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A Short Route To Benzyl Beta-D-Glycosides Of 2-Amino-2-Deoxy-D-Glucose And -D-Allose And Elimination Of The 3-Sulfonate From Benzyl 4,6-O-Benzylidene-2-Benzyloxycarbonylamido-2-Deoxy-3-O-(Methylsulfonyl)- Beta-D-Glucopyranoside

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A SHORT ROUTE TO BENZYL β-D-GLYCOSIDES OF 2-AMINO-2-DEOXY-D-GLUCOSE AND -D-ALLOSE AND ELIMINATION OF THE 3-SULFONATE FROM BENZYL 4,6-O-BENZYLIDENE-2-BENZYLOXYCARBONYLAMIDO-2-DEOXY-3-O-(METHYLSULFONYL)-β-D-GLUCOPYRANOSIDE

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CHAPTER I

INTRODUCTION

Aminosugars have been known and studied for nearly a century. Ledderhose (53), in 1876, was first to isolate, from chitin, the aminosugar D-glucosamine. Since that time many aminosugars have been synthesized in vitro. Aminosugars of the glucose, galactose, altrose, allose, mannose, talose, gulose, idose, ribose, arabinose, xylose, and lyxose series, and several hundred derivatives have been reported in the literature up to 1959 (36). Since then, the number of known aminosugars and their derivatives have been increased at least by a factor of four to six, so that one can say about 80% of all aminosugar chemistry has been done in the last eight years. The importance of aminosugars in living organisms cannot be over-emphasized. In their recent treatise on aminosugars Balazs and Jeanloz (5) have extensively reviewed their role and distribution in metabolic and biological systems. Aminosugars, as moieties, have been found in skeletal substances such as glucosamine in crustacean chitin (53); in the glycoproteins of bacterial cell walls such as glucosamine incorporated with muramic acid and protein (70); in antibiotics such as N-methyl-L-glucosamine in streptomycin (44); in antigenes such as hexosamine in kidney glomerulus antibodies (14); and in chondroitin sulfates such as galactosamine and glucosamine

sulfate in kidney tissue acid glycosaminoglycans (1).

Many biologically active aminosugars are found as 1,4-linked oligosaccharides (5). In the past decade a great variety of blocking groups and reactive groups have been found which enable the chemist to block and/or react selectively certain positions of an aminosugar. Synthesis of aminosugar derivatives with positions 1 and 4 available for coupling could lead to synthetic oligosaccharides with possible biological activity such as a new synthetic antibiotic. Dutcher (18) has recently reviewed this area of aminosugar chemistry. Aminosugars were found as moieties in 61 antibiotics up to 1962. In the last few years several more have been reported (5).

The work in our laboratory has, for a long time, centered around benzyl glycosides of aminosugars. In 1957, McCloskey (56) reviewed the chemistry of benzyl ethers and benzyl glycosides. Benzyl ethers of sugars are of great value in synthetic work because the benzyl group can be readily removed under mild conditions by hydrogenolysis. Mild hydrogenolysis also removes selectively the benzyl group from a benzyl glycoside without altering the remainder of the sugar molecule.

Steric factors seem to play an important role in hydrogenolysis. Ballou, Roseman, and Link (6) have shown that the relative rates of hydrogenolysis of anomeric

benzyl glycosides is quite different. With D-glucose derivatives, the β-D-glycoside is cleaved in three minutes, but the α anomer requires eight hours under comparable conditions. This difference has been linked to the stereochemistry of the groups at positions 1 and 2. In the β anomer, the groups are trans; in the α anomer the groups are cis. Generally one finds that the anomer with the trans configuration is cleaved faster than the one with the cis configuration. Steric or neighboring group effects are thus probably responsible for the observed difference in rates. The benzyl glycosides of D-allosamine are also in the trans configuration, relative to the 2-amino group in the β anomers. Facile preparation of these β anomers would allow an easy approach to derivatives which, after selective removal of the benzyl glycoside moiety, could be coupled at the 1 position.

Several methods are currently available for the preparation of β glycosides. The method of Fischer is the most generally used and involves protection of the amino group and subsequent glycosidation with alcohol in the presence of a mineral acid (59, 15). The amino group must be protected to prevent development of a positive charge on the nitrogen by salt formation with the mineral acid. If this charge is present, glycosidation will not take place because of ammonium ion-proton repulsion. Another method employed

is that of Koenigs' and Knorr's (43) which involves protection of hydroxy and amino groups with subsequent glycosyl halide formation using a hydrogen halide in acetic anhydride. Protection of hydroxy and amino groups prevents, under mild conditions, introduction of the halogen into positions other than C_1. The β glycoside is then prepared from the α glycosyl halide by glycosidation with alcohol in the presence of mercuric cyanide or silver carbonate (49, 73, 33).

The method of Fischer (59, 15) has severe limitations since a mixture of anomers is usually obtained. This mixture usually contains predominantly the α anomer. Kuhn, Zilliken, and Gauhe (51) found that when they allowed 2-acetamido-2-deoxy-D-glucopyranose to react with methanol and hydrochloric acid, they obtained a mixture of methyl glycosides consisting of 85% of the α anomer and 15% of the β anomer. Using benzyl alcohol and hydrochloric acid, Gross and Zimmerman (27) also reported 85% of the α anomer and 15% of the β anomer when they prepared the benzyl glycoside of 2-benzyloxycarbonylamido-2-deoxy-D-glucopyranose. Fractional recrystallization methods, often of a derivative, must be employed to separate these anomeric mixtures into the pure anomers.

On the other hand, the preparation of a glycoside from the α halide (49, 73, 33) will yield the pure β anomer but is time consuming and overall yields are low. For example,

methyl 2-acetamido-2-deoxy-α-D-glucopyranoside is prepared from 2-amino-2-deoxy-α-D-glucose hydrochloride by a series of reactions involving first the preparation of 2-acetamido-2-deoxy-3,4,6-tri-O-acetyl-1-chloro-1,2-dideoxy-α-D-glucopyranose, then preparation of methyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside and finally deacetylation of the above precusor (20, 52, 49). The overall yield from 2-amino-2-deoxy-α-D-glucose hydrochloride is 8% (13).

A less commonly used method for the preparation of β anomers is their preparation from a β glycosyl fluoride (38). Treatment with alkoxide will yield the β glycoside if the 1-fluoro and 2-hydroxy groups are trans. The proposed mechanism for the formation of the β glycoside is formation of an ethylene oxide ring bridging C_1 and C_2 followed by trans cleavage with alkoxide.

Horton, Wolfrom, et. al., have investigated several routes to glycosyl halides (72, 71, 37, 38). They utilized conversion of N-substituted 1-thio-D-glycosides to glycosyl bromides or chlorides and have contributed to the area of β glycoside preparations.

Recently Inch and Fletcher (40) have employed solvolysis of esters to prepare methyl β glycosides. If 2-acetamido-1-O-acyl-3,4,6-tri-O-benzyl-2-deoxy-β-D-glucopyranose is treated with methanol, methyl 2-acetamido-3,4,6-tri-O-benzyl-2-deoxy-β-D-glucopyranoside is obtained. The

reaction fails to yield the glycoside if the α-1-acetate is used.

Another method for the preparation of β glycosides, which was developed by Helferich (32), involves treatment of the penta-acetate of an α-D-glycoside with phenol in the presence of zinc chloride. It is, however, used extensively for preparation of α-arylglycosides; and the preparation of β-arylglycosides is an exception rather than the rule.

Several good methods, in addition to those already mentioned, are available for the preparation of α glycosides and should be listed for comparison. Condensation with alcohols in the presence of cation-exchange resins (16, 10, 60), anomerization reactions employing a Lewis acid such as zinc chloride (39), stannic chloride (63) or titanium tetrachloride (64) and methylation with diazomethane (55) or dimethylsulfate (35) all yield predominantly the α glycoside.

It can be seen from the above discussion that a good overall method for the preparation of β glycosides is not available. It is one purpose of this dissertation to introduce a facile method for the preparation of β glycosides of D-glucose and D-allose.

A particularly good protection group for position 6 of an aminosugar is the trityl (triphenylmethyl) group. Trityl chloride in pyridine will react only with primary hydroxyl groups of a carbohydrate (31); i.e., in normal

hexopyranoses only with the hydroxyl group in the 6 position. As mentioned earlier, the 1,4-linked aminohexopyranoses are important in biologically active systems. The selective blocking of position 1 by the β benzyl group, which can later be removed, and of position 6 by the trityl group leaves positions 2, 3, and 4 unprotected. If a cyclic protection group for positions 2 and 3 were readily available, the synthesis of such 1,4-linked compounds would be aided. In the past few years it has been observed that the oxazolidone derivative of an aminosugar shows promise as a good protective group. Baker and Joseph (3) employed a 2-oxazolidone blocking group in their study of the controlled step-wise degradation of the purine ring system in puromycin like compounds. They found that the oxazolidone protection group was relatively stable and not easily cleaved. They were able to generate the oxazolidone bridge between C_2 and C_3 without inversion of configuration by heating a mixture of 6-dimethyl-9-(3'-benzyloxycarbonylamido-3'-deoxy-β-D-ribofuranosyl)-purine and sodium methoxide in dimethylformamide. A 2-oxazolidone bridging C_2 and C_3 of a carbohydrate was generated with inversion by Baker, Hewson, Goodman, and Benitez (2). These investigators utilized a route involving mesylation of methyl 4,6-O-benzylidene-3-phenylthiourethan-α-D-glucopyranoside to yield methyl 4,6-O-benzylidene-2-O-(methylsulfonyl)-3-phenylthiourethan-α-D-glucopyranoside. Ring closure was then accomplished by treatment with

methanolic sodium methoxide. Subsequent treatment of the product, methyl 2-anilino-4,6-O-benzylidene-2-deoxy-α-D-mannopyranoside 2,3-thiocarbonate, with mercuric acetate in absolute ethanol yielded the corresponding 2-oxazolidone. Gross, Brendel, and Zimmerman (26), Noorzad and Gross (62), and Shryock and Zimmerman (66) reported generation of the 2,3-oxazolidone group with inversion by heating benzyl 2-benzyloxycarbonylamido-2-deoxy-3,4-anhydro-α and -β-D-glucopyranosides in aqueous acetic acid media.

Several methods are currently available for the preparation of oxazolidones in general. Dyen and Swern (19) have recently reviewed this subject. Preparation may be from β-amino alcohols with phosgene, diethyl carbonate, carbon dioxide, urea, isocyanates, ethyl chloroformate, carbonyl sulfide, carbon monoxide and sulfur, carbon tetrachloride, cyanogen bromide and base, carbon bisulfide and methyl chloroformate or N,N'-carbodiimidazole, β-aminoalkylsulfuric acids with inorganic carbonate or bicarbonate and base, and β-haloamines with silver carbonate, sodium carbonate or sodium bicarbonate and sodium hydroxide.

It is the second purpose of this dissertation to investigate the preparation of 2-oxazolidones forming a bridge between C_2 and C_3 of allopyranose. This preparation, along with the facile preparation of β-benzyl glycosides of D-glucosamine and D-allosamine, should lead to compounds which, in a few steps, can conceivably be used for coupling at positions 1 and 4.

