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SYNTHESIS WITH THIO SUGARS:
FORMATION AND DECOMPOSITION OF ACETYLATED
GLYCOSYLSULFENYL BROMIDES

DISSERTATION
Presented in Partial Fulfillment of the Requirements for
the Degree Doctor of Philosophy in the Graduate
School of The Ohio State University

By
Reuben Hays Bell, B.S., M.S.

The Ohio State University
1969

Approved by

Advisor
Department of Chemistry
DEDICATION

To my mother, Alma Hays Bell, and
my late father, Duane Hazlett Bell.
ACKNOWLEDGMENTS

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PUBLICATIONS

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Dimethylthiocarbamates as a Route to Deoxy-sugars," Chem. Commun.,
323 (1968).

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R. H. Bell, D. Horton, and Martha J. Miller, "Reactions of Tetra-
α-Acetyl-β-D-Glucopyranosylsulfenyl Bromide," Carbohyd. Res., 2,
201 (1969).

FIELDS OF STUDY

Major Field: Organic Chemistry
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INTRODUCTION
AND
STATEMENT OF THE PROBLEM

This project was planned as part of a major study on the reactivity with halogen of protected 1-thialdose sugars having various substituents on the sulfur atom, and to explore the reaction as a function of the substituent at the sulfur atom and the nature of the glycosyl group. The study was intended, in part, to extend our knowledge of acetylated glycosylsulfenyl bromides as related to their utility and scope in synthesis of pharmacologically important compounds. A further extension of the program was pointed toward exploring similar reactions in which the sulfur atom was located on carbon atoms other than C-1 of an aldose sugar. When the sulfur atom is located at C-1 of an aldose it is part of a hemithioacetal group. When it is located at positions other than C-1 it becomes a primary, or secondary thiol. One route from a secondary alcohol group in a sugar ring to the corresponding secondary thiol is by pyrolysis of a xanthate ester: \( R-O(C=S)SEt \rightarrow R-S(C=O)SEt \), but the reaction gives low yields and is not of general utility. It was proposed to explore the photolysis of compounds of this type, in particular the related dimethylthiocarbamates \(^1\) - \( R-O(C=S)NMMe_2 \) - to

determine whether such a rearrangement could be effected photolyt-
ically. It is known that C-S bonds in carbohydrate derivatives can be cleaved by light and a possibility existed that the photolysis might alternatively give rise to a deoxy sugar (RH), itself a useful synthetic objective in carbohydrate chemistry.
HISTORICAL

The classical work on thio sugars was reviewed by Raymond\textsuperscript{2} in 1945. More recent reviews have been made by Reid\textsuperscript{3} and by Horton\textsuperscript{4}.


\textsuperscript{4} General preparative methods for 1-thio sugars, and their 1-S-alkyl and aryl derivatives\textsuperscript{5} as well as a review of the 1-thioglycosides\textsuperscript{6} were described by Horton.


\textsuperscript{6} D. Horton, \textit{ibid.}, 2, 368 (1963).
A. Naturally occurring l-thio-
D-glucosides

The most common source of naturally occurring glycosides of
l-thio-D-glucose is found in the mustard-oil glucosides of the
Cruciferae, Capparidaceae, and Resedaceae plant families. This
subject has been reviewed by Raymond, Zinner, Kjaer, and


Horton and Hutson. The first example of this series was isolated in
1831 by Robiquet and Boutron. The most thoroughly studied example


of this group has been sinigrin. This compound was isolated in 1839
from seeds of black mustard, Brassica nigra Koch. Structure (I) for
sinigrin, proposed by Gadamer, was accepted for many years. The

(12) J. Gadamer, Arch. Pharm., 235, 44 (1897).

structure assignment was based on the enzymic hydrolysis of sinigrin
to allyl isothiocyanate, D-glucose, and hydrogen sulfate ion. The
structure was supported by the cleavage of sinigrin with silver nitrate to give D-glucose and silver sinigrate\textsuperscript{13} and by treatment of

\begin{equation}
\text{Structure I}
\end{equation}

sinigrin with sodium methoxide\textsuperscript{14} to obtain 1-thio-D-glucose. Ettlinger

\textsuperscript{(14) W. Schneider and F. Wrede, Ibid., 47, 2225 (1914).}

and Lundeen\textsuperscript{15} pointed out that structure (I) contradicted the fact that sinigrin yielded a nitrile and carboxylic acid having the same number of carbon atoms as the enzymically formed isothiocyanate, and not the amine expected from (I). When sinigrin was reduced with

\textsuperscript{(13) W. Schneider, H. Fischer, and W. Specht, Ber., 62, 2787 (1930).}

Raney nickel, n-butylamine was formed and isolated in 47% yield as the p-nitrobenzamide. Acid hydrolysis of sinigrin gave vinylacetic acid and hydroxylamine. Ettlinger and Lundeen\textsuperscript{15} proposed structure (II) for the mustard-oil D-glucosides.

\[
\text{Structure (II)}
\]

The enzymic breakdown of the mustard-oil D-glucosides to iso-thiocyanates can be described as an initial loss of the glycosyl moiety followed by a 1,2-intramolecular shift.

\[
\begin{align*}
\text{II} &\quad \xrightarrow{\text{H}_2\text{O}} \\
\begin{bmatrix}
\text{S}^- \\
\text{R-C=N-O}_3
\end{bmatrix} &\quad \text{R-N=C=S} \\
\text{HSO}_4^- &+ 
\end{align*}
\]
Ettlinger and Lundeen later verified the newly proposed structure by synthesizing glucotropaeolin (structure II, R=C₆H₅CH₂-).

Waser and Watson confirmed the proposed structure for sinigrin (structure II, R=CH₂=CH-CH₂-) by X-ray crystallographic analysis, and established the syn disposition between the sulfate group and the l-thio-D-glucose moiety about the C=N double bond. The first synthesis of the classical example, sinigrin, was accomplished by Benn and Ettlinger. Benn reported a new synthesis of mustard-oil D-glucosides and the major reaction sequence is given on the following page for glucoaubrietin. Benn and co-workers have synthesized glutinosinalbin (II, R=HOC₆H₄CH₂), glucoaubrietin (II, R=CH₃OC₆H₄CH₂), glucotropaeolin (II, R=PhCH₂), glucoapparin (II, R=CH₃), gluconasturin (II, R=PhCH₂CH₂), glucoputranjivin [II, R=(CH₃)₂CH], glucocochlearin [II, R=(CH₃CH₂)(CH₃)CH] as potassium or tetramethylammonium salts by this method.
R = CH₃

Structure II (R=CH₃O-CH₂CH₂)
Glucoaubriëtine
The similarity of several side-chains of the mustard-oil D-glucosides to those of amino acids in proteins suggests a common pathway in biogenesis.9,15,23,25 (see Table 1). Other mustard-oil D-glucosides have no obvious relationship to known amino acids (see Table 2), suggesting either that they were formed by a different biosynthetic pathway, or that α-amino acids exist in Nature that have not been recognized as yet.23 Recent workers26-29 have linked certain α-amino acids as biogenetic precursors

(21) M. H. Benn, ibid., 42, 163 (1964).
### TABLE 1

**GROUPS COMMON TO AMINO ACIDS AND MUSTARD-OIL D-GLUCOSIDES**

<table>
<thead>
<tr>
<th>R*</th>
<th>Amino acid</th>
<th>Mustard-oil D-glucosides</th>
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<tr>
<td>C₆H₅CH₂</td>
<td>phenylalanine</td>
<td>glucotropaeolin</td>
</tr>
<tr>
<td>E-HO-C₆H₄CH₂</td>
<td>tyrosine</td>
<td>glucosinalbin</td>
</tr>
<tr>
<td>CH₃</td>
<td>alanine</td>
<td>glucopapparin</td>
</tr>
<tr>
<td>CH₃CH₂CH(CH₃)</td>
<td>isoleucine</td>
<td>glucocochlearin</td>
</tr>
<tr>
<td>(CH₃)₂CH</td>
<td>valine</td>
<td>glucoputranjivin</td>
</tr>
</tbody>
</table>

*R is the group common to amino acids of the general structure, R-CH(NH₂)CO₂H, and to the mustard-oil 1-thio-D-glucosides, structure II.*
<table>
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<th>$R^*$</th>
<th>Mustard-oil D-glucoside</th>
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<tr>
<td>$\text{CH}_3\text{S(CH}_2\text{)}_5$</td>
<td>glucoberteron</td>
</tr>
<tr>
<td>$\text{CH}_3\text{SO(CH}_2\text{)}_5$</td>
<td>glucoalyssin</td>
</tr>
<tr>
<td>$\text{CH}_3\text{SO(CH}_2\text{)}_8$</td>
<td>glucohirsutin</td>
</tr>
<tr>
<td>$\text{CH}_3\text{SO(CH}_2\text{)}_9$</td>
<td>glucoarabin</td>
</tr>
</tbody>
</table>

* See structure II for mustard-oil D-glucosides with substituent $R^*$. 
It has been suggested\textsuperscript{4} that the D-glucosyl substituent exists as a removable blocking group for biological stabilization of reactive thiol derivatives. The D-glucosyl group can be enzymically cleaved when the thiol derivative is required in a biological system.

Most 1-thio sugar derivatives do not commonly react by cleavage between the aglycon and the sulfur atom\textsuperscript{4} (bond b, structure III). Scission usually occurs between the sugar and the sulfur atom.

\[
\text{Sugar-}^{\text{a}}S^{\text{b}}R
\]

Structure III

(bond a, structure III). Chemical cleavage of mustard-oil thiogluco-sides as first shown by Schneider\textsuperscript{13,14} is an example of the former (cleavage at bond b) to yield 1-thio-D-glucose. Many 1-thio sugars have been synthesized in the laboratory; however, a review of the entire field of thio sugars is beyond the scope of this dissertation.

Examples of thio sugars having the sulfur atom at positions in the sugar molecule other than C-1 have been synthesized\textsuperscript{4} but have not yet been demonstrated to occur naturally, with the sole exception of 5-thio-D-ribose, which is a component fragment of "S-adenosyl-methionine" the factor involved in methyl group-transfer in biological reactions.
B. Synthesis of acetylated 1-thioglycosides and acetylated 1-thio sugars

The first recorded preparation of a 1-thioglycoside\(^\text{30}\) was that of phenyl 1-thio-\(\beta-D\)-glucopyranoside obtained by condensation of tetra-O-acetyl-\(\alpha-D\)-glucopyranosyl bromide with the sodium salt of benzenethiol, a reaction that involved concomitant deacetylation. This reaction of a poly-O-acetylglucosyl halide with a salt of a thiol has become a general method for the preparation of 1-thioglycosides. Various workers have used this method or slight modifications thereof to prepare 1-thio-\(\beta-D\)-glucopyranosides,\(^{31,33,34-37,39}\) 1-thio-\(\beta-D\)-galactopyranosides,\(^{32}\) 1-thio-\(\beta-D\)-xylopyranosides,\(^{38}\) and 1-thio-\(\alpha-L\)-arabinopyranosides.\(^{40}\) The condensation of potassium...
\begin{align*}
\text{AcOCH}_2 & \quad \rightarrow \quad \text{KSAc} \\
\text{AcO} & \quad \rightarrow \quad \text{AcOCH}_2 \\
\text{Ac} & \quad \rightarrow \quad \text{Ac}
\end{align*}


(32) B. Helferich and O. Türk, Ber., 82, 2215 (1946).

(33) W. Schneider, D. Clibbens, G. Hüllweck, and W. Steibelt, ibid., 47, 1258 (1914).


(37) W. Schneider, J. Sepp, and O. Stiehler, Ber., 51, 220 (1917).


thiolacetate with tri-O-acetyl-β-D-xylopyranosyl bromide gave 1-thio-
β-D-xylopyranose tetraacetate. The method was extended for
the β-D-xylopyranose tetraacetate. The method was extended for
the preparation of 1-thio-β-D-glucopyranose pentaacetate, (42) (43)
M. Gehrke and W. Kohler, Ber., 64, 2696 (1931).
and 1-thio-β-D-galactopyranose pentaacetate. The stereochemical
outcome at C-1 in these condensations is not the result of an SN2
type of reaction but is governed by the formation of an intermediate,
cyclic, 1,2-acetoxonium ion which is opened stereospecifically by
the thiolacetate nucleophile.
In order to obtain the α-D anomer it is necessary to effect a condensation in a system wherein the C-2 substituent is a less effective participating group, and with the proper orientation of the halide group so that an SN2 type of displacement can be effected.

Accordingly, Tejima and co-workers\textsuperscript{44} condensed potassium thiolacate with 3,4,6-tri-O-acetyl-β-D-glucopyranosyl chloride with subsequent acetylation to give 1-thio-α-D-glucopyranose pentaacetate.

Schneider and Eisfeld\textsuperscript{45} refluxed tetra-\(\text{O}\)-acetyl-\(\alpha\)-\(\text{D}\)-gluco-
pyranosyl bromide in dry toluene with thiourea to obtain a product in moderate yield designated as 2-(2,3,4,6-tetra-\(\text{O}\)-acetyl-\(\beta\)-\(\text{D}\)-glucopyranosyl)-2-thiopseudourea hydrobromide. They observed a similar condensation reaction when phenylthiourea was used instead of thiourea. Bonner and Kahn\textsuperscript{46} modified the method by substituting isopropyl alcohol for toluene as the reaction solvent, and increased the yield of the 2-glucosyl-2-thiopseudourea hydrobromide to 64%. They\textsuperscript{46} extended the method to the preparation of 2-(2,3,4,6-tetra-\(\text{O}\)-acetyl-\(\beta\)-\(\text{D}\)-galactopyranosyl)-2-thiopseudourea hydrobromide, 2-(2,3,4-tri-\(\text{O}\)-acetyl-\(\beta\)-\(\text{D}\)-xylopyranosyl)-2-thiopseudourea hydrobromide, and to a polyacetylated celllobiosyl pseudourea hydrobromide.
Corny, Vrkoc, and Stanek further improved the yield of the


2-glucosyl-2-thiopseudourea hydrohalide by substituting acetone for isopropyl alcohol as the reaction solvent. These workers prepared 2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiopseudourea hydrocarbonate, a compound previously described by Schneider and Eisfeld, by adding a solution of sodium hydrogen carbonate to an aqueous solution of the glucosyl thiopseudourea hydrobromide. The 2-glucosyl-2-thiopseudourea hydrocarbonate was then decomposed to 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranose by heating with sodium hydrogen sulfite in ethyl acetate. The 1-thio-β-D-glucopyranose derivative was also obtained when an aqueous solution of the thiopseudourea hydrobromide was combined with a saturated aqueous solution of sodium hydrogen sulfite. The preliminary investigation led to a general procedure for the preparation of per-O-acetylated glycosyl
thiols. The latter could be $\beta$-acetylated to give peracetylated
1-thioaldopyranoses.\(^{47-49}\) The method consisted of dissolving an

\[ \text{(48) J. Staněk, M. Šindlerová, and M. Černý, ibid., 30, 297 (1965).} \]


acetylated glycosylthiopseudourea hydrohalide in aqueous sodium
hydrogen sulfite. The $\beta$-acetylated 1-thio sugar formed was immedi­
ately partitioned by way of an heterogeneous solvent system between
water and either carbon tetrachloride or chloroform. This method
was used followed by acetylation of the 1-thio sugar to prepare 1-thio-β-D-glucopyranose pentaacetate and 1-thio-α-D-arabinopyranose tetraacetate from their corresponding 2-glycosyl-2-thio-pseudourea hydrobromides. Horton and co-workers prepared 1-thio-β-D-ribofuranose tetraacetate and 1-thio-α-L-arabinofuranose tetraacetate from their corresponding thiopseudourea hydrobromides by an adaptation of this method. Černý and co-workers extended the generality of the method to include the preparation of 2,3,4-tri-α-acetyl-1-thio-β-D-xylopyranose and 2,3,4,6-tetra-α-acetyl-1-thio-β-D-galactopyranose.

A previous preparative route for tetra-β-acetyl-1-thio-β-D-glucopyranose had been by reductive cleavage of bis(β-D-glucopyranosyl) disulfide octaacetate.

---

(50) W. Schneider and A. Bansa, Ber., 64, 1321 (1931).
The 1-thio-β-D-glucopyranose pentaacetate was obtained by acetylation of the 1-thio group. Another route was by cleavage of tetra-O-acetyl-β-D-glucopyranosyl ethylxanthate with methanolic ammonia followed by acetylation.\(^{(52)}\)

\(^{(52)}\) W. Schneider, R. Gille, and K. Eisfeld, Ber., \textit{61}, 1244 (1928).
C. Synthesis of l-thioglycosides by acid-catalyzed glycosidation

The reaction of an alcohol with the aldehyde group of a sugar in the presence of an acid catalyst to produce a glycoside is a well-known reaction. Fischer repeated this procedure.

(53) E. Fischer, ibid., 26, 2400 (1893).
(54) E. Fischer, ibid., 27, 673 (1894).

with various thiols in place of alcohols, but obtained instead the corresponding dithioacetals.
Schneider and Sepp\textsuperscript{55} synthesized an ethyl 1-thio-\textsubscript{D}-glucoside (55) W. Schneider and J. Sepp, Ber., 49, 2054 (1916).

by decomposing \textsubscript{D}-glucose diethyl dithioacetal in the presence of mercuric chloride and base. Pacsu and co-workers\textsuperscript{56,57} favored an


(57) E. Pacsu and E. J. Wilson, Jr., \textit{ibid.}, 61, 1450 (1939).

\alpha-\textsubscript{D}-furanoside structure for the ethyl 1-thio-\textsubscript{D}-glucoside by optical rotary evidence based on Hudson's rules of rotation and by ease of hydrolysis in 0.01N hydrochloric acid. Wolfrem and co-workers\textsuperscript{58}


subjected the ethyl 1-thio-\textsubscript{D}-glucoside to periodate oxidation and showed that 1 mole of formaldehyde was produced, thus establishing the furanoside structure.

Under extended times of reaction and at higher temperatures, the acid-catalyzed mercaptalation reactions of sugars may give 1-thioglycosides in moderate yields. Fried and Walz\textsuperscript{59} were able to

obtain a moderate yield of ethyl 1-thio-β-D-mannopyranoside (isolated as the tetraacetate) when methyl α- or β-D-mannopyranoside was equilibrated for 18 hours with ethanethiol and hydrochloric acid at room temperature. A small proportion of the α-D anomer was obtained in the reaction with methyl β-D-mannopyranoside. A slightly better yield was obtained when the free sugar was used.

Wolfrom, Horton, and Garg\textsuperscript{60} obtained a 31% yield of ethyl


1-thio-α- and β-D-mannopyranosides (isolated as the tetraacetates) upon prolonged treatment of D-mannose with ethanethiol and concentrated (12N) hydrochloric acid at room temperature. They were able to show by paper chromatographic evidence that after 5 minutes all of the mannose had reacted and the major product was the diethyl dithioacetal accompanied by minor proportions of the two thioglycosides. At longer reaction times the zones corresponding to the
l-thioglycosides increased in intensity while the intensity of the dithioacetal zone decreased and an additional zone appeared corresponding to D-mannose.

The reaction of the diethyl dithioacetals of D-glucose 61,62


(62) P. Brigl, K. Gronemeier, and A. Schulz, Ber., 72, 1052 (1939).

and D-galactose 59 with a mineral acid gave low yields of l-thio-D-glycopyranosides. As a preparative route for l-thioaldopyranosides the aldose dialkyl dithioacetals have not proven to be satisfactory precursors for a general, high-yielding method.

Brigl and Schinle 63 treated β-D-glucopyranose pentabenzolate

(63) P. Brigl and R. Schinle, ibid., 65, 1890 (1932).

with ethanethiol in the presence of hydrochloric acid, but obtained a complex mixture of products. Wolfrom and Thompson 64,65 modified


(65) M. L. Wolfrom and A. Thompson, ibid., 56, 1804 (1934).

Brigl and Schinle's conditions by the use of zinc chloride as the catalyst in the presence of a drying agent to minimize acid
hydrolysis of acetyl groups in the mercaptolysis of β-D-fructose pentaacetate. They showed that β-D-fructose pentaacetate undergoes mercaptolysis in the presence of ethanethiol to form ethyl 2-thio-β-D-fructoside tetraacetate. Lemieux\(^66\) extended the procedure to include the use of α- and β-D-glucopyranose pentaacetate and -D-galactopyranose pentaacetate to form their corresponding ethyl 1-thio-glycoside tetraacetates. He obtained a 71.2\% yield of ethyl 1-thio-β-D-glucopyranoside tetraacetate and a 75.6\% yield of ethyl 1-thio-β-D-galactopyranoside tetraacetate from their respective β-D-aldopyranose pentaacetates, but found mercaptolysis of the α-pentaacetates was not a practicable method for synthesis of 1-thioglycosides. The reaction was described\(^67\) as abstraction of the O-acetyl group at C-1 with


synchronous attack of the 2-acetyl group to form the cyclic carbonium ion followed by attack of the sulfur atom of ethanethiol to give the ethyl 1-thio-β-D-glycoside tetraacetate.

The reaction method has been extended to formation of ethyl tetra-O-acetyl-1-thio-a-D-mannopyranoside.68,69 Fletcher and co-workers70 have demonstrated the applicability of the method for preparation of tert-butyl 1-thio-β-D-glucopyranoside tetraacetate from β-D-glucopyranose pentaacetate.

D. Formation and reactivity of tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide

A sulfenyl compound may be defined71-73 as a compound that


can undergo reactions typical of the polarization \( \text{RS}^+ - \text{X}^- \) and the compound where \( X \) is a halide ion is known as a sulfenyl halide. Arylsulfenyl chlorides have been known for over 50 years\(^7^4\) and methanesulfenyl chloride was described by Rathke\(^7^5\) in 1870.

\[ \text{(74) T. Zincke, Ber., 44, 769 (1911).} \]
\[ \text{(75) B. Rathke, ibid., 3, 858 (1870).} \]

The first carbohydrate sulfenyl halide was reported by Horton, Wolf from, and Garg.\(^7^6\) They brominated a carbon tetrachloride solution of 1-thio-\( \beta \)-D-glucopyranose pentaacetate and were able to obtain tetra-O-acetyl-\( \beta \)-D-glucopyranosylsulfenyl bromide in high yield. These workers\(^7^6\) explained the formation of the sulfenyl bromide as shown below.
The reaction proceeds with initial halogenation of sulfur followed by heterolysis of the sulfur to acetyl bond (bond a) to give corresponding glucosylsulfenyl bromide and acetylium ion, which combines with the halide to form acetyl bromide. Heterolysis of the C-1 to S bond (bond b), and subsequent attack of the bromide ion at C-1 would have formed tetra-O-acetyl-\(\alpha\)-D-glucopyranosyl bromide. Bonner\(^{77}\) described the latter type of reaction in the bromination of phenyl tetra-O-acetyl-1-thio-\(\beta\)-D-glucopyranoside.

\[
\begin{align*}
\text{AcOCH}_2\text{AcOCH}_2\text{SPh} & \quad \text{AcOCH}_2\text{Br} \quad \text{Br}^+ \quad \text{AcOCH}_2\text{OAc} \\
\text{AcO} & \quad \text{AcO} \\
\text{OAc} & \quad \text{PhSBr}
\end{align*}
\]

Horton and Miller\(^{78}\) and Bell\(^{73}\) demonstrated the general reactivity of tetra-O-acetyl-\(\beta\)-D-glucopyranosylsulfenyl bromide by forming adducts with benzenethiol, \(\alpha\)-toluenethiol, \(\alpha\)-chloroaniline,


and cyclohexene. The yield of glucosylsulfonyl bromide was almost quantitative when a small portion (0.5 g) of 1-thio-β-D-glucopyranose pentaacetate was brominated, but the yield and purity of the product were erratic with larger bromination reactions. It was demonstrated that the glucosylsulfonyl bromide could be obtained in large amounts (∼20 g) if the carbon tetrachloride suspension of 1-thio-β-D-glucopyranose pentaacetate were cooled to about 15°C before bromination.
E. Photochemistry of carbohydrates

Chemists have been concerned with the photochemistry of carbohydrate derivatives for many years. A detailed review of the early work, mainly on degradations of the free sugars, their alditols, and glycosides, is given by G. O. Phillips and is not elaborated upon in this dissertation.


Noyes, Porter, and Jolley have defined a primary photochemical process as "the series of events beginning with the absorption of a photon by a molecule and ending either with the disappearance of that molecule or with its conversion to a state such that its reactivity is statistically no greater than that of similar molecules in thermal equilibrium with their surroundings."

The energy values for single bonds occurring most frequently in carbohydrate compounds are given in Table 3.


TABLE 3
ENERGY VALUES FOR SINGLE BONDS

<table>
<thead>
<tr>
<th>Bond</th>
<th>Bond energy (Kcal/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-C</td>
<td>83.1</td>
</tr>
<tr>
<td>C-H</td>
<td>98.8</td>
</tr>
<tr>
<td>C-N</td>
<td>69.7</td>
</tr>
<tr>
<td>C-O</td>
<td>84.0</td>
</tr>
<tr>
<td>C-S</td>
<td>62.0</td>
</tr>
<tr>
<td>C-I</td>
<td>57.4</td>
</tr>
</tbody>
</table>

Phillips and Barber\(^\text{82}\) irradiated aqueous solutions of D-glucitol for extended periods of time and obtained various degradation products. They showed that light from a medium-pressure mercury arc lamp of 2300-2537Å, corresponding to 124-113 kcal/mole was sufficient to cause degradation of D-glucitol. Light in this wavelength range is sufficient to rupture any bond listed in Table 3.

Recent photochemical reactions with carbohydrates have been undertaken from either a mechanistic or preparative approach. Horton and Turner\(^\text{83}\) reported the formation of 6-\(\underline{\text{S}}\)-acetyl-5-deoxy-1,2-\(\underline{\text{O}}\)-


isopropylidene-6-thio-\(\alpha\)-D-\(\alpha\)-D-xylo-hexofuranose by the photocatalyzed addition of thiolactic acid to 5,6-dideoxy-1,2-\(\alpha\)-isopropylidene-\(\alpha\)-D-xylo-hex-5-enofuranose. The reaction proceeded with net anti-Markownikoff addition, presumably by a free-radical mechanism.

\[
\begin{align*}
\text{CH}_2 & \quad \text{MeCOSH} \quad \text{hv} \\
\text{CHO} & \quad \text{CH}_3\text{SAC} \\
\text{OH} & \quad \text{OH} \\
\text{O} & \quad \text{O}
\end{align*}
\]

In an analogous reaction, Whistler, Wang, and Inokawa \(^{84}\) described the photochemical addition of phosphines to 5,6-dideoxy-1,2-\(\alpha\)-isopropylidene-\(\alpha\)-D-xylo-hex-5-enofuranose to give bis(5,6-dideoxy-1,2-\(\alpha\)-isopropylidene-\(\alpha\)-D-xylo-hexofuranose-6-yl)phosphine oxide. Another major product was postulated as the primary phosphine and a minor product was the phosphonous acid. It was not possible to isolate the phosphine from the phosphonous acid because of apparent air oxidation of the former to the latter. The phosphonous acid was isolated as its cyclohexylammonium salt.

Photoaddition of phenyl phosphine to the sugar olefin gave a good yield of a secondary phosphine oxide. It was postulated

that the phosphine oxide formed by air oxidation of the secondary phosphine.

Irradiation of the sodium salt of 2-deoxy-2-(2,4-dinitroanilino)-D-gluconic acid in either water or aqueous sodium hydrogen carbonate gave D-arabinose. Irradiation of an aqueous methanolic
solution of 1-deoxy-1-(2,4-dinitroanilino)-D-glucitol for 96 hr gave no decomposition.

Binkley and Binkley\textsuperscript{87} photolyzed a methanolic solution of 6-deoxy-6-iodo-1,2,3,4-di-\textalpha-D-galactopyranose and reported an 83\% yield of 6-deoxy-1,2,3,4-di-\textalpha-D-galactopyranose and an unidentified product. When isopropyl alcohol
was substituted for methanol as solvent, the yield of 6-deoxy-
1,2,3,4-di-O-isopropylidene-α-D-galactopyranose was 32% and an
additional product, 6-deoxy-1,2:3,4-di-O-isopropylidene-L-arabino-
hex-5-enopyranose, was obtained in 36% yield.

Generation of an aldehyde group was effected in a protected
sugar by photolysis of a primary azide.\(^{88a}\) Irradiation of methyl

2,3,4-tri-0-acetyl-6-azido-6-deoxy-\( \alpha -D \)-glucopyranoside in cyclo-hexane, followed by mild hydrolysis gave 2,3,4-tri-0-acetyl-6-
aldehyde-\( \alpha -D \)-gluco-hexodialdo-1,5-pyranose, characterized by means of its (2,4-dinitrophenyl)-hydrazone and its acetylated aldehyde.

\[
\begin{align*}
\text{CH}_2\text{N}_3 & \xrightarrow{1) \text{hv}} \text{CHO} \\
\text{AcO} & \quad \text{AcO} \\
\text{O} & \quad \text{O} \\
\text{OAc} & \quad \text{OCH}_3 \\
\text{AcO} & \quad \text{AcO}
\end{align*}
\]

The reaction has been utilized for preparing the 6-aldehydo derivative of the polysaccharide amylose, a component of starch.\(^{88b}\)

A photochemically induced ring contraction has been reported by Collins.\(^{89}\) Irradiation of a pentane solution of methyl 6-deoxy-

\[\text{2,3-O-isopropylidene-\( \alpha -L \)-lyxo-hexopyranosid-4-ulse} \]

yield of two products. The major product (55%) was identified as 5-deoxy-2,3-O-isopropylidene-\( \beta -D \)-ribo-furanoside and the minor product (5%) was identified as 5-deoxy-2,3-O-isopropylidene-\( \alpha -L \)-lyxo-furanoside.

