. Elemental analyses were performed by the Abbott analytical department. Ir, nmr, and mass spectra were recorded by the Abbott structural chemistry department. E Merck silica gel (70-230 mesh) obtained from VWR Scientific was used for column chromatography. Preparative chromatography was performed on selected examples using a 20x20 60F-254 Merck preparative plate in accordance with the following standard procedure: the sample was loaded onto the plate using 0.5-1.0 mL methylene chloride and the dried plate was immersed in 100 mL of a mobile phase, the plate was run to 1 cm from the origin, thoroughly dried and the UV(+) bands were carefully extracted using a single edged razor blade. The silica was crushed with a motor and pestle and immersed in a 50/50 mixture of methanol/ethyl acetate for 1 h, gravity filtered and

concentrated. Preparative HPLCs were run using YMS semi-preparative (C_{18}; 20x250 mm) columns.

Nmr spectra were determined on a General Electric GN-300 spectrometer operating at 300.1 MHz. Chemical shifts were expressed in ppm downfield from internal tetramethylsilane. Significant ^1H Nmr data were tabulated in the order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad, ex, exchangeable with D_2O), number of protons, designation and coupling constants where applicable. Most of the ^1H Nmr data were run on diastereomeric mixtures of compounds. As a result, the ^1H Nmr data collected was fairly complex and the integration of protons was estimated based upon these mixtures. Some selected compounds were analyzed on a General Electric GN-500 spectrometer operating at 500.1 MHz. ^{13}C nmr spectra were all proton-decoupled and carbons were assigned using DEPT experiments. The IR spectra were recorded on a Perkin-Elmer Model 710A infrared spectrometer. The carbon tetrachloride used as a solvent in the IR analysis contained less than 0.03% H_2O while the chloroform used contained 0.5-1 % ethanol. The IR spectra run in 0.15% carbon tetrachloride were also run with 3mm cells. Mass spectra were obtained with a Hewlett-Packard 5985A mass spectrometer or a Kratos Ms-50 with El source (70eV).

All solvents and reagents were purified when necessary according to standard literature methods. Air- or water-sensitive reactions were conducted under nitrogen atmosphere utilizing standard techniques. All substrates were dried for 48 h *in vacuo* over P_2O_5.

As with any chemical experimentation, the utmost care should be taken when working with known sensitizers, mutagens and teratogens such as lead tetracetate, aceloin, acetaldehyde, chlorinated hydrocarbons and toluene. Working in a ventilated hood while wearing gloves and a lab coat is highly recommended.

PART A. The synthesis of compounds

1. 1,2,5,6-bis-O-isopropylidene-D-mannitol (2).

D-mannitol 5.46 g; (30 mM Aldrich) was added to an oven dried, round bottom flask containing 9 mL of rapidly stirring DMSO. p-Toluene sulfonic acid (0.03 g; 0.157 mM) was added to the white slurry and the mixture was stirred at RT under nitrogen. 2,2-Dimethoxypropane 9.2 mL; (2.49 equiv) was added to the slurry via syringe. After 45 min the slurry turned to a clear solution and stirring was continued at RT for 18 h. The reaction was judged complete via tlc analysis and the clear solution was poured into a separatory funnel containing 200 mL ethyl acetate and 150 mL of 5% $NaHCO_3$. A white precipitate formed in the aqueous phase. The aqueous phase was washed

with 3x100 mL portions of ethyl acetate and the organic washes were combined, extracted with brine and dried with anhydrous Na_2SO_4. The organic phase was gravity filtered and the solvent was evaporated *in vacuo* to give a dense, white solid. The residue was crystallized with the minimum amount of boiling hexane and cooled at RT to give 5.1 g of fluffy white crystals. Procedure yields 95% after crystallization. R_f=0.31 (toluene:methanol, 10:2 mL). m.p. 119° C; $[\alpha]^{25}_D$ +1.6° (c=1, MeOH) lit[16] $[\alpha]^{25}_D$ +1.9° (c= 2, MeOH). ^{1}H-NMR (CD_3OD): δ 4.25-4.15 (m ,4H), 3.95 (m, 2H), 3.65 (m, 2H), 1.35 (s, 6H), 1.33 (s, 6H). ^{13}C-NMR (CD_3OD): δ 109, 76, 71, 67(CH_2O), 26, 25. IR (KBr): 3450-3300, 3000-2950, 1390-1380(d), 1260, 1220, 1185 cm^{-1}. Mass spectrum (DCI/NH_3): m/e 280 (m+17), 263 (m+1). Anal. Calcd for $C_{12}H_{22}O_6$(262.30): 54.95 %C, 8.45 %H; Found: 55.16 %C, 8.59 %H.

2. 2,3-O-isopropylidene-2-(R)-glyceraldehyde (**3**).

To an oven dried, 500 mL round bottom flask was added dried 4 angstrom molecular sieves followed by 100 mL of dry methylene chloride. Lead tetraacetate (3.8 g; 8.5 mM; 1.12 equiv.) was added to the solvent and the yellow-orange mixture was stirred at RT under nitrogen. The substrate (2 g; 7.6 mM) was dissolved in 100 mL methylene chloride and added portionwise to the lead tetracetate mixture. After 15 min, the reaction progress was checked with KI paper. A negative

response was interpreted as complete reaction. The yellow-orange slurry was filtered *in vacuo* through celite giving a clear, light-yellow solution. The filtrate was stirred rapidly with a magnetic stirrer while 50 g of K_2CO_3 was added portionwise to the solution. The mixture was stirred for 0.5 h at RT. The yellow solution turned deep, rusty brown in color and a brown precipitate formed in the solution. Note: this phenomenon only occurred roughly 50% of the time, otherwise, the solution remained colorless. The slurry was suction filtered through celite and concentrated down to a yellow oil that contained some methylene chloride residue. The residue was fractionally distilled between 139 ^oC and 143 ^oC to give a colorless liquid. The aldehyde was stored at -25 ^oC for several weeks without observed significant decomposition or racemization. 35-40% yield, R_f=0.34 (toluene:methanol, 10:2 mL). ^1H-NMR ($CDCl_3$): δ 9.8 (s, 1H), 4.2 (m, 1H), 4.07 (m, 2-H), 1.3 (s, 3H), 1.2 (s, 3H), ^{13}C-NMR ($CDCl_3$): δ 210, 115, 83, 77, 69, 29, 25. IR (0.15%, CCl_4, 3mm cell): 3500-3450, 2950-2800, 1735 cm^{-1}. Mass spectrum (DCI/NH_3): m/e 148 (m+17), 131 (m+1). Anal. Calcd for $C_6H_{10}O_3$ (130): %C 55.37, %H 7.74; Found %C 55.38, %H 7.67.

3. 1,2-isopropylidene L-ascorbic acid (**5**).

L-ascorbic acid (10 g; 56.7 mM) and 40 mL anhydrous acetone were combined in an oven dried 100 mL

flask. This slurry was stirred at RT for 5-10 min. Acetyl chloride (1 mL; 14 mM) was added to the slurry and the mixture was stirred at RT. At 15 min, the reaction slurry began to form a clear solution. In 1 h, the clear solution began to reform a flocculant, white slurry. After 18 h, the reaction was analyzed by tlc and was shown to be complete. The slurry was suction filtered and the residue crystals were dried *in vacuo*. 98% yield R_f=0.1 (toluene:methanol, 10:2 mL). m.p. 214-218 (dec.)^{o} C; lit[21] 217-222^{o} C ; $[\alpha]^{25}_{D}$ -47.70^{o} (c=1.35, MeOH). ^{1}H-NMR (CD_3OD): δ 4.65-3.9(m, 6H), 1.35 (m, 6H). ^{13}C-NMR (CD_3OD): δ 173, 154, 120, 111, 76, 75, 67(CH_2O), 27, 26. IR (KBr): 3300, 3000, 1720, 1630, 1330, 1170 cm^{-1}. Mass spectrum (DCI/NH_3): m/e 234 (m+17), 217 (m+1). Anal. Calcd $C_9H_{12}O_6$ (216.19): %C 50.00, %H 5.59; Found %C 49.98, %H 5.57.

4. 1,2-isopropylidene-L-gulonic-γ-lactone (**8**).

L-gulonic-γ-lactone (0.221 g; 1.24 mM) was dissolved in DMF and stirred at RT. p-Toluene sulfonic acid (1.8 mg) was added to the substrate solution, under nitrogen, and the reaction mixture was cooled to 10 ^{o}C with an ice/water bath. 2-Methoxypropane (154 mL; 1.61 mM) was added dropwise to the substrate solution and this mixture was stirred at 10 ^{o}C for 15 min. The cooling bath was removed and the mixture was stirred at RT for 24 h. After 24 h, tlc analysis showed complete reaction to a more non-polar product. The reaction

was quenched with 0.28 g anhydrous Na_2CO_3 and the slurry was stirred for 2 h, suction filtered and evaporated to a yellow oil. The oil was transferred to a round bottom flask and placed under reduced pressure for 24 h to give a pale, orange solid that was suspended in 3 mL acetonitrile and concentrated to a solid. The solid was crystallized using 0.5 mL hot toluene. The white-orange plates were washed repeatedly with hexane:ethanol (9:1) and dried to give 98.6 mg of the desired compound. 50% yield R_f=0.14 (toluene:methanol, 10:2 mL). m.p. 167-170 °C, 167-168 °C (lit)[22] $[\alpha]^{25}_D$ +38.3° (c=0.7, MeOH) $[\alpha]^{25}_D$ +39.0° (c=1, MeOH).(lit)[22]. ^{1}H-NMR ($CDCl_3$): δ 4.5-3.6(m, 4H), 4.2 (m, 1H), 3.85 (m, 1H), 1.35 (s, 3H), 1.3 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 177, 111, 83, 76, 71, 70, 65 (CH_2O), 26, 25. IR (KBr): 3518, 3459, 1770, 1760 cm^{-1}. Mass spectrum. (DCI/NH_3): 236 (m+17), m/e 219 (m+1). Anal. Calc for $C_9H_{14}O_6$(218.20): %C 49.54, %H 6.47; Found %C 49.50, %H 6.52.

5. 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfenyl butane (**9**).

Thioanisole (3.8 mL; 32.4 mM; 1.2 equiv.) was added to a 500 mL round bottom flask containing 38.5 mL anhydrous THF and dried 4 angstrom molecular sieves under N_2. The thioanisole solution was cooled to -10 °C with an acetone/ice bath and (11.3 mL; 32.4 mM; 1.2 equiv.) of n-BuLi (2.5 M in hexane) was added portionwise. The resulting light yellow

anion solution was stirred at -10 °C for 30 min prior to the addition of aldehyde (**3**). After 0.5 h, aldehyde (**3**) (3.5 g; 26.9 mM) was added to the anion solution whereupon the color of the solution changed from a light yellow color to colorless and finally to a brighter yellow color over the course of 10 min. The cooling bath was removed and the reaction mixture was stirred at RT for 15 min. Mini-work-up and tlc indicated that the reaction was near 85% complete resulting in 3-4 more non-polar, UV(+) products. The yellow solution was poured into a separatory funnel containing 150 mL of 10% NH_4Cl. The aqueous mixture was washed with 2x50 mL portions of ether. The ether layers were combined and washed with 100 mL of 5% $NaHCO_3$ followed by 100 mL brine. The ether layer was dried over anhydrous Na_2SO_4, gravity filtered and concentrated *in vacuo* to give 4 g of a smelly, yellow oil. The crude oil was purified via chromatography on a silica gel gravity column (solvent system composed of $CHCl_3$:ethyl acetate, 40:1 mL) affording 1.87 g of clear, odorless oil of (**9**). Procedure afforded a 28% yield of an epimeric mixture of the desired products after chromatography.

R_f=0.48 (toluene:methanol, 10:2 mL). ^{1}H-NMR ($CDCl_3$): δ 7.4-7.18 (m, 10H, aromatic), 4.25 (m, 1H), 4.05 (m, 1H), 3.8-4.1 (m, 3H), 3.85 (m, 1H), 3.65 (m, 2H), 3.35 (m, 1H), 3.09 (m, 2H), 2.9 (m, 1H), 2.55 (m, 1H) 2.53 (m, 1H) 1.35-1.45 (s, 12H). ^{13}C-NMR ($CDCl_3$): δ 129-126, 109, 77, 70, 66(CH_2O), 37(CH_2S), 26, 25.

IR (0.15%, CCl_4, 3mm cell): 3560, 3080-3060(s), 3000-2880 cm^{-1}. Mass spectrum (DCI/NH_3): m/e 272 (m+17), 255 (m+1), 197, 162. Anal. Calcd for $C_{13}H_{18}O_3S$ (254.346): 61.39 %C, 7.13 %H; Found 61.11 %C, 6.94 %H

6. 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfinyl butane (**11**).

Methyl phenyl sulfoxide (3.23 g; 23 mM; 1.2 equiv.) was added to a 500 mL round bottom flask containing 31.5 mL anhydrous THF and dried 4 angstrom molecular sieves under N_2. The sulfoxide solution was cooled to -10 ^oC with an acetone/ice bath and 9.23 mL (23 mM; 1.2 equiv.) of 2.5 M n-BuLi (in hexane) was added portionwise to the sulfoxide solution. The resulting light yellow anion solution was stirred at -10 ^oC for 15 min. Aldehyde (**3**) (2.5 g; 19.2 mM) was added to the anion solution whereupon the color of the solution changed from a light yellow color to colorless and finally to a brighter yellow color over the course of 10 min. The cooling bath was removed and the reaction mixture was stirred at RT for 10 min. Mini-work-up and tlc indicated that the reaction was near 95% complete resulting in 3-4 more non-polar, UV(+) products. The yellow solution was poured into a separatory funnel containing 150 mL of 10% NH_4Cl. The quenched reaction mixture was washed with 2x50 mL portions of ether. The ether layers were combined, washed with 100 mL of 5% $NaHCO_3$, and

100 mL brine. The ether layer was dried over anhydrous Na_2SO_4, gravity filtered and concentrated down *in vacuo* to give 3.5 g of a smelly, off-white oil. The crude oil was purified via chromatography on a silica gel gravity column (toluene:ethyl acetate, 16:1 mL). After 1 Liter of 10 mL fractions, the solvent system was changed to ethyl acetate. The procedure afforded 12% yield of an epimeric mixture of desired product (**11**). R_f=0.27 (ethyl acetate). ^{1}H-NMR ($CDCl_3$): δ 7.7-7.5 (m, 5H, aromatic), 4.4-3.9 (m, 4H), 3.1-3.25 (m, 1H), 2.85-3.0 (m, 1H), 1.45 (s, 3H), 1.32 (s, 3H), 1.27 (s, 3H), 1.1 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 132-124, 109, 77, 70, 66(CH_2O), 60(CH_2SO), 26, 25. IR (Film): 3450-3300, 3000-2900, 1420(s), 1380-1390, 1260, 1210, 1060, 850(s), 750(s), 690(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 288 (m+17), 271 (m+1), 255, 197, 158. Anal. Calc for $C_{13}H_{18}O_4S$ (270.346): %C 57.76, %H 6.71; Found %C 57.42, %H 6.59.

7. 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfonyl butane (**12**).

Thioether (**9**) was dried for 48 h *in vacuo* over P_2O_5. Compound (**9**) (2.2 g; 8.66 mM; 1.0 equiv.) was added to a 500 mL round bottom flask containing 105 mL anhydrous methylene chloride, dried 4 angstrom molecular sieves and crushed K_2CO_3 (1.43 g; 10.3 mM; 1.2 equiv.). Next, m-CPBA (3.29 g; 17.3 mM; 2 equiv.) was added to the solution. The cloudy, white reaction

mixture was stirred at RT under N_2 for 20 min and was analyzed by tlc and the reaction was found to be 85% complete giving 2-3 more polar, UV(+) products. The white solution was poured into a separatory funnel containing 200 mL of 5% $NaHCO_3$. The solution was carefully swirled and vented. The quenched reaction mixture was backwashed with 2x50 mL portions of methylene chloride. The methylene chloride layers were combined and washed with 200 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give 1.75 g of a white solid. The crude solid was purified via chromatography on a silica gel gravity column ($CHCl_3$:ethyl acetate, 9:1 mL). The procedure afforded 39% yield of an epimeric mixture of desired product (**12**). Characterization (See 7b).

7b. 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfonyl butane (**12**).

Sulfoxide (**11**) was dried for 48 h *in vacuo* over P_2O_5. Compound (**11**) (3.97 g; 1.47 mM; 1.0 equiv.) was added to a 100 mL round bottom flask containing 16 mL anhydrous methylene chloride dried 4 angstrom molecular sieves and crushed K_2CO_3 (0.121 g; 0.88 mM; 0.6 equiv.). Next, m-CPBA 0.253 g; (1.47 mM; 1 equiv.) was added to the solution. The cloudy, white reaction mixture was stirred at RT under N_2 for 20 min and was analyzed by tlc and the reaction was found to be 25% complete. An additional 0.1 g of m-CPBA was added to

the reaction mixture in an effort to advance the reaction to completion. The reaction was checked via tlc at 15 min after the last addition of m-CPBA and was found to be around 90% complete to give 2-3 more polar, UV(+) products. The white solution was poured into a separatory funnel containing 100 mL of 5% $NaHCO_3$. The quenched reaction mixture was washed with 2x25 mL portions of methylene chloride. The methylene chloride layers were combined and were then washed with 100 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give 0.34 g of a white solid. The crude solid was purified via chromatography on a silica gel gravity column ($CHCl_3$:ethyl acetate, 9:1 mL). The procedure afforded 44% yield of an epimeric mixture of desired product (**12**). R_f=0.44 ($CHCl_3$:ethyl acetate, 9:1 mL). ^{1}H-NMR ($CDCl_3$): δ 7.95-7.55 (m, 10H, aromatic), 4.1-3.9 (m, 4H), 3.49-3.6 (m, 2H), 3.2 (m, 2H), 1.27 (s, 3H), 1.1 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 139-129, 109, 76, 67, 66(CH_2O), 59(CH_2SO_2), 26, 25. IR (Film): 3300-3450, 2900-3000, 1420(s), 1380-1390(s), 1260, 1210, 1060, 850(s), 750(s), 690(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 304 (m+17), 287(m+1). 218. Anal. Calcd for $C_{13}H_{18}O_5S$ (286.345): %C 54.53, %H 6.34; Found %C 54.14, %H 6.28.

General Procedure for Beta-Hydroxy Sulfone Dianion Generation For Alkyl Halides.

Sulfone (**12**) (59.7 mg; 0.21 mM, 1.0 equiv.) was added to a 10 mL round bottom flask containing 1.3 mL

anhydrous THF and dried 4 angstrom molecular sieves under N_2. The sulfone solution was cooled to -78 ^oC with an acetone/dry ice bath. n-BuLi (2.5 M in hexane) (0.183 mL; 0.46 mM; 2.2 equiv.) was added portionwise to the sulfone solution. DMPU (55 microliters; 0.46 mM; 2.2 equiv.) was added dropwise to the basic solution. The resulting light yellow-green dianion solution was stirred at -78 ^oC for 30 min prior to the addition of electrophile. After 30 min, the electrophile (1.5 equiv.) was added to the dianion solution whereupon the color of the solution changed from a light yellow-green color to colorless and finally to a brighter yellow color over the course of 30 min. The cooling bath was removed and the reaction mixture was stirred at RT for 1.5 h. The yellow solution was poured into a separatory funnel containing 10 mL of 10% NH_4Cl. The quenched reaction mixture was washed with 2x10 mL portions of ether. The ether layers were combined and washed with 10 mL of 5% NaHCO3 followed by 10 mL brine. The ether layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give a crude oil. The crude oil was purified via preparative or column chromatography.

8. 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfonyl-5-heptene (**13**). Reaction with allyl bromide.

40 mg of crude (**13**) was purified using a preparative chromatography with the procedure affording 8.2 mg of an epimeric mixture of desired product (**13**). 15% yield. R_f=0.49 (ethyl acetate). ^{1}H-NMR ($CDCl_3$): δ 7.9-7.5 (m, 5H, aromatic), 5.85-5.65 (m, 2H), 5.2-5.0 (m, 4H), 4.61-4.55 (m, 1H), 3.9 (m, 1H), 3.7 (m, 1H), 3.3 (m, 1H), 3.15 (m, 1H), 2.95 (m, 1H), 2.7-2.6 (m, 2H), 1.45-1.35 (s, 6H). IR (Film): 3600-3500, 3000-2950, 1640-1660(s), 1445(s), 1380-1370(s), 1170, 1060, 850(s), 750(s), 690(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 344 (m+17), 326 (m+1). Anal. Calcd for $C_{16}H_{22}O_5S$ (326.410): %C 58.88, %H 6.79; Found %C 59.20, %H 6.81.

General Method for Beta-Hydroxy Methyl Phenylsulfinyl Dianion Generation For Alkyl Halides and Deuterated Electrophiles.

Sulfoxide (**11**) (0.215 g; 0.797 mM;1.0 equiv.) was added to an oven dried, 10 mL round bottom flask containing 2.5 mL anhydrous THF and dried 4 angstrom molecular sieves under N_2. The sulfoxide solution was cooled to -78 °C with an acetone/dry ice bath. n-BuLi (2.5 M in hexane) (0.7 mL; 1.75 mM; 2.2 equiv.) was added portionwise to the sulfone solution followed by DMPU (2.5 mL; 1.75 mM; 2.2 equiv.). The resulting light yellow-green dianion solution was stirred at -78 °C for 30 min prior to the addition of electrophile. After 30 min, the electrophile(1.19 mM; 1.5 equiv.) was added to the dianion

solution whereupon the color of the solution changed from a light yellow-green color to colorless and finally to a brighter yellow color over the course of 30 min. The cooling bath was removed and the reaction mixture was stirred at RT for 2 h. Mini-work-up and tlc indicated that the reaction was near 95% complete resulting in at least 2-3 more non-polar, UV(+) products. The yellow solution was poured into a separatory funnel containing 50 mL of 10% NH_4Cl. The quenched reaction mixture was washed with 2x20 mL portions of ether. The ether layers were combined and were then washed with 50 mL of 5% $NaHCO_3$ followed by 50 mL brine. The ether layer was dried over anhydrous Na_2SO_4, and concentrated *in vacuo* . The crude oil was chromatographed via silica gel chromatography (toluene:ethyl acetate 10:6 mL; ethyl acetate) or preparative chromatography.

9. 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-deutero-4-phenylsulfinyl butane (**14**). Reaction with deuterated methanol.

R_f=0.45 (ethyl acetate). ^{1}H-NMR ($CDCl_3$): δ 7.7-7.5 (m, 5H, aromatic), 4.25-4.2 (m, 1H), 4.1 (m, 1H), 4.05-3.9 (m, 4H), 3.3-3.15 (m, 1H), 3.0-2.85(m, 2H), 1.41 (s, 3H), 1.32 (s 3H), 1.25 (s, 3H), 1.05 (s, 3H). IR ($CDCl_3$): 3450-3300, 3000-2900, 1420(s), 1380-1390, 1260, 1210, 1060, 850(s), 750(s), 690(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 288 (m+17), 272 (m+1), 255, 197, 162.

10. 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfinyl-5-heptene (**15**). Reaction with allyl bromide.

The procedure afforded 13% of (**15**) (mixture of isomers) after silica gel chromatography (toluene:ethyl acetate 100:6 mL ethyl acetate). Rf=0.40 (ethyl acetate). ^{1}H-NMR ($CDCl_3$): δ 7.7-7.5 (m, 5H, aromatic), 5.85-5.65 (m, 1H), 5.55-5.45 (m, 1H), 5.25-4.95 (m, 3H), 4.65 (m, 1H), 4.25-3.9 (m, 4H), 3.15-3.05 (m, 1H), 2.95-2.89 (m, 1H), 2.8-2.6 (m, 2H) ,2.45-2.35 (m, 1H), 2.1-2.0 (m, 1H), 1.72 (s, 3H), 1.45 (s, 3H), 1.35 (s, 3H), 1.15 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 134, 131-125, 119(CH_2O), 109, 77, 76, 70, 67(CH_2O), 60(CH_2SO), 27, 25. Mass spectrum (DCI/NH_3): m/e 328 (m+17), 311 (m+1), 202, 184. Anal. Calcd for $C_{16}H_{22}O_4S$ (310.411): %C 61.91, %H 7.14; Found %C 61.50, %H 6.91.

11. 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-methyl-4-phenylsulfinyl pentane (**16**). Reaction with methyl iodide.

The procedure afforded 13% of (**16**) (mixture of isomers) after silica gel chromatography(toluene:ethyl acetate, 100:6; ethyl acetate). Rf=0.31 (toluene:MeOH, 10:2 mL). ^{1}H-NMR ($CDCl_3$): δ 7.7-7.5 (m, 5H, aromatic), 4.25-4.2 (m, 1H), 4.15-4.1 (m ,1H), 4.05-3.9 (m, 4H), 3.3-3.15 (m, 1H), 3.0-2.85 (m, 2H), 1.41 (s, 3H), 1.32 (s, 3H), 1.25 (s, 3H), 1.05 (s, 3H).

^{13}C-NMR ($CDCl_3$): δ 132-124, 110, 77, 75, 70, 66.5(CH_2O), 27, 25, 7 . Mass spectrum (DCI/NH_3): m/e 299 (m+17), 285 (m+1), 265, 147, 131. Anal. Calcd for $C_{14}H_{20}O_4S$ (284.373): %C 59.13, %H 7.09; Found %C 59.25, %H 6.91.

General Method for Beta-Hydroxy Methyl Phenylsulfinyl Dianion Generation

Sulfoxide (**11**) (0.215 g; 0.797 mM; 1.0 equiv.) was added to an oven dried, 10 mL round bottom flask containing 2.5 mL anhydrous THF and dried 4 angstrom molecular sieves under N_2. The sulfoxide solution was cooled to -78 °C with an acetone/dry ice bath. n-BuLi (2.5 M in hexane) (0.7 mL;1.75 mM; 2.2 equiv.) was added portionwise to the sulfone solution followed by DMPU (2.5 mL; 1.75 mM; 2.2 equiv.). The resulting light yellow-green dianion solution was stirred at -78 °C for 30 min prior to the addition of electrophile. After 30 min, the electrophile (1.19 mM; 1.5 equiv.) was added to the dianion solution whereupon the color of the solution changed from a light yellow-green color to colorless and finally to a brighter yellow color over the course of 1.5 hr. The cooling bath was removed and the reaction mixture was stirred at RT for 5-10 min. Reaction progress was monitored via mini-work-up and tlc. The yellow solution was poured into a separatory funnel containing 50 mL of 10% NH_4Cl. The quenched reaction mixture was washed with 2x20 mL portions of ether. The ether layers

were combined and washed with 50 mL of 5% $NaHCO_3$ followed by 50 mL brine. The ether layer was dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give an oil. The crude oil was purified using column or preparative chromatography (toluene:ethyl acetate, 100:6 mL;ethyl acetate).

12. 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-tetrahydroxy-4-phenylsulfinyl hexane (**17**). Reaction with acetaldehyde.

The procedure afforded 10% yield of (**17**) (mixture of isomers) after silica gel chromatography (toluene:ethyl acetate, 100:6 mL; ethyl acetate). R_f=0.44 (ethyl acetate). ^1H-NMR ($CDCl_3$): δ 7.7-7.5 (m, 5H, aromatic), 4.4-4.35 (m, 1-2H), 4.3 (m, 1H), 4.1-3.95 (m, 4-5H), 3.15 (m,1H), 2.95-2.85 (m, 1H), 1.6 (m, 1H), 1.4-1.3(s, 6H), 1.15 (s, 2H), 0.9 (s, 1H). IR ($CDCl_3$): 3450, 3000-2950, 1420(s), 1385-1390(s), 1250, 1220, 1150, 1070, 850(s), 690(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 315 (m+1), 255. Anal. Calcd for $C_{15}H_{22}O_5S$ (314.399): %C 57.31, %H 7.05; Found %C 57.53, %H 6.91.

13. 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-tetrahydroxy-4-phenylsulfinyl-octane (**18**). Reaction with butyraldehyde.

The procedure afforded 13% of (**18**) (mixture of isomers) after silica gel chromatography(toluene/ethyl acetate, 10/0.6mL; ethyl acetate). R_f=0.4 (ethyl acetate).

$[\alpha]^{25}_D$ -47.70° (c=1.35, MeOH). ^{13}C-NMR ($CDCl_3$): δ 141, 131-129, 124, 110, 75, 71, 69(CH_2O), 37(CH_2SO), 26, 25, 19(CH_2), 14. ^{1}H-NMR ($CDCl_3$): δ 7.7-7.5 (m, 5H, aromatic), 4.45 (m, 1H), 4.25 (m, 1H), 4.15-4.0 (m, 4H), 3.8 (m, 1H), 3.0 (m, 1H), 1.8 (m, 1H), 1.65(m, 1H), 1.4 (s, 3H), 1.35 (s, 3H), 1.05-0.9 (m ,4H), 0.3 (m, 1H). IR (Film): 3500-3250, 3000-2950, 1540(s), 1370-1390(s), 1250, 1210, 1065(s), 1010-1025(s), 850(s), 750(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 360 (m+17), 343 (m+1), 216, 199, 162. Anal. Calcd for $C_{17}H_{26}O_5S$ (342.453): %C 59.63, %H 7.65; Found %C 59.83, %H 7.86

14. 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-tetrahydroxy4-phenylsulfinyl-5-phenyl hexane (**19**). Reaction with benzaldehyde.

The procedure afforded 5% yield of (**19**) (mixture of isomers) after silica gel chromatography(toluene/ethyl acetate, 100:6 mL; ethyl acetate). R_f=0.38 (ethyl acetate). ^{1}H-NMR ($CDCl_3$): δ 7.75-7.2 (m, 10H, aromatic), 5.4 (m, 1H), 4.4 (m, 1H), 4.15-3.9 (m, 4H), 3.45 (m, 1H), 3.15 (m, 1H), 2.35 (m, 1H), 1.55 (s, 6H), 1.1 (s, 3H), 0.9 (s, 3H) IR (0.15%, CCl_4, 3mm cell): 3600-3300, 3100-2950, 1450(s), 1380(s), 1245, 1220, 1150, 1065, 850(s), 740(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 377 (m+1), 271, 250, 162, 138. Anal. Calcd for $C_{20}H_{25}O_4S$ (377.479): %C 63.64, %H 6.68; Found %C 63.50, %H 6.91.

15. The synthesis of 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-tetrahydroxy-4-phenylsulfinyl-5-methyl hexane (**20**). Reaction with acetone.

The procedure afforded 2% yield of (**20**) (mixture of isomers) after silica gel chromatography(toluene/ethyl acetate, 10/0.6mL;ethyl acetate). R_f=0.38 (ethyl acetate). ^{1}H-NMR ($CDCl_3$): δ 7.7-7.5 (m, 5H, aromatic), 4.0 (m, 4H), 3.25 (m, 2H), 2.95-2.85 (m, 2H), 1.7 (s, 3H), 1.6 (s, 2-3H), 1.4 (s, 3H), 1.3 (s, 3H), 1.05. ^{13}C-NMR ($CDCl_3$, 500 MHz): δ 132-124, 109, 73, 71, 62, 58(CH_2SO), 56, 30, 25, 22, 14. Mass spectrum (DCI/NH_3): m/e 346 (m+17), 329 (m+1), 288, 271.

16. 1,2-O-isopropylidene-2-(R)-3-(R,S)-trimethylsiloxy-4-phenylsulfenyl butane (**23**).

Sulfide (**9**) (1.1 g; 4.3 mM; 1.0 equiv.) was added to an oven dried, 250 mL round bottom flask containing 100 mL anhydrous DMF (distilled over CaH_2). Imidazole (0.198 g; 2.85 mM; 0.66 equiv.) was added to the sulfide solution and the mixture was stirred at RT. Trimethylsilylchloride (1.0 mL; 12.9 mM; 3 equiv.) was added to the sulfide solution via syringe over a period of 5 min. The resulting solution was stirred at RT for 18 hrs. The reaction mixture was analyzed by tlc and found to be about 85% complete affording a more non-polar, UV (+) product. The clear solution was poured into a separatory funnel containing 200 mL ethyl acetate. 5% $NaHCO_3$ was added to this

solution and the mixture was vigorously shaken. A white precipitate formed in the aqueous phase. The aqueous phase was backwashed with 3x100 mL portions of ethyl acetate and the organic washes were combined and dried with 150 mL brine and anhydrous Na_2SO_4. The organic phase was filtered and the solvent was evaporated *in vacuo* to give a colorless oil. The crude oil was purified via chromatography on a silica gel gravity column. The procedure afforded 42% yield of (**23**) (mixture of isomers) after silica gel chromatography (petroleum ether:ethyl acetate, 9:1 mL). R_f=0.77 (toluene:methanol, 10:2 mL). ^{1}H-NMR ($CDCl_3$): δ 7.4-7.2 (m, 5H), 4.15-4.1 (m, 1H), 4.05-4.0, (m, 1H), 3.85-3.8 (m, 2H), 3.3-3.2 (m 1H), 3.0-2.9 (m, 1H), 1.4, (s, 3 H), 1.3, (s, 3 H) 0.1-0.3(s, 9H). ^{13}C-NMR ($CDCl_3$): δ 136-126, 109, 78, 72, 66(CH_2O), 38, 36 (CH_2S), 26, 25, 0.3-0.5. Mass spectrum (DCI/NH_3): m/e 344 (m+17), 327 (m+1). Anal. Calcd for $C_{16}H_{26}O_3SSi$ (326.529): %C 58.85, %H 8.03; Found %C 59.00, %H 7.77.

17. 1,2-O-isopropylidene-2-(R)-3-(R,S)-acetoxy-4-phenylsulfenyl butane (**25**).

Sulfide (**9**) (0.15 g; 0.59 mM, 1.0 equiv.) was added to an oven dried, 50 mL round bottom flask containing 17 mL anhydrous pyridine. Acetic anhydride (0.12 mL; 1.24 mM; 2.1 equiv.) was added to the sulfide solution via a syringe over a period of 5 min. The resulting solution was stirred at RT for

18 hrs. After 18 hrs, the reaction mixture was analyzed by tlc (toluene:methanol 10:2 mL) and was found to be 85% complete to a more non-polar, UV (+) product. The clear solution was poured into a separatory funnel containing 100 mL saturated copper sulfate solution. The aqueous phase was backwashed with 2x50 mL portions of methylene chloride and the organic washes were combined and dried with 50 mL brine and anhydrous Na_2SO_4. The organic phase was filtered and the solvent was evaporated *in vacuo* to give a colorless oil. The crude oil was purified via chromatography on a silica gel gravity column. The procedure afforded 66% yield of epimeric mixture of (**25**) after silica gel chromatography (petroleum ether:ethyl acetate, (9:1 mL). R_f=0.72 (toluene:methanol, 10:2 mL). ^{1}H-NMR ($CDCl_3$): δ 7.4-7.2 (m, 5H), 5.05 (m, 2H), 4.15-4.1 (m, 1H), 4.05-4.0, (m, 1H), 3.85-3.8 (m, 2H), 3.3-3.2 (m, 1H), 3.0-2.9 (m, 1H), 2.05 (s, 3H), 1.98 (s, 2H), 1.4, (s, 3H), 1.3, (s, 3H) 1.3 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 170, 136-126, 109, 78, 72, 66(CH_2O), 36.5(CH_2S), 26, 25, 20. IR (Film): 3100-2950, 1740, 1450-1445(s), 1380-1375, 1245, 1210, 1150, 1065, 850(s), 740(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 314 (m+17), 297 (m+1). Anal. Calcd for $C_{15}H_{20}O_4S$ (296.384): %C 60.79, %H 6.80; Found %C 60.78, %H 6.91.

18. 1,2-O-isopropylidene-2-(R)-3-oxo-4-methyl-phenylsulfenyl butanone (**26**).

Sulfide (**9**) (7.22 g; 28.4 mM; 1 equiv.) was dissolved in 24 mL of dry toluene and set aside. NCS (10.2 g; 76.2 mM; 2.68 equiv) was dissolved in 80 mL sieve dried toluene and cooled to -10 ^{o}C with an acetone/ice bath. DMS (7.69 mL; 110 mM; 3.9 equiv) was added to the stirring slurry. The mixture was stirred for 20 min at -10 ^{o}C. After 20 min, the substrate solution was added to the slurry and this was stirred for 15 min at -10 ^{o}C. The reaction was analyzed by tlc via mini work-up and the reaction was shown to be 85% complete resulting in 3-4 new UV(+) products. The reaction was quenched by adding $(Et)_3N$ (4.75 mL, 34.1mM, 1.2 equiv) to slurry. After stirring for 3-5 min at -10 ^{o}C, the reaction mixture was poured into a separatory funnel containing toluene and was washed once with 150 mL 5% $NaHCO_3$. The aqueous phase was washed with 2x50 mL portions of toluene and the organic phases were combined and dried over anhydrous Na_2SO_4. The toluene layer was filtered and evaporated to a smelly, brown-yellow oil. The crude oil was purified via chromatography on a silica gel gravity column. The procedure afforded 30% yield of (**26**) after silica gel chromatography (hexane:ethyl acetate, 100:7.5 mL). R_f=0.17 (toluene:methanol, 10:2 mL) ^{1}H-NMR ($CDCl_3$): δ 7.4-7.2 (m, 5H), 4.65 (m ,1H), 4.2-3.85 (m, 4H), 1.49, (s, 3H), 1.4, (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 204, 130-127, 111, 79, 72, 66(CH_2O), 40(CH_2S), 26, 24.5. IR (15%, CCl_4, 3mm cell) 3700, 3500,

3080-3060(s), 3000-2900, 1720 cm^{-1}. Mass spectrum (DCI/NH_3): m/e 270 (m+17), 254 (m+1).

19. 1,2-O-isopropylidene-2-(R)-3-oxo-4-phenylsulfenyl-5-(R,S)-hydroxy hexanone (**28**).

Sulfide (**26**) (0.750 g; 2.97 mM; 1.0 equiv.) was added to an oven dried, 100 mL round bottom flask containing 15 mL anhydrous THF. The sulfide solution was cooled to -78 ^{o}C with an acetone/dry ice bath. t-BuLi (1.3 M in pentane) (2.0 mL; 3.87 mM; 1.3 equiv.) was added portion-wise. After each t-BuLi addition, the substrate solution turned bright yellow and disappeared after a few seconds. After all the t-BuLi was added to the solution, the color remained bright yellow for most of the duration of the reaction. The reaction mixture was stirred at -78 ^{o}C under nitrogen for 1 hr. Acetaldehyde (0.22 mL; 3.86 mM; 1.3 equiv.) was added to the basic solution over a 2-3 minute period. The color of the reaction mixture changed from a yellow color to a light yellow color. The cooling bath was removed and the reaction mixture was stirred at RT for 5-10 min. Mini-work-up and tlc indicated that the reaction was near 75% complete resulting in 2-3 more non-polar, UV(+) products. The light yellow solution was poured into a separatory funnel containing 150 mL of 10% NH_4Cl. The quenched reaction mixture was backwashed with 2x50 mL portions of ether. The ether layers were combined and were

then washed with 150 mL of 5% $NaHCO_3$ followed by 100 mL brine. The ether layer was dried over anhydrous Na_2SO_4, filtered and evaporated *in vacuo* to give 800 mg of a off-white oil. The crude oil was purified via chromatography on a silica gel gravity column. The procedure afforded 30% yield of (**28**) after silica gel chromatography (hexane:ethyl acetate ,100:75 mL). Rf=0.7 (toluene:methanol, 10:2 mL) epimeric mixture of (**28**) and unreacted starting material. ^{1}H-NMR ($CDCl_3$): δ 7.5-7.2 (m, 10H), 5.05 (m, 1H), 4.65 (m, 1H), 4.2 (m, 2H), 4.1 (m ,1H), 3.95-3.85 (m, 2H), 2.1 (m, 2H), 1.55 (s, 3H), 1.45 (s, 3H), 1.4, (s, 3H), 1.38, (s, 3H), 1.35 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 204, 196, 149, 130-126, 111, 79, 78, 72, 66(CH_2O), 40(CH_2S), 26, 25, 17. IR (Film) 3700, 3500, 3080-3060(s), 3000-2900, 1715 cm^{-1}. Mass spectrum (DCI/NH_3): 296 (m+1), 279, 270.

20. 1,2-O-isopropylidene-2-oxo-3-phenylsulfenyl-5-phenyl-4-pentenone (**29a**).

Sulfide (**26**) (0.3 g; 1.19 mM; 1.0 equiv.) was added to an oven dried, 100 mL round bottom flask containing 12 mL anhydrous THF. The sulfide solution was cooled to -78 °C with an acetone/dry ice bath. t-BuLi (1.7 M in pentane) (0.98 mL; 1.55 mM; 1.3 equiv.) was added portion-wise to the sulfide solution. After each t-BuLi addition, the substrate solution turned bright yellow and disappeared after a few seconds. After all the t-BuLi was added to the solution, the color

remained bright yellow for most of the duration of the reaction. The reaction mixture was stirred at -78 ^{o}C under nitrogen for 30 min. Benzaldehyde (0.29 mL; 2.86 mM; 2.4 equiv.) was added to the basic solution over a 2-3 minute period. The color of the reaction mixture changed from a yellow color to a bright yellow color. The cooling bath was removed and the reaction mixture was stirred at RT for 5-10 min. Mini-work-up and tlc indicated that the reaction was near 95% complete resulting in 2-3 more non-polar, UV(+) products. One half of the reaction was worked up in the usual fashion. Acetic anhydride (0.18 mL; 1.9 mM; 1.6 equiv.) was added via syringe to the other half of the reaction mixture and this was stirred at RT under nitrogen for 15 min before quenching in the usual fashion. Mini work-up a tlc of the acetic anhydride quenched reaction suggested that the product make-up was identical to the product make-up obtained from the other half of the reaction indicating no hydroxyls remained. The bright yellow solution was poured into a separatory funnel containing 150 mL of 10% NH_4Cl. The quenched reaction mixture was backwashed with 2x50 mL portions of ether. The ether layers were combined and were then washed with 150 mL of 5% $NaHCO_3$ followed by 100 mL brine. The ether layer was dried over anhydrous Na_2SO_4, filtered and evaporated *in vacuo* to give 400 mg of a smelly, orange-yellow oil. The crude oil was purified via chromatography on a silica gel gravity column. The procedure

affords 26% yield of eliminated, desired product (**29a**) and unreacted benzaldehyde after silica gel chromatography (hexane:ethyl acetate, 20:1 mL). Rf=0.62 (toluene:methanol, 10:2 mL) ^{1}H-NMR ($CDCl_3$): δ 7.5-7.1 (m, 10H), 5.25 (m, 1H), 5.1 (m, 1H), 4.65 (m, 1H), 4.25-4.1 (m, 2H), 4.0-3.9 (m, 1H), 2.2 (m, 3H), 1.45 (s, 3H), 1.4, (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 167, 145, 130-127, 115, 110, 74, 57(CH_2O), 40, 21, 18, 15. IR (Film) 3450-3350, 3000-2950, 1760, 1380-1375(s), 1200-1190, 1150, 1050, 850, 695 cm^{-1}. Mass spectrum (DCI/NH_3): m/e 358 (m+17), 341 (m+1), 312, 254.

21. 1,2-O-isopropylidene-2-(R)-3-(R,S)-acetoxy-4-phenylsulfenyl-3-hexenone (**30a**).

Sulfide (**26**) (0.3 g; 1.19 mM; 1.0 equiv.) was added to an oven dried, 100 mL round bottom flask containing 12 mL anhydrous THF. The sulfide solution was cooled to -78 °C with an acetone/dry ice bath and t-BuLi (1.7 M in pentane) (0.98 mL; 1.55 mM; 1.3 equiv.) was added portion-wise to the sulfide solution. After each t-BuLi addition, the substrate solution turned bright yellow and disappeared after a few seconds. After all the t-BuLi was added to the solution, the color remained bright yellow for most of the duration of the reaction. The reaction mixture was stirred at -78 °C under nitrogen for 30 min. Acetone (0.21 mL; 2.86 mM; 2.4 equiv.) was added to the basic solution over a 2-3 minute period. The color of the

reaction mixture changed from a yellow color to a dull yellow color. The cooling bath was removed and the reaction mixture was stirred at RT for 5-10 min. Mini-work-up and tlc (toluene:methanol 10:2 mL or hexane:ethyl acetate 10:2 mL) indicated that the reaction was near 95% complete resulting in 2-3 more non-polar, UV(+) products. One half of the reaction was worked up in the usual fashion. Acetic anhydride (0.18 mL; 1.9 mM; 1.6 equiv.) was added via syringe to the other half of the reaction mixture and this was stirred at RT under nitrogen for 15 min before quenching in the usual fashion. Mini work-up and tlc of the acetic anhydride quenched reaction suggested that the product make-up was different than the product make-up obtained from the other half of the reaction. The bright yellow solution was poured into a separatory funnel containing 150 mL of 10% NH_4Cl and the reaction mixture was backwashed with 2x50 mL portions of ether. The ether layers were combined and were then washed with 150 mL of 5% $NaHCO_3$ followed by 100 mL brine. The ether layer was dried over anhydrous Na_2SO_4, filtered and evaporated *in vacuo* to give 200 mg of a smelly, orange-yellow oil. The crude oil was purified via chromatography on a silica gel gravity column. The procedure afforded 26% yield of an epimeric mixture of elimination and the isolation of 50 mg of acetylated enol ether of the starting material (**30a**) after silica gel chromatography (hexane:ethyl acetate, 20:1 mL). R_f=0.72 (toluene:methanol,

10:2 mL). ^{1}H-NMR ($CDCl_3$): δ 7.4-7.25 (m, 5H), 6.3 (m, 1H), 4.65 (m, 1H), 4.1 (m, 1H), 4.0-3.9 (m, 1H), 2.2 (m, 3H), 1.45 (s, 3H), 1.4. (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 167, 145, 130-127, 115, 110, 76, 67(CH_2O), 26, 25, 19. IR (Film) 3000-2950, 1760, 1380-1375(s), 1200-1190, 1150, 1050, 850, 695 cm^{-1}. Mass spectrum (DCI/NH_3): m/e 311 (m+1), 292, 253.

22. 3-(R,S)-hydroxy-4-phenylsulfinyl-1-butene (**31**).

Methyl phenyl sulfoxide (3.77 g; 27 mM; 1.2 equiv.) was added to an oven dried, 100 mL round bottom flask containing 19 mL anhydrous THF. The methyl phenyl sulfoxide solution was cooled to -10 °C with an acetone/ice bath. n-BuLi (2.5 M in hexane) (10.7 mL; 27 mM; 1.2 equiv.) was added portion-wise to the sulfoxide solution. The resulting light yellow anion solution was stirred at -10 °C for 20 min prior to the addition of 97% acrolein. After 20 min, acrolein (1.5 mL; 22.4 mM; 1 equiv.) was added to the anion solution whereupon the color of the solution changed from a light yellow color to colorless and finally to a brighter yellow color over the course of 15 min. The cooling bath was removed and the reaction mixture was stirred at RT for 1-2 min. Mini-work-up and tlc indicated that the reaction was near 95% complete resulting in 3-4 more non-polar, UV(+) products. The yellow solution was poured into a separatory funnel containing 100 mL of 10% NH_4Cl. The quenched reaction mixture was backwashed with 2x50 mL portions of ether. The ether layers were combined and

were then washed with 100 mL of 5% $NaHCO_3$ followed by 100 mL brine. The ether layer was dried over anhydrous Na_2SO_4, filtered and evaporated *in vacuo* to give 3.5 g of a smelly, off-white oil. The procedure afforded 45% yield of an epimeric mixture of (**30**) after silica gel chromatography (hexane:ethyl acetate, 20:1 mL). R_f=0.4 (ethyl acetate). ^{1}H-NMR ($CDCl_3$): δ 7.7-7.5 (m, 5H), 6.0-5.8 (m, 1H), 5.4-5.2 (m, 2H), 4.85-4.7.(m, 1H), 3.9-3.7 (m, 1H), 3.1-2.75 (m, 2H), 1.7 (s, 1H). ^{13}C-NMR ($CDCl_3$): δ 143, 137-130, 124, 116(CH_2), 110, 69, 66, 63(CH_2SO). IR (Film) 3400-3330, 3000-2950, 1420, 1030-1020(s), 1000, 920, 770, 690 cm^{-1}. Mass spectrum (DCI/NH_3): m/e 214 (m+17), 197 (m+1).

23. 2-methyl-3-(R,S)-hydroxy-4-phenylsulfinyl-1-butene (**32**).

Methyl phenyl sulfoxide (3.04 g; 21.7 mM; 1.2 equiv.) was added to an oven dried, 100 mL round bottom flask containing 19 mL anhydrous THF. The methyl phenyl sulfoxide solution was cooled to -10 °C with an acetone/ice bath. n-BuLi (2.5 M in hexane) (8.7 mL; 21.7 mM; 1.2 equiv.) was added portion-wise to the sulfoxide solution. The resulting light yellow anion solution was stirred at -10 °C for 20 min prior to the addition of methacrolein. After 20 min, methacrolein (1.5 mL 18.1 mM; 1 equiv.) was added to the anion solution whereupon the color of the solution changed from a light yellow

color to colorless and finally to a brighter yellow color over the course of 15 min. The cooling bath was removed and the reaction mixture was stirred at RT for 1-2 min. Mini-work-up and tlc indicated that the reaction was near 95% complete resulting in 3-4 more non-polar, UV(+) products. The reaction was worked up as cited in example 23. The ether layer was dried over anhydrous Na_2SO_4, filtered and evaporated *in vacuo* to give white solid. The white solid was purified via chromatography on a silica gel gravity column. The procedure afforded 70% yield of an epimeric mixture of (**32**) after silica gel chromatography (hexane:ethyl acetate, 100:6 mL). R_f=0.36 (ethyl acetate). H-NMR ($CDCl_3$): δ 7.65-7.5 (m, 5H), 5.1 (s, 1H), 4.9 (s, 1H), 4.6 (m, 1H), 3.7 (m, 1H), 3.15-3.05 (m, 1H), 2.85-2.75 (s, 1H), 1.7(s, 3H). ^{13}C-NMR ($CDCl_3$): δ 145, 143, 129-124, 112(CH_2), 69, 63(CH_2SO), 18. IR (KBr) 3400-3250(b), 3100-2900, 1660-1620, 1440(s), 1080(s), 1060(s), 1020-1010(s), 900(s), 750(s), 690(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 228 (m+17), 211 (m+1), 195, 177. Anal. Calcd for $C_{11}H_{14}O_2S$(210.293): %C 62.83, %H 6.71; Found %C 62.74, %H 6.72.

24. 1-phenyl-trans-2-methyl-(R,S)-3-hydroxy-4-phenylsulfinyl-1-butene (**33**).

