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Diverse Applications Of Carbohydrate Acids In Organic Synthesis (Polyamides).

Tsu-Hsing Lin
University of Alabama at Birmingham

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Diverse applications of carbohydrate acids in organic synthesis

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The University of Alabama in Birmingham, 1987

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UMI

DIVERSE APPLICATIONS OF CARBOHYDRATE ACIDS IN ORGANIC SYNTHESIS

by

TSU-HSING LIN

A DISSERTATION

Submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Chemistry in the Graduate School, The University of Alabama at Birmingham

BIRMINGHAM, ALABAMA

1987

ABSTRACT OF DISSERTATION
GRADUATE SCHOOL, UNIVERSITY OF ALABAMA AT BIRMINGHAM

Degree Ph.D. Major Subject Chemistry

Name of Candidate Tsu-Hsing Lin

Title Diverse Applications of Carbohydrate Acids in Organic Synthesis

This dissertation is concerned with the use of carbohydrates in novel synthetic procedures. The research is presented in three parts: (I) aldonic acids are employed for the preparation of "glycamines," (II) uronic aicds are converted to ε-lactams and unsaturated products thereof, and (III) aldaric acids are monomer precursors for new acyclic polymers.

(I) A new synthetic route to the synthesis of glycamines was developed. The synthesis began with the electrolytic oxidation of aldoses to aldonic acids, which were then esterified to mixtures of esters and lactones. The latter mixtures were then subjected to ammonolysis yielding aldonamides, which were trimethylsilylated with a standard reagent. Trimethylsilyl (TMS) groups were selectively removed from the amide nitrogens by methanolysis to give per-O-TMS aldonamides, which were reduced with borane-THF. Residual borate and TMS groups were removed with methanolic HCl to give the glycamines as their hydrochlorides. Five glycamines were synthesized by this method: 1-amino-1-deoxyglucitol, -galactitol, -mannitol, -ribitol, and -xylitol.

(II) A broad interest in this laboratory is the study of difunctional compounds synthesized from carbohydrates. As part of this study, we undertook the synthesis of two ε-lactams; ε-L-gulonolactam and ε-L-galactonolactam and their corresponding tetra-O-acetyl and tetra-O-TMS derivatives from D-glucurono-6,3-lactone and D-galacturonic acid, respectively. The synthesis of the two lactams was based on a procedure of Weidmann and Fauland (Ann. Chem., 679, 192 [1964]). An improved synthesis of ε-L-gulonolactam and the first synthesis of ε-L-galactonolactam was sucessfully completed. The lactam tetraacetates were considered as potential starting molecules for an unusual aromatic heterocyclic system, an azatropolone.

(III) The primary objective of this research was to develop methods for the synthesis of polyhydroxypolyamides from carbohydrate precursors. Two general methods for polymerization were investigated: (1) ring-opening polymerization of TMS hydroxyl protected ε-lactams derived from uronic acids and (2) condensation polymerization of esterified aldaric acids with diamines.

Abstract Approved by: Committee Chairman _____

Program Director _____

Date 8/27/87 Dean of Graduate School _____

DEDICATION

I Dedicate this work to

my loving wife, Sue-Yuan, and

my lovely daughter, Pei-Hsin.

ACKNOWLEDGMENTS

I express my deepest thanks to my parents, Mr. Tsan-Don Lin and Mrs. Yuh-Bor Lin, who support me in every way, with encouragement and great love. I also express my thanks to my guide and teacher, Professor Donald E. Kiely for the professional and personal directions he has given me during the years. I am very proud to consider him my teacher and good friend. I thank all the members of my graduate committee, Drs. Charles Watkins, Jack Lemons, Wayne Brouillette, and Professor Fred Benington for their direction, understanding and guidance during my graduate career, and especially Dr. Watkins for the NMR simulation experiment. Special regards to the late Dr. Thomas St. Pierre, for his special guidance and friendship. I also thank Mr. Ken Hope for his help in 300 MHz NMR work and the patience to teach me the operation. I also thank Mr. Fred Fish for the mass spectra data included in this dissertation. Finally, I would also like to thank the Graduate School and the Department of Chemistry at the University of Alabama at Birmingham for the financial support during my study.

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LIST OF ABBREVIATIONS

^{13}C NMR	Carbon-13 Nuclear Magnetic Resonance
d	doublet
DMSO	Dimethyl Sulfoxide
Dp	Degree of Polymerization
GC	Gas Chromatography
^{1}H NMR	Proton Nuclear Magnetic Resonance
HMDS	Hexamethyldisilazane
IR	Infrared Spectrum
m	multiplet
mp	Melting Point
MS	Mass Spectrum
s	singlet
t	triplet
THF	Tetrahydrofuran
TMCS	Trimethylchlorosilane
UV	Ultraviolet Spectrum

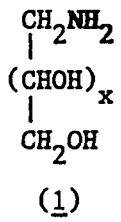
The nomenclature used in this dissertation is based on standard IUPAC conventions. For convenience, compound trivial names are sometimes used in place of systematic names.

INTRODUCTION

Part I: "Synthesis of 1-Amino-1-deoxyalditols from Aldonic Acids"

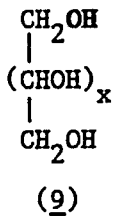
This research was done as an extension of the general synthetic method developed in our laboratory for the preparation of terminal diaminodideoxyalditols, employing trimethylsilyl protecting groups.[1-4]

Glycamines (1), 1-amino-1-deoxy derivatives of alditols (9), are compounds in which the hydroxyl group on carbon 1 of an alditol has been replaced by an NH_2 group.



(1)

Glycamines



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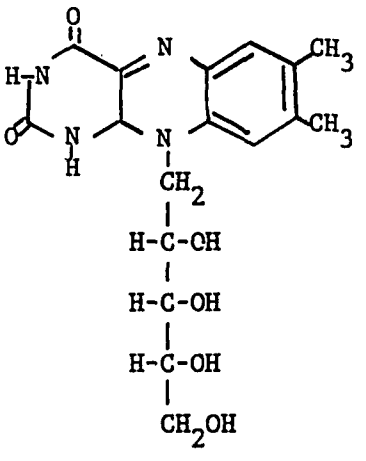
Alditols

Although amino sugars are found in abundance throughout the plant and animal kingdoms, 1-amino-1-deoxyalditols, or glycamines, are rare as natural products. Riboflavin (vitamine B_2) (10), however, can be regarded as a derivative of 1-amino-1-deoxy-D-ribitol (D-ribamine) (11).[5]

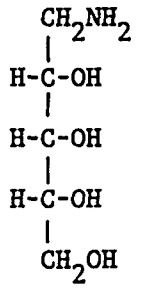
Synthetically prepared glycamines and their derivatives have been used in a number of applications: riboflavin analogues derived from D-glucamine, D-xylamine, D-arabinamine, and D-mannamine[6] have been tested as anti-cancer agents; N-methyl-D-glucamine has been used pharmaceutically in converting sparingly soluble products into forms

possessing better solubility;[7] 1-acrylamido-1-deoxy-D-glucitol and 1-deoxy-1-methacrylamido-D-glucitol derived from 1-amino-1-deoxy-D-glucitol (D-glucamine) have been polymerized.[8]



(10)

Riboflavin (Vitamine B_2)



(11)

D-Ribamine

The glycamines can be synthesized in a number of ways including reductive amination employing high pressure hydrogenation of aldoses in the presence of ammonia over Raney nickel catalyst (Scheme 1).[9] Due to the considerable number of side reactions that can occur using this method, the products are generally impure but can be purified through their salicylidene derivatives (Scheme 2).[9]

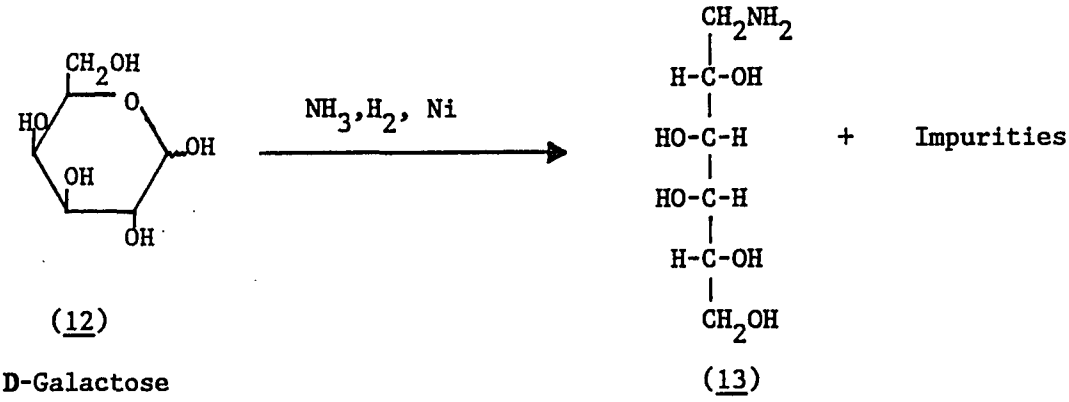
A modification of this reductive amination procedure uses benzylamine rather than ammonia in the reaction mixture[9] to afford the N-benzylglycamine subtantially free of impurities (Scheme 3), e.g. 16 by way of the glycosylamine 15. The benzylglycamine can be converted to the glycamine by catalytic hydrogenation over palladium catalyst. Two other modifications of the reductive amination method are the hydrogenation of aldoses in the presence of hydrazine[10] and the

reductive cleavage of aldose phenylhydrazones and oximes (Scheme 4),[11] the latter being a convenient laboratory procedure.

Additional methods of glycamine preparation are: (a) catalytic reduction of 1-deoxy-1-nitroalditols (Scheme 5),[12,13] (b) the reduction of 1-alkylamino or 1-arylamino ketones formed in the Amadori rearrangement (Scheme 6),[14] and (c) the reduction of protected D-gluconamide with lithium aluminum hydride (Scheme 7).[15]

This research sought to establish another synthetic route to glycamines, a method based on BH_3-THF reduction of per-O-TMS aldonamides. The latter compounds are readily available from the corresponding aldonic acids (Scheme 8).

Scheme 1

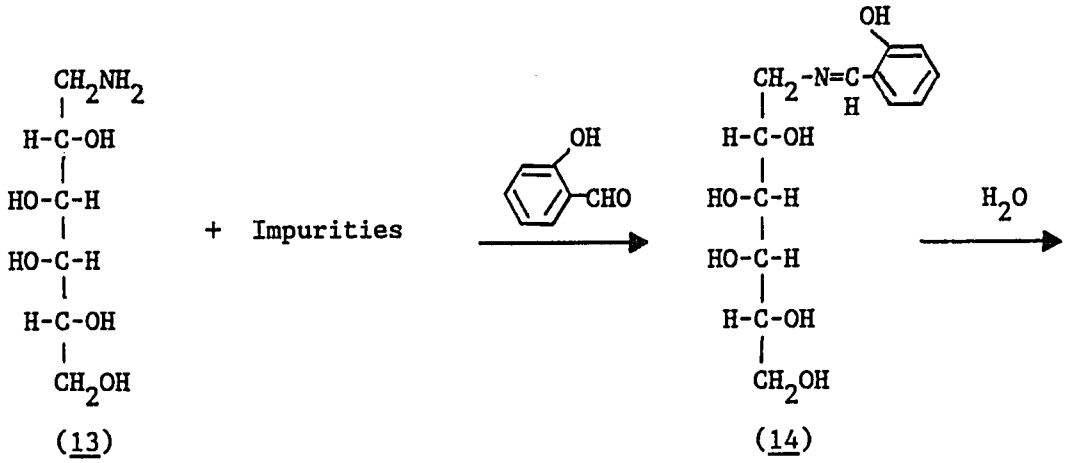


(12)

D-Galactose

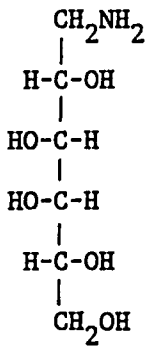
(13)

Scheme 2



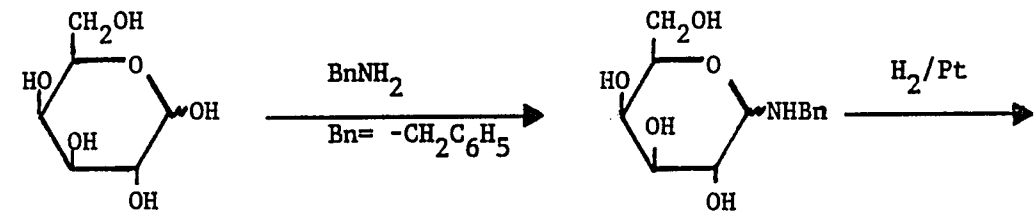
(13)

(14)



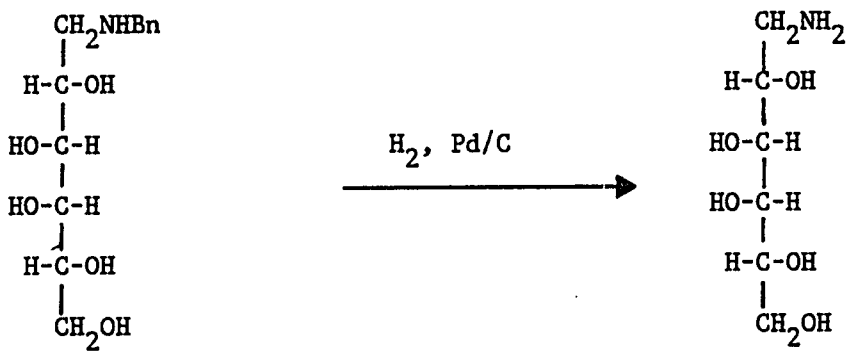
(13)

Scheme 3



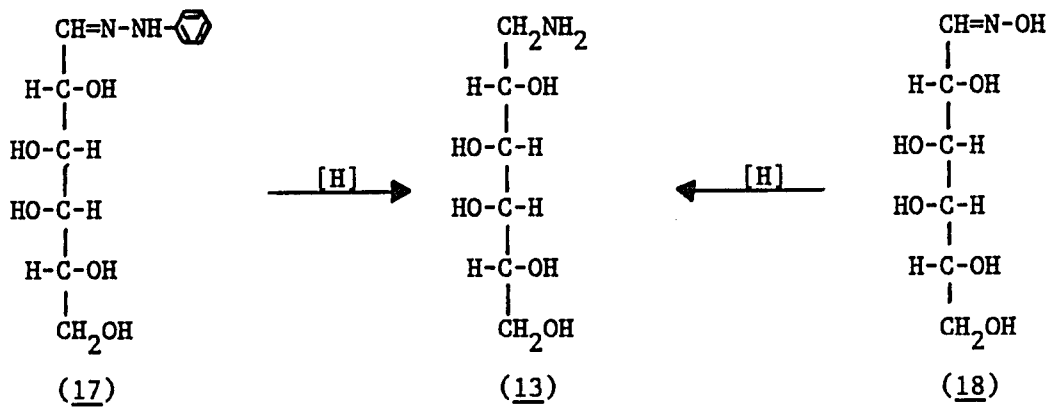
(12)
D-Galactose

(15) Bn= $-CH_2C_6H_5$



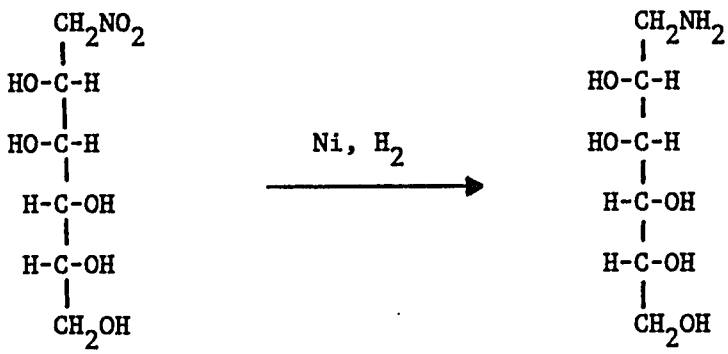
(16) (13)

Scheme 4



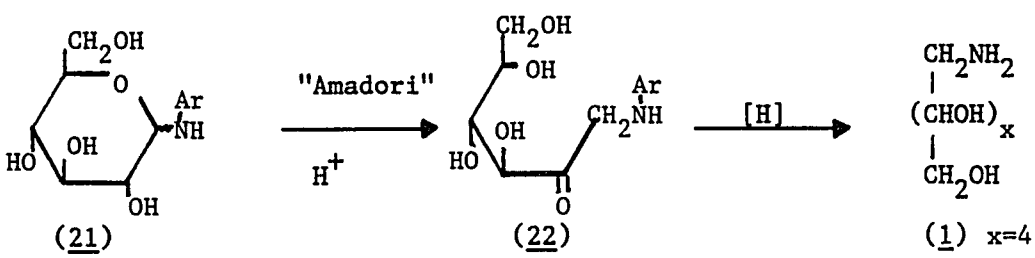
(17) (13) (18)

Scheme 5



(19) (20)

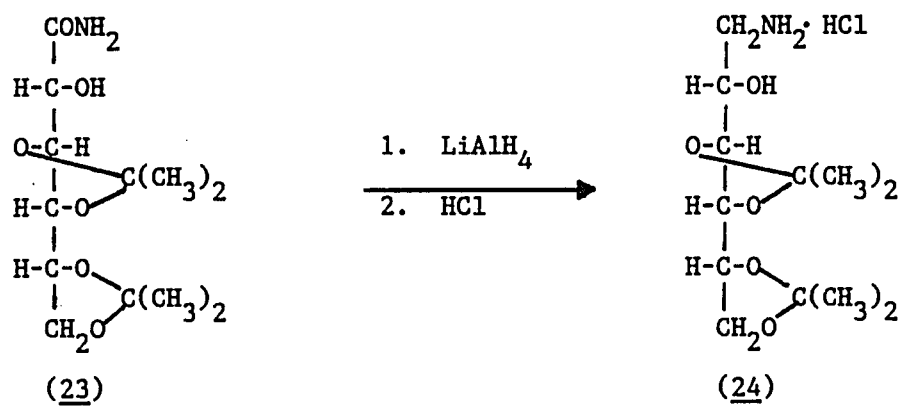
Scheme 6



(21) (22) (1) x=4

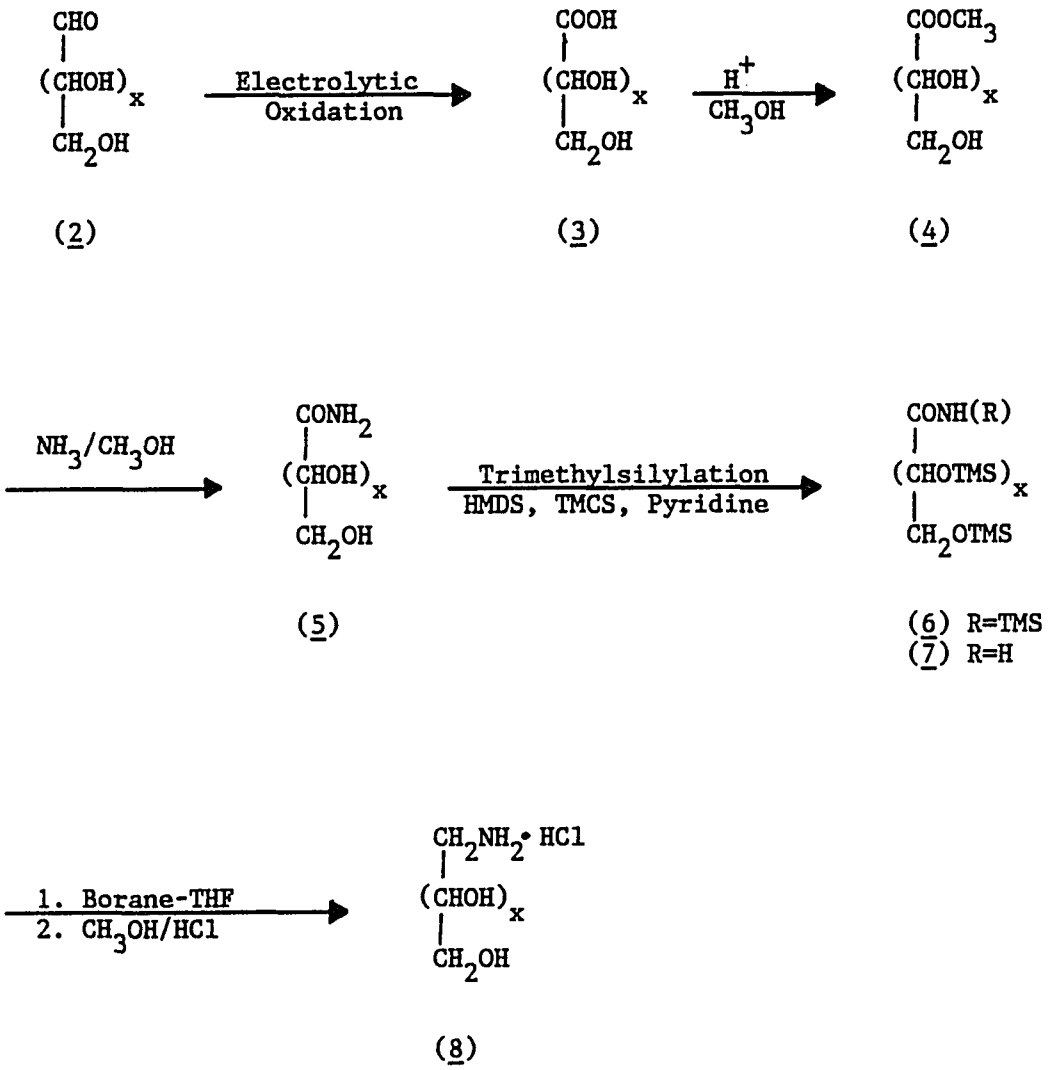
glycosylamine 1-amino-1-deoxy-2-ketose glycamines

Scheme 7



(23) (24)

Scheme 8



RESULTS AND DISCUSSION

Part I: "Synthesis of 1-Amino-1-deoxyalditols from Aldonic Acids"

Synthesis of the 1-amino-1-deoxyalditols (glycamines) originated from the aldoses (Figure 1). Aldonic acids, isolated as their calcium salts, were prepared electrolytically as described by Frush and Isbell.[16] Filtering the reaction mixture and concentrating the aqueous filtrate gave calcium aldonate as a syrup which sometimes crystallized on standing at room temperature overnight. For those salts that did not crystallize, the addition of methanol to the syrup and stirring the resultant mixture at room temperature gave the solid product, which was then washed with deionized water and dried. Acidification of the calcium aldonates was accomplished by passing 0.06-0.10 moles of the salts in 250-300 mL of deionized water through a column containing 250 mL of Amberlite IR-120 (H^+) resin. The effluent was passed through the column twice more to ensure good exchange. After solvent removal, the crude acid/lactone was used directly in the esterification step.

The acids were then esterified with methanolic HCl to yield crude methyl esters. Decolorization of the syrup in methanol with activated charcoal was commonly carried out at this stage. The crystalline aldonamides were prepared by ammonolysis of the crude esterification products in methanol solution saturated with ammonia. Ammonia gas was bubbled through the solution during the reaction time. The

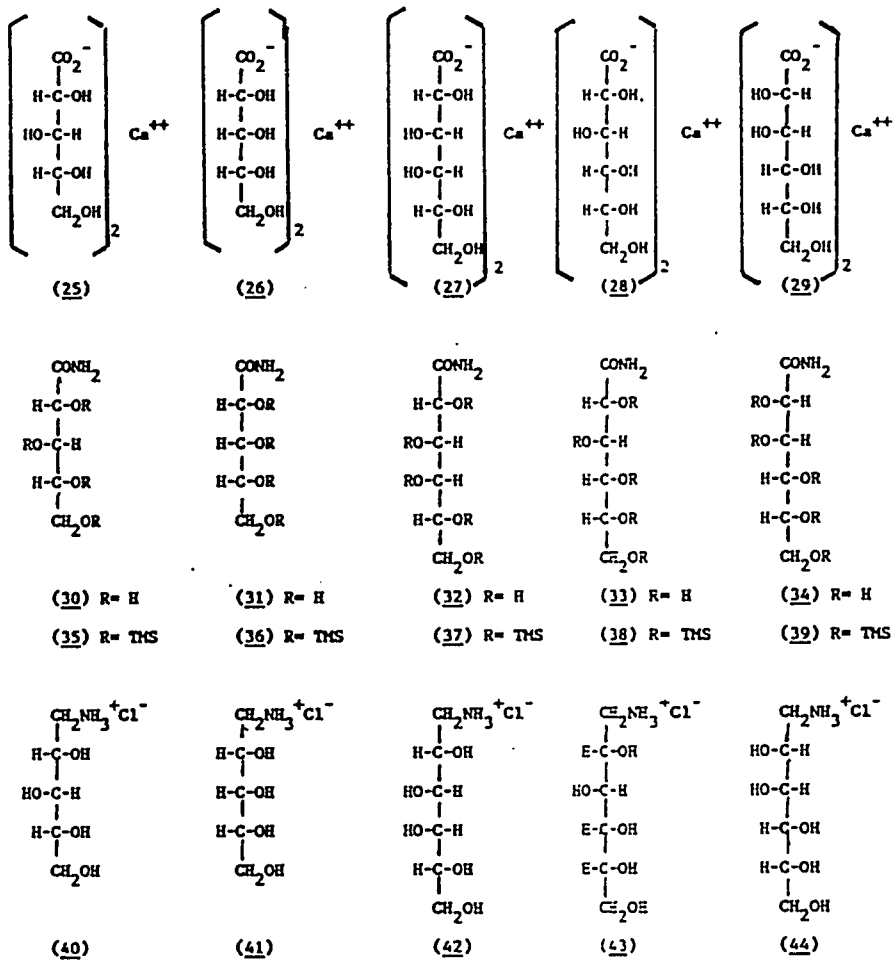


Figure 1. Synthesized 1-Amino-1-deoxyalditol Hydrochlorides and Precursors.

pertrimethylsilylation of the aldonamides was done at room temperature with trimethylchlorosilane (TMCS) and hexamethyldisilazane (HMDS) in pyridine.[17,18] Attempts at reducing the silylated products with borane-THF, followed by methanolic HCl workup and deprotection, gave only the starting aldonamides. These results suggested that the terminal amido TMS groups on the aldonamides were sterically preventing reduction from occurring. Because amido TMS groups are known to be easily deprotected by alcohols,[19,20] a method was then developed to remove the TMS group from the nitrogen of these trimethylsilylated aldonamides while retaining the O-TMS groups. This method involved dissolving the silylated aldonamide in chloroform-d, to which was added a drop of methanol-d_4 containing a trace of water to exchange the acidic deuterium in methanol-d_4 for a proton. This deprotection was carried out for the crude silylation product of aldonamides, and the reaction was monitored by 90 MHz NMR. The spectrum at t=0 is that of a crude product prior to deprotection of pertrimethylsilylated aldonamide. Generally, the spectrum of the crude pertrimethylsilylated aldonamides initially contained several N-H peaks, but deprotection for 12 hours generated a spectrum with the two broad signals characteristic of a primary amide. Typical deprotection monitoring experiments are shown in Figures 2, 3, and 4.

The selective amide deprotection of the pertrimethylsilylated aldonamides was readily scaled up for preparative purpose, with dichloromethane containing a small amount of methanol substituted for the deuterated solvents. The O-TMS aldonamides were then reduced with borane-THF. The glassware assembly for the generation of diborane was patterned after that described by Brown,[21] although Brown's

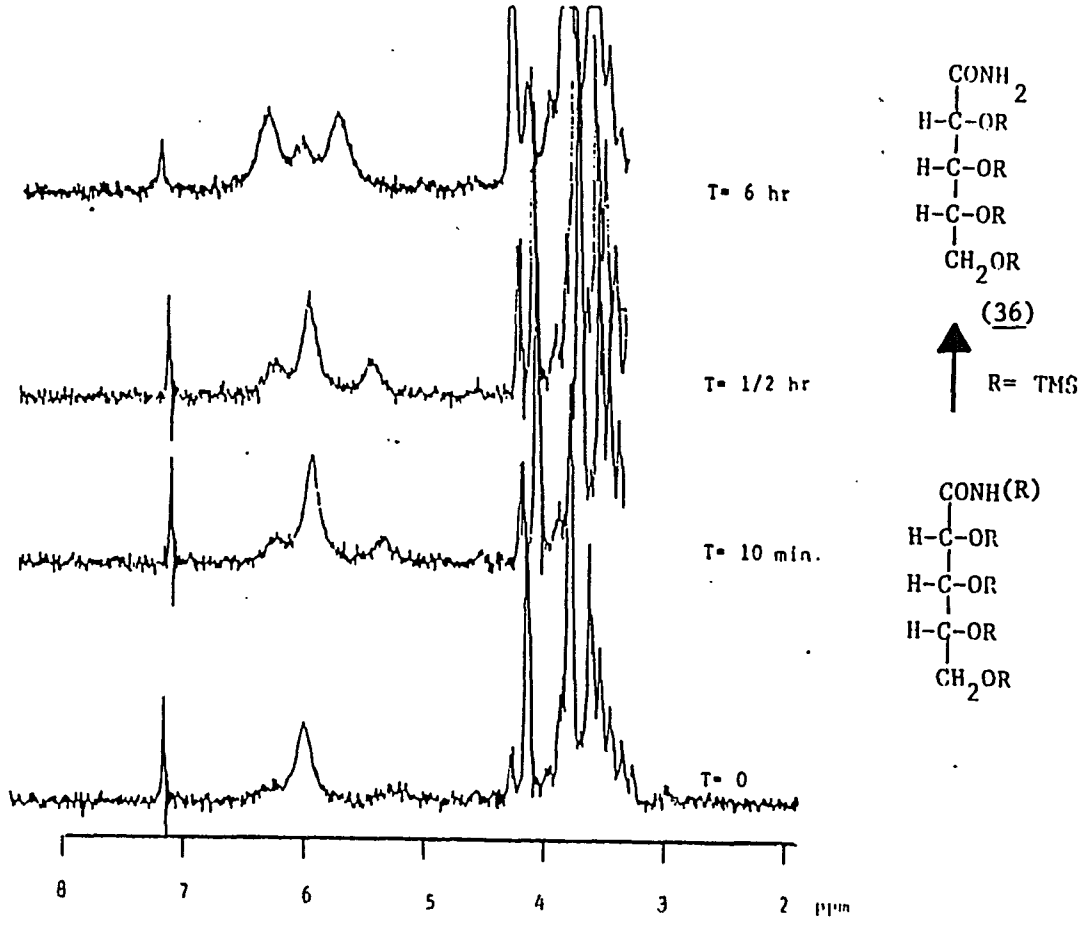


Figure 2. Selective Removal of the Amide TMS Group to Give Compound 36 ($CDCl_3$) as Observed by ^1H NMR Spectra Changes.

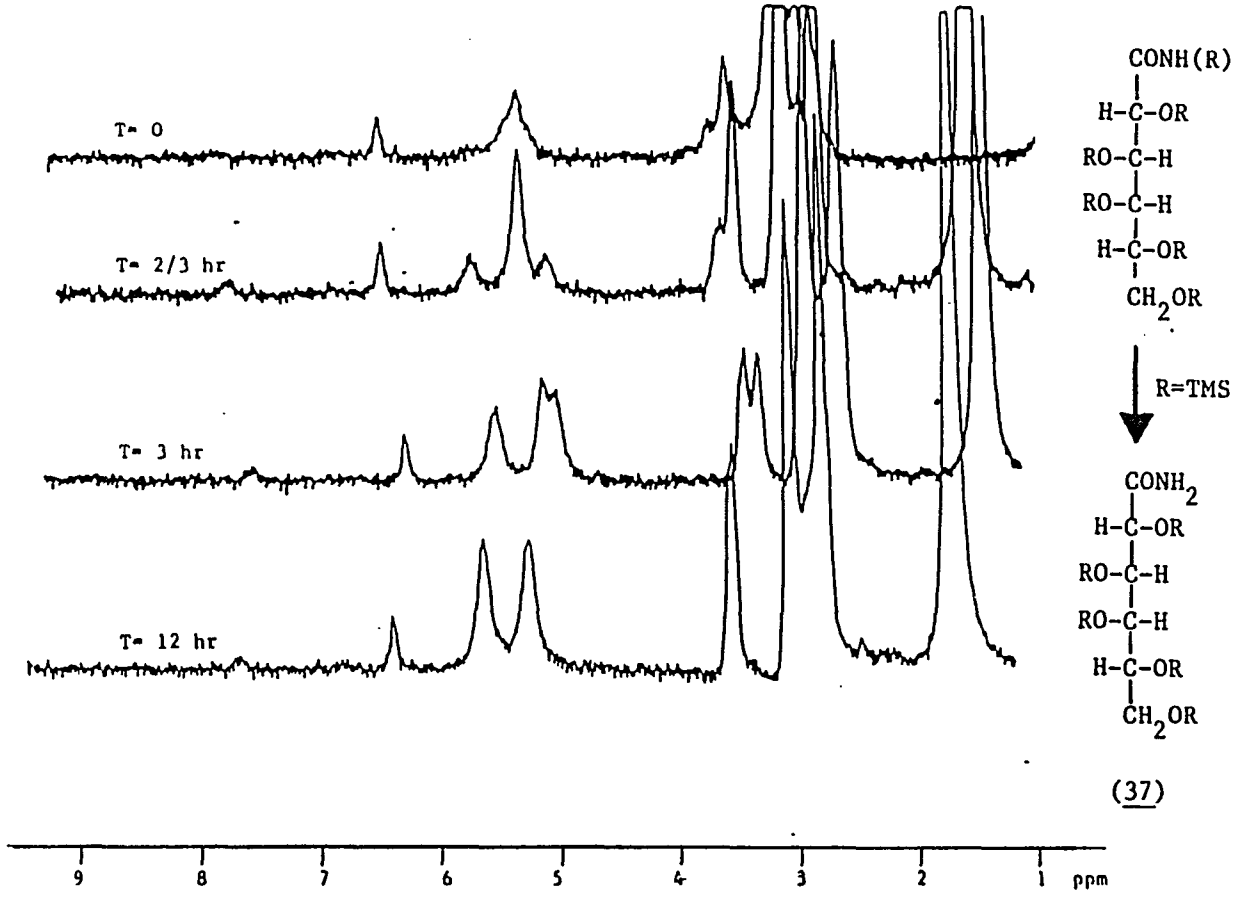


Figure 3. Selective Removal of the Amide TMS Group to Give Compound 37 ($CDCl_3$) as Observed by ^1H NMR Spectra Changes.

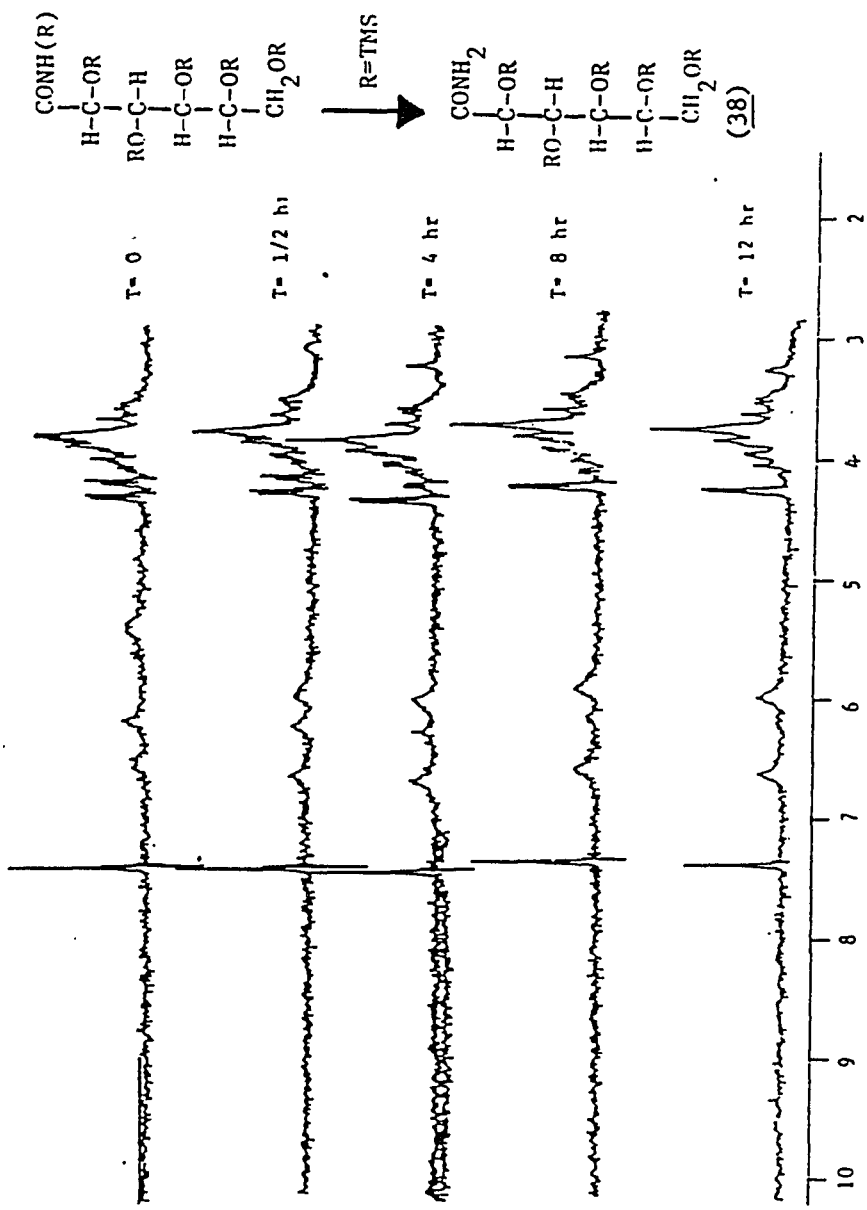


Figure 4. Selective Removal of the Amide TMS Group to Give Compound 38 ($CDCl_3$) as Observed by ^1H NMR Spectra Changes.

procedure employed BF_3 etherate and sodium borohydride to generate diborane. Although borane-THF is commercially available, the best results were achieved using reagent freshly prepared from iodine and sodium borohydride. Glycamines were isolated as their hydrochloride salts, with isolated yields ranging from 49% for 1-amino-1-deoxy-D-ribitol hydrochloride (41) to 92% for 1-amino-1-deoxy-D-galactitol hydrochloride (42) from the corresponding per-O-trimethylsilylaldonamides (Table 1).

Reduction of O-Trimethylsilylated Aldonamides with Externally Generated Diborane.

The reduction of the O-trimethylsilylated amides was carried out with borane-THF[22-24] generated externally by the reduction of iodine with sodium borohydride in THF as follows.

$$2\ NaBH_4 + I_2 \longrightarrow 2\ NaI + 2\ BH_3 + H_2$$

The assembly for borane production is that of Navia's[1] and is shown in Figure 5. This method was chosen in preference to the use of commercial borane-THF solution because the commercial borane-THF solution decomposed on storage in the refrigerator after the Sure/Seal cap had been punctured by a syringe needle. This problem can be eliminated when the commercial reagent is not stored for more than three weeks after the seal is broken. The borane-THF solutions prepared in this manner are on the order of 1 M solutions of borane in THF. An approximately five-fold excess of BH_3 was used in each reduction.

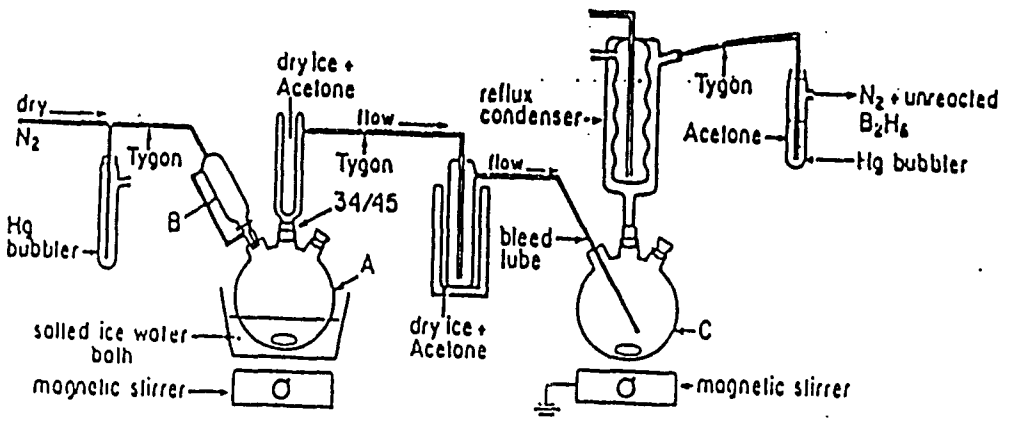


Figure 5. Equipment Assembly to Generate B_2H_6 for Borane Reduction of Amides. (A, C are 1-Liter 3-neck round-bottomed flasks; B is a side-arm addition funnel).

SUMMARY AND CONCLUSIONS

Part I: "Synthesis of 1-Amino-1-deoxyalditols from Aldonic Acids"

A number of general synthetic approaches to 1-amino-1-deoxyalditols (glycamines) have been reported which employed the reduction of a nitrogenous carbohydrate precursor. In this research, a new synthetic route to glycamines was undertaken based on reduction of aldonamides. Aldonic acids, isolated as their calcium salts, were conveniently prepared by electrolytic oxidation of aldoses. The aldonic acid/aldonolactones, prepared by acidification of the corresponding calcium aldonates, were esterified with methanolic HCl, and the crude esterification products were treated with methanolic ammonia to give the crystalline aldonamides. Pertrimethylsilylation of the aldonamides followed by amide TMS deprotection, gave the O-(trimethylsilyl)-aldonamides, which were then reduced by BH_3-THF. Methanolic HCl workup and deprotection yielded the 1-amino-1-deoxyalditol hydrochlorides.

The glycamines prepared by this series of reactions were (1) 1-amino-1-deoxy-D-xylitol (xylamine), (2) 1-amino-1-deoxy-D-ribitol (ribamine), (3) 1-amino-1-deoxy-D-glucitol (glucamine), (4) 1-amino-1-deoxy-D-galactitol (galactamine), and (5) 1-amino-1-deoxy-D-mannitol (mannamine).

SUGGESTIONS FOR FURTHER RESEARCH

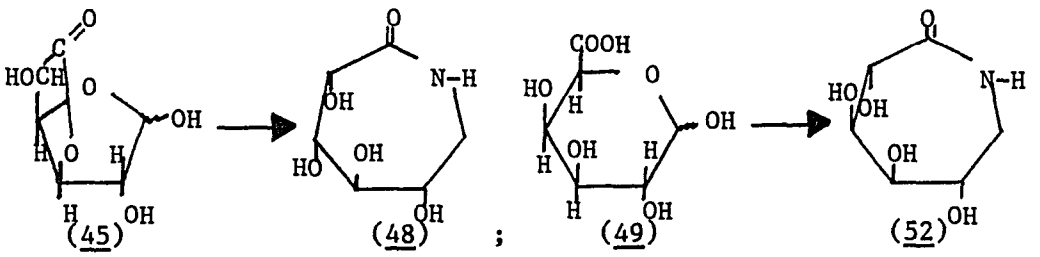
Part I: "Synthesis of 1-Amino-1-deoxyalditols from Aldonic Acids"

Borane-THF has been proved to be a useful reagent for reduction of O-TMS-aldonamides. The reduction procedure was previously employed by Navia[1] to prepare terminal diaminoaididеoxyalditols. It should be possible to use the same reduction methodology to reduce N-alkyl carbohydrate amides, but without hydroxyl protection, to N-alkyl carbohydrate amines since the presence of alkyl group(s) on the amido nitrogen(s) would increase the solubility of the N-alkyl carbohydrate amides in the moderately polar THF. Such carbohydrate secondary amines may be of interest because of their potential liquid crystal and/or surfactant properties.

INTRODUCTION

Part II: "Synthesis and Some Chemistry of Seven-membered Lactams Derived from Carbohydrates"

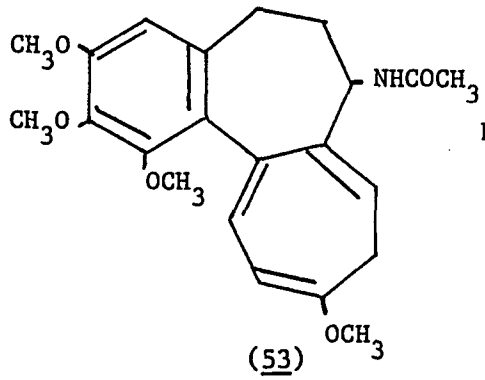
A broad interest of this laboratory is the study of difunctional compounds synthesized from carbohydrates. As part of this study, the synthesis of two seven-membered lactams was undertaken: ε-L-gulonolactam (48), and ε-L-galactonolactam (52), from D-glucurono-6,3-lactone (45) and D-galacturonic acid (49) respectively.



(45) (48) ; (49) (52)

These lactams were envisioned as potential precursors for two very different synthetic objectives: (1) the synthesis of azatropolones (e.g. 57) and (2) the preparation of polyhydroxy nylon-6. The first objective, the synthesis of azatropolones, is the theme of this part of the dissertation.

Frequent medical, chemical, and botanical references have marked the long history of the active ingredient of the plant, Colchicum Autumnal L. (Liliaceae).[25] The most common active principle, Chochicine (53), has been used for a long time in the treatment and diagnosis of gout. Although colchicine is remarkably effective, the mechanism of its action is still uncertain.



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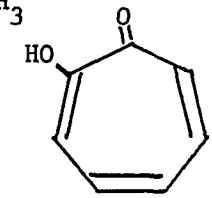

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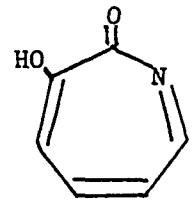
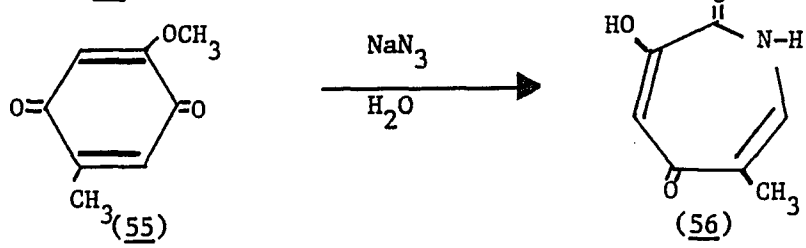


(57)

Colchicine Tropolone 3-Azatropolone

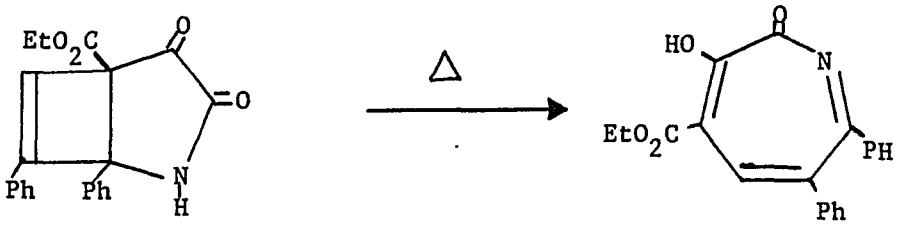
The name colchicine is derived from an area near the Black Sea (Colchis). Colchicum species are common throughout Europe and the middle east. A major structural component of colchicine is **tropolone** (54), a seven-membered ring with 6π electrons, pseuaromatic compound.

Given that the lactams 48 and 52 are seven-membered ring systems, we considered them potential precursors for nitrogen analogs of tropolone, namely azatropolones. Examples of azatropolone ring systems have been reported. Hughes and co-workers prepared the azatropolone derivative 56 by the Schmidt reaction between 2-methoxy-5-methylbenzoquinone (55) and sodium azide.[26]



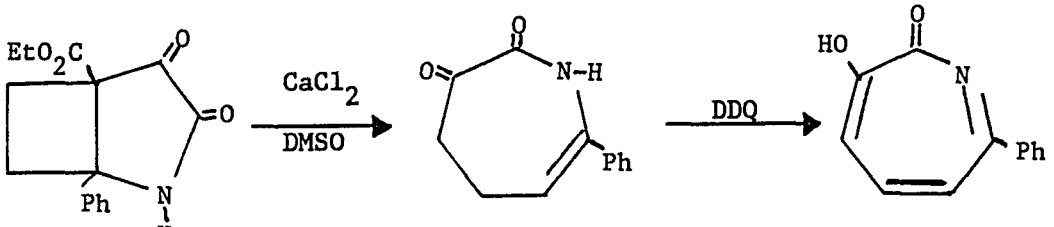
(55) (56)

Sano and co-workers,[27] using a different approach, prepared sevveral 3-azatropolone derivatives (e.g., 59) by ring opening of 2-azabicyclo[3.2.0]heptan-6-one derivatives (e.g. 58).