\(^{89}\) P. M. Collins, \textit{ibid.}, 403 (1968).
\[
\text{hv, pentane} \rightarrow \text{-CO}
\]
RESULTS AND DISCUSSION

General

In this discussion Sections A, B, and C deal with preparation of the 1-thiocaldose derivatives used. Reactions of certain of these products with bromine to give tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide are given in Section D. The use of n.m.r. spectroscopy to follow the general course of the reactions of a range of 1-thialdose derivatives with bromine is given in Section E. Sections F and G deal with characterization of disulfide derivatives and acetylated glycosyl bromides, respectively, as products of the reaction of 1-thialdose derivatives with bromine under certain conditions. Reactions for characterization of tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromides are given in Section H, and similar reactions for other acetylated glycosylsulfenyl bromides are given in Section I. Sections J and K deal with the photolysis of dimethylthiocarbamates of sugars.

A. Acetylated glycosyl halides

The acetylated glycosyl bromides were prepared directly from the free aldoses essentially according to the procedure of Bárczai-Martos and Kőrösy. The physical data measured on the

products were in good agreement with values in the literature. A summary of the mode of characterization of the acetylated glycosyl bromides is given in Table 4.

Tri-α-acetyl-β-D-xylopyranosyl chloride (5) was prepared according to the method of Hudson and Johnson. The compound gave a m.p. and rotation corresponding with the known values.

The method used for the preparation of 3,4,6-tri-α-acetyl-2,6-dichloroacetyl-β-D-glucopyranosyl chloride (6) was essentially that adapted by Lemieux and Howard and Lemieux and Huber from the original procedure of Brigl. The reported yield of 40 g was impossible to repeat by the conditions given and the literature values of m.p. 140-142°, [α]D +8.9° (c 1.4, chloroform) were only obtained after two recrystallizations of crude 6 from ether. Compound 6, which was difficult to crystallize, was only obtained crystalline by periodic agitation of the cold ethereal
TABLE 4

ACETYLATED GLYCOSYL BROMIDES

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mode of characterization</th>
<th>Literature reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetra-O-acetyl-α-D-glucopyranosyl bromide (1)</td>
<td>m.p.; [α]_D(CHCl_3); other</td>
<td>91,92</td>
</tr>
<tr>
<td>Tetra-O-acetyl-α-D-galactopyranosyl bromide (2)</td>
<td>82-83° +213° n.m.r.</td>
<td>93,92</td>
</tr>
<tr>
<td>Tri-O-acetyl-β-L-arabinopyranosyl bromide (3)</td>
<td>138-140° +279° n.m.r.</td>
<td>94,92</td>
</tr>
<tr>
<td>Tri-O-acetyl-α-D-xylopyranosyl bromide (4)</td>
<td>101-102° +211° n.m.r.</td>
<td>95,96,92</td>
</tr>
</tbody>
</table>

(94) M. Gehrke and F. X. Aichner, Ber., 69, 918 (1927).
crystallizing mixture over a two day period. Various modifications of the method, including purification of the starting material, (penta-O-acetyl-β-D-glucopyranose, 2), and increased time of evaporation under vacuum at an elevated temperature of 85° to eliminate unwanted side products, did not increase the yield of 6.

3,4,6-Tri-O-acetyl-β-D-glucopyranosyl chloride (8) from 3,4,6-tri-O-acetyl-2-O-trichloroacetyl-β-D-glucopyranosyl chloride was prepared by Brigl's method as described by Lemieux and Howard. The reported values for the m.p. and rotation were obtained after a lengthy purification process for the glucopyranosyl chloride (8).

B. Preparation of 2-glycosyl-2-thiopseudouracil hydrohalides

The 2-(acylated glycopyranosyl)-2-thiopseudouracil hydrohalides were prepared according to the method of Černý, Vrkoč, and Stančk, (a modification of the original procedure of Schneider and Eisfeld). The acetylated glycosyl halides were condensed with thiourea in acetone to give the corresponding thiopseudouracil hydrohalide derivatives. A summary of the mode of characterization of the thiopseudouracil hydrohalides is given in Table 5.

An attempt was made to obtain 100 MHz n.m.r. spectra of the 2-glycosyl-2-thiopseudouracil hydrohalide derivatives in deuterium oxide solution with sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) as an internal standard and to correlate the structure of each compound with its n.m.r. data. Compound 9 precipitated
<table>
<thead>
<tr>
<th>Compound</th>
<th>Mode of characterization</th>
<th>Literature reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thio- = pseudourea hydrobromide (2)</td>
<td>m.p. 205°, [α]_D -8.7° (H_2O)</td>
<td>45,46,47</td>
</tr>
<tr>
<td>2-(2,3,4,6-tetra-O-acetyl-3-D-galactopyranosyl)-2-thiopseudourea hydrobromide (10)</td>
<td>m.p. 169.5°, [α]_D +16.9° (EtOH) n.m.r.</td>
<td>46</td>
</tr>
<tr>
<td>2-(2,3,4-tri-O-acetyl-α-L-arabinopyranosyl)-2-thiopseudourea hydrobromide (11)</td>
<td>m.p. 174-175°, [α]_D +6.8° (H_2O) n.m.r.</td>
<td>39</td>
</tr>
<tr>
<td>2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-2-thiopseudourea hydrobromide (12)</td>
<td>m.p. 173°, [α]_D -36° (H_2O) n.m.r.</td>
<td>48</td>
</tr>
<tr>
<td>2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-2-thiopseudourea hydrochloride (13)</td>
<td>m.p. 181°, [α]_D -89° (H_2O) n.m.r.</td>
<td>46</td>
</tr>
</tbody>
</table>
from solution when a sufficient amount of DSS was added to obtain a
lock signal for the 100 MHz n.m.r. spectrometer. N.m.r. spectra
were obtained for compounds 10, 11, 12, and 13. As was anticipated,
the protons attached to the nitrogen atoms underwent deuterium ex-
change with the solvent and their signals were not observed. In
each case the n.m.r. spectrum was not amenable to complete first-
order analysis, but partial analyses made were based upon known chemi-
cal-shift data for acetylated 1-thio-aldopyranoses.39

The ring protons of the 2-galactosyl-2-thiopseudourea hydro-
bromide (10) gave rise to a 4-proton multiplet at 74.39-4.77 and a
3-proton multiplet at 75.45-5.85. The low-field multiplet was
assigned to H-1, 2, 3, and 4 and the higher-field multiplet was
assigned to H-5, 6, and 6'. The higher-field multiplet was partially
masked by appearance of the HOD signal. The methyl protons of
the acetyl groups of 10 were assigned to four sharp singlets, at 77.79,
7.86, 7.91, and 7.98. No attempt was made to assign these signals to
specific acetyl groups.101

(101) D. Horton and J. H. Lauterbach, J. Org. Chem., 34,

The n.m.r. spectrum of 2-(tri-O-acetyl-α-L-arabinosyl)-2-
thiopseudourea hydrobromide 11 showed a low-field multiplet 74.44-
4.79. This multiplet was assigned to H-1, 2, 3, and 4. Two
quartets at higher field, 75.76 and 5.97 were designated as H-5a
(lower field) and H-5b (higher field). The J4,5 couplings were
then $J_{4,5a} = 3.2$ Hz, $J_{4,5b} = 1.8$ Hz, and $J_{5a,5b} = 13.0$ Hz. These constants were in agreement for those reported\(^3^9\) for a benzene-$d_6$ solution of 1-thio-$\alpha$-L-arabinopyranose tetraacetate (14), which showed $J_{4,5a} = 3.9$ Hz, $J_{4,5b} = 2.0$ Hz, $J_{5a,5b} = 12.4$ Hz. The protons at C-5 were not clearly differentiated as equatorial or axial since both of these protons are gauche-disposed to the vicinal protons at C-4.

The n.m.r. spectra of the 2-D-xylopyranosyl-2-thiopseudourea hydrobromide 12 and the 2-D-xylopyranosyl-2-thiopseudourea hydrochloride 13 were similar. Each showed a doublet at $\gamma_{4.26}$ assigned to H-1 with a spacing of 5.0 Hz. The multiplets at $\gamma_{4.66-5.13}$ and $\gamma_{4.66-5.16}$ were assigned to H-2, 3, and 4 of the respective compounds 12 and 13. Two quartets at higher field, $\gamma_{5.60}$ and $\gamma_{6.17}$ in the case of 12 and $\gamma_{5.59}$ and $\gamma_{6.17}$ in the case of 13, were designated as H-5a (low field) and H-5b (high field) for the low and high field H-5 protons of each compound. The coupling constants for $J_{4,5a}$, $J_{4,5b}$, and $J_{5a,5b}$ were similar for the two examples, thus for 12, $J_{4,5a} = 3.6$ Hz, $J_{4,5b} = 6.0$ Hz, and $J_{5a,5b} = 12.3$ Hz, and for 13, $J_{4,5a} = 3.9$ Hz, $J_{4,5b} = 6.1$ Hz, and $J_{5a,5b} = 12.3$ Hz. The small coupling constants for $J_{1,2}$ and $J_{4,5a}$ and $J_{4,5b}$ for 12 and 13, compared with those for a chloroform-$d_6$ solution of 1-thio-$\beta$-D-xylopyranose tetraacetate\(^3^9\) (15) ($J_{1,2} = 8.1$ Hz, $J_{4,5e} = 4.7$ Hz, and $J_{4,5a} = 8.3$ Hz), indicated that there is very probably a conformational equilibrium between chair conformers for 12 and 13, with the observed spectrum representing a time average of the chair conformers.
S-substituent would account for a greater amount of the \( \text{Ig} \) (\( 3 \)) conformer for 12 or 13 as opposed to the relatively minor amount of \( \text{Ig} \) (\( 3 \)) conformer observed in the n.m.r. study of 1-thio-\( \beta \)-D-xylopyranose tetraacetate\(^{39} \) (15). A more complete n.m.r. study of 2-glycosyl-2-thiopseudourea hydrohalides of this type needs to be made before meaningful conclusions can be obtained.
C. Peracetylated 1-thio sugars

a. From acetylated 2-glycosyl-2-thiopseudourea hydrohalides.—The method for preparation of most of the polyacetylated 1-thio sugars was that of Černý, Vrkoč, and Staněk. This method involved the decomposition of the 2-glycosyl-2-thiopseudourea hydrohalides to the corresponding 1-thiol by sodium hydrogen sulfite, followed by acetylation of the resulting thiol with pyridine and acetic anhydride. The compounds prepared in this manner are given in Table 6.

1-Thio-\(\beta\)-D-glucopyranose pentaaceta 47 (16) and 1-thio-c-L-arabinopyranose tetraacetate 39 (14) have previously been prepared from their corresponding 2-glycosyl-2-thiopseudourea hydrobromides. The corresponding thiol has been prepared from 2-D-galactosyl-2-thiopseudourea hydrobromide, but to the author's knowledge this preparation of 1-thio-\(\beta\)-D-galactopyranose pentaacetate is the first complete transformation of 10 into 17. This process also represents the first preparation of 1-thio-\(\beta\)-D-xylopyranose tetraacetate (15) from the 2-xylopyranosyl-2-thiopseudourea hydrobromide and the hydrochloride.

b. From acetylated aldoses.—The acid-catalyzed equilibration of penta-O-acetyl-\(\beta\)-D-glucopyranose pentaacetate (7) with zinc chloride in thiolacetic acid gave 92% yield of crystalline 1-thio-\(\beta\)-D-glucopyranose pentaacetate (16). The compound was identified by comparison of the m.p., optical rotation, and n.m.r. spectrum with that previously reported in the literature. 39,42,43 An n.m.r. spectrum (60 MHz) of the crude reaction product showed only the
<table>
<thead>
<tr>
<th>Compound</th>
<th>Mode of characterization</th>
<th>Literature reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Thio-β-D-glucopyranose pentaacetate (16)</td>
<td>118-119° +10° n.m.r.</td>
<td>39,42,99</td>
</tr>
<tr>
<td>1-Thio-β-D-galactopyranose pentaacetate (17)</td>
<td>114-115° +30.1° n.m.r.</td>
<td>39</td>
</tr>
<tr>
<td>1-Thio-α-L-arabinopyranose tetracetate (14)</td>
<td>77-78° +33.3 n.m.r.</td>
<td>39</td>
</tr>
<tr>
<td>1-Thio-β-D-xylopyranose tetracetate (15)</td>
<td>99-100° -7.0° n.m.r.</td>
<td>39,41</td>
</tr>
</tbody>
</table>
presence of \( \text{1-thio-\( \beta \)-D-glucopyranose pentaaceta te (16)} \) and no signal was visible at low field (\( \gamma \text{3.76} \)) that would have indicated the presence of \( \text{1-thio-\( \alpha \)-D-glucopyranose pentaaceta te (18)} \).

The method employed for the equilibration reaction was analogous to that described by Wolfrom and Thompson\(^{64}\) for the mercaptolysis of \( \beta \)-D-fructose pentaaceta te with ethanethiol and a Lewis acid (zinc chloride) and to the method described by Wood, Coxon, Diehl, and Fletcher\(^{70}\) for the preparation of tert-butyl \( \text{1-thio-\( \beta \)-D-glucopyranose tetraaceta te (19)} \). Lemieux\(^{66}\) obtained a 71.2\% yield of ethyl tetra-O-acetyl-1-thio-\( \beta \)-D-glucopyranoside by the zinc chloride-catalyzed mercaptolysis of \( \gamma \) with ethanethiol. The reaction is thought\(^{66,67}\) to proceed by a route analogous to that of the ethanethiol with mercaptolysis of \( \beta \)-D-glucopyranose pentaaceta te (\( \gamma \)). Loss of the 1-acetoxy group with synchronous participation of the 2-acetoxy group forms a cyclic carbonium ion. The carbonium ion is then attacked by the sulfur atom of thiolacetic acid.
The method offers a potential route for a one-step preparation of 1,2-trans peracetylated 1-thioaldopyransides.

c. By reaction of potassium thiolacetate with 3,4,6-tri-O-acetyl-β-D-glucopyranosyl chloride (8).--The preparation of 1-thio-α-D-glucopyranose pentaacetate (18) presents special problems because the substituents at C-1 and C-2 are cis-disposed. Potassium thiolacetate was condensed with 8 in acetone and the product was acetylated according to the procedure of Tejima et al. The desired 1-thio-α-D-glucopyranose pentaacetate (18) was isolated from a mixture of three products and the m.p. and specific rotation were consistent with the values of Tejima et al. The rotation, [α]_D^20 +135° (c 1.0, chloroform), differed somewhat from that reported by Schneider and co-workers, [α]_D^20 +120.2° (c 0.416, chloroform). The German workers obtained 18 by acetylation of a mutarotated sample of 1-thio-β-D-glucopyranose and separation of the mixture of products. Their product may not have been separated completely from the β-D anomer.

The signal observed for H-1 in the 60 MHz n.m.r. spectrum of the 1-thio-α-D-pentaacetate 18 in chloroform-d was an apparent quartet (T3.76) having spacings of about 1.2 Hz. When the spectrum was measured at 100 MHz, the signal for H-1 was observed as a triplet having spacings of about 2.1 Hz. When the solvent was changed to benzene-d_6 the H-1 signal appeared as a sharp doublet, T3.49, J_{1,2} = 4.7 Hz. The perturbed signal for H-1 in chloroform-d was attributed to virtual coupling of H-1 with H-3 as the result of close proximity of the H-2 and H-3 signals. For further details of the n.m.r. spectra of 18 see the Experimental section.


d. Preparation of phenyl (20) and benzyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranoside (21).—These compounds, 20 and 21, were prepared by condensation of the corresponding benzenthio and α-toluenethiol with tetra-O-acetyl-α-D-glucopyranosyl bromide (1). The physical constants obtained were in agreement with reported values for 2030,31 and 2137,39.

D. Tetra-O-acetyl-β-D-glucopyranosyl-sulfenyl bromide (22)

The original preparation of tetra-O-acetyl-β-D-glucopyranosyl-sulfenyl bromide (22)76 was described in the author’s Master of Science thesis.73 The sulfenyl bromide 22 was also obtained by brominating tert-butyl 1-thio-β-D-glucopyranose tetraacetate (19). The compound isolated was identical with an authentic sample of 2273,76,78 by comparison of physical constants, and was characterized by trapping with benzenethiol to give the known phenyl tetra-O-acetyl-β-D-glucopyranosyl disulfide (23).73,78 Formation of the sulfenyl
bromide 22 from the tert-butyl thio-\(D\)-glucoside 19 as well as from

\[
\begin{align*}
\text{AcOCH}_2 & \quad \text{AcOCH}_2 \\
\text{O} & \quad \text{O} \\
\text{SCMe}_3 & \quad \text{SBr} \\
\text{OAc} & \quad \text{OAc} \\
\text{OAc} & \quad \text{OAc} \\
\end{align*}
\]

the thiolacetate 16, support the mechanistic rationale (see Scheme I) originally proposed\(^{71}\) for the formation of the sulfenyl bromide 22, based on the heterolysis of an intermediate bromosulfonium ion at point b, if \(R^+\) is a cation more stable than the glycosyl cation that would result from scission at point a. The reaction requires more than one molecule of bromine per molecule; therefore, the actual transition state may involve an additional molecule of bromine that interacts with the bromosulfonium ion. Conversion of the sulfenyl bromide 22 into the tetra-\(\text{O}\)-acetyl-\(\alpha\)-\(D\)-glucopyranosyl bromide (4) is, predictably a slower process than formation of 1, because the sulfur atom in 22 would be expected to be much less susceptible to attack by (positive) bromine than the sulfur atom in the thiolacetate 16 or thio-\(D\)-glucoside 19. It was decided to investigate the bromination of a number of acetylated 1-thioaldopyranoses and acetylated 1-thioglycosides and to attempt to follow the reaction by the use of n.m.r. spectroscopy.
Scheme I. -- Mechanistic rationale for formation of tetra-O-acetyl-β-D-glucosylsulfenyl bromide (22) and tetra-O-acetyl-α-D-glucopyranosyl bromide (1).
E. N.m.r. spectral studies of the bromination of various acetylated 1-thioaldose derivatives in carbon tetrachloride

a. For 1-thio-β-D-glucopyranose pentaacetate 16.---Treatment of thioacetate 16 with a 6.3-molar excess of bromine caused complete cleavage of the S-acetyl group from 16 within 1 min, as shown by the disappearance of the 3-proton singlet at 7.59 (SAc)39 observed in the spectrum of 16, and the appearance of a signal corresponding to acetyl bromide at 7.19. Tetra-O-acetyl-α-D-glucopyranosyl bromide (1) was definitely absent from the reaction mixture at this stage, because no low-field doublet (for H-1 of 1)92 was observed in the spectrum. The spectrum indicated the product was the sulfonyl bromide 22. The data from elemental analysis and the reactivity of

the product isolated clearly establish that it is 22 and not bis(tetra-O-acetyl-β-D-glucopyranosyl) disulfide 24.73 The n.m.r. spectra of the sulfonyl bromide 22 and the disulfide 24 differ only in minor details, and in neither case can the H-1 signal be observed clearly to the low-field side of the "envelope" of signals for the methine protons, because the sulfur atom at C-1 exerts a much smaller deshielding effect than an oxygen or halogen atom.39
b. For 1-thio-α-D-glucopyranose pentaacetate (18).—As in the case of 16, treatment of thioacetate 18 with a 7-molar excess of bromine at 34° caused cleavage of most of the S-acetyl group from 18 within 1 min as shown by the disappearance of the 3-proton singlet at 77.60 (SAc) observed in the spectrum of 18, and the appearance of a signal at 77.19 that corresponded to acetyl bromide. A low-field doublet was present, 74.12 having a coupling constant of 4.0 Hz. The signal for H-1 of 18 was not observed in the initial spectrum before bromination due to the low solubility of 18 in carbon tetrachloride, however H-1 of 18 gave a complex signal at 73.76 in chloroform-d. It is not likely that the change in solvent systems from chloroform-d to carbon tetrachloride would cause a shift of this magnitude for the H-1 signal. An additional low-field doublet, 73.28, J1,2 = 4.0 Hz (H-1 of tetra-O-acetyl-α-D-glucopyranosyl bromide92) was present in less than 55 sec after bromination and the signal at 77.60 (S-acetyl) had completely disappeared. The signal at 74.12 gradually decreased in intensity and the signal at 73.28 increased in intensity until the low-field doublet was the only signal observed. Three compounds that could conceivably account for the doublet at 74.12, are tetra-O-acetyl-α-D-glucopyranosyl-bromide (25), bis(α-D-glucopyranosyl) disulfide octaacetate (26), and tetra-O-acetyl-β-D-glucopyranosyl bromide (27). German workers107 reported the H-1 signal as part of a multiplet, 74.6-5.0

for a chloroform-d solution of 27. They observed the H-l signal of 27 by dissolving the compound in acetonitrile followed by addition of tetramethylammonium chloride. No chemical shift was recorded for H-1 because the shift changed with chloride-ion concentration; however, a coupling constant of 8 Hz was recorded. Thus, the doublet at T4.12 cannot be attributed to H-1 of 27.

The thioacetate 18 was converted almost entirely into the a-D-glucopyranosyl bromide 1 in less than 1 hr at 34°, as determined by the integrated intensity of the H-1 signal relative to that of the acetyl methyl protons. Isolation of 1 from the reaction mixture in a yield of 36% substantiated the conversion of 18 into 1. Quantitative isolation of 1 was difficult due to the instability of 1.
to possible decomposition on silica gel, and failure to crystallize in the presence of minor impurities. T.l.c. showed $\text{I}$ as the major reaction product.

c. For 1-thio-$\beta$-D-galactopyranose pentaacetate (17), 1-thio-$\alpha$-L-arabinopyranose tetraacetate (14), 1-thio-$\beta$-D-xylopyranose tetraacetate (15), and 1-thio-$\beta$-D-ribopyranose tetraacetate $^{39}$ (28).--Treatment of the 1-thioacetates, 17, 14, 15, and 28, in carbon tetrachloride with 7, 4.2, 5.9 and 5.9 molar equivalents of bromine, respectively, caused complete cleavage of the S-acetyl groups at a rate faster than was measurable by the n.m.r. technique described. The appearance of signals corresponding to acetyl bromide and to H-1 for the respective acetylated glycosyl halides were observed in each experiment. Integration of the
spectra, in less than 10 min after bromination, indicated complete conversion of the thioacetates into their respective acetylated glycosyl halides as determined by the integrated intensities of the H-1 signals relative to those of the acetyl methyl protons. T.l.c. indicated that the major reaction component was the acetylated glycosyl halide and the identity of the reaction product was verified by isolation of the acetylated glycosyl halide in each experiment.

d. For phenyl 2,3,4,6-tetra-O-acetyl-1-thio-a-D-glucopyranoside (20) and benzyl 2,3,4,6-tetra-O-acetyl-1-thio-ß-D-glucopyranoside (21).--Bonner77 had previously described the bromination of 20 in acetic acid to yield tetra-O-acetyl-a-D-glucopyranosyl bromide (1). This n.m.r. spectral study also shows the formation of 1. Other workers 69,108,109 showed that various acetylated alkyl thioglycosides gave glycosyl bromides on bromination.
The insolubility of the phenyl l-thioglucoside 20 in carbon tetrachloride made the bromination reaction difficult to follow. A scan of the n.m.r. spectrum was initiated 40 sec after the addition of bromine to the suspension of 20 and a low-field doublet was observed for H-1 of tetra-O-acetyl-α-D-glucopyranosyl bromide (1). Integration after 7 min indicated complete conversion of 20 into 1.

T.l.c. of the reaction product showed the major reaction product to be 1 and isolation of crystalline 1 confirmed the identity of the reaction product.

Bromination of the benzyl l-thio-D-glucoside 21 in carbon tetrachloride at 34° caused complete cleavage of the benzyl group from 21 within one min as indicated by the shift of the benzylic CH₂
protons from \( \text{76.44} \) to \( \text{75.77} \). No low-field doublet for H-1 of the glycosyl halide 1 was observed until 7 min 30 sec after bromination. At this time the H-1 signal of 1 began to appear. After 25 min the H-1 signal of 1 had an integrated intensity of 0.34 relative to the acetyl protons and after 1 hr 30 min the integrated intensity of the H-1 signal increased to 1. T.l.c. of the reaction mixture showed the glycosyl halide 1 was the major reaction product of extended bromination of 21. The reaction product was verified as 1 when it was isolated in crystalline form.

The immediate shift of the benzylic protons upon bromination of 21 and the absence at that time of a low-field signal for the glycosyl bromide 1 suggest that the sulfenyl bromide 22 was formed initially. However if the sulfenyl bromide had been present at this point it would certainly have been converted into the glycosyl bromide 1 at the relatively slow rate described for the conversion of 22 into 1 in the bromination of 1-thio-\( \beta \)-D-glucopyranose pentacetate (16). Possibly, the reaction proceeds by bromination of the
benzylic CH₂ position of the thioglycoside 21, followed by bromination of the resulting species to give the glycosyl halide 1.

e. For 2,3,4,6-tetra-O-acetyl-l-S-benzoyl-l-thio-β-D-glucopyranose (29). —Treatment of the l-thiobenzoate 29 with bromine was difficult to follow because of the initial insolubility of 29 in carbon tetrachloride. A signal of low intensity was present for H-1 of the glucosyl bromide 1 after 1 min. The low-field doublet was clearly visible 2 min 20 sec after the addition of bromine. The integrated intensity of the low-field doublet relative to the acetyl methyl signal was 1 after 7 min. T.l.c. of the reaction mixture showed 1 as the major reaction product and the conversion of 22 to 1 was verified by isolation of crystalline tetra-O-acetyl-α-D-glucopyranosyl bromide 1.
F. Formation of bis(tetra-O-acetyl-β-D-
glucopyranosyl) disulfide (24) and
bis(tetra-O-acetyl-β-D-glucopyranosyl)
disulfide mono-oxide (30)

Treatment of tert-butyl 1-thio-β-D-glucopyranoside tetra-
acetate (19) in carbon tetrachloride with dropwise addition of
bromine during 3 hr (instead of rapid addition, which gives the
sulfenyl bromide) gave a high yield of bis(tetra-O-acetyl-β-D-
glucopyranosyl) disulfide (24). It may be supposed that bromine
reacts with 19 to give the sulfenyl bromide 22, which then reacts
with excess 1-thioglycoside 19 to give the glucosyl disulfide 24
and tert-butyl bromide. Such a reaction would be facilitated by

\[ 22 + 19 \rightarrow 24 + \text{Me}_3\text{CBr} \]

the ease of heterolysis of the C-1-S bond in 19 during attack of
the electrophilic sulfur atom of 22 on the nucleophilic sulfur
atom of 19. Support for this mechanism is provided by the observa-
tion that, in carbon tetrachloride, compound 22 reacts with 19 to
give the disulfide 24 in high yield, and a volatile tert-butyl
derivative is produced.

The sulfenyl bromide 22 was decomposed rapidly by dry ethanol,
and the major product of reaction after 0.5 hr at 25° was bis(tetra-
O-acetyl-β-D-glucopyranosyl) disulfide 24; none of the sulfenyl
bromide 22 could be detected. Water, also, caused rapid decomposi-
tion of the sulfenyl bromide 22, but in this case the principal
crystalline product, isolated in 59% yield, was a compound having
the empirical formula \( \text{C}_{28}\text{H}_{38}\text{O}_{19}\text{S}_2 \), corresponding to a mono-oxide of
the disulfide 24; compound 24 was obtained concurrently, in 6%
yield. The mono-oxide 30 migrated more slowly than the disulfide 24 on t.l.c., and was absent from the product of reaction of the sulfenyl bromide 22 with dry ethanol. Separation of the mono-oxide 30 from the disulfide 24 could be effected readily, because of the extreme low solubility of the former in cold ethanol. The n.m.r. spectra of 24 and the mono-oxide 30 were very closely similar, and different noticeably only in the pattern of the acetyl-group signals at high resolution; the two compounds were readily differentiated, however, by their i.r. spectra (see Figure 1) and X-ray powder diffraction patterns.

Oxidation of the disulfide 24 with m-chloroperoxybenzoic acid gave a mono-oxide derivative identical with that obtained by treating the sulfenyl bromide 22 with water. An excess of the oxidant did not appear to cause oxidation to a more highly oxygenated derivative. Treatment of the sulfenyl bromide 22 with 95% ethanol gave a mixture of the mono-oxide and the disulfide 24.

The mono-oxide may be formulated either as a sulfenic anhydride (R-S-O-S-R) or as a thiosulfinate [R-S-S(O)-R]; the formulation R-O-S-S-R is excluded by the n.m.r. data. By analogy with work on simple compounds of related structure, the

Scheme II.—Formation of bis(tetra-O-acetyl-β-D-glucopyranosyl) disulfide (24) and bis(tetra-O-acetyl-β-D-glucopyranosyl) disulfide mono-oxide (30).
thiolsulfinate structure (30) may be considered the more probable, although this supposition has not been proved rigorously. A compound having structure (30) should be capable of existence in two diastereoisomeric forms. In various preparations of the mono-oxide, the crude product had a melting point much lower than that of the product after recrystallization from hot ethanol. Possibly, the crude product was a different structural isomer of the mono-oxide or a mixture of diastereoisomers of 30.

