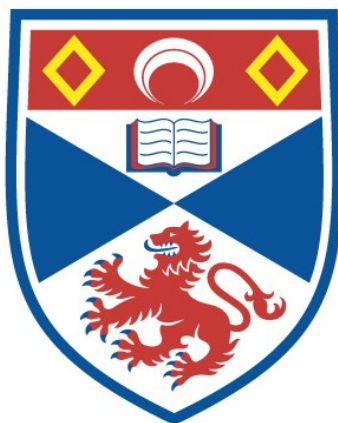# A CONTRIBUTION TO THE CHEMISTRY OF XYLOSE

Thomas Hall Speedie

A Thesis Submitted for the Degree of PhD
at the
University of St Andrews

1934

A CONTRIBUTION TO THE CHEMISTRY

OF XYLOSE.

BEING A THESIS

PRESENTED BY

THOMAS HALL SPEEDIE, B.Sc.

TO THE UNIVERSITY OF ST. ANDREWS

IN APPLICATION FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY.

DECLARATION.

I hereby declare that the following Thesis is a record of the results of experiments carried out by me and, further, that the Thesis is my own composition and has not previously been presented for a Higher Degree.

The Research was carried out in the Chemical Research Laboratory of the University of St. Andrews, under the direction of George James Robertson, Esq., M.A., B.Sc., Ph.D.

St. Andrews,

16th May, 1934.

C E R T I F I C A T E.

I certify that Mr. Thomas Hall Speedie, B.Sc., has spent nine terms at Research Work under my direction, that he has fulfilled the conditions of Ordinance No. 16, (St. Andrews), and is qualified to submit the accompanying Thesis in application for the degree of Ph.D.

Director of Research.

St. Andrews,

May, 1934.

UNIVERSITY CAREER.

I graduated B.Sc., with Second Class Honours in Chemistry in the University of St. Andrews in 1931.
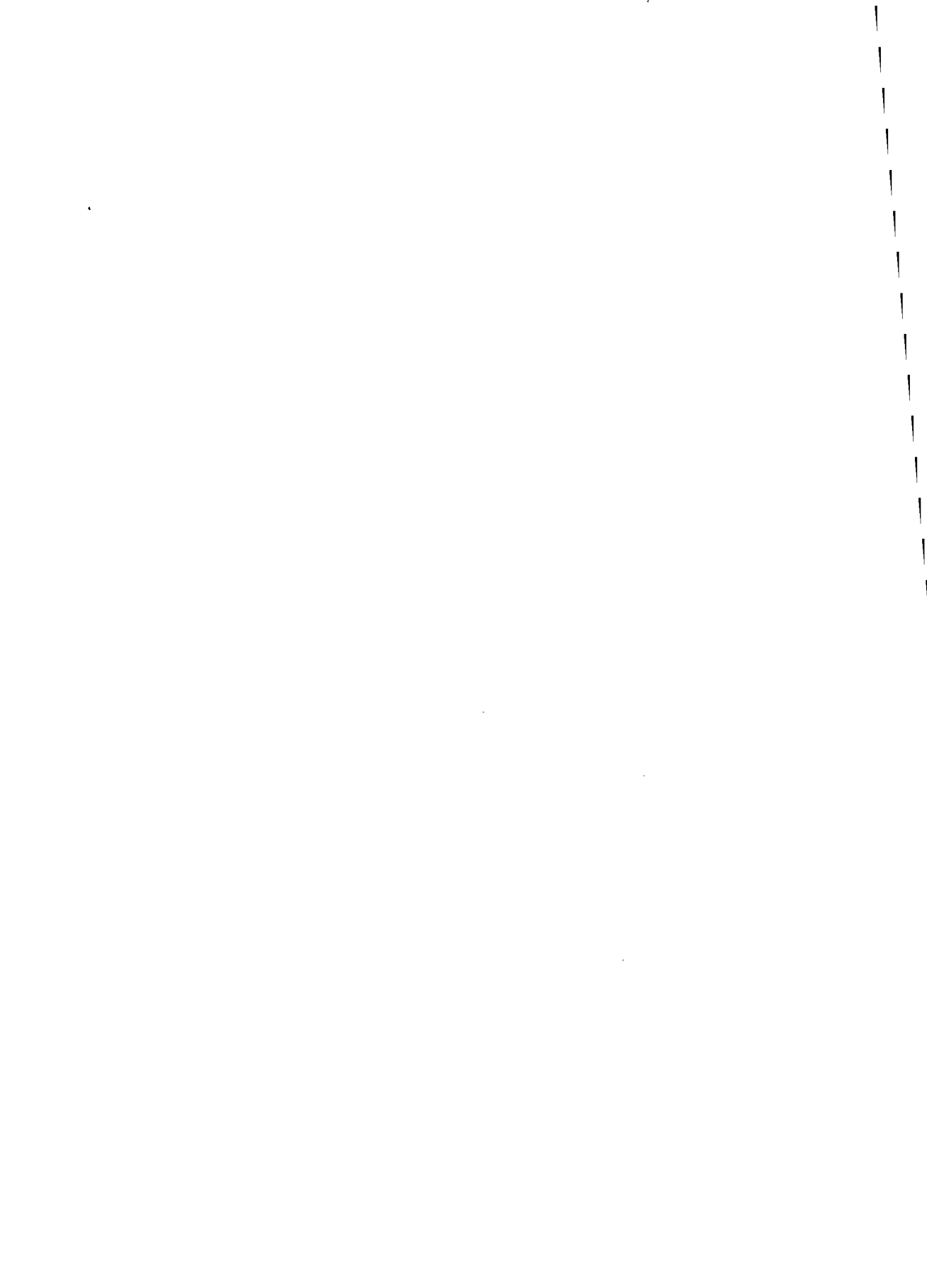
I commenced the research which is now being submitted as a Ph.D. Thesis in October, 1931 and was admitted a Research Student of the University of St. Andrews from that date.

In 1931 I was awarded a Carnegie Research Scholarship which I have held for three years.

The results of this research are being published in a forthcoming issue of the Journal of the Chemical Society.

CONTENTS.

INTRODUCTION.

.

A CONTRIBUTION TO THE CHEMISTRY OF XYLOSE.

The wide distribution of xylose in nature coupled with its important structural relationship to other naturally occurring sugars, are factors which invite speculation on the mechanism of transformations within the sugar molecule, and place this pentose in the first rank of importance.

```
CHO      1.         CHO      1.         CHO      1.
 |                   |                   |
H-C-OH   2.        H-C-OH   2.        H-C-OH   2.
 |                   |                   |
HO-C-H   3.        HO-C-H   3.        H-C-OH   3.
 |                   |                   |
H-C-OH   4.        H-C-OH   4.        H-C-OH   4.
 |                   |                   |
H-C-OH   5.        CH₂OH   5.         CH₂OH   5.
 |
CH₂OH   6.
```

GLUCOSE (II)   XYLOSE (I)   RIBOSE (III)
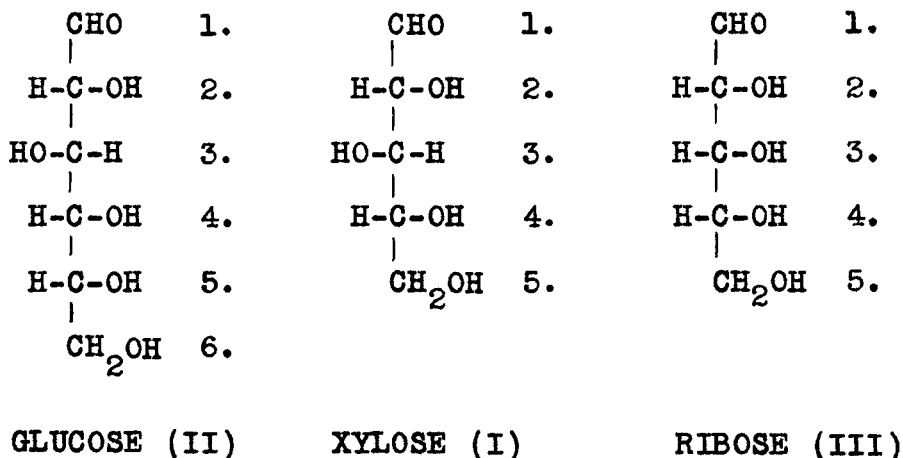
An examination of the configuration assigned to the aldehydic form of xylose (I) shows that it closely resembles that of glucose (II), since (I) may be obtained from (II) merely by the omission of carbon atom 6, while in turn, ribose (III) is obtained from xylose (I) by the inversion of the groups attached to carbon atom 3.

The close association of glucose and xylose in the vegetable kingdom has suggested the idea that xylose may result from the degradation of glucose. It is known that glucose (IV), where the reducing end of the molecule is protected by glucoside formation, may undergo a process of oxidation to give glucuronic acid (V) which, in

(IV)   (V)   (VI)
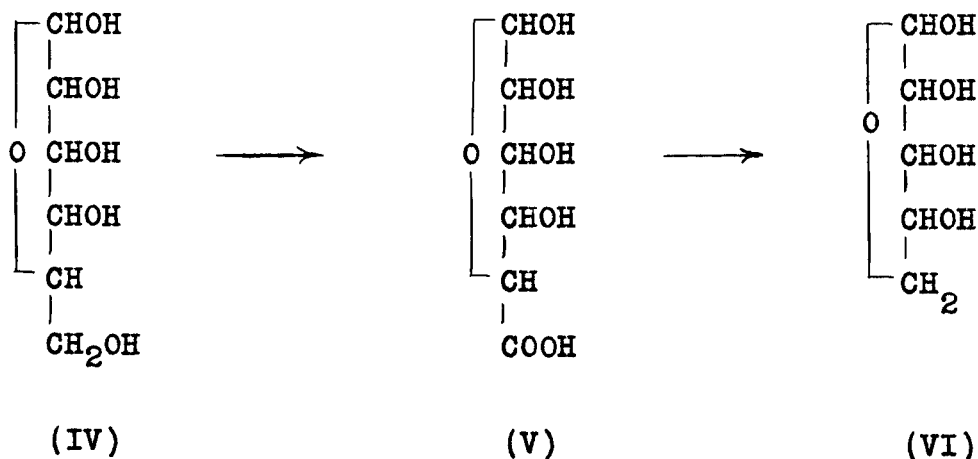
contact with certain bacteria, loses carbon dioxide and passes into xylose (VI).

The above scheme of transformation may not be that effected by nature but it is at least suggestive that glucose and xylose occur in conjunction in many natural products eg., in esparto cellulose, as a disaccharide in glycosides and associated together with glucuronic acid in certain saponins. In addition, crystalline xylose and glucuronic acid are also found in the shoot juices of certain species of bamboo.
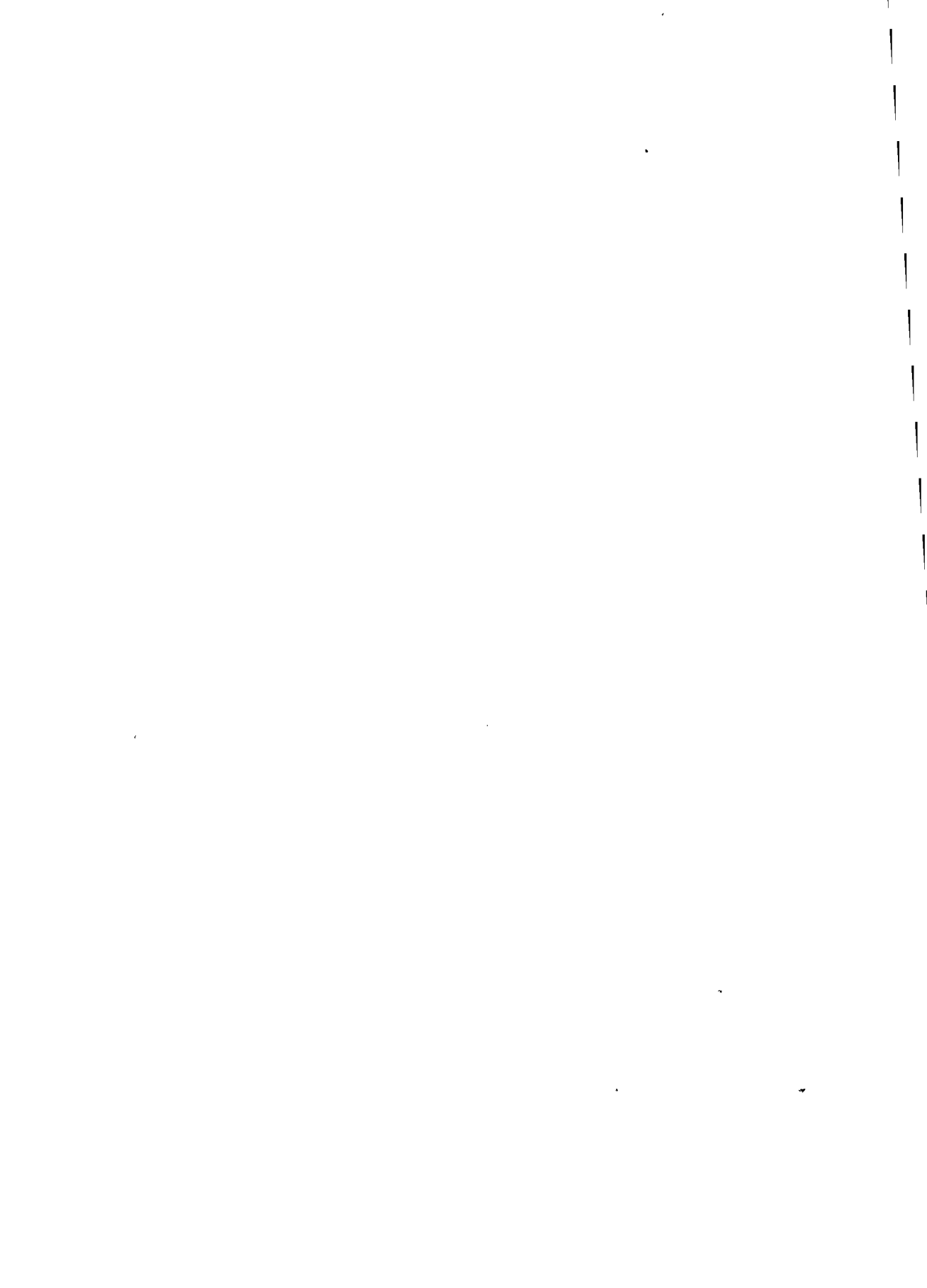
Further, Robinson (Nature, 7th July, 1927) has suggested that the pentose of plant nucleic acid, which has been isolated by Levene in the form of the rare sugar d-ribose, is formed by a Walden inversion during the enzymatic hydrolysis of a xylose 3-phosphate. It should be added that Levene does not accept this view.

The importance of xylose in nature, therefore, cannot be overestimated and it is surprising to discover that only a comparatively small number of its partially methylated derivatives have been prepared and characterised and the present research was undertaken with a view to extending knowledge in this direction.

```
        H    OH   1.                    ┌─CHOH   1.
          C                             │
          │                             │  H-C-OH  2.
         H-C-OH    2.                 O  │
          │                             │  HO-C-H  3.
    O  HO-C-H     3.                    │
          │                             └─CH      4.
         H-C-OH    4.                      │
          │                              CH₂OH  5.
         CH₂        5.
```
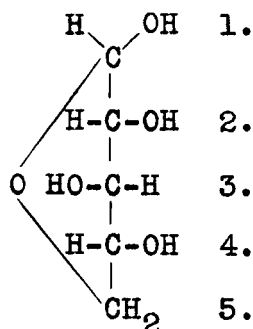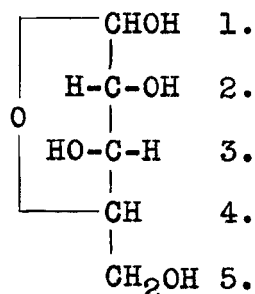
        α-xylose (VII)   α and β(γ)-xylose (VIII)

The structure of xylose (VII) was established by Hirst and Purves (J., 1923, 123, 1352) who showed that it possessed the amylene oxide ring, while it was later shown by Haworth and Westgarth (J., 1926, 880) to be
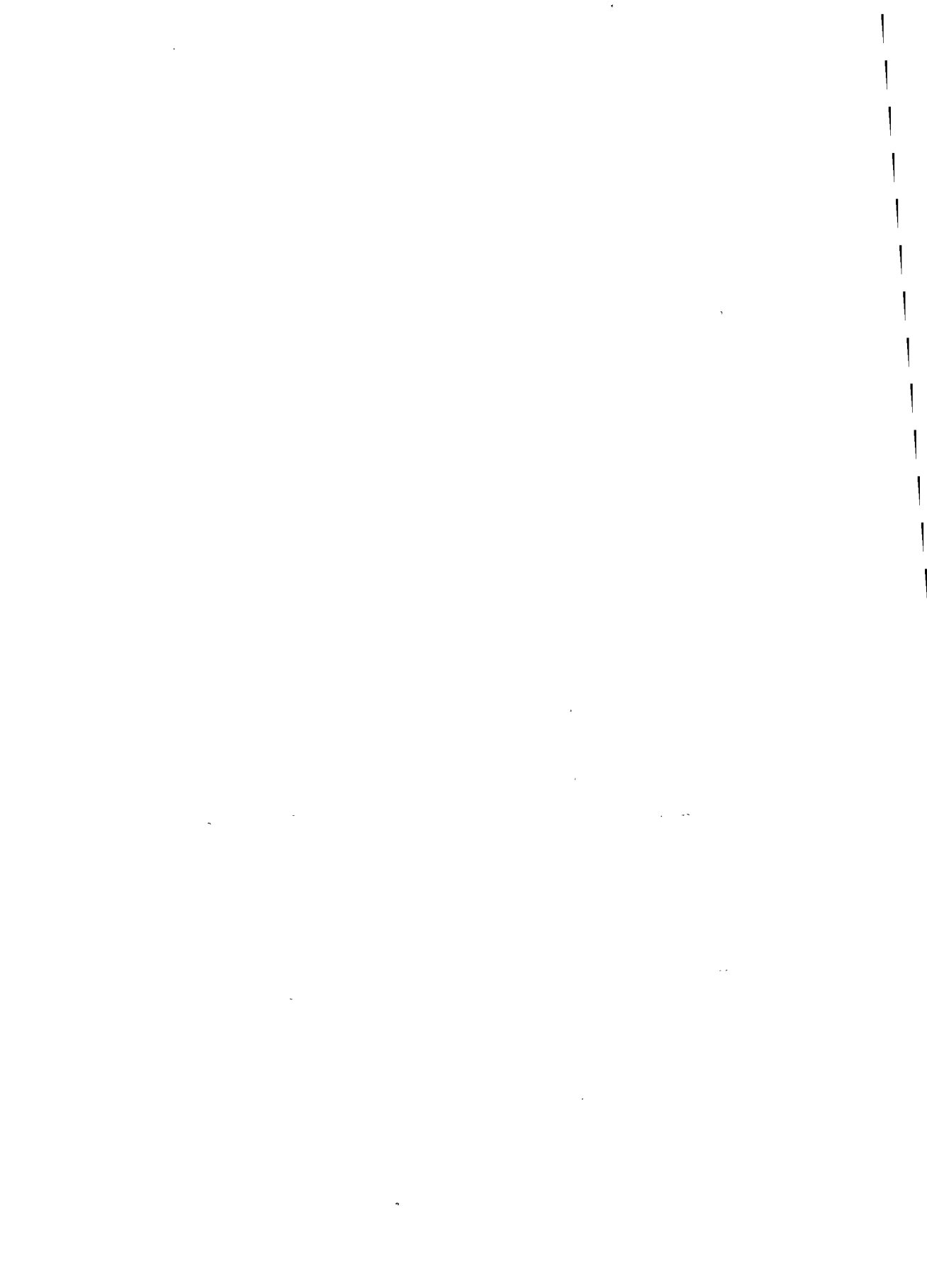
capable of entering into reactions in a second form
(γ-form, VIII) in which the oxygen atom is linked to
carbon atoms 1 and 4.   The methylation of xylose was effect-
ed by Carruthers and Hirst (J., 1922, <u>121</u>, 2299) when the
properties of the resultant 2:3:4-trimethyl xylose were
investigated and the derivative fully characterised.
This investigation was of value later when 2:3:5-trimethyl-
γ-xylose was isolated by Haworth and Westgarth (<u>loc. cit.</u>)
as it was shown that the properties of 2:3:5-trimethyl-γ-
xylose differed entirely from those of 2:3:4-trimethyl
xylose and the fundamental difference in structure of the
two parent sugars was emphasised.

Earlier work had resulted in the isolation of two
acetone compounds of xylose.   Diacetone-xylose (IX)
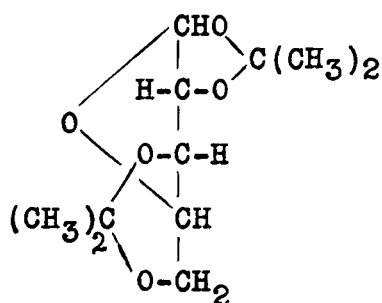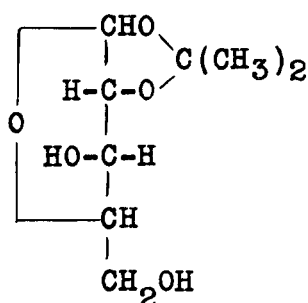
(IX)   (X)

prepared by Svanberg and Sjöberg (Ber., 1923, <u>56</u>, 863 and
1448) is a compound in which the <u>iso</u>propylidene residues
are attached through the 1:2 and 3:5 positions (cf. Haworth

and Porter, J., 1928, 611) thus showing that diacetone-xylose is a derivative of the γ-form. The same authors record the isolation of monacetone-xylose (X), prepared by the partial hydrolysis of the diacetone compound, where the acetone substituent is subsequently proved to occupy positions 1 and 2.

The first attempt at the partial methylation of xylose was made by Svanberg (Ber., 1923, 56, 2195) utilising monacetone-xylose, when by partial methylation, a mixture of mono and dimethyl-monacetone xyloses was obtained. The isolation of these impure syrupy products could not be said to have advanced the problem to any great extent. An important communication was, however, contributed by Levene and Raymond (J. Biol. Chem., 1933, 102, 317) who succeeded in isolating 3-methyl xylose and 5-methyl-γ-xylose. These authors, using Svanberg's monacetone-xylose as a starting point, and making use of the fact that the primary alcoholic group in position 5 is susceptible to preferential substitution, succeeded in isolating a series of derivatives in which the hydroxyl group in position 3 or position 5 were substituted with acetyl, benzoyl, or p-toluenesulphonyl groups. Having fully established the structure of each of these monosubstituted derivatives, they utilised 5-benzoyl-monacetone-xylose for the preparation of methylated compounds. During the

course of these experiments, it was shown that, owing to
the instability of the benzoyl group in the 5 position
during methylation, it was possible to isolate 3-methyl
and 5-methyl-γ-xylose.   This is noteworthy in the light
of the work now to be described.

Researches on the methylated compounds of xylose
were further extended by Haworth and his collaborators
(J., 1929, 1739) who showed that naturally ocurring xylan
consisted entirely of xylose residues.   By fully methyl-
ating the polysaccharide with dimethyl sulphate, dimethyl
xylan was isolated and yielded 2:3-dimethyl xylose on
hydrolysis, thus showing that the xylose units were link-
ed together through positions 1 and 4 in the complex
molecule.   By this means they were able to suggest a
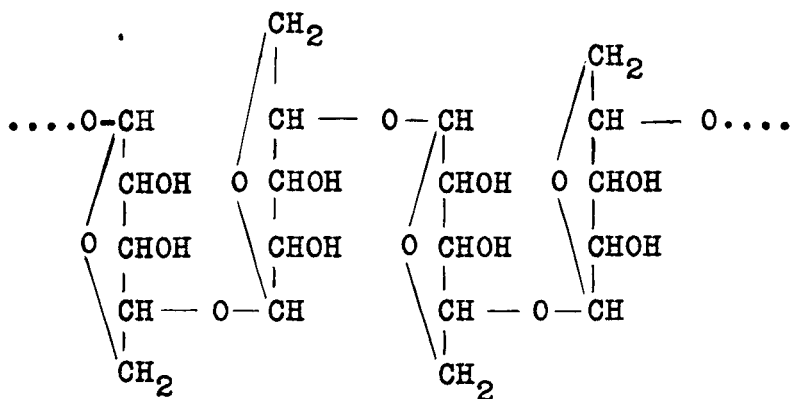
(XI)

structural formula (XI) for the complex molecule of
xylan.

The characterisation of 3-methyl xylose and 5-methyl-γ-xylose by Levene and Raymond (<u>loc</u>. <u>cit</u>.) and the preparation of 2:3-dimethyl xylose (Hampton, Haworth and Hirst, <u>loc</u>. <u>cit</u>.) when considered with the results now to be discussed, which include the preparation of 2-methyl xylose, 2:4-dimethyl-β-methylxyloside, and 3:4-dimethyl xylose, it is obvious that an advance has been made in this particular branch of xylose chemistry. The present position of the problem therefore is that of all the mono and dimethyl xyloses which may be expected to exist only 4-methyl xylose, 2:5-dimethyl-γ-xylose and 3:5-dimethyl-γ-xylose remain to be synthesised.

THEORETICAL

P A R T 1.

THE SYNTHESIS OF 2-METHYL XYLOSE.

THE SYNTHESIS OF 2-METHYL XYLOSE.

β-Methylxyloside was selected as the starting material in these researches for a variety of reasons. In the first place, the methods available for the preparation of α-methylxyloside were limited, while the substance exhibits a low melting point and is not readily obtained in a pure crystalline form. In addition, from analogy with glucose derivatives of the β series, it was considered probable that the β-compound and its derivatives would exert a much stronger crystallising power than the α-isomerides.

Previous to the commencement of this study, few observations had been made on the preparation of this important xyloside since Fischer (Ber., 1893, 26, 2407 1895, 28, 1157) first pointed out that a mixture of α- and β-methylxylosides results when xylose is heated under pressure with methyl alcohol containing dry hydrogen chloride. From the mixture obtained he was able to isolate β-methylxyloside in poor yield. This method was considered wholly unsuitable for the present range of work.

Later, Dale (J. Am. Chem. Soc., 1915, 37, 2745)

described the preparation of triacetyl-β-methylxyloside, but by a somewhat drastic method and a modified form of his procedure was adopted at the beginning of these researches. This modification was analogous to that described by Fischer, (Ber., 1916, 49, 584) for the isolation of β-methylglucoside.