CHAPTER II

METHODS AND DISCUSSION

In order to prepare pure benzyl 2-benzyloxycarbonylamido-2-deoxy-β-D-glucopyranoside (VIII), it was first necessary to protect the amino group. The carbobenzoxy group was used for this purpose. 2-Benzyloxycarbonylamido-2-deoxy-D-glucopyranose (II) was first prepared by Chargaff and Bovarnick (11). D-glucosamine hydrochloride (I) (See Figures 2.1 and 2.2.) was treated with carbobenzoxychloride and sodium bicarbonate to yield (II). An anomeric mixture of benzyl glycosides (IV) was then prepared by the usual method of heating a mixture of II with benzyl alcohol containing 2% hydrochloric acid at 60-70° for 3-4 hours (34). This method involved neutralization of the HCl by lead carbonate and subsequent crystallization of IV by addition of large amounts of diisopropylether. The glycoside obtained in this way contains usually β and α anomer in a ratio of 1:7. In an attempt to simplify the procedure by eliminating the neutralization step, the concentration of acid was decreased to a level of 0.05%. Only starting material was obtained when diethyl ether was added to the reaction mixture. The acid concentration was then increased to 0.5% and diethyl ether used to precipitate the product. An anomeric mixture of α and β benzyl glycosides was obtained which contained β and α anomers in the ratio of 1:4.

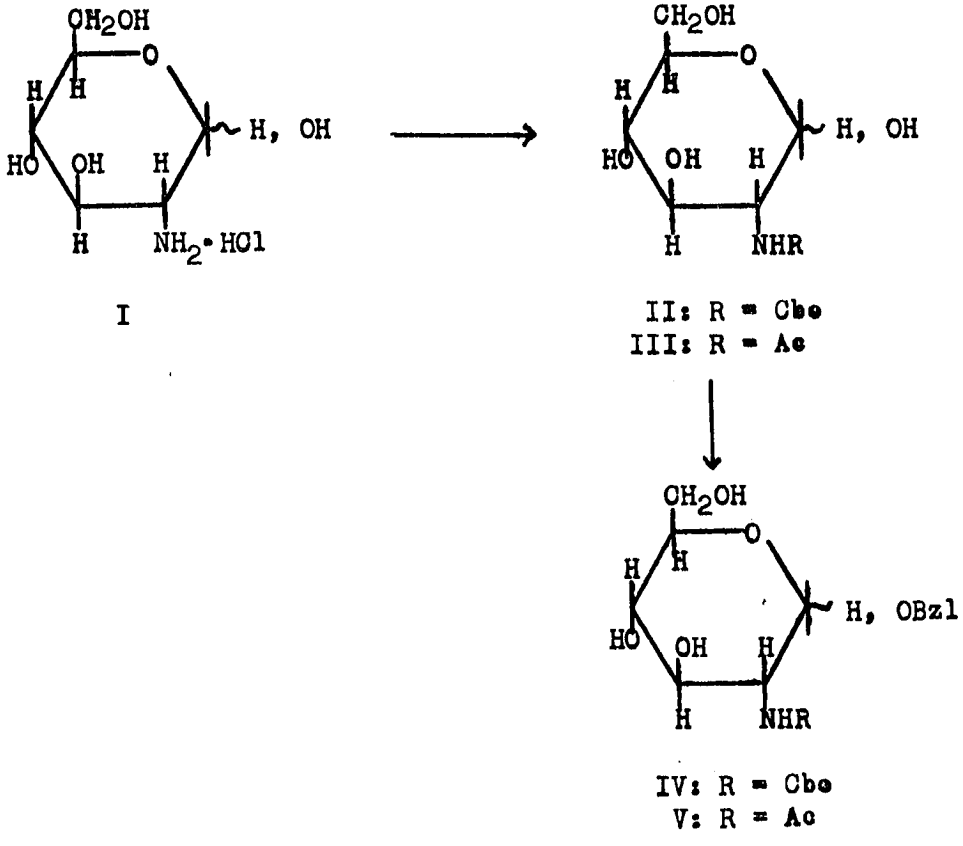
FIGURE 2.1

EXPLANATION OF SYMBOLS

-Ac	=	$-COCH_3$
-Bz	=	$-COC_6H_5$
-Bzl	=	$-CH_2C_6H_5$
-Cbo	=	$-COCH_2C_6H_5$
-Ph	=	$-C_6H_5$
-Ms	=	$-SO_2CH_3$
-Ts	=	$-p\text{-}SO_2C_6H_4CH_3$
-Tr	=	$-C(C_6H_5)_3$

FIGURE 2.2

PREPARATION OF BENZYL 2-ACYLAMIDO-2-DEOXY-β-D-GLUCOPYRANOSIDE



Relative percentages were determined both by semi-quantitative thin layer chromatography, using 10% methanol in chloroform as the eluting solvent, and by polarimetric methods assuming a linear relationship between specific rotation and composition of the mixture (69).

More often than not, it is found that the β anomer of a glucosamine derivative is less soluble than the α anomer in a given solvent (25). Slow recrystallization of the acidic anomeric mixture might have led to a crystalline product which was enriched with the less soluble β anomer. In testing this hypothesis, such conditions were further studied by adding with slow stirring in a closed system at 30-40° diethyl ether in portions to the acidic solution containing the anomeric mixture. A 100 watt light bulb placed a few inches away from the flask was used to maintain this temperature. By systematic variation of reaction conditions, a general method was developed in this way for the preparation of an anomeric mixture of benzyl 2-benzyloxycarbonylamido-2-deoxy-α and -β-D-glucopyranoside (IV), which was enriched with β anomer up to a ratio of 2:1. Table 2.1 lists results of this study. Conditions which led to mixtures enriched with β anomer were also found for the glycosidation of 2-acetamido-2-deoxy-D-glucopyranose (III) with benzyl alcohol. The usual method, using benzyl alcohol and 2% hydrochloric acid, yields only 10-12% benzyl 2-acetamido-2-deoxy-β-D-glucopyranoside (25). Similar conditions, as described above,

TABLE 2.1

PREPARATION OF BENZYL 2-BENZYLOXYCARBONYLAMIDO-2-DEOXY-α AND -β-D-GLUCOPYRANOSIDE

Catalyst	Reaction Temperature	Reaction Time	Days for diethylether addition	Yield of Crude Anomeric Mixture	Percentage β anomer In Crude Mixture
0.5% hydrochloric acid	90-95°	3 hrs.	2	45%	80
0.5% hydrochloric acid	90-95°	5 hrs.	2	63%	67
0.5% trifluoroacetic acid	90-95°	6 hrs.	2	71%	67
1.0% trifluoroacetic acid	90-95°	5 hrs	2	63%	68
1.0% trifluoroacetic acid	90-95°	7 hrs.	4	48%	68
1.5% trifluoroacetic acid	90-95°	5 hrs.	2	62%	68
0.5% paratoluene sulfonic acid	90-95°	5 hrs.	2	76%	44
1.0% borontrifluoride etherate (shelf sample)	90-95°	5 hrs.	2	43%	42

TABLE 2.1 (continued)

Catalyst	Reaction Temperature	Reaction Time	Days for Di-ethylether Addition	Yield of Crude Anomeric Mixture	Percentage β anomer In Crude Mixture
0.5% boron-trifluoride etherate (redistilled)	90-95°	5 hrs.	2	42%	5
1.5% boron-trifluoride etherate (redistilled)	90-95°	4 hrs.	2	10%	0
0.5% 70% per-chloric acid	70-80°	4 hrs.	4	38%	0
0.5% 70% per-chloric acid	70-80°	4 hrs.	4	46%	10 (β anomer seed crystal used)
1.0% 70% per-chloric acid	90-95°	4 hrs.	4	19%	0

TABLE 2.2

PREPARATION OF BENZYL 2-ACETAMIDO-2-DEOXY-α AND -β-D-GLUCOPYRANOSIDE

Catalyst	Reaction Temperature	Reaction Time	Days for diethylether Addition	Yield of Crude Anomeric Mixture	Percentage β anomer In Crude Mixture
1.0% trifluoroacetic acid	90-95°	7 hrs.	2	84%	21
1.5% trifluoroacetic acid	90-95°	9 hrs.	4	86%	29
2.0% trifluoroacetic acid	90-95°	7 hrs.	2	77%	30
1.5% boron-trifluoride etherate (redistilled)	90-95°	3 hrs.	4	56%	5

were used in the preparation of benzyl 2-acetamido-2-deoxy-α and -β-D-glucopyranoside (V). Data are summarized in Table 2.2.

Since anomeric mixtures of benzyl 2-benzyloxycarbonylamido-2-deoxy-D-glucopyranoside (IV) were obtained, separation by fractional recrystallization of a derivative was employed to obtain pure benzyl 2-benzyloxycarbonylamido-2-deoxy-β-D-glucopyranoside (VIII). The method of Gross and Zimmerman (27) was employed for this purpose, as shown in Figure 2.3. Acetylation of IV with acetic anhydride in pyridine followed by fractional recrystallization of V from pyridine-toluene/petroleum ether yielded pure benzyl 2-benzyloxycarbonylamido-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucopyranoside (VI) or pure benzyl 2-benzyloxycarbonylamido-2-deoxy-3,4,6-tri-O-acetyl-α-D-glucopyranoside (VII).

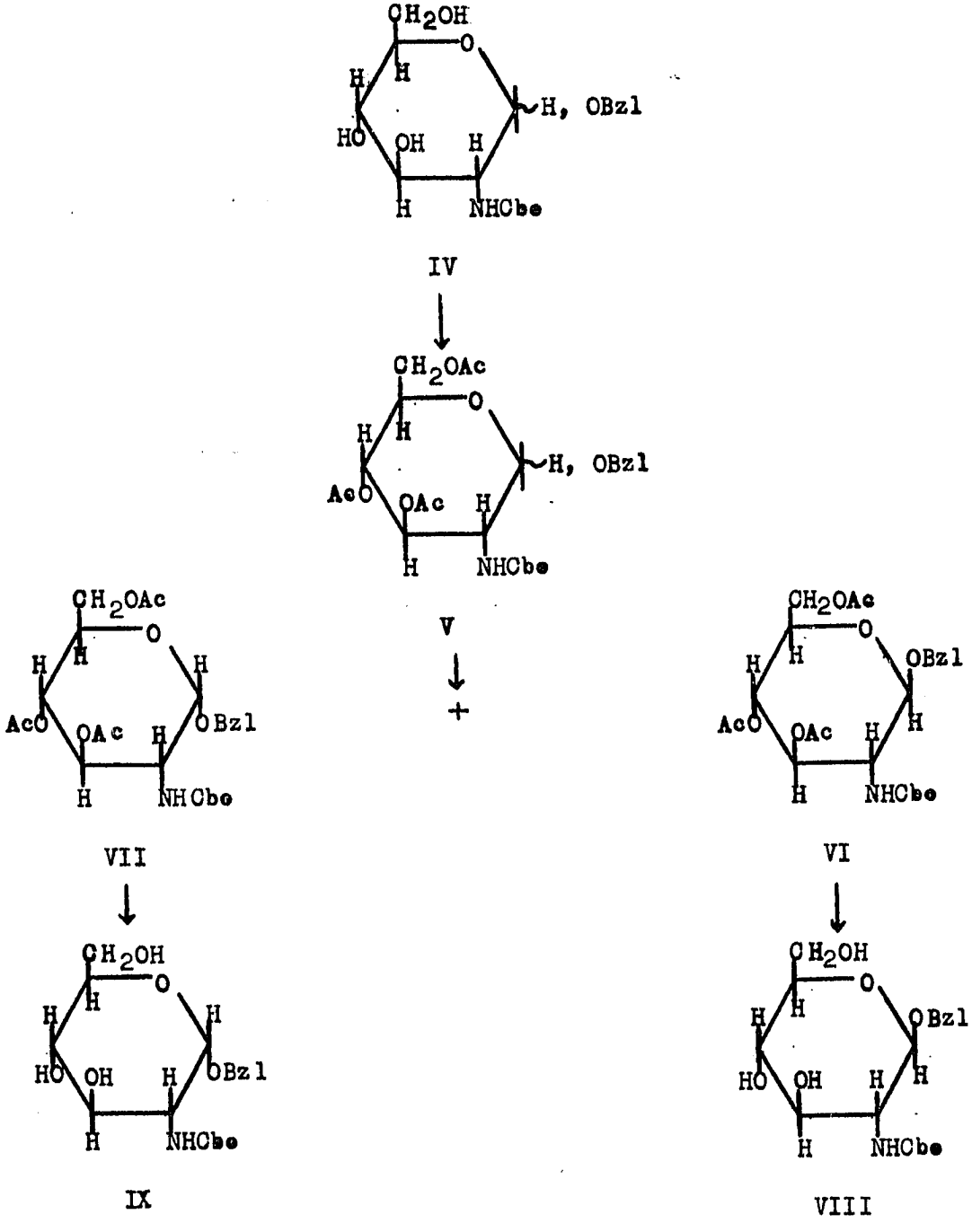
Other methods for the separation of pure anomers of IV, developed by Gross and Zimmerman (27), involved fractional recrystallization of either the 4,6-O-benzylidene or 4,6-O-benzylidene-3-O-mesyl derivatives of IV.