A plausible route for the formation of the mono-oxide 30 in the reaction of the sulfinyl bromide 22 with water would involve hydrolysis of one molecule of 22 to the sulfonic acid, followed by reaction of the latter with a second molecule of 22 to give the

\[ R-S-Br + H_2O \overset{HBr}{\rightarrow} R-S-OH \]

thiolsulfinate. In the reaction with ethanol, it is conceivable that the observed disulfide 24 may arise by the reaction of a molecule of an ethyl sulfenate with a molecule of the sulfinyl bromide, with formation of ethyl hypobromite by sulfur-oxygen
bond-cleavage, since the Et-0 bond would not be susceptible to

\[ \text{R-S-Br} + \text{EtOH} \rightarrow \text{R-S-OEt} \rightarrow \text{R-S-S-R} + \text{EtOBr} \]

abstraction of the Et group by bromide ion. These rationalizations
have not been proved experimentally.

G. Extended bromination of 1-thio sugar derivatives

Bromination of the \( \text{tert-butyl 1-thio-D-glucoside} \) \( \text{19} \), the
disulfide \( \text{24} \), or the disulfide mono-oxide \( \text{30} \) in carbon tetrachloride
for an extended period of time gave tetra-\( \text{O-acetyl-}\alpha-\text{D-}
glucopyranosyl bromide (1)\). It had previously been demonstrated\( ^{73} \)
that the sulfenyl bromide \( \text{22} \) and 1-thio-\( \beta-\text{D-glucopyranose}
pentacetate (16) also formed tetra-\( \text{O-acetyl-}\alpha-\text{D-glucopyranosyl bromide}
when reacted with an excess of bromine in carbon tetrachloride for
an extended period of time. A possible mechanistic rationale is
outlined in Scheme I.

H. Reaction of tetra-\( \text{O-acetyl-}\beta-
glucopyranosylsulfenyl bromide
(22) with electron-rich centers

a. Reaction of 22 with aniline.—The sulfenyl bromide 22
reacted readily with aniline to give the crystalline sulfenamide
31 in 82% yield. A trace of the disulfide 24 was formed in the
reaction mixture as indicated by t.l.c. The elemental analyses of
the product established that it had been formed by condensation of
one molecule of the amine with one molecule of sulfenyl bromide with
the loss of a molecule of hydrogen bromide. This evidence does not
prove the sulfenamide structure, because attack of the sulphenyl bromide \( \sim \) on the aryl ring-positions cannot be excluded. The n.m.r. spectra provided clear confirmation of the sulfenamide structure. A one-proton singlet was observed (at \( \gamma 4.76 \), with chloroform-\( d \) as solvent) that could be assigned to the NH proton of a sulfenamide, because it was exchanged slowly when the sample was deuterated. The region for aryl protons integrated for five protons thus proving that substitution on the aryl nucleus had not taken place.

The n.m.r. spectrum of \( 31 \) was analyzed completely for the ring protons on the sugar moiety by first-order inspection (see Tables 8 and 9). The assignments were verified by spin decoupling. A striking feature of the spectrum is the high field-position of the H-1 signal. Because the H-1 signal is shifted away from the H-2, H-3, and H-4 signals, it is possible to analyze the latter signals readily. In most of the acetylated derivatives of 1-thio-\( \beta-D \)-glucopyranose, the proximity of the H-1 signal to those of H-2, H-3, and H-4 makes detailed spectral analysis difficult.\(^{39}\) It has
not been established whether the unusual shielding of H-1 is an inductive effect of the sulfenamide group, or whether it is the effect of the location of H-1 in the shielding region of the n-cloud above or below the aromatic ring.

b. Reaction of the sulfenyl bromide \( \text{22} \) with an activated aryl derivative.—The sulfenyl bromide \( \text{22} \) was allowed to react in a carbon tetrachloride medium with two molar equivalents of \( \text{N},\text{N}-\text{dimethylaniline} \). The latter was selected as an activated, aromatic molecule that readily undergoes substitution, principally at the para position, by electrophilic reagents. The major product isolated was, the glucosyl disulfide \( \text{24} \) (yield 62%), although the anticipated product, \( 4-(\text{dimethylamino})\text{phenyl tetra-}\text{O-acyl-1-thio-}\beta-\text{D-glucopyranoside (22)} \), was formed simultaneously, in low yield. The structure of the product was apparent from the data of elemental analysis and n.m.r. spectroscopy; the spectrum was amenable to first-order analysis of the carbohydrate portion, and the assignments (see Tables 8 and 9) were confirmed by spin decoupling. Chemical confirmation of the structure of \( \text{22} \) was obtained by independent synthesis through coupling of tetra-\( \text{O-acyl-1-thio-}\beta-\text{D-glucopyranosyl bromide with p-dimethylaminobenzenethiol, as first described by Montgomery, Richtmyer, and Hudson.}^{35} \) The procedure was improved by preparing the thiol from \( 4-(\text{dimethylamino})\text{phenyl thiocyanate by reduction with lithium aluminum hydride instead of tin and acid.} \)

A complex series of secondary reactions ensued if, after the sulfenyl bromide \( \text{22} \) had been treated with two molar portions of \( \text{N},\text{N}-\text{dimethylaniline}, \) the reaction mixture (presumably
containing the product \(32\); \(N,N\)-dimethylaniline hydrobromide; probably the glucosyl disulfide \(24\); and, possibly other products) was heated for 20 min at a relatively high temperature (105°). Fractionation of the reaction mixture gave (see Scheme III) in addition to

\[
bis(tetra-O-acetyl-\beta-D-glucopyranosyl)\text{ disulfide} (24), \quad p\text{-bromo-}N,N\text{-dimethylaniline} (33), \quad bis(p\text{-dimethylaminophenyl})\text{ disulfide} (34),
\]

tetra-O-acetyl-\(\alpha-D\)-glucopyranosyl bromide \(1\), and a product closely resembling the adduct of \(32\) in its n.m.r. spectral data, but containing an additional sulfur atom; it was formulated as \(p\text{-}(\text{dimethylamino})\text{phenyl} \text{ tetra-O-acetyl-}\beta-D\text{-glucopyranosyl disulfide} (35).\) These products probably arise by a series of metathetical reactions between primary reaction products, and free-radical bromination of the amine by \(22\) is a possible route to \(33\). The factors controlling the distribution of these products were not investigated.

c. **Reaction of the sulfonyl bromide 22 with ketones and phenol.** To determine whether the sulfonyl bromide would react with enolizable ketones by attack of the sulfur at the \(\alpha\)-position to the carbonyl group, separate experiments were conducted with \(22\) and acetophenone, acetone, and cyclohexanone, respectively. In each case, the reaction gave \(bis(tetra-O-acetyl-\beta-D-glucopyranosyl)\text{ disulfide} (24)\) in high yield. Possible, free-radical bromination of the ketones provides a more favored reaction-pathway than electrophilic attack by sulfur on the enolic forms of the ketones. The glucosyl disulfide \(24\) was obtained in high
Scheme III.—High temperature (105°) reaction of tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide (22) and N,N-dimethyl-aniline.
yield in the reaction between the sulfenyl bromide and phenol, and no product of attack on the aryl ring by sulfur was detected.

I. Reaction of peracetylated 1-thio sugars with bromine and isolation of trapping products

The n.m.r. spectral study of the bromination of 1-thio sugars in carbon tetrachloride was used as a guide for determining reaction times in an attempt to trap unstable sulfenyl bromide intermediates. It was demonstrated by the n.m.r. study that bromination of 1-thio-β-D-xylopyranose tetraacetate (15) or 1-thio-α-L-arabinopyranose tetraacetate (14) gave immediate formation of the corresponding glycosyl bromide at a probe temperature of 34°. Thus, the reaction mixture was cooled to about -10° before bromination in an attempt to retard formation of the glycosyl bromide. The utility of this method was demonstrated earlier in the large scale preparation of tetra-α-acetyl-β-D-glucopyranosylsulfenyl bromide (22).

1-Thio-β-D-xylopyranose tetraacetate (15) was brominated at low temperature and volatile reaction components were immediately removed by evaporation. An excess of benzenethiol was added in an attempt to trap any tri-α-acetyl-β-D-xylopyranosylsulfenyl bromide (38) present. T.l.c. showed the presence of a major component, Rf 0.89, but an n.m.r. spectrum of the crude syrup in chloroform-d showed more than one major reaction product. A low-field doublet was assigned to H-1 of tri-α-acetyl-α-D-xylopyranosyl bromide (4), and the integrated intensity of this proton to the acetyl protons was in a ratio of 1:16, which indicated that 4 was the principal
reaction product. In an analogous experiment the bromide 4 was isolated in 61% yield.

Phenyl tri-\(\alpha\)-acetyl-\(\beta\)-\(\varepsilon\)-xylopyranosyl disulfide (39) was present in the reaction mixture and was isolated in 3% yield after decomposition of the xylosyl bromide 4.

Trapping of the xylosylsulfenyl bromide 38 with \(\alpha\)-toluene-thiol gave an 18% yield of benzyl tri-\(\alpha\)-acetyl-\(\beta\)-\(\varepsilon\)-xylopyranosyl disulfide (40) isolated by column chromatography and crystallized from ether—petroleum ether.

The structures of the trapping products 32 and 40 were established by elemental analysis and n.m.r. spectral data at 100 MHz with chloroform-\(d\) as solvent (see Figure 2, and Tables 8 and 9). Each compound showed a low-field region for the aryl protons with an integrated intensity of five protons and an acetyl region with an integrated intensity of nine protons. A two-proton singlet was assigned to the benzylic \(\text{CH}_2\) protons for 40. The C-5 methylene groups were analyzed as the AB portion of an ABXY system and the higher-field quartet was assigned to the axial H-5 in the \(\text{Cl}_{(\varepsilon)}\) conformation on the basis of a large coupling constant \(J_{4,5a} = 8.9\) Hz for 32 and 9.0 Hz for 40 and the lower-field quartet was assigned to the equatorial H-5 based on the smaller coupling constant, \(J_{4,5e} = 5.0\) Hz for 32 and 5.0 Hz for 40. This system was analogous to that reported for 1-thio-\(\beta\)-\(\varepsilon\)-xylopyranose tetraacetate\(^{39}\) (15).

Tri-\(\alpha\)-acetyl-\(\alpha\)-\(\varepsilon\)-xylopyranosyl bromide (4) can conceivably be formed directly by cleavage of the sugar to sulfur bond or by way of tri-\(\alpha\)-acetyl-\(\beta\)-\(\varepsilon\)-xylopyranosylsulfenyl bromide. Perhaps
Scheme IV.—Formation of phenyl tri-O-acetyl-β-D-xylo-pyranosyl disulfide (39) and benzyl tri-O-acetyl-β-D-xylo-pyranosyl disulfide (40).
both mechanisms are operative. A definite mechanism cannot be
determined from the experimental evidence available.

Low-temperature bromination of 1-thio-α-L-arabinopyranose
tetraacetate (14) followed by trapping with benzenethiol gave re-
sults similar to those encountered in the formation of the phenyl
D-xylosyl disulfide 39. It was demonstrated that tri-O-acetyl-β-
L-arabinopyranosyl bromide (3) was formed in high yield, even with
bromination of 14 at low temperature. Phenyl tri-O-acetyl-α-L-
arabinopyranosyl disulfide (41) was isolated from the reaction
mixture in 45% yield. N.m.r. spectral data showed the presence
of a compound similar in structure to 41 and this compound is probably
phenyl 1-thio-\(\alpha\)-L-arabinopyranoside triacetate (42). Reaction of excess benzenethiol and tri-\(\Omega\)-acetyl-\(\beta\)-L-arabinopyranosyl bromide (3) present in the reaction mixture could account for the presence of 42.

The structure of 41 was established by elemental analysis and n.m.r. spectral data at 100 MHz for a solution of 41 in chloroform-\(d\). A wide doublet at 75.27 was assigned to H-1 of 41. The coupling constant of 7.2 Hz is in accord with the diaxial relationship of H-1 to H-2 in the \(C_1\) (\(L\)) conformer for 41. The spectrum showed aryl and acetyl regions consistent with the assigned structure. Quartets at higher field were assigned to H-5,5', however, no attempt was made to differentiate between axial and equatorial protons due to the small difference in coupling observed (see Figure 3 and Tables 8 and 9).

T.l.c. of the reaction product of low-temperature bromination of 1-thio-\(\beta\)-D-galactopyranose pentaacetate (17) showed that incomplete bromination of 17 had occurred, although the n.m.r. spectral study of the bromination of 18 at a probe temperature of 34° showed formation of tetra-\(\Omega\)-acetyl-\(\alpha\)-D-galactopyranosyl bromide (2) at a rate faster than was measurable by the n.m.r. technique applied. Bromination of 17 at room temperature followed by trapping with benzenethiol gave a mixture of three products, as indicated by t.l.c. One of the components corresponded to starting material 17 and was less intense than the corresponding component observed for the bromination experiment at low temperature. A 60-MHz n.m.r. spectrum of a solution of the crude reaction product in chloroform-\(d\)
showed the presence of starting material and a benzenethiol adduct, as indicated by the aryl region present in the spectrum. No low-field doublet was present to indicate the presence of tetra-O-acetyl-α-D-galactopyranosyl bromide (2) and verification was made by the lack of decomposition of the product during a process designed to decompose the relatively unstable 2. A low yield (6%) of phenyl tetra-O-acetyl-β-D-galactopyranosyl disulfide (43) was isolated crystalline from the reaction mixture. Structure assignment for 43 was based on elemental analysis and spectral data. A 100 MHz spectrum for a chloroform-d solution of 43 showed the aryl-proton signals as a characteristic low-field multiplet. H-2 and H-4 gave a complex multiplet, and a quartet at 74.91 was assigned to H-3. A wide doublet having a spacing of 10 Hz was assigned to H-1. The wide coupling is attributed to the axial-axial relationship for H-1 and H-2 in the Cl-(D) conformer for 43. A multiplet at 75.87-6.06 was assigned to H-5, 6, and 6'. The acetyl signals were in accord with the structure of 43 (see Figure 4 and Tables 8 and 9).
The poor yield of 43 can be attributed to its difficulty in crystallization except when relatively pure. Separation of 43 from the mixture of reaction products was difficult.

Bromination of 1-thio-α-D-glucopyranose pentaacetate (18) at a probe temperature of 34° gave either tetra-O-acetyl-α-D-glucopyranosylsulfenyl bromide (25) or bis(tetra-O-acetyl-α-D-glucopyranosyl) disulfide (26) as evidenced by the n.m.r. spectral data. An attempt was made to brominate 18 at room temperature and to trap 25. Spectral evidence was obtained that an aryl trapping product had formed (see Figure 5), however the product could not be isolated pure. Therefore, it cannot be stated definitely that 25 was a reaction product in the bromination of 1-thio-α-D-glucopyranose pentaacetate (18).

Bromination of 2,3,4,6-tetra-O-acetyl-1-S-benzoyl-1-thio-β-D-glucopyranose (29) at room temperature followed by trapping of the product with benzenethiol gave a 29% yield of phenyl tetra-O-acetyl-β-D-glucopyranosyl disulfide (23), identical with an authentic sample by m.p., n.m.r. data, and X-ray powder diffraction pattern. Formation of 23 as a trapping product of tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide (22) further supported the mechanistic rationale proposed for the formation of the sulfenyl bromide 22 (see Scheme I). If the aglycon is a cation more stable than the glycosyl cation, the glucosylsulfenyl bromide forms. However, if the aglycon forms a cation less stable than the glycosyl cation, then tetra-O-acetyl-α-D-glucopyranosyl bromide (2) is the
reaction product. This rationale appears to be true with 1-thio-β-D-glucose precursors as demonstrated by the formation of the glucosylsulfenyl bromide 22, identified by isolation of crystalline 22 or by trapping with electron-rich reagents such as thiols or amines.

The sulfenyl bromide 22 was found to be a product of the bromination of 1-thio-β-D-glucopyranose pentaacetate (16), tert-butyl 1-thio-β-D-glucopyranoside tetraacetate (19), and 2,3,4,6-tetra-O-acetyl-l-S-benzoyl-1-thio-β-D-glucopyranose (29). In each case extended bromination, with carbon tetrachloride as solvent, gave tetra-O-acetyl-α-D-glucopyranosyl bromide (1).

The bromination of phenyl (20) and benzyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranoside (21) gave no evidence that 22 had formed. The bromination of 21 apparently proceeded by way of the benzyl protons of the aglycon. In each case extended bromination gave the glycosyl bromide 1.

Trapping products with benzenethiol were obtained from the bromination of 1-thio-β-D-xylopyranose tetraacetate (15),
l-thio-α-L-arabinopyranose tetraacetate (14), and l-thio-β-D-galactopyranose pentaacetate (17). Formation of these trapping products indicated the presence of the respective sulfenyl bromides. Tetra-O-acetyl-β-D-galactopyranosylsulfenyl bromide (44) appeared to be more stable than tri-O-acetyl-β-D-xylopyranosylsulfenyl bromide (38) or tri-O-acetyl-α-L-arabinopyranosylsulfenyl bromide (45), as evidenced by the lack of formation of the galactosyl bromide 2 at room temperature in the short-term bromination of 17.

J. Photolysis of sugar dimethyl-thiocarbamates

The Freudenberg rearrangement113 of sugar xanthates has been known for many years and gives relatively low yields of rearrangement product.113,114

(113) K. Freudenberg and A. Wolf, Ber., 60, 232 (1927).

Horton and Prihar\textsuperscript{1} synthesized various dimethylthiocarbamates of sugars and Prihar\textsuperscript{115} has demonstrated by thermolytic studies on the dimethylthiocarbamates that these compounds do not offer significant advantage over the xanthates for rearrangement to give a thio-substituted sugar ring. It had been demonstrated that carbon to sulfur bond cleavage occurs\textsuperscript{85} under photolytic conditions with carbohydrate molecules to give deoxy sugars. It was anticipated that photolysis of sugar N,N-dimethylthiocarbamates might lead to a Freudenberg type of rearrangement, giving carbohydrate derivatives with sulfur attached to the sugar ring, or give a new photolytic route to deoxy sugars.

a. **Preparation of dimethylthiocarbamates.**--The dimethylthiocarbamates were synthesized according to the method of Horton and Prihar.\textsuperscript{1} The sugars used for these preparations were blocked so that only one free OH group was available for reaction with N,N-dimethylthiocarbamoyl chloride. The physical data of the dimethylthiocarbamates prepared were in reasonable agreement with those previously reported (see Table 7 for compounds prepared and mode of characterization).

b. **Photolysis of the dimethylthiocarbamates 46, 47, and 48.**--Methanolic solutions of 46, 47, and 48 were photolyzed for extended periods of time with intermittent processing to eliminate polymeric
<table>
<thead>
<tr>
<th>Compound</th>
<th>Mode of characterization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>m.p.</td>
</tr>
<tr>
<td>3-0-Dimethylthiocarbamoyl-1,2:5,6-di-0-isopropylidene-$\alpha$-D-glucopyranose (46)</td>
<td>105-106°</td>
</tr>
<tr>
<td>1,6-Anhydro-4-0-dimethylthiocarbamoyl-2,3-0-isopropylidene-$\beta$-D-mannopyranose (47)</td>
<td>136-137°</td>
</tr>
<tr>
<td>6-0-Dimethylthiocarbamoyl-1,2:3,4-di-0-isopropylidene-$\alpha$-D-galactopyranose (48)</td>
<td>90-91°</td>
</tr>
</tbody>
</table>
residue formed. The reactions were monitored by n.m.r. and t.l.c. to determine necessary photolysis times and product formation. T.l.c. in each experiment showed the presence of an array of products; however, two major products were present in each photolysis mixture, and were separated by column chromatography and identified.

Photolysis of 3-O-dimethylthiocarbamoyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (46) gave a 17% yield of 3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexofuranose (49) and a 26% yield of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (50). When the reaction was repeated, respective yields of 22.5% and 32% were obtained.

\[ \text{46} \rightarrow \text{49} + \text{50} \]

Compound 50 was identical with an authentic sample by m.p., n.m.r. spectrum,\(^1\) and by X-ray powder diffraction pattern.

The 3-deoxy-α-D-hexofuranose was purified by distillation. The optical rotation of 49 was in good agreement with the known value and the n.m.r. data (60 MHz) were consistent


with those reported for a carbon tetrachloride solution of 49.


A crystalline derivative, 3-deoxy-1,2-0-isopropylidene-α-D-ribo-hexofuranose (51), was prepared by partial hydrolysis of 40 by the procedure of Hedgley, Overend, and Rennie.

An authentic sample of 3-deoxy-1,2:5,6-di-0-isopropylidene-α-D-ribo-hexofuranose (52) was prepared according to the method of Brown and Jones from 3-deoxy-3-iodo-1,2:5,6-di-0-isopropylidene-α-D-glucofuranose. 1,2:5,6-Di-0-isopropylidene-3-0-ethylsulfonyl-α-D-glucofuranose (53) was treated with hydrazine

(120) K. Freudenberg and O. Ivers, Ber., 55, 929 (1922).


to form 3-deoxy-3-hydrazone-1,2;5,6-di-Q-isopropylidene-a-D-
allofuranose (54).\(^{123,124}\) Reaction of 54 with iodine gave


3-deoxy-3-iodo-1,2;5,6-di-Q-isopropylidene-a-D-glucofuranose
(52).\(^{119}\) Reduction of 52 with Raney nickel\(^{119}\) gave 3-deoxy-1,2;5,6-di-Q-isopropylidene-a-D-ribo-hexofuranose (49). Partial acid
hydrolysis of 49 gave an authentic sample of 3-deoxy-1,2-Q-
isopropylidene-a-D-ribo-hexofuranose (51)\(^{117,118}\) (see Scheme V)
identical with 51 prepared from 49 by the photolysis of 46 by com-
parison of m.p., X-ray powder diffraction pattern and n.m.r.
spectra.

Černý and Pacák\(^{117}\) reported \([\alpha]_D^{18} = -37.8^\circ\) (c 0.635, ethanol)
for 3-deoxy-1,2-Q-isopropylidene-a-D-ribo-hexofuranose (51); however,
the optical rotation for this preparation of 51 was \([\alpha]_D^{23} = -12.6^\circ\)
(c 1.1, ethanol) and \([\alpha]_D^{21} = -19.0^\circ\) (c 1.7, chloroform).

Desulfurization of bis(1,2;5,6-di-Q-isopropylidene-a-D-
glucofuranose) disulfide (55)\(^{113}\) with Raney nickel gave 1,2;5,6-di-Q-
isopropylidene-a-D-ribo-hexofuranose (49) identical with authen-
tic 49 by optical rotation and n.m.r. spectrum. Partial acid
hydrolysis of 49 gave 3-deoxy-1,2-Q-isopropylidene-a-D-ribo-
hexofuranose (51) identical with an authentic sample.

Photolysis of a methanolic solution of 6-Q-dimethylthio-
carbamoyl-1,2;3,4-di-Q-isopropylidene-a-D-galactopyranose (48)
Scheme V.—Preparation of 3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexofuranose (49) and 3-deoxy-1,2-O-isopropylidene-α-D-ribo-hexofuranose (51) by a known route.
gave a 15% yield of 6-deoxy-1,2:3,4-di-Ω-isopropylidene-α-D-galactopyranose (56) and a 35.5% yield of 1,2:3,4-di-Ω-isopropylidene-α-D-galactopyranose (57).

6-Deoxy-1,2:3,4-di-Ω-isopropylidene-α-D-galactopyranose (56) crystallized neat and was identical with an authentic sample prepared according to Freudenberg and Raschig.125

125 K. Freudenberg and K. Raschig, Ber., 60, 1633 (1927).
The n.m.r. spectrum of an acetone-$d_6$ solution of 56 was identical to that described by Cone and Hough.


Compound 57, a syrup, was purified by distillation and was identified as \(1,2:5,6\)-di-$\alpha$-isopropylidene-$\alpha$-$D$-galactopyranose (57) by comparison of the optical rotation \(^{127,128}\) and n.m.r. spectrum \(^{126}\) with those previously reported. The syrupy product was characterized as its \(6$-$\alpha$-toluenesulfonate (58) and the m.p., X-ray powder diffraction pattern, and n.m.r. spectrum of a chloroform-$d$ solution of 58 were in good agreement with literature values. \(^{128}\)

Photolysis of a methanolic solution of \(1,6\)-anhydro-$4$-$\alpha$-dimethylthiocarbamoyl-2,3-$\alpha$-isopropylidene-$\beta$-$D$-mannopyranose (47) gave a 19% yield of a product formulated as \(1,6\)-anhydro-$4$-deoxy-2,3-$\alpha$-isopropylidene-$\beta$-$D$-$\alpha$-lyxo-hexopyranose (59) and a 17% yield of \(1,6\)-anhydro-2,3-$\alpha$-isopropylidene-$\beta$-$D$-mannopyranose (60). The reaction was repeated and gave 26% and 29% of 59 and 60 respectively.

Formulation of 59 as the 4-deoxy sugar was based on
elemental analysis, n.m.r. spectral data (see Tables 10 and 11),
and by analogy with the foregoing photolysis reactions.

The 1,6-anhydro-2,3-O-isopropylidene-β-D-mannopyranose
(60) was identical with an authentic sample.129,130

(129) A. E. Knauf, R. M. Hann, and C. S. Hudson, J. Amer.

(1966).

c. Photolysis of 3-deoxy-3-ido-1,2:5,6-di-O-isopropylidene-
α-D-glucofuranose (52).—Binkley and Binkley87 showed that photolysis
of a primary iodo-substituted sugar in methanol gave a deoxy sugar
in high yield. It was anticipated that photolysis of a secondary
iodo-sugar would give similar results and this was demonstrated by
photolysis of a methanolic solution of 3-deoxy-3-iodo-1,2:5,6-di-
O-isopropylidene-α-D-glucofuranose (52). T.l.c. of the crude
photolysis reaction product revealed the presence of three components.
One of the major components, $R_2^2 0.85$, was isolated in 32% yield by column chromatography and was identified as 3-deoxy-1,2:5,6-di-O-

\[
\text{MeC}_2\text{OCH}_2
\]

isopropylidene-$\alpha$-D-ribo-hexofuranose (49) by comparison of n.m.r. spectral data and optical rotation with those of a known sample. Compound 49 was further characterized by conversion into a known crystalline derivative, 3-deoxy-1,2-O-isopropylidene-$\alpha$-D-ribo-

\[
\text{MeC}_2\text{OCH}_2
\]

hexofuranose\textsuperscript{117,118} (51).

Photolysis of 3-deoxy-3-iodo-1,2:5,6-di-O-isopropylidene-$\alpha$-

\[
\text{MeC}_2\text{OCH}_2
\]

glucofuranose (52) is thought to proceed by homolysis of the C-I bond followed by abstraction of a proton from the solvent, methanol, as was described for formation of a deoxy sugar from 6-deoxy-6-iodo-

\[
\text{MeC}_2\text{OCH}_2
\]

1,2:3,4-di-O-isopropylidene-$\alpha$-D-galactopyranose.\textsuperscript{87}

Photolysis of dimethylthiocarbamates of various protected sugars in methanol solution thus affords a preparative method for deoxy sugars. Although the yields are not high the alcohol side-product can be re-esterified and recycled in the photolysis, and the net yields compare favorably with those that can be achieved by conventional multi-step routes. The reaction appears to proceed by
Rearrangement of S-dimethylcarbamoyl derivatives of the corresponding thio sugars and subsequent C-S scission to give a deoxy sugar; a concurrent process involves simple cleavage of the dimethylthiocarbamoyl group to give the alcohol. These rationalizations have not been proved experimentally.

K. N.m.r. spectral study of deoxy sugars

a. 3-Deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexofuranose (49).—Brown and Jones\(^{119}\) reported 60 MHz n.m.r. data for a carbon tetrachloride solution of 49. The spectrum for a chloroform-d solution of 49 showed signals of H-1, H-2, and H-3a, 3b\(^*\) clearly; however, the H-4, H-5, and H-6a, 6b signals were observed as multiplets. The H-1 signal was a doublet with \(J_{1,2} = 4.0\) Hz; that of H-2 was a triplet which indicated lack of coupling between one of the H-3 protons and H-2. Irradiation of the high-field H-3 multiplet resulted in perturbation of the H-2 signal, and the low-field H-3 multiplet. Irradiation of the H-2 signal resulted in collapse of the H-1 doublet to a singlet and perturbation of the high-field H-3 signal; however, no change was observed in the

\(^*\) a, low-field signal; b, high-field signal.
low-field H-3 multiplet. No advantage was gained by the use of acetone-\textit{d}_6 as solvent for \textit{H}_2. When benzene-\textit{d}_6 was used as solvent, the H-4 signal was observed as a multiplet, 76.69-6.90. Spin decoupling of the lower-field H-3 quartet (77.82) caused perturbation of the H-4 signal. The high-field H-3 signal was shifted under the signals of the isopropylidene protons (see Figure 6.

b. 6-Deoxy-1,2:3,4-di-0-isopropylidene-\textit{\alpha-D}-galactopyranose (56).—Cone and Hough\textsuperscript{126} reported 60 MHz n.m.r. data for an acetone-\textit{d}_6 solution of \textit{56}. Protons were assigned on a first-order basis for a 100 MHz spectrum of an acetone-\textit{d}_6 solution of \textit{56}. The C-6 methyl protons gave a doublet at 78.84 with an integrated intensity of three protons indicating that the H-6 protons were equivalent and were coupled with H-5. Additional narrow splitting (~1.0 Hz) was observed for the principal quartets of H-2 and H-3. The additional coupling is probably long-range coupling\textsuperscript{131-135}

although no attempt was made to assign this coupling to specific protons. The 100 MHz n.m.r. data for a chloroform-d solution was similarly first-order with the exception that a slight overlap of H-4 and H-5 occurred and additional small coupling (presumably long-range coupling) was observed for the principal quartets of H-2 and H-3. All proton assignments were verified by spin-decoupling experiments (see Tables 10 and 11 for further spectral details).

c. 1,6-Anhydro-4-deoxy-2,3-O-isopropyldene-β-D-lyxo-hexopyranose (59).—The 100 MHz n.m.r. spectrum in either chloroform-d or acetone-d₆ was complex. For a chloroform-d solution of 59, H-1 was observed as a broadened doublet. In addition to coupling of H-1 with H-2, the possibility exists for long-range coupling with H-3, H-5, and possibly H-6 (exo). The signal for H-2 is a sharp quartet with J₁,₂ = 3.0 Hz and J₂,₃ = 5.9 Hz. A multiplet, T₅.₄₁-₅.₇₀ was assigned to H-6a* and H-3. The high-field multiplets, T₇.₇₀ and 7.₉₂ were assigned to H-4a* and H-4b*. H-5 was assigned to a multiplet, T₆.₂₅. The principal structure of the multiplet appeared as a triplet. The additional splitting of the triplet can be attributed to long-range coupling with H-1 and H-3. A quartet at T₅.₉₄ with J₅,₆b = 0, J₆a,₆b = 6.₄ was assigned to H-6b and an additional coupling was present of 1.₅ Hz with either H-1 or H-4.