(58) (59)

An alternate synthesis of the 3-azatropolone system by Sano[28] et al. was by oxidation (DDQ, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone) of the dihydroazatropolones (61) formed from ring opening and de-ethoxycarbonylation of 60.



(60) (61) (62)

Our approach to the synthesis of azatropolones is based on base-initiated β-eliminations of acetic acid from the lactam tetraacetates 63 and 64, respectively. It was envisioned that under appropriate basic conditions a series of eliminations from these acetates (e.g., 63) might be effected leading to the O-acetylazatropolone (Figure 6).

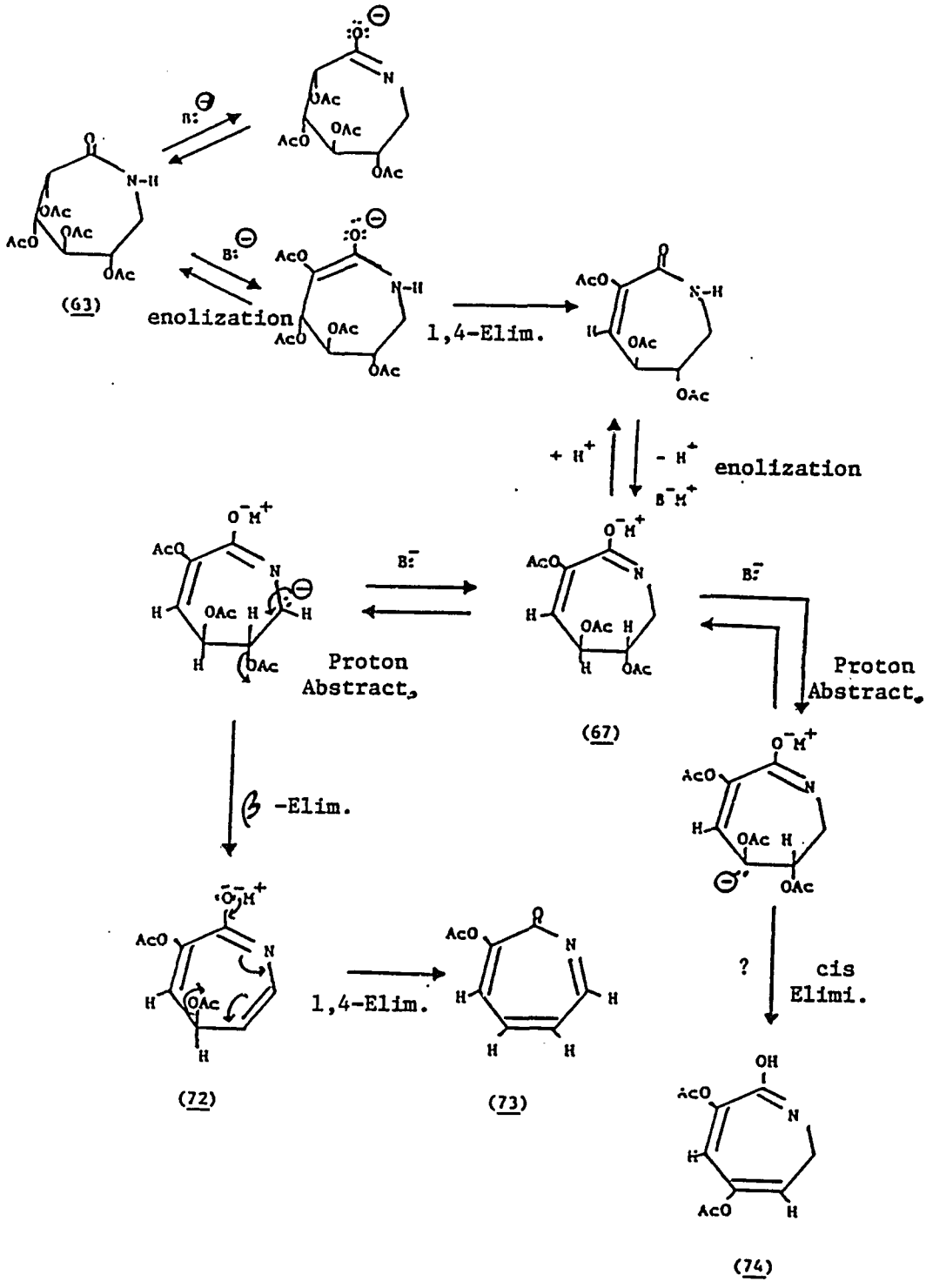


Figure 6. Hypothetical Mechanistic Scheme for the Conversion of 63 to the Azatropolone 73.

RESULTS AND DISCUSSION

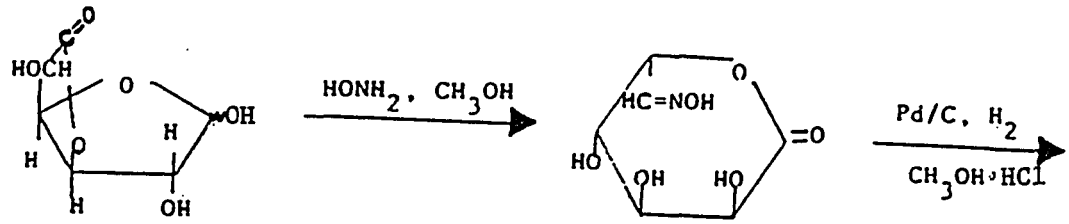
Part II: "Synthesis and Some Chemistry of Seven-membered Lactams Derived from Carbohydrates"

The initial synthetic objective of this project was the synthesis of two seven-membered sugar lactams, ε-L-gulonolactam (48) and ε-L-galactonolactam (52) from D-glucurono-6,3-lactone (45) and D-galacturonic acid monohydrate (49), respectively. The two seven-membered sugar lactams 48 and 52 were prepared by a procedure based on that of Weidmann and Fauland (Schemes 9 & 10).[29] The strategy involved three steps: (1) preparation of 1-oximidouronic acids, (2) reduction of the latter compounds to the corresponding 6-amino-6-deoxy-L-aldonic acids, and (3) cyclization of these amino acids to the lactams.

Oximation of the Uronic Acids.

The oximation of D-glucurono-6,3-lactone (45) and D-galacturonic acid monohydrate (49) were carried out in a slightly acidic methanol solution of hydroxylamine. The oxime from D-glucurono-6,3-lactone (45) crystallized directly from the reaction mixture, mp 147-155 °C (lit.[29] 143 °C), in 87% yield. The infrared (IR) spectrum of the oximation product 46 contained strong absorption peaks at 3300 cm^{-1} (OH) and 1735 cm^{-1} (lactone C=O). The -C=N- oxime stretching frequency, which is normally a weak band in the 1650-1685 cm^{-1} region,[30] was obscured by the broad carbonyl absorption. The result of the elemental analysis of this product indicated the molecular formula, $C_6H_9NO_6$, a molecular formula consistent with an oxime of the lactone form of the

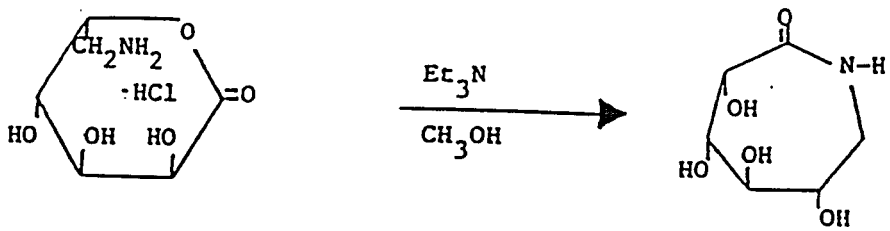
Scheme 9



(45)

(46)

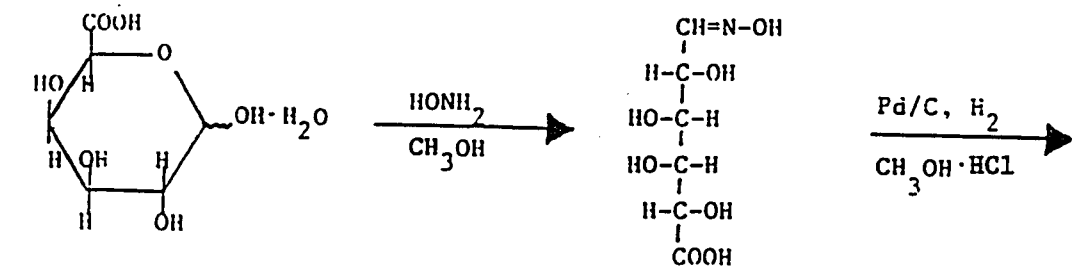
D-Glucurono-6,3-lactone



(47)

(48)

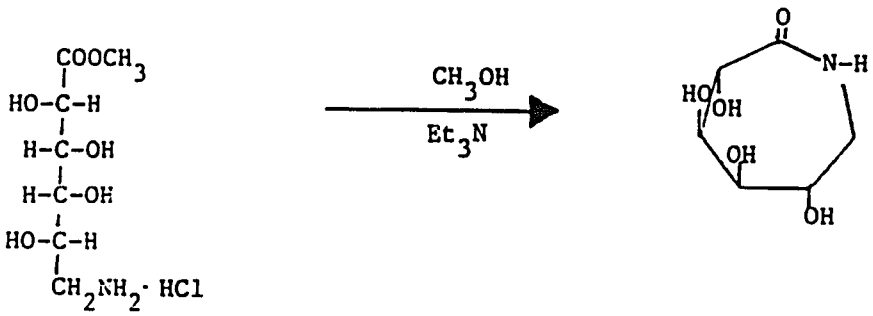
Scheme 10



(49)

D-Galacturonic Acid Monohydrate

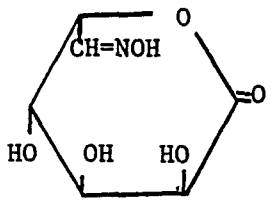
(50)



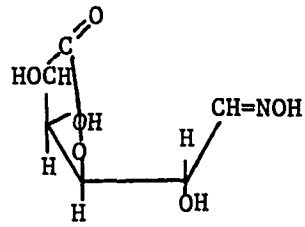
(51)

(52)

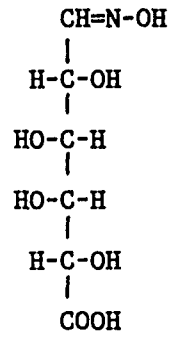
uronic acid. The low frequency for the carbonyl absorption (1735 cm^{-1}) suggests a six-membered lactone, i.e., 1-oximido-D-glucurono-6,2-lactone (46).[31]



(46)



(46c)



(50)

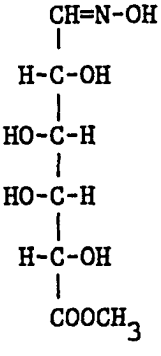
The five-membered lactone structure, i.e. 46c is less likely considering the carbonyl absorption, but it is interesting to note that the IR of the parent lactone, D-glucurono-6,3-lactone (45), has the carbonyl absorption peak at 1750 cm^{-1}, low for a five-membered lactone.

The oxime from D-galacturonic acid monohydrate (49) crystallized directly from the reaction mixture, mp 156-163 °C, in 65% yield. The IR spectrum of this oximation product 50 contained strong absorption peaks at 3300 cm^{-1} (OH) and 1715 cm^{-1} (acid C=O). The result of the elemental analysis of this product indicated the molecular formula, $C_6H_{11}NO_7$, a molecular formula consistent with an oxime of the uronic acid, i.e., 1-oximido-D-galacturonic acid (50).

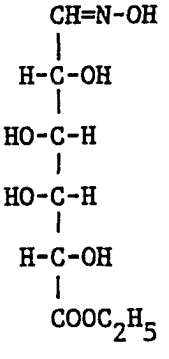
The ^1H NMR spectra of 46 and 50 each showed two isomeric vinylic protons (H-C=N-OH) with a ratio of approximately 4 to 1 corresponding to the syn and anti forms of the oximes 46a, 46b and 50a, 50b. Warming the oxime mixture 46a, 46b and 50a, 50b in D_2O resulted in conversion to the predominant and more stable syn isomers 46a and 50a,

respectively. The stereochemical assignments for these oximes is based on findings of Phillips[32] who correlated the ^{1}H NMR chemical shifts of the H-C=NOH protons with their geometric (syn and anti) isomers (Figure 7). On theoretical grounds, the signals at the lower field were assigned to the syn (E) isomers and those at higher field to the anti (Z) isomers.

For the oximation of D-galacturonic acid monohydrate (49), it was observed that under different reaction conditions we were able to isolate the ester forms of the oxime, 50c and 50d.



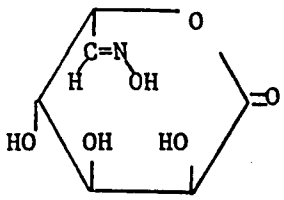
(50c)



(50d)

Reduction of Oximes 46 and 50 with Hydrogen over Palladium on Carbon (10%).

The reduction of the oximes was carried in methanolic HCl solution to the corresponding sugar amino acid hydrochlorides, 47 and 51. The very hydroscopic reduction product 47 from 1-oximido-D-glucurono-6,2-lactone (46) was used directly for the next (cyclization) step without any further purification. The reduction product 51 from 1-oximido-D-galacturonic acid (50) was obtained as a crystalline product, mp 169-173 ^{o}C, in 81% yield. The IR spectrum of this product 51 contained strong absorption peaks at 3300 cm^{-1} (OH) and 1725 cm^{-1} (ester C=O); ^{1}H NMR spectrum showed a methyl singlet at δ= 3.8 ppm, and the elemental analysis indicated the molecular formula $C_7H_{16}NO_6Cl$.

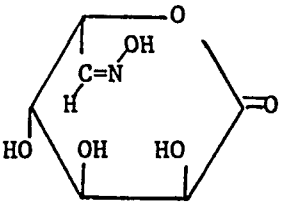


Syn(E)-1-Oximido-D-glucurono-6,2-lactone

(46a)

7.58 ppm

80%

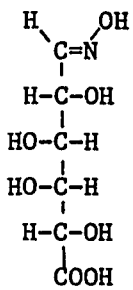


Anti(Z)-1-Oximido-D-glucurono-6,2-lactone

(46b)

6.96 ppm

20%

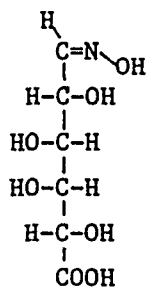


Syn(E)-1-Oximido-D-galacturonic Acid

(50a)

7.56 ppm

80%



Anti(Z)-1-Oximido-D-galacturonic Acid

(50b)

6.95 ppm

20%

Figure 7. ^{1}H NMR H-C=NOH Chemical Shifts for Oximes 46a, 46b, 50a and 50b.

Based on these results, 51 is methyl 1-amino-1-deoxy-D-galacturonate hydrochloride (51).

Cyclization of the Sugar Amino Acid Hydrochlorides 47 and 51.

The amine hydrochlorides 47 and 51 were treated with triethylamine in methanol to form the lactam ring. The product derived from D-glucurono-6,3-lactone (45), ε-L-gulonolactam (48), crystallized directly from the reaction mixture, mp 195 °C (lit.[29] 195 °C), in 90% yield. The IR spectrum of 48 showed strong OH (3360 cm^{-1}) and lactam C=O (1640 cm^{-1}) absorptions. The elemental analysis supported the molecular formula $C_6H_{11}NO_5$ for the ε-L-gulonolactam (48). The ^1H NMR and ^{13}C NMR spectra also supported the assigned structure for 48.

The cyclization product derived from D-galacturonic acid monohydrate (49), ε-L-galactonolactam (52) crystallized directly from the reaction mixture, mp 186-190 °C, in 83% yield. The IR spectrum of this product had strong absorption peaks at 3320 cm^{-1} (OH) and 1640 cm^{-1} (lactam C=O). The infrared spectrum carbonyl (C=O) absorption of the lactams with six-membered rings or larger is near 1650 cm^{-1}.[33] ^1H NMR (D_2O) showed peaks at δ= 4.46 ppm (d, 1H, H5); 3.88 ppm (broad, 1H, H3); 3.74 ppm (q, 2H, H2& H4); 3.52 ppm & 3.15 ppm (2d, 2H, H1).

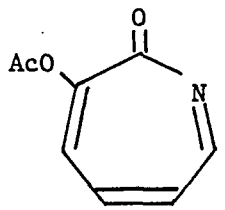
Acetylation of ε-L-Gulonolactam (48) and ε-L-Galactonolactam (52).

The acetylation was carried out at room temperature with acetic anhydride in pyridine overnight. 2,3,4,5-Tetra-O-acetyl-ε-L-gulonolactam (63), melting point of 213-215 °C (lit.[29] 215 °C), was isolated in 92% yield. The IR spectrum has absorption peaks at 3230 cm^{-1} (N-H), and 1740 cm^{-1} (ester C=O) and 1645 cm^{-1} (lactam C=O). The ^1H NMR and ^{13}C NMR spectra also indicated four acetate groups on 63. 2,3,4,5-Tetra-O-acetyl-ε-L-galactonolactam (64) was isolated in 86%

yield and has a melting point of 165 °C. The IR spectrum has absorption peaks at 3300 cm^{-1} (N-H), 1730 cm^{-1} (ester C=O), and 1650 cm^{-1} (lactam C=O). The ^1H NMR spectrum was consistent with the assigned structure. It is interesting to note that the results of the elemental analysis of these two tetraacetates, 63 and 64, showed that the tetraacetates each crystallized with a half mole of H_2O.

Base Catalyzed Elimination of Acetic Acid from the Lactam Tetraacetates 63 and 64.

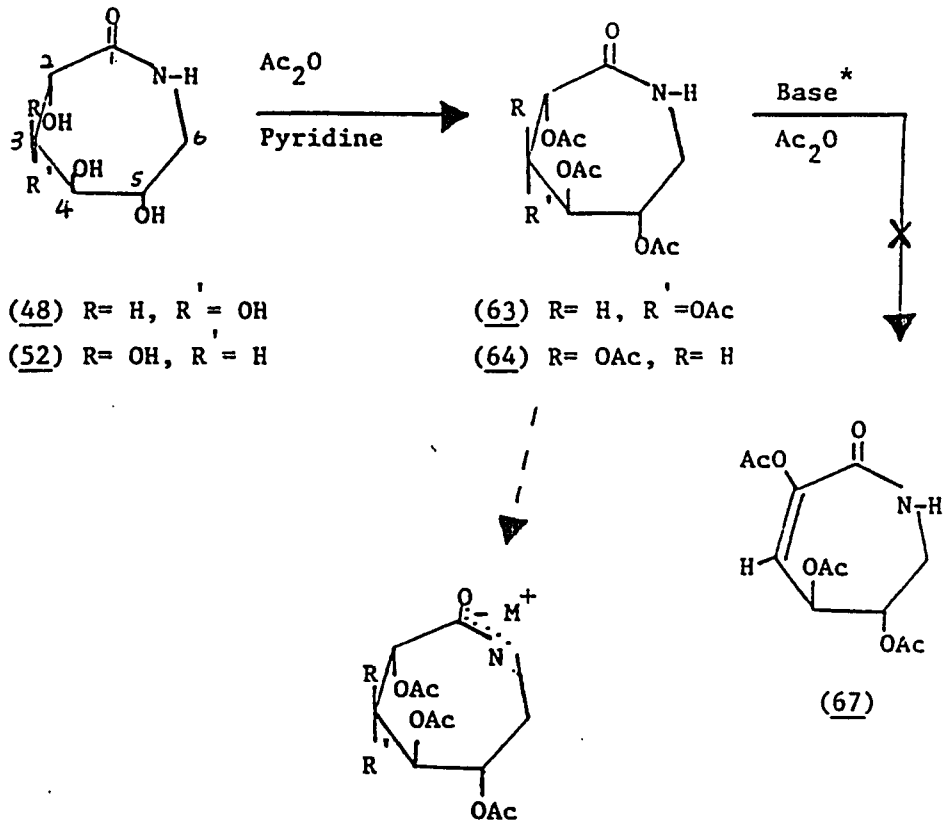
Our original goal was the base catalyzed elimination of acetic acid from either of the lactam tetraacetates 63 and 64 to the azatropolone 73 according to the hypothetical elimination mechanism shown in Figure 6.



(73)

Our initial β-elimination experiments were carried out with several different bases: pyridine, sodium acetate, triethylamine, or 1,8-diaza-bicyclo[5.4.0]undec-7-ene (DBu), in acetic anhydride. The reactions were directly monitored by ^1H NMR. Starting from either 63 or 64, a broad peak at δ= 6.3 ppm (N-H) and a singlet at δ= 5.2 ppm corresponding to the proton on carbon 2 diminished during the course of the reaction, while a new singlet at δ= 5.7 ppm appeared and increased in intensity. After the disappearance of the 6.3 & 5.2 ppm peaks and the appearance of the 5.7 ppm peak, the reaction stopped. It was concluded that the 63 or 64 formed a salt with the base after the proton on the nitrogen was abstracted, and the alternate β-elimination to 67 did not occur at all (Scheme 11).

Scheme 11



(48) R= H, R' = OH
(52) R= OH, R' = H

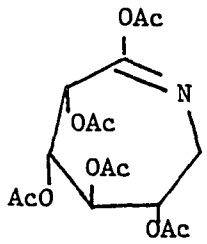
(63) R= H, R' =OAc
(64) R= OAc, R= H

(67)

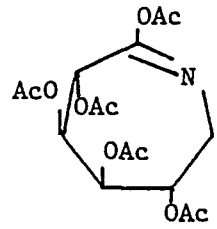
(76) R= H, R' = OAc
(77) R= OAc, R' = H

*Base= Pyridine
Sodium Acetate
Triethylamine
1,8-Diazabicyclo[5,4,0]undec-7-ene

An alternate route to the azatropolone ring system was undertaken based on initial O-acetylation of the lactams 63 and 64. It was reasoned that if the enol form of the lactam could be oxygen protected, then the desired β-elimination reactions might be accomplished. The lactams 2,3,4,5-tetra-O-acetyl-ε-L-gulonolactam (63) and 2,3,4,5-tetra-O-acetyl-ε-L-galactonolactam (64) were O-acetylated in acetic anhydride with acid catalyst using Nafion membrane (a perfluorosulfonic acid membrane) at room temperature overnight. The reaction was monitored by ^{1}H NMR, and the broad N-H signal at δ= 6.3 ppm was observed to diminish as the reaction proceeded. The enol actates 65 and 66 were very stable in acidic acetic anhydride, but all attempts to isolate these compounds by removal of the acetic anhydride under vacuum distillation yielded only the starting lactams.



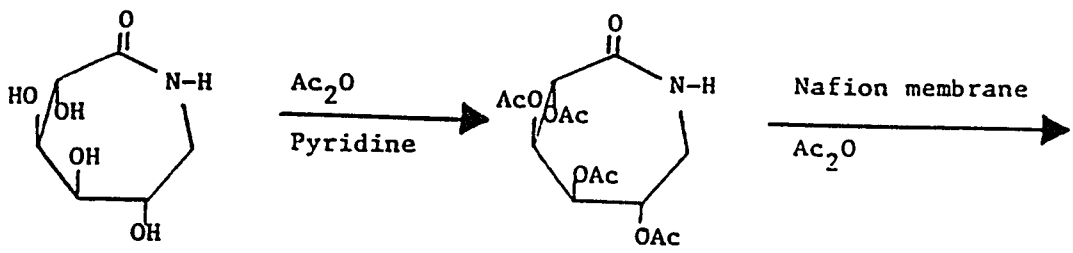
(65)



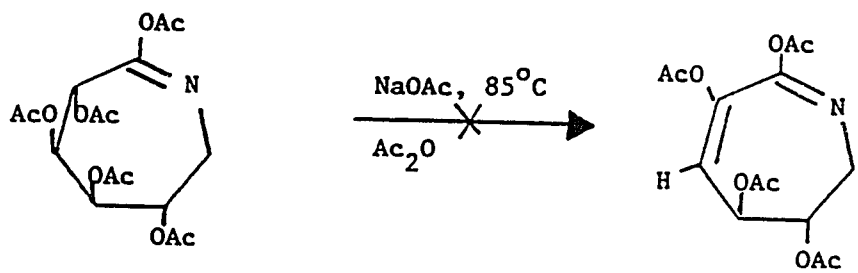
(66)

Upon complete formation of the enol acetates 65 and 66, the membrane was removed from the reaction mixture, and anhydrous sodium acetate was added. The reaction mixture was then heated up to 85 °C. However, no reaction was observed for the penta-O-acetyl compound 66. It was concluded that the syn relationship between the proton at C-3 and the O-acetyl group at C-4 was unfavorable for acetate β-elimination (Scheme 12). However, from the pentaacetate 65, the product 68 was isolated as a slightly brown colored solid in quantitative yield

Scheme 12



(52) (64)



(66) (68)

after 36 h. The reaction was monitored by ^{1}H NMR by observing the disappearance of a singlet at δ= 5.7 ppm (H-3 of 65) and the appearance of a new doublet at δ= 6.0 ppm (H-4 of 68). Further reaction with sodium acetate in acetic anhydride did not give any further change in product.

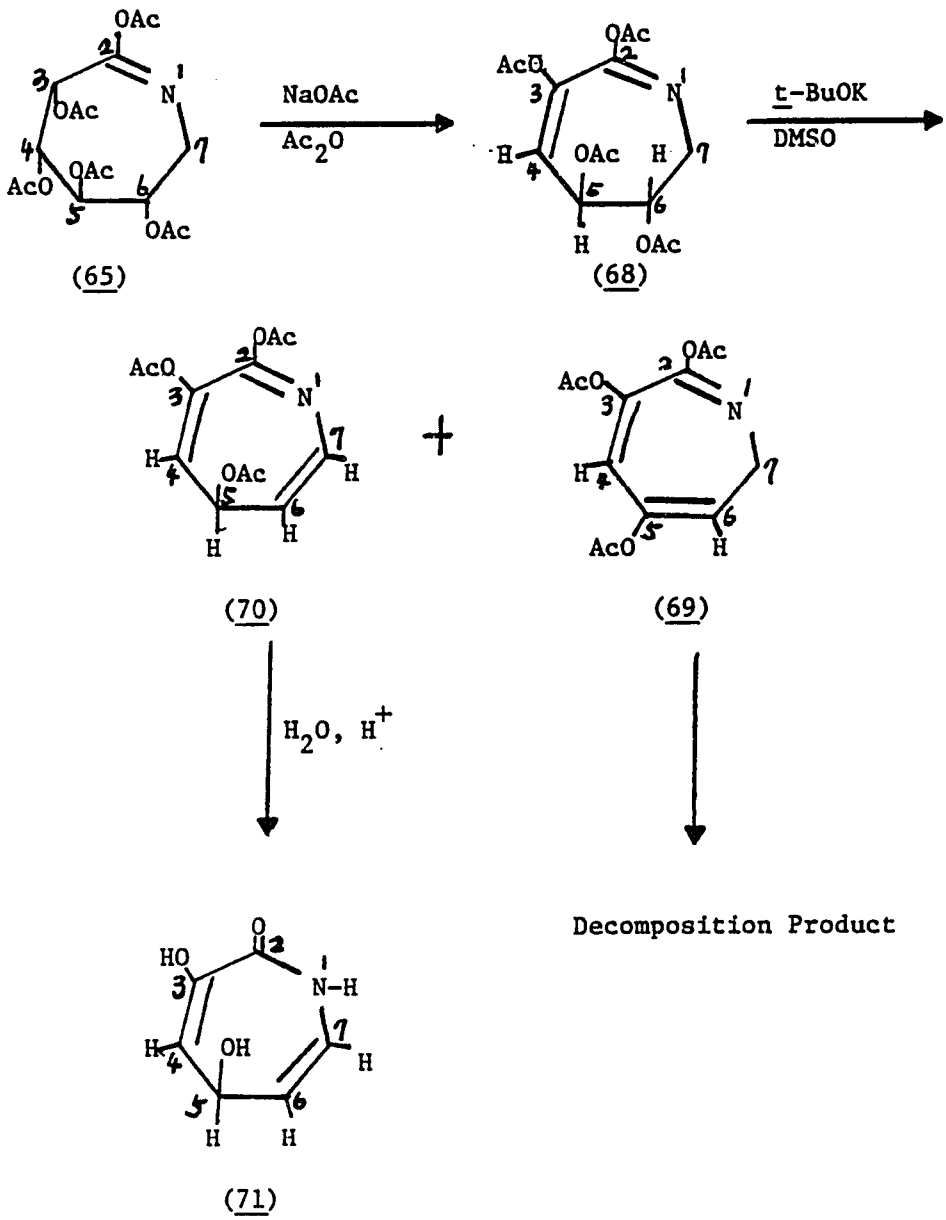
A stronger base, potassium t-butoxide in dimethyl sulfoxide was chosen for the base-catalyzed elimination reaction of acetic acid from 68. The reaction was complete at room temperature after 2 h as observed by ^{1}H NMR (60 MHz); the doublet at δ= 6.0 ppm (H-4 of 68) disappeared and a new doublet at δ= 6.5 ppm appeared (H-4 of 70). After the reaction stopped, glacial acetic acid was added to the reaction mixture to neutralize any excess base. The solvent and the salts were removed, and the ^{1}H NMR spectrum (300 MHz) of the crude product in $CDCl_3$ showed a mixture of two components with a ratio of approximately 2 to 1 (Figure 51). The major product is assigned the structure of triene 69, and the minor product the triene structure 70 (Scheme 13).

However, it was observed that, after several days, the major component 69 dissolved in $CDCl_3$ decomposed to an insoluble black precipitate, leaving the minor component in the chloroform. The ^{1}H NMR spectrum showed four doublets at δ= 7.01 (1H, $J_{6,7}$ = 9.9 Hz, H-6), 5.85 (1H, $J_{6,7}$ = 9.9 Hz, H-7), 5.64 (1H, $J_{4,5}$ = 4.5 Hz, H-4), and 5.10 (1H, $J_{4,5}$ = 4.5 Hz, H-5). The spectrum also showed the presence of some residual dimethyl sulfoxide.

Hydrolysis of Compound 70.

The hydrolysis of the acetates of 70 was carried out with a mixture of 1:1 D_2O and acetic acid-d_6 at 50 °C overnight. The three singlets near δ=2 ppm for the acetate groups and a singlet for the

Scheme 13



(65) (68) (70) (69) (71)

solvent in the reaction mixture converted to a single large singlet. When solvent was removed, the ^{1}H NMR spectrum of product 71 showed no remaining acetate group; δ= 7.01 (d, 1H, $J_{4,5}$ = 10.3 Hz, H-4) and 6.94 (dd, 1H, $J_{5,6}$ = 2.6 Hz, $J_{6,7}$ = 13.1 HZ, H-6), 6.88 (d, 1H, $J_{6,7}$ = 13.1 Hz, H-7) 5.94 ppm (dd, 1H, $J_{4,5}$ = 10.3 Hz, $J_{5,6}$ = 2.6 Hz). The simulated ^{1}H NMR spectrum (Figure 52) for H-4 to H-7 of 71 was generated using the NMCSIM program supplied by Nicolet Instrument. Iterative analysis was performed using the Nicolet ITRCAL program. The rms error was 0.008, the number of assigned trasitions was 12. The ultraviolet (UV) spectrum of 71 had a λ_{max} = 280 nm, with a molar absorptivity ε= 700. The calculated λ_{max} = 285 nm based on α,β-unsaturated lactam (250 nm) with an α-substituted OH group (+ 35 nm).[33]

We propose that a 1,4-elimination of a molecule of water from compound 71 would allow us to obtain 3-azatropolone (57). Attempts to eliminate water from 71 have thus far failed. The first attempts to remove water from 71 were under acid-catalyzed dehydration conditions: (1) in D_2O with Nafion membrane at 85 °C, (2) in DMSO-d_6 with Nafion membrane and dry molecular sieves at 85 °C. No reaction was observed in either case. A base catalyzed elimination employing triethylamine-thionyl chloride patterned after a 1,2-dehydration of cyclitol derivatives according to Riordan and Kiely[34] also was unsuccessful.

SUMMARY AND CONCLUSIONS

Part II: "Synthesis and Some Chemistry of Seven-membered Lactams Derived from Carbohydrates"

Two seven-membered sugar lactams, ε-L-gulonolactam (48) and ε-L-galactonolactam (52), were synthesized from D-glucurono-6,3-lactone (45) and D-galacturonic acid (49), respectively.

The improved synthesis of ε-L-gulonolactam (48) and the first synthesis of ε-L-galactonolactam (52) were carried out by a procedure based on that of Weidmann and Fauland.[29] 1-Oximidouronic acids, prepared by the oximation of 45 and 49, were reduced to the corresponding esterified 6-amino-6-deoxy-L-aldonic acid hydrochlorides in methanolic HCl using hydrogen over palladium on carbon (10%). Intramolecular aminolysis of the esterified 6-amino-6-deoxy-L-aldonic acid hydrochlorides gave the corresponding sugar lactams.

Conversion of sugar lactams 48 and 52 to the lactam tetraacetates 63 and 64 was carried out in pyridine with acetic anhydride. The lactam tetraacetate 65 was the starting material for a planned synthesis of 3-azatropolone 57, a nitrogen analogue of the naturally occurring tropolone ring system. The lactam tetraacetate 63 was enol O-acetylated to the pentaacetate 65 in acetic anhydride in the presence of an acidic catalyst, Nafion membrane (a perfluorosulfonic acid polymeric membrane). Double bonds were introduced into the ring system by base catalyzed eliminations. The first β-elimination was carried out in acetic anhydride with anhydrous sodium acetate at 85 °C to give

(5R,6S)-2,3,5,6-tetra-O-acetyl-1,3-azacycloheptadiene (68). The base-catalyzed elimination (t-BuOK in DMSO) of acetic acid from 68 gave a mixture of two components, 2,3,5-tri-O-acetyl-1,3,5-azacycloheptatriene (69) and (5R)-2,3,5-tri-O-acetyl-1,3,6-azacycloheptatriene (70) in a ratio of 2 to 1. However, the major component 69 decomposed while in chloroform-d precipitating as a black tarry material, leaving the minor component 70 in chloroform-d. The hydrolysis of 70 gave unsaturated diene lactam (5R)-3,5-dihydroxy-2-oxo-3,5-azaheptadiene (71).

Attempts to eliminate water from 71 under acidic or basic condition to give 3-azatropolone (57) have thus far been unsuccessful. However, acetylation of the two hydroxyl groups of 71 under basic condition followed by 1,4-elimination of acetic acid should lead to the target 3-azatropolone (57).

The use of a carbohydrate derived precursor 65 for the preparation of the unsaturated seven-membered heterocyclic products 68 - 71 represented a novel synthetic approach to azatropolones and related compounds.

SUGGESTIONS FOR FURTHER RESEARCH

Part II: "Synthesis and Some Chemistry of Seven-membered Lactams Derived from Carbohydrates"

It recommended that the lactams 48 and 52 be converted to tetra-O-triflates and the latter compounds be subjected to base catalyzed eliminations. Beta-elimination of triflate should occur under very mild conditions, and a one pot conversion to 3-azatropolone (57) may be possible.

The syn/anti composition of the oximidouronic acids in solution is temperature dependent. An NMR study of this composition/temperature dependency might be carried out. Consideration should be given to the preparation of carbohydrate amino acid esters that will undergo intramolecular aminolysis, rather than intermolecular aminolysis, for the preparation of carbohydrate-based polyamides.

INTRODUCTION

Part III: "Synthesis Directed Toward the Preparation of Polyhydroxylated Polyamides"

Naturally occuring carbohydrate polymers are termed polysaccharides and are polymers with monomeric monosaccharide units connected by glycosidic (acetal) bonds. In such polymers, the monosaccharide units are found as six-membered (pyranose) rings and to a lesser extent as five-membered (furanose) rings. Our interests in dicarbonyl sugar chemistry lead us to consider the preparation of synthetic carbohydrate-based polymers derived from acyclic carbohydrate monomers. Long-term objectives of this approach to the synthesis of carbohydrate-based polymers are production and control of the properties of a range of synthetic polymers, taking into account the particular carbohydrate(s) used in the synthesis.

The target polymers for this research were carbohydrate-based polyamides modeled after (1) nylon-6,6 and (2) nylon-6. The parent nylon-6,6 is the product of a condensation polymerization process, whereas nylon-6 is prepared by an anionic ring-opening polymerization process.

An important commercial process for the preparation of polyamide copolymers is by melt polycondensation of dicarboxylic acids or diesters with diamines at elevated temperatures. The polycondensations are carried out at melting points above that of the resulting polymers

so that the equilibrium of the polycondensation is shifted toward polymer formation by eliminating water or alcohol from the reaction system. A second common method involves condensation of a diacid dichloride with an appropriate diamine. This method also has been used with protected carbohydrate diacid dichlorides (aldaryl dichlorides) to prepare a variety of carbohydrate-based polyamides. By using this method, Wolfrom, Toy, and Chaney[35] synthesized polyamides from the densation of tetra-O-acetylgalactaroyl dichloride with ethylenediamine or piperazine (Scheme 14). Dewar and co-workers[36,37] prepared a large number of polyamides in this way. Among them are those derived from: (1) 1,6-diamino-1,6-dideoxy-di-O-methylenehexitols with sebacoyl or adipoyl dichloride (Scheme 15), (2) hexamethylenediamine or decamethylenediamine with di-O-methylenehexaroyl dichlorides (Scheme 16), (3) a polyamide containing isopropylidene blocked sugar residues (Scheme 17),[38] and (4) a polyamide containing O-methylene and benzylidenedideoxy sugar derivatives (Scheme 18).[39-42]

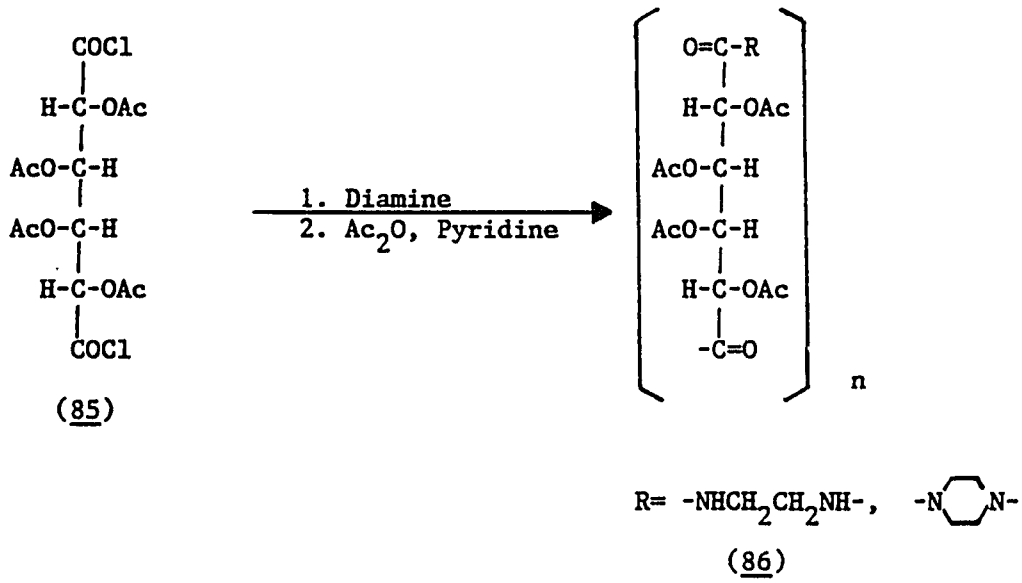
An alternate and more convenient approach to carbohydrate-based polyamides was first described by Ogata.[44] Ogata described that diesters of carbohydrate diacids (aldaric acids) condense directly under mild conditions in polar solvents with diamines. In general, Ogata observed that diesters having heteroatoms such as oxygen or sulfur atoms at the position α to the carbonyl groups undergo polycondensation with diamines under mild conditions to form the corresponding polyamides.[43-45] Hoagland[46] recently reported employing the aminolysis of carbohydrate diacids diesters (aldarates) according to the Ogata procedure. Hoagland's explanation for the ease of this reaction

involves a mechanism that proceeds through an intermediate five-membered lactone. In contrast, simple aliphatic diesters such as diethyl adipate which have no hydroxyl groups are unable to form intermediate lactones. Aminolysis of these latter esters proceeds at a very slow rate. Ogata reported polyamides synthesized from dimethyl L-tartarate with hexamethylenediamine[47,48] and from diethyl mucate (galactarate) with hexamethylenediamine (Scheme 19).[49]

The synthesis of 12 polyamides is described in this part of the dissertation. They were prepared by the aminolysis of the esters of galactaric, D-glucaric, and xylaric acids with the diamines hexamethylenediamine, dodecamethylenediamine, octamethylenediamine, and 2-methylpentamethylenediamine.

The synthetic approach to nylon-6 type carbohydrate-based polyamides was fashioned after that used to prepare the parent nylon-6, i.e., anionic ring-opening of an ε-caprolactam. The lactams synthesized for this study were 2,3,4,5-tetrahydroxy-ε-caprolactams of the L-gulono and L-galactono configurations. These lactams, as their O-trimethylsilyl (TMS) derivatives, were then subjected to anionic ring-opening polymerization conditions designed to produce the hydroxylated, but O-TMS protected nylon-6 polymers.

Scheme 14

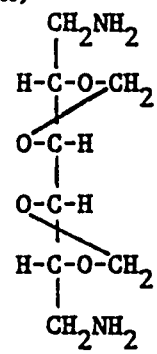


(85)

(86)

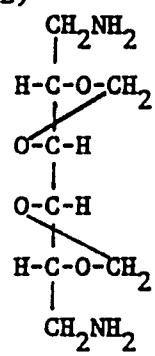
Scheme 15

(A)



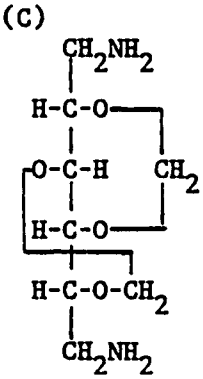
(78) + Cl-C(=O)-$(CH_2)_8$-C(=O)-Cl ⟶ $[C_{18}H_{30}N_2O_6]_n$

(B)



(78) + Cl-C(=O)-$(CH_2)_4$-C(=O)-Cl ⟶ $[C_{14}H_{22}N_2O_6]_n$

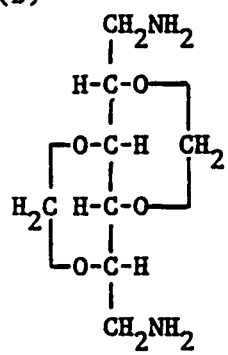
(C)



(79) + Cl-C(=O)-$(CH_2)_8$-C(=O)-Cl ⟶ $[C_{18}H_{30}N_2O_6]_n$

Scheme 15 (Continued)

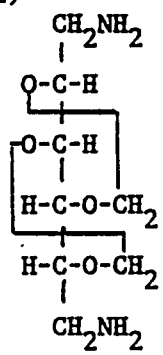
(D)



(80)

+ $Cl\text{-}\overset{O}{\overset{\|}{C}}\text{-}(CH_2)_8\text{-}\overset{O}{\overset{\|}{C}}\text{-}Cl$ ⟶ $[C_{18}H_{30}N_2O_6]_n$

(E)

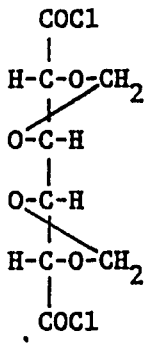


(81)

+ $Cl\text{-}\overset{O}{\overset{\|}{C}}\text{-}(CH_2)_8\text{-}\overset{O}{\overset{\|}{C}}\text{-}Cl$ ⟶ $[C_{18}H_{30}N_2O_6]_n$

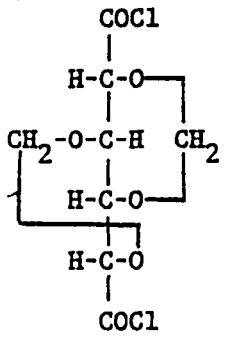
Scheme 16

(A)



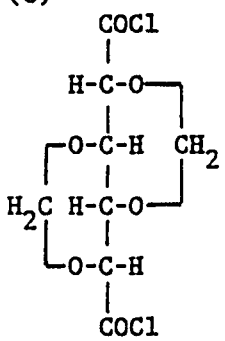
(82) + $H_2N-(CH_2)_6-NH_2$ ⟶ $[C_{14}H_{22}N_2O_6]_n$

(B)



(83) + $H_2N-(CH_2)_6-NH_2$ ⟶ $[C_{14}H_{22}N_2O_6]_n$

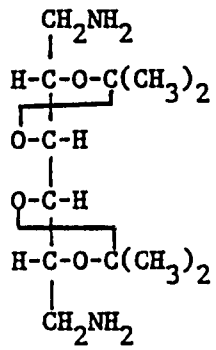
(C)



(84) + $H_2N-(CH_2)_6-NH_2$ ⟶ $[C_{14}H_{22}N_2O_6]_n$

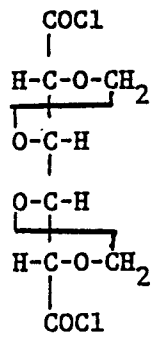
Scheme 17

(A)

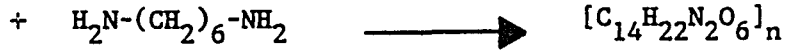


(87)

Scheme 18

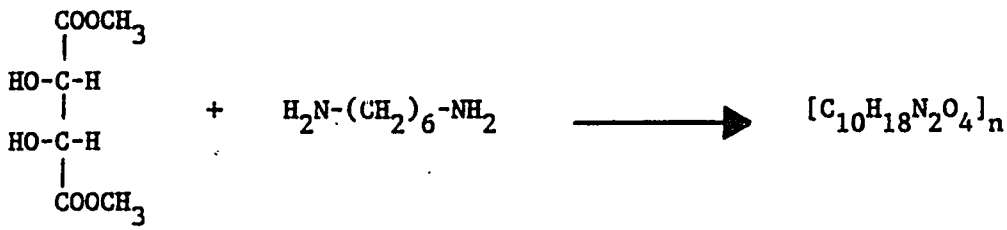


(82)



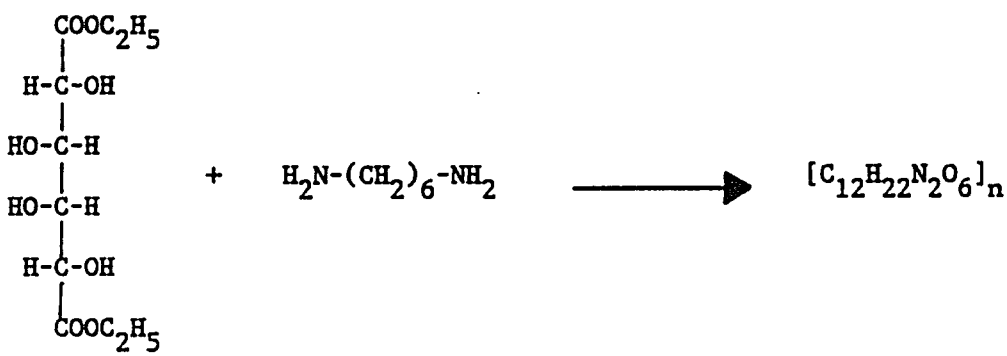
Scheme 19

(A)



(88)

(B)



(89)

RESULTS AND DISCUSSION

Part III: "Synthesis Directed Toward the Preparation of Polyhydroxylated Polyamides"

Aldaric Acids by Nitric Acid Oxidation of Aldoses.

