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OPTICAL ROTATORY DISPERSION STUDY OF THE OZOTRIAZOLE DERIVATIVES OF THE ALDO SUGAR FAMILY

MATTEO JOSEPH PIAZZA

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OPTICAL ROTATORY DISPERSION STUDY OF THE OSOTRIAZOLE DERIVATIVES OF THE ALDO SUGAR FAMILY

BY

MATTEO JOSEPH PIAZZA

Assoc., Erie County Technical Institute, 1960

B. S., University of Mississippi, 1962

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This thesis has been examined and approved.

Dana W. Ellis

R. W. Schreber

J. J. Abel

Alexander R. Campbell

Paul R. Jones

Gloria G. Lyle
Research Director

August 9, 1966
Date

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INTRODUCTION

INTRODUCTION

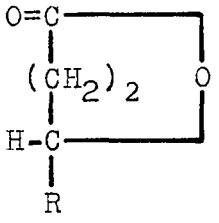
The search for methods of assigning stereochemistry has long been a subject of interest and concern. Therefore, the development of empirical rules of optical rotation which could indicate configuration of asymmetric centers was received with enthusiasm and in turn generated increased interest in optical properties of compounds. However, in spite of the considerable experimental investigations into the relationship between the specific or molar rotation and chemical structures, very few general rules have been derived.

The basic concept for all of these rules is that of the principle of "optical superposition," which was first proposed by J. H. van't Hoff in 1894.[1] The rotatory power of a substance is, according to the principle, the algebraic sum of the contribution of each separate asymmetric carbon atom, the value of which is a definite amount and is independent of the configuration of the other atoms.

In 1909, C. S. Hudson proposed his now famous "isorotation rules".[2] These rules represent an advance on van't Hoff's principles of superposition, particularly in regard to their wider applicability. These rules are still frequently used in the determination of anomeric configuration and in some cases to determine ring size.

C. S. Hudson published his most significant "lactone rule of rotation"[3] in the following year. He observed in his work with aldonic acids that the configuration of an aldonic

acid determined the rotation of the derived lactone. This rule was one of the earliest generalizations of configuration and optical properties and was inferred from very extensive data. In its simplest form the rule states that "the γ-lactone derived from an aldonic acid will be strongly dextrorotatory if the γ-hydroxy group that engages in lactone formation is on the right of the Fischer projection of the aldonic acid". As an example, lactone I should have a more positive rotation than lactone II. This rule was later extended to include amides[5] and phenylhydrazides.[6,7]



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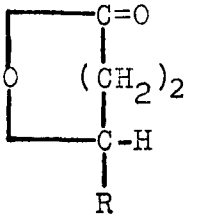


II

In 1942 N. K. Richtmyer and C. S. Hudson observed an empirical correlation between the sign of rotation and configuration of the benzimidazole derivatives. The benzimidazole rule states[8] that "whenever the hydroxyl group on the second carbon atom of an aldonic acid is written on the right in the conventional projection formula, the rotation of the derived benzimidazole is positive and, conversely, when the hydroxyl is written on the left, the rotation of the benzimidazole is negative." This correlation between sign of rotation and configuration appears to hold true irrespective of the con-

figuration of other asymmetric centers in the molecule.

The benzimidazole rule allows one to discern the configuration of the first hydroxyl group of reducing sugars by converting them to benzimidazole derivatives (Fig.1) and observing the sign of rotation at the sodium D-line. The rule has been of great value in elucidating C-2 stereochemistry of new sugars, especially the synthetic heptoses prepared by hydrogen cyanide addition to hexoses, in which case, two epimeric heptoses are obtained. Hudson's benzimidazole rule is known to give the correct prediction in 31 test cases.[8,9]

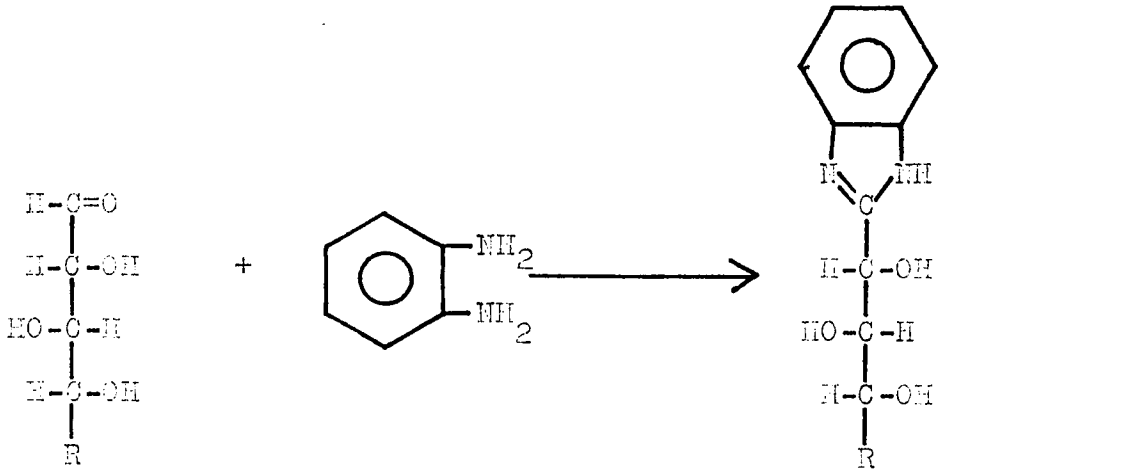
During the development of this thesis, Khadem[10] and Hills[11] extended the benzimidazole rule by formulating a corresponding "phenyl osotriazole rule." This rule again relates configuration with the sign of rotation at the sodium D-line. It states that "when the hydroxyl group attached to C-3 of the sugar residue is to the right in the Fischer projection formula, the sign of rotation of the derived osotriazole is positive, and when to the left, it is negative."[12,13] This rule has since been generalized to correlate the sign of rotation with the configuration of the asymmetric carbon atom adjacent to a heterocyclic or aromatic ring.[14]

Although these rules are strictly empirical correlation of rotation at a single wavelength (589 mμ) with configuration at a single asymmetric center, no known exception to them has as yet been reported. Extension of the rules to predict the configuration of additional centers of asymmetry in the molecule has shown that the contributions to the rotation of the centers are not strictly additive, as would be assumed

from van't Hoff's principle, but that considerations of polarizability[15] and conformational[16] factors are vital to the success of the calculations.

The "benzimidazole rule", together with the "phenyl osotriazole rule", both of which correlate sign of rotation with configuration of a hydroxyl group, make it possible by their separate and collective use to assign the configuration of the C-2 and C-3 positions of a reducing sugar (Fig. 1 & 2).

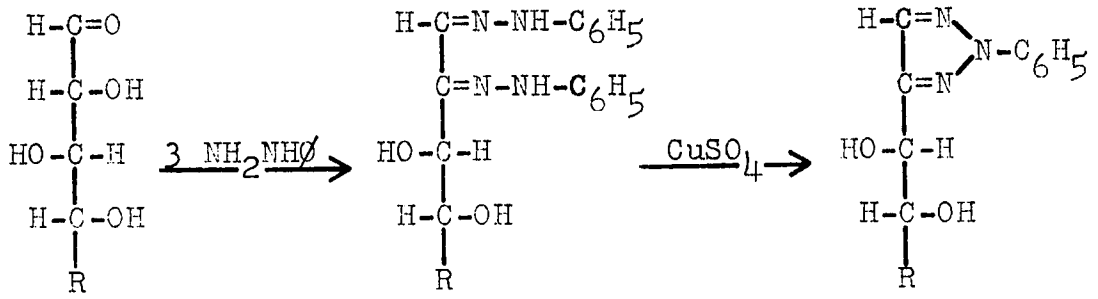
C-2



III IV V (+)-Rotation

Fig. 1. Assignment of Configuration at C-2 of a Reducing Sugar

C-3



III VI VII (-)-Rotation

Fig. 2. Assignment of Configuration at C-3 of a Reducing Sugar.

It seemed desirable to examine these sugar derivatives with the view of correlating the configuration with the optical rotatory dispersion (O.R.D.) curve. As Djerassi[17] pointed out, "Configurational assignments based on rotations obtained at the D-line are at times equivocal or even impossible, especially when a plain dispersion curve crosses the zero rotation line somewhere below 589 mμ. This change in sign is, of course, not known to the experimentalist relying only on a measurement of $[\alpha]_D$ and several such examples have been encountered by Sjoberg,[18] who demonstrated the utility of plain dispersion curves for settling certain configurational relationship."

It was felt that such an investigation would allow one to ascertain if the correlation of sign of rotation and configuration observed at the sodium D-line reflects the sign of an anticipated Cotton effect in the O.R.D. Since the 2-phenyl-

2,1,3-triazoles have an aromatic system which absorbs at approximately 268 mμ, this class of compounds should produce Cotton effects at accessible wavelengths in the O.R.D. due to a weak absorption band in an asymmetric environment. It was further hoped that a detailed study of the optical rotation of the 2-phenyl-2,1,3-triazoles of the complete aldo sugar family could produce some further correlations between strength of rotation and configuration of secondary alcohols as well as information on the partial rotation of secondary hydroxyl groups at varying distances from a chromophoric group and in differing conformational environments. This latter comparison was suggested by J. A. Mills in a communication[11] published during the course of this investigation. In this communication he stated: "Attempts to correlate the magnitude of rotation of lactones and 2-(polyhydroxyalkyl)-benziminazoles with the configuration at several contiguous asymmetric centers have been partially successful, and the rotations of the benziminazoles show a trend broadly similar to that shown by the phenylosotriazoles. The latter are, however, the only acyclic derivatives of sugars that show such wide differences between the molecular rotations of different configurational groups. The main reason for this may merely be that pyridine has been the preferred solvent for phenylosotriazoles, whereas water has normally been used for obtaining the rotations of the other derivatives. It is very desirable that more extensive data should be provided for the optical rotatory properties of all these derivatives in several solvents, because of the practical value of more precise configurational deductions, and con-

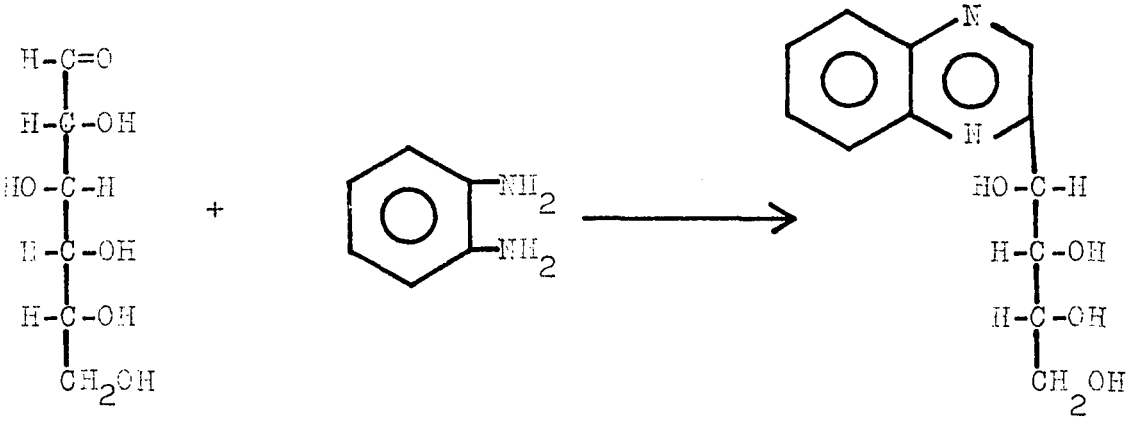
tributions that might be made to theories of conformational analysis and optical rotatory power. The rotations of the 2-(polyhydroxyalkyl)quinoxalines derived from reducing sugars may also be a source of configurational correlations when more data are available."

To determine information on the partial rotation of secondary hydroxyl groups it would be necessary to assume the existence of some sort of additivity relationship in optical rotation. In reference to this Djerassi[19] stated: "Until now, it has been difficult to inquire into the extent of validity of such an assumption. Numerical values of individual rotational strengths do, however, provide the proper criterion for such an investigation, and it is in this broad sense that the concept of the rotational strength may play its most important role. First, it opens up the possibility of a reliable set of empirical rules for the structural chemist, and second, the theoretician will at last have an experimental guide with which to test his hypotheses of the intramolecular interactions that affect optical activity." The synthesis of these aryl-substituted polyhydroxylated compounds in a systematic manner would permit a relatively complete analysis of the physical and optical properties of the 2-phenyl-2,1,3-triazoles of all of the members of the aldotetrose, aldopentose, and aldohexose families and could lead to correlation between stereochemistry and strength of rotation in the O.R.D. Such correlations could be of considerable value in assigning stereochemistry to new sugars.

DISCUSSION

DISCUSSION

The current investigation involves the systematic study of the optical and physical properties of an aryl-substituted polyhydroxy system. The investigation was expected to lead to a correlation between the stereochemistry and strength of rotation of polyhydroxy systems. To accomplish this end, the D-aldo sugar family as shown in Fig. 3 was chosen as the polyhydroxy moiety. It was then necessary to decide upon a convenient aryl derivative for this system. A literature search for such an aryl substituent produced the possibility of the quinoxaline derivatives.



VIII IV IX

In 1934, H. Ohle[20] obtained a quinoxaline derivative of an aldo sugar by the direct combination of ortho-phenylenediamine (IV) with D-glucose (VIII) yielding 2-(D-arabino-tetrahydroxybutyl)quinoxaline (IX). This aromatic derivative was very stable and showed no mutarotation in acid or base. These

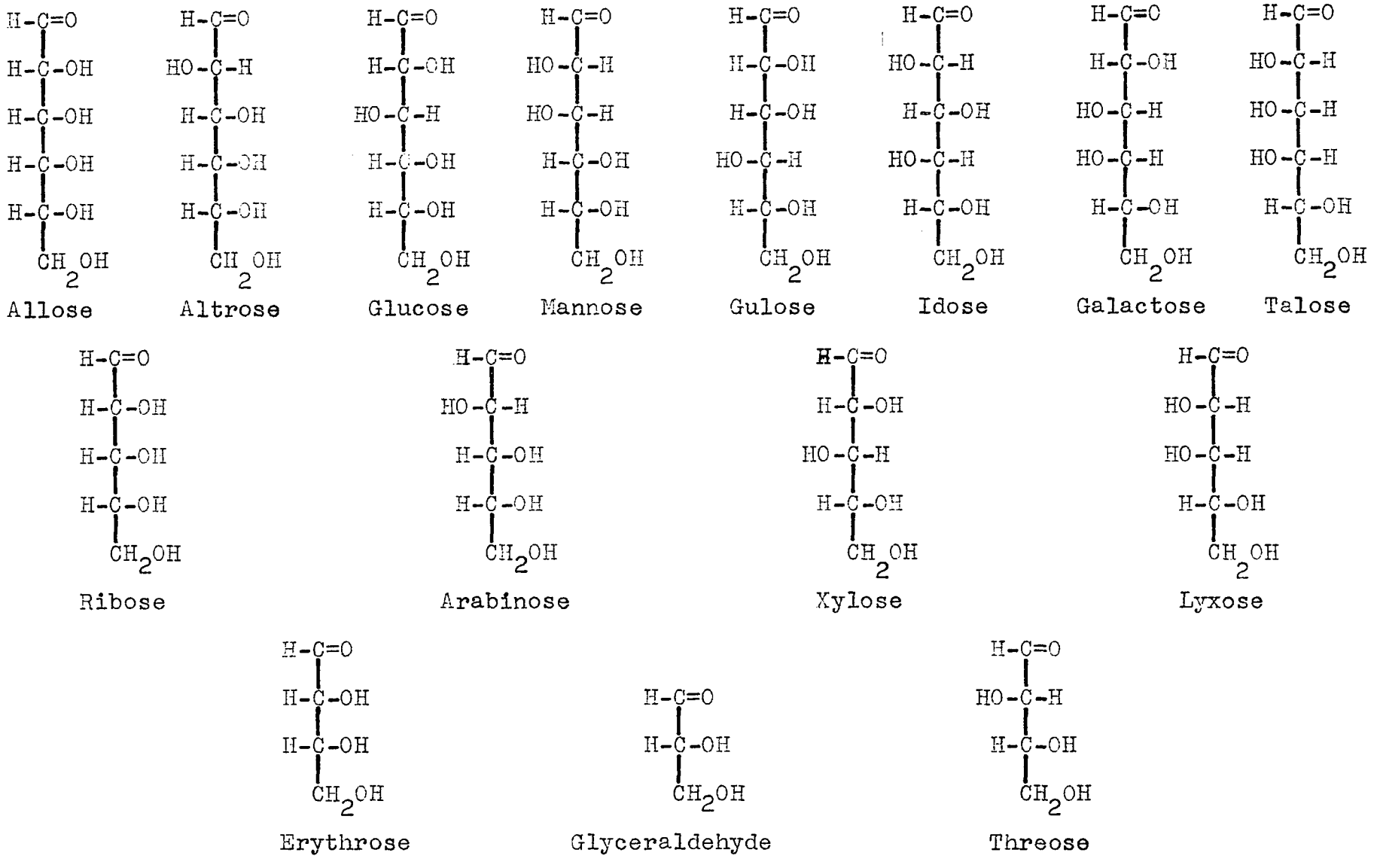


Fig. 3. D-Aldo Sugar Family

features made the quinoxaline derivatives desirable for the aromatic moiety for this investigation.

features made the quinoxaline derivatives desirable for the aromatic moiety for this investigation.

In the initial study of this reaction, it was observed that many of the quinoxaline compounds were produced in low yield along with a substantial quantity of other side reaction products, presumed to be the compounds indicated in Fig. 4. Since separation of the quinoxaline derivatives from the side products was not possible by crystallisation, a more desirable aryl system was sought.

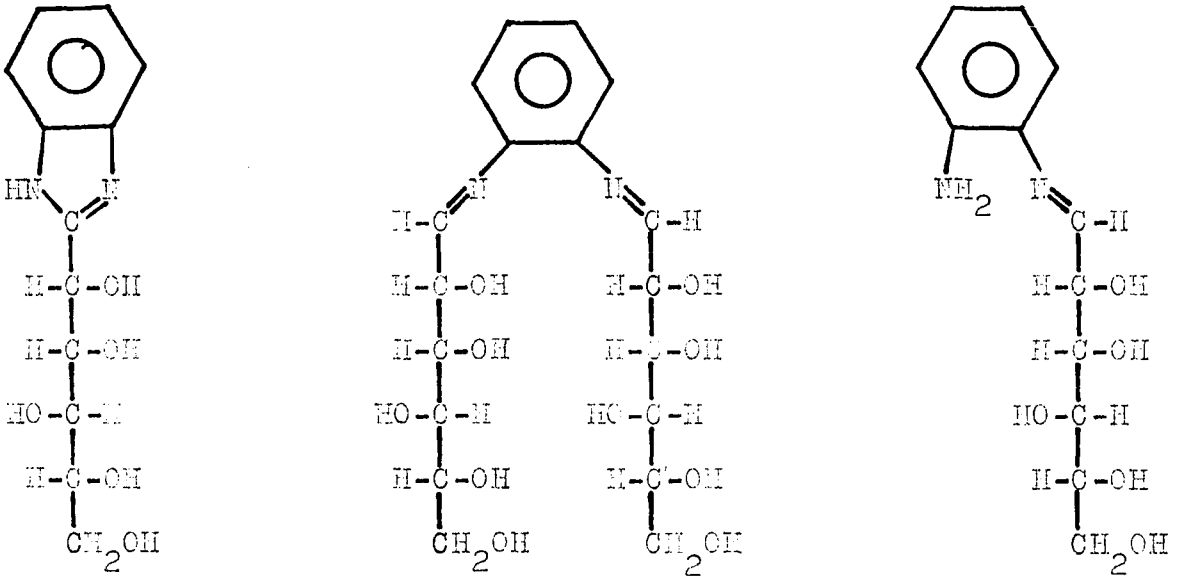
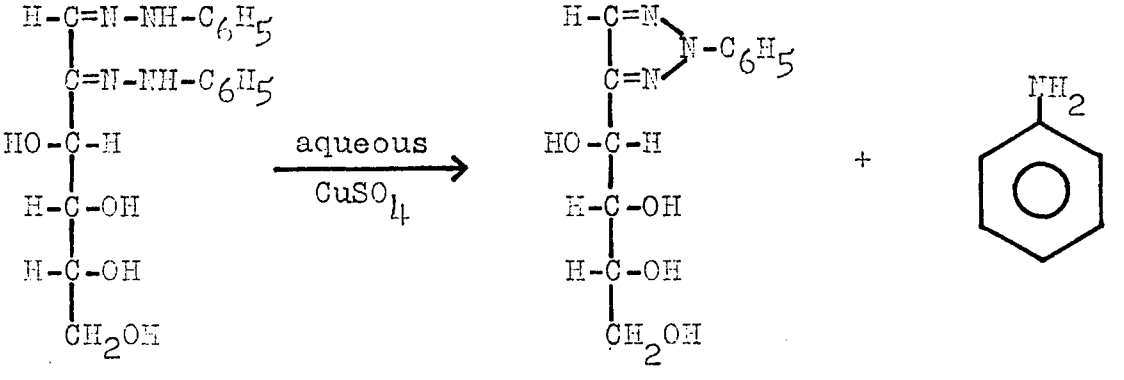


Fig. 4. Side Reaction Products from the Preparation of Quinoxaline Derivatives

2-PHENYL-2,1,3-TRIAZOLE DERIVATIVES

2-PHENYL-2,1,3-TRIAZOLE DERIVATIVES

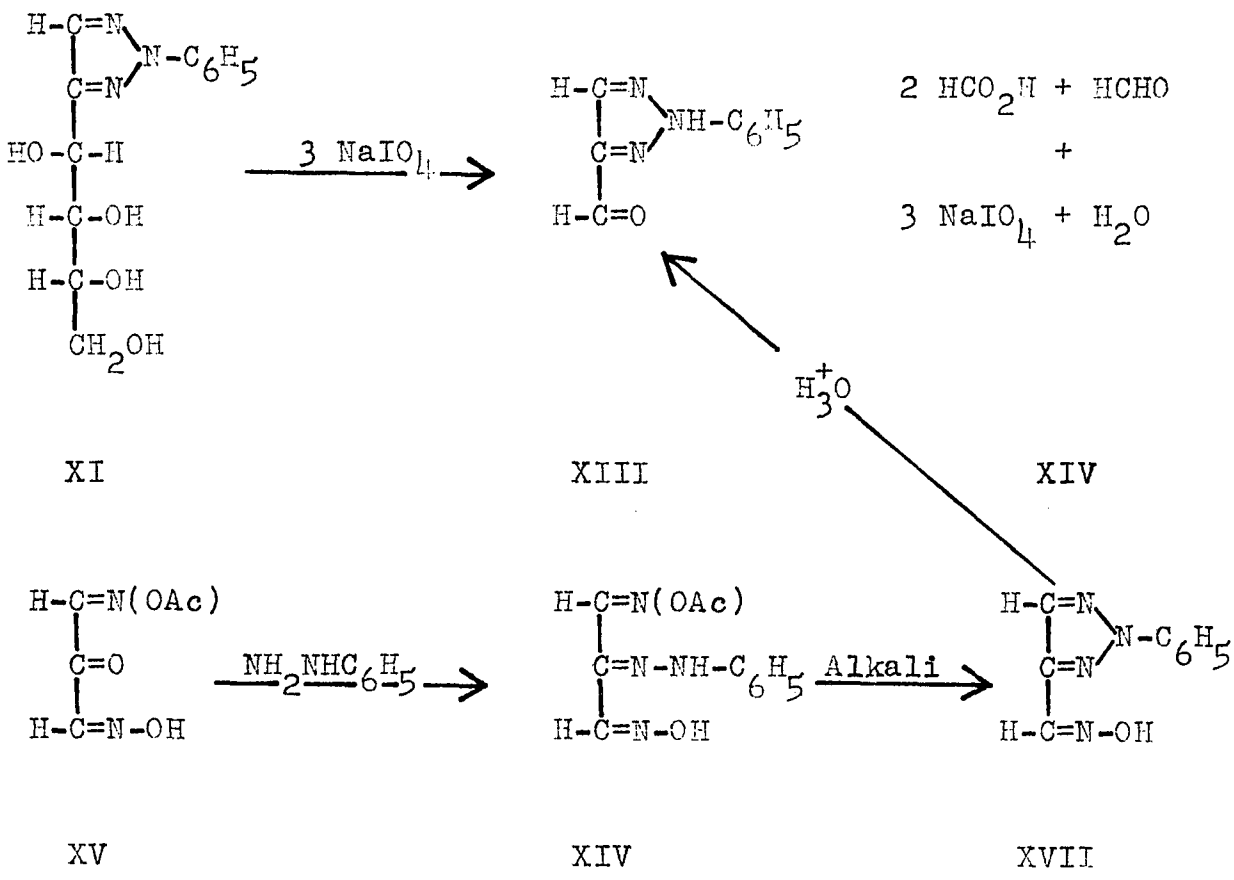
During the course of their work with aldonic acids, Hann and Hudson found that a satisfactory procedure for converting phenylhydrazides of aldonic acids was possible by decomposing the phenylhydrazide in hot aqueous copper sulfate solution to the free sugar acid, nitrogen, and benzene.[21] The reaction appeared to be a quantitative one. These investigators next tested the action of aqueous copper sulfate on the phenylosazones of the aldo sugars. However, unlike the hydrazides, the sugar osazones such as X were cyclized to the corresponding 2-phenyl-2,1,3-triazole derivative XI and aniline (XII).[22]



X XI XII

Hann and Hudson based their structural assignments on the fact that the product XI had a molecular formula of $C_{12}H_{15}N_3O_4$ which differed from the formula of the starting

osazone X by C_6H_7N. The product gave a tetraacetate and a tetrabenzoate both of which could be hydrolyzed with mineral acid to the starting 2-phenyl-2,1,3-triazole, thus indicating the presence of four hydroxyl groups. When one mole of the free material was oxidized with sodium metaperiodate, three moles of periodate were consumed with the production of one mole of formaldehyde, two moles of formic acid and one mole of a white crystalline material which was found to be an aldehyde. The compound was compared with 2-phenyl-4-formyl-2,1,3-triazole (XIII) which was first prepared in 1891 by von Pechmann,[23] from mesoxaldehyde-1-β-acetyloxime (XV). The compounds were found to be identical, thus indicating that the osazone had been cyclized into a 2-phenyl-2,1,3-triazole ring system.



All of the 2-phenyl-2,1,3-triazole derivatives, when subjected to sodium metaperiodate oxidation gave 2-phenyl-4-formyl-2,1,3-triazole with modifications of the other oxidative by-products depending upon the number of hydroxyl groups.

Mechanism of Osotriazole Derivative Formation

Hann and Hudson proposed a mechanism for this reaction in which the copper ion formed a complex with the osazone.[21,22] This was evidenced by the production of a red color upon the addition of copper ions to the osazone which faded as the formation of the 2-phenyl-2,1,3-triazole derivative proceeded. The copper ion presumably complexes with the π-system of the osazone, and in so doing holds the two bulky phenylhydrazine groups in one plane and <u>cis</u> with each other. This would be in contrast to the more desirable <u>trans</u> configuration which they would presumably be in if they were not coordinated with the copper ion (Fig. 5). This planer <u>cis</u> configuration of the phenylhydrazine moiety thus allows for the elimination of aniline from the osazone with the production of a highly resonance stabilized 2-phenyl-2,1,3-triazole ring. It has been shown that copper readily forms complexes with semicarbazones[24] and hydrazones,[25] thus offering further support for the complexing of copper with the osazone.

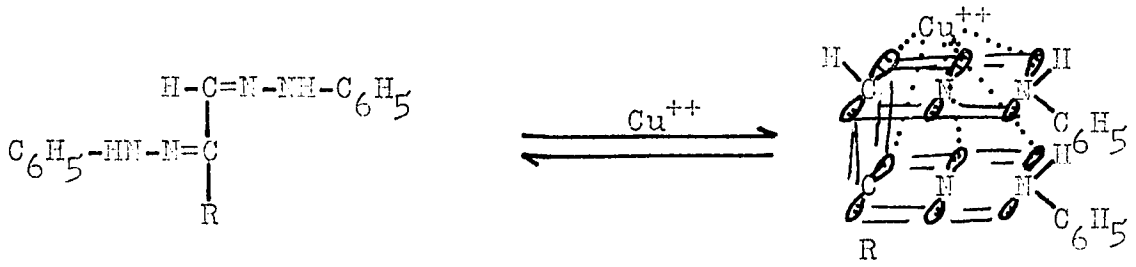


Fig. 5. Complexing of the Copper Ion With an Osazone

Hann and Hudson[22] also noted the precipitation of a small portion of copper as cuprous oxide which they attributed to reductive side reactions. Subsequent work showed that ferric chloride, ferric sulfate, and potassium ferricyanide, all of which contain iron(III) cause 2-phenyl-2,1,3-triazole formation. However, ferrous chloride, ferrous sulfate, and potassium ferrocyanide, all of which contain iron(II), fail to cause 2-phenyl-2,1,3-triazole formation. The authors stated that these results showed that an oxidizing agent was necessary, thus indicating that an oxidation is involved in at least one step of the mechanism.[26,27,28]

The second question involved in the mechanism of the 2-phenyl-2,1,3-triazole formation was whether aniline was removed from the hydrazone residue of C-1 or C-2. This question was solved independently by Weygaud[29] and Henseke.[30] Weygaud examined the question by using the p-bromophenylosazones. When they were treated with ^{82}Br-labeled (p-bromophenyl)hydrazine, the transhydrazination[31] proceeded unequally, such that most of the label appeared on C-1 (Fig. 6). Cleavage of this transhydrazinated (p-bromophenyl)hydrazone showed that 23% of the label was on C-2. When the unequally labeled osazone was subjected to 2-phenyl-2,1,3-triazole formation, it was found that only 18% of the label remained, indicating that the C-1 hydrazone residue had been eliminated. Henseke and co-workers[30] also obtained similar results by the use of mixed substituted osazones.

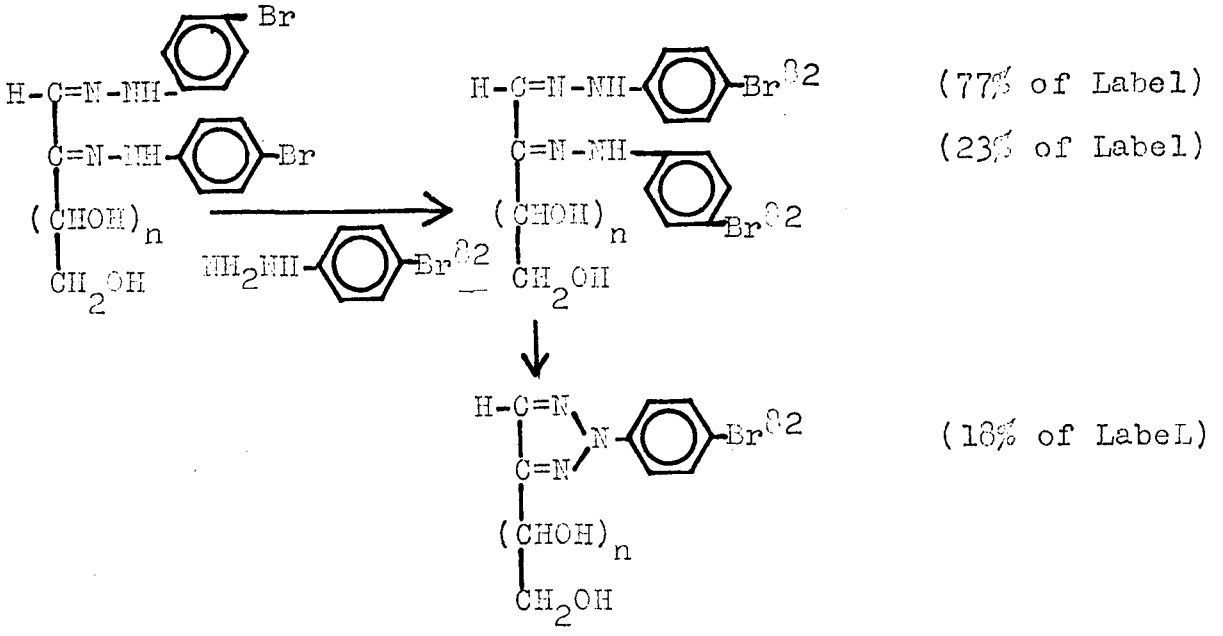


Fig. 6. ^{82}Br Study of Cyclization Mechanism

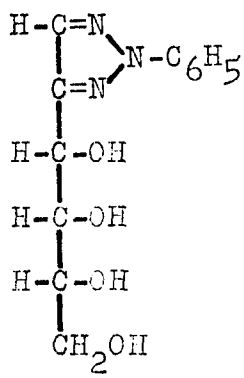
The conclusion is, therefore, inescapable that the conversion of osazones into 2-phenyl-2,1,3-triazole derivatives involves an oxidation, at least at one stage of the reaction, and complexes of the metal ion with the osazone may also be involved. The exact mechanism of this cyclization, however, is still uncertain.