Spin decoupling was an aid in assignment of protons. Irradiation of the signal assigned to H-2 caused collapse of the H-1 signal to a singlet and perturbation of the multiplet assigned to H-3 and H-6a.

* The low-field H-6 proton is indicated by a and the high-field H-6 proton is indicated by b.
Irradiation of the signal assigned to H-4a and H-4b resulted in perturbation of the H-3 and H-6a multiplet in addition to narrowing the multiplet assigned to H-5. Irradiation of the H-5 multiplet resulted in possible perturbation of the H-3 and H-6a multiplet, collapse of the H-6b signal, and collapse of the H-4a and H-4b signals to quadruplets, $J_{3,4a} = 5.0$ Hz, $J_{3,4b} = 2.8$ Hz, and $J_{4a,4b} = 15.0$ Hz. Assignments were difficult to make due to the complex nature of the spectrum (see Figure 8 and Tables 10 and 11 for further details).

d. 3-Deoxy-3-ido-D-1-0-isopropylenone-1-D-glucofuranose (52).—A 100 MHz spectrum of 52 with chloroform-d as solvent showed the H-1, 2, and 3 signals as doublets at 7.408, 4.99 and 5.58 respectively. Brown and Jones assigned a high-field multiplet, 7.685, to H-5 for a carbon tetrachloride solution of 52. Irradiation of the high-field multiplet collapsed the doublet assigned to H-3 to a singlet. Irradiation of the H-3 signal caused perturbation of the high-field multiplet. Irradiation of the H-1 doublet collapsed the H-2 doublet to a singlet. Irradiation of the H-2 doublet collapsed the H-1 doublet to a singlet and no change was observed for the H-3 signal, which showed that the H-2 and H-3 protons are trans disposed and that $J_{2,3}$ is approximately equal to zero. Thus, the gluco configuration assigned by Brown and Jones was reaffirmed. A multiplet, 7.58-6.08, was assigned to H-5, 6, and 6'.
EXPERIMENTAL - PART A

General methods. -- Evaporations were performed under diminished pressure (~10 mm) on a rotary evaporator. Specific rotations were measured in either a 1-dm tube (Perkin-Elmer 141 photoelectric polarimeter) or a 2-dm tube (Rudolph manual polarimeter). Melting points were determined with a Thomas Hoover Unimelt apparatus. I.r. spectra were measured with a Perkin-Elmer "Infracord" infrared spectrophotometer. N.m.r. spectra were measured at 60 or 100 MHz with Varian A-60 or HA-100 n.m.r. spectrometers. Chemical shifts refer to an internal standard of tetramethyldisilane (TMS) (r=10.00) for organic solutions and sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) (r=10.00) for aqueous solutions. Spin-decoupling experiments were performed with the HA-100 instrument operating in the frequency-sweep mode. Ultraviolet spectra were measured with a Bausch and Lomb "Spectronic 505" recording spectrometer. Micro-analyses were determined by W. N. Rond. X-ray powder diffraction data give interplanar spacings, Å, for CuKα radiation. The camera diameter was 114.59 mm. Relative intensities were estimated visually: m, moderate; s, strong; v, very; w, weak. The strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities. Thin layer chromatography (t.l.c.) was performed with Desaga equipment and Silica Gel G (E. Merck, Darmstadt, Germany)
activated at 120° as the adsorbent, 3:1 dichloromethane—ether as
developer (unless specified otherwise) and sulfuric acid as the indi-
cator. Column chromatography was performed with silica gel No. 7734
(0.05-0.2 mm) of E. Merck AG, Darmstadt, Germany with 1 g of the mix-
ture to be separated per 30 g of adsorbent. Columns were packed by
allowing a slurry of the adsorbent in the eluent to settle under
gravity. The eluent was 3:1 dichloromethane—ether (solvent A) or
9:1 dichloromethane—ether (solvent B). Solvent A is the eluent of
choice where no specific eluent is indicated. Petroleum ether used
in recrystallizations was a fraction having a boiling range 60-110°.

Preparation of tetra-O-acetyl-β-D-glucopyranosyl bromide (1).—
Compound 1 was prepared essentially according to the procedure of
Bárczai-Martos and Körösy90 as described by Lemieux.91 Acetic an-
hydride (400 ml) was cooled (~10°) and 70% perchloric acid (2.4 ml)
was added dropwise. The cooled solution was brought to room
temperature and D-glucose (100 g, 55.5 mmole) was added to
the vigorously stirred solution over a period of 30 min as to
control the temperature between 30 and 40°. The reaction mixture
was cooled below 20° and red phosphorus (32 g) was added to the
reaction mixture followed by the dropwise addition of bromine (62 ml,
193.4 g) over a period of 1 hr. Water (36 ml) was added dropwise
over a 30 min period so as to maintain the reaction temperature be-
low 20°. The mechanical stirrer was removed from the reaction
mixture and the reaction mixture was removed from the ice bath and
allowed to remain undisturbed at room temperature for a period of
2 hr. Dichloromethane (300 ml) was added to the mixture, which
was then filtered through Celite to remove excess phosphorus. The filtrate was added with caution to ice and water (~700 g). The organic phase was separated and washed successively with an ice-cold, saturated solution of sodium hydrogen carbonate (~600 ml), and water (~600 ml). The dried (magnesium sulfate) solution was evaporated to give a crystalline, white mass. The crude product was digested with 250 ml of ether, warmed on a steam bath, and refrigerated overnight. The product was collected in three crystal crops, yield 182.8 g, 44.5 mmoles (80%), m.p. 88-89°, \([\alpha]_D^{22} +198° (c 1.2, \text{chloroform})\) \([\text{lit.}]^{91} \text{m.p. } 88-89°, [\alpha]_D^{20} +198° (c 2, \text{chloroform})\]. The n.m.r. data for a chloroform-d solution coincided with that reported previously by Horton and Turner.\(^{92}\)

Preparation of tetra-O-acetyl-a-D-galactopyranosyl bromide \((2)\).—Acetic anhydride was cooled to ~10° and 2.4 ml of a 70% solution of perchloric acid was added dropwise with stirring. The cooled solution was brought to room temperature and D-galactose (100 g, 55.5 mmoles) was added to the reaction mixture over a 30 min period in order to maintain the temperature between 30-40°. The reaction mixture was treated with red phosphorus (32 g), bromine (62 ml, 193.4 g), and then water (36 ml), by the procedure used in the foregoing experiment and the work-up was essentially the same as that described for \(1\), however, a syrup was obtained instead of a crystalline product. The syrup would not crystallize from ether or ether—petroleum ether. A small amount (~1 g) of the syrup was passed down a column of silica gel with solvent \(A\) as
eluent. Fractions that contained the product were collected and evaporated to give a colorless syrup. The syrup was dissolved in a few ml of ether (~2 ml) and refrigerated overnight. White needles formed and they were added to an ether solution of the major syrupy product. The product crystallized overnight as a white crystalline mass, yield 90.0 g, 21.9 mmoles (40%), m.p. 82-83°, [a]D 212.9° (c 2.9, chloroform) [lit. 93 m.p. 83-84°, [a]D 215° (c 1, chloroform)]. The n.m.r. spectrum of 2 in a chloroform-d solution was consistent with that reported previously.92

The filtrate was evaporated to a syrup and the syrup was re-dissolved in ether and seeded with crystalline 2. The solution was refrigerated, but further crystallization did not occur. The ether solution was re-evaporated to a syrup, 108.4 g, 26.4 mmoles (48%).

**Preparation of tri-O-acetyl-β-L-arabinopyranosyl bromide (3).**

Acetic anhydride (300 ml) was cooled to about 20° and 1.8 ml of 70% perchloric acid was added dropwise. The reaction solution was stirred and L-arabinose (75.0 g, 50.0 mmoles) was added over a 30 min period and the temperature was not allowed to exceed 30°. The reaction mixture was treated with red phosphorus (22.5 g), bromine (52 ml, 162.2 g), and water (27 ml) by the procedure used for the preparation of tetra-O-acetyl-α-D-glucopyranosyl bromide (1) and the work-up was the same as described for (1). The dichloromethane extract was evaporated to give a crude, crystalline product. The crude product was diluted with ether (400 ml), warmed to effect solution, and diluted with petroleum ether (50 ml). The product
crystallized after refrigeration overnight to give 3 as fine white needles, yield 84.7 g, 25.0 mmoles (50%), m.p. 138-140°, \([\alpha]_D^{23} +278.9°\) (c 2.1, chloroform) [lit.\(^{94}\) m.p. 139°, \([\alpha]_D^{20} +283.6°\) (in chloroform)]. The n.m.r. data for a chloroform-\(d\) solution were consistent with those reported previously.\(^{92}\)

**Preparation of tri-O-acetyl-\(\beta\)-D-xylopyranosyl bromide (4).—**

The method used for the preparation of 4 was essentially that of Bárczai-Martos and Kőrösy\(^{90}\) as described by Weygand.\(^{95}\) Acetic anhydride was cooled to 10° and 70% perchloric acid (2.4 ml) was added to the stirred, cooled solution followed by D-xylose (100 g, 66.6 mmoles) at a rate such that the reaction temperature did not exceed 40°. Red phosphorus (32 g), bromine (62 ml, 193 g), and water (36 ml) were added to the cooled solution as described for the preparation of 1. The work-up was the same as described previously for 1 and a dichloromethane solution of the product was evaporated to a syrup. The syrup was diluted with ether (200 ml) and refrigerated overnight. A white mass of needles formed and was filtered, yield 105.2 g, 31.0 mmoles (47%), m.p. 101-102°, \([\alpha]_D^{23} +211°\) (c 1.2, chloroform) [lit.\(^{95}\) m.p. 102°, \([\alpha]_D^{20} +272°\) (c 2.5, chloroform) and lit.\(^{96}\) m.p. 102°, \([\alpha]_D^{20} +212.2°\) (c 2.5, chloroform)]. An n.m.r. spectrum of the product in a chloroform-\(d\) solution was identical with that reported by Horton and Turner.\(^{92}\)

**Preparation of tri-O-acetyl-\(\alpha\)-D-xylopyranosyl chloride (5).—**

Compound 5 was prepared essentially according to the method of Hudson and Johnson.\(^{97}\) To D-xylose (100.0 g, 66.6 mmoles) was added acetyl chloride (410 ml, 454 g) and a catalytic portion of
freshly fused zinc chloride. The reaction mixture was refluxed until
dissolution occurred (about 2 hr). The solution was cooled, diluted
with dichloromethane (300 ml), and poured onto about 1 kg of ice
and water. The organic phase was separated and washed with a satu-
rated solution of sodium hydrogen carbonate until the organic phase
was neutral. The organic phase was washed with water (200 ml),
dried (magnesium sulfate), and evaporated to a light-yellow syrup.
The syrup was dissolved in ether (150 ml) and diluted with petroleum
ether (50 ml). The solution was refrigerated overnight to give
white needles, in two crystal crops, yield 90.9 g, 30.8 mmoles (46%),
m.p. 101-102°, \([\alpha]_{D}^{18} +171.4^\circ (c \, 2.4, \text{ chloroform}) \) [lit. \textit{97} m.p. 95-97°,
\([\alpha]_{D}^{20} +165^\circ (c \, 12, \text{ chloroform})\)]. N.m.r. data (60 MHz, CDCl$_3$):
\(7^3.92\) (one-proton doublet, \(J_{1,2} \, 3.7 \, \text{Hz}, \, \text{H}-1\)), \(7^6.44\) (one-proton
triplet, \(J_{2,3} \, =J_{3,4} \, 10 \, \text{Hz}, \, \text{H}-3\)), \(7^4.69-5.21\) (two-proton multiplet,
H-2 and H-4), \(7^5.61-6.32\) (two-proton multiplet, H-5, 5'), \(7^7.88, 
7.95\) (three-and six-proton singlets, OAc).

**Preparation of 3,4,6-tri-O-acetyl-2-O-trichloroacetyl-\(\beta\)-D-
\text{glucopyranosyl chloride (6).}** The method used for the preparation
of 6 was essentially that adapted by Lemieux and Howard\textit{98} from the
original procedure of Brigl.\textit{100} Finely powdered penta-O-acetyl-\(\beta\)-
\(\text{D-glucopyranose (7, 78.0 g, 200 mmoles, m.p. 129-131°, Pfanstiehl}
Laboratories, Inc., Waukegan, Illinois) was mixed with 177 g of
powdered phosphorus pentachloride, and carbon tetrachloride (40 ml)
was added to the reaction mixture. The reaction vessel was equipped
with a condenser and drying tube and the mixture was refluxed for
5 hr at a temperature of 120° (oil bath). The resulting light-yellow solution was evaporated under diminished pressure (water aspirator) until the bath temperature had risen to 85°. The syrup was dissolved in anhydrous ether (160 ml) and refrigerated overnight at -15°. The crystalline precipitate was barely visible on the flask bottom. The cold ethereal solution was shaken vigorously periodically over a two day period. A crystalline mass was observed on the flask bottom and was collected in two crystal crops, yield 21.3 g, 45.3 mmoles (22.7%), m.p. 129-132°, (lit.98 m.p.132-138°). The product was re-crystallized twice from ether to give fine, white needles, m.p. 140-141°, [\(\alpha\)]\(_D\)\(^{30}\) +8.49° (c 1.15 chloroform) [lit.100 m.p. 142° and lit.99 m.p. 140-142°, [\(\alpha\)]\(_D\) +8.9° (c 1.4, chloroform)]. N.m.r. data (100 MHz, CDCl\(_3\)): \(\nu\)4.48-4.94 (four-proton multiplet (H-1, 2,3,4), \(\nu\)6.6 (one-proton quartet, \(\mathcal{J}_{5,6}\) 4.9 Hz, H-6\(_a\) low field), \(\nu\)6.82 (one-proton quartet, \(\mathcal{J}_{5,6}\) 2.5 Hz, \(\mathcal{J}_{6a,6b}\) 2.5 Hz, H-6\(_b\) high field), \(\nu\)7.89, 7.97, and 7.99 (three-proton singlets, OAc).

The experiment was repeated several times with the conditions and amounts of starting material and reagents remaining the same as in the previous experiment. The yield did not improve when \(\mathcal{Z}\) was purified by recrystallization from ethanol to give m.p. 132°, nor did the yield improve when evaporation time at 85° was extended to 1 hr. The yields ranged from 12.5 g to 22.5 g and were mostly near the former value. In all attempts to prepare \(\mathcal{Z}\), several days of cooling at -15° with intermittent shaking was required for crystallization to occur.
Preparation of 3,4,6-tri-O-acetyl-β-D-glucopyranosyl chloride (8).—The method used for the preparation of 8 was that described by Lemieux and Howard.\(^9\) Anhydrous ether (200 ml) was saturated at room temperature with anhydrous ammonia. The solution was cooled to 0\(^\circ\) and finely powdered 3,4,6-tri-O-acetyl-2-O-tri-chloroacetyl-β-D-glucopyranosyl chloride (6, 10.0 g, 21.3 mmoles) was added to the cooled solution. The mixture was shaken vigorously for about 20 min at room temperature and at no time was complete dissolution observed as described by Lemieux and Howard.\(^9\) The reaction mixture was cooled for 5 min in ice and the white crystalline residue was collected to yield 6.8 g, m.p. 129-134\(^\circ\) [lit.\(^9\) yield 6.7 g, m.p. 156-158\(^\circ\), \([\alpha]_D^{20} +29\(^\circ\) (c, 1, chloroform)]. The white, crystalline residue was swirled in chloroform (50 ml) and the insoluble residue was filtered off. The filtrate was evaporated to a crystalline residue and redissolved in chloroform. This procedure was repeated four times and the resultant residue was crystallized from ether to yield 8, 2.5 g, 7.7 mmoles (36\%), as white needles, m.p. 152-154\(^\circ\), \([\alpha]_D^{30} +26.3\(^\circ\) (c 1.49, chloroform).

Preparation of 2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiopseudourea hydrobromide (9).—The method used for the preparation of 9 was according to the general method of Černý and co-workers.\(^4\) Tetra-O-acetyl-α-D-glucopyranosyl bromide (1, 164 g, 399 mmoles) was dissolved in warm acetone (300 ml) and thiourea (30.5 g, 401 mmoles) was added to the solution. The reaction mixture was refluxed for 15 min and solid began to form in the solution. The reaction mixture
appeared to be completely solid with crystals after refluxing for an additional 15 min. The solid was digested with an additional 75 ml of acetone and refrigerated overnight. The yield of 2 as a white solid was 148.7 g, 305 mmoles (76%). A small portion of the solid (20 g) was refluxed in acetone (100 ml) and filtered to give 2 as a white solid, m.p. 204°, [α]$_D^{29}$ -8.65° (c 2.08, water) [lit.$^{47}$ m.p. 178° from acetone, lit.$^{46}$ m.p. 205° from isopropyl alcohol, [α]$_D^{23}$ -7.6° (c 1.443, water), and lit.$^{45}$ m.p. 192° from ethanol, [α]$_D^{20}$ -8.72° (c 5.102, water)]. An attempt was made to obtain the n.m.r. spectrum with deuterium oxide as solvent and DSS as an internal standard, however the compound was not soluble.

Preparation of 2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-2-thiopseudourea hydrobromide (10).—Compound 10 was prepared essentially according to the method of Bonner and Kahn$^{46}$ except acetone was used as solvent instead of isopropyl alcohol. Crystalline tetra-O-acetyl-α-D-galactopyranosyl bromide (88.5 g, 215 mmoles) was dissolved in acetone (300 ml) and thiourea (16.6 g, 218 mmoles) was added to the solution. The reaction mixture was refluxed for 40 min when solid product began to reappear. The reaction mixture was diluted with petroleum ether to opalescence and refrigerated overnight to give a solid mass of crystals, yield 91.8 g, 188 mmoles (87%), m.p. 161-163°. A 10-g portion of the product was refluxed in acetone for an additional 1 hr and allowed to stand at room temperature. The white, crystalline product gave m.p. 169.5°, [α]$_D^{22}$ +16.9° (c 1.46, ethanol) [lit.$^{46}$ m.p. 169.5° after four crystallizations from isopropyl alcohol, [α]$_D^{25}$ +16.0°
(c 1.560, ethanol)]. N.m.r. data (100 MHz, deuterium oxide):

\[
T_{4.39-4.77} \text{ (four-proton multiplet, H-1, 2, 3, 4), } T_{5.45-5.85} \text{ (three-proton multiplet, H-5, 6, 6') }, T_{7.79, 7.86, 7.91, \text{ and } 7.93} \text{ (three-proton singlets, OAc).}
\]

The reaction was repeated with syrupy tetra-O-acetyl-a-D-galactopyranosyl bromide (2, 108.4 g, 264 mmoles) and thiourea (20.1 g, 264 mmoles). The yield of crystalline 10 was 89.1 g, 183 mmoles (69%).

**Preparation of 2-(2,3,4-tri-O-acetyl-a-L-arabinopyranosyl)-2-thiopseudourea hydrobromide (11).**—Compound 11 was prepared essentially according to Horton and co-workers.\(^{39}\) A mixture of tri-O-acetyl-\(\beta\)-L-arabinopyranosyl bromide (84.0 g, 248 mmoles) was dissolved in warm acetone (300 ml) and thiourea (19.0 g, 249 mmoles) was added to the solution. The mixture was refluxed and the product began to crystallize out of solution after 15 min. The mixture was refluxed for an additional 15 min and the solution was cooled to room temperature. Petroleum ether (50 ml) was added and the mixture was refrigerated overnight. The product crystallized as fine white needles, yield 83.1 g, 200 mmoles, 81%, m.p. 174-175\(^{0}\), \([\alpha]_{D}^{22} +6.8^{0}\) (c 1.63, water) [lit.\(^{39}\) m.p. 169-171\(^{0}\), \([\alpha]_{D}^{21} +8.8^{0}\) (c 1.3, water)].

N.m.r. data (100 MHz, deuterium oxide solution): \(T_{4.44-4.79}\) (four-proton multiplet, H-1, 2, 3, 4), \(T_{5.76}\) (one-proton quartet, \(J_{4,5a} 3.2\) Hz, \(J_{5a,5b} 13.0\) Hz, H-5a low field), \(T_{7.97}\) (one-proton quartet, \(J_{4,5b} 1.8\) Hz, H-5b high field), \(T_{7.84, 7.85, \text{ and } 7.94}\) (three-proton singlets, OAc).
Preparation of 2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-2-thiopseudourea hydrobromide (12).—Compound 12 was prepared essentially according to the procedure of Stanek, Sindlerova, and Černý.48 An acetone solution of (30 ml) 2,3,4-tri-O-acetyl-α-D-xylopyranosyl bromide (104 g, 307 mmoles) and thiourea (23.4 g, 307 mmoles) was refluxed 15 min and solid product formed in the reaction mixture. The reaction mixture was refluxed an additional 30 min and the solid mass was diluted with acetone (100 ml) and refrigerated overnight. White crystals were collected in two crystal crops, yield 105.1 g, 253 mmoles, 82%. A 10-g portion of the product was refluxed in acetone (100 ml) and filtered from warm acetone. The crystals had m.p. 173°, [α]D28 = -36.0 (c 1.3, water) [lit.48 m.p. 176-178°, [α]D = -71.0° (c 0.27, ethanol-water, 1:1). N.m.r. data (100 MHz, deuterium oxide): δ4.26 (one-proton doublet, J1,2 5.0 Hz), δ4.68-5.13 (three-proton multiplet, H-2, 3, 4), δ5.60 (one-proton quartet, J4,5a 3.6 Hz, J5a,5b 12.3 Hz, H-5a low field), δ6.17 (one-proton quartet, J4,5b 6.0 Hz, H-5b high field), δ7.85, 7.87, and 7.89 (three-proton singlets, OAc).

Preparation of 2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-2-thiopseudourea hydrochloride (13).—The method used for preparation of 13 was that of Bonner and Kahn,46 however acetone was used as solvent instead of isopropyl alcohol. Tri-O-acetyl-α-D-xylopyranosyl chloride (2, 85.6 g, 290 mmoles) was dissolved in warm acetone (200 ml) and thiourea (22.1 g, 290 mmoles) was added to the solution. The mixture was refluxed for 0.5 hr and the reaction
mixture appeared as a white solid mass. Another 250 ml of acetone was added and the reaction mixture was refluxed an additional 1.5 hr. The reaction mixture was cooled, diluted with petroleum ether (50 ml), and refrigerated to give fluffy needles in three crystal crops, yield 76.6 g, 207 mmoles (71%), m.p. 163-165°. The product (5 g) was refluxed in acetone (500 ml) for 6.5 hr. The product did not dissolve and was filtered from the hot acetone solution to give m.p. 181°, $\left[\alpha\right]_{D}^{21} = -89.2° (c 2.6, \text{ water}) \left[\text{lit.} \left[\alpha\right]_{D}^{46} \text{ m.p. } 181°, \left[\alpha\right]_{D}^{25} = -71.5° (c 0.587, \text{ ethanol})\right]; \lambda_{\text{Br max}}^{X} = 5.69 (\text{OAc}), -3.2 (\text{ broad }), 6.01 \mu m (\text{amidinium})^{39}; \lambda_{\text{OH max}}^{X} = 214 nm (\epsilon 6000); \text{n.m.r. data (100 MHz, deuterium oxide): } 74.26 (\text{one-proton doublet, } J_{1,2} = 5.0 \text{ Hz}, \text{ H-1, 74.66-5.16 (three-proton multiplet, } \text{H-2, 3, 4}), 75.59 (\text{one-proton quartet, } J_{4,5a} = 3.9 \text{ Hz, } J_{5a,5b} = 12.3 \text{ Hz, H-5a low field}), 76.17 (\text{one-proton quartet, } J_{4,5b} = 6.1 \text{ Hz, H-5b high field}), 77.85, 7.86, \text{ and 7.88 (three-proton singlets, OAc). X-ray powder diffraction data: } 16.66 \text{ w, 8.88 s (1,1), 7.89 s (1,1), 6.30 \text{ w}, 5.89 \text{ w, 5.57 w, 5.30 s (2), 4.90 s (3), 4.56 m, 4.29 m, 3.86 s (5,5), 3.69 s (5,5), 3.53 m, 3.29 s (4).}

\text{Anal. Calcd. for } C_{12}H_{19}ClN_2O_7S: \text{ C, 38.87; H, 5.16; Cl, 9.56; N, 7.56; S, 8.65. Found: C, 38.75; H, 5.17; Cl, 9.73; N, 7.64; S, 8.89.}

\text{Preparation of 1-thio-β-D-glucopyranose pentaacetate (16).—The general procedure of Černý and co-workers\textsuperscript{47} was essentially followed. Sodium hydrogen sulfite (35.3 g) was dissolved in water (300 ml) and the solution was heated to } 85°. \text{ To the solution was added 2-(2,3,4,6-tetra-0-acetyl-β-D-glucopyranosyl)-2-thiopseudocurea}
hydrobromide (2, 127 g, 261 mmoles) followed by carbon tetrachloride (300 ml). The heterogeneous solution was refluxed 30 min and cooled to room temperature. The organic layer was separated and the aqueous layer was extracted twice with 100-ml portions of carbon tetrachloride. The combined organic extract was washed with water (300 ml), dried (magnesium sulfate), and evaporated to a syrup. The syrup was dissolved in a mixture of pyridine (200 ml) and acetic anhydride (175 ml) and refrigerated overnight. The solution was poured onto ice and water (about 1000 g) with vigorous stirring. White crystals formed and were collected after 1 hr. The crystals were washed with water (200 ml), dried in air, and recrystallized from ethanol to give 16 as white needles, yield 86.0 g, 212 mmoles (81%), m.p. 118-119°, [α]_D^{28} +10° (c 1.1, chloroform) [lit.43 m.p. 120°, [α]_D^{19} +12.4° (c 5, tetrachloroethane and lit.42 m.p. 119-120° [α]_D^{23} +10.5° (c 0.6, chloroform)]. The n.m.r. data (100 MHz, CDCl_3) were consistent with those previously reported.39

1-Thio-β-D-galactopyranose pentaacetate (17) from 2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-2-thiopseudourea hydrobromide.—Sodium hydrogen sulfite (40 g) was dissolved in water (200 ml) and the solution was heated to 85°. To the solution was added 2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-2-thiopseudourea hydrobromide (10, 120 g, 246 mmoles) followed by addition of carbon tetrachloride (300 ml). The reaction conditions and work-up were the same as described in the foregoing experiment. The yield of white, coarse needles was 81.5 g, 201 mmoles, 82%, m.p. 114-115° [α]_D^{22} +30.1°
Preparation of 1-thio-α-L-arabinopyranose tetraacetate (14).—Compound 14 was prepared from 2-(2,3,4-tri-O-acetyl-α-L-arabinopyranosyl)-2-thiopseudourea hydrobromide (11, 73.0 g, 176 mmoles) by the method described by Horton and co-workers. The method was essentially that described for the preparation of 16 from 9. The acetylated mixture did not crystallize when poured onto ice and water (1000 g). The syrupy product adhered to the sides of the flask and the aqueous solution was decanted. The syrup was dissolved in dichloromethane (200 ml) and the organic solution was washed with water (100 ml), aqueous sodium hydrogen carbonate (100 ml), dried (magnesium sulfate), and evaporated to a syrup. The syrup was distilled twice from 100-ml portions of toluene and twice from 100-ml portions of carbon tetrachloride. The resulting syrup was dissolved in ethanol, seeded, and refrigerated overnight. White needle-like crystals of 14 were collected in two crops, yield 25.3 g, 76 mmoles (43%), m.p. 77-78°, [α]D +33.3° (e 1.7, chloroform) [lit.39 m.p. 81.5-82°, [α]D +39.4° (e 2.2, chloroform)]. The n.m.r. data (100 MHz, CDCl3) were consistent with those previously reported.39

Preparation of 1-thio-β-D-xylopyranose tetraacetate (15).—From 2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-2-thiopseudourea hydrobromide (12).—Compound 15 was prepared from (81.0 g, 195 mmoles) by the method described for the preparation of
1-thio-β-D-glucopyranose pentaacetate (16) from its corresponding thiopseudourea hydrobromide (9). The acetylated mixture did not crystallize when poured onto ice and water (~1000 g) and the work-up described in the foregoing experiment was used. The crystalline yield of 15 was 21.5 g, 64 mmoles (33%). The product had m.p. 99-100° and [α]_D^24 -7.0° (c 1.1, chloroform) [lit. 41 m.p. 99°, [α]_D^24 -6.88° (chloroform) and lit. 39 m.p. 103°, [α]_D^20 -7.7° (c 1.4, chloroform)]. The n.m.r. data (100 MHz, CDCl_3) were the same as previously reported. 39

B. From 2-(2,3,4-tri-O-acetyl-β-D-xylopyanosyl)-2-thiopseudourea hydrochloride (13).—Compound 13 (70.0 g, 189 mmoles) when treated essentially as described in the foregoing experiment gave 15 (39.9 g, 119 mmoles, 63%) as white, stout needles, m.p. 99-100° after one recrystallization from ethanol.