Treatment of VI and VII with KOH in dioxane (27) yielded benzyl 2-benzyloxycarbonylamido-2-deoxy-β-D-glucopyranoside (VIII) and benzyl 2-benzyloxycarbonylamido-2-deoxy-α-D-glucopyranoside (IX). High yields of the β anomer supported the findings of thin layer chromatographic analysis and polarimetric measurements.

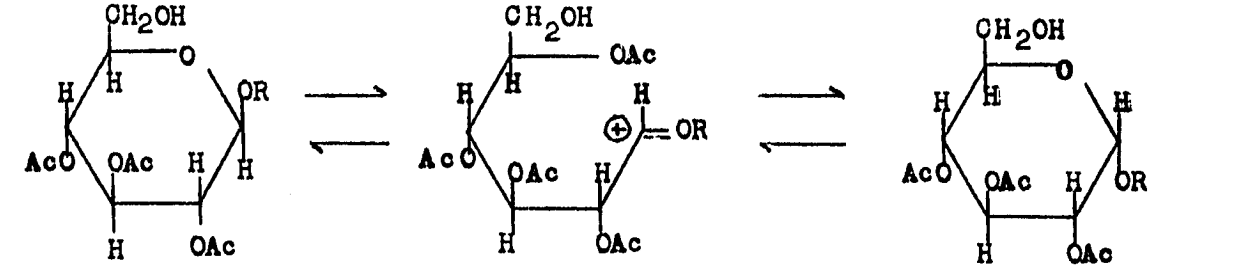
The finding of an increased proportion of β anomer in

FIGURE 2.3

PREPARATION OF BENZYL 2-BENZYLOXYCARBONYLAMIDO-2-DEOXY-β-D-GLUCOPYRANOSIDE

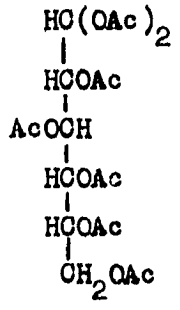


the mixtures of glycosides is easily explained, if several facts are considered. Anomerization of glycosides to an equilibrium mixture was first noted by Fischer (21, 22) in his work with the methyl glycosides of several carbohydrates. Lindberg (54) was first to propose a mechanism for the anomerication of glycosides, which was later supported by the work of Painter (65). Lindberg found that in the anomerization of acetylated alkyl aldopyranosides with strong acid catalysts in an acetylating medium some aldehydo-1,1-diacetate of the acetylated sugar structure X was always formed as a by-product. He assumed, therefore, that the pyranose ring opens and closes in acidic media.



β-D-glucopyranoside tetraacetate

α-D-glucopyranoside tetraacetate



Aldehydro-D-glucose heptaacetate

X

During the closure to the pyranoside ring, the -OR group can be either in the axial position (α) or equatorial position (β). Selective removal of one of the anomers by crystallization results in a disturbance of the anomeric equilibrium in the solution. This, according to Le Chateliers Principle, leads to the production of the removed anomer.

The process of selectively crystallizing an equilibrium mixture in favor of the least soluble compound, which may be the minor component in solution, is not new. Dimroth (17), in 1910, proposed the following equation which related solubility and concentrations of isomers in solution:

$$\frac{[A]}{[B]} = \frac{L_A}{L_B} \cdot G$$

The principle of Dimroth, as it is called, states that if one has two isomers, A and B which are readily interconvertible, then the ratio of their concentrations, [A] and [B] in solution, is related to their solubilities, L_A and L_B, through a constant G which is dependent only on the nature of the solute.

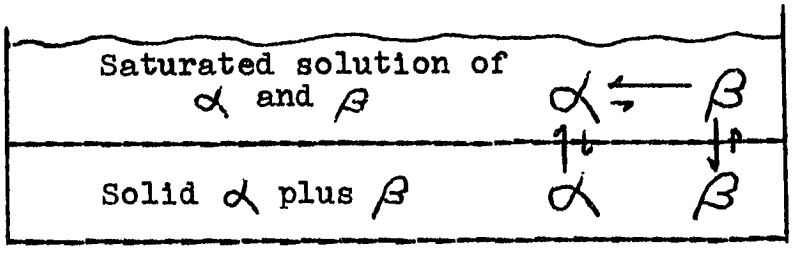
Recently Kuhn and Jochims (48) applied the Principle of Dimroth to the synthesis of allosamine and talosamine. If D-ribose is treated with a primary amine and hydrogen cyanide, a pair of epimers of 2-amino-2-deoxy-hexonic acid nitriles is obtained (47). By fractional recrystallization, hydrolysis and catalytic reduction 7% allosamine and 28% altrosamine may be obtained. Similarly if the process is applied to lyxose, 29%

galactosamine and 9% talosamine may be obtained (46, 50). Both of these systems yield, as the predominant product, the aminosugar in which the amino group is trans to the adjacent hydroxyl group (45). If ribose and lyxose are allowed to react with 9-amino-fluorene and hydrogen cyanide, a mixture of epimers of the 2-[fluorenyl-(9)-amino]-2-deoxy-hexonic acid nitriles results. These epimers have quite different solubilities. The precursors which lead to allosamine and talosamine are the least soluble. Kuhn and Jochims employed slow recrystallization techniques, at elevated temperatures, and obtained products enriched in allosamine and talosamine.

The Principle of Dimroth may be applied to the preparation of mixtures of benzyl 2-benzyloxycarbonylamido-2-deoxy-α and -β-D-glucopyranoside and benzyl 2-acetamido-2-deoxy-α and -β-D-glucopyranoside, respectively, which are enriched with the β anomer. Since the Principle of Dimroth is valid for an equilibrium system, any precipitation of one of the anomers will result in an imbalance of the system. Anomerication will occur in order to re-establish the equilibrium. If conditions are favorable for slow crystallization, the least soluble β anomer will thus crystallize with the resultant formation of more of the β anomer.

Table 2.1 (see page 13) lists results of studies with several acid catalysts. Conditions which favor the formation of samples, enriched with the β anomer, were met using hydrochloric acid, trifluoroacetic acid and para-toluenesulfonic

acid. Boron trifluoride and perchloric acid favor α anomer predominance. It is possible that the two latter catalysts change the respective solubilities or bring about degradation of the more sensitive β glycoside. The total yields found in those cases are also quite low. The results using trifluoroacetic acid are of special interest. It will be noted that in every case the crude anomeric mixture contained from 67 to 68% of the β anomer of benzyl 2-benzyloxycarbonylamido-2-deoxy-D-glucopyranoside. These data indicate that a true equilibrium system may have been established. The following drawing illustrates the principle of the new method. Let us assume that, during the process of crystallization, a mixture of solid α and β benzyl glycosides exists as well as a solution which is saturated with respect to this mixture.



Since the Gibbs phase rule states for the degrees of freedom (variables) of a chemical system:

$$F = C - P + 2$$

we have in the above drawing C = 1. Because of the equilibrium $\alpha \rightleftharpoons \beta$, only one component is necessary to describe the system. Moreover, we have P = 3 (liquid, solid α and solid β). Therefore F = 1 - 3 + 2 leaves no degree of

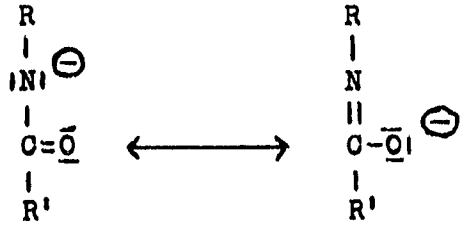
freedom. In other words this system with 3 phases can only exist at an invariance point with a certain temperature and pressure. At all other temperatures, one phase has to vanish. The one solid phase left must not necessarily be a pure anomer; it may be a solid solution of both. It was indeed observed before (51, 27) and in this work that the two anomers co-crystallize readily if one anomer is in large excess. In the intermediate composition range only gelatinous, amorphous precipitates are formed.

In order to prepare the 3-o-(methylsulfonyl) derivative of benzyl 2-benzyloxycarbonylamido-2-deoxy-β-D-glucopyranoside (VIII), (see Figure 2.4.) it was first necessary to protect the 4 and 6 positions. They may be protected by bridging with benzaldehyde, acetone, or boric acid (68). The procedure used by Gross and Zimmerman (27), which involves reaction of VIII with benzaldehyde in the presence of anhydrous zinc chloride, was also used here to prepare benzyl 4,6-O-benzylidene-2-benzyloxycarbonylamido-2-deoxy-β-D-glucopyranoside (XI). Benzyl 4,6-O-benzylidene-2-benzyloxycarbonylamido-2-deoxy-3-O-(methylsulfonyl)-β-D-glucopyranoside (XII) was then prepared by mesylation of XI with methane sulfonylchloride in pyridine solution (67).

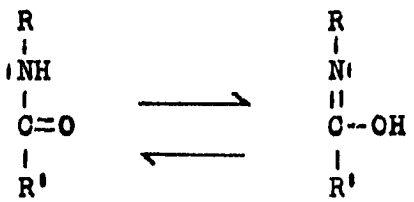
Because the 4,6-O-benzylidene group is cleaved under acidic conditions (67, 23, 61), elimination experiments of the 3-sulfonate of XII were limited to either neutral or basic conditions. Elimination of the 3-sulfonate of XII,

under strongly basic conditions, (sodium isopropoxide in isopropanol), led to the formation of benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranoside (XIII). Treatment of benzyl 2-benzamido-4,6-O-benzylidene-2-deoxy-3-O-(methylsulfonyl)-β-D-glucopyranoside (XIV), under the same conditions, yielded a compound identical in all respects to XIII.