Crystalline galactaric acid (90) and xylaric acid (93) were each prepared according to literature procedures. Galactaric acid was prepared by the oxidation of lactose using concentrated nitric acid as the oxidizing agent.[50] Usually the yield for this oxidation was around 33%-35%, mp 223 °C (decomp.); (lit.[50] mp 211-212 °C). Xylaric acid was prepared by the oxidation of D-xylose (92)[51] also with concentrated nitric acid as the oxidizing agent, the yield being typically around 35%, mp 142-145 °C (lit.[51] 145-147 °C).

D-Glucaric acid, as D-glucaro-6,3-lactone (96) was generated from its calcium salt (95) purchased from the Sigma Chemical Company. This compound is sold as D-saccharic acid, calcium salt. A suspension of calcium D-glucarate (95) in water was deionized with fresh cation exchange resin (Amberlite IR-120, H^+ form). Deionization solubilized the D-glucaric acid as it was formed, which, after solvent removal was obtained as the syrupy product D-glucaro-6,3-lactone (96), which is the lactone form of D-glucaric acid.[55] Syrupy 96 was used for esterification without purification (Scheme 20).

Esterification of Aldaric Acids.

The conversion of aldaric acids to dimethyl aldarates and/or methyl aldarolactones was carried out in acidic methanol solution. For

D-glucaro-6,3-lactone (96) and xylaric acid (93) esterifications, acetyl chloride was added to cold reagent grade methanol for *in situ* HCl generation. The solution was brought to room temperature, and to it was added xylaric acid (93) or D-glucucaro-6,3-lactone (96). The reaction mixture was then refluxed overnight, and the resultant solution concentrated to a syrup. Residual water was azeotroped with benzene. These products were used directly in the polymerization reactions without further purification. For galactaric acid (90), esterification was carried out in methanol containing concentrated sulfuric acid. The reaction mixture was refluxed overnight, but during this time, no solid appeared to dissolve. However, the insoluble material obtained was dimethyl galactarate (91) (90%, mp 205 °C); (lit.[50] mp 205 °C). The crude dimethyl galactarate (mp 205 °C) was recrystallized from methanol containing triethylamine to give purified ester, mp 220-222 °C (83 %).

Polycondensation of Methyl Aldarates with Certain Aliphatic Diamines.

Polycondensation of the esterified aldaric acids with aliphatic diamines was carried out under mild conditions. Typically a methanol solution of the esterified aldaric acid, a slight molar excess of an appropriate aliphatic diamine, and triethylamine were stirred at room temperature or under reflux for 2 hours to yield the insoluble white polyamide, isolated by simple flitration. Four diamines, hexamethylenediamine, octamethylenediamine, dodecamethylenediamine, and 2-methylpentamethylenediamine, were condensed with the aldaric acid esters dimethyl galactarate (91), the mixture of dimethyl xylarate (94a) and methyl xylaro-1,4-lactone (94b), and the esterified D-glucaric acid represented as methyl D-glucaro-6,3-lactone (97). Of the 12

condensations carried out (Scheme 21), only the condensations of 2-methylpentamethylenediamine with methyl D-glucaro-6,3-lactone (97) and the esterified xylaric acid did not produce insoluble polyamide directly. In these condensations the product polyamides were isolated by removal of solvent and washing the residue with methanol. IR spectra of all the polyamides gave a strong absorption band at about 1640 cm^{-1}, characteristic of an Amide I carbonyl and at about 1540 cm^{-1}, an Amide II band. The absence of ester or lactone carbonyl absorptions in IR spectra of these products implies that the polymer end groups are primary amine fuctions.

The ^{1}H NMR spectrum (Figure 58) of O-TMS of hexamethylenegalactaramide pentamer (98) supported this, in that it has no resonance for a methyl ester methyl group. In addition the ratio of $(CH_2)_6$ to NH was measured from the spectrum to be 5.8. This value corresponds to an oligomer of degree of polymerization (Dp) on the order of 5-7. The calculated value for Dp 5= 6.0 and that for Dp 7= 5.33. The elemental analysis of this product was very close to an oligomer of Dp 5; $C_{30}H_{60}N_6O_{12}$ Calcd: C, 51.71; H, 8.68; N, 12.06. Found: C, 51.50; H, 8.73; N, 12.18. Condensation of dimethyl galactarate with octamethylenediamine and dodecamethylenediamine also gave oligomeric products according to elemental analytical results; octamethlyenegalactaramide nonamer (107) and dodecamethylenegalactaramide (104), respectively. The results of the elemental analyses of the remaining condensation products suggested that these products are polymeric with Dp's >30. The oligomeric character of the galactaramide polymers probably results from the low solubility of these oligomers in the reaction medium, thus limiting the condensation. The low solubility

characteristic is typically of a variety of galactaric acid derivatives.

Trimethylsilylation of the ε-Lactams 48 and 52.

The procedure for making the O-trimethylsilylated aldonamides previously described in this dissertation was used here to synthesize the O-TMS ε-lactams (110 and 111). O-trimethylsilylation of ε-L-gulonolactam (48) produced a syrupy tetra-O-TMS lactam (110) and some minor tri-O-TMS lactam. Trimethylsilylation of ε-L-galactonolactam (52) gave the fully trimethylsilylated product, 2,3,4,5-tetra-O-TMS-ε-L-galactonolactam (111), mp 107-108 °C; Anal. Calcd for $C_{18}H_{43}NO_5Si_4$: C, 46.41; H, 9.30; N, 3.01. Found : C, 46.48; H, 9.33; N, 2.97. IR spectra of these two compounds contained similar absorption peaks at 3220 cm^{-1} (N-H) and 1670 cm^{-1} (lactam C=O). GC/MS of trimethylsilylated 48 indicated a mixture of compounds of a major product (68%, 7.2 min) and several minor products (32%, 6.88 min, 7.15 min, and 7.5 min). The major product was 2,3,4,5-tetra-O-TMS-ε-L-gulonolactam (110) with m/e at 465 (M), 450 (M-15), 375 (M-90), 360 (M-90-15), and 285 (M-90-90). Two minor products (6.88 and 7.5 min) were assigned as tri-O-TMS-ε-L-gulonolactams with m/e at 393 (M), 378 (M-15), and 375 (M-18), 303 (M-90). The peak at 7.15 min corresponded to the tetra-O-TMS-N-TMS-ε-L-gulonolactam with m/e at 423 (M-72-14-28), 333 (423-90). For 2,3,4,5-tetra-O-TMS-ε-L-galactonolactam (111) GC/MS showed the presence of one compound with m/e at 465 (M), 450 (M-15), and 378 (M-87).

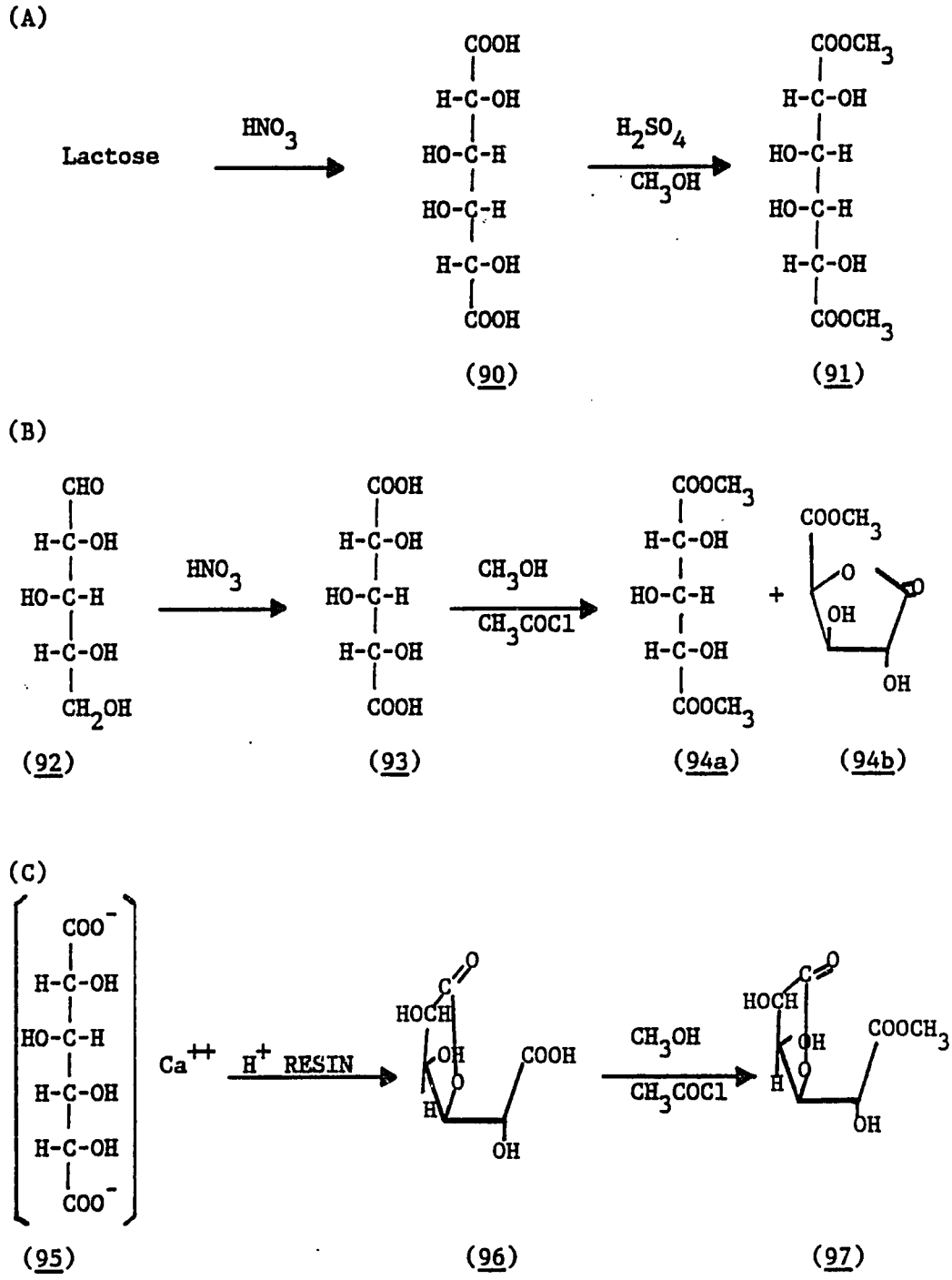
Attempted Polymerization of 2,3,4,5-Tetra-O-TMS-ε-L-aldonolactam 110 and 111.

The attempted anionic polymerization of the O-TMS aldonolactams 110 and 111 (Scheme 22) was carried out in a manner similar to that

described for polymerization of ε-caprolactam.[56] The lactam 111 was placed in a sidearm test tube, and nitrogen was slowly bubbled through the lactam via a Pasteur pipette fitted to the test tube with a rubber stopper. After the lactam was melted (about at 120 °C, oil bath temperature), a small piece of sodium metal was added, and warming was continued. A few drops of acetic anhydride were added to the lactam, and the reaction mixture was heated to 200 °C (oil bath) for a few minutes to effect the polymerization. IR and ^{1}H NMR spectra of the product were essentially the same as the starting material, indicating that polymerization had not occurred. A similar result was obtained by attempted polymerization of compound 110.

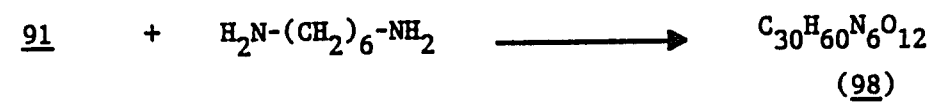
Preliminary results from attempted polymerization of 111 initiated by sodium hydride suggest polymerization of this lactam is possible. The polymerization setup was the same as described except that sodium hydride was substituted for sodium metal and acetic anhydride was omitted. The resultant product had a clearly different ^{1}H NMR spectrum (Figure 76) from that of the starting 111. Additional experiments are planned to determine the nature of the final product.

Scheme 20

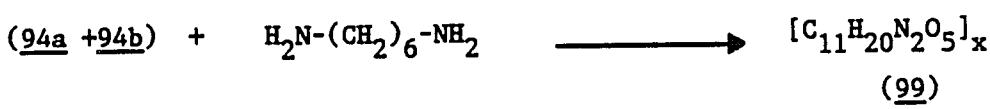


Scheme 21

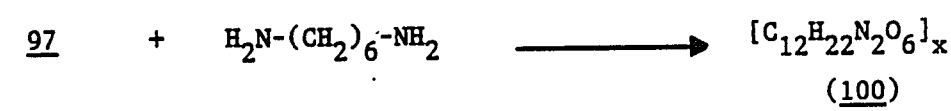
(A)



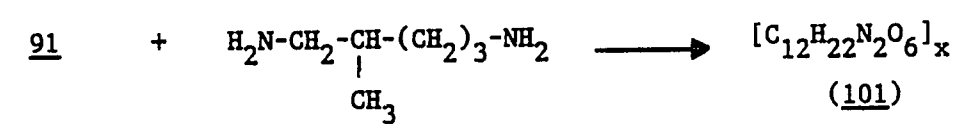
(B)



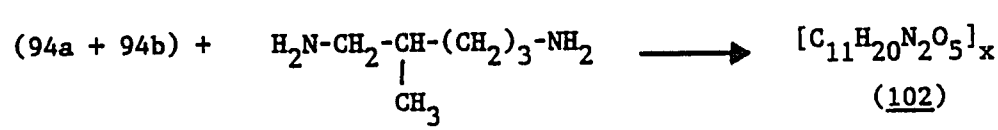
(C)



(D)

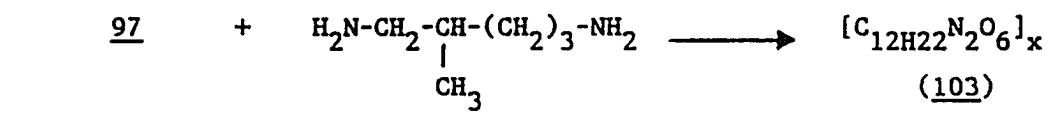


(E)

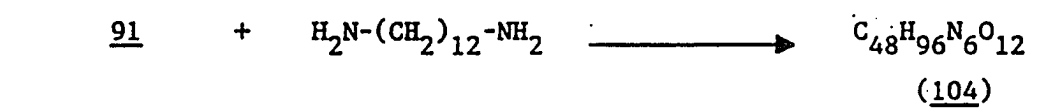


Scheme 21 (Continued)

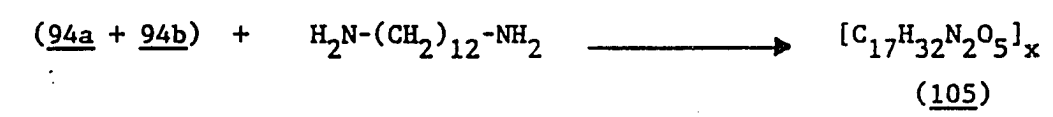
(F)



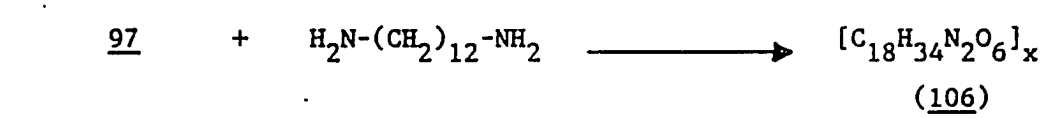
(G)



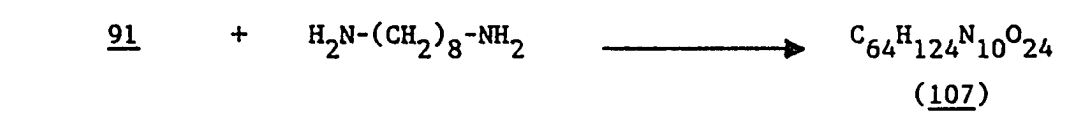
(H)



(I)

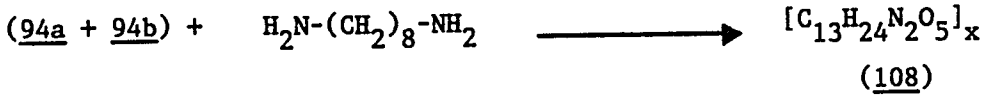


(J)

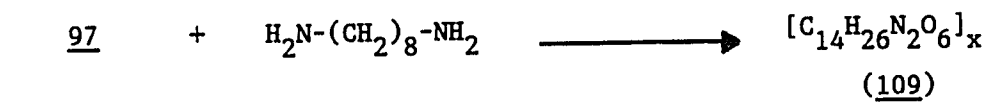


Scheme 21 (Continued)

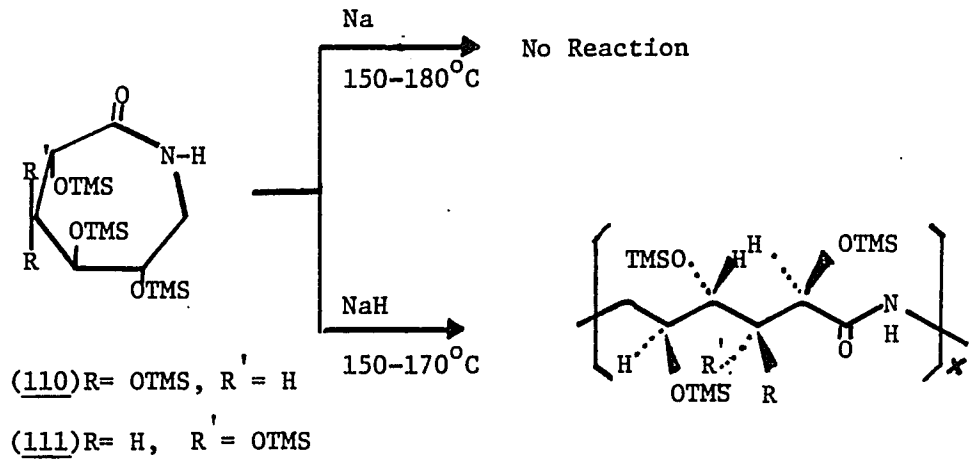
(K)



(L)



Scheme 22



SUMMARY AND CONCLUSIONS

Part III: "Synthesis Directed Toward the Preparation of Polyhydroxylated Polyamides"

A series of acyclic carbohydrate-based polyamides was prepared. Twelve carbohydrate-based polyamides were synthesized in methanol containing triethylamine by condensation polymerization between the methanol esterified aldaric acids, galactaric acid, xylaric acid, and D-glucaric acid, and four aliphatic diamines: 2-methylpentamethylenediamine, hexamethylenediamine, octamethylenediamine, and dodecamethylenediamine. This method of carbohydrate polyamide synthesis, in comparison to most of the reported synthetic routes of this class of polymers, does not require carbohydrate hydroxyl protection. In general, the polyamides formed in this way precipitate from the reaction mixture in a short time and can be isolated by simple filtration.

The lack of ester carbonyl absorption (1750-1735 cm^{-1}) in the IR of the polyamides suggests that the end groups of the polyamides are primary amine functions.

Trimethylsilylation of the pendant polymer OH groups makes the polyamides readily soluble in organic solvent, and subject to standard ^{1}H and ^{13}C NMR studies. Based on elemental analytical results, the degree of polymerization (Dp) of poly(hexamethylenegalactaramide), poly(octamethylgalactaramide), and poly(dodecamethylenegalactaramide are approximately 5-9. For the remaining carbohydrate based polyamides, the Dps appear to be > 30.

Advantages of the described method for the preparation acyclic cabohydrate-based polyamides are as follows: (1) the polymers are easily prepared and isolated, (2) the physical properties of the polymers can be varied by the choice of the esterified aldaric acids and diamines, (3) the physical properties of the polymers can be modified by functionalizing the pendant OH groups, e.g., trimethylsilylation of the resulting polyamides, and (4) simple sugars (precursors of the aldaric acids) are available from renewable resources.

SUGGESTIONS FOR FURTHER RESEARCH

Part III: "Synthesis Directed Toward the Preparation of Polyhydroxylated Polyamides"

Some of the acyclic carbohydrate-based polyamides melt before they decomposed. This property may be very important in the fabrication of these polyamides into fibers or films. The carbohydrate-based polyamides also might be used to prepare a variety of graft polymers through the available pendant OH groups and block polymers by reaction at terminal amine functions. Further characterization of these polyamides is necessary and should include ^{1}H and ^{13}C NMR studies, viscosity measurements, molecular weight distribution using gel permeation chromatography, and differential scanning colorimetry measurements.

Finally, this research and future research should bring to the attention of academic and industrial synthetic carbohydrate chemists and polymer chemists the importance of ultilizing carbohydrates for the preparation of new polymeric materials.

EXPERIMENTAL

General Methods

Melting points reported were determined on a Fischer-Johns melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded at 60 MHz, Varian EM 360; 90 MHz, Varian EM 390; or at 300 MHz, GE 300 WB (NT Series). IR spectra were obtained on Beckman Acculab-4 & Perkin-Elmer 283 IR Spectrophotomers. Solutions were concentrated at reduced pressure on a rotary evaporator. Elemental analyses were performed by Atlantic Microlabs, P.O. Box 80569, Atlanta, GA 30366. Gas chromatography/mass spectroscopy (GC/MS) was carried using a Hewlett-Packard 5985 system. Ultraviolet (UV) spectrum was obtained on a Varian Cary 17 spectrophotometer.

Part I: "Synthesis of 1-Amino-1-deoxyalditols from Aldonic Acids"

Aldonic Acids by Electrolytic Oxidation of Aldoses.

Aldonic acids, isolated as their calcium salts, were prepared as described by Frush and Isbell.[16] In a 2-liter kettle equipped with a stirrer and two graphite rods of 3/4" diameter and 12" length, aldose (0.25 mole), water (1 liter), calcium bromide (8 g, 0.4 mole), and calcium carbonate (13.5 g, 0.14 mole) were combined. A steady current of 0.5 Amp (5-15 Volts) was passed through a mechanically well-stirred reaction mixture for 27 h. The polarity was reversed periodically (every 1.5 h) to remove the calcareous deposited on the cathode. The reaction mixture was then filtered, and the filtrate concentrated on a

rotary evaporator to give a thin syrup which sometimes crystallized on standing at room temperature overnight. For those salts that did not crystallize, the addition of methanol (100 mL) to the syrup, followed by stirring the resultant mixture at room temperature, gave the solid product, which was then washed with deionized water and dried. The yield of salts ranged from 74% for calcium ribonate (26) to 96% for calcium mannonate (29). Acidification of the calcium aldonates was accomplished by passing 0.06-0.10 mol of the salt in 250-300 mL of deionized water through a column containing 250 mL Amberlite IR-120 (H^+) resin. The effluent was passed through the column twice more to ensure good exchange. After the solvent removal, the crude acid/lactone was used directly in the esterfication step.

Esterification of the Aldonic Acids.

Conversion of the aldonic acids to their methyl esters was carried out in methanolic HCl. Acetyl chloride was added to cold (5 ^{o}C) reagent grade methanol for in situ HCl generation. The solution was brought to room temperature, and to it was added the aldonic acid. The reaction mixture was then refluxed overnight, and the resultant solution concentrated on a rotary evaporator to a syrup. Decolorization of the syrup in methanol with activated charcoal was commonly carried out at this stage. As a final step, residual water was removed azeotropically at reduced pressure with benzene. The yields of methyl ester ranged from 94% for methyl xylonate to 65% for methyl ribonate.

Ammonolysis of Aldonic Acid Esterification Products.

The crude esterification products were used directly for conversion to the respective aldonamides. In a typical ammonolysis

experiment, the crude esterification product (0.1 mole based on starting aldonic acid) in methanol (50 mL) was added dropwise to a cold (5 °C) solution of methanol (150 mL) saturated with ammonia. Ammonia was bubbled through the solution during the addition and for 1 h after the addition was completed. The reaction mixture was kept open to the atmosphere in a fumehood overnight. The aldonamides usually crystallized directly from the reaction mixture and were removed by filtration. The yields (based on crude ester and lactone) and mp's (°C) are as follows: ribonamide (31) (83%, 136-138), galactonamide (32) (70%, 174-176), gluconamide (33) (79%, 144-147), mannonamide (34) (80%, 170-172).

Xylonamide (30).

The preparation of the previously unreported xylonamide was carried out according to the procedure described for the general preparation of aldonamides. However, the syrupy product resisted crystallization until it was observed that stirring the syrup with methanol at room temperature for several hours rendered crystalline 30; 9.5 g (88% based on ester/lactone), mp 80-85 °C. Trituration of the crude product with methanol gave an analytical sample: mp 83-85 °C; IR (Nujol) 1650 cm^{-1} (amide C=O); $[\alpha]_D^{25}$ +51.42° (c 1.2, DMSO); Anal. Calcd for $C_5H_{10}N_2O_5$: C, 36.36; H, 6.71; N, 8.48. Found : C, 36.15; H, 6.74; N, 8.40.

Trimethylsilylation and Amide Deprotection of Aldonamides.

The silylation procedure was based on that of Sweeley and coworkers[17] but was performed at room temperature according to Loewus.[18] The following trimethylsilylation procedure for ribonamide is representative. To a 250-mL Erlenmeyer flask, with a standard tapered

opening, was added pyridine (200 mL), hexamethyldisilazane (140 mL), and trimethylchlorosilane (45 mL) in that order. Ribonamide (31) (12 g, 72.7 mMol) was added to the silylation medium, the flask was stoppered, and the reaction mixture was stirred at room temperature for at least 24 h. The highly turbid mixture was vacuum filtered through a fine sintered glass funnel, and the filtrate was concentrated to a clear syrup under reduced pressure. The syrup was dissolved in dry hexane (150 mL), the slightly turbid mixture was filtered, and the hexane solution was concentrated to a clear, colorless syrup (37.9 g, 99%). The syrup was then dissolved in dichloromethane (250 mL) containing methanol (9 mL). The reaction mixture was left overnight at room temperature and then vacuum filtered to remove a small amount of colored precipitate. The clear filtrate was concentrated to give tetra-O-(trimethylsilyl)ribonamide (36, 30 g, 92%).

After ^{1}H NMR verification that the selective deprotection was completed, the compounds were used in the reduction step without further purification or attempted recrystallization. The yields of the O-TMS aldonamides were generally about 90%.

Typical Diborane Reduction of an O-(Trimethylsilyl)aldonamide. The Synthesis of 1-Amino-1-deoxy-D-galactitol Hydrochloride (42).

The glassware assembly (Figure 5) for the generation of diborane was patterned after that described by Brown,[21] although Brown's procedure employed BF_3 etherate and sodium borohydride to generate diborane. Crude pentakis-O-(trimethylsilyl)galactonamide (37, 12.6 g, 22.7 mmol, mp 64-66 ^{o}C) was prepared by N-deprotection of fully trimethylsilylated galactonamide (14.9 g) in a solution of dichloromethane (100 mL) and methanol (5 mL) at room temperature for 24 h. To an ice-bath cooled, 500-mL round-bottomed flask, containing sodium

borohydride (9.0 g, 240 mMol) suspended in diglyme (45 mL), was added dropwise a solution of iodine (30 g, 118 mMol) in diglyme (30 mL). The diborane was flushed with nitrogen into a flask containing 37 in THF (150 mL). The nitrogen flow was continued for 1 h after the addition of iodine solution was completed, and the reaction mixture was refluxed overnight. Methanol (10 mL) and the methanolic HCl solution (70 mL, 5 M) were then added successively to the cooled (ice-bath) reaction mixture. The acidified reaction mixture was refluxed for 1 h and then concentrated to a syrup. Methanol (15 mL), then methanolic HCl solution (80 mL, 5 M), were added to the crude syrupy product, and the resultant solution brought just to boiling. The mixture was allowed to cool to room temperature, the solvent removed, and to the syrupy product was added absolute ethanol (40 mL). The mixture was stirred overnight to give 1-amino-1-deoxy-D-galactitol hydrochloride (42), mp 141-142 °C (lit.[40] 143-145 °C), 4.5 g (92%).

Table 1

Yields of Monoaminoalditol Hydrochlorides Based on Starting Per-O-Trimethylsilylaldonamides

O-TMS Amide	Amine Hydrochloride	Percent Yield
35	40	88
36	41	49
37	42	92
38	43	75
39	44	72

1-Amino-1-deoxy-D-xylitol Hydrochloride (40), 1-Amino-1-deoxy-D-ribitol Hydrochloride (41), 1-Amino-1-deoxy-D-glucitol Hydrochloride (43), 1-Amino-1-deoxy-D-mannitol Hydrochloride (44).

The 1-amino-1-deoxyalditol hydrochlorides 40, 41, 42, and 44 were prepared using the procedure described for the preparation of 42; 40

mp 108-113 °C (lit.[52] mp 139-140 °C), 41 mp 128-133 °C (lit.[53] mp 129 °C), 43 mp 114-119 °C (lit.[9] 122-126 °C), and 44 mp 156-158 °C (lit.[54] 161.5-162.5 °C). The percent yields of these hydrochlorides are based on the per-O-trimethylsilylaldonamides given in Table 1.

Part II: "Synthesis and Some Chemistry of Seven-membered Lactams Derived from Carbohydrates"

1-Oximido-D-glucurono-6,2-lactone (46).

Sodium methoxide (5.4 g, 0.1 mole) was dissolved in methanol (150 mL) in a 250-mL Erlenmeyer flask with heating if necessary to dissolve the base. Hydroxylamine hydrochloride (19.1 g, 0.25 mole) was slowly added to the solution until the solution become acidic to pH paper. The mixture was still heated while the hydroxylamine hydrochloride was added and the precipitate removed by vacuum filtration. D-Glucurono-6,3-lactone (45, Aldrich Chemical Co., mainly β-anomer) (17.6 g, 0.1 mole) was slowly added to the hot methanol solution and then dissolved by boiling the reaction mixture for a few minutes. The reaction mixture was transfered to a 500-mL round-bottomed flask and the product crystallized. The product was removed by vacuum filtration, and the filtrate concentrated on a flash evaporator. The residue was washed with a small amount of methanol to give additional product, yield 16.7 g (87%): mp 147-155 °C (lit.[29] mp 143 °C); IR (KBr) 3300 cm^{-1} (OH) and 1735 cm^{-1} (lactone C=O); ^1H NMR (D_2O) for the E-isomer 46a (Figure 40) δ 7.50 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1), 4.75 (d, 1H, $J_{4,5}$ = 5.4 Hz, H-5), 4.65 (dd, 2H, $J_{1,2}$ = 5.1 Hz, $J_{4,5}$ = 5.4 Hz, H-2 & H-4), 4.56 (dd, 1H, H-3). The ^1H NMR of a sample of 46 in D_2O that was not heated was typically a mixture of E:Z (4:1). The ^1H NMR NMR spectrum of such a mixture is shown in Figure 41. Anal. Calcd for $C_6H_9NO_6$: C, 37.70; H, 4.75; N, 7.33. Found : C, 37.44; H, 4.73; N, 7.15.

ε-L-Gulonolactam (48).

Acetyl chloride (1 mL) was added to cold (5 °C) reagent grade methanol (150 mL) in a pressure bottle for in situ HCl generation. The solution was then brought to room temperature and to it was added (46) (2.1 g, 11 mMol) and 10% Pd/C (1.2 g). The reaction bottle was put in the Parr Shaker, and after flushing with hydrogen three times the hydrogen gas pressure was maintained at about 50 psi overnight. After the reduction was completed, catalyst was removed by vacuum filtration and the solvent removed on a rotary evaporator to give a very hydroscopic product in quantitative yield. The hydroscopic product 47 was redissolved in methanol (100 mL) in a 250-mL round-bottomed flask, and to this was added triethylamine (2 mL, 22 mMol) dropwise with stirring. During this addition, precipitation of the product occurred. The reaction mixture was concentrated to dryness, and the residue was triturated with ethanol (20 mL) to give crystalline 48 (1.75 g, 90%): mp 195 °C (lit.[29] 195 °C); IR (KBr) 3360 cm^{-1} (OH), 1656 cm^{-1} (lactam C=O); ^1H NMR (D_2O) δ 4.78 (d, 1H, $J_{2,3}$ = 3.9 Hz, H-2), 4.06 (d, 1H, $J_{2,3}$ = 3.9 Hz, H-3), 3.99 (d, 1h, $J_{4,5}$ = 3.9 Hz, H-4), 3.79 (q, 1H, $J_{4,5}$ = 3.9 Hz, H-5), 3.65 (m, 1H, $J_{6a,6b}$ = 12 Hz, H-6a), 3.42 (m, 1H, $J_{6a,6b}$ =12 Hz, H-6b); ^{13}C NMR (D_2O) δ 180 (C=O), 78 (C-2), 75 (C-3), 73 (C-4 & C-5), 44 (C-6). Anal. Calcd for $C_6H_{11}NO_5$: C, 40.67; H, 6.26; N, 7.90. Found : C, 40.57; H, 6.28; N, 7.88.

2,3,4,5-Tetra-O-acetyl-ε-L-gulonolactam (63).

To a 100-mL round-bottomed flask equipped with a magnetic stirrer was added pyridine (30 mL) and acetic anhydride (6 mL). ε-L-Gulonolactam (48) (1.0 g, 5.6 mMol) was added to the acetylation reagents and the flask stoppered and contents stirred at room temperature

overnight. During this time, all the crystals of 48 dissolved. The acetylation reagents were removed by short path vacuum distillation at about 45 °C. The product was washed with chloroform, and any residue that was not soluble in chloroform was removed by filtration. The chloroform was evaporated, and the product was recrystallized from chloroform-hexane to give 63 (1.8 g, 92 %): mp 213-215 °C (lit.[29] 215 °C); IR (KBr) 3230 cm^{-1} (N-H), 1740 cm^{-1} (ester C=O), and 1645 cm^{-1} (lactam C=O); ^1H NMR ($CDCl_3$) δ 5.86 (t, 1H, N-H), 5.73 (s, 1H, H-2), 5.24 (m, 2H, $J_{3,4}$ = 3.3 Hz, $J_{4,5}$ = 2.1 Hz, H-3 & H-4), 4.81 (m, 1H, $J_{4,5}$ = 2.1 Hz, $J_{5,6a}$ = 4.5 Hz, $J_{5,6b}$ = 5.4 Hz, H-5); 3.50 (m, 2H, $J_{5,6a}$= 4.5 Hz, $J_{5,6b}$ = 5.4 Hz, $J_{6a,6b}$ = 15.6 Hz, H-6a & H-6b); ^{13}C NMR ($CDCl_3$) δ 170 (C-1), 69.5 (C-2 & C-3), 68.3 (C-4), 67.5 (C-5); 38.7 (C-6). Anal. Calcd for $C_{14}H_{19}NO_9$ 1/2 H_2O : C, 47.46; H, 5.69; N, 3.95. Found : C, 47.66; H, 5.42; N, 3.95.

(3S,4R,5R,6S)-2,3,4,5,6-Penta-O-acetylazacycloheptene (65).

To a small sample vial equipped with a small stirring bar was added 2,3,4,5-tetra-O-acetyl-ε-L-gulonolactam (63) (0.4 g) and acetic anhydride (10 mL). A small piece of Nafion membrane (ca. 1 cm x 2 cm) was added to the sample vial. The progress of the acetylation was monitored by ^1H NMR at 60 MHz below 4 ppm noting disappearance of the N-H at δ= 6.3 ppm from 63. After 24 h, the reaction was complete. The product, which was general not stable when solvent was removed, was used in the next step (base-catalyzed elimination) without further purification.

(5R,6S)-2,3,5,6-Tetra-O-acetyl-1,3-azacycloheptadiene (68).

The crude acetic anhydride solution of (3S,4R,5R,6S)-2,3,4,5,6-penta-O-acetylazacyclohetene (65) from the previous reaction was

heated at 65 °C for 36 h in the presence of anhydrous sodium acetate (0.3 g). The course of this reaction was monitored by ^{1}H NMR at 60 MHz NMR below 4 ppm by noting the disappearance of the H-3 singlet of 65 (δ = 5.7 ppm) and the appearance of the H-4 doublet of 68 (δ= 6.0 ppm). After 36 h, the undissolved base was removed by vacuum filtration, the solvent was removed at ca. 50 °C under reduced pressure (vacuum pump), and the residue washed with chloroform (20 mL). The chloroform was then removed by flash evaporation, and the residue further dried in a dessicator to give 1.0 g of 67 (quant): ^{1}H NMR ($CDCl_3$) δ 6.03 (d, 1H, $J_{4,5}$ = 4.8 Hz, H-4), 5.54 (dd, 1H, $J_{4,5}$ = 4.8 Hz, $J_{5,6}$ = 6.9 Hz, H-5), 5.26 (m, 1H, $J_{5,6}$ = 6.9 Hz, $J_{6,7a}$ = 3.3 Hz, $J_{6,7b}$ = 3.9 Hz, H-6), 4.06 (dd, 1H, $J_{6,7a}$=3.3 Hz, $J_{7a,7b}$= 15.3 Hz, H-7a), 3.94 (dd, 1H, $J_{6,7b}$= 3.9 Hz, $J_{7a,7b}$= 15.3 Hz, H7-b); ^{13}C NMR ($CDCl_3$) δ 171.1 (C-2), 123.7 (C-3), 123.6 (C-4), 75.9 (C-5), 69.8 (C-6), 43.0 (C-7).

(5R)-2,3,5-Tri-O-acetyl-1,3,6-azacycloheptatriene (70).

Compound 68 obtained from the previous reaction was used directly in this step. In a small sample vial equipped with a tiny magnetic stirring bar was added compound 67 in chloroform. Nitrogen was used to evaporate the chloroform, and the sample further dried in a vacuum dessicator. To the sample vial was added dimethyl sulfoxide (3 mL) and a dimethyl sulfoxide solution (3 mL) containing potassium tert-butoxide (120 mg). The reaction mixture was kept at room temperature for 2 h after which time the reaction was complete. The course of the reaction was monitored by ^{1}H NMR at 60 MHz by noting the disappearance of the H-4 doublet from 68 (δ = 6.0 ppm) and the appearance of the H-4 doublet from 70 (δ = 6.5 ppm). A few drops of acetic acid were then added to the reaction mixture to neutralize the base. The bulk of the

solvent was removed under reduced pressure (vacuum pump). Chloroform (10 mL) was added to extract the product from the residue. A small amount of suspended precipitate was removed by filtration. ^{1}H NMR ($CDCl_3$) at 300 MHz showed the product to be a mixture of two components in a ratio of 2:1 (Figure 51). The major product was assigned the structure of 2,3,4-tri-O-acetyl-1,3,5-azacyclohetatriene (69) based on the ^{1}H NMR spectrum ($CDCl_3$) δ 6.25 (s, 1H, H-4), 6.09 (t, 1H, $J_{6,7}$ = 4.2 Hz, H-6), 4.33 (broad, 2H, H-7). However, 69 was unstable and precipitated from the solution as a black amorphous solid. The minor product (5R)-2,3,5-tri-O-acetyl-1,3,6-azacycloheptatriene (70) was stable in $CDCl_3$ and gave the following ^{1}H NMR spectrum: ($CDCl_3$) δ 7.01 (d, 1H, $J_{6,7}$ = 9.9 Hz, H-6), 5.85 (d, 1H, $J_{6,7}$ = 9.9 Hz, H-7), 5.64 (d, 1H, $J_{4,5}$ = 4.5 Hz, H-4); 5.10 (d, 1H, $J_{4,5}$ = 4.5 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 165 (C-2), 144 (C-3), 127 (C-4), 113 (C-6), 112 (C-7), 71 (C-5); EI Mass spectrum has shown molecular ion M/e = 267.

(5R)-3,5-Dihydroxy-2-oxo-3,6-azacycloheptadiene (71).

Compound 70 from the previous reaction was dissolved in deuterium oxide (1 mL) and acetic acid-d_6 (1 mL). The hydrolysis reaction mixture was kept at 50 °C for 24 h, and solvents were removed by lyophilyzation to give an amorphous product 71: ^{1}H NMR (D_2O) δ 7.01 (d, 1H, $J_{4,5}$ = 10.3 Hz, H-4), 6.94 (dd, 1H, $J_{5,6}$ = 2.6 Hz, $J_{6,7}$ = 13.1 Hz, H-6), 6.88 (d, 1H, $J_{6,7}$ = 13.1 Hz , H-7), 5.94 (dd, 1H, $J_{4,5}$ = 10.3 Hz, $J_{5,6}$ = 2.6 Hz, H-5); ^{13}C NMR (CD_3COOD) δ 145, 138, 135, 115 (C-4 to C-7 unassigned); UV spectrum of 71 in H_2O was obtained on a Varian Cary 17 spectrophotometer λ_{max} = 280 nm, ε = 700.

1-Oximido-D-galacturonic acid (50).

The procedure used to prepare 50 was the same as that described for 46. To a 250-mL Erlenmeyer flask equipped with a magnetic stirrer was added hydroxylamine hydrochloride (7.65 g, 0.11 mol) and ethanol (100 mL). To this mixture was added anhydrous sodium acetate (8.84 g, 0.065 mole). The insoluble sodium chloride was removed by vacuum filtration, and D-galacturonic acid monohydrate (49, 10.6 g, 0.05 mol) was added to the above solution. The reaction mixture was then brought to boiling for a few minutes, transferred to a 250-mL round-bottomed flask, and kept at room temperature overnight. The product crystallized during this time and was isolated by vacuum filtration to give 50 (6.8 g, 65%), mp 156-163 °C; IR (KBr) 3360-3240 cm^{-1} (broad, OH), 1715 cm^{-1} (acid C=O); ^1H NMR (D_2O) δ 7.62 (d, 1H, $J_{1,2}$ = 2.4 Hz, H-1), 4.58 (q, 1H, $J_{1,2}$ = 2.4 Hz, H-2), 4.18 (s, 1H, H-5), 4.15 (m, 1H, $J_{3,4}$ = 9.6 Hz, H-4), 3.55 (d, 1H, $J_{3,4}$ = 9.6 Hz, H-3); The ^1H NMR of a sample of 50 in D_2O also showed a mixture of E : Z (4:1); Anal. Calcd for $C_6H_{11}NO_7$: C, 34.46; H, 5.30; N, 6.70. Found : C, 34.35; H, 5.35; N, 6.69.

Methyl 1-Amino-1-deoxy-D-galacturonate Hydrochloride (51).

Acetyl chloride (1 mL) was added to cold (5 °C) reagent grade methanol (150 mL) in a pressure bottle for in situ HCl generation. The solution was allowed to cool to room temperature, and to the above solution 50 (2.1 g, 11 mMol) and 10% Pd/C (1.2 g) were added. After flushing the reaction bottle with H_2 gas three times, the hydrogen gas pressure was maintained at about 50 psi overnight while the pressure bottle was continuously shaken. After removal of the catalyst by vacuum filtration, the filtrate was concentrated on a rotary evaporator

to dryness, and the crystals washed with a small amount of methanol to give 1.9 g (81 %) of 51: mp 169-173 °C; IR (KBr) 3360-3280 cm^{-1} (OH), 1725 cm^{-1} (ester C=O); ^1H NMR (D_2O) δ 4.63 (d, 1H, $J_{4,5}$ = 0.6 Hz, H-5), 4.20 (dd, 1H, $J_{1,2}$ = 5.4 Hz, $J_{2,3}$ = 0.8 Hz, H-2), 4.1 (dd, 1H, $J_{3,4}$ = 9.6 Hz, $J_{4,5}$ = 0.6 Hz, H-4), 3.8 (s, 3H, OCH_3), 3.7 (dd, 1H, $J_{2,3}$ = 0.8 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 3.2 (d, 2H, $J_{1,2}$ = 5.4 Hz, H-1). Anal. Calcd for $C_7H_{16}NO_6Cl$: C, 34.22; H, 6.52; N, 5.70. Found : C, 34.00; H, 6.58; N, 5.62.

ε-L-Galactonolactam (52).

To a 250-mL round-bottomed flask equipped with a magnetic stirrer was added 51 (2 g, 11.3 mMol), methanol (150 mL), and triethylamine (3.14 mL, 22.6 mMol). The reaction mixture was then refluxed overnight, cooled to room temperature, and the insoluble product isolated by vacuum filtration and washed with cold methanol (10 mL) to give 52 (1.2 g, 83%): mp 186-190 °C; IR (KBr) 3400-3240 cm^{-1} (OH), 1640 cm^{-1} (lactam C=O); ^1H NMR (D_2O) δ 4.46 (d, 1H, $J_{2,3}$ = 10.2 Hz, H-2), 3.88 (broad, 1H, H-4), 3.74 (m, 2H, $J_{2,3}$ = 10.2 Hz, H-3 & H-5), 3.52 & 3.15 (2d, 2H, $J_{6a,6b}$ = 16.2 Hz, H-6a & H-6b).

2,3,4,5-Tetra-O-acetyl-ε-L-galactonolactam (64).

To a 100-mL round-bottomed flask equipped with a magnetic stirrer was added 52 (0.36 g, 2 mMol), pyridine (10 mL), and acetic anhydride (2 mL). The reaction mixture was stirred at room temperature overnight, during which time all the crystals dissolved. The same work-up procedure was used as for 63 to give 64 (0.58 g, 86%): mp 165 °C; IR (KBr) 3300 cm^{-1} (N-H), 1730 cm^{-1} (ester C=O) and 1650 cm^{-1} (lactam C=O); ^1H NMR ($CDCl_3$) δ 6.61 (broad, 1H, N-H), 5.61 (d, 1H, $J_{2,3}$ = 8.4 Hz, H-2), 5.50 (dd, 1H, $J_{2,3}$ = 8.4 Hz, $J_{3,4}$ = 2.1 Hz, H-3), 5.35 (dd,

1H, $J_{3,4}$ = 2.1 Hz, $J_{4,5}$ = 7.2 Hz, H-4), 4.93 (broad, 1H, H-5), 3.78 & 3.47 (m, 2H, $J_{5,6}$ = 5.4 Hz, $J_{6a,6b}$ = 15.9 Hz, H-6a & H-6b); Anal. Calcd for $C_{14}H_{19}NO_9$ 1/2 H_2O : C, 47.46; H, 5.69; N, 3.95. Found : C, 47.87; H, 5.40; N, 3.93.

(3S,4S,5R,6S)-2,3,4,5,6-Penta-O-acetylazacycloheptene (66).

To a 50-mL Erlenmeyer flask equipped with a magnetic stirrer was added 64 (0.43 g, 1.25 mMol), acetic anhydride (15 mL), and 5 mL of cationic resin (Dowex 50W-X8, H^+, 20-50 mesh). The reaction mixture was then stirred at room temperature overnight. During this time, the progress of the reaction was monitored directly by running ^1H NMR spectra below 4 ppm. After removal of the catalyst and the solvent, the amorphous residue was washed with a small amount of $CDCl_3$; ^1H NMR ($CDCl_3$) δ 5.6 (s, 2H, H-2 & H-5), 5.1 (s, 2H, H-3 & H-4), 5.0 & 3.6 (2d, 2H, H-1). This product appears to rapidly convert to starting material upon standing.

Part III: "Synthesis Directed Toward the Preparation of Polyhydroxylated Polyamides"

Xylaric Acid (93).

D-Xylose (92) (101 g, 0.673 mol) and deionized water (78 mL) were added to a 1-liter 3-neck round-bottomed flask equipped with a thermometer, a condensor, and a magnetic stirrer. Concentrated nitric acid (70%, 203 mL, 3.19 mol) was added to the flask, and the contents stirred. D-Xylose (92) dissolved after several minutes, and the reaction mixture was warmed slowly in a water bath. At about 60 °C the reaction became exothermic and the temperature began to rise rapidly. The reaction mixture was quickly put into an ice bath until the reaction mixture was no longer warming on its own. The reaction mixture was then allowed to remain at room temperature for 15 min and then put

back into the oil bath where the temperature was brought slowly to 60 °C and kept at this temperature for 2 h. The temperature was then raised to 90 °C over 30 min and kept at 90 °C for no more than 10 min. The reaction mixture was then cooled to 60 °C and 2-propanol (200 mL) was added in 20 mL portions for the first 100 mL. The first addition of 20 mL of 2-propanol raised the temperature to 100 °C. A readily available icebath was used to cool the reaction mixture. The last 100 mL of 2-propanol was added more rapidly. The reaction mixture was then stirred for 15 min at 55-60 °C, diluted with water (100 mL) and concentrated hydrochloric acid (10 mL) added followed by stirring at 60-70 °C for 30 min. The reaction mixture was concentrated on the rotary evaporator at 50-70 °C until it became a thick syrup or semi-crystalline mass. The resulting syrup was then placed in the refrigerator overnight. Deionized water (40 mL) was added to the syrup, and the mixture again concentrated on the rotary evaporator. The resulting syrup was refrigerated overnight again, and during this time a small portion of the syrup crystallized out in the flask. Reagent grade acetone (50 mL) was added to the flask, and the mixture stirred at room temperature to complete the crystallization. The product was isolated by vacuum filtration to give 42 g (35%): mp 142-145 °C (lit.[51] mp 145-147 °C); IR (KBr) 3500-2500 cm^{-1} (OH), 1710 cm^{-1} (acid C=O); ^{1}H NMR (DMSO-d_6) δ 4.06 (d, 2H, $J_{2,3} = J_{3,4}$ = 3.9 Hz, H-2 & H-4), 4.00 (t, 1H, $J_{2,3} = J_{3,4}$ = 3.9 Hz, H-3); ^{13}C NMR (DMSO-d_6) δ 174 (C=O), 73 (C3), 71 (C2 & C4).