Methyl phenyl sulfoxide (1.8 g; 12.7 mM; 1.2 equiv.) was added to an oven dried, 100 mL round bottom flask

containing 19 mL anhydrous THF. The methyl phenyl sulfoxide solution was cooled to -10 ^{o}C with an acetone/ice bath. n-BuLi (2.5 M in hexane) (5.1 mL; 12.7 mM; 1.2 equiv.) was added portion-wise to the sulfoxide solution The resulting light yellow anion solution was stirred at -10 ^{o}C for 10 min prior to the addition of α-methyl-trans-cinnamaldehyde. After 10 min, (1.5 mL; 10.7 mM; 1 equiv.) of α-methyl-trans-cinnamaldehyde was added to the anion solution whereupon the reaction color progressed as usual. The reaction monitoring and workup proceeded as previously cited in example (**31**). The procedure afforded an off-white oil that was purified via chromatography on a silica gel gravity column. The procedure afforded 80% yield of epimeric mixture of (**33**) after silica gel chromatography (toluene:ethyl acetate, 25:1 mL:ethyl acetate). R_f=0.49 (ethyl acetate). ^{1}H-NMR ($CDCl_3$): δ 7.7-7.1 (m, 10H), 6.65 (m, 1H), 6.6 (m, 1H), 5.1 (s 1H), 4.85 (m, 1H), 4.72 (m, 1H), 3.95-3.85 (s, 1H), 3.25-3.15 (m, 3H), 2.95 (m, 1H), 2.85 (m, 1H), 2.35 (s, 3H), 1.87 (s, 3H), 1.8 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 144, 137, 131,-124, 74, 71, 62(CH_2SO), 14, 13. IR (Film) 3250-3300(b), 3100-2810, 1600-1590, 1440(s), 1080(s), 1020-1030(s), 760(s), 700(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 304 (m+17), 287(m+1), 269, Anal. Calcd for $C_{11}H_{14}O_2S$(): Calc. %C 71.30, %H 6.39; Found %C 71.66, %H 6.49.

25. 2-Methyl-3-(R,S)-hydroxy-4-phenylsulfinyl-1,6-hexadiene (**34**).

Sulfoxide (**32**) (50 mg; 0.48 mM; 1.0 equiv.) was added to an oven dried, 10 mL round bottom flask containing 0.65 mL anhydrous THF. The sulfoxide solution was cooled to -78 °C with an acetone/dry ice bath. n-BuLi (2.5 M in hexane) (0.2 mL; 1.05 mM; 2.2 equiv.) of was added portion-wise to the sulfoxide solution. DMPU (63 μliters; 1.05 mM; 2.2 equiv.) was added dropwise to the basic solution. The resulting light yellow-orange dianion solution was stirred at -78 °C for 30 min prior to the addition of allyl bromide. After 30 min, 33 μliters (0.71 mM; 1.5 equiv.) of allyl bromide was added to the dianion solution whereupon the color of the solution changed from a light yellow-orange color to colorless over the course of 30 min. The reaction was monitored and quenched as previously cited in example (**31**). The crude oil was purified via chromatography on a silica gel gravity column. The procedure afforded 9% yield of epimeric mixture of (**34**) after silica gel chromatography (toluene:ethyl acetate, 100:6 mL; ethyl acetate). R_f=0.49 (ethyl acetate). ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.6-7.5 (m, 5H), 6.0-5.9 (m, 1H), 5.55-5.4 (m, 1H), 5.15 (s, 1H), 5.05 (s, 1H), 4.9 (m, 2H), 4.4 (m, 1H), 2.85 (m, 1H), 2.3 (m, 1H), 2.1 (m, 1H), 1.8 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 143, 140, 134, 131-124, 118-117, 114, 112(CH_2), 75, 71, 64-63(CH_2SO),

27, 19, 17. Mass spectrum (DCI/NH_3): m/e 268 (m+17), 251 (m+1).

26. The separation of 1,2-O-isopropylidene-3-(R)-3-(S)-hydroxy-4-phenylsulfonyl butane (**35**) from 1,2-O-isopropylidene-2-(R)-3-(R)-hydroxy-4-phenylsulfonyl butane (**36**) using preparative HPLC.

The substrate was dissolved in 3 mL of methanol and 450 microliter injections were made onto the column. A total of 0.5 gram of a 60/40 mixture of sulfone (**12**) was injected on to a semi-preparative hplc column using water, 65% methanol, 30 g/L $NaOAc*3H_2O$, 1.5 mL/L glacial acetic acid and 20 mL/L ethylene glycol as the mobile phase. The flow rate was 11 mL/minute with the sensitivity set at 16. Two sharp peaks were separated out on the column with a retention time of (1) 12 min and the other with a retention time of (2) of 14 min. The respective samples were poured into separatory funnels containing 100 mL 5% $NaHCO_3$. The aqueous layers were back washed with 2x50 mL portions of methylene chloride, were dried with 100 mL portions of brine and suspended over anhydrous Na_2SO_4. After basic aqueous work-up, the eluents were evaporated to (1) 100 mg colorless oil and (2) 300 mg colorless oil. Upon standing at RT, both samples solidified to give white crystalline solids. The nmr spectra showed the samples to be 97% pure. $[\alpha]^{25}_D$ -5.04° (c=1.3,

MeOH). (**35**). Rf=0.4 (chloroform:ethyl acetate, 9:1 mL). ^{1}H-NMR ($CDCl_3$): δ 7.95-7.55 (m ,10H aromatic), 4.1-3.9 (m, 4H), 3.6-3.49 (m, 2H), 3.2 (m, 1H), 1.27 (s, 3H), 1.1 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 139-129, 109, 76, 67, 66(CH_2O), 59(CH_2SO_2), 26, 25. Mass spectrum (DCI/NH_3): m/e 304 (m+17), 287 (m+1), 218.

(**36**). ^{1}H-NMR ($CDCl_3$): δ 7.95-7.55 (m, 10H aromatic), 4.1-3.9 (m, 4H), 3.6-3.49 (m, 2H), 3.2 (m, 1H), 1.27 (s, 3H), 1.1 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ 139-129, 109 76, 67, 66(CH_2O), 59(CH_2SO_2), 26.3, 25. Mass spectrum (DCI/NH_3): m/e 304 (m+17), 287 (m+1), 218. Anal. Calcd for $C_{13}H_{18}O_5S$ (286.345): %C 54.53, %H 6.34; Found %C 54.04, %H 6.28.

27. The separation of 1,2-O-isopropylidene-2-(R)-3-(R)-hydroxy-4-phenylsulfenyl butane (**37**) from 1,2-O-isopropylidene-2-(R)-3-(S)-hydroxy-4-phenylsulfenyl butane (**38**) using preparative HPLC.

The substrate was dissolved in 3 mL of methanol and 450 microliter injections were made on to the column. A total of 1 gram of a 70/30 mixture of sulfide (**9**) was injected on to a semi-preparative hplc column using water, 60% methanol, and 30 g/L NH_4OAc as the mobile phase. The flow rate was 11 mL/minute with the sensitivity set at 16. Two sharp peaks were separated out on the column with a retention

time of 21 min and 26 min. The respective samples were poured into separatory funnels containing 100 mL 5% $NaHCO_3$. The aqueous layers were back washed with 2x50 mL portions of methylene chloride, were dried with 100 mL portions of brine and suspended over anhydrous Na_2SO_4. After basic aqueous work-up, the eluents were evaporated to 568 mg colorless oil (faster eluting component) and 200 mg colorless oil (slower eluting component). Upon standing at RT, both samples solidified to give white crystalline solids. The nmr spectra showed the samples to be 95% pure. (**37**). R_f=0.5 (chloroform:ethyl acetate, 9:1 mL). $[\alpha]^{25}_D$-46.8° (c=1.19,MeOH). ^{1}H-NMR ($CDCl_3$): δ 7.18-7.4 (m 5H aromatic), 4.25 (m, 1H), 4.05 (m, 1H), 3.85 (m,1H), 3.65 (m, 2H), 3.09 (d, 2H), 2.53 (d, 1H) 1.45-1.35 (s, 6H). Mass spectrum (DCI/NH_3): m/e 272 (m+17), 255 (m+1), 197, 162.

(**38**). ^{1}H-NMR ($CDCl_3$): δ 74-7.18 (m, 5H aromatic), 4.1-3.8 (m, 3H), 3.65 (m, 2H), 3.35 (m, 1H), 2.9 (m, 1H), 2.55 (d, 1H) 1.45-1.35 (s, 12H). ^{13}C-NMR ($CDCl_3$): δ 129-126, 109, 77, 70, 66(CH_2O), 37(CH_2S), 26, 25. IR ($CDCl_3$): 3600-3250(b), 3100-2900, 1660-1620, 1480, 1440(s), 1280, 1220, 1080(s), 1060(s), 900(s), 750(s), 690(s) cm^{-1}. Mass spectrum (DCI/NH_3): m/e 272 (m+17), 255 (m+1), 197, 162. Anal Calcd for $C_{13}H_{18}O_3S$ (254.346): 61.39%C, 7.13%H; Found 61.11%C, 6.94%H.

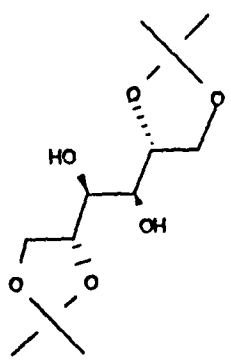
28. 1,2-O-isopropylidene-2-(R)-3-(S)-hydroxy butane (**39**) and 1,2-O-isopropylidene-2-(R)-3-(R)-hydroxy butane (**40**).

Substrate (**37**) or (**38**) respectively, (0.112 g; 0.44 mM) were dissolved in 10 mL methanol and stirred at RT. Plugs of activated #28 wet Raney nickel (3 mL) were added to the substrate solution rinsing the nickel into the reaction vessel with water. The grey slurry was stirred at RT and the reaction progress was monitored via tlc analysis. At 30 min, the reaction mixture was analyzed by tlc and was shown to be 98% complete to a more polar, UV(-) product. The slurry was poured into 200 mL methanol and was carefully gravity filtered making sure that all of the nickel residue remained moistened with methanol wash. The filtrate was refiltered over a micropore filtration apparatus and this filtrate was evaporated *in vacuo* to a clear colorless oil which solidified upon standing at RT (**39**). Rf=0.4 (toluene:MeOH, 10:2 mL). $[\alpha]^{25}_{D}$=33.8° (c=1.6, C_6H_6) (lit)[47], $[\alpha]^{25}_{D}$ =33.9° (c=0.73, C_6H_6) . ^{1}H-NMR ($CDCl_3$): δ 4.1-3.82 (m, 4H), 2.09 (m, 1H), 1.42-1.36 (s, 6H), 1.16(d, 3H, *J* =6.5 Hz). ^{13}C-NMR ($CDCl_3$): δ 129-126, 109, 77, 70, 66(CH_2O), 37(CH_2S), 26, 25. Mass spectrum (DCI/NH_3): m/e 164 (m+17), 147 (m+1).

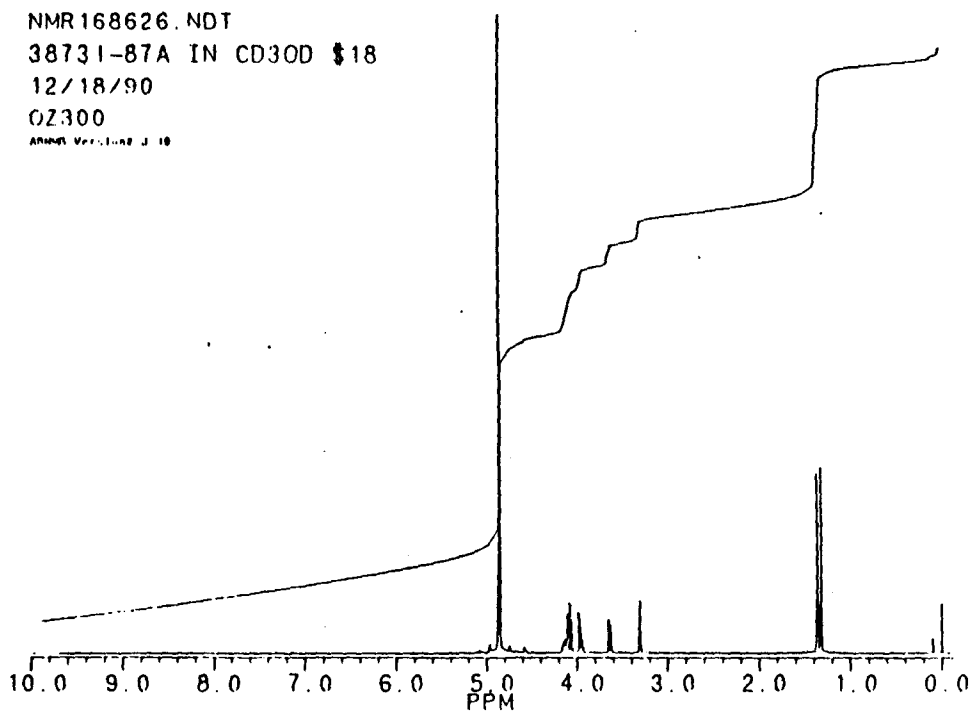
(**40**). $[\alpha]^{25}_D$ =5.9° (c=1.4,C_6H_6) (lit)[47], $[\alpha]^{25}_D$ =2.9° (c=1.14, C_6H_6). ^{1}H-NMR ($CDCl_3$): δ 4.01 (dd, 1H, *J* 1'1=7.5 Hz, *J* 1'2=6.5 Hz). 3.93 (m, 2H), 3.67 (dd, 1H*J* 1'1=7.5 Hz, *J* 1'2=6.5 Hz), 3.72-3.61 (m, 3H), 2.73 (s, 1H), 1.45-1.35 (s, 6H), 1.14 (d, 3H, *J* =6.5 Hz). ^{13}C-NMR ($CDCl_3$): see example (**39**). Mass spectrum (DCI/NH_3): m/e 164 (m+17), 147(m+1). Anal. Calcd for $C_7H_{14}O_3$ (146.20): 57.51%C, 9.65%H; Found %C 57.62, %H 9.85.

CHAPTER VI

SPECTRAL APPENDICES


HO
OH
O
O
O
O
O

(2)


NMR168626.NDT
38731-87A IN CD3OD $18
12/18/90
QZ300
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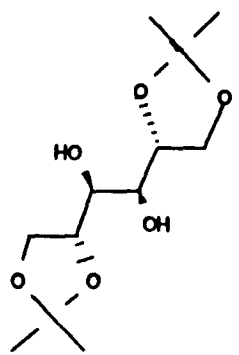
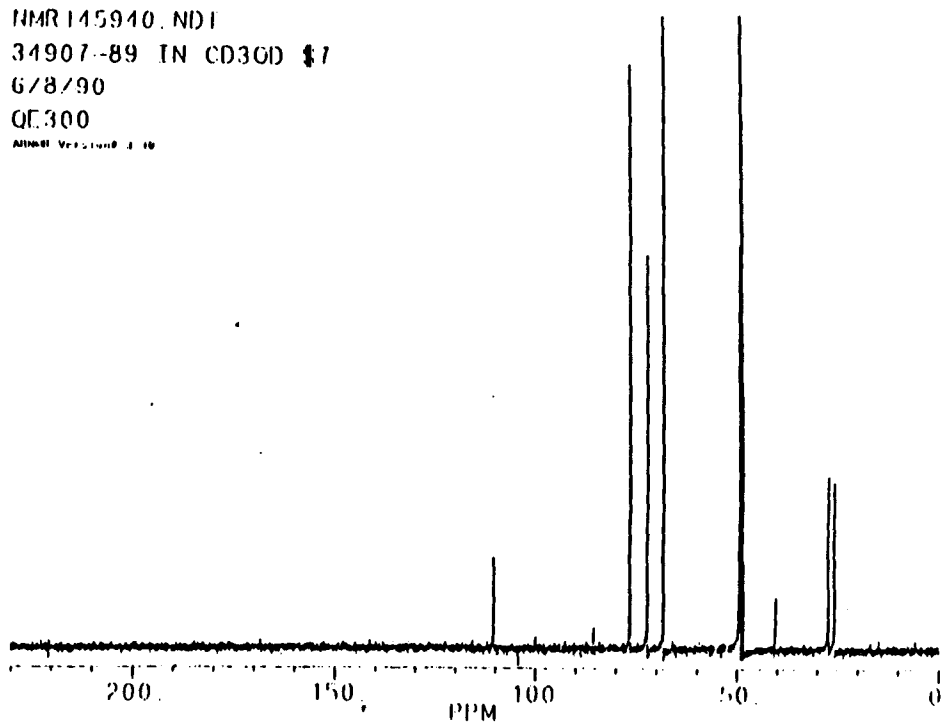
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM


HO
OH
O
O
O
O

(2)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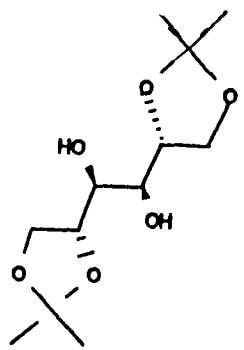
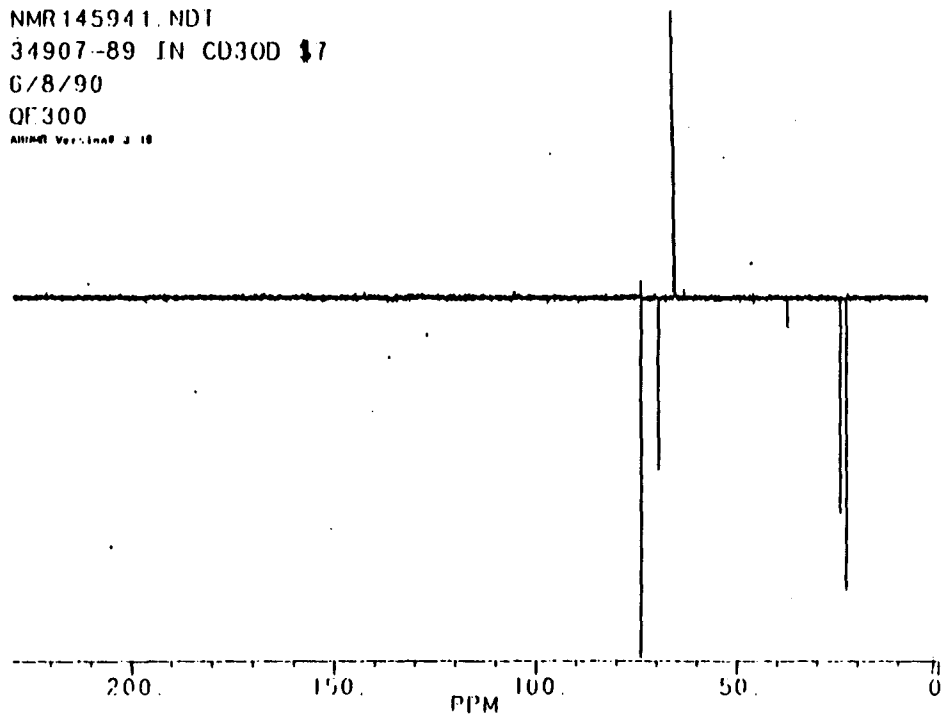
34907-89 IN CD3OD $7
6/8/90
QE300
200.
150.
100
50.
0
PPM


HO
OH
O
O
O
O

(2)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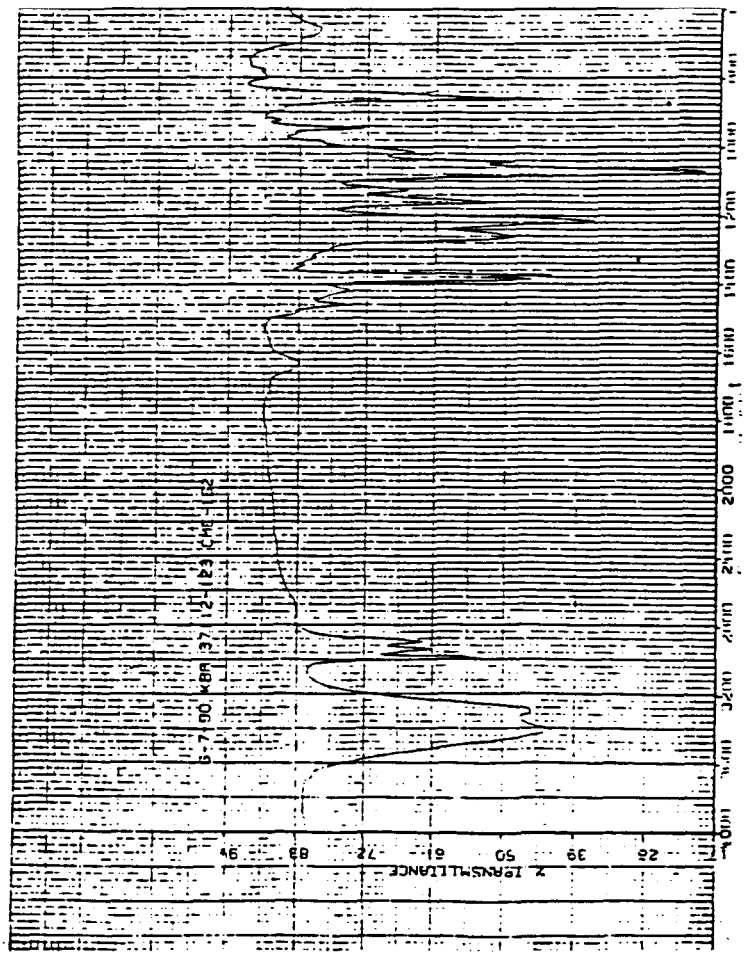
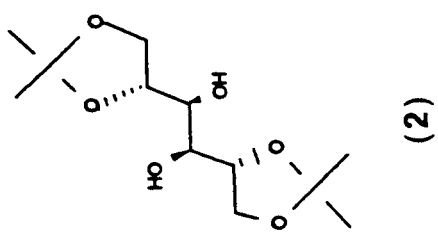
6/8/90
QE300
200.
150.
100.
50.
0.
PPM





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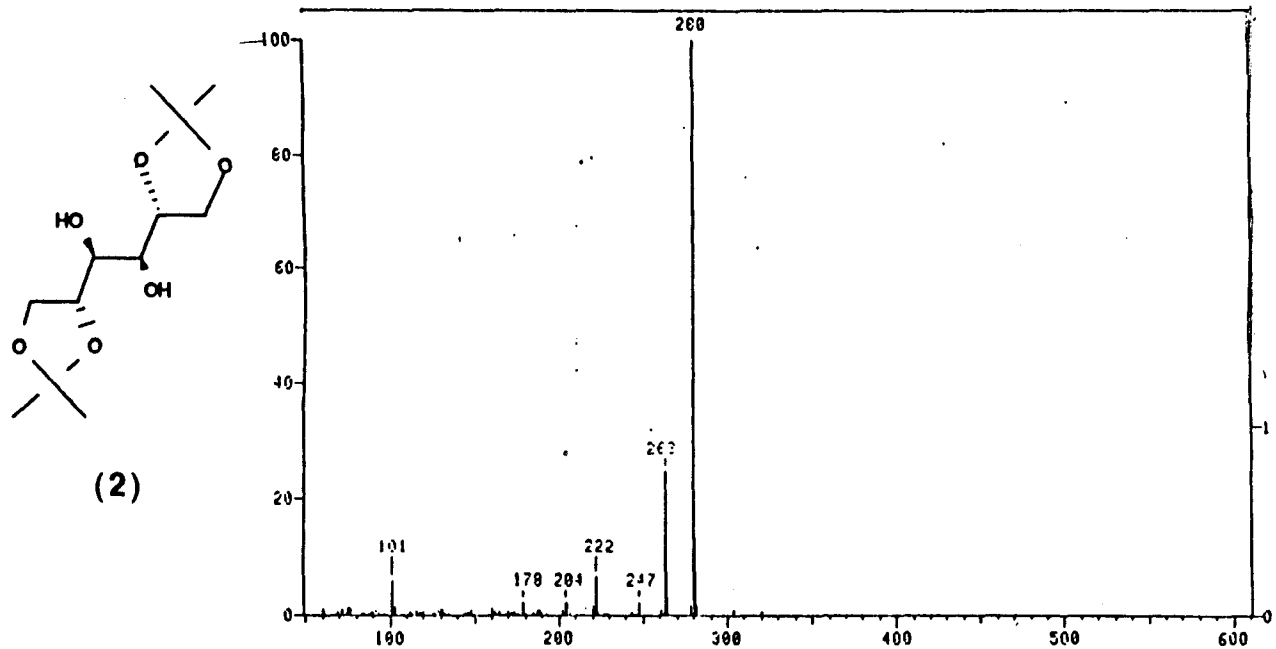
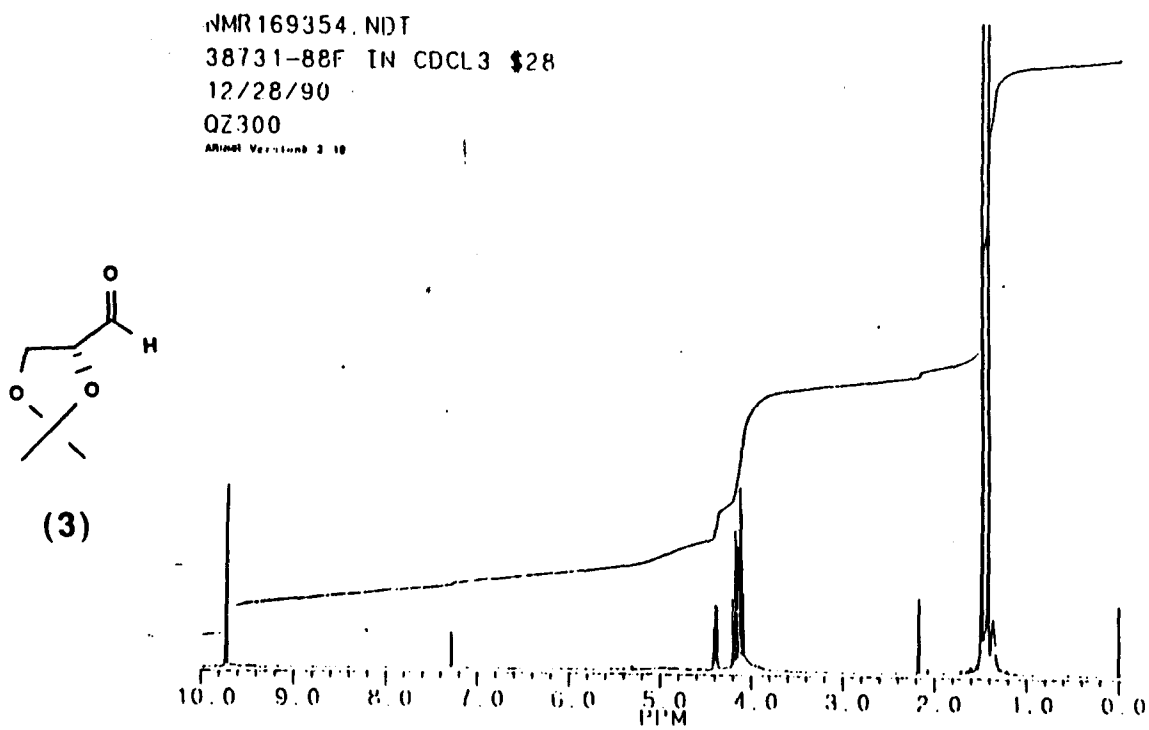
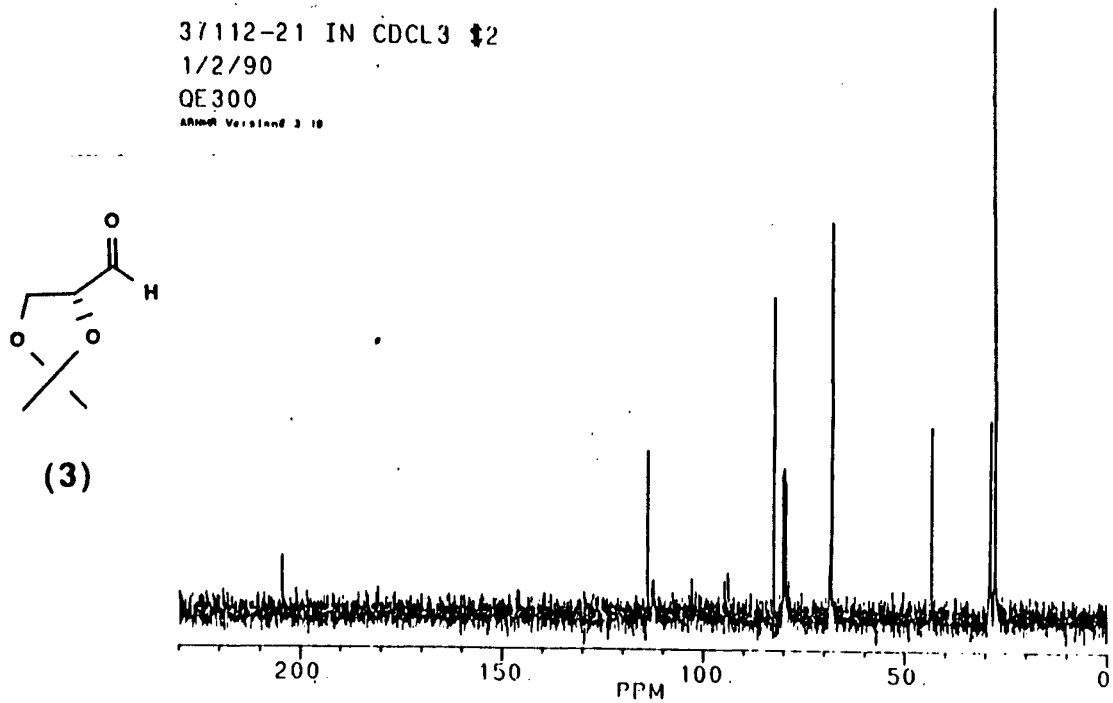

HO
OH
O
O
O
O
(2)
100
80
60
40
20
0
101
178
204
222
247
263
280
100
200
300
400
500
600


NMR169354.NDT
38731-88F IN CDCL3 $28
12/28/90
QZ300
O
H
O
O
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

(3)



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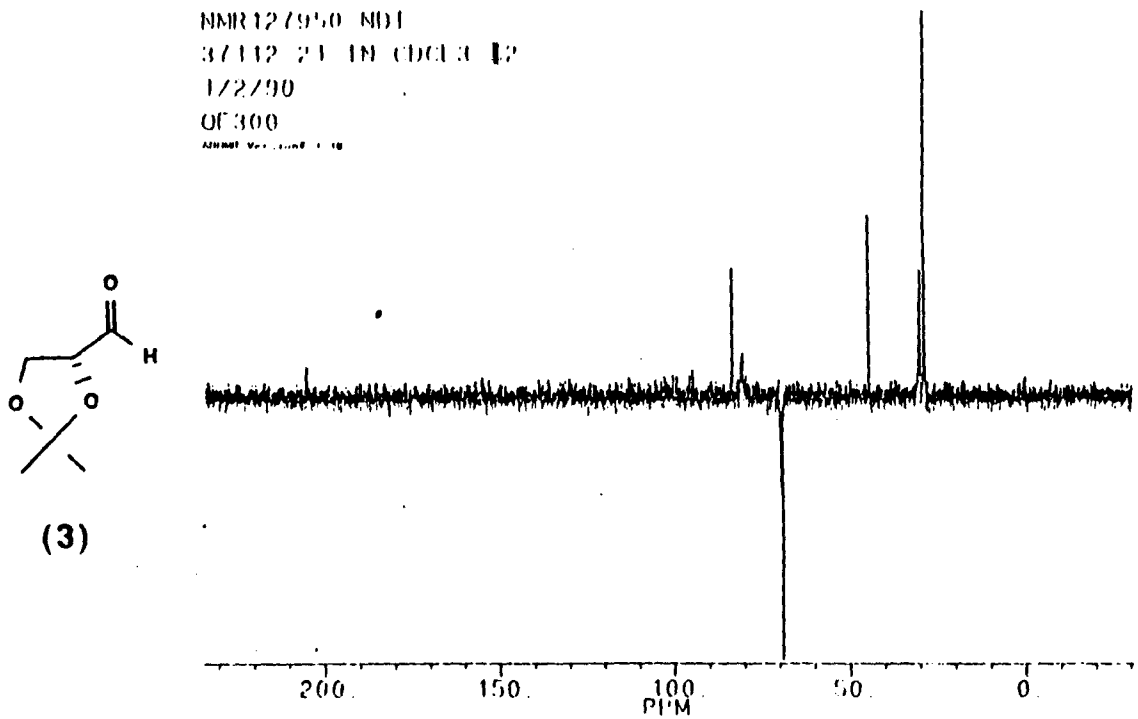
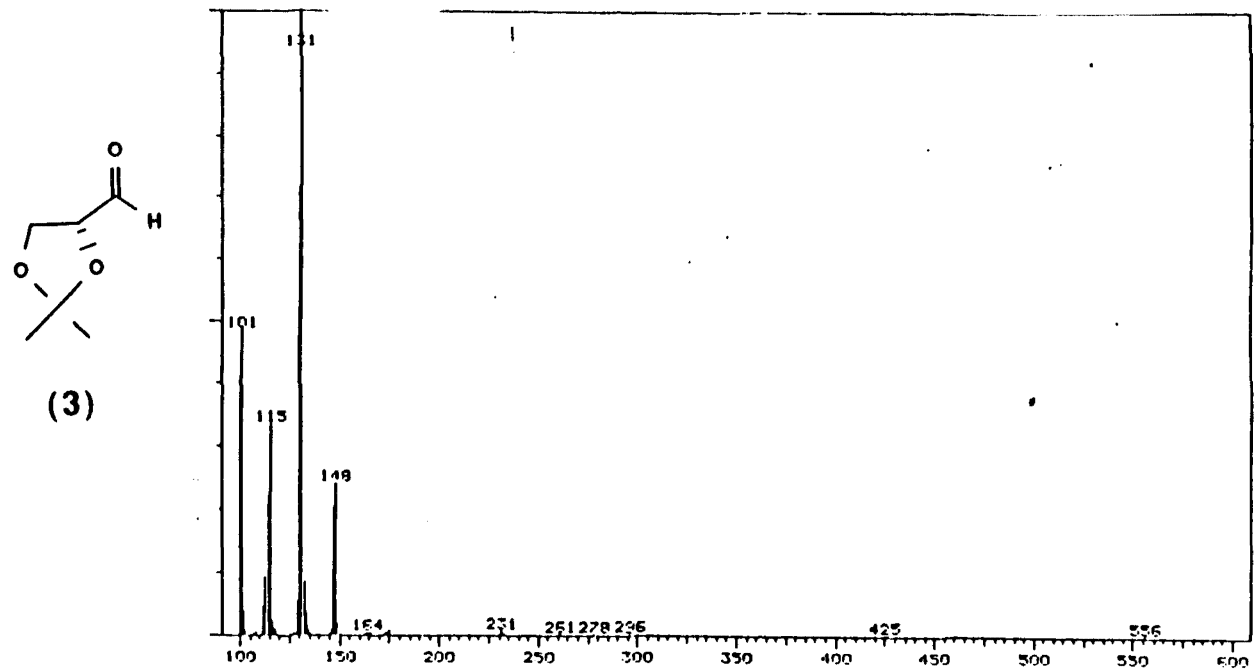
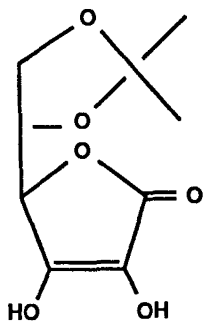


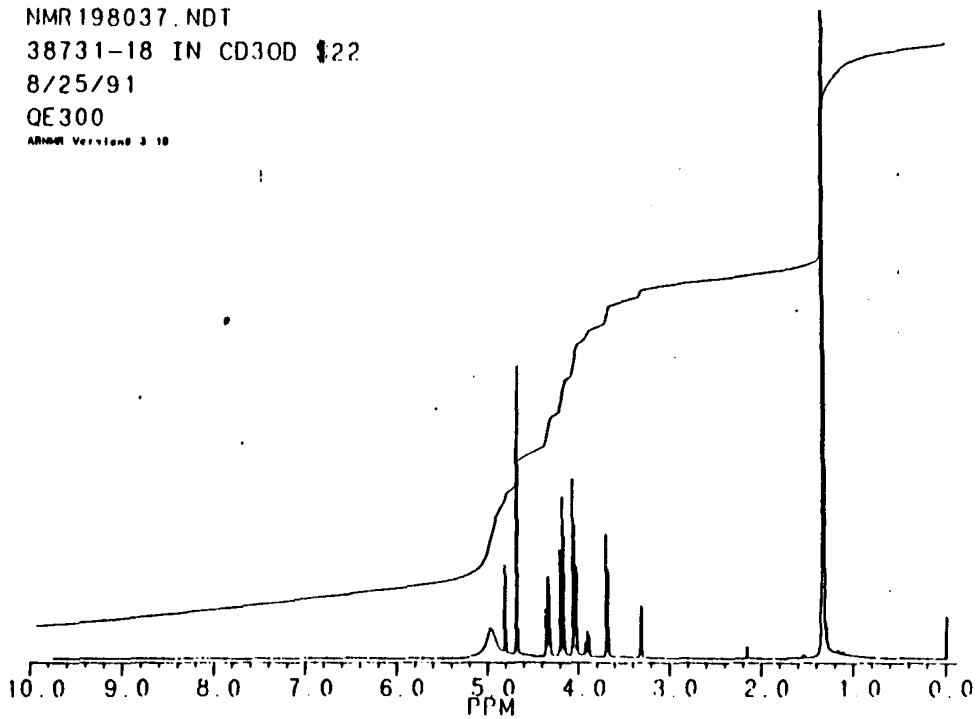
(3)

(3)


O
H
O
O
(3)
131
101
115
148
164
231
261 278 296
425
556
100
150
200
250
300
350
400
450
500
550
600


O
O
O
O
HO
OH

(5)


NMR198037.NDT
38731-18 IN CD3OD $22
8/25/91
QE300
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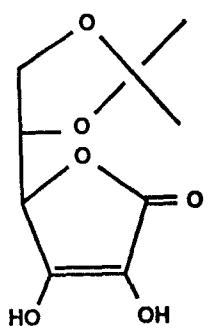
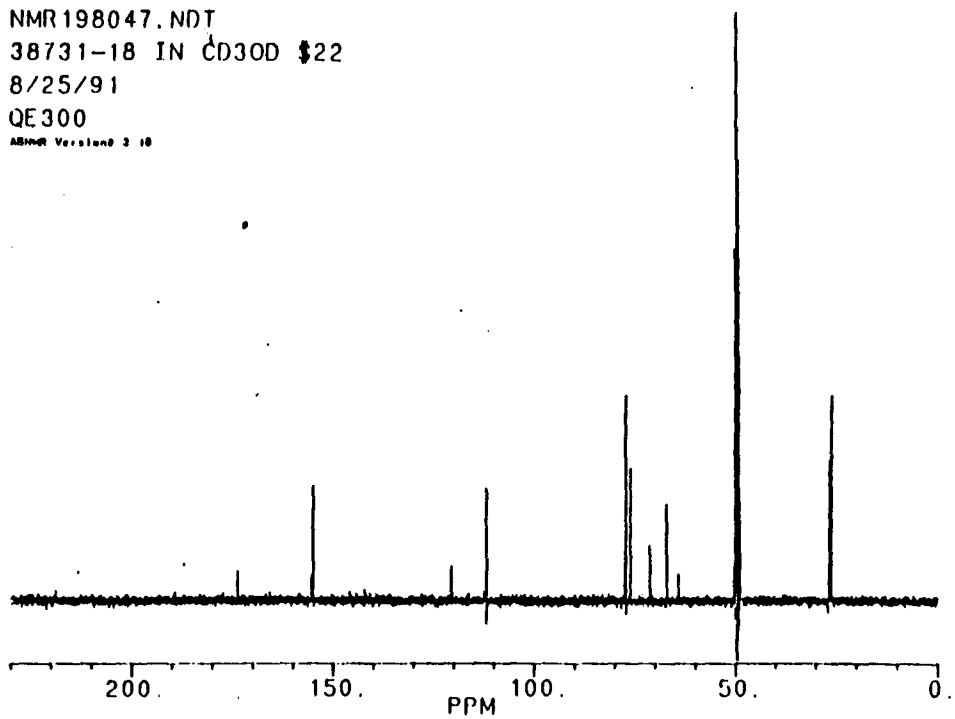
PPM


O
O
O
O
HO
OH

(5)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38731-18 IN CD3OD $22
8/25/91
QE300
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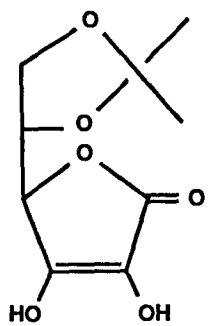
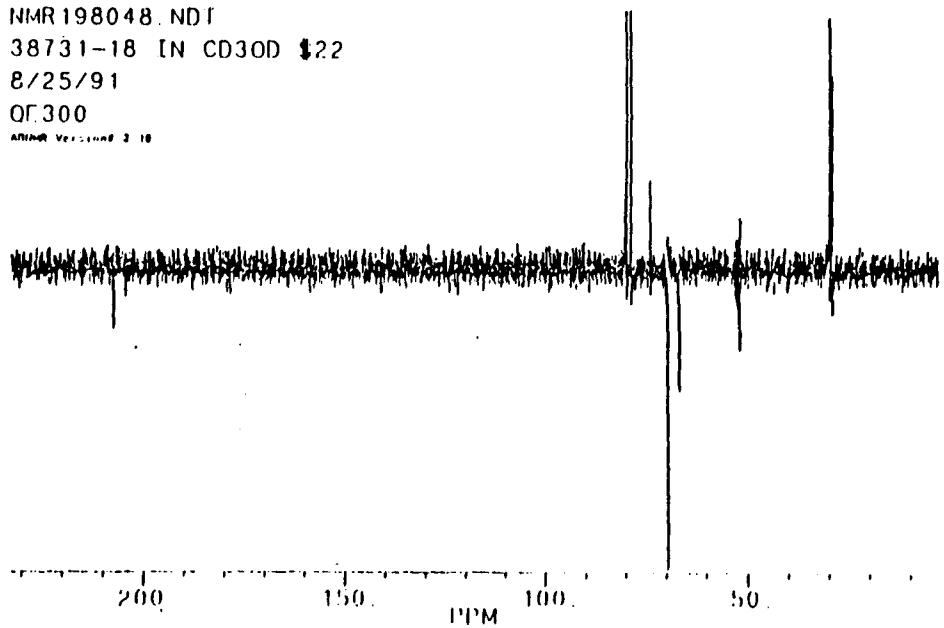
150.
100.
50.
0.
PPM


O
O
O
O
HO
OH

(5)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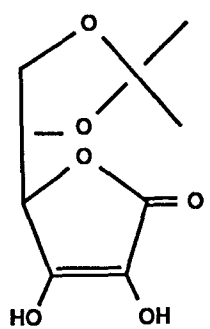
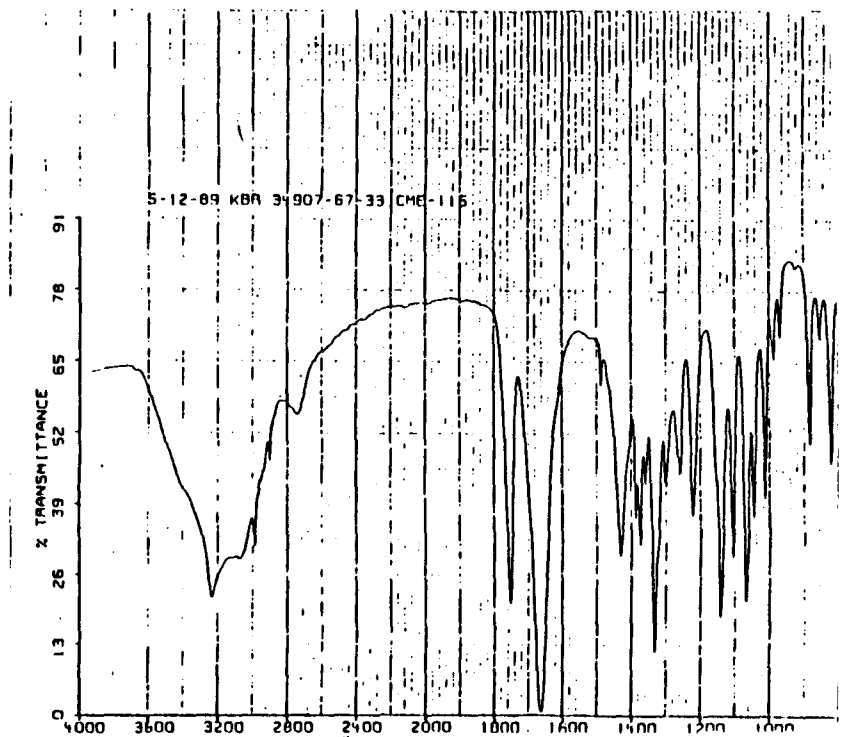
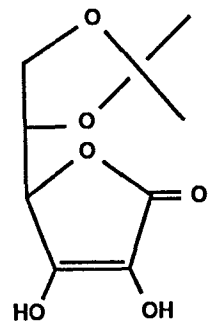
38731-18 IN CD3OD $22
8/25/91
QE300
200
150
100
50
PPM

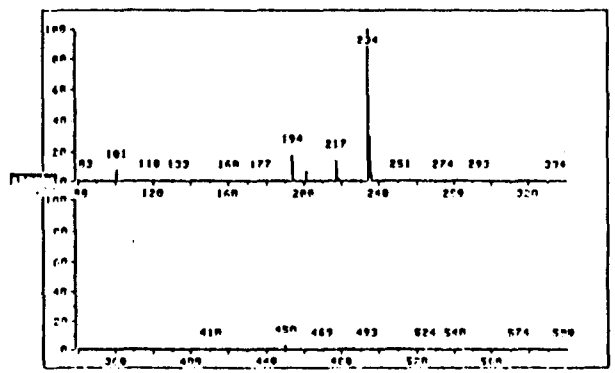

O
O
O
O
HO
OH

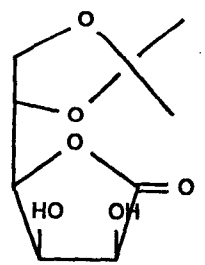
(5)


5-12-89 KBR 34907-67-33 CME-116
% TRANSMITTANCE
0
13
26
39
52
65
78
91
4000
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000

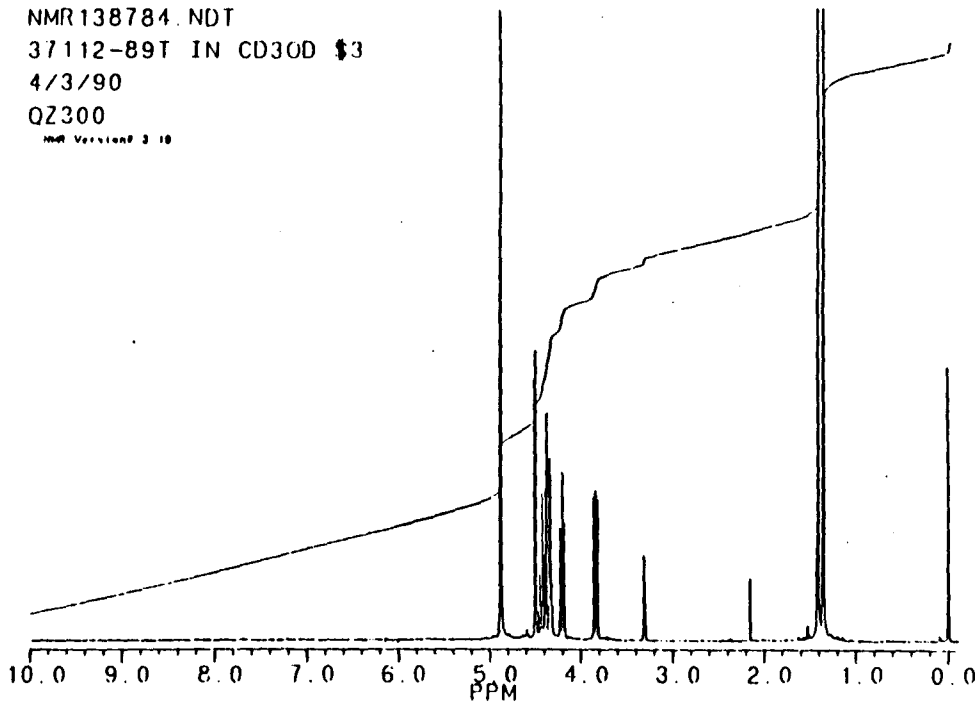


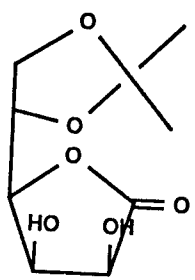
(5)



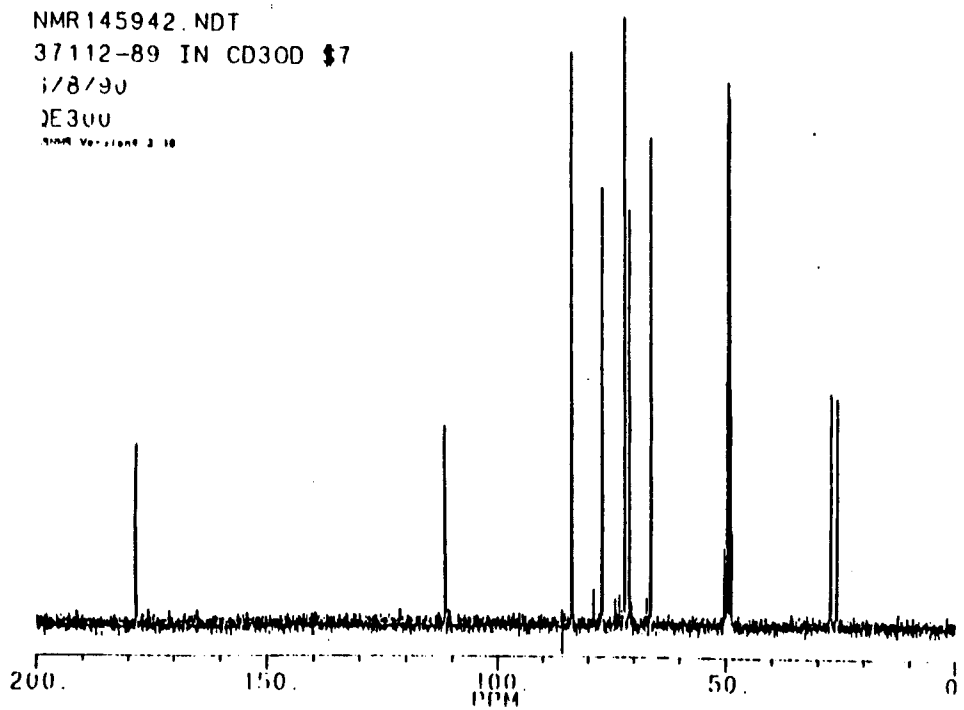

O
O
O
O
HO
OH

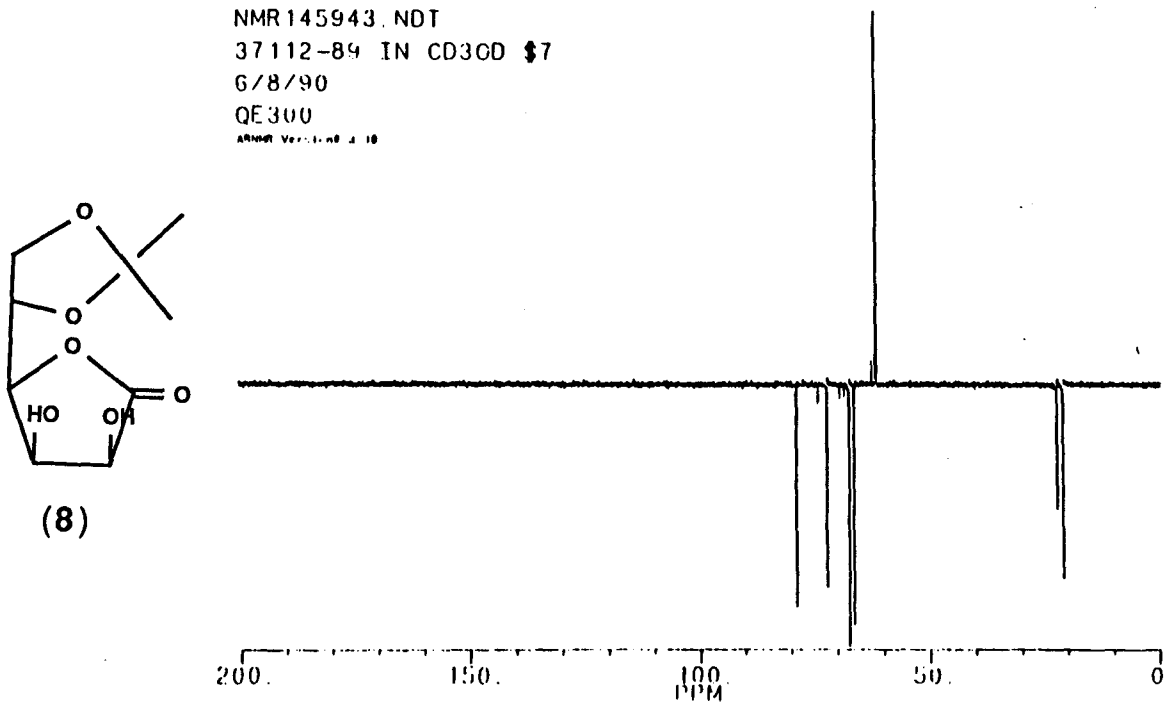
(8)