The formation of benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranoside (XIII) by the elimination of the 3-sulfonate of benzyl 4,6-O-benzylidene-2-benzyloxycarbonylamido-2-deoxy-3-O-(methylsulfonyl)-β-D-glucopyranoside (XII) or benzyl 2-benzamido-4,6-O-benzylidene-2-deoxy-3-O-(methylsulfonyl)-β-D-glucopyranoside (XIV) under basic conditions is not unexpected. Under basic conditions the electron pair on the nitrogen is apparently more available for nucleophylic attack at the 3 position, because of the removal of the acidic amide proton. The amide anion has two resonance structures:



while the amide itself has the two corresponding tautomeric structures:

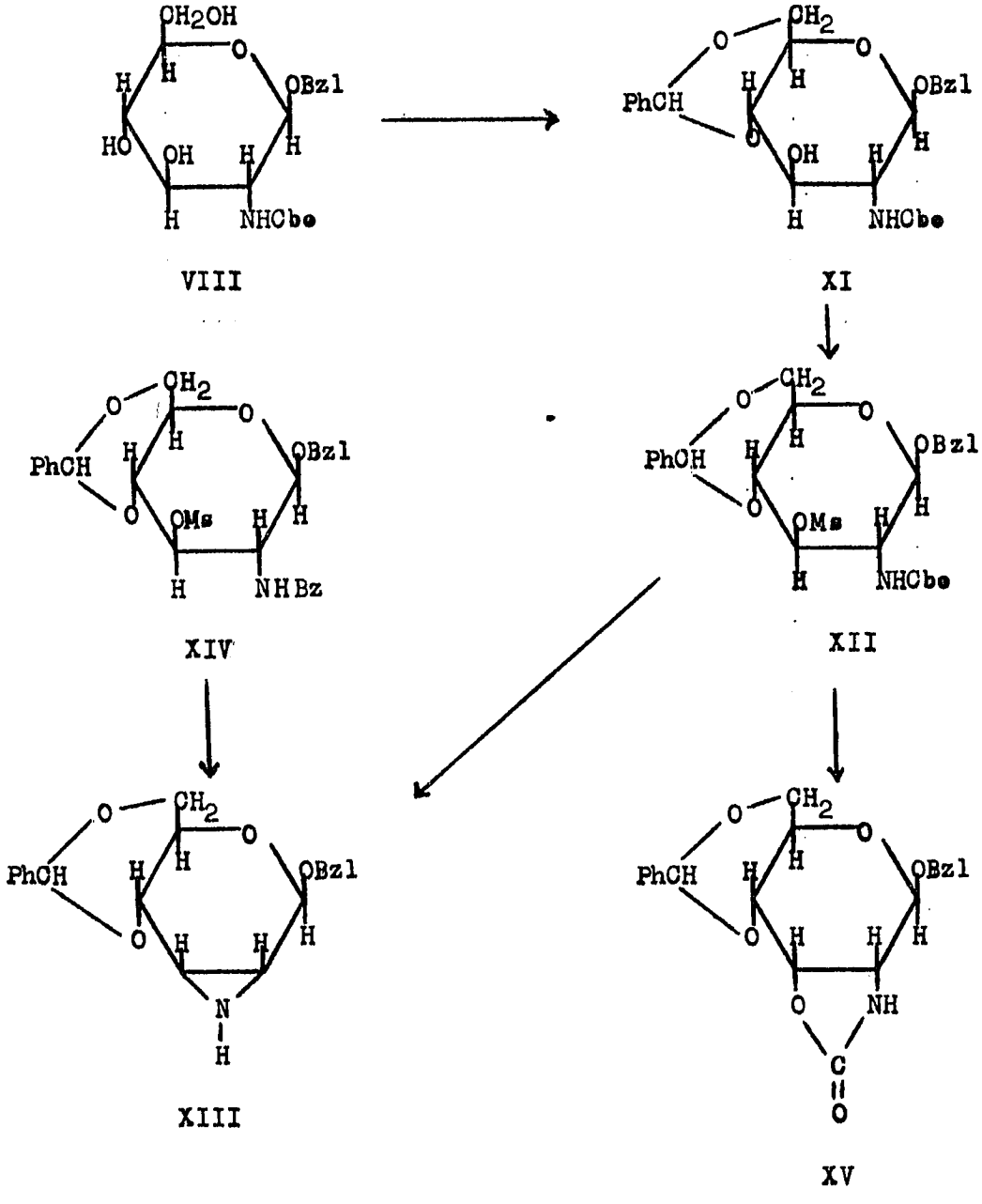


In view of the larger electronegativity of the oxygen it was not predictable that this change would cause preferential epimine formation. However, this was found.

The synthesis of 2,3-epimino sugars has been accomplished only recently. In 1960 Christensen and Goodman (12) reported the first synthesis of a 2,3-epimino sugar. They were able to prepare methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-α-D-alloside by ammonolysis of methyl 2,3-anhydro-4,6-O-benzylidene-2,3-dideoxy-α-D-mannoside. Guthrie and Murphy (28) reacted hydrazine hydrate and Raney nickel in methanol with methyl 2-azido-4,6-O-benzylidene-2-deoxy-3-O-(methylsulfonyl)-α-D-altroside and obtained methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannoside. Buss, Hough, and Richardson (9) observed that lithium aluminum hydride and methyl 2-benzamido-4,6-O-benzylidene-2-deoxy-3-O-(methylsulfonyl)-α-D-altropyranoside yielded methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannoside. They

FIGURE 2.4

PREPARATION AND REACTIONS OF BENZYL 4,6-O-BENZYLIDENE-2-BENZYLOXYCARBONYLAMIDO-2-DEOXY-3-O-(METHYLSULFONYL)-β-D-GLUCOPYRANOSIDE



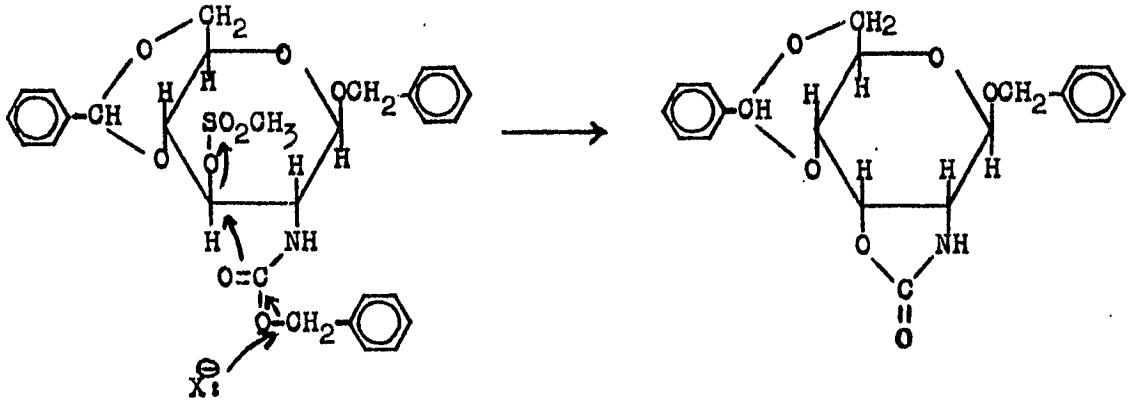
also observed that if methyl 2-acetamido-4,6-O-benzylidene-2-deoxy-3-O-(methylsulfonyl)-α-D-altropyranoside was treated with sodium ethoxide in ethanol, a mixture of methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-(2-methyl-1-oxa-3-azaprop-2-ene)-α-D-mannopyranoside (60%) and methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-α-D-mannopyranoside (40%) was obtained (9). The use of a stronger base, such as sodium isopropoxide or lithium aluminum hydride, seems to eliminate oxazoline formation.

Difficulty was experienced in attempts to open the aziridine ring of the epimino sugar XIII. Only starting material was obtained when a mixture of XIII and ammonia in methanol was heated in a Parr bomb for 48 hours at 165°. Attempts to open the aziridine ring with sodium azide failed to yield a clean product. Reaction did take place; but thin layer chromatographic analysis indicated that at least six products, as well as starting material, were present in the reaction mixture. Heine (30) has shown that N-acylepimines are relatively unstable and have a tendency to undergo ring opening in the presence of nucleophiles. Aziridine opening with sodium azide was therefore investigated, using benzyl 2,3-acetepimino-4,6-O-benzylidene-2,3-dideoxy-β-D-allopyranoside (XVI). When a mixture of XVI, sodium azide and ammonium chloride in dimethylformamide was refluxed for three hours, only benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranoside (XIII) was obtained. Guthrie and Murphy

(29) observed that treatment of N-acetylepimines with sodium azide in 2-methoxyethanol or in dimethylformamide yielded products identical to those obtained on azidolysis of the parent epimines. They attribute their results to hydrolysis of the acetyl group followed by opening of the epimine ring. The unusual stability of the aziridine ring of benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranoside (XIII) is not understood.

Because basic conditions lead to the epimino sugar (XIII) and acidic conditions would cleave the 4,6-O-benzylidene group of XII, preparation of benzyl 4,6-O-benzylidene-2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XV) was limited to near neutral conditions. Great difficulty was encountered in elimination of the 3-sulfonate. However, the oxazolidone was obtained after 100 hours of reflux at high temperatures, by the method of Baker and Schaub (4), which involves solvolysis of N-acetyl-3-O-sulfonyl derivatives of 2-aminosugars, and results in inversion of configuration at the sulfonyl position. This method has been utilized extensively by Jeanloz, et. al. (41, 24, 42). He reacted, for instance, methyl 2-acetamido-4,6-O-benzylidene-2-deoxy-3-O-(methylsulfonyl)-α-D-glucopyranoside with sodium acetate trihydrate in a solution of 2-methoxyethanol containing 5% water. Methyl 2-acetamido-4,6-O-benzylidene-2-deoxy-α-D-allopyranoside was obtained in 62% yield. In our experiments potassium acetate in aqueous 2-ethoxyethanol was used.

A mechanism for the formation of benzyl 2-deoxy-α-D-gulopyranosido-[2.3:4'.5']-oxazolidone-(2') from benzyl 3,4-anhydro -2-benzyloxycarbonylamido-2,3,4-trideoxy-α-D-galactopyranoside was proposed by Gross, Brendel, and Zimmerman (26). This same mechanism may be applied to the formation of benzyl 4,6-O-benzylidene-2-deoxy-β-D-allo-pyranosido-[2.3:4'.5']-oxazolidone-(2') (XV) from benzyl 4,6-O-benzylidene-2-benzyloxycarbonylamido-2-deoxy-3-O-(Methylsulfonyl)-β-D-glucopyranoside (XII):



XII XV

A concerted mechanism is represented above where the carbonyl oxygen of the carbobenzoxy moiety approaches the 3 position as the O-mesyl group leaves. A relatively stable benzyl carbonium ion finally leaves which may then react with a nucleophile, such as water, and the 2-oxazolidone is formed.

In the work of Jeanloz N-acetyl derivatives were employed. It is quite possible that the carbonyl oxygen here

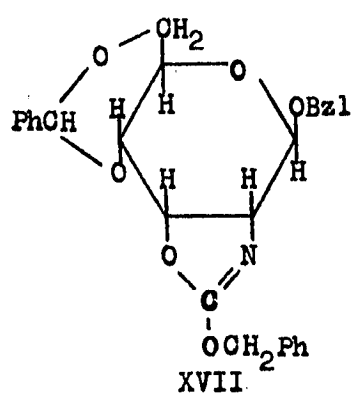
also attacks the 3 position; but the leaving of an unstable methyl carbonium ion, which would thereby create an electron sextett on the carbonyl carbon atom, is unlikely. Solvolysis is thus the favored path with N-acetyl derivatives. In any case, the methanesulfonyl group and the participating acylamido group have to be arranged trans to each other for the reaction to occur. The product then carries the substituents in a 2,3-cis arrangement.

Infrared spectra were used to confirm the oxazolidone (XV) structure. Oxazolidones show an amide I band at 1750 cm^{-1}, their NH stretching absorption band at 3300-3250 cm^{-1} and no amido II band at 1500 cm^{-1} (7). Compound XV had such an infrared spectrum.