Mixed Methyl Esters of Xylaric Acid.

In a 250-mL round-bottomed flask equipped with a magnetic stirrer was added reagent grade methanol (150 mL), and the flask cooled to

5 °C. Acetyl chloride (5 mL) was added to the cold methanol for *in situ* HCl generation. The solution was allowed to cool to room temperature, and to it was added xylaric acid (93) (18 g, 0.1 mole) all at once. The reaction mixture was refluxed overnight, and the slightly yellow solution was then concentrated to a syrup. The syrup was dissolved in methanol (50 mL) and the solution stirred overnight, and then concentrated to a syrup. Residual water was azeotroped with benzene at reduced pressure. The resulting thick syrup was further dried at room temperature under vacuum (vacuum pump) overnight to give a syrup which did not crystallize; ^{1}H NMR (DMSO-d_6) showed the product to be a mixture of dimethyl xylarate (94a) and methyl xylaro-1,4-lactone (94b) in a ratio of 5:3 (Figure 94). The major product was assigned the structure of 94a; ^{1}H NMR (DMSO-d_6) δ 4.12 (d, 2H, $J_{2,3} = J_{3,4} = 4.5$ Hz, H-2 & H-4), 3.90 (t, 1H, $J_{2,3} = J_{3,4} = 4.5$ Hz, H-3), 3.63 (s, 6H, OCH_3). This product was used without further purification for the polycondensation with diamines.

Galactaric Acid (90).

A solution of lactose (62.5 g, 0.18 mole), concentrated nitric acid (100 mL), and water (37.5 mL) in a 1-liter 3-neck, round-bottomed flask equipped with a thermometer, a magnetic stirrer, and a condenser was heated to 70 °C while stirring. The solution appeared transparent and then dark yellow as the reaction became exothermic at 70 °C. The reaction flask was quickly removed from the heating mantle and swirled in an ice water bath until the boiling subsided. The flask was returned to the heating mantle, the solution was heated to 85 °C, and the heating mantle was removed. The temperature of the solution continued to rise to about 100 °C over 30 minutes on its own.

During this time, the product began to precipitate. After being maintained for 1 h at 100 °C without the benefit of external heating, the temperature of the solution began to drop, and when the temperature reached 85 °C, the reaction mixture was cooled to 50 °C by swirling the flask in an ice water bath. When the solution reached 50 °C, the contents were transfered to a 500-mL round-bottomed flask and concentrated to half of its volume at 50 °C. The mixture was filtered, and the solid product washed with water and dried overnight in a vacuum dessicator. The yield of 90 was 12.8 g (33.5%): mp 223 °C (decomp.) (lit.[50] mp 211-212 °C); IR (KBr) 3260-2500 cm^{-1} (OH), 1710 cm^{-1} (acid C=O); ^1H NMR (DMSO-d_6) δ 7.5 (broad, OH), 4.2 (s, 2H, H-2 & H-5), 3.67 (s, 2H, H-3 & H-4).

Dimethyl Galactarate (91).

Galactaric acid (90) (10 g, 0.048 mol), methanol (300 mL), and concentrated sulfuric acid (1 mL) was added to a 500 mL round-bottomed flask. The contents of the flask were refluxed overnight with stirring. During this time, no solid appeared to dissolve. The reaction mixture was then allowed to cool to room temperature, and filtration gave a powder, white solid 9.5 g (83%), purified by recrystallizing from hot methanol containing triethylamine: mp 220-222 °C (lit.[50] mp 205 °C); IR (KBr) 3420-3260 cm^{-1} (OH), 1720 cm^{-1} (ester C=O); ^1H NMR (D_2O) δ 4.5 (s, 2H, H-2 & H-5), 3.98 (s, 2H, H-3 & H-4), 3.7 (s, 6H, OCH_3).

Mixed Methyl Esters of D-Glucaric (Saccharic) Acid.

A suspension of D-saccharic acid as its calcium salt (95) (30 g, 105.6 mMol) in 1 liter of water was swirled with fresh ion exchange resin (Amberlite IR-120, H^+ form, 700 mL) in a 2-L Erlenmeyer flask

until all the calcium salt dissolved. The resin was removed by vacuum filtration, and the filtrate concentrated at 50-60 ^{o}C to a thin syrup. The syrup was stored in the freezer overnight, then frozen with dry ice in acetone and lyophilized to a slightly yellow, thick, sticky mass which appeared to retain some water. The syrup was dried in the lyophilizer for two more days and did not crystallize from either acetone or ethanol, with a yield 16.6 g of 96 (82%). Crude D-glucaro-6,3-lactone (96) was used directly in the esterification without further purification. To a 500-mL round-bottomed flask, equipped with a condenser and a magnetic stirrer, was added methanol (200 mL). The flask was cooled to 5 ^{o}C by putting the flask in an ice-water bath. HCl was generated *in situ* by slowly adding acetyl chloride (20 mL) to the cold methanol solution and allowing the solution to warm up to room temperature by itself. Crude D-glucaro-6,3-lactone (96) in methanol (50 mL) was added to the methanolic HCl, and the reaction mixture was refluxed overnight. After the removal of the solvent, methanolic HCl (100 mL methanol with 1 mL acetyl chloride) was added to the residue, and the reaction mixture stirred overnight to ensure that esterification was complete. The reaction mixture was concentrated on a rotary evaporator to dryness, and benzene was added to the residue to azeotrope residual water; the yield of syrupy ester/lactone was 18.8 g (86%), represented as methyl D-glucaro-6,3-lactone (97). IR spectrum showed absorption peaks at 3200-3500 cm^{-1} (OH), 1775 cm^{-1} (lactone C=O), and 1735 cm^{-1} (ester C=O). This product was dissolved in methanol to make a 200 mL solution, which was used in the polycondensation with diamines.

2,3,4,5-Tetra-O-TMS-ε-L-gulonolactam (110).

ε-L-gulonolactam (48) (1.0 g, 5.6 mMol) was added while stirring to the mixture of HMDS (10 mL) and TMCS (4 mL) in pyridine (40 mL). The reaction mixture was stirred at room temperature for two days, then filtered through a sintered glass funnel and concentrated to dryness under reduced pressure to give a syrupy product (2.49 g, 95 %): IR (neat) 3220 cm^{-1} (N-H), 1670 cm^{-1} (lactam C=O); GC/MS of trimethylsilylated 48 indicated a mixture compound of a major product (68%, 7.2 min) and several minor products (32%, 6.88 min, 7.15 min, 7.5 min). The major product was 2,3,4,5-tetra-O-TMS-ε-L-gulonolactam (110) with m/e at 465 (M), 450 (M-15), 375 (M-90), 360 (M-90-15), and 285 (M-90-90). Two minor products (6.88 and 7.5 min) were assigned as tri-O-TMS-ε-L-gulonolactams with m/e at 393 (M), 378 (M-15), 375 (M-18), and 303 (M-90). The peak at 7.15 min corresponding to the tetra-O-TMS-N-TMS-ε-L-gulonolactam with m/e at 423 (M-72-14-28), 333 (423-90); ^{1}H NMR ($CDCl_3$) δ 5.59 4.55, 3.71, 3.62, and 3.44 (each a broad singlet, unassigned ring protons H-2 to H-6); ^{13}C NMR ($CDCl_3$) δ 174.8 (C-1, 110), 76.2, 73.9, 71.0, 68.3 (C-2 to C-5 unassigned), and 41.6 (C-6).

2,3,4,5-Tetra-O-TMS-ε-L-galactonolactam (111).

ε-L-Galactonolactam (52) (0.5 g, 2.8 mMol) was added to a solution of pyridine (20 mL), HMDS (5 mL), and TMCS (2 mL). The reaction mixture was stirred at room temperature for two days. The reaction mixture was vacuum filtered to remove any undissolved salts, and the filtrate was concentrated under reduced pressure to give 1.2 g of 111 (93 %): mp 107-108 °C; IR (KBr) 3220 cm^{-1} (NH), 1670 cm^{-1} (lactam C=O); GC/Ms (electron impact) showed the presence of one compound

with peaks at 465 (M), 450 (M-15), and 378 (M-87); ^{1}H NMR ($CDCl_3$) δ 6.19 (t, N-H), 4.60-3.70 (4H, complex multiplets, H-2 to H-5), 3.56 and 2.83 (2H, each complex multiplets from H-6a and H6b); Anal. Calcd for $C_{18}H_{43}NO_5Si_4$: C, 46.41; H, 9.30; N, 3.01. Found : C, 46.48; H, 9.33; N, 2.97.

Hexamethylenegalactaramide Pentamer (98).

1,6-Hexanediamine (98% pure) was purchased from Aldrich Chemical Company. It was purified by vacuum distillation at <60 °C, 0.05 mm Hg. Dimethyl galactarate (91) (5.23 g, 22 mMol) and methanol (150 mL) were added to a 250-mL round-bottomed flask equipped with a magnetic stirrer. To the mixture was added triethylamine (1 mL), and the reaction mixture refluxed for 20 min. During this time, part of the dimethyl galactarate (91) dissolved. To the mixture was added 14.5 mL of a 1.7 M methanol solution of 1,6-hexanediamine (24 mMol) in methanol. Within 10 min the contents of the flask were all mixed in the solution, and then a white solid began to precipitate from the reaction mixture. The mixture was then refluxed for 2 h. After the reaction mixture was cooled to room temperature, the product was isolated by vacuum filtration and washed with a small amount of methanol to give 6.5 g of 98 (82% based on the total weight of monomers): mp > 220 °C (decomp.); IR (KBr) 3350 cm^{-1} (OH), 1640 cm^{-1} (C=O Amide I band), 1540 cm^{-1} (Amide II band); Anal. Calcd for the Pentamer $C_{30}H_{60}N_6O_{12}$: C, 51.71; H, 8.68; N, 12.06. Found : C, 51.50; H, 8.73; N, 12.18.

Poly(hexamethylenexylaramide) (99).

A methanol solution (60 mL) of mixed methyl esters of xylaric acid (94a and 94b) (4.6 g, ca. 22 mMol) was added to a 250-mL

round-bottomed flask equipped with a magnetic stirrer. To this solution was added 14.5 mL of a methanol solution containing 1,6-hexanediamine 24 mMol) and triethylamine (1 mL). The reaction mixture was refluxed for 1 h. During this time, precipitation started within 10 min. After the reaction mixture was cooled to room temperature, the product was isolated by vacuum filtration and washed with a small amount of methanol to give 5.2 g of 99 (72 % based on the total weight of the monomers): mp 198-202 °C; IR (KBr) 3410 & 3290 cm^{-1} (OH), 1640 cm^{-1} (C=O Amide I band), 1545 cm^{-1} (Amide II band); Anal. Calcd for $[C_{11}H_{20}N_2O_5]_x$: C, 50.76; H, 7.74; N, 10.76. Found : C, 50.52; H, 7.81; N, 10.66.

Poly(hexamethylene-D-glucaramide) (100).

To a 250-mL round-bottomed flask was added a 50 mL methanol solution of mixed methyl esters of D-glucaric acid represented as methyl D-glucaro-6,3-lactone (97) (4.7 g, ca. 22.8 mMol), triethylamine (1 mL), and 15 mL of a 1.7 M methanol solution of 1,6-hexanediamine (25.5 mMol). A white solid precipitate began to form immediately. The reaction mixture was refluxed for 2 h. After the reaction mixture was cooled to room temperature, the product was isolated by vacuum filtration and washed with a small amount of methanol to give 5.5 g of 100 (72% based on the total weight of the monomers): mp 190-205 °C; IR (KBr) 3300 cm^{-1} (broad, OH), 1635 cm^{-1} (C=O Amide I band), 1530 cm^{-1} (Amide II band). Anal. Calcd for $[C_{12}H_{22}N_2O_6]_x$: C, 49.65; H, 7.64; N, 9.65. Found : C, 49.70; H, 7.90; N, 10.20.

Poly(2-methylpentamethylenegalactaramide) (101).

To a 250-mL round-bottomed flask equipped with a magnetic stirrer was added dimethyl galactarate (91) (5.23 g, 22 mMol), methanol

(150 mL), and triethylamine (1 mL). The reaction mixture was then refluxed for 30 min. During this time, part of the dimethyl galactarate (91) dissolved. 2-Methylpentamethylenediamine (3.3 mL, 2.88 g, 24.8 mMol) obtained from E. I. DuPont De Nemours & Co., Inc., 98% pure with 2% of isomers, was added to the reaction mixture and the mixture refluxed for 2 h. The contents of the flask dissolved within 10 min and then precipitation of white solid in 20 min. The reaction mixture was cooled to room temperature, and the product was isolated by vacuum filtration and washed with a small amount of methanol to give 7 g of 101 (86% based on the total weight of the monomers): mp 204-210 ^{o}C; IR (KBr) 3300 cm^{-1} (broad, OH), 1625 cm^{-1} (C=O Amide I band), 1525 cm^{-1} (Amide II band). Anal. Calcd for $[C_{12}H_{22}N_2O_6]_x$: C, 49.65; H, 7.64; N, 9.65. Found : C, 49.57; H, 8.00; N, 10.03.

Poly(2-methylpentamethylenexylaramide) (102).

To a methanol solution (60 mL) of mixed methyl esters of xylaric acid (94a, 94b) (4.6 g, ca. 22 mMol) in a 250-mL round-bottomed flask equipped with a magnetic stirrer was added 2-methylpentamethylenediamine (3.3 mL, 2.88 g, 24.8 mMol) and triethylamine (1 mL). The reaction mixture was refluxed for 1 h. Precipitation of white solid began within 30 min. The reaction mixture was cooled to room temperature, and the product was isolated by vacuum filtration and washed with a small amount of methanol to give 2.3 g of 102 (31% based on the total weight of the monomers): mp 163-210 ^{o}C; IR (KBr) 3300 cm^{-1} (broad, OH), 1625 cm^{-1} (C=O Amide I band), 1535 cm^{-1} (Amide II band); Anal. Calcd for $[C_{11}H_{20}N_2O_5]_x$: C, 50.76; H, 7.74; N, 10.76. Found : C, 50.55; H, 7.81; N, 10.57.

Poly(2-methylpentamethylene-D-glucaramide) (103).

To a methanol solution (100 mL) of mixed methyl esters of D-glucaric acid represented as methyl D-glucaro-6,3-lactone (46) (5.0 g, ca. 25 mMol) in a 250-mL round-bottomed flask equipped with a magnetic stirrer was added 2-methylpentamethylenediamine (3.65 mL, 3.19 g, 27.5 mMol). The reaction mixture was then refluxed for 2 h with a syrupy precipitate starting to form within 10 min. After refluxing was completed, the solvent was decanted carefully to another flask. The syrupy material was dried in the desiccator to give a yellowish, glassy solid, which weighed 6.0 g of 103 (73% based on the total weight of the monomers): mp 75-80 °C; IR (KBr) 3320 cm^{-1} (broad,OH), 1650 cm^{-1} (C=O Amide I band), 1540 cm^{-1} (Amide II band); Anal. Calcd for $[C_{12}H_{22}N_2O_6]_x$: C, 49.65; H, 7.64; N, 9.65. Found : C, 49.68; H, 8.06; N, 10.40.

Dodecamethylenegalactaramide Pentamer (104).

1,12-Dodecanediamine (98% pure) was purchased from Aldrich Chemical Company. To a 250-mL round-bottomed flask equipped with a magnetic stirrer was added dimethyl galactarate (91) (5.23 g, 22 mMol), methanol (100 mL), and triethylamine (1 mL). The mixture was refluxed for 30 min. During this time, part of the dimethyl galactarate (91) dissolved in the solution. To the mixture was added a solution of 1,12-dodecanediamine (4.85 g, 24 mMol) in methanol (50 mL). The reaction mixture was refluxed for 2 h. After the reaction mixture was cooled to room temperature, the solid product was isolated by vacuum filtration and washed with a small amount of methanol to give 8.0 g of 104 (80% based on the total weight of the monomers): mp >240 °C (decomp.); IR (KBr) 3300 cm^{-1} (broad, OH), 1625 cm^{-1} (C=O Amide

I band), 1525 cm^{-1} (Amide II band); Anal. Calcd for the Pentamer $C_{48}H_{96}N_6O_{12}$: C, 60.73; H, 10.19; N, 8.85. Found : C, 60.90; H, 10.31; N, 8.96.

Poly(dodecamethylenexylaramide) (105).

To a 250-mL round-bottomed flask equipped with a magnetic stirrer was added a methanol solution (60 mL) of mixed methyl esters of xylaric acid (94a, 94b) (4.6 g, ca. 22 mMol) and a solution of 1,12-dodecanediamine (4.85 g, 24.2 mMol) in methanol (50 mL) and triethylamine (1 mL). The reaction mixture was refluxed for 1 h. During refluxing, precipitation started in 10 min. After the reaction mixture was cooled to room temperature, the solid product was isolated by vacuum filtration and was washed with a small amount of methanol to give 7 g of 105 (73% based on the total weight of the monomers): mp 208-220 °C (decomp.); IR (KBr) 3290 cm^{-1} (broad, OH), 1625 cm^{-1} (C=O Amide I band), 1530 cm^{-1} (Amide II band); Anal. Calcd for $[C_{17}H_{32}N_2O_5]_x$: C, 59.28; H, 9.36; N, 8.13. Found : C, 58.06; H, 9.23; N, 7.90.

Poly(dodecamethylene-D-glucaramide) (106).

To a 250-mL round-bottomed flask equipped with a magnetic stirrer was added a methanol solution (50 mL) of mixed methyl esters of D-glucaric acid represented as methyl D-glucaro-6,3-lactone (97) (4.7 g, ca. 22.8 mMol), triethylamine (1 mL), and a solution of 1,12-dodecanediamine (5.03 g, 25.1 mMol) in methanol (50 mL). The reaction mixture was then refluxed for 2 h. During refluxing, precipitation started in 10 min. After the reaction mixture was cooled to room temperature, the solid product was isolated by vacuum filtration and washed with a small amount of methanol to give 8.0 g of 106 (82% based on the total

weight of the monomers): mp 205 °C (decomp.); IR (KBr) 3300 cm^{-1} (broad, OH), 1640 cm^{-1} (C=O Amide I band), 1540 cm^{-1} (Amide II band); Anal. Calcd for $[C_{18}H_{34}N_2O_6]_x$: C, 57.73; H, 9.15; N, 7.48. Found : C, 57.82; H, 9.16; N, 7.46.

Octamethylenegalactaramide Nonamer (107).

1,8-Octanediamine (98% pure) was purchased from Aldrich Chemical Company. To a 250-mL round-bottomed flask equipped with a magnetic stirrer was added dimethyl galactarate (91) (5.23 g, 22 mMol), methanol (100 mL), and triethylamine (1 mL). The mixture was then refluxed for 30 min. A solution of 1,8-octanediamine (3.48 g, 24 mMol) in 50 mL of methanol was then added to the mixture, and refluxing was continued for 2 h. After the reaction mixture was cooled to room temperature, the solid product was isolated by vacuum filtration and washed with a small amount of methanol to give 6.2 g of 107 (72% based on the total weight of the monomers): mp >240 °C (decomp.); IR (KBr) 3310 cm^{-1} (broad, OH), 1680 cm^{-1} (C=O Amide I band), 1530 cm^{-1} (Amide II band); Anal. Calcd for the Nonamer $C_{64}H_{124}N_{10}O_{24}$: C, 54.22; H, 8.82; N, 9.88. Found : C, 54.19; H, 8.91; N,10.00.

Poly(octamethylenexylaramide) (108).

To a 250-mL round-bottomed flask equipped with a magnetic stirrer was added a methanol solution (60 mL) of mixed methyl esters of xylaric acid (94a, 94b) (4.6 g, ca. 22 mMol), triethylamine (1 mL), and 1,8-octanediamine (3.48 g, 24 mMol) in methanol (50 mL). The reaction mixture was then refluxed for 2 h. After the reaction mixture was cooled to room temperature, the solid product was isolated by vacuum filtration and washed with a small amount of methanol to give 6.0 g of 108 (74% based on the total weight of the monomers):

mp 203-207 °C (decomp.); IR (KBr) 3410 cm^{-1} (broad, OH), 1645 cm^{-1} (C=O Amide I band), 1540 cm^{-1} (Amide II band). Anal. Calcd for $[C_{13}H_{24}N_2O_5]_x$: C, 54.15; H, 8.39; N, 9.72. Found : C, 53,70; H, 8.46; N, 9.84.

Poly(octamethylene-D-glucaramide) (109).

To a 250-mL round-bottomed flask equipped with a magnetic stirrer was added a methanol solution (50 mL) of mixed methyl esters of D-glucaric acid represented as methyl D-glucaro-6,3-lactone (97) (4.7 g, 22.8 mMol), triethylamine (1 mL), and 1,8-octanediamine in methanol (50 mL). The reaction mixture was then refluxed for 2 h. After the reaction mixture was cooled to room temperature, the product was isolated by vacuum filtration and washed with a small amount of methanol to give 5.9 g of 109 (71% based on the total weight of the monomers): mp 195-200 °C (decomp.); IR (KBr) 3350 cm^{-1} (broad, OH), 1640 cm^{-1} (C=O Amide I band), 1545 cm^{-1} (Amide II band). Anal. Calcd for $[C_{14}H_{26}N_2O_6]_x$: C, 52.02; H, 8.23; N, 8.80. Found : C, 51.88; H, 8.30; N, 8.74.

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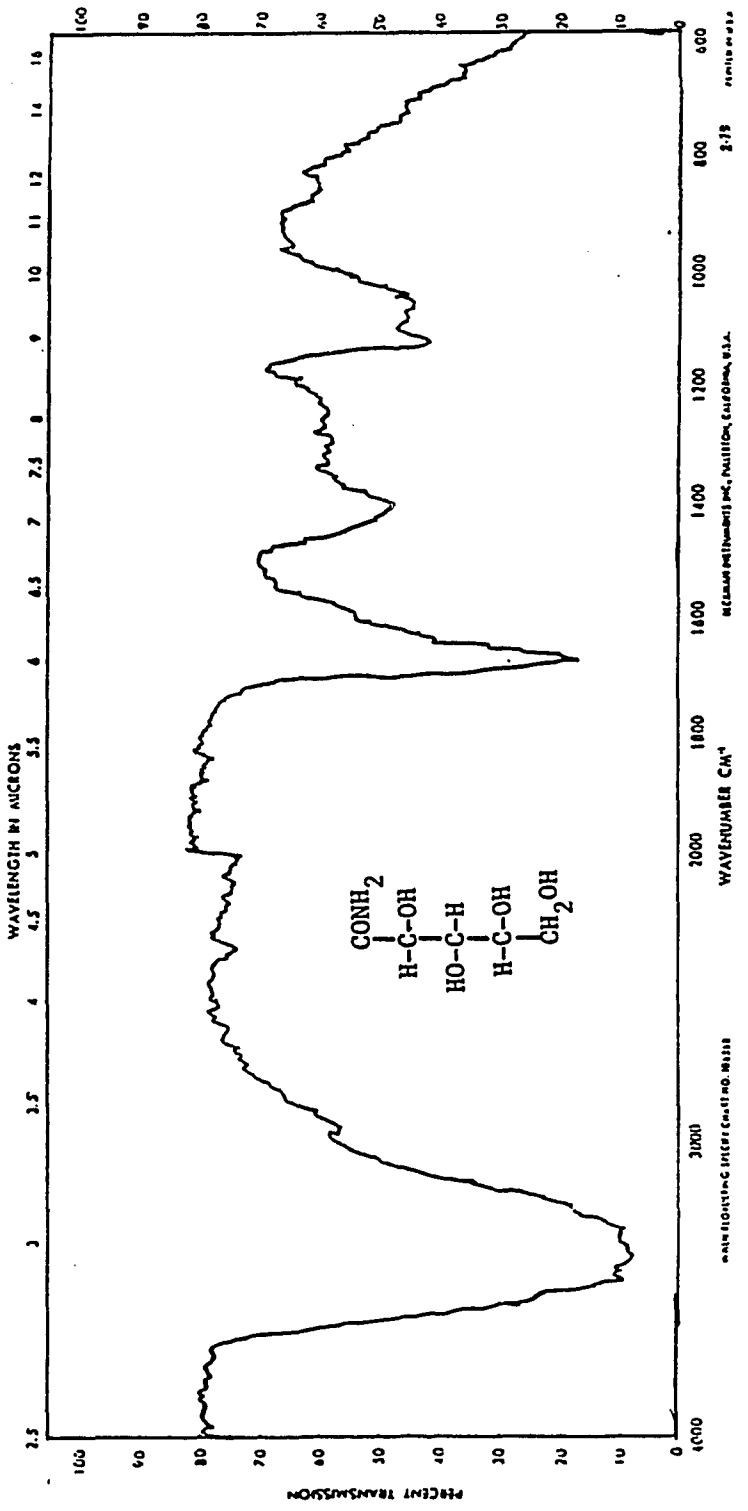

Figure 8. IR Spectrum of Compound 30 (KBr).

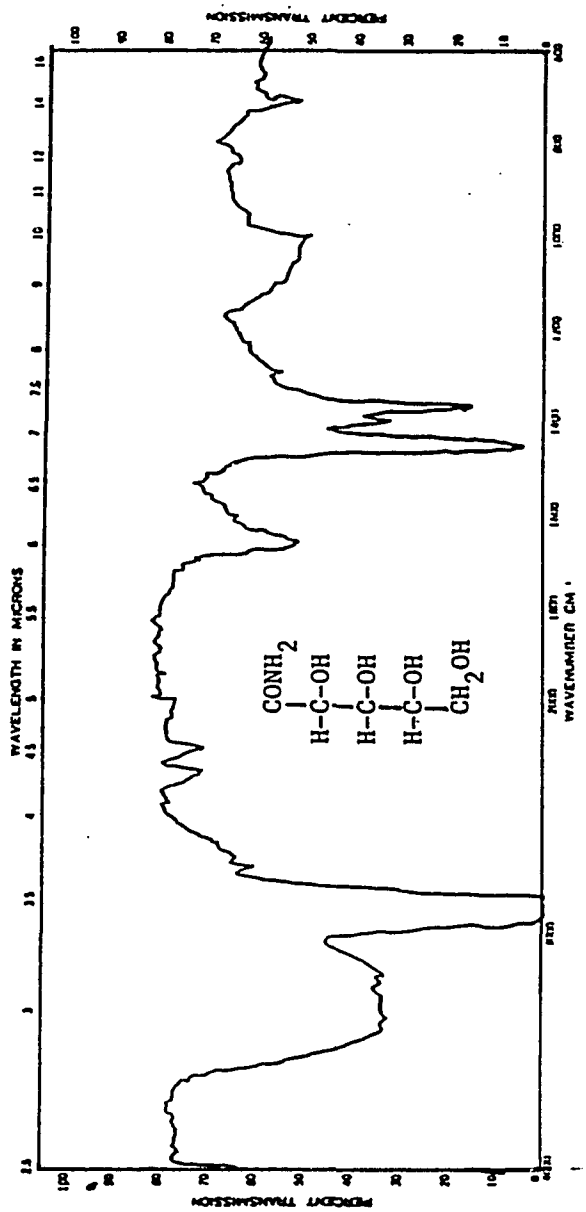

Figure 9. IR Spectrum of Compound 31 (Mineral Oil).

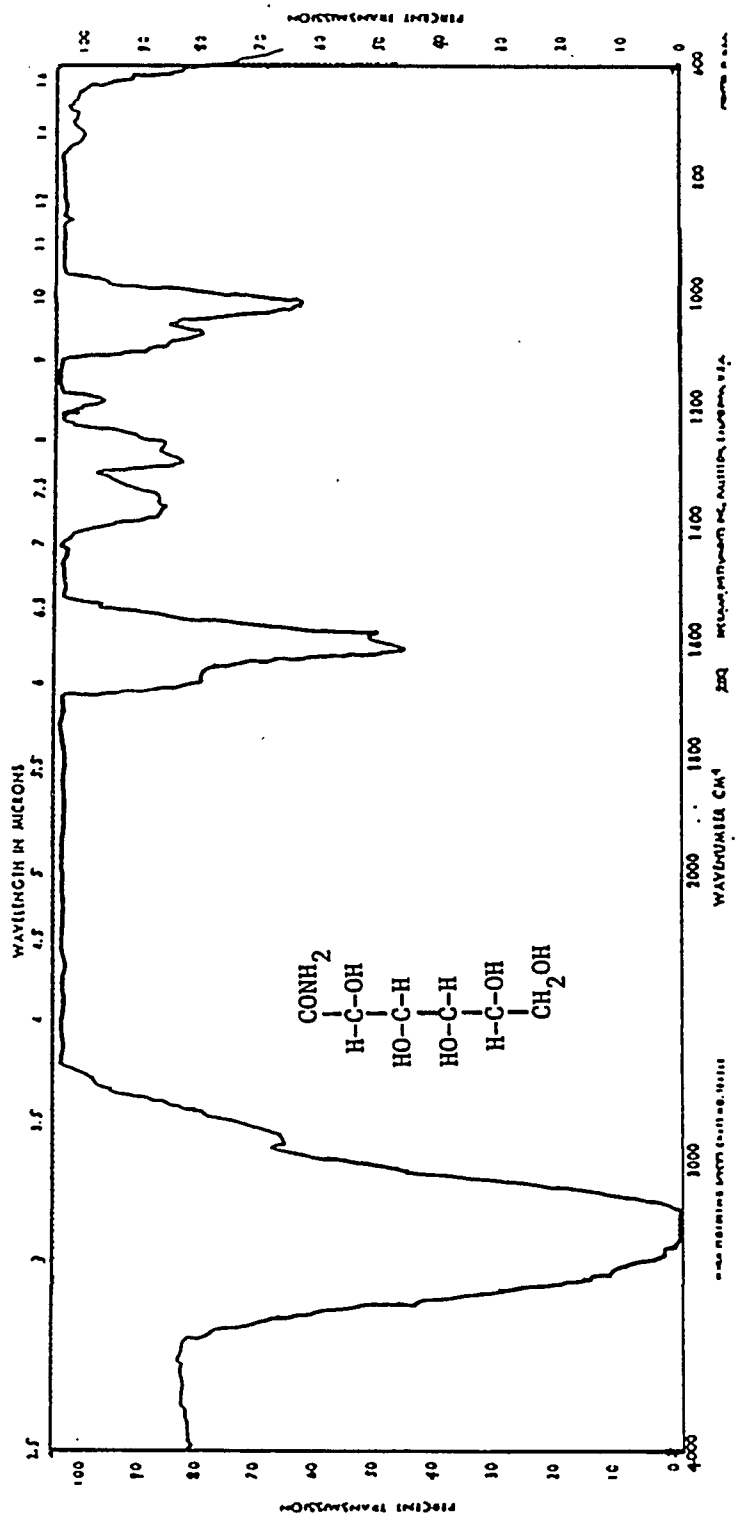

Figure 10. IR Spectrum of Compound 32 (KBr).

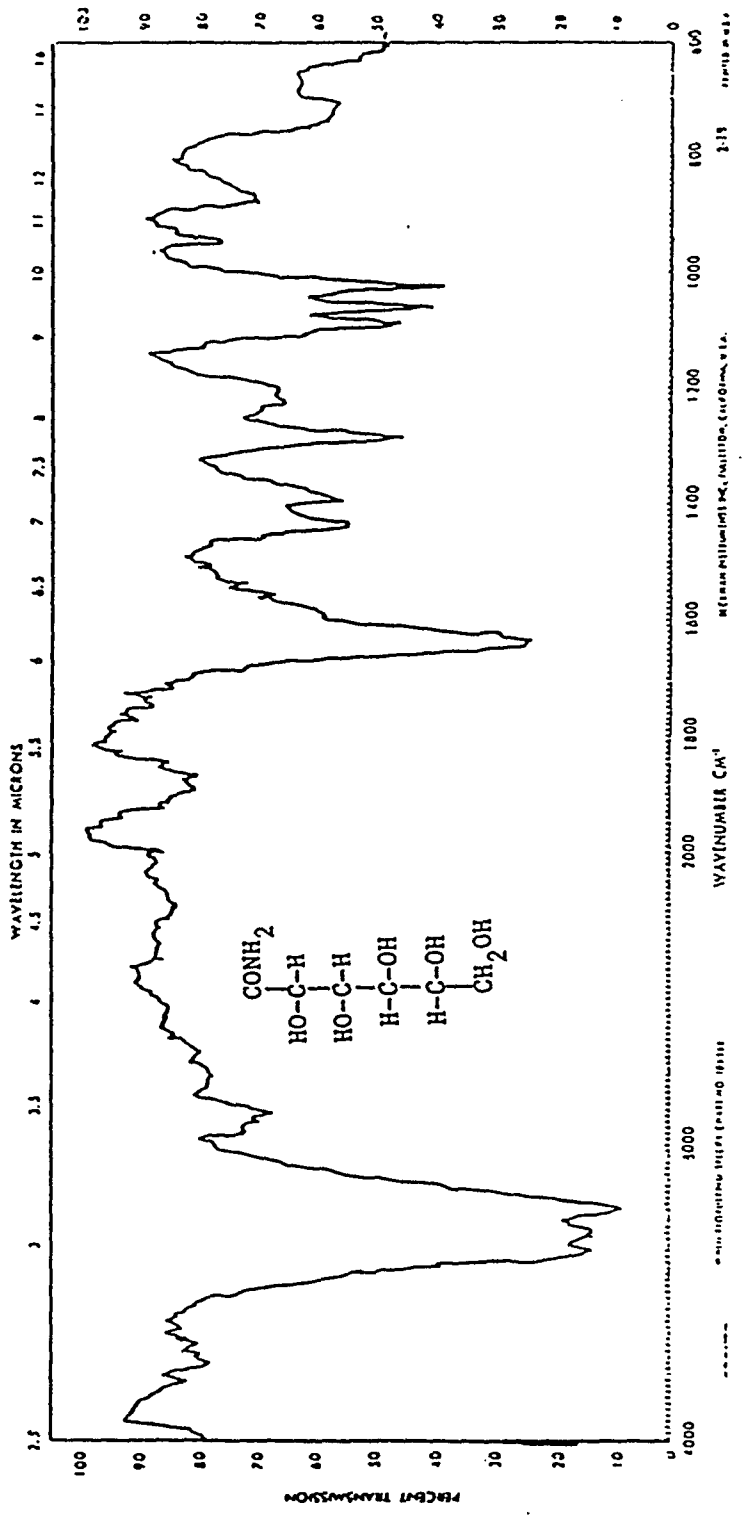

Figure 11. IR Spectrum of Compound 34 (KBr).

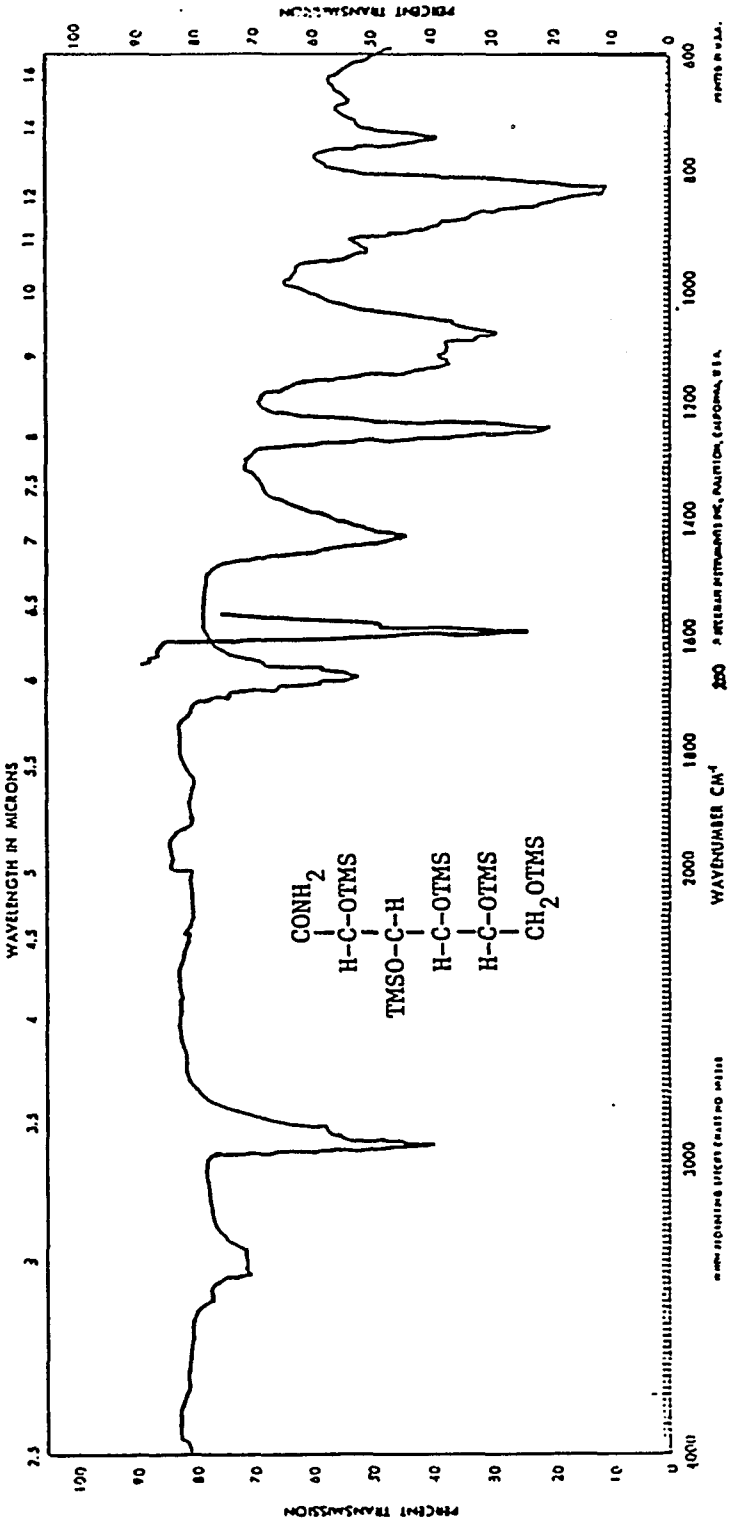

Figure 12. IR Spectrum of Compound 38 (KBr).

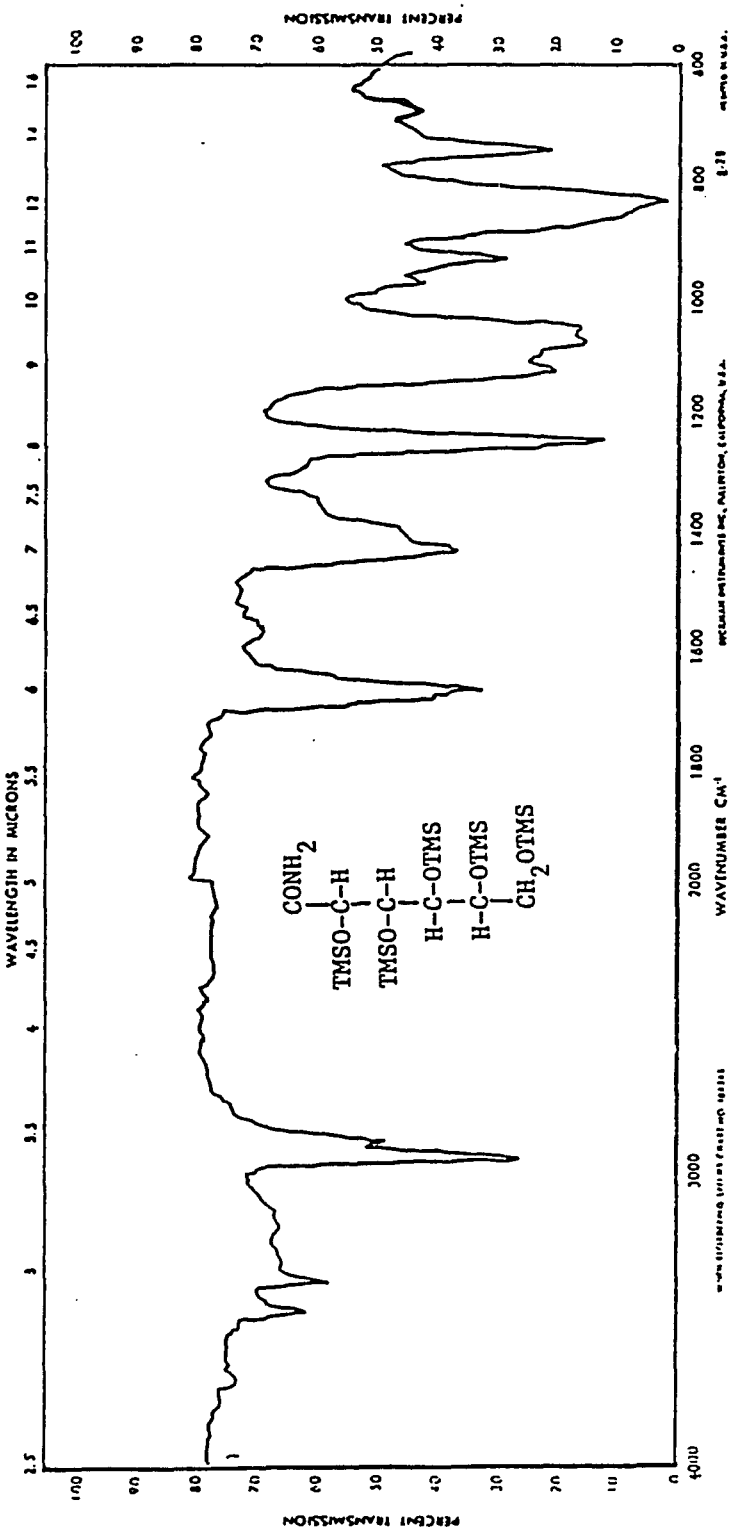

Figure 13. IR Spectrum of Compound 39 (KBr).

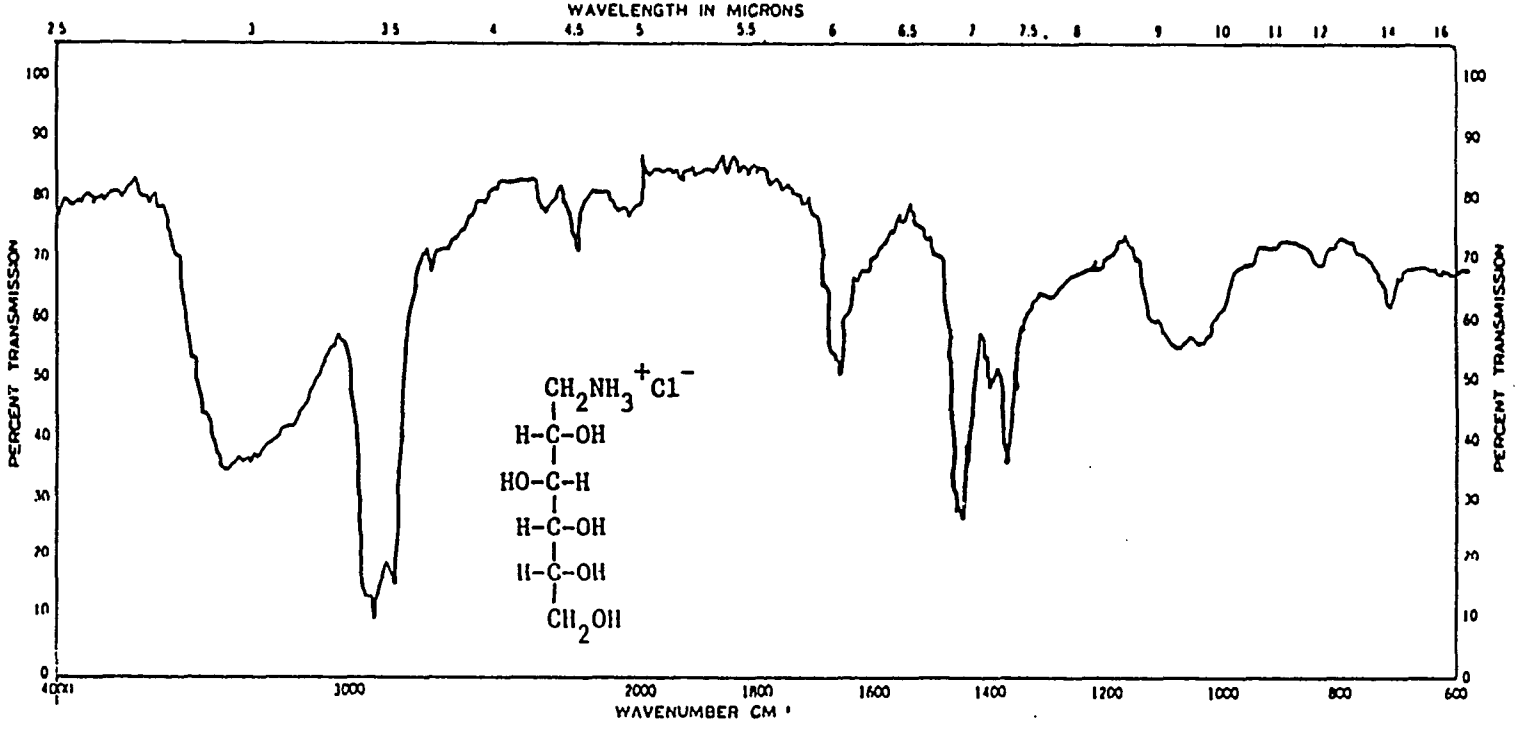

Figure 14. IR Spectrum of Compound 43 (Mineral Oil).