The 2-phenyl-2,1,3-triazole derivatives are colorless, crystalline compounds with sharp melting points. They are very stable toward strong oxidizing agents, concentrated alkalis or acids and exhibit no mutarotation. This system has a strong absorption in the 260-270 mμ region of the ultraviolet and, therefore, should produce Cotton effects at an accessible wavelength in the O.R.D. Although the preparation of the 2-phenyl-2,1,3-triazole derivatives from the aldo sugar family requires an additional step over that of the quinoxaline de-

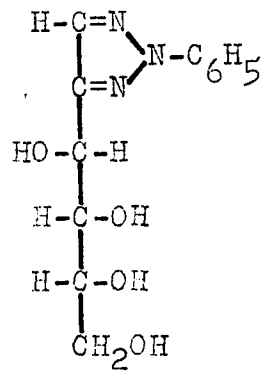
rivatives, the overall yield of their preparation was reported to be much higher and the products were less contaminated with side products thus indicating the desirability of these derivatives.

Nomenclature of Derivatives

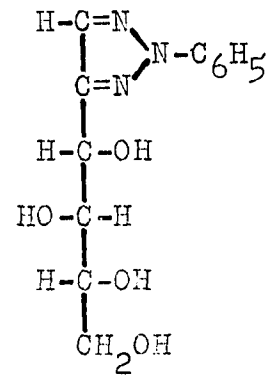
The current investigation involved the synthesis of the 2-phenyl-2,1,3-triazole derivatives (Fig. 7) of the D-aldo sugar family. Due to the expense of D-arabinose and D-gulose, however, L-arabinose and L-sorbose (L-sorbose being the conjugate of L-gulose in the keto sugar family) were used as the starting sugars for preparing these two respective 2-phenyl-2,1,3-triazole derivatives. Thus, L-enantiomers will be designated by a L after the compound number. For example 2-phenyl-4-(D-erythrose-trihydroxypropyl)-2,1,3-triazole's number is XXI and its L-enantiomer will be XXI-L. Also, when referring to the 2-phenyl-2,1,3-triazole derivatives, they will be called by their common names (which in most cases is the name of the sugar from which the osazone was prepared) instead of the systematic name. When the compound is mentioned, the number assigned to the common name (corresponding to the systematic name used in the experimental section) will also be given. Therefore, for example, 2-phenyl-4-(D-arabino-tetrahydroxybutyl)-2,1,3-triazole which was prepared from D-glucose will be referred to in this dissertation as D-glucose osotriazole (XI) and that of 2-phenyl-4-(L-erythro-trihydroxypropyl)-2,1,3-triazole which was prepared from L-arabinose will be named L-arabinose osotriazole (XXI-L).



XVIII



XI



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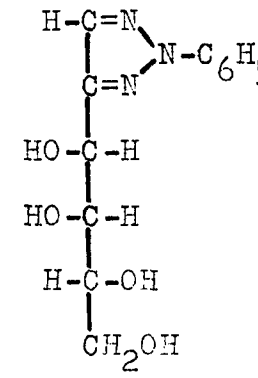
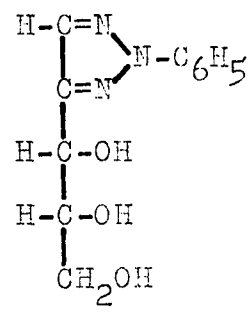
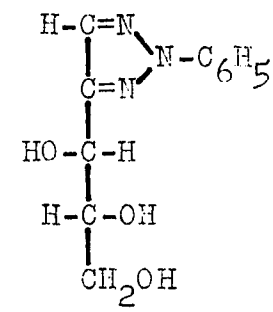


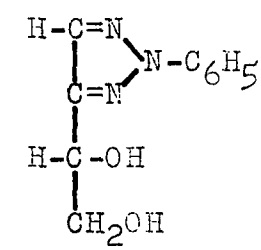
XX



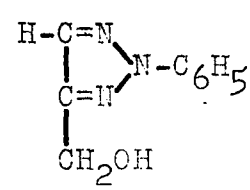
XXI



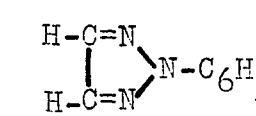
XXII



XXIII



XXIV

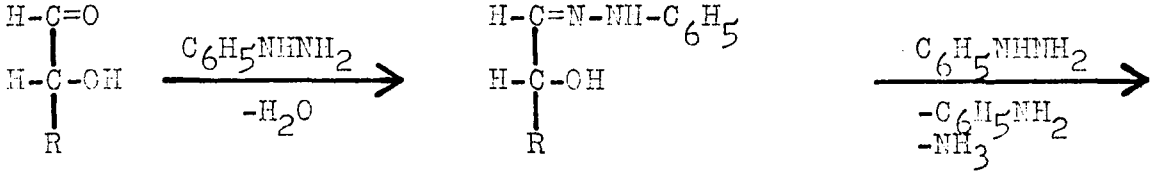


XXV

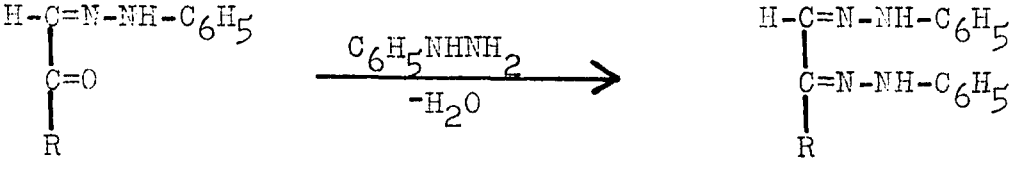
Fig. 7. Osotriazole Derivatives of the D-Aldo Sugar Family

Mechanism of Osazone Formation

The first step in making the osotriazole is to make the phenylosazone derivative of the aldo sugar. Osazones are usually prepared[32] by the action of three molar equivalents of hydrazine (or its hydrochloride) on one mole of the carbohydrate in aqueous acetic acid (or sodium acetate). Fischer[33] described the steps leading to the osazone as occurring in three parts: (1) the formation of a phenylhydrazone XXVII from the aldose, (2) the oxidation of the phenylhydrazone with a second mole of phenylhydrazine to XXVIII, (3) the reaction of XXVIII with a third molecule of phenylhydrazine to form the osazone.



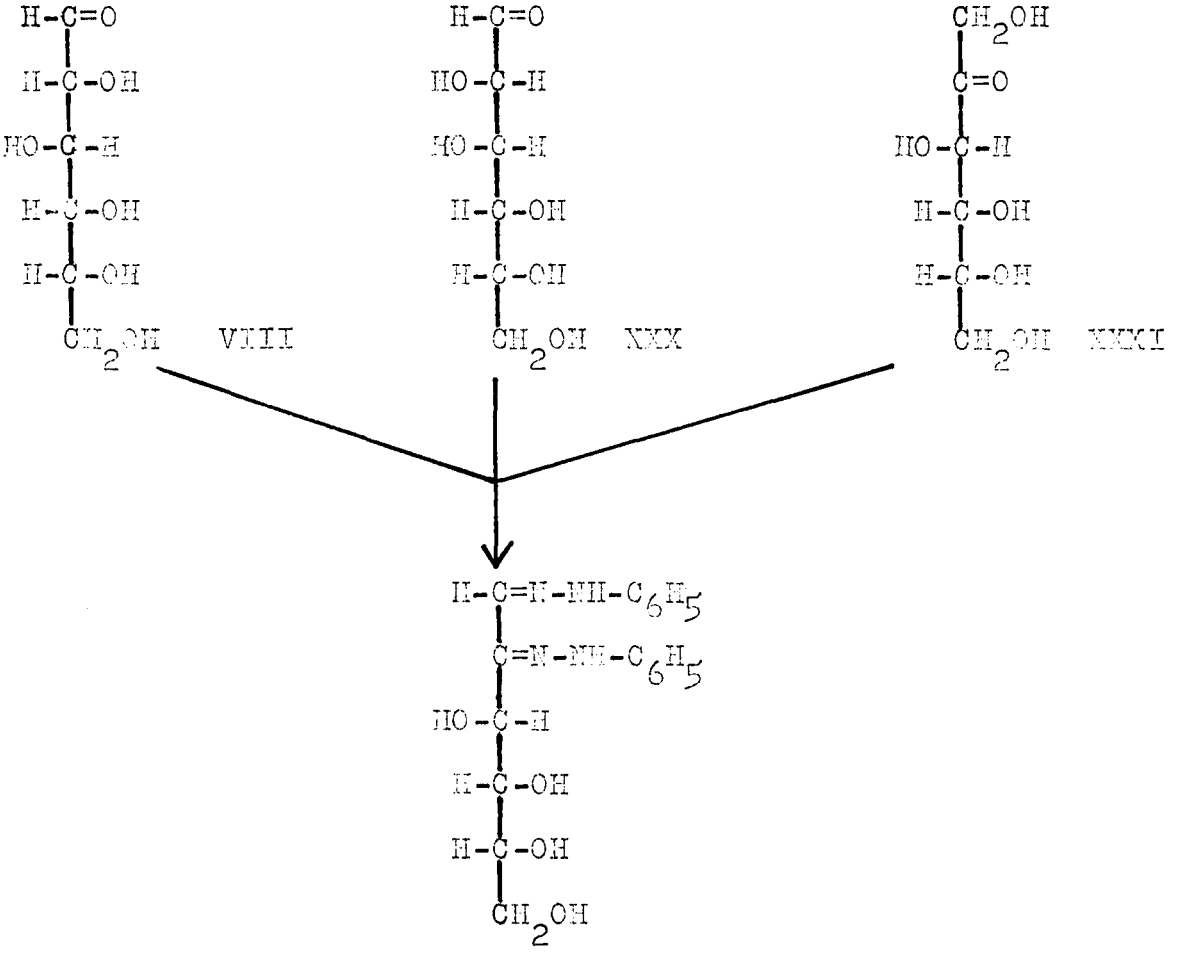
XVI XXVII

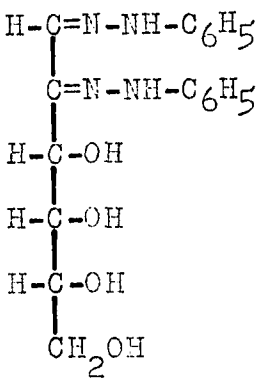


XXVIII XXIX

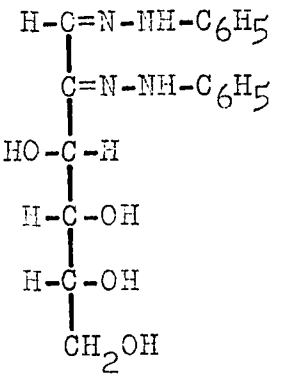
Since the second step in the formation of the osazones involves oxidation of C-2 and thus destroys the asymmetric center, epimeric carbohydrates will produce the same phenylosazone.

For example, both D-mannose (XXX) and D-glucose (VIII) yield osazone X. The same osazone was also formed from D-fructose (XXXI), thus indicating that the conjugate carbohydrate in the keto sugar family also produces the same osazone. The structural formulas for the osazone derivatives are shown in Fig. 8. The names of the two aldo sugars and one keto sugar from which each osazone is derived are given in Table I.

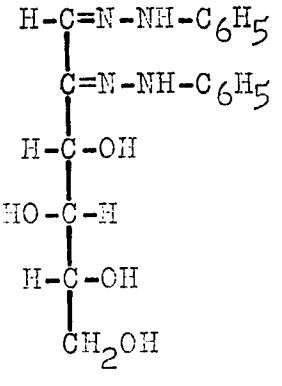




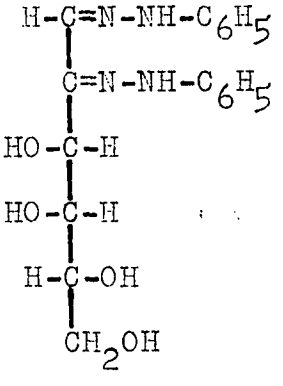
XXXII



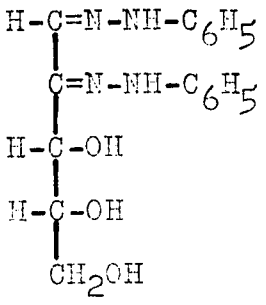
X



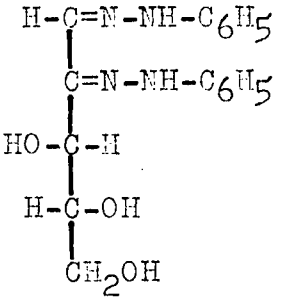
XXXIII



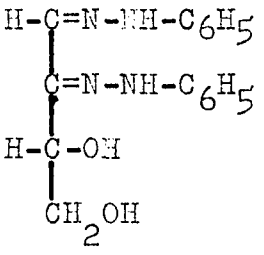
XXXIV



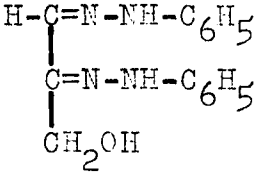
XXXV



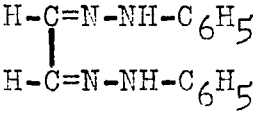
XXXVI



XXXVII



XXXVIII



XXXIX

Fig. 8. Osazone Derivatives of the D-Aldo Sugar Family

TABLE I

Relationship of Sugars to Derived Osotriazoles

Osotriazole*	Osazone** from which Osotriazole May be Prepared	D-Aldo Sugars*** from which Osazone May be Prepared	D-Ketose Sugars from which Osazone May be Prepared
XVIII	XXXII	D-Allose D-Altrose	D-Allulose
XI	X	D-Glucose D-Mannose	D-Fructose
XIX	XXXIII	D-Gulose D-Idose	D-Sorbose
XX	XXXIV	D-Galactose D-Talose	D-Tagatose
XXI	XXXV	D-Arabinose D-Ribose	D-Ribulose
XXII	XXXVI	D-Xylose D-Lyxose	D-Xylulose
XXIII	XXXVII	D-Erythrose D-Threose	D-Erythrulose
XXIV	XXXVIII	D-Glyceraldehyde	Dihydroxyacetone

*For structures of osotriazoles see Fig. 7.
**For structures of osazones see Fig. 8.
***For structures of D-aldo sugars see Fig. 3.

The Nature of the Osazone Intermediate

Fieser[34] suggested, on theoretical grounds, that osazones exist in tautomeric, chelated forms which stabilize these unsaturated compounds and prevent the reaction of hydrazines with carbohydrates from proceeding beyond C-2 (Fig. 9).

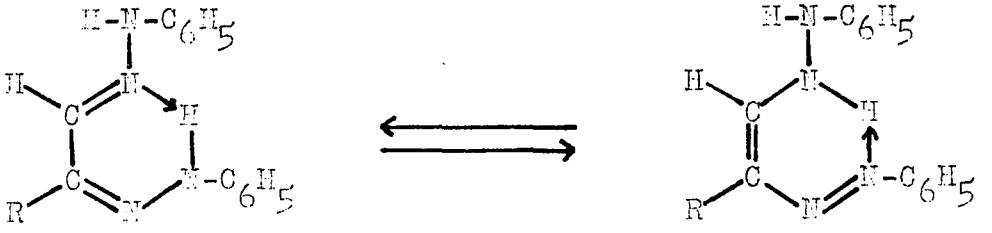
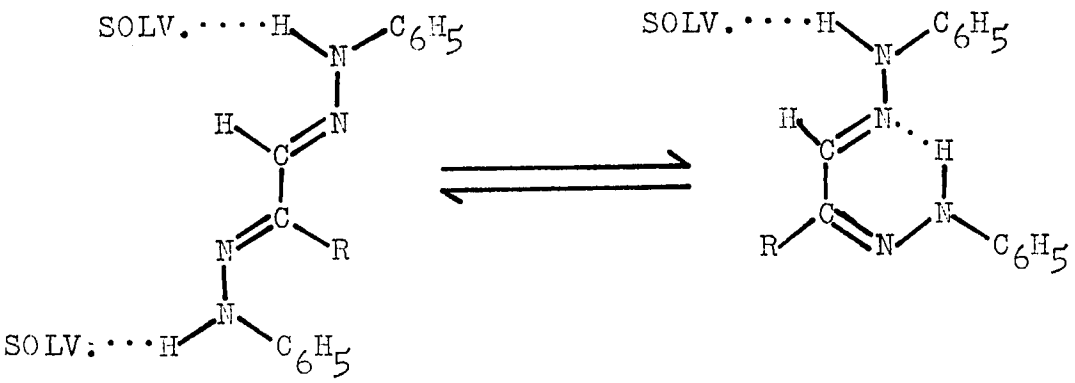


Fig. 9. Fieser's Tautomeric, Chelated Forms of Osazones

O. L. Chapman[35] has presented evidence which shows that there exists an equilibrium between a non-chelated structure XL, which is stabilized by hydrogen bonding to the solvent, and a chelated structure XLI, which is stabilized by intramolecular hydrogen bonding. This equilibrium between structures XL and XLI is dependent upon the size of the R group and on the strength of the hydrogen bonding of the solvent. The author further presents evidence as to the lack of aromaticity of this chelated structure due to the absence of a ring current, and concludes by saying: "The major portion of the stabilization of the chelate form (which is still small) in poor hydrogen bonding solvents thus is primarily due to the chelate hydrogen bond and not to a substantial difference in π-electron delocalization energies in the two isomers."



XL XLI

Synthesis of Osazones

The preparation of the osazones was effected as previously indicated by the direct combination of the aldo sugar with phenylhydrazine hydrochloride in a sodium acetate solution. It was found, however, that the yield could be increased by preparing the sodium bisulfite addition product of the aldehyde and then proceeding as above.

In all cases prolonged contact of the osazone with the reaction mixture produced substantial decomposition of the osazone. It was, therefore, necessary to separate the precipitate by filtration shortly after the reaction was complete and wash it very well with acetic acid and water to remove all traces of unreacted phenylhydrazine. The best procedure found was to wash the osazone and recrystallize it immediately before allowing it to dry.

In the case of L-arabinose osazone (XXXV-L), this decomposition from contact of the osazone with phenylhydrazine was so rapid that the osazone could not be collected. To cor-

rect this problem the osazone was prepared as a solution. Methyl cellosolve was found to be an excellent solvent for this preparation as it meets the three necessary requirements, namely: (1) the starting materials are soluble in methyl cellosolve; (2) the final product is soluble in methyl cellosolve; (3) methyl cellosolve is miscible with water and the osazone is water insoluble, therefore the product can be easily precipitated by the addition of water to the mixture. This technique was found to be very successful for both L-arabinose osazone (XXXV-L) and glyoxal osazone (XXXIX).

Due to the expense of erythrose and threose an indirect procedure for obtaining the osazone of these tetroses was undertaken. It was observed in the literature[36] that when starch is oxidized with sodium metaperiodate, the glyoxal linkages are oxidized to oxystarch which readily hydrolyzes to aldehyde sugar groups (Fig. 10).

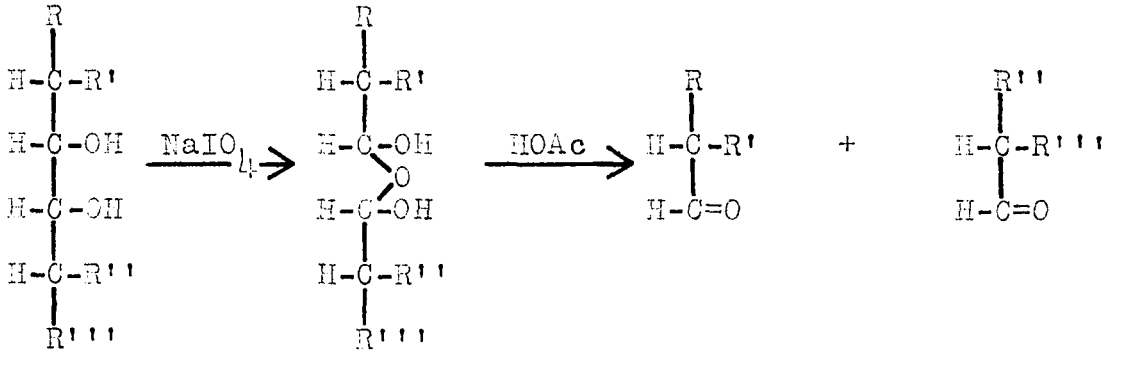
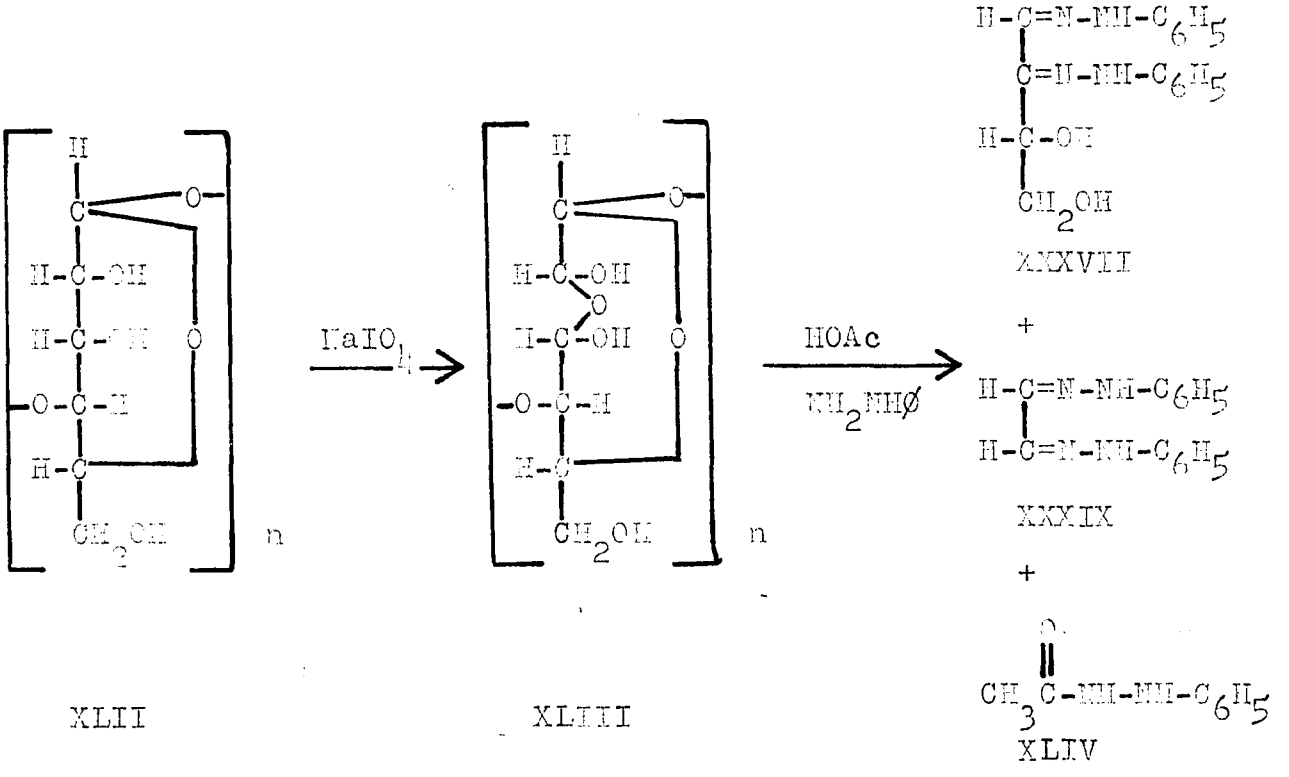


Fig. 10. Oxidative Cleavage of the Glyoxal Linkages of Starch

When potato starch was subjected to the above oxidative degradation followed by hydrolysis with acetic acid in the presence of phenylhydrazine, components of the degraded linkage were D-erythrose phenylosazone (XXXVII) and glyoxal phenylosazone (XXXIX) along with some β-acetyl phenylhydrazine (XLIV). The latter compound was produced from the reaction of phenylhydrazine with acetic acid.



XLII XLIII

XXXVII + XXXIX + XLIV

These components can be separated on a neutral alumina column to obtain the free D-erythrose phenylosazone (XXXVII) or the mixture can be subjected to osotriazole formation conditions leading directly to D-erythrose osotriazole (XXIII). This was the one remaining unknown osotriazole of the aldo sugar family and is the most important link in the current investigation.

Synthesis of Osotrizoles from Osazones

The preparation of the osotriazoles was effected as previously indicated by a cyclization reaction on the isolated osazone (with the exception of D-erythrose osotriazole (XXIII)). In all cases, the cyclization was accomplished by the use of copper sulfate in an aqueous medium. The aqueous solution of copper sulfate was added to a water suspension of the insoluble osazone. Solution of the osazone and the concurrent development of a red color occurred in the first few minutes of refluxing. Some of the osazone was decomposed by the copper sulfate as evidenced by the black insoluble residue produced during the reaction. When the osazone was finely powdered, it dissolved much more readily, and decomposition of it was kept to a minimum. If this decomposition was not extensive, at the completion of the reaction an emerald green colored solution indicating the presence of free copper ions was produced. In either case, filtration of the solution at completion of the reaction to remove the black decomposition products and the small quantity of red copper oxide also present yielded an emerald green solution.

Due to a problem in solubility and the complexing of the copper sulfate with the osotriazoles, the best procedure found to isolate the osotriazole product was to remove the copper sulfate. This was achieved by precipitation of the copper ions with hydrogen sulfide and the sulfate ions with barium carbonate, thus leaving the media free of inorganic ions. Concentration of this slightly basic, yellow solution usually produced a syrup which was dried thoroughly and recrystallized from an appropriate solvent.

OPTICAL ROTATORY DISPERSION STUDY

OPTICAL ROTATORY DISPERSION STUDY

In order to obtain the optical rotatory dispersion curves of the optically active osotriazoles, it was necessary to employ three different spectropolarimeters. It is interesting to compare the results from these three instruments.

Rudolph Recording Spectropolarimeter

From the ultraviolet data it was observed that the 2-phenyl-2,1,3-triazole ring system absorbs in the region of 265-270 mμ with a rather large extinction coefficient of 15,000-20,000. Although this region is accessible to the Rudolph instrument the absorption of the 2-phenyl-2,1,3-triazole ring system proved to be too strong for its 450 watt xenon light source. As a consequence, no appreciable data below 300 mμ could be obtained due to the lack of transmittance even with very low concentrations (1×10^{-4} M) of the absorbing material. The long wavelength data, however, appeared to be reproducible from samples of relatively high concentrations. The molecular rotation at the 589 mμ wavelength of the O.R.D. curves obtained on the Rudolph instrument compared very closely with those reported in the literature (Table II). Therefore, in the following study, the long wavelength data obtained from the Rudolph instrument will be taken as quantitative. This fact makes the Rudolph an excellent instrument for conducting a solvent study in the long wavelength region.

TABLE II

Comparison of Sodium D-Line Rotation Values

Osotriazole of:	Molecular Rotation $[M]_D$*	Molecular Rotation $[M]_D$**
L-Arabinose (XXI-L)	-76 (P)	-61 (P)[a]
L-Arabinose (XXI-L)	-51 (W)	-54 (W)[a]
D-Xylose (XXII)	-74 (W)	-76 (W)[b]
L-Sorbose (XIX-L)	-133 (P)	-133 (P)[b]
D-Glucose (XI)	-219 (P)	-218 (P)[c]

*Values from the Rudolph Instrument
**Literature values (P) = Pyridine; (W) = Water

[a] W. T. Haskins, R. M. Hann, and C. S. Hudson, J. Am. Chem. Soc., 68, 1766 (1946).

[b] W. T. Haskins, R. M. Hann, and C. S. Hudson, J. Am. Chem. Soc., 67, 939 (1945).

[c] R. M. Hann and C. S. Hudson, J. Am. Chem. Soc., 66, 735 (1944)

Cary Recording Spectropolarimeter

The low concentrations (1 X 10^{-6} M) handled by the Cary made it possible to obtain transmittance of the polarized light through the solution in spite of the strong absorption of the media. Therefore, O.R.D. curves through one Cotton effect in the cases of the stronger rotating compounds such as D-glucose osotriazole (XI) could be obtained (Fig. 21). These shorter wavelength data tended to couple quite nicely with the long wavelength data obtained from the Rudolph instrument, and the

midpoint of the peak and trough of the Cotton effect coincided with the maximum absorption wavelength in the ultraviolet. In the case of the more weakly rotating compounds such as D-galactose osotriazole (XX) and L-arabinose osotriazole (XXI-L), less favorable results were obtained (Fig. 18). Although these curves indicated the presence of a negative Cotton effect, the strong absorption producing low transmittance made it necessary to use a high sensitivity setting such that the "background noise" was extensive and thus the amplitude, zero point crossing and midpoint wavelength of the first Cotton effect were uncertain. L-Arabinose osotriazole (XXI-L) possessed such a weak rotation compared to its absorption that no worthwhile data could be obtained on the Cary in the short wavelength region. However, it was observed that the shape and amplitude of the curve appeared to be similar to that of D-galactose osotriazole (XX).

Bellingham-Stanley Recording Spectropolarimeter.

The O.R.D. curves of D-galactose osotriazole (XX), L-arabinose osotriazole (XXI-L) and D-erythrose osotriazole (XXIII) were also obtained on the Bellingham-Stanley instrument (Fig. 13,16 & 17). Here again however, the light source was not sufficiently strong to permit quantitative data. This point was exhibited by the poor agreement of the midpoint of the first Cotton effect with the maximum absorption wavelength in the ultraviolet and also by the lack of coincidence of the long wavelength data with those obtained from the Rudolph in-

strument. These results indicate that only the shapes and signs of these Cotton effects are of value in this comparison.

From studying the results of these three instruments it appears that the following generalizations can be made concerning them:

Rudolph Recording Spectropolarimeter

1. This instrument requires too high a concentration and has too weak a light source to obtain short wavelength data for strongly absorbing compounds.
2. It appears to give quantitative results in the region outside of the absorption band which, in this study, is at wavelengths longer than 300 mμ.

Cary 60 Recording Spectropolarimeter

1. The low concentrations necessary for satisfactory results from this instrument permit data to be obtained at low wavelengths on compounds having strong absorption bands if they have strong rotations.
2. It appears, however, to give quantitative results only for strongly rotating compounds.
3. The agreement of the midpoint of the Cotton effect with the wavelength of the maximum absorption in the ultraviolet indicated its excellent resolution.

Bellingham-Stanley Recording Spectropolarimeter

1. It is able to obtain data on weakly rotating compounds having strong absorption of ultraviolet light.
2. The lack of agreement of the midpoint of the Cotton effect with the wavelength of the maximum absorption in the ultraviolet indicates its lack of resolution and points to the fact

that the data are not quantitative.

3. Only the shape of the curves can be used in any comparison of data. The accuracy of the results has been taken to be [illegible] of significance to only one figure. The data reported in this study support this limitation.

Analysis of Cotton Effect Curves

All O.R.D. data in the region below 300 mμ of the osotriazoles were obtained from the Cary 60 and the Bellingham-Stanley using methanol as the solvent. These data were used to calculate the molecular rotation [M] of these compounds and were plotted as molecular rotation versus wavelength (mμ).