Xylose was acetylated in the usual manner to give tetracetyl-xylose (Stone, J. Am. Chem. Soc., 1894, 15, 653) in 52% yield. Treatment of the acetate with hydrogen bromide in glacial acetic acid solution yielded presumably triacetylbromoxylose which was not isolated. The bromine atom was replaced by a methyl radical and triacetyl-β-methylxyloside identical with that obtained by Stone (loc. cit.) was obtained. β-Methylxyloside was isolated in a readily crystalline form by the removal of the acetyl groups, the constants of which agreed closely with those already quoted. Although this method of preparation was necessarily lengthy it proved to be exceedingly useful and was employed in the present research until a more economic method, which will be discussed later, was discovered.

The preparation of a partially methylated xylose from β-methylxyloside entailed the temporary protection of one or more hydroxyl groups by a radical which could easily be eliminated when methylation had been effected.

For this purpose, benzaldehyde was employed as the condensing agent and a scrutiny of the structural formula assigned to β-methylxyloside (XII) showed that three possibilities existed.

$$CH_3O-C-H \quad 1.$$
$$H-C-OH \quad 2.$$
$$O \quad HO-C-H \quad 3.$$
$$H-C-OH \quad 4.$$
$$CH_2 \quad 5.$$

(XII)

$$CH_3O-C-H$$
$$H-C-O$$
$$O \quad HO-C-H \quad CH.C_6H_5$$
$$H-C-O$$
$$CH_2$$

(XIII)

$$CH_3O-C-H$$
$$H-C-O$$
$$O \quad O-C-H \quad CH.C_6H_5$$
$$H-C-OH$$
$$CH_2$$

(XIV)

$$CH_3O-C-H$$
$$H-C-OH$$
$$O \quad O-C-H$$
$$H-C-O \quad CH.C_6H_5$$
$$CH_2$$
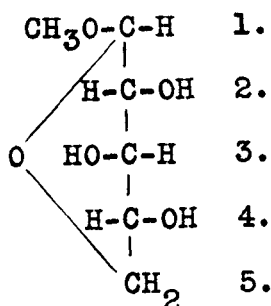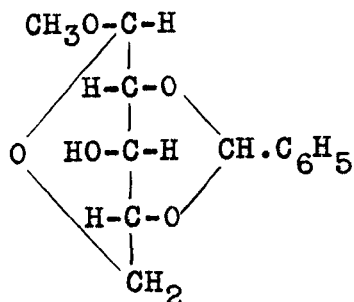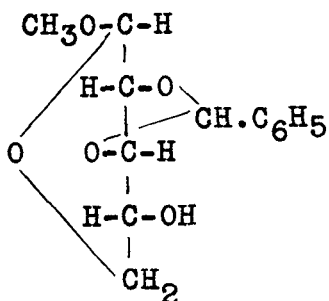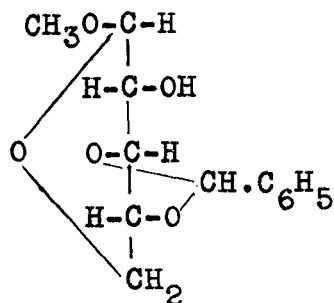
(XV)

Freudenburg's method (Ber., 1928, 61, 1750) for the formation of benzylidene compounds was utilised, whereby β-methylxyloside was shaken with benzaldehyde in the presence of anhydrous zinc chloride but condensation failed to take place. In an effort to increase the tendency for condensation β-methylxyloside was heated with benzaldehyde in an atmosphere of carbon dioxide

(Irvine and Scott, J., 1913, 103, 585), but this method also proved unsuccessful.

By this means it was shown that the benzylidene residue was unable to enter the molecule through condensation with neighbouring hydroxyl groups in the trans position to give products (XIV) and (XV) and also that condensation through hydroxyl groups 2 and 4 did not take place. At first sight, this result appeared rather unusual but a closer study of the similarity of the structures of β-methylxyloside (XII) and β-methyl glucoside (XVI) suggested an explanation of the negative results quoted above.

$$CH_3O-C-H \qquad 1.$$
$$H-C-OH \qquad 2.$$
$$HO-C-H \qquad 3.$$
$$H-C-OH \qquad 4.$$
$$CH \qquad 5.$$
$$CH_2OH \qquad 6.$$
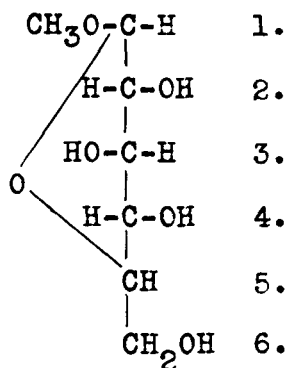
(XVI)

It will be observed that β-methylxyloside is identical in configuration with β-methylglucoside except for the addition of the 6th carbon atom and attached hydroxyl group. Further, when β-methylglucoside is condensed with benzaldehyde, 4:6-benzylidene-β-methylglucoside is

is the only product isolated, a fact which points to
the idea that the hydroxyl group attached to the 6th
carbon atom of β-methylglucoside is definitely required
before condensation can take place.

The matter was followed up by a study of the
condensation of benzaldehyde with xylose itself, since
the existence of analogous acetone-xyloses was known
(Freudenburg and Svanberg, Ber., 1922, 55, 3233,
Svanberg and Sjöberg, Ber., 1923, 56, 863, and Haworth
and Porter, J., 1928, 611), and the structure of these
derivatives established. It was hoped by this means
to prepare dibenzylidene-xylose which would afford a
mono-benzylidene derivative when subjected to partial
hydrolysis.

Freudenburg's method (loc. cit.) was again em-
ployed and a crystalline derivative obtained which was
ultimately proved to be dibenzylidene-xylose (XIX),
since an acetylated derivative could not be isolated.
It was apparent that xylose (XVII) had reacted in the γ-
form (XVIII), thus permitting of easy condensation in the
1:2 and 3:5 positions.

All attempts to partially hydrolyse the di-
benzylidene compound proved unsuccessful and complete
hydrolysis to xylose took place in each experiment
owing to the sensitivity of the dibenzylidene compound

to acid.

$$
\begin{array}{ccc}
\text{(XVII)} & \text{(XVIII)} & \text{(XIX)}
\end{array}
$$

Structure XVII: a ring with O, bearing CHOH, CHOH, CHOH, CHOH, CH$_2$.

Structure XVIII: a ring with O, bearing CHOH, CHOH, CHOH, CH, CH$_2$OH.

Structure XIX: a ring with O, bearing CHO (with CH.C$_6$H$_5$), CHO, CHO, CH, CH$_2$O (with CH.C$_6$H$_5$).
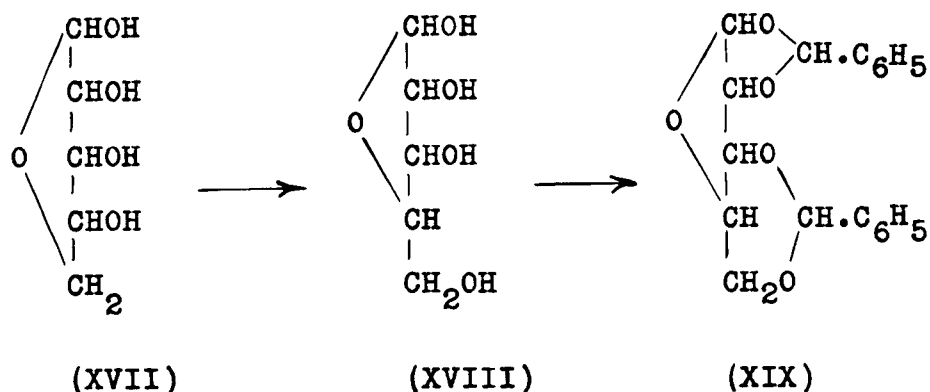
It may be noted in passing that the acetone compounds of xylose, to which reference has already been made, could have been utilised in the preparation of partially methylated xyloses but that method was already in the course of exploration (Levene and Raymond, J. Biol. Chem., 1933, 102, 331).

An investigation was then instituted on the preparation of γ-methylxyloside which had first been described by Haworth and Porter (J., 1928, 611). The method adopted by these workers entailed the condensation of dry xylose with methyl alcohol at the ordinary temperature, in the presence of 1% dry hydrogen chloride when the time required to complete the reaction was noted to vary from five to seven days. The main principles of this method were adopted but in an attempt to decrease the time required, the concentration of

hydrogen chloride was increased to 2% when it was discovered that condensation was usually complete within four days. Isolation of the product in the usual manner yielded a mobile syrup from which a crystalline precipitate separated on treatment with acetone. This crystalline material was later identified as β-methylxyloside and was generally obtained in approximately 30% yield from similar experiments. The residue which consisted of crude γ-methylxyloside was now condensed with acetone when a poor yield of 3:5-monacetone-γ-methylxyloside was obtained. The yield of the condensation product was variable and depended upon the actual amount of γ-methylxyloside formed in the first condensation with methyl alcohol. The analytical details of the syrup showed it to be almost pure 3:5-monacetone-γ-methylxyloside while the slightly low methoxyl content of the substance was doubtless due to traces of the diacetone compound formed by the expulsion of the methyl group in the reducing position followed by additional condensation with a further quantity of acetone. Generally, a separation within limits could be obtained by distilling the mixture of compounds under diminished pressure, but an analytically pure specimen of 3:5-monacetone-γ-methylxyloside was never obtained.

α and β

CHOCH₃
|
CHOH
|
CHOH
|
CHOH
|
CH₂

$$\text{CHOCH}_3 - \text{CHOH} - \text{CHOH} - \text{CHOH} - \text{CH}_2$$

(XX)

CHOH 1.
|
CHOH 2.
|
CHOH 3.
|
CHOH 4.
|
CH₂ 5.

(XXI)

CHOCH₃
|
CHOH
|
CHOH
|
CH
|
CH₂OH

(XXII)

CHOCH₃
|
CHOH
|
CHO
|
CH   C—CH₃
| |
CH₂O CH₃

(XXIII)

CHOCH₃
|
CHOCH₃
|
CHO
|
CH   C—CH₃
| |
CH₂O CH₃

(XXIV)

CHOH
|
CHOCH₃
|
CHOH
|
CHOH
|
CH₂

(XXV)
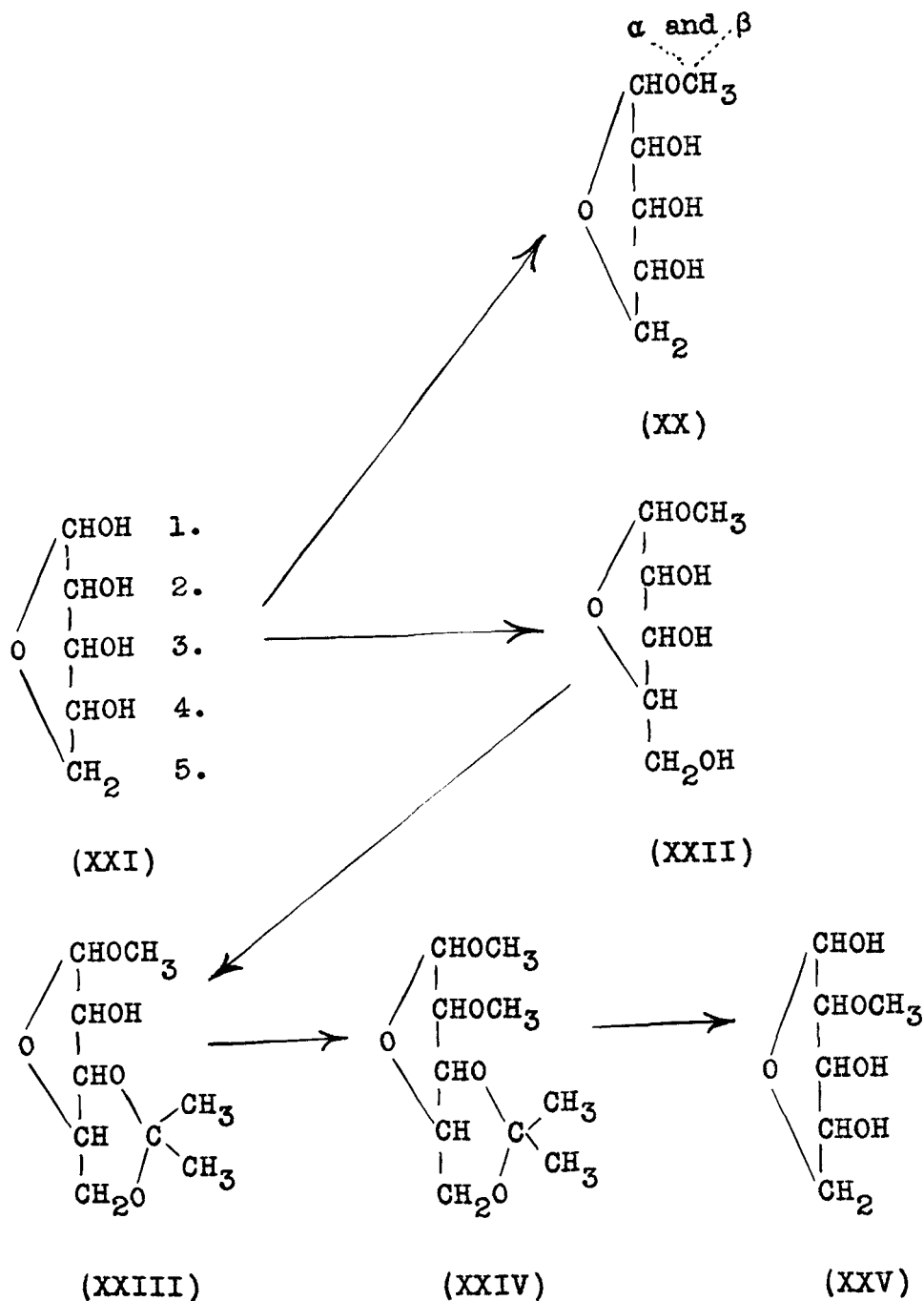
Methylation of the monacetone compound (XXIII)
by Purdie's method proceeded smoothly and was generally
found to be complete in three methylations when the
refractive index remained unaltered.   The product

distilled readily in a high vacuum to give a mobile syrup
of watery consistency, which analysed as 2-methyl-3:5-
monacetone-γ-methylxyloside (XXIV).

It is a well-known fact that the hydrolysis of
pentosides with acidic reagents is always fraught with
difficulties since furfuraldehyde or its derivatives
are frequently produced during the course of the reaction.
In the present instance, hydrolysis was effected with
oxalic acid solution in order to minimise this tendency
and as the acid could be easily removed in the form of
the calcium salt in the later stages of extraction.
By the hydrolysis of this γ-derivative (XXIV), the iso-
propylidene residue was eliminated as was also the methyl
group in the reducing position and the resulting unstable
compound immediately reverted to the normal form giving
normal 2-methyl xylose (XXV).   The first partially
methylated xylose now synthesised was obtained in the
form of colourless needles, m.p. 132-133° which analysed
for a pure monomethyl pentose.   A scrutiny of the
muta-rotation curve of the substance showed it to be a
β-form.

The method of preparation must go far in proving
the constitution of this new methylated derivative of
xylose but additional evidence was procured by forming
the osazone.   It suffices to say that the osazone

obtained from 2-methyl xylose was identical in all respects with that obtained from an authentic specimen of xylose, in as much as the osazone contained no methoxyl group and did not depress the melting point of xylos-azone itself.   From this argument it must be concluded that the methyl group in 2-methyl xylose was in a react-ing position, and was thus displaced during osazone formation.

With the aim of supplying further characterisation to 2-methyl xylose, 2-methyl-β-methylxyloside was pre-pared in the following manner :-

(XXVI)   (XXVII)   (XXVIII)

(XXIX)   (XXX)
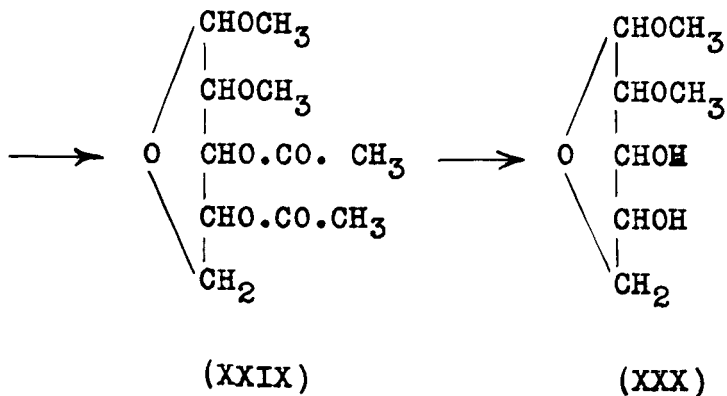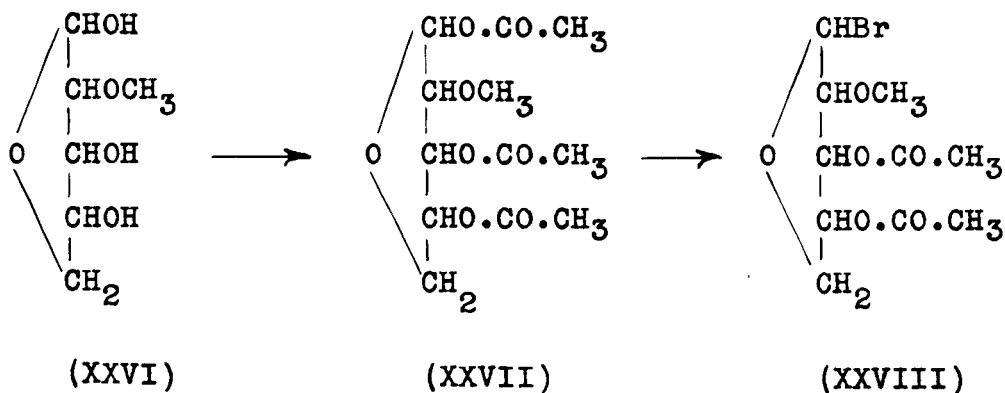
This preparation (Fischer, Ber., 1916, 49, 584) en-
tailed the intermediate formation of triacetyl-2-
methyl xylose (XXVII) and 3:4-diacetyl-2-methyl-β-
methylxyloside (XXIX) both of which were obtained in
the crystalline state.   With regard to triacetyl-2-
methyl xylose however, both α and β forms of the acetyl
derivative were necessarily present, a mixture of prisms
and needles being clearly visible through the microscope.
In contrast, 3:4-diacetyl-2-methyl-β-methylxyloside (XXIX)
was obtained in the pure β-form.   2-Methyl-β-methyl-
xyloside (XXX) was isolated in the form of glistening
plates m.p. 111-112° while the p-toluenesulphonyl
derivative of the compound showed m.p. 123°.

It was of interest to examine the condensation
of 2-methyl xylose with acetone when the course of the
reaction could have followed one of four possibilities
(see formula scheme p. 19).   In the first place,
2-methyl xylose (XXXI) might have combined with acetone
in the 1:3 position to give product (XXXII) or in the
3:4 position to give product (XXXIII) while reversion
to the γ-form and subsequent condensation with acetone
would have led to the possible production of compounds
(XXXIV) and (XXXV).   Condensation to give (XXXIII)
was highly improbable since neither xylose nor β-methyl-
xyloside condense with acetone in the 3:4 position and

$$
\begin{array}{c}
\text{CHOH} \\
\text{CHOCH}_3 \\
\text{O} \quad \text{CHO} \quad \text{CH}_3 \\
\text{CHO} \quad \text{O} \quad \text{CH}_3 \\
\text{CH}_2
\end{array}
$$

(XXXIII)

$$
\begin{array}{c}
\text{CHOH} \\
\text{CHOCH}_3 \\
\text{O} \quad \text{CHOH} \\
\text{CHOH} \\
\text{CH}_2
\end{array}
$$

(XXXI)

$$
\begin{array}{c}
\text{CHO} \\
\text{CHOCH}_3 \quad \text{O} \quad \text{CH}_3 \\
\text{O} \quad \text{CHO} \quad \text{CH}_3 \\
\text{CHOH} \\
\text{CH}_2
\end{array}
$$

(XXXII)

$$
\begin{array}{c}
\text{CHO} \\
\text{CHOCH}_3 \quad \text{C} \quad \text{CH}_3 \\
\text{O} \quad \text{CHO} \quad \text{CH}_3 \\
\text{CH} \\
\text{CH}_2\text{OH}
\end{array}
$$

(XXXIV)

$$
\begin{array}{c}
\text{CHOH} \\
\text{CHOCH}_3 \\
\text{O} \quad \text{CHO} \quad \text{CH}_3 \\
\text{CH} \quad \text{C} \quad \text{CH}_3 \\
\text{CH}_2\text{O} \quad \text{CH}_3
\end{array}
$$

(XXXV)

$$
\begin{array}{c}
\text{CHO} \\
\text{CHOCH}_3 \quad \text{C} \quad \text{CH}_3 \\
\text{O} \quad \text{CHO} \quad \text{CH}_3 \\
\text{CHOCH}_3 \\
\text{CH}_2
\end{array}
$$

(XL)

$$
\begin{array}{c}
\text{CHO} \\
\text{CHOCH}_3 \quad \text{C} \quad \text{CH}_3 \\
\text{O} \quad \text{CHO} \quad \text{CH}_3 \\
\text{CH} \\
\text{CH}_2\text{OCH}_3
\end{array}
$$

(XXXVI)

$$
\begin{array}{c}
\text{CHOCH}_3 \\
\text{CHOCH}_3 \\
\text{O} \quad \text{CHO} \quad \text{CH}_3 \\
\text{CH} \quad \text{C} \quad \text{CH}_3 \\
\text{CH}_2\text{O} \quad \text{CH}_3
\end{array}
$$

(XXXVIII)

$$
\begin{array}{c}
\text{CHOH} \\
\text{CHOCH}_3 \\
\text{O} \quad \text{CHOH} \\
\text{CHOCH}_3 \\
\text{CH}_2
\end{array}
$$

(XLI)

$$
\begin{array}{c}
\text{CHOH} \\
\text{CHOCH}_3 \\
\text{O} \quad \text{CHOH} \\
\text{CH} \\
\text{CH}_2\text{OCH}_3
\end{array}
$$

(XXXVII)

$$
\begin{array}{c}
\text{CHOH} \\
\text{CHOCH}_3 \\
\text{O} \quad \text{CHOH} \\
\text{CHOH} \\
\text{CH}_2
\end{array}
$$

(XXXIX)

this possibility was dismissed without further discussion.

The justifiable assumption was then made that the
other three possible products, namely (XXXII), (XXXIV),
and (XXXV) could be easily identified by the use of the
methylation process and subsequent hydrolysis of the
resulting methylated compounds.   Under such conditions
(XXXII) would furnish a normal dimethyl xylose (XLI),
(XXXIV) a dimethyl xylose of the γ-type (XXXVII) and
so distinguishable from that obtained from (XXXII),
while (XXXV) would yield a substance (XXXIX) identical
with the starting material 2-methyl xylose.

2-Methyl xylose was shaken with acid acetone
in the usual manner and the condensation product isolated
as a pale yellow syrup which reduced Fehling's solution
slightly.   The product was not, however, obtained pure
at this stage, and showed a low methoxyl content owing
to the presence of mesityl oxide or phorone.   The product
was methylated and yielded a mobile syrup which distilled
in a high vacuum to give a colourless, mobile syrup
which had no reducing action on Fehling's solution but
which did not analyse well for a dimethyl-monacetone
xylose.   The substance was then submitted to hydrolysis
in the presence of oxalic acid solution when a syrup
was obtained which could not be induced to crystallise
and which showed a lower methoxyl content than a mono-

methyl xylose.   While these experiments proved unsatis-
factory from a strictly synthetical point of view, it
cannot be doubted that the condensation of 2-methyl
xylose with acetone proceeded in the 3:5 position to
give 3:5-monacetone-2-methyl xylose (XXXV) in the first
instance.   The analyses were, to a large extent,
rendered useless owing to the formation of other con-
densation products in the reaction mixture e.g. mesityl
oxide and phorone etc., which were difficult to eliminate
throughout the course of the investigation.

These results were all the more striking since
Miss M. A. Ross (Dissertation, 1931) reported the
formation of 2-methyl-3:4-monacetone arabinose (XLII)
from the condensation of 2-methyl arabinose (XLIII)
with acetone as follows :-

(XXXII)   (XLII)
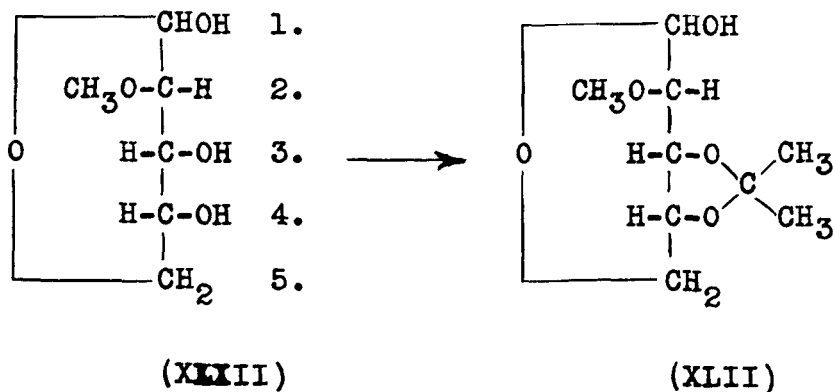
The position of the _iso_-propylidene residue was proved
by the same sequence of reactions as has been described

above, the explanation lying in the fact that in the analogous derivative of arabinose the reactive hydroxyl groups are in the _cis_ position.

P A R T II.

THE DIMETHYL XYLOSES.

THE DIMETHYL XYLOSES.

The isolation of 3:5-monacetone-γ-methylxyloside played an important part in suggesting the synthesis of 3:4-dimethyl xylose.   By the benzoylation of 3:5-monacetone-γ-methylxyloside with subsequent removal of the iso-propylidene residue and resultant conversion of the substance to the normal form, positions 3 and 4 in the molecule could then be methylated.   Removal of the benzoyl residue and the methyl group in the reducing position, ultimately furnished 3:4-dimethyl xylose.

3:5-Monacetone-γ-methylxyloside (I), see p. 24, was benzoylated in the usual manner with benzoyl chloride when a clear, viscous syrup, namely 2-benzoyl-3:5-monacetone-γ-methylxyloside (II) was obtained.   The product showed a distinct tendency to crystallise on standing, but, since the initial material existed in α and β forms, the condensation product necessarily contained both types.   Accordingly, purification by crystallisation was not attempted at this stage since a large loss in material would have taken place.   The difficult problem of hydrolysing away the iso-propylidene

FORMULA SCHEME FOR SYNTHESIS OF 3:4-DIMETHYL XYLOSE.