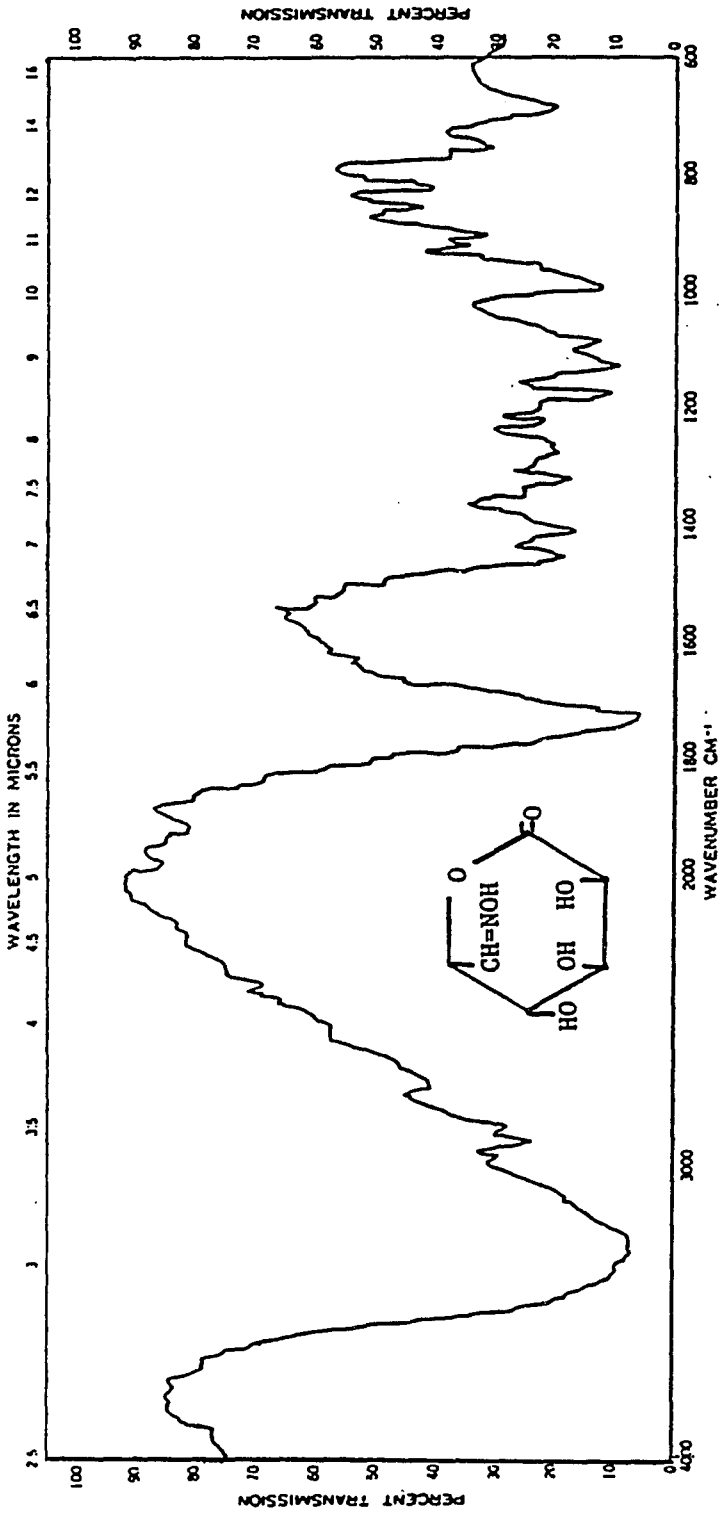

Figure 15. IR Spectrum of Compound 46 (KBr).

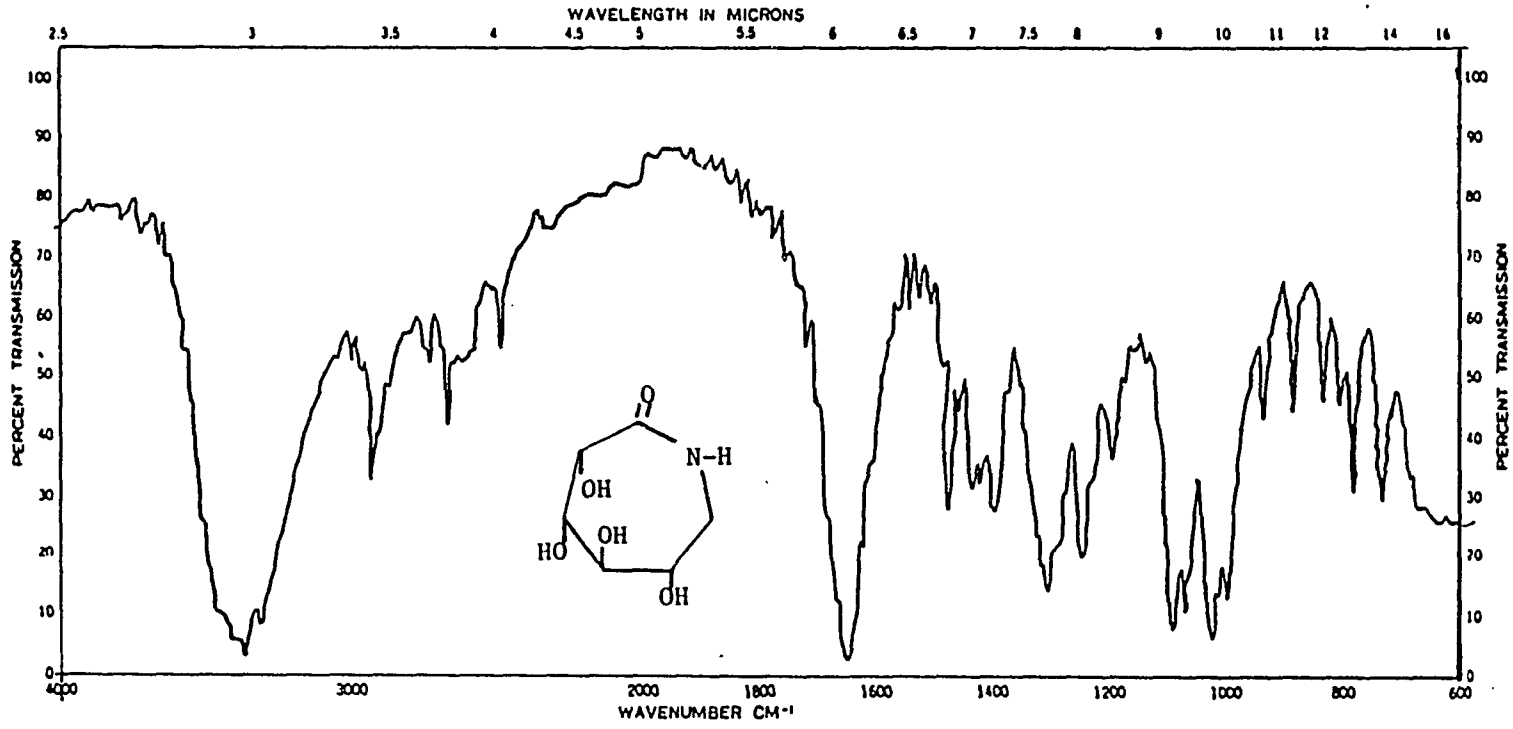

Figure 16. IR Spectrum of Compound 48 (KBr).

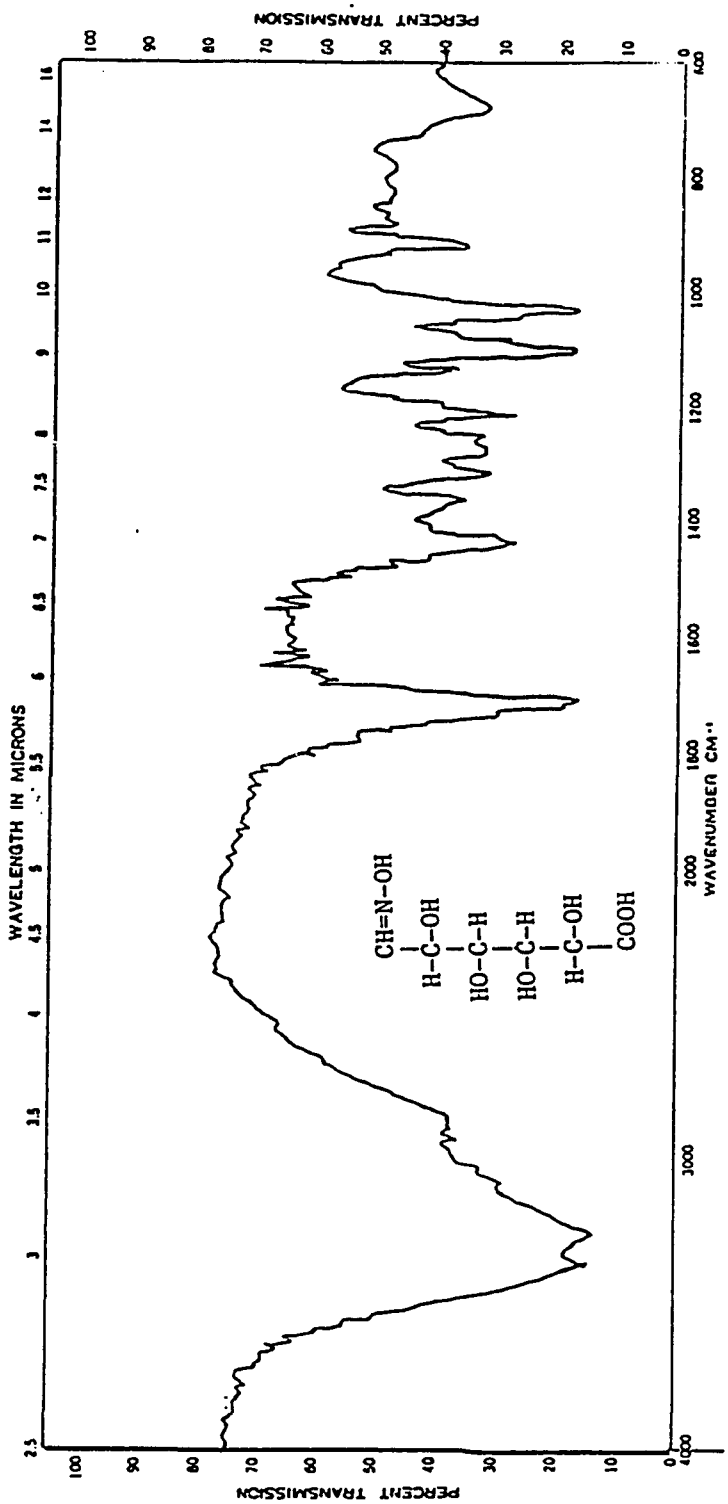

Figure 17. IR Spectrum of Compound 50 (KBr).

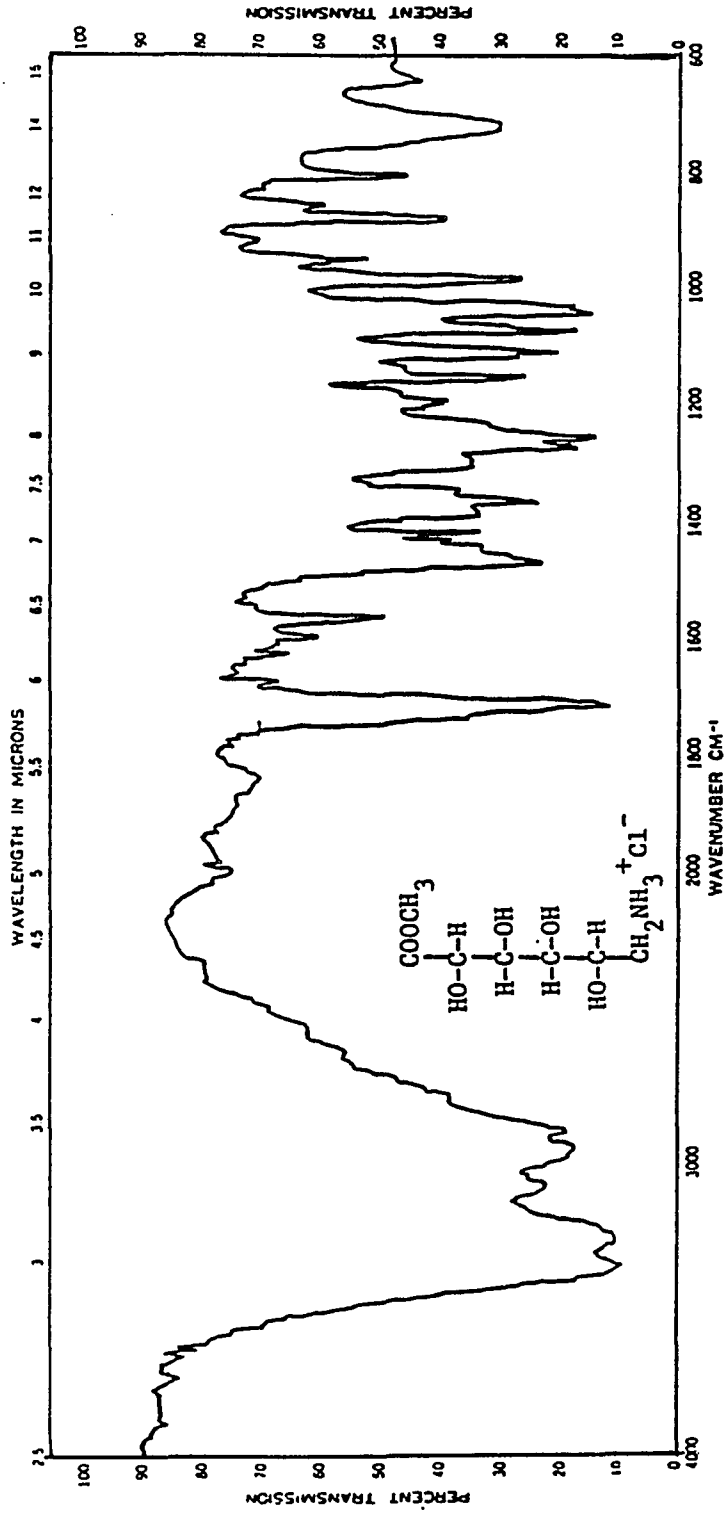

Figure 18. IR Spectrum of Compound 51 (KBr).

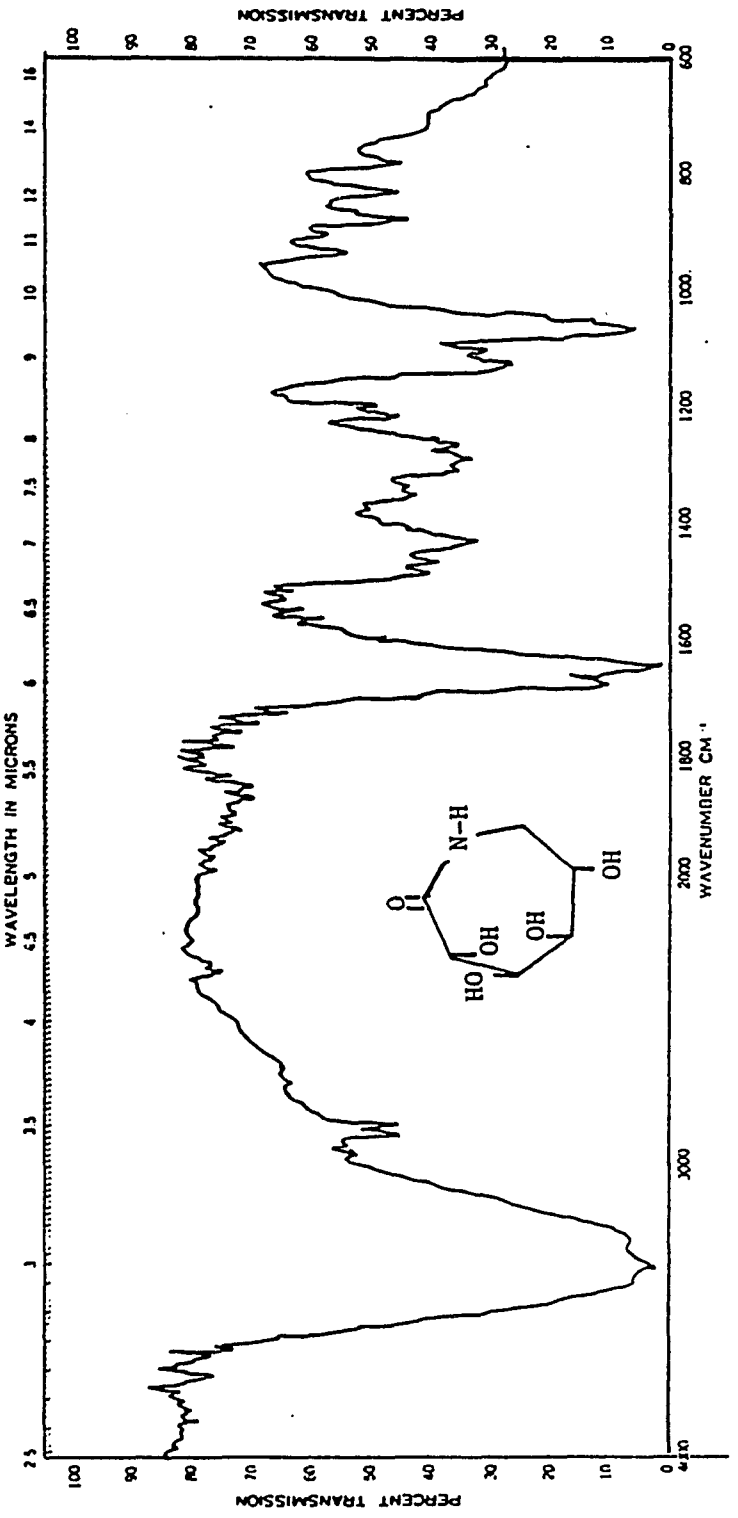

Figure 19. IR Spectrum of Compound 52 (KBr).

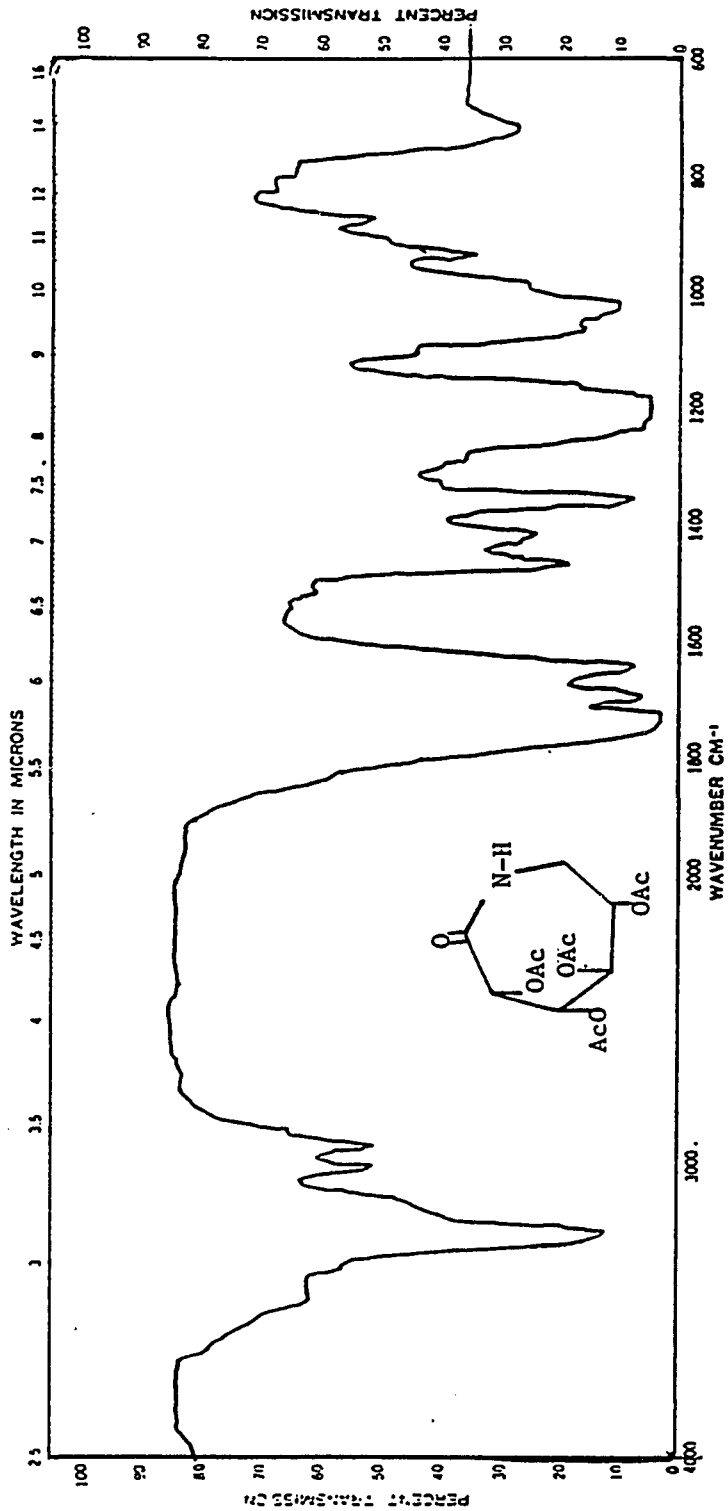

Figure 20. IR Spectrum of Compound 63 (KBr).

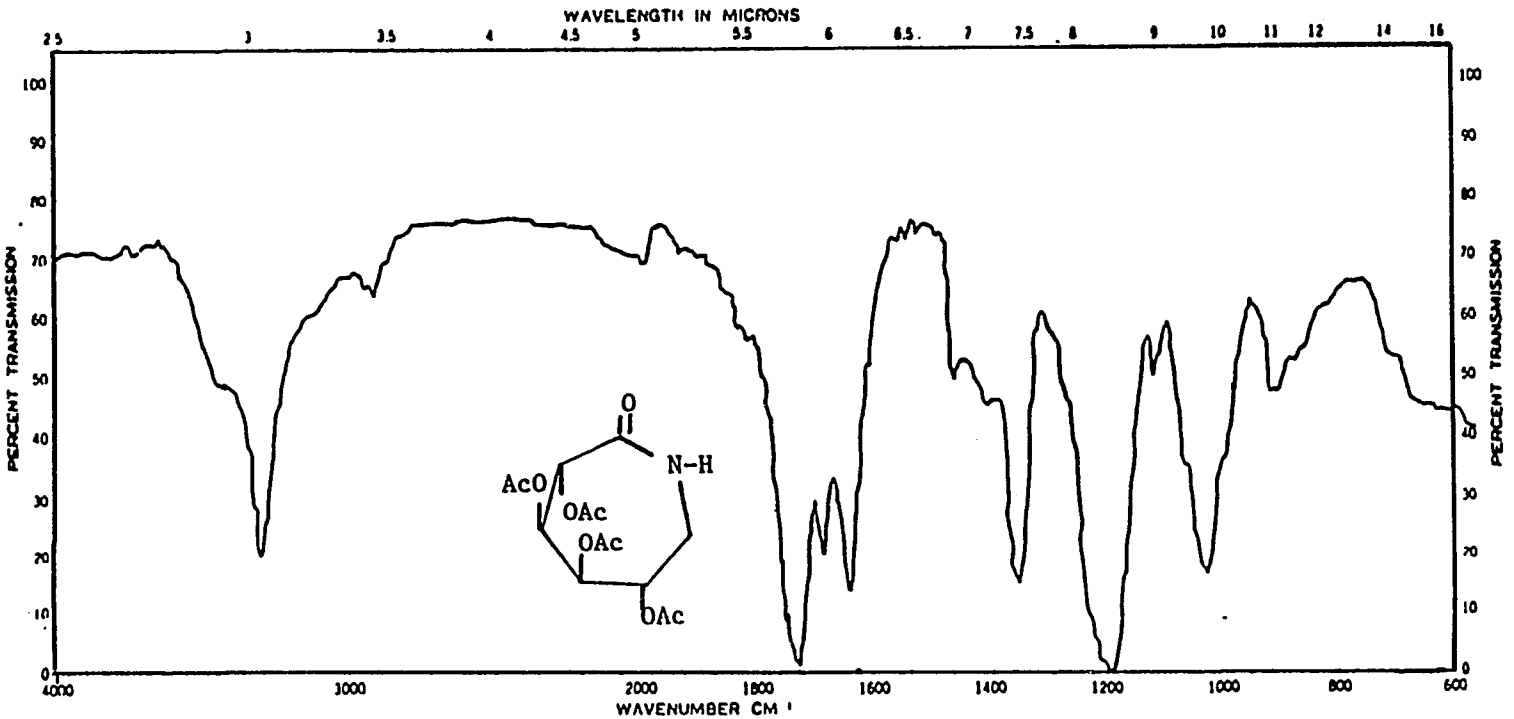

Figure 21. IR Spectrum of Compound 64 (KBr).

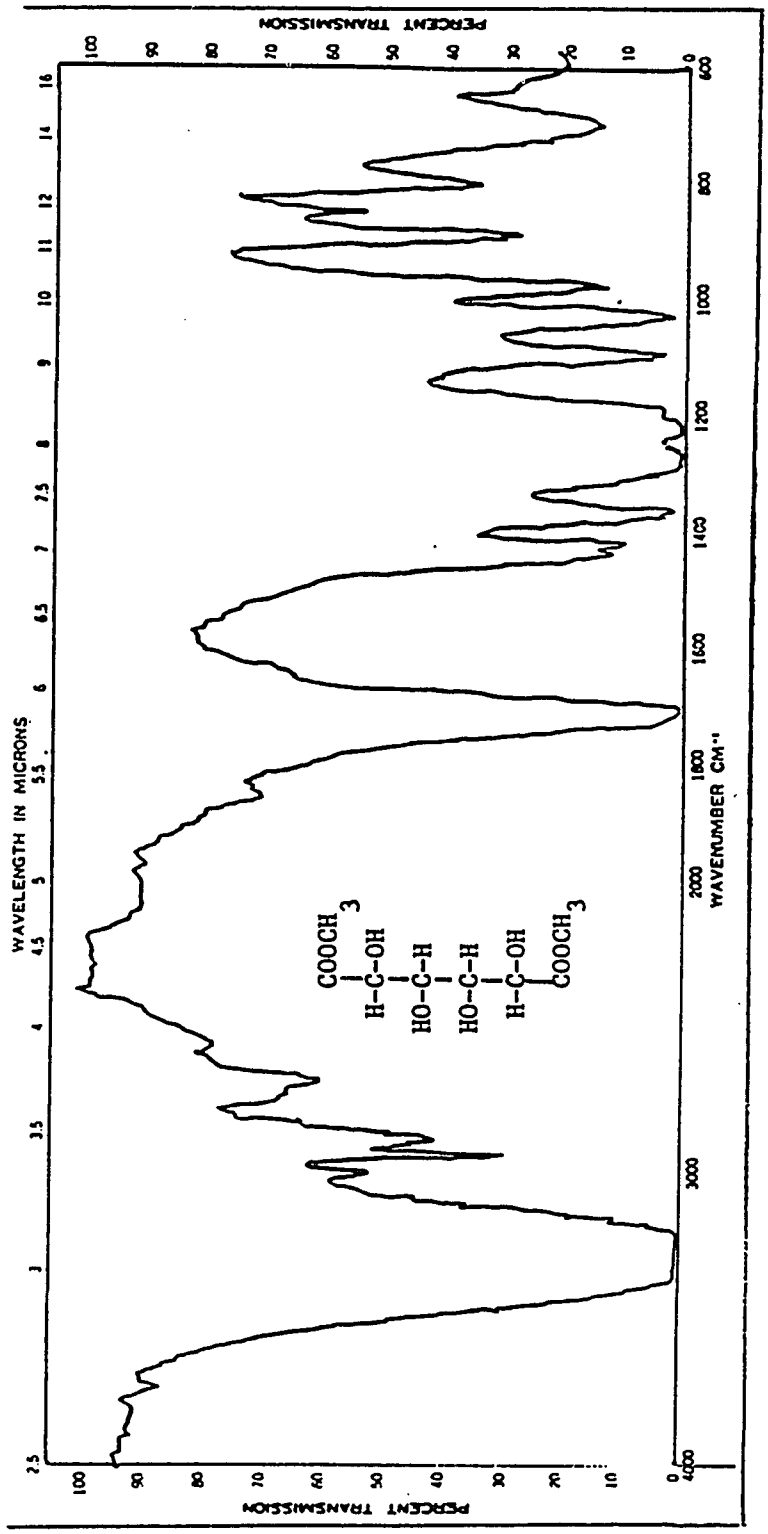

Figure 22. IR Spectrum of Compound 91 (KBr).

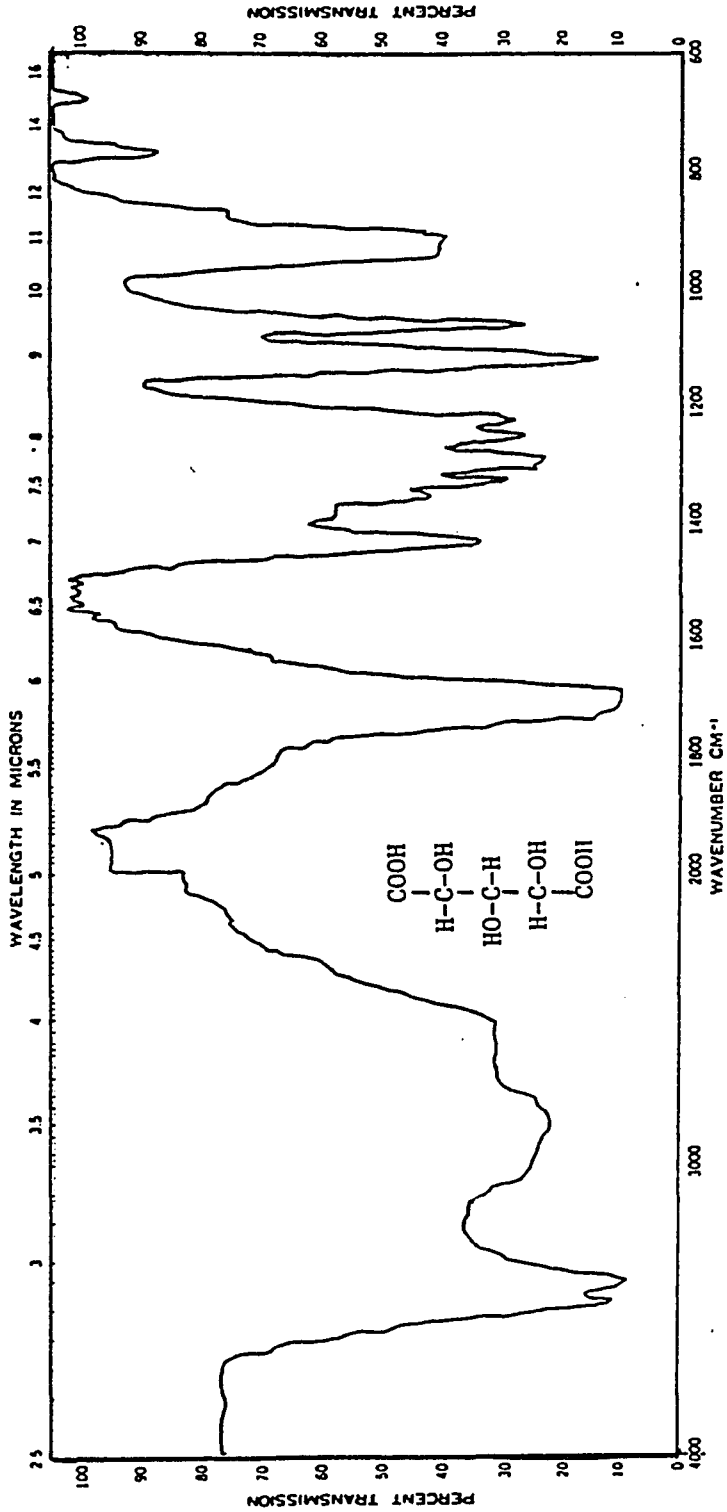

Figure 23. IR Spectrum of Compound 93 (KBr).

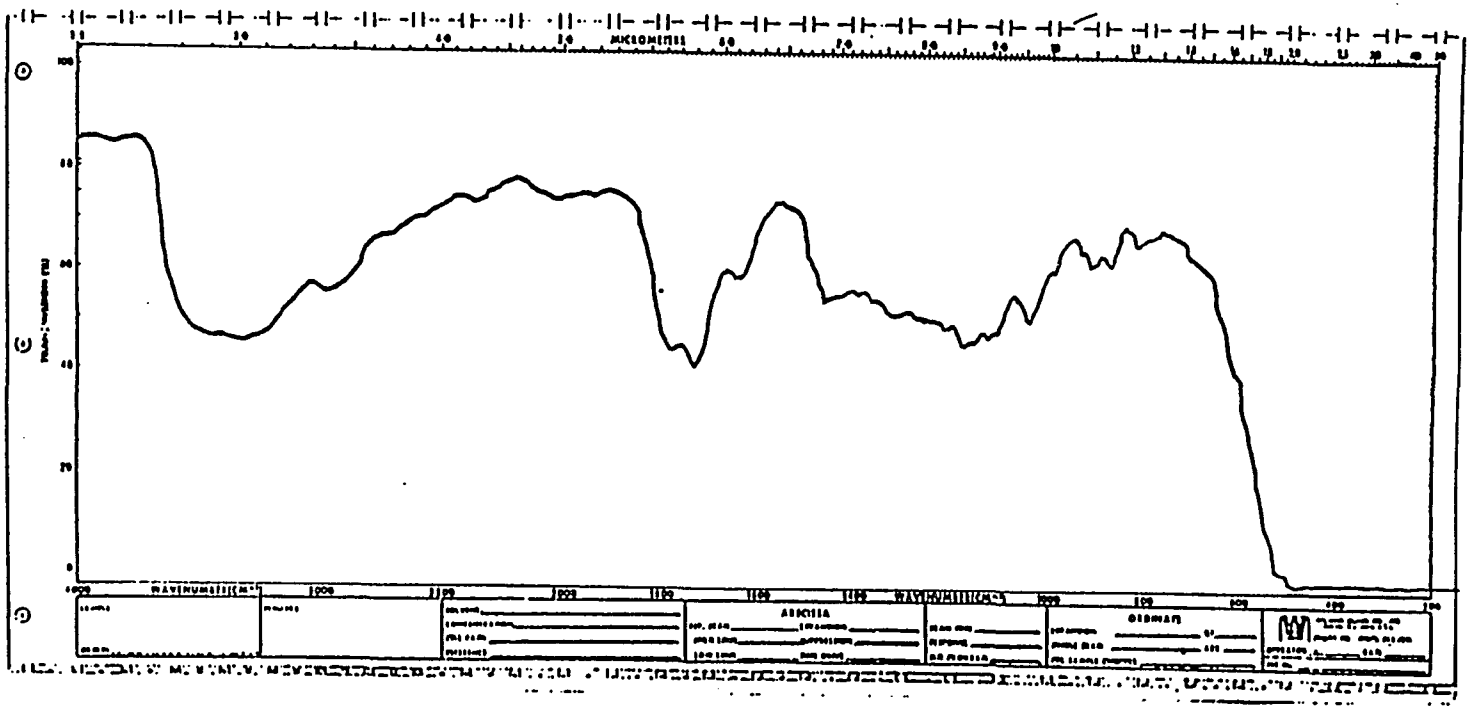

Figure 24. IR Spectrum of Methyl Esters of D-Glucaric Acid (Neat).

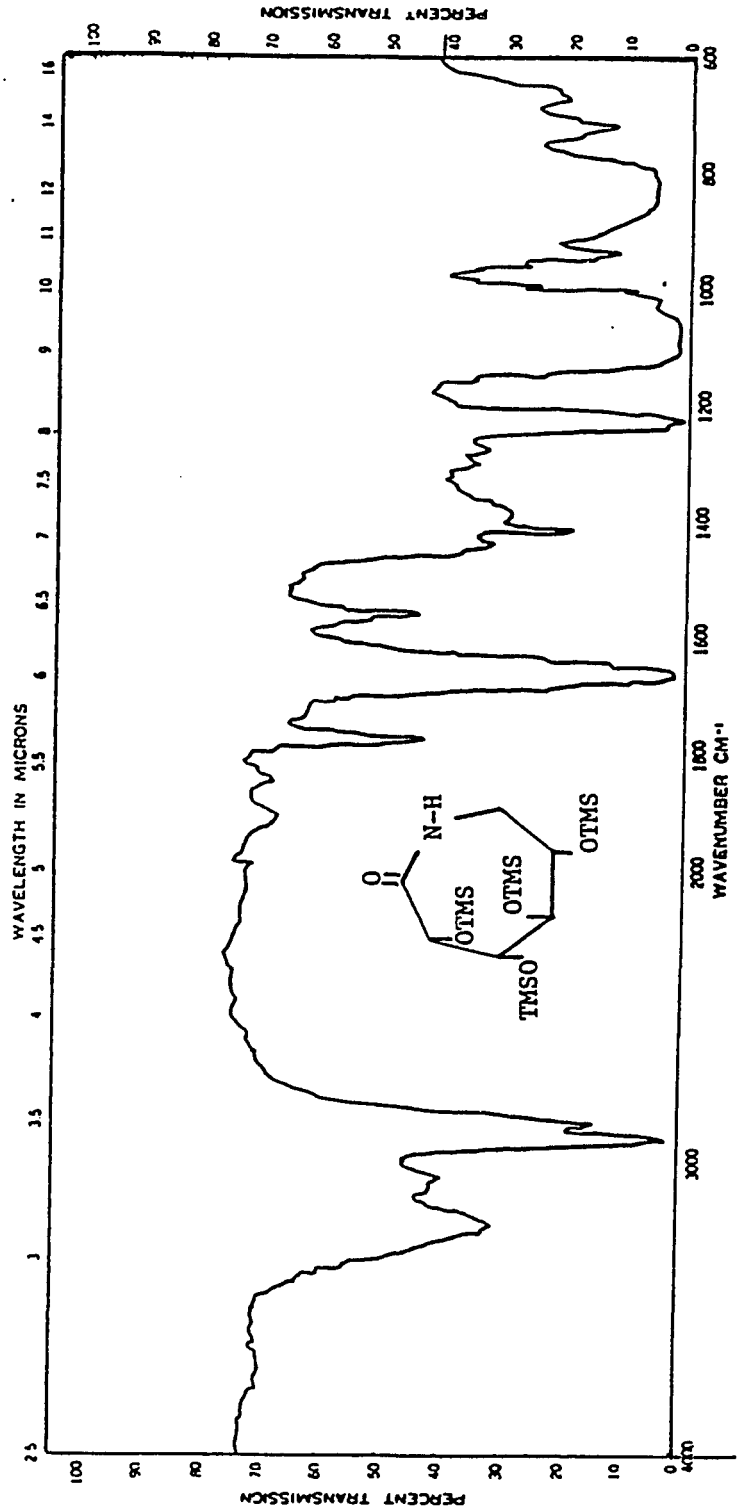

Figure 25. IR Spectrum of Compound 110 (Neat).

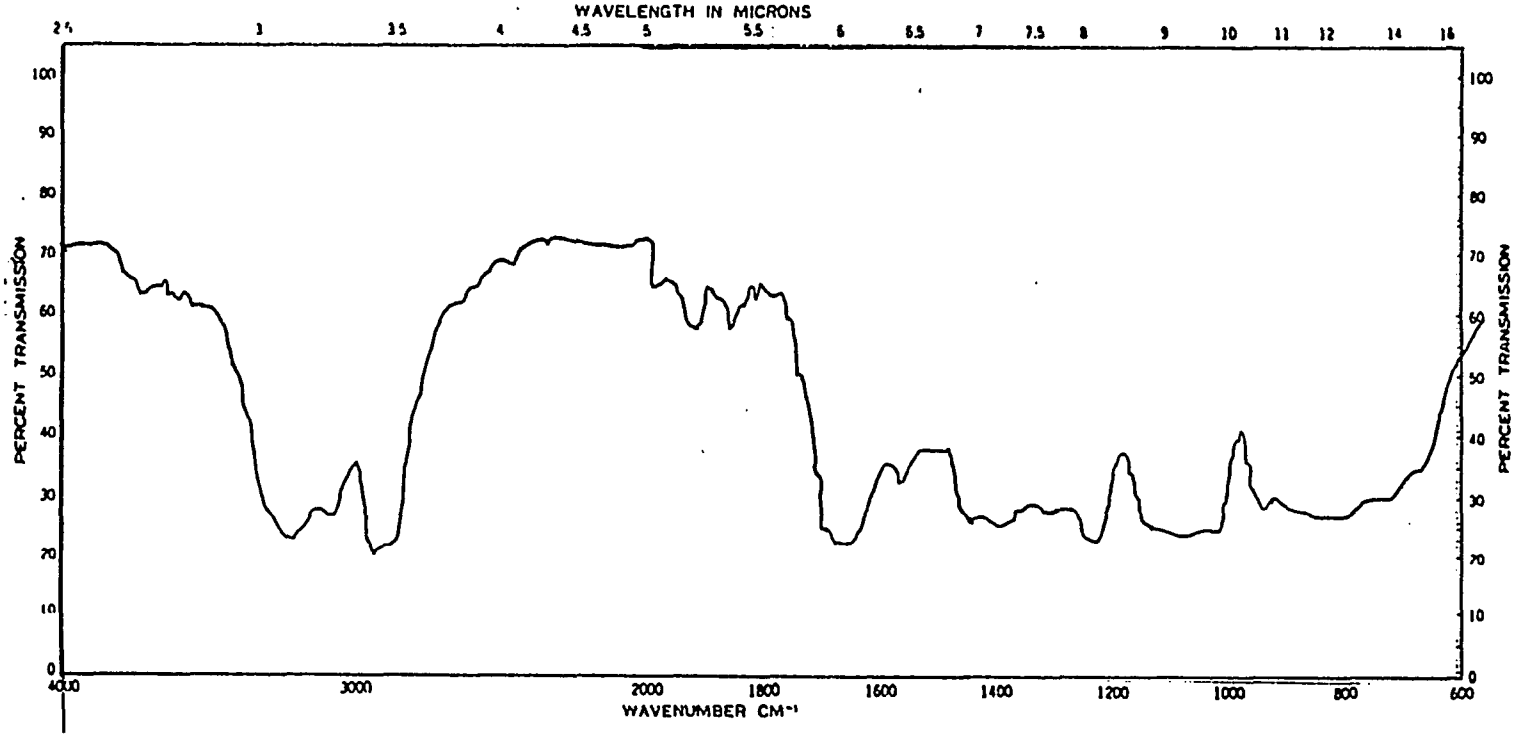

Figure 26. IR Spectrum of the Product from Attempted Ring-opening Polymerization of Compound 110 (Neat).

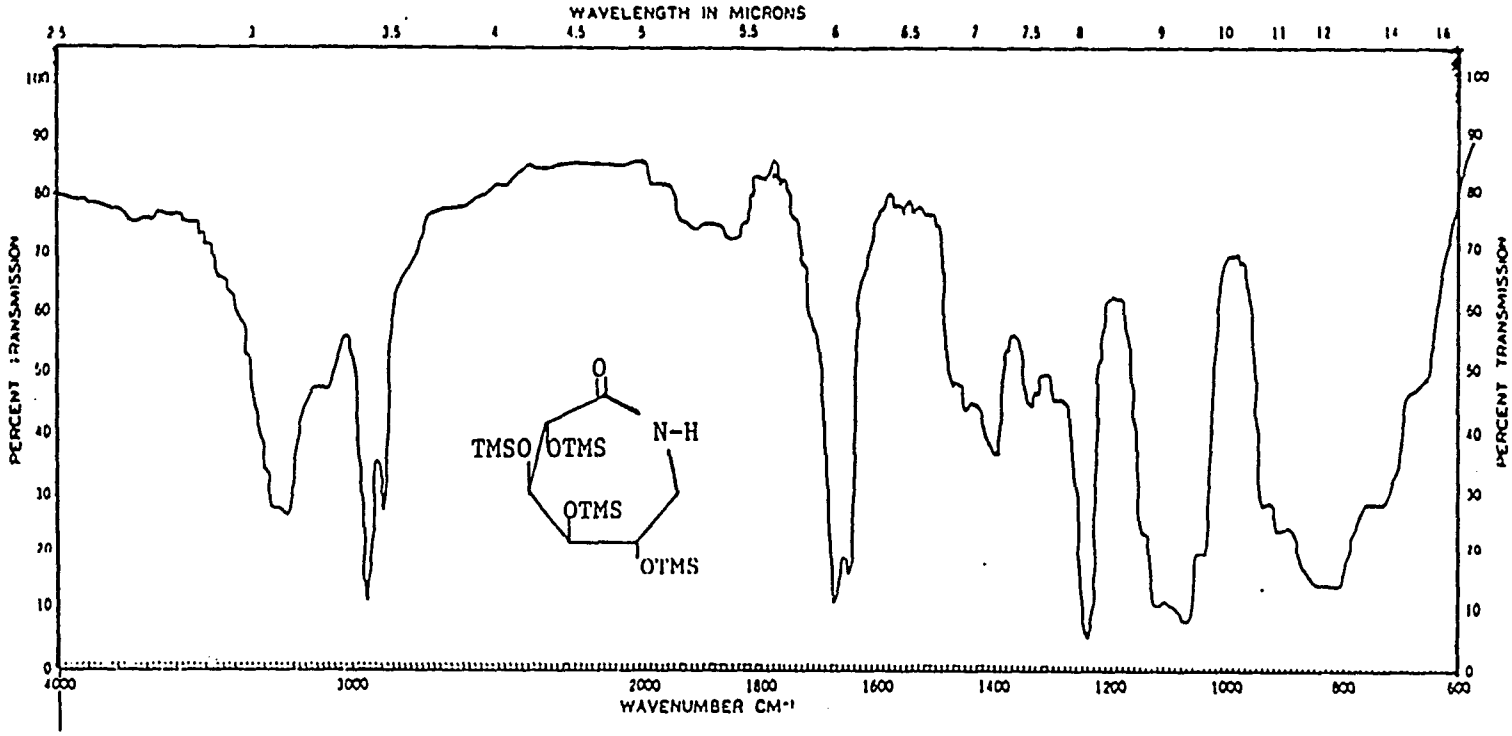

Figure 27. IR Spectrum of Compound 111 (KBr).

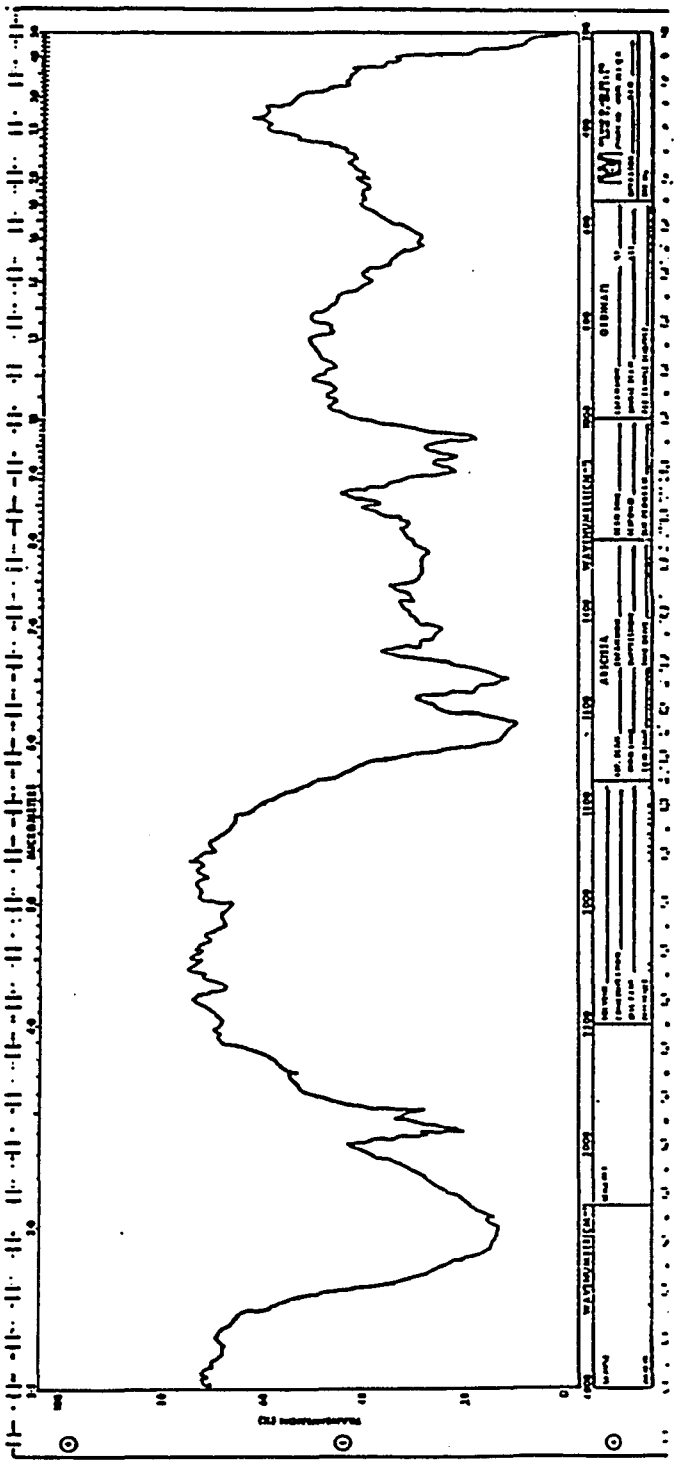

Figure 28. IR Spectrum of Compound 98 (KBr).