Recently Miyai and Gross (58) have prepared benzyl 4,6-O-benzylidene-2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XV) by an independent route. When they allowed benzyl 2-amino-4,6-O-benzylidene-2-deoxy-β-D-allopyranoside to react with phosgene, a compound identical in all respects to XV was obtained.

Preparation of the oxazolidone XV from XII was extensively studied using a variety of conditions. Reactions involving acetates of basic ion-exchange resins, barium acetate in aqueous 2-ethoxyethanol, potassium acetate in aqueous dimethylsulfoxide, potassium acetate in aqueous dimethylformamide, 1,5-diazabicyclo-[4.3.0]-5-nonene in aqueous dimethylsulfoxide, tetramethylammonium acetate in aqueous

2-ethoxyethanol and lithium acetate in 2-ethoxyethanol failed to give results superior to the preparation with potassium acetate in aqueous 2-ethoxyethanol. In all the variations studied, the oxazolidone and starting material were present. Thin layer chromatographic analysis also showed the presence of one or more other products from the dimethylsulfoxide and dimethylformamide reactions. In the reaction with acetates of basic ion-exchange resin a total of eleven products, as well as starting material, was obtained. One possible side product would be the oxazoline represented by structure XVII. Bromund and Herbst (8) reported the synthesis of similar compounds in 1945. Mild heating, in 0.02N KOH, of



XVII

the N-carbobenoxy-1,3,4,6-tetraacetate derivative of 2-deoxy-D-glucosamine yielded an oxazoline bridging carbon atoms C_1 and C_2. Two other possible side products are also likely: formation of the epimine and formation of the N-carbobenzoxyepimine. It was shown before that the epimine may be the exclusive product under more basic conditions.

Attempts to prepare the oxazolidone corresponding to XV in the α series were fruitless. Several of the methods mentioned before were tried. Only starting material was recovered. Removal of the 4,6-O-benzylidene group from benzyl 4,6-O-benzylidene-2-benzyloxycarbonylamido-2-deoxy-3-O-(methylsulfonyl)-α-D-glucopyranoside and subsequent attempts to form the oxazolidone, either under neutral or acidic conditions, led only to tarry products consisting of at least eight compounds, as shown by thin layer chromatographic analysis.

The inertness of the α anomer toward oxazolidone formation is not understood. Complex intramolecular interactions must be present.

For further characterization, derivatives of benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranoside (XIII) and benzyl 4,6-O-benzylidene-2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XV) were prepared. (See Figures 2.5 and 2.6.) When XIII was treated with 1-fluoro-2,4-dinitrobenzene and sodium bicarbonate, benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-(2,4-dinitrophenyl)-epimino-β-D-allopyranoside (XVIII) was obtained. Treatment of XIII with p-toluenesulfonylchloride in absolute pyridine yielded benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-(p-toluenesulfonyl)-epimino-β-D-allopyranoside (XIX). Debenzylidenation of XV yielded benzyl 2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XX). Treatment of

FIGURE 2.5

PREPARATION OF DERIVATIVES OF BENZYL 4,6-O-BENZYLIDENE-2,3-DIDEOXY-2,3-EPIMINO-β-D-ALLOPYRANOSIDE

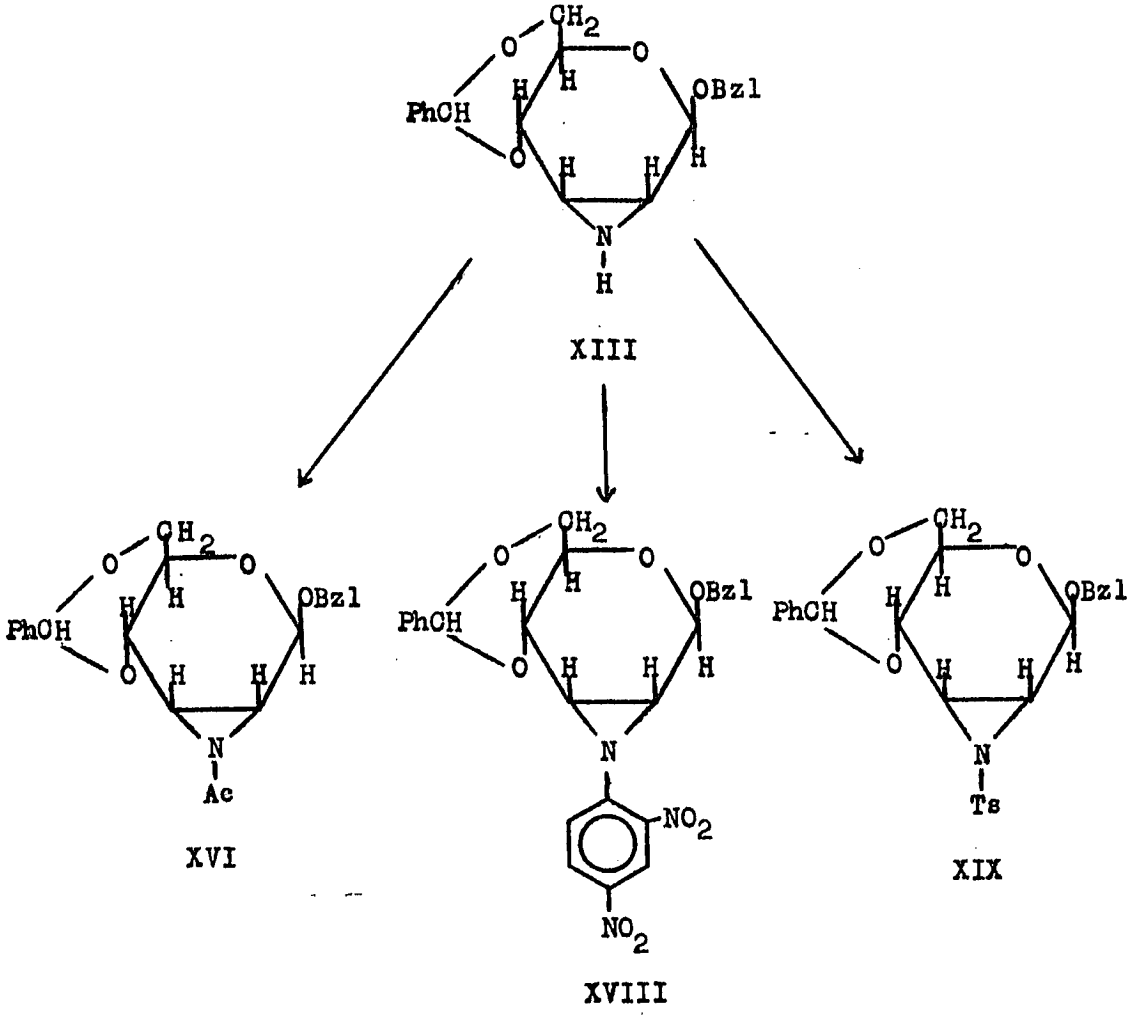
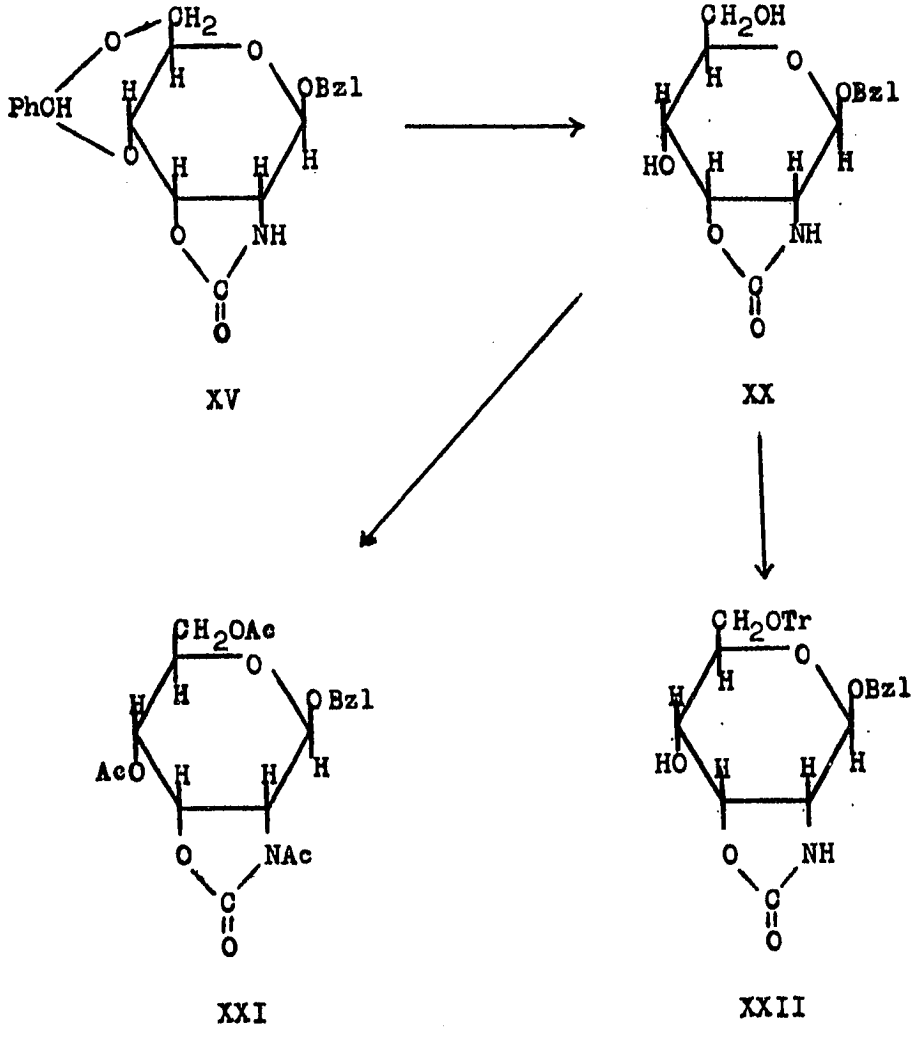


FIGURE 2.6

PREPARATION OF DERIVATIVES OF BENZYL 2-DEOXY-β-D-ALLOPYRANOSIDO-[2.3:4'.5']-OXAZOLIDONE-(2')



XX with acetic anhydride in pyridine yielded benzyl 1',4,6-triacetyl-2-deoxy-β-D-allopyranoside-[2.3:4'.5']-oxazolidone-(2') (XXI). When XX was allowed to react with chlorotriphenylmethane in pyridine, benzyl 2-deoxy-6-triphenylmethyl-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XXII) was obtained. Selective hydrogenolysis of the β benzyl glycoside in XXII could yield a sugar which is fully protected at all positions except 1 and 4. This compound would then be ready for coupling reactions which could lead to 1,4-linked oligosaccharides.

CHAPTER III

EXPERIMENTAL

Melting points were determined in a Thiele tube and are uncorrected.

Infrared spectra were determined on a Perkin-Elmer 137 spectrophotometer using KBr pellets.

All compounds were found to be uniform by thin layer chromatography on silica gel plates, using chloroform/methanol as the solvent. Detection of spots was by extinction of the UV-fluorescence of an admixed Zn_2SiO_4 indicator and finally by spraying with H_2SO_4 and subsequent charring.