NMR138784.NDT
37112-89T IN CD3OD $3
4/3/90
QZ300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

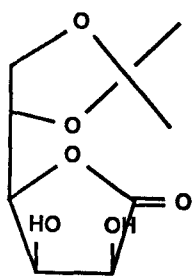

O
O
O
O
HO
OH

(8)

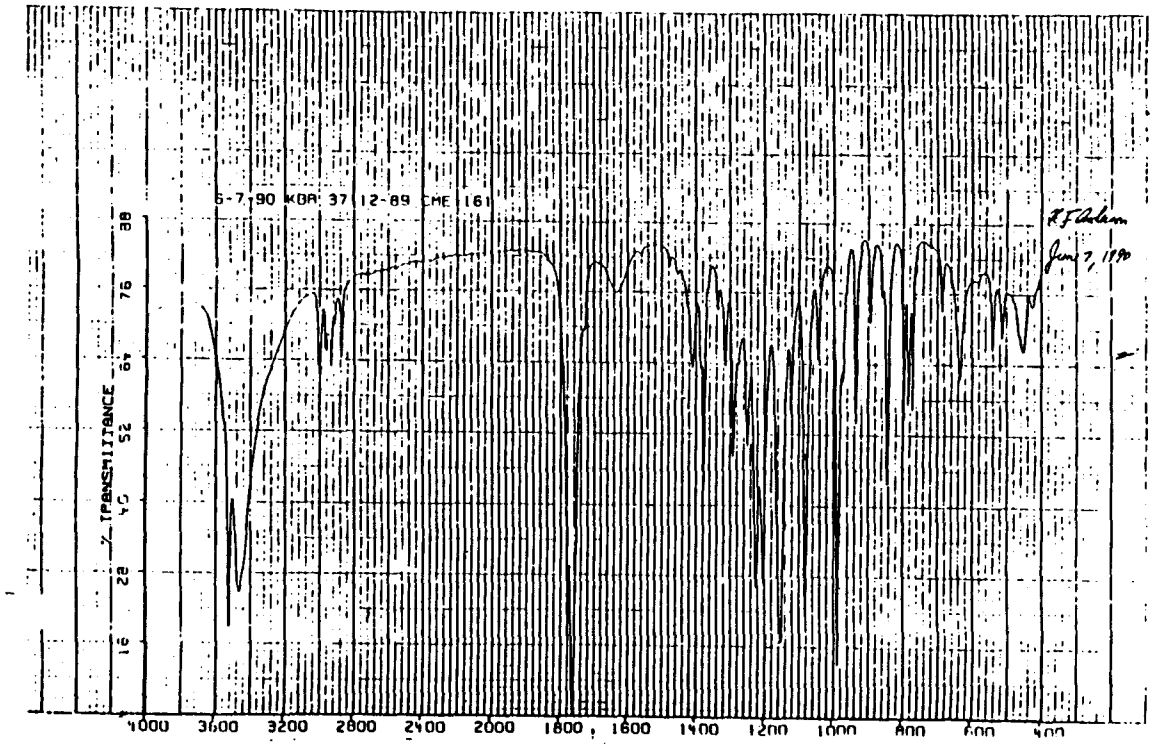

NMR145942.NDT
37112-89 IN CD3OD $7
200.
150.
100.
50.
0.
PPM


NMR145943.NDT
37112-89 IN CD3OD $7
6/8/90
QE300
O
O
O
O
HO
OH
200.
150.
100.
50.
0.
PPM

(8)


O
O
O
O
HO
OH

(8)


5-7,90 KBR 37 12-89 CHE 161
% TRANSMITTANCE
88
76
64
52
40
28
16
4000
3600
3200
2800
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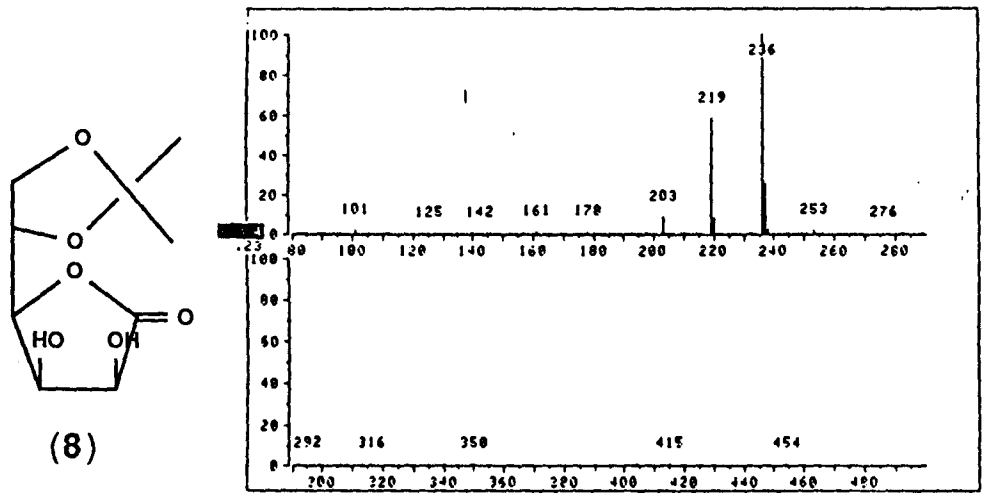
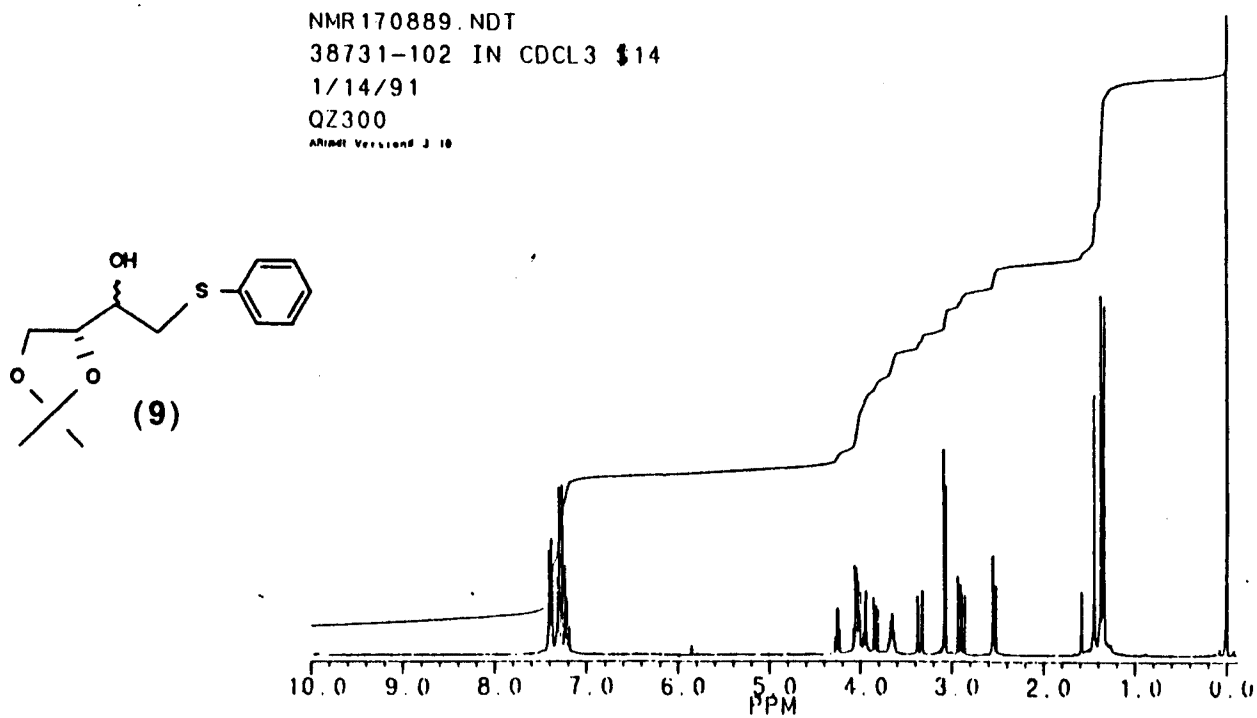
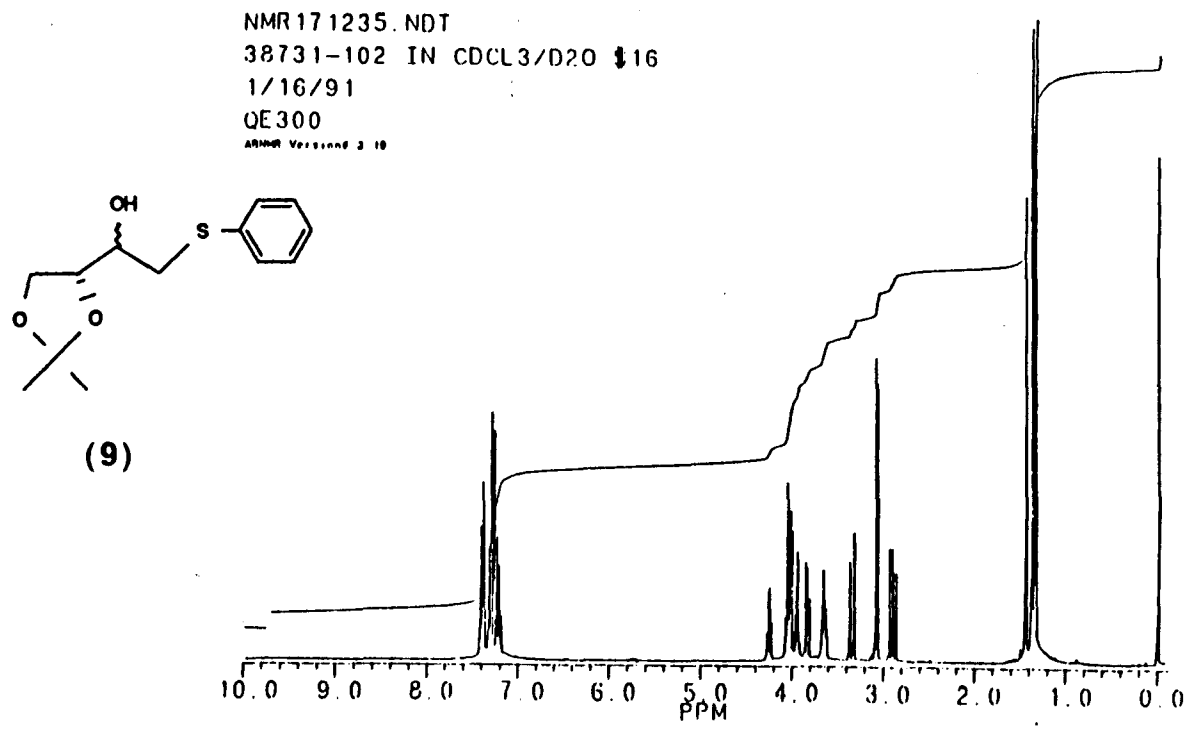
2000
1800
1600
1400
1200
1000
800
600
400

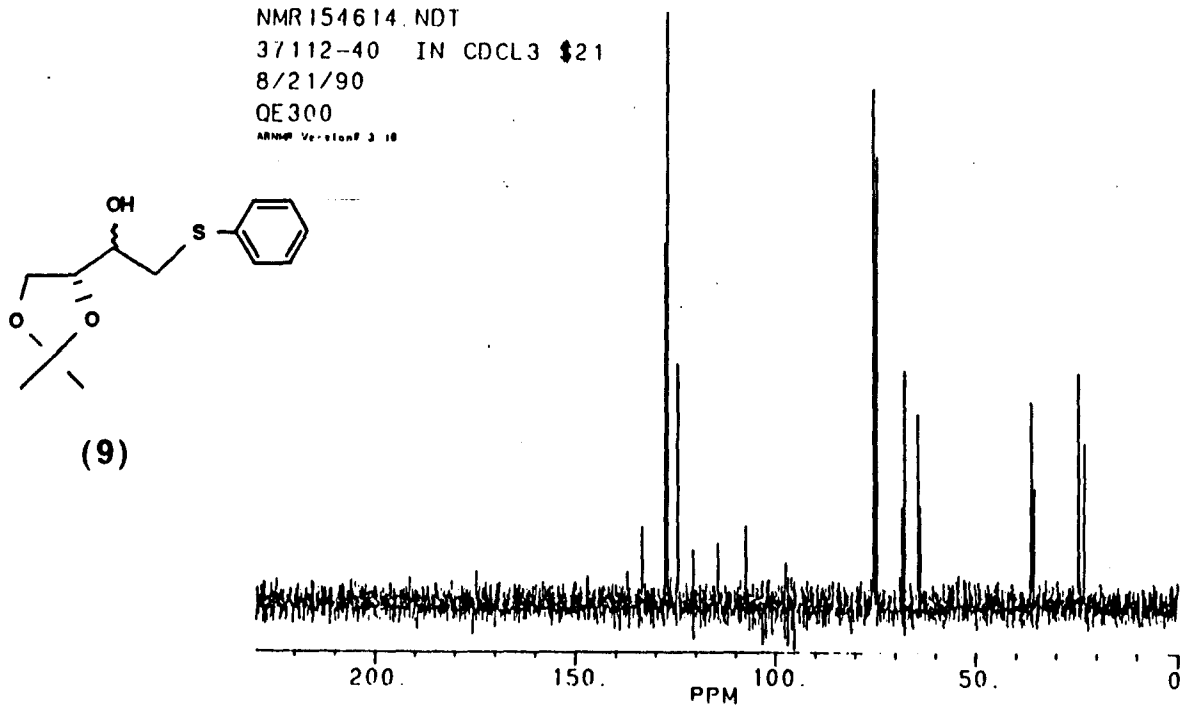

O
O
O
O
HO
OH
100
80
60
40
20
0
236
219
203
101
125
142
161
178
253
276
80
100
120
140
160
180
200
220
240
260
280
292
316
350
415
454
300
320
340
360
380
400
420
440
460
480

(8)

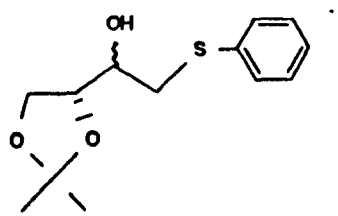

NMR170889.NDT
38731-102 IN CDCL3 $14
1/14/91
QZ300
OH
S
O
O
(9)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM


NMR171235.NDT
38731-102 IN CDCL3/D2O #16
1/16/91
QE300
OH
S
O
O
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
PPM

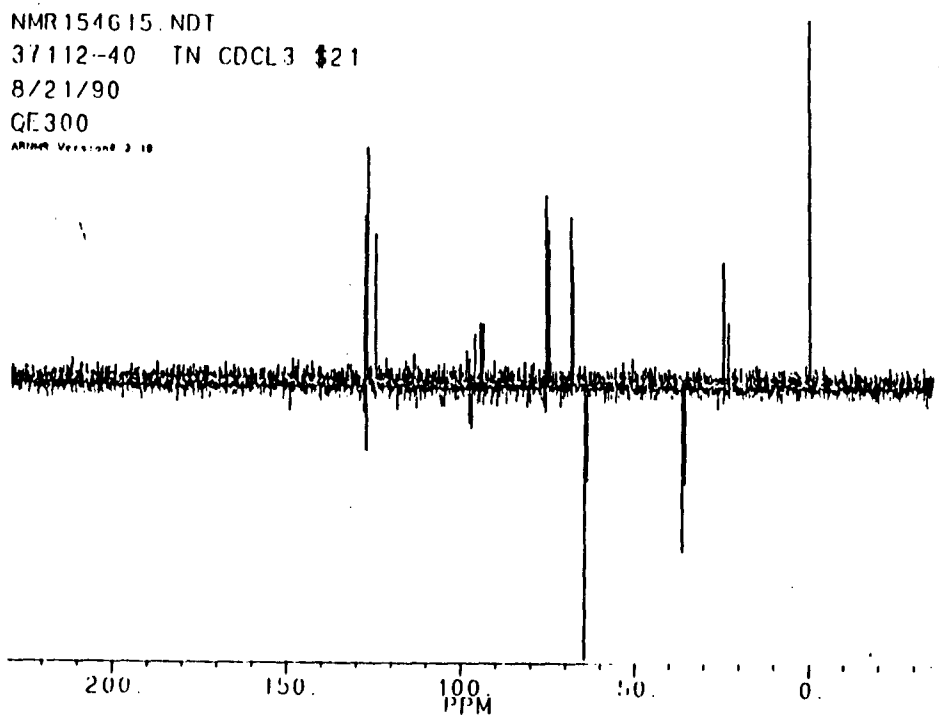
(9)

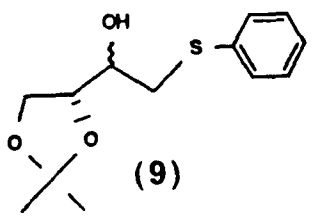

NMR154614.NDT
37112-40 IN CDCL3 $21
8/21/90
QE300
OH
S
O
O
200.
150.
100.
50.
0
PPM

(9)

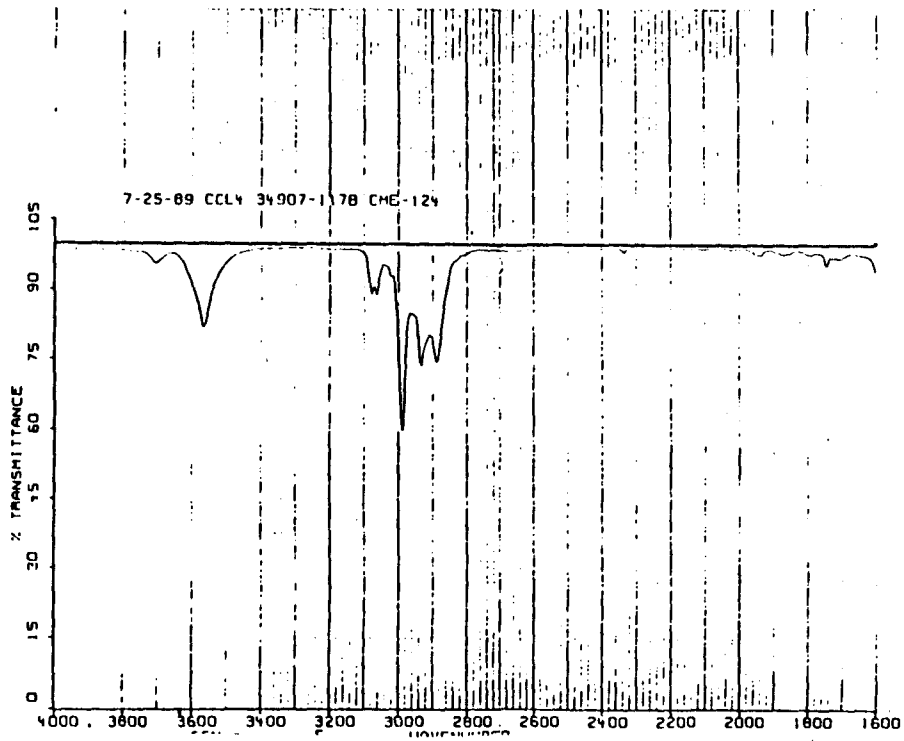

OH
S
O
O

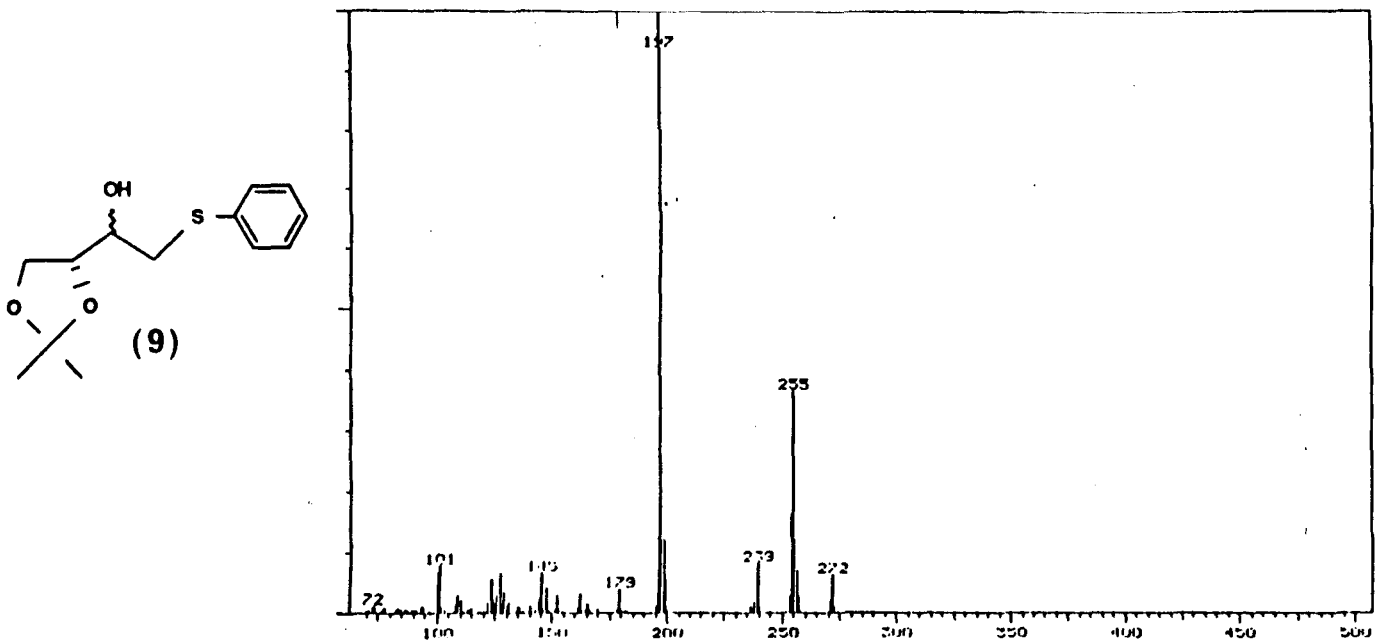
(9)

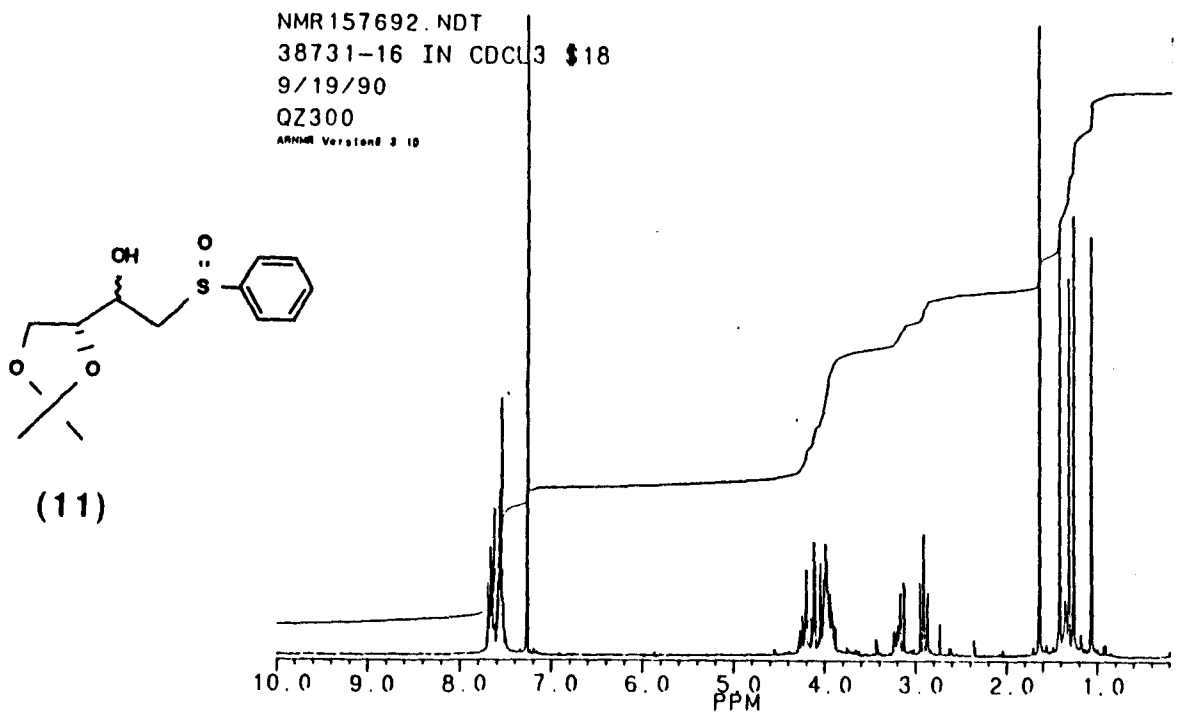

NMR154G15.NDT
37112-40 TN CDCL3 $21
8/21/90
QE300
200.
150.
100.
50.
0.
PPM


OH
S
O
O

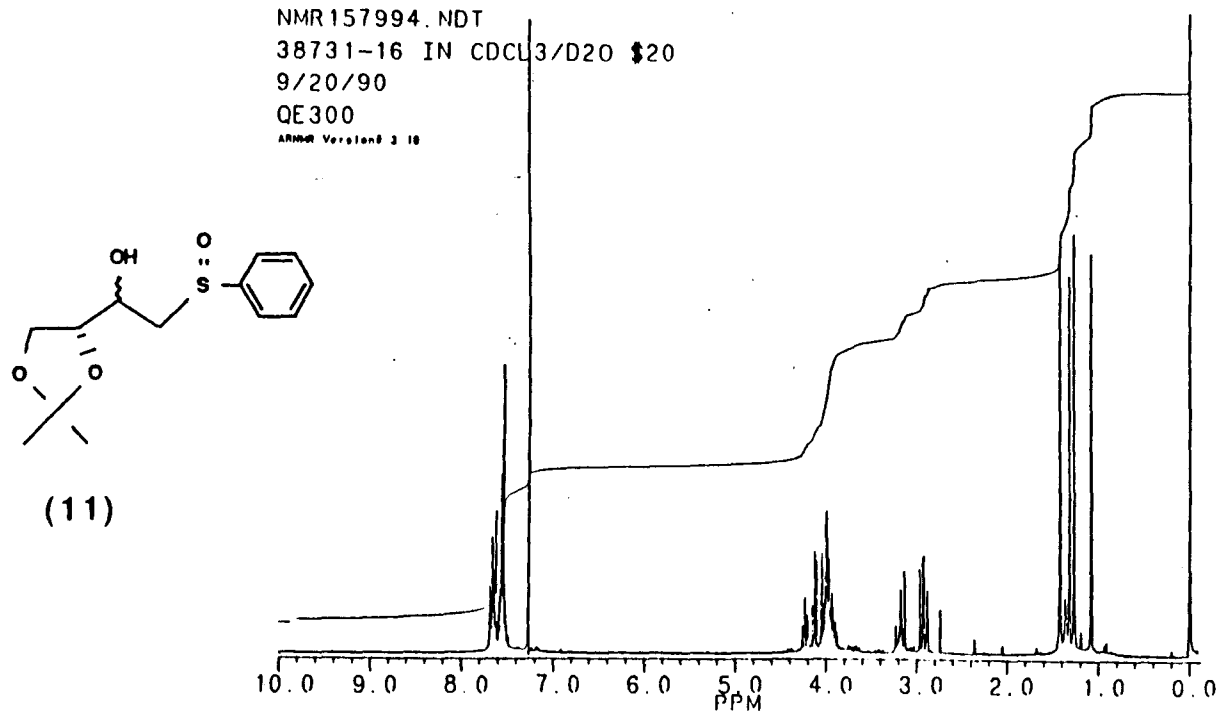
(9)


7-25-89 CCL4 34907-1178 CME-124
% TRANSMITTANCE
105
90
75
60
45
30
15
0
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600

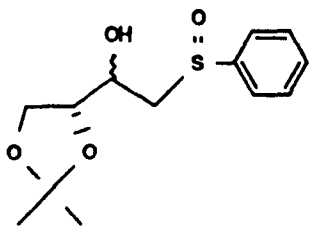

OH
S
O
O
(9)
197
255
101
179
273
272
72
100
150
200
250
300
350
400
450
500


NMR157692.NDT
38731-16 IN CDCL3 $18
9/19/90
QZ300
OH
O
S
O
O
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
PPM

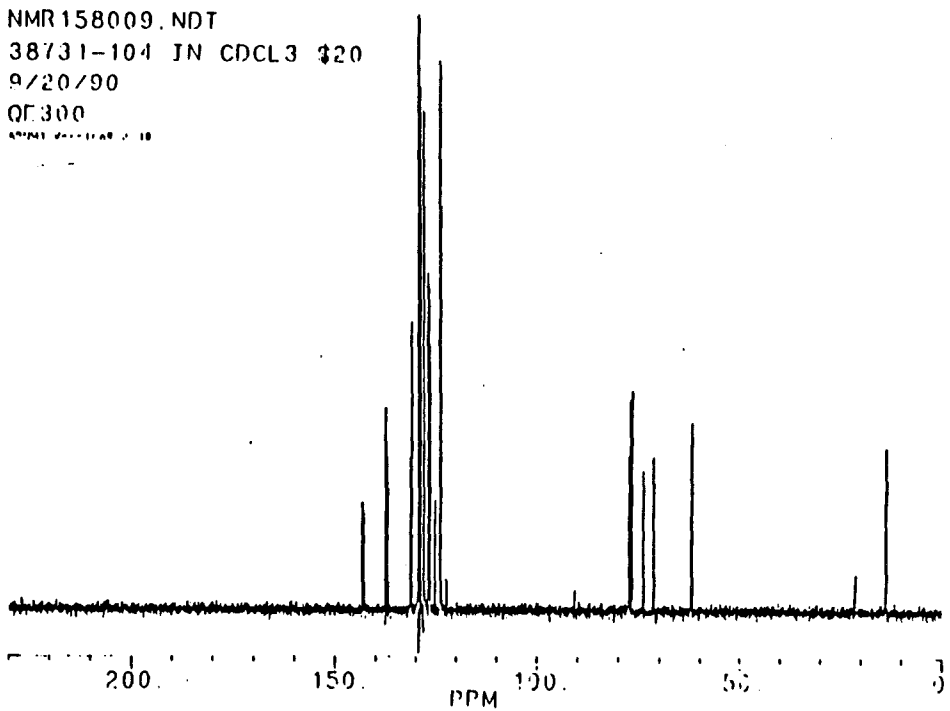
(11)

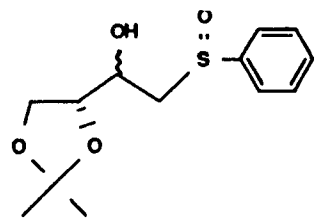

NMR157994.NDT
38731-16 IN CDCL3/D2O $20
9/20/90
QE300
OH
O
S
O
O
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

(11)

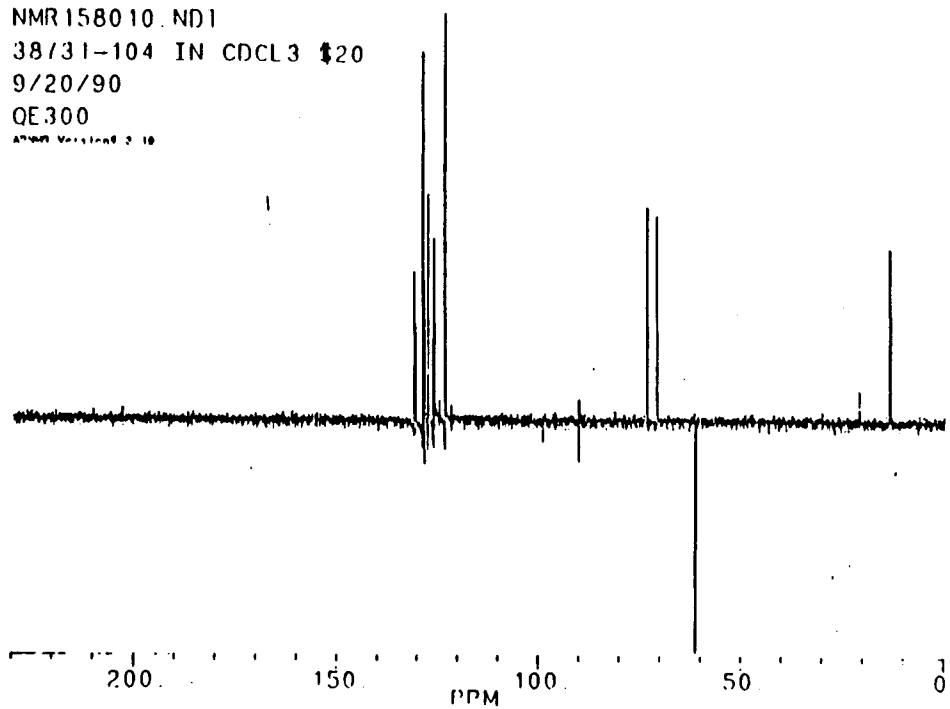

OH
O
S
O
O

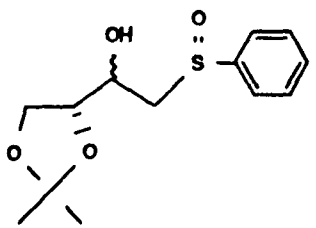
(11)


NMR158009.NDT
38731-104 IN CDCL3 #20
9/20/90
QE300
200.
150.
100.
50.
0.
PPM

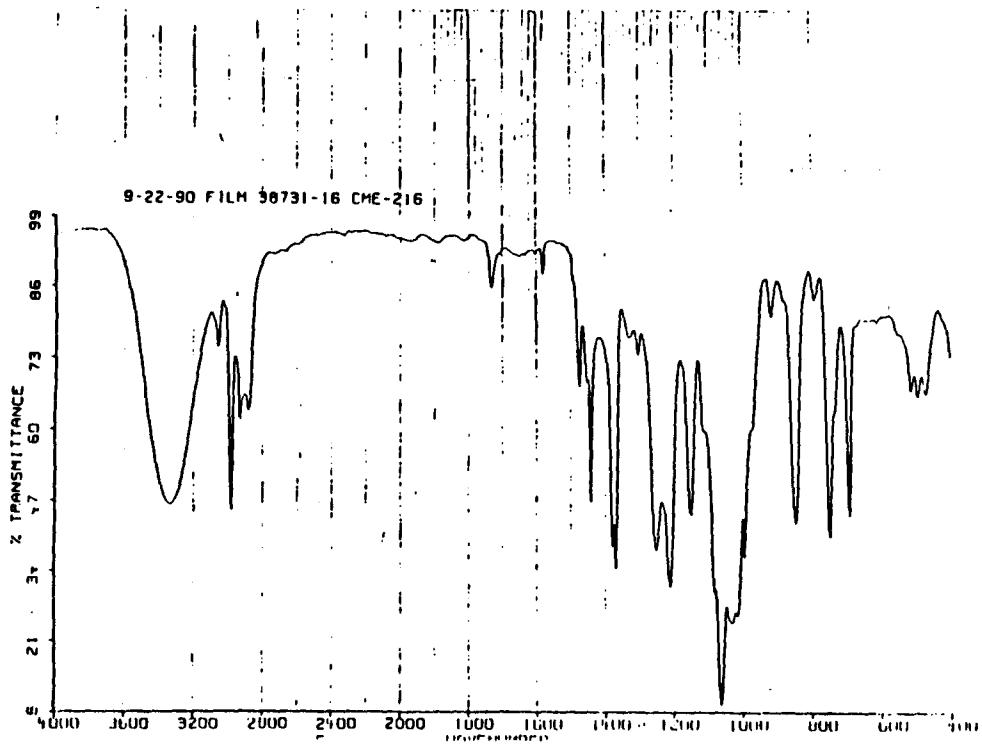

OH
O
S
O
O

(11)


NMR158010.ND1
38/31-104 IN CDCL3 #20
9/20/90
QE300
200
150
100
50
0
PPM


OH
O
S
O
O

(11)


9-22-90 FILM 38731-16 CME-216
% TRANSMITTANCE
99
86
73
60
47
34
21
8
4000
3600
3200
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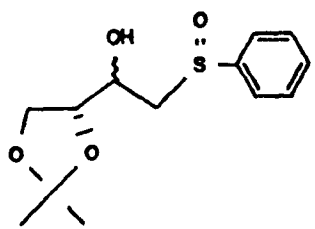
2400
2000
1800
1600
1400
1200
1000
800
600
400



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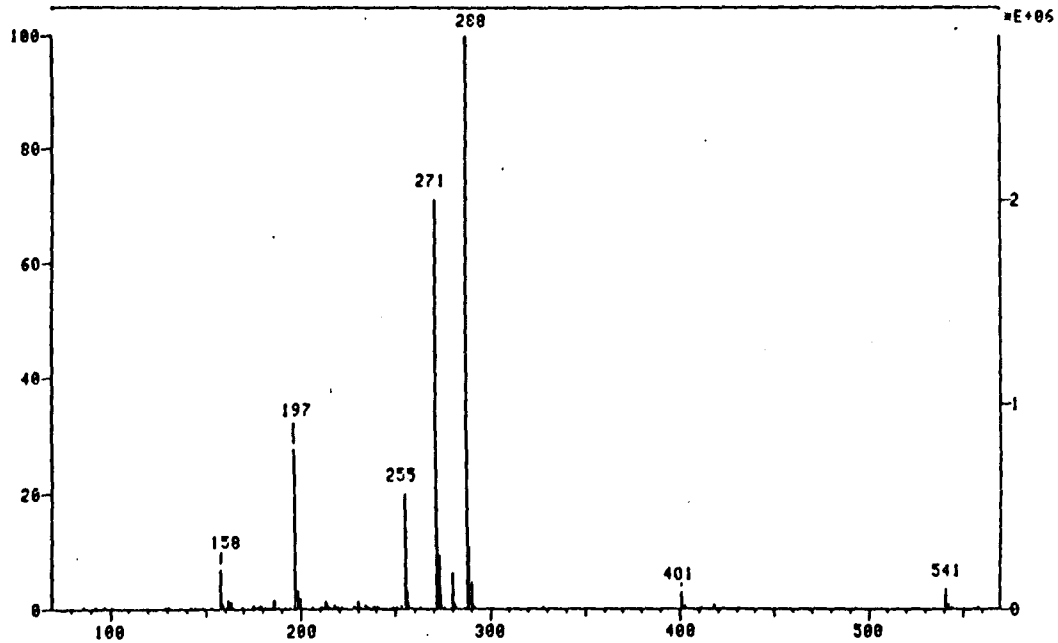
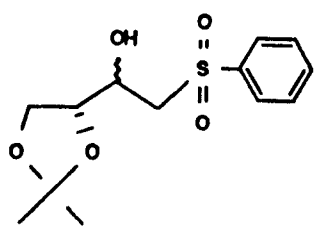
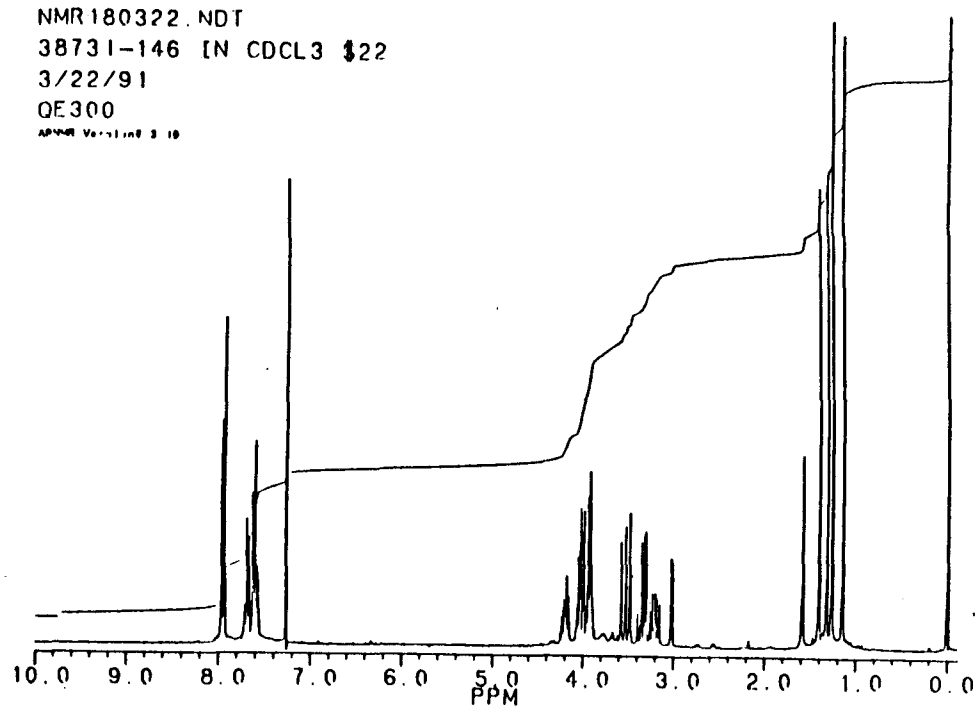



OH
O
S
O
O
O

(12)


NMR180322.NDT
38731-146 IN CDCL3 $22
3/22/91
QE300
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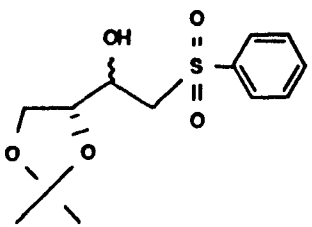
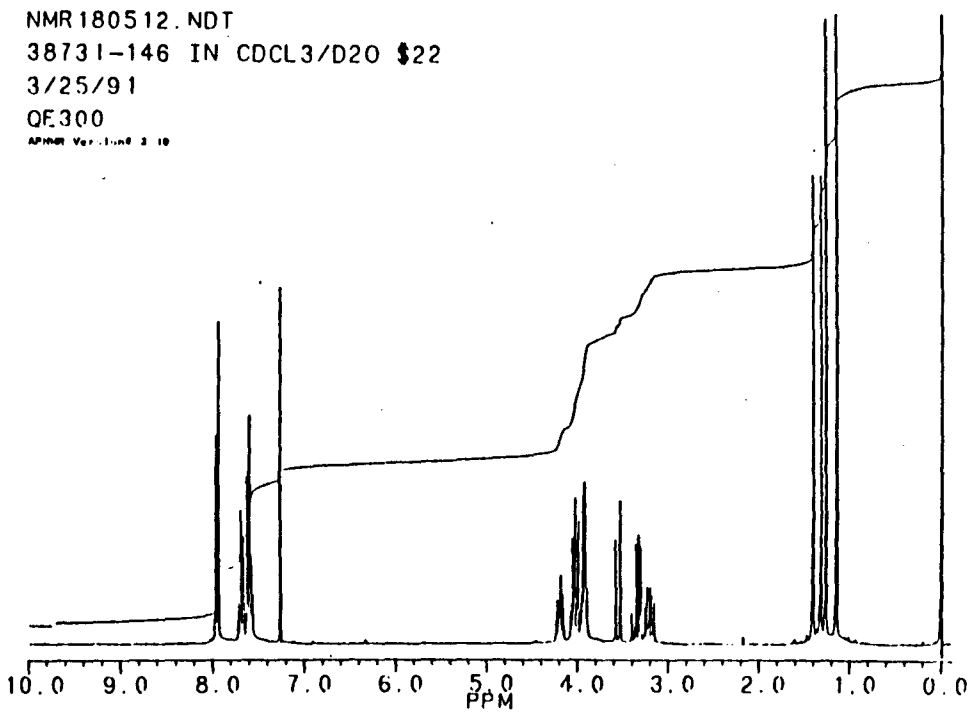
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM


OH
O
S
O
O
O

(12)


NMR180512.NDT
38731-146 IN CDCL3/D2O $22
3/25/91
QE300
10.0
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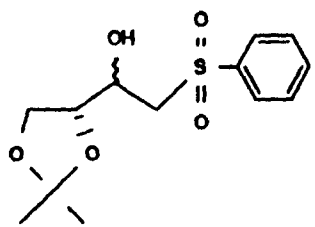
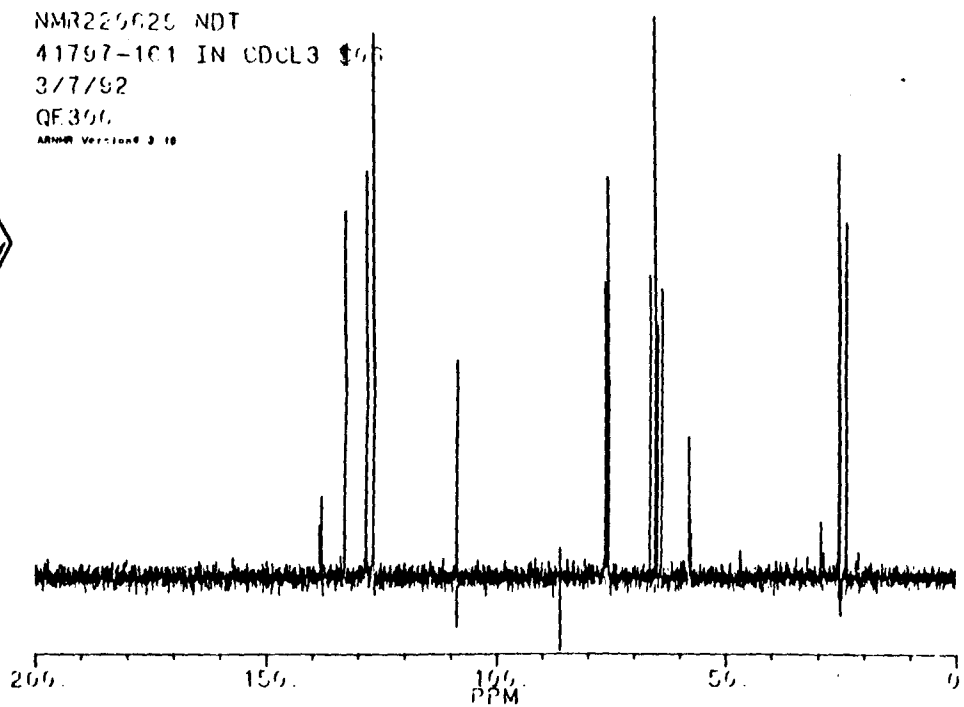
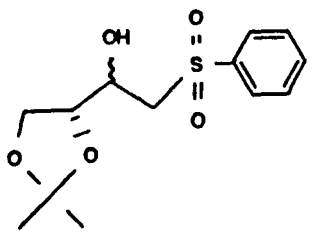
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

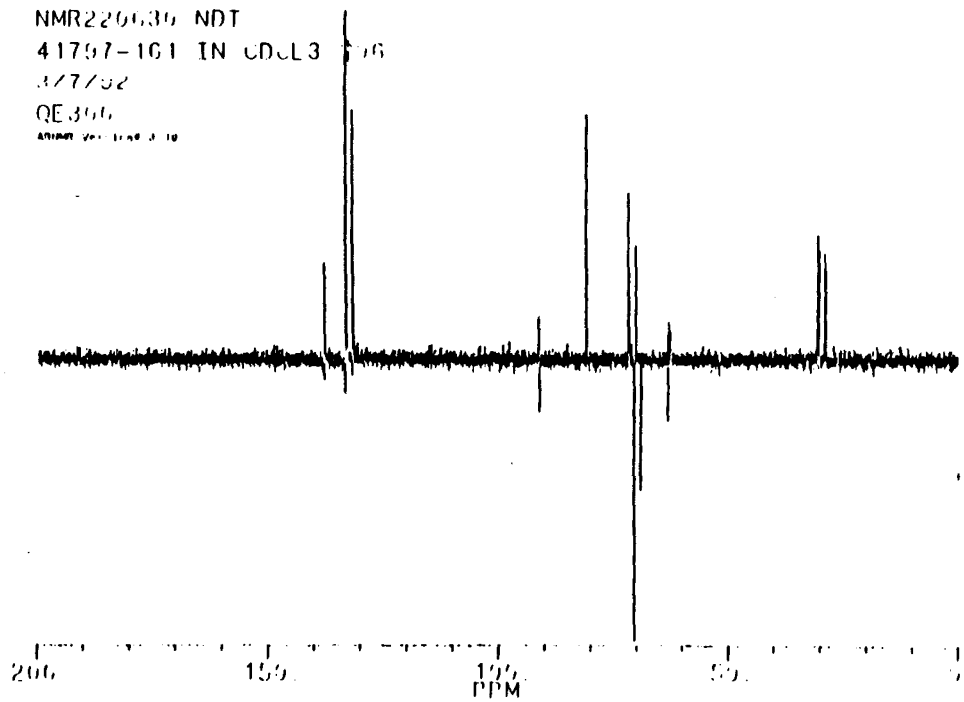

OH
O
S
O
O
O

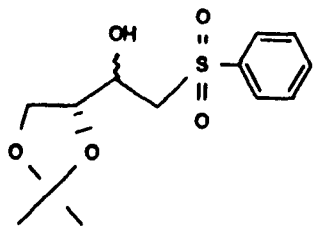
(12)


NMR220628 NDT
41797-101 IN CDCL3
3/7/92
QE300
200.
150.
100.
50.
0
PPM


OH
O
S
O
O
O

(12)