The O.R.D. curves for the osotriazoles were expected to show a Cotton effect due to the aromatic chromophore in the presence of an asymmetric center. D-Erythrose osotriazole (XXIII) contains only a single center of asymmetry at C-3. The hydroxyl group is adjacent to the aromatic system and lies on the right side in the Fischer projection. The O.R.D. curve of XXIII as obtained from the Bellingham-Stanley showed two Cotton effects (Fig. 13). As shown in Table III, the first Cotton effect is positive and has an amplitude* of +52.0 with the midpoint at 268 mμ. The second Cotton effect has an amplitude of +31.8 with a midpoint at 224 mμ. This double Cotton effect suggests that two separate electronic transitions are occurring in the ultraviolet region. Examination, however, of the ultraviolet spectrum obtained from a Cary Model 15 recording spectrophotometer showed no fine structure in the 225-

*Amplitude of a Cotton effect is defined by the expression.[37]

$$\frac{[M]_{\text{first extremum}} - [M]_{\text{second extremum}}}{100} = \text{amplitude } (\underline{a})$$

TABLE III

O.R.D. and U.V. Data of the Osotriazoles

Osotriazole of	No. of Carbons	Config. at C-3	Sign of C.E.*	Amplitude of C.E.*	Midpoint of C.E. (mμ)*	Ultraviolet*** $\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	Instrument
D-Erythrose (XXIII)	4	Right	+	+52.0	268	265	20,147	Bellingham-Stanley
			+	+31.8**	224			
				+44.6	263			Cary 60
D-Xylose (XXII)	5	Left	-	-59.2	261	267	20,239	Cary 60
L-Arabinose (XXI-L)	5	Left	-	-76.3	248	266	19,827	Bellingham-Stanley
D-Galactose (XX)	6	Left	-	-47.3	249	266	19,545	Bellingham-Stanley
			-	-21.9	258			Cary 60
L-Sorbose (XIX-L)	6	Left	-	-68.8	268	266	18,812	Cary 60
D-Glucose (XI)	6	Left	-	-195.0	267	267	24,450	Cary 60
D-Galactose Tetraacetate (XLVI)	6	Left	-	-37.7	279	264	22,070	Cary 60
			-	-44.8	258**			

*Data for First Cotton Effect **Data for Second Cotton Effect ***In 95% Ethanol

275 mμ region which would be indicative of two separate electronic transitions.

The curiously shaped curve for D-erythrose osotriazole (XXIII) could actually have been composed of a negative Cotton effect superimposed on a positive background curve. In this case, the peak at 279 mμ would not be related to the peak of the absorption band but would represent the partial, positive rotation in the longer wavelength region now falling under the influence of a stronger, negative partial rotation owing to entry into the optically active absorption band around 250 mμ, the first extremum of which is the trough at 256 mμ.[38]

The possibility that the double Cotton effects were the result of instrumental error must be considered. In an attempt to distinguish between these two possibilities, the O.R.D. of D-erythrose osotriazole (XXIII) was also obtained from the Cary 60 (Fig. 14 & 22). The curve obtained from the Cary 60 possessed a single, positive Cotton effect which had an amplitude of +44.6 and a midpoint of 263 mμ. Therefore, the curve obtained from the Bellingham-Stanley (Fig. 13) was probably due to instrumental error, caused by the strong absorption of the chromophore in the 215-290 mμ region and thus causing loss of transmittance of the polarized light.

Both the non-symmetrical shape and the breadth of the Cotton effect curve would indicate that more than a single electronic transition contributed to the O.R.D. Furthermore, lack of agreement of the λ_o value obtained from the solution of a one term Drude equation (see page 55) and the λ_o value (midpoint of Cotton effect) obtained from the O.R.D. curve sup-

ported this fact. Therefore the Cotton effect curve obtained from an osotriazole ring system attached to an asymmetric carbon atom possessing a hydroxyl group probably is composed of more than a single electronic transition. This question could best be resolved by examination of the circular dichroism of erythrose osotriazole (XXIII).

It is significant that the "phenyl osotriazole rule" correlating the configuration of the hydroxyl group alpha to the aromatic moiety with the rotation at the sodium D-line has been observed to apply to a large number of derivatives. One may assume, therefore, that this rule reflects a more fundamental relationship evidenced in the Cotton effect curves of these sugar derivatives. If this is true, it should be possible to devise a more general explanation for the correlation in the form of a simple Partition Rule analogous to the Octant Rule which has been devised for ketones.

The phenylosotriazole system contains the aromatic ring system attached to an asymmetric center, the original C-3 of the sugar. The phenyl and triazole rings must be coplanar in order to provide maximum resonance stabilization. The unsubstituted rings (R=H) possess two planes of symmetry (XY and YZ, Fig. 11a), but only that plane which passes through all atoms of the rings will also include R or the asymmetric center C-3, i.e., plane XY. These symmetry planes are also nodal planes of the aromatic chromophore and the atoms in the plane will not affect the Cotton effect curve. Atoms outside of the nodal planes, however, will perturb the orbitals asymmetrically if they are not free to rotate equally over opposite nodes.

Orienting the phenyl osotriazole on a Partition Diagram shows that the substituents at the C-3 asymmetric center will perturb the nodes to different extents. Due to the free rotation of the C-2, C-3 bond, the relative free energies of the possible rotomers determine the time a given group has one particular orientation. It is necessary, therefore, for an external force to play a role in the conformational choice, and the most logical force is the possible hydrogen bond which can be established between the nitrogen attached to C-2 of the original sugar and one of the hydroxyl groups.

The orientation of the aromatic chromophore must be selected to conform with experimental results. Two possible arrangements are shown in Fig. 11b, c.

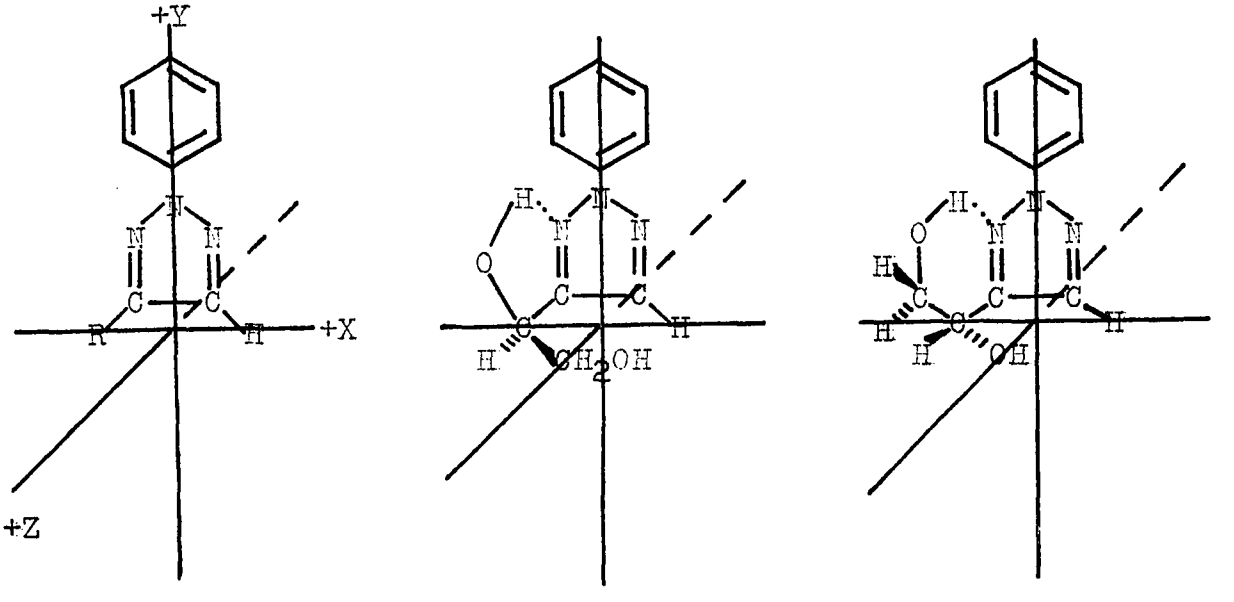
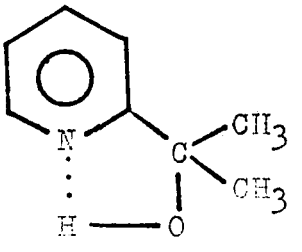


Fig. 11. Comparison of the Orientation of the Osotriazoles on an Octant and a Partition Diagram

If the sign of the quadrants is the same as those designated by the Octant Rule, conformation (b) would be expected to show a positive Cotton effect since the CH_2OH substituent would be in the lower left front quadrant (-X,-Y,+Z) while conformation (c) which has the hydroxyl group at lower left rear quadrant (-X,-Y,-Z) would have a negative Cotton effect. An unequivocal decision between these two conformations will require much additional data, but a logical choice between them can be made on the basis of the "phenyl osotriazole rule." Since this rule has been shown to apply in a large number of cases, it is evident that the dominant factor is the absolute configuration of C-3. Since conformation (b) would be much more seriously altered by a change at C-3 than would conformation (c), it seems logical that the major conformation involves hydrogen bonding between the C-3 hydroxyl and the nitrogen attached to C-2. There is evidence of such bonding in similar systems, such as 2-α-pyridylpropan-2-ol (XLV).[39]



XLV

Such a diagram as drawn in Fig. 11 may be an oversimplification, but it is consistent with the experimental

results. D-Erythrose osotriazole (XXIII) which has the configuration shown in the illustration (Fig. 11) shows a positive Cotton effect centered at 263 mμ, a wavelength which is in good agreement with the maximum absorption in the ultraviolet. If the chain of this tetrose is lengthened as in the 5- or 6- carbon sugar series, the additional atoms will have little effect on the sign of the Cotton effect. The conformation shown by Fig. 11b would not be changed by lengthening the chain, but the size of the group in the lower left front quadrant (-X,-Y,+Z) would be increased. Thus, one would predict a larger amplitude for the Cotton effects of the larger sugars. Above 6-carbon sugars, however, the chain may become so involved that a maximum in amplitude would be reached.

If model Fig. 11c were the correct one, the prediction would be much more complex since substituents at C-4 would cause marked alteration of the sign of the Cotton effect. In other words, there should be no consistency of sign of Cotton effect with configuration at C-3 for model (c). On this basis, model (c) was eliminated from consideration.

The Partition Diagram selected on the basis of D-erythrose osotriazole (XXIII) predicts a positive Cotton effect in the region of maximum absorption by the aromatic substituent for any osotriazole having the hydroxyl group alpha to the aromatic system to the right in a standard Fischer projection. The rule, therefore, predicts a positive Cotton effect for osotriazoles derived from D-erythrose, D-arabinose, D-allose and D-gulose. Unfortunately, D-allose osotriazole (XVIII) has not yet been prepared in a pure form. D-gulose osotriazole (XIX)

was actually prepared from L-sorbose, a keto sugar, and is referred to by that name below, and L-arabinose osotriazole (XXI-L) was actually used in the synthesis. The consistency of results is discussed in the sequel.

The asymmetric hydroxyl group attached to C-3 of D-xylose osotriazole (XXII) is on the left in the Fischer projection formula. The O.R.D. curve for this compound is shown in Fig. 15. It contains a negative Cotton effect with an amplitude of -59.2 and a midpoint of 261 mμ. This compared fairly well with the maximum absorption at 267 mμ obtained from the ultraviolet spectrum. The amplitude of its Cotton effect is very similar to that of D-erythrose osotriazole (XXIII). The additional asymmetric center at C-4 produced the effect of increasing the Cotton effect amplitude by 7.2 over that for D-erythrose osotriazole (XXIII). This would indicate that the asymmetric center at C-4 has only a 14% effect on the magnitude of the Cotton effect, and is consistent with the prediction that the amplitude of the Cotton effects of the pentose osotriazoles will exceed that of the tetrose derivatives.

L-Arabinose osotriazole (XXI-L) also contains an asymmetric hydroxyl group at C-3 which is on the left in the Fischer projection formula, and the O.R.D. curve for this compound (Fig. 16) also showed a negative Cotton effect. The midpoint of the Cotton effect is 248 mμ. This is compared with a maximum obtained from the ultraviolet spectrum of 266 mμ. This poor agreement of midpoint absorption coupled with the poor resolution indicated by the "background noise" in

the originally recorded curve indicated that the amplitude of this curve is not quantitative and that only the sign and shape of the Cotton effect are meaningful. Thus, its amplitude of -76.3 is not a quantitative value; however it indicates that its amplitude is probably larger than the +52.0 obtained for D-erythrose osotriazole (XXIII).

The curves for D-galactose osotriazole (XX) were obtained from the Bellingham-Stanley and the Cary 60 as shown in Fig. 23. The discrepancy in Cotton effect amplitude as obtained from the two instruments is again due to the strong absorption of the chromophore in the region of the Cotton effect. This amplitude discrepancy is reflected in the disagreement of the midpoint absorption of the Cotton effect and the λmaximum of the ultraviolet spectrum. The curve however does indicate that the compound which possesses a hydroxyl group on the left at C-3 in the Fischer projection formula gave a negative Cotton effect in the O.R.D.

L-Sorbose osotriazole (XIX-L), which again contained a hydroxyl group on the left at C-3 in the Fischer projection, also yields a negative Cotton effect in the O.R.D. (Fig. 20). The first Cotton effect had an amplitude of -68.8 and a midpoint absorption of 268 mμ as compared with the 266 mμ obtained from its ultraviolet spectrum. This compound has a C-3 and C-4 configuration equal to that of D-xylose osotriazole (XXII). However, it contains an additional asymmetric center at C-5. Its Cotton effect amplitude is 9.6 higher than that for D-xylose osotriazole (XXII) indicating that the hydroxyl group attached to the asymmetric center at C-5 has only

a 10% effect on the magnitude of the Cotton effect.

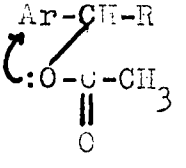
D-Glucose osotriazole (XI), which also has a hydroxyl group at C-3 on the left in the Fischer projection, gave a negative Cotton effect in the O.R.D. of exceptionally high amplitude of -195 (Fig. 21) and a midpoint absorption at 267 mμ as compared with maximum absorption at 267 mμ in the ultraviolet spectrum. Its amplitude is more than two and a half times greater than any of the other osotriazoles. This high amplitude indicates that no calculations of hypotheoretical contribution to the Cotton effect amplitude will be meaningful, for if it is assumed from D-erythrose osotriazole (XXIII) that C-3 contributes ±52.0 to the amplitude of the O.R.D., then C-4 and C-5 must contribute more than ±52.0 each in order to give a total rotation of -195. As the model from the Partition Rule indicated, however, and subsequent data will also show, all facts support the hypothesis that C-3 must be the strongest rotational center in the molecule.

It may be of some significance to point out also that all of the osotriazoles except D-glucose osotriazole (XI) had an exceptionally small ultraviolet extinction range (from 19,000-20,000) and also a small O.R.D. amplitude range (from +52.0-+68.8). D-glucose osotriazole (XI) on the other hand has an extinction of approximately 25,000 and an amplitude of -195.

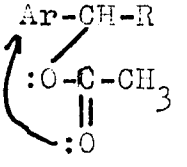
D-galactose osotriazole tetraacetate (XLVI) gave an O.R.D. curve (Fig. 19) containing two Cotton effects. The first Cotton effect had an amplitude of -37.7 and a midpoint of 279 mμ while the second Cotton effect had an amplitude of -44.8 and a midpoint of 258 mμ. This represents a considera-

ble shift in the midpoint of the first Cotton effect from that of D-galactose osotriazole (XX). This shift in midpoint absorption coincides with the increased steric requirement which attend the exchange of hydroxyl for acetate, and thereby suggests that conformational factors may be important. In going from D-galactose osotriazole (XX) to D-galactose osotriazole tetraacetate (XLVI), the possibility of a hydrogen bonded conformation is removed by acetylation of the hydroxyl groups. This would cause a change in conformation of the molecule with probably an increase in the random form and thus a loss in amplitude of the Cotton effect (Fig. 19 & 24). However, in destroying the possibility of hydrogen bonding, the steric requirement of the former hydroxyl group has been drastically increased. This increased steric requirement would now produce conformationally preferred structures of a zig-zag form, such as to reduce steric interactions as much as possible. Therefore, a comparison of the amplitude of the Cotton effect with respect to the effect of hydrogen bonding as an important factor in the molecular conformation of XX is not possible.

The two Cotton effects of D-galactose osotriazole tetraacetate (XLVI) could be due to two separate possible electronic transitions, namely:



A



B

The second Cotton effect has a midpoint absorption of 258 mμ which is identical to that of the osotriazole XX having free hydroxyl groups and this could be indicative of an electronic transition of Type A. Thus the first transition could then have been due to a transition of Type B.

The conclusions obtained from this study are as follows:

(a) The asymmetric centers other than that at C-3 have only small effects on the O.R.D. curves.

(b) The shapes of the molecules of the osotriazoles are relatively similar.

(c) The similarity of the D-galactose osotriazole (XX) curve with that of the D-galactose osotriazole tetraacetate (XLVI), relative to the long wavelength Cotton effect, may indicate a relative unimportance of conformation to the O.R.D. curves. The D-galactose osotriazole tetraacetate (XLVI) would be expected to be quite different from the tetrahydroxy compound in shape (H-bonding etc.) and yet the amplitudes are approximately equal if one considers only one Cotton effect. However, this is a comparison of two different electronic transitions and two different types of conformational structures. The tetrahydroxy compound would possess a conformational structure which allows for intramolecular hydrogen bonding whereas the D-galactose osotriazole tetraacetate (XLVI) possesses a different conformational structure which better accommodates the increased steric requirements of the hydroxyl group.

(d) Hudson's rule points to the correlation between the stereochemistry of an optically active group adjacent to a chromophore and the sign of rotation at the sodium D-line.

The most significant fact from the O.R.D. curves is that this investigation shows that Hudson's rule can be extended to cover the sign of the Cotton effects of the osotriazoles and may be stated as follows: Whenever the hydroxyl group attached to C-3 of the sugar residue is to the right in the Fischer projection formula, the sign of the Cotton effect obtained from the derived osotriazole is positive, and when the hydroxyl group is on the left, it is negative. It is anticipated that this rule may have general application and thus include the correlation of sign of the Cotton effect with the configuration of an asymmetric carbon atom adjacent to a heterocyclic or aromatic ring.

Furthermore, for the rule to hold true, the hydroxyl group at C-3 must dominate the sign of rotation and amplitude of the Cotton effect. Therefore, C-3 must be greater in rotation than the total sum of the individual rotations of all other centers in the molecule.

The Long Wavelength Region Solvent Study

The long wavelength solvent study data of this work were obtained on the Rudolph instrument using methanol, acetic acid, pyridine and water as solvents. Although other solvents may also have been desirable for this investigation these compounds have the handicap of being insoluble in most solvents and, in addition, their solubility varies quite markedly from the larger molecular weight members to the lower molecular weight members.

The long wavelength solvent study of the osotriazoles

was carried out in a 0.1 dcm. tube from 300 to 600 mμ. All of the curves obtained within this spectral range of experimental observation exhibited no maximum (peak) or minimum (trough) and were therefore all plain curves (Fig. 25-42).

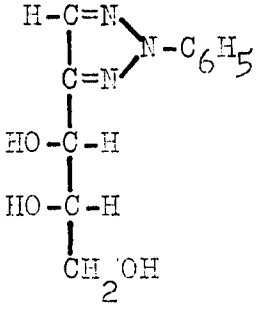
Pyridine. D-Erythrose osotriazole (XXIII) is the lowest molecular weight, optically active osotriazole. It contains a hydroxyl group attached to an asymmetric carbon atom which is adjacent to the triazole ring. This hydroxyl group attached to the optically active group C-3 is on the right in the Fischer projection and, as predicted by Hudson's rule, the sodium D-line was positive. The O.R.D. for this compound as shown in Fig. 25 showed that it possessed a positive plain curve above 283 mμ.

D-Xylose osotriazole (XXII) is the next optically active member osotriazole of the aldo sugar family. It contains two optically active centers at C-3 and C-4 respectively. In the Fischer projection the hydroxyl groups attached to these centers are trans to one another. The C-3 hydroxyl group adjacent to the triazole ring is on the left. Again, as predicted by Hudson's rule it gives a negative rotation at the sodium D-line and also gives a negative plain O.R.D. curve above 286 mμ (Fig. 25).

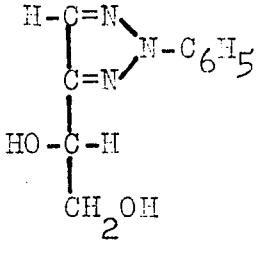
In order to compare more easily the positive curve of D-erythrose osotriazole (XXIII) with the negative curves obtained for the other osotriazole compounds, the data for D-erythrose osotriazole (XXIII) have been plotted as negative values. This mirror image curve would be that expected for L-erythrose osotriazole (XXIII-L). Therefore, hereafter this

negative plotting of the data obtained for D-erythrose osotriazole (XXIII) will be referred to as L-erythrose osotriazole (XXIII-L). A comparison of the O.R.D. obtained for D-xylose osotriazole (XXII) with that obtained for L-erythrose osotriazole (XXIII-L) shows it to be symmetrical to the latter but higher in rotatory power.

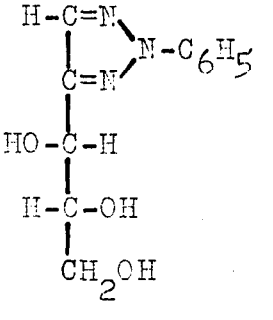
L-Arabinose osotriazole (XXI) also contains two hydroxyl groups at C-3 and C-4. However, unlike D-xylose osotriazole (XXII), in the Fischer projection these two hydroxyl groups are <u>cis</u> to each other. When this curve was compared with the O.R.D. curve for L-erythrose osotriazole (XXIII-L) it was found to be similar in shape but lower in intensity (Fig. 28). The symmetrical spacing of these curves suggested a possible pattern. If this pattern is compared with the different pattern in stereochemistry of the osotriazole family, it is observed that there is a similarity in the two patterns such that the rotational amplitude for the osotriazole family can be correlated with their conformation in the Fischer projection formulas.



XXI-L



XXIII-L



XXII

However, Djerassi[40] has pointed out that an O.R.D. containing a Cotton effect is made up of contributions from the partial rotations of the asymmetric centers in the compound and also from the "background rotation" produced by the chromophore in the presence of an asymmetric center. This "background rotation" will be most significant in the region of the absorption band. Therefore, in making a comparison of the stereochemistry of the members of the osotriazole family to their rotatory power in the O.R.D. curves one is dealing with the same chromophore such that the effect of the "background rotation" produced by it should be nearly the same in each compound. Furthermore, since the solvent study has been conducted in the long wavelength region, the background effect in this area should be insignificant and almost negligible. In this comparison of plain curves the differences in rotatory power between the curves rather than the absolute intensity of the curves are of most significance.

Mathematically the difference in magnitude of rotation between L-arabinose osotriazole (XXI-L) and L-erythrose osotriazole (XXIII-L) at equal wavelengths on their respective curves is approximately equal to the difference between L-erythrose osotriazole (XXIII-L) and D-xylose osotriazole (XXII) at the same wavelength. Since the only structural difference in these three compounds is that of the second asymmetric center (C-4) then this difference in intensity is due to the effect of the asymmetric center C-4. This equal spacing may imply the existence of some sort of additive re-

lationships for optical rotations. Since L-erythrose osotriazole (XXIII-L) contains only the one optically active center at C-3 adjacent to the chromophore and since the rotation is negative, it indicates that an hydroxyl group on the left at C-3 gives a negative rotation which is in agreement with Hudson's rule.

L-Arabinose osotriazole (XXI-L) possesses the L-erythrose osotriazole (XXIII-L) structure at C-3 plus a second hydroxyl group C-4 cis to the C-3 group. Since L-arabinose osotriazole (XXI-L) gave an optical rotation curve less negative in rotation, this would imply two facts about C-4 in L-arabinose osotriazole (XXI-L) if the additivity relationship is valid. First, it contributes a rotation opposite in sign to that of C-3. Second, its rotational strength is numerically less than that of C-3.

D-Xylose osotriazole (XXII) possesses the L-erythrose osotriazole (XXIII-L) configuration plus a second group at C-4 trans to the C-3 hydroxyl group in the Fischer projection. In this case the O.R.D. curve was more negative in value than that of L-erythrose osotriazole (XXIII-L), thus indicating that C-4 in D-xylose osotriazole (XXII) contributes a rotation the same in sign as that of the C-3 center.

From this comparison the following correlations between stereochemistry and strength of rotation are indicated:

1. When the hydroxyl group is on the left at C-3, a negative rotational contribution is observed; conversely, when on the right, a positive rotation is observed.
2. When a hydroxyl group is on the left at C-4 a negative

rotational contribution is observed. If the hydroxyl is on the right at C-4, a positive rotational contribution is observed approximately equal in magnitude to that observed for the hydroxyl group on the left.

3. The rotational contribution for the asymmetric center at C-4 is lower in magnitude than the rotation contribution for the asymmetric center at C-3.

Since L-sorbose osotriazole (XIX-L) is composed of the same stereochemistry at C-3 and C-4 as D-xylose osotriazole (XXII) with an additional asymmetric center at C-5 containing a hydroxyl group on the left in the Fischer projection, the difference in their rotational strengths may be indicative of the effect of this hydroxyl group at C-5. The O.R.D. curve for L-sorbose osotriazole (XIX-L) is less negative in amplitude than that for D-xylose osotriazole (XXII) (Fig. 27), thus indicating that the C-5 hydroxyl group on the left in the Fischer projection may be correlated with rotatory contribution positive in sign. Conversely, the O.R.D. curve of D-glucose osotriazole (XI) is more negative in intensity than that for D-xylose osotriazole (XXII), thus indicating that the C-5 hydroxyl group on the right in the Fischer projection may be correlated with a negative rotatory contribution.

If the above correlation is valid, D-galactose osotriazole (XX) which has its C-3, C-4 configuration identical to that of L-arabinose osotriazole (XXI-L) and its C-5 hydroxyl group on the right in the Fischer projection should be more negative in amplitude than L-arabinose osotriazole

(XXI-L). A comparison of these two O.R.D. curves in Fig. 27 shows the above correlation to be valid.

The data indicate the following correlations between stereochemistry of the hydroxyl groups of the osotriazole derivatives of the aldo sugar family in the Fischer projection and the rotational amplitudes in the 600-400 mμ region of the O.R.D.:

1. The asymmetric center at C-3 dominates the sign of rotation.
2. The further the asymmetric center from the aryl group the smaller its effect on the amplitude of the O.R.D. Thus C-3 > C-4 > C-5.
3. The rotational strength of the asymmetric center at C-3 is greater in amplitude than the total rotation of all the other asymmetric centers in the molecule. Thus C-3 > (C-4 + C-5).
4. The following stereochemistry of the hydroxyl group in the Fischer projection coincides with the sign of rotation as shown in Table IVa.
5. The correlations between stereochemistry and rotational amplitudes which have been observed in this investigation were applied to other osotriazole derivatives on the basis of their sodium D-line rotations in pyridine which are reported in the literature (Table IVb & Fig. 12). A comparison showed continued agreement of this correlation and extended to additional asymmetric carbon atoms the correlation of the stereochemistry of the hydroxyl group in the Fischer projection with the sign of rotation.

Table IVa

Correlation of Stereochemistry at Asymmetric Centers and Their Signs of Rotation

Osotriazole of:	Config. of OH group in Fischer Projection C-3	C-4	C-5	Sign of Rotation C-3	C-4	C-5	$[M]_D$ In Pyridine From ORD curve
L-Arabinose (XXI-L)	Left	Left		-	+		-76
D-Galactose (XX)	Left	Left	Right	-	+	-	-88
L-Erythrose (XXIII-L)	Left			-			-109
L-Sorbose (XIX-L)	Left	Right	Left	-	-	+	-133
D-Xylose (XXII)	Left	Right		-	-		-147
D-Glucose (XI)	Left	Right	Right	-	-	-	-219

TABLE IVb

Correlation of Stereochemistry at Asymmetric Centers and Their Signs of Rotation

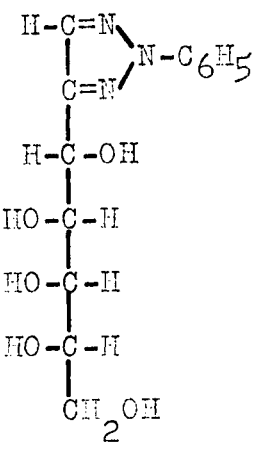
Osotriazole Structure	Configuration of OH group in Fischer Projection					Sign of Rotation					$[M]_D$
	C-3	C-4	C-5	C-6	C-7	C-3	C-4	C-5	C-6	C-7	In Pyridine
L	Right	Right	Left	Right		+	-	+	+		+47[a]
LII	Right	Right	Left	Right	Right	+	-	+	+	+	+58[b]
XLVIII	Right	Left	Right	Right		+	+	-	+		+138[c]
XLVII	Right	Left	Left	Left		+	+	+	-		+211[c]
XLIX	Right	Left	Left	Right		+	+	+	+		+231[c]
LI	Right	Left	Left	Right	Right	+	+	+	+	+	+251[d]

[a] L. C. Stewart, N. K. Richtmyer, and C. S. Hudson, J. Am. Chem. Soc., 74, 2210 (1952).

[b] N. K. Richtmyer, T. S. Bodenheimer, J. Org. Chem., 27, 1892 (1962).

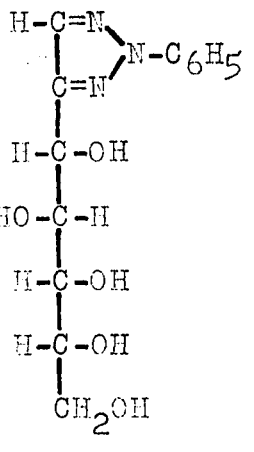
[c] W. T. Haskins, R. M. Hann and C. S. Hudson, J. Am. Chem. Soc., 69, 1050 (1947).

[d] J. V. Karabinos, H. M. Hann and C. S. Hudson, J. Am. Chem. Soc., 75, 4320 (1953).



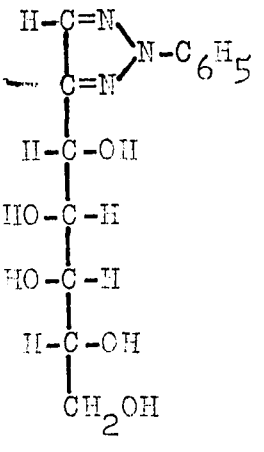
+211°

XLVII



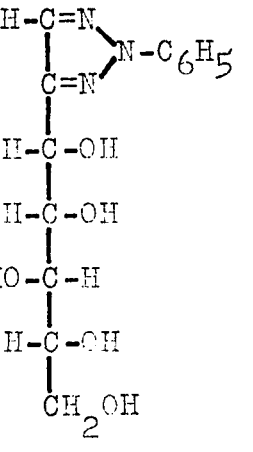
+138°

XLVIII



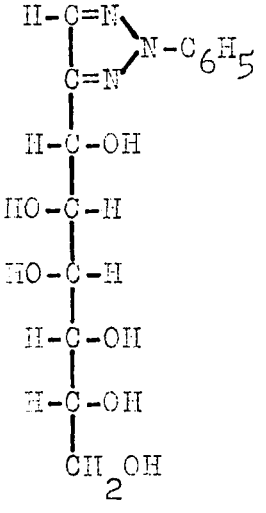
+231°

XLIX



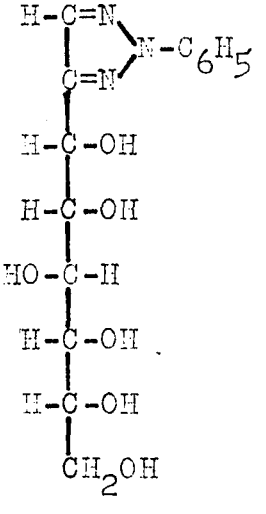
+47°

L



+251°

LI



+58°

LII

Fig. 12. Sodium D-Line Molecular Rotations of Osotriazoles in Pyridine

Methanol. The methanol curves tended to converge in the long wavelength region (Fig. 28-30). However, in the 450 mμ region, the curves begin to take on their own characteristic shape and intensity. This trend of the curves to converge in the 500-600 mμ region exemplified the need for studying rotatory power of an asymmetric carbon atom by use of the complete plain curve where the differences in intensity became more pronounced and characteristic of the compound. The rotation at an arbitrary wavelength (such as 589 mμ) could not be chosen to make such an investigation without first looking at the O.R.D. curve because this wavelength would have to be one outside of the convergence. Also if the arbitrary wavelength was outside of the convergence region, there would still remain the uncertainity of locating the wavelength at which the background rotation contribution became pronounced. It was felt that in a study of solvent effects on rotatory power two things must be done. First, the study must be made at high concentrations in order to obtain maximum accuracy in readings and second, the overall plain curves should be analyzed rather than the rotation at an arbitrary wavelength.