General method for the preparation of Benzyl 2-benzyloxycarbonylamido-2-deoxy-β-glucopyranoside (VIII). A mixture of 5.0 grams (0.016 mole) 2-benzyloxycarbonylamido-2-deoxy-D-glucopyranose (II), 60 ml. of anhydrous doubly distilled benzyl alcohol and the acid catalyst (see Table 2.1, page 13) were stirred at elevated temperatures until a clear solution was obtained. Stirring, with heating (Table 2.1), was then continued for an additional hour. The contents of the flask, which was equipped with a condenser and calcium chloride drying tube, were cooled to about 35° and diethyl ether added in increments to a total of 175 ml. Increment additions were at 24-hour intervals. The stoppered flask was stirred at 30-40° continuously. The gelatinous material which had deposited was collected by suction filtration,

washed and digested with diethyl ether to remove traces of benzyl alcohol, and air dried.

Benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranosido (XIII). (Method A): Metallic sodium, 0.2 gram (0.0087 mole), which had previously been washed with isopropanol, was dissolved in 10 ml. of isopropanol and added to a solution of 2.3 grams (0.0040 mole) benzyl 4,6-O-benzylidene-2-benzyloxycarbonylamido-2-deoxy-3-O-(methylsulfonyl)-β-D-allopyranoside (XII) in 30 ml. of dioxane, and the mixture boiled under reflux for 18 hours. The reaction mixture was allowed to cool and filtered to remove the gelatinous basic by-products. The solvents were removed by vacuum rotatory evaporation, and traces of dioxane removed by additions of water followed by vacuum rotatory evaporation. The white residual crystals were finally dried by azeotropic distillation of the water, with ethanol and toluene in vacuo. Recrystallization from methanol yielded 0.8 gram (62%) of white flaky crystals. (Method B): To a solution of 2.5 grams (0.0057 mole) of benzyl 2-benzamido-4,6-O-benzylidene-2-deoxy-3-O-(methylsulfonyl)-β-D-glucopyranoside (XIV) in 100 ml. of absolute dioxane was added a solution of 20 ml. of isopropanol containing 0.33 gram (0.0143 mole) metallic sodium, which had previously been washed with isopropanol. The reaction mixture was boiled, under reflux, for 17 hours, cooled and the gelatinous basic by-products removed by suction filtration. The solvents were then

removed from the filtrate by vacuum rotatory evaporation. Treatment of the oily residual crystals with water yielded white crystals which were collected, washed with water and air dried. Recrystallization from redistilled methanol yielded 1.2 gram (63%) of white flaky crystals, M.P. = 148-150° ; $[\alpha]_D^{23}$ = -5.0°, (c = 1.0 in pyridine).

$C_{20}H_{21}NO_4$ (339.40)

Calculated:	70.80% C	6.24% H	4.15% N	18.85% O
Found:	70.93% C	6.38% H	4.20% N	19.02% O

Benzyl 4,6-O-benzylidene-2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XV). A solution of 3.0 grams (0.0054 mole) of benzyl 4,6-O-benzylidene-2-benzyloxycarbonyl-amido-2-deoxy-3-O-(methylsulfonyl)-β-D-allopyranoside (XII) and 3.0 grams (0.031 mole) potassium acetate in 90 ml. of 2-ethoxyethanol containing 5% water was heated under reflux for 94 hours. The reaction mixture was allowed to stand at 0° for 24 hours and filtered to remove any insoluble material. Most of the solvent was removed by vacuum rotatory evaporation and the syrupy residue treated with excess water. The tan crystals which formed were collected by suction filtration, washed with water and air dried. Two recrystallizations from absolute ethanol yielded 0.9 gram (43%) of long white needles, M.P. = 205-206°; $[\alpha]_D^{25}$ = +7.0°, (c = 1.0 in pyridine.)

$C_{21}H_{21}NO_6$ (383.41)

Calculated:	65.78% C	5.52% H	3.65% N	25.04% O
Found:	65.55% C	5.83% H	3.66% N	24.97% O

Benzyl 2,3-acetepimino-4,6-O-benzylidene-2,3-dideoxy-β-D-allopyranoside (XVI). To a stirred solution containing 0.45 gram (0.0014 mole) of benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranoside (XIII) in 5 ml. absolute pyridine was added, over a period of 15 minutes, 0.29 gram (0.0028 mole) of acetic anhydride, while the temperature of the reaction mixture was maintained at 0° by aid of an ice bath. After addition was complete, the reaction mixture was left at room temperature for 3 days, and then poured into 25 ml. of ice/water. The mother liquor was decanted from the syrupy residue. The syrup was washed with water and dried by azeotropic distillation with ethanol and toluene on a vacuum rotatory evaporator. Attempts to crystallize the 0.37 gram (71%) of syrup were fruitless. The infrared spectrum showed the carbonyl absorption at 1710 cm^{-1}. The NH band at 3320 cm^{-1} was absent.

Benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-(2,4-dinitrophenyl)-epimino-β-D-allopyranoside (XVIII). A mixture containing 0.5 gram (0.00152 mole) of benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranoside (XIII), 1.0 gram (0.0122 mole) sodium bicarbonate and 0.31 gram (0.00182 mole) of 1-fluoro-2,4-dinitrobenzene in 7.5 ml. dimethylformamide was stirred, at room temperature, for 22 hours. The reaction mixture was poured into 150 ml. of ice/water and the light yellow crystals collected by suction filtration. Recrystallization from 2-propanol yielded 0.39 gram

(51%) of light yellow crystals, M.P. = 72-74°; $[\alpha]_D^{23}$ = -271.0°, (c = 1.0 in pyridine). The infrared spectrum showed the NH band at 3320 cm^{-1} was absent.

$C_{26}H_{23}N_3O_8$ (505.49)

Calculated:	61.78% C	4.59% H	8.31% N	25.32% O
Found:	61.54% C	4.95% H	8.22% N	25.44% O

Benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-toluene-p-sulfonylepimino-β-D-allopyranoside (XIX). To a solution of 0.5 gram (0.00152 mole) of benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranoside (XIII) in 5 ml. of absolute pyridine, stirred in an ice/salt bath, was added, over a period of 45 minutes, 0.35 gram (0.00183 mole) of p-toluenesulfonylchloride in 5 ml. of absolute pyridine. After complete addition of the p-toluenesulfonylchloride, stirring was continued for an additional hour. The reaction mixture was then left at 0° for 12 hours. The reaction mixture was poured into 100 ml. of ice/water, and the white crystals which formed were collected by suction filtration. Recrystallization from a large volume of 2-propanol yielded 0.44 gram (60%) of white needles, M.P. = 226-227°; $[\alpha]_D^{26}$ = -17.5°, (c = 1.0 in pyridine). The infrared spectrum showed the NH band at 3320 cm^{-1} was absent.

$C_{27}H_{27}NO_6S$ (493.59)

Calculated:	65.70% C	5.51% H	2.84% N	19.45%O
Found:	65.58% C	5.56% H	2.94% N	19.68% O

Benzyl 2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XX). Benzyl 4,6-O-benzylidene-2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XV), 0.6 gram (0.00156 mole), was dissolved in 22 ml. of glacial acetic acid and the solution stirred at 95°. To this solution, over a period of 35 minutes, was added water (12 ml.). After addition was complete the reaction mixture was stirred for an additional 15 minutes and the solvents were then removed by vacuum rotatory evaporation. Residual traces of acetic acid were removed by additions of water followed by vacuum rotatory evaporation. The syrup was dried azeotropically with ethanol and toluene in vacuo. Attempts to crystallize the syrup were fruitless; however, the product was uniform with respect to thin layer chromatography.

Benzyl 1',4,6-triacetyl-2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XXI). Benzyl 2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XX), 0.46 gram (0.00156 mole), was dissolved in the minimum amount of absolute pyridine, the flask equipped with a calcium chloride drying tube and the solution stirred at 0°. To this was added, over a period of 30 minutes, 4.3 grams (0.042 mole) acetic anhydride. The reaction mixture was then kept at room temperature for 4 days, and then poured into 30 ml. of ice/water. The mother liquor was decanted from the residual syrup. The syrup was washed several times with water and

finally dried azeotropically by distillation with ethanol and toluene on a vacuum rotatory evaporator. Recrystallization from isopropanol yielded 0.21 gram (32%) of white flaky crystals, M.P. = 89-91°; $[\alpha]_D^{23}$ = +39.0°, (c = 1.0 in pyridine).

$C_{20}H_{24}NO_9$ (422.42)

Calculated:	57.00% C	5.50% H	3.33% N	34.17% O
Found:	57.09% C	5.58% H	3.16% N	34.53% O

Benzyl 2-deoxy-6-triphenylmethyl-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XXII). A solution containing 0.69 gram (0.0023 mole) of benzyl 2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2') (XX) and 0.70 gram (0.0025 mole) chlorotriphenylmethane in 3 ml. of absolute pyridine was shaken at room temperature for 23 hours. The reaction mixture, which had deposited crystals, was poured into 25 ml. of water. The crystals which formed were collected by suction filtration, washed with water and air dried. Recrystallization from a mixture of toluene, hexane and diethyl ether yielded 0.30 gram (24%) of white crystals, M.P. = 215-217°; $[\alpha]_D^{22}$ = -9.0°, (c = 1.0 in pyridine).

$C_{33}H_{31}NO_6$ (537.62)

Calculated:	73.72% C	5.81% H	2.61% N	17.86% O
Found:	73.88% C	5.87% H	2.80% N	17.93% O