NMR220630 NDT
41797-161 IN CDCL3
QE300
200
150
100
50
PPM



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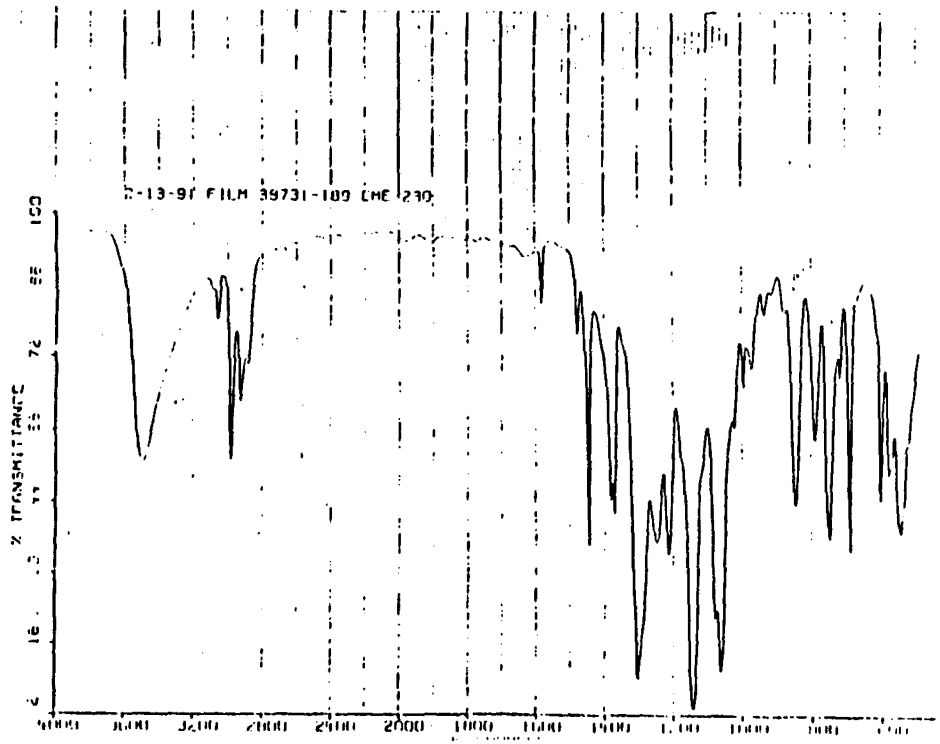
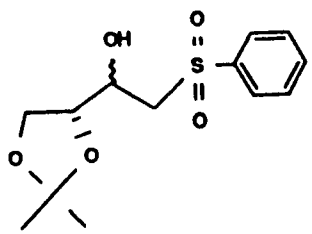
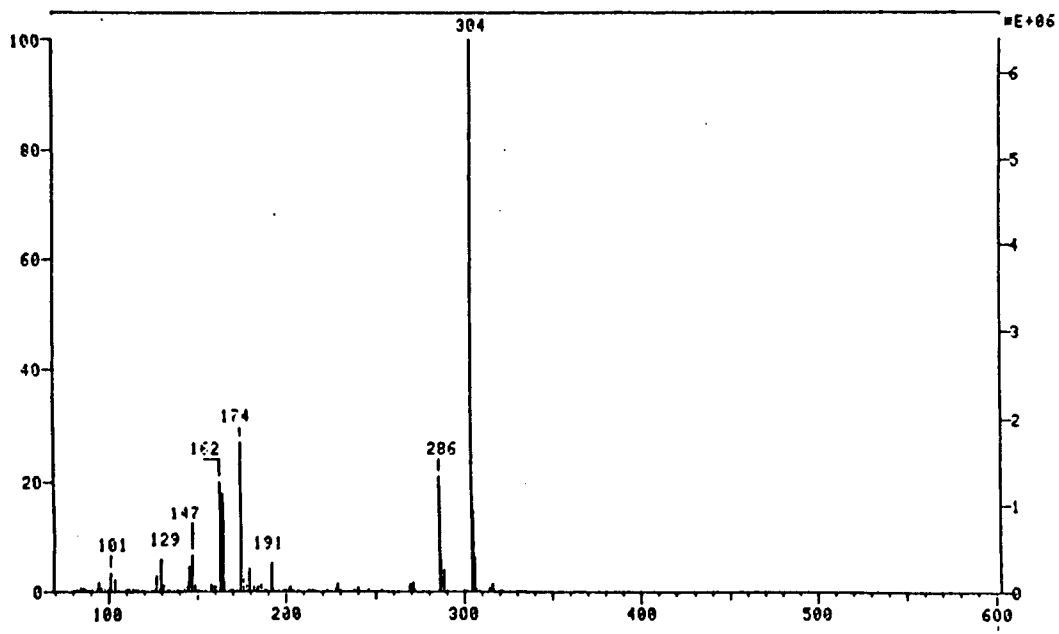



OH
O
S
O
O
O

(12)


304
286
174
162
147
129
101
191
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100
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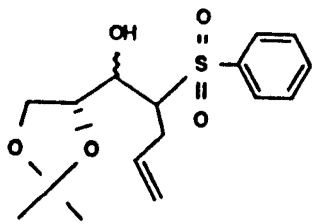
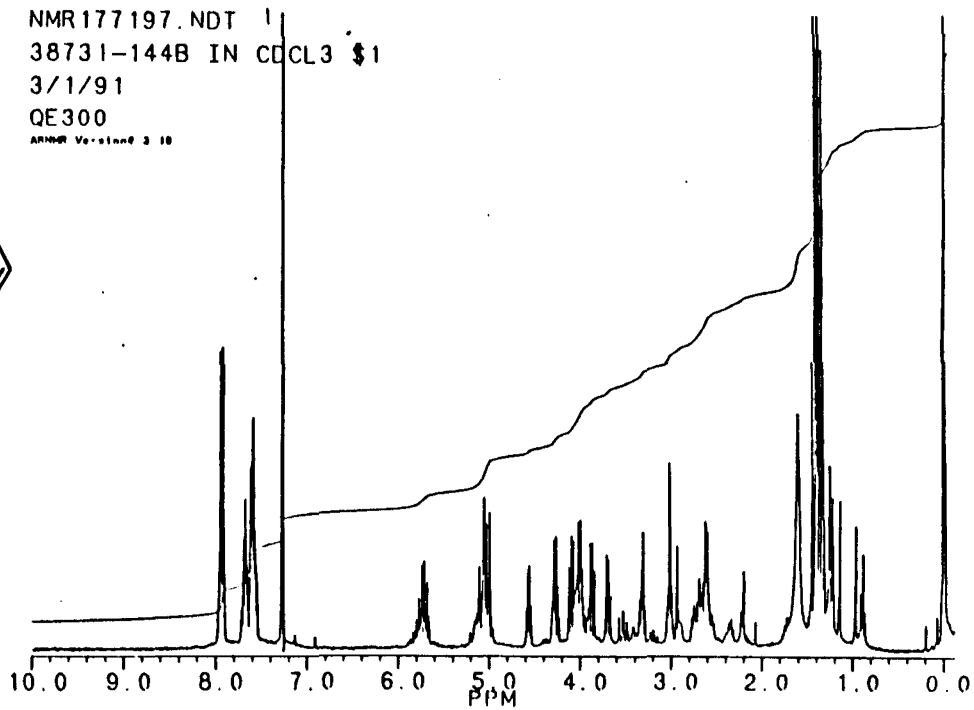
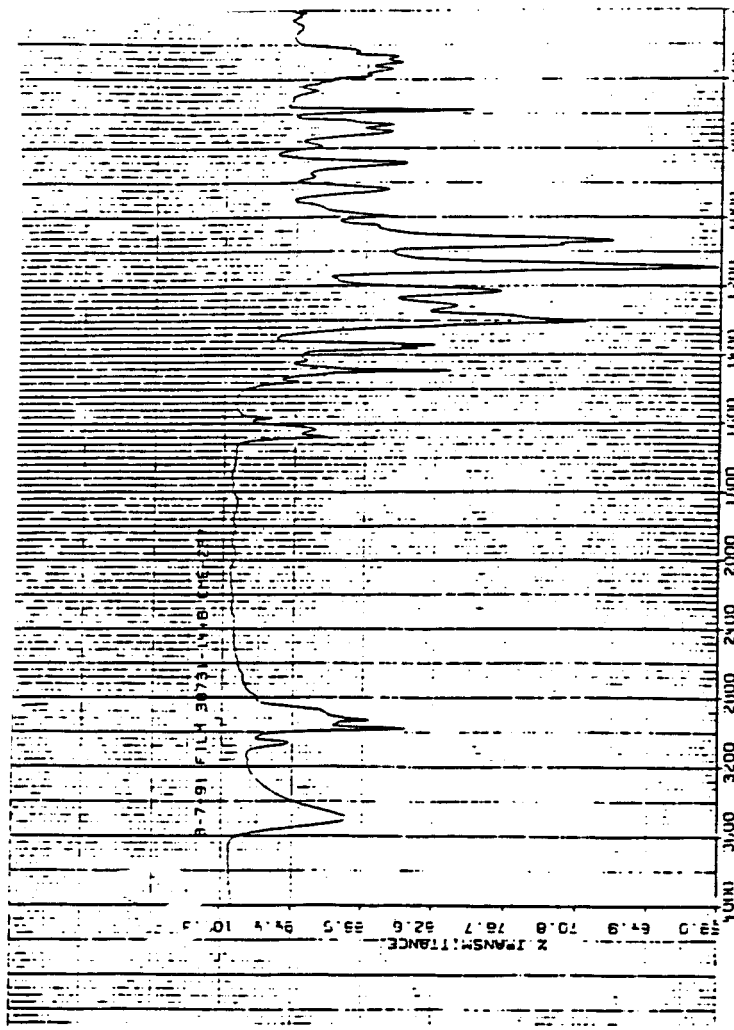
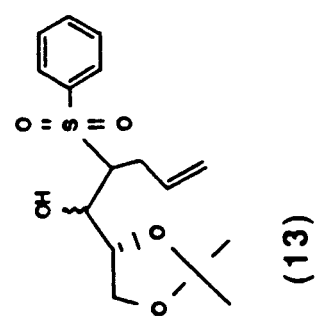
300
400
500
600
E+06
6
5
4
3
2
1
0


OH
O
S
O
O
O

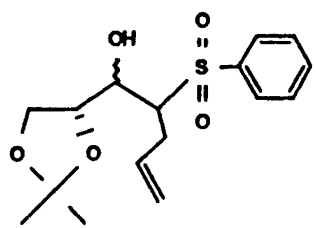
(13)


NMR177197.NDT 1
38731-144B IN CDCL3 $1
3/1/91
QE300
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
PPM

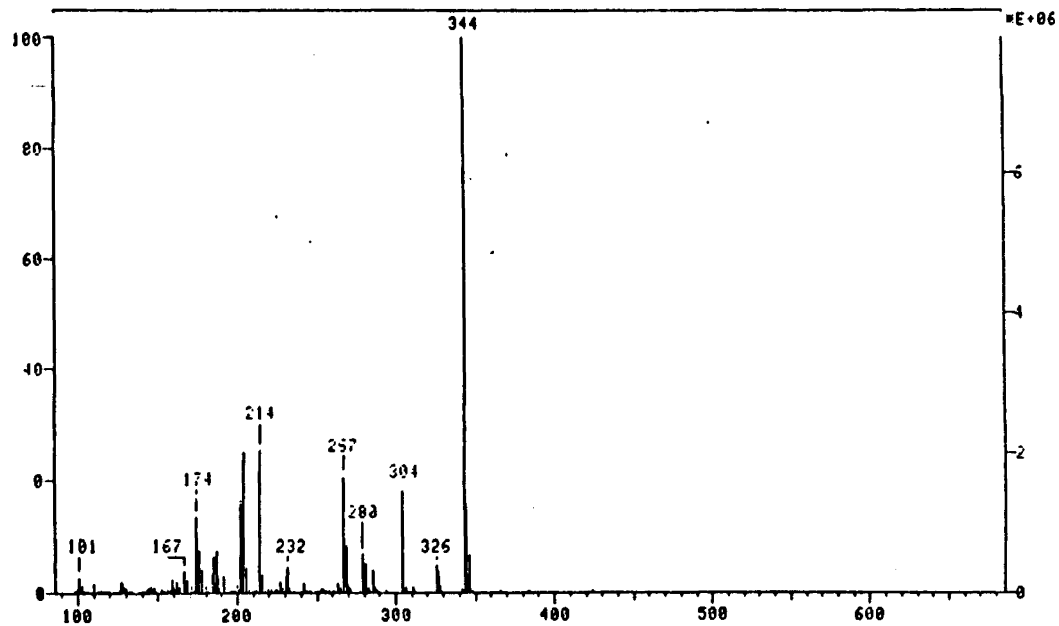




(13)


OH
O
S
O
O
O

(13)


344
E+06
100
80
60
40
0
6
4
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0
214
257
304
174
280
101
167
232
326
100
200
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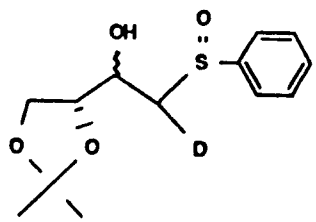
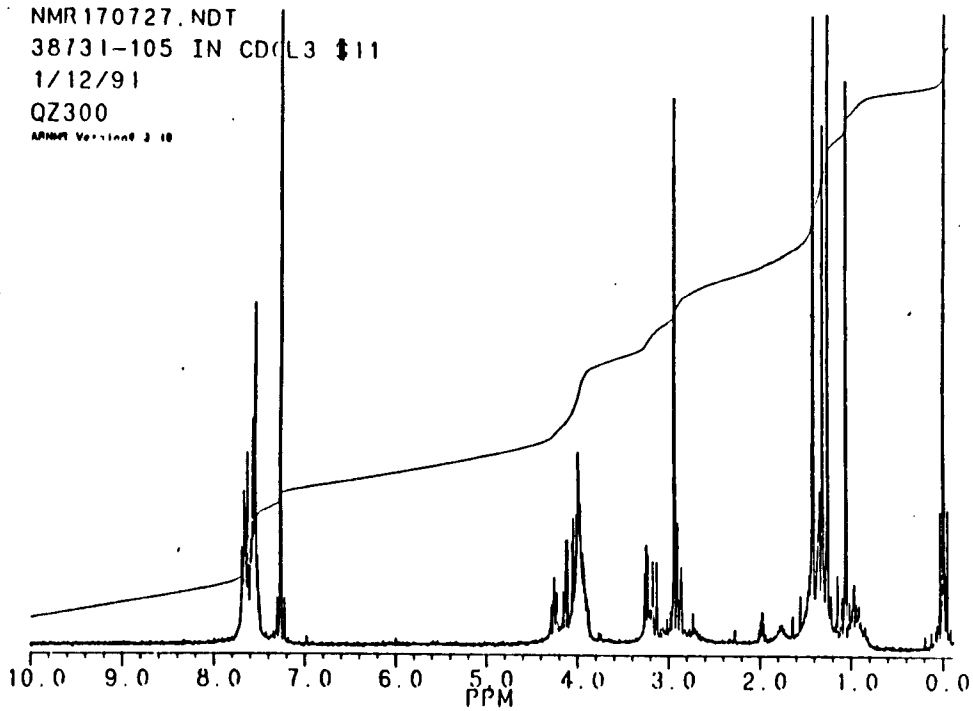
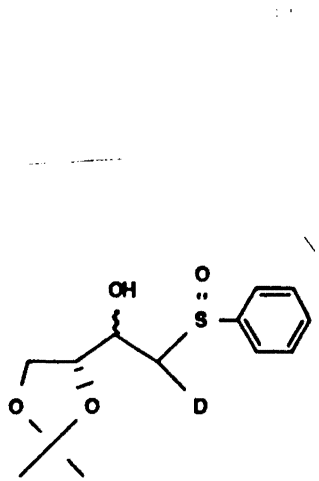
500
600

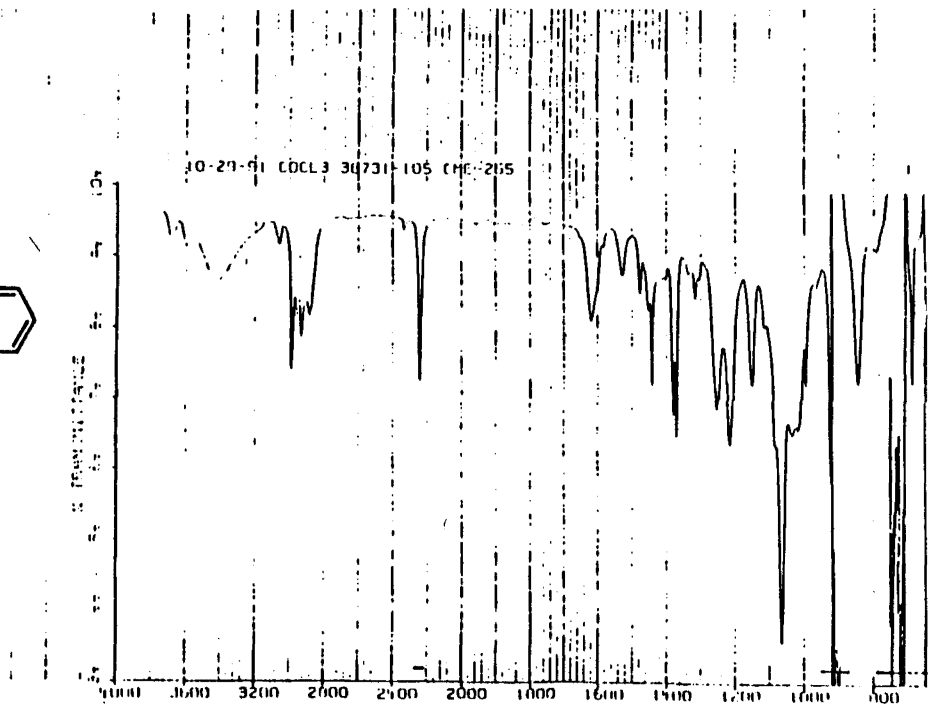

OH
O
S
O
O
D

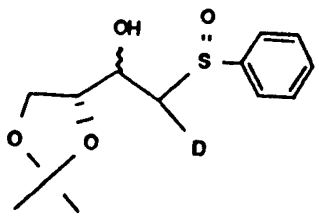
(14)


NMR170727.NDT
38731-105 IN CDCL3 #11
1/12/91
QZ300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

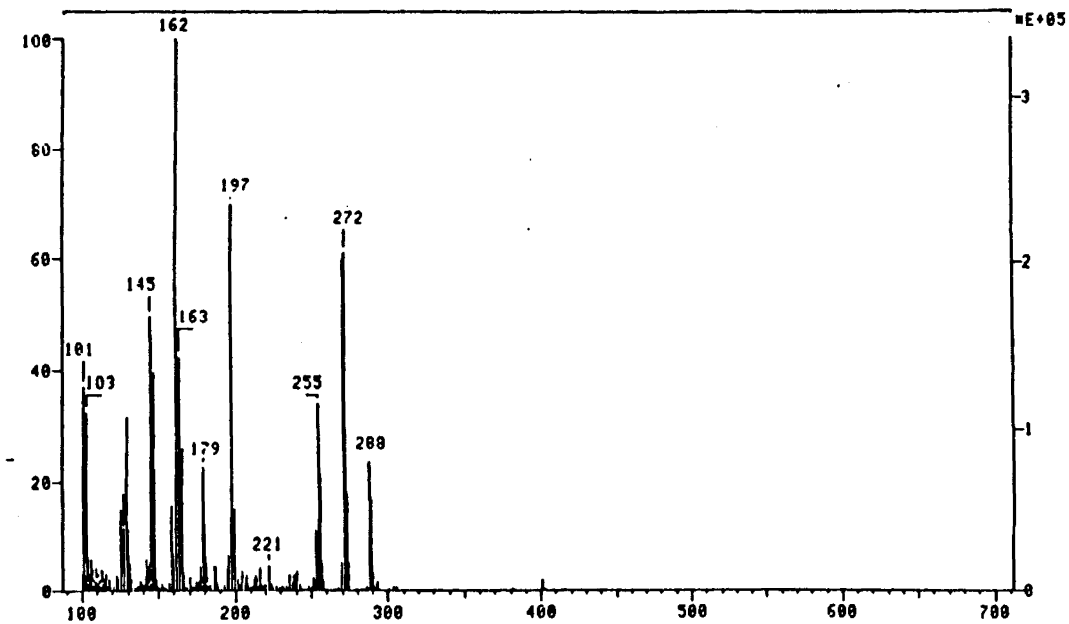

OH
O
S
O
O
D

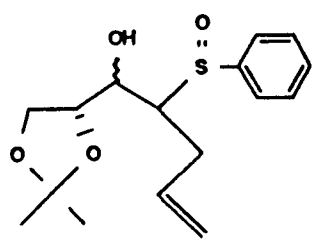
(14)


10-29-91 CDCL3 30731-105 CHE-265
4000
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800

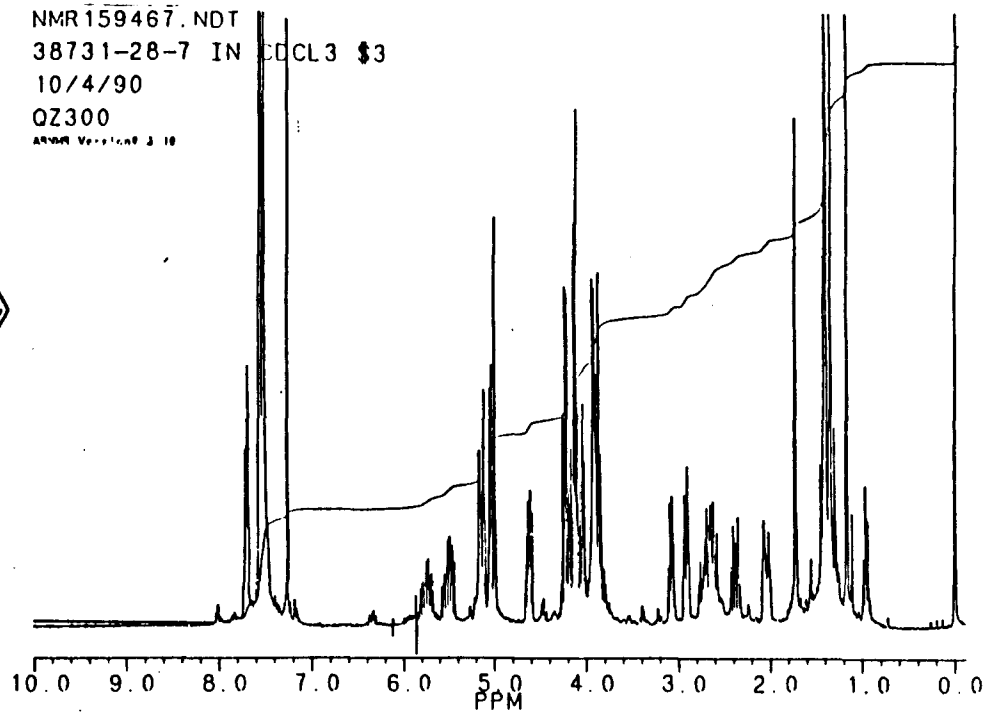

OH
O
S
O
O
D

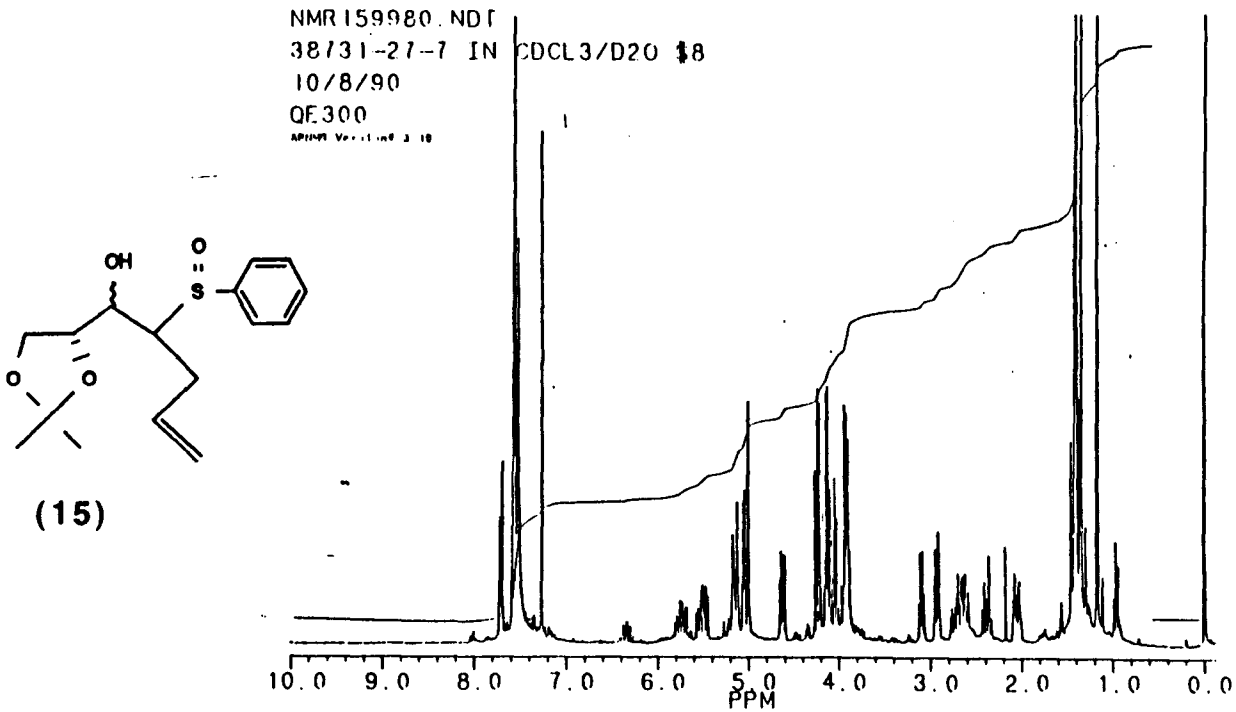
(14)


162
197
272
145
163
101
103
255
179
288
221
100
60
40
20
0
200
300
400
500
600
700
3
2
1
0

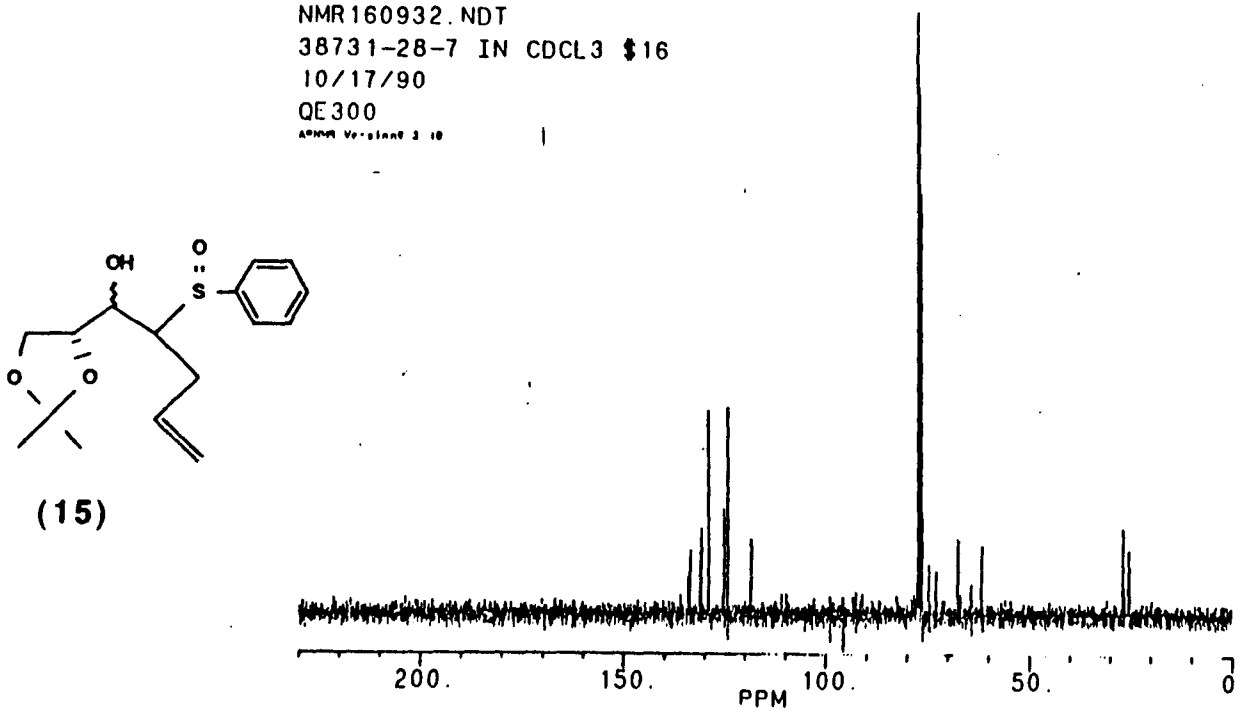

OH
O
S
O
O

(15)

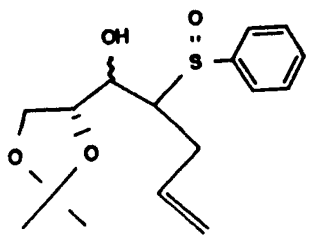

NMR159467.NDT
38731-28-7 IN CDCL3 $3
10/4/90
QZ300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM


NMR159980.NDT
38/31-27-7 IN CDCL3/D2O #8
10/8/90
QE300
OH
O
S
O
O
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

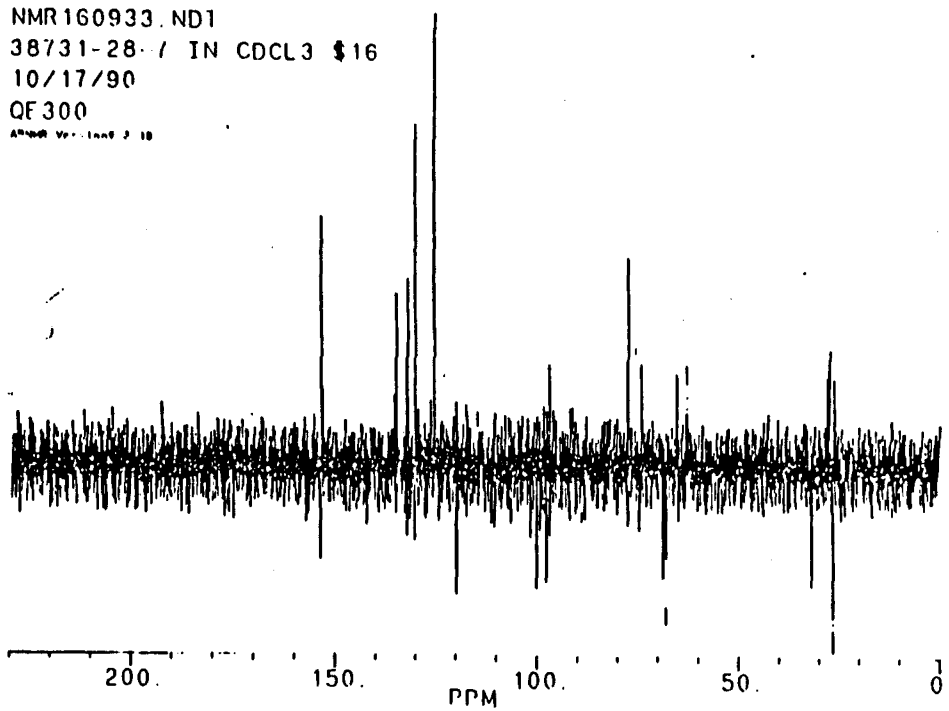
(15)

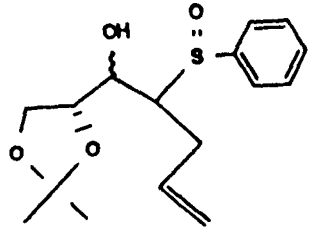

NMR160932.NDT
38731-28-7 IN CDCL3 $16
10/17/90
QE300
OH
O
S
O
O
200.
150.
100.
50.
0.
PPM

(15)

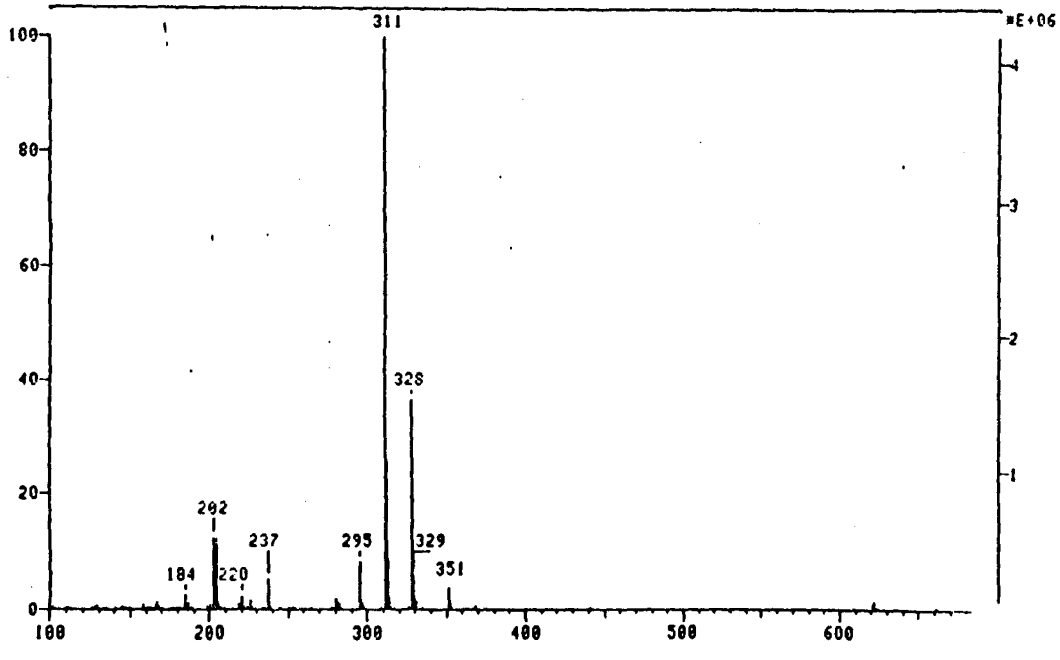

OH
O
S
O
O

(15)


NMR160933.ND1
38731-28-1 IN CDCL3 $16
10/17/90
QE300
200.
150.
100.
50.
0
PPM


OH
O
S
O
O

(15)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328
202
237
295
329
351
184
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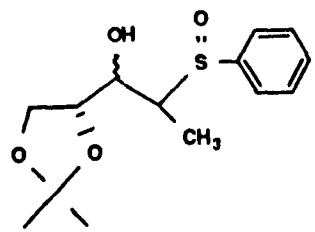
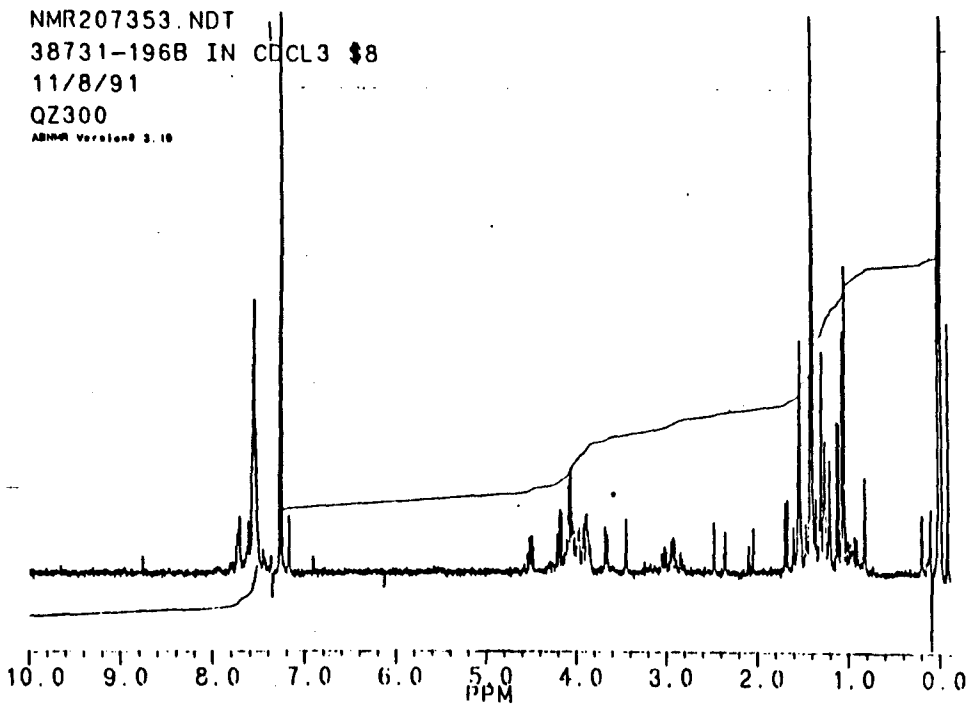
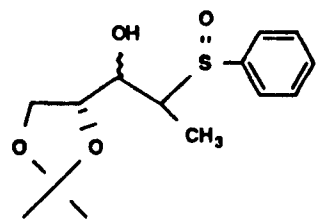
40
20
0
100
200
300
400
500
600
E+06
4
3
2
1

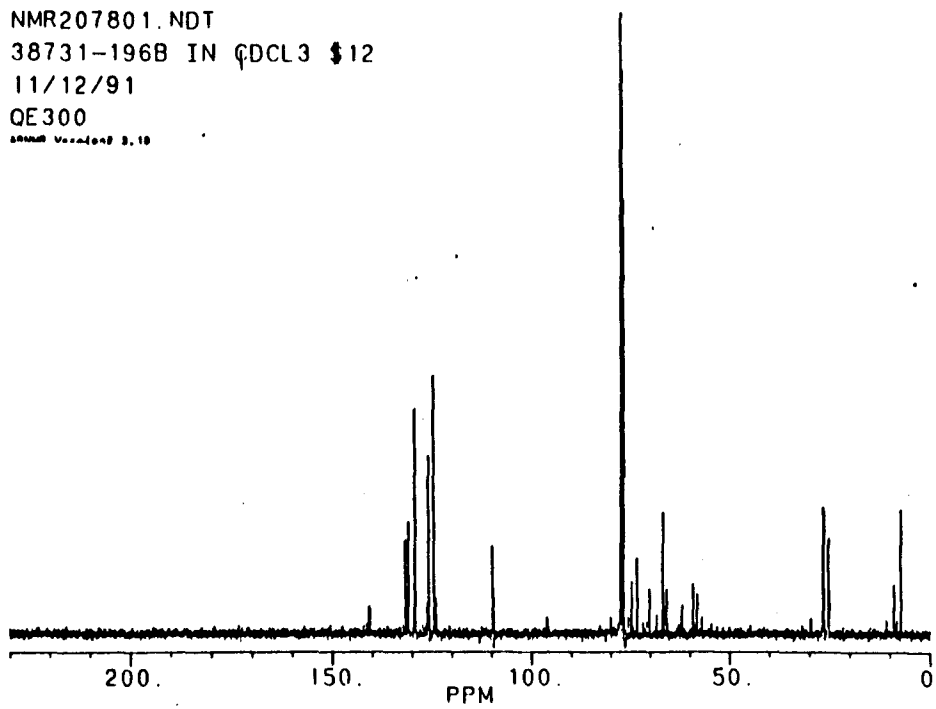

OH
O
S
CH3
O
O

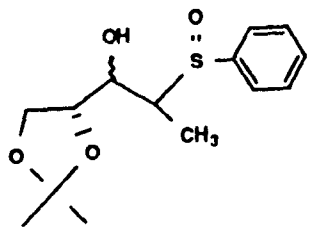
(16)


NMR207353.NDT
38731-196B IN CDCL3 $8
11/8/91
QZ300
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
PPM

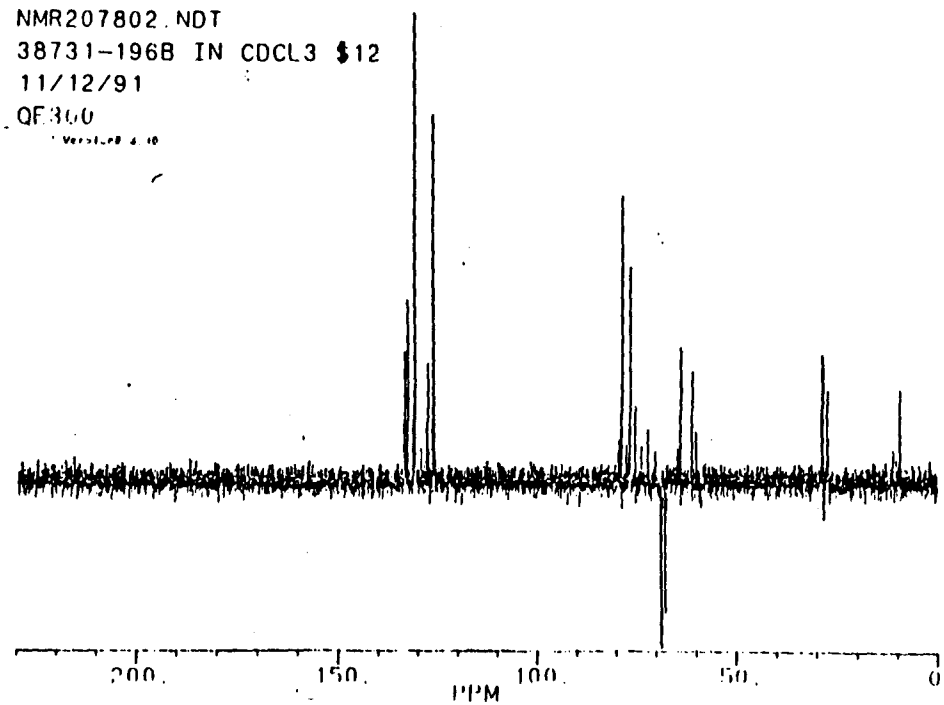

OH
O
S
CH3
O
O

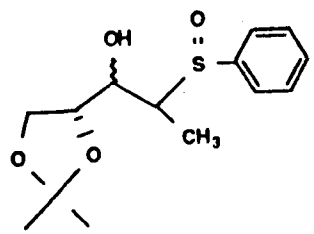
(16)


NMR207801.NDT
38731-196B IN CDCL3 $12
11/12/91
QE300
200.
150.
100.
50.
0
PPM

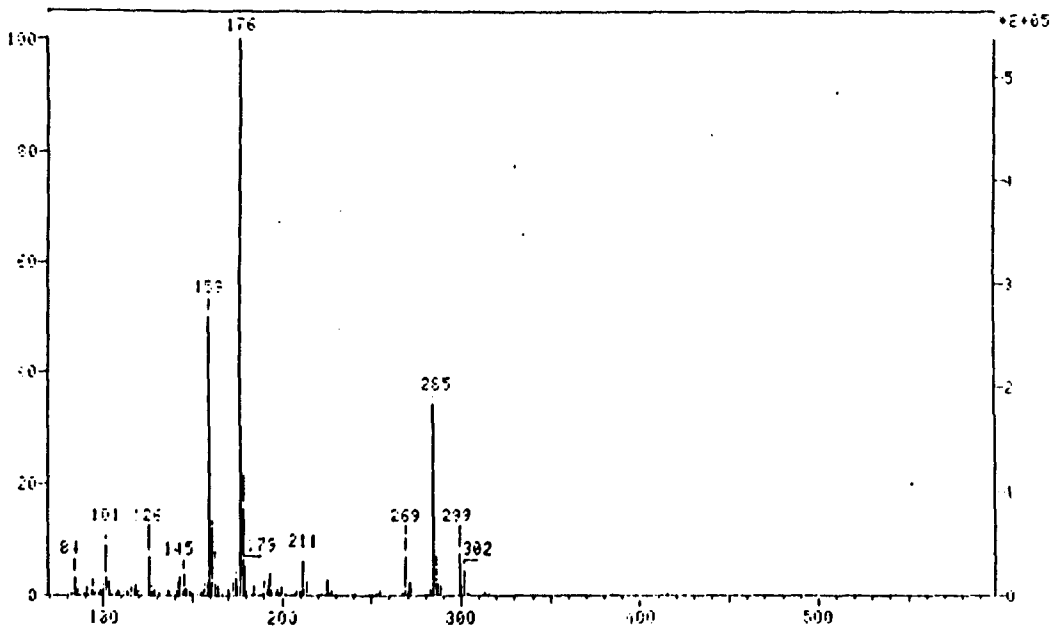

OH
O
S
CH3
O
O

(16)


NMR207802.NDT
38731-196B IN CDCL3 $12
11/12/91
QE300
200.
150.
100.
50.
0
PPM


OH
O
S
CH3
O
O

(16)


176
159
265
269
299
302
211
145
101
84
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60
40
20
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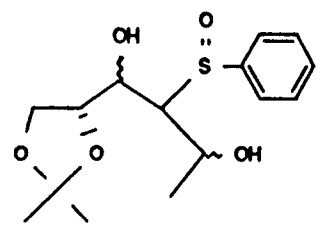
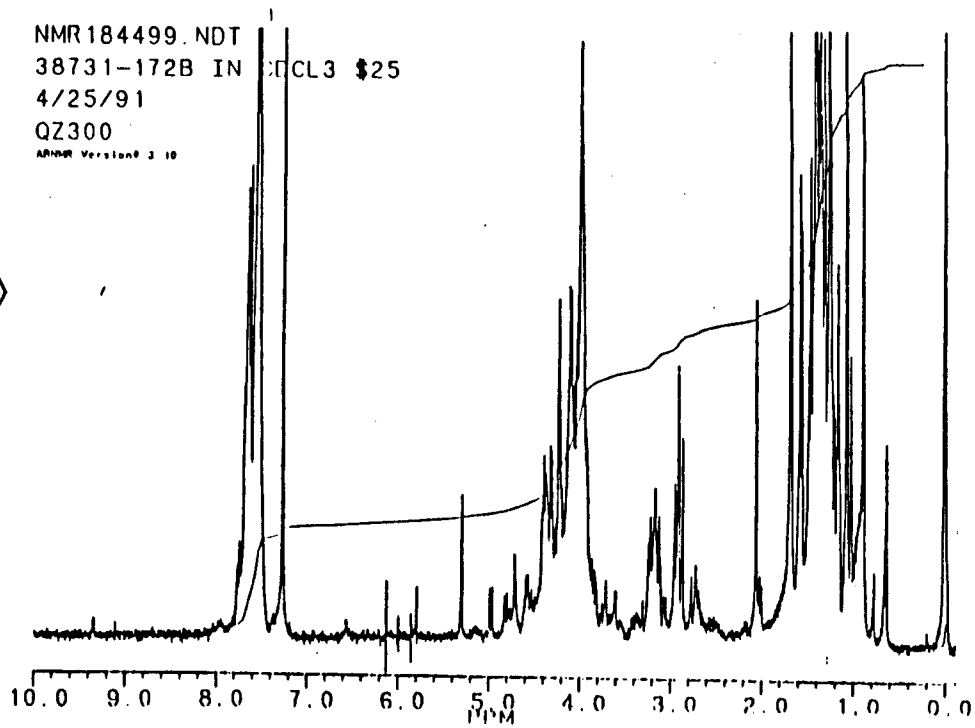
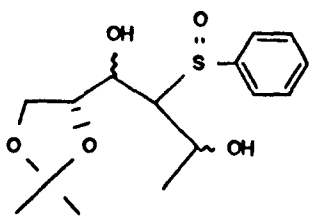
150
200
300
400
500
*2+05
5
4
3
2
1
0

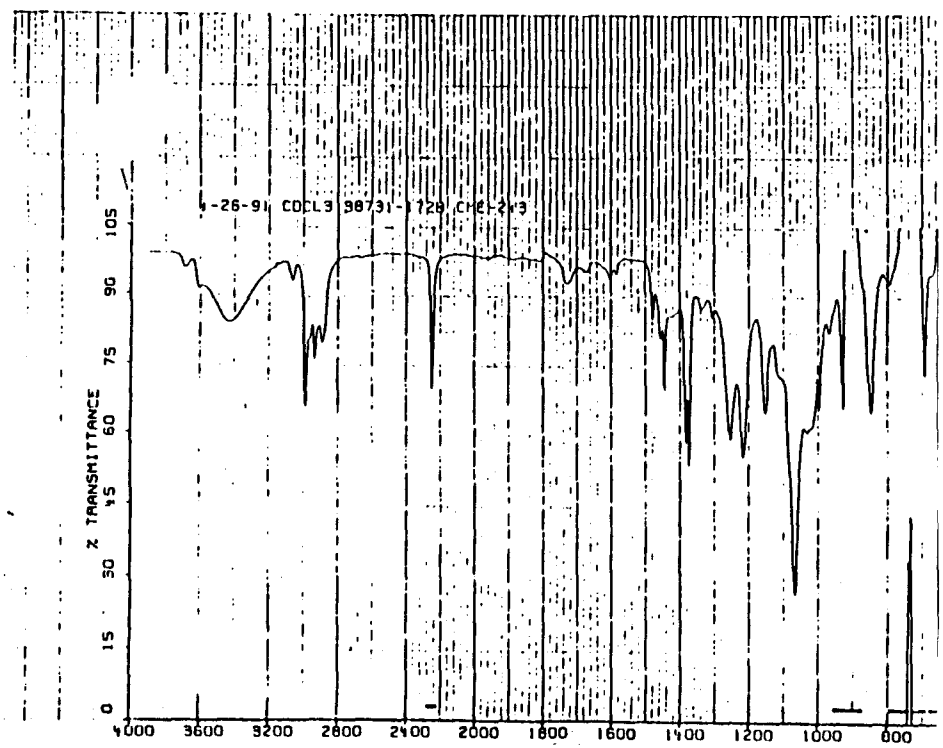

OH
O
S
O
O
OH

(17)


NMR184499.NDT
38731-172B IN CDCL3 $25
4/25/91
QZ300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM


OH
O
S
O
O
OH

(17)