The correlation between rotatory strengths and stereochemistry described in the pyridine solvent study was not as apparent in the methanol curves. This pattern was lost in the long wavelength region due to the convergence of the curves. However, as the curve approached the shorter wavelength region this pattern was again observed.

Acetic Acid. The Rotatory Dispersion (RD) curves obtained from the osotriazoles using acetic acid as the solvent

also showed the convergence of plain curves in the longer wavelength region. The pattern first described for pyridine however, is also evident here in the shorter wavelength region. (Fig. 31-33). The most striking point observed from the acetic acid curves was the comparison of these curves with those obtained for the same compounds in methanol (Fig. 36-42). This comparison showed that both solvents yielded RD curves which possessed the same shape and intensity, although these solvents have polarities and refractive indexes which are quite different. The fact that the osotriazoles would be protonated in acetic acid would change the nature of the chromophore under consideration here. The extent of protonation is unknown, and no detailed study of the system was attempted. Further study of solvent effects would yield information that could, hopefully, be correlated with the conformation of the osotriazoles in different solvents.

Water. The plain curves obtained from the solvent study using water as a solvent were somewhat different from those obtained from the other solvents (Fig. 34 & 35). These curves tended to be much flatter in shape and showed very little difference in intensity through the spectral range examined. These features may not be characteristic of the compounds in this solvent but they may arise from the accuracy of the instrument at the low rotations of these compounds in water. This factor has no doubt introduced error into the results and due to the low solubility of the osotriazoles in this solvent, this problem could not be overcome by increasing the concentration to increase the rotation. The

data, however, indicated that the solvent effect is such as to produce lower intensity curves than those obtained from other solvents for similar concentrations of the compound.

In a comparison of the solvent effects (differences between the four solvents), the increasing order of intensity of RD curves of the compounds in these solvents as shown in Fig. 36-42 was as follows:

water < methanol = acetic acid < pyridine

These solvent effects are attributed to bathochromic solvent shifts of the O.R.D. curves. This would imply that the solvents showing higher intensities of rotation in the longer wavelength region were those in which the larger bathochromic shift of the ultraviolet absorption occurred; therefore, the curves obtained in pyridine were of much higher rotatory strength than those obtained in water, acetic acid or methanol. Such a hypothesis would imply the observance of a shift of the first extremum of the Cotton effect in different solvents which should parallel the ultraviolet absorption. Unfortunately, due to the spectral properties of pyridine and of the osotriazoles in acetic acid, no data below 300 mμ could be obtained and this shift of the first extremum could not be investigated.

Drude Equation Study

In 1906 P. Drude published a book entitled "Lehrbuch der Optick" in which he presented a mathematical relationship between optical rotatory power and wavelength outside the region of an optically active absorption band. This theoretical

equation was experimentally proven by many investigators among whom were T. M. Lowry and T. W. Dickson. A one term Drude equation,

$$[M]_\lambda = \frac{A}{\lambda^2 - \lambda_o^2}$$

defines the contribution to the total molecular rotation [M] at any specific wavelength, λ, of a single optically active chromophore which possesses a maximum absorption band, λ_o, A being a constant.

If the Drude equation is applicable to a specific rotatory dispersion curve, the λ_o value obtained from solution of this equation should be in agreement with the midpoint of the Cotton effect at longest wavelength (this being the experimental value) and with the wavelength of the absorption band of the compound's ultraviolet absorption spectrum.

Analysis of the rotatory dispersion curves was made with respect to a one-term Drude equation. The data were evaluated by the least squares method with the assistance of an I.B.M. 1620 computor using 16 points from 600-400 mμ (Tables VIII-XVI). The results are summarized in Table V below and the λ_o values are compared with the long ultraviolet absorption bands of the osotriazoles. A solution of the equation graphically shows that λ_o^2 is the intercept and λ_o is the square root of the intercept which is in microns and may be assumed to indicate the wavelength at which the compound has a maximum absorption band. The constant A is the slope of the straight line which should be obtained on plotting the data as $1/[M]$ versus λ^2.

TABLE V

Physical Constants of RD Curves From One-Term Drude Equation

Osotriazole of:	Pyridine			Methanol		
	λ_o^2	λ_o (μ)	A	λ_o^2	λ_o (μ)	A
L-Erythrose XXIII-L	0.074	0.272	-30.3	0.005	0.073	-38.6
D-Xylose XXII	0.107	0.327	-35.7	0.104	0.323	-24.5
L-Arabinose XXI-L	0.009	0.094	-26.6	0.087	0.295	-21.8
D-Galactose XX	0.122	0.349	-19.6	0.036	0.189	-30.1
L-Sorbose XIX-L	0.083	0.288	-35.2	0.020	0.141	-31.9
D-Glucose XI	0.076	0.275	-60.0	0.068	0.261	-37.3
D-Galactose Tetraacetate XLVI	0.136	0.369	-25.1	0.109	0.330	-25.2

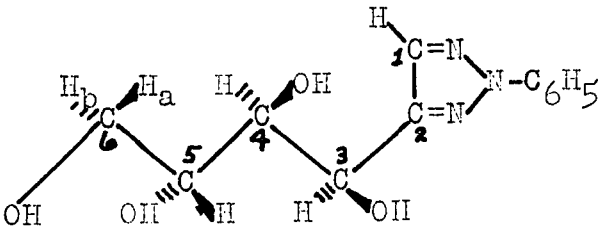
TABLE V Cont.

Physical Constants of RD Curves From One-Term Drude Equation

Osotriazole of:	Acetic Acid			Water		
	λ_o^2	λ_o (μ)	A	λ_o^2	λ_o (μ)	A
L-Erythrose XXIII-L				0.062	0.249	-18.6
D-Xylose XXII	16.1	4.02	-20.0	0.028	0.168	-30.7
L-Arabinose XXI-L	0.176	0.420	-4.66	0.140	0.374	-10.5
D-Galactose XX	0.122	0.349	-20.0	0.024	0.156	-31.8
L-Sorbose XIX-L	0.039	0.197	-33.8	0.016	0.245	-28.7
D-Glucose XI	0.118	0.344	-24.1	0.144	0.379	-31.3
D-Galactose Tetraacetate XLVI	0.059	0.244	-40.0	-	-	-

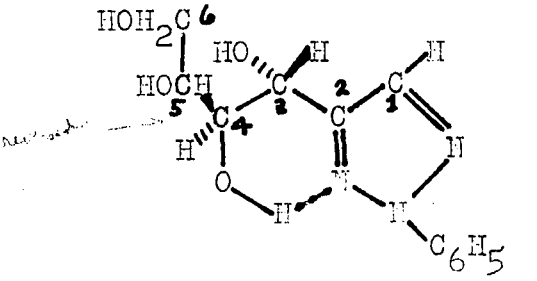
NUCLEAR MAGNETIC RESONANCE STUDY

In the analysis of the O.R.D. of the osotriazoles the hypothesis of a Partition Rule was put forth. It was further stated that such a rule would require the assumption of a preferential conformation of the acyclic side chain. The most apparent factors which could determine a preferred conformation of the side chain would be, first, steric requirements (alignment into a conformation which would produce the least steric interference).and second intramolecular hydrogen bonding. Compliance with the first factor would place the side chain into a zig-zag conformation such as A or a hydrogen bonding conformation such as C. The second factor would produce a conformation involving one or more rings in which hydrogen bonding could be formed between O---H-O or N---H-O atoms. The N---H-O hydrogen bond is much stronger than the O---H-O hydrogen bond[41] therefore the N---H-O bond between the C-2 nitrogen and the C-4 group would produce a six-membered ring (B) while bonding with the C-3 hydroxyl would produce a five-membered ring (A or C). The C-conformation combines the chelate ring of conformation A along with additional rings formed by hydrogen bonding involving the remaining hydroxyl groups and would be predicted to be the most stable because of the combination of the small number of unfavorable steric interactions and the stabilization due to maximum hydrogen bonding.



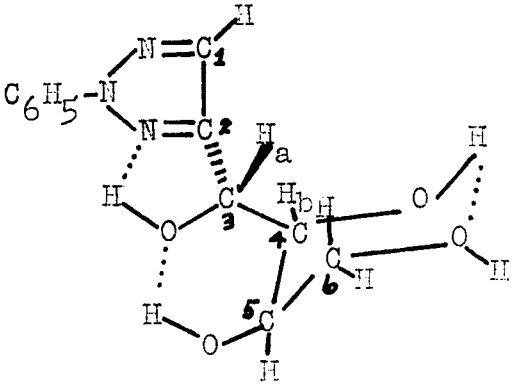
Zig-Zag Conformation

A



C-2, C-4 Hydrogen bonded Conformation

B



Maximum Hydrogen Bonded Conformation

C

In an attempt to determine which of these factors, if any, played the more important role in producing conformational preference in the osotriazole derivatives, the N.M.R. spectra of the osotriazoles were analyzed (Table XIV).

The spectrum of D-glucose osotriazole (XI) in pyridine showed a sharp low-field proton singlet at τ1.65 (1H) which may be assigned to the C-1 proton of the osotriazole ring. This was confirmed by the N.M.R. spectrum of 2-phenyl-2,1,3-triazole (XXV) which showed a sharp low-field, proton singlet (2H) at τ2.09. The phenyl ring protons are masked by the resonance of the solvent.

The C-3 proton of D-glucose osotriazole (XI) appears at τ 3.94 as a doublet by coupling with the C-4 proton, $J_{3,4}$= 1.5 c.p.s. Studies of acetylated sugars have shown that coupling of an axial and an equatorial proton ($J_{a,e}$) or between two equatorial protons ($J_{e,e}$) on adjacent carbons resulted in observed values of 2-3.5 c.p.s. Axial-axial proton coupling, however, results in larger coupling constants ($J_{a,a}$ ~5-9 c.p.s.). Examination of the three models for glucose osotriazole (XI) shows that the zig-zag conformation (A) would have an anticipated dihedral angle of 180° which by the Karplus correlation[42] would predict a very large coupling constant. Conformation B should have a cyclohexene-like geometry and the dihedral angle between the pseudo equatorial proton and the equatorial hydrogen must be approximately 80°.[43] The C-conformation would be the one in which the dihedral angle between these C-H bonds is approximately 60°, the ideal angle of the diequatorial hydrogens of cyclohexane. The spectra of cyclohexane derivatives have shown diequatorial coupling constants of 2-3.5 c.p.s. Conformation A can be eliminated on this basis, however, it does not allow a choice between conformation B or C. The C-4 and C-5 protons appear as an indiscernible overlapping multiplet at τ 5.38. The two protons of the methylene group are nonequivalent because of the adjacent asymmetric center and give rise to a multiplet, the AB part of an ABX system, centered at τ 5.31. This type of nonequivalence of methylene protons in a terminal group has been observed in acetylated sugar phenylhydrazine derivatives,[44] however, it is remarkable that the nonacetylated sugar should

show this nonequivalence with coupling constants of nearly the same magnitude as that of an acetylated derivative. This could imply that the hydroxyl group's steric requirement is of the same magnitude as that for the acetylated product and is large enough to dominate the rotamer state.

If the osotriazole is in the zig-zag conformation, the tetraacetate osotriazole should also be in a similar conformation and show a splitting pattern similar to the nonacetylated osotriazole. However, if the conformation is produced by hydrogen bonding, acetylation, which would preclude any possibility of hydrogen bonding, may produce a different coupling constant at C-3.

The spectrum of D-glucose osotriazole tetraacetate (LIII) showed that the coupling constant for the C-3 proton is of much larger magnitude than that of the nonacetylated osotriazole as shown in the Table below. Furthermore, the spectrum obtained for D-glucose osotriazole tetraacetate (LIII) is identical in splitting pattern and coupling constants to that obtained for D-glucose quinoxaline tetraacetate (LIV) by Horton and Miller.[45] These authors analyzed the spectrum for D-glucose quinoxaline tetraacetate (LIV) and found that the spectrum indicated a high degree of conformational purity, and it was in agreement with an extended planar zig-zag arrangement as the favored conformation. D-Glucose osotriazole tetraacetate (LIII) showed this same coupling constant and splitting pattern; therefore, it may be assumed that it also is in the zig-zag conformation. The nonacetylated osotriazole possesses coupling constants for the C-3 proton of a

different magnitude from that of the acetylated structure; therefore, this would tend to discount the zig-zag conformation in the hydroxyl compound.

TABLE VI

N.M.R. Spectral Data on D-Glucose Quinoxaline Tetraacetate[45] (LIV) and D-Glucose Osotriazole Tetraacetate (LIII) in $DCCl_3$

Protons of LIII & LIV	Chemical Shift τ LIII	LIV	Integral Protons of LIII & LIV	Multiplicity[a] of LIII & LIV	Coupling[b] Constant (c.p.s.) of LIII & LIV
C-1	1.10	2.13	1	s	
C-3	3.58	3.55	1	d	$J_{3,4}=3.0$
C-4	4.14	4.18	1	q	$J_{3,4}=3.0$ $J_{4,5}=8.5$
C-5	4.50	4.58	1	m	
C-6	5.66	5.72	2	m	$J_{6a,6b}=12.0$ $J_{5,6a}=3.0^c$ $J_{5,6b}=5.5^c$

[a] d, doublet; m, multiplet; q, quartet; s, singlet.

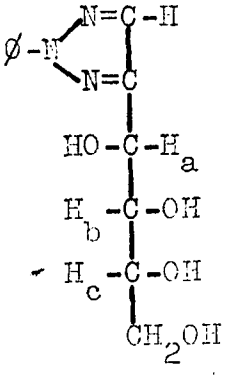
[b] The spectra have been analyzed on a first-order basis, and the recorded coupling constants are the observed splittings. The relative chemical shifts of the methine protons in A (p. 60) are sufficiently different than the recorded and J parameters should be close to the theoretical values.

[c] The absolute magnitudes may be larger, owing to second-order effects.

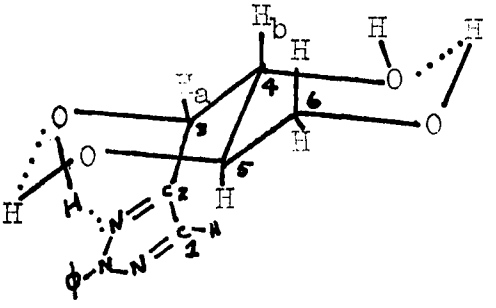
A choice between the hydrogen bonded conformations (B & C) may be made from some data obtained for the three hexose sugar derivatives (Table VIII and XIV). If D-glucose

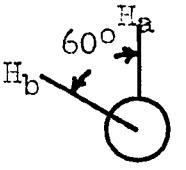
TABLE VIII

Hydrogen Bonding in the Hexose Osotriazoles



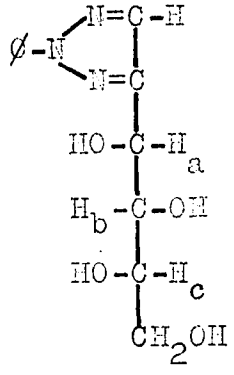
D-Glucose (XI)



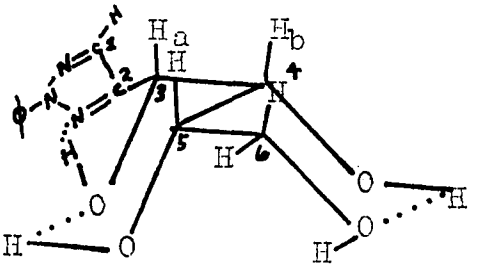


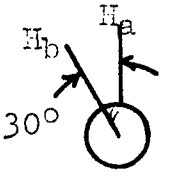
$J_{H_aH_b}$ *

Predicted=2c.p.s.
Found=1.5c.p.s.



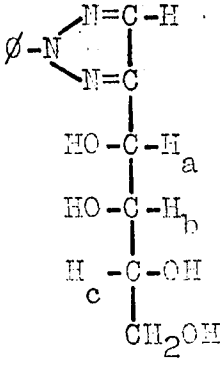
L-Sorbose (XIX-L)



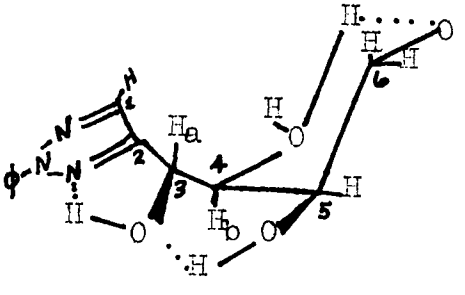


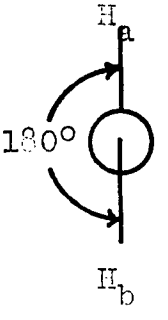
$J_{H_aH_b}$ *

Predicted=6c.p.s.
Found=5c.p.s.



D-Galactose (XX)





$J_{H_aH_b}$ *

Predicted=9c.p.s.
Found=6.5c.p.s.

Sugar:	Type C Conformation:	Approx. Dihedral Angles:

*Spectra were recorded by means of a Perkin-Elmer 60 mc instrument Model using pentadeutero pyridine (Merck, purity > 99%) as solvent. The author thanks Mrs. E. Richards & Mr. P. Cherry of the Dyson Perrins Lab., Oxford, England for obtaining the spectra.

osotriazole (XI) and L-sorbose osotriazole (XIX-L) is placed in conformation B the dihedral angle between the C-3 and C-4 protons in both compounds would be the same and therefore the coupling constants for them should be nearly the same. The data shows this to be inconsistant.

In Table VIII D-glucose, D-galactose and L-sorbose osotriazole are placed into a conformation of type C. The coupling constants predicted by the Karplus correlation for the dihedral angles produced between the C-3 and C-4 protons are compared with those obtained experimentally.

These results suggest that the preferred conformation of D-glucose osotriazole (XI) may be C. Conformation B cannot be unquestionably eliminated on this basis, but the weight of the O.R.D. and N.M.R. data favors the C form. Acetylation of the hydroxyl groups undoubtedly produces the zig-zag conformation A in which the maximum dihedral angle of the protons is maintained since each conformation would be such to avoid steric interactions of the bulky substituents on the asymmetric carbon atoms. Acceptance of these conclusions must necessarily await confirmation by the synthesis of some deoxy analogs of these derivatives where hydrogen bonding would be limited to a few selected sites.

This initial investigation of the N.M.R. spectra of the osotriazoles indicated that a more detailed study of the splitting patterns and coupling constants of the complete aldo sugar family osotriazole derivatives could give further data to indicate if a Partition Rule could correlate the configuration of an osotriazole and sign of Cotton effects.

SUMMARY

SUMMARY

The O.R.D. curves obtained from the aldo sugar family osotriazole derivatives prepared in this investigation gave Cotton effects due to the aromatic chromophore in the presence of an asymmetric center. A comparison of these Cotton effects showed that the asymmetric centers other than those at C-3 have only small effects on the magnitude of the Cotton effect of the O.R.D. curves. It was also noted that the conformations of the osotriazoles must be relatively similar.

There was observed a correlation between the stereochemistry of an optically active group adjacent to a chromophore and the sign of its Cotton effect. This correlation may be stated as follows: Whenever the hydroxyl group attached to C-3 of the sugar residue is to the right in the Fischer projection formula, the sign of the Cotton effect obtained from the derived osotriazole is positive, and when the hydroxyl group is on the left, it is negative.

It is anticipated that this rule may have general application and thus include the correlation of sign of the Cotton effect with the configuration of an asymmetric carbon atom adjacent to a heterocyclic or aromatic ring. This correlation between stereochemistry and sign of Cotton effect was explained by means of a Partition Rule which is similar in nature to the Octant Rule in that it attempts to

predict the sign of the Cotton effect by locating the molecule on Cartesian coordinates, the signs of the substituent groups leading to the sign of the Cotton effect with the maximum effect resulting from asymmetry at the carbon alpha to the osotriazole ring.

In obtaining the O.R.D. curves of the optically active osotriazoles three different spectropolarimeters were employed and the following generalizations are made concerning them. The Rudolph Spectropolarimeter gave quantitative results in the 600-300 mμ region, but the absorption of the osotriazole ring system was too strong to allow data below 300 mμ. The Cary 60 Spectropolarimeter gave nearly quantitative results for the strongly rotating compounds and was able to obtain data on all but the very weakly rotating, strongly absorbing compounds. The Bellingham-Stanley Spectropolarimeter was able to obtain data on all of the osotriazoles, but the data were not quantitative and in any comparison only the sign and shape of the Cotton effects would be significant.

In an investigation of the solvent effect a comparison of the differences in magnitude of rotation with configuration in the Fischer projection indicated that the asymmetric center at C-3 dominates the sign of rotation and the further the asymmetric center from the aryl group the smaller is its effect "on the rotatory power." The rotational strength of the asymmetric center at C-3 is greater than the total rotatory power of all the other asymmetric centers in the molecule. The stereochemistry of the hydroxyl groups in

the Fischer projection coincides with the indicated signs of rotation as shown below:

	Left	Right
C-3	-	+
C-4	+	-
C-5	+	-

This correlation between the stereochemistry of the optically active centers and the magnitude of rotation of the compound further indicates evidence of the existence of the additivity relationship in optical rotation. Although the symmetry of the RD curves allowed the correlation of the stereochemistry of secondary hydroxyl groups with strength of rotation, the attempt to establish absolute partial rotational values from secondary hydroxyl groups at varying distances from a chromophoric group and in differing conformational environments will await more detailed analysis with instruments of higher resolution.

In a comparison of the solvent effects among pyridine, methanol, acetic acid and water the increasing order of intensity of RD curves of the compounds in these solvents was as follows: water < methanol = acetic acid < pyridine. These solvent effects are attributed to characteristic bathochromic shifts of the O.R.D. curves paralleling the change in solvent.

The data obtained from the long wavelength solvent study were analyzed using a one term Drude equation. The λ_o values from the solution of the one term Drude equation did not agree with the values obtained experimentally. The data indicated that the optically active chromophores must

have at least two major contributions of electronic perturbation.

The conformations of the osotriazoles were analyzed by means of their N.M.R. spectra. A comparison of D-glucose osotriazole (XI) and its tetraacetate LIII to that of D-glucose quinoxaline tetraacetate (LIV) which has been shown to possess a zig-zag conformation indicated that the acetylated osotriazole also possessed the zig-zag structure. It also indicated that the nonacetylated osotriazoles do not possess this conformation but in fact possess hydrogen bonded structures. Further investigation of the N.M.R. spectra of osotriazoles, both acetylated and nonacetylated as well as deoxy derivatives, may be rewarding by indicating the conformation of polyhydroxy side chains. This conformational analysis coupled with the sign of the Cotton effects could give further evidence by which to evaluate the Partition Rule.

EXPERIMENTAL

EXPERIMENTAL

General

Melting Points. Melting points were determined using either a Kofler hot-stage melting point apparatus equipped with a polarizing microscope or with a Thomas-Hoover Unimelt capillary melting point apparatus and are corrected.

Infrared Absorption Spectra. The infrared absorption spectra were determined using a Perkin-Elmer Model 337 infrared spectrophotometer. The position of the absorption bands is given in wavenumber units, $cm.^{-1}$. The spectra were calibrated with a polystyrene film versus air standard with absorption bands at 2851 $cm.^{-1}$, 1603 $cm.^{-1}$ and 906 $cm.^{-1}$. The spectra of liquids were determined as films, and the spectra of solids were determined as mulls in Halocarbon oil from 4000 $cm.^{-1}$ to 1300 $cm.^{-1}$ and in Nujol from 1300 $cm.^{-1}$ to 650 $cm.^{-1}$. Halocarbon oil was purchased from Halocarbon Products Corp., Hackensack, New Jersey and Nujol from Plough, Inc., San Francisco, California.

Ultraviolet Absorption Spectra. The ultraviolet absorption spectra of the osotriazole products were determined using a Perkin-Elmer Model 4000 recording spectrophotometer or a Cary Model 15 recording spectrophotometer. Those spectra determined on the Perkin-Elmer Model 4000 are indicated by No.$_4$ and those determined on the Cary Model 15 are indicated by No.$_{15}$. The spectra were determined in 95% ethanol.

Optical Rotatory Dispersion Data. The optical rotatory dispersion curves were determined on:

(a) Rudolph recording spectropolarimeter Model 260/655/850/810-614, using a 0.1 dcm. tube. Those curves determined on the Rudolph are indicated by No.$_R$.

(b) Cary Model 60 recording spectropolarimeter standardized according to the data reported by Y. Tominatau and W. Gaffield, Biopolymers 3, 509 (1965). Those curves determined on the Cary are indicated by No.$_C$.

(c) Bellingham and Stanley Bendix-Ericsson Spectropolarimeter "Polarmatic 62". These curves are indicated by No.$_B$.

The solvent, concentration (g. per 100 ml. solution), and path length are indicated for each curve and the data are expressed as molecular rotations [M].

Nuclear Magnetic Resonance Spectra. The nuclear magnetic resonance spectra were determined using a Varian Model A-60 proton resonance spectrometer. The spectra were obtained in a Varian Associates micro cell, Kit No. 906733 using pentadeuteriopyridine as the solvent, which was obtained from Isotropic products, Merck Sharp & Dohme of Canada Limited, Montreal, Canada. The chemical shifts are given in p.p.m. relative to tetramethylsilane, an internal standard.

Gas Chromatographic Analysis Data. The gas chromatographic analyses were determined on an Aerograph M. 90-PC, 154 vapor fractometer using helium as the carrier gas. The column was a 5 ft. x ¼ in., 20% SF-96, 60/80 mesh chro. P.

Analytical Data. Microanalyses were determined by Schwarzkopf Microanalytical Laboratory, Woodside, New York.

2-Phenyl-2,1,3-Triazole (XXV)

Glyoxal bis(Phenylhydrazone) (XXXIX). To 100 ml. of methyl cellosolve was added 67 ml. of 30% aqueous glyoxal. The solution was heated to 80° and 150 ml. of phenylhydrazine was added and the mixture heated on a steam bath for 1 hr. The red solution was cooled to room temperature, and 1000 ml. of ice water was added to it with stirring. The fine, yellow precipitate which was formed was separated by filtration, washed with cold water, and recrystallized from 95% ethanol yielding 62 g. (65%) of glyoxal bis(phenylhydrazone) (XXXIX), m.p. 180°; lit.[46] m.p. 179-180°.

2-Phenyl-2,1,3-Triazole (XXV). In a solution of 7 g. of copper sulfate pentahydrate and 350 ml. of water was suspended 7 g. of glyoxal bis(phenylhydrazone) (XXXIX). The solution was heated under reflux for 1.5 hr. and steam distilled. The distillate (yellow oil) was extracted with two 100 ml. portions of ether. The ether layer was washed with dilute hydrochloric acid to remove aniline, and the ether layer was dried over sodium sulfate. The solution was concentrated to a yellow oil by removing the ether under reduced pressure. The oily residue thus obtained was purified by repeated vacuum distillation yielding 2.8 g. (62%) of 2-phenyl-2,1,3-triazole (XXV), b.p. 79° at approximately 12 mm.; lit.[28] b.p. 80° at 12 mm. The sample was analyzed by V.P.C. and showed only one peak.

U.V. Spectrum No.$_{15}$-$\lambda_{max.}$ 265 mμ, $\epsilon_{max.}$ 24,324;
$\lambda_{max.}$ 207 mμ, $\epsilon_{max.}$ 21,621

I.R. Spectrum-Fig. 43 N.M.R. Values-Table XIV

2-Phenyl-4-methanol-2,1,3-Triazole (XXIV)

2-Phenyl-4-formyl-2,1,3-Triazole (XIII). A suspension of 0.5078 g. of 2-phenyl-4-(D-arabinose-tetrahydroxybutyl)-2,1,3-triazole (XI) in a mixture of 50 ml. of water and 15 ml. of 0.428 M. of aqueous sodium periodate solution (3.35 molecular equivalents) was agitated at 25° for 24 hr. The appearance of the suspended crystals changed from that of long, fine needles to shorter and more thickened ones. The crystals were removed by filtration, washed well with cold water, and recrystallized from 50% ethanol-water to yield 0.28 g. (78%) of 2-phenyl-4-formyl-2,1,3-triazole (XIII), m.p. 67-68°; lit.[22] m.p. 68-69°.

2-Phenyl-4-methanol-2,1,3-Triazole (XXIV). To a suspension of 0.5 g. of lithium aluminum hydride in 50 ml. of dry ether was added 0.28 g. of 2-phenyl-4-formyl osotriazole (XIII). The reaction mixture was stirred until the reaction subsided and wet ether was added until all of the lithium aluminum hydride was destroyed. Several drops of water were added and the mixture stirred until all of the grey solid was replaced by white salts. The mixture was separated by filtration, and the ethereal solution was dried over sodium sulfate and air concentrated to yield a solid residue. When recrystallized from hot carbon tetrachloride, the solution deposited on cooling 0.25 g. (90%) of 2-phenyl-4-methanol-2,1,3-triazole (XXIV), m.p. 64-65°; lit.[47] 64-65°.

U.V. Spectrum No.4-$\lambda_{max.}$ 266 mμ, $\varepsilon_{max.}$ 18,219

I.R. Spectrum-Fig. 44 N.M.R. Values-Table XIV

2-Phenyl-4-(D-Glyceraldehyde-dihydroxyethyl)-2,1,3-Triazole (XXIII).

Potato Oxystarch (XLIII). A colloidal suspension of 4.5 g. of potato starch (XLII) and 6.18 g. of sodium metaperiodate was kept stirring in the dark for 48 hr. At the end of this time the insoluble oxystarch was separated by filtration and washed with water until free from periodate and iodate. The gelatinous solid was washed with absolute alcohol until a white powder was obtained. The powder was washed with ether and dried by passing air through the filter cake. The yield was quantitative.

Phenylosazone of Potato Oxystarch (LV). A mixture of 2.3 g. of potato oxystarch (XLIII) in 100 ml. of water was heated under reflux in 200 ml. of ethanol, 25 ml. of phenylhydrazine and 30 ml. of glacial acetic acid. Solution of the oxystarch took place in about 10 min. after which time the ethanol was removed under reduced pressure. To the remaining solution was added with rapid stirring 500 ml. of cold water producing a golden yellow precipitate. The precipitate was collected by filtration and washed with 50 ml. portions of 10% acetic acid followed by two 50 ml. portions of cold water, yielding 3.5 g. of the phenylosazone (LV) which was used without further purification in the following experiment.

D-Erythrose Osazone (XXXVII). A solution of 2 g. of the crude potato oxystarch osazone (LV) was dissolved in 100 ml. of benzene and absorbed on a 150 g. neutral alumina column. The column was eluted with 1 l. of ether or until the initial wide yellow band came off the column. The ether eluted the

glyoxal osazone (XXXIX) and β-acetyl phenylhydrazine (XLIV) as one band. The column was washed free of the remaining solid with 95% ethanol. The ethanol solution was concentrated under reduced pressure and the erythrose osazone (XXXVII) was precipitated by the addition of water to the rapidly stirring solution. The yellow precipitate was collected by filtration and recrystallized from 60% ethanol-water yielding 0.42 g. of D-erythrose phenylosazone (XXXVII), m.p. 175-177°; lit.[22,36] m.p. 175-177°.

2-Phenyl-4-(D-Glyceraldehyde-dihydroxyethyl)-2,1,3-Triazole (XXIII). A suspension of 20 g. of the crude potato starch phenylosazone (LV) and 1800 ml. of water was heated to boiling and a solution of 16.7 g. of copper sulfate pentahydrate in 100 ml. of boiling water was added. After 30 min. of heating under reflux, the solution was allowed to cool to room temperature. The solution was set free of decomposition products by filtration. Hydrogen sulfide was bubbled through the solution as long as a black precipitate continued to form. The black precipitate was separated by filtration leaving a yellow solution which was boiled with 20 g. of barium carbonate until the solution was slightly basic to litmus. After cooling, the mixture was separated by filtration and the filtrate concentrated to a syrup under reduced pressure. The syrup was extracted with two 250 ml. portions of carbon tetrachloride. The combined extracts of carbon tetrachloride were concentrated under reduced pressure and cooled for two hours under refrigeration. The white voluminous precipitate was dried on the filter. The solid was dissolved in hot isopropyl

ether and n-hexane was added until the first sign of turbidity appeared. The solution was allowed to cool to room temperature and then refrigerated overnight. The white precipitate was separated by filtration and washed with two 25 ml. portions of n-hexane yielding 2.5 g. of D-erythrose osotriazole (XXIII), m.p. 64-65°.