I

$$CHOCH_3$$
$$CHOH$$
$$CHO$$
$$CH$$
$$C(CH_3)(CH_3)$$
$$CH_2O$$

II

$$CHOCH_3$$
$$CHO.CO.C_6H_5$$
$$CHO$$
$$CH$$
$$C(CH_3)(CH_3)$$
$$CH_2O$$

IIa

$$CHOCH_3$$
$$CHO.NO_2$$
$$CHO$$
$$CH$$
$$C(CH_3)(CH_3)$$
$$CH_2O$$

III

$$CHOCH_3$$
$$CHO.CO.C_6H_5$$
$$CHOH$$
$$CHOH$$
$$CH_2$$

IIIa

$$CHOCH_3$$
$$CHO.NO_2$$
$$CHOH$$
$$CHOH$$
$$CH_2$$

IV

$$CHOCH_3$$
$$CHO.CO.C_6H_5$$
$$CHOCH_3$$
$$CHOCH_3$$
$$CH_2$$

V

$$CHOCH_3$$
$$CHOH$$
$$CHOCH_3$$
$$CHOCH_3$$
$$CH_2$$

IVa

$$CHOCH_3$$
$$CHO.NO_2$$
$$CHOCH_3$$
$$CHOCH_3$$
$$CH_2$$

VI

$$CHOH$$
$$CHOH$$
$$CHOCH_3$$
$$CHOCH_3$$
$$CH_2$$
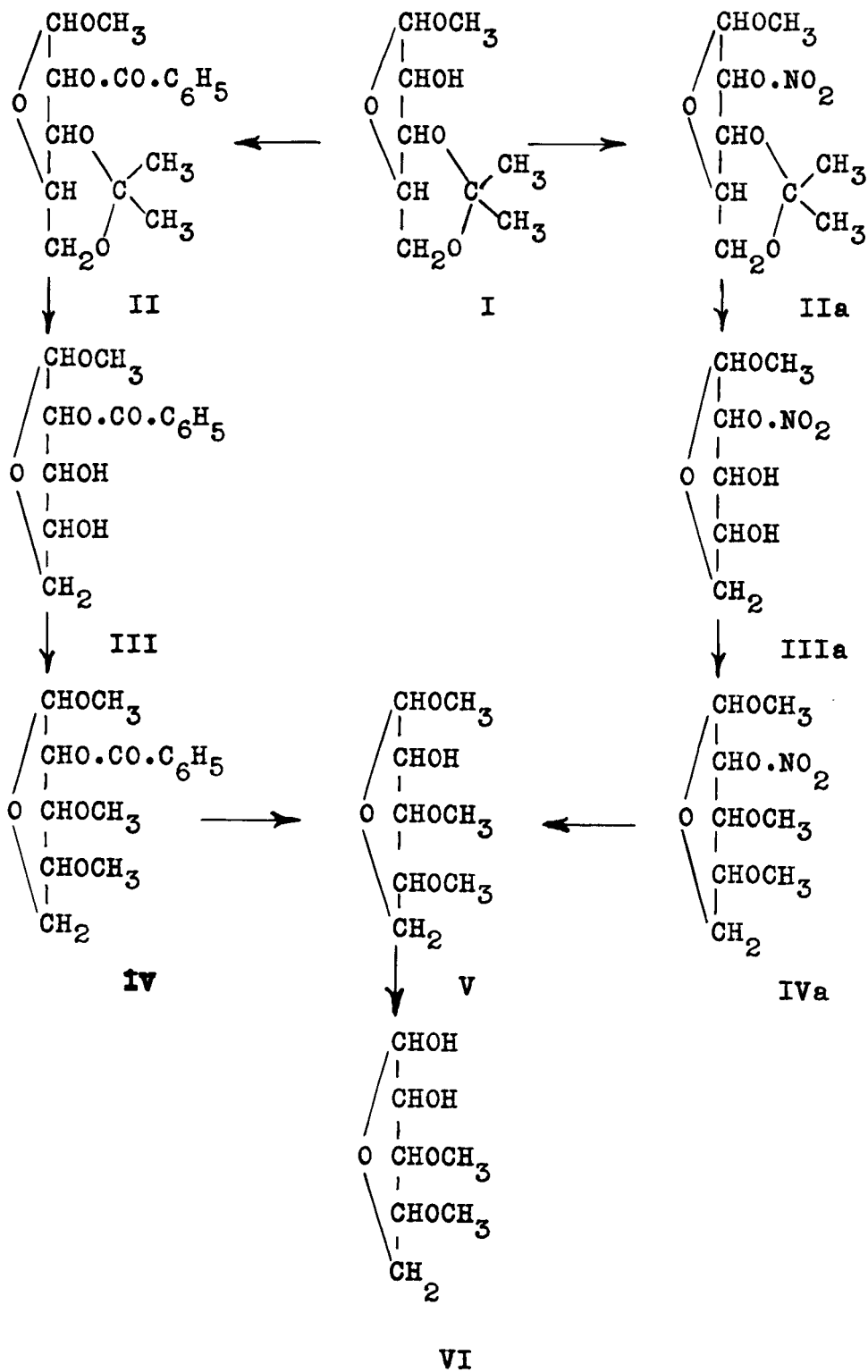
residue without affecting the benzoyl group was now
entered upon and for this purpose methyl alcohol
containing 1% dry hydrogen chloride was employed, the
hydrolysis being controlled polarimetrically.   A strong
smell of methyl benzoate showed that the benzoyl group
had also been hydrolysed away to some extent, although
this discovery was not unexpected.   The product, on
isolation, proved to be a hard glass which smelt keenly
of methyl benzoate, the presence of which accounted for
the somewhat low methoxyl value of the substance.
Methylation was completed in the usual manner with
silver oxide and methyl iodide when four methylations
were usually required.   The syrup was now subjected to
purification by solution in benzene followed by extraction
of the benzene solution with water.   In this way,
any trimethylmethylxyloside formed through the loss of
the benzoyl group during hydrolysis and subsequent
methylation was successfully eliminated from the system.
By this means, a pure specimen of 2-benzoyl-3:4-dimethyl-
methylxyloside (IV) was obtained.

The process of debenzoylation was essentially
similar to that described by Zemplen (Ber., 1929, 62, 1613)
and consisted in the catalytic removal of the benzoyl
group with sodium methylate after which methyl benzoate
was removed by steam distillation and the product ex-

tracted from the aqueous solution with chloroform.
Unchanged material was eliminated by solution of the
syrup in benzene and extracting the benzene solution with
water. Extraction of the aqueous solution with
chloroform yielded the required product, namely 3:4-
dimethylmethylxyloside (V) as a mobile syrup which
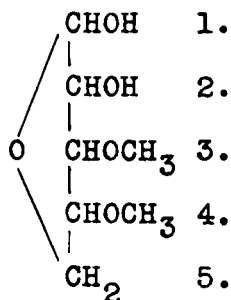distilled readily in a high vacuum.

Hydrolysis of the product to 3:4-dimethyl xylose (VI)
was effected using 3% hydrochloric acid and the reaction
controlled polarimetrically when the product was isolated
as a pale yellow syrup which could not be induced to
crystallise. Mutarotation of the substance was ob-
served both in aqueous and chloroform solutions.

In seeking to prove the structure of the partially
methylated xylose now isolated, an attempt was made
to condense the substance with methyl alcohol containing
1% dry hydrogen chloride at the ordinary temperature.
Failure to obtain such a product was attributed to the
inability of 3:4-dimethyl xylose to adopt the γ-structure,
thus demonstrating that position 4 was occupied.
Osazone formation from the partially methylated derivative
was also considered unsatisfactory in so far as a non-
crystalline material was obtained, although analysis
showed that both methoxyl groups were still present in
the molecule. This investigation showed that neither

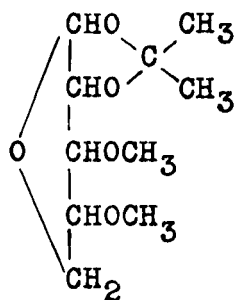of the methoxyl groups occupied a position affected
by osazone formation and proved that the substance was
in reality 3:4-dimethyl xylose. Characterisation of
3:4-dimethyl xylose was afforded by the formation of
3:4-dimethyl-β-methylxyloside which was obtained in
a crystalline form, whilst an additional crystalline
derivative was obtained by the p-toluenesulphonation
of 3:4-dimethyl-β-methylxyloside.

Condensation of 3:4-Dimethyl Xylose with Acetone.

The condensation of 3:4-dimethyl xylose with acetone was investigated in the hope that an acetone derivative would be obtained where the iso-propylidene residue occupied positions 1 and 2 in the molecule.
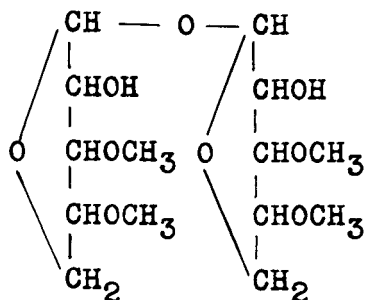
<table>
<tr><td>

CHOH   1.
CHOH   2.
O CHOCH$_3$ 3.
CHOCH$_3$ 4.
CH$_2$ 5.

(VII)

</td><td>

CHO CH$_3$
    C
CHO CH$_3$
O CHOCH$_3$
CHOCH$_3$
CH$_2$

(VIII)

</td></tr>
<tr><td>

CH — O — CH
CHOH   CHOH
O CHOCH$_3$ O CHOCH$_3$
CHOCH$_3$ CHOCH$_3$
CH$_2$ CH$_2$

(IX)

</td><td>

CH O
CH
O CHOCH$_3$
CHOCH$_3$
CH$_2$

(X)

</td></tr>
</table>

Acetone condensation was effected in the usual way and the product was isolated as a syrup which distilled in a high vacuum but which could not be induced to crystallise.   Analysis showed, however, that although the syrup did not reduce Fehling's solution, the de-

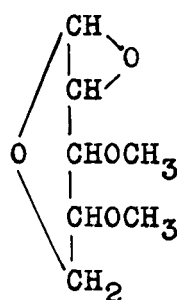sired condensation product had not been obtained, since the methoxyl content was greater than could be accounted for theoretically. The supposition was made that the condensation had proceeded in such a fashion as to give tetramethyl-dixylose (IX) probably admixed with traces of the desired 3:4-dimethyl-mon-acetone xylose, although the ease with which the product distilled was in complete disagreement with this view. An alternative suggestion pointed to the idea that the product was 1:2-anhydro-3:4-dimethyl xylose (X) since the changes obtained in the refractive index and boil-ing point corresponded with such changes in analogous compounds of glucose. No means could be devised for the purification of the material obtained.

It will have been observed that the foregoing
synthesis of 3:4-dimethyl xylose entails the methyl-
ation of 2-benzoyl-methylxyloside (III) and it is well-
known that in such a case, owing to the slight alkalinity
of the methylating system, migration of the benzoyl group
may take place to give a mixture of products, with the
result that in the present research a mixture of
benzoylated dimethylmethylxylosides might result.
In other words, can we be certain that the final product,
described as 3,4-dimethyl-β-methylxyloside, does contain
the methyl groups in the positions indicated or alter-
natively in the other two possible positions for a
dimethyl derivative of β-methylxyloside.

To settle the question, it was decided to intro-
duce a non-migratory group into /3:5-monacetone-γ-
methylxyloside (I) and to follow the same scheme of re-
actions as has been described for the preparation of
3:4-dimethyl-β-methylxyloside. It was hoped that a
comparison of the final products obtained would indicate
definitely the positions of the methyl groups.

The non-migratory group employed was the nitrate
group since it was stable during methylation and any
decomposition in the sugar molecule could be readily de-
tected. The ordinary method of nitration using fuming
nitric acid could not be used since the iso-propylidene

group in 3:5-monacetone-γ-methylxyloside was readily

affected in an acid medium and recourse was had to

the rather drastic nitrating reagent, nitrogen pent-

oxide.   3:5-Monacetone-γ-methylxyloside-2-nitrate (IIa)

was isolated as an impure syrup, the impurities being

accounted for by the loss of the acetone group or by the

loss of the methyl group in the reducing position with

subsequent replacement by a nitrate radical.

Hydrolysis of the product was again effected

with methyl alcohol containing 1% dry hydrogen chloride,

whereby the acetone group was eliminated and the sub-

stance simultaneously converted to the normal form.

Subsequent methylation by the Purdie reagents afforded

3:4-dimethylmethylxyloside-2-nitrate (IVa) as an impure

syrup.   The nitrate group was then eliminated by re-

duction processes to give 3:4-dimethylmethylxyloside (V),

which was also shown by analysis to contain impurities.

In an endeavour to eliminate as far as possible these

impurities, the substance was subjected to an alkaline

treatment since it was thought that partial oxidation of

the molecule had taken place at some point in the syn-

thesis whereby an acid derivative had been formed.

The alkaline treatment was continued until a product was

isolated which analysed closely for 3:4-dimethylmethyl-

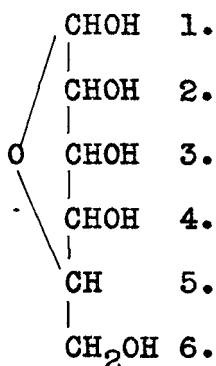xyloside (V).   The product was now treated to acid

hydrolysis in the same manner as has been described
for the isolation of 3:4-dimethyl xylose in the alter-
native method, when a pure product was obtained which
compared favourably with that already isolated, as far
as could be ascertained at this stage, since both products
were syrups.   An attempt was made to characterise the
syrupy material obtained by the formation of the osazone
and the β-methylxyleside derivative but none of these
products could be induced to crystallise.

Thus a comparison of the final products obtained
by these methods was rendered valueless while an adverse
criticism of the second method of preparation of 3:4-
dimethyl xylose was inevitable since the intermediate
products isolated during the course of the work appeared
to be complicated by uncertain secondary reactions
which were rendered apparent by the analytical data
observed.   The observations made during the present
attempted synthesis of 3:4-dimethyl xylose would point
to the idea that one of the subsidiary reactions taking
place was one of oxidation of the pentose molecule while
nitration was being effected.   It was also apparent
that more extensive knowledge was required before
definite assertions could be made with regard to the
nitration of pentoses with nitrogen pentoxide as the
nitrating reagent.
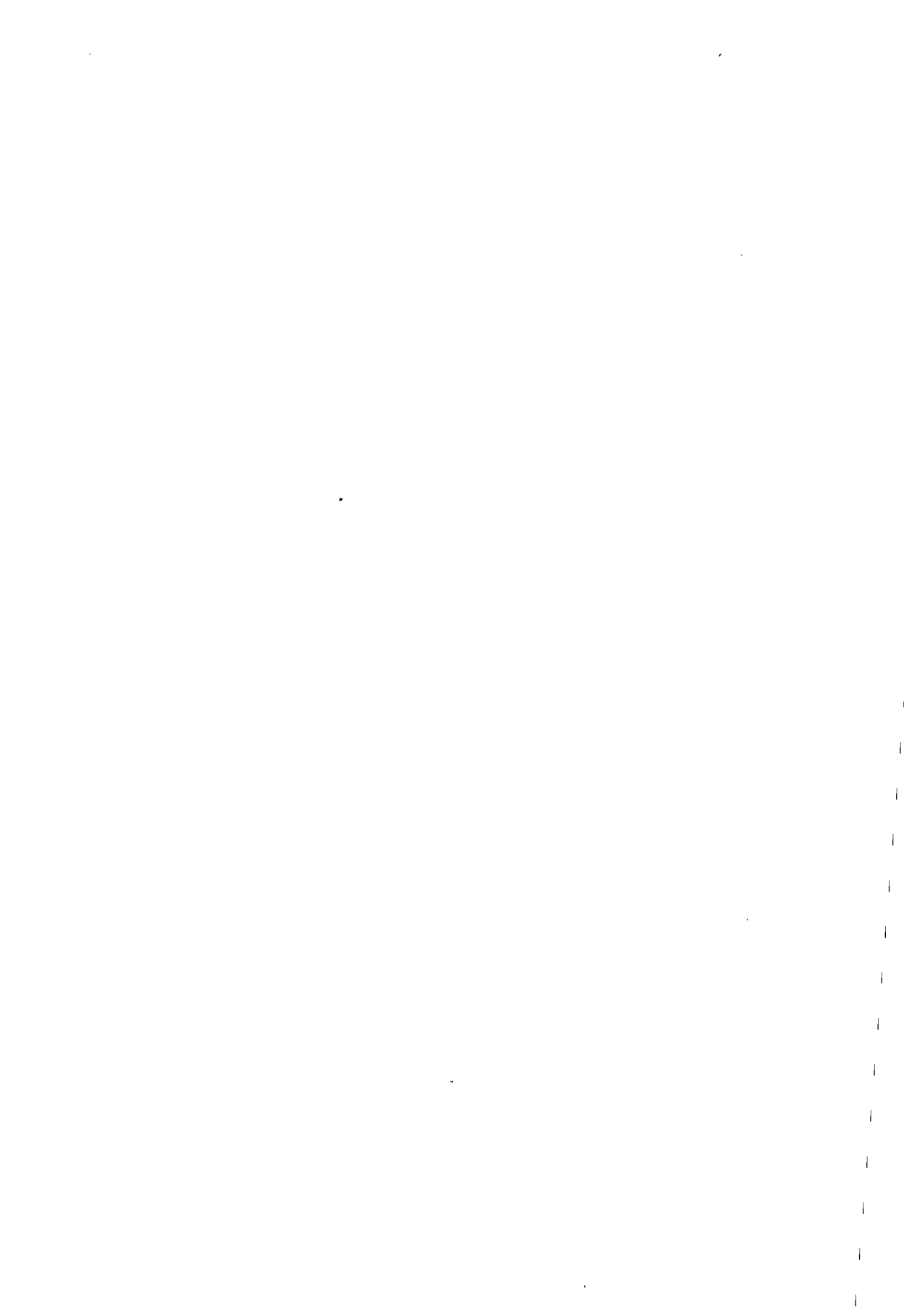
SYNTHESIS OF 2:4-DIMETHYL-β-METHYLXYLOSIDE.

Helferich (Ann., 1924, <u>140</u>, 1, and Ber., 1925, <u>58</u>, 872) has stated that when triphenylchloromethane reacts with glucose or α- and β-methylglucoside the 6 position is occupied preferentially. From work carried out in this Laboratory, however, Oldham and Rutherford (J.,Am. Chem. Soc., 1932, <u>54</u>, 366) state that they

```
  /CHOH  1.
  |
  /CHOH  2.
  |
O  CHOH  3.
  |
 .\CHOH  4.
  |
  \CH     5.
  |
  CH₂OH 6.
```

have reason to suggest "that the aromatic residue is capable of entering positions other than 6."

More recently, Hudson and Hockett (J. Am. Chem. Soc., 1931, <u>53</u>, 4456) describe the isolation of a condensation product of triphenylchloromethane with β-methyl-xyloside which could not be induced to crystallise. It was decided to utilise this condensation material in a further attempt to complete the synthesis of the dimethyl xyloses.

β-Methylxyloside was therefore condensed with triphenylchloromethane as described by Helferich (Ber., 1925, <u>58</u>, 877) when the syrupy product described by

Hudson and Hockett (<u>loc</u>. <u>cit</u>.) was obtained, which was subsequently acetylated in the usual manner.   No crystallisation could be affected at this stage but with the removal of the trityl residue, the substance was readily converted into a crystalline diacetyl-β-methylxyloside-mononitrate, where the nitrate group may be considered as having replaced the trityl group since acyl rearrangement was precluded by the experimental conditions involved.

The deacetylation of diacetyl-β-methylxyloside-mononitrate was accomplished with difficulty since the ordinary methods of deacetylation would have led to the simultaneous removal of the nitrate group.   The process finally adopted was a modified form of that described by Zemplen, (Ber., 1929, 62, 1613) and consisted of the addition of sodium methylate which acted as a catalytic deacetylation reagent.   The modification consisted in the immediate addition of glacial acetic acid in an attempt to grade the reaction since the nitrate group would also be susceptable.   The crude isolated material was then submitted to methylation when no crystallisation could be effected when it was deduced from the syrupy nature of the product obtained, that deacetylation had been incompletely performed.

Further treatment with sodium methylate being considered
inadvisable, the product was treated with dimethylamine
at the ordinary temperature when the isolated material
was again methylated.   The experimental conditions were
then so adjusted that a separation of any fully methylated
pentose was effected.   No crystallisation of the main
product dimethyl-β-methylxyloside-mononitrate took
place and analysis showed that a slight impurity was
present in the final substance probably consisting of
unchanged diacetyl-β-methylxyloside-mononitrate.

Elimination of the nitrate group was accomplished
in a similar manner to that described by Irvine and
Rutherford (J. Am. Chem. Soc., 1932, 54, 1491) when
dimethyl-β-methylxyloside was obtained in the form of
long colourless needles, m.p. 60-61° from which further
characterisation was afforded by the formation of
dimethyl-β-methylxyloside-p-toluenesulphonate.

The proof that the derivative of the dimethyl
xylose now synthesised was 2:4-dimethyl-β-methylxyloside
was furnished by the comparison of this product with
those obtained from 3:4-domethyl xylose and 2:3-dimethyl
xylose now to be described.

ISOLATION OF 2:3-DIMETHYL XYLOSE.

The preparation of 2:3-dimethyl xylose was carried out as described by Hampton, Haworth, and Hirst (J., 1929, 1746). Crude xylan was precipitated from an aqueous solution of soda-lye, obtained from esparto grass, by the addition of rectified spirit and subsequently purified by treatment with acetic acid, alcohol and ether. The substance was obtained as a dark brown powder which was generally subjected to the purification process a second time and finally obtained as a light brown fibrous powder.

Methylation of the xylan was effected using dimethyl sulphate and the process repeated three times when the methoxyl content had increased to 30.4%(dimethyl xylan OCH_3= 38.8%). Purification was effected by solution of the methylated product in the least amount of chloroform and subsequent precipitation with dry ether when the substance was separated as an almost yellowish flocculent precipitate but which rapidly darkened on standing. The product was hydrolysed by boiling in methyl alcohol containing 1.2% dry hydrogen chloride and extracted in the usual manner when 2:3-dimethylmethyl -xyloside was submitted to purification by distillation

in a high vacuum.   Further hydrolysis to the parent
sugar was carried out by boiling with 3% aqueous hydro-
chloric acid and 2:3-dimethyl xylose isolated as a
yellow, viscid syrup.

2:3-Dimethyl-β-methylxyloside was prepared in
the usual manner for β-methylxyloside formation
(Fischer, Ber., 1916, 49, 584) and isolated as a mobile
syrup which could not be induced to crystallise although
a crystalline derivative was readily obtained by the
preparation of 2:3-dimethyl-4-p-toluenesulphonyl-β-
methylxyloside which completed the data required for
comparison and identification of the dimethyl derivative
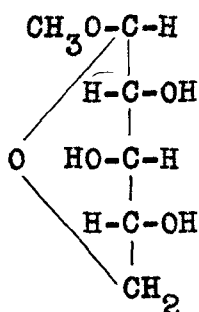described.

P A R T   III.

SUMMARY   OF   RESULTS.

SUMMARY OF RESULTS.

The methods available for the preparation of
β-methylxyloside have been amplified.   Fischer's
method (loc. cit.) for the preparation of the anal-
ogous β-methylglucoside has been applied successfully
to the formation of β-methylxyloside, which was ob-
tained in theoretical yield from xylose tetracetate,
and although the method was lengthy and somewhat tedious
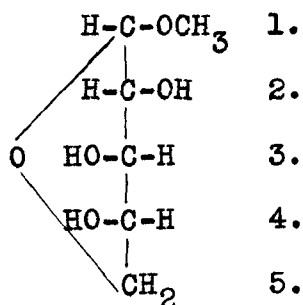it was found to be thoroughly trustworthy.

It was found however, that β-methylxyloside
could be obtained in 30% yield when dry xylose was
condensed with methyl alcohol containing 2% dry hydrogen
chloride at the ordinary temperature.   In experiments
where 1% hydrogen chloride was employed. β-methylxyloside
was again obtained and it would seem that a proportion
of β-methylxyloside is always formed to some extent
when xylose condenses with methyl alcohol under these
conditions.   At the same time, the results obtained
would point to the idea that when stronger concentrations
of acid are employed, the yield of the β-derivative is
increased at the expense of γ-methylxyloside.   In the
experiments quoted, γ-methylxyloside was generally obtained

in poor yield, judging from the amount of 3:5-monacetone-
γ-methylxyloside derived, since no means could be devised
of separating γ-methylxyloside from the crude mixture
of normal and γ-forms.