% TRANSMITTANCE
0
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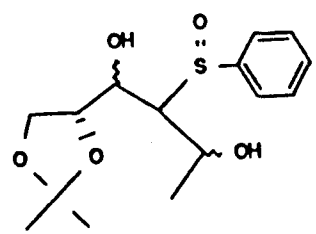
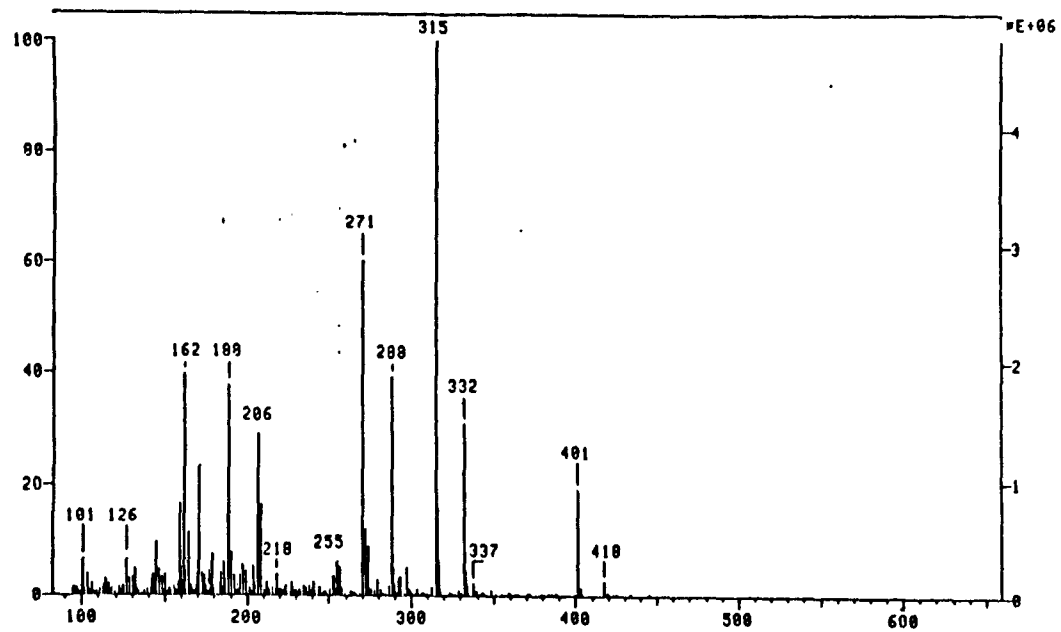
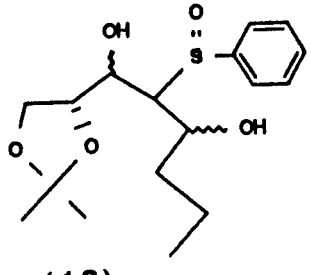
30
45
60
75
90
105
4000
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800

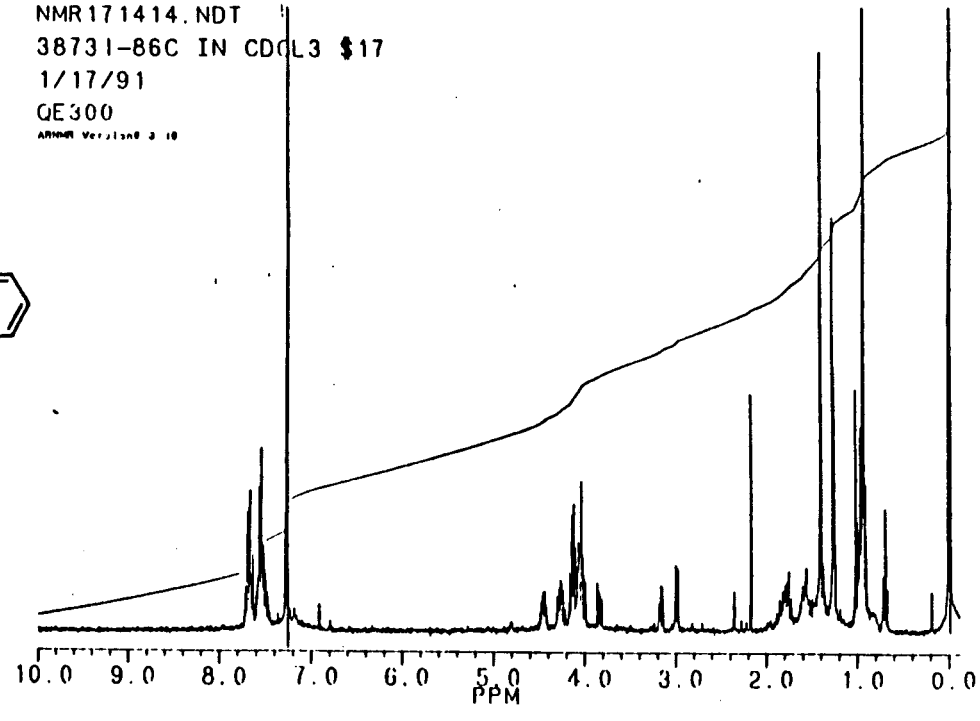

OH
O
S
O
O
OH

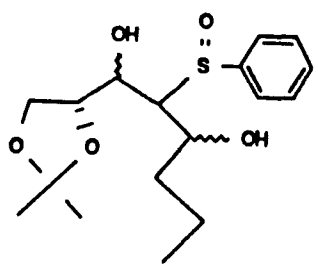
(17)


315
271
162
189
288
206
332
401
101
126
218
255
337
410
100
200
300
400
500
600
E+06

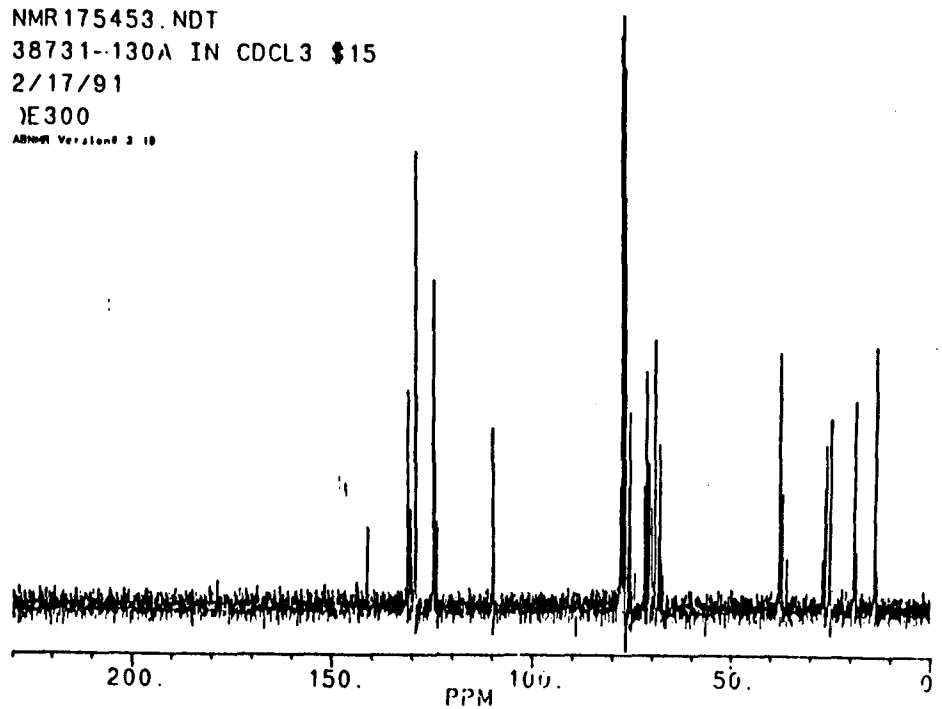

OH
O
S
OH
O
O

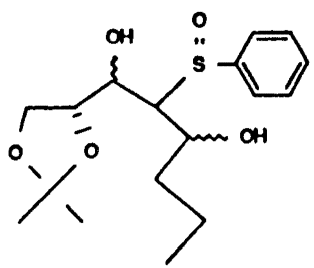
(18)


NMR171414.NDT
38731-86C IN CDCL3 $17
1/17/91
QE300
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
PPM

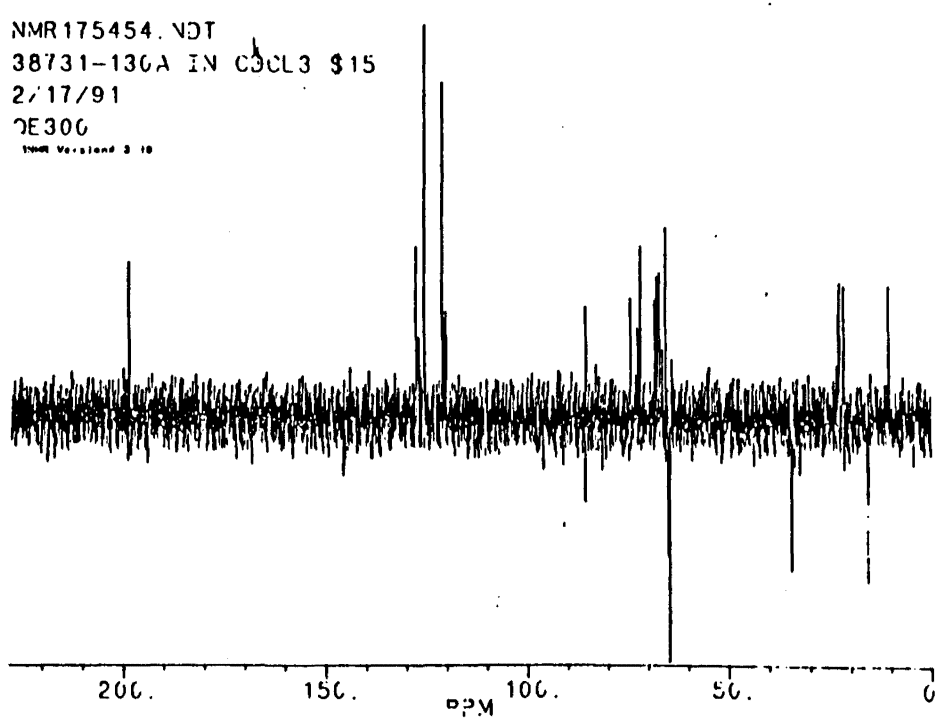

OH
O
S
O
O
OH

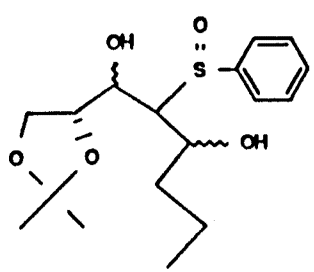
(18)


NMR175453.NDT
38731-130A IN CDCL3 $15
2/17/91
)E300
200.
150.
100.
50.
0
PPM

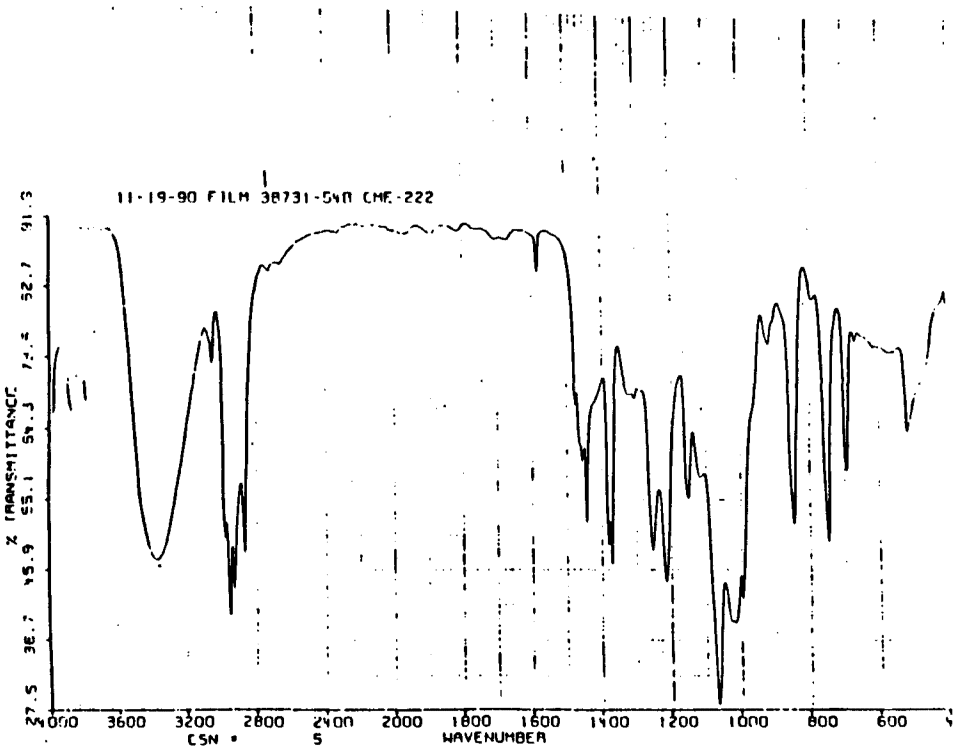

OH
O
S
OH
O
O

(18)


NMR175454.NDT
38731-130A IN CDCL3 $15
2/17/91
QE300
200.
150.
100.
50.
0
PPM


OH
O
S
OH
O
O

(18)


11-19-90 FILM 38731-54A CME-222
% TRANSMITTANCE
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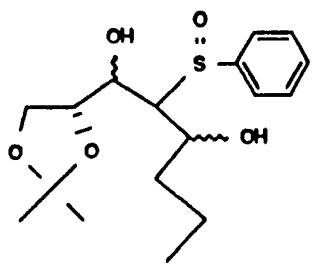
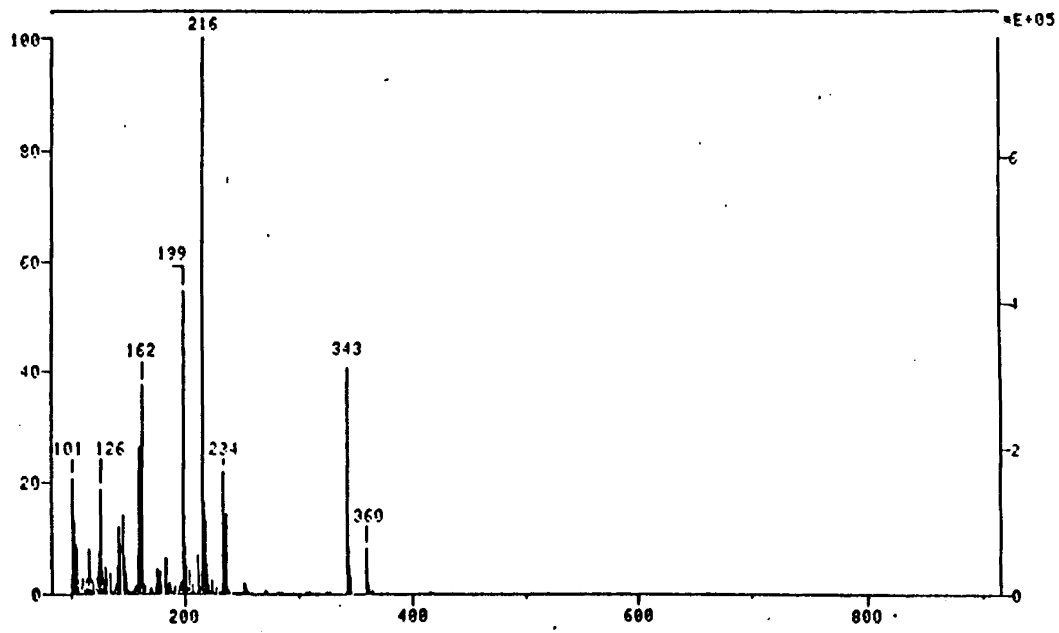
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
WAVENUMBER


OH
O
S
OH
O
O

(18)


216
199
162
343
101
126
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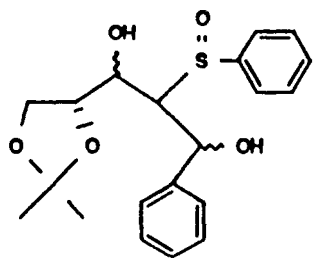
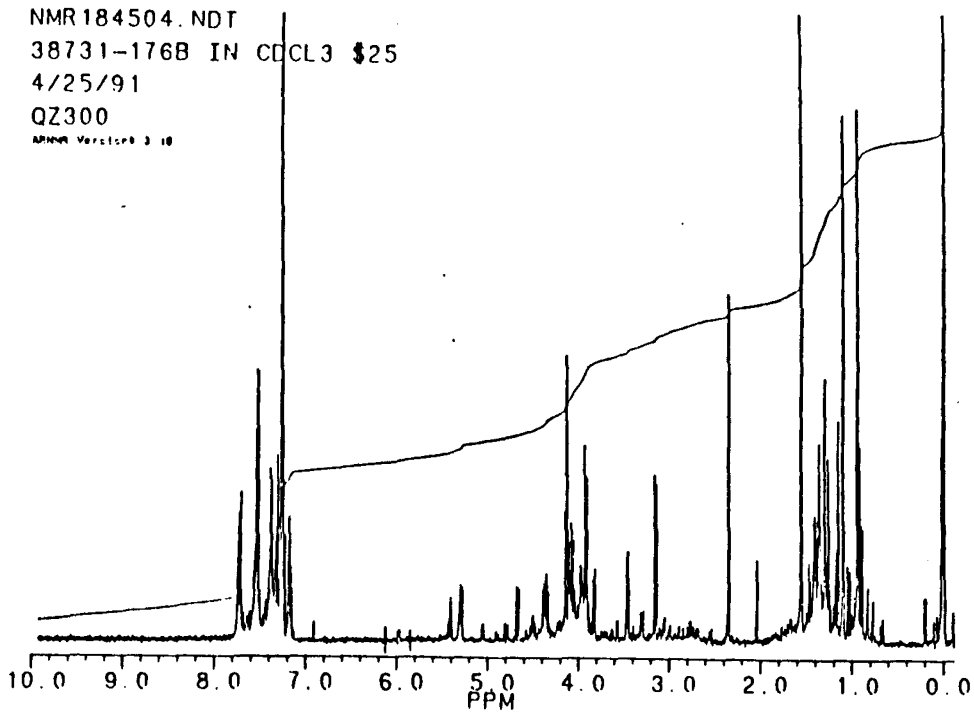
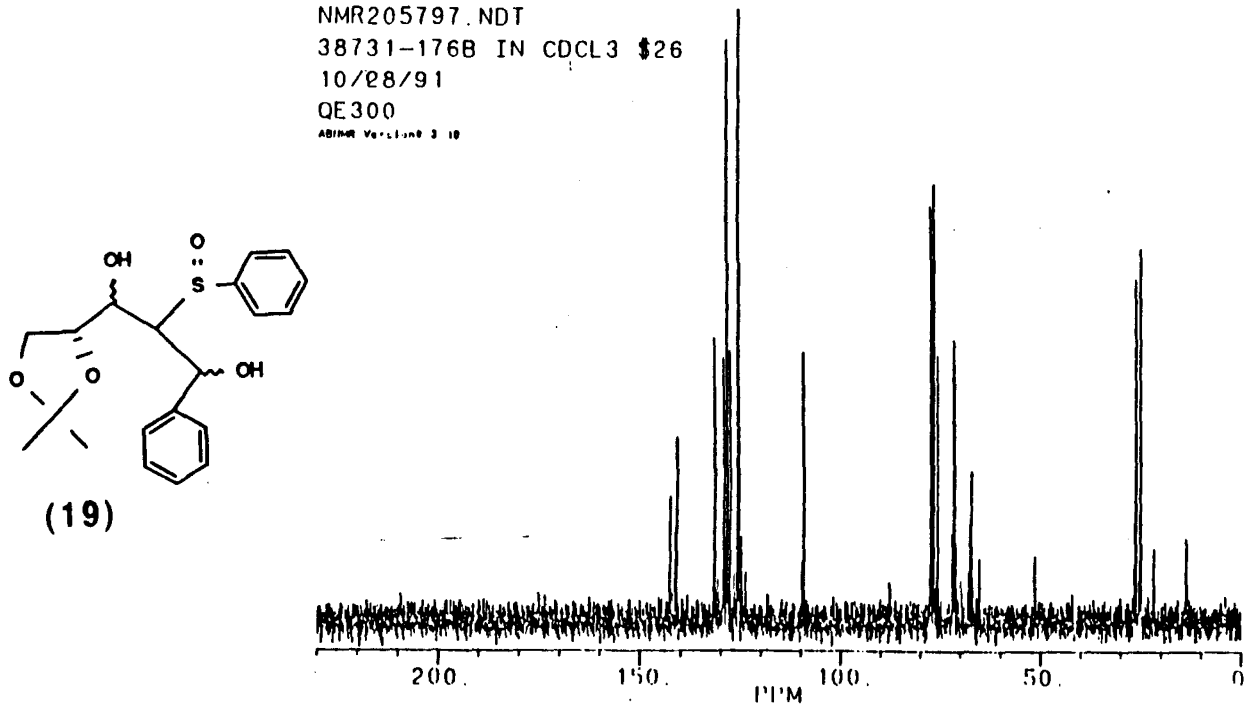
360
100
80
60
40
20
0
200
400
600
800
*E+05
6
4
2
0

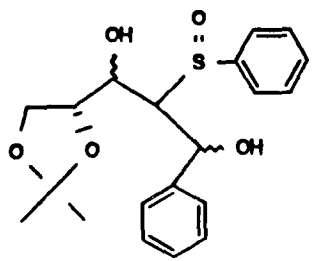

OH
O
S
O
O
OH

(19)

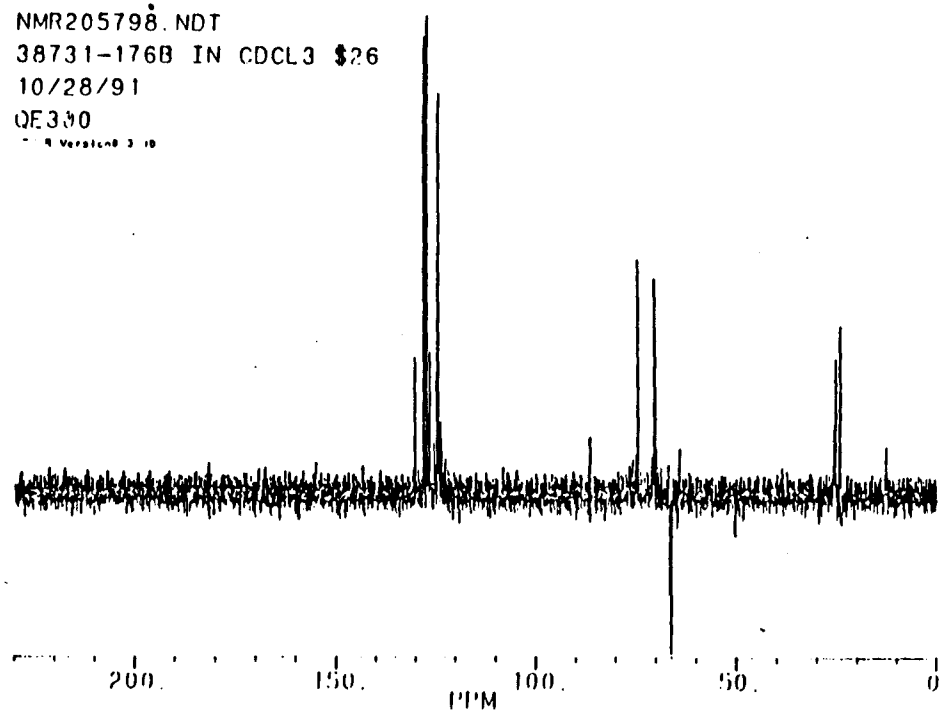

NMR184504.NDT
38731-176B IN CDCL3 $25
4/25/91
QZ300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

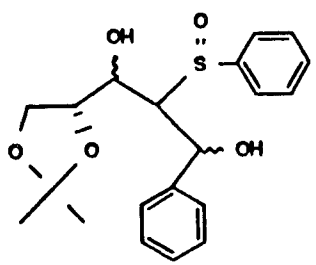

NMR205797.NDT
38731-176B IN CDCL3 $26
10/28/91
QE300
OH
O
S
O
O
OH
200.
150.
100.
50.
0
PPM

(19)

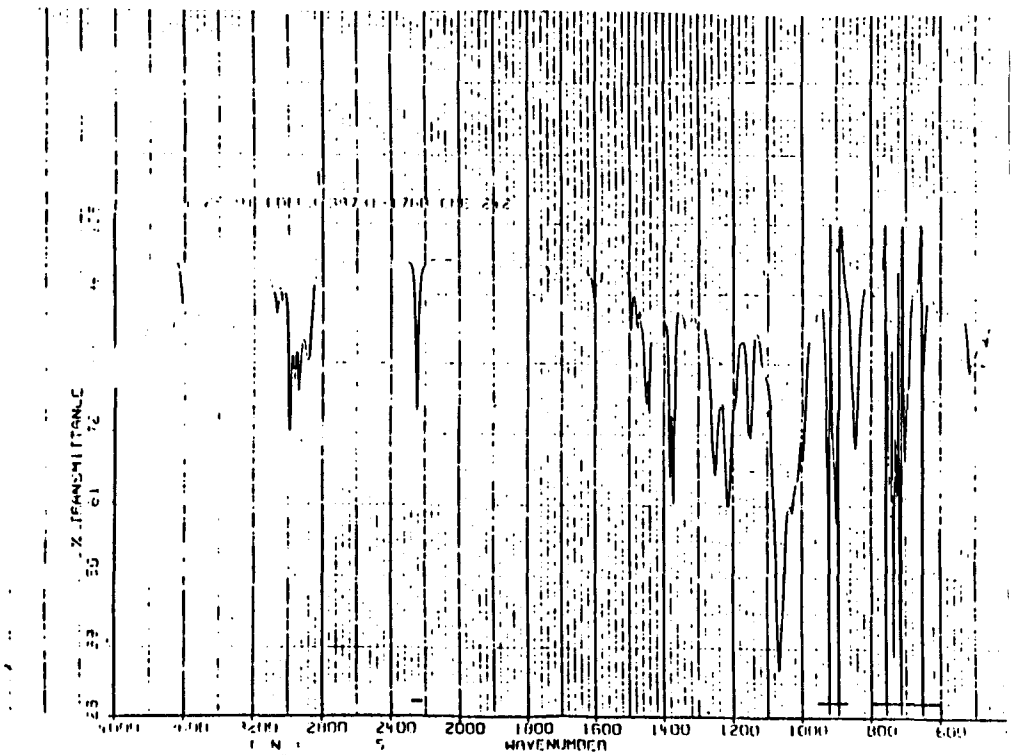

OH
O
S
O
O
OH

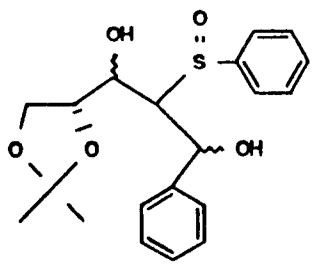
(19)


NMR205798.NDT
38731-176B IN CDCL3 $26
10/28/91
QE300
200.
150.
100.
50.
0.
PPM

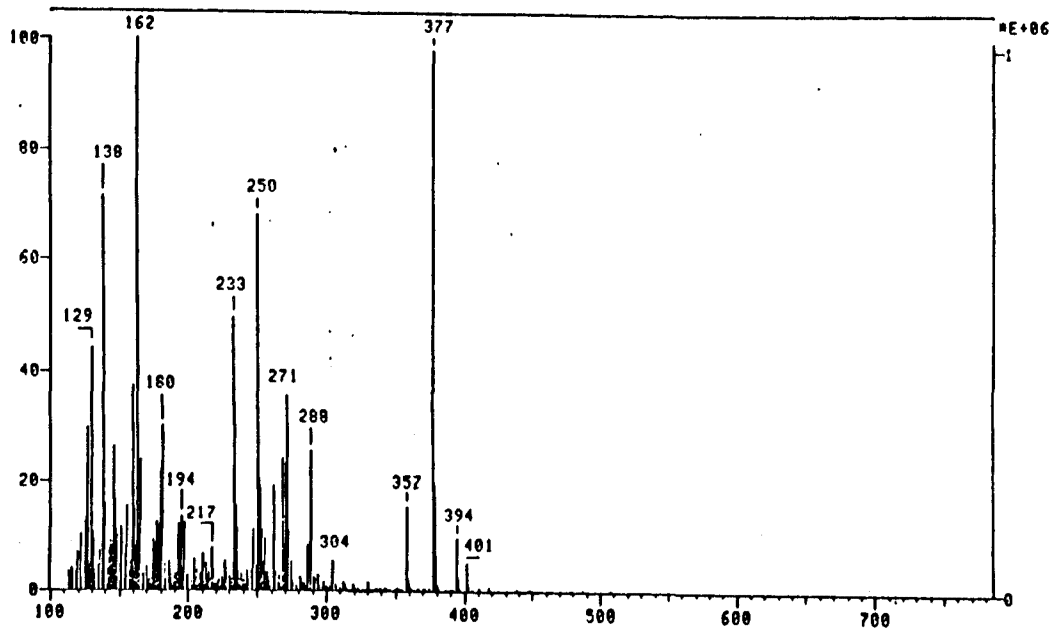

OH
O
S
O
O
OH

(19)


% TRANSMITTANCE
WAVENUMBER
2400
2000
1800
1600
1400
1200
1000
800


OH
O
S
O
O
OH

(19)


162
377
138
250
233
129
271
180
288
194
357
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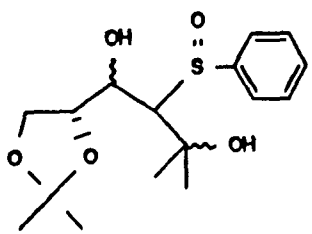
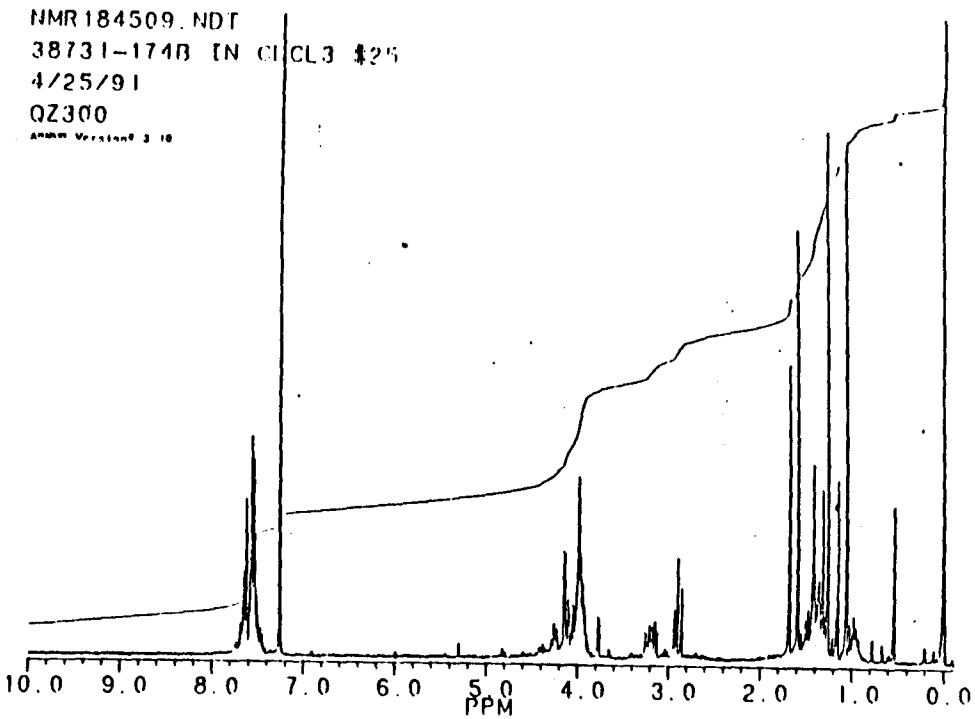
394
304
401
100
80
60
40
20
0
100
200
300
400
500
600
700
E+06
1
0


OH
O
S
O
O
OH

(20)


NMR184509.NDT
38731-174B IN CDCL3 #25
4/25/91
QZ300
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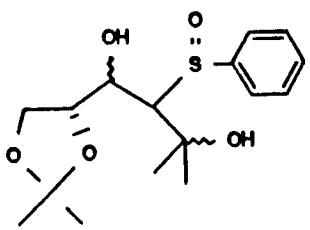
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM



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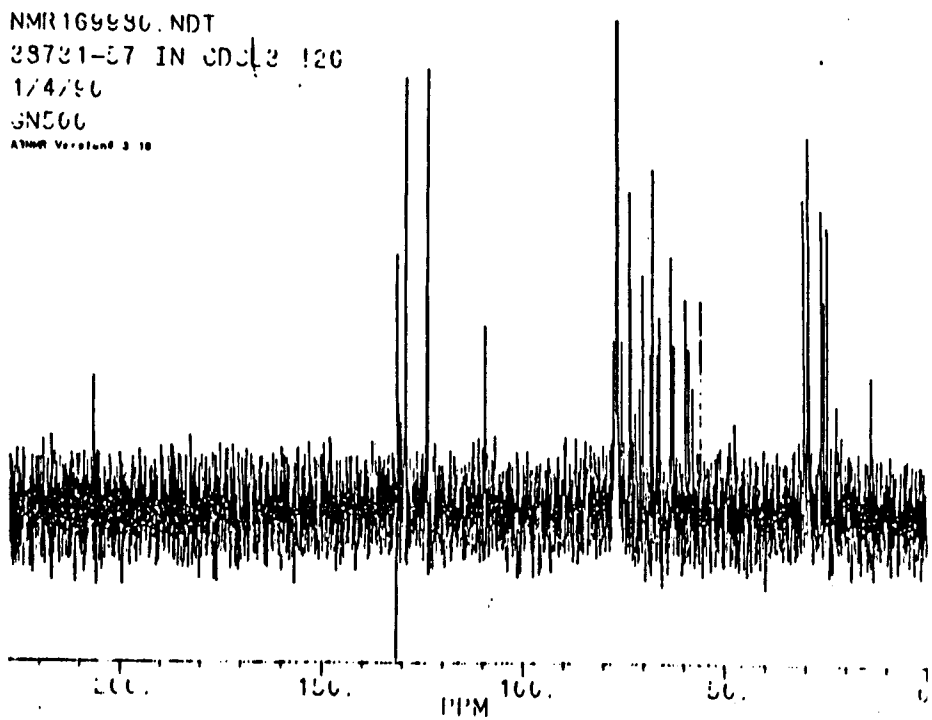
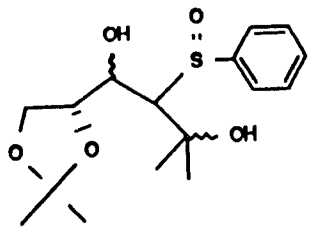
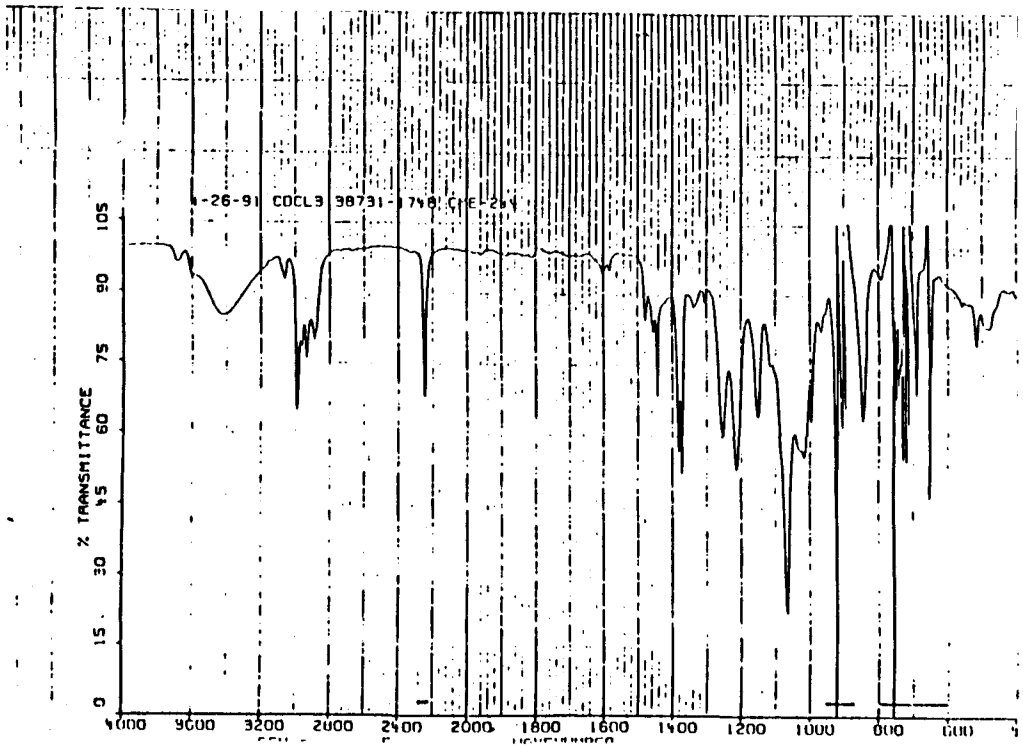



OH
O
S
O
O
OH

(20)


% TRANSMITTANCE
0
15
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90
105
4000
3600
3200
2800
2400
2000
1800
1600
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1200
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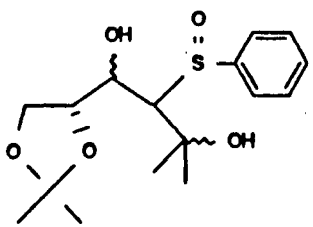
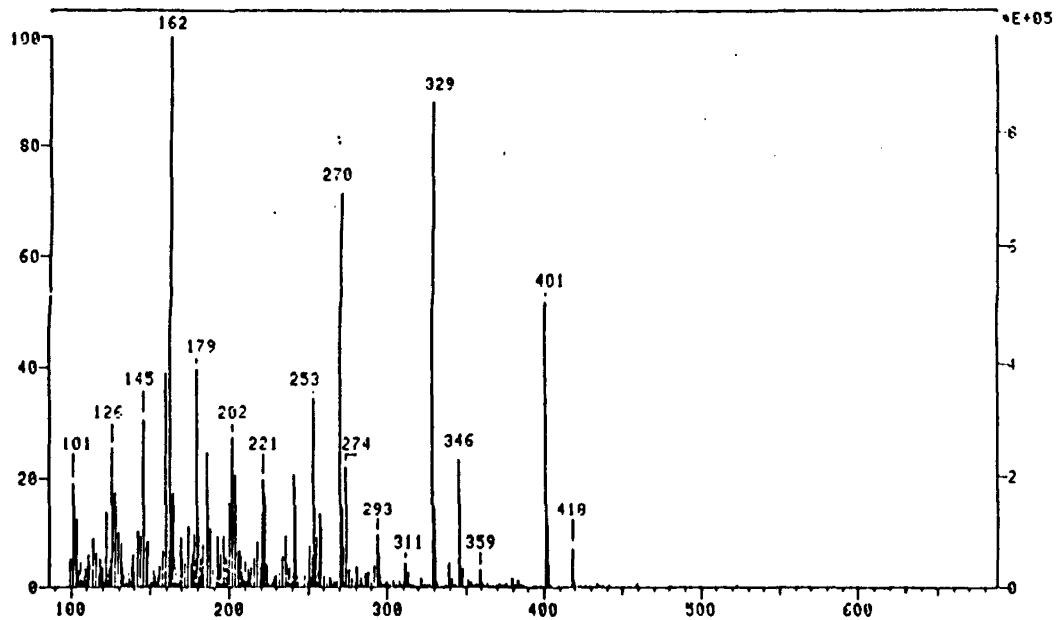
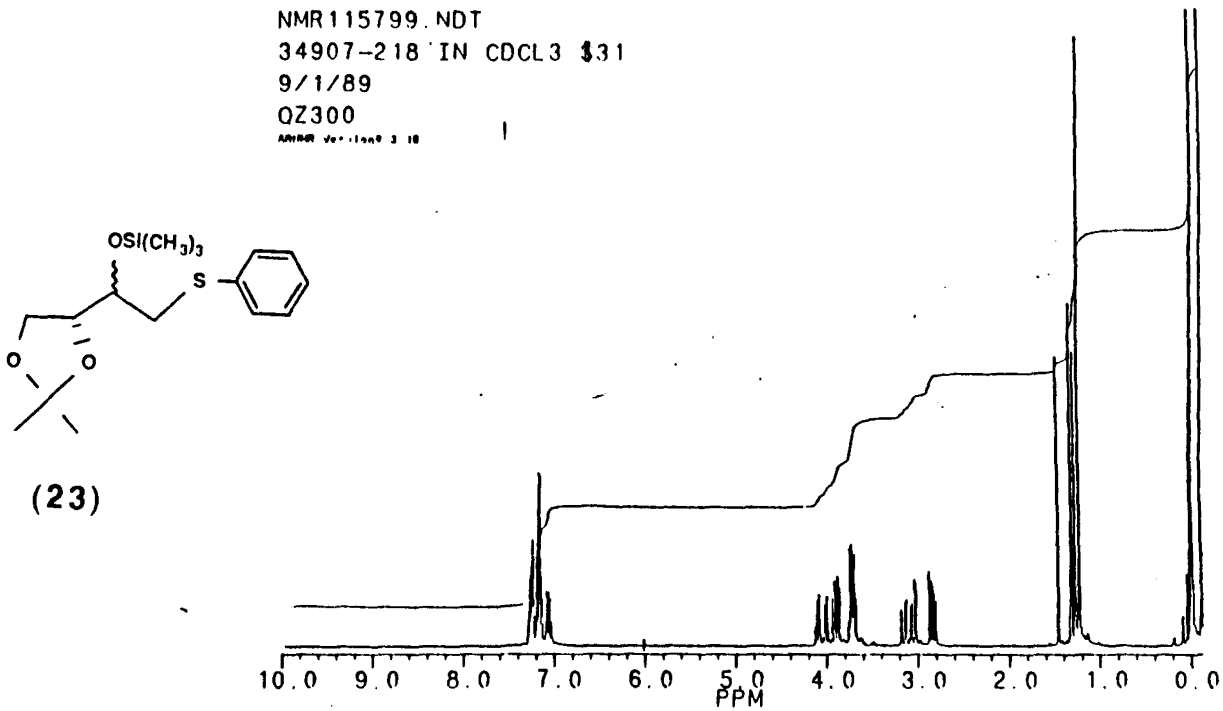
800
600

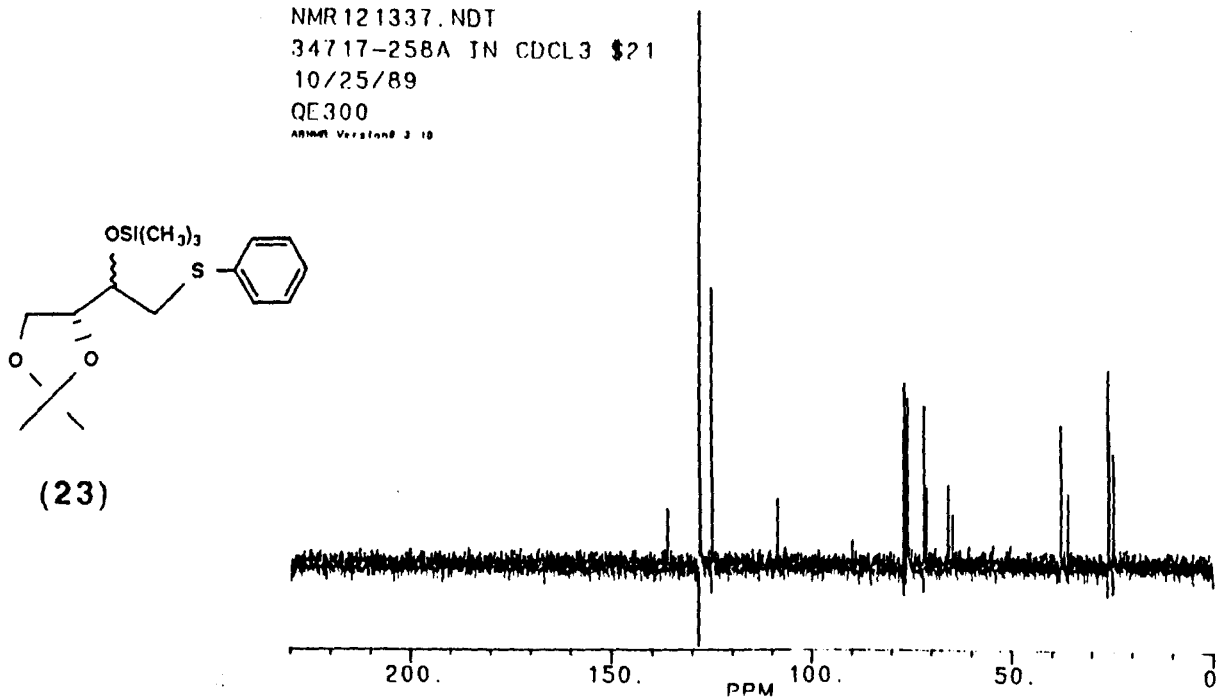

OH
O
S
OH
O
O

(20)

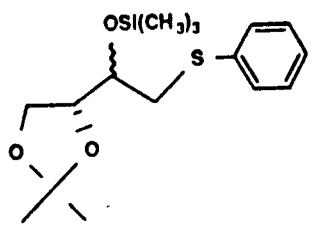

100
80
60
40
20
0
162
329
270
401
179
145
253
126
202
101
221
274
346
293
311
359
418
100
200
300
400
500
600
*E+05
6
5
4
2
0


NMR115799.NDT
34907-218 IN CDCL3 $31
9/1/89
QZ300
OSI(CH3)3
S
O
O
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

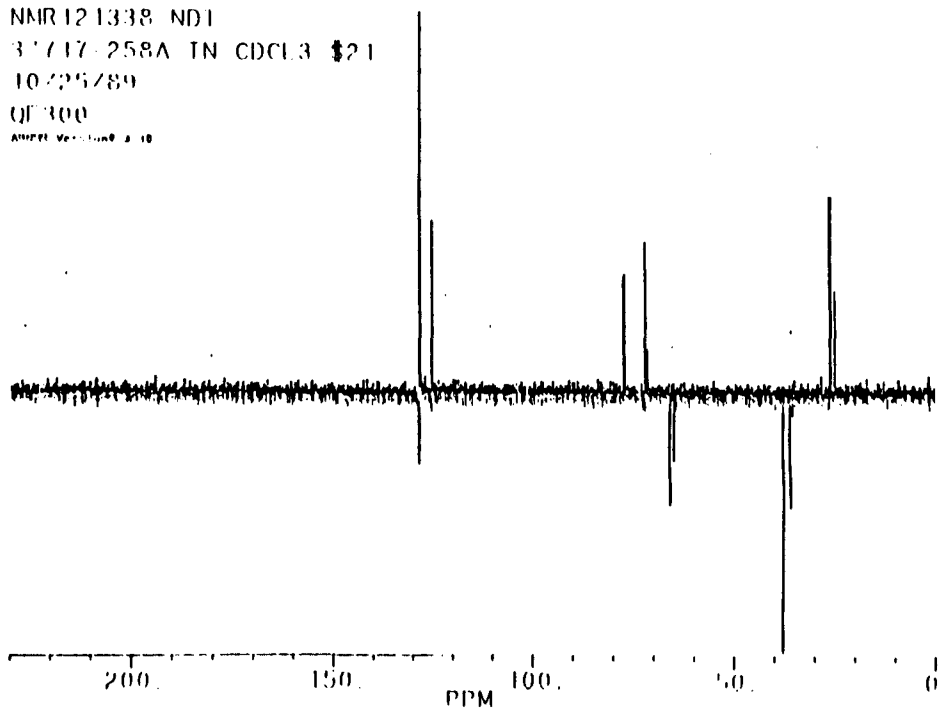
(23)

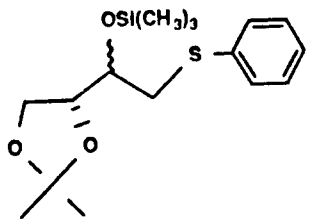

NMR121337.NDT
34717-258A IN CDCL3 $21
10/25/89
QE300
OSI(CH3)3
S
O
O
200.
150.
100.
50.
0
PPM

(23)

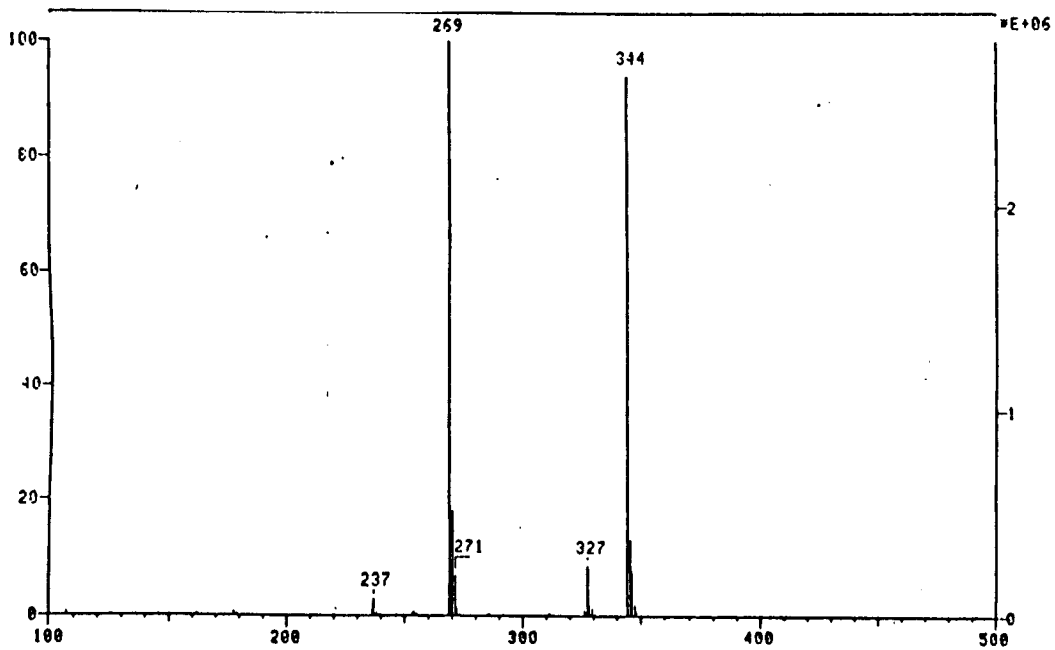

OSI(CH3)3
S
O
O

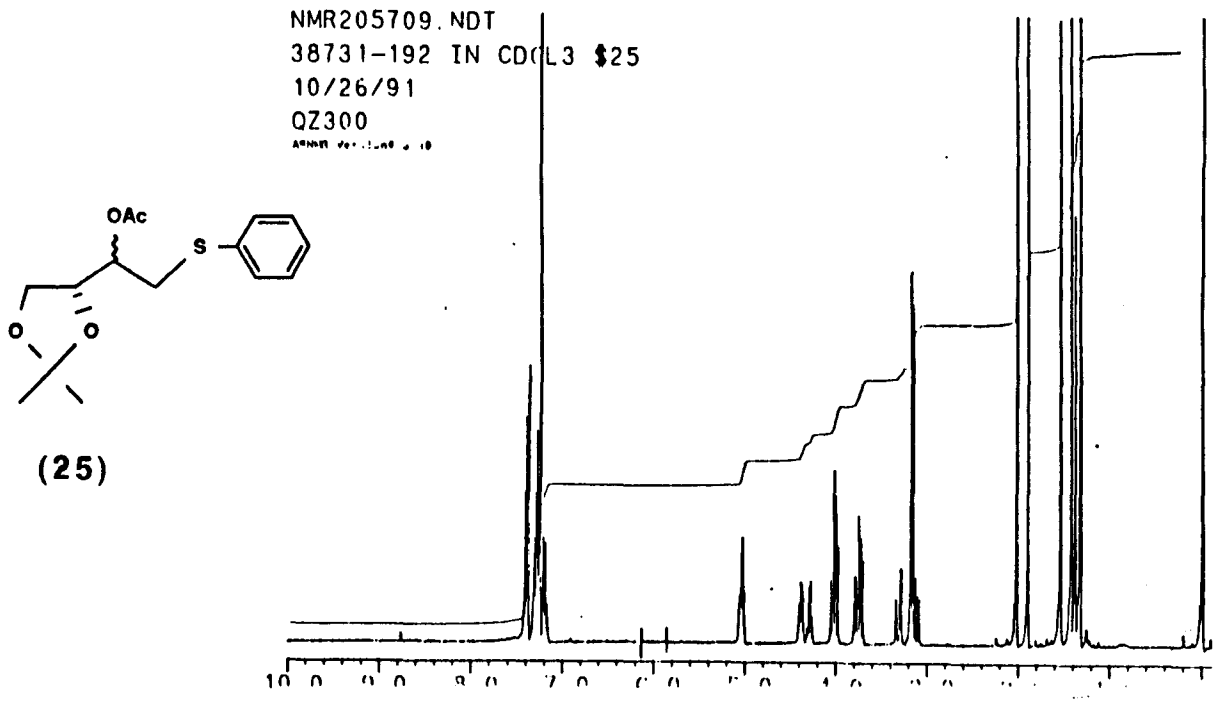
(23)