Anal. Calcd. for $C_{10}H_{11}N_3O_2$: C, 58.53; H, 5.40; N, 20.48. Found: C, 59.10; H, 5.23; N, 19.83.

U.V. Spectrum No. 15-$\lambda_{max.}$ 265 mμ, $\epsilon_{max.}$ 20,147;
$\lambda_{max.}$ 208 mμ, $\epsilon_{max.}$ 14,117

I.R. Spectrum-Fig. 45 N.M.R. Values-Table XIV

O.R.D. Spectrum-Fig. 13 & 14

2-Phenyl-4-(D-Threose-trihydroxypropyl)-2,1,3-Triazole (XXII)

D-Xylose Phenylosazone (XXXVI). The D-xylose phenylosazone (XXXVI) was obtained in a yield of 13.5 g. (62%) upon treatment of 10 g. of D-xylose by the method employed for the preparation of D-glucose phenylosazone (X). The yellow solid melted at 162-164; lit.[48] m.p. 163°.

2-Phenyl-4-(D-Threose-trihydroxypropyl)-2,1,3-Triazole (XXII). A solution of 20.0 g. of D-xylose phenylosazone (XXXVI) and 16.7 g. of copper sulfate pentahydrate in 1200 ml. of water was heated to boiling under reflux for 30 min. The mixture was allowed to cool to room temperature and the fine red precipitate which had been deposited was separated by filtration. The copper still present in solution was precipitated as sulfide by passing in hydrogen sulfide, and the copper sulfide was separated by filtration. The solution was

boiled with 15 g. of barium carbonate until it was neutral to litmus paper. The yellow filtrate from removal of the barium salt was concentrated under reduced pressure to a volume of 25 ml. and allowed to stand in the refrigerator overnight. The precipitate thus formed was separated by filtration and recrystallized with seeding from warm ether yielding 5.8 g. (40%) of D-xylose osotriazole (XXII), m.p. 87-88.5°; lit.[49] m.p. 88-89°.

U.V. Spectrum-No. 4-$\lambda_{max.}$ 267 mu, $\epsilon_{max.}$ 20,239

I.R. Spectrum-Fig. 47 N.M.R. Values-Table XIV

O.R.D. Spectrum-Fig. 15

2-Phenyl-4-(L-Erythrose-trihydroxypropyl)-2,1,3-Triazole (XXI-L)

L-Arabinose Phenylosazone (XXXV-L). A suspension of 25 g. of L-arabinose in 100 ml. of freshly distilled methyl cellosolve and 32.5 ml. of glacial acetic acid was heated on a steam bath to 80° at which time 65 ml. of phenylhydrazine was added. Solution of the sugar took place almost immediately and a reddish solution developed during the next hour, after which the solution was poured into 1600 ml. of ice water with vigorous stirring. A voluminous yellow precipitate was obtained which was separated by filtration with suction and washed with two 50 ml. portions of 10% acetic acid and four 100 ml. portions of cold water. The precipitate was separated by filtration, partially dried by passing air through it, and dissolved in 100 ml. of boiling ethanol. The hot solution was filtered, cooled and the precipitate separated and washed with three 25 ml. portions of ice cold alcohol yielding 33 g.

(60%) of L-arabinose phenylosazone (XXXV-L), m.p. 170-171°; lit.[50] m.p. 171-172°.

2-Phenyl-4-(L-Erythrose-trihydroxypropyl)-2,1,3-Triazole (XXI-L). A suspension of 10 g. of L-arabinose phenylosazone (XXXV-L) in 1000 ml. of water was heated to boiling and a solution of 8.4 g. of copper sulfate pentahydrate in 100 ml. of boiling water added. A cherry red color developed at once and after 15 min. heating under reflux the color changed to green, at which time all of the osazone was dissolved and the fine red precipitate had settled. Heating was continued for an additional 15 min. and the mixture was cooled and separated by filtration. The copper still present in solution was removed as sulfide and the filtrate was neutralized with 10 g. of barium carbonate and again filtered. The solution was concentrated on a rotary evaporator to a syrup which was dried by three successive evaporations with absolute alcohol. A solution of the syrup in 25 ml. of warm chloroform was filtered to remove a small amount of insoluble material and diluted just to turbidity with a 50% mixture of dry ether and hexane. The solution was cooled at room temperature for several hours without disturbance, scratched to induce precipitation, and cooled in the refrigerator overnight. The dark colored precipitate was separated by filtration and recrystallized from ether yielding 5 g. (70%) of L-arabinose osotriazole (XXI-L), m.p. 65-68.5°; lit.[22] m.p. 69-70°.

U.V. Spectrum No.4-$\lambda_{max.}$ 266 mμ, $\varepsilon_{max.}$ 19,827

I.R. Spectrum-Fig. 46 N.M.R. Values-Table XIV

O.R.D. Spectrum-Fig. 16

2-Phenyl-4-(D-Lyxose-tetrahydroxybutyl)-2,1,3-Triazole (XX)

D-Galactose Phenylosazone (XXXIV). The D-galactose phenylosazone (XXXIV) was obtained in a yield of 20 g. (60%) upon treatment of 10 g. of D-galactose by the method employed for the preparation of D-glucose phenylosazone (X). The yellow solid melted at 201-202°; lit.[48] m.p. 201°.

2-Phenyl-4-(D-Lyxose-tetrahydroxybutyl)-2,1,3-Triazole (XX). A solution of 20.0 g. of D-galactose phenylosazone (XXXIV) and 15.4 g. of copper sulfate pentahydrate in 1200 ml. of water was heated under reflux for 1 hr. The precipitate was separated by filtration and the solution allowed to cool to room temperature. Hydrogen sulfide was bubbled through the solution until no more black precipitate was formed. The precipitate was separated by filtration leaving a yellow solution which was neutralized by boiling with 15 g. of barium carbonate until the solution tested neutral or slightly basic to pH paper. After cooling the solution was filtered and concentrated to a syrup under reduced pressure. The syrup was extracted with warm chloroform until no further color appeared in the chloroform layer. After cooling the precipitate was separated by filtration, and the mother liquid concentrated to half of its original volume and refrigerated overnight. The precipitate was again separated and the two fractions combined giving 7 g. (47%) of D-galactose osotriazole (XX), m.p. 108-109°; lit.[49] m.p. 110-111°.

U.V. Spectrum No.$_4$-$\lambda_{max.}$ 266 mμ, $\varepsilon_{max.}$ 19,545

I.R. Spectrum-Fig. 4[illegible] N.M.R. Values-Table XIV

O.R.D. Spectrum-Fig. 17 & 18

2-Phenyl-4-(D-Lyxose-tetraacetoxybutyl)-2,1,3-Triazole (XLVI)

2-Phenyl-4-(D-Lyxose-tetraacetoxybutyl)-2,1,3-Triazole (XLVI). To a solution of 0.2 g. of phenyl D-galactose osotriazole (XX) in 2.5 ml. of pyridine was added 2.5 ml. of acetic anhydride. The acetylation was allowed to proceed with stirring at 20° for 48 hr. The mixture was extracted with chloroform and the water-washed extract was dried over calcium chloride. The solution was concentrated in a stream of air to a semicrystalline material which was dissolved in hot dioxane and sufficient water was added to induce turbidity. The turbid solution was allowed to stand overnight at room temperature during which time crystallization began. The white precipitate was filtered and dried, yielding 0.3 g. (92%) of the tetraacetate XLVI, m.p. 104-105°; lit.[49] m.p. 105-106°.

U.V. Spectrum No_{15}-$\lambda_{max.}$ 264 mμ, $\epsilon_{max.}$ 22,070;
$\lambda_{max.}$ 205 mμ, $\epsilon_{max.}$ 17,241

I.R. Spectrum-Fig. 48. O.R.D. Spectrum-Fig. 19.

2-Phenyl-4-(L-Xylose-tetrahydroxybutyl)-2,1,3-Triazole (XIX-L)

L-Sorbose Phenylosazone (XXXIII-L). The L-sorbose phenylosazone (XXXIII-L) was obtained in a yield of 11.2 g. (56%) upon treatment of 10 g. of L-sorbose by the method employed for the preparation of D-glucose phenylosazone (X). The yellow solid melted at 162-163°; lit.[51] m.p. 168°.

2-Phenyl-4-(L-Xylose-tetrahydroxybutyl)-2,1,3-Triazole (XIX-L). A suspension of 10 g. of sorbose phenylosazone (XXXIII-L) in a solution of 7.7 g. of copper sulfate pentahydrate in 1200 ml. of water was heated to boiling under reflux.

Solution of the osazone and the concurrent development of a red color occurred in 10 min. Shortly thereafter a fine, red precipitate was deposited from the solution and, after 30 min. additional heating, it was separated by filtration. The solution was allowed to cool to room temperature, and hydrogen sulfide was bubbled through the solution as long as a black precipitate continued to form. The black precipitate was separated by filtration leaving a yellow solution which was neutralized by boiling for 15 min. with 10 g. of barium carbonate or until the solution tested neutral to pH paper. After cooling the mixture was separated by filtration and the filtrate concentrated to a syrup under reduced pressure. The syrup was extracted with hot ethyl acetate until no further color appeared in the ethyl acetate layer. After cooling the solution was filtered and the mother liquid was concentrated to half of its volume and cooled. The precipitate was again separated and the two fractions combined giving 3.0 g. (40%) of XIX-L, m.p. 151-152°; lit.[49] m.p. 158-159°.

U.V. Spectrum No. 4-$\lambda_{max.}$ 266 mμ, $\epsilon_{max.}$ 18,812

I.R. Spectrum-Fig. 50 N.M.R. Values-Table XIV

O.R.D. Spectrum-Fig. 20

2-Phenyl-4-(D-Arabinose-tetrahydroxybutyl)-2,1,3-Triazole (XI)

D-Glucose Phenylosazone (X). A mixture of 10.0 g. of D-glucose, 20.0 g. of phenylhydrazine hydrochloride, 25 ml. of a saturated solution of sodium bisulfite, 30 g. of crystalline sodium acetate and 200 ml. of distilled water was heated with stirring on a steam bath for 0.5 hr. The precipitate was

separated by filtration and washed well with cold water. The mother liquor was returned to the flask and heated for several hours. The mixture was cooled for 1 hr., separated by filtration and the precipitate washed with water. The combined solids were recrystallized from 60% ethanol-water and yielded 25 g. (75%) of D-glucose phenylosazone (X), m.p. 208° (dec.); lit.[52] m.p. 208° (dec.).

2-Phenyl-4-(D-Arabinose-tetrahydroxybutyl)-2,1,3-Triazole (XI). To a solution of 180 ml. of water and 10 ml. of 0.5 N sulfuric acid, 6.0 g. of copper sulfate pentahydrate, 120 ml. of isopropyl alcohol and 2 g. of powdered D-glucose phenylosazone (X) were added. The mixture was refluxed for 1 hr. The osazone dissolved after 15 min. and the solution became a deep red which in the next half hour changed to green and finally to a yellowish green. The red precipitate was separated by filtration and the solution concentrated under reduced pressure to a volume of 50 ml. during which a tan precipitate crystallized. The solution was cooled for 3 hr. and the tan precipitate separated and washed. The precipitate was dissolved in hot water, decolorized with norite, and the mixture separated by filtration and the filtrate cooled overnight. The long white needles of pure D-glucose osotriazole (XI), 300 mg. (20%), were separated and dried, m.p. 193-193.5°; lit.[22] m.p. 195-196°.

U.V. Spectrum-No.$_4$-$\lambda_{max.}$ 267 mμ, $\varepsilon_{max.}$ 24,450

I.R. Spectrum-Fig. 51 N.M.R. Values-Table XIV

O.R.D. Spectrum-Fig. 21

2-Phenyl-4-(D-Arabino-tetraacetoxybutyl)-2,1,3-Triazole (LIII)

2-Phenyl-4-(D-Arabino-tetraacetoxybutyl)-2,1,3-Triazole (LIII). The D-glucose osotriazole tetraacetate (LIII) was obtained in quantitative yield upon treatment of 0.6 g. of D-glucose osotriazole (XI) by the method employed for the preparation of D-galactose osotriazole tetraacetate (XLVI). The white solid which was recrystallized from methanol melted at 81-82°; lit.[22] m.p. 81-82°.

N.M.R. Values-Table VI

APPENDIX

OPTICAL ROTATORY DISPERSION CURVES

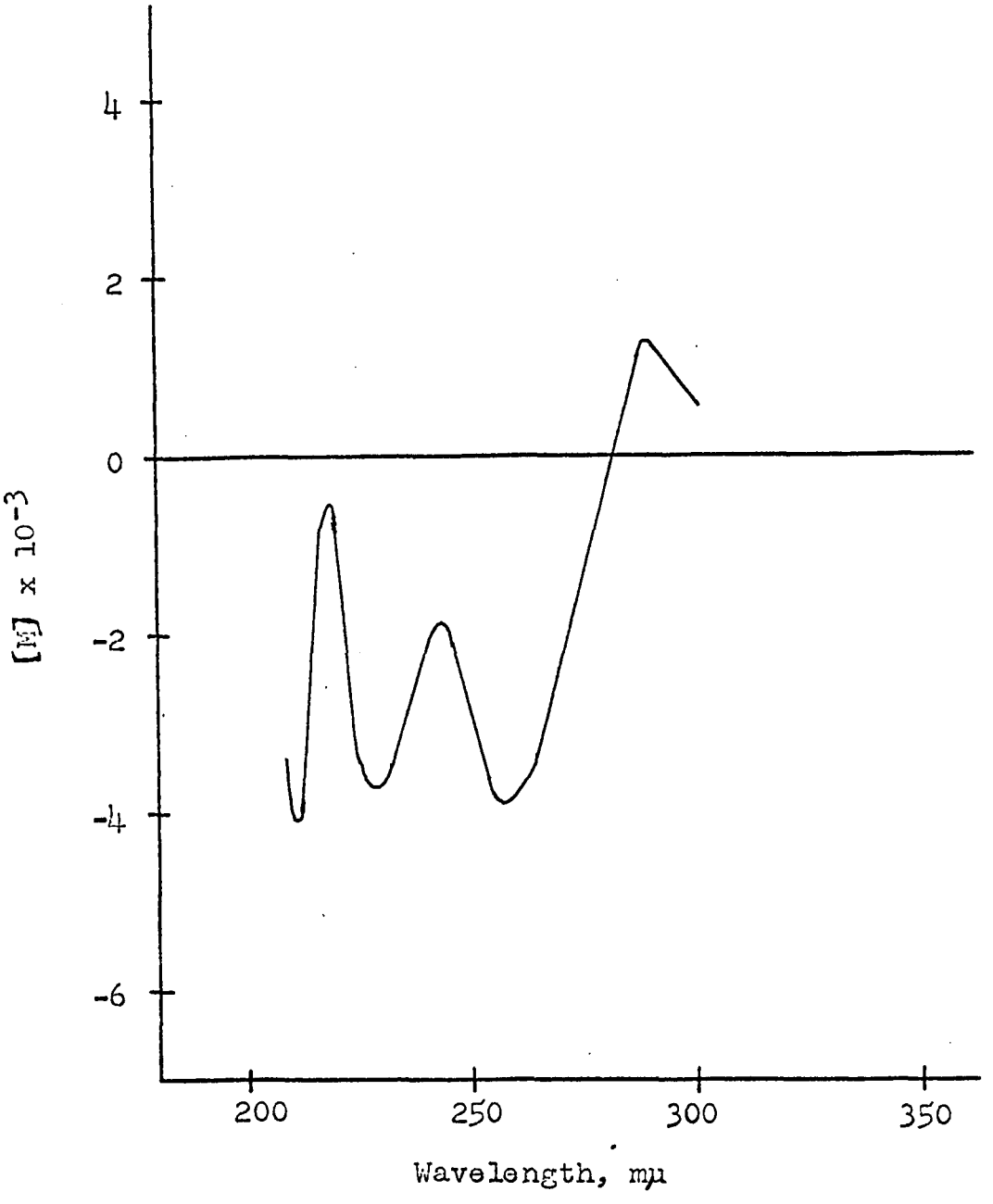


Fig. 13. Optical Rotatory Dispersion Curve of D-Erythrose Osotriazole (XXIII). The curve was obtained from the Bellingham-Stanley using methanol as the solvent. (Table VIII)

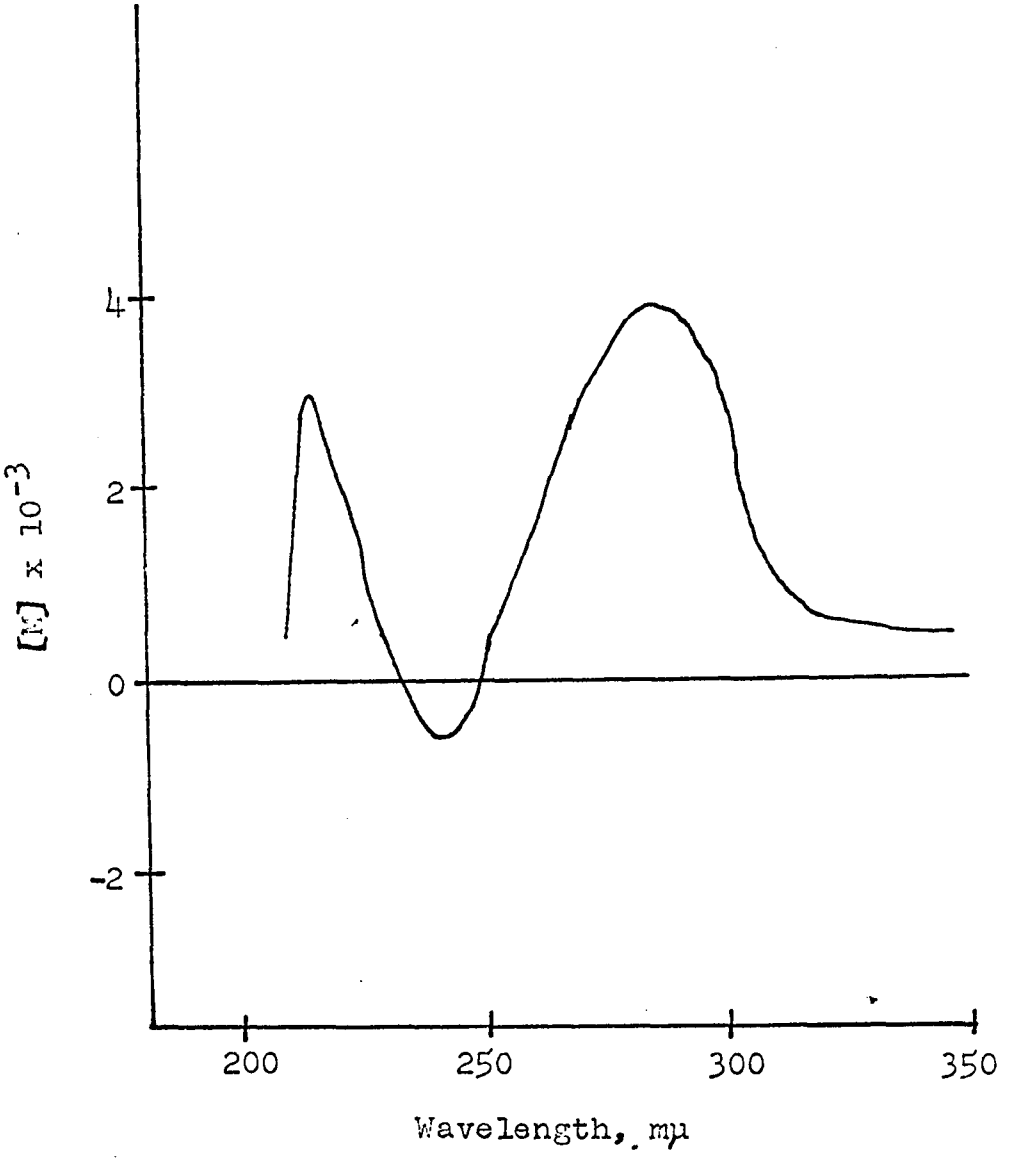


Fig. 14. Optical Rotatory Dispersion Curve of D-Erythrose Osotriazole (XXIII). The curve was obtained from the Cary 60 using methanol as the solvent. (Table VIII)

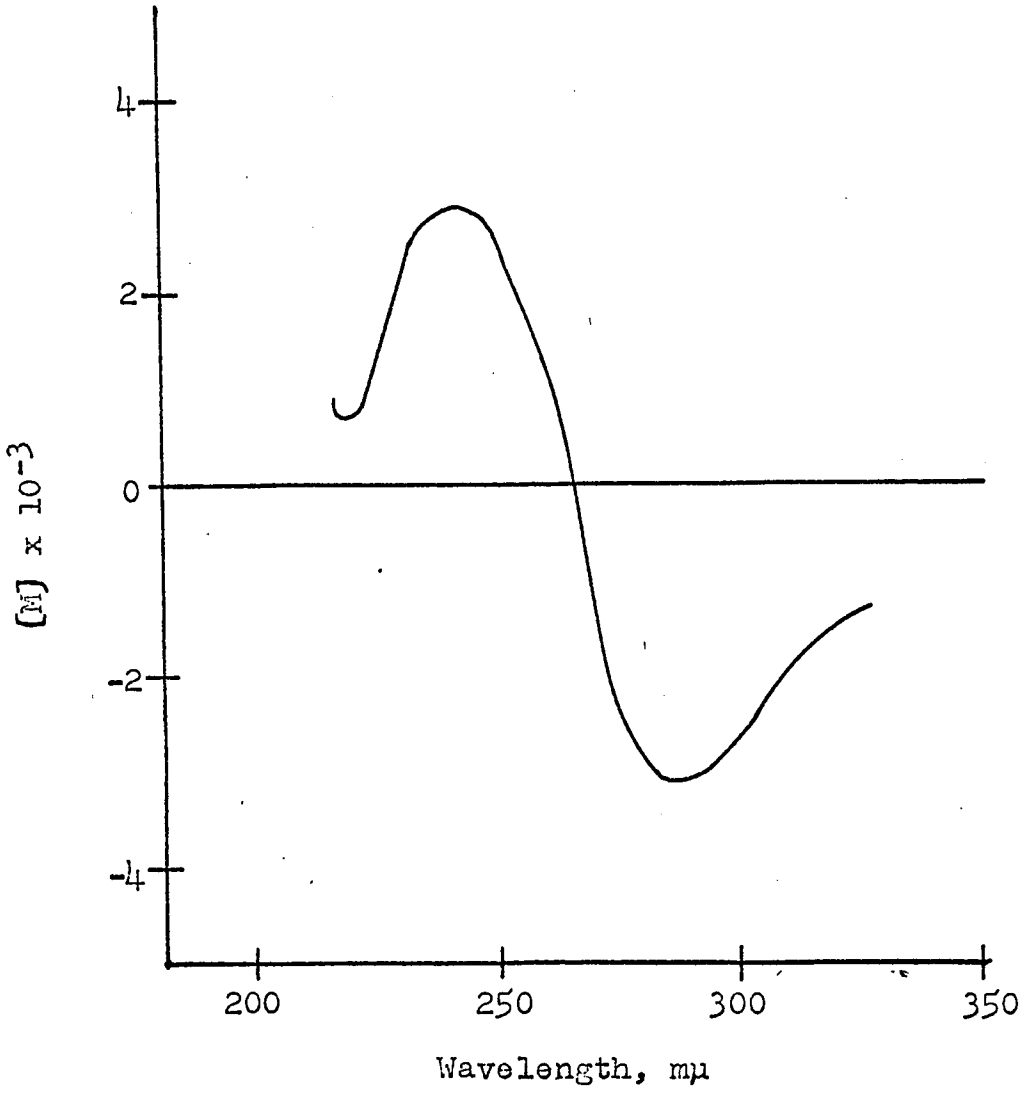


Fig. 15. Optical Rotatory Dispersion Curve of D-Xylose Osotriazole (XXII). The curve was obtained from the Cary 60 using methanol as the solvent. (Table VIII)

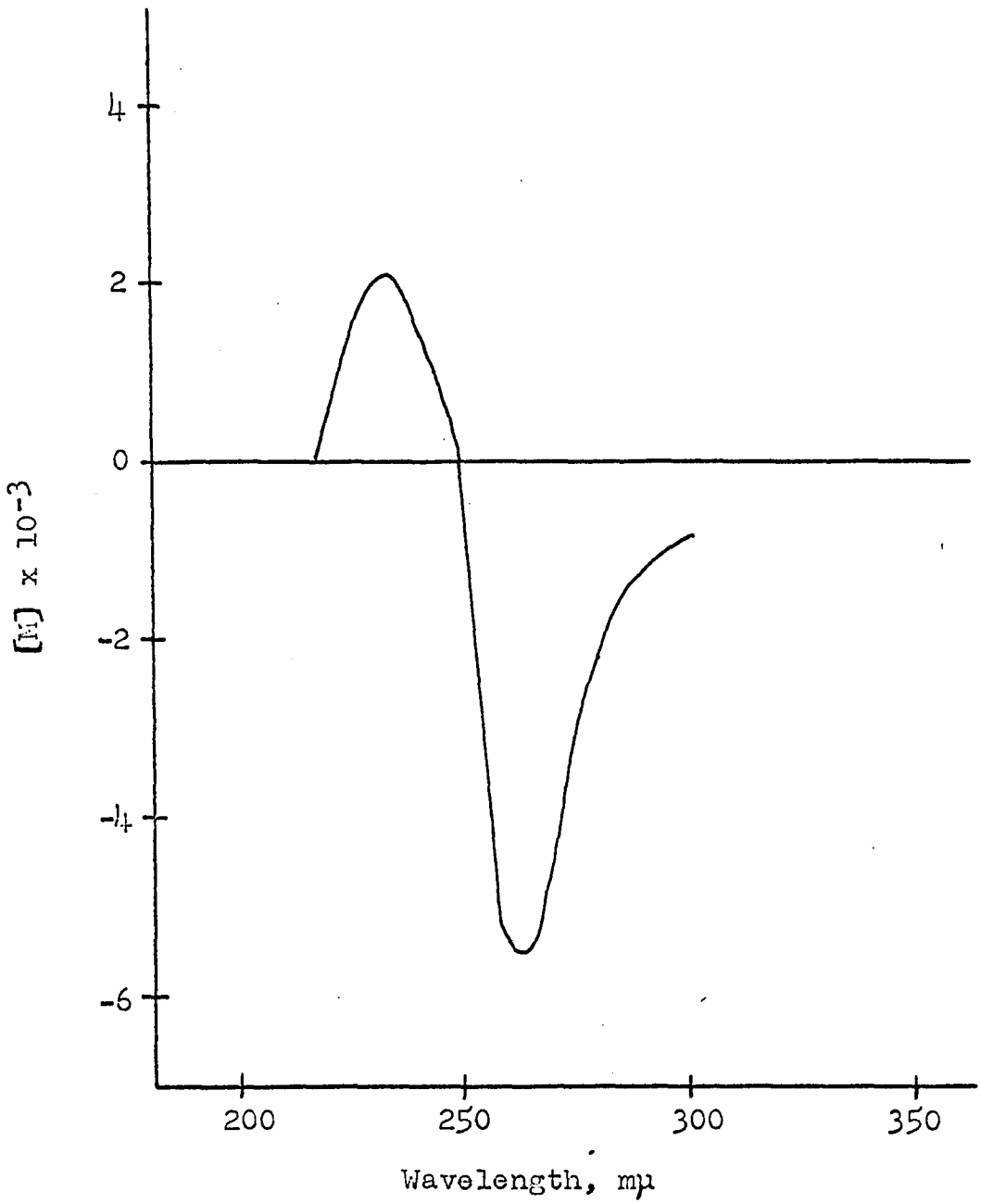


Fig. 16. Optical Rotatory Dispersion Curve of L-Arabinose Osotriazole (XXI-L). The curve was obtained from the Bellingham-Stanley using methanol as the solvent. (Table VIII)

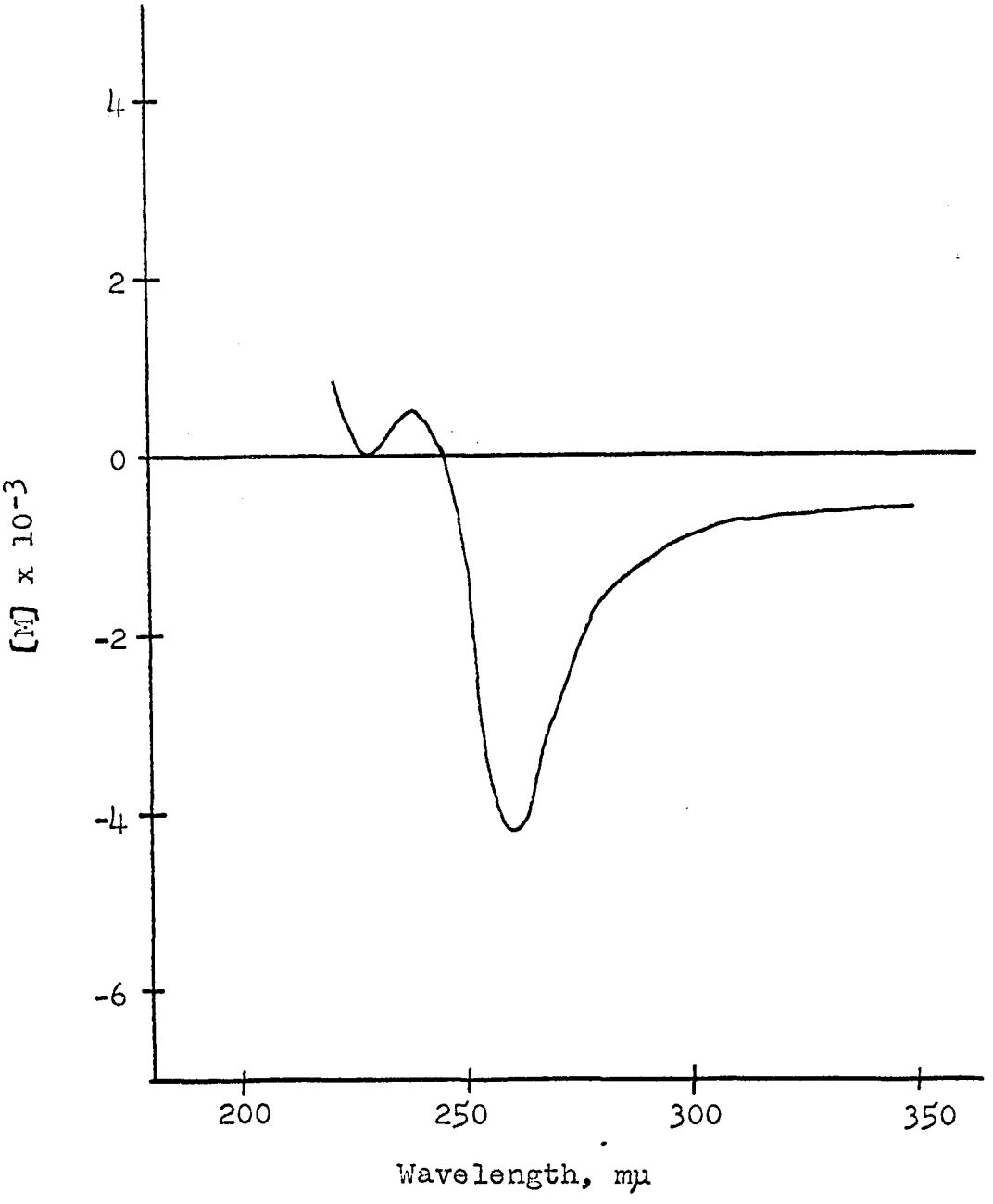


Fig. 17. Optical Rotatory Dispersion Curve of D-Galactose Osotriazole (XX). The curve was obtained from the Bellingham-Stanley using methanol as the solvent. (Table VIII)