A point of more than usual interest arises in
that β-methylxyloside does not condense with benzaldehyde
whilst it may be recalled that α-methylarabinoside
condenses with benzaldehyde to give 3:4-benzylidene-
α-methylarabinoside.

$$
\begin{array}{ll}
CH_3O\text{-}C\text{-}H & \\
H\text{-}C\text{-}OH & \\
HO\text{-}C\text{-}H & \\
H\text{-}C\text{-}OH & \\
CH_2 & \\
\end{array}
$$

$$
\begin{array}{ll}
H\text{-}C\text{-}OCH_3 & 1. \\
H\text{-}C\text{-}OH & 2. \\
HO\text{-}C\text{-}H & 3. \\
HO\text{-}C\text{-}H & 4. \\
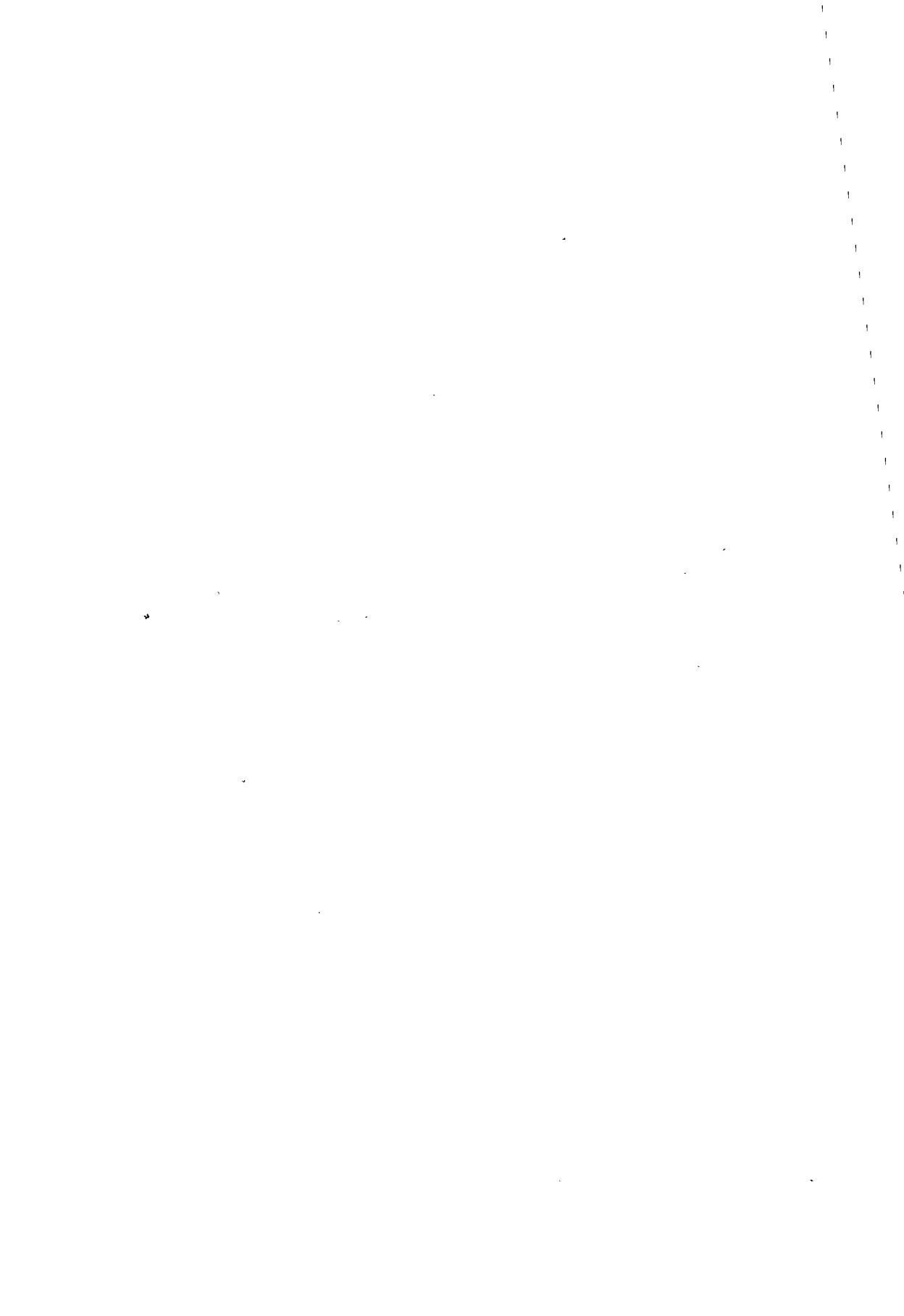CH_2 & 5. \\
\end{array}
$$

(XI)   (XII)

A study of the structural formulae assigned
to these substances, shows that β-methylxyloside (XI)
contains the hydroxyl groups in the _trans_ positions
whilst hydroxyl groups 3 and 4 in α-methylarabinoside
(XII) are in the _cis_ position.   The _trans_ disposition
of the hydroxyl groups in β-methylxyloside was thus
proved to be unfavourable to the entry of the benzyl-
idene resdiue.   The condensation of xylose with
benzaldehyde proceeded however to form a dibenzylidene-

xylose. These results could only be explained by
inferring that xylose reacted with benzaldehyde in the
γ-form to give a dibenzylidene derivative of structure
(XIII) analogous with that assigned to diacetone-xylose
by Haworth and Porter (loc. cit.). In contrast with
diacetone xylose, dibenzylidene-xylose could not be
partially hydrolysed to give a monobenzylidene derivative.

$$\begin{array}{c}
\text{H-C-O} \\
\text{|} \quad \text{CH.C}_6\text{H}_5 \\
\text{H-C-O} \\
\text{|} \\
\text{O-C-H} \quad \text{O} \\
\text{|} \\
\text{C}_6\text{H}_5\text{.CH} \quad \text{H-C} \\
\text{|} \\
\text{O-CH}_2
\end{array}$$
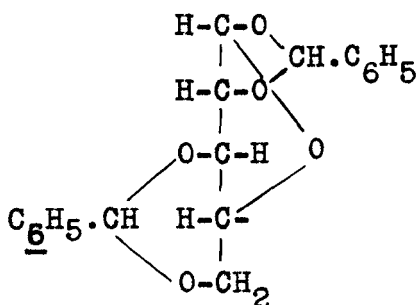
(XIII)

The structure of 2-methyl xylose has been
definitely established since the derived osazone is
identical with the xylosazone showing that the methyl
group in 2-methyl xylose occupied a reacting position
in the molecule.

The study of the condensation of 2-methyl xylose
with acetone was complicated to such an extent by un-
known side-reactions, that the entering position of the
acetone residue could not be ascertained, although it
would seem probable that 2-methyl xylose would assume
the γ-form and effect condensation in the 3:5 position.

Such a procedure would again furnish 2-methyl xylose as already outlined. In this respect also arabinose shows a marked contrast, since 2-methyl arabinose condenses with acetone to give 2-methyl-3:4-monacetone-arabinose which could only be accounted for by assuming that the cis position of the hydroxyl groups 3 and 4 was more favourable to the entry of the acetone residue.

Since 3:4-dimethyl xylose was prepared by the methylation of a partially benzoylated compound, it was all important to prove the structure of the sugar obtained, since acyl migration could have occurred (Levene and Raymond, J. Biol. Chem., 1933, 102, 331, and Robertson, J., 1933, 737). The first attempt in this direction was the substitution of the nitrate group in 3:5-monacetone-γ-methylxyloside in place of the benzoyl residue during the synthesis of 3:4-dimethyl xylose, since, so far as it was known, the nitrate group was stable towards methylation while any decomposition occurring in the molecule could be readily detected. Unfortunately, the introduction of the nitrate group was attended by obscure complications and analyses of the compounds obtained point to the idea that one of these side reactions is oxidation. In the end, where a crystalline derivative was naturally expected a syrupy product was obtained which thus rendered further comparison with
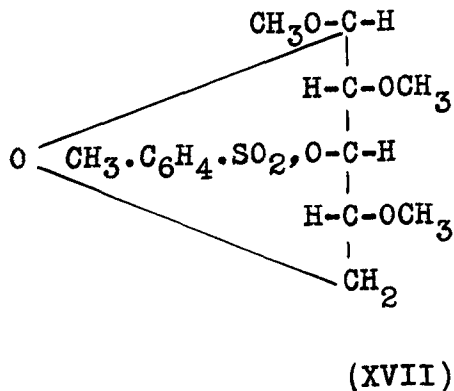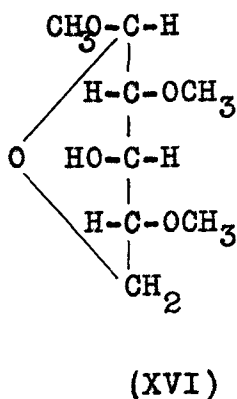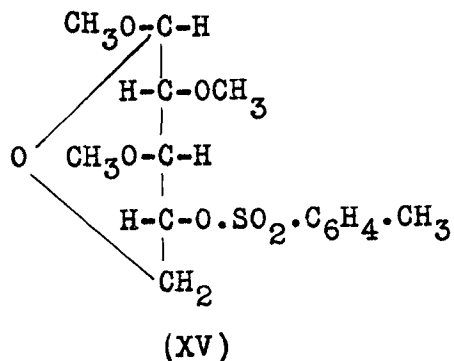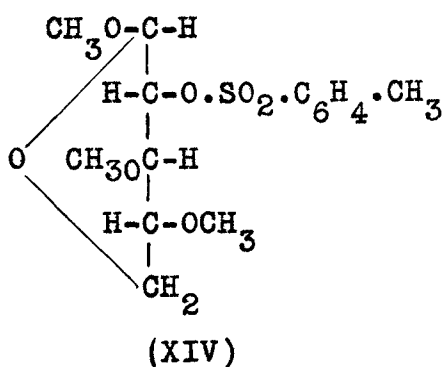
the crystalline material isolated through the benzoyl
method of preparation of 3:4-dimethyl xylose impossible.

Osazone formation from the dimethyl sugar was also
considered unsatisfactory in so far as no crystallisation
could be effected but the methoxyl estimation of the
syrup showed that no loss of methoxyl group had taken
place during osazone formation and therefore that these
methyl groups did not occupy a reacting position in the
molecule.

2:3-Dimethyl xylose has already been isolated
(Hampton, Haworth and Hirst, loc. cit.) and character-
ised so that the structure of 2:3-dimethyl-β-methylxyloside
now prepared is well established and by p-toluenesulphon-
ation 2:3-dimethyl-4-p-toluenesulphonyl-β-methylxyloside
is obtained.

The constitution of the dimethyl-β-methylxyloside
isolated from the initial condensation of β-methylxyl-
oside with triphenylchloromethane naturally rests upon
the position occupied by the trityl group, since the
nitrate group may be considered to have replaced the tri-
tyl radical in the acetylated trityl compound, the ex-
perimental conditions throughout precluding any possibility
of acyl rearrangement. The dimethyl-β-methylxyloside
was readily obtained in a crystalline form from which
a dimethyl-β-methylxyloside-p-toluenesulphonate was

derived.   That this product was entirely different from 2-p-toluenesulphonyl-3:4-dimethyl-β-methylxyloside (XIV) and 4-p-toluenesulphonyl-2:3-dimethyl-β-methylxyloside (XV) already isolated, was readily seen by comparison. The product was therefore assigned the 2:4-configuration so that the compounds isolated were 2:4-dimethyl-β-methyl-xyloside (XVI) and 2:4-dimethyl-3-p-toluenesulphonyl-β-methylxyloside (XVII).

$$CH_3O\text{-}C\text{-}H$$
$$H\text{-}C\text{-}O.SO_2.C_6H_4.CH_3$$
$$CH_3O\text{-}C\text{-}H$$
$$H\text{-}C\text{-}OCH_3$$
$$CH_2$$
(XIV)

$$CH_3O\text{-}C\text{-}H$$
$$H\text{-}C\text{-}OCH_3$$
$$CH_3O\text{-}C\text{-}H$$
$$H\text{-}C\text{-}O.SO_2.C_6H_4.CH_3$$
$$CH_2$$
(XV)

$$CH_3O\text{-}C\text{-}H$$
$$H\text{-}C\text{-}OCH_3$$
$$HO\text{-}C\text{-}H$$
$$H\text{-}C\text{-}OCH_3$$
$$CH_2$$
(XVI)

$$CH_3O\text{-}C\text{-}H$$
$$H\text{-}C\text{-}OCH_3$$
$$CH_3.C_6H_4.SO_2,O\text{-}C\text{-}H$$
$$H\text{-}C\text{-}OCH_3$$
$$CH_2$$
(XVII)

EXPERIMENTAL.

PREPARATION OF β-METHYLXYLOSIDE.

(a)   This method of preparation of β-methylxyloside
is an application of that described by Fischer (B.,
1916, <u>49</u>, 584) for the preparation of β-methyl-
glucoside.

10 g. Xylose (m.p. 143-144°) were mixed with
5 g. anhydrous sodium acetate and covered with acetic
anhydride.   Heat was applied until a vigorous reaction
began when the source of heat was removed and the mixture
allowed to cool.   While still warm the solution was
poured into water and extracted five times with benzene.
The benzene solution was washed with dilute sodium hydr-
oxide until the washings were only slightly coloured,
once with dilute hydrochloric acid and finally once with
water.   The benzene solution was then dried over anhydrous
sodium sulphate and taken to dryness in a vacuum and the
product crystallised from hot absolute alcohol.
Yield of tetracetyl xylose 11.2 g. = 53%.   m.p. = 124-125°.

20 g. Tetracetyl xylose were dissolved in 150 cc.
sodium dried benzene when 20 cc. (10% by volume) of a
40% solution of hydrobromic acid in glacial acetic acid
and 30 cc. (15% by volume) of sodium dried ether were
added, thus making a 10% solution of tetracetyl xylose.

The solution was allowed to remain out of contact with air for five hours when the rotation became constant at $\alpha_D = +20.4°$. Thereafter, the solution was quickly washed twice with water and once with a strong solution of potassium bicarbonate, dried over anhydrous sodium sulphate, filtered and one-third volume of methyl alcohol added with 18 g. freshly prepared silver carbonate and the mixture shaken from 4-5 hours in a mechanical shaker. After removal of the silver residue, the solution was taken to dryness under diminished pressure when a viscous syrup was obtained (14.4 g.) which showed a slight reducing action towards Fehling's solution. The syrup was now dissolved in 5 cc. benzene and methylated once with 9 cc. methyl iodide and 14 g. silver oxide. After filtration from the inorganic residue the solvent was removed under diminished pressure and the product isolated as a hard glass (14.2 g.) which crystallised from a mixture of absolute alcohol and petroleum ether (b.p. 40-60°). Yield 9.1 g.   m.p. 115°.

A concentrated solution of 10 g. triacetyl-β-methylxyloside in absolute alcohol was treated with 0.2 g. potassium in alcoholic solution. The solution was boiled for one minute and poured into water containing slightly less than the theoretical amount of tartaric acid necessary to precipitate the potassium as potassium

hydrogen tartrate (0.7 g.). The ethyl acetate formed
in the catalytic reaction was now extracted with chloro-
form and the water solution taken to dryness under dim-
inished pressure. The β-methylxyloside formed was extract-
ed with boiling absolute alcohol, the bulk of the alcohol
removed under diminished pressure and the product allowed
to crystallise. After two crystallisations from absolute
alcohol the substance gave the correct m.p. 156-157°.
The yield of the product was almost theoretical.

The above method of preparation of β-methyl-
xyloside was discontinued when it was discovered that
β-methylxyloside could also be isolated during the
preparation of γ-methylxyloside.

(b)   Isolation of β-methylxyloside during the
        formation of γ-methylxyloside.

γ-Methylxyloside was first described by Haworth
and Westgarth (J., 1926, 880) and their experiment was
slightly modified in order to reduce the time taken to
complete the reaction.

30 g. Xylose were dissolved in 750 cc. methyl
alcohol containing 12 g. dry hydrogen chloride thereby
forming a 5% sugar solution with 2% acid present and the
mixture allowed to remain at room temperature till the
solution no longer reduced Fehling's solution. The time
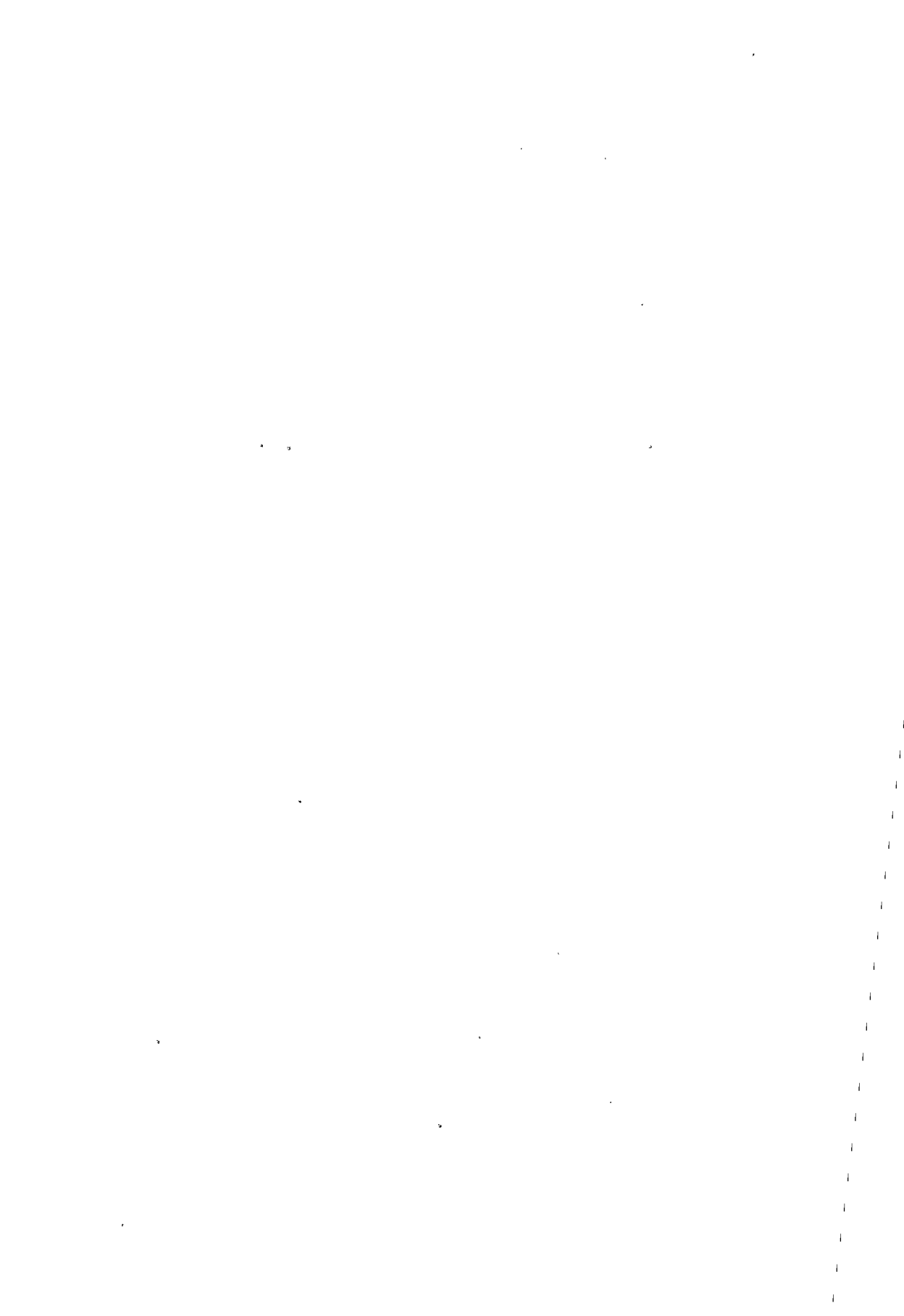
required to complete the reaction varied in different experiments from three to four days, whereas Haworth's experiment (Haworth and Westgarth, loc. cit.) required from five to seven days using 1% acid methyl alcohol. The colour of the solution during the experiment was noticed to change from a greenish tinge to a distinctly yellow colour.   The acid was now neutralised in the cold by shaking the solution with excess lead carbonate for one hour in a mechanical shaker and then by slowly raising the temperature to boiling point.   After removal of the inorganic material, the solvent was removed under diminished pressure and the product obtained as a yellow, viscous syrup (32 g.).   25 cc. Acetone were now added and the syrup allowed to crystallise when a thick bed of colourless crystals was obtained.   After filtration and one recrystallisation from absolute alcohol, β-methylxyloside was obtained with m.p. 156°.   The yield of β-methylxyloside varied in different experiments but approximated to 30%.   The acetone was taken to dryness under diminished pressure when a pale yellow mobile syrup was obtained consisting of a mixture of α- and γ-methylxylosides contaminated possibly with traces of β-methylxyloside.

PREPARATION OF MONACETONE-γ-METHYLXYLOSIDE.

The above α and γ-methylxyloside mixture (20 g.) was dissolved in 200 g. acetone containing 2 g. dry hydrogen chloride and the solution allowed to remain at room temperature for ten minutes. The solution was then neutralised by pouring the mixture into water containing twice the theoretical amount of potassium bicarbonate (11 g.) necessary to neutralise the acid present and extracted five times with chloroform. The extract was dried over anhydrous sodium sulphate and the solvent removed under diminished pressure when monacetone-γ-methylxyloside was obtained as a coloured mobile syrup (8.7 g.) which distilled in a vacuum at 102-107° (bath temperature)/0.1 mm. to give a colourless, mobile syrup (5.2 g.), 21%.

Methoxyl estimation:-

Monacetone-γ-methylxyloside requires OCH_3 = 15.2%

Found OCH_3 = 14.2%

Rotation:-

$[\alpha]_D$ = +17.3° in chloroform, c = 4.39%.

CONDENSATION OF β-METHYLXYLOSIDE WITH BENZALDEHYDE.

(a)   Freudenburg's method (B., 1928, 61, 1750) for
the formation of benzylidene compounds was used.

2.5 g. β-Methylxyloside was shaken with 2 g.
powdered anhydrous zinc chloride in 8 cc. freshly
distilled benzaldehyde for four hours in a mechanical
shaker.   The reaction was poured into water and extracted
three times with chloroform, the chloroform extract
dried over anhydrous sodium sulphate, filtered and the
solvent removed under diminished pressure.   A small
residue was obtained which did not crystallise and which
showed no rotation, showing that no condensation had taken
place between β-methylxyloside and benzaldehyde.

(b)   The following method (Irvine and Scott, J., 1913,
103, 585) for the condensation of sugars with benzalde-
hyde was also investigated in order to discover whether
an increase of temperature would promote the condensation.

3 g. β-Methylxyloside was heated with 15 cc.
freshly distilled benzaldehyde in an oil-bath to 150°
in an atmosphere of carbon dioxide.   This was accomplished
by heating the solution under slightly reduced pressure
and drawing carbon dioxide through the capillary tube
used.   Heating was continued for four hours when the
temperature was raised and the vacuum increased in order

to distil over unchanged benzaldehyde. A syrup remained which crystallised from absolute alcohol but proved to be β-methylxyloside by a mixed melting point determination with an authentic specimen of β-methylxyloside. No condensation product was isolated.

CONDENSATION OF XYLOSE WITH BENZALDEHYDE.

3 g. Pure dry xylose was shaken for four hours with 2.5 g. powdered zinc chloride and 9 cc. freshly distilled benzaldehyde. The condensation product was isolated by pouring the reaction mixture into water and extracting the solution three times with chloroform, drying the extract over anhydrous sodium sulphate and removing the solvent under diminished pressure. A slightly coloured syrup was obtained (2.1 g.) which crystallised readily from absolute alcohol. Acetylation in the usual manner and recovery of the material unchanged showed that the condensation product was dibenzylidene-xylose, m.p. 135-136°, $[\alpha]_D = +21.5°$ in chloroform, c = 3.4.

(cf. Van Ekenstein, Rec. Trav. Pays-Bas, 25, 153)

Attempted Partial Hydrolysis of Dibenzylidene-xylose.

After preliminary experiments with different concentrations of hydrochloric acid, the hydrolysis was finally attempted with N/50 hydrochloric acid.

Accordingly, dibenzylidene-xylose (1 g.) was dissolved in acetone (45 cc.), water (4 cc.) and normal hydrochloric acid (1 cc.), thus making N/50 hydrochloric acid solution with 10% water present. After an initial rotation, the solution was boiled for 15 minutes, cooled and the rotation of the solution again recorded. This process was repeated until a constant value was obtained.

Time	l	α_D	$[\alpha]_D$
Initial	1 dm	+1.76°	+88°
15 mins.	"	+1.66°	+83°
30 mins.	"	+1.42°	+71°
45 mins.	"	+1.22°	+61°
60 mins.	"	+1.02°	+51°
75 mins.	"	+1.02°	+51°
90 mins.	"	+0.95°	+47.5°
105 mins.	"	+0.79°	+39.5°
120 mins.	"	+0.79°	+39.5°
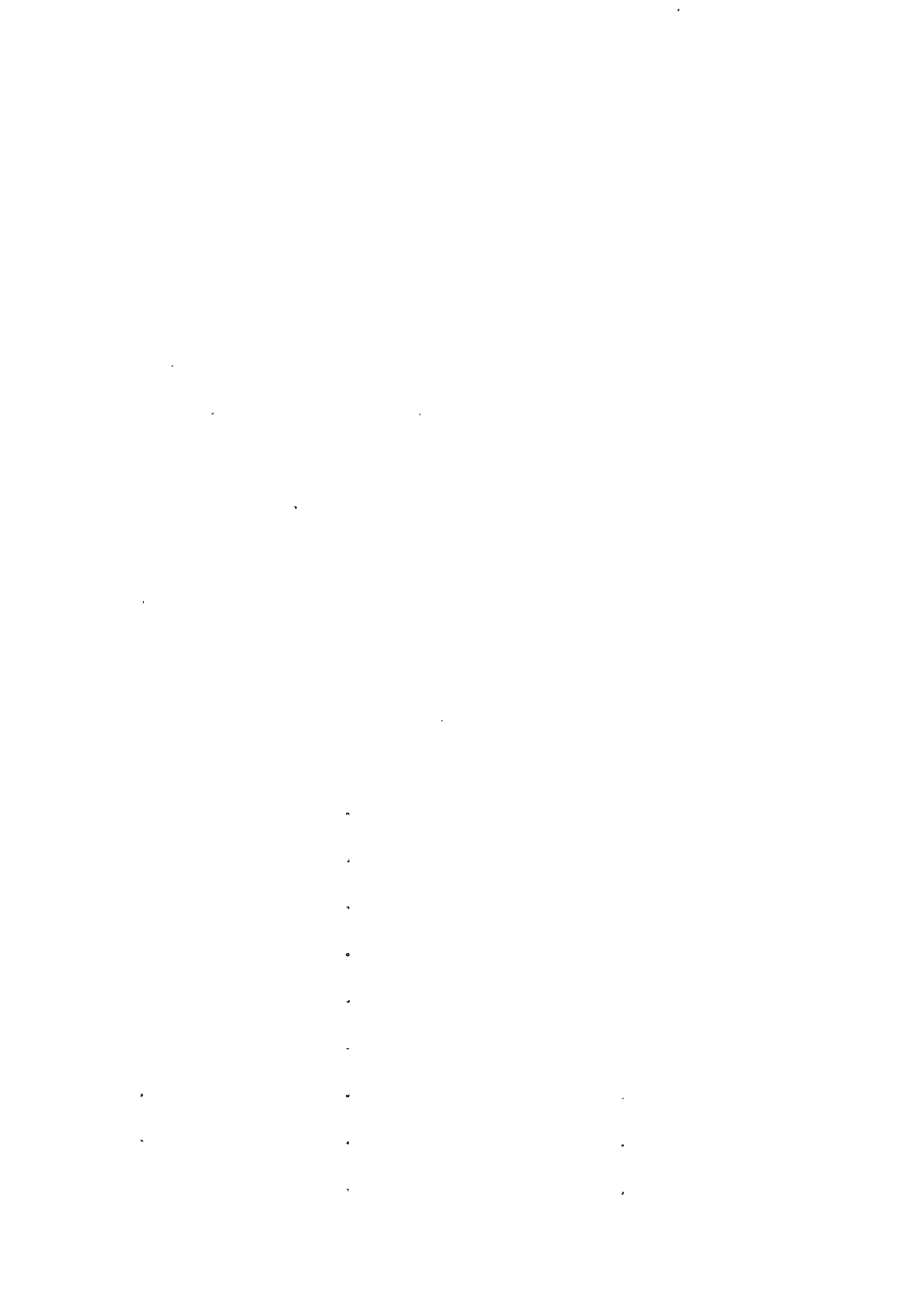
On plotting the values for a complete hydrolysis
it was deduced that after hydrolysing under the same
conditions for one hour, a monobenzylidene derivative would
be present.   On repeating the experiment, however,
limiting the hydrolysis to one hour, no monobenzylidene
derivative could be isolated, the product being a mixture
of xylose and the dibenzylidene derivative.