Preparation of 1-thio-α-D-glucopyranose pentaacetate (18).—The method used for the preparation of 18 was essentially that of M. Sakata, M. Haga, S. Tejima, and M. Akagi. 44 To an acetone solution (50 ml) of crude 3,4,6-tri-O-acetyl-β-D-glucopyranosyl chloride (5, 6.2 g, 19.1 mmoles, m.p. 129-134°) was added potassium thiolacetate (2.16 g, 19.1 mmoles) and the mixture was refluxed for 5 min. The precipitate of potassium chloride was filtered off and the acetone filtrate was evaporated to a syrup. The syrup was dissolved in pyridine (20 ml), acetic anhydride (15 ml) was added to the solution, and the solution was kept overnight at room temperature. The solution was poured onto ice and water (~500 g) and stirred for 1 hr. The aqueous solution was decanted and the remaining syrup
was dissolved in dichloromethane (100 ml). The organic solution was washed with a saturated solution of sodium hydrogen carbonate (100 ml), water (100 ml), dried (magnesium sulfate), and evaporated to a syrup. The syrup was evaporated twice from 100-ml portions of toluene, and twice from 100-ml portions of carbon tetrachloride.

T.l.c. of the syrupy product revealed three components, $R_f$ 0.86 (major), 0.73, and 0.54 (very minor). The syrup was crystallized from ethanol to give fluffy, needle-like crystals that were difficult to filter, yield 2.5 g, m.p. 102-105°. T.l.c. of the crystalline product and the filtrate revealed the same three components described for the crude syrupy product. Recrystallization from ethanol gave needle-like crystals, m.p. 105-108°. The reaction product was subjected to column chromatography with silica gel as the adsorbent and solvent A as eluent. The separation was monitored by t.l.c. and the fractions that contained the component having $R_f$ 0.86 were combined, evaporated to a syrup, and crystallized from ethanol to give fluffy, white needles. The yield of crystalline $\bar{\lambda}$ was 2.193 g, 5.4 mmoles (28.3%), m.p. 125°, $[\alpha]_{D}^{28}$ +135° (c 1.12, chloroform) [lit. 44 m.p. 125°, $[\alpha]_{D}^{20}$ +135° (c 1.0, chloroform) and lit. 52 m.p. 126-127° $[\alpha]_{D}^{20}$ +120° (c 0.416, chloroform)]. N.m.r. data (100 MHz, CDCl$_3$): \( \gamma \) 3.76 (apparent triplet, H-1, spacing \(-2.1\) Hz), \( \gamma \) 4.68-5.03 (multiplet, H-2, 3, 4), \( \gamma \) 5.70, 5.95 (quartets, H-6a and H-6b, low- and high-field respectively, \( J_{5,6a} \) 4.0 Hz, \( J_{5,6b} \) 2.0 Hz), \( \gamma \) 5.92-6.14 (multiplet overlapping H-6b, H-5), \( \gamma \) 7.58 (singlet, SAc), \( \gamma \) 7.94, 7.98 (three- and nine-proton singlets, OAc): The H-1 signal at 60 MHz was an apparent quartet at \( \gamma \) 3.76 with spacings of \(-1.2\) Hz;
(100 MHz, benzene-d$_6$): $\gamma$ 3.49 (doublet, H-1, $J_{1,2} 4.7$ Hz), $\gamma$ 4.36-4.86 (multiplet, H-2; 3, 4), $\gamma$ 5.68 (quartet, H-6a, $J_{5,6a} 4.8$ Hz), $\gamma$ 5.88-6.13 (multiplet, H-6b, H-5) $\gamma$ 8.17, 8.26, and 8.36 (singlets, three-, nine-, and three-protons, acetyl methyl protons). X-ray powder diffraction data: 12.54 vu, 9.40 s (1), 7.19 vu, 5.44 s (2,2), 5.09 s (2,2), 4.69 m, 4.40 m, 4.15 m, 3.58 m, 3.44 s (3), 3.29 w, 3.12 m, 2.99 w.

Acid-catalyzed equilibration of penta-O-acetyl-$\beta$-D-glucopyranose (2) in thiolactic acid with zinc chloride. Freshly fused zinc chloride (5 g) was added to anhydrous ether (25 ml). The flask was stoppered and the suspension was stirred at room temperature until the solid was evenly dispersed on the bottom of the flask. Thiolactic acid (15 ml) and penta-O-acetyl-$\beta$-D-glucopyranose (7, 10.0 g, 25.6 mmoles) (Pfanstiehl Laboratories, Inc., Waukegan, Ill.) were added to the reaction mixture and stirring was continued for 16 hr at room temperature. Carbon tetrachloride (25 ml) was added and the solvent was removed under vacuum. The resulting crude, syrupy reaction product was diluted with water (100 ml) and carbon tetrachloride (100 ml) and filtered. The residue was washed with carbon tetrachloride (50 ml) and the organic phase was separated from the aqueous phase and washed with two 100-ml portions of an aqueous solution of sodium hydrogen carbonate, water (100 ml), and dried (magnesium sulfate), and evaporated to a dark yellow syrup. An n.m.r. spectrum (60 MHz) of a solution of the syrup in chloroform-d showed only the presence of 1-thio-$\beta$-D-glucopyranose pentaacetate (16) and no low field signal, $\gamma$ 3.76, for the anomeric proton of
l-thio-α-D-glucopyranose (18). The syrup was crystallized from ethanol to give the thioaceta te 16 in three crystal crops, yield 9.6 g, 23.6 mmoles (92%), m.p. 117-118°, $[\alpha]_D^{28} + 9.5^o$ (c 1.1, chloroform) [lit.43 m.p. 120°, $[\alpha]_D^{19} + 12.4^o$ (c 5, tetrachloroethane and lit.39 m.p. 119-120°, $[\alpha]_D^{23} + 10.5^o$ (c 0.6, chloroform)]. The n.m.r. spectral data (100 MHz, CDCl₃) corresponded to that previously reported for l-thio-β-D-glucopyranose pentaacetate (16).39

Preparation of benzyl 2,3,4,6-tetra-O-acetyl-l-thio-β-D-glucopyranoside (21).—This compound was prepared according to the method described by Horton and co-workers.39 Tetra-O-acetyl-α-D-glucopyranosyl bromide (100 g, 240 mmoles) was dissolved in 320 ml of warm absolute ethanol and the ethanol solution was added to a solution of α-toluenethiol (30 ml, 240 mmoles) in 3 N ethanolic potassium hydroxide (80 ml). The mixture was shaken for 5 hr at room temperature, concentrated to a syrup, and dissolved in 170 ml of acetic anhydride containing 10 g of sodium acetate. The solution was refluxed and poured onto ice and water (-1000 g) and stirred for 2 hr. Crystallization did not occur and the aqueous solution was decanted. The syrupy residue was dissolved in dichloromethane (200 ml) and the organic solution was washed with two 100-ml portions of a saturated solution of sodium hydrogen carbonate, water (100 ml), dried (magnesium sulfate), and re-evaporated to a syrup. The syrup was crystallized from methanol to give 21 as white needles, collected in two crystal crops, yield 60.1 g, 132 mmoles, (55%), m.p. 97-99°, $[\alpha]_D^{28} - 88^o$ (c 1.5, chloroform) [lit.39 m.p. 100-101°, $[\alpha]_D^{20} - 94^o$ (c 0.6, chloroform) and lit.37 m.p. 98°, $[\alpha]_D^{24} - 93.1^o$
(1,1,2,2-tetrachloroethane)]. The n.m.r. data (60 MHz, CDCl₃) were consistent with those reported previously. T.l.c. of the filtrate showed the presence of a major component, R₄ 0.88, which corresponded to the product, however further crystallization did not occur.

Preparation of phenyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranoside (20).—Preparation of 20 was analogous to that for preparation of 21 described in the foregoing experiment. Benzene-thiol (3 ml, 29 mmoles) in 3 N ethanolic potassium hydroxide (8 ml) was added to tetra-O-acetyl-α-D-glucopyranosyl bromide (10.0 g, 24 mmoles), that had been dissolved in warm absolute ethanol (25 ml). The mixture was shaken for 5 hr at room temperature and was concentrated to give a crude white solid. The solid was dissolved in acetic anhydride (20 ml), sodium acetate (1 g) was added, and the mixture was refluxed for 2 hr and then poured onto ice and water (500 g). The aqueous layer was decanted and the remaining residue was dissolved in dichloromethane (200 ml) and washed with saturated sodium hydrogen carbonate (100 ml), water (100 ml), and dried (magnesium sulfate). The dichloromethane solution was concentrated to a syrup. The syrup crystallized to give 20 in two crystal crops as white needles, yield 7.4 g, 17 mmoles (71%), m.p. 116-117°, [α]D²³ -15.8° (c 2.2, chloroform) [lit. [α]D²⁰ -40.1° (toluene) and lit. [α]D²⁰ -17.5° (c 2.5, chloroform)].

Preparation of 2,3,4,6-tetra-O-acetyl-1-S-benzoyl-1-thio-
β-D-glucopyranose (29).—Compound 29 was prepared by C. V. Holland
according to the procedure described by Holland, Horton, Miller,
and Bhacca. The compound had m.p. 130-131°, [α]D20 -12.5°
(g 1, chloroform) [lit. m.p. 126°, [α]D20 -12.44° (1,1,2,2-
tetrachloroethane)].

N.m.r. spectral study of the reaction of 1-thio-β-D-gluco-
pyranose pentaacetate (16) in carbon tetrachloride with bromine.—
A suspension of the thioacetate (16, 126 mg) in carbon tetrachloride
(1 ml) was prepared in an n.m.r. sample tube, and a small drop of
tetramethyldisilane was added. The spectrum at 60 MHz showed a 3-
proton singlet at 7.59 (SAc), peaks (12 protons) at 7.92, 7.98,
and 8.00 (OAc) and no signals below 7.5. From a stock solution
of bromine (15.60 g, 5.0 ml) in carbon tetrachloride (20 ml) a
250-μl aliquot (corresponding to 6.3 mmoles of bromine per mole of
16 was added by means of a syringe to the suspension of 16 at ~40°.
The suspended material dissolved rapidly. A scan of the n.m.r.
spectrum was initiated 60 sec after addition of the bromine, and
was completed 100 sec later. The spectrum showed no signals below
7.5, but the SAc signal had disappeared completely and a 3-proton
singlet at 7.19 had appeared (acetyl bromide in carbon tetrachloride
shows its proton signal at 7.19). A 12-proton multiplet was ob-
served at 7 ~7.9 (OAc). The spectrum was rescanned 200 sec after
the addition of the bromine: this scan, completed 100 sec later,
resembled the previous one, except that a low-intensity doublet at
7.3, having J1,2 4.0 Hz (H-1 of the glycosyl bromide 12), was
The latter signal increased in intensity with time, and, after 1 hr, it had an integrated intensity of one proton (relative to the 12-proton signal at \( \gamma \sim 7.9 \)). At this time, the spectrum was identical with that of the glycosyl bromide 2 in carbon tetrachloride, except for the additional 3-proton singlet at \( \gamma 7.19 \) (AcBr).* The reaction solution was evaporated to dryness and the residue was dissolved in carbon tetrachloride. The n.m.r. spectrum of the solution was unchanged, except that the signal at \( \gamma 7.19 \) had disappeared.

**N.m.r. spectral study of the reaction of 1-thio-a-D-glucopyranose pentaacetate (18) in carbon tetrachloride with bromine.**—The thioacetate (18, 114 mg) was suspended in carbon tetrachloride (2 ml) in an n.m.r. sample tube and a small drop of tetramethylsilane was added. Although the thioacetate (18) was quite insoluble in carbon tetrachloride, the spectrum at 60 MHz showed a broadened 3-proton singlet at \( \gamma \sim 7.60 \) (SAc) and a 9-proton multiplet at \( \gamma \sim 8.05 \) (OAc). A signal for H-1 of 18 was not observed because of the low solubility of 18 in carbon tetrachloride and no other signal was observed below \( \gamma 4.0 \). From the stock solution of bromine described in the foregoing experiment, a 250-\( \mu l \) aliquot (corresponding to 7 moles of bromine per mole of 18) was added to the suspension of 18 and the n.m.r. tube was shaken vigorously to aid dissolution. A scan of the n.m.r. spectrum at a probe temperature of \( 34^\circ \) was initiated 35 sec after the addition of bromine and completed 50 sec.

*An n.m.r. spectrum of acetyl bromide in carbon tetrachloride with TMS as a standard showed its signal at \( \gamma 7.19 \). The exact field position was determined by the normal sidebanding technique with TMS as the internal standard.*
later. The spectrum showed no signals below 7.4,0, but a doublet was present at 7.4,12 having $J_{1,2}$ 4.0 Hz. Most of the SAc signal at 7 ~7.60 had disappeared and a singlet was present at 7.7.19 (AcBr). A second scan was initiated 1 min 35 sec after the addition of bromine and completed 50 sec later. The spectrum was the same as that described for the first scan with the exception that the signal corresponding to SAc at 7 ~7.60 was absent. No signals were observed below 7.4,0. A third scan was initiated 2 min 35 sec after the addition of bromine and completed 50 sec later. A low intensity doublet at 7.3.28 having $J_{1,2}$ 4.0 Hz (H-1 of the glycosyl bromide 1) was present in addition to the signal at 7.4.12. The latter signal was the more intense signal. A fourth scan was initiated 3 min 50 sec after the addition of bromine and completed 100 sec later. The doublet at 7.4,12 was more intense than the doublet at 7.3.28 and the remaining portion of the spectrum was analogous to that of the third scan. At 5 min 50 sec after bromine addition and at a scan time of 250 sec the low field doublets, 7.3.28 and 7.4.12, were of approximately equal intensity. At 10 min 20 sec after bromine addition and at a scan time of 250 sec, the low field doublet 7.3.28 was much more intense than the doublet at 7.4.12. At 14 min 50 sec after bromine addition and at a scan time of 250 sec, no signal was observed at 7.4.12 and the doublet at 7.3.28 prevailed. At 42 min after the addition of bromine, the spectrum was identical with that of 1 in carbon tetrachloride, except for the additional 3-proton singlet at 7.7.19 (AcBr). The doublet at 7.3.28 had an integrated intensity of one proton (relative to the 12-proton signal
at γ ~7.9). The carbon tetrachloride solution was evaporated to a syrup and the syrup was redissolved in chloroform-d. The 3-proton singlet at γ7.19 was absent and the n.m.r. spectrum was identical to that reported previously.\(^{92}\) T.l.c. of the solution revealed a very major component at \(R_f\) 0.87 and five very minor components, \(R_f\) 0.69, 0.49, 0.41, 0.33, and 0.22. The solvent was evaporated to give a syrupy residue that was subjected to column chromatography on silica gel (5 g) with solvent A as eluent. The separation was monitored by t.l.c. and ~2 ml fractions were collected. Component, \(R_f\) 0.87, was collected and evaporated to a syrup. The syrup crystallized from ether—petroleum ether to give tetra-O-acetyl-\(\alpha\)-D-glucopyranosyl bromide (1), yield 42 mg, 0.1 mmoles (36%), m.p. 84-85°, lit.\(^{91}\) m.p. 88-89°. The i.r. spectrum was superposable with that of an authentic sample of 1.

\textbf{N.m.r. spectral study of the reaction of 1-thio-\(\beta\)-D-galactopyranose pentaacetate (17) in carbon tetrachloride with bromine.---} A suspension of the thioacetate (17, 119 mg) in carbon tetrachloride (1 ml) was prepared in an n.m.r. sample tube, and a drop of tetramethylsilane was added. The spectrum at 60 MHz showed a 3-proton singlet at γ7.64 (SAc), peaks (12 protons) at γ7.87, 7.93, 8.02, and 8.07 (OAc), and no signals below γ4.5. From the stock solution of bromine in carbon tetrachloride, described for the bromination of 16, a 250-µl aliquot (corresponding to 7 moles of bromine per mole of 17) was added to the suspension of 17 at 34°. The suspended material dissolved. A scan of the n.m.r. spectrum was initiated 30 sec after addition of bromine, and was completed 50 sec later. The
spectrum showed a doublet at 73.33, having $J_{1,2} = 3.4$ Hz ($\text{H}-1$ of the glycosyl bromide 2).\(^{92}\) The SAc signal had disappeared completely and a 3-proton singlet at 77.19 had appeared (AcBr). A 12-proton multiplet was observed at 7 \sim 7.9 (OAc). Scanning of the n.m.r. spectrum was continued with no significant change in the spectrum. After 7 min the low field doublet, 73.33, had an integrated intensity of one proton (relative to the 12-proton signal at 7 \sim 7.9). After about 2 hr the solution in the n.m.r. tube was evaporated to a syrup. T.l.c. revealed the presence of a principal component, $R_f 0.82$ and three very minor components, $R_f 0.44$, 0.32, and 0.21. The syrup was dissolved in chloroform-\(d\) and the n.m.r. spectrum showed the absence of the 3-proton singlet at 77.19 (AcBr). The n.m.r. spectrum was identical with that reported previously for tetra-\(O\)-acetyl-\(\alpha\)-\(D\)-galactopyranosyl bromide (2).\(^{92}\) The chloroform-\(d\) solution was re-evaporated to a syrup and the syrup was subjected to column chromatography on silica gel (5 g) with solvent A as eluent. The separation was monitored by t.l.c. and the major component ($R_f 0.82$) was collected, evaporated to a syrup, and crystallized from ether—petroleum ether to give tetra-\(O\)-acetyl-\(\alpha\)-\(D\)-galactopyranosyl bromide (2), yield 53.7 mg, 0.13 mmoles (45%), m.p. 81-82\(^{\circ}\), $[\alpha]_{D}^{28} +2060$ (c 1.76 chloroform) lit.\(^{93}\) m.p. 83-84\(^{\circ}\), $[\alpha]_{D}^{20} +2150$ (c 1, chloroform).

N.m.r. spectral study of the reaction of 1-thio-\(\alpha\)-\(L\)-arabinopyranose tetraacetate (14) in carbon tetrachloride with bromine.—

A solution of the thioacetate (14, 155 mg) in carbon tetrachloride (1 ml) was prepared in an n.m.r. tube, and a small drop of
tetramethyldisilane was added. The spectrum at 60 MHz showed a 3-
proton singlet at 77.66 (SAc) peaks (12 protons) at 77.93 and 8.00
(0Ac) and no peaks below 74.4. From a stock solution of bromine,
described previously for the bromination of 16, a 250-μl aliquot
(corresponding to 4.2 moles of bromine per mole of 14) was added
to the solution. A scan of the n.m.r. spectrum at a probe tempera-
ture of 34⁰ was initiated 25 sec after addition of bromine, and was
completed 50 sec later. The spectrum showed a doublet at 73.37,
having 1,2 3.7 Hz (H-1 of the glycosyl bromide 3). The SAc signal
had disappeared completely and a 3-proton singlet at 77.19 had
appeared (AcBr). A 9-proton multiplet was observed at 7 7.9 (0Ac).
Further scanning of the n.m.r. spectrum over a 5 min period revealed
no significant change in the spectrum. After 5.5 min the low field
doublet, 73.37 and an integrated intensity of one proton (relative
to the 9-proton signal at 7 7.9). After about 3 hr the solution
in the n.m.r. tube was evaporated to a yellow syrup. T.l.c. of the
syrup revealed the presence of four components. There was one major
component, R₉ 0.92 and three minor components, R₉ 0.44, 0.37, and
0.21. The syrup was dissolved in chloroform-d and an n.m.r. spec-
trum was made of the solution. The spectrum was identical with
that reported by Horton and Turner⁹² for tri-0-acetyl-3-D-arabinopyranosyl bromide. The chloroform-d solution was evaporated to a
syrup and the syrup was crystallized from ether—petroleum ether to
give 3, yield 45 mg, 0.13 mmoles (28%), m.p. 138-139⁰, [α]D ²⁸ +279⁰
(c 1.24 chloroform) [lit.⁹⁴ m.p. 139⁰, [α]D ²⁸ +283.6⁰ (chloroform)].
N.m.r. spectral study of the reaction of 1-thio-\(\beta\)-D-xylo-pyranose tetraacetate (15) in carbon tetrachloride with bromine.---

The thioacetate (15, 109 mg) was mostly dissolved in carbon tetrachloride (1 ml) in an n.m.r. sample tube and a drop of tetramethylsilane was added. The spectrum at 60 MHz showed a 3-proton singlet at \(\tau 7.63\) (SAc) and a 9-proton broadened singlet at \(\tau 8.00\) (OAc) and no signals below \(\tau 4.5\). From the stock solution of bromine in carbon tetrachloride described for the bromination of 16 was added a 250-\(\mu\)l aliquot (corresponding to 5.9 moles of bromine per mole of 15) to the solution of 15. A scan of the n.m.r. spectrum at a probe temperature of \(34^\circ\) was initiated 30 sec after addition of bromine and was completed 50 sec later. The spectrum showed a doublet at \(\tau 3.44\), having \(\Delta_{1,2} 4.0\) Hz (H-1 of the glycosyl bromide 4). The SAc signal had disappeared completely and a 3-proton singlet at \(\tau 7.19\) had appeared (AcBr). A 9-proton multiplet was observed at \(\tau \approx 7.95\) (OAc). Scanning of the n.m.r. spectrum was continued for 7 min with no significant change in the spectrum. After 7 min the low field doublet, \(\tau 3.44\), had an integrated intensity of one proton (relative to the 9-proton signal at \(\tau \approx 7.95\)). After about 2 hr the solution in the n.m.r. tube was evaporated to a syrup. T.l.c. of the syrup revealed the presence of four components, \(R_f 0.92\) (very major) and 0.52, 0.44, and 0.21 (minor). The syrupy residue was dissolved in chloroform-\(d\) and the n.m.r. spectrum was identical with that reported previously\(^92\) for tri-\(\omega\)-acetyl-\(\alpha\)-D-xylopyranosyl bromide (4). The chloroform-\(d\) solution was evaporated to a crystalline residue. The residue was recrystallized from ether—petroleum ether to give the bromide 4.
as fine needles, yield 75.1 mg, 0.22 mmoles (67%), m.p. 99-100°, 
$[\alpha]^28_D +215^0$ (c 1.4, chloroform) [lit.96 m.p. 102°, $[\alpha]^20_D +212.2^0$ (c 2.5, chloroform).

N.m.r. spectral study of the reaction of 1-thio-\(\beta\)-D-ribo-
pyranose tetraacetate (28) in carbon tetrachloride with bromine.—

The thioacetate (28, 110 mg) was dissolved in carbon tetrachloride
(1 ml) in an n.m.r. tube and a drop of tetramethylsilane was added
to the solution. The spectrum at 60 MHz showed a 3-proton singlet
at \(\gamma 7.67\) (SAC), and peaks (9 protons) at 77.92 and 8.02 (OAc) and
no signals below 74.4. From the stock solution of bromine described
for the bromination of \(16, \) was added a 250-\(\mu\)l aliquot (corresponding to 5.9 moles of bromine per mole of 28) to the solution
of 28. A scan of the n.m.r. spectrum at a probe temperature of 34°
was initiated 13 sec after the addition of bromine and was completed
50 sec later. A broadened singlet was observed at \(\gamma 3.70\) (H-1 of
the glycosyl bromide \(36\)). The SAC signal had disappeared completely
and a 3-proton signal at \(\gamma 7.19\) had appeared (AcBr). A 9-proton
multiplet was observed at \(\gamma \sim 8.0\) (OAc). Scanning of the n.m.r.
spectrum was continued for 7 min with no significant change in the
spectrum. After 7 min the low field, broadened singlet, \(3.70,\)
had an integrated intensity of one proton (relative to the 9-proton
signal at \(\gamma \sim 8.0\)). After about 4 hr the carbon tetrachloride solu-
tion was evaporated to a syrupy residue. T.l.c. of the residue
revealed a major component, \(R_f^\perp, 0.84\) and three minor components,
\(R_f^\perp 0.37, 0.34,\) and \(0.23.\) The residue was dissolved in chloriform-d
and the n.m.r. spectrum was identical with that previously
reported for tri-\(\text{O}-\text{acetyl-}\beta-\text{D-ribopyranosyl bromide} (36). The width at half-height of the H-1 signal was 3.0 Hz. After about 4 hr the chloroform-\(d\) solution was evaporated to a syrup and the syrup was crystallized from ether to give 36 as colorless, stout crystals, yield 39 mg, 0.11 mmoles (33%), m.p. 95°, \([\alpha]_{D}^{28} -208° (c 1.3, \text{chloroform}) [\text{litr.}^{136} \text{m.p. 96°, } [\alpha]_{D}^{25} -209.3° (\text{chloroform})].


N.m.r. spectral study of the reaction of benzyl 2,3,4,6-tetra-\(\text{O}-\text{acetyl-}\text{l-thio-}\beta-\text{D-glucopyranoside} (21) in carbon tetrachloride with bromine.---The l-thio-\(\beta-\text{D-glucoside (21, 122 mg) was partly dissolved in carbon tetrachloride (1 ml) in an n.m.r. sample tube and a drop of tetramethylsilane was added. The 60 MHz spectrum showed a 5-proton singlet, \(72.80 \text{ (Ph)}), 74.83-5.28 and 5.60-5.99 \text{(multiplets, three and three protons, H-1, 2, 3, 4, 6, 6')}, \(76.14 \text{ (2-proton doublet, benzylic CH}_2\text{)}, 76.28-6.69 \text{(multiplet, H-5)}, \(77.94, 8.05, \text{and 8.08 (three, six, and three proton singlets, OAc). From the stock solution of bromine in carbon tetrachloride described for the bromination of 16 was added a 250-\text{ul aliquot (corresponding to 7.2 moles of bromine per mole of 21). A scan of the n.m.r. spectrum at a probe temperature of 34° was initiated 17 sec after addition of bromine and was completed 50 sec later. The spectrum showed the absence of a doublet at \(76.14 \text{ (benzylic CH}_2\text{)}\) and the appearance of a broadened singlet at \(75.77\) and no low-field doublet...
was present to indicate the presence of glycosyl bromide 1. The spectrum was scanned for 7 min 30 sec after the addition of bromine and no appreciable change in the spectrum occurred. The spectrum was scanned at 8 min 35 sec after the addition of bromine at a scan speed of 250 sec and a low-field doublet appeared as a weak signal \( \gamma 3.40 \), having \( \delta 1,2 4.0 \text{ Hz (H-1 of the glycosyl bromide 1)} \). The spectrum was scanned 25 min after the addition of bromine and the low-field doublet, \( \gamma 3.40 \), had an integrated intensity of 0.32 protons (relative to OAc protons). The low-field doublet had an integrated intensity of 1 proton (relative to OAc protons) 1 hr 30 min after the addition of bromine. At this time, the spectrum was identical with that of the glycosyl bromide 1 in carbon tetrachloride, except for the additional 5-proton singlet at \( \gamma 2.71 \) and a 2-proton singlet at \( \gamma 5.57 \). The carbon tetrachloride solution was evaporated to a syrupy residue. T.l.c. of the residue revealed a major component, \( R_f 0.83 \) and three minor components, \( R_f 0.51, 0.43, \) and \( 0.32 \). The residue was dissolved in chloroform-d and the n.m.r. spectrum was essentially the same as reported previously for 1 with the exception of the presence of a 5-proton singlet at \( \gamma 2.72 \) and a 2-proton singlet \( \gamma 5.53 \). The chloroform-d solution was evaporated to a syrup and the syrup was chromatographed on silica gel (5 g) with solvent A as eluent. The separation was monitored by t.l.c. and the compound \( R_f 0.83 \) was isolated and evaporated to a colorless syrup. The syrup crystallized from ether—petroleum ether to give tetra-\( \beta \)-acetyl-\( \alpha \)-D-glucopyranosyl bromide (2), yield 31 mg, 0.07 mmol (26%).
m.p. 86-87°, [α]_D^28 +188° (c 1.0, chloroform) [lit. m.p. 88-89°, [α]_D^28 +198° (c 2, chloroform)]. The crystalline compound was dissolved in chloroform-d. Its n.m.r. spectrum was identical with that previously reported. The i.r. spectrum was superposable on that of an authentic sample of 1.