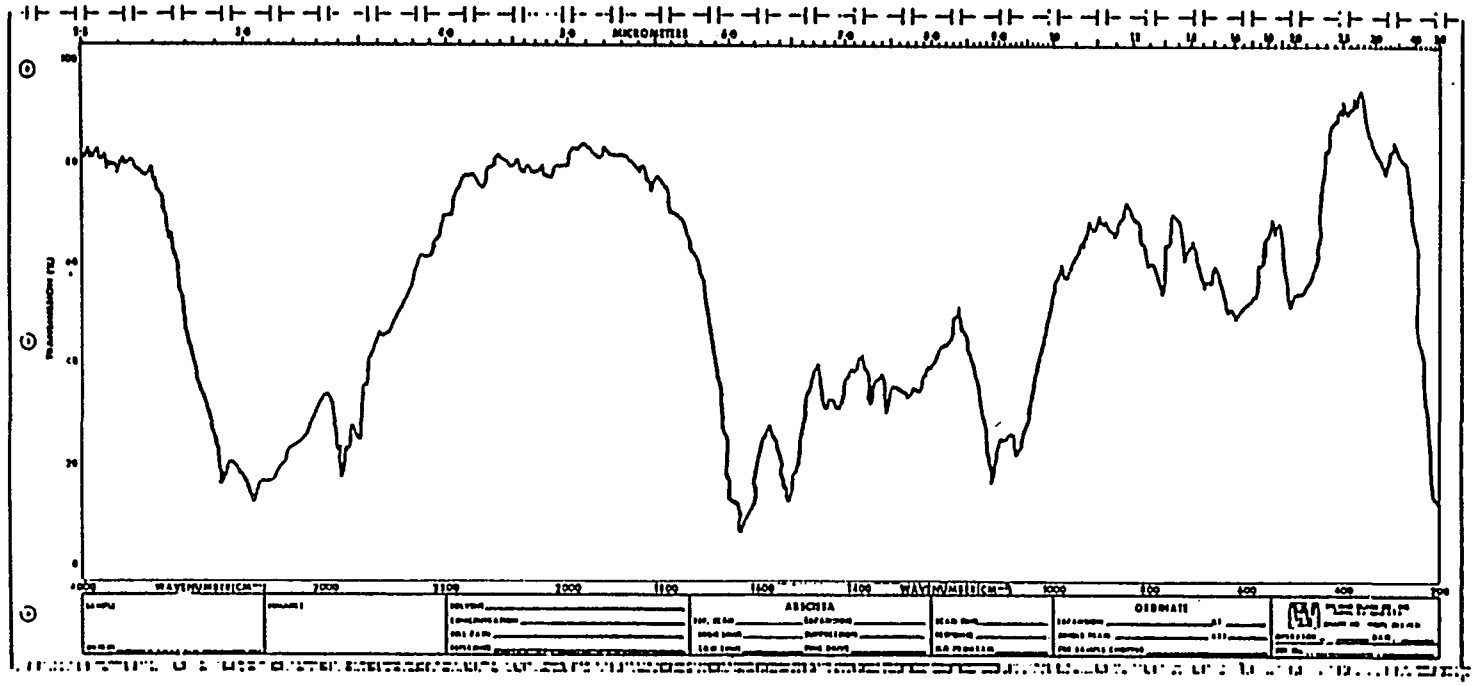

Figure 29. IR Spectrum of Compound 99 (KBr).

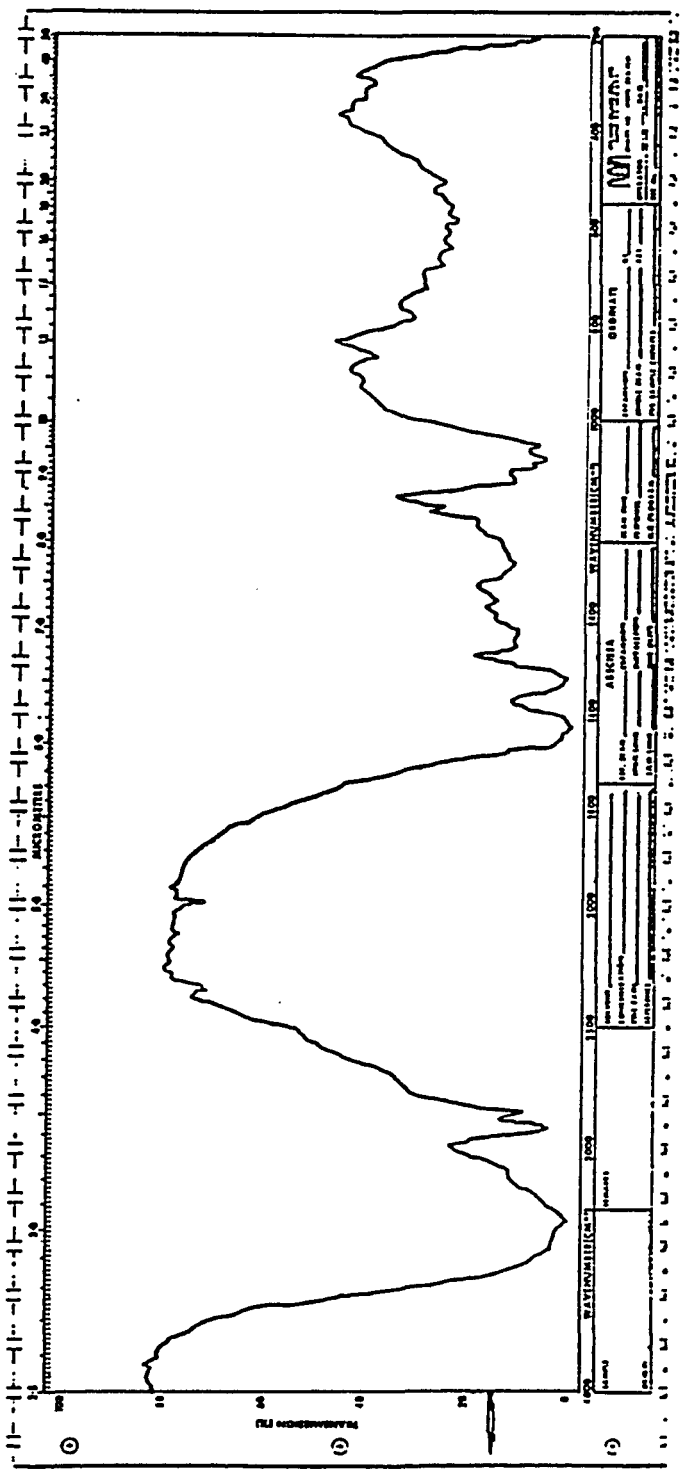

Figure 30. IR Spectrum of Compound 100 (KBr).

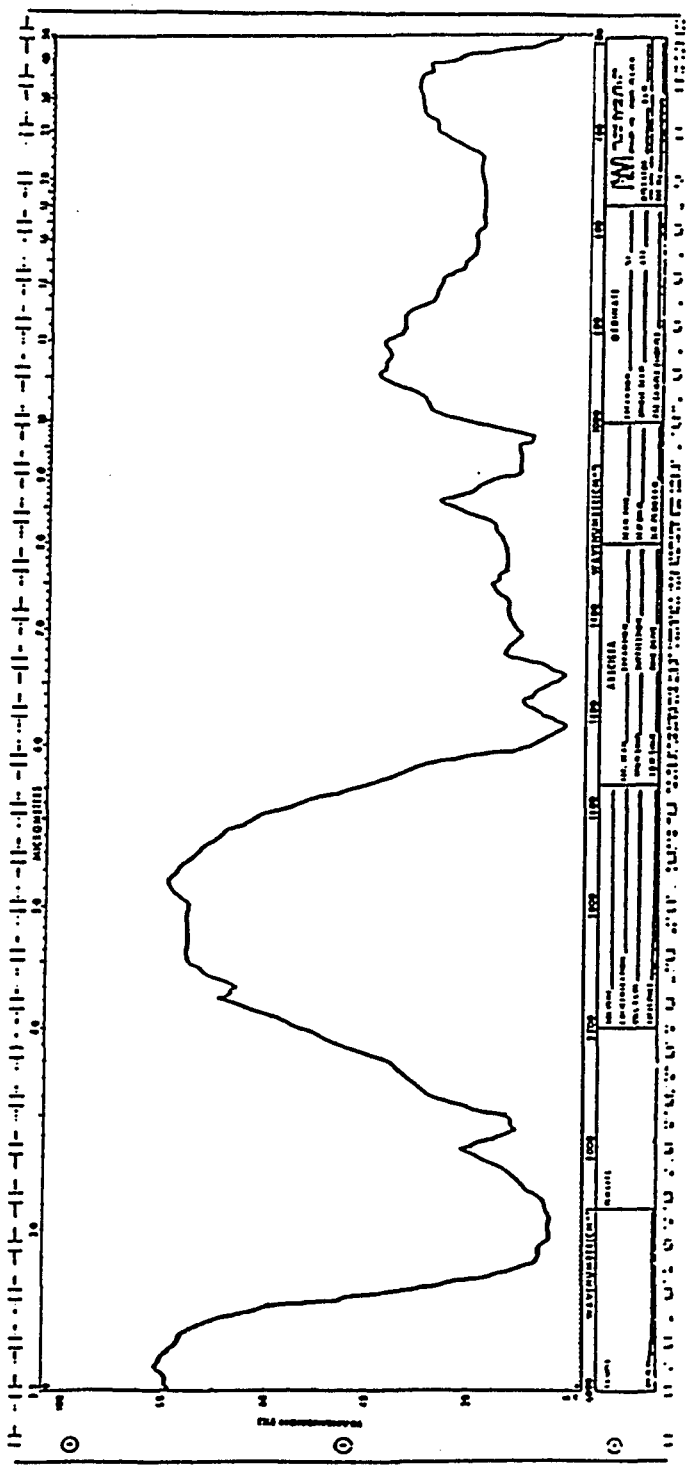

Figure 31. IR Spectrum of Compound 101 (KBr).

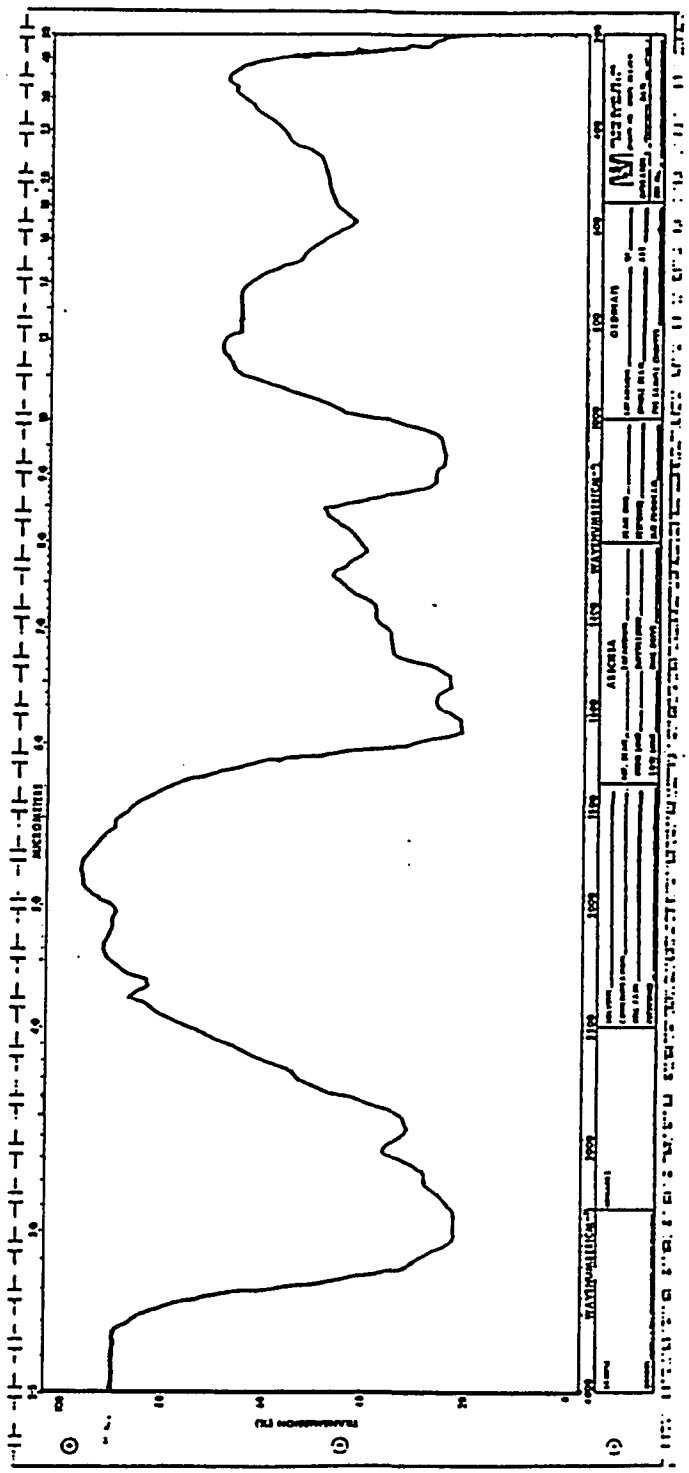

Figure 32. IR Spectrum of Compound 102 (KBr).

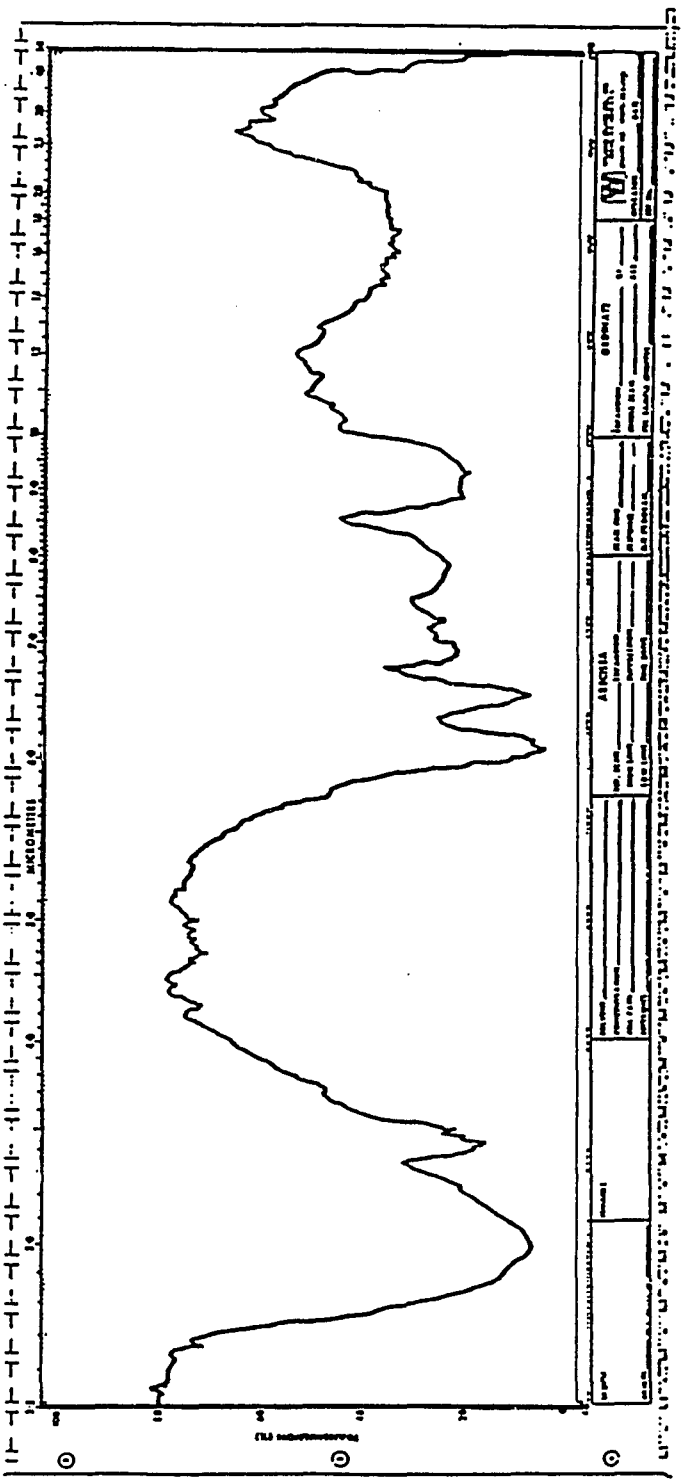

Figure 33. IR Spectrum of Compound 103 (KBr).

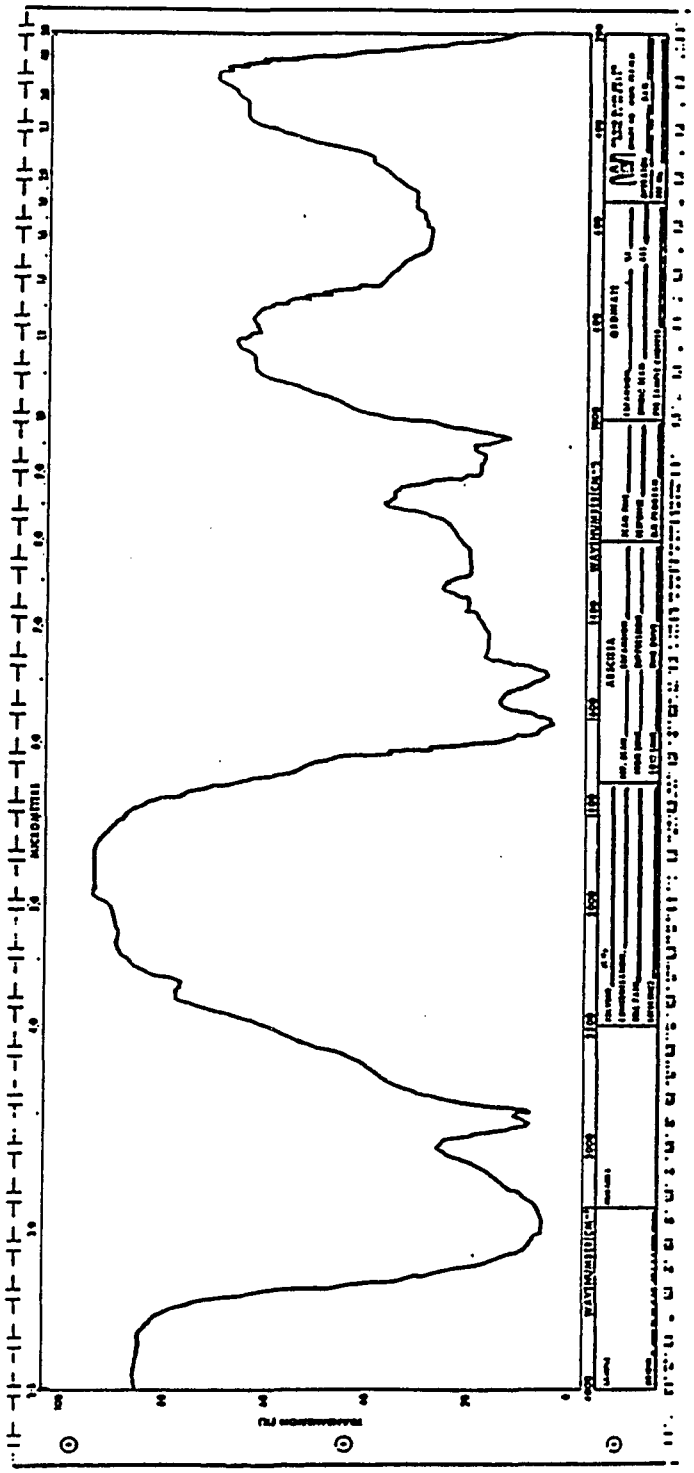

Figure 34. IR Spectrum of Compound 104 (KBr).

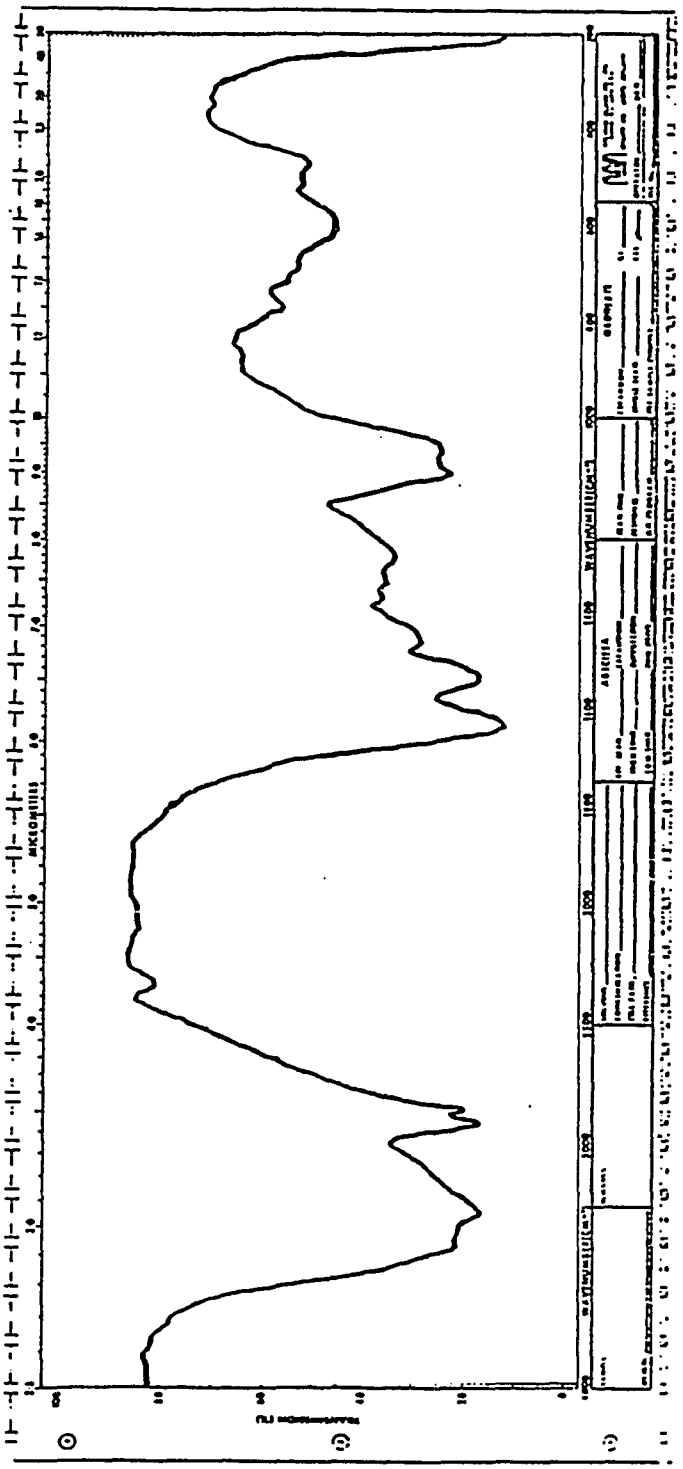

Figure 35. IR Spectrum of Compound 105 (KBr).

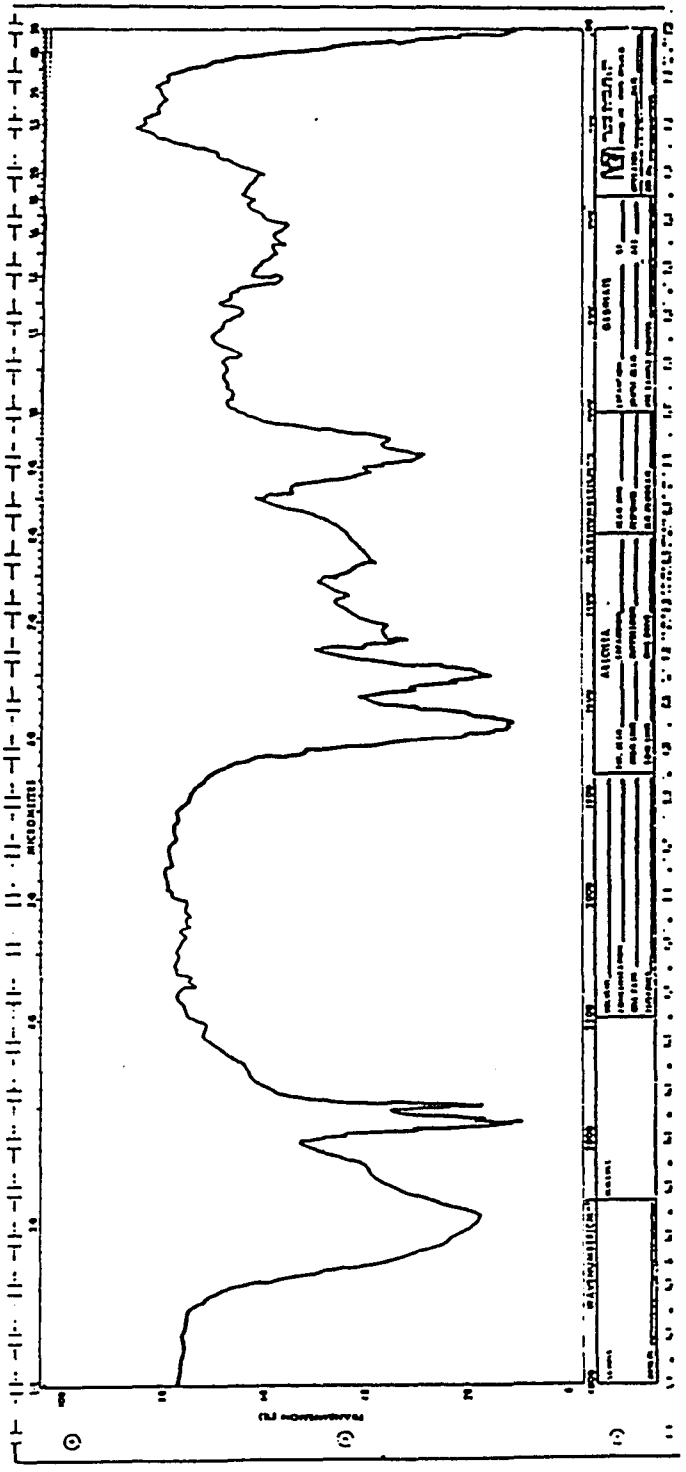

Figure 36. IR Spectrum of Compound 106 (KBr).

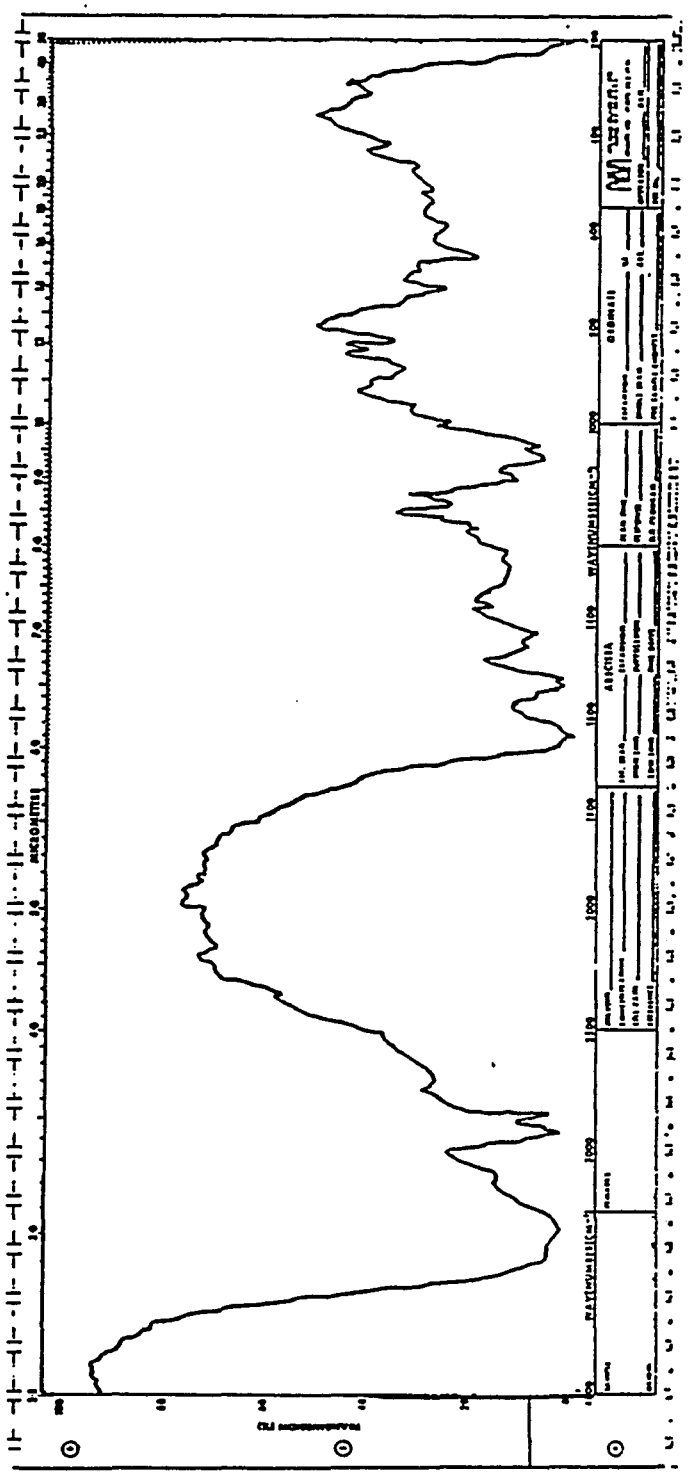

Figure 37. IR Spectrum of Compound 107 (KBr).

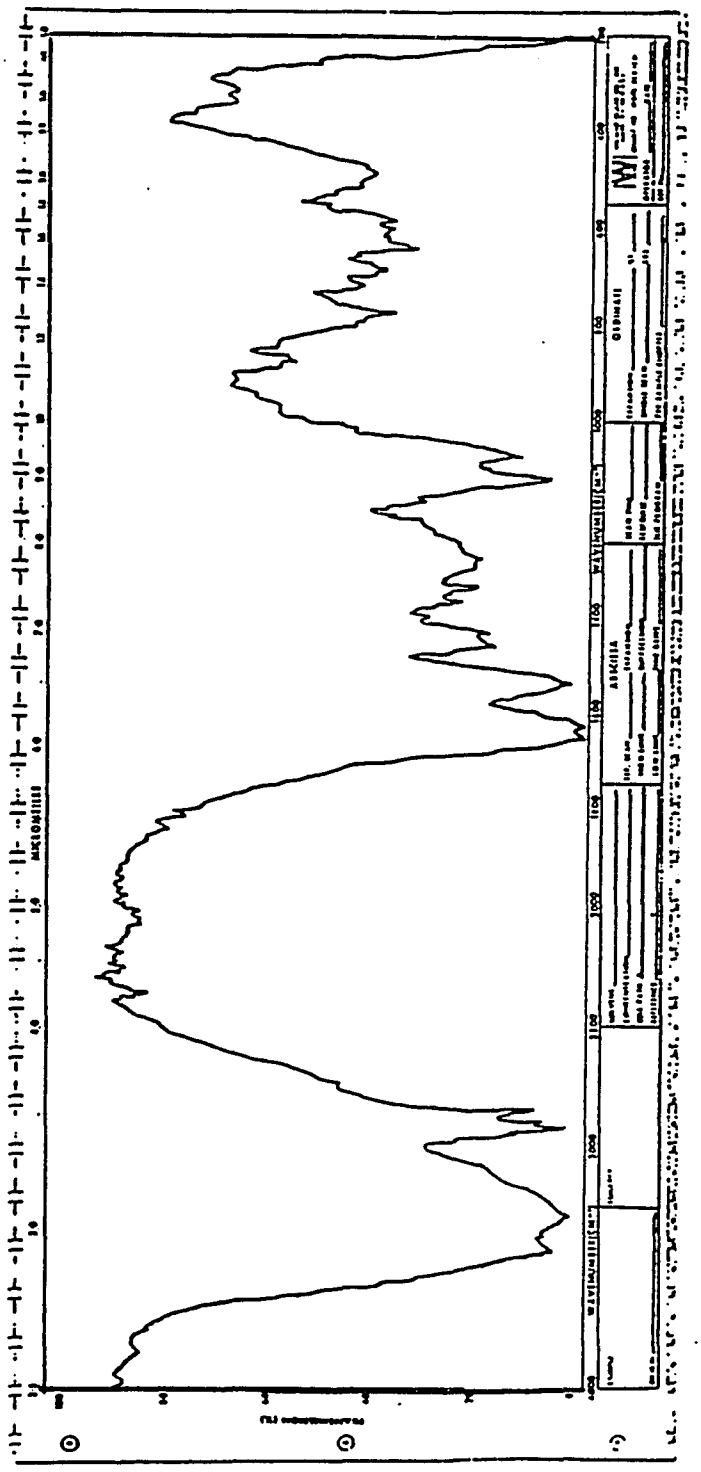

Figure 38. IR Spectrum of Compound 108 (KBr).

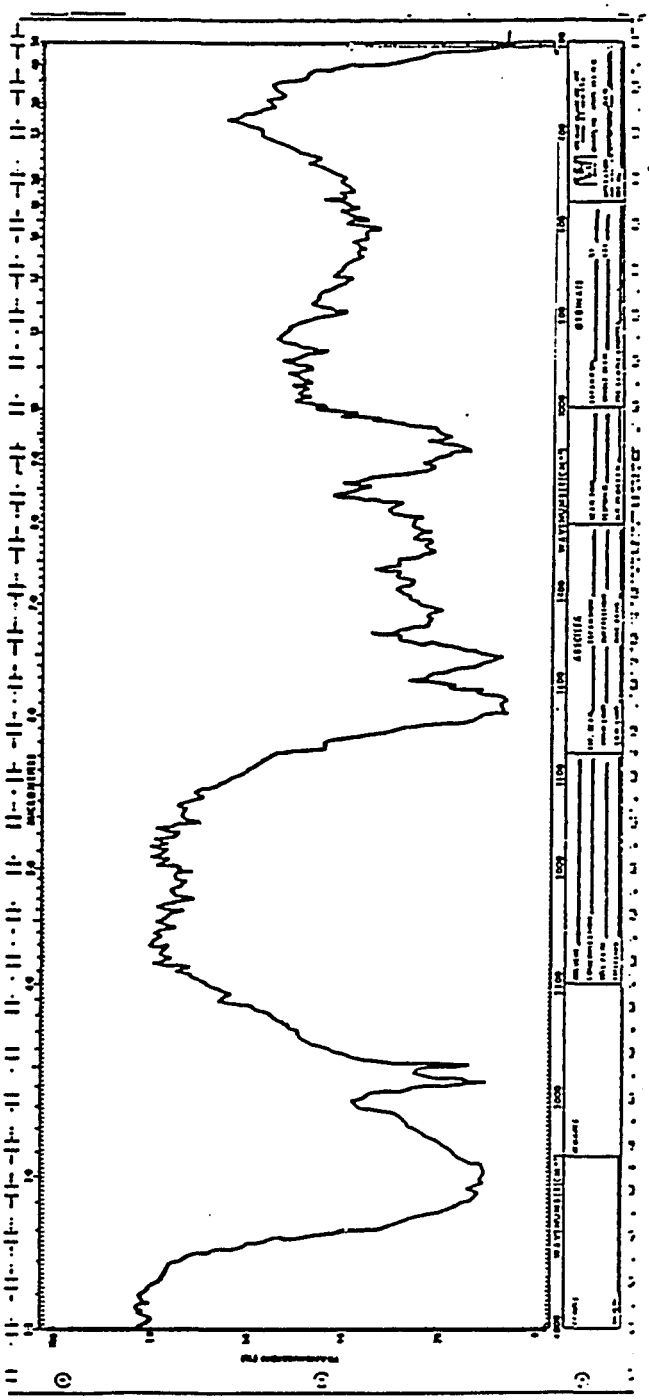

Figure 39. IR Spectrum of Compound 109 (KBr).

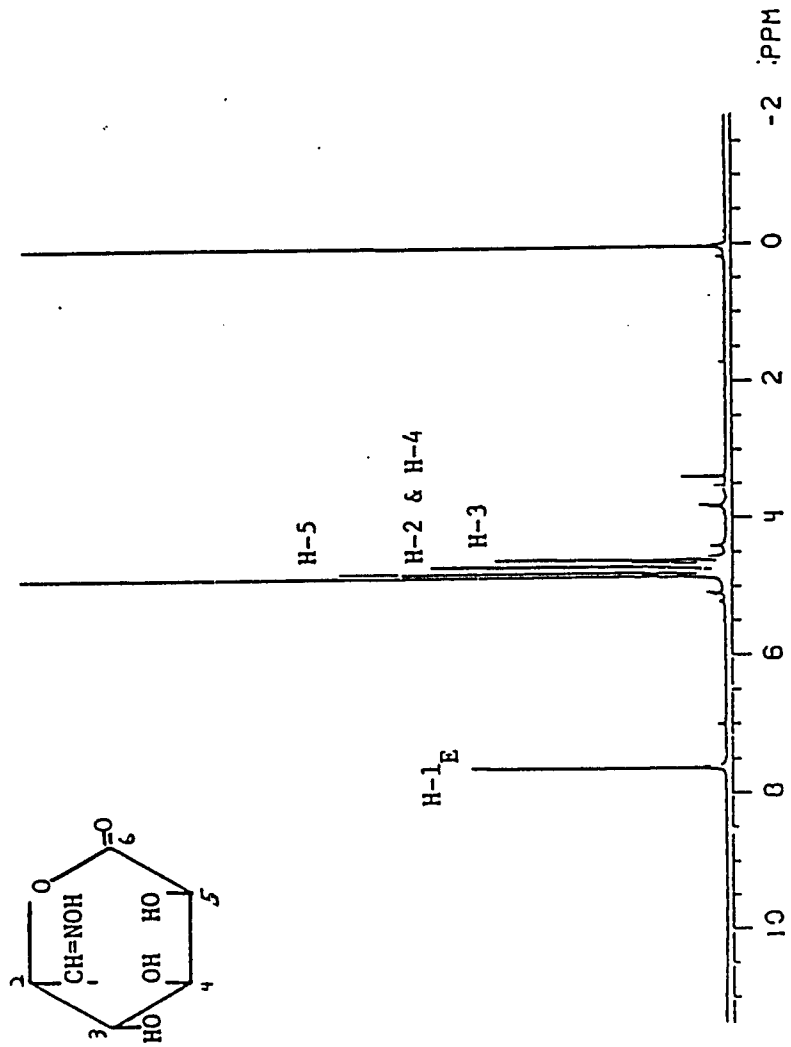

Figure 40. ^{1}H NMR of Compound 46 (After Heating) (D_2O).

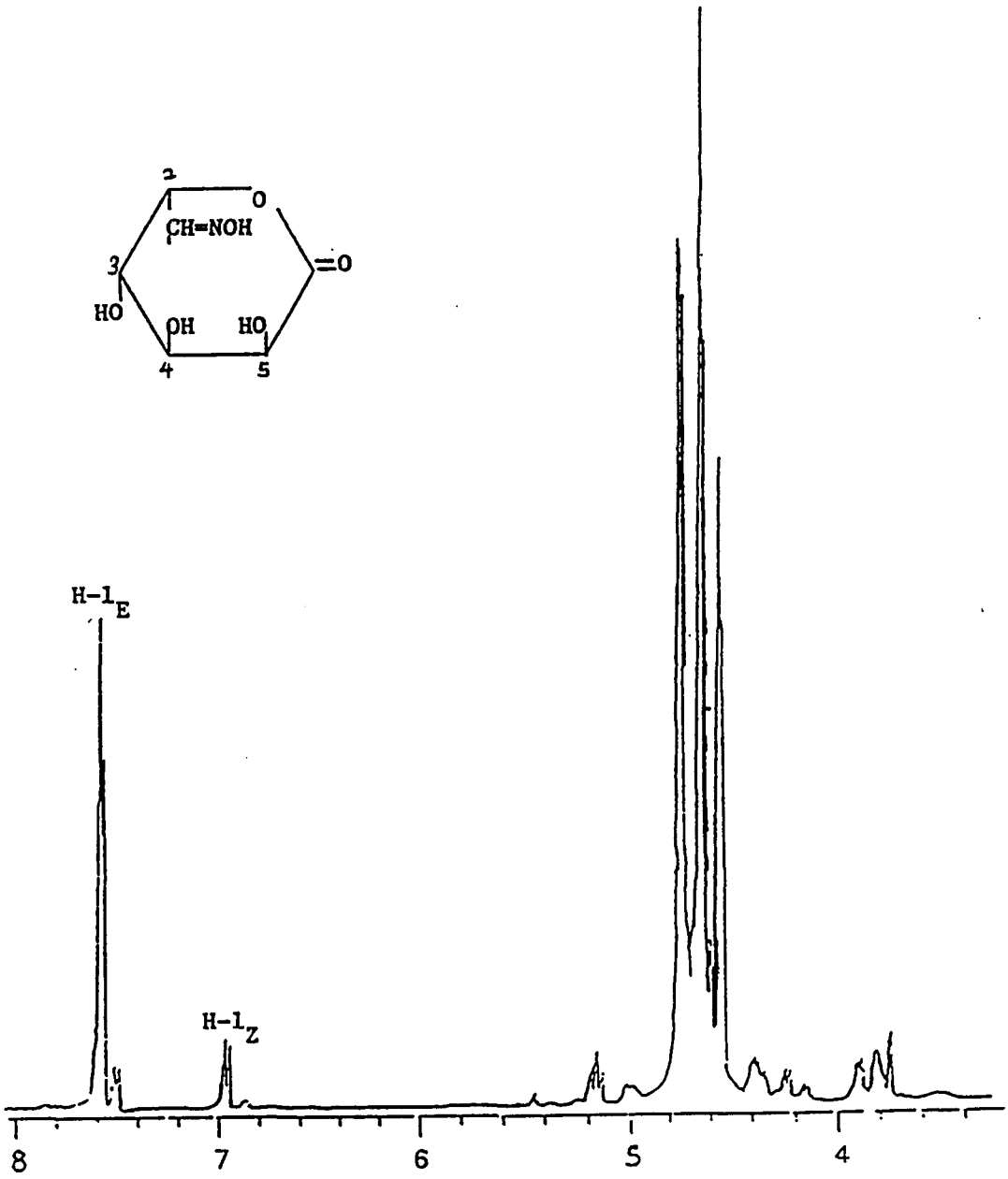

Figure 41. ^{1}H NMR of Compound 46 (No Heating) (D_2O).

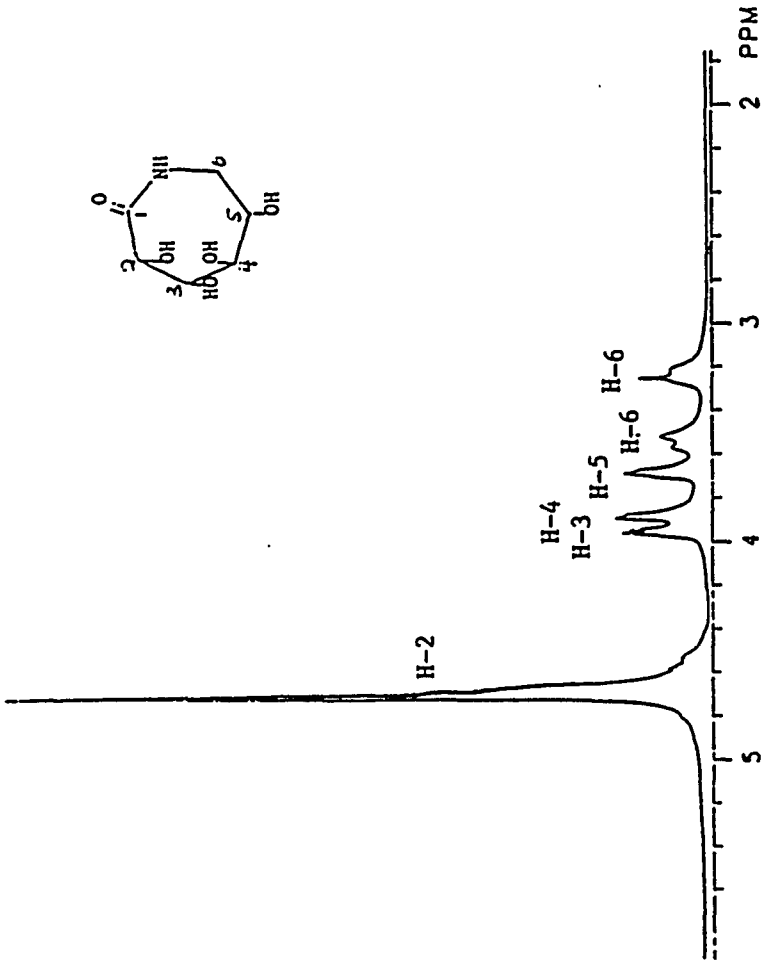

Figure 42. ^{1}H NMR of Compound 48 (D_2O).

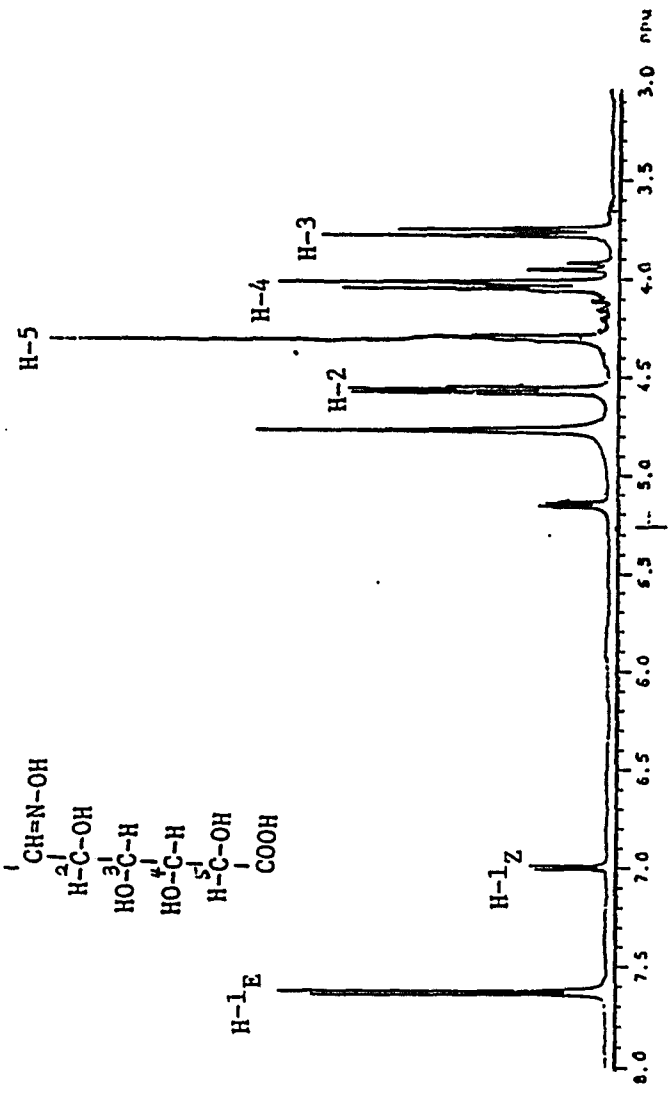

Figure 43. ^{1}H NMR of Compound 50 (D_2O).