NMR121338 ND1
3'717-258A TN CDCL3 $21
10/25/89
QE300
200.
150.
100.
50.
0.
PPM

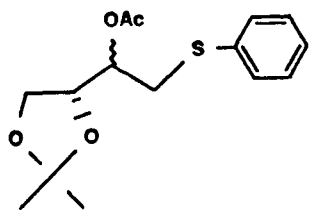

OSi(CH3)3
S
O
O

(23)

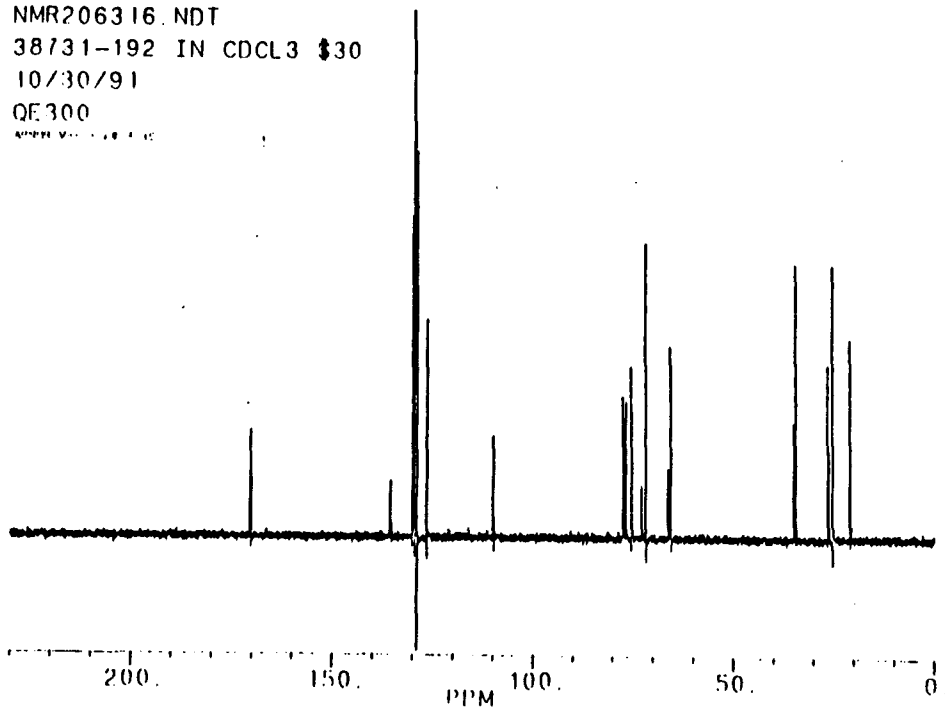

269
344
271
327
237
100
80
60
40
20
0
100
200
300
400
500
2
1
0

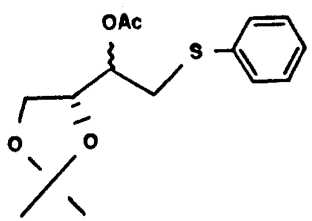


(25)

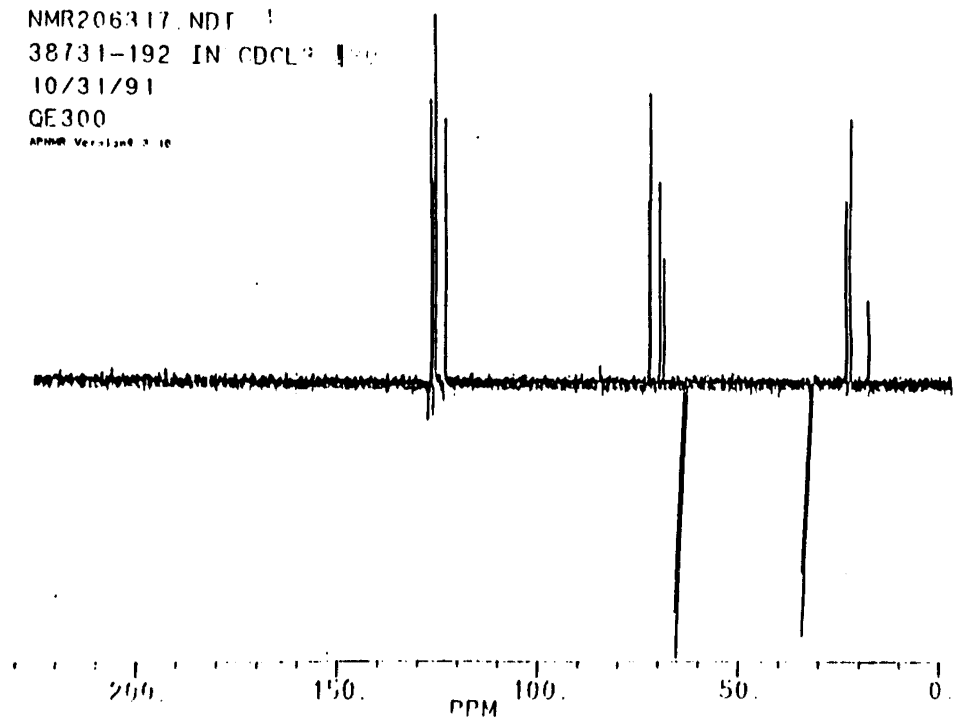

OAc
S
O
O

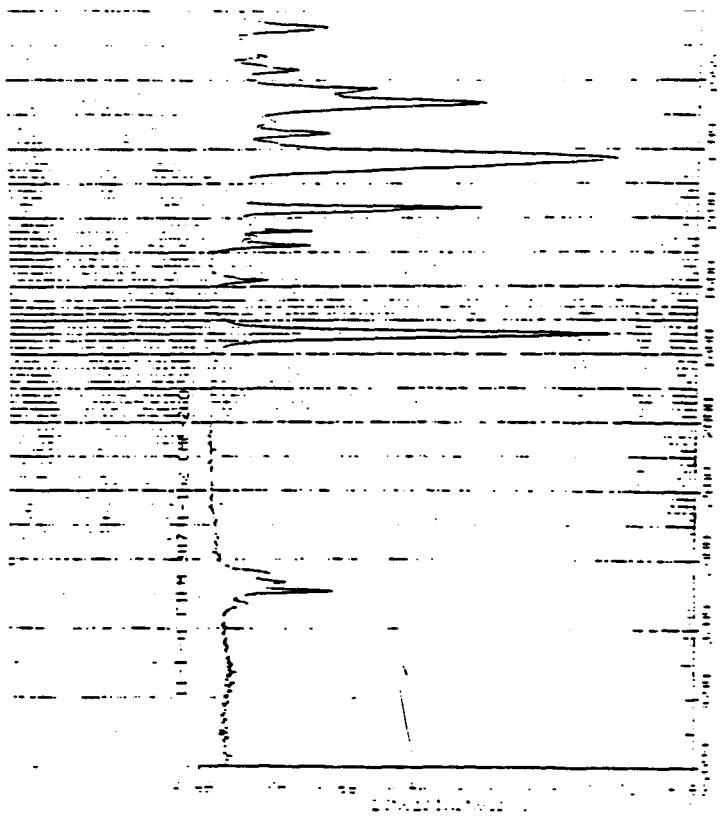
(25)

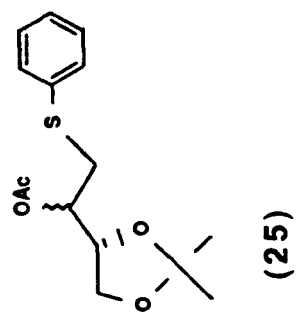

NMR206316.NDT
38731-192 IN CDCL3 $30
10/30/91
QE300
200.
150.
100.
50.
0.
PPM


OAc
S
O
O

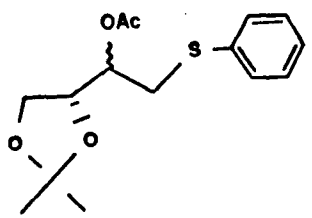
(25)


NMR206317.NDT
38731-192 IN CDCL3
10/31/91
QE300
200.
150.
100.
50.
0.
PPM

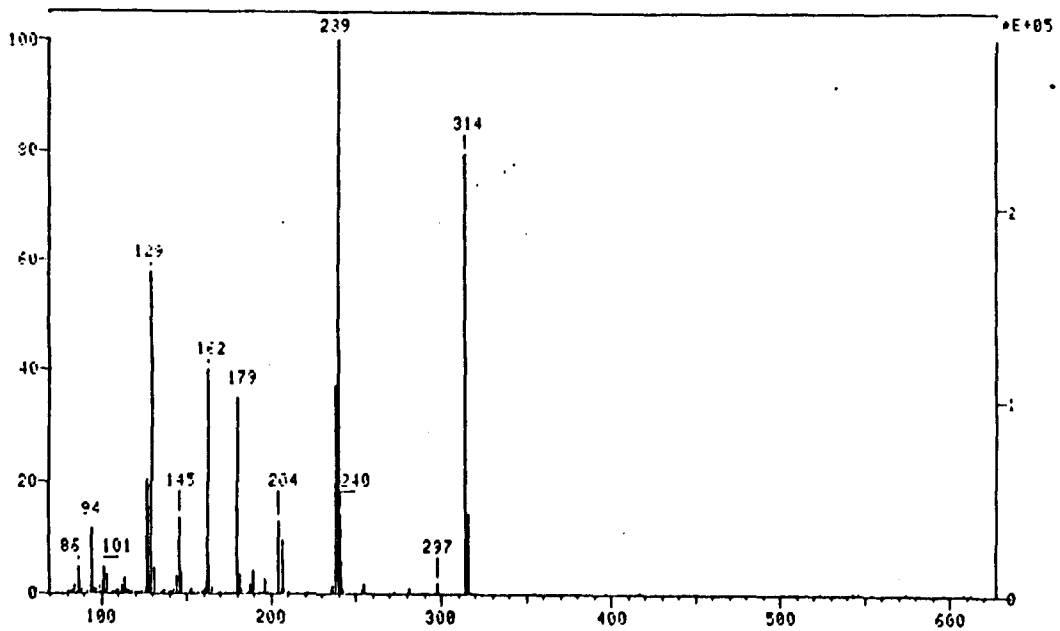


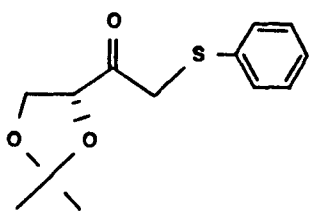


(25)

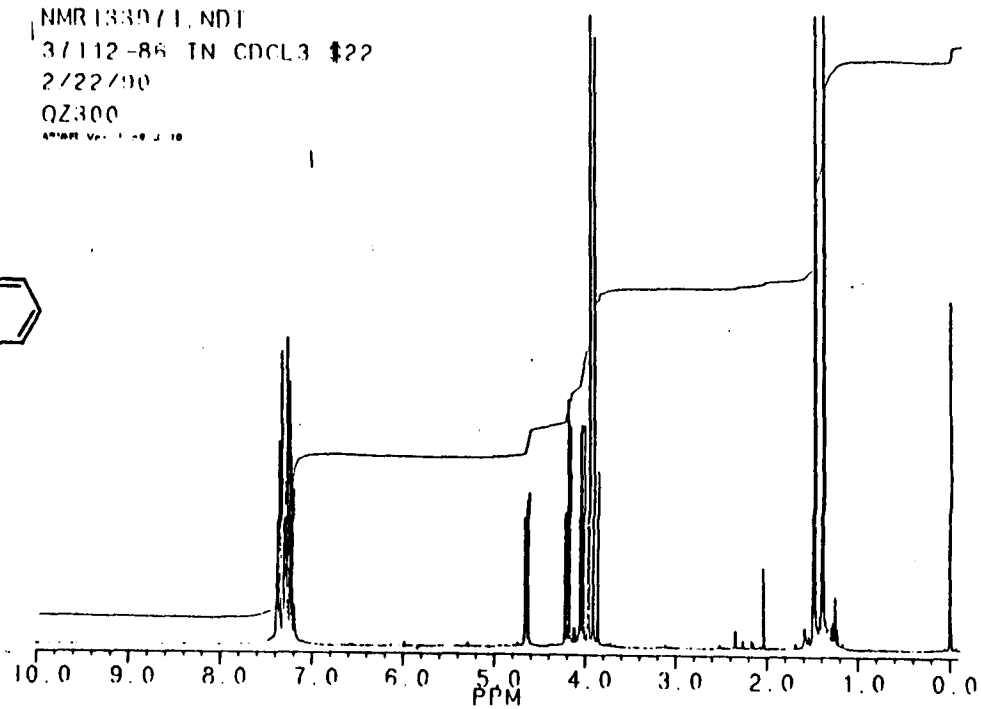

OAc
S
O
O

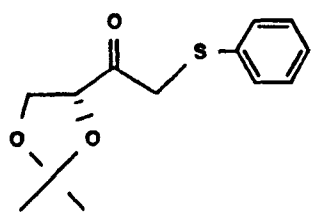
(25)


239
314
129
162
179
145
204
240
94
85
101
297
100
80
60
40
20
0
100
200
300
400
500
600
E+05
2
1
0

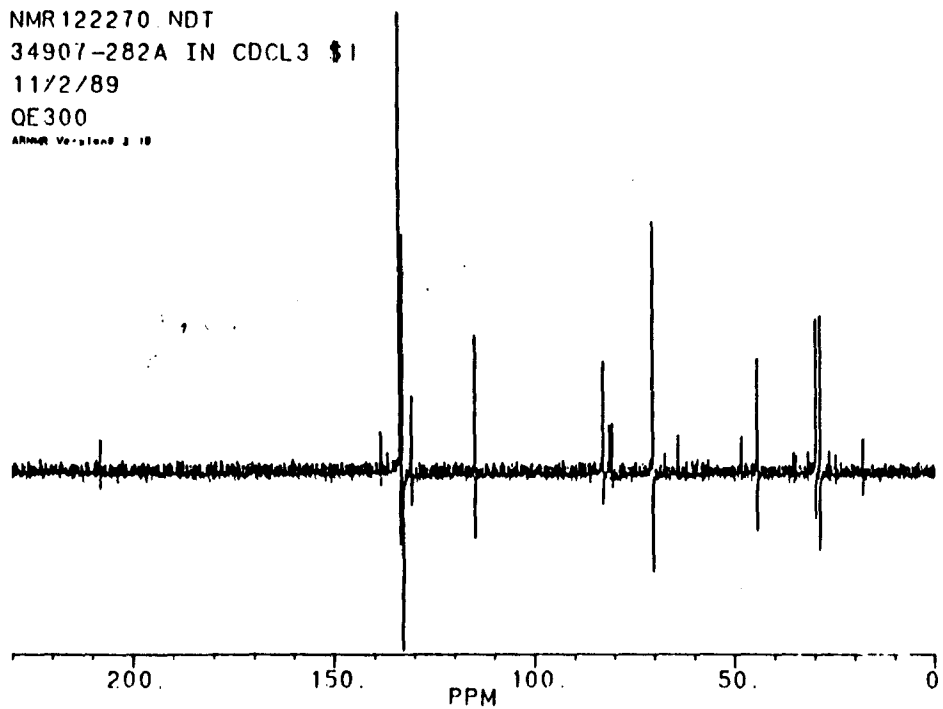

O
S
O
O

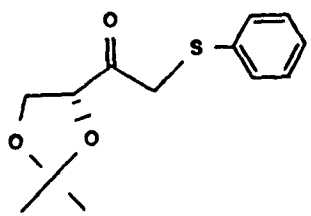
(26)


NMR1339/1.NDT
3/112-86 TN CDCL3 #22
2/22/90
QZ300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

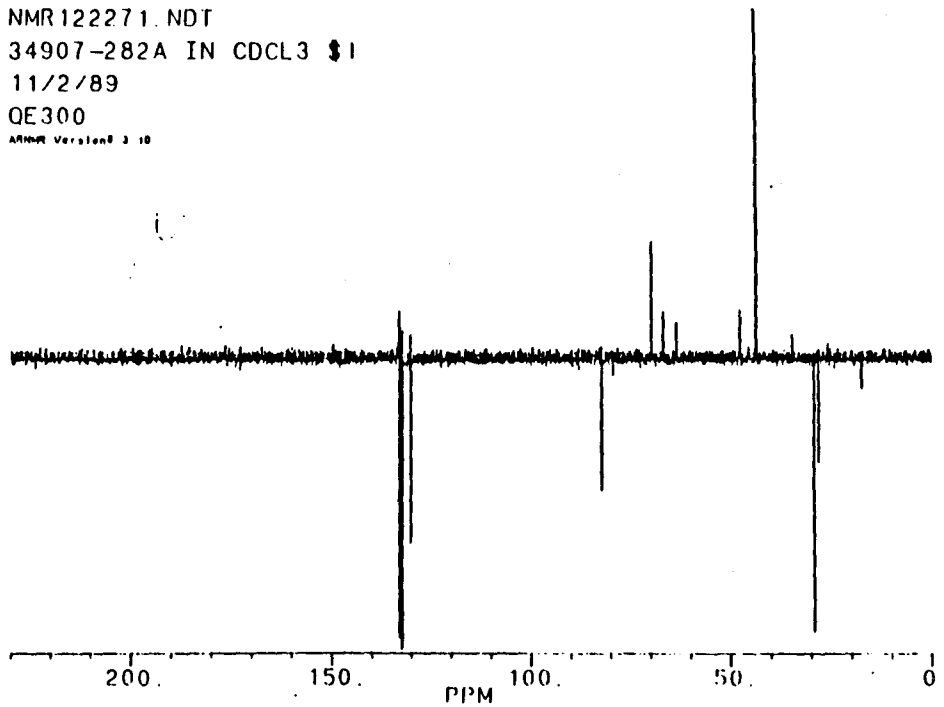

O
S
O
O

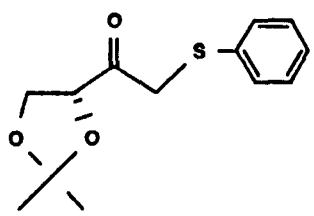
(26)


NMR122270 NDT
34907-282A IN CDCL3 $1
11/2/89
QE300
200.
150.
100.
50.
0.
PPM

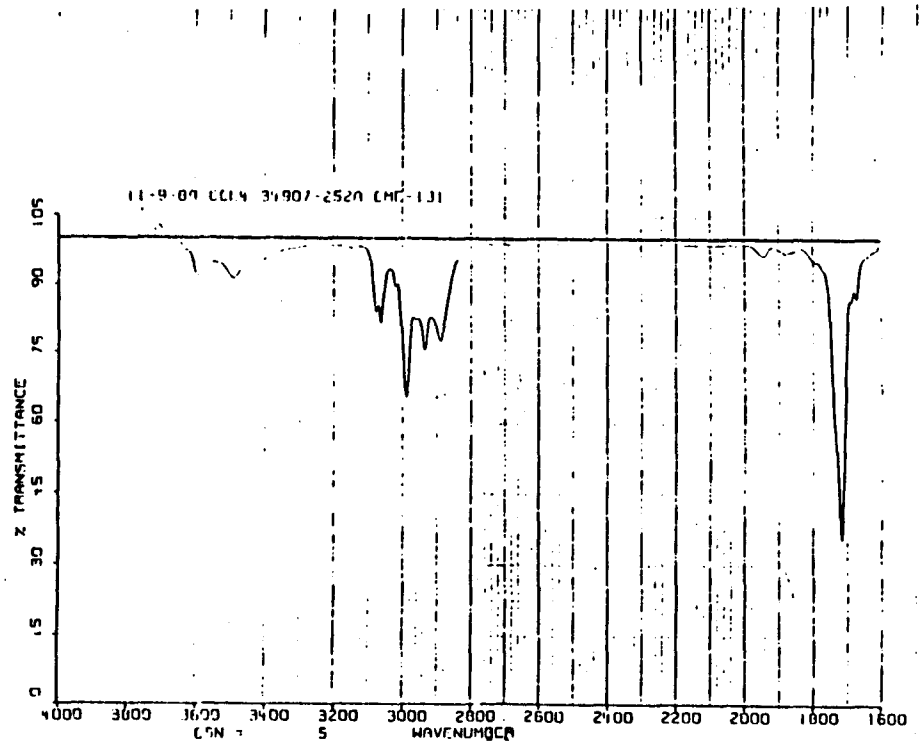

O
S
O
O

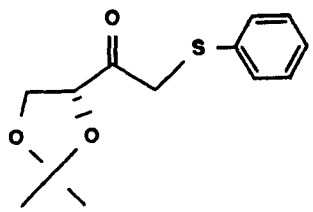
(26)


NMR122271.NDT
34907-282A IN CDCL3 $1
11/2/89
QE300
200.
150.
100.
50.
0.
PPM

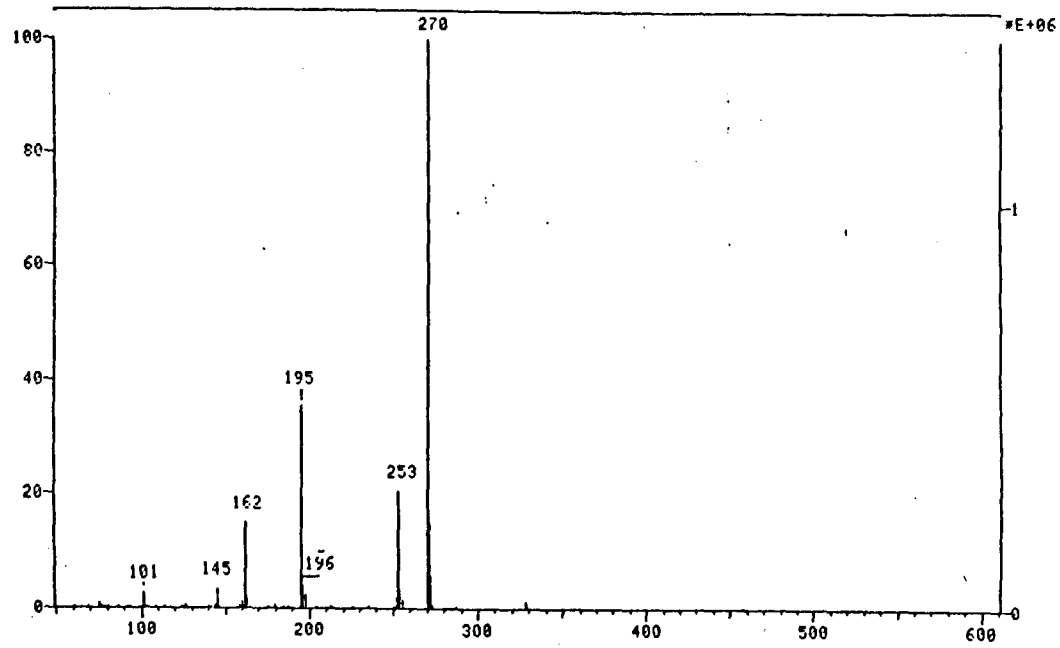

O
S
O
O

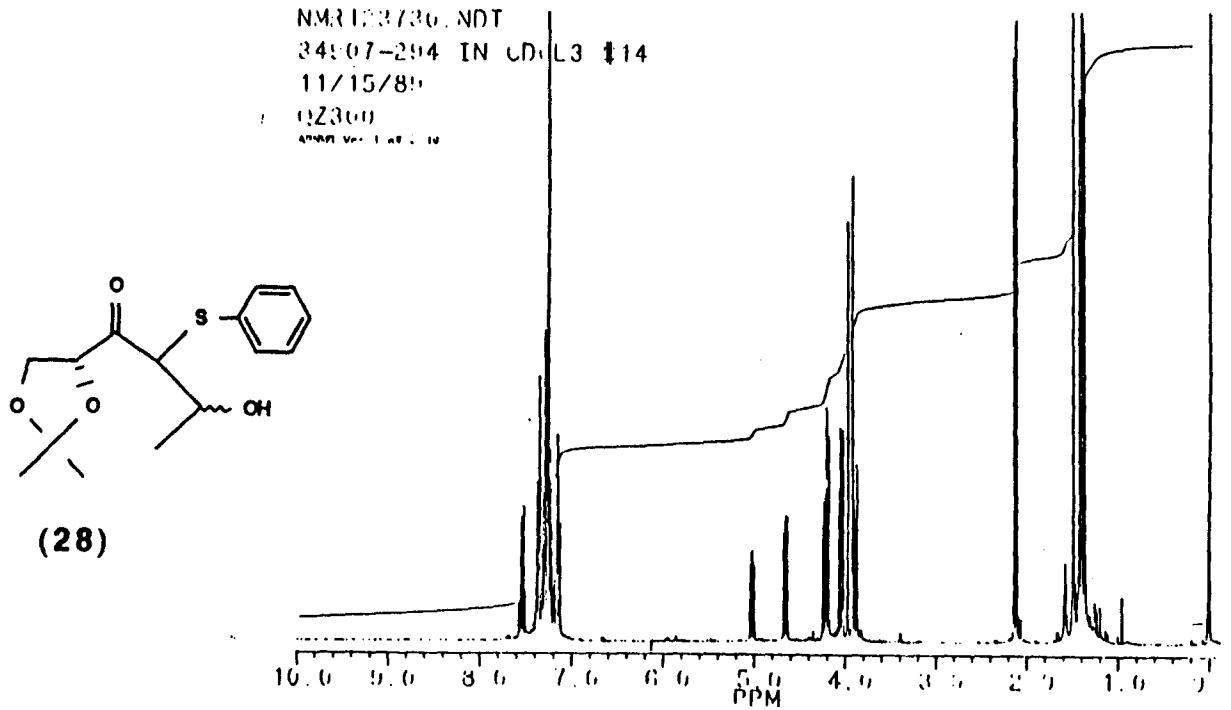
(26)


% TRANSMITTANCE
105
90
75
60
45
30
15
0
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
WAVENUMBER

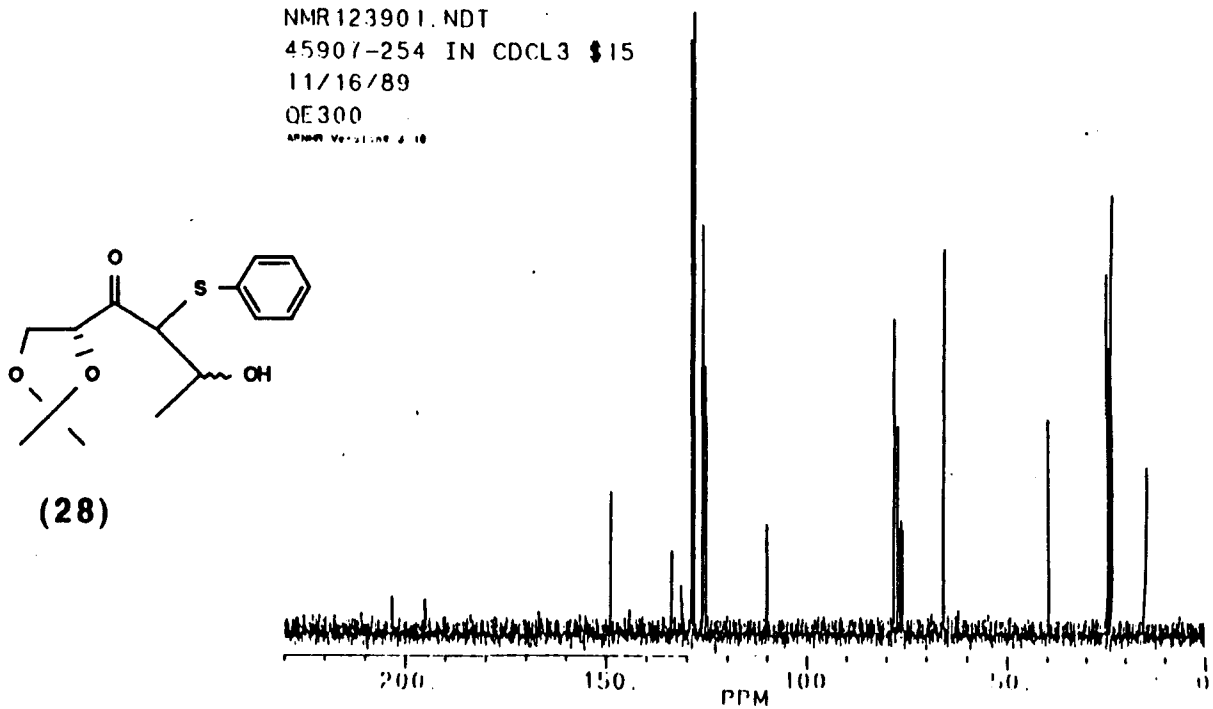

O
S
O
O

(26)

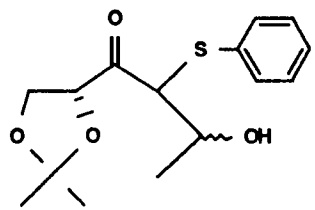

270
#E+06
100
80
60
40
20
0
195
253
162
101
145
196
1
0
100
200
300
400
500
600


NMR[illegible]30.NDT
34907-294 IN CDCL3 #14
11/15/89
QZ300
O
S
O
O
OH
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
PPM

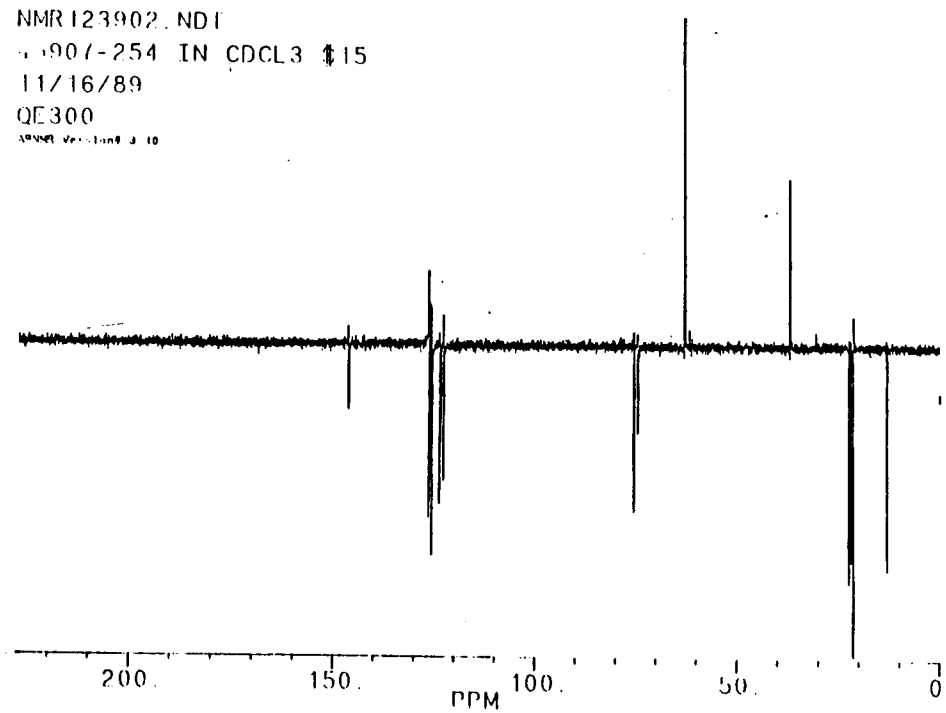
(28)


NMR123901.NDT
45907-254 IN CDCL3 $15
11/16/89
QE300
O
S
O
O
OH
200.
150.
100
50.
0
PPM

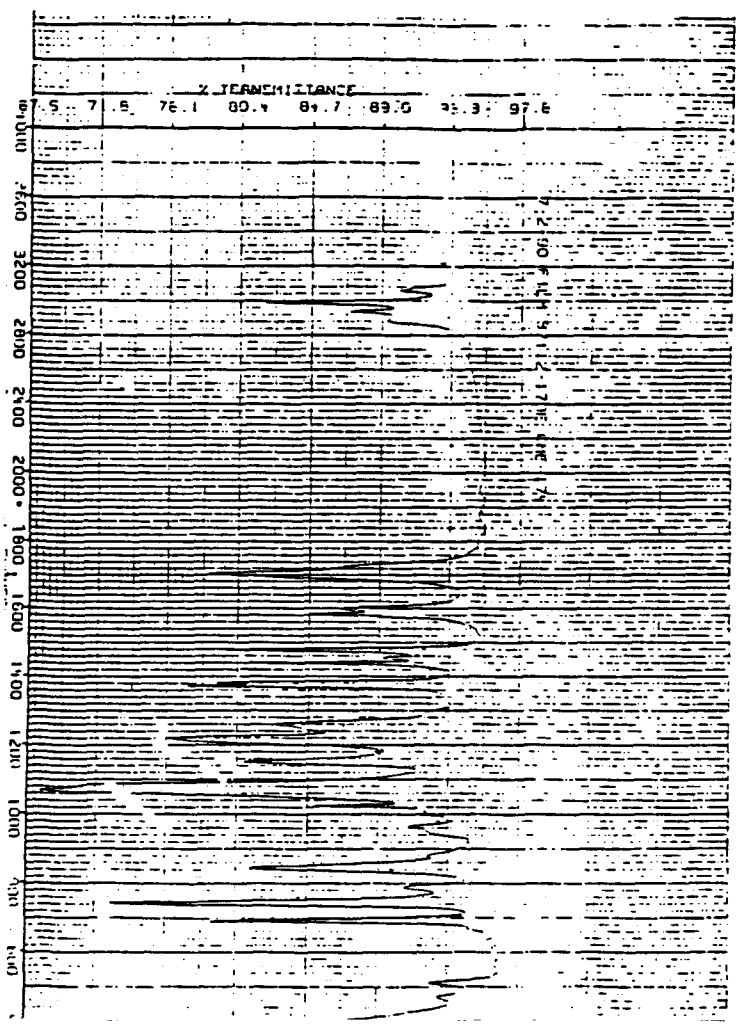
(28)

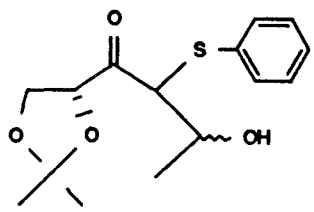

O
S
O
O
OH

(28)

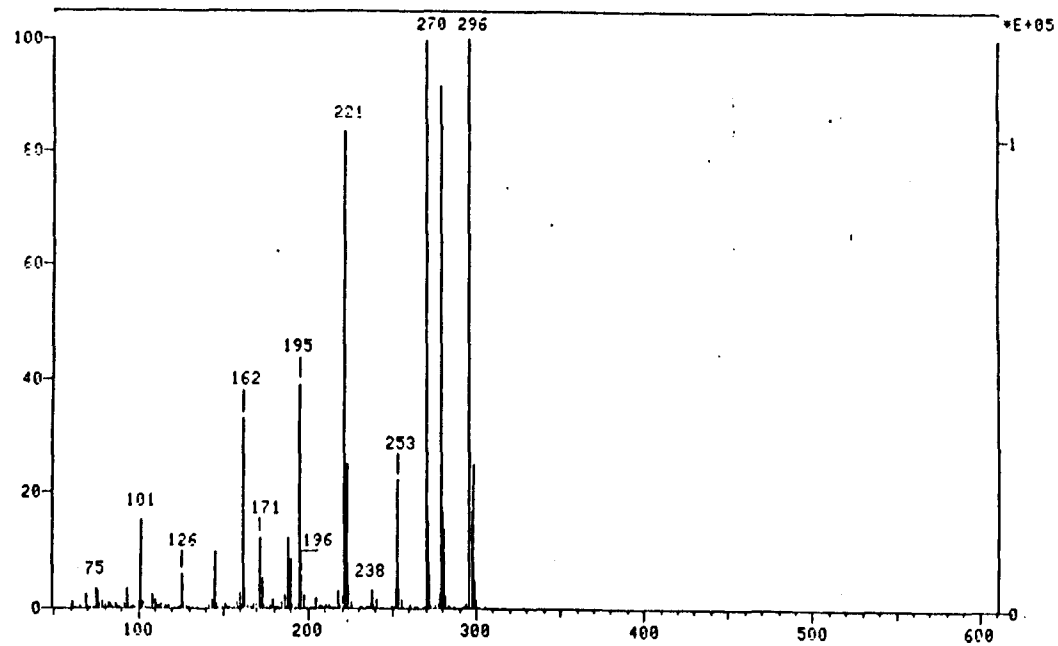

NMR123902.NDT
907-254 IN CDCL3 $15
11/16/89
QE300
200.
150.
100.
50.
0.
PPM

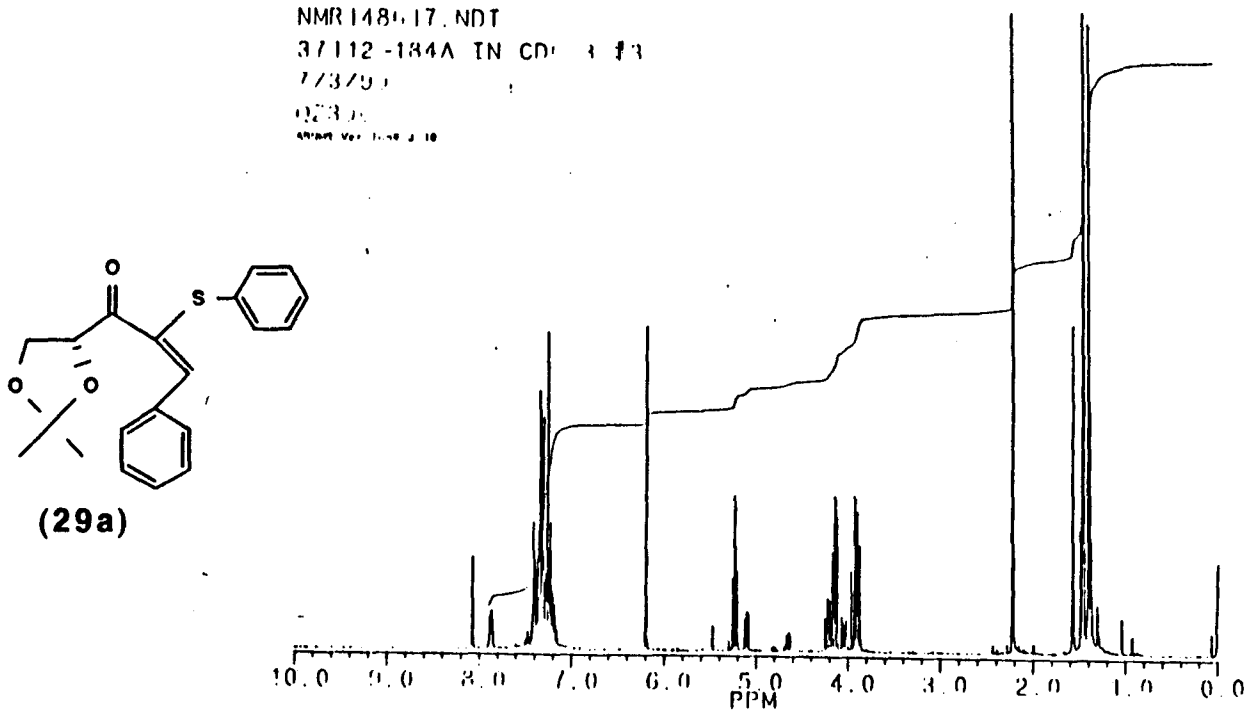
(28)


% TRANSMITTANCE
7.5 7.8 76.1 80.4 84.7 89.0 93.3 97.6
4000
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400

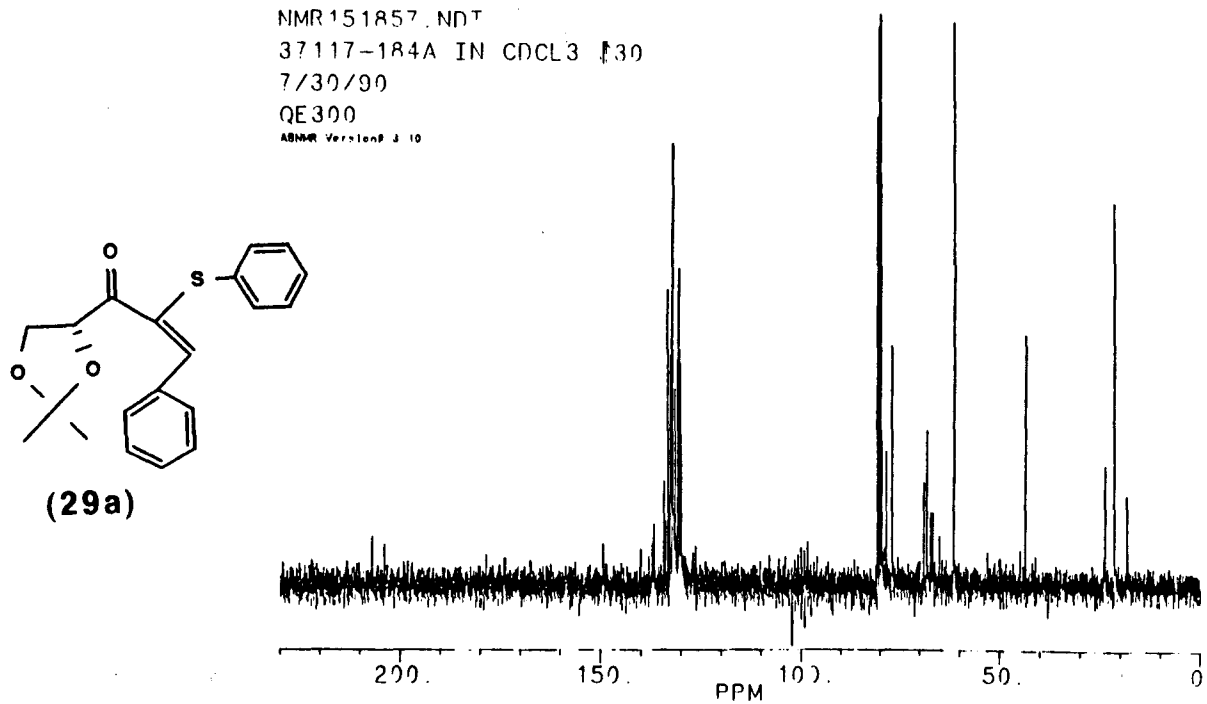

O
S
O
O
OH

(28)

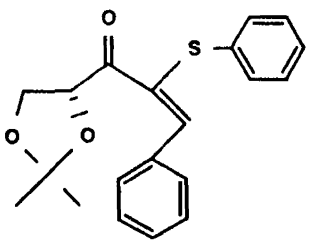

*E+05
100
80
60
40
20
0
1
0
270 296
221
195
162
253
101
171
126
196
75
238
100
200
300
400
500
600


NMR148-17.NDT
37112-184A IN CD
O
S
O
O
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

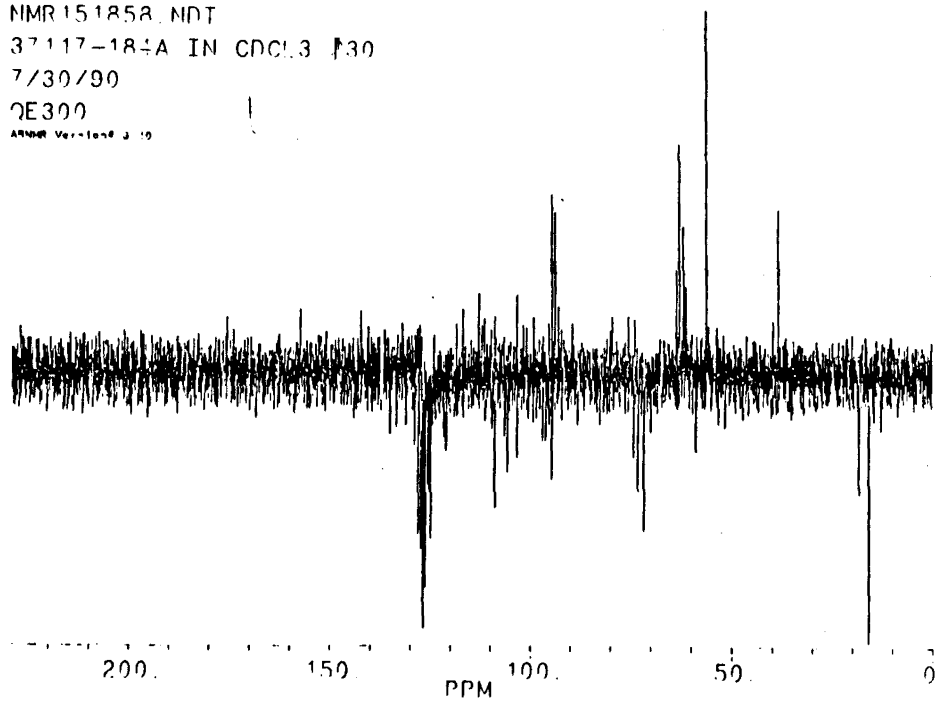
(29a)

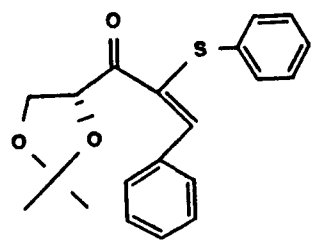

NMR151857.NDT
37117-184A IN CDCL3 #30
7/30/90
QE300
O
S
O
O
200.
150.
100.
50.
0
PPM

(29a)

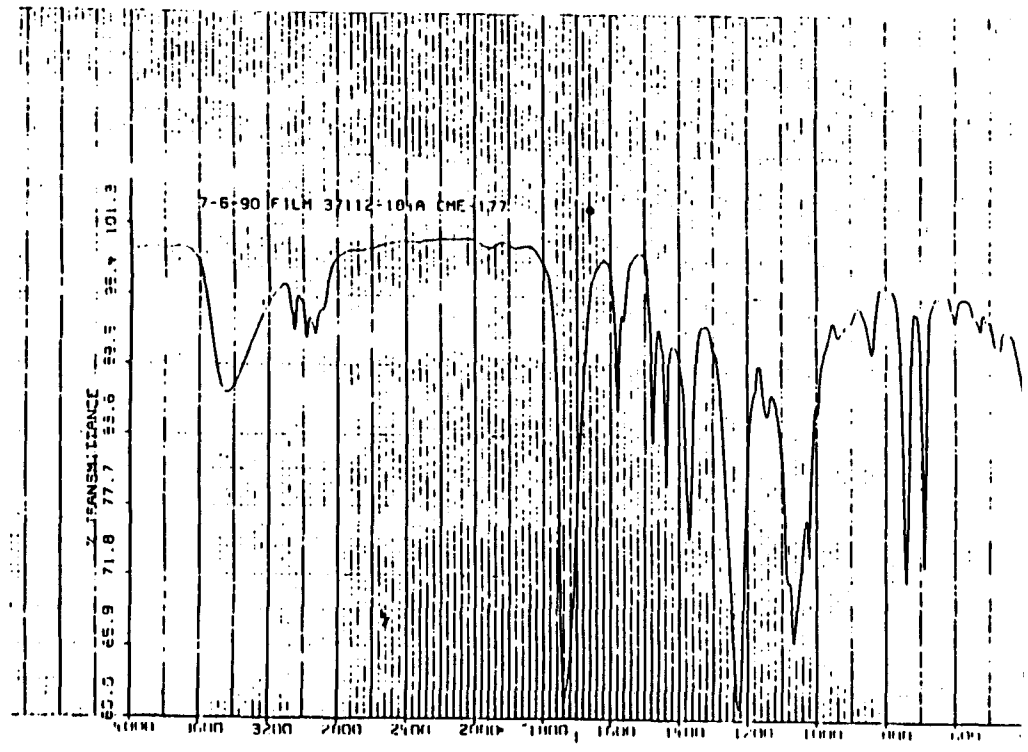

O
S
O
O

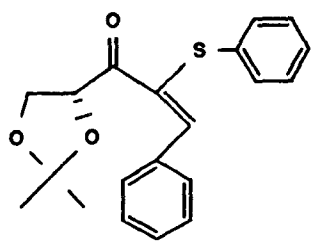
(29a)


NMR151858.NDT
37117-184A IN CDCL3 #30
7/30/90
QE300
200.
150.
100.
50.
0
PPM

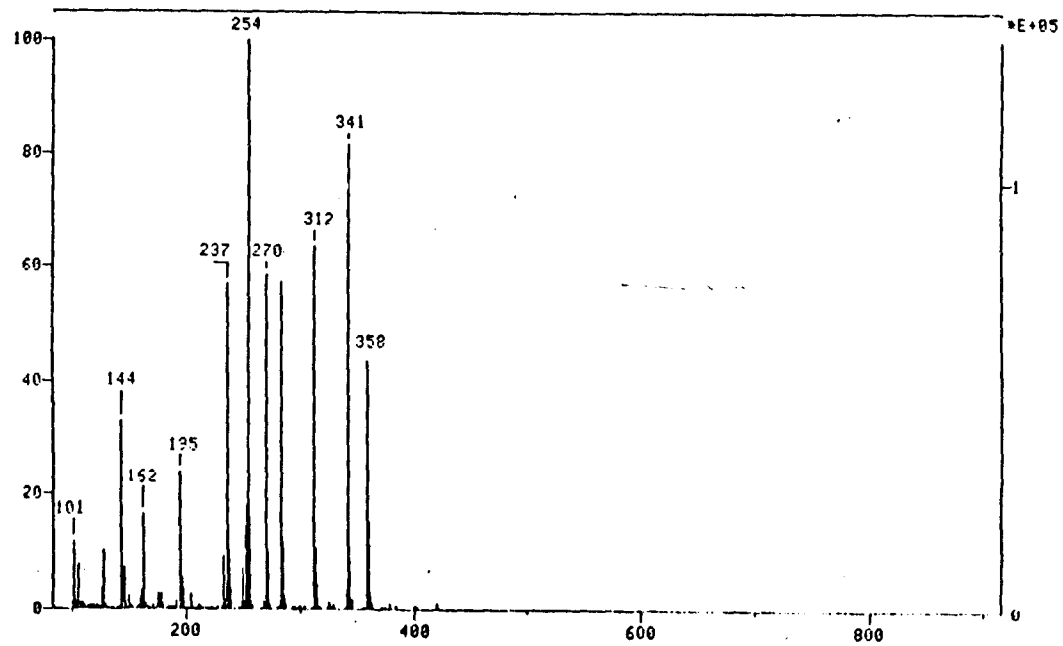


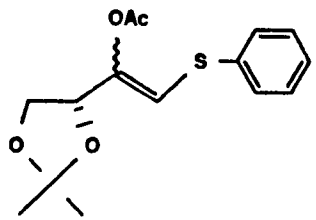
(29a)