SYNTHESIS OF 2-METHYL XYLOSE.

(a) 3:5-Monacetone-2-methyl-γ-methylxyloside.

Methylation of 3:5-monacetone-γ-methylxyloside
(4.4 g.) see p. 48, was carried out in the usual
manner, using silver oxide (4 g.), methyl iodide (4 cc.)
and acetone (2 cc.) and refluxing gently for four
hours. The methylation process was repeated three times
omitting the addition of acetone at the second and
third operation, while the product was isolated in
each case by filtering away the silver residue and
taking the solution to dryness in a vacuum. After
the fourth methylation, the yellowish syrup obtained
(4.8 g.) showed n_D = 1.4531.

Methoxyl estimation:-

3:5-Monacetone-2-methyl-γ-methylxyloside requires

$$OCH_3 = 28.4\%$$

$$\text{Found } OCH_3 = 26.9\%$$

High vacuum distillation at $77°/0.07$ mm. raised the
methoxyl content to 27.1% and gave n_D = 1.4500, the
product at this stage being a colourless, mobile
syrup.

Robation:- $[\alpha]_D$ = +24.6° in chloroform, c = 3.532%

(b) <u>2-Methyl xylose.</u>

A 10% solution of 3:5-monacetone-2-methyl-γ-
methylxyloside (13 g.) in normal oxalic acid solution
was boiled for one hour, under reflux, when the rotation
became constant.   The cold solution was neutralised
with pure calcium carbonate and heated gently, the
inorganic material removed by filtration and the solution
taken to dryness in a vacuum.   The residue was powdered
and extracted with boiling alcohol, the alcoholic extract
filtered through charcoal and evarporated to smaller
volume when 2-methyl xylose gradually crystallised out
 on cooling.   After repeated crystallisation from hot
absolute alcohol, the product was finally obtained in the
form of colourless needles, m.p. 132-133°.

<u>Methoxyl estimation:-</u>

2-Methyl xylose requires OCH_3 = 18.9%

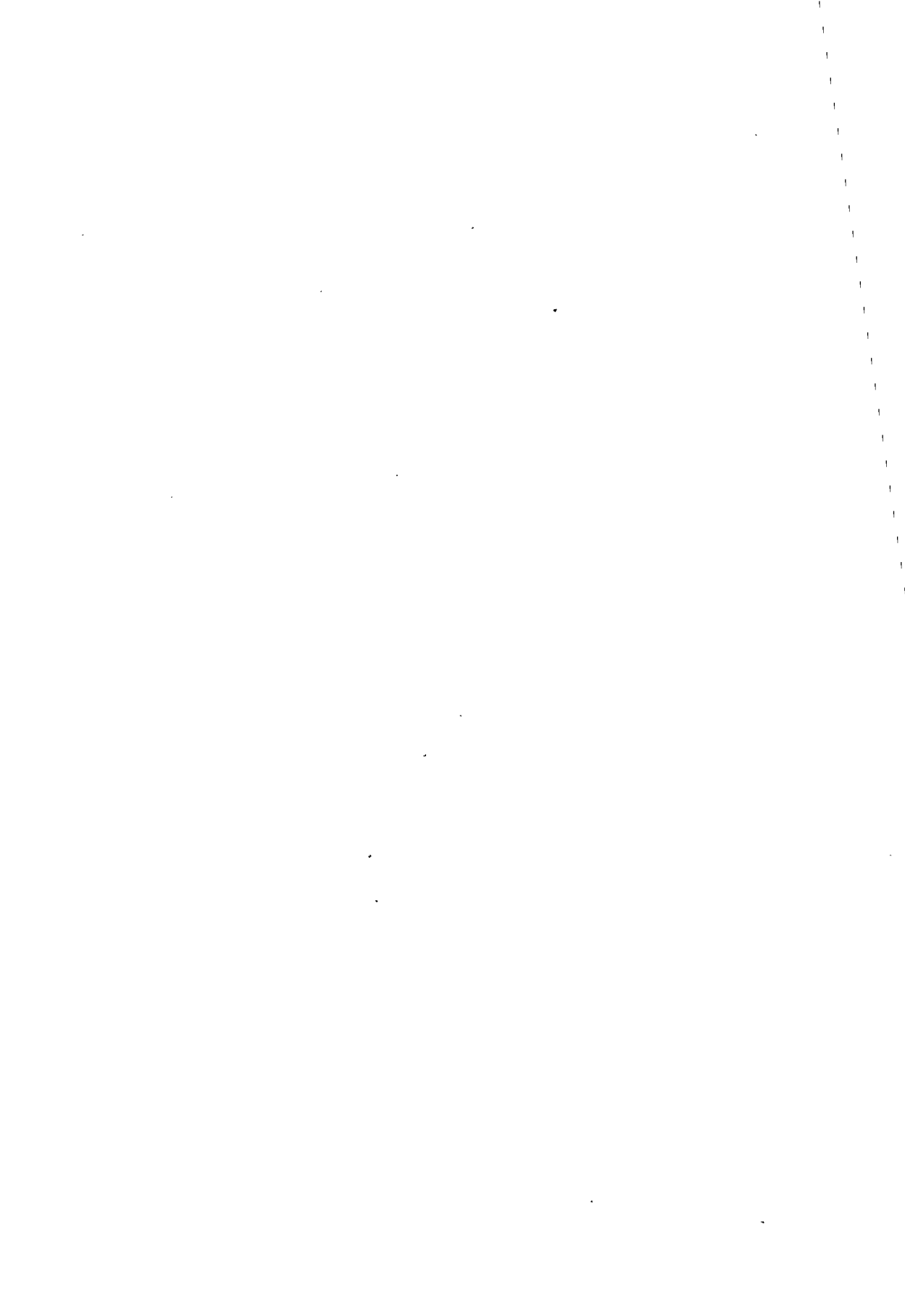Found OCH_3 = 18.3%

<u>Solubility:-</u>

Soluble in hot methyl and ethyl alcohols, hot acetone,
and benzene.   Insoluble in other common solvents.

<u>Rotation:-</u>

The mutarotation curve of 2-methyl xylose is shown on the
following page, where it is seen that an initial rotation
in water of $[\alpha]_D = -23.9°$ changed to a final value of
$[\alpha]_D = +35.9°$ in three hours, showing that the sugar is

MUTAROTATION CURVE OF 2:METHYL XYLOSE IN WATER.

SPECIFIC ROTATION.

+35°
+25°
+15°
+5°
-5°
-15°
-25°

TIME IN MINUTES.

30   60   90   120
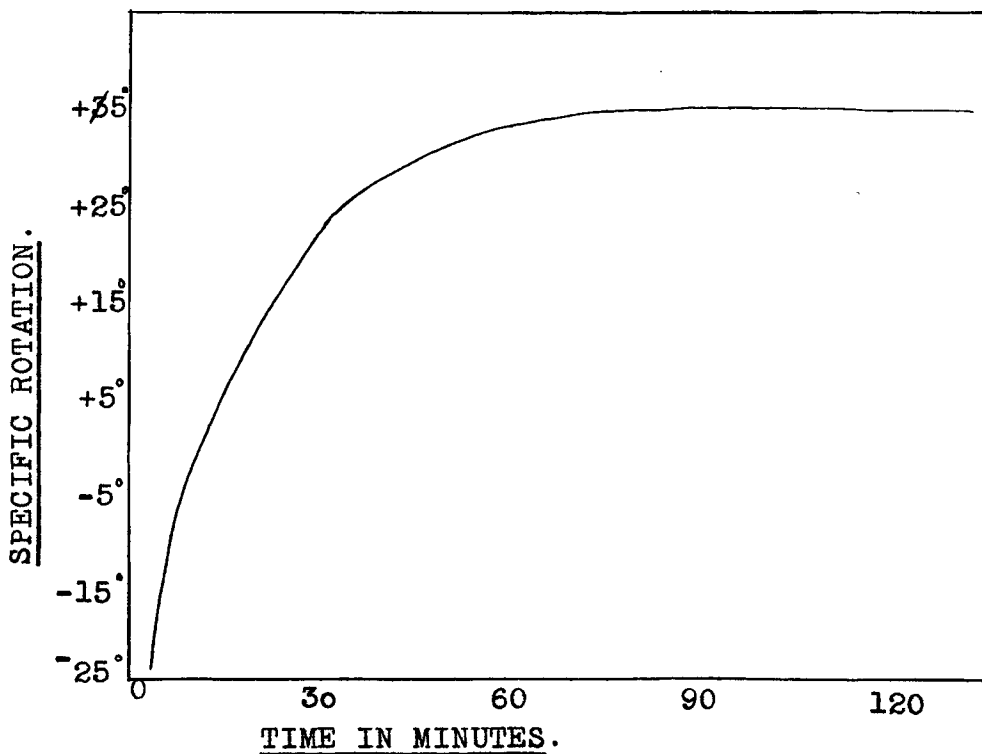
a β-form.

Mutarotation of 2-Methyl Xylose in Water.

Time	α_D	$[\alpha]_D$
3 mins.	-1.74°	-23.9°
4 mins.	-0.84°	-11.5°
5 mins.	-0.84°	-11.5°
6 mins.	-0.71°	-9.8°
7 mins.	-0.60°	-8.3°
8 mins.	-0.39°	-5.4°
9 mins.	-0.17°	-2.4°
10 mins.	-0.10°	-1.4°
11 mins.	+0.13°	+1.8°
12 mins.	+0.19°	+2.6°
14 mins.	+0.36°	+4.9°
16 mins.	+0.61°	+8.4°
18 mins.	+0.76°	+10.5°
20 mins.	+0.99°	+13.7°
22 mins.	+1.12°	+15.4°
24 mins.	+1.30°	+17.9°
26 mins.	+1.50°	+20.7°
28 mins.	+1.6°	+21.9°
30 mins.	+1.70°	+22.9°
45 mins.	+2.16°	+29.8°
1 hr.	+2.43° ......+	33.5°
1 hr.15 mins.	+2.5°	+34.3°
1 hr.30 mins.	+2.53°	+34.8°
2 hr.	+2.53°	+34.8°
2 hr.30 mins.	+2.53°	+34.8°
20 hrs.	+2.61°	+35.97°
Final with NH_4OH	+2.61°	+35.97°

OSAZONE FORMATION FROM 2-METHYL XYLOSE.

2-Methyl xylose when treated with phenyl-
hydrazine in the usual manner for osazone formation,
yielded an osazone melting at 157-158° which contained
no methoxyl group.   The osazone prepared from xylose
gave m.p. 160-161° while a mixed melting point of these
two osazones showed 159-160°.   Thus it was shown
that the osazone from 2-methyl xylose was identical
with that obtained from xylose itself and that the
methoxyl group had been displaced from the pentose
molecule during osazone formation.   This displace-
ment would only occur if the methyl group occupied
a reacting position, namely position 2 in the
molecule.

PREPARATION OF 2-METHYL-β-METHYLXYLOSIDE.

(a) Triacetyl-2-methyl xylose.

2-Methyl xylose (6.5 g.) was dissolved in dry pyridine (50 cc.) and acetic anhydride (15 cc.) added gradually and the solution allowed to remain at room temperature overnight. After pouring into water the solution was extracted three times with benzene, the benzene extract washed twice with dilute hydrochloric acid, once with dilute sodium hydroxide, once with water and finally dried over anhydrous sodium sulphate. Removal of the solvent under diminished pressure gave a syrup (8.5 g.) which crystallised slowly from aqueous alcohol. Two recrystallisations from absolute alcohol gave triacetyl-2-methyl xylose in the form of colourless prisms m.p. 95°.

Methoxyl estimation:-

Triacetyl-2-methyl xylose requires OCH_3 = 10.7%

Found OCH_3 = 11.2%

Rotation:-

$[\alpha]_D$ = -2.2° in chloroform, α_D = +0.08°, $\underline{L}$ = 2, c = 2.27.

Solubility:-

Soluble in hot water, hot alcohols and other common solvents except petroleum ether.

(b) <u>3:4-Diacetyl-2-methyl-β-methylxyloside.</u>

Triacetyl-2-methyl xylose (7.8 g.) was dissolved
in dry benzene (118 cc.) and a 40% solution of hydrogen
bromide in glacial acetic acid (15 cc.) with dry ether
(23 cc.) added and the solution allowed to remain at the
ordinary temperature for five hours out of contact with
air. No optical readings could be observed due to the
effect of the solution on the polarimeter tube and the
gradual darkening in colour of the solution. The
solution was quickly washed with water and again with a
concentrated solution of potassium bicarbonate to remove
the acid tendency absolutely and dried over anhydrous
sodium sulphate. After removal of the inorganic
material, one third volume of methyl alcohol (60 cc.)
was added with silver carbonate (12 g.) and the solution
shaken in a mechanical shaker for four hours when a
further quantity of silver carbonate (6 g.) was added
and the solution again shaken for four hours. The reaction
was shown to be complete by testing a few drops of the
clear solution with alcoholic silver nitrate in the presence
of methyl alcohol when no turbidity ensued. The silver
residue was then removed by filtration and the solvent
evapobated under diminished pressure when a brownish
coloured syrup was obtained which was found to reduce
Fehling's solution to a slight extent. Thereupon, the

syrup was methylated in the usual manner with methyl iodide (6 cc.) and silver oxide (10 g.) and upon extraction the material (6.5 g.) was found to have no action on Fehling's solution and crystallised from a mixture of ether and petroleum ether in the form of colourless needles.   After two recrystallisations the substance showed m.p. 78-79°.

Methoxyl estimation:-

3:4-Diacetyl-2-methyl-β-methylxyloside requires OCH_3 = 23.7%

Found OCH_3 = 22.7%

Rotation:-

$[\alpha]_D$ = -38.1° in chloroform, α_D = -3.06°, $\underline{1}$ = 2 and c = 4.02.

Solubility:-

Soluble in chloroform, acetone, benzene, methyl and ethyl alcohols, warm ether but insoluble in petroleum ether (b.p. 40-60°).

(c)   2-Methyl-β-methylxyloside.

3:4-Diacetyl-2-methyl-β-methylxyloside (5 g.) was dissolved in acetone (10 cc.) and N/2 sodium hydroxide (80 cc.) added and the solution boiled for 15 minutes. After the addition of a large amount of potassium carbonate, the solution was extracted five times with chloroform, the chloroform extract dried over anhydrous sodium sulphate

and taken to dryness under diminished pressure when a
white crystalline mass was obtained (2.9 g.) which
crystallised readily from a mixture of dry ether and a
small quantity of absolute alcohol, in the form of
glistening plates (2.4 g.) m.p. 111-112°. Yield 71%.

Methoxyl estimation:-

2-Methyl-β-methylxyloside requires OCH_3 = 34.8%

Found OCH_3 = 34.2%

Rotation:-

$[\alpha]_D$ = -67.7° in chloroform, α_D = -1.82°, $\underline{l}$ = 2, c = 1.37.

Solubility:-

Insoluble in ether and petroleum ether but soluble in
the other common solvents.

Preparation of 3:4-Di-p-toluenesulphonyl-2-methyl-β-methylxyloside.

2-Methyl-β-methylxyloside (0.2 g.) was dissolved in the least amount of dry pyridine, p-toluenesulphonic chloride (0.7 g.) added and shaken till dissolved when the solution was allowed to stand in a warm room for four days. The product was extracted by treating the solution with aqueous benzene, washing the benzene extract twice with dilute hydrochloric acid and once with dilute caustic soda solution, drying over anhydrous sodium sulphate and taking to dryness under diminished pressure. A pale viscous syrup was obtained (0.5 g.) which crystallised readily from absolute alcohol. Two recrystallisations from absolute alcohol gave the substance (0.35 g.) melting at 123°.

Methoxyl estimation:-

3:4-Di-p-toluenesulphonyl-2-methyl-β-methylxyloside

requires $OCH_3 = 12.8\%$

Found $OCH_3 = 13.0\%$

Rotation:-

$[\alpha]_D = -16.0°$ in chloroform, $\alpha_D = -0.53°$, $\underline{1} = 1$, $c = 3.3\%$

Solubility:-

May be recrystallised from hot methyl and ethyl alcohols, but soluble in the other common solvents except petroleum ether.

CONDENSATION OF 2-METHYL XYLOSE WITH ACETONE.

2-Methyl xylose (3.3 g.) was shaken for six
hours in a mechanical shaker with acetone (125 cc.)
containing 0.2% dry hydrogen chloride.   The solution,
after filtration from undissolved 2-methyl xylose, showed
only a slight trace of reduction with Fehling' s solution.
The amount of recovered 2-methyl xylose was 0.6 g.   The
acetone solution was poured into water containing
twice the theoretical amount of potassium bicarbonate
required to neutralise the acid present and extracted
five times with chloroform.   The chloroform solution,
after drying over anhydrous sodium sulphate, was then
taken to dryness under diminished pressure when a yellow-
ish coloured syrup (1.5 g.) was obtained shewing slight
reducing properties towards Fehling's solution.   The
residue was dissolved in dry ether and decolourised
with charcoal and again taken to dryness.

Methoxyl estimation:-

Monacetone-2-methyl xylose requires OCH_3 = 15.2%

$$\text{Found } OCH_3 = 11.8\%$$

The low methoxyl content could be accounted for by the
presence of mesityl oxide, the presence of which could
not be disputed.

Methylation of the Product obtained from the Condensation of 2-Methyl Xylose with Acetone.

The condensation product (1.2 g.) was submitted to the methylation process in the customary manner, using silver oxide (5 g.), methyliodide (3 cc.) and dry ether (2 cc.). The methylation process was repeated twice omitting the extraneous solvent with the quantities of silver oxide and methyl iodide remaining the same. On extraction, the syrup (1.4 g.) showed $n_D = 1.4578$, after having been heated on a boiling water-bath for two hours under a good vacuum as obtained on the water-pump. The product was distinctly mobile and showed no reaction towards Fehling's solution.
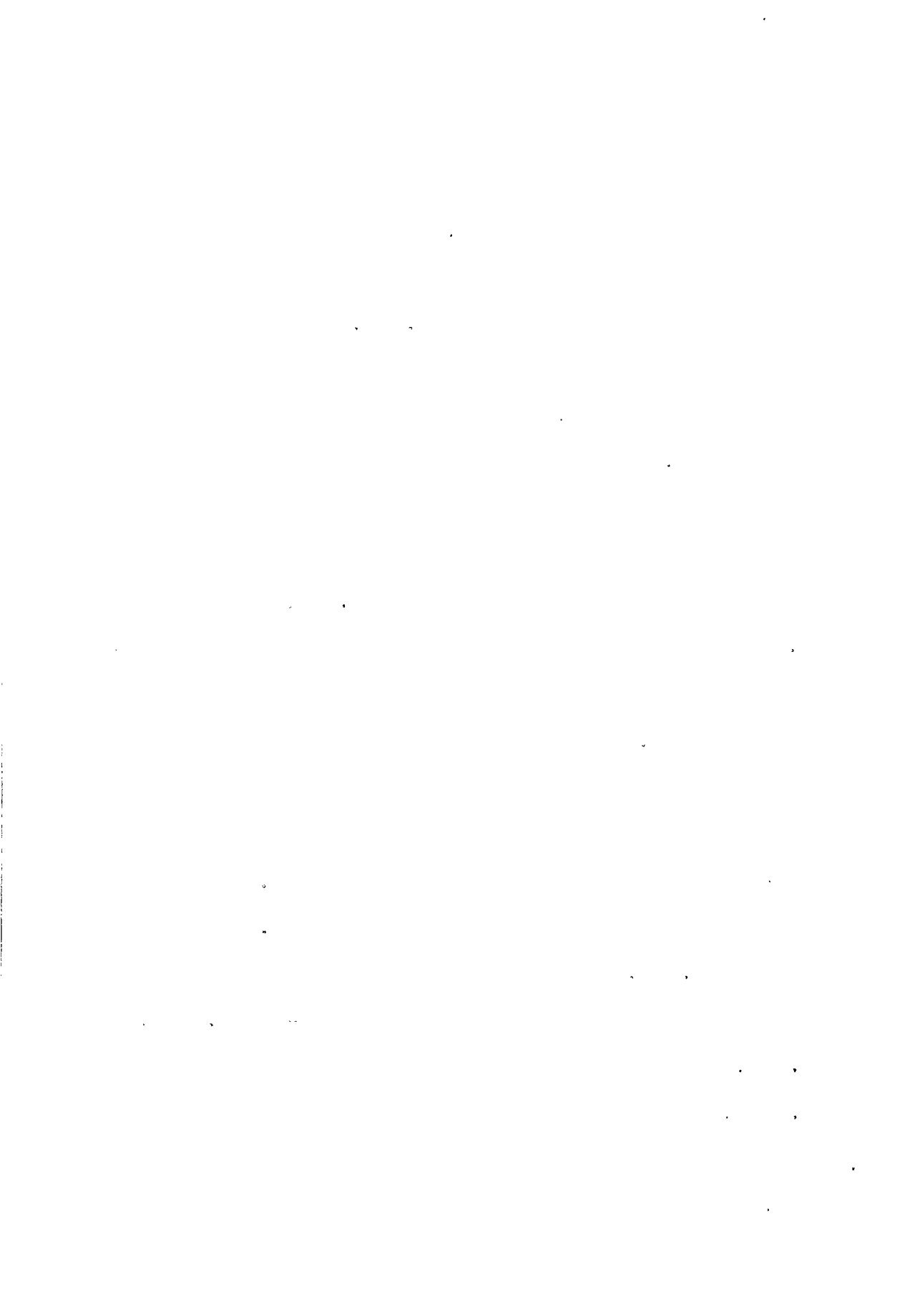
Methoxyl estimation:-

Dimethyl-monacetone xylose requires $OCH_3 = 28.4\%$

Found $OCH_3 = 19.6\%$

The product (1.1 g.) as obtained above was distilled using a high vacuum and bath temperature 90-95°/0.1 mm. when 0.9 g. colourless, mobile syrup was obtained. $n_D = 1.4550$. The syrup showed no reducing properties while the residue consisted of a dark coloured viscous material.

Methoxyl estimation:-

Dimethyl-monacetone xylose requires OCH_3 = 28.4%

Found OCH_3 = 20.2%

Hydrolysis of the Methylated Product obtained from the Condensation of 2-Methyl Xylose with Acetone.

The methylated material (0.75 g.) was now subjected to hydrolysis using normal oxalic acid (15 cc.) and boiling under a reflux condenser in the presence of animal charcoal. The following polarimetric observations were noted:-

Time	$\underline{1}$	T	α_D	$[\alpha]_D$
Initial	1	21°	+2.49°	+49.8°
30 mins.	1	21°	+1.28°	+25.6°
1 hr.	1	21°	+1.30°	+25.9°
1 hr. 30 mins.	1	21°	+1.34°	+26.8°
1 hr. 45 mins.	1	21°	+1.34°	+26.8°

The acid solution was then neutralised with pure calcium carbonate at the boiling point, the solution cooled, filtered and extracted three times with chloroform in order to remove any unhydrolysed material. The water

residue was taken to dryness under diminished pressure
and repeatedly extracted with boiling alcohol.   The
alcoholic solution, after filtration through charcoal,
was taken to dryness under reduced pressure when a hard
glass was obtained (0.3 g.).   No crystallisation could
be effected.

Methoxyl estimation:-

A Dimethyl xylose requires OCH_3 = 34.8%

A Monomethyl xylose requires OCH_3 = 18.9%

$$\text{Found } OCH_3 = 14.0\%$$

These experiments were to a large extent
rendered useless owing to the formation of other con-
densation products in the reaction mixture, e.g.,
mesityl oxide and phorone etc., which were difficult
to eliminate and thus rendered analysis inaccurate.
No definite conclusions could be based on these experiments.

SYNTHESIS OF 3:4-DIMETHYL XYLOSE.

The synthesis of 3:4-dimethyl xylose was
accomplished by utilising monacetone-γ-methylxyloside,
the isolation of which has already been described.
By the benzoylation of monacetone-γ-methylxyloside with
subsequent removal of the iso-propylidene residue and
resultant conversion of the substance to the normal
form, positions 3 and 4 could be methylated.   Removal
of the benzoyl group in position 2 with the methyl-
xylosidic group completed the synthesis of 3:4-dimethyl
xylose.

(a)   <u>2-Benzoyl-3:5-monacetone-γ-methylxyloside.</u>

3:5-Monacetone-γ-methylxyloside (2.7 g.) was
dissolved in pyridine (6 cc.), cooled by immersing the
flask in crushed ice and benzoyl chloride (1.7 cc.)
added drop by drop, when after shaking, the solution was
allowed to stand overnight at room temperature.   The
product was extracted by adding a few drops of pyridine
and water to destroy any benzoyl chloride present followed
by solution in aqueous benzene.   The benzene extract

after washing with acid and alkali, was dried over
anhydrous sodium sulphate and taken to dryness under
diminished pressure when a clear viscous syrup was obtained
in theoretical yield.

The product showed a distinct tendency to crystallise
from the parent syrup on standing, but, since the product
was prepared from γ-methylxyloside originally, the syrup
must have contained α and β forms of the material which
would undoubtedly have led to a large loss of product
if crystallisation to purity had been attempted at
this stage.

Methoxyl estimation:-

2-Benzoyl-3:5-monacetone-γ-methylxyloside requires $OCH_3 = 10.1\%$

Found $OCH_3 = 10.4\%$

(b) 2-Benzoylmethylxyloside.

An attempt was made to hydrolyse away the acetone
group in 2-benzoyl-3:5-monacetone-γ-methylxyloside and
for this purpose methyl alcohol containing 1% dry
hydrogen chloride was used.   It was hoped by this
means to effect the required hydrolysis and to convert
the substance from the γ-form to the normal form
simultaneously.