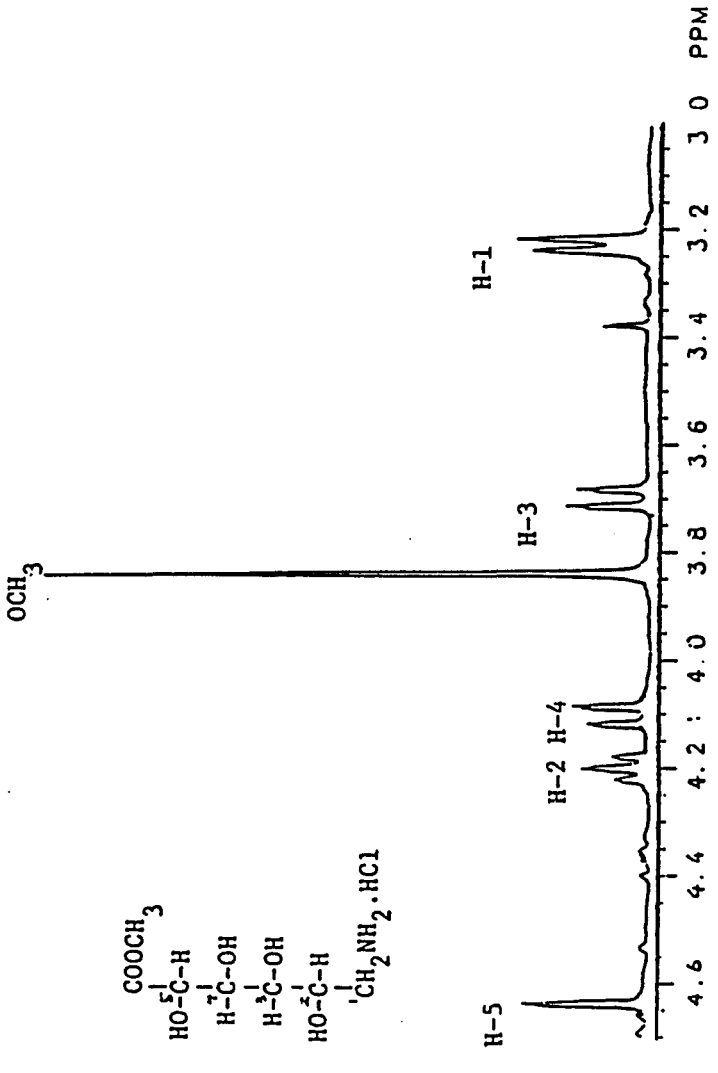

Figure 44. ^{1}H NMR of Compound 51 (D_2O).

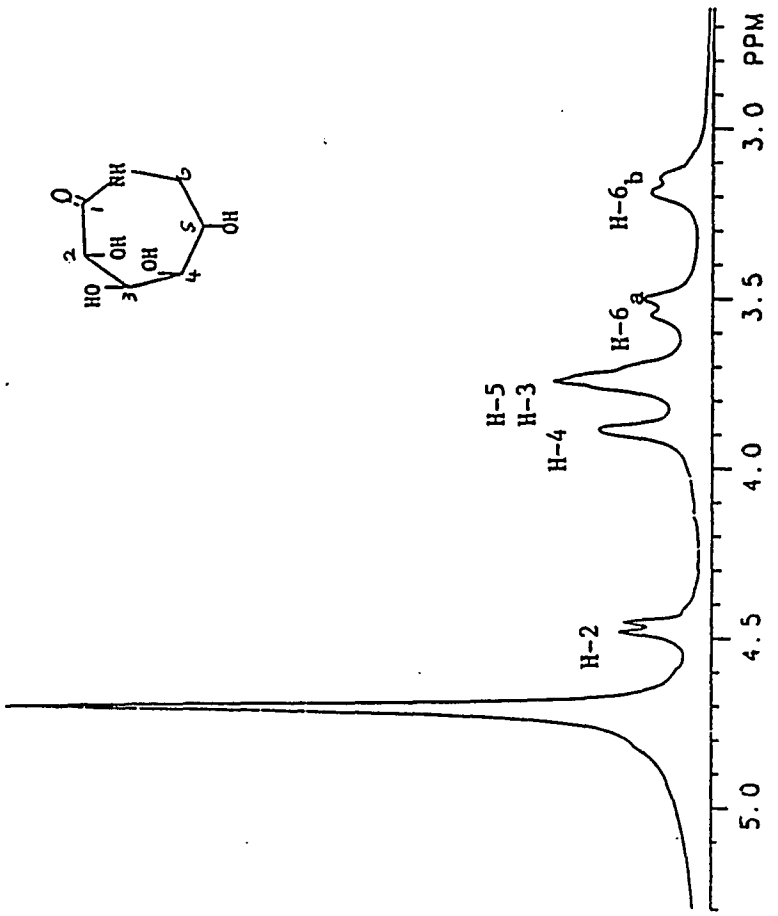

Figure 45. ^{1}H NMR of Compound 52 (D_2O).

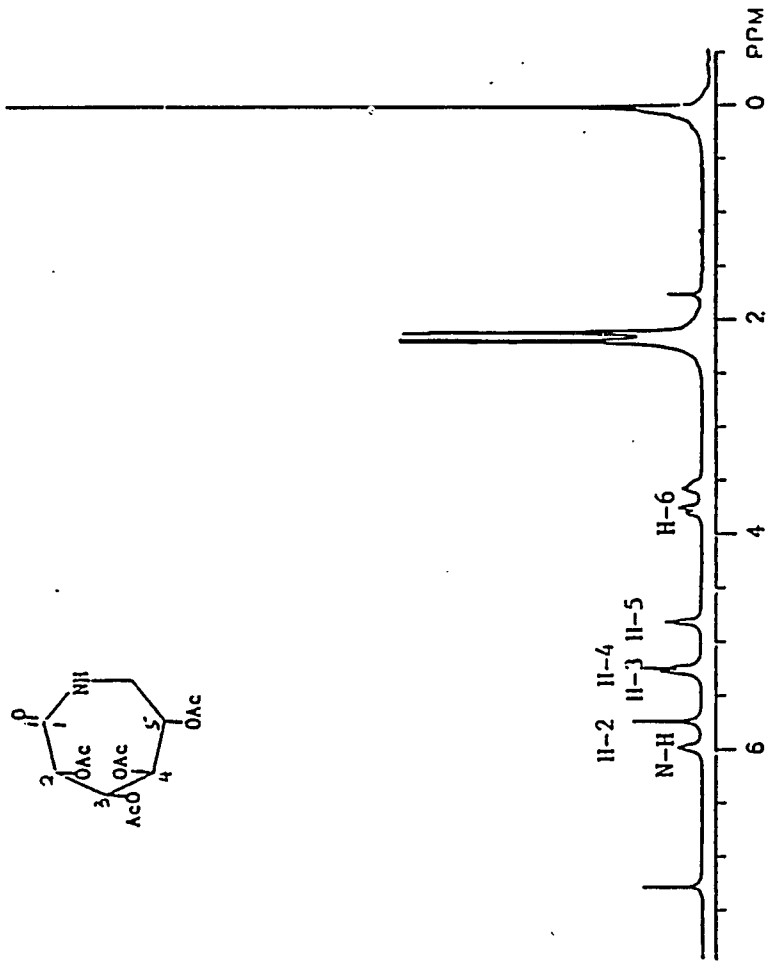

Figure 46. ^{1}H NMR of Compound 63 ($CDCl_3$).

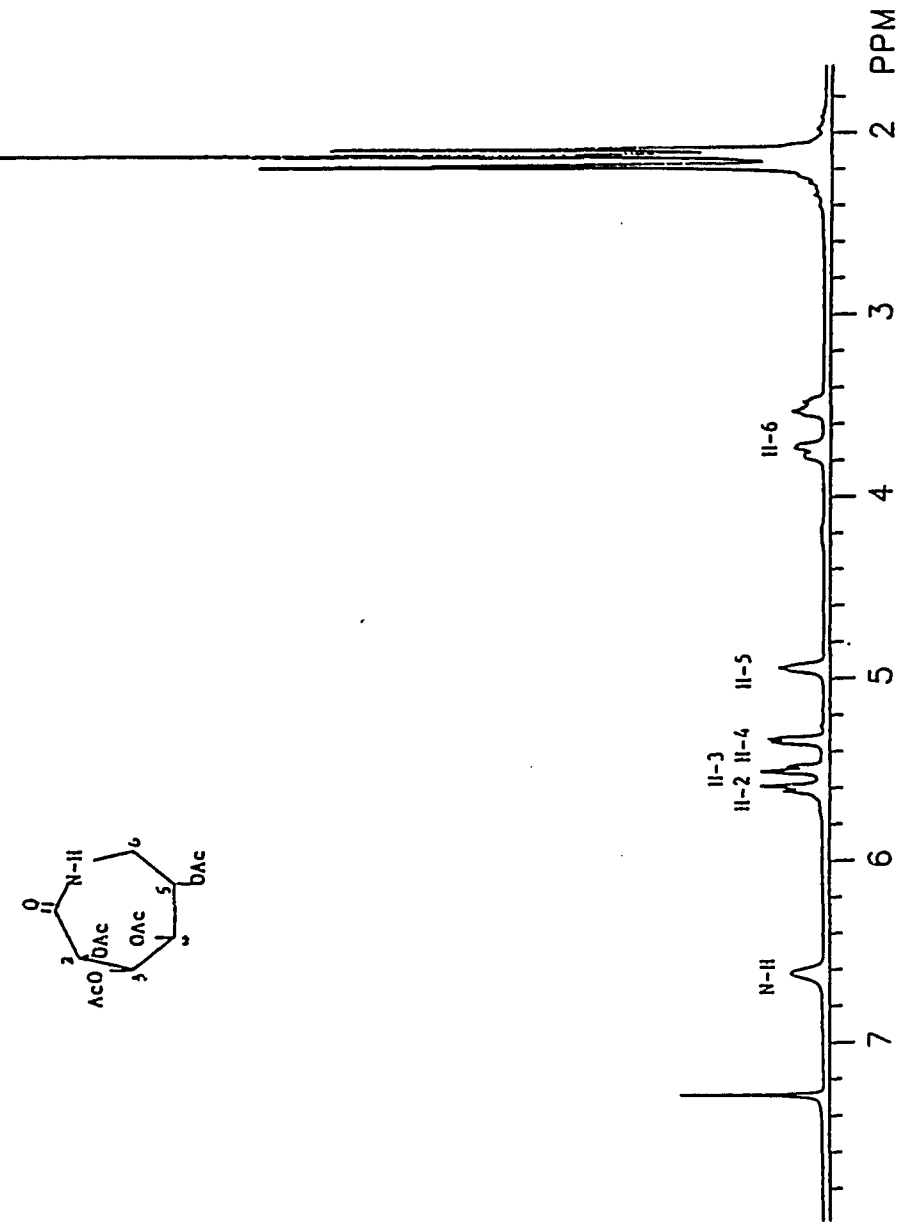

Figure 47. ^{1}H NMR of Compound 64 ($CDCl_3$).

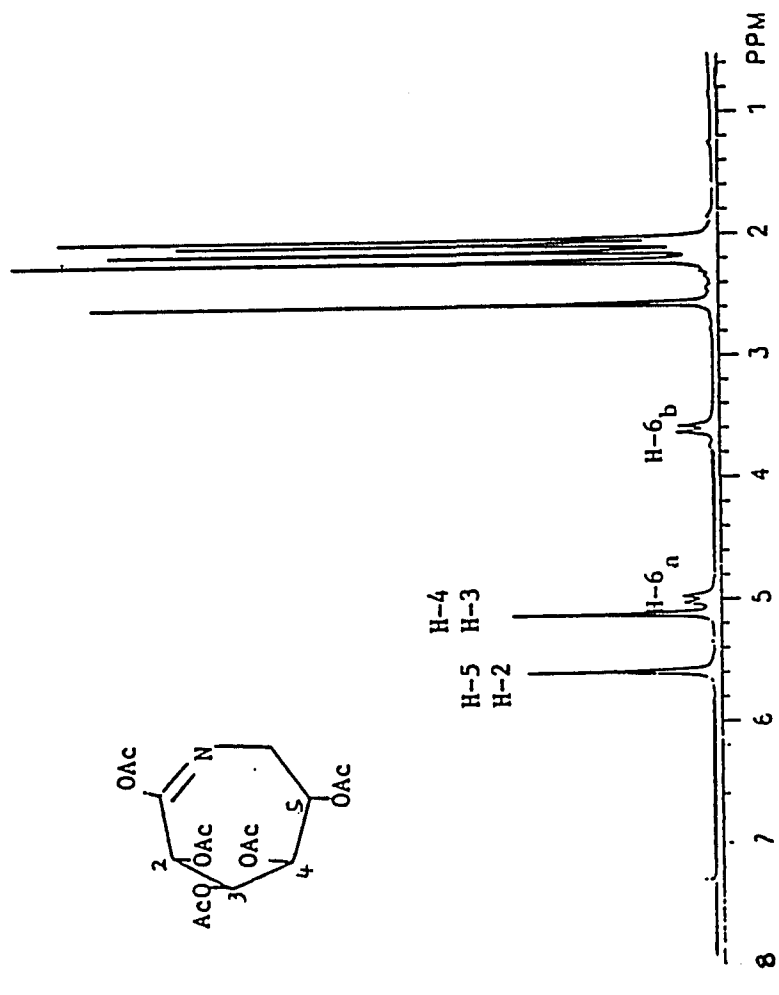

Figure 48. ^{1}H NMR of Compound 66 ($CDCl_3$).

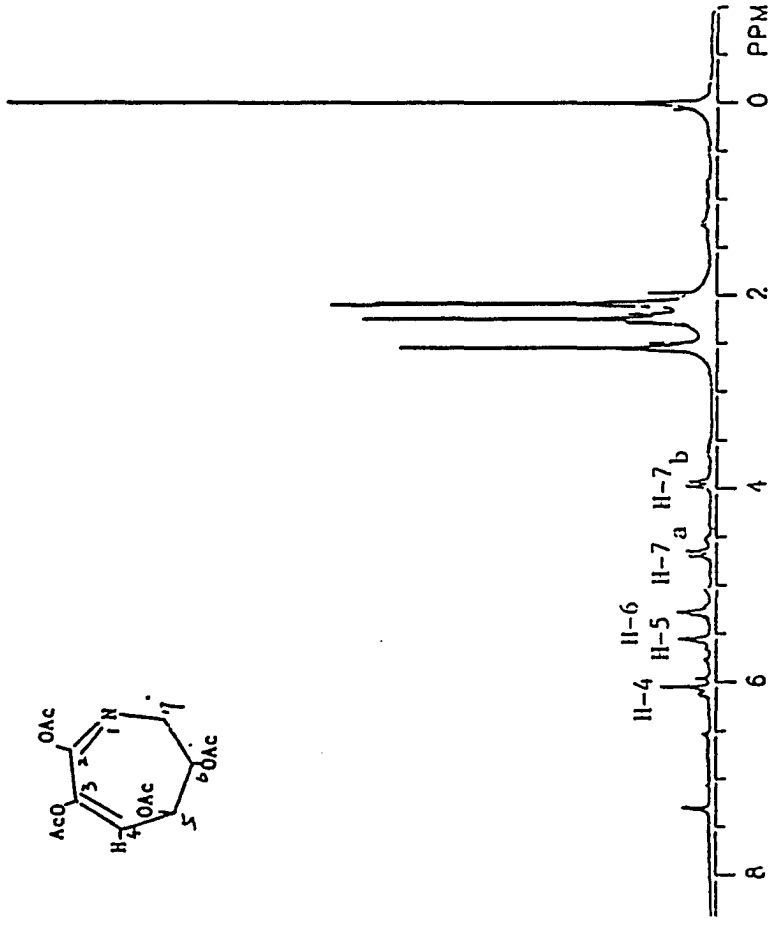

Figure 49. ^{1}H NMR of Compound 68 ($CDCl_3$).

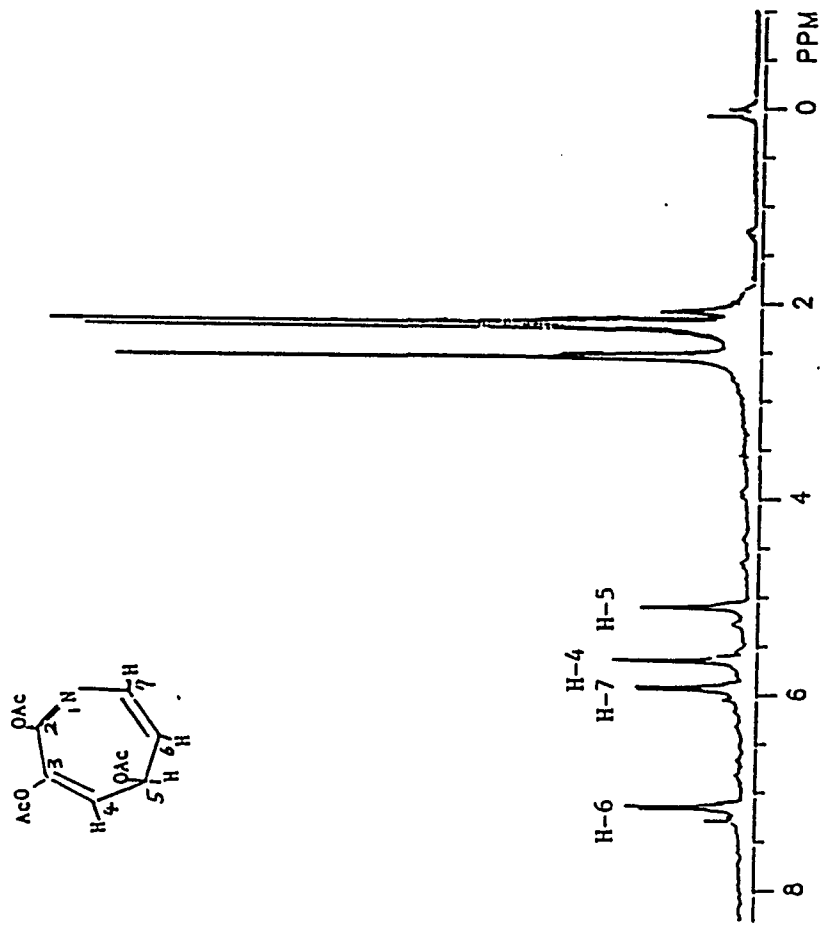

Figure 50. ^{1}H NMR of Compound 70 ($CDCl_3$).

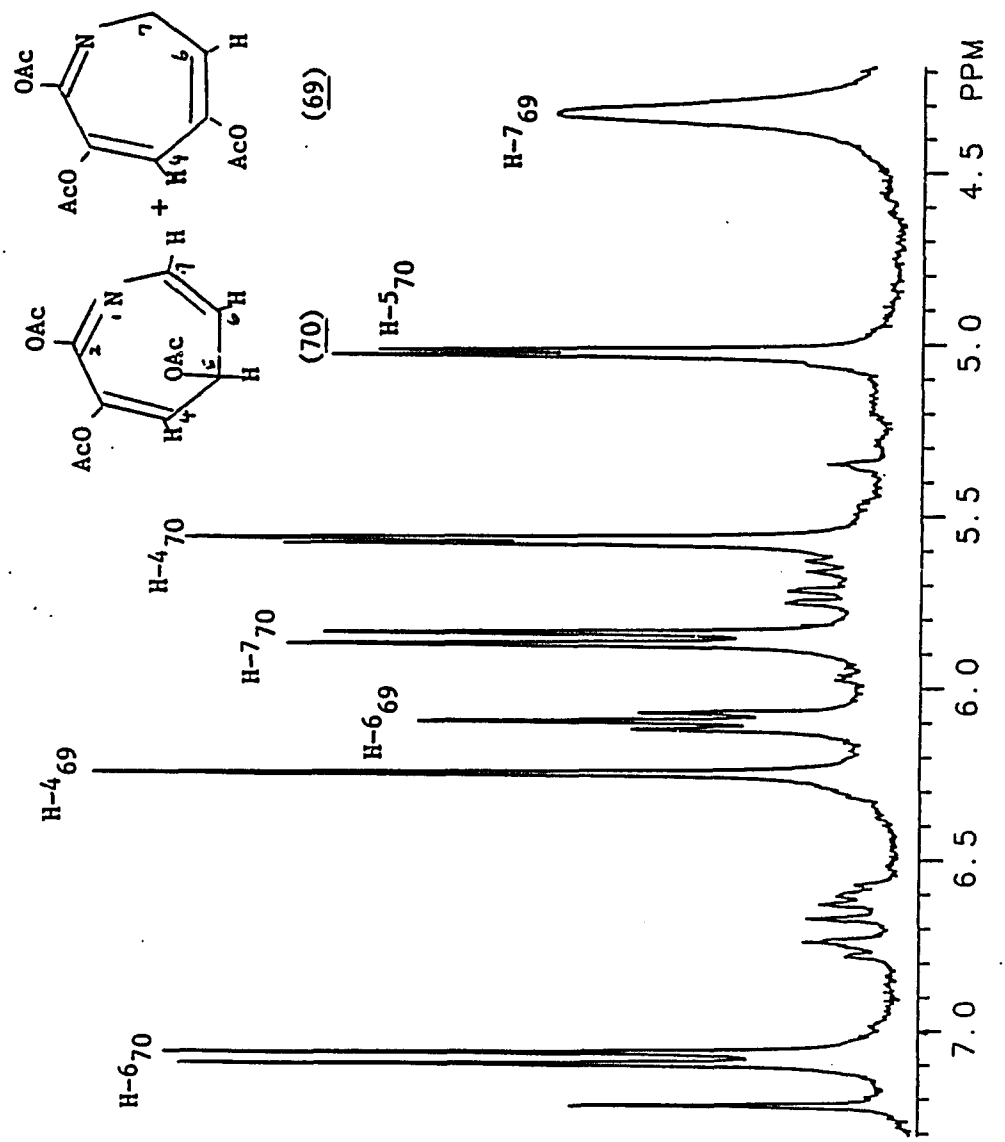

Figure 51. ^{1}H NMR of the Mixture of Compound 69 and 70 ($CDCl_3$).

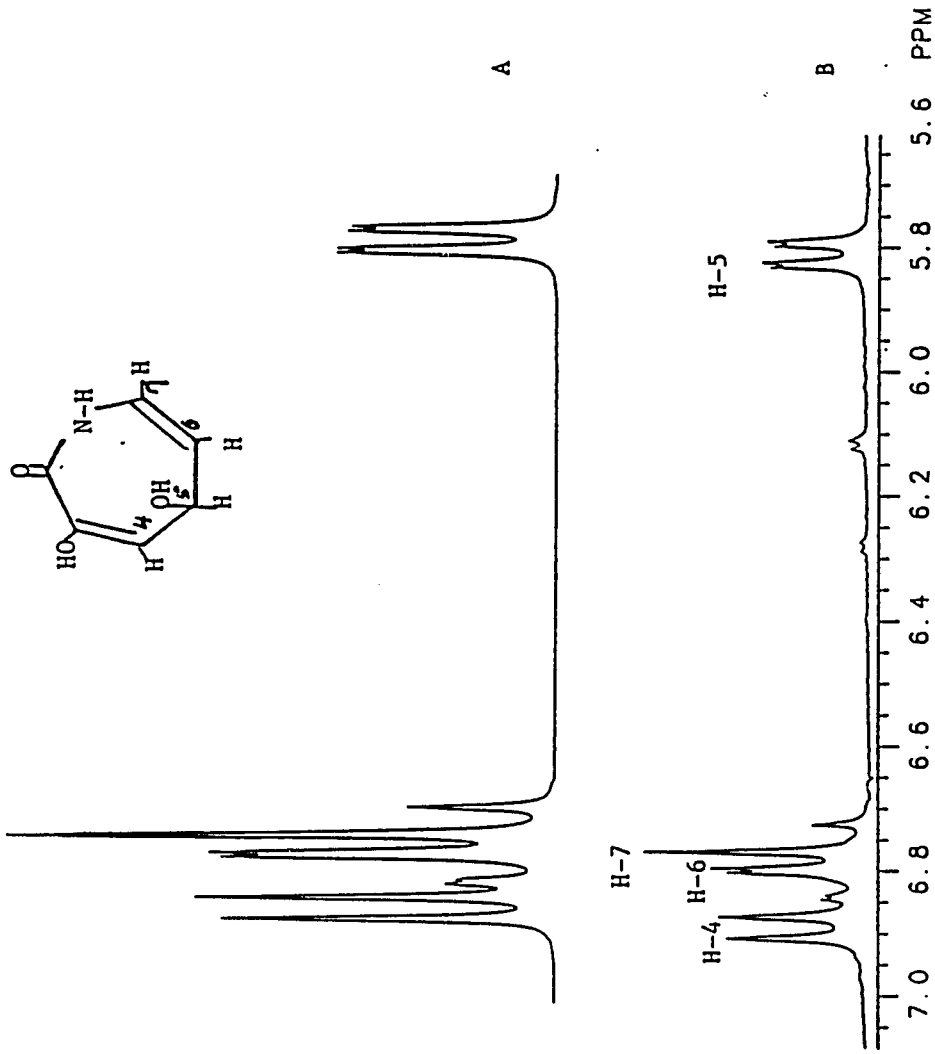

Figure 52. Simulated (A) and Recorded (B) ^{1}H NMR (D_2O) of 71, H-4 to H-7.

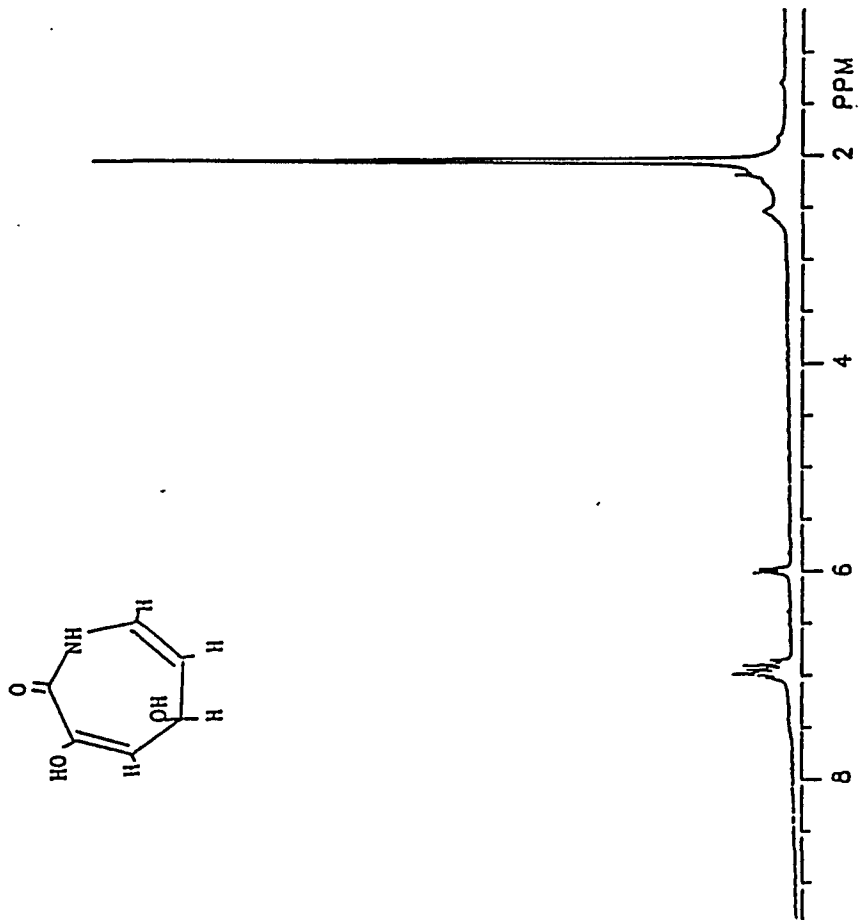

Figure 53. ^{1}H NMR of Compound 71 (CD_3COOD).

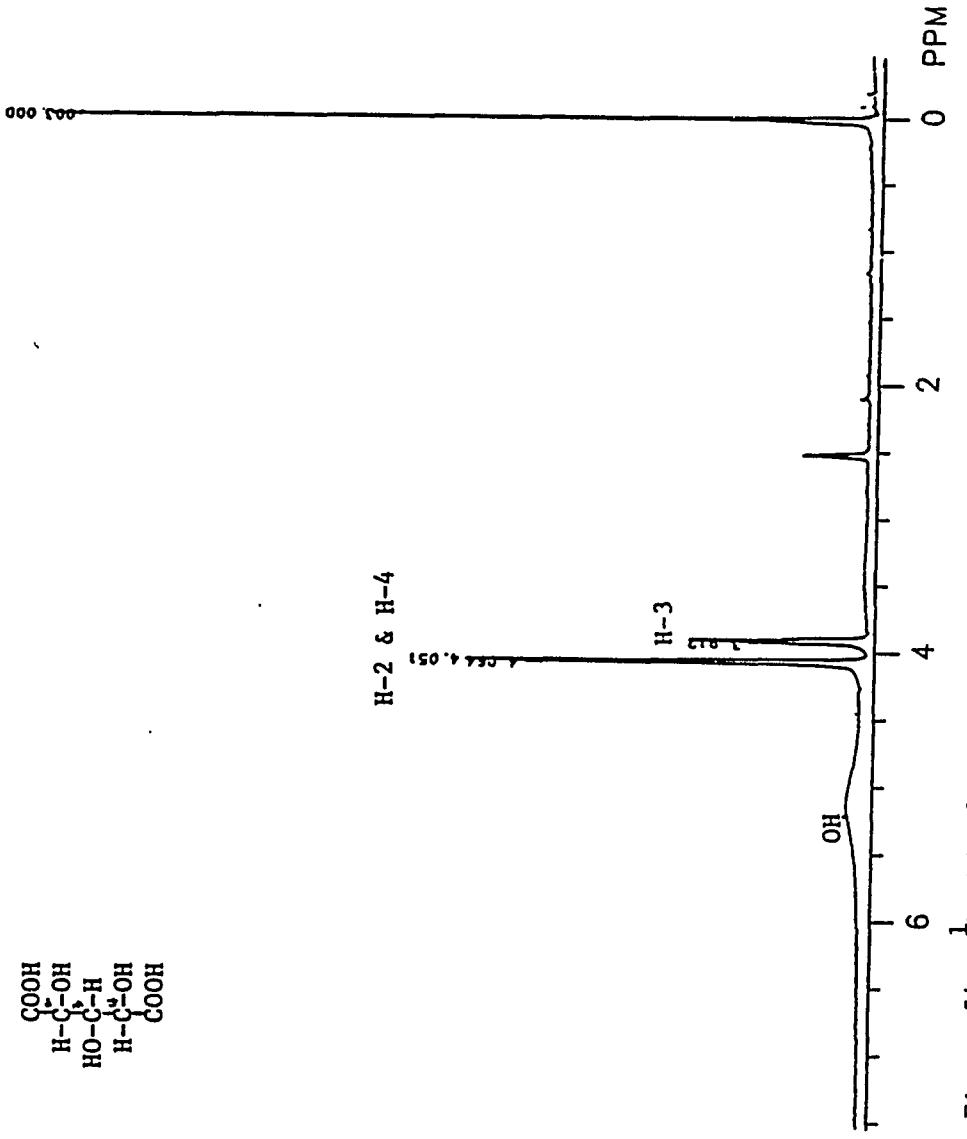

Figure 54. ^{1}H NMR of Compound 93 (DMSO-d_6).

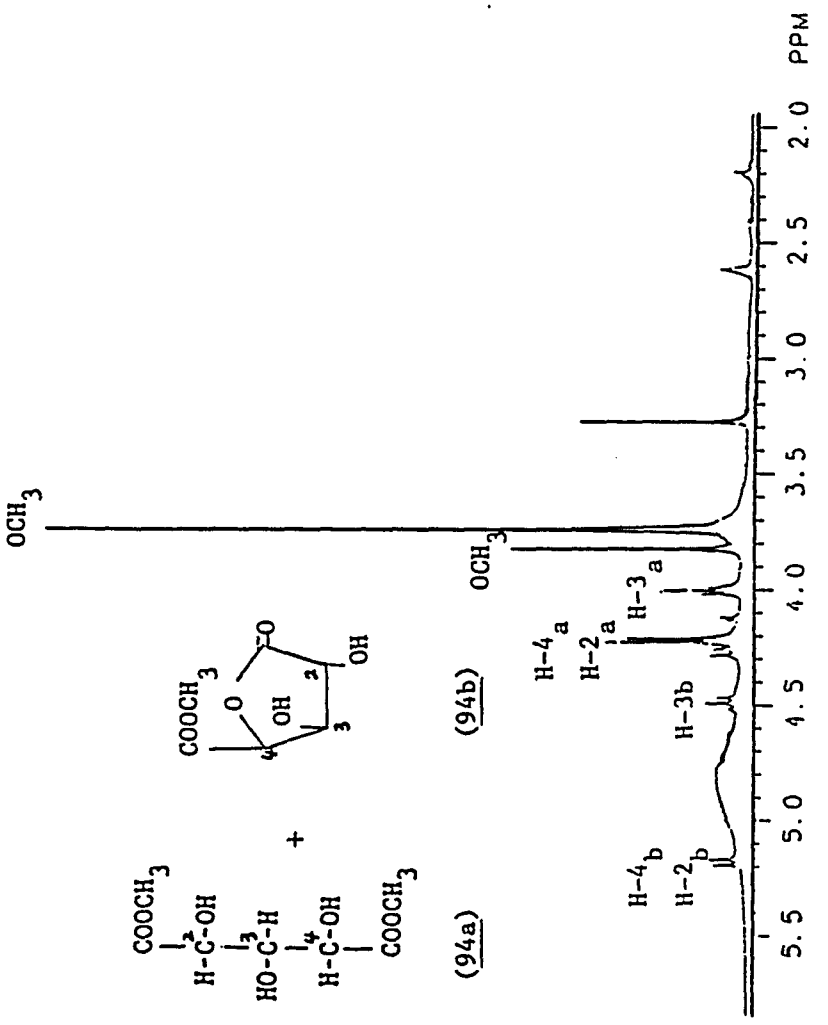

Figure 55. ^{1}H NMR of Methyl Esters of Xylaric Acid (DMSO-d_6).

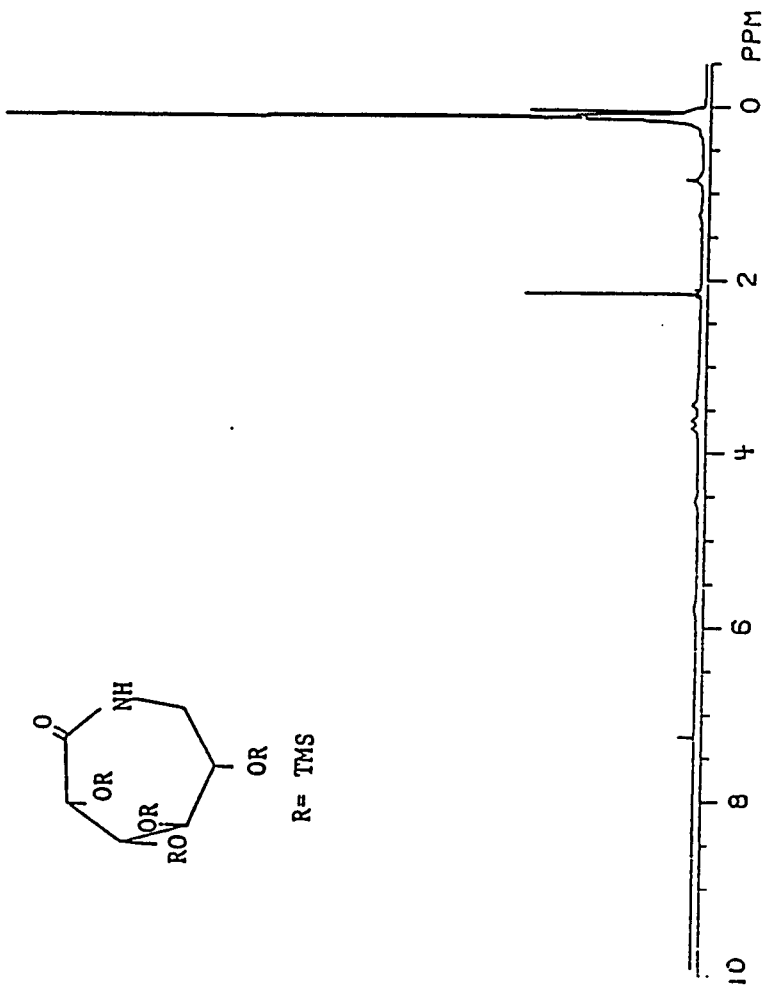

Figure 56. ^{1}H NMR of Compound 110 ($CDCl_3$).

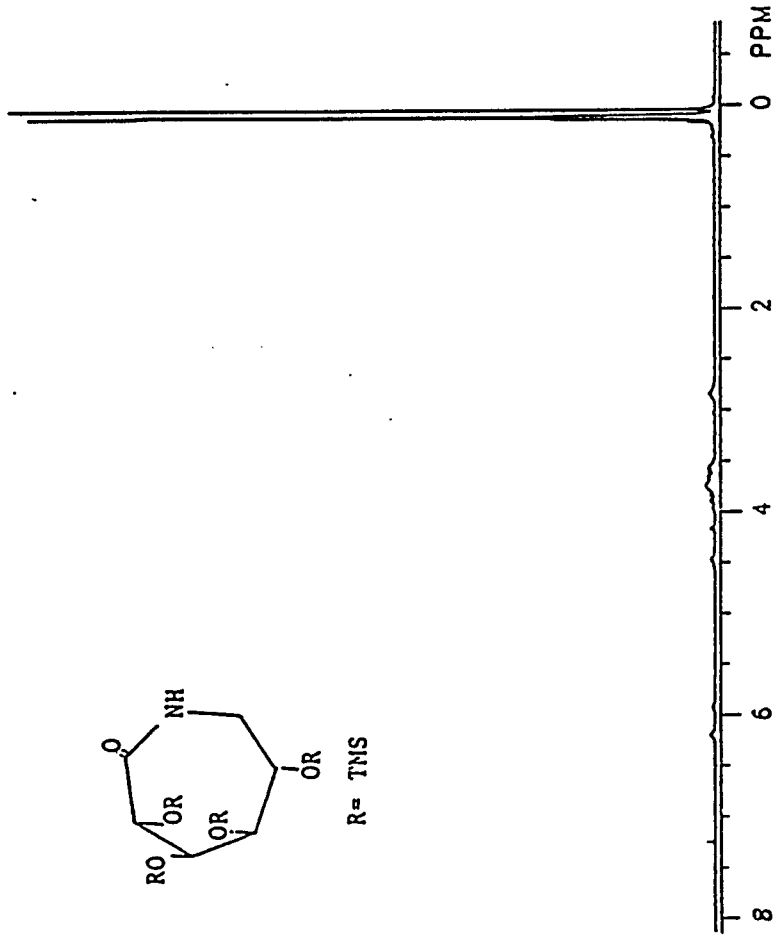

Figure 57. ^{1}H NMR of Compound 111 ($CDCl_3$).

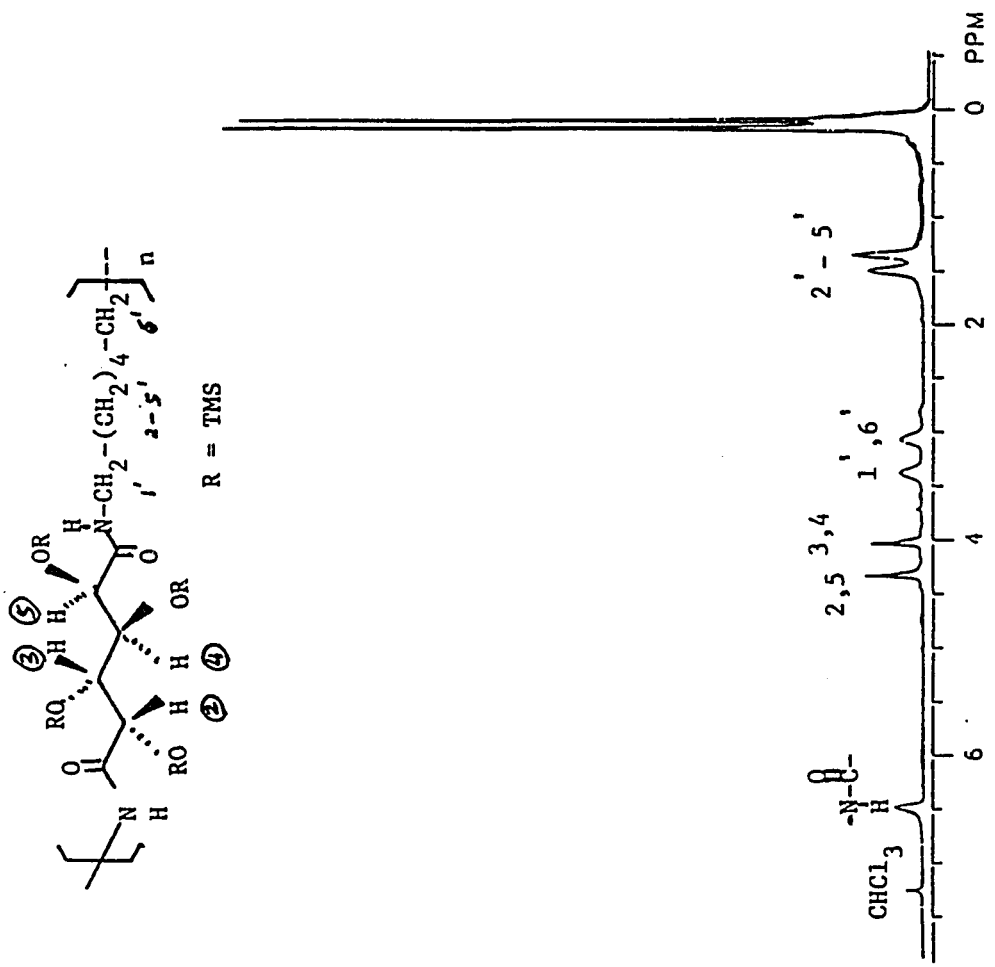

Figure 58. ^{1}H NMR of O-TMS of Compound 98 ($CDCl_3$).

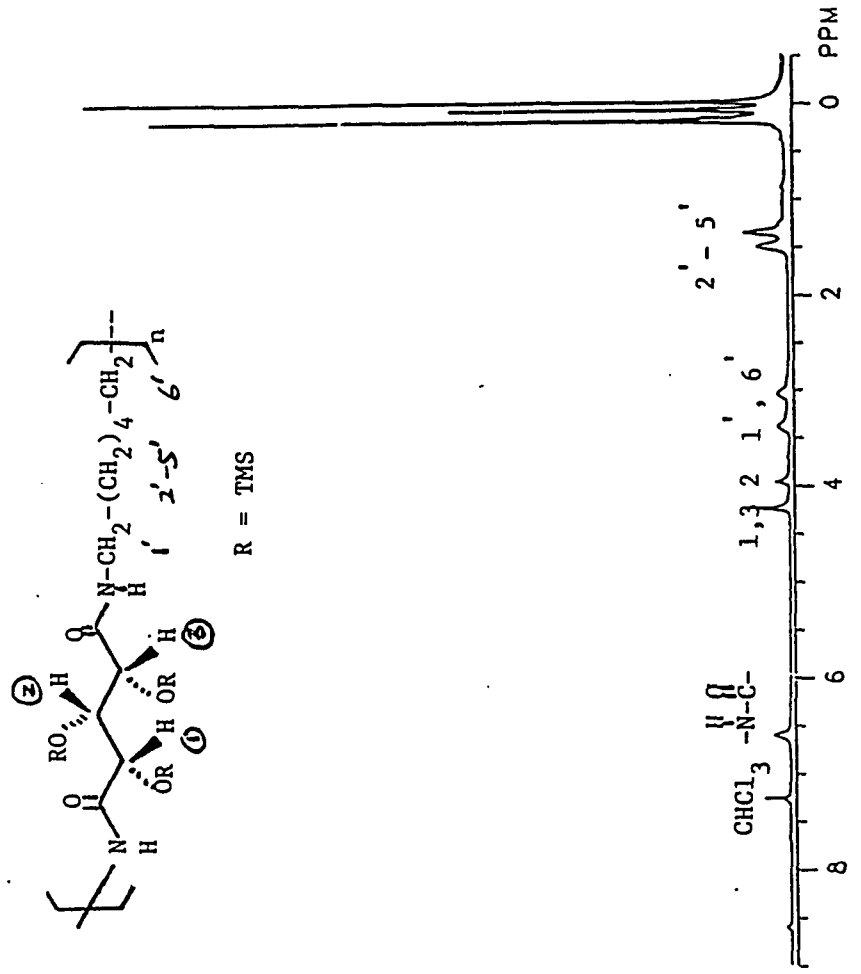

Figure 59. ^{1}H NMR of O-TMS of Compound 99 ($CDCl_3$).

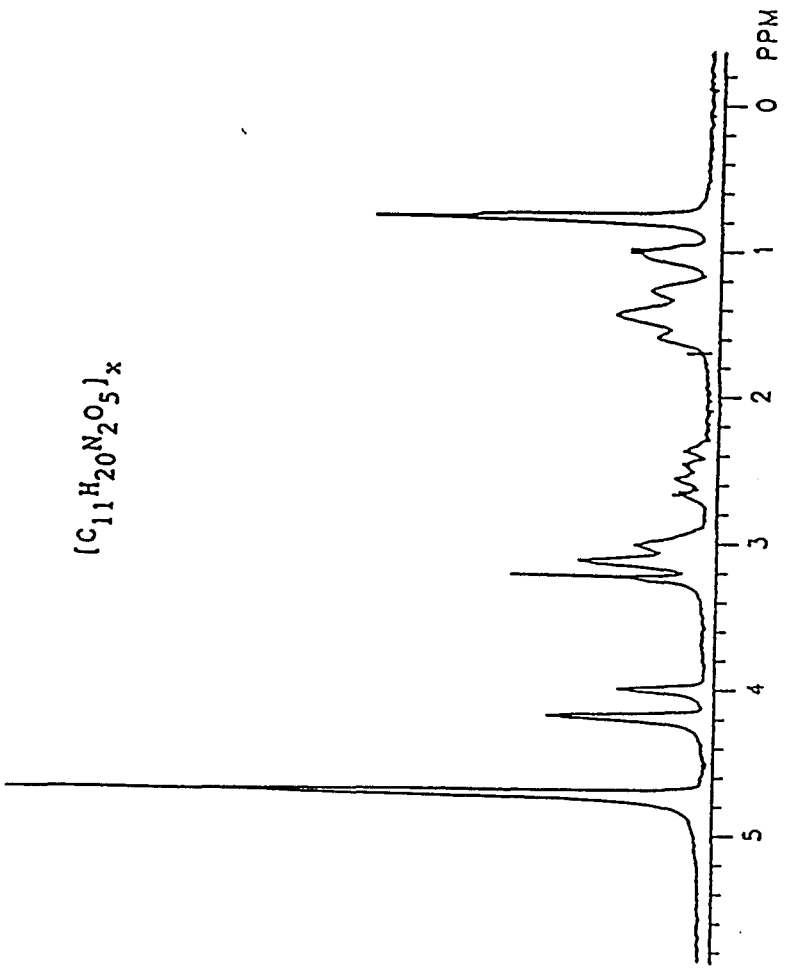

Figure 60. ^1H NMR of Compound 102 (D_2O).

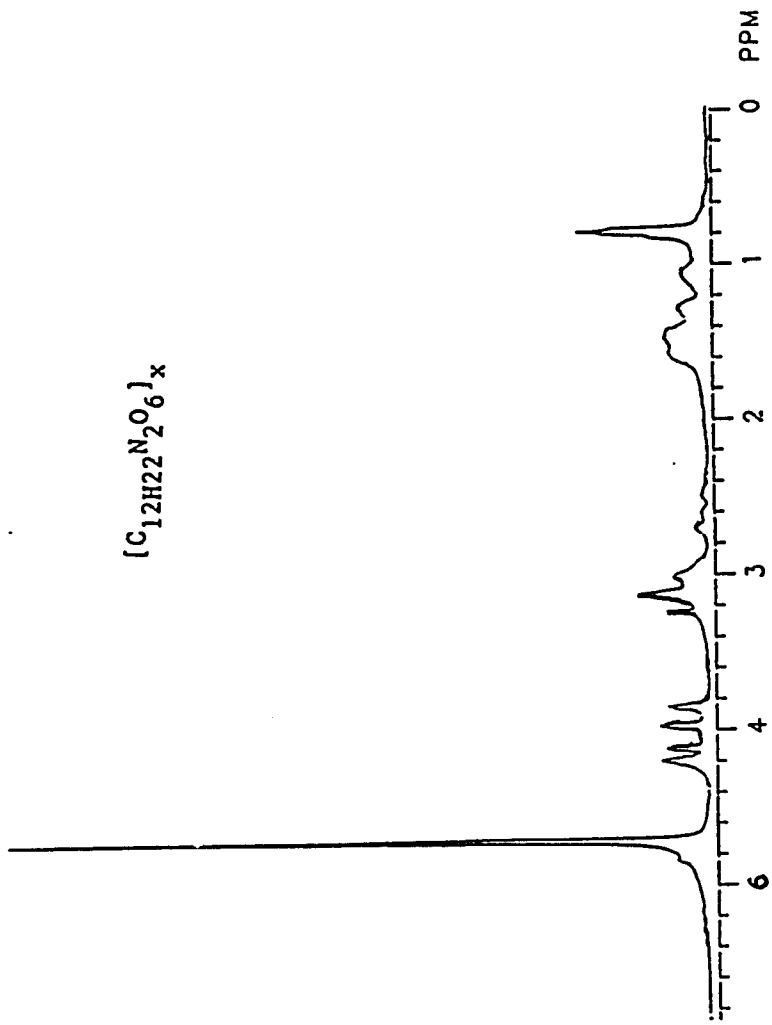

Figure 61. ^1H NMR of Compound 103 (D_2O).