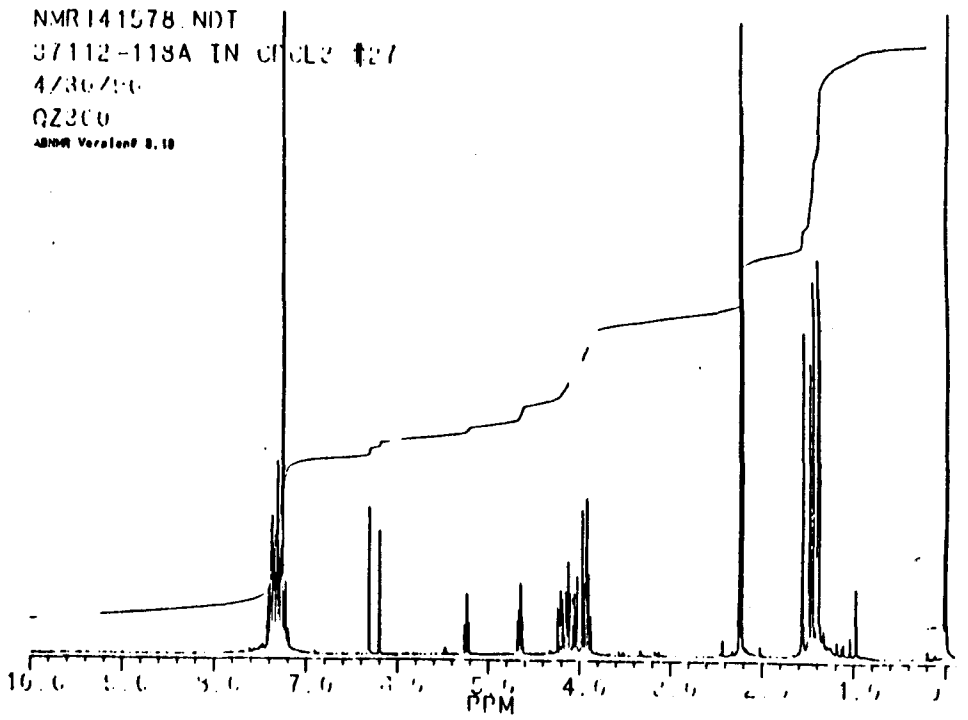


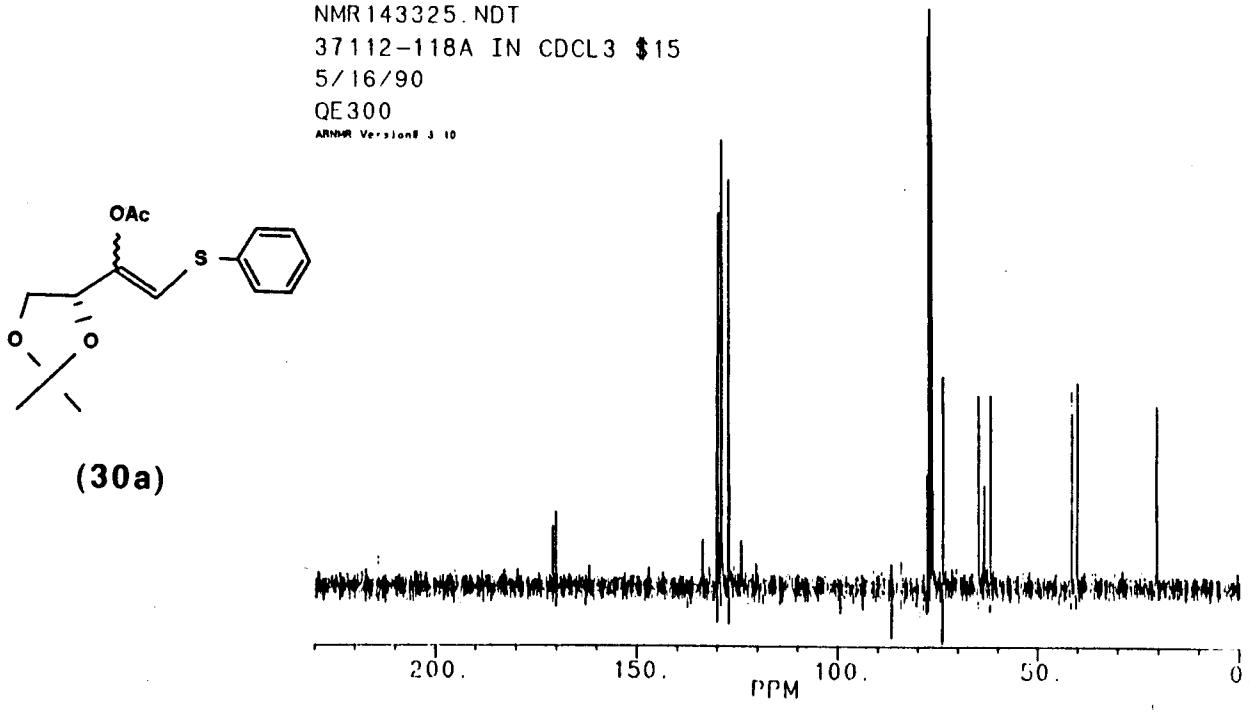
(29a)


254
341
312
237
270
358
144
135
152
101
100
80
60
40
20
0
200
400
600
800
*E+05
1
0

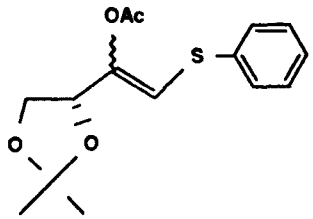


(30a)

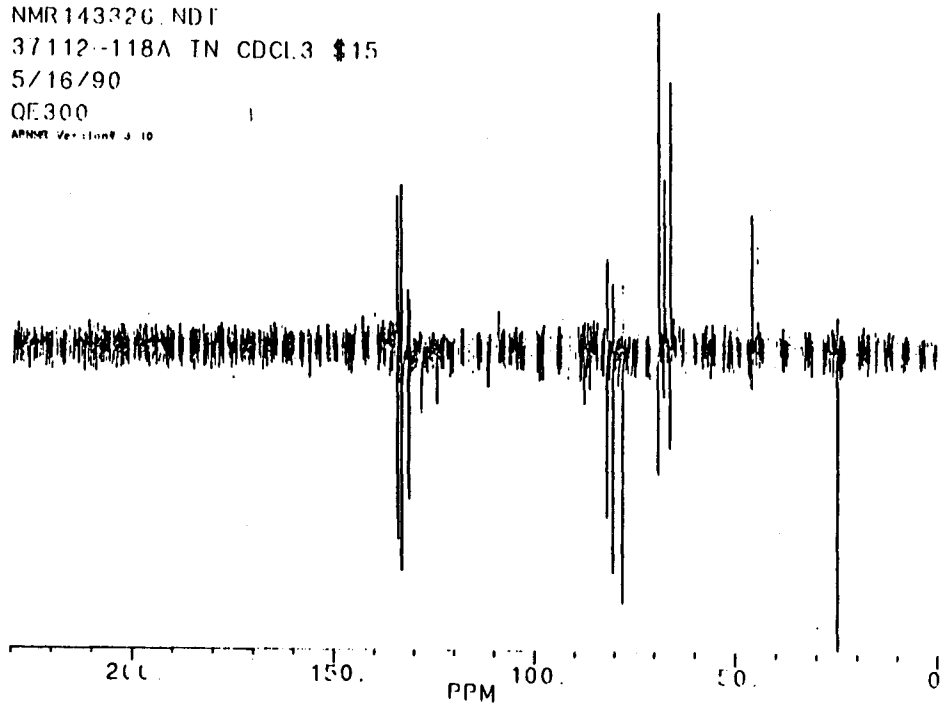


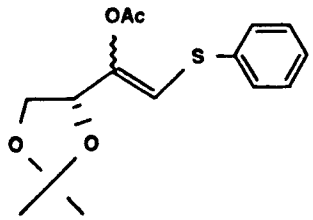

NMR143325.NDT
37112-118A IN CDCL3 $15
5/16/90
QE300
OAc
S
O
O
200.
150.
100.
50.
0.
PPM

(30a)

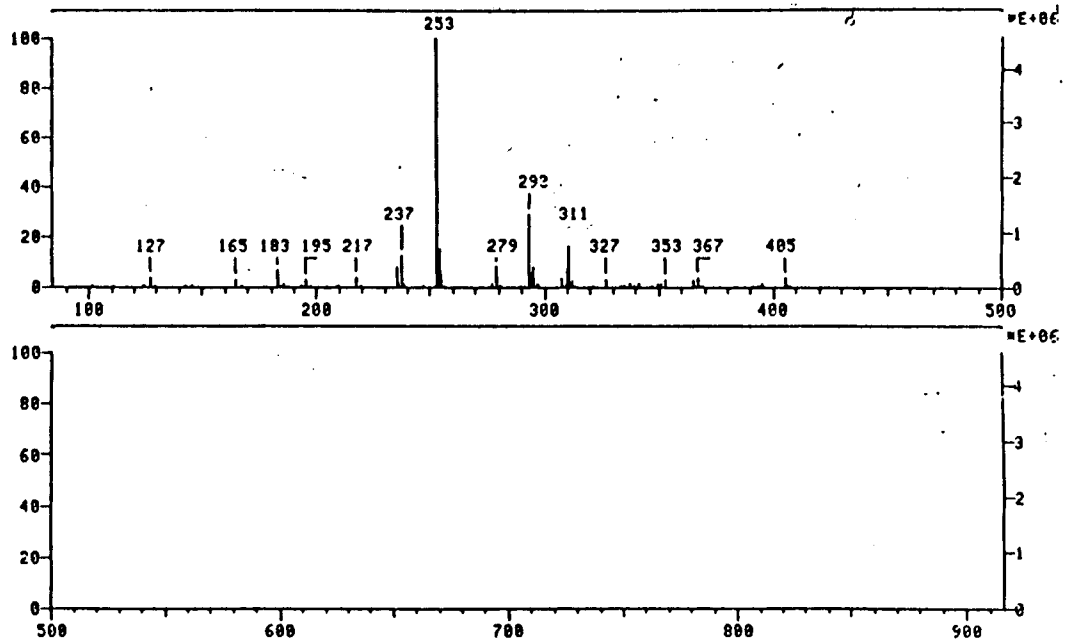

OAc
S
O
O

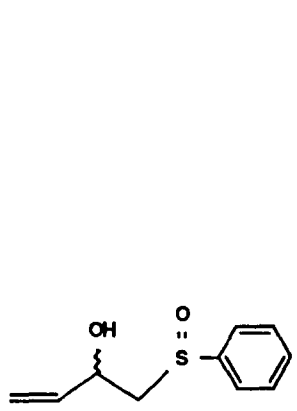
(30a)


NMR143326.NDT
37112-118A TN CDCL3 $15
5/16/90
QE300
200.
150.
100.
50.
0.
PPM

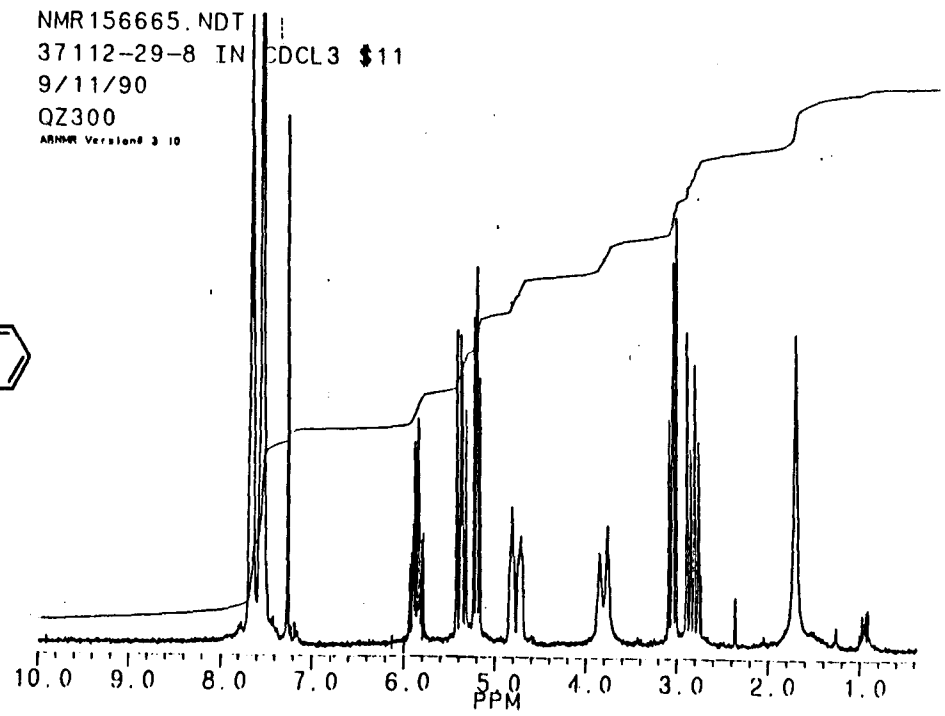

OAc
S
O
O

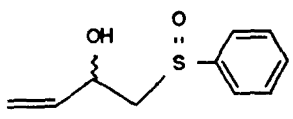
(30a)


253
293
311
237
127
165
183
195
217
279
327
353
367
405
100
200
300
400
500
600
700
800
900

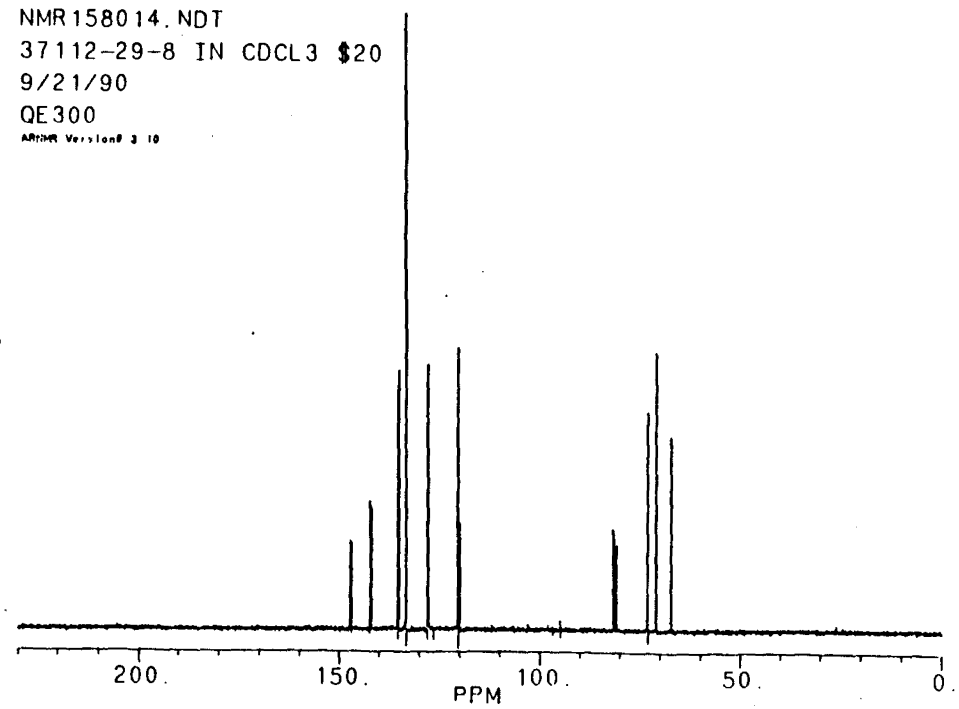

OH
O
S

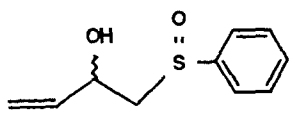
(31)


NMR156665.NDT
37112-29-8 IN CDCL3 $11
9/11/90
QZ300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
PPM

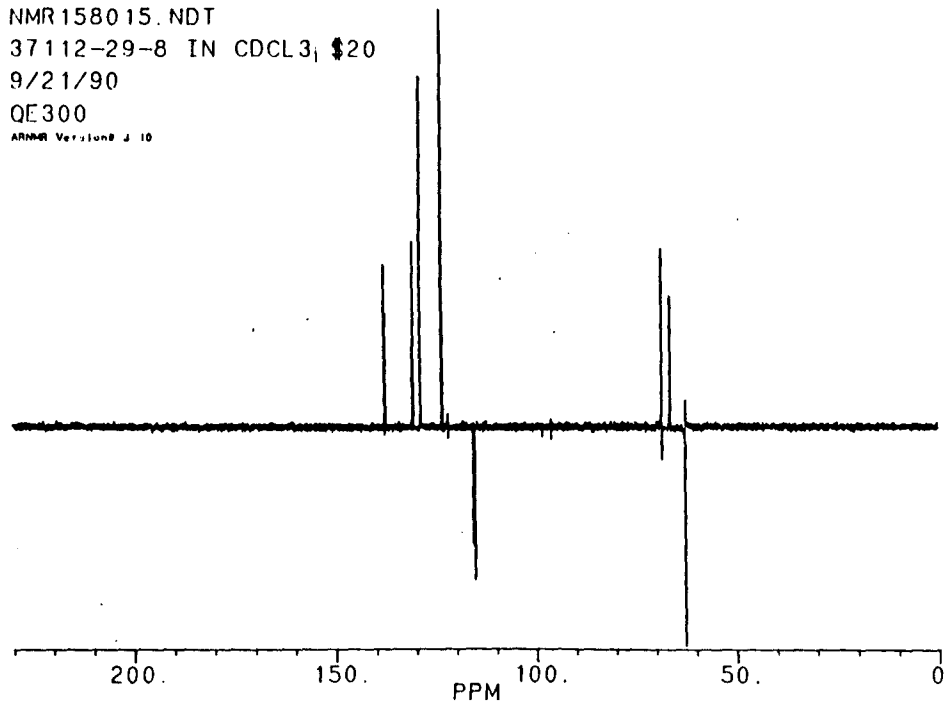

OH
O
S

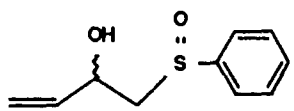
(31)


NMR158014.NDT
37112-29-8 IN CDCL3 $20
9/21/90
QE300
200.
150.
100.
50.
0.
PPM

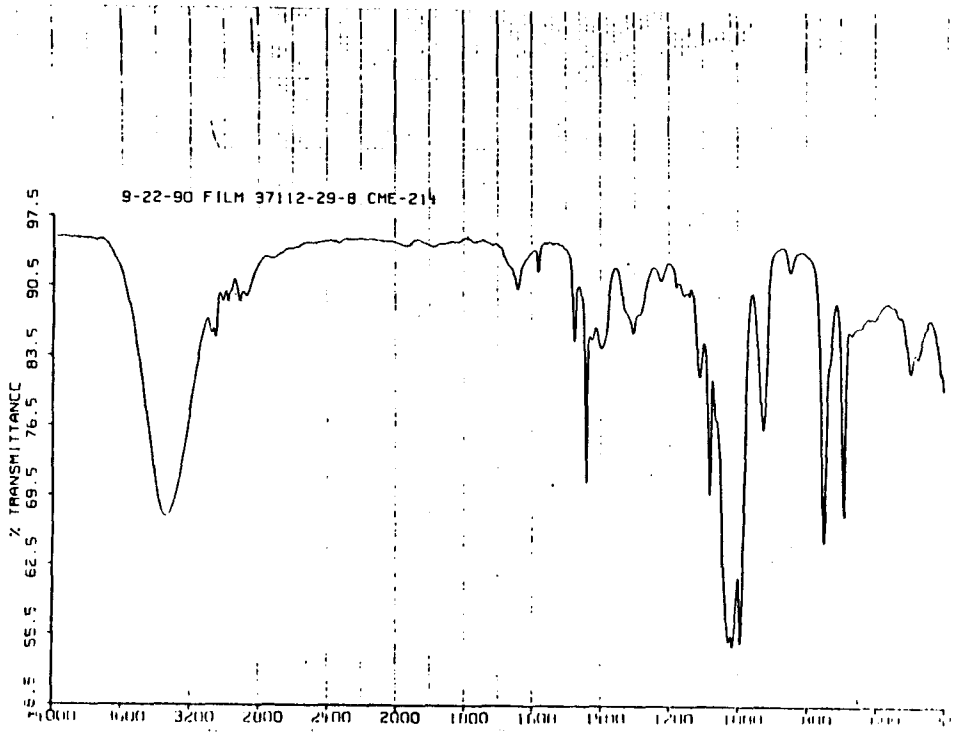

OH
O
S

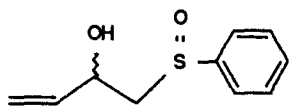
(31)


NMR158015.NDT
37112-29-8 IN CDCL3, $20
9/21/90
QE300
200.
150.
100.
50.
0.
PPM

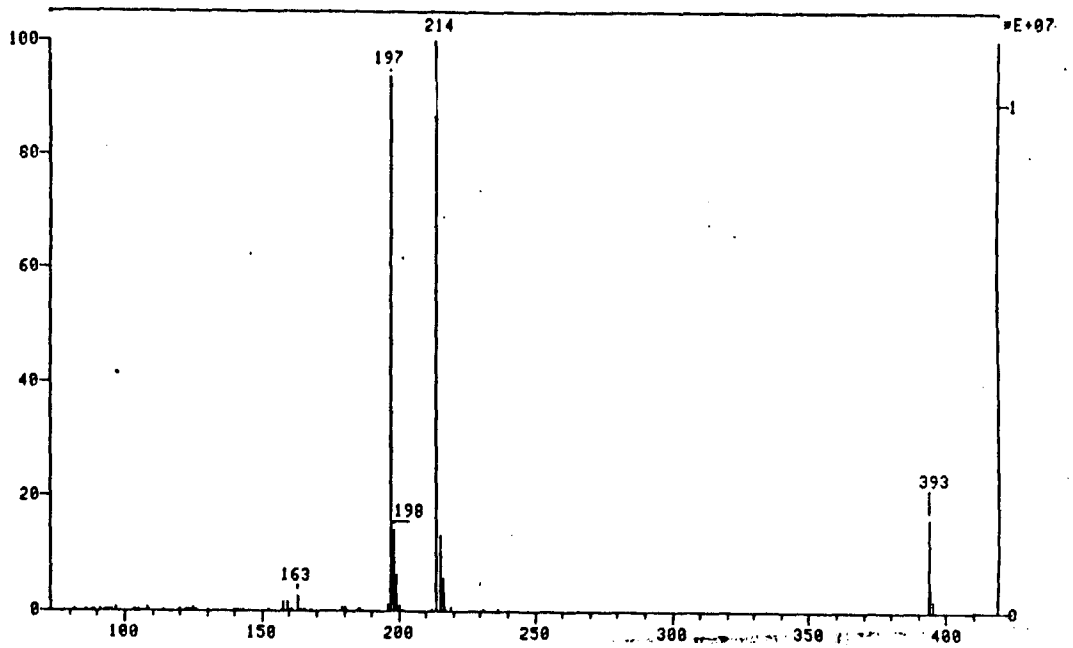

OH
O
S

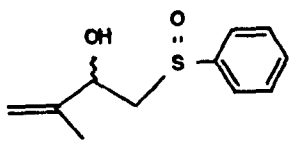
(31)


9-22-90 FILM 37112-29-8 CME-214
% TRANSMITTANCE
97.5
90.5
83.5
76.5
69.5
62.5
55.5
4000
3200
2800
2400
2000
1600
1400
1200
1000
800

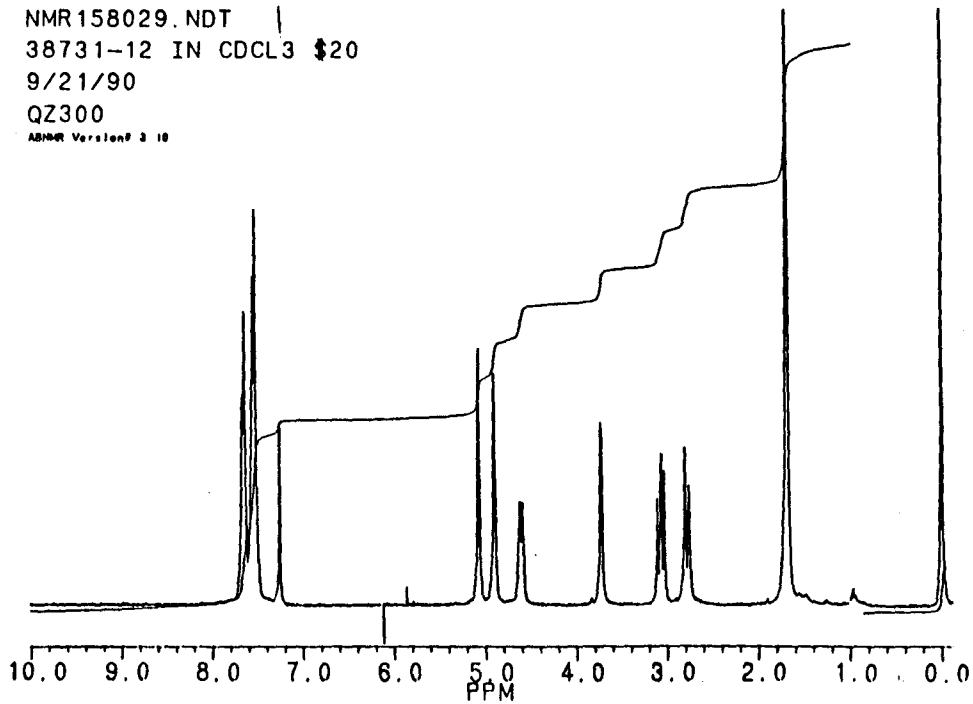

OH
O
S

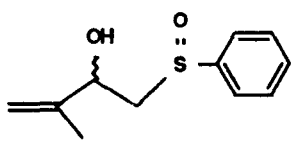
(31)


214
197
198
163
393
100
80
60
40
20
0
100
150
200
250
300
350
400
1
0

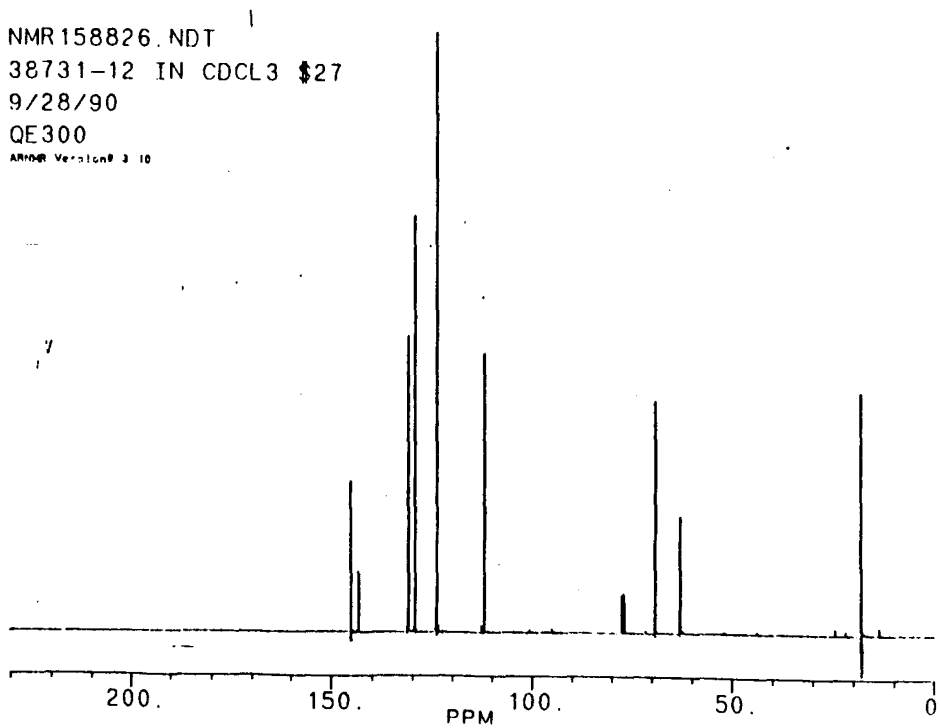

OH
O
S

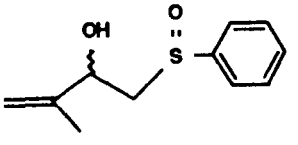
(32)


NMR158029.NDT
38731-12 IN CDCL3 $20
9/21/90
QZ300
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
PPM

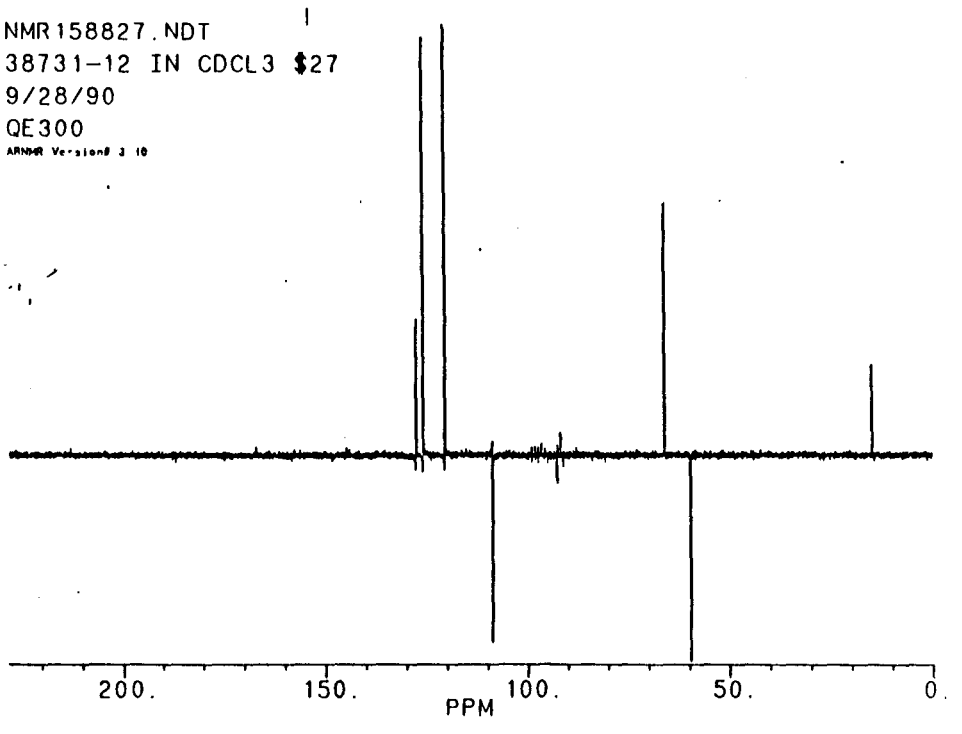

OH
O
S

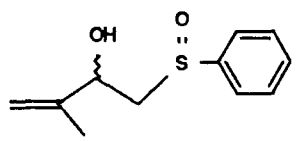
(32)


NMR158826.NDT
38731-12 IN CDCL3 $27
9/28/90
QE300
200.
150.
100.
50.
0
PPM

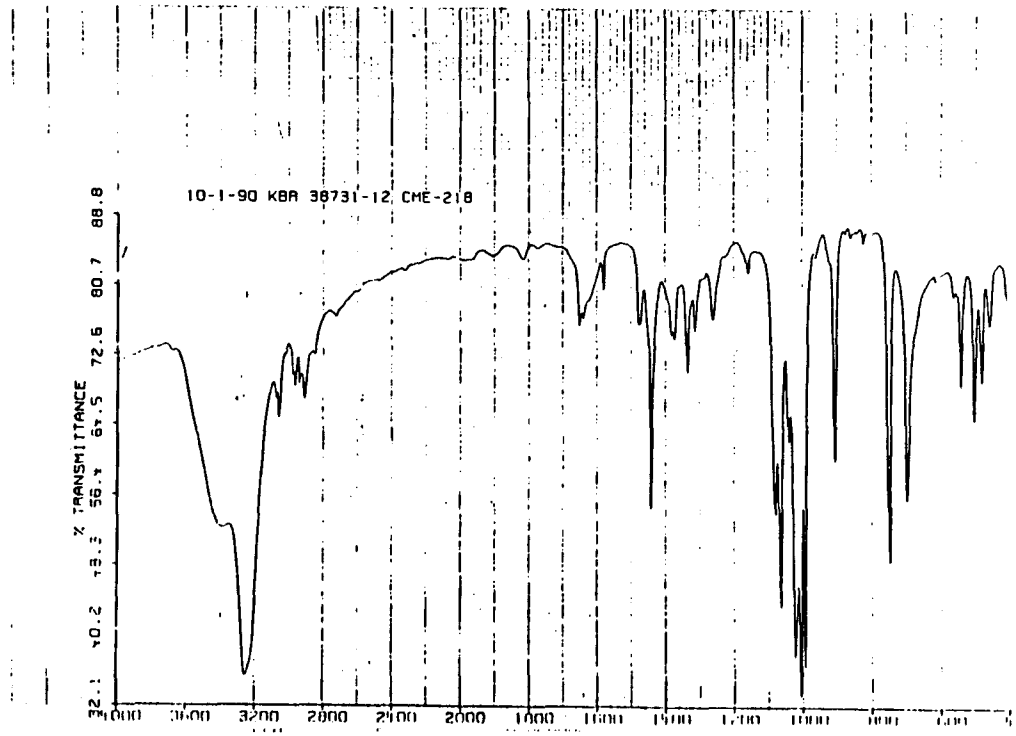

OH
O
S

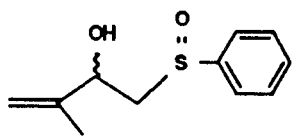
(32)


NMR158827.NDT
38731-12 IN CDCL3 $27
9/28/90
QE300
200.
150.
100.
50.
0.
PPM

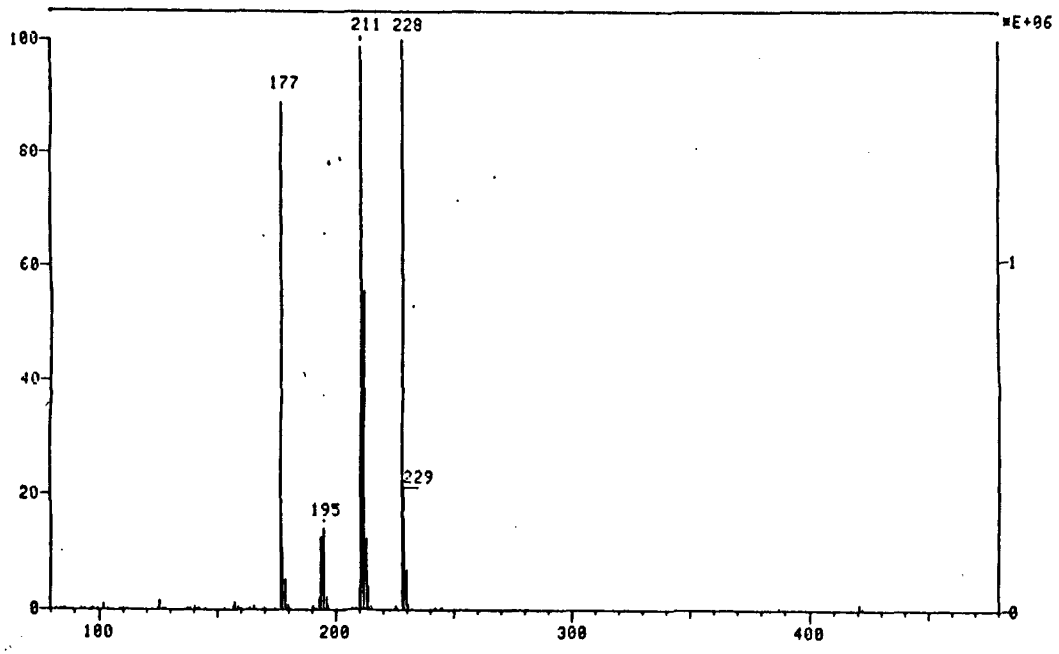

OH
O
S

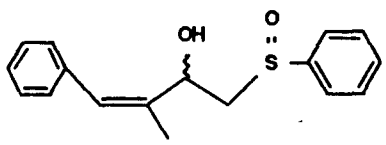
(32)


10-1-90 KBR 38731-12 CME-218
% TRANSMITTANCE
88.8
80.7
72.6
64.5
56.4
48.3
40.2
32.1
4000
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400

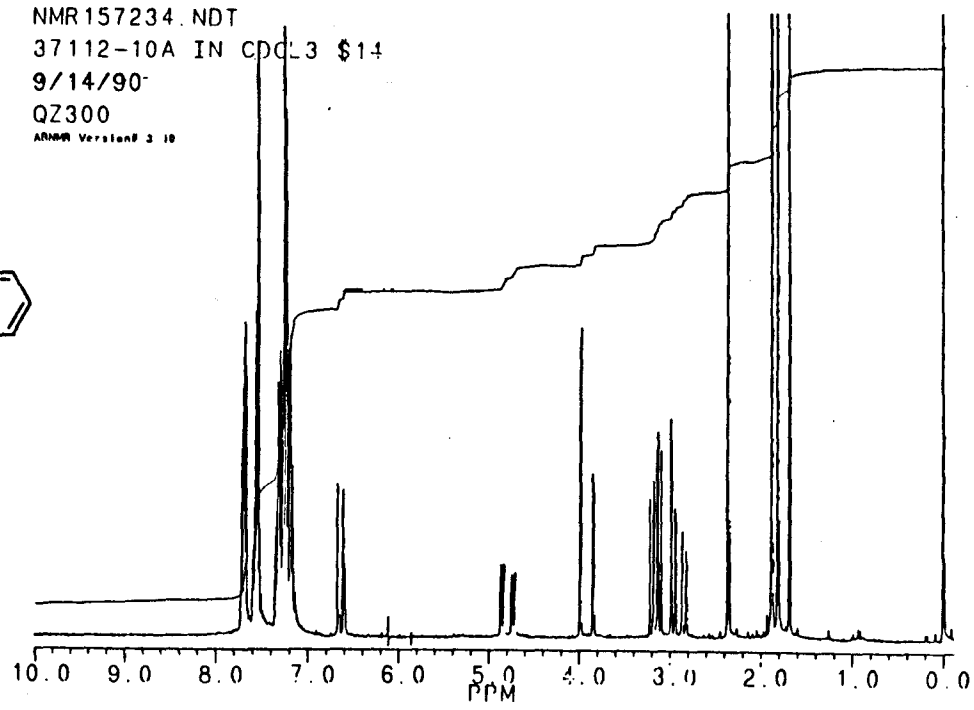


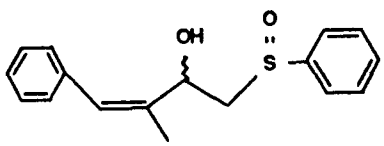
(32)



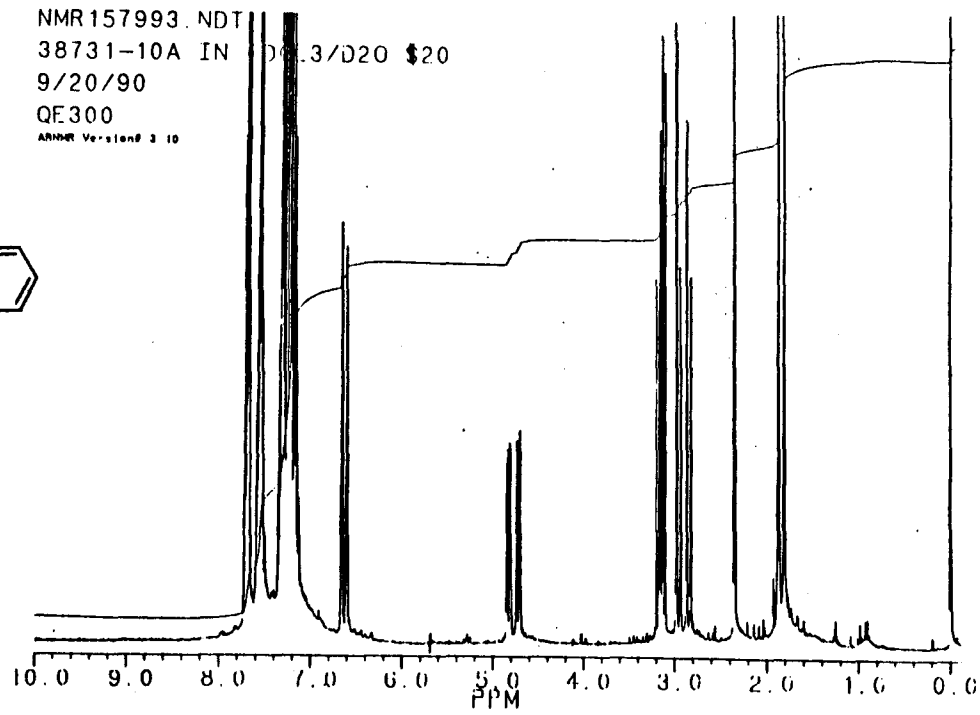

OH
O
S

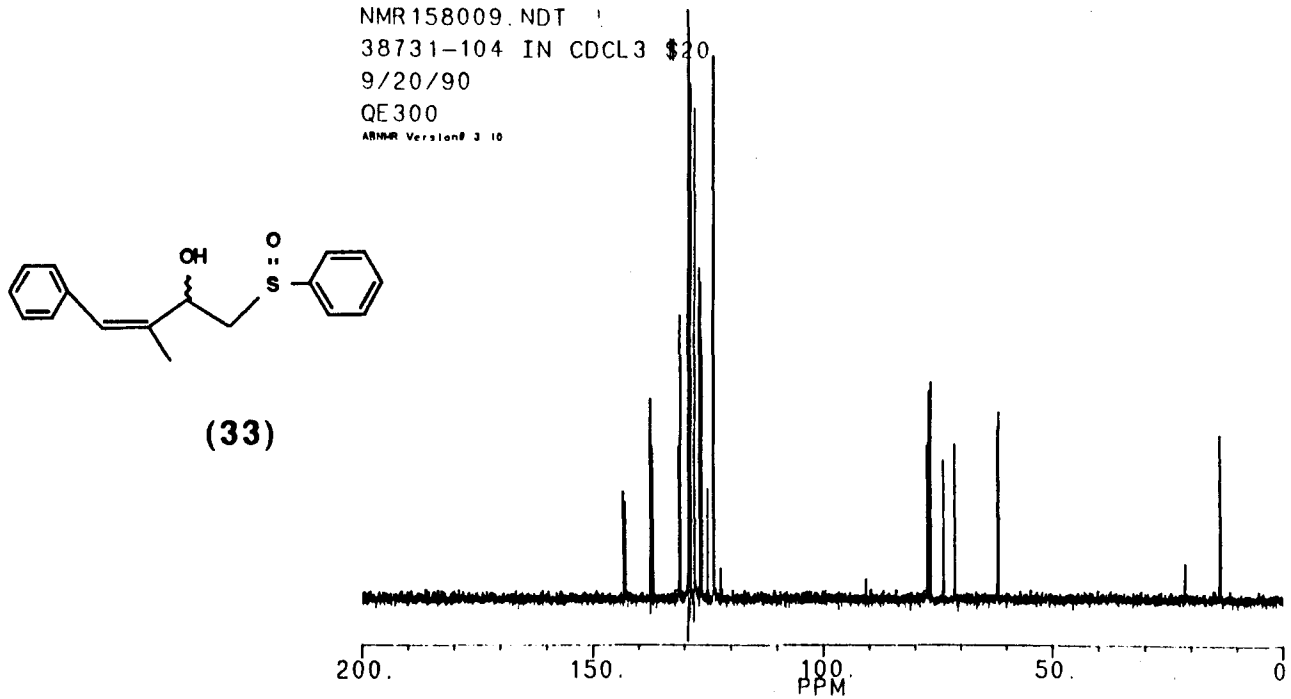
(33)


NMR157234.NDT
37112-10A IN CDCL3 $14
9/14/90
QZ300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

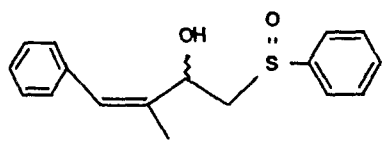

OH
O
S

(33)

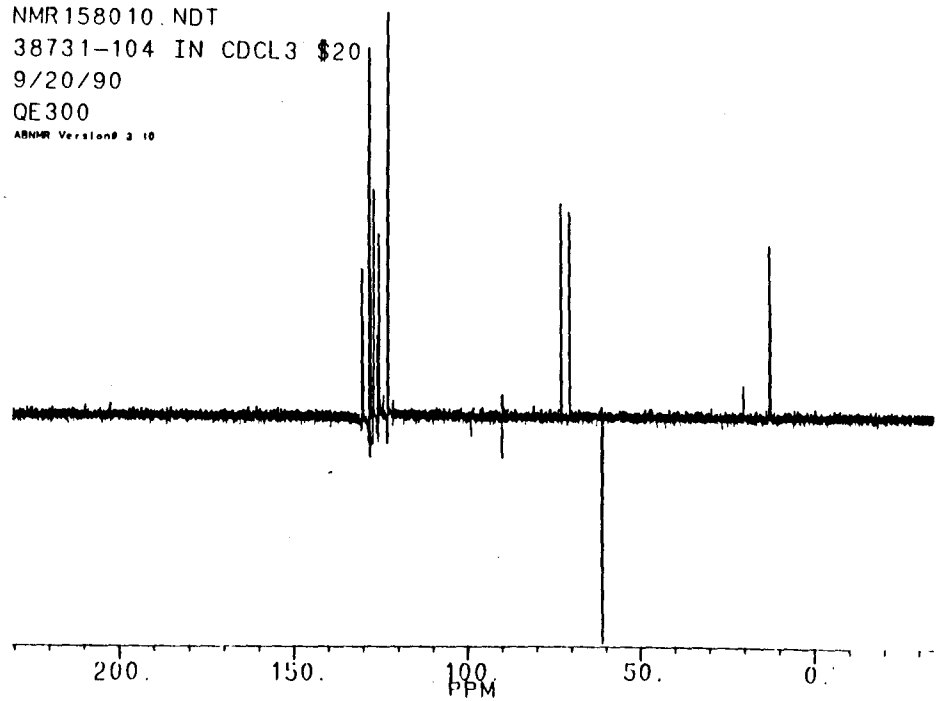

NMR157993.NDT
38731-10A IN
9/20/90
QE300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

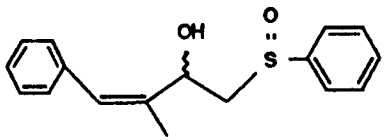

NMR158009.NDT
38731-104 IN CDCL3 $20
9/20/90
QE300
OH
O
S
200.
150.
100.
50.
0.
PPM

(33)

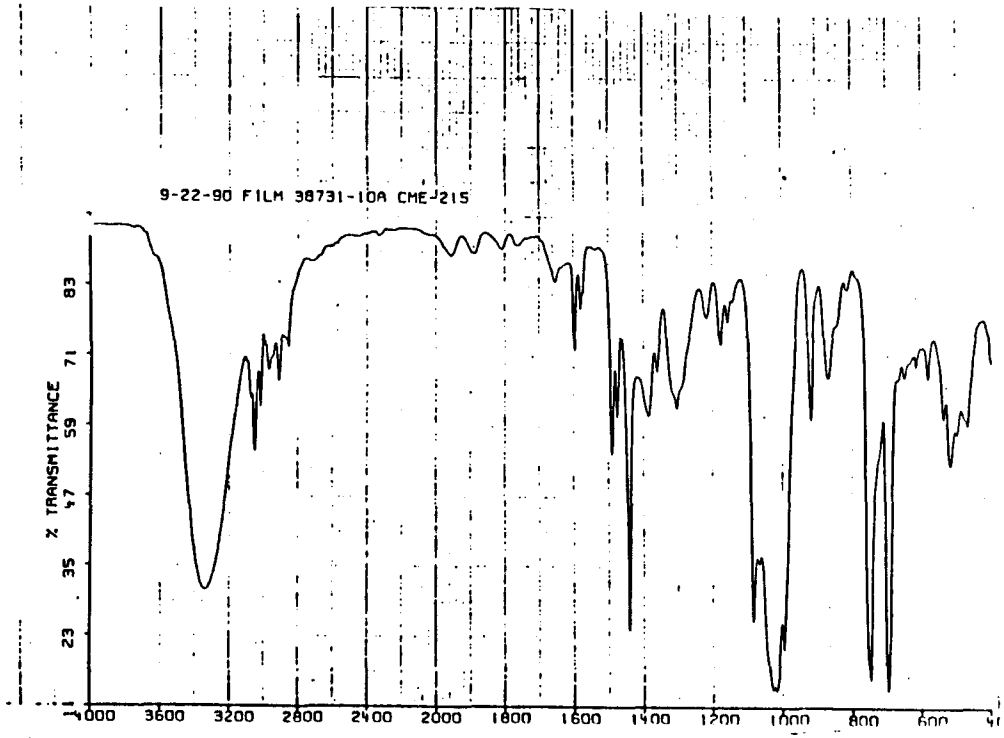

OH
O
S

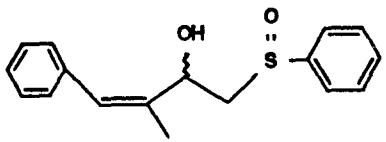
(33)