N.m.r. spectral study of the reaction of phenyl 2,3,4,6-tetra-O-acetyl-1-thio-D-glucopyranoside (20) in carbon tetrachloride with bromine. The 1-thio-D-glucoside (20, 103 mg) was almost insoluble in carbon tetrachloride (2 ml) in an n.m.r. sample tube. A drop of tetramethylsilane was added to the carbon tetrachloride. The 60 MHz spectrum showed a weak acetyl signal as a broadened doublet \( \gamma \approx 8.0 \) and a weak aryl signal as a very broad singlet, \( \gamma \approx 2.7 \). From the stock solution of bromine in carbon tetrachloride described for the bromination of 11° was added a 250-µl aliquot (corresponding to 8.5 moles of bromine per mole of 20). The n.m.r. tube and its contents were shaken vigorously to aid dissolution. A scan of the n.m.r. spectrum at a probe temperature of 34° was initiated 40 sec after addition of bromine and was completed 50 sec later. The spectrum showed a low-field doublet, \( \gamma_{3.42} \) (H-1 of the glycosyl bromide 1), having \( J_{1,2} 4.0 \) Hz and a low field multiplet \( \gamma_{2.13-2.69} \) (aryl protons). Scanning of the spectrum was continued with no observable change. At 7 min after the addition of bromine the integrated intensity of the low field doublet, \( \gamma_{3.42} \), was 1 proton (relative to the OAc). The carbon tetrachloride solution was evaporated to a syrup. T.l.c. of the syrup revealed a major component R_f 0.80 and four minor components,
The syrup was dissolved in chloroform-d. The n.m.r. spectrum of the product was the same as that reported by Horton and Turner\textsuperscript{92} with the exception of a low-field multiplet centered at 72.68. The chloroform-d solution was evaporated to a syrup and the syrup was chromatographed on silica gel (5 g) with solvent A as eluent. Component $R_f$ 0.80 was separated and crystallized from ether—petroleum ether to yield tetra-O-acetyl-α-D-glucopyranosyl bromide (1), 23 mg, 0.06 mmoles (26\%), m.p. 87-88\(^\circ\), $[\alpha]_D^{28}$ +199\(^o\)  (c 0.76, chloroform) [lit.\textsuperscript{91} m.p. 88-89\(^o\), $[\alpha]_D^{28}$ +198\(^o\)  (c 2, chloroform)].

A chloroform-d solution of the product gave the same n.m.r. spectrum as that reported previously for tetra-O-acetyl-α-D-glucopyranosyl bromide (1).\textsuperscript{92}

**N.m.r. spectral study of the action of bromine on 2,3,4,6-tetra-O-acetyl-1-S-benzoyl-1-thio-β-D-glucopyranose (29) in carbon tetrachloride.**—A suspension of 29 (123 mg) in carbon tetrachloride (1 ml) was prepared in an n.m.r. tube, and a drop of tetramethylsilane was added. The spectrum at 60 MHz showed a low field multiplet, 72.0-2.7 (aryl protons) and singlets, 77.99, 8.02, and 8.05 (three, three, and six protons, OAc). The remaining portion of the spectrum was not observable because of the low solubility of 29 in carbon tetrachloride. From the stock solution of bromine in carbon tetrachloride described for the bromination of 16 was added a 250-μl aliquot (corresponding to 7.5 moles of bromine per mole of 29). A scan of the n.m.r. spectrum at a probe temperature of 34\(^o\) was initiated 17 sec after bromine addition and was completed 50 sec later. The n.m.r. spectrum showed a weak signal for a low field
doublet at $73.40$, having $\frac{3}{2}, 4.0$ Hz (H-1 of the glycosyl bromide $\frac{1}{2}$).

A second scan of the n.m.r. spectrum was initiated 1 min 80 sec after the addition of bromine and completed 50 sec later. The low-field doublet was clearly discernible. Scanning of the n.m.r. spectrum was continued for 7 min with no appreciable change in the spectrum. At this time the integrated intensity of the low field doublet was one proton (relative to the acetyl signals at $\gamma \sim 7.9$) and the spectrum was identical with that of the glycosyl bromide $\frac{1}{2}$ in carbon tetrachloride, except for a multiplet $\gamma 1.34-2.60$. The solution was evaporated to a syrupy residue. T.l.c. of the syrup revealed a major component, $R_F 0.82$ and three minor components, $R_F 0.51, 0.43$, and 0.22. The syrup was dissolved in chloroform-d and the n.m.r. spectrum was identical with that previously reported by Horton and Turner $^{92}$ with the exception of the presence of a low field multiplet, $\gamma 1.94-2.80$. The solution was evaporated to a syrup and the syrup was chromatographed on silica gel (5 g) with solvent A as eluent. The component, $R_F 0.82$ was isolated and crystallized from ether—petroleum ether to yield $\frac{2}{2}$, 27 mg, 0.07 mmole (27%), m.p. 85-86$^\circ$ [lit. $^{91}$ m.p. 88-89$^\circ$]. A solution of the product in chloroform-d gave the same n.m.r. data as reported previously $^{92}$ and the i.r. spectrum was superposable with that of an authentic sample of tetra-$O$-acetyl-$\alpha$-$D$-glucopyranosyl bromide ($\frac{1}{2}$).

Tetra-$O$-acetyl-$\beta$-$D$-glucopyranosylsulfenyl bromide ($\frac{22}{2}$)

A. From $16$ in carbon tetrachloride.--The sulfenyl bromide $\frac{22}{2}$ was prepared according to the method described by the author in his Master of Science thesis. $^{73}$ To a suspension of
1-thio-β-D-glucopyranose pentaacetate (16, 20.00 g, 49.2 mmoles) in anhydrous carbon tetrachloride (200 ml) cooled to about -10° was added a solution of bromine (9.0 ml, 176 mmoles) in carbon tetrachloride (40 ml) and the mixture was stirred for 2-3 min at about -10°. Volatile materials were then rapidly removed on a rotary evaporator at ~30°/<10 torr., to give 22 as a pale-yellow, crystalline residue, yield 22.27 g (102%, m.p. 102-104°, [a]D15\textsuperscript{15} = -66.7° (c 2.1, tetrahydrofuran) changing to -114° after 14 hr; λmaxKBr = 5.72 (0Ac), 11.20 μm (axial H at C-1), SAc absent; 42 n.m.r. data (100 MHz, chloroform-d): \nu5.55-5.02 (3-proton multiplet), 5.35 (1-proton multiplet (H-1, 2, 3, 4)), \nu5.63-5.99 (2-proton multiplet, H-6, 6'), \nu6.14 (1-proton multiplet, H-5), \nu7.90, 7.92, 7.97, 8.00 (12 protons, acetyl's).

Anal. Calcd. for C\textsubscript{14}H\textsubscript{19}BrO\textsubscript{9}S: C, 37.93; H, 4.32; Br, 18.03; S, 7.23. Found: C, 37.99; H, 4.39; Br, 17.52; S, 7.51.

The product gave an X-ray powder diffraction pattern identical with that previously reported.\textsuperscript{76} Rapid recrystallization of the product from carbon tetrachloride gave an almost quantitative recovery of 22, having physical constants essentially identical with those of the material first isolated. T.l.c. of 22 showed a principal component having Rf 0.45 and minor components having Rf 0.76, 0.71, and 0.29, although none of these components could actually be attributed to 22 itself, because of the probability that 22 undergoes decomposition on the adsorbent.

Compound 22 prepared by the above procedure was used in all preparations described in this dissertation, unless stated otherwise.
B. By bromination of tert-butyl tetra-O-acetyl-1-thio-β-D-glucopyranoside (19) in carbon tetrachloride. To a solution of 1-thioglycoside 19 (516 mg, 1.23 mmoles) in carbon tetrachloride (20 ml) at -10° was added bromine (0.75 ml, 15 mmoles); after 1.5 min at -10°, the mixture was rapidly evaporated at 30° to give the sulphenyl bromide as a yellow, crystalline solid, yield 548 mg (101%), m.p. 97-99°. By comparative i.r. and n.m.r. spectra, and by X-ray powder diffraction data, this product was identical with 22 prepared by method A.

To a suspension of the product (463 mg) in carbon tetrachloride (40 ml) was added a solution of benzenethiol (0.5 g) in carbon tetrachloride (9.5 ml), and the mixture was kept 1 hr at 25°. The resulting solution was washed successively with water, saturated aqueous sodium hydrogen carbonate, and water, dried (magnesium sulfate), and evaporated to dryness. The residue was crystallized from ethanol—petroleum ether to give phenyl tetra-O-acetyl-β-D-glucopyranosyl disulfide (23),73,78 yield 200 mg (34%), m.p. 123-125°, identical with an authentic sample73,78 by mixed m.p., comparative i.r. and n.m.r. spectra, and X-ray powder diffraction data.73

Extended bromination of tert-butyl tetra-O-acetyl-1-thio-β-D-glucopyranoside (19).--To a suspension of the 1-thioglycoside 19 (534 mg, 1.27 mmoles) in carbon tetrachloride (20 ml) was added bromine (1.5 ml, 29 mmoles). The resultant, clear solution was kept for 60 hr at 25°, and evaporated to dryness; a solution of the resultant syrup in dichloromethane was washed with aqueous
sodium hydrogen carbonate, dried (magnesium sulfate), decolorized with carbon, and evaporated to a syrup. Crystallization of the syrup from ether—petroleum ether gave tetra-O-acetyl-α-D-glucopyranosyl bromide (1), yield 167 mg (32%), m.p. 82-85°, identical with an authentic sample of 1 by t.l.c. and i.r. and n.m.r. spectra. T.l.c. of the mother liquors indicated that 1 was the principal component, a minor component had $R_f$ 0.46.

When the reaction was followed by n.m.r. spectroscopy at ~40°, the 9-proton signal at $\gamma$8.61 for the tert-butyl group of 19 was absent 1 min after the addition of bromine, and the spectrum showed no signal below $\gamma$4.5. A 9-proton signal at $\gamma$8.19 was observed. After 14 hr, the spectrum showed a 1-proton doublet at 3.27, $J_{1,2}$ 4.1 Hz, and was closely similar to that of the glucosyl bromide 1, except for the presence of the 9-proton singlet at $\gamma$8.19.

Formation of bis(tetra-O-acetyl-β-D-glucopyranosyl) disulfide (24) by slow bromination of the 1-thioglycoside (19).—Bromine (0.35 ml, ~7 mmoles) was added dropwise during 3 hr to a solution of 19 (544 mg, 1.29 mmoles) in carbon tetrachloride (30 ml), and the reaction was monitored by t.l.c. At the end of the 3-hr period, only a trace of 19 remained, and the major component corresponded to the diglucosyl disulfide 24; a trace of the product having $R_f$ 0.39 was also present. Evaporation of the solution, and crystallization of the residue from ether—petroleum ether, gave the diglucosyl disulfide 24, yield 358 mg (76%), m.p. (one recrystallization) 140-141°, identical with authentic 24 by mixed m.p., i.r. and n.m.r. spectra, and X-ray powder diffraction pattern.
Fractional recrystallization of the mother liquors gave 13.4 mg (2.5%) of the starting material 19.

Reaction of the sulfonyl bromide 22 with tert-butyl tetra-0-acetyl-1-thio-β-D-glucopyranoside (19) to give the disulfide (24).—A suspension of the glucosyl sulfonyl bromide 22 (1.151 g, 2.60 mmoles) in carbon tetrachloride (50 ml) was mixed with a solution of 19 (1.060 g, 2.52 mmoles) in carbon tetrachloride (20 ml) and the mixture was shaken for 16 hr at room temperature. The resultant, clear solution was washed successively with aqueous sodium hydrogen carbonate and water, dried (magnesium sulfate) and evaporated to dryness. Crystallization of the residue from ethanol—petroleum ether gave the diglucosyl disulfide 24; yield (in three crops) 1.314 g (70%), identical with an authentic sample by t.l.c., mixed m.p., i.r. and n.m.r. spectra, and X-ray powder diffraction pattern.

T.l.c. of the mother liquors showed a major component corresponding to 24 and a minor component corresponding to 19.

An aliquot of the reaction mixture after 16 hr was examined by n.m.r. spectroscopy at 60 MHz. The 9-proton singlet at 7.861 (SCMe3) present in the spectrum of the starting l-thioglycoside 19 had diminished to low intensity, and a sharp singlet at 7.819, corresponding to tert-butyl bromide formed, was observed. The reaction mixture was evaporated, and the residue was dissolved in carbon tetrachloride. The signal at 7.819 (Me3CBr) was no longer observable in the n.m.r. spectrum of this solution.
Reaction of the sulfenyl bromide 22 with dry ethanol to give the disulfide 24.—Dry ethanol (50 ml) was added to the sulfenyl bromide 22 (prepared from 1.90 g of 16), and the yellow reaction mixture was kept for 20-30 min at room temperature; white needles were then present, and t.l.c. indicated the presence of a single component, $R_F$ 0.53, corresponding to the disulfide 24. No component having $R_F$ 0.39 (corresponding to the oxide 30) was detected. To the reaction mixture was added 50 ml of saturated aqueous sodium hydrogen carbonate solution, and the mixture was concentrated to remove ethanol. The resulting aqueous suspension was extracted with two 50-ml portions of dichloromethane, and the extracts were combined, washed with water, dried (magnesium sulfate), and evaporated. Crystal- lization of the residue from ethanol gave the diglucosyl disulfide 24, yield 847 mg (50%), m.p. (after recrystallization from ethanol) 141-142°, identical with authentic 24 by t.l.c. and X-ray powder diffraction pattern.

T.l.c. of the mother liquors showed a major component having the mobility of the disulfide 24, and traces of components having $R_F$ 0.77 and 0.12. No component corresponding to the oxide 30 ($R_F$ 0.39) was present.

The experiment was repeated with sulfenyl bromide 22 (from 2.32 g of 16) in dry ethanol (50 ml). After 20 min, the white needles of 24 that had formed were filtered off, yield 548 mg (26%) m.p. 142-143°. The filtrate was collected in a flask containing α-toluenethiol (1 ml) in dry ethanol (10 ml). After 10 min at
25\(^\circ\), t.l.c. of the mixture showed no component having the mobility 
\((R_f 0.88)\) of benzyl tetra-O-acetyl-\(\beta\)-D-glucopyranosyl disulfide 
\((37)\)\(^73,78\) indication that the sulfenyl bromide 22 had been com-
pletely decomposed by ethanol within 20 min.

Bis(tetra-O-acetyl-\(\beta\)-D-glucopyranosyl disulfide mono-oxide

(30) by oxidation of disulfide 24 with m-chloroperoxybenzoic acid.--

A solution of the disulfide 24 \((264 \text{ mg, } 360 \text{ \textmu moles})\) and m-
chloroperoxybenzoic acid \((49 \text{ mg, } 80\% \text{ pure by t.l.c.}, 230 \text{ \textmu moles of oxidant})\) 
in chloroform \((50 \text{ ml})\) was kept at 25\(^\circ\). After 40 min, t.l.c. indi-
cated the presence of two components, \(R_f 0.51\) and 0.39, in approxi-
mately equal amounts; no change was noted after 4 hr. Additional 
oxidant \((-50 \text{ mg, } 230 \text{ \textmu moles})\) was added, and after 1 hr t.l.c. 
indicated no significant change in the mixture; it was therefore 
 washed successively with aqueous sodium hydrogen carbonate solution 
\((50 \text{ ml})\) and water \((50 \text{ ml})\), dried \((\text{magnesium sulfate})\), and evaporated 
to dryness, and the residue was triturated with ethanol \((10 \text{ ml})\), 
whereupon the mono-oxide 30 crystallized as colorless, microscopic 
needles, yield 110 mg \((41\%)\), m.p. 150-151\(^\circ\). Recrystallization 
from hot ethanol gave pure 30, m.p. 152.5-153\(^\circ\), \([\alpha]_D^{22} -52.1^{\circ}\) 
g \(2.5\), chloroform); \(R_f 0.39\); \(\lambda \text{KBr } 5.72 \mu \text{m (OAc); } \)\(\text{n.m.r. data}\) 
\((100 \text{ MHz, chloroform-d)}: \gamma 4.36-5.18 \text{ (multiplets, H-1, 2, 3, 4),} \) 
\(\gamma 5.76 \text{ (multiplet, H-6), } \gamma 6.17 \text{ (multiplet, H-5), } \gamma 7.90, 7.95,\) 
7.96, and 7.98 \((\text{singlets, acetyl)s); X-ray powder diffraction data:} \) 
11.86 s \((2,2), 10.45 s \((2,2), 7.68 s \((2,2), 5.43 s \((3,3), 5.07 m,\) 
4.95 s \((3,3), 4.67 vw, 4.64 vs \((1), 4.29 w.\)
Anal. Calcd. for $C_{28}H_{38}O_{19}S_2$: C, 45.28; H, 5.16; S, 8.63; O, 4.92. Found: C, 45.17; H, 5.18; S, 8.86; O, 4.09.

The product 30 had extremely low solubility in cold ethanol, in contrast to the disulfide 24, which was moderately soluble; the two compounds were readily separable because of this difference.

**Reaction of the sulfenyl bromide 22 with water to give the disulfide mono-oxide 30.**--A suspension of 22 prepared from 1.043 g of 16 in carbon tetrachloride (40 ml) was shaken with water (3 ml) for 40 min at 25°. The solvents were evaporated from the resultant white suspension, the residue was dissolved in dichloromethane (100 ml), and the solution was washed successively with saturated aqueous sodium hydrogen carbonate solution and water, dried (magnesium sulfate), and evaporated to a syrup. Addition of ethanol to the syrup caused immediate crystallization, to give the oxide 30, yield 560 mg (59%), m.p. 151°, identical with an authentic sample by t.l.c., i.r. and n.m.r. spectra, and X-ray powder diffraction data.

T.l.c. of the mother liquors showed that essentially all of the oxide 30 had been removed by crystallization, but a component having the mobility ($R_f$ 0.51) of the diglucosyl disulfide 24 was present. Column chromatographic fractionation of the mother liquors gave the disulfide 24, yield 60 mg (6%), m.p. 140°, identical with an authentic sample by t.l.c., i.r. and n.m.r. spectra, and X-ray powder diffraction pattern.
Reaction of the sulfonyl bromide 22 with 95% ethanol to give the disulfide 24 and the mono-oxide 30.---To the sulfonyl bromide 22 (prepared from 2.317 g of 16) was added 95% ethanol (40 ml) at room temperature. The mixture became clear after a few min, and then became turbid and deposited white, fluffy needles. After 8 hr, the reaction mixture was processed as in the preceding experiment, to give the mono-oxide 30, yield 1.239 g (59%), m.p. (after recrystallization from hot ethanol) 151-152°, identical with an authentic sample by mixed m.p., i.r. and n.m.r. spectra, and X-ray powder diffraction pattern.

The mother liquors from the reaction contained a single component, chromatographically identical with the disulfide 24; t.l.c. of the initial reaction-product indicated that 24 and 30 were present in approximately equal amounts.

The foregoing experiment and the preceding one were repeated several times, either by the procedure described or by filtering off directly the product that crystallized from the reaction mixture. Frequently, the ethanol-insoluble product obtained initially had a melting point lower than that of the material obtained after recrystallization from hot ethanol; values of 101-103°, 111-113°, 113-114°, 132-134°, and 138-139° were observed in different experiments. In each instance, the product was free from the disulfide 24 (t.l.c.), and after refluxing with ethanol, recrystallization gave the oxide 30 having m.p. 152.5-153°, with recoveries of ~60%. A second form of 30, having m.p. 157-158°, was also encountered.
Bromination of the disulfide 24 to give the bromide 1.---

To a suspension of 24 (196 mg, 270 mmoles) in carbon tetrachloride (30 ml) was added bromine (1.5 ml, 29 mmoles), and the resultant solution was kept for 23 hr at 35°. The solution was evaporated to dryness at 30°, carbon tetrachloride was added to, and evaporated from, the residue, and the latter was dissolved in dry chloroform-d. The n.m.r. spectrum of the solution was identical with that of the tetra-O-acetyl-α-D-glucopyranosyl bromide 1, and the integrated intensities of the H-1 signal (T 3.25, J 1,2 4.0 Hz) and of the acetyl-group signals were in the ratio of 1:12. T.l.c. of the solution showed a principal component (Rf 0.80) chromatographically indistinguishable from 1; very minor side-products, having Rf 0.42, 0.31, 0.29, 0.20, and 0.1 were also present.

Bromination of the mono-oxide 30 to give the bromide 1.---

The mono-oxide 30 (133 mg, 180 mmoles) was treated with bromine (1.5 ml, 29 mmoles) by exactly the procedure used in the preceding experiment, and identical results were obtained.

Tetra-O-acetyl-β-D-glucopyranosylsulfenamidobenzene (31).---

To a suspension of the sulfenyl bromide 22 (3.24 g, 7.3 mmoles) in carbon tetrachloride (40 ml) was added aniline (1.4 ml, 15.4 mmoles), and the mixture was kept for 1 hr at room temperature. Water (100 ml) was added to the cloudy, yellow, reaction mixture, and the mixture was shaken. The organic layer was separated, dried (magnesium sulfate), and evaporated to a syrup. The syrup was dissolved in ether (50 ml), and the solution was decolorized
with carbon, concentrated to one-half volume and petroleum ether was added to opalescence. Refrigeration of the solution gave \( \text{as colorless, fine needles; yield 2.76 g (83\% \text{), m.p. (after one recrystallization)116-117}^{\circ}, [\alpha]_{D}^{21} -330^{\circ} \text{(g 2.4, chloroform); } R_f \text{0.85 homogeneous); } \lambda_{	ext{max}}^{\text{KBr}} 5.72 \text{ (OAc), 6.23, and 6.70 } \mu\text{m (aryl); } \lambda_{\text{max}}^{\text{EtOH}} 288 \text{ (e 2.000) (shoulder), 24.4 (10.300), and 206 nm (13.900); n.m.r. data, see Tables 8 and 9; X-ray powder diffraction data: 12.53 v.v., 10.13 vs (1), 7.16 w, 6.40 w, 5.69 w, 5.31 s (2), 5.14 m, 4.49 m, 4.27 m, 3.96 w, 3.67 m, and 3.52 m.}

\text{Anal. Calcd. for C}_{33}\text{H}_{25}\text{NO}_{9}\text{S: C, 52.73; H, 5.53; N, 3.08; S, 7.04. Found: C, 52.78; H, 5.45; N, 3.28; S, 6.85.}

\text{T.l.c. of the mother liquors indicated the presence of } \text{and a minor component having the mobility of the diglucosyl disulfide 24.}

4-(Dimethylamino)phenyl tetra-O-acetyl-1-thio-\( \beta \)-D-glucopyranoside (32).--A. \text{From sulfoxyl bromide 22 and N,N-dimethyl-aniline.}--To a suspension of the sulfoxyl bromide 22 (2.972 g, 6.7 mmoles) in carbon tetrachloride (50 ml) was added N,N-dimethyl-aniline (2 ml, 15.8 mmoles); the mixture turned green. After 1 hr at room temperature, the mixture was evaporated (bath temperature 43\(^\circ\), and the resultant syrup was dissolved in dichloromethane (100 ml). The solution was treated as described in the foregoing experiment. The resultant, green syrup was dissolved in ether, and petroleum ether was added to opalescence. Several crops of crystals were collected; the first three (total yield 1.522 g, 62\%, m.p.}
126-127°) were recrystallized to give pure bis(tetra-O-acetyl-β-D-glucopyranosyl) disulfide \(24\) (1.348 g), m.p. 141-142°, indistinguishable from an authentic sample\(^73\) by t.l.c., i.r. spectra, and X-ray powder diffraction pattern. The fourth and fifth crystal fractions, yield 206 mg, were shown by t.l.c. to contain \(24\) as a minor component, together with a principal component \((32)\) having \(R_f\) 0.81. Recrystallization (twice) from ethanol gave \(32\) as colorless needles, m.p. 150°, \([\alpha]_{D}^{20} -54.7° (c 0.9, \text{chloroform})\) [lit.\(^{35}\) m.p. 150-151°, \([\alpha]_{D}^{20} -47° \text{in chloroform} \)]; \(R_f\) 0.81; 
\(\lambda_{\text{KBr}}^{\text{max}} 5.72 (0\text{Ac}), 6.23 \text{ and } 6.68 \mu \text{m (aryl)}; \lambda_{\text{EtOH}}^{\text{max}} 276 (c 12,500)\) and 208 nm (16,900); n.m.r. data, see Tables 8 and 9; X-ray powder diffraction data: 15.63 \(vw\), 12.71 \(vw\), 10.58 \(vs\) (1,1), 8.48 \(vs\) (1,1) 6.96 \(m\), 5.60 \(m\), 5.27 \(m\), 5.00 \(m\), 4.74 \(w\), 4.51 \(w\), 4.39 \(s\) (2,2), 4.23 \(s\) (2,2), and 4.04 \(w\).

Anal. Calcd. for \(C_{22}H_{29}NO_{9}S\): C, 54.64; H, 6.05; N, 2.90; S, 6.63. Found: C, 54.87; H, 6.11; N, 3.21; S, 6.96.

B. From tetra-O-acetyl-α-D-glucopyranosyl bromide (1) and p-dimethylaminobenzenethiol.—The procedure of Montgomery, Richtmyer, and Hudson\(^{35}\) was modified. p-Dimethylaminophenyl thiocyanate (18 g, 101 mmoles) in dry ether (200 ml) was added with stirring to a suspension of lithium aluminum hydride (4.0 g, 105 mmoles) in dry ether (200 ml) that was maintained at 0°, and stirring was continued for 45 min. The mixture was processed by the general procedure \(^{137}\)

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used for the reduction of nitriles with lithium aluminum hydride. The resultant, ethereal solution was decanted from the gray-white residue, and evaporated to give p-dimethylaminobenzenethiol (9.0 g, 59 mmoles). The latter was not purified, because of the ease with which it undergoes oxidative dimerization, and it was condensed immediately with tetra-0-acetyl-a-D-glucopyranosyl bromide (20 g, 48.6 mmoles) by the general method of Purves. Evaporation of the yellow, turbid reaction-mixture gave a yellow syrup, which was partitioned between dichloromethane (100 ml) and water (100 ml). The turbid mixture was filtered, and the organic phase was separated, dried (magnesium sulfate), and evaporated to give a yellow syrup. Crystallization of the syrup from ether—petroleum ether gave yield 5.2 g (22%), m.p. (after recrystallization) 149-150°, identical by mixed m.p., i.r. spectrum, and X-ray powder diffraction pattern with prepared by method A.

Reaction of sulfenyl bromide 22 with N,N-dimethylaniline to give p-(dimethylamino)phenyl tetra-0-acetyl-a-D-glucopyranosyl disulfide (35).—To a suspension of 22 (3.086 g, 7.0 mmoles) in carbon tetrachloride (50 ml) was added N,N-dimethylaniline (2 ml, 15.8 mmoles), and the mixture was kept for 0.5 hr at 30°. The resultant solution was evaporated to a syrup at ~90°, the syrup was dissolved in dichloromethane (100 ml), and the solution was processed as described for compound 21. The syrup obtained showed major components having \( R_f \) 0.88 and 0.51 (t.l.c.). The mixture was subjected to column chromatography. The first fractions eluted from the column were evaporated to a syrup that was distilled at 180° (bath)/0.15 torr
to give p-bromo N,N-dimethylaniline \((\text{33})\); yield 0.168 g, m.p. 52-54° [lit.\(^{138,139}\) m.p. 54.7°], \(R_f\) 0.99 (detected very slowly)

\(^{138}\) A. Weber, Ber., \(\text{8},\) 714 (1875).


by sulfuric acid.

**Anal.** Calcd. for \(\text{C}_8\text{H}_{10}\text{BrN}\): C, 48.02; H, 4.89; Br, 39.82; N, 7.00. Found: C, 47.85; H, 4.89; Br, 39.94; N, 7.09.

Continued elution of the column gave a chromatographically homogeneous component, \(R_f\) 0.88, that crystallized from ethanol to give the disulfide \(2\) as pale-yellow needles; yield 307 mg (8.5%), m.p. (after one recrystallization) 156-157°, \([\alpha]_D^{22}\) -324° (c 1.6, chloroform); \(R_f\) 0.9; \(\lambda_{\text{max}}^{\text{kBr}}\) 5.72 (0Ac), 6.25, and 6.65 μm (aryl); \(\lambda_{\text{max}}^{\text{EtOH}}\) 311 (e 11,500), 268 (8,800), and 208 nm (12,700); n.m.r. data, see Tables 8 and 9; X-ray powder diffraction data: 16.50 vvw, 15.22 vvw, 10.84 vs (1), 8.48 s (3,3), 7.76 w, 6.76 vvw, 6.05 w, 5.74 vvw, 5.40 m, 5.09 m, 4.80 s (2), 4.41 w, 4.22 w, 4.06 s (3,3), 3.78 s (3,3), and 3.68 m.

**Anal.** Calcd. for \(\text{C}_{22}\text{H}_{29}\text{NO}_{9}\text{S}_2\): C, 51.25; H, 5.67; N, 2.72; S, 12.44. Found: C, 51.06; H, 5.78; N, 2.97; S, 12.13.

Continued elution of the column gave, first, a mixture of components having \(R_f\) 0.88 and 0.50, and then the component having \(R_f\) 0.50 alone; from the latter fractions, the crystalline diglucosyl disulfide \(2\) was obtained, yield 1.11 g (44%) m.p. (after
recrystallization from ethanol) 141-142°, identical with authentic 24 by mixed m.p., i.r. and n.m.r. spectra, and X-ray powder diffraction pattern.

A second experiment was performed under similar conditions, except that 5.0 g (11.3 mmoles) of 22 and 5 ml (39.4 mmoles) of N,N-dimethylaniline was used, and the initial syrupy product was heated for ~20 min at 105°/0.2 torr. Column-chromatographic fractionation of the product gave, in the early fractions, bis-(p-dimethylaminophenyl) disulfide (24), isolated crystalline from ether; yield 566 mg, m.p. 117.5-118.5° [lit. 140 m.p. 118°].

(140) V. Merz and W. Weith, Ber., 12, 1570 (1886).