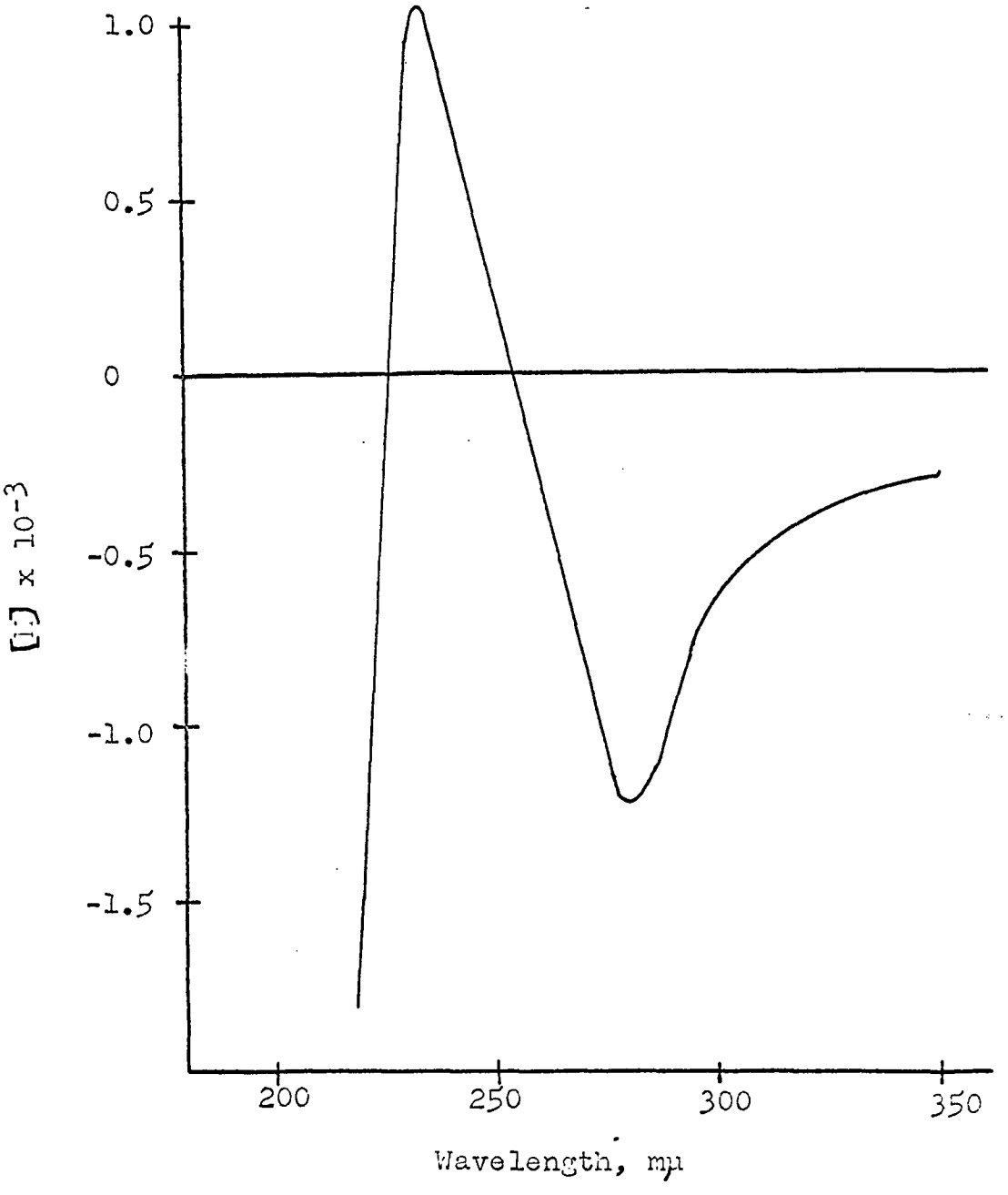


Fig. 18. Optical Rotatory Dispersion Curve of D-Galactose Osotriazole (XX). The curve was obtained from the Cary 60 using methanol as the solvent. (Table VIII)

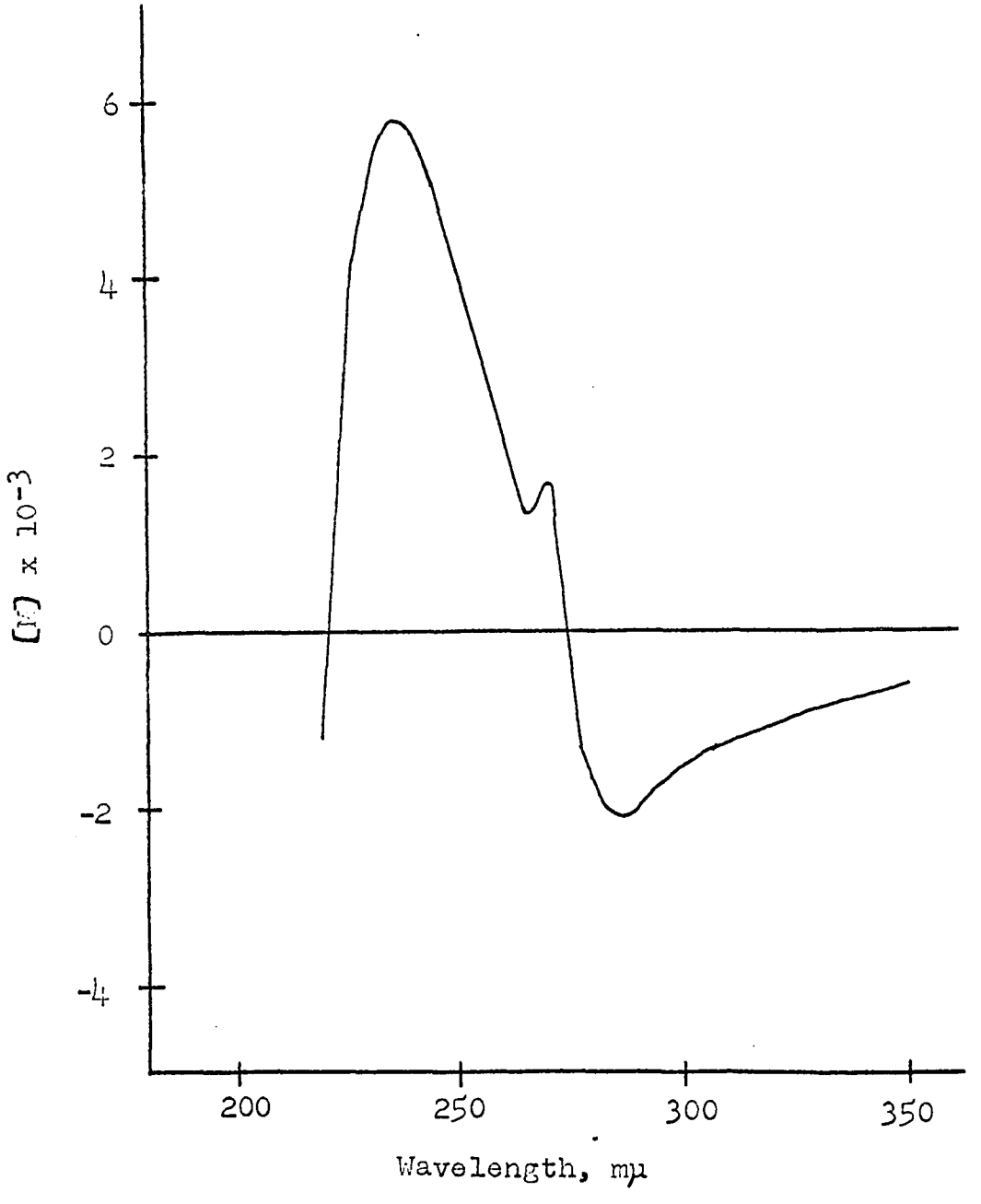


Fig. 19. Optical Rotatory Dispersion Curve of D-Galactose Tetraacetate Osotriazole (XLVI). The curve was obtained from the Cary 60 using methanol as the solvent. (Table VIII)

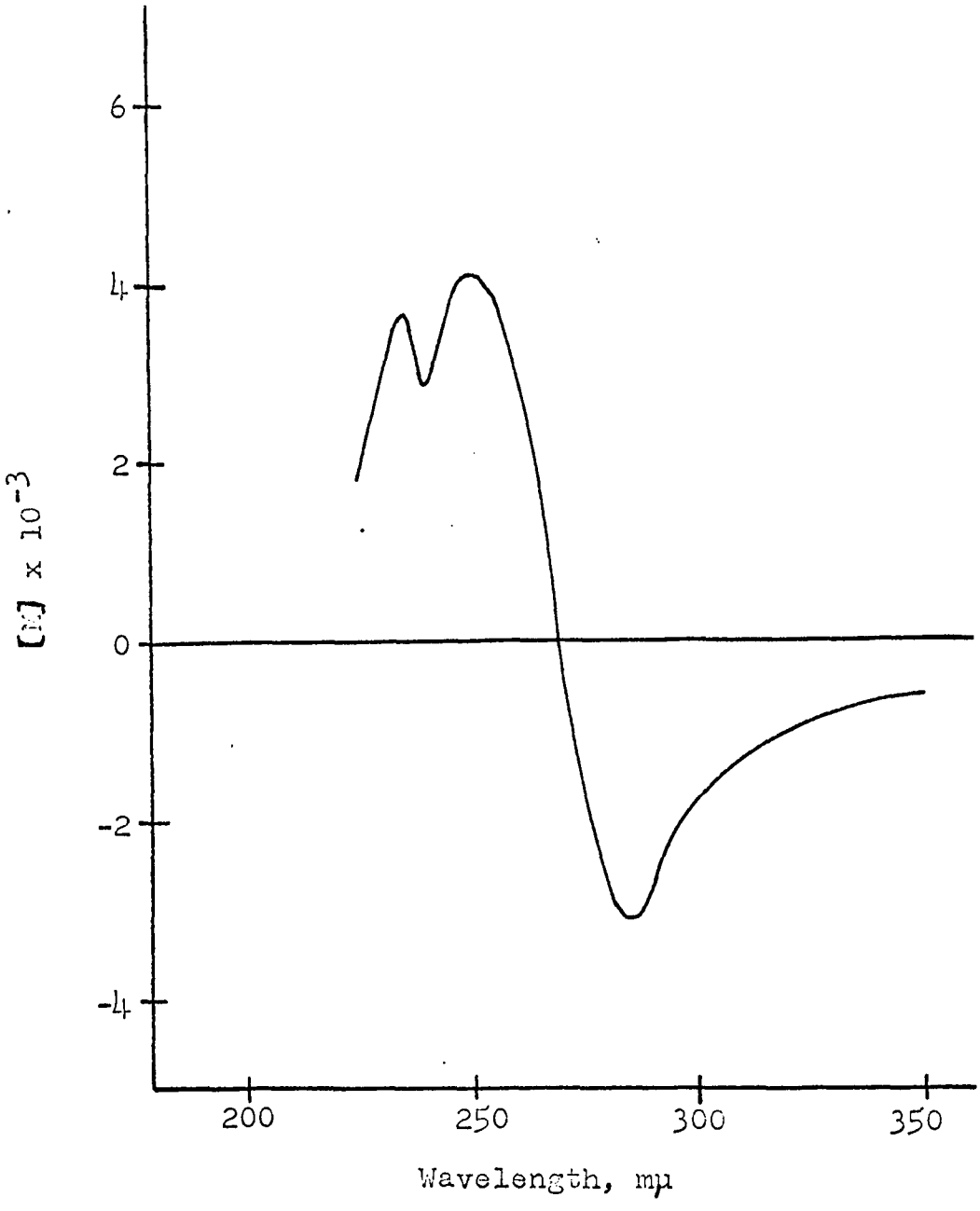


Fig. 20. Optical Rotatory Dispersion Curve of L-Sorbose Osotriazole (XIX-L). The curve was obtained from the Cary 60 using methanol as the solvent. (Table VIII)

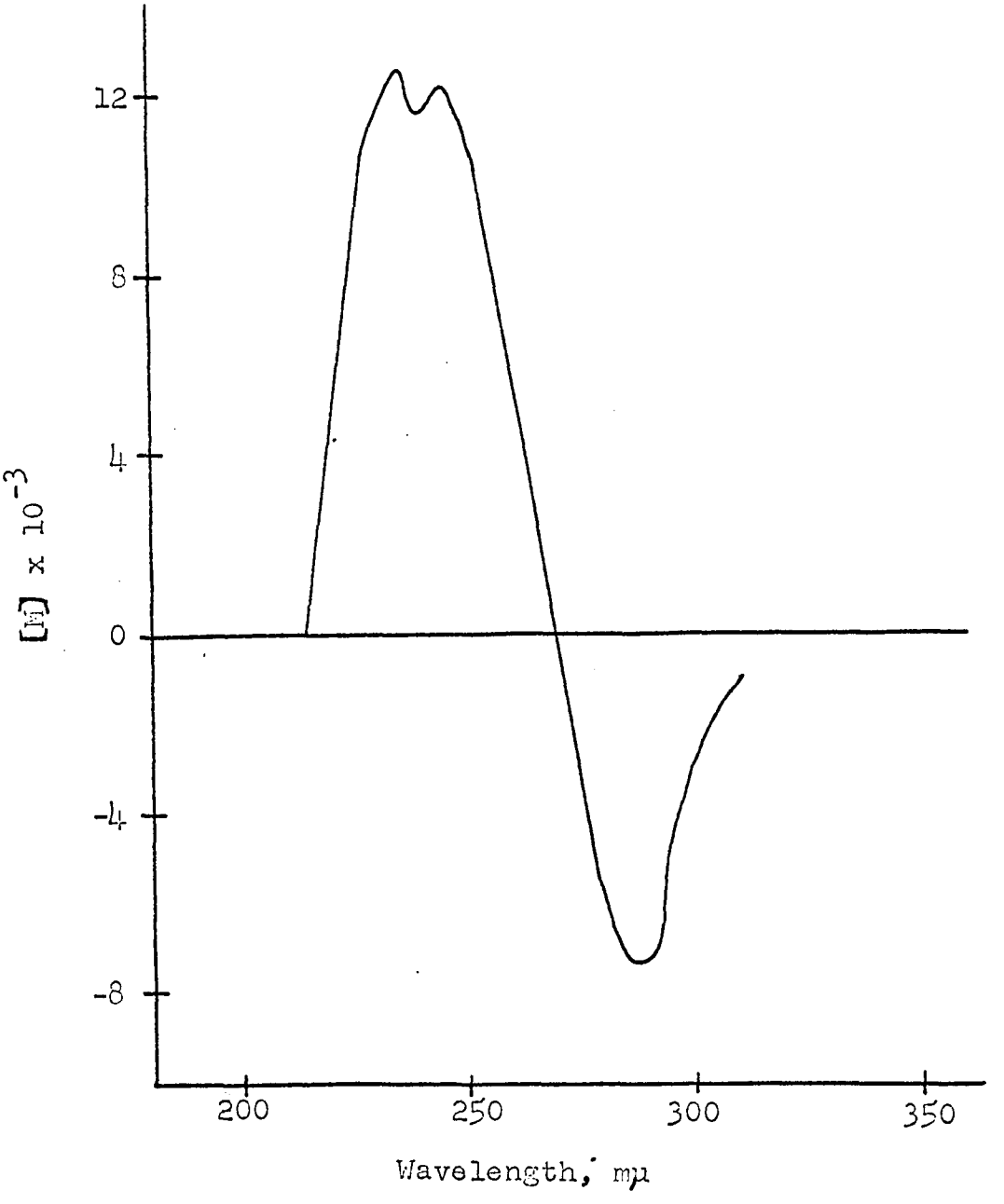


Fig. 21. Optical Rotatory Dispersion Curve of D-Glucose Osotriazole (XI). The curve was obtained from the Cary 60 using methanol as the solvent. (Table VIII)

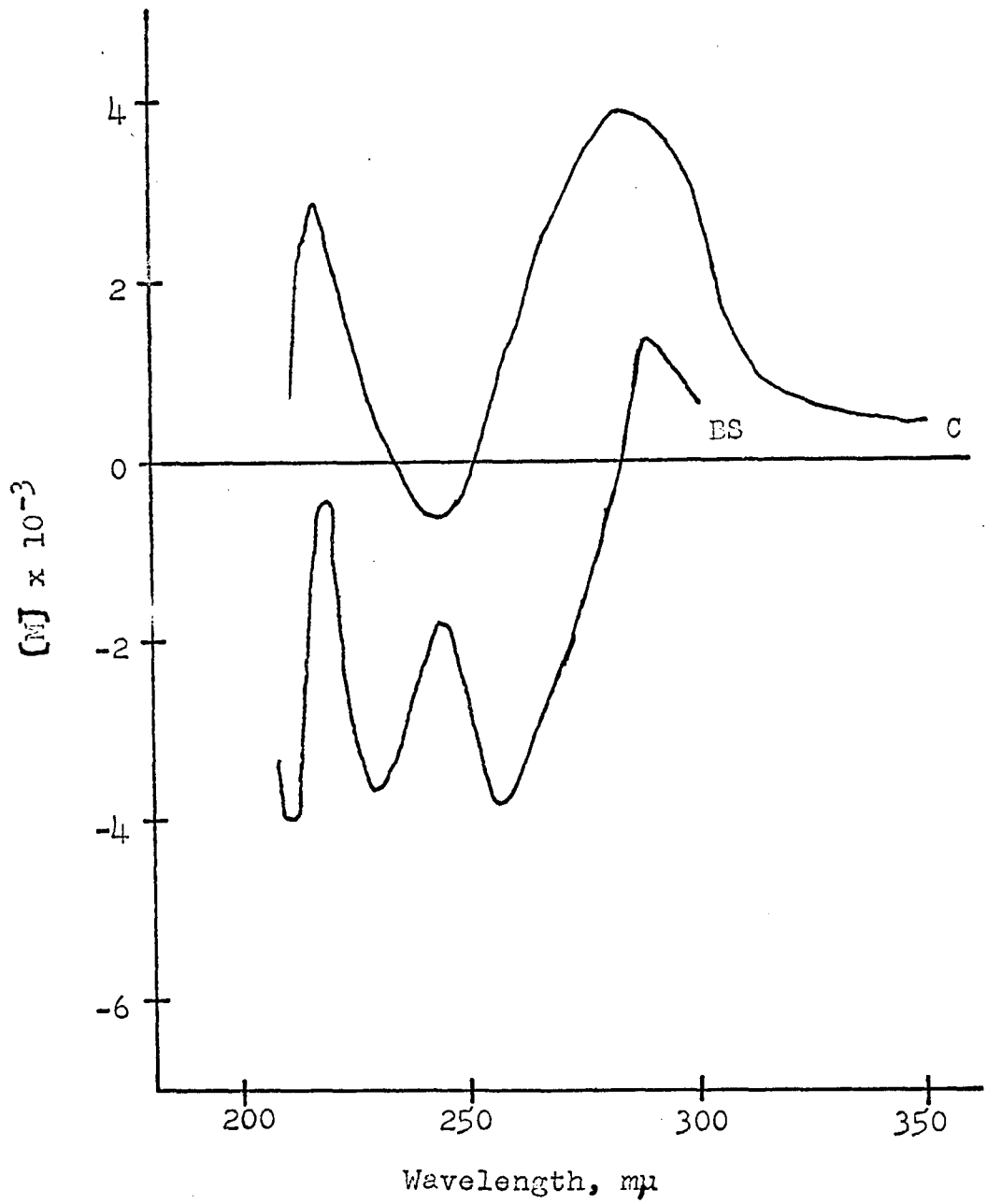


Fig. 22. Optical Rotatory Dispersion Curves of D-Erythrose Osotriazole (XXIII) obtained from the Cary 60 (C) and the Bellingham-Stanley (BS) using methanol as the solvent. (Table VIII)

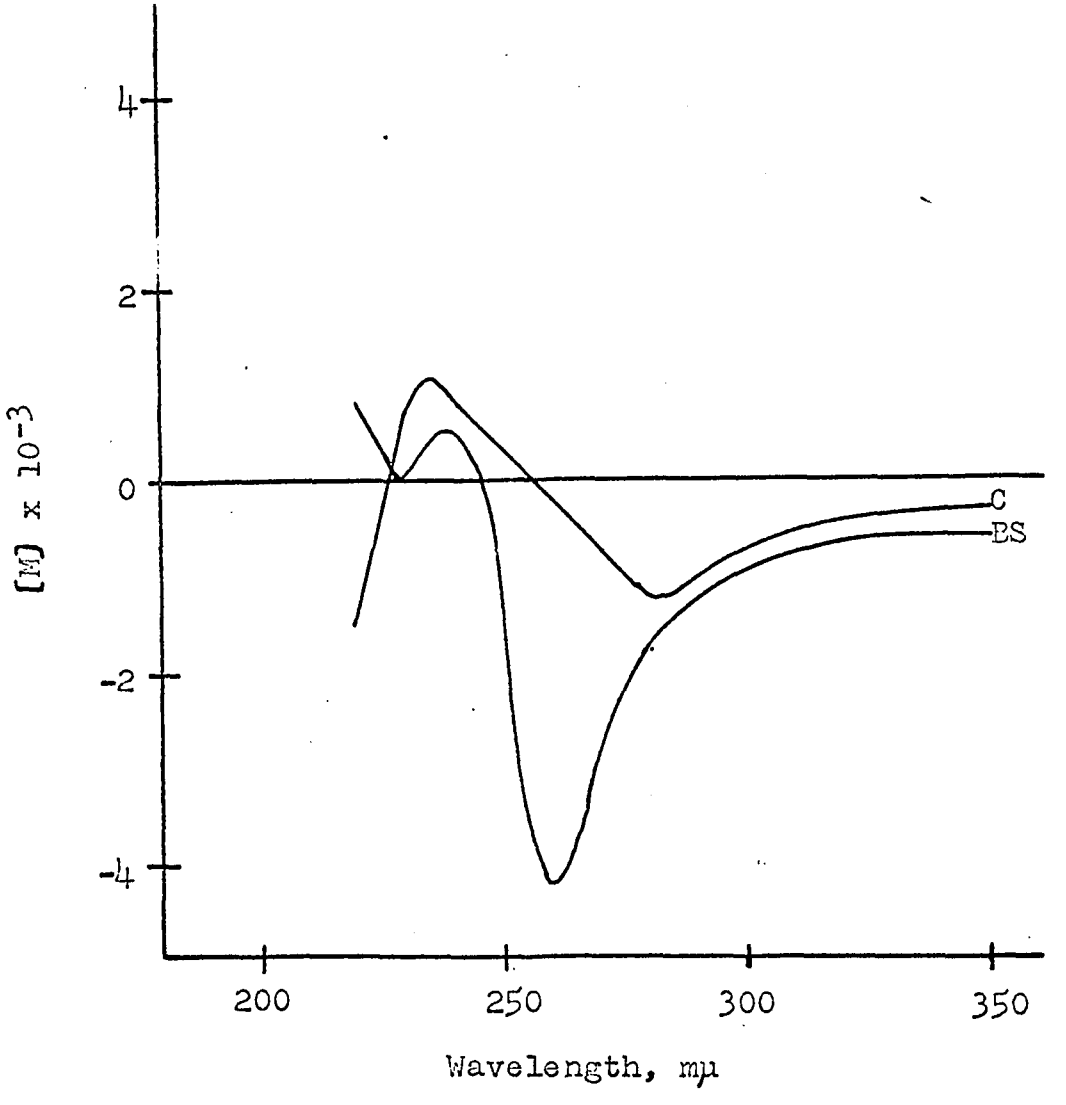


Fig. 23. Optical Rotatory Dispersion Curves of D-Galactose Osotriazole (XX) obtained from the Cary 60 (C) and the Bellingham-Stanley (BS) using methanol as the solvent. (Table VIII)

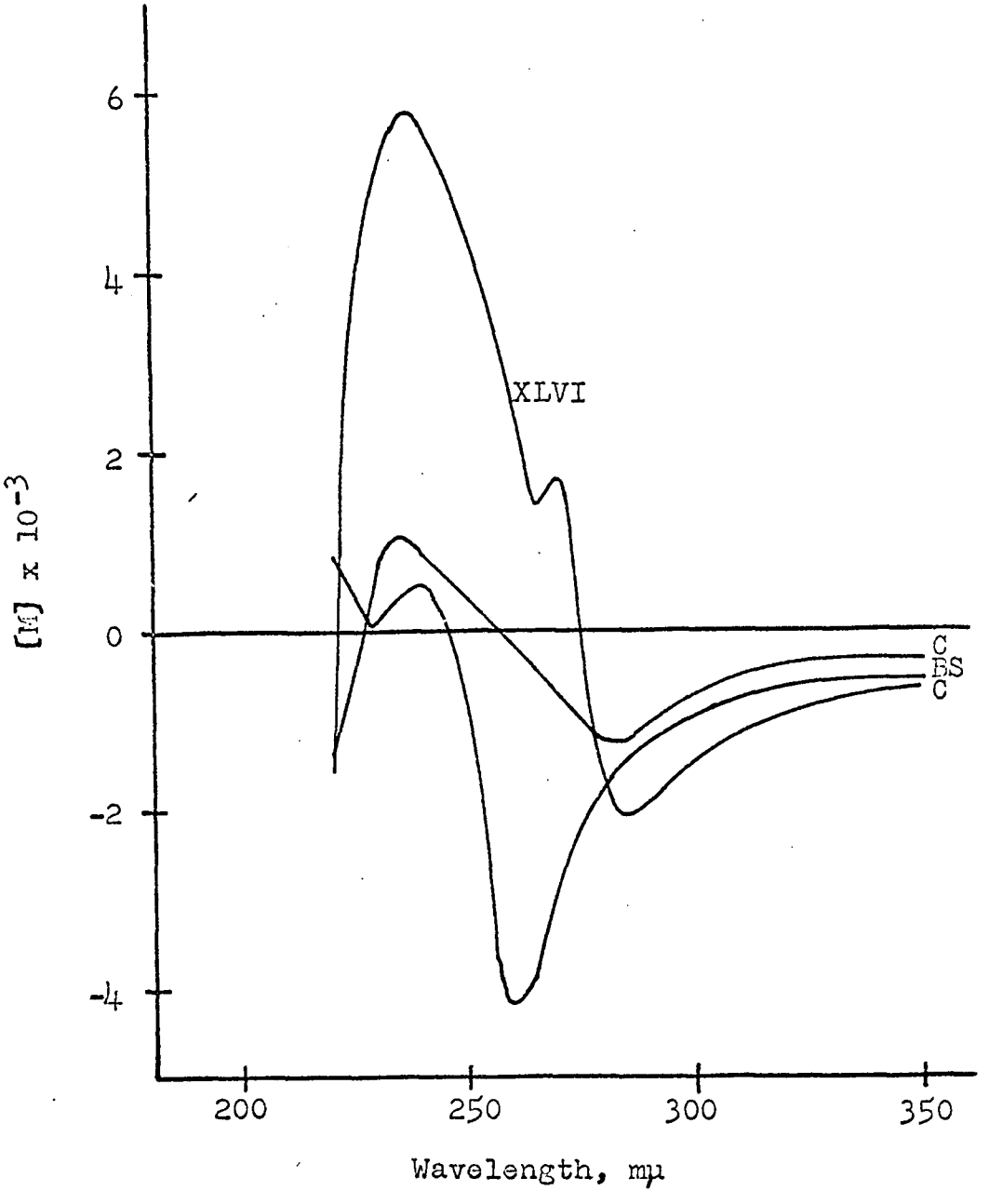


Fig. 24. Optical Rotatory Dispersion Curves of D-Galactose Osotriazole (XX) obtained from the Cary 60 (C) and the Bellingham-Stanley (BS) and D-Galactose Osotriazole Tetraacetate (XLVI) obtained from the Cary 60. Methanol was employed as the solvent. (Table VIII)

SOLVENT STUDY ROTATORY DISPERSION CURVES

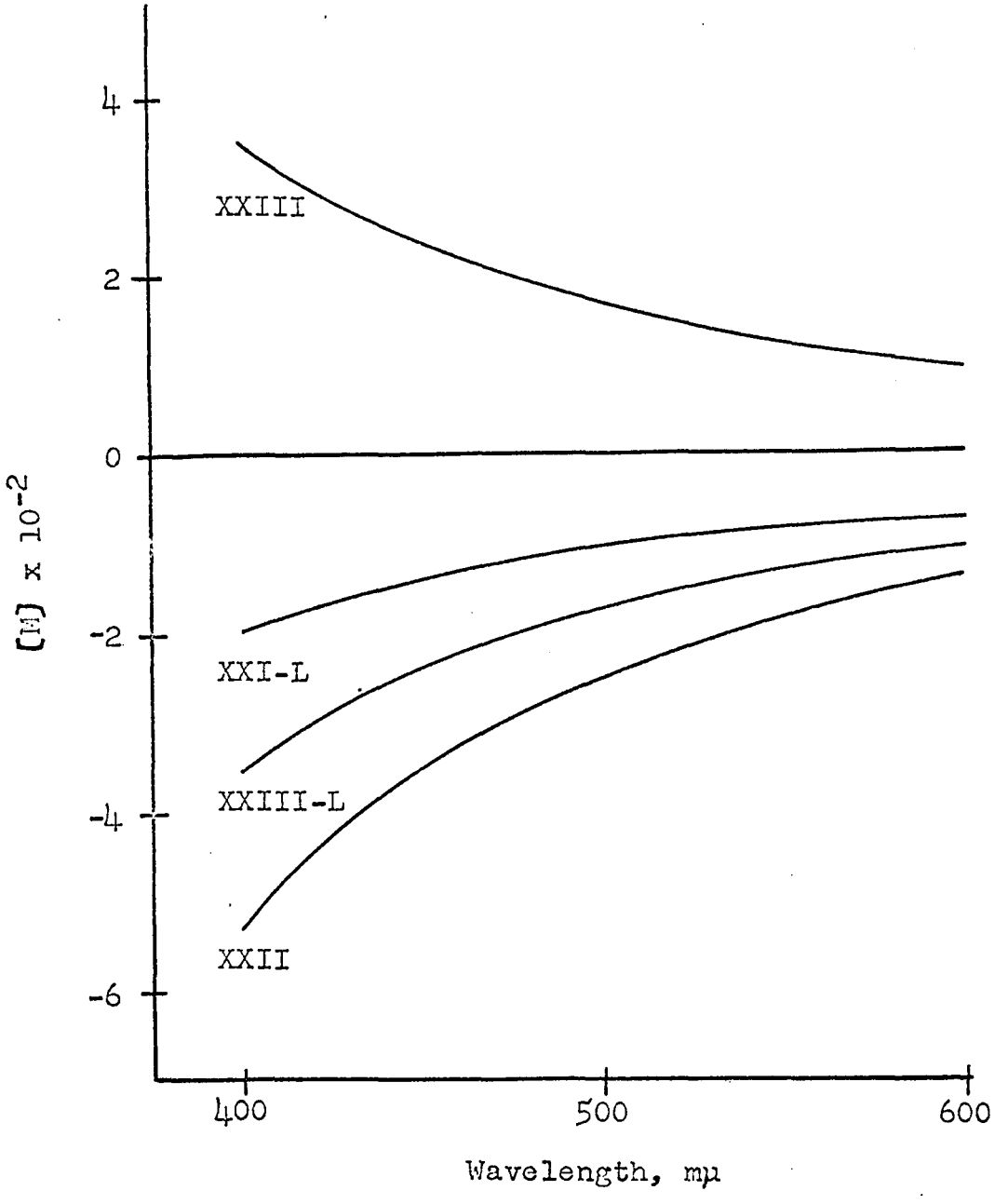


Fig. 25. RD Curves of D-Erythrose Osotriazole (XXIII), L-Erythrose Osotriazole (XXIII-L), D-Xylose Osotriazole (XXII) and L-Arabinose Osotriazole (XXI-L). The curves were obtained from the Rudolph instrument using pyridine as the solvent. (Table IXa)