2-Benzoyl-3:5-monacetone-γ-methylxyloside (1 g.)
in a 5% solution of methyl alcohol containing 1% dry

hydrogen chloride, was boiled for 45 minutes under a
reflux condenser when an initial rotation of α_D = +2.79°
changed to a constant value α_D = +.81°. A strong smell
of methyl benzoate showed that the benzoyl group had
also been hydrolysed away to some extent as had been
expected. The solution was neutralised with lead
carbonate at the boiling point, filtered through animal
charcoal and taken to dryness under diminished pressure.
The residue was dissolved in acetone, the solution filtered
through a bed of animal charcoal and the solvent removed
in a vacuum when a hard glass (0.6 g.) was obtained.

Methoxyl estimation:-

2-Benzoylmethylxyloside requires OCH_3 = 11.5%

Found OCH_3 = 13.0%

(The high methoxyl content recorded was in all probability
due to the presence of methyl benzoate (OCH_3 = 22.8%).

(c)   2-Benzoyl-3:4-dimethylmethylxyloside.

2-Benzoylmethylxyloside (3.6 g.) was now methylated
in the usual manner with silver oxide (5 g.), methyl
iodide (4 cc.) and acetone (1 cc.). The process was
repeated three times omitting the extraneous solvent to
the methylating mixture when the refractive index of the
product became constant at n_D = 1.4890. The syrup
was dissolved in benzene, the benzene extract washed five

times with water to remove any trimethylmethylxyloside
formed through the loss of the benzoyl group with
subsequent methylation of the hydroxyl group thus
exposed.   The benzene solution was dried over anhydrous
sodium sulphate and finally taken to dryness in a vacuum
when a dark-coloured mobile syrup (3 g.) was obtained
having n_D = 1.4992.

Methoxyl estimation:-

2-Benzoyl-3:4-dimethylmethylxyloside requires OCH_3 = 31.4%

Found OCH_3 = 31.2%

(d)   3:4-Dimethylmethylxyloside.

The process of debenzoylation of 2-benzoyl-3:4-
dimethylmethylxyloside was essentially similar to that
described by Zemplen (Ber., 62, 1613).

2-Benzoyl-3:4-dimethylmethylxyloside (2.7 g.)
was dissolved in a few cubic centimetres of methyl
alcohol and sodium (0.1 g.) also dissolved in methyl
alcohol added to the solution and the mixture boiled for
one minute.   After dilution with water, the solution
was distilled in a vacuum until the oily drops of methyl
benzoate ceased to come over into the distillate.
After cooling the solution remaining in the flask,
potassium carbonate was added and the solution extracted
five times with chloroform, the chloroform extract
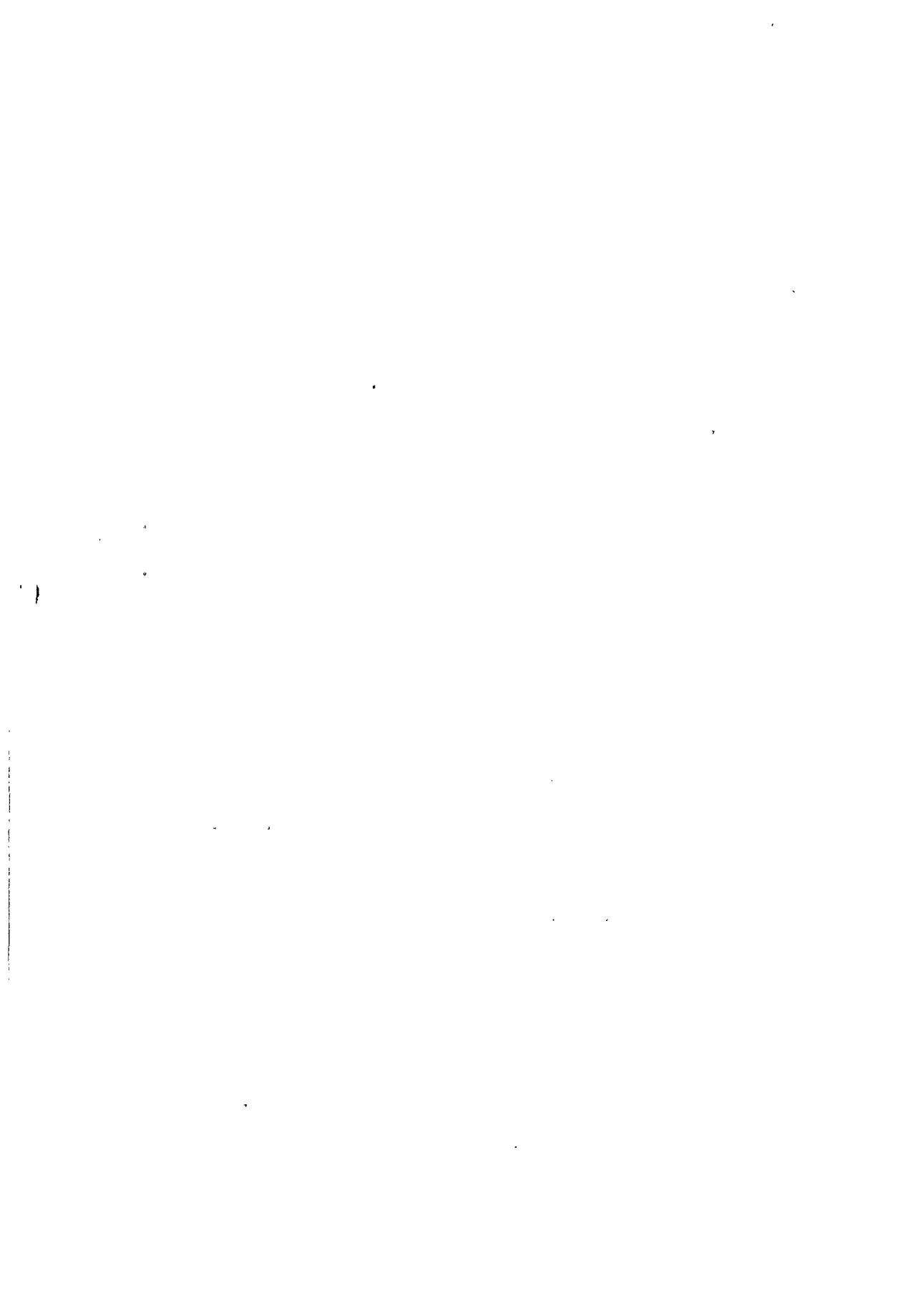
dried over anhydrous sodium sulphate and the solvent

removed under diminished pressure.   The residue was

then dissolved in benzene[x] and this solution repeatedly

extracted with water when the water extract was finally

extracted with chloroform after the addition of potassium

carbonate.   The chloroform extract was again dried

over anhydrous sodium sulphate and taken to dryness

in a vacuum when the product was isolated as a pale

yellow syrup (0.9 g.) which was distilled in a high

vacuum to give a colourless, very mobile syrup (0.75 g.)

at bath temperature 110-115°/0.2 mm.   This syrup

showed n_D = 1.4520 and partially crystallised from

the parent syrup on standing to give syrupy crystals.

Methoxyl estimation:-

3:4-Dimethylmethylxyloside requires OCH_3 = 48.4%

$\qquad\qquad\qquad\qquad\qquad$ Found OCH_3 = 48.6%

---

[x]
  The benzene layer was also dried over anhydrous sodium

sulphate and taken to dryness under diminished pressure

when a brownish coloured syrup (0.3 g.) was obtained

which, by the method of extraction appeared to be un-

changed 2-benzoyl-3:4-dimethylmethylxyloside.   This

was neglected.

(e) 3:4-Dimethyl Xylose.

3:4-Dimethylmethylxyloside (7 g.) was boiled
under a reflux condenser with 3% hydrochloric acid
(140 cc.) and the hydrolysis controlled polarimetrically.

Time	$\underline{1}$	α_D	$[\alpha]_D$
Initial	1	+0.50°	+10.0°
30 mins.	1	+0.96°	+19.2°
45 mins.	1	+1.02°	+20.4°
50 mins.	1	+1.02°	+20.4°

The solution was then decolourised by the addition
of animal charcoal, filtered and the acid present
neutralised by the addition of barium carbonate at the
boiling point.   After filtration, the solution was
extracted five times with chloroform in order to remove
any unhydrolysed material.   Thereafter the aqueous
solution was taken to dryness in vacuo and the solid
residue obtained powdered and repeatedly extracted with
boiling acetone.   The acetone solution was then decolour-
ised with charcoal and taken to dryness under diminished
pressure when the residue was dissolved in sodium dried
ether, again decolourised, filtered and taken to dryness.
The product consisted of a colourless, viscous syrup (5.4 g.)

which, however, failed to crystallise from any of the common solvents. $n_D = 1.4690$.

Methoxyl estimation:-

3:4-Dimethyl xylose requires $OCH_3 = 34.8\%$

Found $OCH_3 = 34.8\%$

Rotation:-

$[\alpha]_D = +5.32°$ changing to $+7.50°$ in 18 hours in chloroform, $\underline{1} = 2$, $c = 4.13\%$.

The following optical readings were observed using water as the solvent, where $c = 2.164\%$

Time	$\underline{1}$	t.	α_D	$[\alpha]_D$
7 mins.	2	23°	+1.30°	+24.9°
47 mins.	2	23°	+1.15°	+22.0°
2 hrs. 27 mins.	2	21.5°	+1.10°	+21.0°
4 hrs. 1 min.	2	18°	+1.07°	+20.5°

Solubility:-

Insoluble in petroleum ether but soluble in all other common solvents tested.

CONDENSATION OF 3:4-DIMETHYL XYLOSE WITH METHYL ALCOHOL CONTAINING 1% HYDROGEN CHLORIDE.

3:4-Dimethyl xylose (0.5406 g.) was dissolved in methyl alcohol (20 cc.) containing hydrogen chloride when the progress of the condensation was observed polarimetrically at 22.5°.

Time	l	α_D	$[\alpha]_D$	Action on Fehling's solution.
Initial	1	+0.60°	+22.2°	Strong reduction.
1 hr. 5 min.	1	+0.60°	+22.2°	Strong reduction.
18 hrs. 50 min.	1	+0.71°	+26.3°	Strong reduction.
1 day 3 hrs.	1	+0.71°	+26.3°	Strong reduction.
1 day 18 hrs.	1	+0.71°	+26.3°	Strong reduction.
2 days 12 hrs.	1	+0.69°	+25.5°	Strong reduction.
No further change.				

The only interpretation from these results was, that 3:4-dimethyl xylose did not condense with methyl
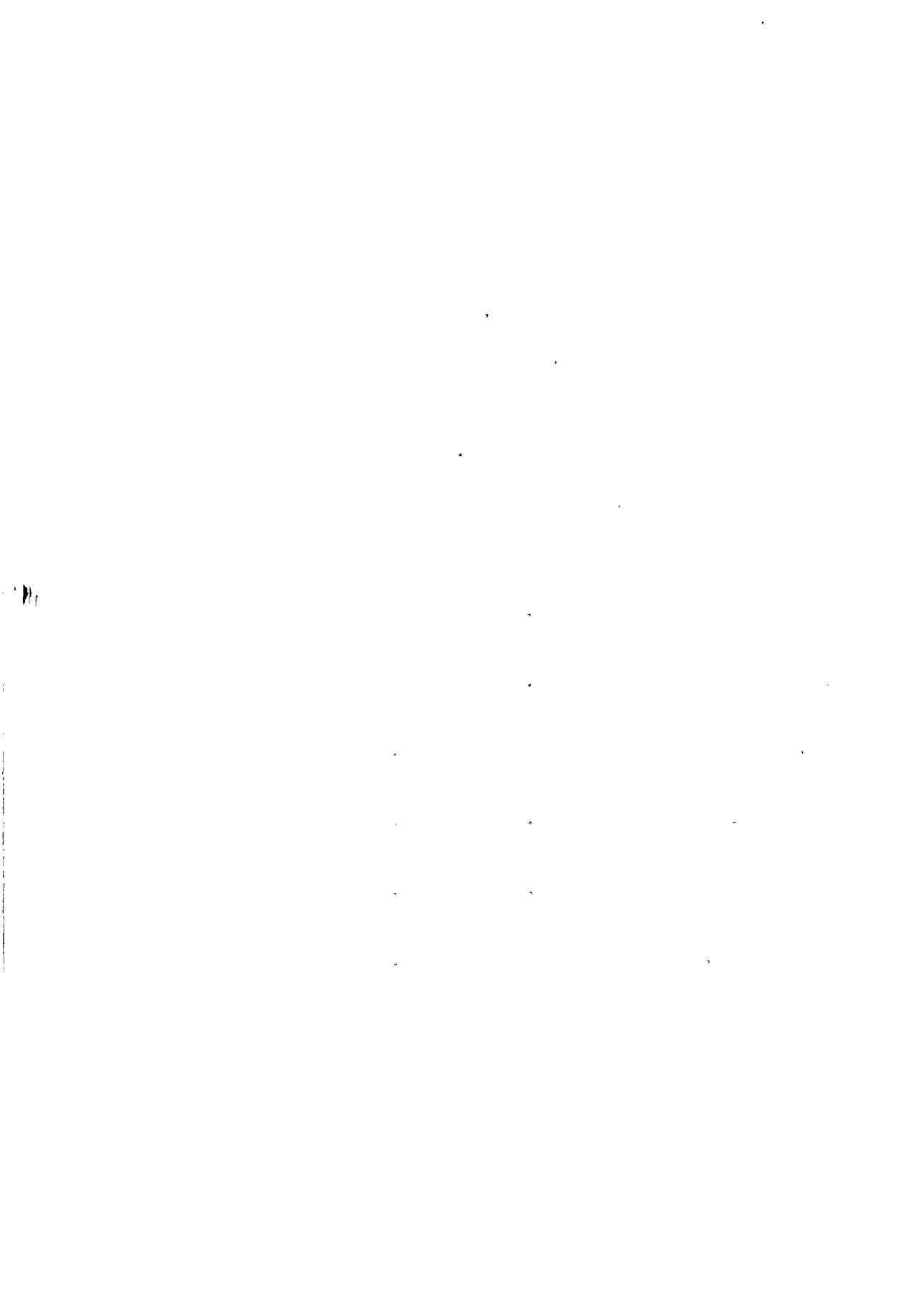
alcohol containing 1% hydrogen chloride which was
no doubt due to the inability of the substance to
assume the γ structure necessary for such condensation.

The acid solution was then neutralised after
three days with barium carbonate and taken to dryness
under diminished pressure when the product was dissolved
in acetone in order to free the material from any
inorganic matter present.   The solution was filtered
and taken to dryness in vacuo when a viscous syrup
(0.4 g.) was obtained. n_D = 1.4673.

Methoxyl estimation:-

3:4-Dimethyl xylose requires OCH_3 = 34.8%

Found OCH_3 = 33.4%

The syrup reduced Fehling's solution in a
similar manner to 3:4-dimethyl xylose and it was
concluded that no condensation with methyl alcohol
had been effected.

It is interesting to note in passing that when
3:4-dimethyl arabinose is condensed with methyl alcohol
containing 0.2% hydrogen chloride in a similar manner
to the experiment described above, a condensation product
a methoxyl content of 44.6% was obtained whereas dimethyl-
methylarabinose requires 48.4%.   This difference was
attributed to incomplete condensation while the optical
observations indicated that methylarabinosides of the
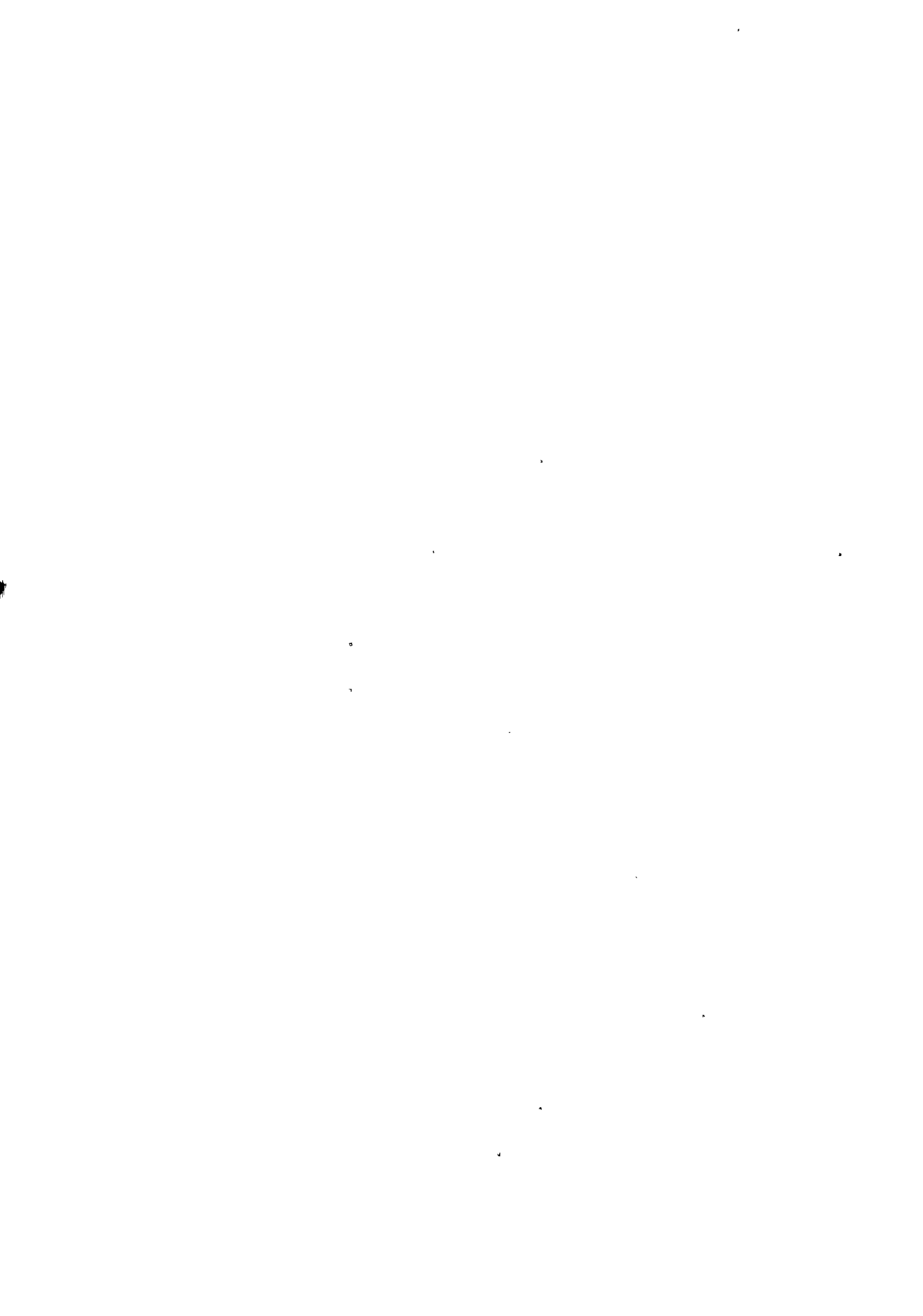
normal type only were produced during condensation. It is not possible to draw a similar conclusion from the work on 3:4-dimethyl xylose.
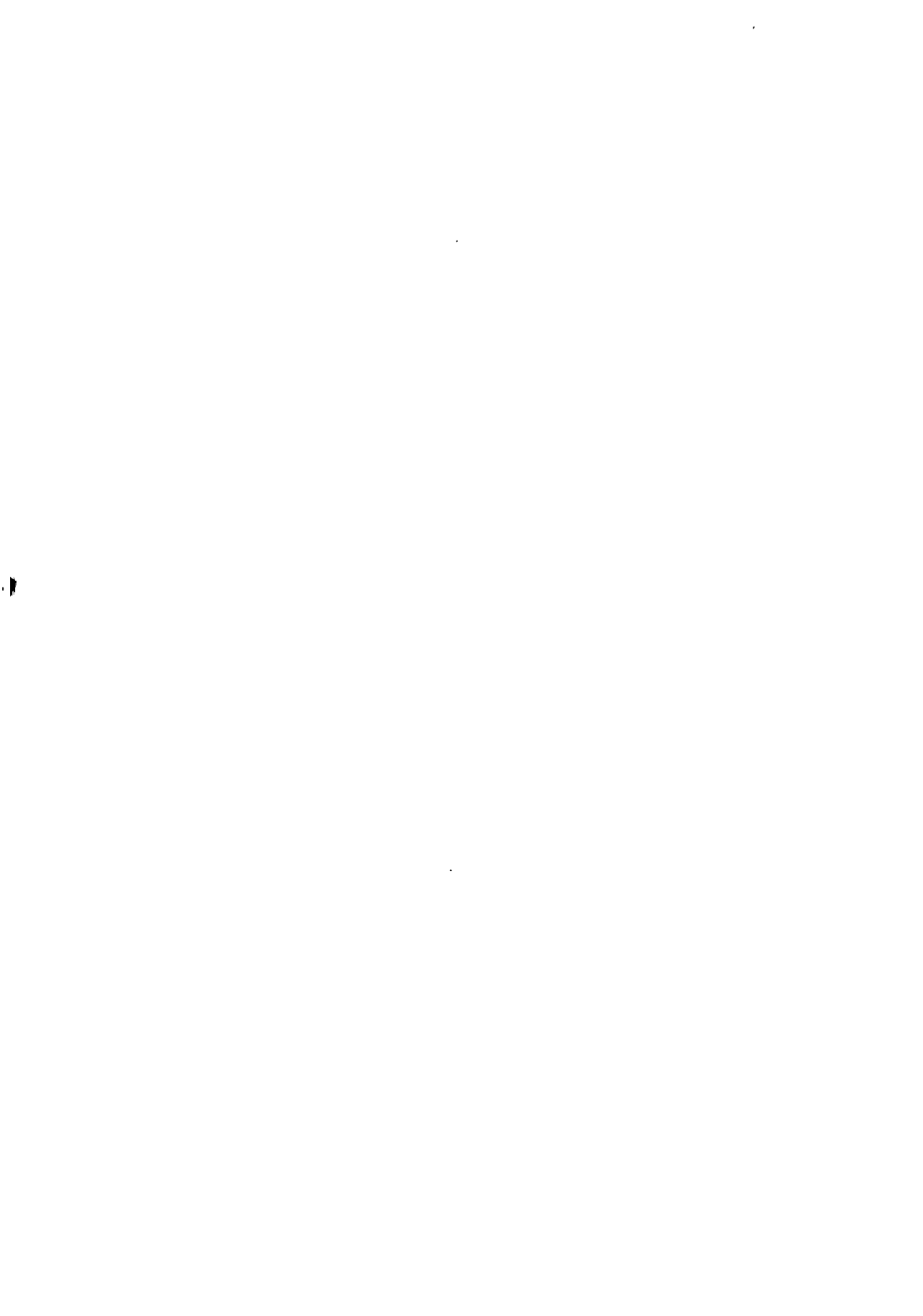
PHENYLOSAZONE   FORMATION   FROM   3:4-DIMETHYL XYLOSE.

3:4-Dimethyl xylose was treated with phenyl-
hydrazine acetate in the usual manner for osazone
formation and the product obtained as a yellowish-
brown syrup which could not be induced to crystallise
from any of the common solvents.

Methoxyl estimation:-

3:4-Dimethyl xylosazone requires OCH_3 = 17.4%

Found OCH_3 = 13.4%

Nitrogen estimation:-

3:4-Dimethyl xylosazone requires N = 15.9%

Found N = 14.7%

PREPARATION OF 3:4-DIMETHYL-β-METHYLXYLOSIDE.

A pyridine solution of 3:4-dimethyl xylose
(1 g.) was carefully treated with a 10% excess of
benzoyl chloride, the addition of the chloride being
slow while the solution was kept cool by running tap-
water. After standing at room temperature overnight
the product was isolated by treatment with aqueous
benzene, the benzene layer separated and washed twice
with dilute hydrochloric acid inorder to remove traces
of pyridine and finally washed once with dilute caustic
soda solution. After drying over anhydrous sodium
sulphate the benzene solution was taken to dryness
under diminished pressure and the benzoyl derivative
of 3:4-dimethyl xylose obtained as a reddish-coloured
mobile syrup (2 g.) having $n_D = 1.5569$.

The syrup was now dissolved in 45 cc. sodium
dried benzene and treated with a 40% solution of hydro-
bromic acid in glacial acetic acid (6 cc. 10% by volume),
and dry ether (9 cc. 15% by volume), the substance
being present in 5% concentration. The reaction was
allowed to proceed at room temperature keeping the
flask tightly sealed, for two hours on the analogy of a

similar reaction in the glucose series since optical
readings were made impossible owing to the colouration
developed in the polarimeter tube. After the stated
time, the solution was once quickly washed with water
and twice with a concentrated solution of potassium
bicarbonate and thence dried over anhydrous sodium
sulphate. Success with this preparation depends very
largely on the exclusion of moisture as much as possible
at this stage.

After freeing the solution from inorganic
material one third total volume of methyl alcohol
(approx. 20 cc.) was added with freshly prepared silver
carbonate (10 g.) and the mixture shaken in a mechanical
shaker for 5 hours. In order to discover whether
the reaction had been completed the silver residue
was allowed to settle and a few drops of the clear
solution diluted with methyl alcohol. After the
addition of two drops of alcoholic silver nitrate the
solution was boiled when the reaction was shown to be
complete by the absence of a slight milkiness in the
test-tube. Repetitions of the above experiment
sometimes showed that the reaction with silver carbonate
was incomplete at this stage when a further quantity
of silver carbonate was usually added and the shaking
continued for a longer time.

The silver residue was removed by filtration
and the solution taken to dryness under diminished
pressure when a dark-coloured syrup was obtained which
was generally found to reduce Fehling's solution
slightly on warming.   This difficulty was overcome
by methylating the syrup in the usual manner when
reduction towards Fehling's solution was found to
disappear after one methylation.   The syrup was then
dissolved in benzene and washed four times with water,
dried over anhydrous sodium sulphate and taken to dryness
in vacuo.   The product (1.4 g.) was found to crystallise
partially from the parent syrup but could not be induced
to crystallise from any solvent.   The smell of methyl
benzoate was also detected.