FIGURE 3.1

INFRARED SPECTRUM OF BENZYL 4,6-O-BENZYLIDENE-2,3-DIDEOXY-2,3-EPIMINO-β-D-ALLOPYRANOSIDE

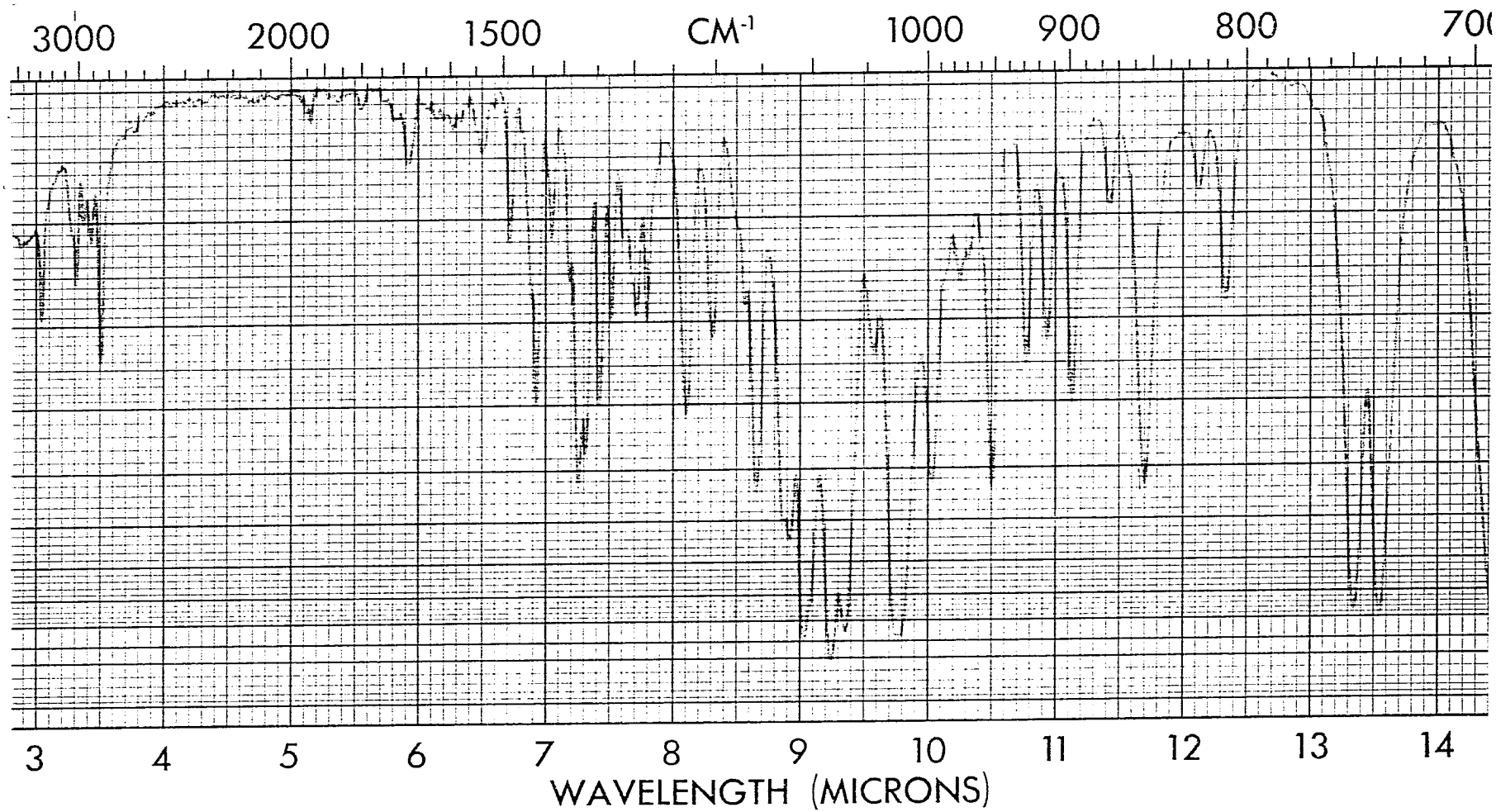


FIGURE 3.2

INFRARED SPECTRUM OF BENZYL 4,6-O-BENZYLIDENE-2-DEOXY-β-D-ALLOPYRANOSIDO-[2.3:4'.5']-OXAZOLIDONE-(2')