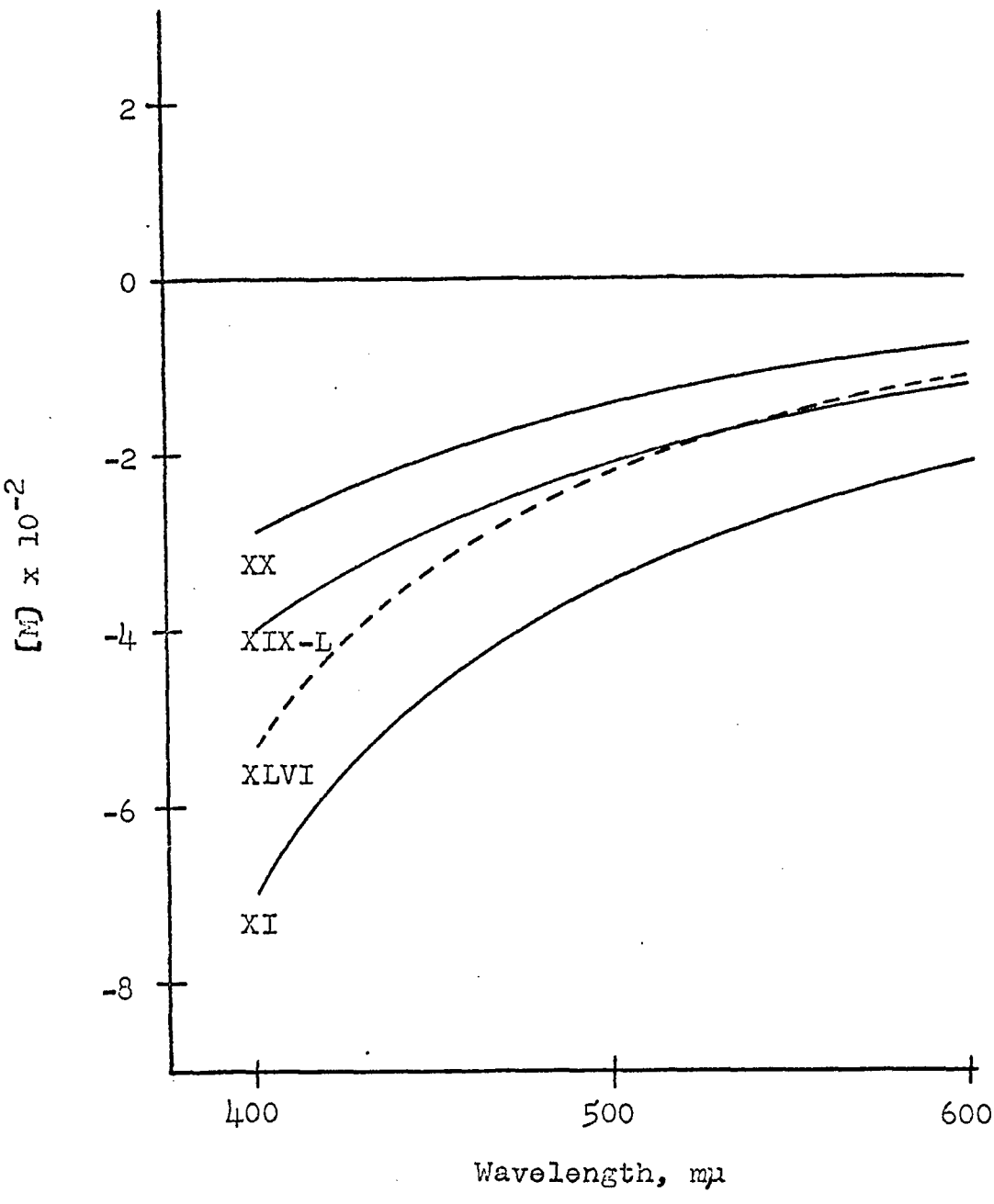


Fig. 26. RD Curves of D-Glucose Osotriazole (XI), L-Sorbose Osotriazole (XIX-L), D-Galactose Osotriazole (XX) and D-Galactose Osotriazole Tetraacetate (XLVI). The curves were obtained from the Rudolph instrument using pyridine as the solvent. (Table IXb & XIII)

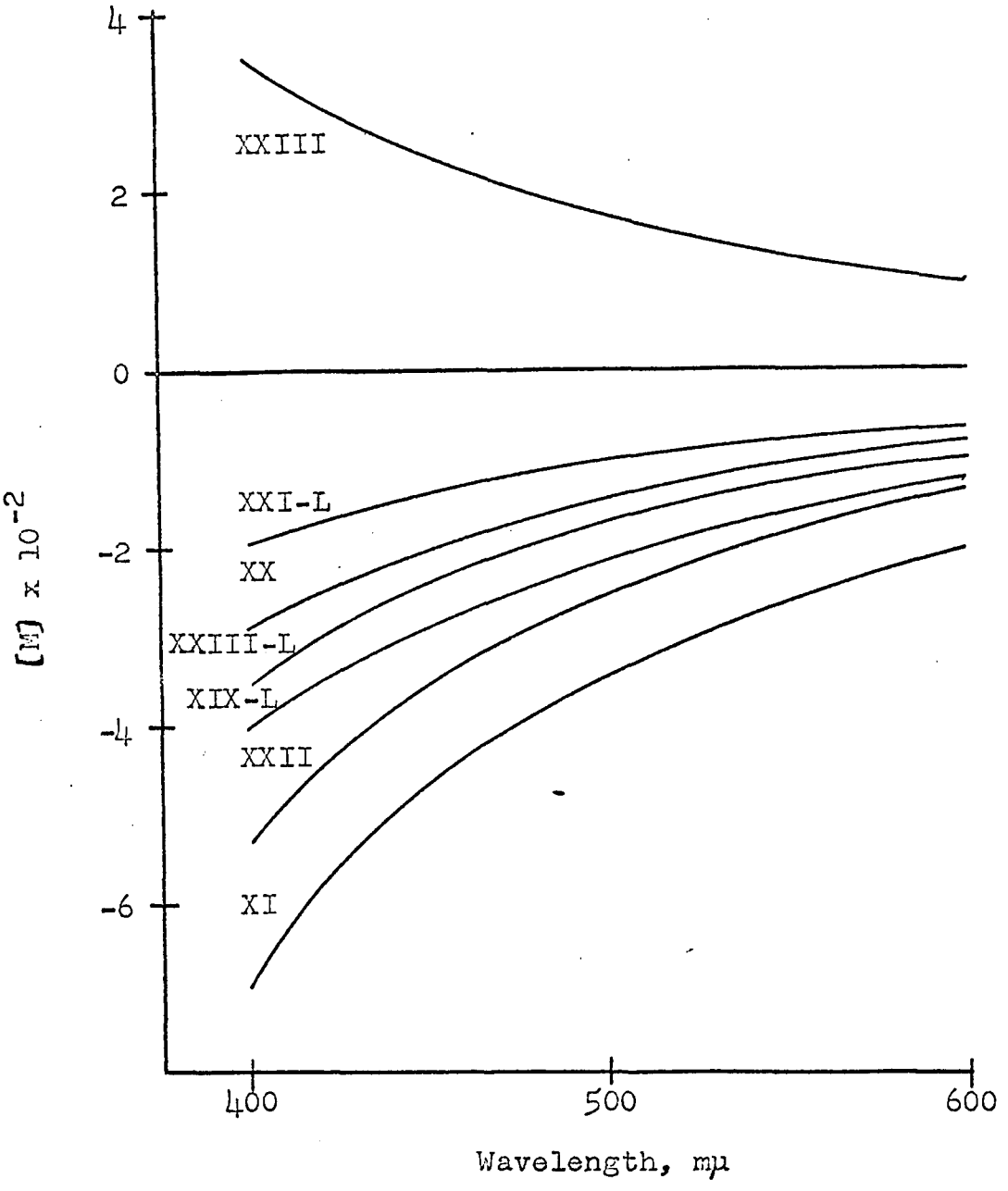


Fig. 27. RD Curves of D-Erythrose Osotriazole (XXIII), L-Arabinose Osotriazole (XXI-L), D-Galactose Osotriazole (XX), L-Erythrose Osotriazole (XXIII-L), L-Sorbose Osotriazole (XIX-L), D-Xylose Osotriazole (XXII) and D-Glucose Osotriazole (XI). The curves were obtained from the Rudolph instrument using pyridine as the solvent. (Table IXa & b)

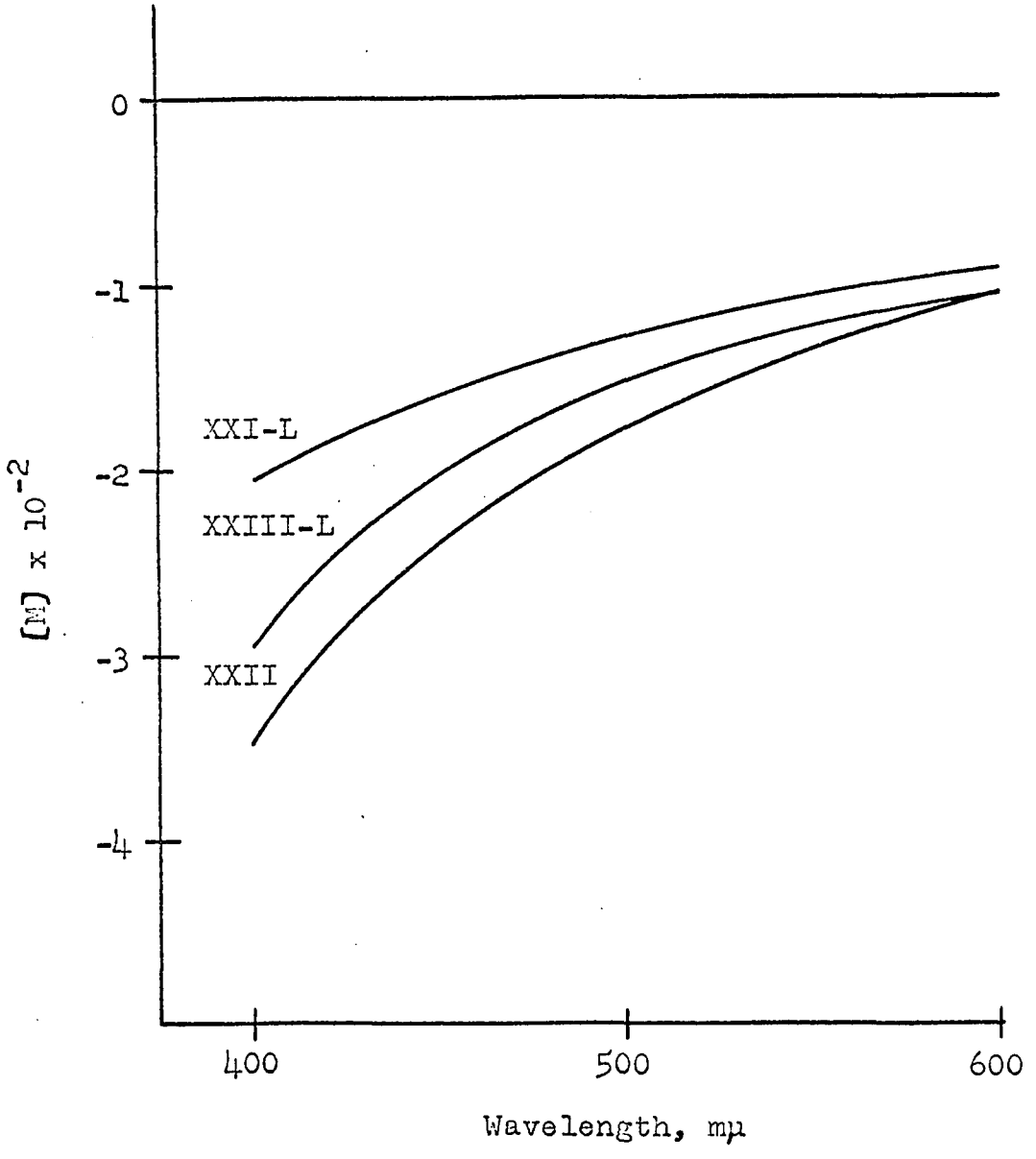


Fig. 28. RD Curves of L-Erythrose Osotriazole (XXIII-L), L-Arabinose Osotriazole (XXI-L), and D-Xylose Osotriazole (XXII). The curves were obtained from the Rudolph instrument using methanol as the solvent. (Table Xa)

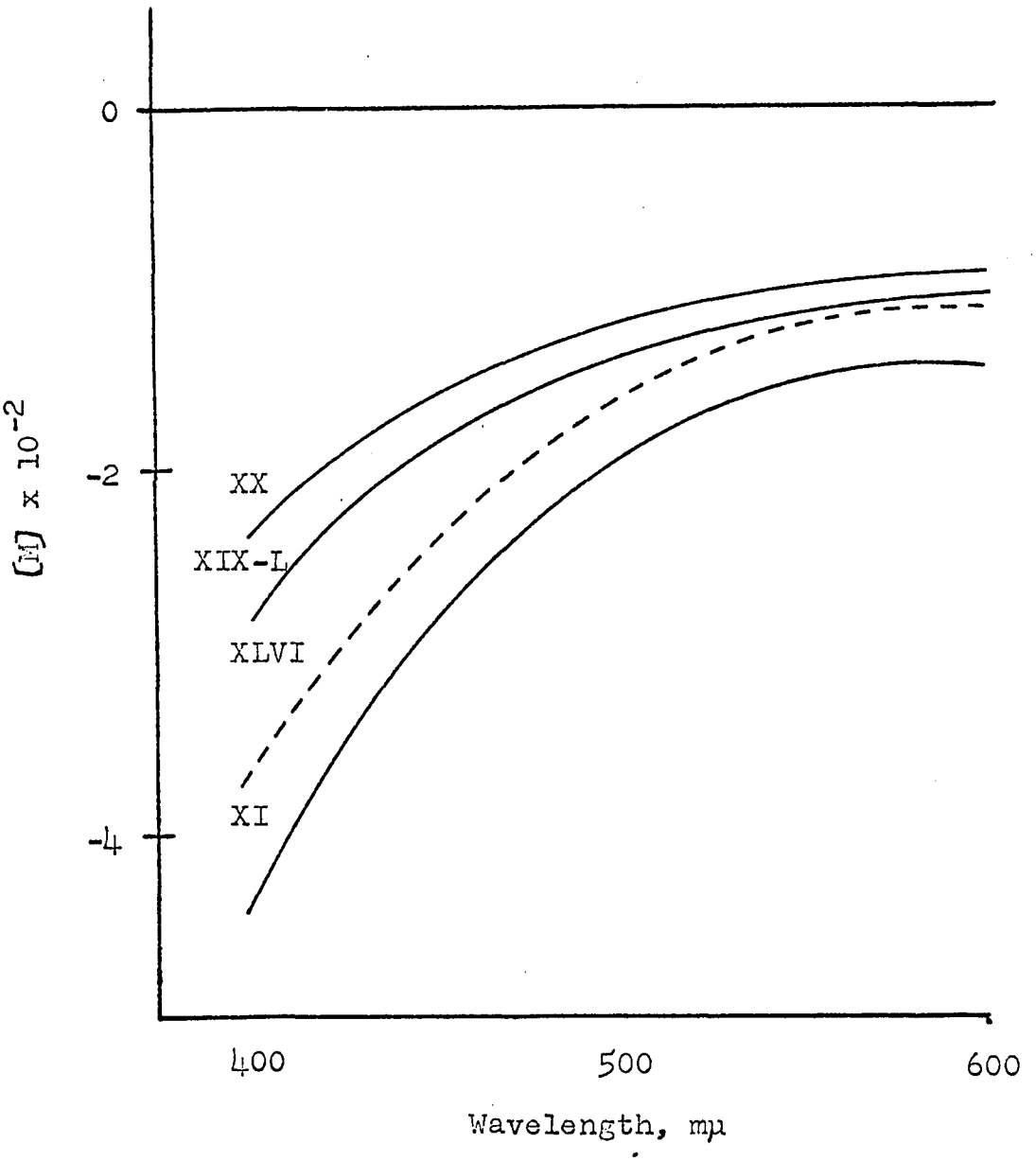


Fig. 29. RD Curves of D-Galactose Osotriazole (XX), L-Sorbose Osotriazole (XIX-L), D-Galactose Osotriazole Tetra-acetate (XLVI) and D-Glucose Osotriazole (XI). The curves were obtained from the Rudolph instrument using methanol as the solvent. (Table Xa & XIII)

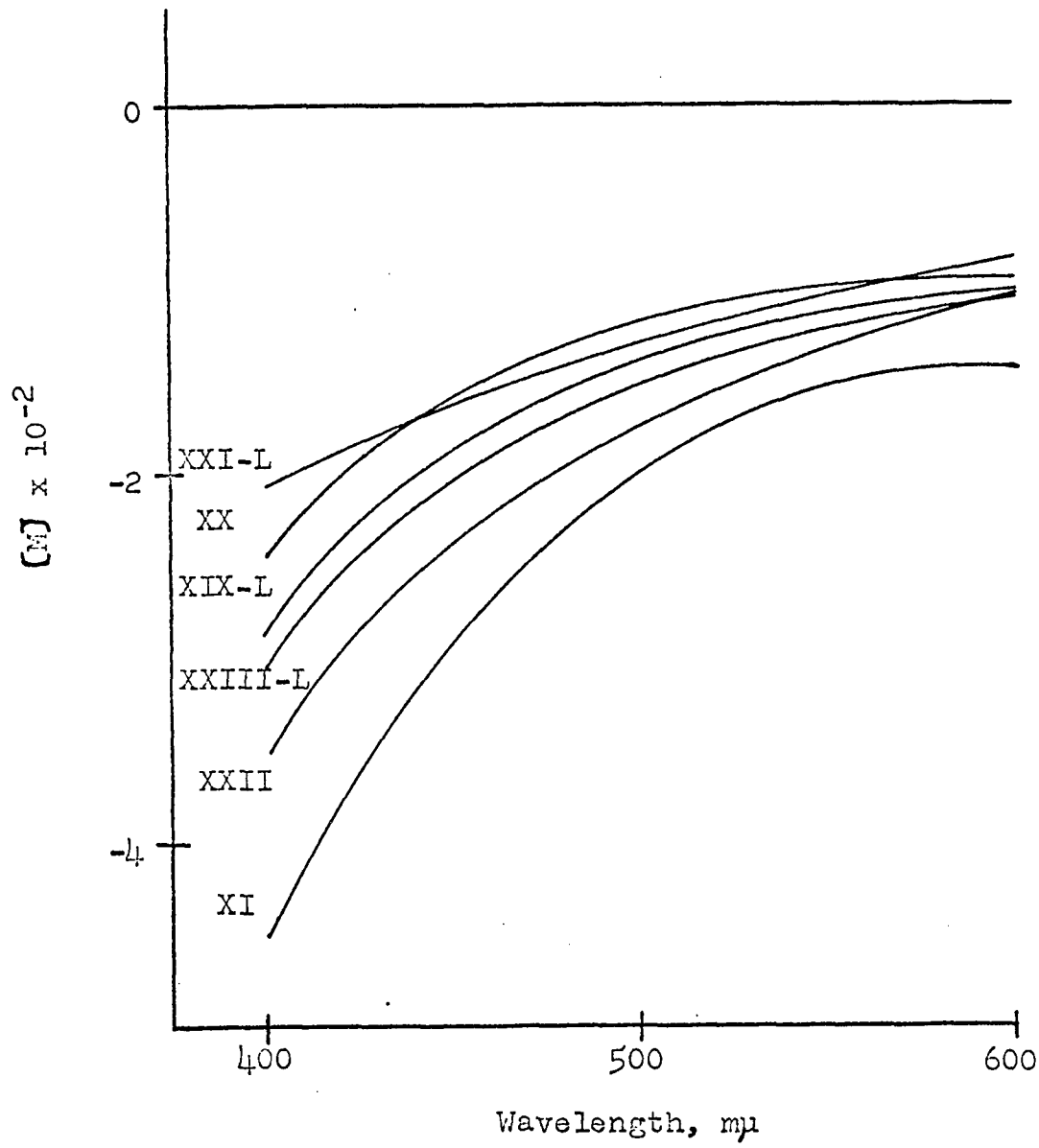


Fig. 30. RD Curves of L-Arabinose Osotriazole (XXI-L), D-Galactose Osotriazole (XX), L-Sorbose Osotriazole (XIX-L), L-Erythrose Osotriazole (XXIII-L), D-Xylose Osotriazole (XXII) and D-Glucose Osotriazole (XI). The curves were obtained from the Rudolph instrument using methanol as the solvent. (Table Xa & b)

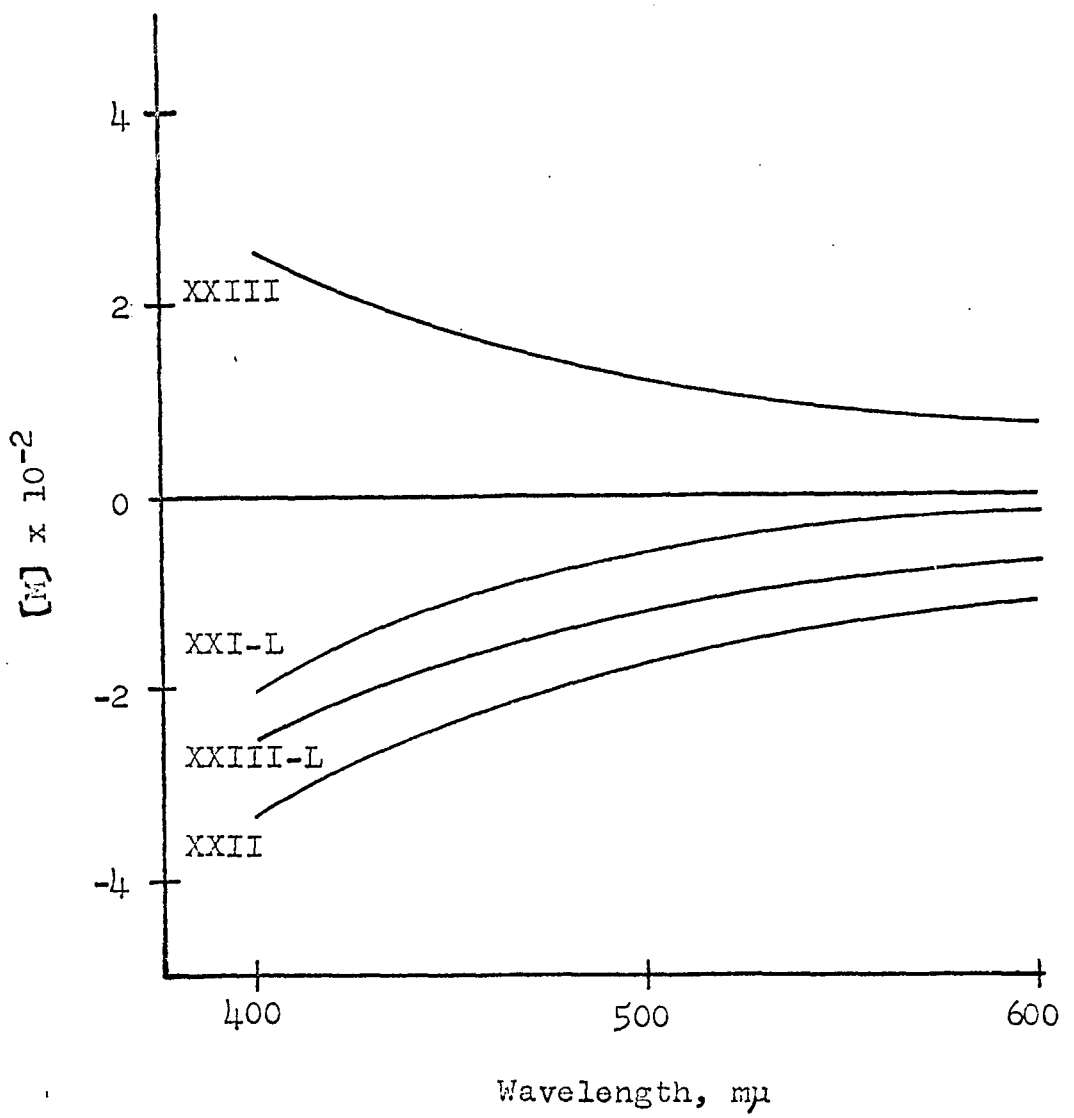


Fig. 31. RD Curves of D-Erythrose Osotriazole (XXIII), L-Arabinose Osotriazole (XXI-L), L-Erythrose Osotriazole (XXIII-L) and D-Xylose Osotriazole (XXII). The curves were obtained from the Rudolph instrument using acetic acid as the solvent. (Table XIa)

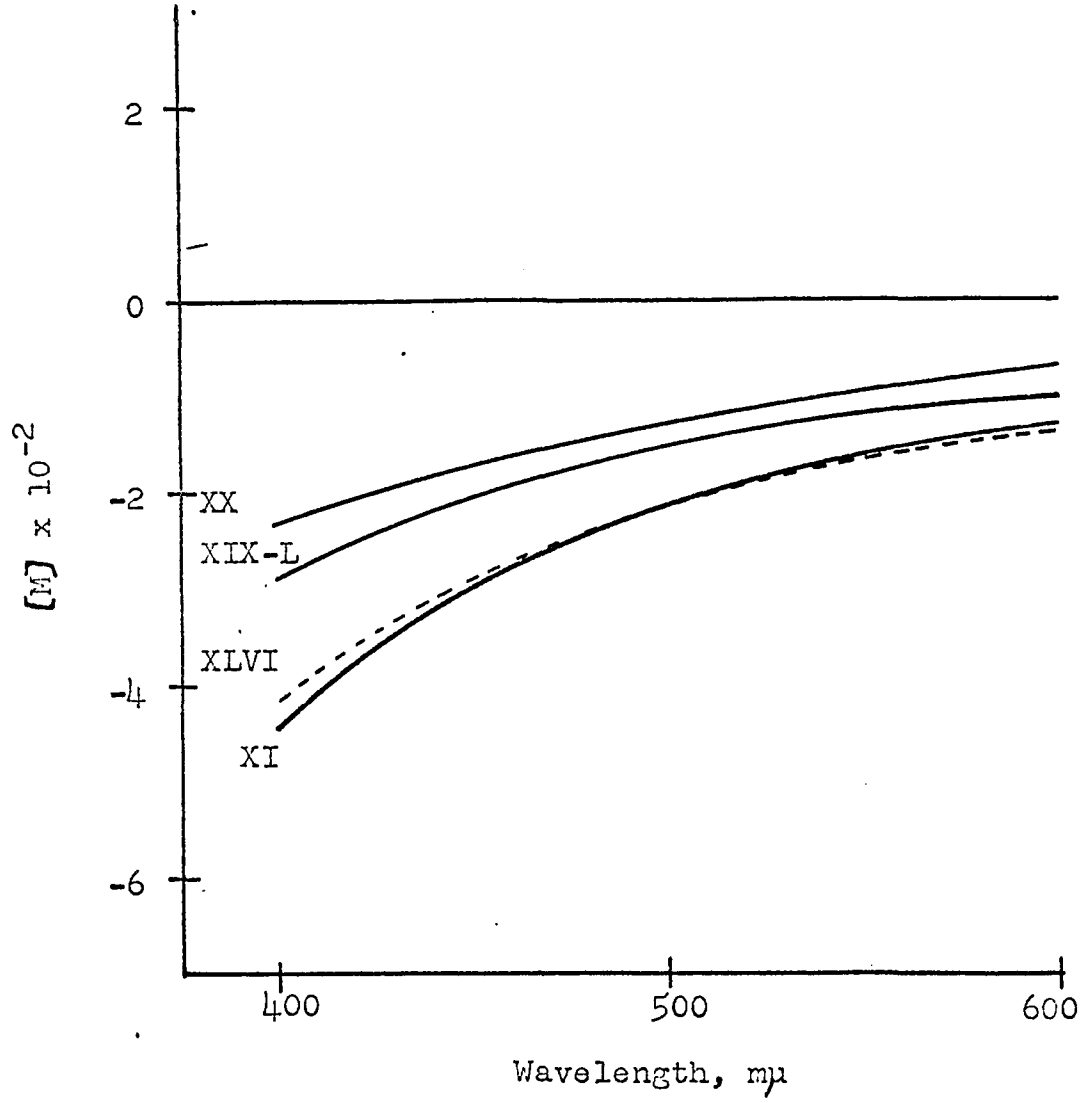


Fig. 32. RD Curves of D-Glucose Osotriazole (XI), L-Sorbose Osotriazole (XIX-L), D-Galactose Osotriazole (XX) and D-Galactose Osotriazole Tetraacetate (XLVI). The curves were obtained from the Rudolph instrument using acetic acid as the solvent. (Table XIb & XIII)

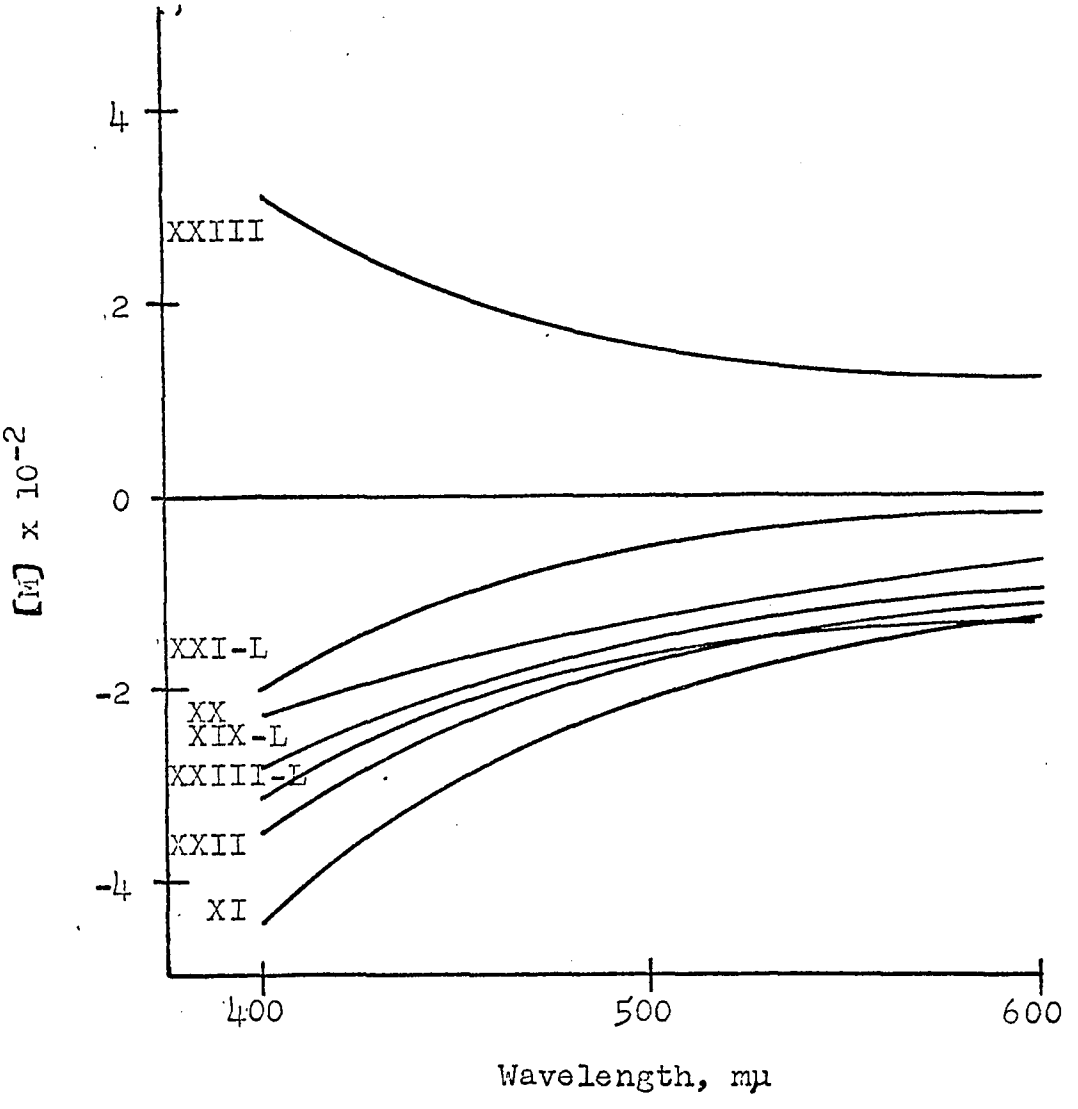


Fig. 33. RD Curves of D-Erythrose Osotriazole (XXIII), L-Arabinose Osotriazole (XXI-L), D-Galactose Osotriazole (XX), L-Sorbose Osotriazole (XIX-L), L-Erythrose Osotriazole (XXIII-L), D-Xylose Osotriazole (XXII) and D-Glucose Osotriazole (XI). The curves were obtained from the Rudolph instrument using acetic acid as the solvent. (Table XIa & b)