NMR158010.NDT
38731-104 IN CDCL3 $20
9/20/90
QE300
200.
150.
100.
50.
0.
PPM

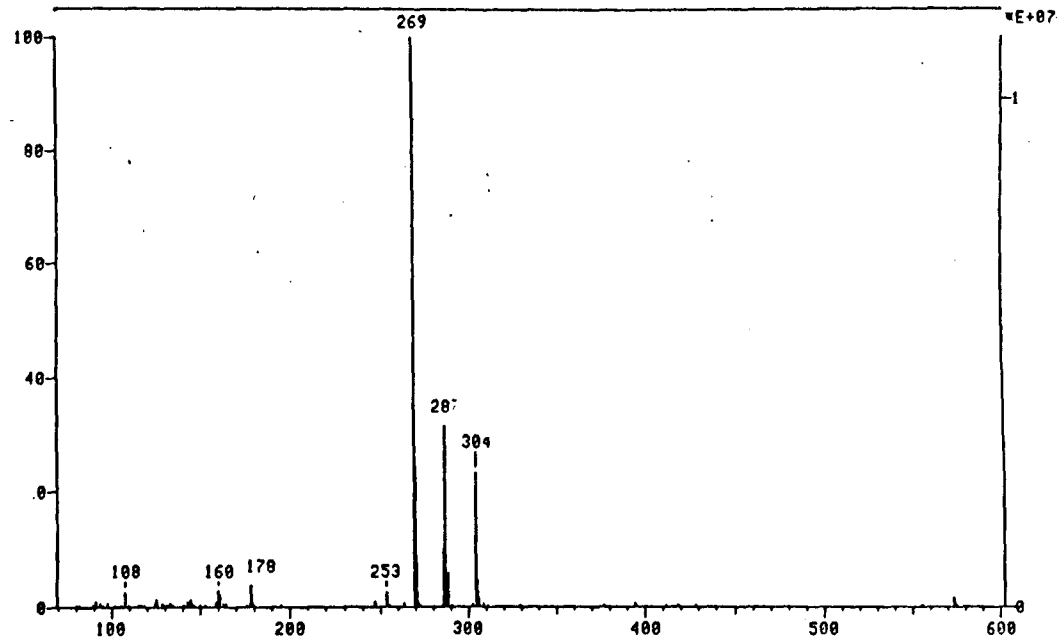

OH
O
S

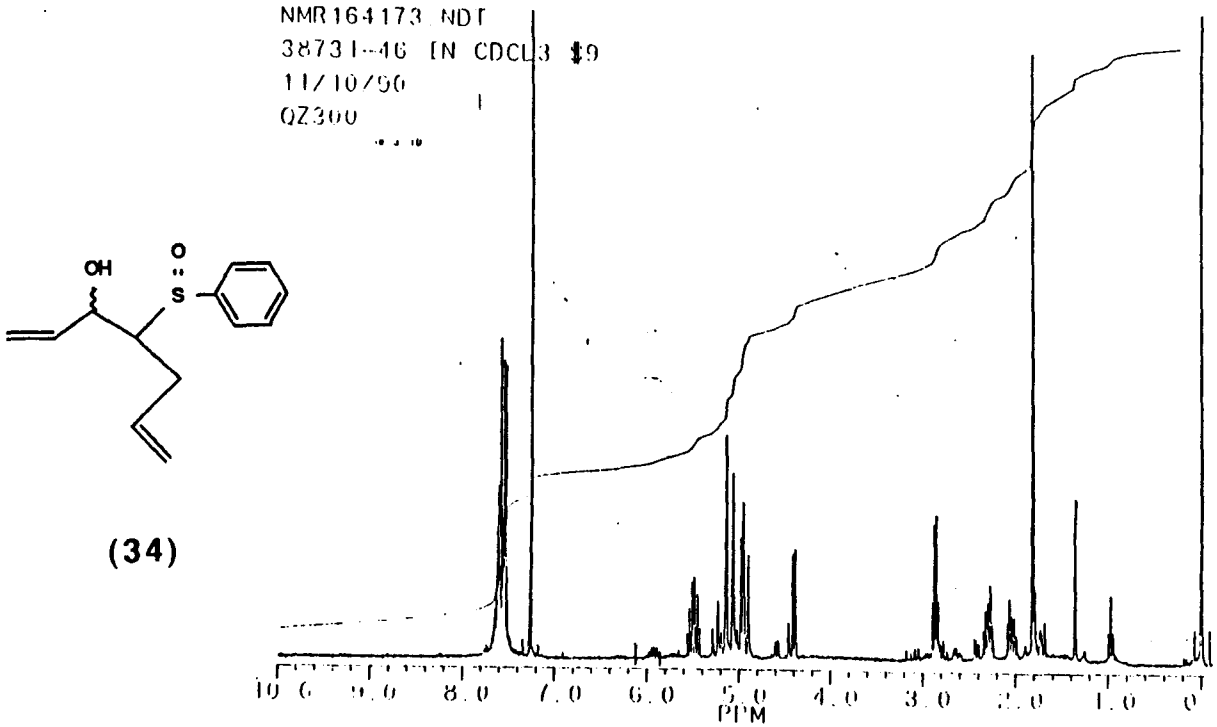
(33)


9-22-90 FILM 38731-10A CME-215
% TRANSMITTANCE
11
23
35
47
59
71
83
4000
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600

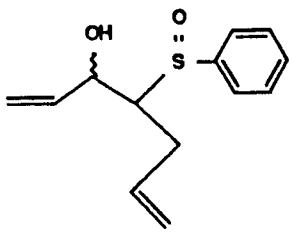

OH
O
S

(33)

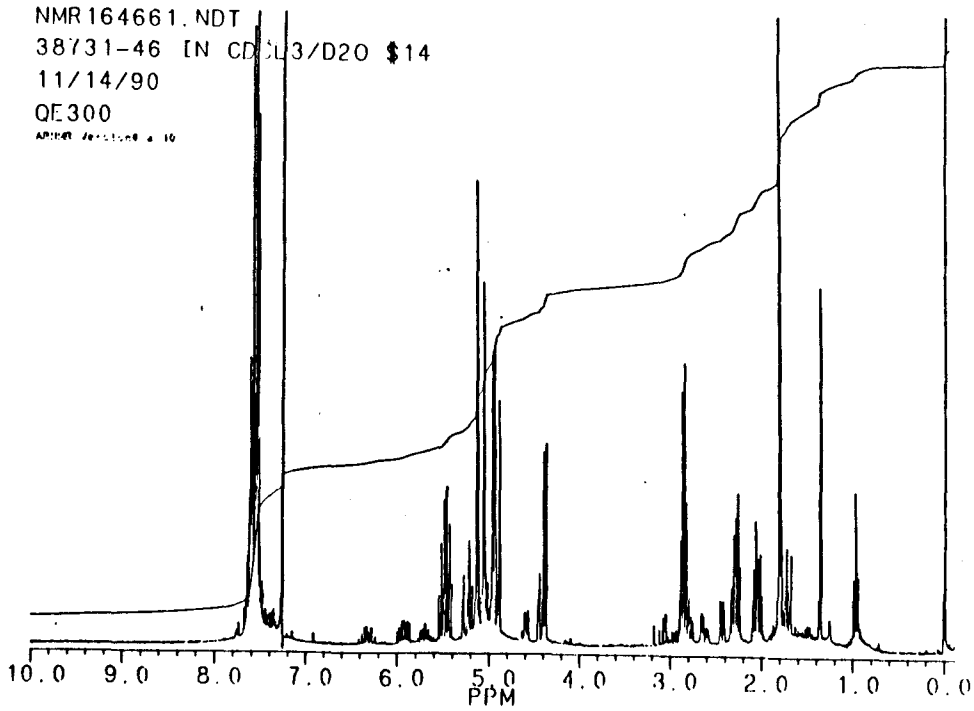

269
287
304
108
160
178
253
100
80
60
40
0
100
200
300
400
500
600
1
0

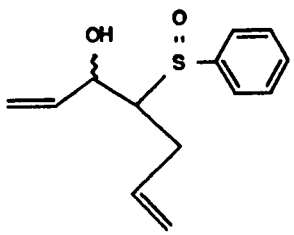

NMR164173 NDT
38731-46 IN CDCL3 $9
11/10/90
QZ300
OH
O
S
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
PPM

(34)

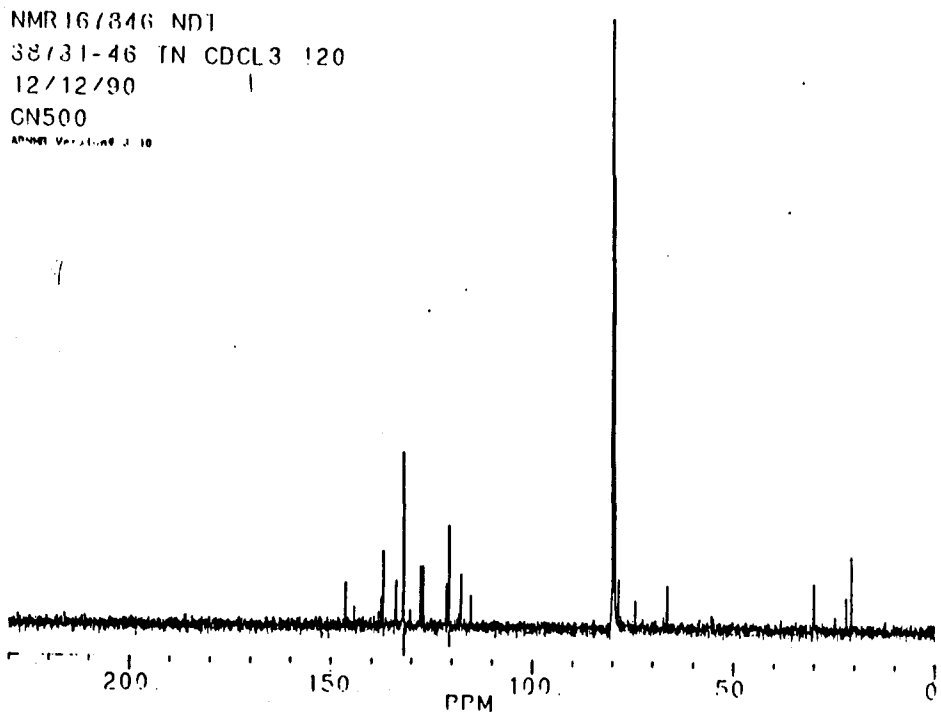

OH
O
S

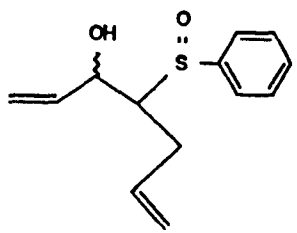
(34)


NMR164661.NDT
38731-46 [N CDCL3/D2O $14
11/14/90
QE300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

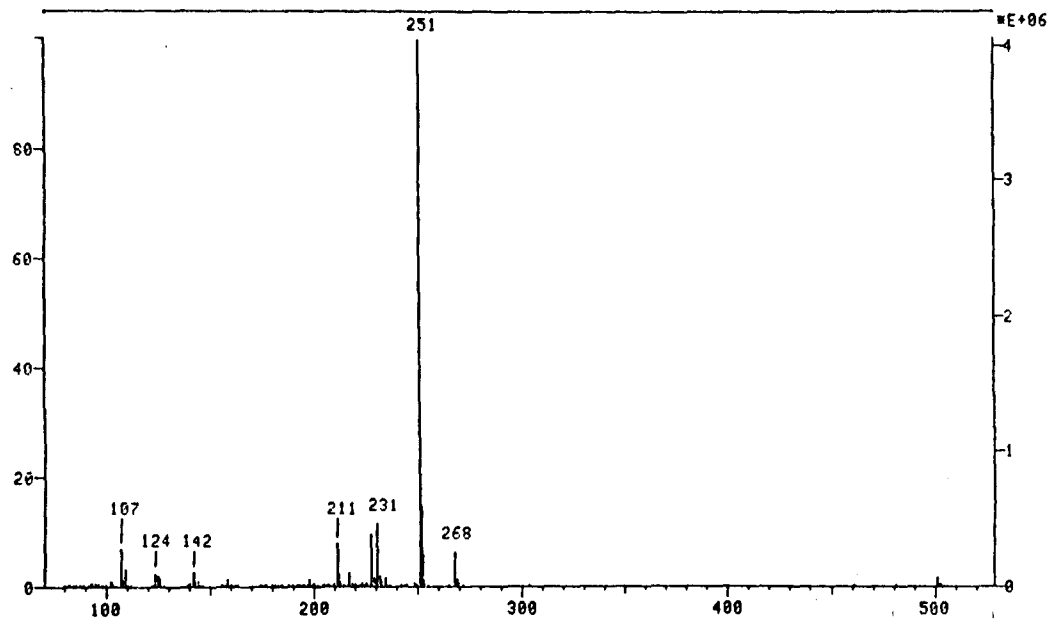

OH
O
S

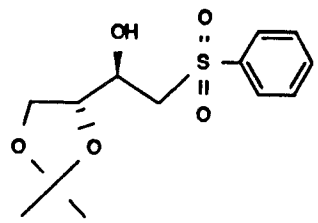
(34)


NMR16/846 ND1
38/31-46 IN CDCL3 120
12/12/90
CN500
200
150
100
50
0
PPM

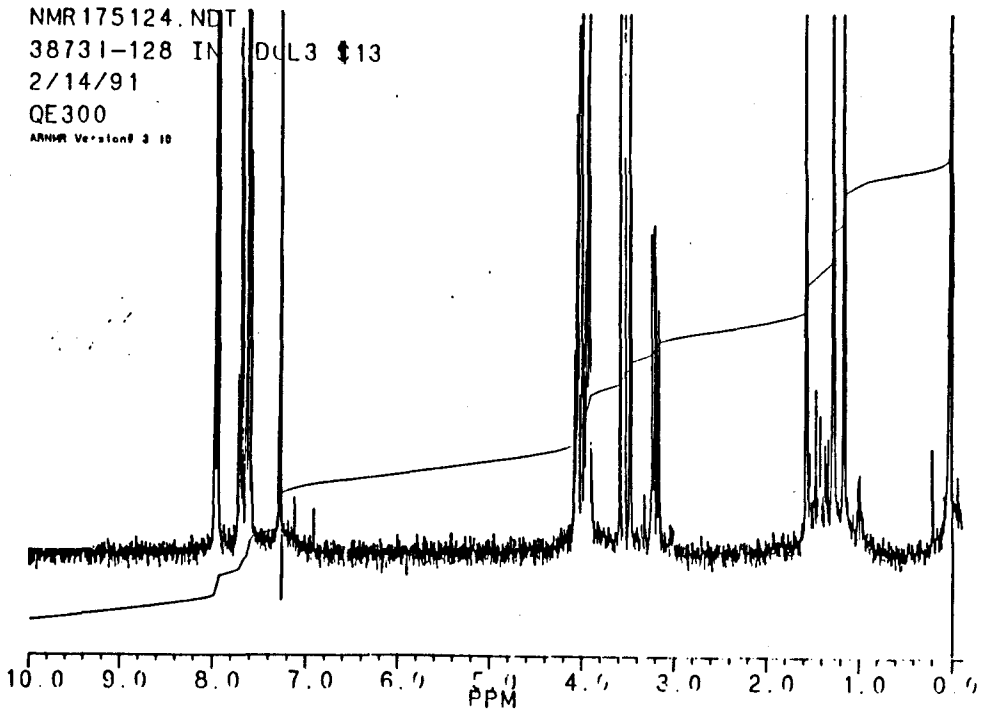

OH
O
S

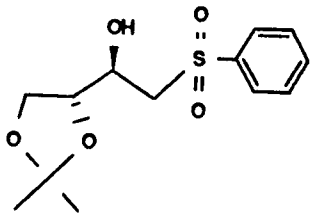
(34)


251
E+06
80
60
40
20
0
4
3
2
1
0
107
124
142
211
231
268
100
200
300
400
500

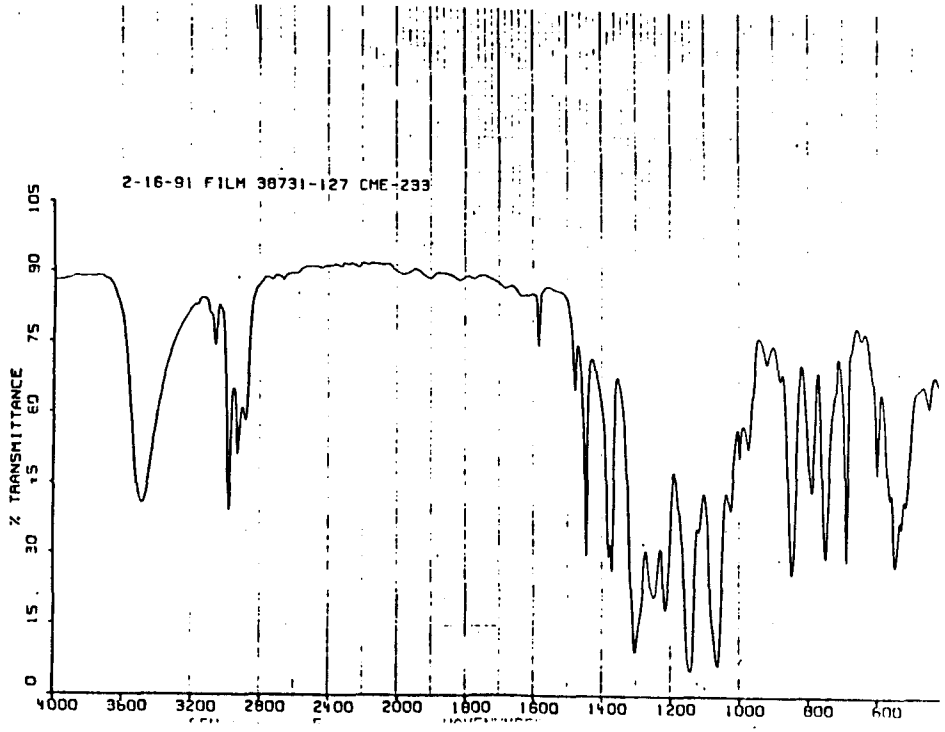

OH
O
S
O
O
O

(35)


NMR175124.NDT
38731-128 IN CDCL3 $13
2/14/91
QE300
10.0
9.0
8.0
7.0
6.0
4.0
3.0
2.0
1.0
PPM


OH
O
S
O
O
O

(35)


2-16-91 FILM 38731-127 CME-233
% TRANSMITTANCE
0
15
30
45
60
75
90
105
4000
3600
3200
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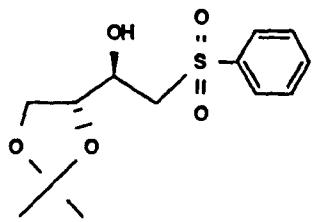
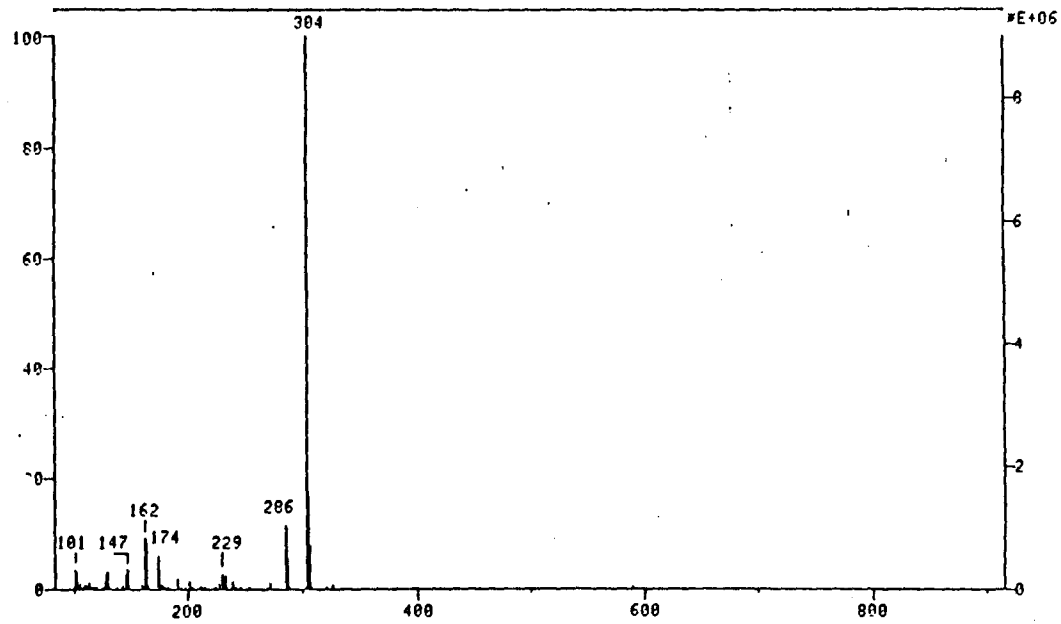
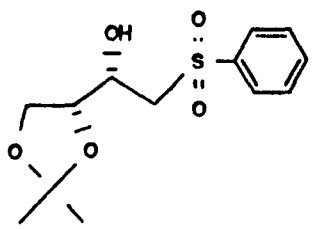
2400
2000
1800
1600
1400
1200
1000
800
600

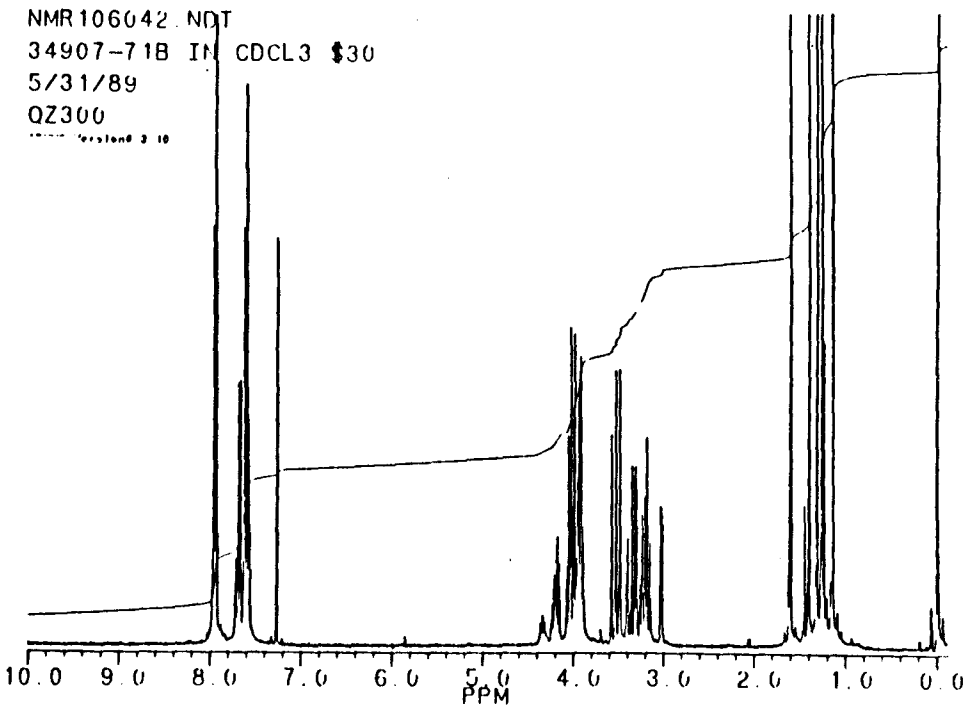

OH
O
S
O
O
O

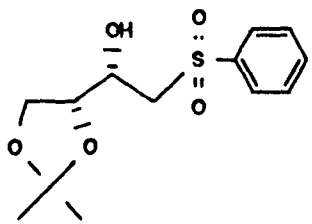
(35)


304
#E+06
100
80
60
40
20
0
8
6
4
2
0
162
286
101
147
174
229
200
400
600
800

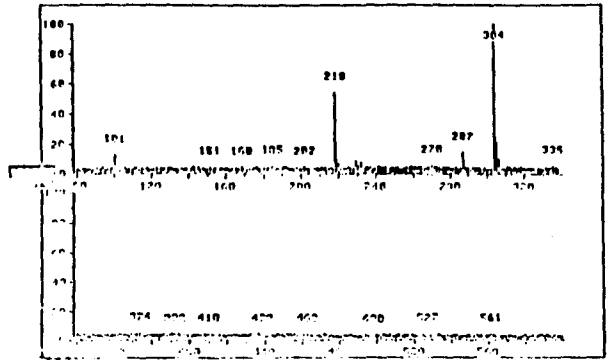

OH
O
S
O
O
O

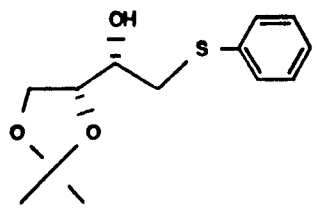
(36)


NMR106042.NDT
34907-71B IN CDCL3 $30
5/31/89
QZ300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

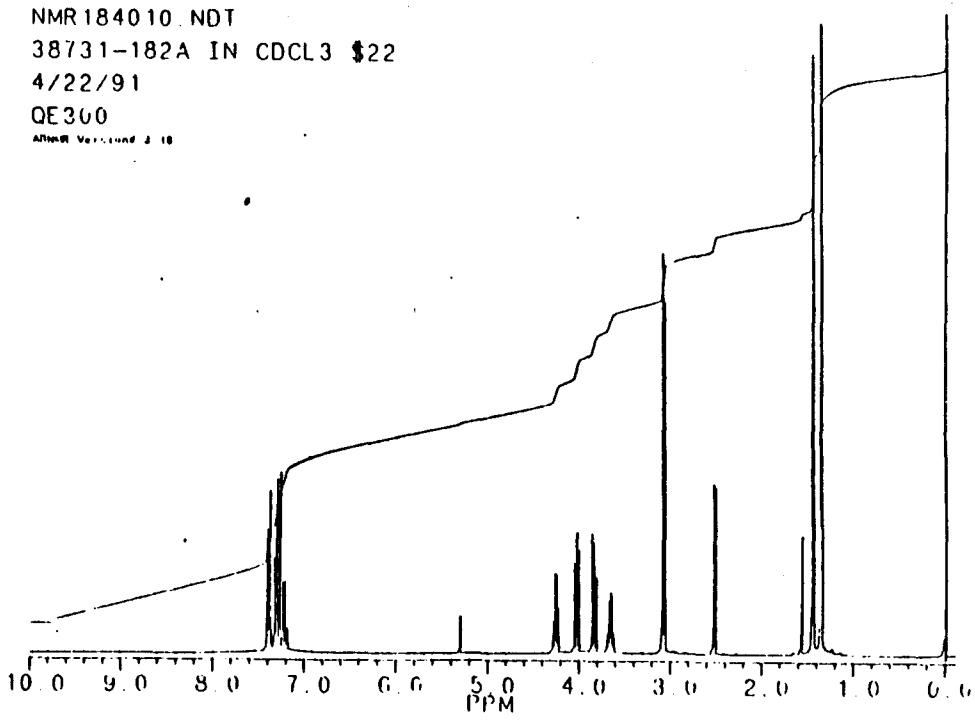


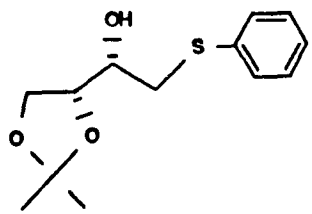
(36)



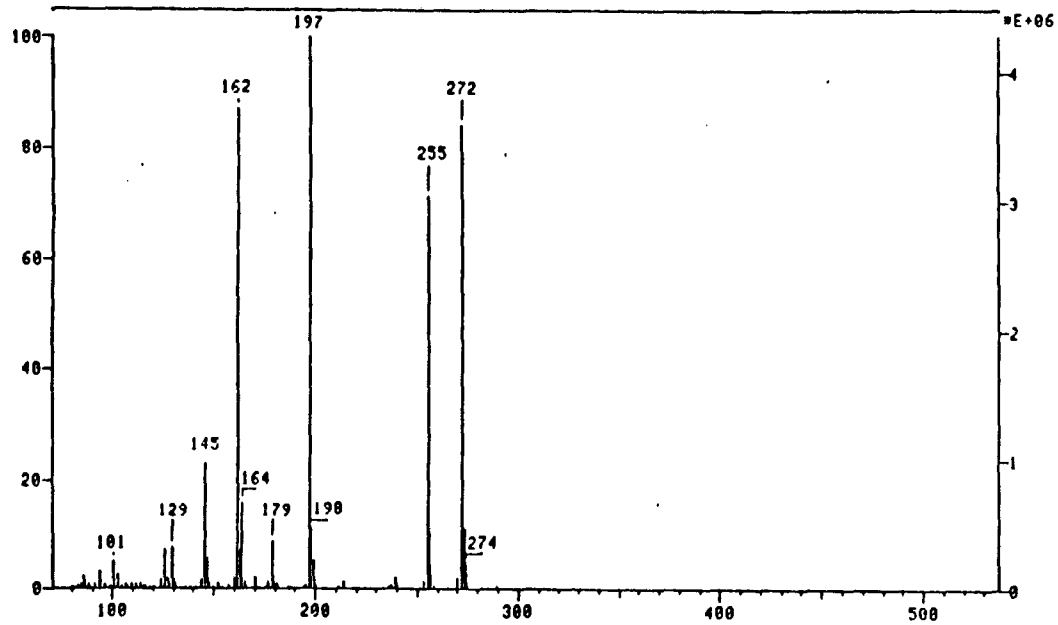

OH
S
O
O

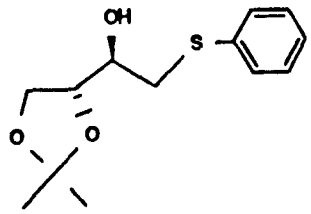
(37)


NMR184010.NDT
38731-182A IN CDCL3 $22
4/22/91
QE300
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
PPM


OH
S
O
O

(37)


197
162
272
255
145
164
129
179
198
101
274
100
80
60
40
20
0
100
200
300
400
500
4
3
2
1
0
*E+06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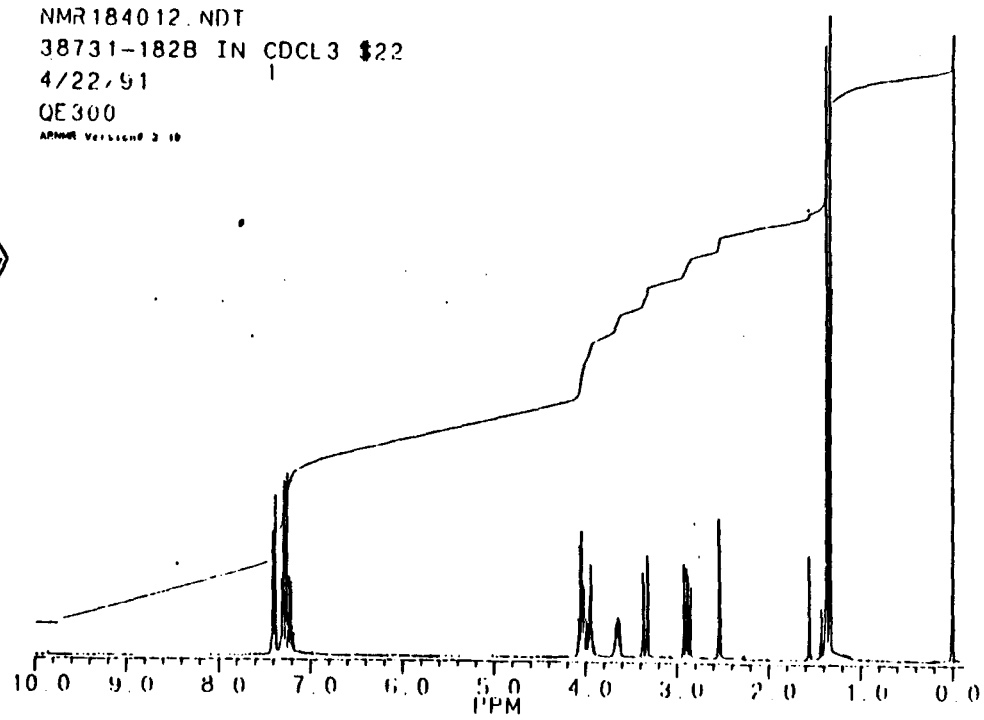
O

(38)


NMR184012.NDT
38731-182B IN CDCL3 $22
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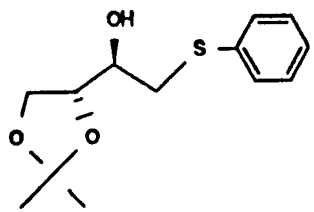
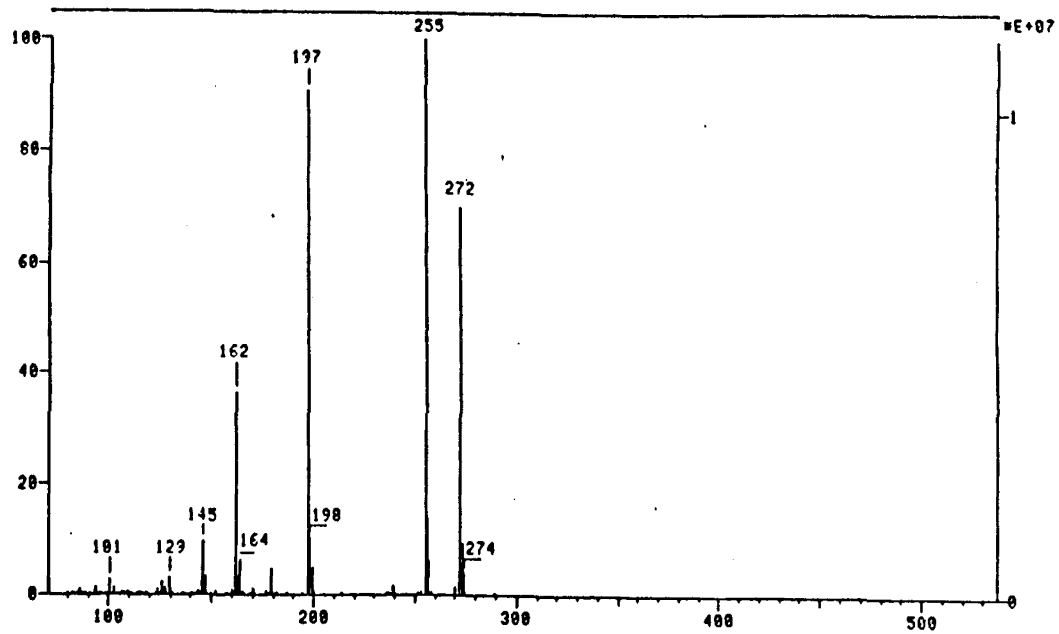
4/22/91
QE300
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
PPM


OH
S
O
O

(38)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164
101
129
274
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60
40
20
0
100
200
300
400
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E+07
1
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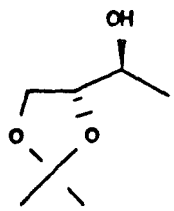
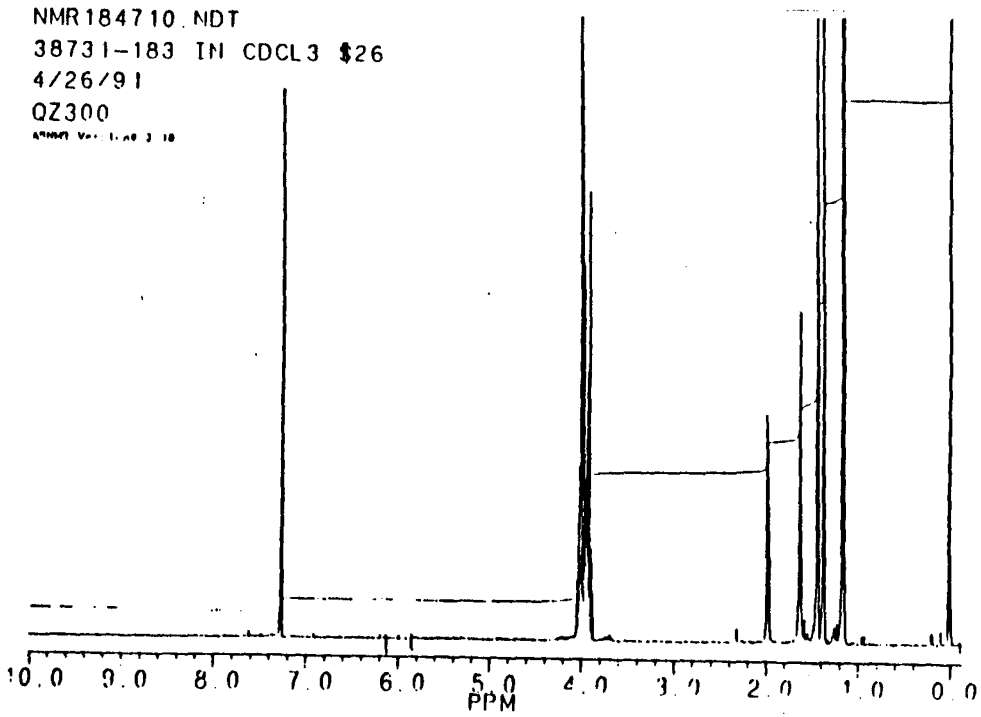

OH
O
O

(39)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38731-183 IN CDCL3 $26
4/26/91
QZ300
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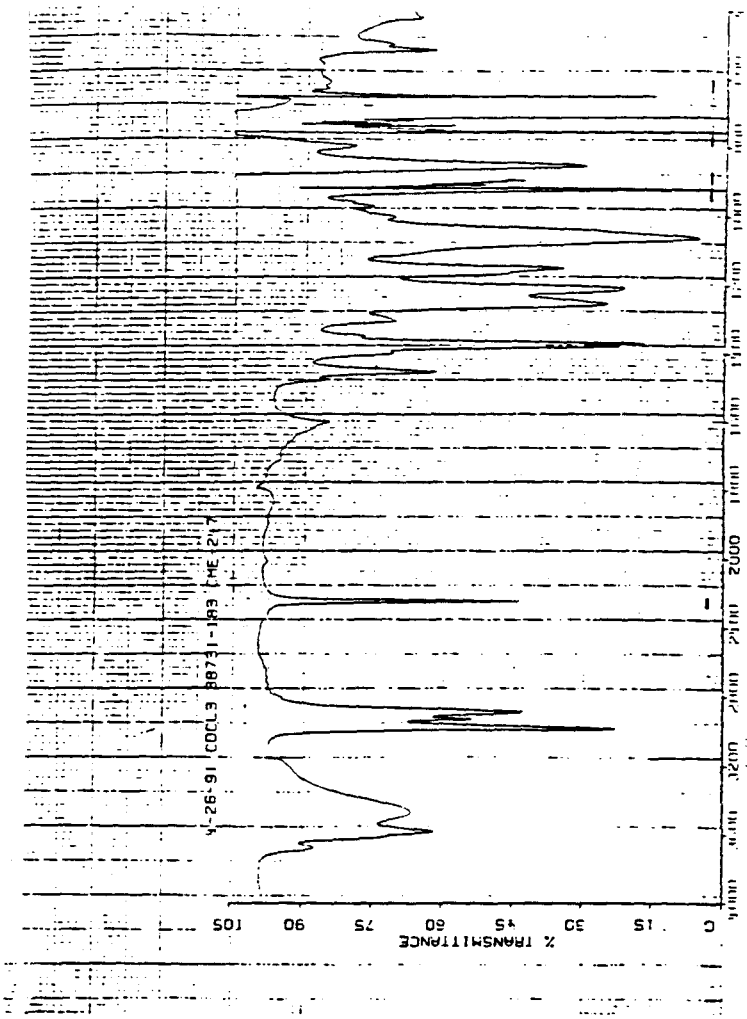
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM


% TRANSMITTANCE
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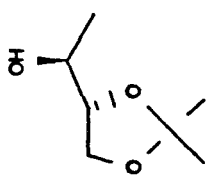
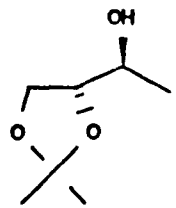
15
30
45
60
75
90
105
4-26-91 CDCL3 8871-183 HE 21.7
2000


OH
O
O

(39)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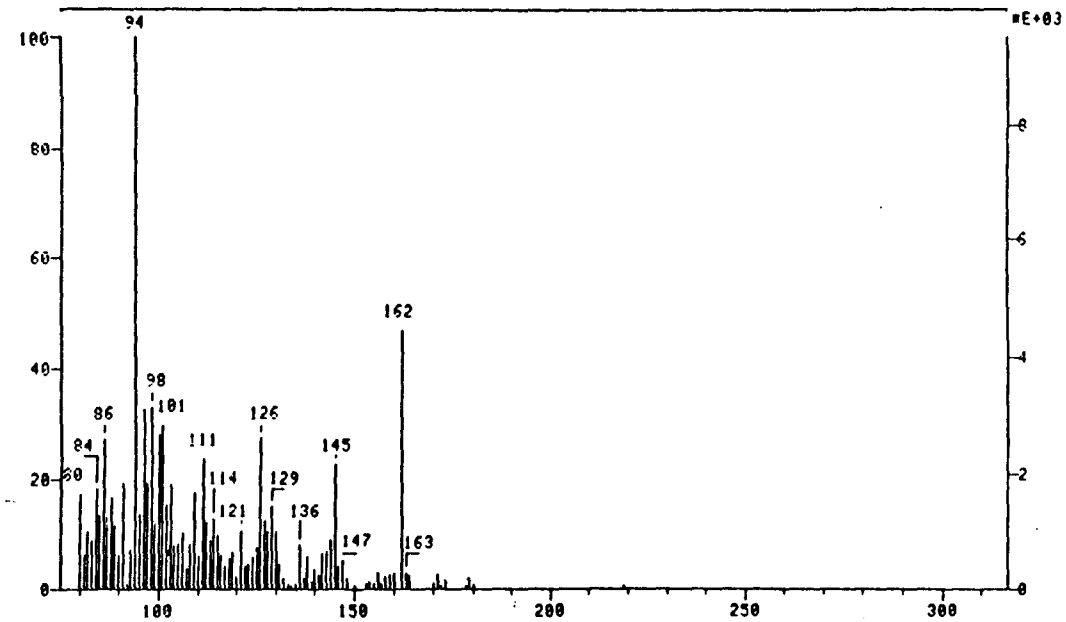
O
O

(39)


94
98
101
86
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80
111
114
121
126
129
136
145
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40
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0
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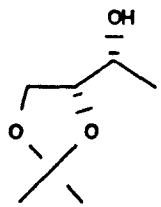
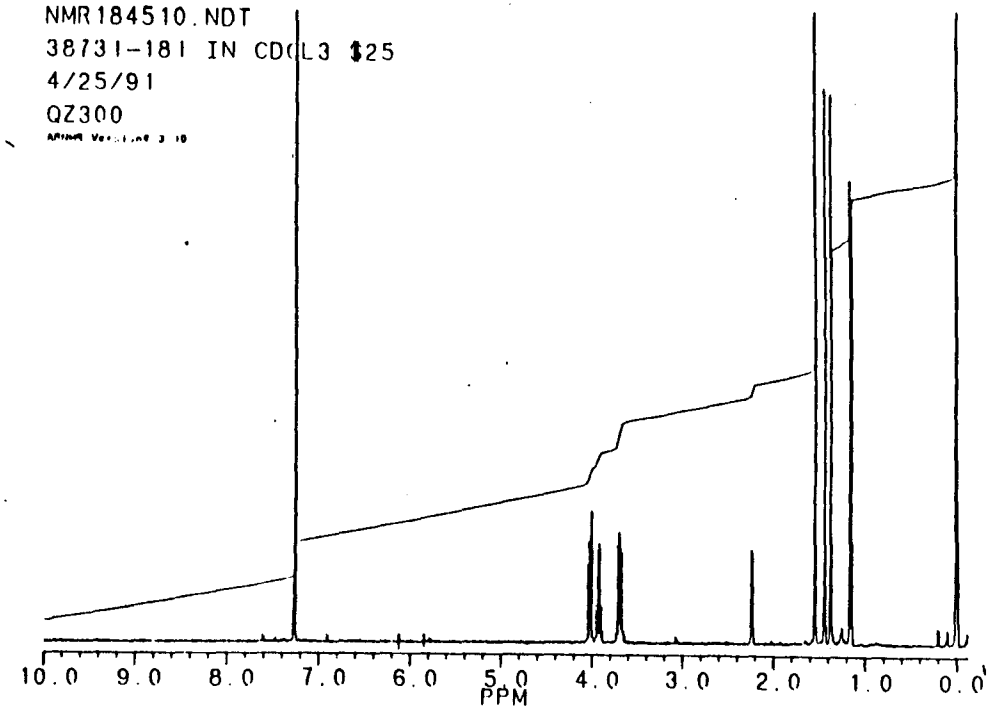
150
200
250
300
E+03
8
6
4
2
0


OH
O
O

(40)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8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

OH
O
O

(40)

4-26-91 COCL3 38731-181 CME-246
% TRANSMITTANCE
0
15
30
45
60
75
90
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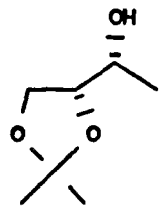
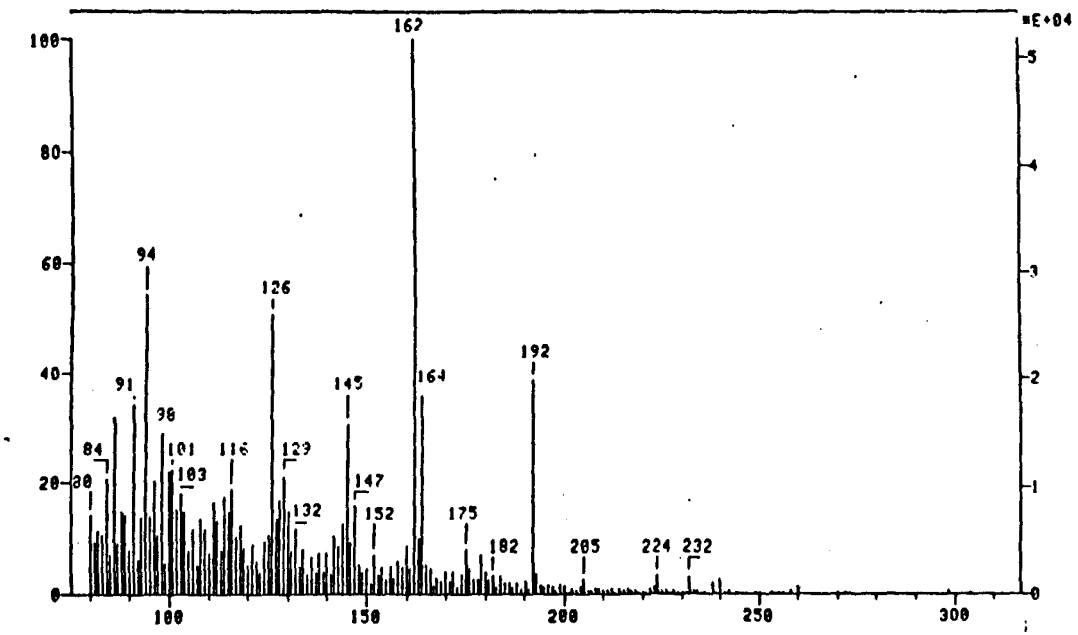
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
WAVENUMBER


OH
O
O

(40)


E+04
100
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60
40
20
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5
4
3
2
1
0
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94
126
192
91
164
145
98
84
101
116
129
103
147
80
132
152
175
182
205
224
232
100
150
200
250
300

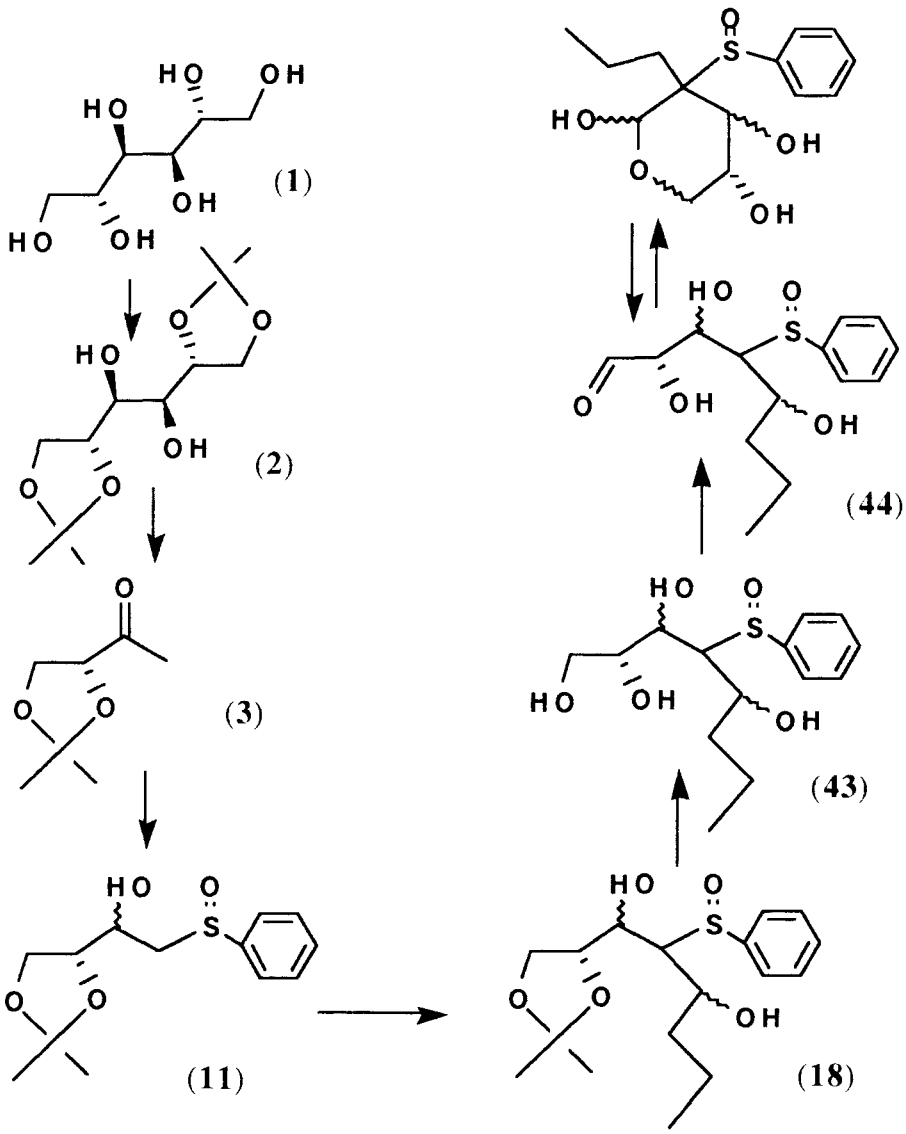
CHAPTER VII

SUMMARY

The objective of this project was to prepare pro-sugar building blocks in a stereoselective synthesis using beta-hydroxy sulfoxide dianions. This goal was realized with the successful preparation of 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-tetrahydroxy-4-phenylsulfinyl hexane (**17**), 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-tetrahydroxy-4-phenylsulfinyl-octane (**18**), 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-(R,S)-tetrahydroxy-4-phenylsulfinyl-6-phenyl hexane (**19**), and 1,2-O-isopropylidene-2-(R)-3-(R,S)-5-tetrahydroxy-4-phenylsulfinyl-5-methyl hexane (**20**). Additionally, we were able to extend dianion chemistry to other structurally related compounds. However, we were unable to prepare the dianion of the beta-hydroxy sulfide (**9**). We also explored the chemistry of the beta-keto phenyl sulfide derivative (**26**) in order to investigate the reactivity of the alpha protons under strongly basic conditions. The stereochemistry at the 2-hydroxy position was assigned for the preparation of 1,2-O-isopropylidene-2-(R)-3-(R,S)-trihydroxy-4-phenylsulfenyl butane (**9**). Finally, we were unable to form an unnatural sugar using an unprotected building block (**18**) in the synthesis.

(**Scheme 26**) We attempted this synthesis only once using a small amount (15 mg) of 75% pure substrate. We are confident that given an adequate supply of pure substrate, further experimentation will give the desired unnatural sugar products.

Scheme 26



CHAPTER VIII

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THESIS/DISSERTATION APPROVAL SHEET

The THESIS submitted by Robert Edwards has been read and approved by the following committee:

Dr. Charles M. Thompson, Director
Associate Professor, Chemistry
Loyola University of Chicago

Dr. Duarte Mota De Freitas
Associate Professor, Chemistry
Loyola University of Chicago

Dr. Ken Olsen
Associate Professor, Chemistry
Loyola University of Chicago

The final copies have been examined by the director of the RESEARCH and the signiture which appears below verifies the fact that any necessary changes have been incorporated and that the Thesis is now given final approval by the Committee with reference to content and form.
The Thesis is, therefore, accepted in partial fulfillment of the requirements for the degree of Masters of Science.

April 20, 1992
Date

Charles M. Thompson
Director's Signature