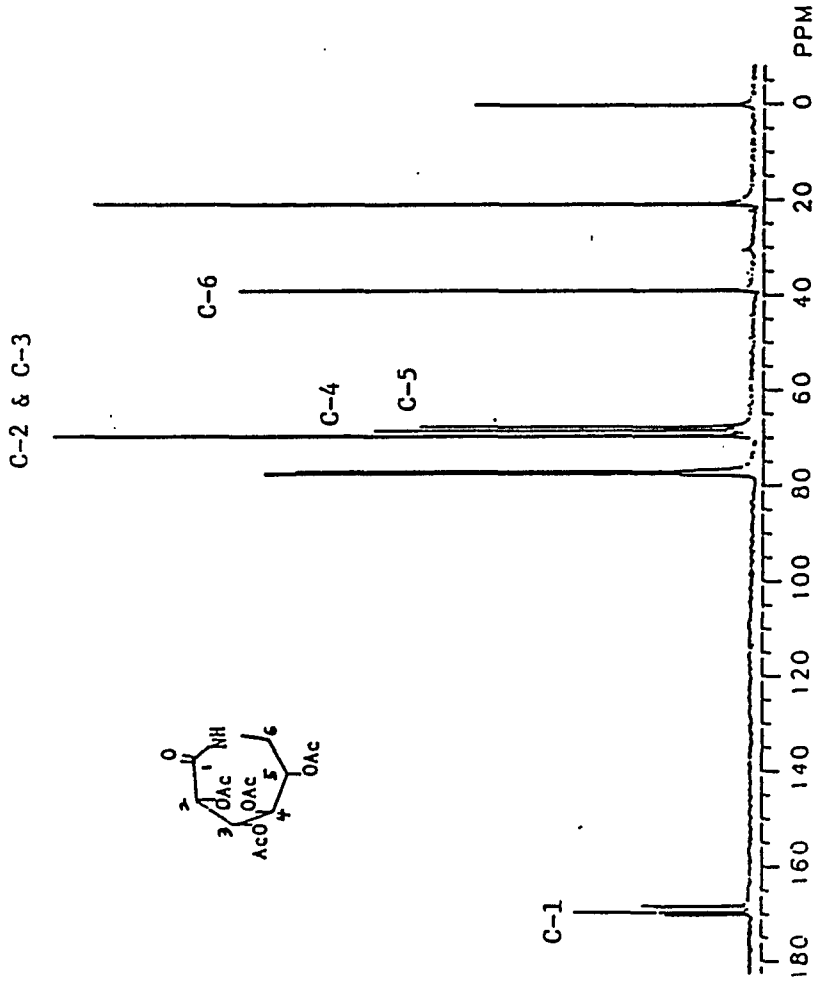

Figure 62. ^{13}C NMR of Compound 63 ($CDCl_3$).

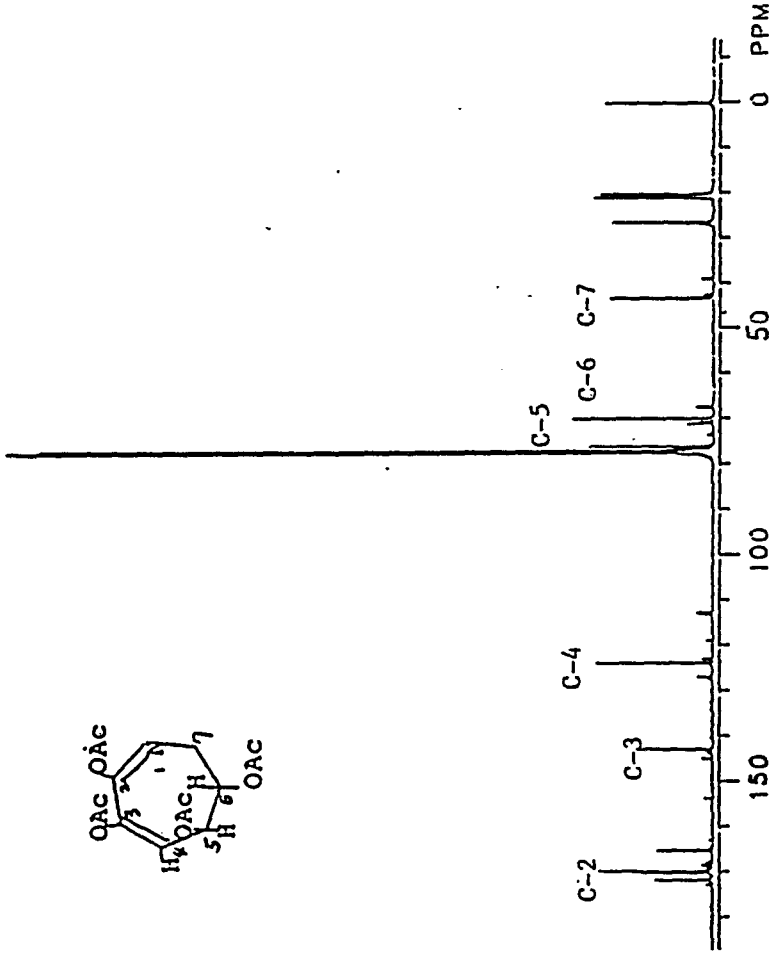

Figure 63. ^{13}C NMR of Compound 68 ($CDCl_3$).

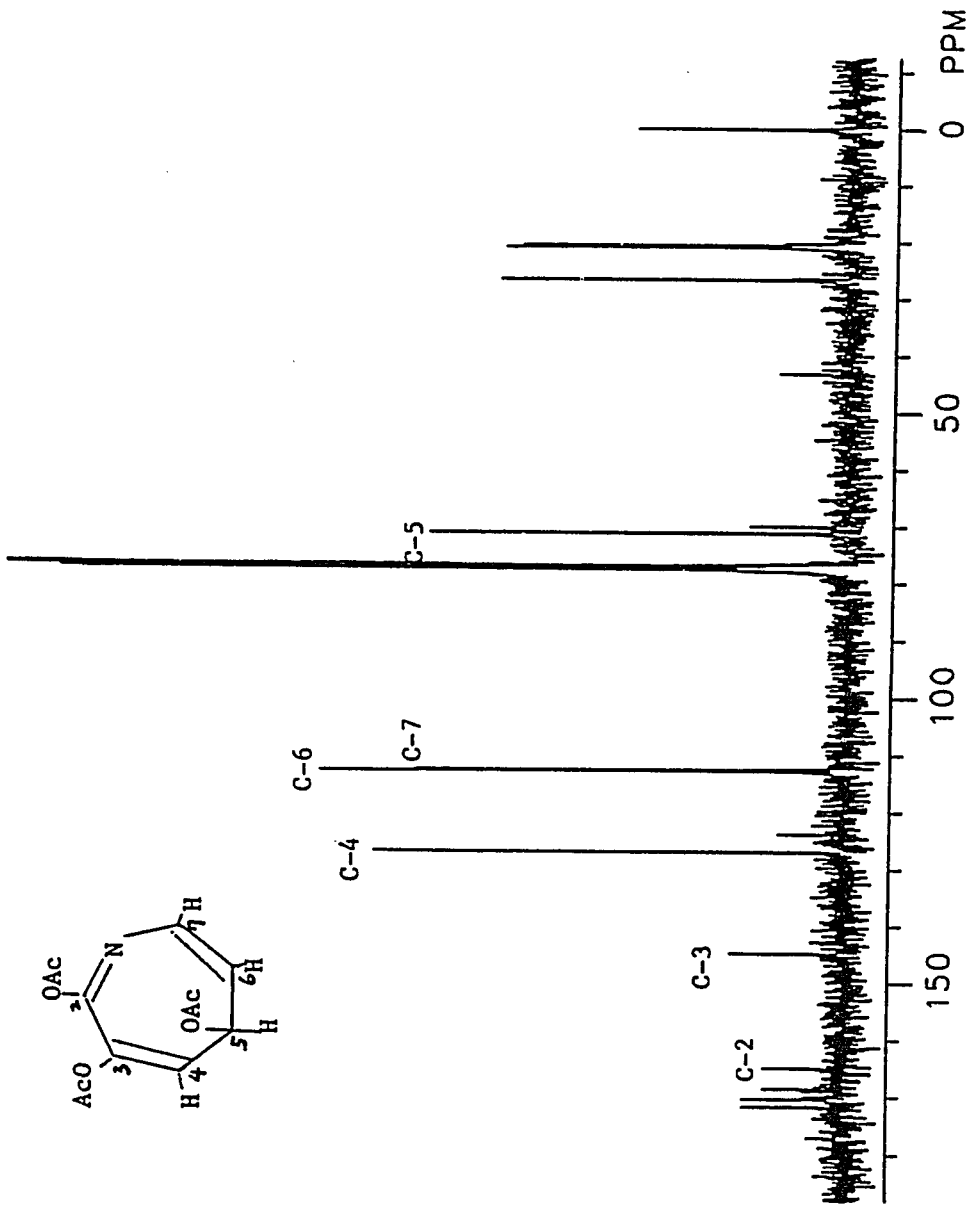

Figure 64. ^{13}C NMR of Compound 70 ($CDCl_3$).

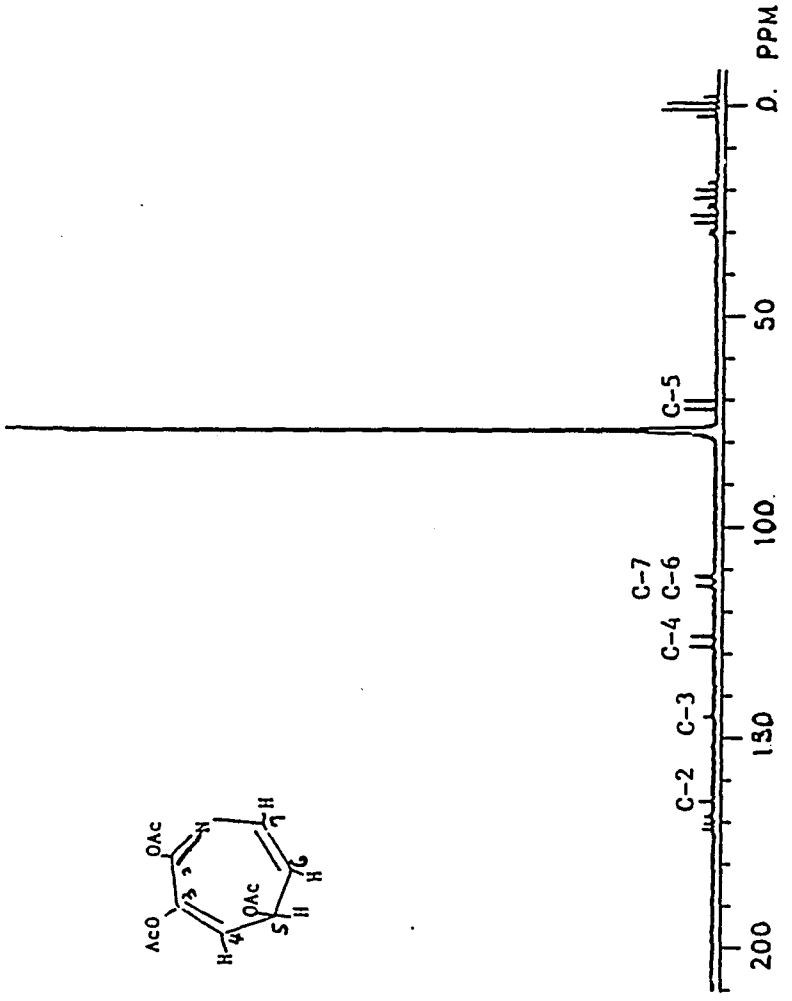

Figure 65. ^{13}C NMR (C, H Coupled) of Compound 70 ($CDCl_3$).

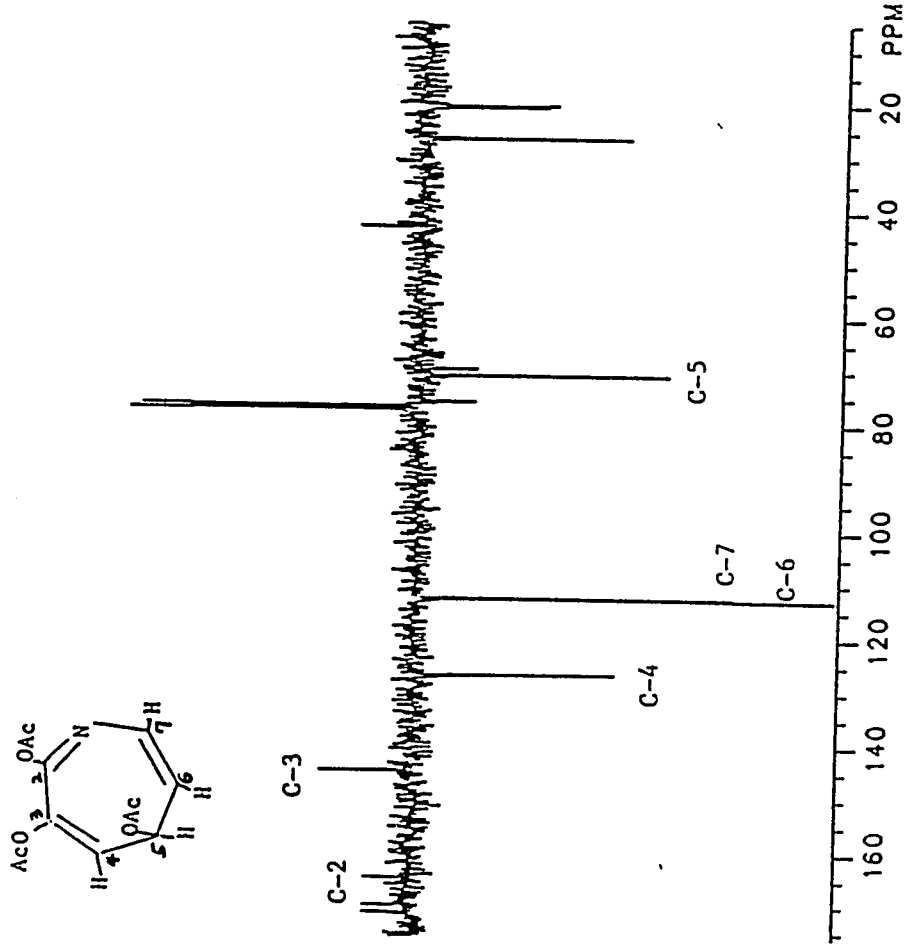

Figure 66. ^{13}C NMR Attached Proton Test (ATP) of Compound 70 ($CDCl_3$).

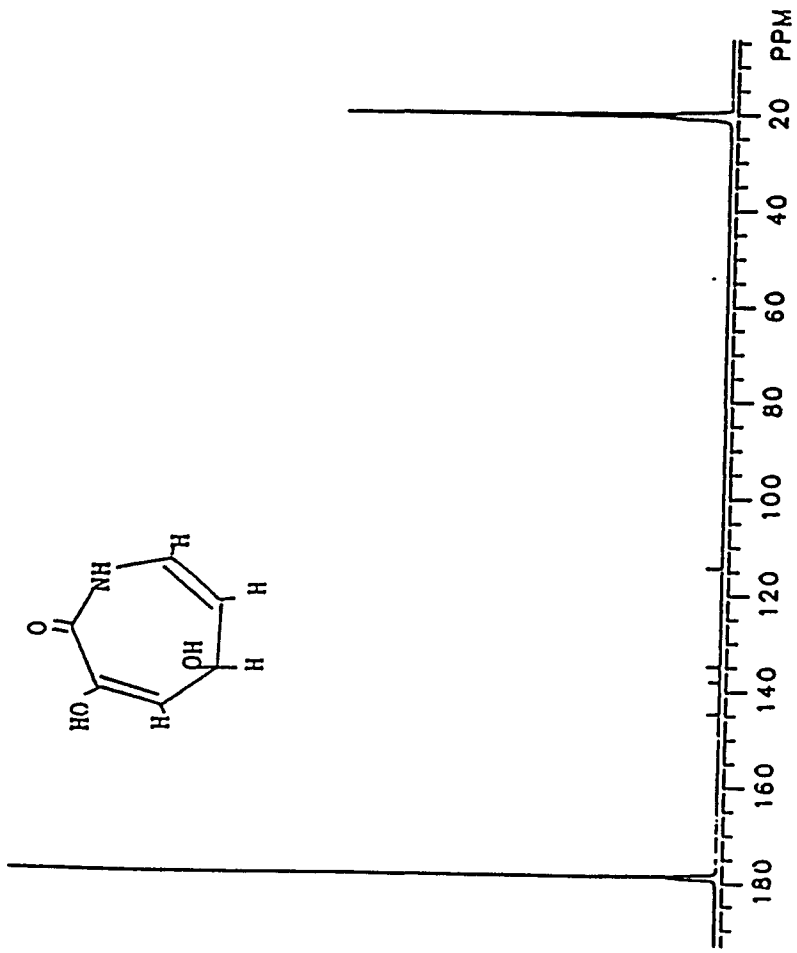

Figure 67. ^{13}C NMR of Compound 71 (CD_3COOD).

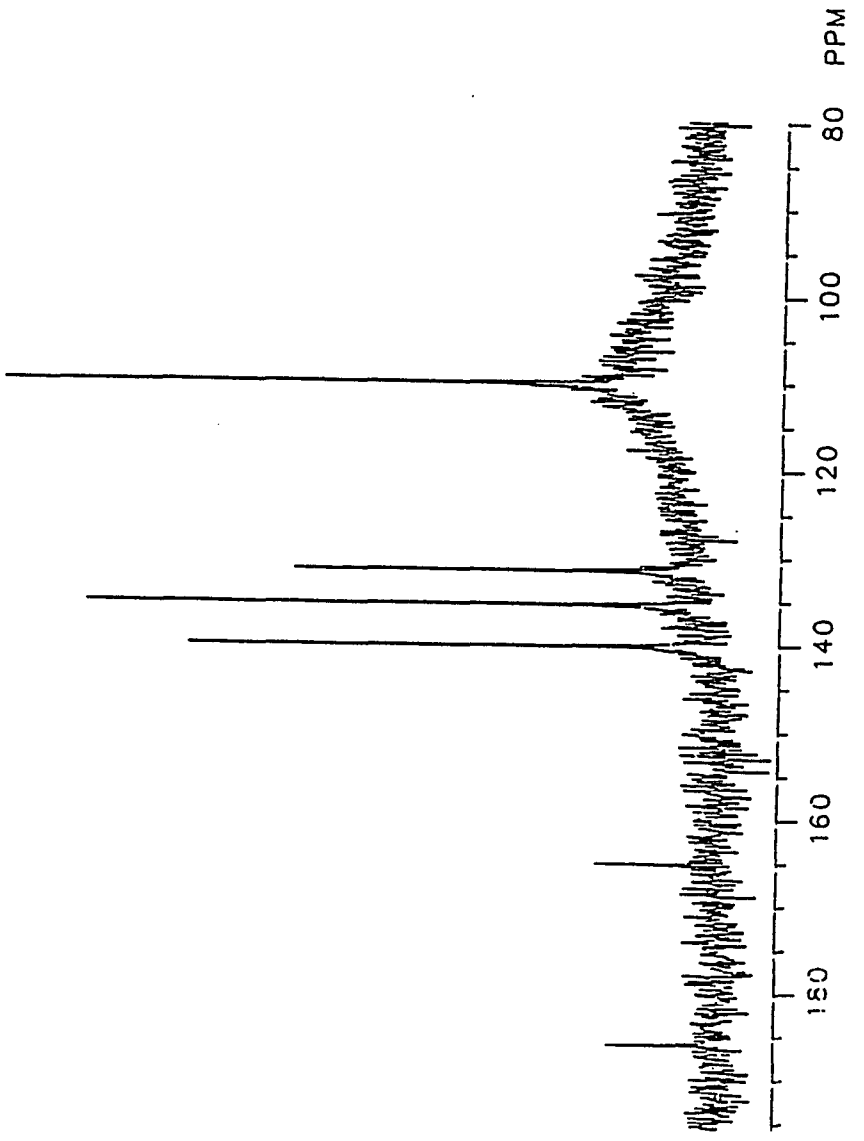

Figure 68. ^{13}C NMR of Compound 71 (D_2O).

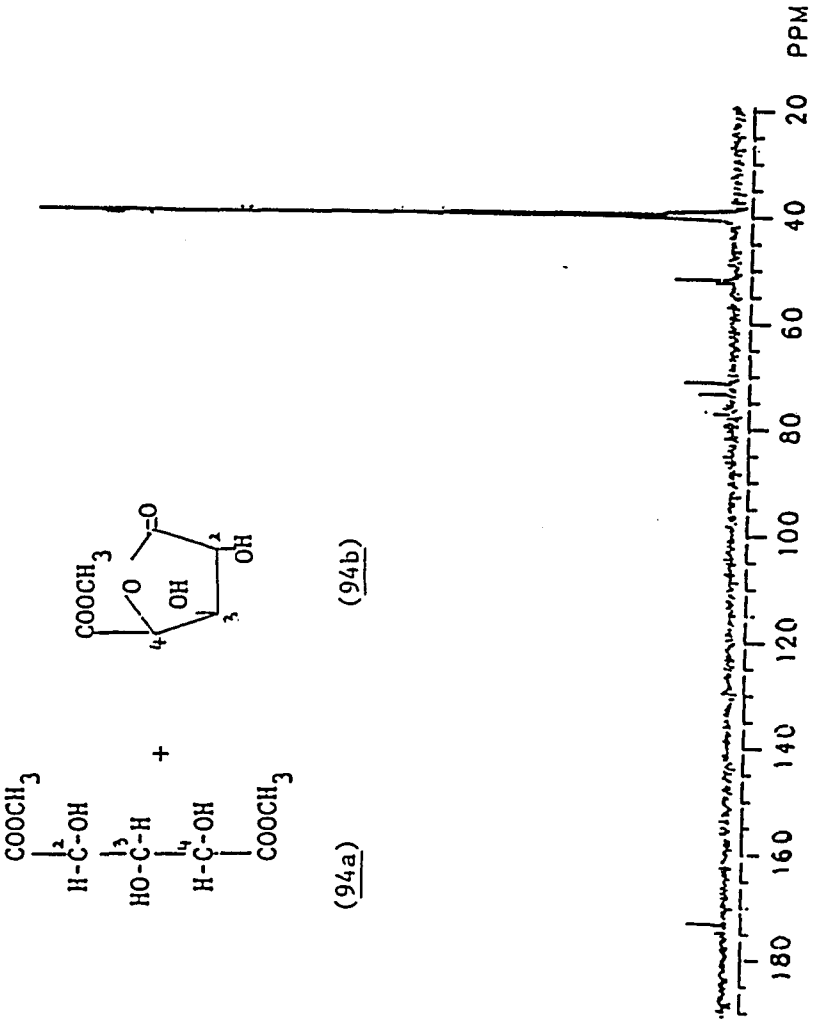

Figure 69. ^{13}C NMR of Methyl Esters of Xylaric Acid (DMSO-d_6).

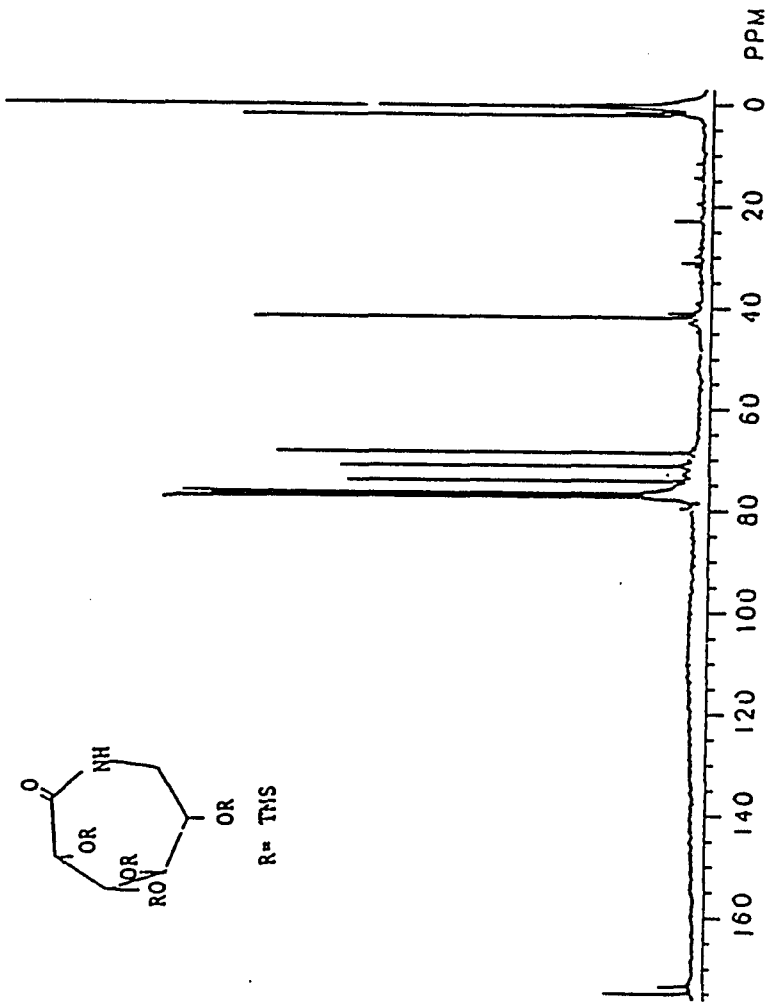

Figure 70. ^{13}C NMR of Compound 110 ($CDCl_3$).

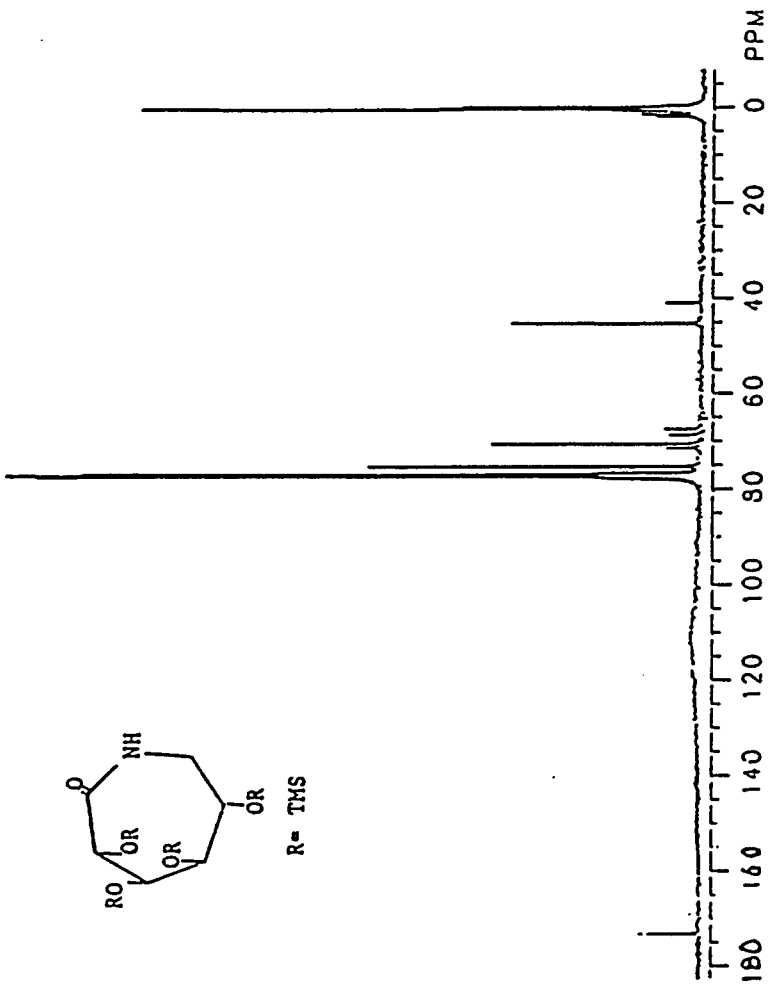

Figure 71. ^{13}C NMR of Compound 111 ($CDCl_3$).

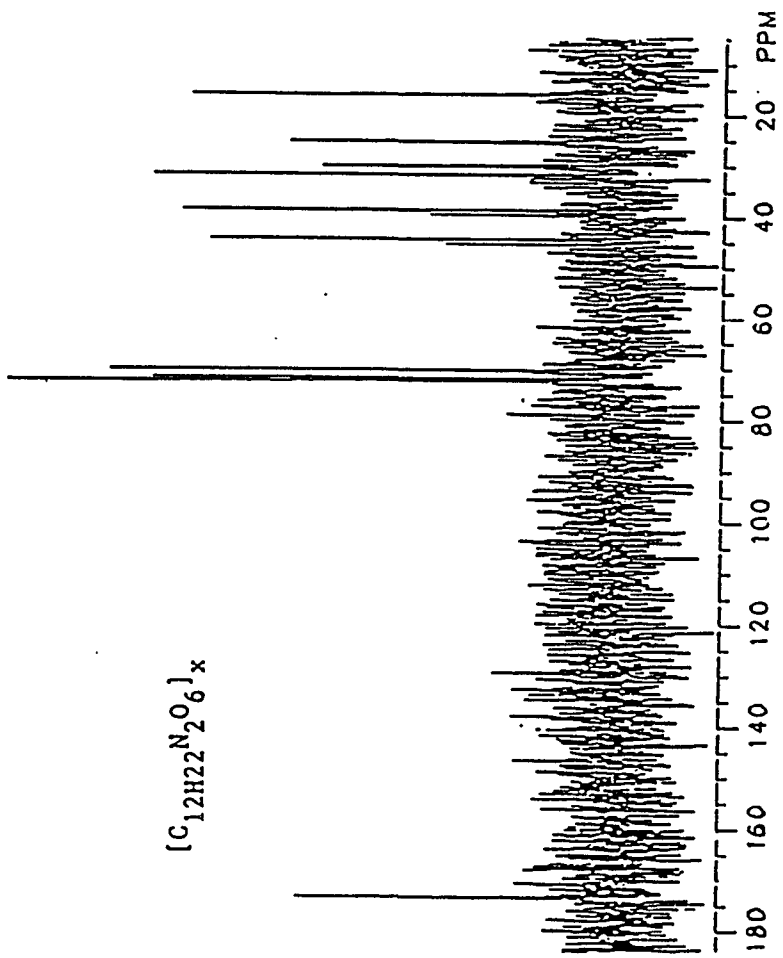

Figure 72. ^{13}C NMR of Compound 103 (D_2O).

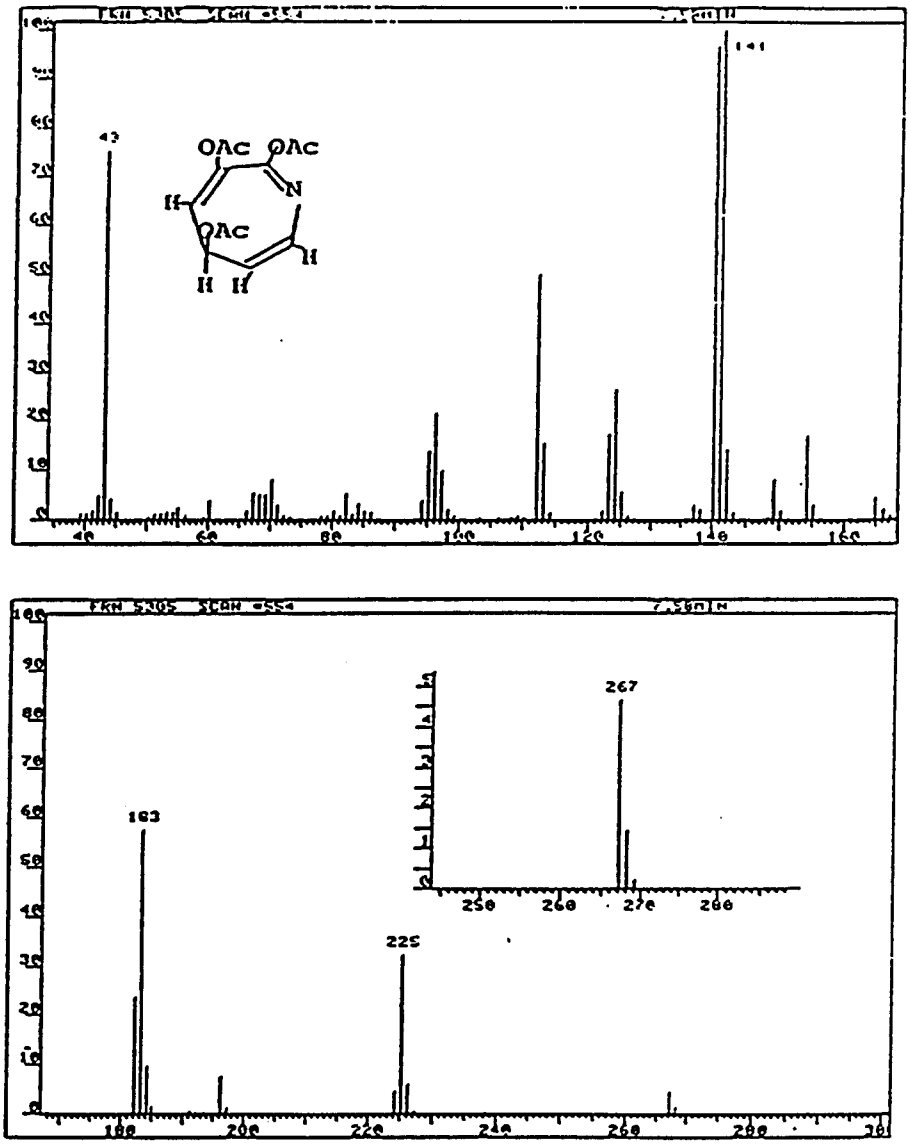

Figure 73. EI Mass Spectrum of Compound 70.

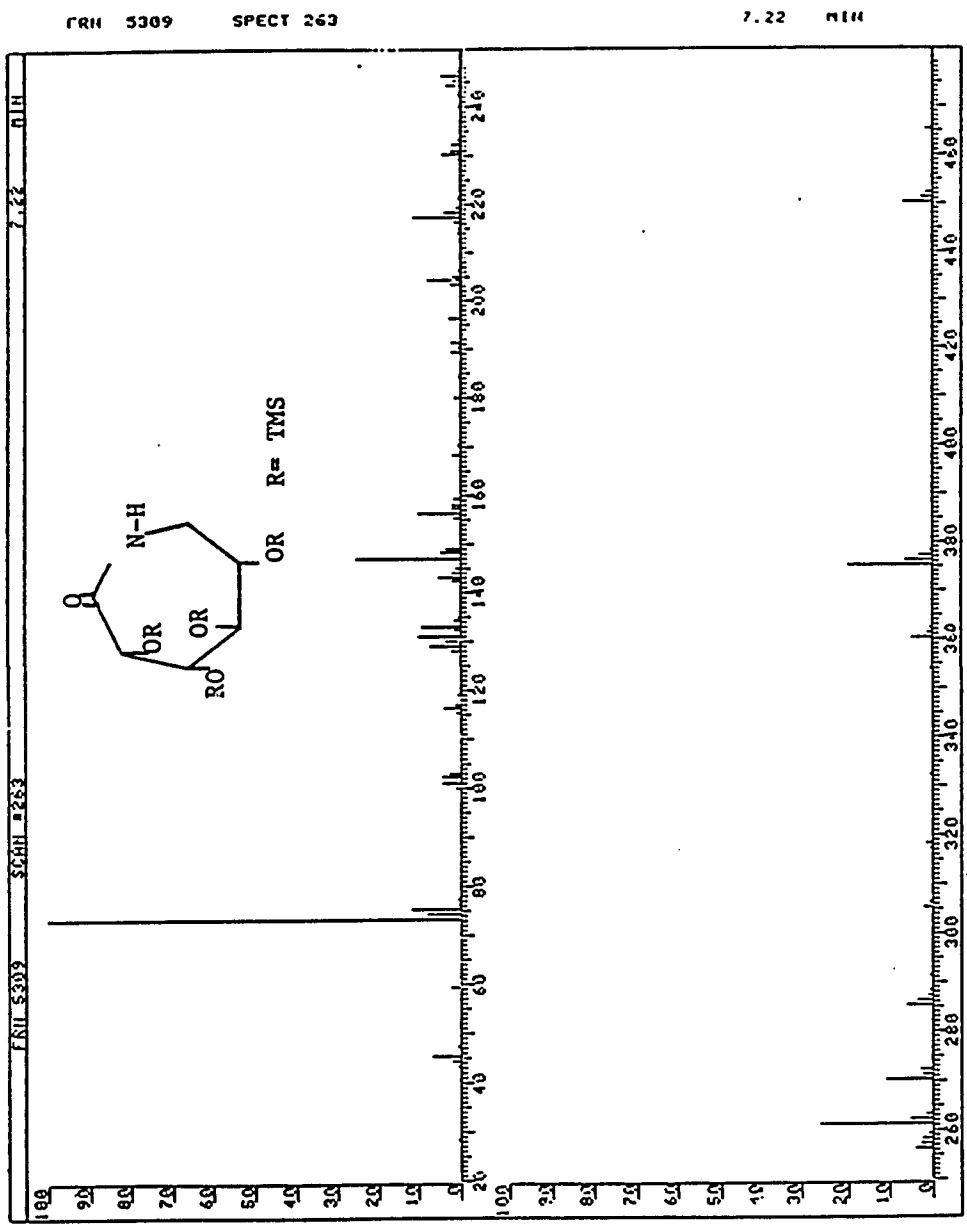

Figure 74. EI Mass Spectrum of Compound 110.

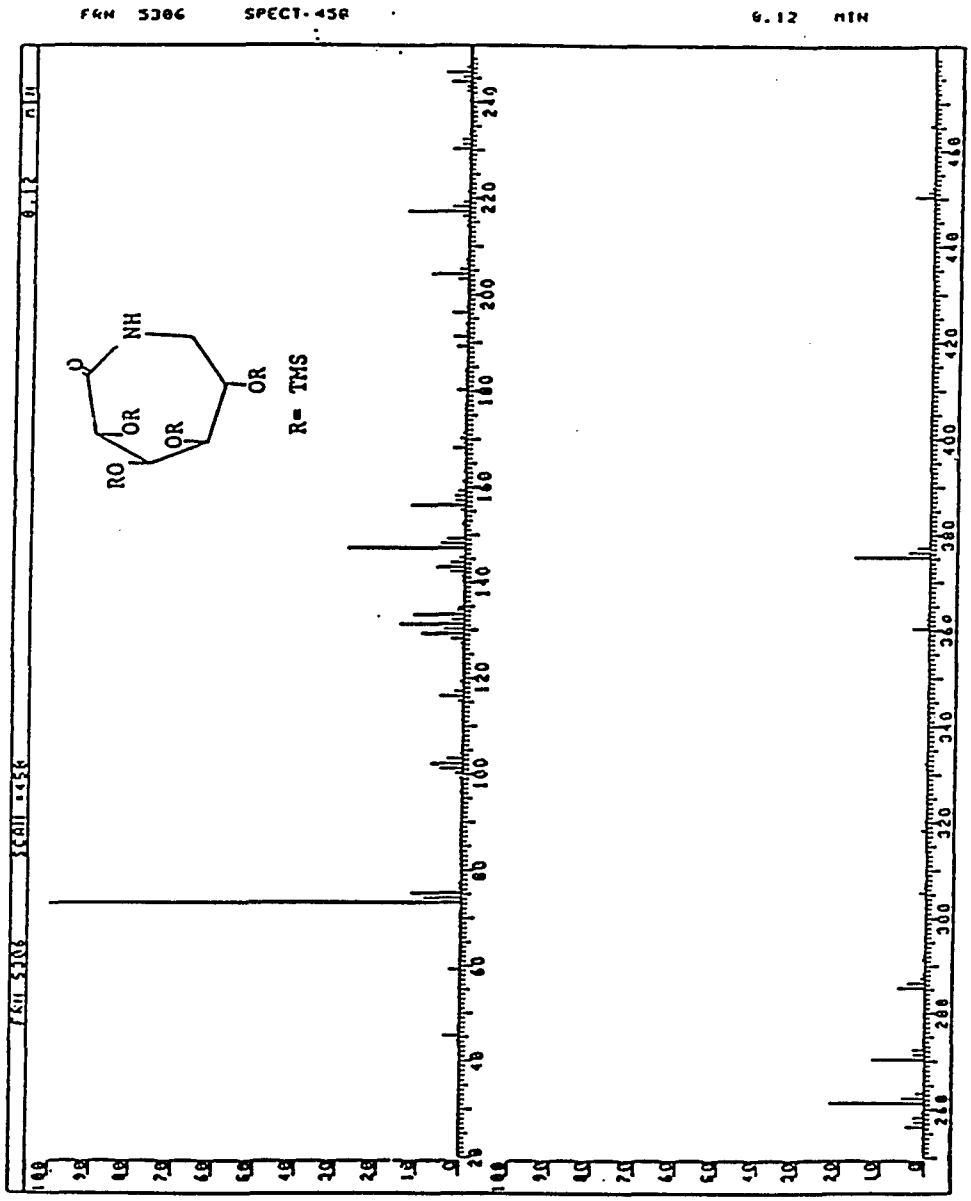

Figure 75. EI Mass Spectrum of Compound 111.

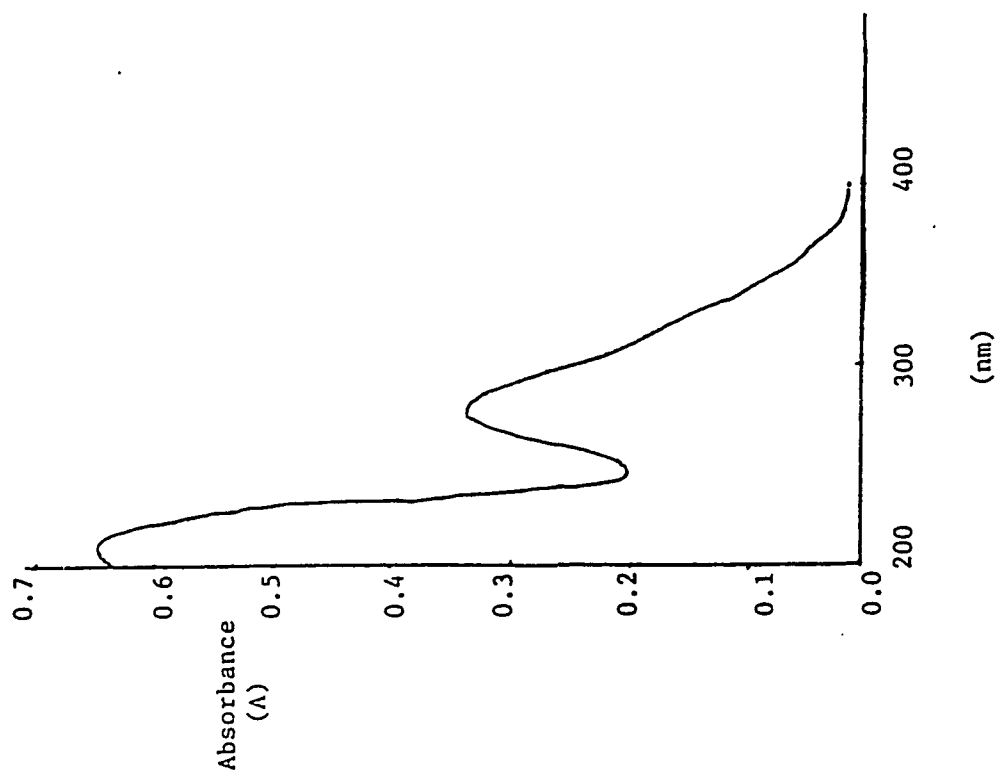

Figure 76. UV Spectrum (H_2O) of Compound 71.

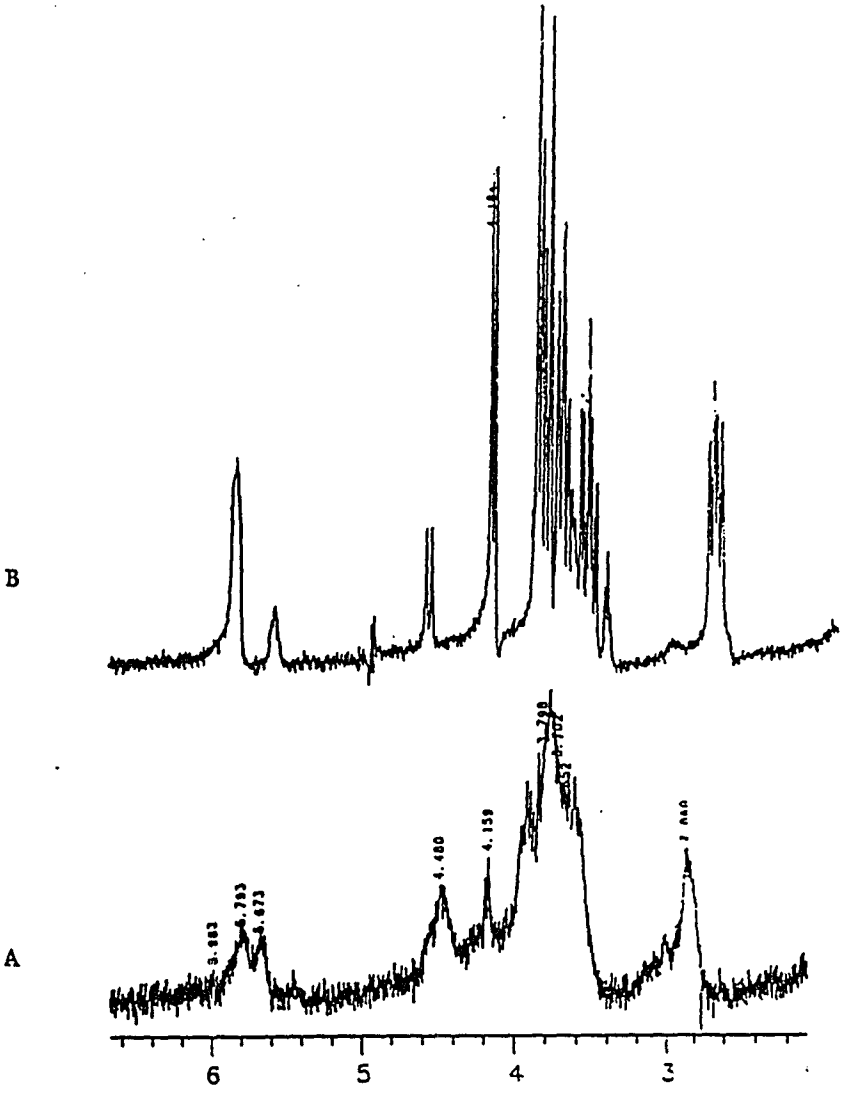

Figure 77. ^{1}H NMR of the Product from Attempted Ring-opening Polymerization of Compound 111 (A) ($CDCl_3$) and the Starting Material Compound 111 (B) ($CDCl_3$).

GRADUATE SCHOOL
UNIVERSITY OF ALABAMA AT BIRMINGHAM
DISSERTATION APPROVAL FORM

Name of Candidate Tsu-Hsing Lin

Major Subject Chemistry

Title of Dissertation Diverse Applications of Carbohydrate Acids in Organic Synthesis

Dissertation Committee:

Donald E. Kiely, Chairman

Edith Simmons

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Wayne J. Brouillette

Director of Graduate Program

Dean, UAB Graduate School

Date 8/27/87

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