Anal. Calcd. for C_{16}H_{20}N_{2}S_{2}: C, 63.11; H, 6.62; N, 9.20; S, 21.06. Found: C, 63.18; H, 6.56; N, 9.20; S, 20.98.

Further elution of the column gave fractions that contained tetra-O-acetyl-α-D-glucopyranosyl bromide (1), yield 2.155 g (46%), identical with an authentic sample by i.r. and n.m.r. spectra.

The next compound to be eluted from the column was the aryl glycosyl disulfide 35, yield 324 mg (6%), identical with the product obtained in the preparation already described. Subsequent fractions yielded the diglycosyl disulfide 24, yield 446 mg (5%), m.p. 141-142°.

In a third experiment, the reaction between 22 (1.17 g) and 2 equivalents of N,N-dimethylaniline was allowed to proceed for 60 hr at 30°, and the product was isolated without heating
it above 40°. Fractionation gave the aryl glycosyl monosulfide 22 (188 mg, 15%), and the diglycosyl disulfide 24 (579 mg, 60%).

Reaction of sulfinyl bromide 22 with (a) acetophenone, (b) acetone, (c) cyclohexanone, and (d) phenol.---Suspensions of the sulfinyl bromide 22 in carbon tetrachloride were treated, in separate experiments, with the following ketones or enols, in the molar proportions indicated (relative to 0.1 of 22): acetophenone (1.0 mole), acetone (4.4 moles), cyclohexanone (1.0 mole), and phenol (1.1 moles). The reaction mixture was kept for 1-3 hr at room temperature, and then processed by the general procedures used for isolating coupling products formed from 22. In each of the four experiments, the principal product, isolated crystalline in 70, 63, 76, and 75% yields, respectively, was bis(tetra-O-acetyl-β-D-glucopyranosyl) disulfide 24, m.p. 142-143°, identical with an authentic sample by mixed m.p., i.r. spectrum, and X-ray powder diffraction data.

Phenyl tri-O-acetyl-β-D-xylopyranosyl disulfide (39) from 1-thio-β-D-xylopyranose tetraacetate (15).---A suspension of 15, (1.867 g, 5.6 mmoles) in carbon tetrachloride (50 ml) was cooled to about -10° and bromine (2 ml) in carbon tetrachloride (8 ml) was added to the cooled suspension. Volatile materials were immediately removed on a rotary evaporator at ~30°/10 torr, to give a semi-crystalline, yellow residue. T.l.c. of a carbon tetrachloride solution (50 ml) of the residue showed three components in about equal intensity, Rf 0.76, 0.50, and 0.43. Benzenethiol
(1 ml) was added to the reaction mixture and an immediate color change, from yellow to colorless, was observed. T.l.c. of the solution, after 10 min at room temperature, showed a major component, $R_f$ 0.89, and three minor components, $R_f$ 1.00, 0.50, and 0.43. The solution was kept for 1 hr at room temperature, washed with aqueous sodium hydrogen carbonate (100 ml), dried (magnesium sulfate), and evaporated to a syrup. An n.m.r. spectrum of a chloroform-d solution of the crude product showed a low-field doublet, $\delta_{3.40}, J_{1,2} 4.0$ Hz [tri-O-acetyl-α-D-xylopyranosyl bromide (4), lit.92 $\delta_{3.30}, J_{1,2} 4.0$ Hz], $\nu$ 2.25-2.90 (aryl protons), $\nu$ 4.25-5.40 (complex multiplet), $\nu$ 5.65-6.70 (complex multiplet), and $\nu$ 7.94, 7.98 (singlets, OAc). The ratio of the integrated intensity of the low-field doublet to the acetyl signal was 1:16. A carbon tetrachloride solution of the product was kept 2 days at room temperature and evaporated to a syrup. Evaporation was continued until the water bath temperature reached 70°. The black, syrupy residue was dissolved in carbon tetrachloride (75 ml), aqueous sodium hydrogen carbonate (75 ml) was added to the solution, and the heterogeneous mixture was kept for 24 hr at room temperature. The phases were separated and the organic phase was dried (magnesium sulfate) and evaporated to a syrup. T.l.c. of the syrup revealed three major components, $R_f$ 0.89, 0.59, and 0.17 (point of application) and two minor components, $R_f$ 1.00 and 0.28. The syrup was subjected to column chromatography and the component, $R_f$ 0.89 was collected, evaporated to a syrup, and crystallized from a small volume of ether—petroleum ether to give a product formulated as
phenyl tri-O-acetyl-β-D-xylopyranosyl disulfide (39), yield 69.6 mg, 0.17 mmoles (3%). Decolorization (activated charcoal) of an ether solution of the product and recrystallization gave 39 as fine, white needles, m.p. 120-121°, [α]_D<sup>28</sup> -242° (c 1.2, chloroform); λ<sub>max</sub><sup>KBr</sup> 5.72 (OAc) and 6.77, 6.96 μm (aryl); λ<sub>max</sub><sup>EtOH</sup> 288 (ε 3,500) (shoulder), 238 (6,500), and 200 nm (10,000); n.m.r. data see Tables 8 and 9 and Figure 2; X-ray powder diffraction data:

13.63 w, 11.94 m, 10.64 s (1), 8.05 s (2), 6.98 vw, 5.33 s (3,3), 4.76 s (3,3), 4.45 m, 4.19 m, 3.99 m, 3.79 w, 3.64 w, 3.45 s (4).

Anal. Calcd. for C<sub>17</sub>H<sub>20</sub>O<sub>7</sub>S<sub>2</sub>: C, 50.98; H, 5.03; S, 16.01.

Found: C, 51.23; H, 5.46; S, 15.86.

In a brief report Horton and Miller gave for m.p. 122°, [α]<sub>D</sub> -250° (chloroform).

The reaction was repeated with 2.04 g (6.1 mmoles) of 15; however, the decomposition procedure was eliminated and the product was worked up 1 hr after addition of benzenethiol as described in the foregoing experiment. The syrupy product was crystallized from ether to give tri-O-acetyl-α-D-xylopyranosyl bromide (4), yield 1.262 g, 3.7 mmoles (61%). The product had m.p. 100-102° [lit. 95, 96 m.p. 102°]. The n.m.r. data were consistent with those previously reported.

Benzyl tri-O-acetyl-β-D-xylopyranosyl disulfide (40) from 1-thio-β-D-xylopyranose tetraacetate (15).--A suspension of 15, (557 mg, 1.67 mmoles) in carbon tetrachloride (30 ml) was brominated under the conditions described in the foregoing
experiment and α-toluenethiol (0.5 ml) was added to a carbon tetrachloride solution (50 ml) of the crude bromination product. After 10 min at room temperature, t.l.c. of the reaction mixture showed a major component, $R_F$ 0.86 and three minor components, $R_F$ 0.51, 0.41, and 0.32. After 1 hr at room temperature the solution was evaporated to a syrup, which was dissolved in dichloromethane (60 ml). The solution was washed with aqueous sodium hydrogen carbonate (50 ml), dried (magnesium sulfate) and evaporated to a syrup. Column chromatography of the product gave the component having $R_F$ 0.86 as a syrup, that crystallized from ether—petroleum ether to give benzyl 2,3,4-tri-O-acetyl-β-D-xylopyranosyl disulfide (40) as white needles, yield 125 mg, 0.30 mmoles (18%). Two re-crystallizations from ether—petroleum ether gave the analytical sample, m.p. 126°, $[\alpha]_D^{22}$ -229° (c 0.8, chloroform); $\lambda_{\text{max}}^{\text{EtOH}}$ 5.72 (0Ac), 6.76 and 6.90 μm (aryl); $\lambda_{\text{max}}^{\text{EtOH}}$ 270 (ε 1,500), 220 (8,500) (shoulder), and 209 nm (10,000); n.m.r. data, see Tables 8 and 9; X-ray powder diffraction data: 10.10 m, 8.54 s (3), 6.55 w, 5.96 w, 5.45 s (2,2), 5.02 s (1), 4.78 s (2,2), 4.39 vvw, 4.12 m, 3.97 vvw, 3.74 w, 3.41 m, 3.26 m, 3.12 w.

**Anal. Calcd. for C_{18}H_{22}O_{7}S_{2}:** C, 52.16; H, 5.35; S, 15.47. **Found:** C, 51.98; H, 5.32; S, 15.20.

**Phenyl tri-O-acetyl-α-L-arabinopyranosyl disulfide (41) from 1-thio-α-L-arabinopyranose tetraacetate (14).**—A solution of 14 (1.977 g, 5.9 mmoles) in carbon tetrachloride (50 ml) was cooled to about -10° and treated by the procedure described for the bromination of 1-thio-β-D-xylopyranose tetraacetate (12).
The product after evaporation was a yellow syrup. T.l.c. of a carbon tetrachloride solution (50 ml) of the syrup showed three components of approximately equal intensity, \( R_f \) 0.72, 0.51, and 0.44. Benzenethiol (1 ml) was added to the carbon tetrachloride solution and the reaction mixture was treated exactly as described for the preparation of the phenyl xylosyl disulfide 39. An n.m.r. spectrum (60 MHz) of a solution of the crude syrup in chloroform-\( d \) showed a low-field doublet, \( \gamma_{3.25} \) (H-1 of tri-O-acetyl-\( \beta \)-L-arabinopyranosyl bromide) [lit. \( \gamma_{3.25} \) for the \( \beta-D \) isomer], \( \gamma \approx 2.25-2.95 \) (aryl protons), \( \gamma \approx 4.4-5.4 \) (complex multiplet), \( \gamma \approx 5.65-6.55 \) (complex multiplet), and \( \gamma 7.89, 7.95, 7.99 \) (multiplet, OAc). The syrup was dissolved in carbon tetrachloride and the solution was treated as described for the preparation of the phenyl xylosyl disulfide 39. T.l.c. of the dark syrup showed a major component, \( R_f 0.89 \) and four minor components, \( R_f 0.55, 0.48, 0.28 \), and 0.18. The product was filtered through silica gel with solvent A as eluent; however, no separation occurred. The product was crystallized from ether—petroleum ether to give 0.564 g of fluffy, white needles. T.l.c. showed only a single component, \( R_f 0.89 \).

An n.m.r. spectrum (100 MHz) of a solution of the product in chloroform-\( d \) showed the compound to be impure by an unexpectedly large number of signals for H-5, 5', \( \gamma_{5.85-6.16} \) (8-line multiplet), \( \gamma_{6.29-6.65} \) (7-line multiplet). A doublet, \( \gamma_{5.29, 7.3} \) Hz was assigned to H-1 of phenyl 2,3,4-tri-O-acetyl-\( \alpha \)-L-arabinopyranosyl disulfide (41); however, the signal had an intensity too great for a single proton. An n.m.r. spectrum (100 MHz) of a solution
of the product in benzene-$d_6$ showed the presence of two doublets, 7.53 and 5.45, each having a spacing of 7.8 Hz. The multiplets assigned to H-5, 5' for the chloroform-$d$ solution were observed as narrower multiplets with benzene-$d_6$ as solvent, 7.65-6.47 (multiplet) and 7.65-7.05 (multiplet).

The product was allowed to crystallize incompletely from ethanol, and pure phenyl tri-O-acetyl-$\alpha$-$L$-arabinopyranosyl disulfide ($\mathcal{L}_2$) was obtained, yield 83.6 mg, 0.21 mmoles (4%), m.p. 124°, $[\alpha]_{D}^{28}$-171° (c 0.8, chloroform); $\lambda_{\text{max}}^{\text{KBr}}$ 5.72 (0Ac), 6.77 and 6.96 μm (aryl); $\lambda_{\text{max}}^{\text{EtOH}}$ 288 (ε 2,300) (shoulder), 238 (9,000), and 200 nm (16,000); n.m.r. data: see Tables 8 and 9 and Figure 4; X-ray powder diffraction data: 10.23 m, 9.22 m, 7.57 m, 7.70 w, 6.91 w, 5.77 m, 5.49 m, 5.05 s (1), 4.42 m, 4.19 m, 4.06 m.

Anal. Calcd. for $\text{C}_{17}\text{H}_{20}\text{O}_{7}\text{S}_2$: C, 50.98; H, 5.03; S, 16.01. Found: C, 50.78; H, 5.05; S, 16.22.

T.l.c. of the residual solution showed component, $\mathcal{R}_2$ 0.89, as the major product; however, further crystallization did not occur. The reaction was repeated with 2.032 g, 6.1 mmoles of $\mathcal{L}_2$, but the decomposition procedure was eliminated and the product was isolated 1 hr after the addition of benzenethiol. After the usual work-up the organic solution was evaporated to give a syrup, that crystallized from ether to yield colorless needles of tri-O-acetyl-$\beta$-$L$-arabinopyranosyl bromide (2), yield 1.257 g, 3.7 mmoles (61%), m.p. 138-139° [lit.94 m.p. 139°]. The n.m.r. data for a solution of the product were consistent with those previously reported for the $\beta$-$D$ isomer.92
Phenyl tetra-O-acetyl-β-D-galactopyranosyl disulfide (43) from 1-thio-β-D-galactopyranose pentaacetate (17).—Compound 17 (1.854 g, 4.56 mmoles) was brominated at low temperature as described for the preparation of the phenyl xylosyl disulfide and benzenethiol (1 ml) was added. T.l.c. of the reaction mixture 10 min after the addition of benzenethiol showed the reaction mixture to contain three components of approximately equal intensity, R_f 0.89, 0.83 (starting material), and 0.63. The reaction was repeated with 17 (2.030 g, 4.99 mmoles); however, the carbon tetrachloride solution of 17 was not cooled before bromination. Bromine (2 ml) in carbon tetrachloride (8 ml) was added to the solution, which was kept for ~30 sec at room temperature before evaporation. After rapid evaporation of the volatile components and dissolution of the syrupy product in carbon tetrachloride (50 ml), t.l.c. showed three minor components, R_f 0.91, 0.83, and 0.40, and a major component, R_f 0.64. Benzenethiol (1 ml) was added to the solution and after 10 min at room temperature t.l.c. showed the same three components described for the low temperature experiment; however, the component, R_f 0.83, was of diminished intensity. After 1 hr at room temperature, the reaction mixture was worked up in the usual manner and an n.m.r. spectrum (60 MHz) of the crude product in chloroform-d showed a complex multiplet, 72.26-3.10 (aryl), multiplets 74.39-5.13 and 75.23-6.25, a singlet at 76.47, a singlet at 77.58 (SaC), and a complex multiplet centered at 7 ~7.95. No low-field doublet was observed at 73.23 that would indicate the
presence of tetra-\(\alpha\)-acetyl-\(\beta\)-\(\delta\)-galactopyranosyl bromide (2).
The syrupy product was dissolved in carbon tetrachloride and

treated as described in the preparation of the phenyl xylosyl
disulfide 39, however, no decomposition was observed. A portion
of the compound having \(R_F\) 0.91, was separated by column chromato-

graphy. Complete separation of the components \(R_F\) 0.91 and 0.83 was

not obtained. The fractions that contained only component, \(R_F\)

0.91 were combined and evaporated to a syrup, which crystallized

as white, stout needles to give a product formulated as phenyl
tetra-\(\alpha\)-acetyl-\(\beta\)-\(\delta\)-galactopyranosyl disulfide (43), yield 161 mg,

0.3 mmole (6%). The product had m.p. 126-127° (after one recrystal-

lization from ether), \([\alpha]_D^{28} -155^\circ (c 1.4,\) chloroform); \(\lambda_{\text{max}}^\text{KBr} 5.75

(\text{OAc}), 6.80, 6.97 \mu\text{m} \) (aryl); \(\lambda_{\text{max}}^\text{EtOH} 288 (c 2,800) \) (shoulder); 238

(7,700), and 200 nm (15,500); n.m.r. data: see Tables 8 and 9 and

Figure 4; X-ray powder diffraction data: 10.52 s (3,3), 7.03 s (1),

6.07 s (2,2), 5.47 m, 5.07 m, 4.70 s (4), 4.37 m, 4.24 m, 4.05 s

(3,3), 3.87 w, 3.67 s (2,2), 3.50 s (3,3).

**Anal. Calcd. for \(\text{C}_{20}\text{H}_{24}\text{O}_9\text{S}_2\): C, 50.83; H, 5.12; S, 13.57.**

**Found:** C, 50.69; H, 5.24; S, 13.19.

Phenyl tetra-\(\alpha\)-acetyl-\(\beta\)-\(\delta\)-glucopyranosyl disulfide (23)

from 2,3,4,6-tetra-\(\alpha\)-acetyl-1-S-benzoyl-1-thio-\(\beta\)-\(\delta\)-glucopyranose

(29).—Bromine (1 ml) in carbon tetrachloride (9 ml) was added to

compound 22 (556 mg, 1.2 mmol) in carbon tetrachloride (50 ml).

The reaction mixture was kept for 3 min at room temperature before

rapid evaporation of volatile components to give a yellow crystal-

line residue. The residue was dissolved in carbon tetrachloride
(50 ml) and benzenethiol (0.3 ml) was added. T.l.c. of the reaction mixture after 10 min at room temperature showed 2 components, Rf 0.89 (major) and 0.56. After 1 hr at room temperature, the reaction mixture was washed with a saturated solution of aqueous sodium hydrogen carbonate, dried (magnesium sulfate), and evaporated to a syrup, that crystallized from ether–petroleum ether to yield phenyl tetra-O-acetyl-β-D-glucopyranosyl disulfide (23), 165 mg, 0.35 mmole (29%), in two crystal crops. The product had m.p. 121-122° (after 1 recrystallization from ethanol), [lit.73 m.p. 123-124°]. The product was identical to an authentic sample by X-ray powder diffraction pattern and by comparison of n.m.r. spectral data for a chloroform-d solution.73

T.l.c. of the mother liquors after 5 days showed a mixture of components, Rf 0.89 (major), 0.70, 0.63, 0.56, 0.32, and 0.19 (major, point of application).

Bromination of 1-thio-a-D-glucopyranose pentaacetate (18) and trapping of the reaction product with benzenethiol.—Compound 18 (360 mg, 0.9 mmole) was suspended in carbon tetrachloride and bromine (~1 ml) was added to the suspension at room temperature. Volatile materials were rapidly evaporated to give a yellow crystalline residue. The residue lost weight on the balance pan, thus attempt at further characterization was terminated. The residue was dissolved in carbon tetrachloride (50 ml) and benzenethiol (0.3 ml) was added. The reaction mixture was kept 1 hr at room temperature and the work-up was in the usual manner. The reaction product, a syrup, was evaporated twice from carbon
tetrachloride (50 ml). An n.m.r. spectrum of a solution of the syrup in chloroform-d showed a multiplet, 72.25-2.75 (aryl protons), \( \tau \approx 3.65 \) (H-1 of \( \mathrm{L}^8 \)), 74.03 (low intensity doublet with a spacing of \( \sim 6.0 \text{ Hz} \), 74.20 doublet, with a spacing of \( \sim 5.8 \text{ Hz} \)), 74.4-5.1 (multiplet), 74.4-5.5 (multiplet), 7.54 (SAc), 7.79 (multiplet, OAc). The ratio of the integrated intensity of the S-acetyl signal to the O-acetyl signal indicated that \( \sim 40\% \) of the starting material was present. T.i.c. of the product showed two major components, \( R_\lambda \approx 0.86 \) and 0.80, and four minor components, \( R_\lambda \approx 0.66, 0.54, 0.28, \) and 0.21 (point of application). The component, \( R_\lambda 0.80 \) corresponded to \( \approx \). The faster moving components, \( R_\lambda 0.86 \) and 0.83 were separated from the mixture with the use of column chromatography. An unsuccessful attempt was made to separate these components by fractional crystallization from ethanol. A mixture of the compounds was obtained as indicated by the n.m.r. spectrum (100 MHz) of the product in a chloroform-d solution. See Figure 5 for the n.m.r. spectrum of the crude product. Further attempts at purification of these compounds were unsuccessful.
EXPERIMENTAL - PART B

Photolysis procedure. -- The ultraviolet source for photolysis experiments was a mercury-arc lamp (Hanovia Type L, Model 697A, Hanovia Lamp Division, Engelhard Hanovia Inc., Newark, N. J.). The lamp was equipped with a water-cooled, quartz immersion-well (Hanovia Model 19431) and the assembly was mounted in a Pyrex reaction vessel. Photolysis was effected with unfiltered light and the solutions undergoing photolysis were stirred with a magnetic stirring bar and the apparatus was continually flushed with nitrogen. The photolysis solvent was methanol (Spectro grade, Eastman Organic Chemicals, Rochester, New York). All N,N-dimethylthiocarbamates were subjected to column chromatography before photolysis to ensure purity. All other general procedures were as described for General methods, Part A.

Preparation of 3-O-dimethylthiocarbamoyl-1,2;5,6-di-O-isopropylidene-α-D-glucopyranose (46). -- Compound 46 was prepared according to the method of Horton and Prihar. A solution of 1,2;5,6-di-O-isopropylidene-α-D-glucofuranose (50, 25.0 g, 96.0 mmoles) in N,N-dimethylformamide (200 ml) was treated with 3.30 g of a 61% sodium hydride dispersion in mineral oil (Metal Hydrides, Inc., Beverly, Massachusetts). The mixture was cooled and maintained below 20°, while being stirred under a nitrogen atmosphere.
for 1 hr. To the stirred mixture was added dimethylthiocarbamoyl chloride (12.3 g). The mixture was stirred 1.5 hr and poured onto ice and water (~500 g) with vigorous stirring. Solid product (27.0 g, 77.6 mmol, 80.8%) separated and was recrystallized from ethanol to give 46, yield 18.0 g, 51.8 mmol (54.0%), m.p. 105-106°, [α]$_D^{28}$ -62.6° (c 1.3, chloroform) [lit. 1 m.p. 105.5°, [α]$_D^{22}$ -70° (c 2, chloroform)]. The n.m.r. data (60 MHz) were consistent with those previously reported. 1

Preparation of 1,6-anhydro-4-O-dimethylthiocarbamoyl-2,3-O-isopropylidene-β-D-mannopyranose (47).—Compound 47 was prepared from 1,6-anhydro-2,3-O-isopropylidene-β-D-mannopyranose 129 according to the method of Horton and Prihar 1 by Diana M. Williams (National Science Foundation Undergraduate Research Participant, Summer, 1967). The n.m.r. data (A-60 n.m.r. spectrometer) were consistent with those previously reported, 1 m.p. 136-137° [α]$_D^{28}$ -83.0° (c 1.080, chloroform) [lit. 1 m.p. 135°, [α]$_D^{20}$ -64.5° (c 2, chloroform)].

Preparation of 6-O-dimethylthiocarbamoyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (48).—Compound 48 was prepared from 1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (57) (Aldrich Chemical Company, Inc., Milwaukee, Wisconsin) according to the method of Horton and Prihar. 1 Compound 57 (14.0 g, 53.8 mmol) was dissolved in N,N-dimethylformamide (200 ml) and treated with a 61% sodium hydride dispersion (1.94 g) and then with dimethylthiocarbamoyl chloride (6.65 g) by the procedure used in the preparation of 46. The crude yield of 48 was 14.5 g, 41.7 mmol, 77.5%. Re-crystallization from ethanol gave 12.0 g, 34.5 mmol (64.1%).
m.p. 90-91°, $\left[a\right]_{D}^{28} -59.4^\circ$ (c 3.1, chloroform). The n.m.r. data were consistent with those reported previously.\(^1\) [Lit.\(^1\) m.p. 88-89°, $\left[a\right]_{D}^{20} -47.3$ (c 2, chloroform)].

Preparation of 1,2:5,6-di-O-isopropylidene-3-O-p-tolylsulfonyl-α-D-glucopyranose (53).—To a solution of 1,2:5,6-di-O-isopropylidene-α-D-glucopyranose (50, 25.0 g, 96.0 mmoles) in pyridine (250 ml) was added p-toluenesulfonyl chloride (21.0 g, 110 mmoles). After 2 days at room temperature, water (25 ml) was added and stirring was continued for an additional 1 hr. The reaction mixture was poured onto vigorously stirred ice and water (~400 g) and the crystalline product was filtered, washed with water, and recrystallized from ethanol to give fine, white needles in two crops, yield 28.0 g, 67.5 mmoles (70.3%), m.p. 120-121°, $\left[a\right]_{D}^{28} -68.8^\circ$ (c 1.03, chloroform) [lit.\(^{120}\) m.p. 120-121°, $\left[a\right]_{D}^{20} -81.7^\circ$ (1,1,2,2-tetrachloroethane)]. The n.m.r. data (60 MHz n.m.r. spectrometer) were consistent with those reported by Jewell, Horton, and Prihar.\(^{21}\)

Preparation of 3-deoxy-3-hydrazino-1,2:5,6-di-O-isopropylidene-α-D-allopyranose (54).—Compound 54 was prepared according to the method of Coxon and Hough\(^{124}\) and Wolfson and co-workers.\(^{123}\) To 97% anhydrous hydrazine (100 ml) was added 1,2:5,6-di-O-isopropylidene-3-O-p-tolylsulfonyl-α-D-glucopyranose (53, 25.0 g, 60.3 mmoles) and the reaction mixture was refluxed under a stream of nitrogen for 40 hr. The solution was cooled and extracted with three 100-ml portions of peroxide-free ether. The combined organic extract was washed with 20 ml of 50% (w/v) potassium
hydroxide and dried (magnesium sulfate). The organic solution was concentrated and fine white needles formed in the flask. The product was filtered to yield 5.8 g, 21.1 mmoles (35.0%) of 54, Rf 0.63, m.p. 90-93°. The product showed signs of decomposition after 4 hr at room temperature. N.m.r. data (CDCl₃, 60 MHz):

\[ \gamma_{4.28} \text{ (doublet, } H-1, J_1, 4.0 \text{ Hz), } \gamma_{5.31} \text{ (triplet, } H-2, J_2, 3 \text{ Hz), } \gamma_{5.69-7.00} \text{ (8-proton multiplet, } H-3, 4, 5, 6, 6',-\text{NH}_2), \gamma_{8.46, 8.57, 8.66} \text{ (3, 3', and 6-proton singlets, } -\text{CMe}_2) ] \text{ [lit.]}^{119}

 Examination of the ethereal mother liquors by t.l.c. revealed the presence of five components, Rf 0.88, 0.75, 0.63 (major), 0.43, and 0.16 (spotting point). Further crystallization did not occur.

**Photolysis of 6-O-dimethylthiocarbamoyl-1,2,3,4-di-O-isopropylidene-\(\alpha\)-D-galactopyranose (48).**—A solution of 48 (4.82 g, 13.9 mmoles) in methanol (150 ml) was photolyzed for 113 hr. The brown photolysis solution was evaporated to yield a brown syrup. The residue was partially dissolved in ether (50 ml) and filtered to give 553 mg of brown solid. The solid remained at the point of application on t.l.c. The filtrate was decolorized with charcoal and evaporated to give a light yellow syrup. The syrup was dissolved in methanol (150 ml) and photolyzed for an additional 48 hr. The above work-up was repeated to give an additional 410 mg of residue and 2.933 g of yellow syrup. An
n.m.r. spectrum (60 MHz) of the crude syrup revealed the absence of a signal for the $-\text{NMe}_2$ protons of 4 at 6.60 and 6.82. T.l.c. (solvent A) revealed four components, $R_f$ 0.98, 0.93 (yellow-brown, major), 0.78, and 0.56 (black). T.l.c. (solvent B) revealed nine components, $R_f$ 0.93 (very weak), 0.86 (very weak), 0.80 (very weak), 0.74 (very weak), 0.70 (major, yellow-brown), 0.54 (weak), 0.41 (very weak), 0.38 (very weak), and 0.32 (major, brown-black).

The syrup was subjected to column chromatography on silica gel with solvent B as eluent. Fractions (10 ml) were collected and monitored by t.l.c. The fractions containing the major component ($R_f$ 0.70) were combined and evaporated to yield 6-deoxy-1,2:3,4-di-O-isopropylidene-a-D-galactopyranose (56) as a light yellow syrup, 505 mg, 2.1 mmoles (15%). The syrup was maintained at -15° and a solid mass of crystals formed overnight. The compound was distilled at a bath temperature of 100-110°/0.2 torr to give a colorless syrup. The syrup crystallized upon seeding, m.p. 33-35°, $[\alpha]_D^{19}$ -53.6° (c 1.2, chloroform). Freudenberg and Raschig reported m.p. 37°, $[\alpha]_D^{19}$ -52.4°. Cone and Hough reported m.p. 30-35° after distillation of the product. The 60 MHz n.m.r. spectrum in acetone-d$_6$ was identical to that described by Cone and Hough. See Tables 10 and 11 for 100 MHz n.m.r. data for chloroform-d and acetone-d$_6$ solutions; X-ray powder diffraction data: 11.86 m, 9.11 s (2,2), 6.57 s (2,2), 6.24 s (3,3), 5.58 s (3,3), 5.22 s (1,1), 4.88 s (1,1), 4.56 s (1,1).
The fractions containing the major component, \( R_p 0.32 \)
were combined and evaporated to yield 1,2:3,4-di-\( \beta \)-isopropylidene-
\( \alpha \)-\( \beta \)-galactopyranose (57), 1.287 g, 4.94 mmoles (35.5%). The light
eyellow syrup was distilled (bath temperature 150-165\(^\circ\)C/0.2-0.3 torr);
\([\alpha]_D^{19} -53.1^\circ\) (c 6.2, chloroform), [lit. \([\alpha]_D^{127} -55^\circ\) (chloroform)]
and \([\alpha]_D^{20} -59^\circ\) (c 1.4, chloroform)]. The n.m.r. spectrum for
a chloroform-d solution of 57 was comparable with that described
by Cone and Hough.