The syrup was dissolved in a small quantity of
methyl alcohol to which was added sodium (0.2 g.)
also dissolved in methyl alcohol and the mixture boiled
for two minutes.   After dilution with water,   the
methyl benzoate formed was eliminated by distillation
under diminished pressure, when potassium carbonate
was added to the cold solution and five extractions
performed with chloroform.   The chloroform extract was
then dried over anhydrous sodium sulphate and taken to
dryness under reduced pressure, the residue dissolved
in benzene and the benzene solution extracted repeatedly

with water.   Potassium carbonate was added to the
water extract and the whole extracted five times with
chloroform.   After drying over anhydrous sodium
sulphate, the chloroform solution was taken to dryness
in vacuo when the product was obtained as a yellowish-
coloured syrup, which distilled readily at bath-temper-
ature 110-115°/0.15 mm. to give a colourless mobile
syrup (0.75 g.) which crystallised from a mixture of
petroleum ether (b.p. 40-60°) in small, colourless
needles, which, after one recrystallisation from the
mixture of solvents, showed m.p. 89-90°.

Methoxyl estimation:-

3:4-Dimethyl-β-methylxyloside requires OCH_3 = 48.4%

Found OCH_3 = 47.8%

Rotation:-

$[\alpha]_D$ = -82.2° in chloroform, $\underline{1}$ = 2, α_D = -3.43°, c = 2.08%

Solubility:-

Insoluble in cold petroleum ether, slightly soluble in
ether but soluble in all other common solvents.

PREPARATION OF 3:4-DIMETHYL-2-p-TOLUENESULPHONYL-β-METHYLXYLOSIDE.

3:4-Dimethyl-β-methylxyloside (0.3 g.) was dissolved in the least amount of dry pyridine and 50% in excess of the theoretical amount of p-toluene-sulphonic chloride (0.45 g.) added and shaken till dissolved. The solution was allowed to stand for four days when the product was isolated by the addition of pyridine and a few drops of water in order to destroy the excess p-toluenesulphonic chloride present in the system, when the solution was extracted with benzene. The benzene layer was washed twice with dilute hydro-chloric acid to remove traces of pyridine and twice with dilute sodium hydroxide, again with dilute hydrochloric acid and finally once with water. After drying the benzene solution over anhydrous sodium sulphate, the solvent was removed under reduced pressure when a yellowish viscous syrup (0.45 g.) was obtained. Crystallisation took place from a mixture of petroleum ether (b.p. 40-60°) and ether and after two recrystallisations from petroleum ether alone, the substance was obtained in small colourless prisms, much like ordinary house-hold sugar in appearance. m.p. 105°.
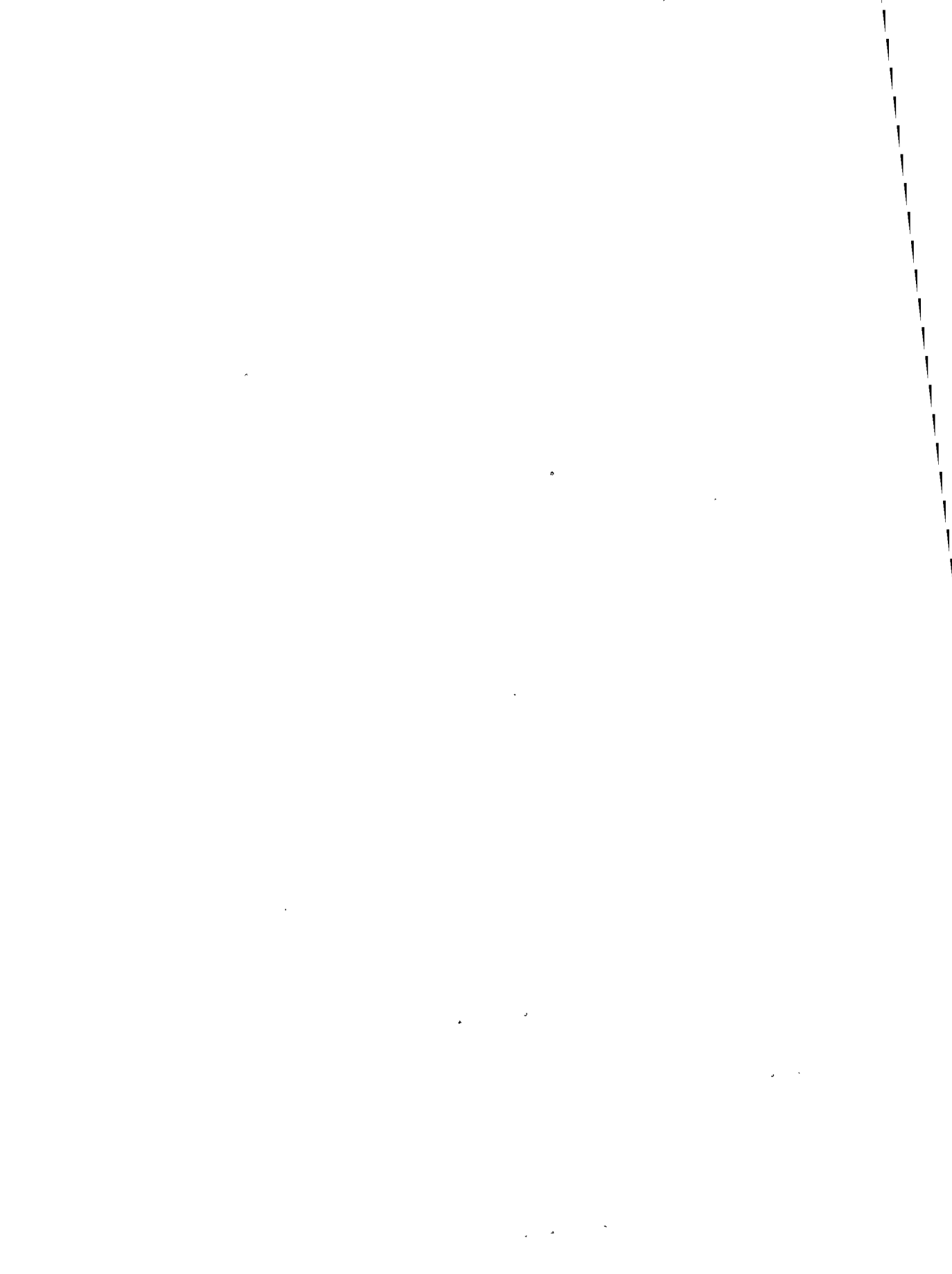
Methoxyl estimation:-

3:4-Dimethyl-2-p-toluenesulphonyl-β-methylxyloside

$$\text{requires } OCH_3 = 26.8\%$$

$$\text{Found } OCH_3 = 26.9\%$$

Rotation:-

$[\alpha]_D = -34.8°$ in chloroform, $\underline{l} = 2$, $c = 1.59\%$, $\alpha_D = -1.11°$.

CONDENSATION OF 3:4-DIMETHYL XYLOSE WITH ACETONE.

3:4-Dimethyl xylose (1.6 g.) was dissolved in acetone (32 cc.) which contained 1.5% dry hydrogen chloride and the solution kept at room temperature for three hours when the following optical readings were observed.

Time	$\underline{1}$	t.	α_D	$[\alpha]_D$
Initial	1	21°	+0.91°	+18.2°
1 hr. 15 m.	1	21°	+1.56°	+31.2°
2 hr. 15 m.	1	21°	+1.66°	+33.2°
2 hr. 45 m.	1	21°	+1.66°	+33.2°

The solution was poured into water containing potassium bicarbonate in excess of the amount required to neutralise the acid present and the solution extracted five times with chloroform. After drying the chloroform extract the solvent was removed under diminished pressure when a yellow, mobile syrup (0.6 g.) was obtained which gave indications of crystallising from the parent syrup but could not be obtained crystalline from any solvent. In addition, 0.9 g.

of the original sugar was recovered from the water
solution unchanged.

<u>Methoxyl estimation</u>:-

3:4-Dimethyl xylose-monacetone requires $OCH_3 = 28.4\%$

Found $OCH_3 = 34.6\%$

The syrup distilled easily at $98-105°/0.15$ mm. to give
a colourless mobile syrup with a methoxyl content of
35.7% and $n_D = 1.4520$ but which, however, failed to
crystallise.

The syrup did not reduce Fehling's solution and was
thought to be a tetramethyl-dixylose ($OCH_3 = 36.7\%$)
although the ease with which the product distilled was
at variance with this view.

ATTEMPTED SYNTHESIS OF 3:4-DIMETHYL XYLOSE.

The reasons for attempting this subsidiary
synthesis of 3:4-dimethyl xylose have already been
outlined in the theoretical discussion and need
not be elaborated here.

3:5-Monacetone-γ-methylxyloside-2-nitrate.

3:5-Monacetone-γ-methylxyloside (6.6 g.) was
dissolved in chloroform (66 cc.), cooled by
surrounding the flask with crushed ice and nitrogen
pentoxide (6.6 g.) in solution in chloroform (66 cc.)
added and the mixture allowed to stand for ten minutes
in the cooling solution.   The mixture was run into
a separating funnel containing ice and water and the
chloroform layer washed with a solution of potassium
bicarbonate containing crushed ice.   Thereafter the
chloroform layer was dried over anhydrous sodium sulphate
and taken to dryness in a vacuum at a temperature not
exceeding 60° when the product was isolated as a
yellowish mobile syrup (7.6 g.) showing a refractive
index of n_D = 1.4682.

<u>Methoxyl estimation</u>:-

3:5-Monacetone-γ-methylxyloside-2-nitrate

requires OCH_3 = 12.5%

Found OCH_3 = 9.8%

The low methoxyl content of the substance could be accounted for by the loss of the acetone group and subsequent replacement with nitrate groups, or by the loss of the methyl group in the reducing position and replacement by a nitrate group since the product did not reduce Fehling's solution. It should be borne in mind, however, that this criterion is not always completely diagnostic.

<u>Methylxyloside-2-nitrate</u>.

3:5-Monacetone-γ-methylxyloside-2-nitrate (1 g.) was dissolved in methyl alcohol (25 cc.) containing 1% dry hydrogen chloride and boiled under a reflux condenser for 45 minutes when the rotation of the solution became constant. After neutralisation with lead carbonate at the boiling point, the solution was filtered and the solvent removed under diminished pressure. The residue was now dissolved in acetone, filtered through animal charcoal to remove traces of inorganic impurities and taken to dryness in a vacuum.
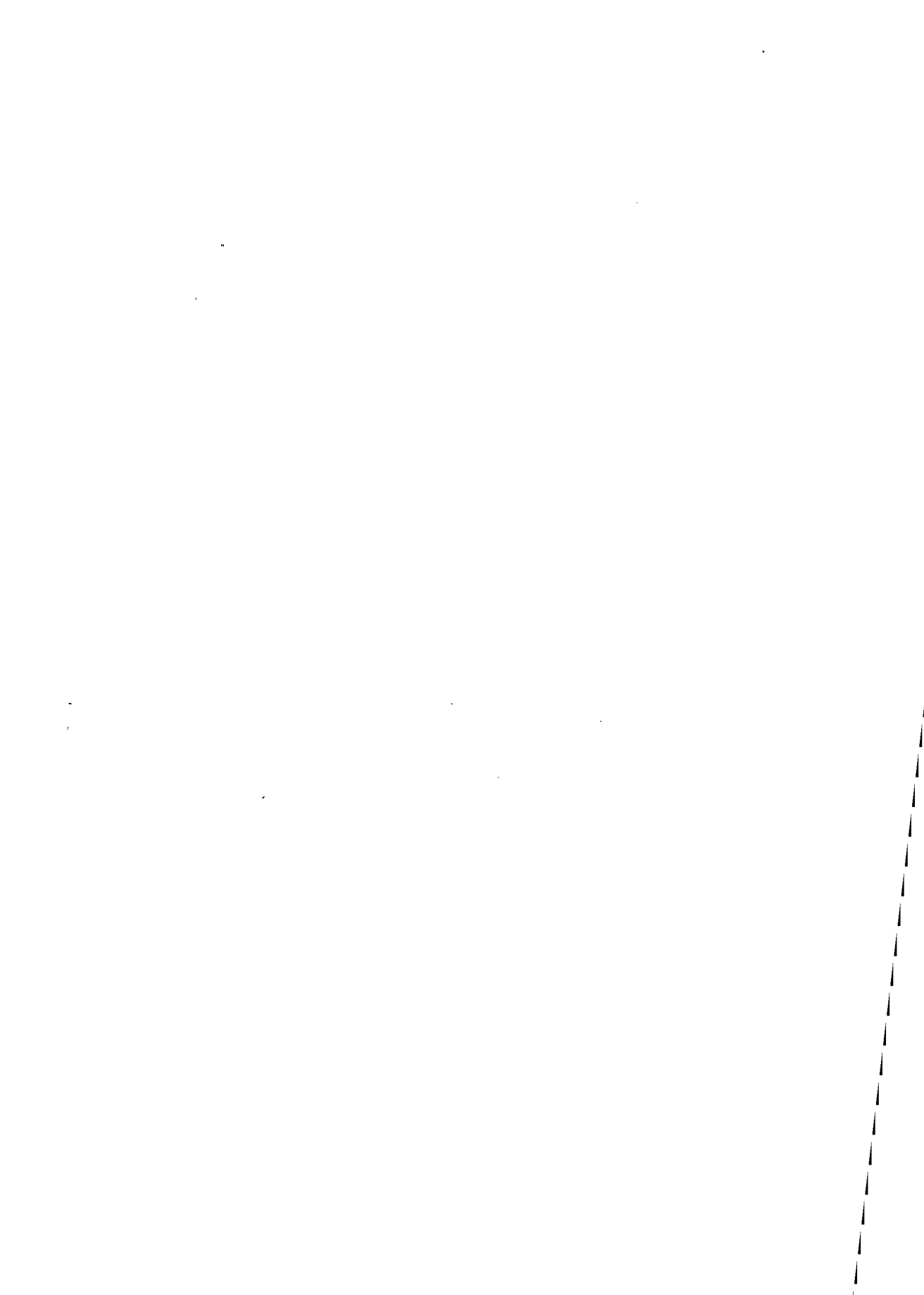
The product was obtained as a yellow syrup (0.8 g.) and showed n_D = 1.4820.

<u>Methoxyl estimation:-</u>

Methylxyloside-2-nitrate requires OCH_3 = 14.8%

Found OCH_3 = 15.2%

Slight loss of the nitrate group would account for the increase in the methoxyl content.

3:4-Dimethylmethylxyloside-2-nitrate.

Methylxyloside-2-nitrate (5.6 g.) was methylated in the usual manner with silver oxide (10 g.), methyl iodide (6 cc.) and acetone (3 cc.). The methylation process was repeated four times (omitting the addition of acetone after the first methylation) when the refractive index remained unaltered at n_D = 1.4525.

<u>Methoxyl estimation:-</u>

3:4-Dimethylmethylxyloside-2-nitrate requires OCH_3 = 39.2%

Found OCH_3 = 36.3%

The syrup was dissolved in benzene and the solution washed five times with water in order to remove any fully methylated material or any anhydro compounds formed. After washing the solution twice with dilute sodium hydroxide, once with dilute hydrochloric acid and twice with water, the product was dried over anhydrous sodium sulphate and the solvent removed in vacuo when a

reddish, mobile syrup (6.1 g.) was isolated.
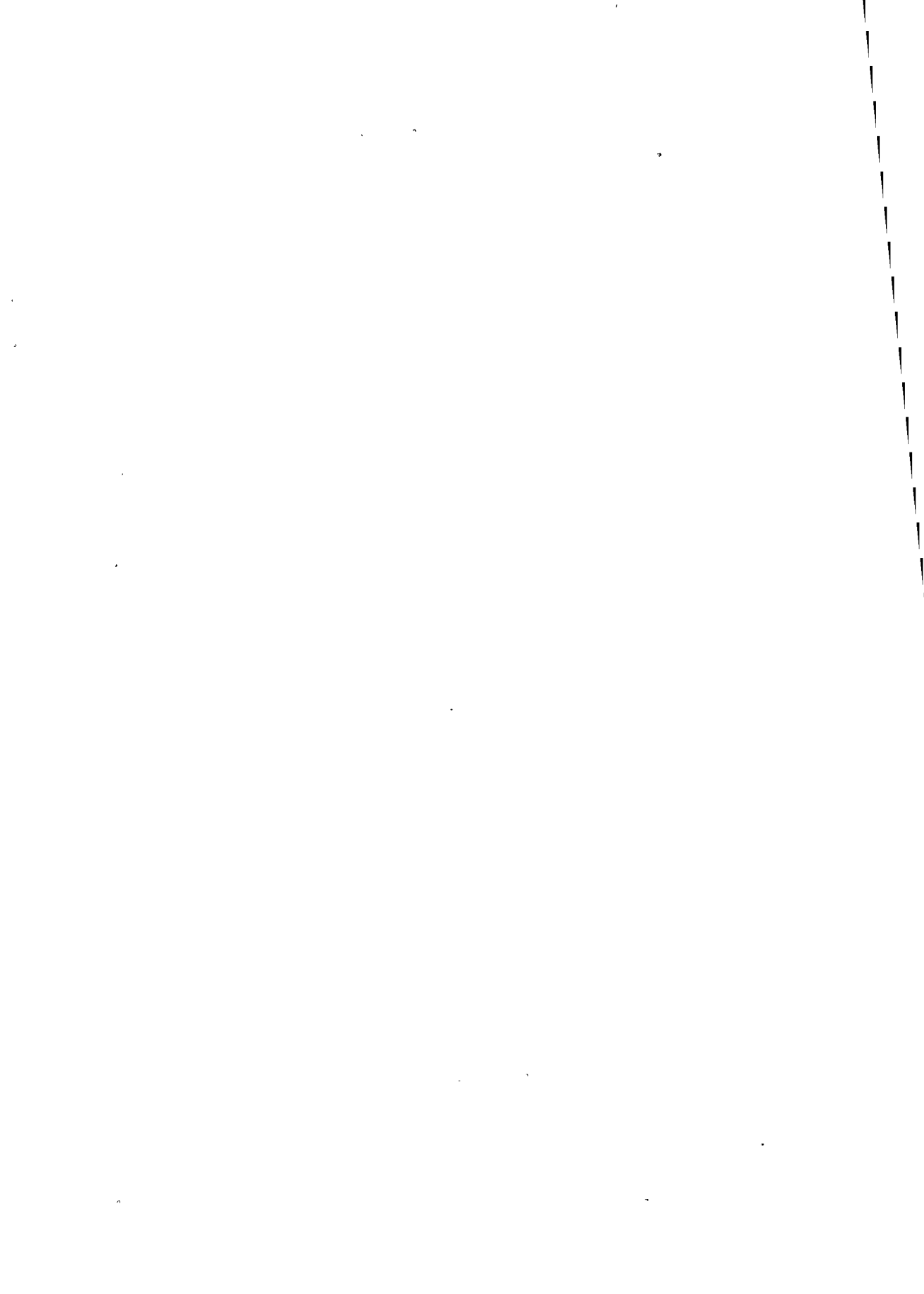$n_D = 1.4530.$

Methoxyl estimation:-

3:4-Dimethylmethylxyloside-2-nitrate requires $OCH_3 = 39.2\%$

Found $OCH_3 = 36.9\%$

3:4-Dimethylmethylxyloside.

3:4-Dimethylmethylxyloside-2-nitrate (1 g.)
was dissolved in glacial acetic acid and the nitrate
group reduced by the action of zinc and iron dust.
The solution was gently heated and the action continued
until a negative colour test was obtained on testing
with diphenylamine. After the removal of the solid
residue and addition of water, the solution was extracted
five times with chloroform. The chloroform extract
was now dried over a mixture of anhydrous potassium
carbonate and sodium sulphate and the solvent removed
under diminished pressure. The residue was finally
taken up in sodium dried ether, filtered through animal
charcoal, dried over anhydrous sodium sulphate and
taken to dryness in a vacuum when a syrup (0.7 g.)
was obtained. $n_D = 1.4519.$
The syrup distilled in a high vacuum at bath-temperature
110/0.15 mm. to give a colourless mobile syrup (0.5 g.)
shewing $n_D = 1.4504$ which partly crystallised from the

parent syrup to give syrupy crystals.

Methoxyl estimation:-

3:4-Dimethylmethylxyloside requires OCH_3 = 48.4%

Found OCH_3 = 46.2%

In a repetition of the above experiment the product
3:4-dimethylmethylxyloside (10.6 g.) (OCH_3 = 46.0%)
was treated with N/10 sodium hydroxide (100 cc.) and
boiled under a reflux condenser for seven minutes.
No optical readings were possible owing to the
turbidity of the solution and the dark colour which
quickly developed. The solution was then cooled and
extracted repeatedly with chloroform, the chloroform
extract dried over anhydrous sodium sulphate and taken
to dryness in a vacuum. The residue (8.4 g.) distilled
in a high vacuum to give a colourless, mobile syrup
(7.7 g.) at bath-temperature 110-115°/0.1 mm.

Methoxyl estimation:-

3:4-dimethylmethylxyloside requires OCH_3 = 48.4%

Found OCH_3 = 47.2%

The product was again boiled with N/10 sodium hydroxide
(77 cc.) for 16 minutes when only a slight change in
colour took place. The solution was cooled and extracted
eight times with chloroform, the chloroform extract
dried over anhydrous sodium sulphate and the solvent
removed under diminished pressure. The product distilled

at the same temperature and pressure as quoted in the previous treatment to give a mobile syrup (6.8 g.), showing $n_D = 1.4490$.
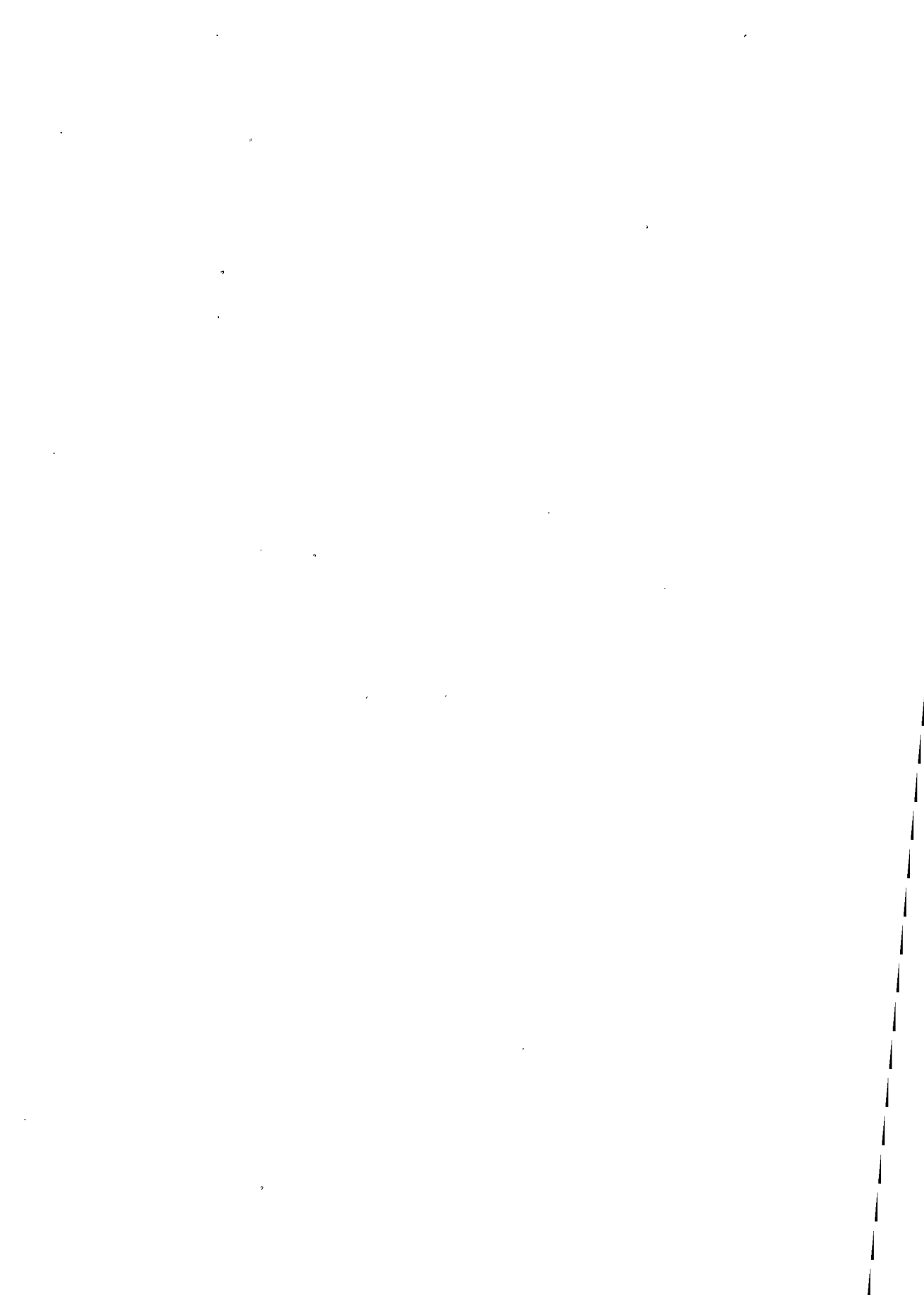
Methoxyl estimation:-

3:4-Dimethylmethylxyloside requires $OCH_3 = 48.4\%$

Found $OCH_3 = 47.5\%$

No further treatment with dilute sodium hydroxide was considered necessary.

3:4-Dimethyl xylose.

3:4-Dimethylmethylxyloside (6.7 g.) was boiled for 90 minutes with normal hydrochloric acid (134 cc.) when the initial rotation of $[\alpha]_D = +42.2°$ changed to a permanent value of $[\alpha]_D = +11.2°$. Decolourisation was effected by animal charcoal and the acid neutralised with barium carbonate, the solution filtered and extracted three times with chloroform in order to remove any unhydrolysed material. The water solution was now taken to dryness under diminished pressure and the residue repeatedly extracted with boiling acetone. After removal of the acetone in a vacuum the residue was dissolved in sodium-dried ether, the solution decolourised with charcoal and taken to dryness when a greenish-tinged viscous syrup was isolated. The syrup (5.3 g.) was obtained in 85% yield. $n_D = 1.4508$.

<u>Methoxyl estimation</u>:-

3:4-Dimethyl xylose requires $OCH_3 = 34.8\%$

Found $OCH_3 = 34.8\%$

<u>Rotation</u>:-

$[\alpha]_D = +8.3°$ in chloroform changing to $+10.3°$ in

20 hours, $\underline{1} = 2$, c = 3.302%.

It will be observed that this rotation differs slightly from the rotation of 3:4-dimethyl xylose prepared from 2-benzoyl-monacetone-γ-methylxyloside which was $+5.32°$ changing to $+7.50°$ in 18 hours using the same solvent.