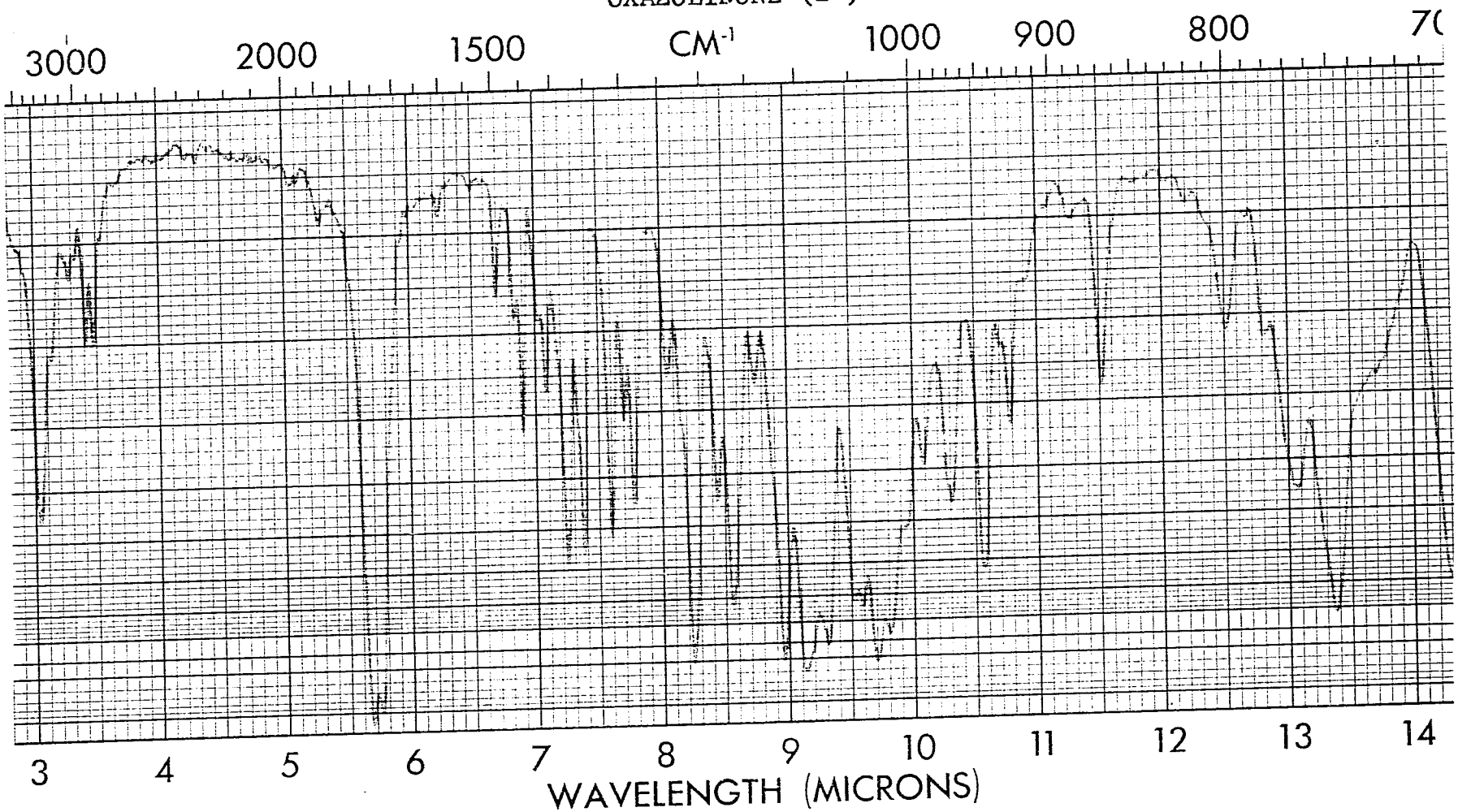


FIGURE 3.3

INFRARED SPECTRUM OF BENZYL 4,6-O-BENZYLIDENE-2,3-DIDEOXY-2,3-(2,4-DINITROPHENYL)-EPIMINO-β-D-ALLOPYRANOSIDE

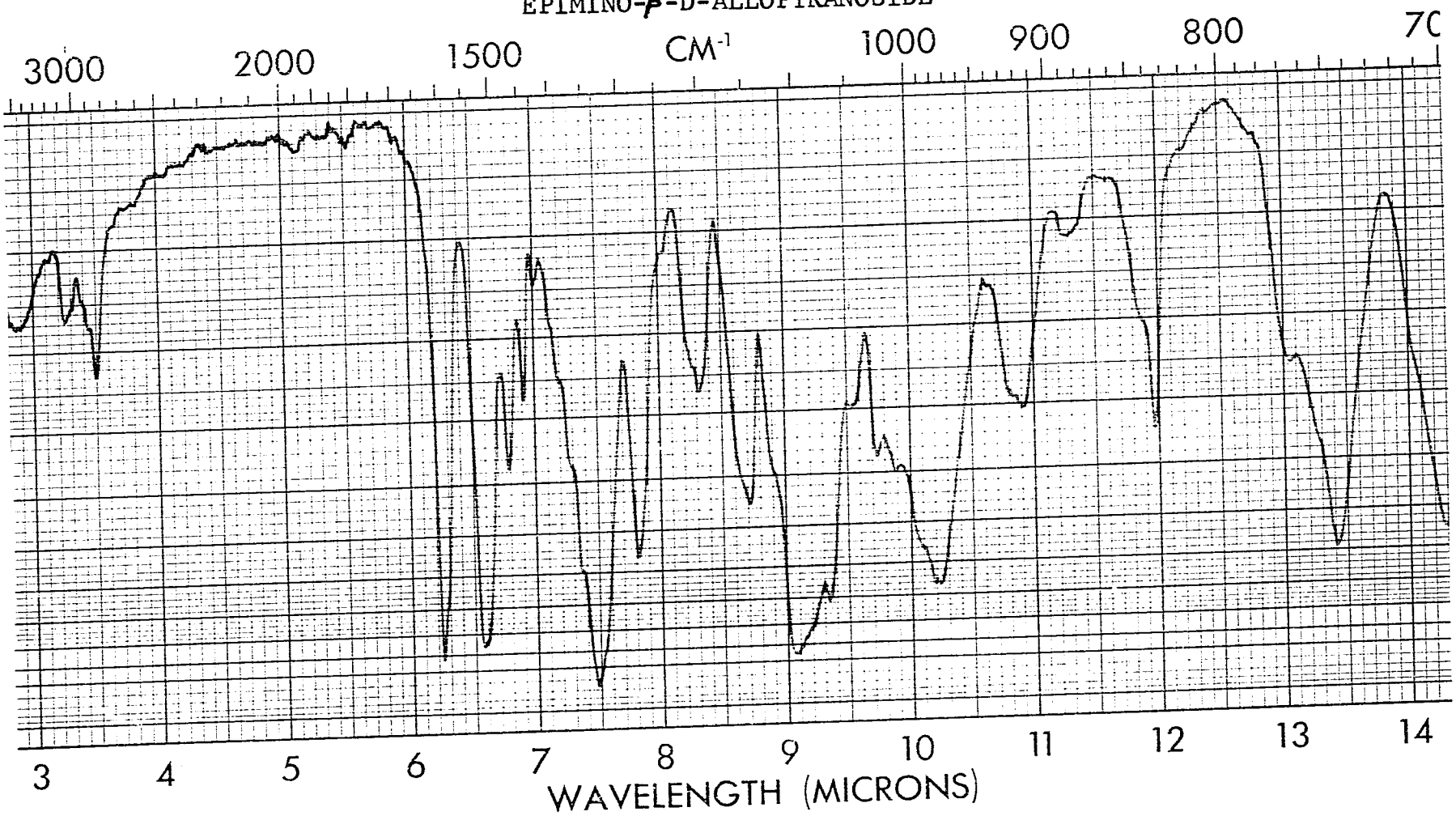


FIGURE 3.4

INFRARED SPECTRUM OF BENZYL 4,6-O-BENZYLIDENE-2,3-DIDEOXY-2,3-TOLUENE-p-SULFONYL-EPIMINO-β-D-ALLOPYRANOSIDE

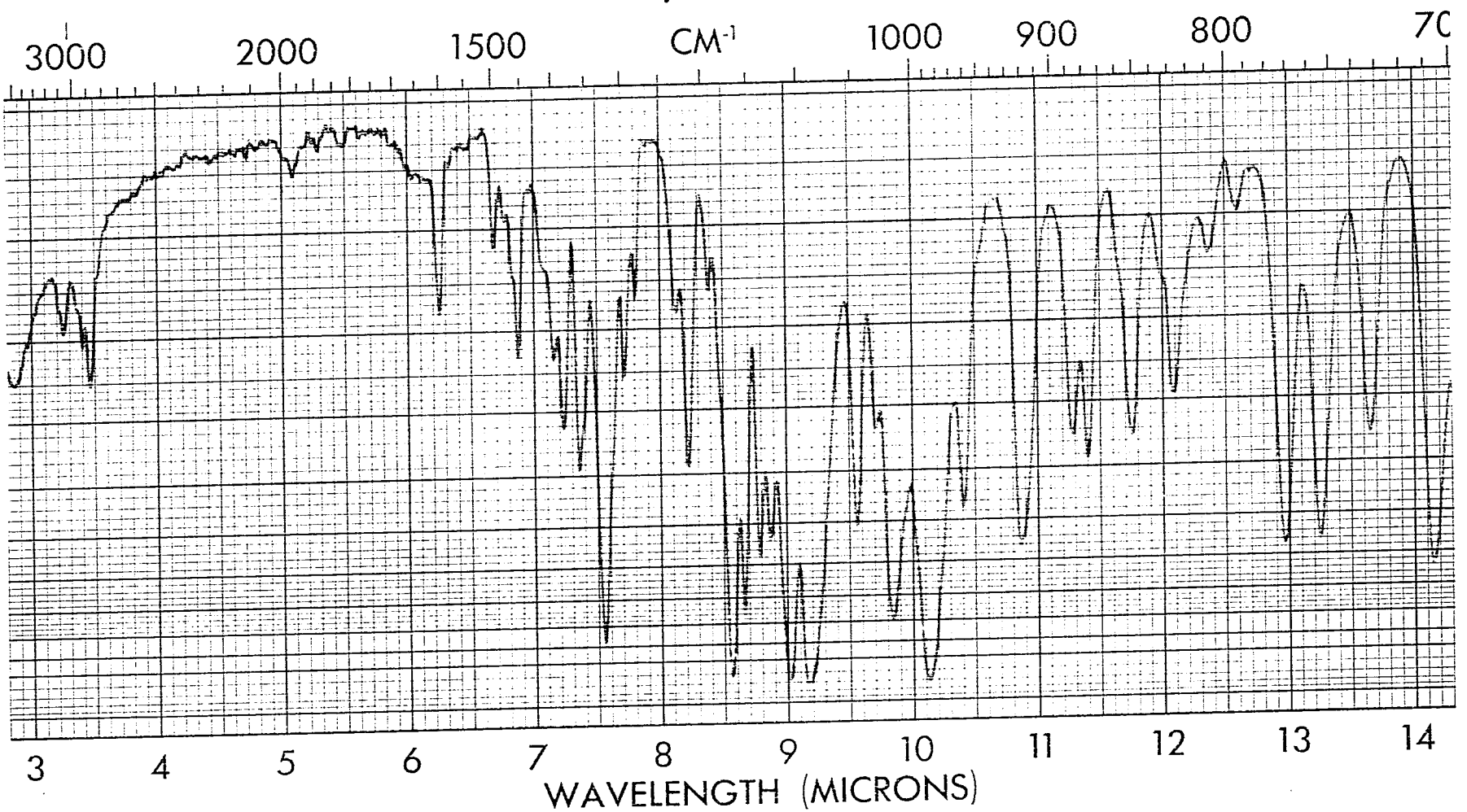


FIGURE 3.5

INFRARED SPECTRUM OF BENZYL 1',4,6-TRIACETYL-2-DEOXY-β-D-ALLOPYRANOSIDO-[2.3:4'.5']-OXAZOLIDONE-(2')

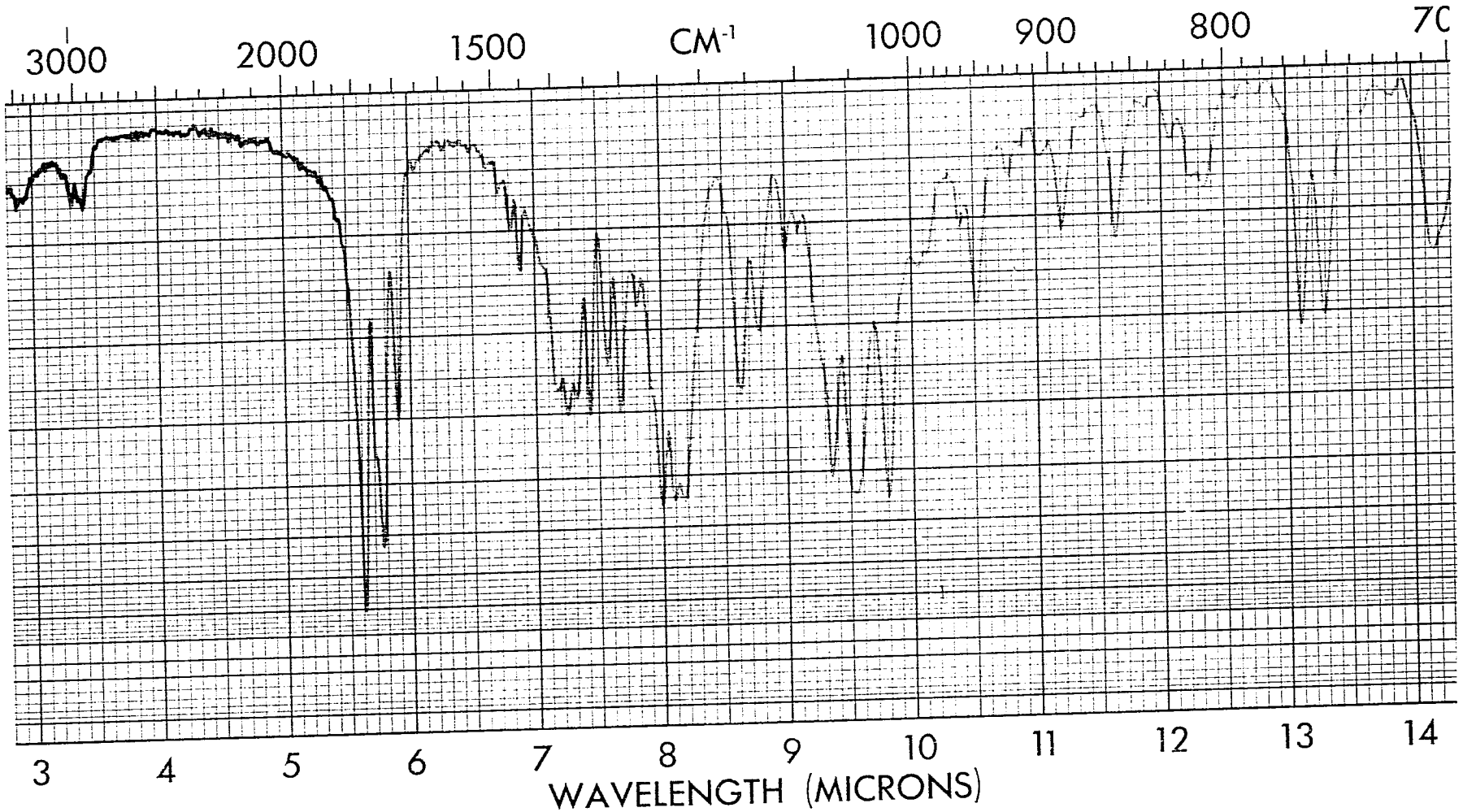
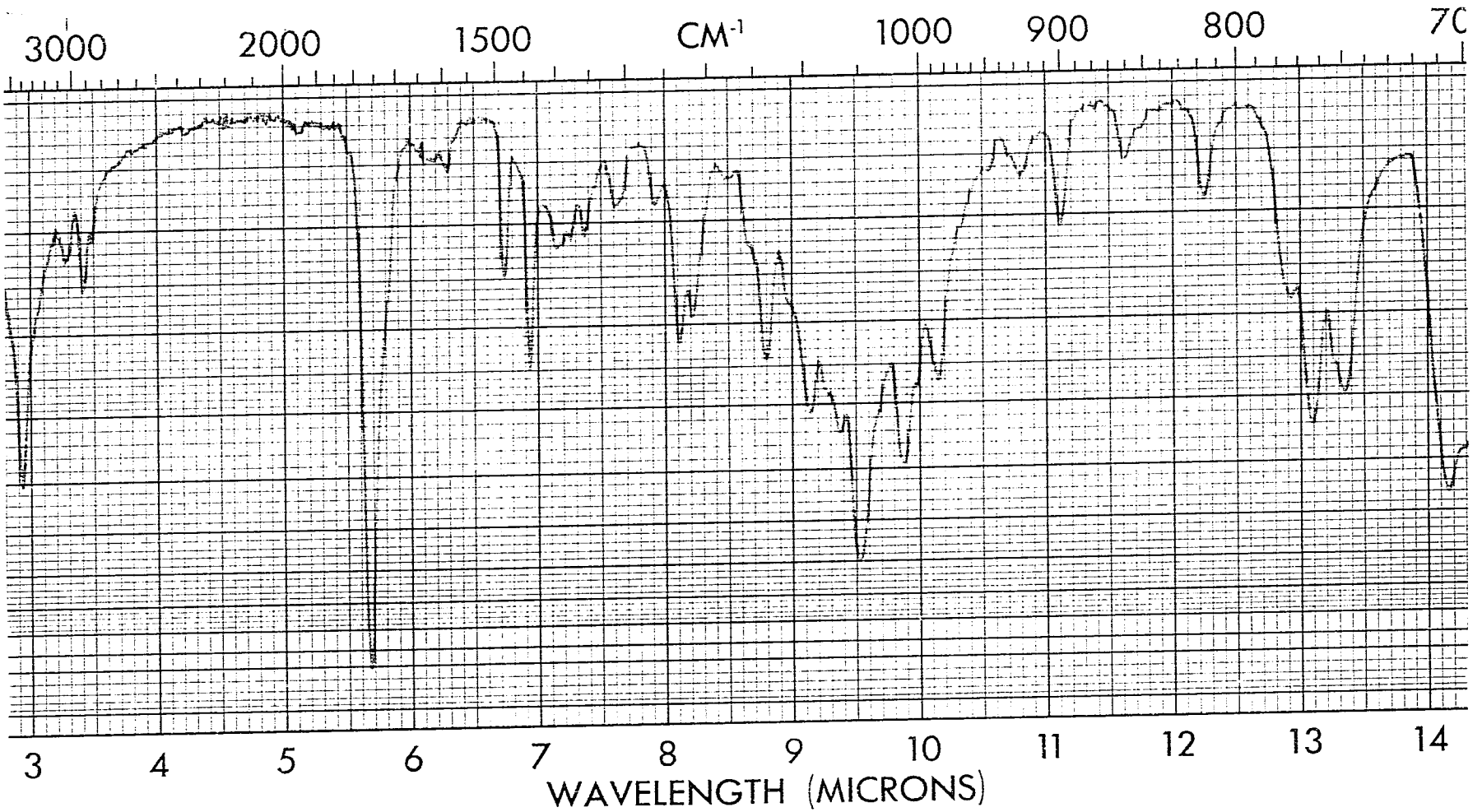


FIGURE 3.6

INFRARED SPECTRUM OF BENZYL 2-DEOXY-6-TRIPHENYLMETHYL-β-D-ALLOPYRANOSIDO-[2.3:4'.5']-OXAZOLIDONE-(2')



CHAPTER IV

SUMMARY

Benzyl β-D-glycosides of 2-acylamido-2-deoxy-D-glucopyranose are usually prepared by multistep processes employing the glycosyl halides. Mixtures of α and β benzyl glycosides result if direct acid catalyzed reactions with benzyl alcohol are carried out. If, however, this latter reaction is carried out in a two phase system with an acid catalyst, the lower solubility of the β-D-anomer becomes the determining factor in the resultant tandem equilibrium, and the β-D-glycoside predominates in the final product.

Benzyl 4,6-O-benzylidene-2-benzyloxycarbonylamido-2-deoxy-3-O-(methylsulfonyl)-β-D-glucopyranoside was obtained by a series of known reactions. Difficulties in elimination of the 3-sulfonate were encountered but proceeded with alkoxide to give benzyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranoside, and with potassium acetate in aqueous 2-ethoxyethanol to give benzyl 4,6-O-benzylidene-2-deoxy-β-D-allopyranosido-[2.3:4'.5']-oxazolidone-(2'). Preparation of derivatives, independent synthesis and infrared spectra confirmed structures.

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