Characterization of 1,2:3,4-di-\( \beta \)-isopropylidene-\( \alpha \)-\( \beta \)-galactopyranose as its 6-p-toluenesulfonate (58).—Compound 58 was
prepared as a crystalline derivative of the photolysis product, 57,
essentially by the method described by Cone and Hough. Compound 57 (311 mg, 1.2 mmoles) obtained from the previous experiment
was dissolved in pyridine (10 ml) and p-toluenesulfonyl chloride
(288 mg, 1.51 mmoles) was added. The reaction mixture was
stirred for 2 days at room temperature and then poured onto ice
and water (~100 g). Crystallization did not occur. The aqueous
solution was decanted and 30-ml portions of toluene were twice
evaporated from the syrupy residue. The syrup was dissolved in
ether (30 ml), decolorized with activated carbon and evaporated
to a syrup. The syrup was dissolved in ethanol (2 ml) and seeded
with 58. Crystallization occurred immediately. The crystallization
mixture was refrigerated and 58 was obtained in two crystal crops
as white platelets, yield 280 mg, 0.7 mmole (58%), m.p. 100-101\(^\circ\)
(lit. 99-100\(^\circ\)). The x-ray diffraction pattern and n.m.r.
spectrum (chloroform-d, 60 MHz) were identical with those
previously reported by Horton, Nakadate, and Tronchet.\textsuperscript{128}

**Preparation of 6-deoxy-1,2:5,6-di-O-isopropylidene-α-D-galactopyranose (56).**—The procedure of Freudenberg and Raschig\textsuperscript{125} was followed for the preparation of an authentic sample of 56. Sulfuric acid (1 ml) was added to 6-deoxy-α-D-galactopyranose (D-fucose, 1.009 g, 6.1 mmoles) (Pfanstiehl Laboratories, Inc., Waukegan, Illinois) in acetone (30 ml). The reaction mixture was kept for 4 hr at room temperature. The solution was neutralized with sodium carbonate, filtered, and evaporated to a syrup. T.l.c. of the syrup revealed a major component, \( R_t \) 0.65 and 0.13 (point of application). Distillation of the syrup at 0.2-0.3 torr (bath temperature 100-116°) gave a colorless syrup, yield 1.15 g, 4.7 mmoles (77%). The syrup was refrigerated (-15°) overnight and white crystals formed immediately upon removal from refrigeration, m.p. 35-36°. This compound was identical with 56 prepared by photolysis of 48 by comparison of n.m.r. spectral data and X-ray powder diffraction data.

**Photolysis of 3-O-dimethylthiocarbamoyl-1,2:5,6-di-O-isopropylidene-α-D-glucopyranose (46).**—A solution of 46 (5.049 g, 14.5 mmoles) in methanol (150 ml) was photolyzed for 37 hr and the brown photolysis solution was treated by the procedure used for preparation of 56 from 48 and the amount of brown residue formed was 393 mg. The yellow syrup obtained after decolorization of the filtrate was redissolved in methanol (150 ml) and the solution was photolyzed for an additional 31 hr. Processing the product as before gave 262 mg of brown residue. An ethereal
solution of the syrup was decolorized and evaporated to yield a yellow syrup. The syrup was redissolved in methanol (150 ml) and photolyzed for 65 hr. Isolation as previously described gave 324 mg of brown residue and 2.746 g of yellow syrup. An n.m.r. spectrum (60 MHz n.m.r. spectrometer) indicated the absence of signals for the -NMe2 protons of 46 at 6 6.61 and 6.86. The residue remained at the spotting point on t.l.c. (solvent A). T.l.c. of the syrup in the same solvent system revealed five components, Rf 0.97, 0.93, 0.85 (major), 0.62 (very minor), and 0.57 (major). T.l.c. of the syrup (solvent B) as eluent gave eight components Rf 0.75 (very minor), 0.71 (very minor), 0.66 (very minor), 0.64 (very minor), 0.60 (major), 0.49 (very minor), and 0.36 (major).

The syrup was subjected to column chromatography on silica gel with solvent A as eluent. Fractions were collected every 10 ml and monitored by t.l.c. The fractions containing the major component Rf 0.85 were combined and evaporated to give 3-deoxy-1,2:5,6-di-α-isopropylidene-α-D-ribo-hexofuranose (49) as a light-yellow syrup, yield 610 mg, 2.50 mmolts (17%). The syrup was distilled at 0.4 torr (bath temperature 115-125°) to give a colorless syrup [α]D21 -6.3° (c 1.9, chloroform). Černý and Pacák117 gave [α]D18 -8.6° (c 3.7, ethanol) and Hedgley, Overend, and Rennie118 gave [α]D18 -5.78° (c 4.2, ethanol). The 60-MHz n.m.r. data for carbon tetrachloride solution of 49 were in agreement with those reported by Brown and Jones.119 (See Tables 10 and 11 for 100 MHz n.m.r. data for chloroform-d, benzene-d6, and acetone-d6 solutions).

A crystalline derivative 3-deoxy-1,2-α-isopropylidene-α-D-ribo-
hexofuranose (51) was prepared from 49 (44 mg, 0.18 mmole) by partial hydrolysis according to the method of Hedgley, Overend, and Rennie. The yield of syrupy 51 was 32 mg, 0.16 mmole (89%). The syrup was crystallized from chloroform—petroleum ether to yield 17 mg, 0.08 mmole (44%) of 51 as white needles, m.p. 82-83°, [lit. m.p. 84°]. The compound was identical by X-ray powder diffraction data with an authentic sample.

The fractions containing the major component (Rf 0.57) were collected and evaporated to give 1,2:5,6-di-O-isopropylidene-\(\alpha\)-D-glucofuranose (50) as a syrup, that crystallized; yield 967 mg, 3.71 mmoles (26%). Recrystallization from cyclohexane gave white needles, m.p. 106° (lit. m.p. 105-109°). The n.m.r. spectrum of 50 in chloroform-d was comparable with that previously reported, and the X-ray powder diffraction pattern data were identical with that of an authentic sample of 50; X-ray powder diffraction data: 11.62 m, 9.73 s (3), 8.07 w, 6.05 w, 5.33 s (1), 4.96 s (2,2), 4.67 w, 4.16 s (2,2), 3.89 w, 3.72 w.

The photolysis of 46 was repeated. The yield of 49 was 22.5% and the yield of 50 was 32%.

Photolysis of 1,6-anhydro-4-O-dimethylthiocarbamoyl-2,3-O-isopropylidene-\(\beta\)-D-mannopyranose (47).--A solution of 47 (1.838 g, 6.4 mmoles) in methanol was photolyzed for 69 hr and the brown photolysis solution was treated by the procedure used for preparation of 56 from 48 and the brown residue collected was 52 mg. The decolorized, ethereal solution was evaporated to give a yellow syrup. An n.m.r. spectrum of the crude syrup in
chloroform-d indicated the absence of the singlets at 76.62 and 76.82 corresponding to the -NMe_2 protons\(^1\) of 47. The syrup crystallized spontaneously to give white needles, 806 mg. The brown residue remained at the point of application on t.l.c. (solvent A). The white needles were dissolved in chloroform. T.l.c. of the solution (solvent A) revealed seven components, \(R_f\) 0.98 (minor), 0.96 (minor), 0.91 (minor), 0.88 (minor), 0.80 (major), 0.73 (very minor), and 0.43 (major). T.l.c. of the solution (solvent B) showed nine components, \(R_f\) 0.93 (very minor), 0.86 (minor), 0.78 (minor), 0.70 (minor), 0.63 (minor), 0.57 (major), 0.46 (minor), 0.33 (minor), and 0.28 (major). The chloroform solution was evaporated to give white crystals of crude product. The product was subjected to column chromatography with solvent A as eluent and 10-ml fractions were collected and monitored by t.l.c. The fractions containing the major component \(R_f\) 0.80 were combined and evaporated to yield a crude crystalline product formulated as 1,6-anhydro-4-deoxy-2,3-O-isopropylidene-\(\beta\)-D-lyxo-hexopyranose (59), yield 228 mg, 1.2 mmoles (19%), m.p. 119-120\(^\circ\). Recrystallization from ethanol gave white needles, m.p. 120-121\(^\circ\), [\(\alpha\)]\(_{D}^{19}\) \(\equiv\) -16.7\(^\circ\) (c 1.05, chloroform). After three recrystallizations from ethanol the product had m.p. 125-126\(^\circ\), [\(\alpha\)]\(_{D}^{23}\) \(\equiv\) -21.9\(^\circ\) (c 0.8, chloroform). N.m.r. data: see Tables 10 and 11 for solutions in chloroform-d and acetone-d\(_6\); X-ray powder diffraction data: 7.42 s (3), 6.14 m, 5.73 s (3), 5.50 s (1), 5.13 m, 4.82 s (2,2), 4.40 vvw, 4.20 s (2,2), 3.96 w, 3.85 vvw, 3.71 w, 3.53 w, 3.09 w, 3.02 w.
Anal. Calcd. for CgH_{14}O_{4}: C, 58.49; H, 7.57. Found: C, 58.52; H, 7.61.

The fractions containing the major component R_f 0.28 were collected and the solvent was evaporated to yield 1,6-anhydro-2,3-isopropylidene-\(\beta\)-D-mannopyranose (60), yield 220 mg, 1.1 mmoles (17%), m.p. 157-159°. Recrystallization from butyl alcohol gave m.p. 160-161° (lit. 129 m.p. 161-162°). The product was identical with an authentic sample by n.m.r. spectrum in chloroform-d and by X-ray powder diffraction pattern. The photolysis of 47 was repeated to yield 26% of 52 and 29% of 60.

Preparation of 3-deoxy-3-iodo-1,2:5,6-di-0-isopropylidene-\(\alpha\)-D-glucofuranose (52).—The procedure of Brown and Jones was followed essentially except that triethylamine was used as a base in place of \(N\)-methylmorpholine, and the product was isolated by column chromatography instead of by distillation. To 3-deoxy-3-hydrazino-1,2:5,6-di-0-isopropylidene-\(\alpha\)-D-glucofuranose (54) (15.0 g, 5.5 mmoles) dissolved in chloroform (100 ml) containing triethylamine (0.77 ml, 560 mg, 5.5 mmoles) was added iodine (870 mg, 11.0 mmoles) in chloroform (200 ml). The solution was kept until t.l.c. showed that 54 had completely reacted. The solution was then washed with aqueous sodium hydrogen sulfite (iodine color disappeared) and dried (magnesium sulfate). Evaporation gave crude 52 as a light yellow syrup, yield 11.0 g, 3.0 mmoles (55%). T.l.c. revealed a principal component, R_f 0.91 and five very minor components, R_f 0.80, 0.49, 0.33, and 0.21. The product having R_f 0.91 was separated by column chromatography with solvent A as
eluent. The solvent was evaporated to give a light yellow syrup. The syrup was dissolved in ether (200 ml), decolorized, and re-evaporated to give 52 as a colorless syrup, yield 8.4 g, 2.3 mmoles (42%). The syrup solidified spontaneously or could be crystallized from a small volume of dichloromethane to give colorless platelets m.p. 38-41°, [α] \textsubscript{D} \textsuperscript{21} = -15.1° (c 3.0, chloroform). The platelets reverted to a syrup in air at room temperature after a short time. The n.m.r. spectrum in carbon tetrachloride was the same as that reported previously\textsuperscript{119} however, the reported proton assignments were incorrect. (See Tables 10 and 11 for 100 MHz n.m.r. data with chloroform-d as the solvent).

Preparation of 3-deoxy-1,2;5,6-di-0-isopropylidene-2-D-ribo-hexofuranose (49).—A reference sample of 49 was prepared from 52 according to the method of Brown and Jones.\textsuperscript{119} Compound 52 (1.964 g, 5.3 mmoles) was dissolved in 50 ml of ethanol and 0.5 g of sodium acetate was added together with 4 g of Raney nickel No. 28 (W. R. Grace and Co., So. Pittsburg, Tenn.). The mixture was hydrogenated at 20 lb in\textsuperscript{-2} until uptake ceased. The solution was filtered and evaporated to a syrup. The syrup was dissolved in dichloromethane (50 ml), washed twice with water, dried (magnesium sulfate), and re-evaporated to a syrup. The syrup was distilled at a bath temperature of 115-130°/0.1 torr to give 1.173 g, 4.80 mmoles (91%) of colorless syrup. T.l.c. revealed the presence of two components, R\textsubscript{L} 0.87 (minor) and 0.74 (major). The syrup was subjected to column chromatography with solvent A as eluent and the separation was monitored by t.l.c. The fractions
containing the component having $R_f$ 0.74 were collected and evaporated to give 642 mg, 2.6 mmoles (49%) of 49 as a colorless syrup, $[\alpha]^D_{20} -6.0^\circ$ (e 5.5, chloroform) [lit. $[\alpha]^D_{18} -8.6^\circ$ (e 3.7 ethanol) and $[\alpha]^D_{18} -5.78^\circ$ (e 4.2, ethanol)]. The n.m.r. data were in agreement with those described previously (see Tables 10 and 11 for n.m.r. data of chloroform-d, benzene-d$_6$, and acetone-d$_6$ solutions.

Preparation of 3-deoxy-1,2-O-isopropylidene-α-D-ribo-hexofuranose (51).—A reference sample of 51 was prepared as a crystalline derivative of 49 prepared from 52 by an established route. The method was a slight modification of the one used by Hedgley, Overend, and Rennie. Compound 49 (266 mg, 1.1 mmole) was dissolved in 10 ml of ethanol and the solution was added to 400 ml of 0.01 N hydrochloric acid. The reaction mixture was kept undisturbed for 5 hr at room temperature and was then neutralized with sodium hydrogen carbonate. The aqueous solution was evaporated to dryness and the residue was extracted with three 30-ml portions of chloroform. The combined extracts were evaporated to give a colorless syrup, yield 0.177 g, 0.87 mmole (79%). T.l.c. of the syrup revealed two very minor components, $R_f$ 0.79 and 0.75 and a major component at the point of application. The syrup was crystallized from chloroform—petroleum ether to yield 51 as white needles, 109 mg, 0.53 mmole (48%), m.p. 82°, $[\alpha]^D_{23} -12.6^\circ$ (e 1.1, ethanol), $[\alpha]^D_{21} -19.0^\circ$ (e 1.69, chloroform) [lit. $[\alpha]^D_{17}$ m.p. 84°]; X-ray powder diffraction data: 9.89 vw, 8.71 vw, 7.51 s (2), 5.42 m, 4.87 s (1,1), 4.35 m, 3.90 w, 3.62 m, 3.45 vw, 3.20 vw. See Tables 10 and 11 for 100 MHz n.m.r. data in chloroform-d.
Photolysis of 3-deoxy-3-ido-1,2:5,6-di-O-isopropylidene-\(\alpha\)-D-glucopyranose (52).-Compound 52 (1.16 g, 3.1 mmoles) was dissolved in methanol (150 ml) containing dissolved sodium hydroxide (163 mg, 4.08 mmoles, 1.3 equivalents). The solution was photolyzed for 4 hr and evaporated to a syrup. The residue was swirled with ether (50 ml) and yellow-white insoluble material (574 mg, presumably sodium iodide and excess sodium hydroxide) was filtered off. T.l.c. of the ether solution revealed a major component (\(R_f^0.85\)), a minor component (\(R_f^0.55\)), and a substantial component having \(R_f^0.47\). Streaking was observed on the t.l.c. plate from the component having \(R_f^0.47\) to the point of application. The ether solution was evaporated to a syrup, which was dissolved in dichloromethane (50 ml). The solution was washed with water (50 ml), dried (magnesium sulfate), and re-evaporated to a syrup; yield 440 mg. The product was subjected to column chromatography with solvent A as eluent. The separation was monitored by t.l.c. and the fractions containing the component having \(R_f^0.85\) were collected and evaporated to give 49 as a colorless syrup, yield 248 mg, 1.0 mmoles (32%). The syrup was distilled at a bath temperature of 100-110\(^\circ\)/0.2 torr; \([\alpha]^21_D^0\) -7.1\(^\circ\) (c 1.6, chloroform) \[\text{lit.}^117 [\alpha]^{18}_D^0\] -8.16\(^\circ\) (c 3.7, ethanol) and \[\text{lit.}^118 [\alpha]^{18}_D\] -5.78\(^\circ\) (c 4.2, ethanol)]. The n.m.r. spectrum coincided with that described previously\(^119\) (see Tables 10 and 11 for n.m.r. data of chloroform-\(d_2\), benzene-\(d_6\), and acetone-\(d_6\) solutions.

The product 49 (45 mg, 0.2 mмоles) was converted into
crystalline (3-deoxy-1,2-0-isopropylidene-\(\alpha\)-D-ribo-hexofuranose) by the method already described. The yield of syrup was 26 mg, 0.13 mmole (65%). Crystallization of the syrup from chloroform—petroleum ether gave 51 as white needles, yield 18 mg, 0.09 mmole (45%), m.p. 80-81°. The compound was identical with an authentic sample of 51 by comparison of n.m.r. spectra and X-ray powder diffraction patterns.

Desulfurization of bis(1,2:5,6-di-0-isopropylidene-\(\alpha\)-D-glucofuranosyl) disulfide (55).\(^{113}\) Compound 55 (328 mg, 0.6 mmole) was dissolved in absolute ethanol (40 ml) and excess Raney nickel No. 28 (W. R. Grace and Company, So. Pittsburg, Tenn.) (10 g) was added to the solution. The reaction mixture was refluxed for 5 hr and the ethanol solution was filtered off. The Raney nickel was refluxed with two additional 30-ml portions of ethanol and the nickel was filtered off. The combined ethanol filtrate was evaporated to a syrup. T.l.c. of the syrup revealed four components, \(R_f\) 0.85 (major), 0.53 (very minor), 0.36 (minor), and a substantial component was observed at the application point. The syrup was subjected to column chromatography with solvent A as eluent. The chromatographic separation was followed by t.l.c. and the fractions containing the major component, \(R_f\) 0.85 were combined and evaporated to yield 49 as a colorless syrup, yield 102 mg, 0.4 mmole (33%); \([\alpha]_{D}^{21}\) -6.3° (c 1.9, chloroform), \([\text{lit.}^{117}\ [\alpha]_{D}^{18}\ -8.6° (c 3.7, ethanol) and \text{lit.}^{118}\ [\alpha]_{D}^{18}\ -5.78° (c 4.2, ethanol)]. An n.m.r. spectrum of the syrup was identical with that of an authentic
sample of 49 (see Tables 10 and 11 for n.m.r. data for chloroform-d, benzene-d₆, and acetone-d₆ solutions).

Partial hydrolysis of the product as already described for characterization of 49 gave 3-deoxy-1,2-L-isopropylidene-a-D-ribo-hexofuranose (51) as white needles from chloroform–petroleum ether, yield 41 mg, 0.20 mmole (57%), m.p. 81-82°. This product was identical with an authentic sample by comparison of n.m.r. spectra and by X-ray powder diffraction data.
TABLE 8
CHEMICAL SHIFT DATA FOR 1-THIO DERIVATIVES

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical shifts (τ) and signal multiplicities</th>
<th>H 5</th>
<th>H 6</th>
<th>OAc integral</th>
<th>Aryl protons integral</th>
<th>Other protons</th>
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<tr>
<td>3₁ ³</td>
<td>5.72d 485t 468t 5.02t</td>
<td>6.310</td>
<td>573q 5.95q 7.86, 7.99(6)</td>
<td>2.74-327(5)</td>
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<tr>
<td>3₂ ²</td>
<td>551d 5.13t 4.80t 5.02t</td>
<td>6.34m 575q 5.87q 7.89, 7.91, 8.00, 8.04</td>
<td>2.47, 256, 2.74, 3.38, 3.47</td>
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<td>7.00</td>
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<td>3₂ ³</td>
<td>537d 4.40-491q 4.40-4.65m 4.65m</td>
<td>5.85-6.13</td>
<td>7.86, 7.89, 8.03(6)</td>
<td>2.22-2.41 and 255-279(5)</td>
<td>7.99, 8.04(6)</td>
<td>6.02(2)</td>
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<td>3₉</td>
<td>4.70-5.39-5.81q 6.62q e</td>
<td>8.97, 8.98</td>
<td>230-251 and 253-280(5)</td>
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<td>3.32, 3.40(4)</td>
<td>NMe₂</td>
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<td>4₁ ³</td>
<td>526d 4.51-4.98-5.90q 6.33q e</td>
<td>784-789, 226-252 and 7.94</td>
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a Data from 100-MHz spectra measured in CDCl₃. 
b Signals are singlets unless a range or multiplicity (d, doublet; m, multiplet; o, octet; q, quartet; t, triplet) is given. 
c Assignments verified by spin decoupling. 
d Signal disappears after deuteration. 
³ Not applicable.
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<th>Compound</th>
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<th>( J_{23} )</th>
<th>( J_{34} )</th>
<th>( J_{45a} )</th>
<th>( J_{45b} )</th>
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$^a$ Data from 100-MHz spectra measured in CDCl$_3$. $^b$ For H-5a 5b 6a 6b (a=high-field and b=low-field protons). $^c$ Not measured due to second order effects. $^d$ Not applicable.
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<td>6.08 m</td>
<td>5.83–</td>
<td>6.08 m</td>
<td>8.54, 8.62,</td>
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<tr>
<td>51</td>
<td>CDCl₃</td>
<td>4.14 d</td>
<td>5.20 t</td>
<td>7.90 q</td>
<td>8.17 o</td>
<td>562</td>
<td>586</td>
<td>559–</td>
<td>639 m</td>
<td>642 q</td>
<td>8.47, 8.66 s</td>
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</tbody>
</table>

a Data from 100-MHz spectra. b Signal multiplicity is given as s, singlet; d, doublet; t, triplet; q, quartet; o, octet; m, multiplet. c Assignments verified by spin decoupling. d Obscured by solvent impurity. e Under another signal.
<table>
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<tr>
<th>Compound</th>
<th>Solvent</th>
<th>Coupling constants in Hz</th>
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<tr>
<td></td>
<td></td>
<td>$J_{12}$ $J_{23}$ $J_{34}$ $J_{45}$ $J_{56}$</td>
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<td>56</td>
<td>CDCl$_3$</td>
<td>5.1 2.3 7.8 c c c c 1.9 6.6 c</td>
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<td></td>
<td>(CD$_3$)$_2$CO</td>
<td>5.2 2.3 7.8 c c c c 1.9 6.6 c</td>
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<td>49</td>
<td>CDCl$_3$</td>
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<tr>
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<td>C$_6$D$_6$</td>
<td>4.0 0 4.3 4.3 d 13.9 c c c d d d</td>
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<td>4.0 0 4.4 3.7 d d c c c d d d</td>
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<td>(CD$_3$)$_2$CO</td>
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<td>CDCl$_3$</td>
<td>3.8 0 4.6 4.9 10.8 13.2 c c c d d 6.0 11.6</td>
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</table>

$^a$Data from 100MHz spectra. $^b$a=low field proton; b=high field proton. $^c$Not applicable
$^d$Not measured due to second order effects. $^e$Obtained from spin decoupling data
Fig. 1.—The i.r. spectra (KBr pellet) of tetra-0-acetyl-β-D-glucopyranosylsulfenyl bromide (22), bis(tetra-0-acetyl-β-D-glucopyranosyl) disulfide (24), and bis(tetra-0-acetyl-β-D-glucopyranosyl disulfide mono-oxide (30).
Fig. 2.—Partial n.m.r. spectrum of phenyl tri-O-acetyl-β-D-xylopyranosyl disulfide (39).
Fig. 3.--Partial n.m.r. spectrum of phenyl tri-O-acetyl-α-L-arabinopyranosyl disulfide (41).
Fig. 4.—N.m.r. spectrum of phenyl tetra-$\alpha$-acetyl-$\beta$-$\dagger$-galactopyranosyl disulfide (43).
Fig. 5.—N.m.r. spectrum of the crude reaction product of tetra-O-acetyl-α-D-glucopyranosyl-sulfenyl bromide (25) and benzenethiol.
Fig. 6.—N.m.r. spectrum of 3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexofuranose (49).
Fig. 7.—N.m.r. spectrum of 6-deoxy-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (56).
Fig. 8.--N.m.r. spectrum of 1,6-anhydro-4-deoxy-2,3-O-isopropylidene-$\beta$-D-lyxo-hexopyranose (59).
The original contributions to chemistry by this author are listed below. List A gives new methods of synthesis developed in conjunction with this research project and List B gives new compounds synthesized as part of this research project.

LIST A. NEW METHODS OF SYNTHESIS

1. 1-Thio-β-D-galactopyranose pentaacetate from 2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-2-thiopseudouracil hydrobromide.

2. 1-Thio-β-D-xylopyranose tetraacetate:
   a. From 2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-2-thiopseudouracil hydrochloride
   b. From 2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-2-thiopseudouracil hydrobromide

3. 1-Thio-β-D-glucopyranose pentaacetate by acid-catalyzed exchange from β-D-glucopyranose pentaacetate in thiolacetic acid.

4. N.m.r. studies of reactions of the following 1-thio sugars and 1-thioglycosides in carbon tetrachloride with bromine:
   a. 1-Thio-β-D-glucopyranose pentaacetate
   b. 1-Thio-α-D-glucopyranose pentaacetate
   c. 1-Thio-β-D-galactopyranose pentaacetate
d. 1-Thio-α-L-arabinopyranose tetraacetate
e. 1-Thio-β-D-xylopyranose tetraacetate
f. 1-Thio-β-D-ribopyranose tetraacetate
g. Benzyl 2,3,4,6-tetra-α-acetyl-1-thio-β-D-glucopyranoside
h. Phenyl 2,3,4,6-tetra-α-acetyl-1-thio-β-D-glucopyranoside
i. 2,3,4,6-Tetra-α-acetyl-1-S-benzoyl-1-thio-β-D-glucopyranose

5. Tetra-α-acetyl-α-D-glucopyranosyl bromide by bromination of:
a. 1-Thio-β-D-glucopyranose pentaacetate
b. Benzyl 2,3,4,6-tetra-α-acetyl-β-D-glucopyranoside
c. 2,3,4,6-Tetra-α-acetyl-1-S-benzoyl-1-thio-β-D-glucopyranose
d. Bis(tetra-α-acetyl-β-D-glucopyranosyl) disulfide
e. Bis(tetra-α-acetyl-β-D-glucopyranosyl) disulfide mono-oxide
f. Tert-butyl-tetra-α-acetyl-1-thio-β-D-glucopyranoside

6. Tetra-α-acetyl-α-D-galactopyranosyl bromide from 1-thio-β-D-galactopyranose pentaacetate

7. Tri-α-acetyl-β-L-arabinopyranosyl bromide from 1-thio-α-L-arabinopyranose tetraacetate
8. Tri-O-acetyl-α-D-xylopyranosyl bromide from 1-thio-β-D-glucopyranose tetraacetate

9. Tri-O-acetyl-β-D-ribofuranosyl bromide from 1-thio-β-D-ribofuranose tetraacetate

10. Tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide from tert-butyl tetra-O-acetyl-1-thio-β-D-glucopyranoside

11. Bis(tetra-O-acetyl-β-D-glucopyranosyl) disulfide by:
   a. Slow bromination of tert-butyl tetra-O-acetyl-1-thio-β-D-glucopyranoside
   b. Reaction of dry ethanol with tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide
   c. Reaction of tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide with tert-butyl tetra-O-acetyl-1-thio-β-D-glucopyranoside
   d. Reaction of tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide with:
      (1) Acetophenone
      (2) Acetone
      (3) Cyclohexanone
      (4) Phenol

12. Bis(tetra-O-acetyl-β-D-glucopyranosyl) disulfide mono-oxide by:
   a. Oxidation of bis(tetra-O-acetyl-β-D-glucopyranosyl) disulfide with m-chloroperoxybenzoic acid
b. Reaction of tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide with water

c. Reaction of tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide with 95% ethanol

13. p-(Dimethylamino)phenyl tetra-O-acetyl-1-thio-β-D-glucopyranoside from tetra-O-acetyl-β-D-glucopyranosylsulfenyl bromide and N,N-dimethylaniline

14. A route to deoxy sugars by photolysis of dimethylthiocarbamates:

a. 6-Deoxy-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose from photolysis of 6-O-dimethylthiocarbamoyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose

b. 1,6-Anhydro-4-deoxy-2,3-O-isopropylidene-β-D-lyxo-hexopyranose from photolysis of 1,6-anhydro-4-O-dimethylthiocarbamoyl-2,3-O-isopropylidene-β-D-mannopyranose

c. 3-Deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexofuranose from photolysis of:

(1) 3-O-Dimethylthiocarbamoyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose

(2) 3-Deoxy-3-iodo-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose

(3) By reduction of bis(1,2:5,6-di-O-isopropylidene-α-D-glucofuranosyl) disulfide with Raney nickel
LIST B. NEW CHEMICAL COMPOUNDS

1. Bis(tetra-α-acetyl-β-D-glucopyranosyl) disulfide mono-oxide
2. Tetra-α-acetyl-β-D-glucopyranosylsulfenamidobenzene
3. p-(Dimethylemino)phenyl tetra-α-acetyl-β-D-glucopyranosyl disulfide
4. Phenyl tri-α-acetyl-β-D-xylopyranosyl disulfide
5. Benzyl tri-α-acetyl-β-D-xylopyranosyl disulfide
6. Phenyl tetra-α-acetyl-β-D-galactopyranosyl disulfide
7. Phenyl tri-α-acetyl-α-L-arabinopyranosyl disulfide
8. 1,6-Anhydro-4-deoxy-2,3-α-isopropylidene-β-D-lyxo-hexopyranose