ATTEMPTED CHARACTERISATION OF 3:4-DIMETHYL XYLOSE

OBTAINED FROM 3:5-MONACETONE-γ-METHYLXYLOSIDE-

2-NITRATE.

Phenylosazone from 3:4-Dimethyl Xylose.

3:4-Dimethyl xylose was treated with phenyl-
hydrazine acetate in the usual manner for osazone
formation when a dark coloured syrup was obtained.

3:4-Dimethyl-β-methylxyloside.

(The full method of preparation of the
β-methylxyloside has already been outlined and it
suffices to give the following data only.)

3:4-Dimethyl xylose (1.2 g.) was benzoylated
in pyridine solution to give the benzoyl derivative
of 3:4-dimethyl xylose (2.4 g.). $n_D = 1.5620$.

The benzoyl derivative was now treated with
hydrobromic acid in glacial acetic acid solution,
followed by treatment with methyl alcohol and silver
carbonate. The product (2.5 g.) was a yellowish

syrup which showed partial crystallisation from the
parent syrup.   Debenzoylation was accomplished
using sodium methylate and the syrup obtained was
distilled in a high vacuum at bath temperature
110-115°/0.2 mm. when 0.45 g. mobile syrup was
isolated having $n_D = 1.4560$.

<u>Methoxyl estimation:-</u>

3:4-Dimethyl-β-methylxyloside requires $OCH_3 = 48.4\%$

Found $OCH_3 = 46.2\%$

The substance could not be induced to crystallise
even after several months and the impurity could not
be determined.

In an attempt to obtain a crystalline
derivative from 3:4-dimethyl xylose, 3:4-dimethyl-
β-methylxyloside as obtained above was p-toluene-
sulphonated but a non-crystallisable syrup was again
isolated.

SYNTHESIS OF 2:4-DIMETHYL-β-METHYLXYLOSIDE.

Condensation of Triphenylchloromethane with β-methyl-xyloside.

The reaction was carried out in a similar manner to the experiment described by Helferich, (Ber., 1925, 58, 877).

β-Methylxyloside (3 g.) and triphenylchloro-methane (5.25 g.), slight excess over the theoretical amount required, were dissolved in pyridine and the solution heated at 100° for 1.25 hours, under a reflux condenser carrying a calcium chloride tube. The hot solution was poured into cold water but the syrup obtained failed to crystallise after washing the residue free from pyridine. Thereafter, the product was dissolved in benzene, the solution dried over anhydrous sodium sulphate and taken to dryness in a vacuum. A pyridine solution of the residue (7.9 g.) was treated with acetic anhydride (5 cc.) in the recognised manner for acetylation and the solution allowed to remain at room temperature overnight. The

product was extracted by the addition of aqueous
benzene, when the benzene layer was washed twice with
dilute hydrochloric acid and once with caustic soda
solution.   After drying over anhydrous sodium sulphate
the solvent was removed under diminished pressure when
a reddish brown viscous syrup was obtained (8.8 g.)
This syrup could not be induced to crystallise, due to
the presence of triphenylcarbinol.   The acetylated
product was then dissolved in benzene (90 cc.) and dry
hydrogen chloride passed into the solution until the
saturation point was reached (no optical readings could
be observed owing to the dark colouration which
quickly developed).   The benzene solution was extracted
repeatedly with water until the final washing (thirteenth)
gave a zero polarimetric reading when the water extract
was neutralised with potassium bicarbonate and extracted
ten times with chloroform.   After drying the extract
over anhydrous sodium sulphate the solvent was removed
under diminished pressure when a syrup (1 g.) was ob-
tained.   The product could not be induced to crystallise.

<u>Methoxyl estimation</u>:-

2:4-Diacetyl-β-methylxyloside requires OCH_3 = 12.5%

Found OCH_3 = 12.1%

<u>Acetyl estimation</u>:-

2:4-Diacetyl-β-methylxyloside requires $CO.CH_3$ = 34.7%

Found $CO.CH_3$ = 36.5%

2:4-Diacetyl-β-methylxyloside-3-nitrate.

The nitration process adopted was that described by Oldham, J., 1925, <u>127</u>, 2840.

A 5% solution of 2:4-diacetyl-β-methylxyloside (1.2 g.) in chloroform containing 30% fuming nitric acid was allowed to stand in ice for one minute and poured quickly into a separating funnel containing ice and water. After shaking, the chloroform layer was run into a second funnel containing ice and potassium bicarbonate solution and finally dried over anhydrous sodium sulphate and taken to dryness in a vacuum at 55-60°. The product was isolated as a pale coloured syrup (1.5 g.) which crystallised readily from absolute alcohol. The product, after two recrystallisations from hot absolute alcohol was obtained in the form of colourless needles, m.p. 120-121°.

<u>Methoxyl estimation</u>:-

2:4-Diacetyl-β-methylxyloside-3-nitrate

$$\text{requires } OCH_3 = 10.6\%$$
$$\text{Found } OCH_3 = 10.3\%$$

<u>Rotation</u>:-

$[\alpha]_D = -57.4°$ in chloroform, $\underline{1} = 2$, $\alpha_D = -2.69°$, $c = 1.843\%$

<u>Solubility</u>:-

Insoluble in petroleum ether, soluble in hot alcohols and

other common solvents.

2:4-Dimethyl-β-methylxyloside-3-nitrate.

The deacetylation of 2:4-diacetyl-β-methyl-xyloside-3-nitrate constituted the most difficult problem in the present item of research.   Removal of the acetyl groups under those conditions governed by the ordinary methods of deacetylation would doubtless have led to the removal of the nitrate group simultaneously, with the result that a modified method of deacetylation was required.

2:4-Diacetyl-β-methylxyloside-3-nitrate (1 g.) was dissolved in a mixture of alcohol and chloroform and the solution cooled by surrounding with crushed ice. A catalytic proportion of sodium (0.025 g.) was dissolved in absolute alcohol (2 cc.), cooled in crushed ice and added to the solution of acetylated material.   The solution was immediately neutralised by adding one drop of glacial acetic acid and thereafter taken to dryness at 60° under diminished pressure.   The product was then methylated in the customary manner with silver oxide (5 g.), methyl iodide (3 cc.) and acetone (2 cc.)   The methylation process was repeated three times omitting the addition of acetone after the first methylation, when the refractive index became constant

at a final value of $n_D = 1.4582$.

The product was thereafter dissolved in benzene and washed three times with water to remove any fully methylated material formed by the loss of the nitrate group with subsequent methylation. The solution was then dried over anhydrous sodium sulphate and taken to dryness in a vacuum at 60°. The isolated material was a yellow, distinctly mobile syrup which could not be crystallised from any solvent. $n_D = 1.4597$. The material (0.8 g.) gave a conclusive test with diphenylamine showing that the nitrate group still existed in the molecule.

In a larger scale experiment however, it was found more difficult to remove the acetyl groups completely under the conditions just outlined when the following method was adopted.

The product (3.4 g.) obtained from the above method of deacetylation was now dissolved in sufficient alcoholic dimethylamine (33% solution) to ensure complete solution (10 cc.) and the mixture allowed to remain overnight at the ordinary temperature. No change in the colour of the solution was observed. The alcohol and the dimethylamine were distilled away while the dimethylacetamide formed was removed by heating the residue at 100° for two hours in a high vacuum.

A dark yellow syrup (2.8 g.) was obtained and
methylation was again carried out using silver oxide
(4 g.), methyl iodide (3 cc.) and acetone (1 cc.)
after which the refractive index showed a value of
n_D = 1.4539. The benzene solution of the product
was then washed five times with water in order to
remove any fully methylated material, dried over
anhydrous sodium sulphate and the solvent removed
under diminished pressure. The syrup (2.4 g.) showed
n_D = 1.4545. The product could not be induced to
crystallise. (It should be noted here that high
vacuum distillation of the product was not attempted
as decomposition would have undoubtedly taken place.
This is known from similar work done in this Laboratory
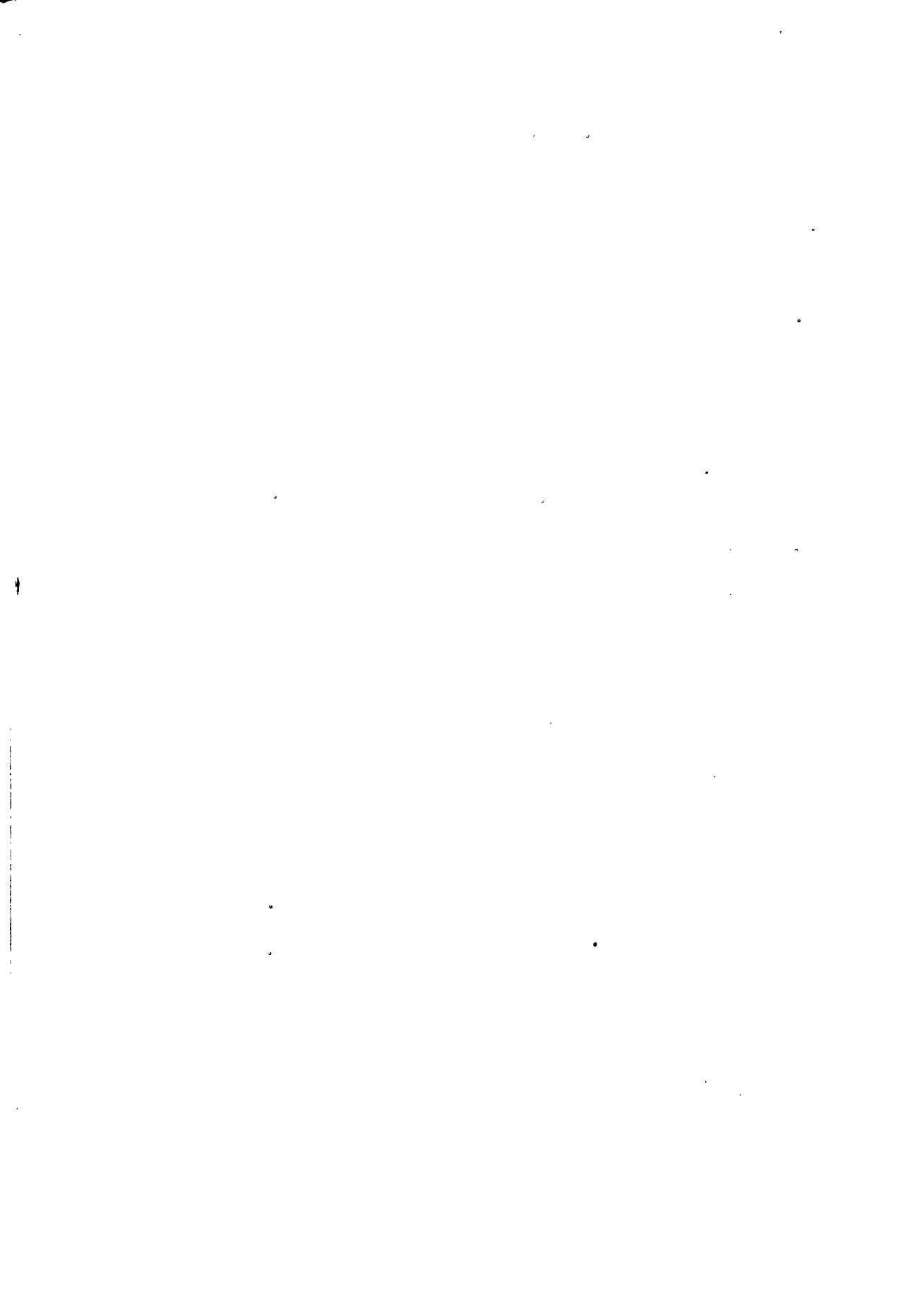on arabinose.)

Methoxyl estimation:-

2:4-Dimethyl-β-methylxyloside-3-nitrate

requires OCH_3 = 39.2%

Found OCH_3 = 37.7%

The methoxyl estimation showed that there was still a
small quantity of unchanged 2:4-diacetyl-β-methyl-
xyloside-3-nitrate present and illustrated the
difficulty of completing deacetylation without incurr-
ing the loss of the nitrate group also.

2:4-Dimethyl-β-methylxyloside.

2:4-Dimethyl-β-methylxyloside-3-nitrate (2.2 g.) was dissolved in aqueous alcohol(sufficient to maintain the substance in solution) and freshly prepared sodium amalgam (80 g.) added in 10 g. portions over 4 hours. A few drops of acetic acid were added at intervals in order to prevent excessive alkalinity. After the stated time, the diphenylamine test for the nitrate radical was almost negative. After separation from mercury, the solution was neutralised with acetic acid, potassium carbonate added and the solution extracted repeatedly with chloroform when the extract was dried over anhydrous sodium sulphate and the solvent removed under diminished pressure. A dark coloured syrup (1.7 g.) was obtained. The benzene solution of the residue was then repeatedly extracted with water, potassium carbonate added to the water washings and the solution extracted eight times with chloroform. The extract was then dried over anhydrous potassium carbonate and taken to dryness in a vacuum when a mobile syrup (1.45 g.) was obtained. The product distilled in a high vacuum at bath temperature 100-105°/0.06 mm. to give a colourless mobile syrup (1.3 g.).

n_D = 1.4535.   Yield 73%.

The syrup crystallised from a mixture of dry ether and petroleum ether (b.p. 40-60°), which on tiling and recrystallisation from petroleum ether gave the substance in long, colourless needles, m.p. 60-61°.

Methoxyl estimation:-

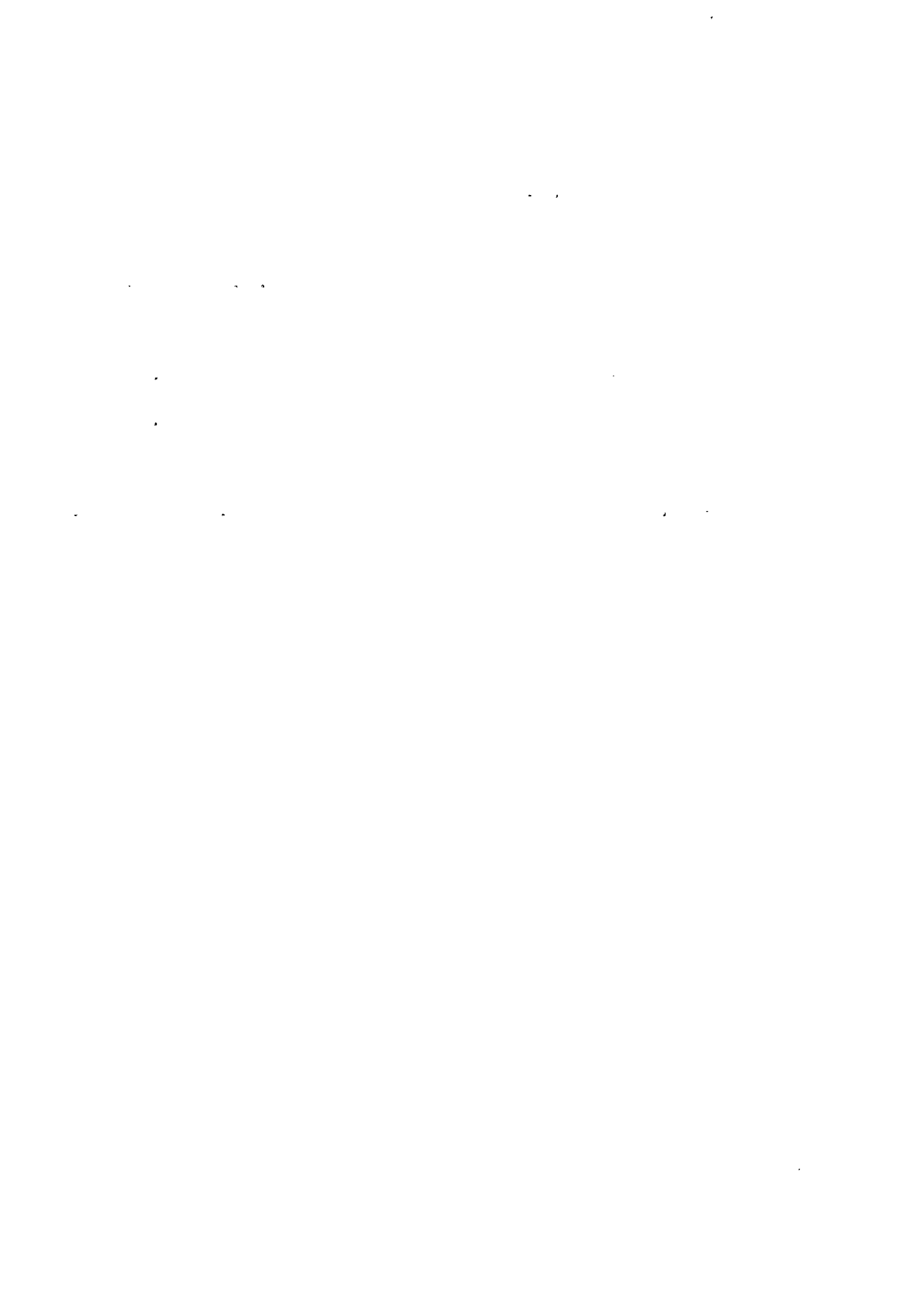2:4-Dimethyl-β-methylxyloside requires OCH_3 = 48.4%

Found OCH_3 = 48.0%

Rotation:-

$[α]_D$ = -82.4° in chloroform, $\underline{l}$ = 2, $α_D$ = -2.27°, c = 1.377%

Solubility:-

Slightly soluble in petroleum ether, but soluble in all other common solvents.

Preparation of 2:4-Dimethyl-β-methylxyloside-
3-p-toluenesulphonate.

2:4-Dimethyl-β-methylxyloside (0.15 g.) was
dissolved in the least amount of pyridine and
p-toluenesulphonic chloride (0.2 g.) added and the
solution allowed to remain at room temperature for
four days.   The product was isolated by the addition
of aqueous benzene, when the benzene layer was washed
twice with dilute hydrochloric acid, twice with caustic
soda solution and finally dried over anhydrous sodium
sulphate.   Removal of the solvent in a vacuum gave a
hard clear glass (0.27 g.) which crystallised from
petroleum ether (b.p. 40-60°) in small colourless
needles.   After two recrystallisations from petroleum
ether the substance had m.p. 88°.

Methoxyl estimation:-

2:4-Dimethyl-β-methylxyloside-3-p-toluenesulphonate

$$\text{requires } OCH_3 = 26.9\%$$
$$\text{Found } OCH_3 = 25.8\%$$

Rotation:-

$[\alpha]_D = -58.9°$ in chloroform, $\underline{1} = 2$, $\alpha_D = -0.97°$,

$$c = 1.0\%$$

Solubility:-

Soluble in most common solvents except petroleum ether.

PREPARATION OF 2:3-DIMETHYL XYLOSE FROM XYLAN.

In general, the scheme of preparation of 2:3-dimethyl xylose was carried out as described by Hampton, Haworth and Hirst (J., 1929, 1746). The preparation is further discussed in a paper by Haworth and Percival (J., 1931, 2850).

Separation of Xylan from Alkaline Liquors.

Concentrated soda-lye (100 g.) was dissolved in water (300 cc.) with heating. After filtration, the solution was cooled to 30° and an equal volume of rectified spirit added gradually from a dropping funnel, while the solution was kept mechanically stirred. A fine brown solid separated which was filtered through muslin, triturated with a mixture of equal volumes of acetic acid and alcohol, washed quickly with water, alcohol and finally with ether when a dark brown powder was obtained (30 g.). The crude xylan was now dissolved in 12% caustic soda solution and reprecipitated with alcohol and treated as before. The product was isolated as a dark brown powder (21 g.).

Methylation of Xylan.

Xylan (20 g.) as obtained above was treated with dimethyl sulphate (194 g.) and caustic soda (150 g.) dissolved in water (500 cc.). The alkali and dimethyl sulphate were added in equimolecular quantities every 30 minutes over a period of 5 hours, the solution being kept mechanically stirred at the ordinary temperature. The temperature was now raised to 100° for 1 hour when the partially methylated xylan was filtered through muslin, well-washed with hot water to remove dimethyl sulphate and dried at 70° in a vacuum oven. Yield 14-16 g.

It was found impractical to extract the liquid with chloroform as the amount of material obtained (0.6 g.) was negligible. A second methylation using the same quantities as above gave the substance as a light brown fibrous powder.

Methoxyl estimation:-

Dimethyl xylan requires OCH_3 = 38.8%

Found OCH_3 = 27.7%

The partially methylated xylan was remethylated twice using the same quantities, filtered through muslin, well-washed with hot-water, dried at 100° under diminished pressure, powdered finely and again washed

with hot water and dried as above.

Methoxyl estimation:-

Dimethyl xylan requires OCH_3 = 38.8%

Found OCH_3 = 30.4%

Purification of Methylated Xylan.

The crude methylated xylan was powdered and dissolved in chloroform, the chloroform solution well dried over anhydrous sodium sulphate, filtered, the solution reduced in volume and the methylated xylan re-precipitated by the addition of dry ether. When first precipitated the methylated xylan was almost white in colour but rapidly turned a brownish colour on standing. On filtering the flocculent precipitate, drying in a vacuum desiccator and powdering, the substance (7.3 g.) was finally obtained as a pale yellow powder.

Methoxyl estimation:-

Dimethyl xylan requires OCH_3 = 38.8%

Found OCH_3 = 31.3%

Hydrolysis of Dimethyl Xylan.

Dimethyl xylan (6.9 g.) was treated with methyl alcohol (437.5 cc.) containing dry hydrogen chloride (4.2 g.) (1.2% solution) and the mixture boiled under a reflux condenser for 18 hours when filtration was carried out while the solution was still hot. A small quantity (0.8 g.) of insoluble residue was obtained. The solution was then allowed to cool when a fine brown precipitate was deposited from the solution. To complete the hydrolysis a further 22.5 cc. dry methyl alcohol containing hydrogen chloride (3.7 g.) was added and the solution again boiled for 8 hours. After allowing to cool a fine brownish precipitate was deposited which was filtered away and the solution decolourised with charcoal and any further hydrolysis followed polarimetrically.

The solution was then neutralised with barium carbonate and taken to dryness under reduced pressure after filtration from inorganic material. The residue was then extracted six times with boiling chloroform the extract dried over anhydrous sodium sulphate and taken to dryness under diminished pressure when a brown syrup (5.5 g.) was isolated. High vacuum distillation of the product gave a colourless, mobile syrup (4.5 g. b.p. 101-105°/0.09 mm.) while a dark coloured viscous

material (0.9 g.) remained as a residue.

The 2:3-dimethylmethylxyloside obtained had n_D = 1.4510.

Methoxyl estimation:-

2:3-Dimethylmethylxyloside requires OCH_3 = 48.4%

Found OCH_3 = 48.4%

2:3-Dimethyl Xylose.

2:3-Dimethylmethylxyloside (4.4 g.) was boiled under reflux with 3% aqueous hydrochloric acid (100 cc.) and the hydrolysis followed polarimetrically.

Time	$\underline{l}$	α_D	$[\alpha]_D$
Initial	1	+1.62°	+36.8°
45 mins.	1	+1.00°	+22.7°
1 hr. 15 mins.	1	+0.93°	+21.1°
1 hr. 30 mins.	1	+0.90°	+20.5°

The solution was neutralised with barium carbonate and decolourised with charcoal and taken to dryness at 65°/10 mm. The residue was then repeatedly extracted with dry boiling ether, filtered and taken to dryness. The resulting residue was dissolved in chloroform, filtered and the solvent removed under diminished pressure when a pale yellow viscid syrup (3.3 g.) was obtained showing n_D = 1.4723. Yield 82%.

Methoxyl estimation:-

2:3-Dimethyl xylose requires OCH_3 = 34.8%

Found OCH_3 = 32.1%

Rotation:-

$[\alpha]_D$ = +19.0° in chloroform changing to a final value
of +20.1° after 10 minutes. $\underline{1}$ = 2, c = 1.4%

Hampton, Haworth and Hirst (<u>loc.cit.</u>) quote $[\alpha]_D$ = +22.6°
in chloroform changing to +24° after 6 minutes.

PREPARATION OF 2:3-DIMETHYL-β-METHYLXYLOSIDE.

2:3-Dimethyl xylose (3.2 g.) was converted to
2:3-dimethyl-β-methylxyloside by the usual method
already described for β-methylxyloside formation.

The benzoylation of 2:3-dimethyl xylose (3.2 g.)
in the usual manner gave a pale yellow syrup (6.9 g.)
which ontreatment with hydrogen bromide in glacial
acetic acid solution and subsequent replacement of the
bromine radical with a methyl group gave 2:3-dimethyl-
4-benzoyl-β-methylxyloside (4.9 g.) as a mobile syrup
which did not crystallise. Debenzoylation of this
product with sodium methylate furnished 2:3-dimethyl-
β-methylxyloside (2.2 g.) as a yellow, mobile syrup
which could not be induced to crystallise. The product
was then distilled in a high vacuum at bath temperature
90-95°/0.03 mm. to give a colourless mobile syrup (2 g.).
$n_D = 1.4540$.

Methoxyl estimation:-

2:3-Dimethyl-β-methylxyloside requires $OCH_3 = 48.4\%$

Found $OCH_3 = 48.5\%$

Rotation:-

$[\alpha]_D = -5.8°$ in chloroform, $\underline{1} = 2$, c = 2.2%

Solubility:-

Miscible with all common solvents except petroleum ether.

2:3-Dimethyl-4-p-toluenesulphonyl-β-methylxyloside.

2:3-Dimethyl-β-methylxyloside (1.8 g.) when treated with 50% in excess of the theoretical amount required of p-toluenesulphonic chloride (2.7 g.) yielded a mobile syrup which on retreatment with p-toluenesulphonic chloride furnished a syrup (3.6 g.) which could not be crystallised from any solvent but slowly crystallised on standing. These syrupy crystals were then dried on a porous plate in a vacuum desiccator for two days when 1.5 g. crystals were obtained in the form of colourless needles. Recrystallisation twice from petroleum ether (b.p. 40- 60°) gave m.p. 56-59° with sintering at 50°.

Methoxyl estimation:-

2:3-Dimethyl-4-p-toluenesulphonyl-β-methylxyloside

$$\text{requires OCH}_3 = 26.9\%$$
$$\text{Found OCH}_3 = 24.9\%$$

Rotation:-

$[\alpha]_D = -8.8°$ in chloroform, $\underline{1} = 2$, $\alpha_D = -0.44°$, $c = 2.5\%$

Solubility:-

Insoluble in petroleum ether.

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