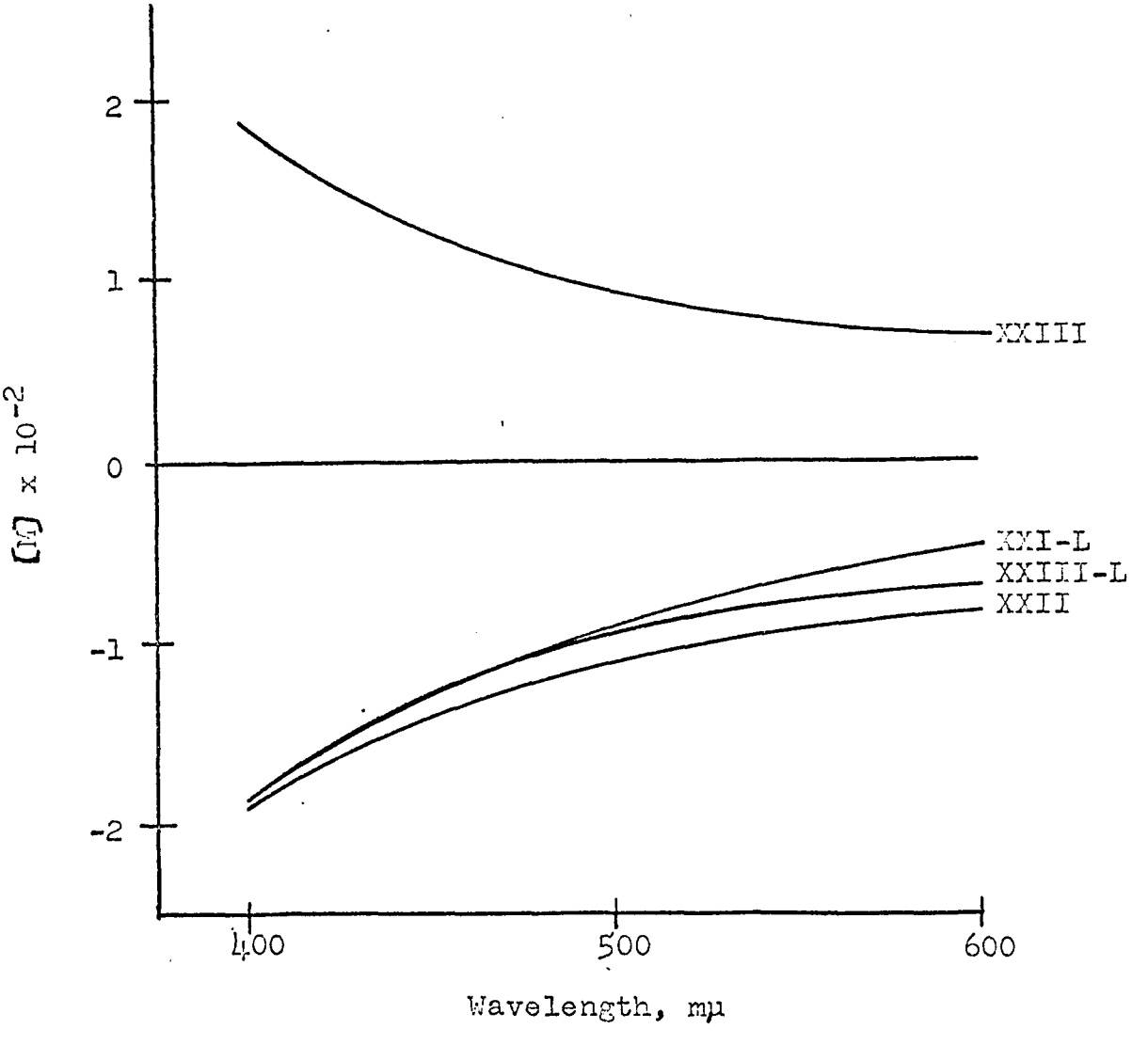


Fig. 34. RD Curves of D-Erythrose Osotriazole (XXIII), L-Arabinose Osotriazole (XXI-L), L-Erythrose Osotriazole (XXIII-L) and D-Xylose Osotriazole (XXII). The curves were obtained from the Rudolph instrument using water as the solvent. (Table XIIa)

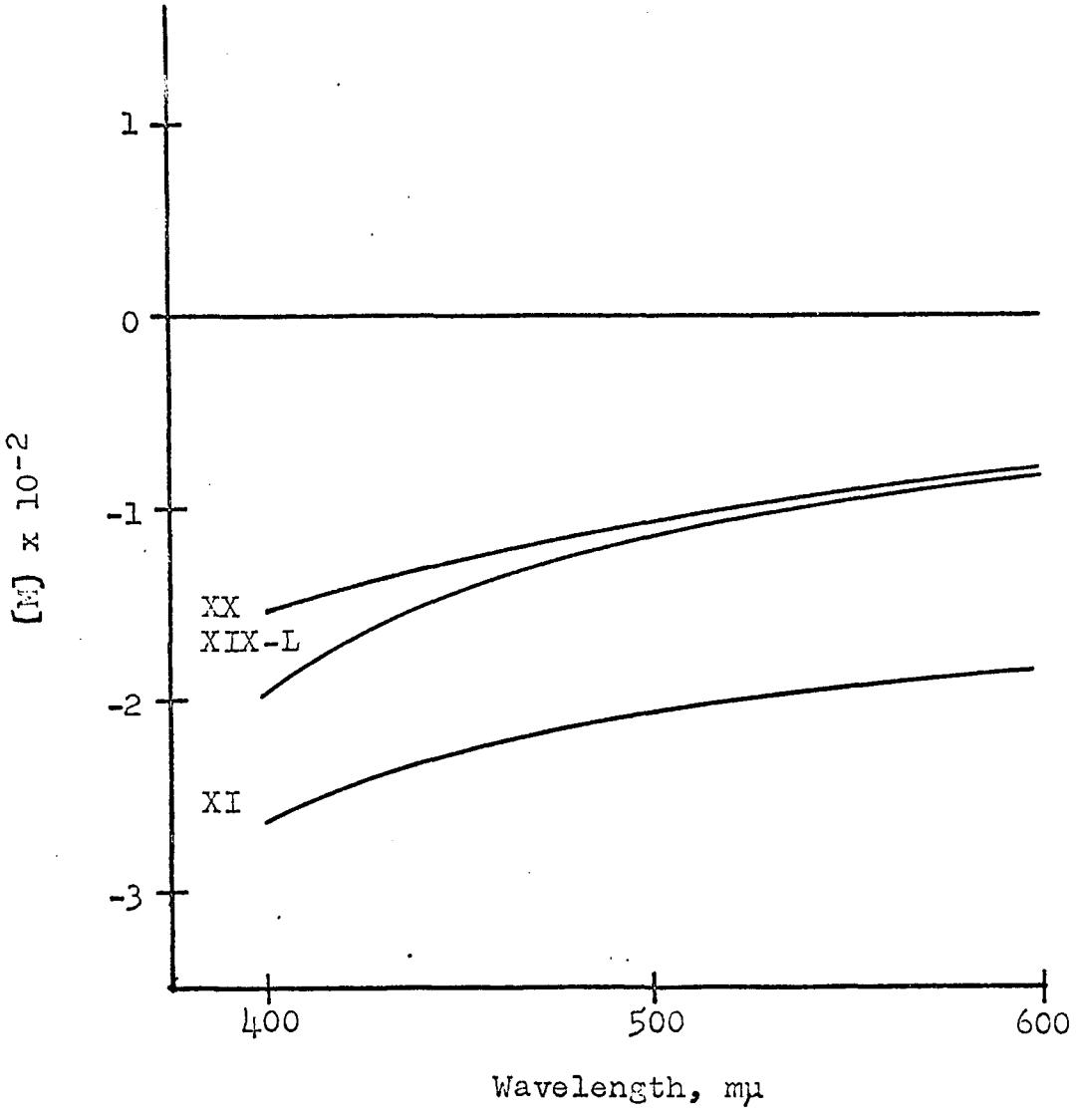


Fig. 35. RD Curves of D-Galactose Osotriazole (XX), L-Sorbose Osotriazole (XIX-L) and D-Glucose Osotriazole (XI). The curves were obtained from the Rudolph instrument using water as the solvent. (Table XIIb)

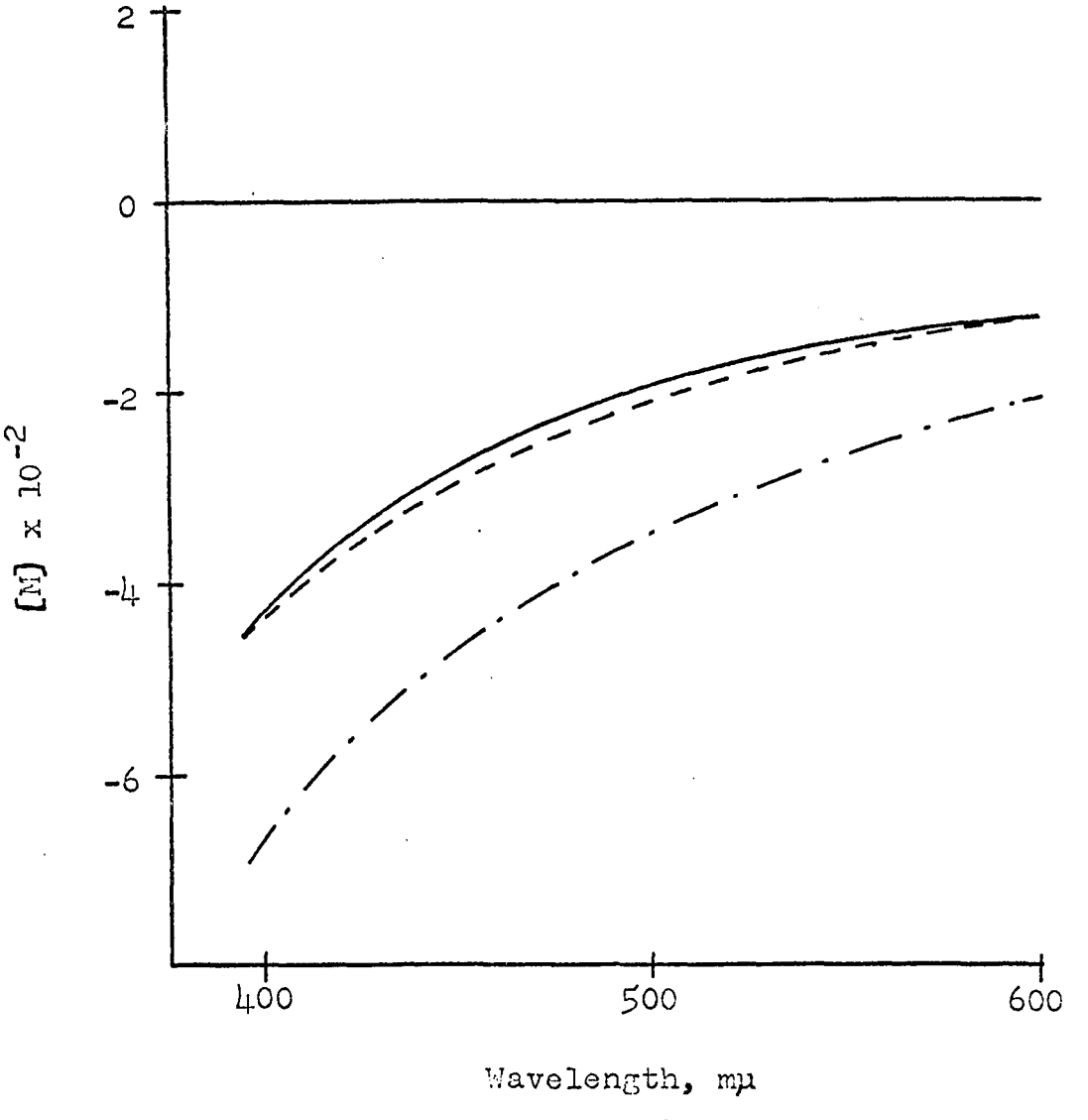


Fig. 36. RD Curves of D-Glucose Osotriazole (XI). The curves were obtained from the Rudolph instrument using acetic acid (— — —), methanol (————), and pyridine (—·—) as the solvents. (Table IXb, Xb, XIb, & XIIb)

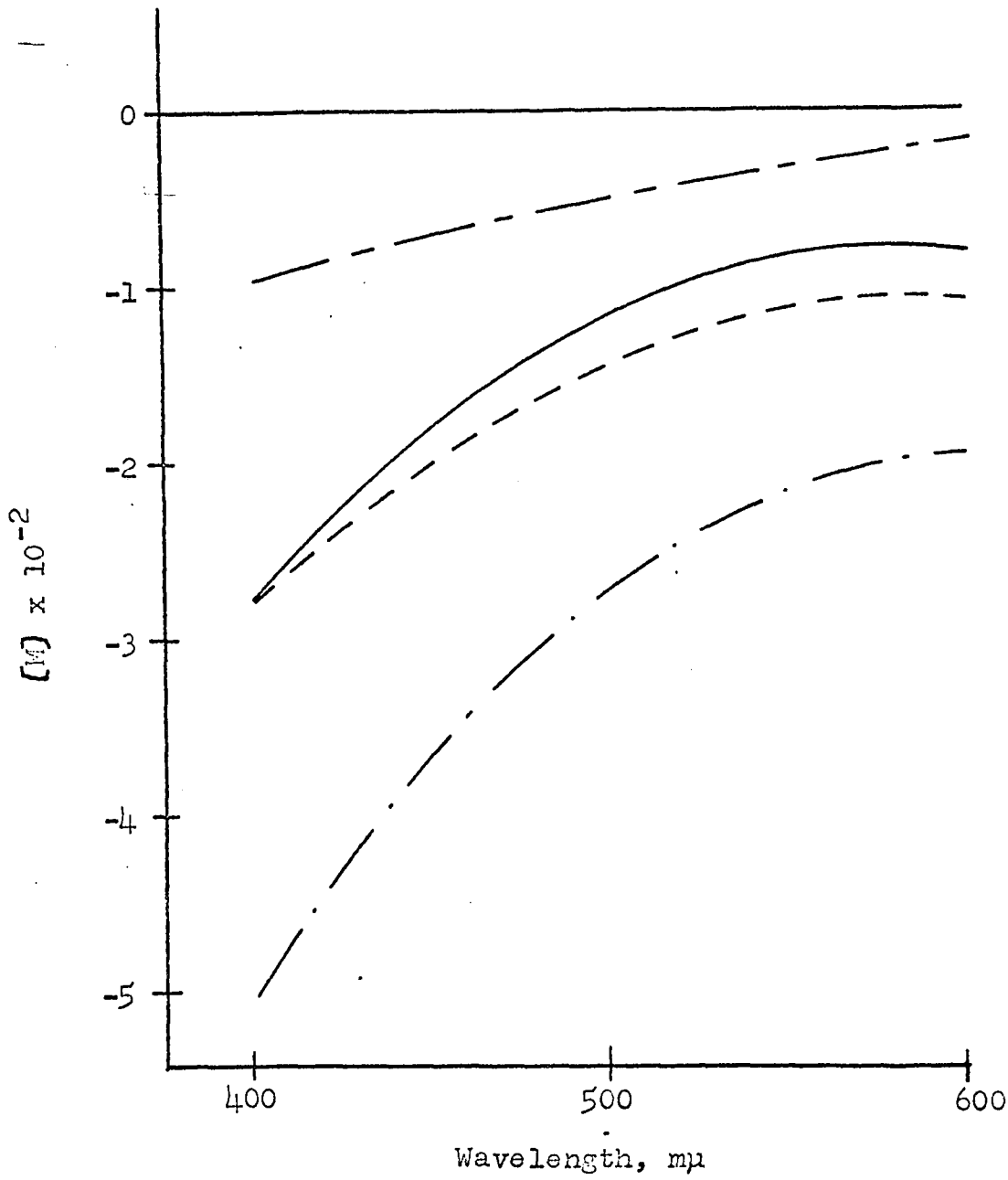


Fig. 37. RD Curves of L-Sorbose Osotriazole (XIX-L). The curves were obtained from the Rudolph instrument using pyridine (— · —), methanol (————), acetic acid (— — —) and water (— - —) as the solvents. (Tables IXb, Xb, XIb, & XIIb)

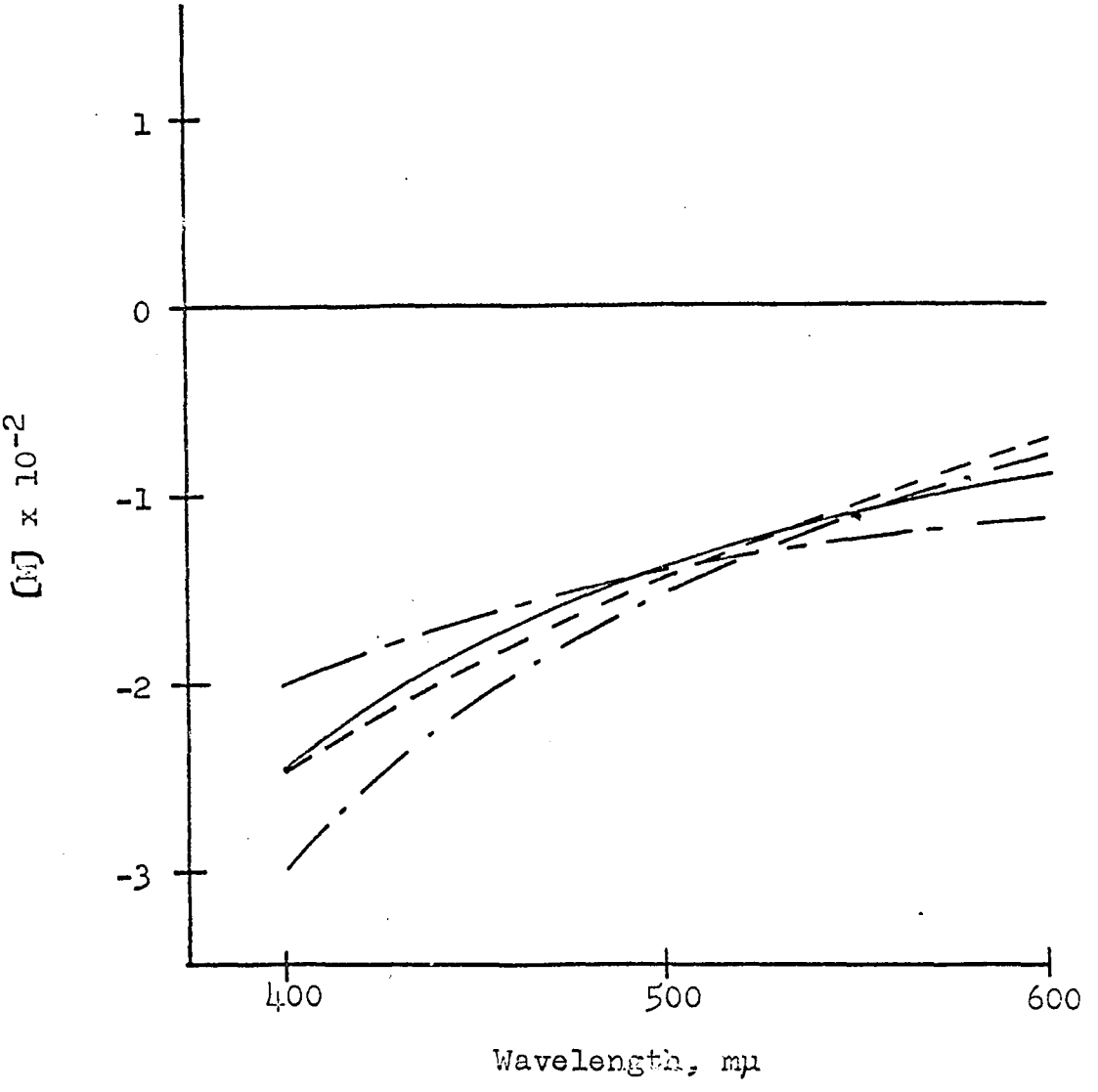


Fig. 38. RD Curves of D-Galactose Osotriazole (XX). The curves were obtained from the Rudolph instrument using pyridine (——·——), methanol (————), acetic acid (— — —) and water (—— - ——). (Tables IXb, Xb, XIb, XIIb)

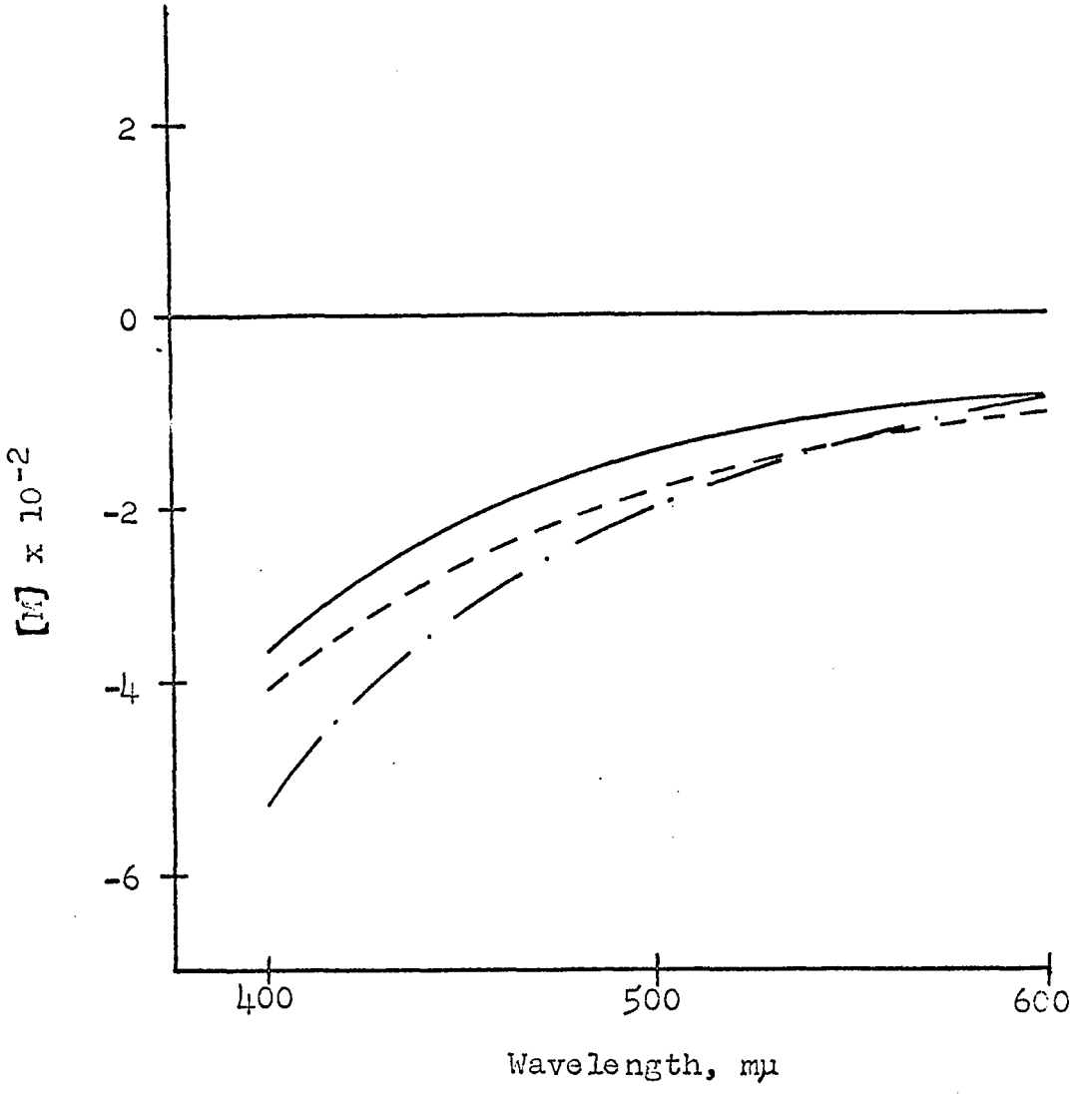


Fig. 39. RD Curves of D-Galactose Osotriazole Tetraacetate (XLVI). The curves were obtained from the Rudolph instrument using pyridine (— · —), methanol (———) and acetic acid (— — —). (Table XIII)

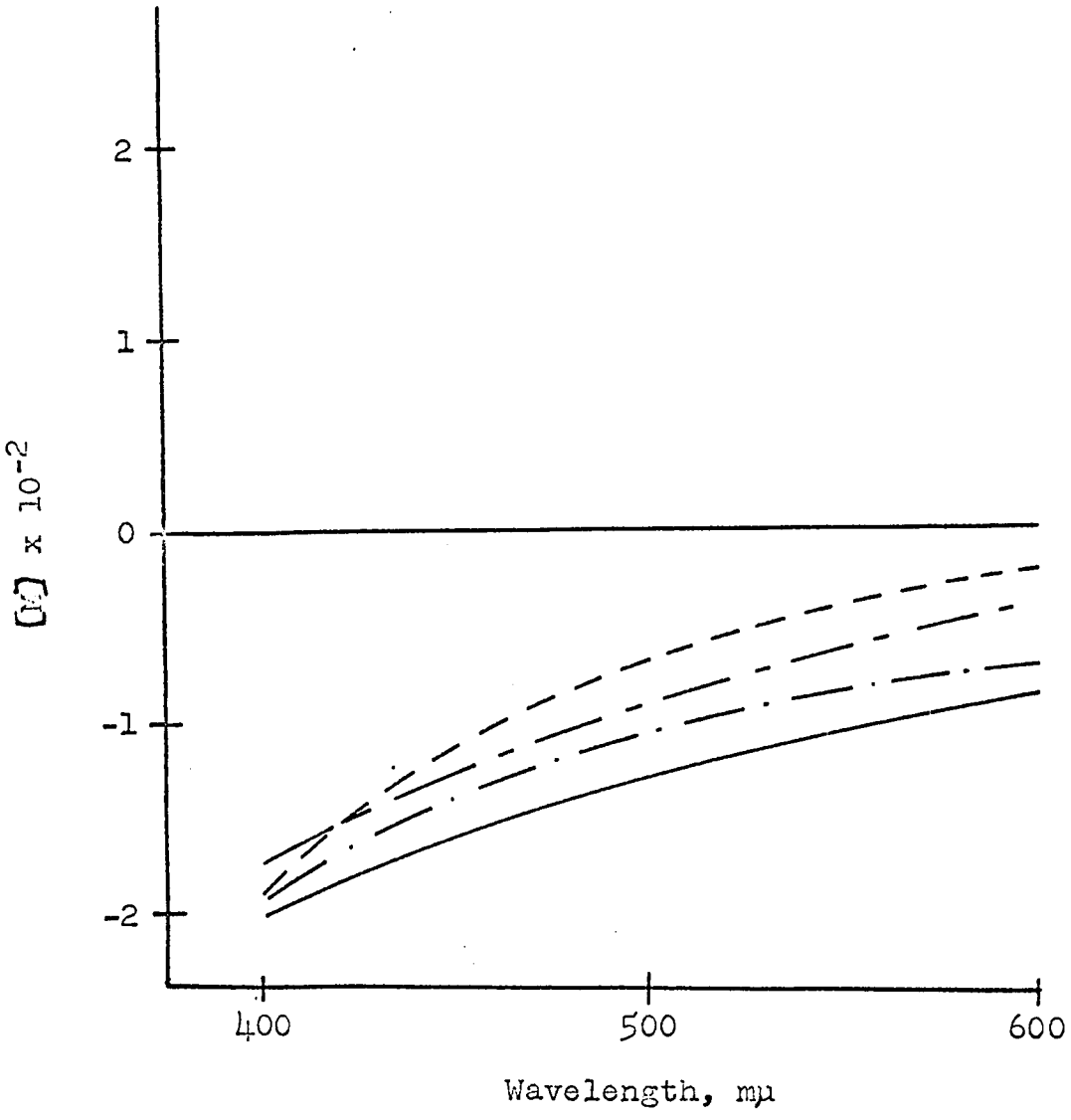


Fig. 40. RD Curves of L-Arabinose Osotriazole (XXI-L). The curves were obtained from the Rudolph instrument using pyridine (— · —), methanol (————), acetic acid (— — —) and water (— - —). (Tables IXa, Xa, XIa, & XIIa)

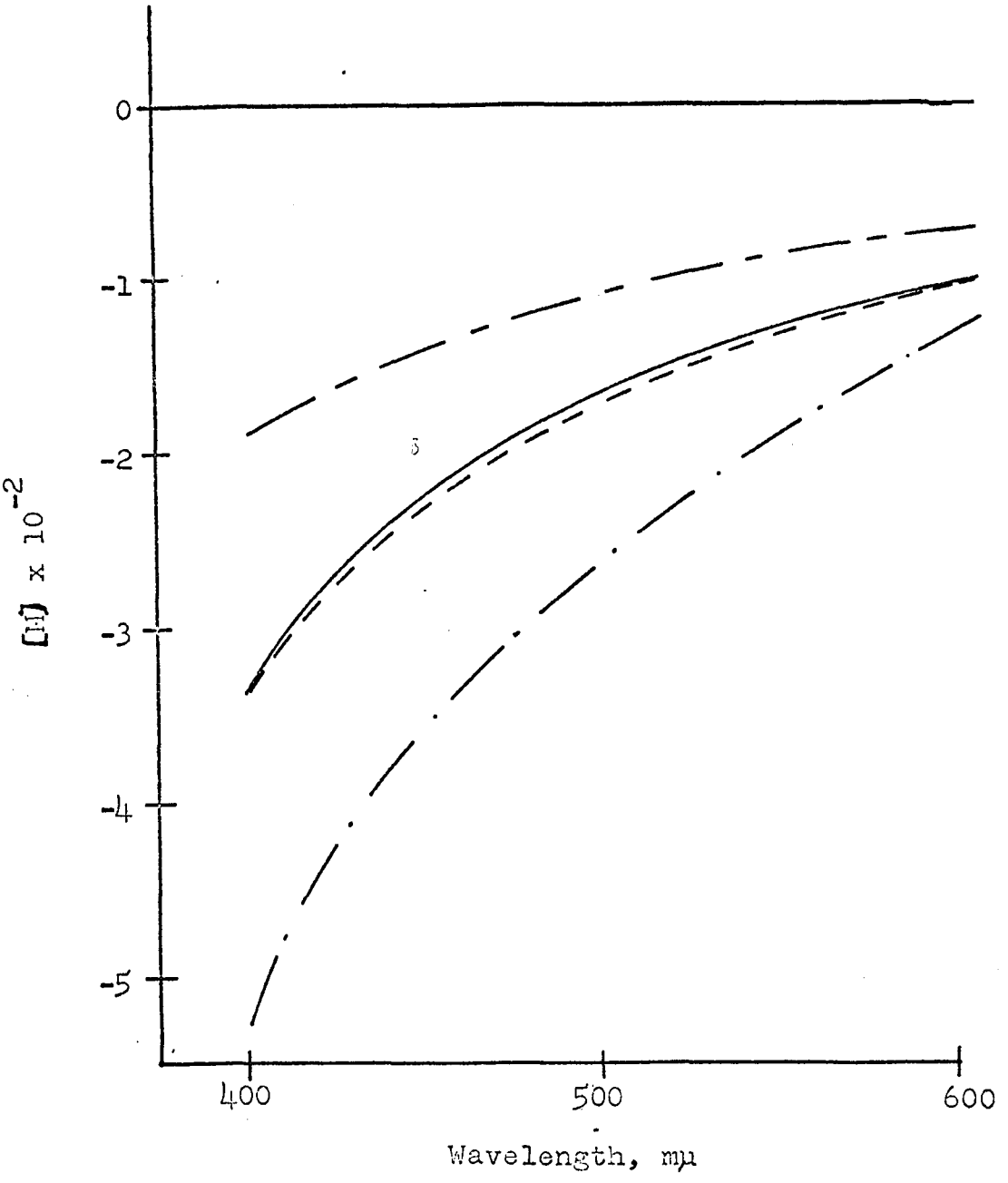


Fig. 41. RD Curves of D-Xylose Osotriazole (XXII). The curves were obtained from the Rudolph instrument using pyridine (—·—), methanol (————), acetic acid (— — —) and water (— - —). (Tables IXa, Xa, XIa & XIIa)

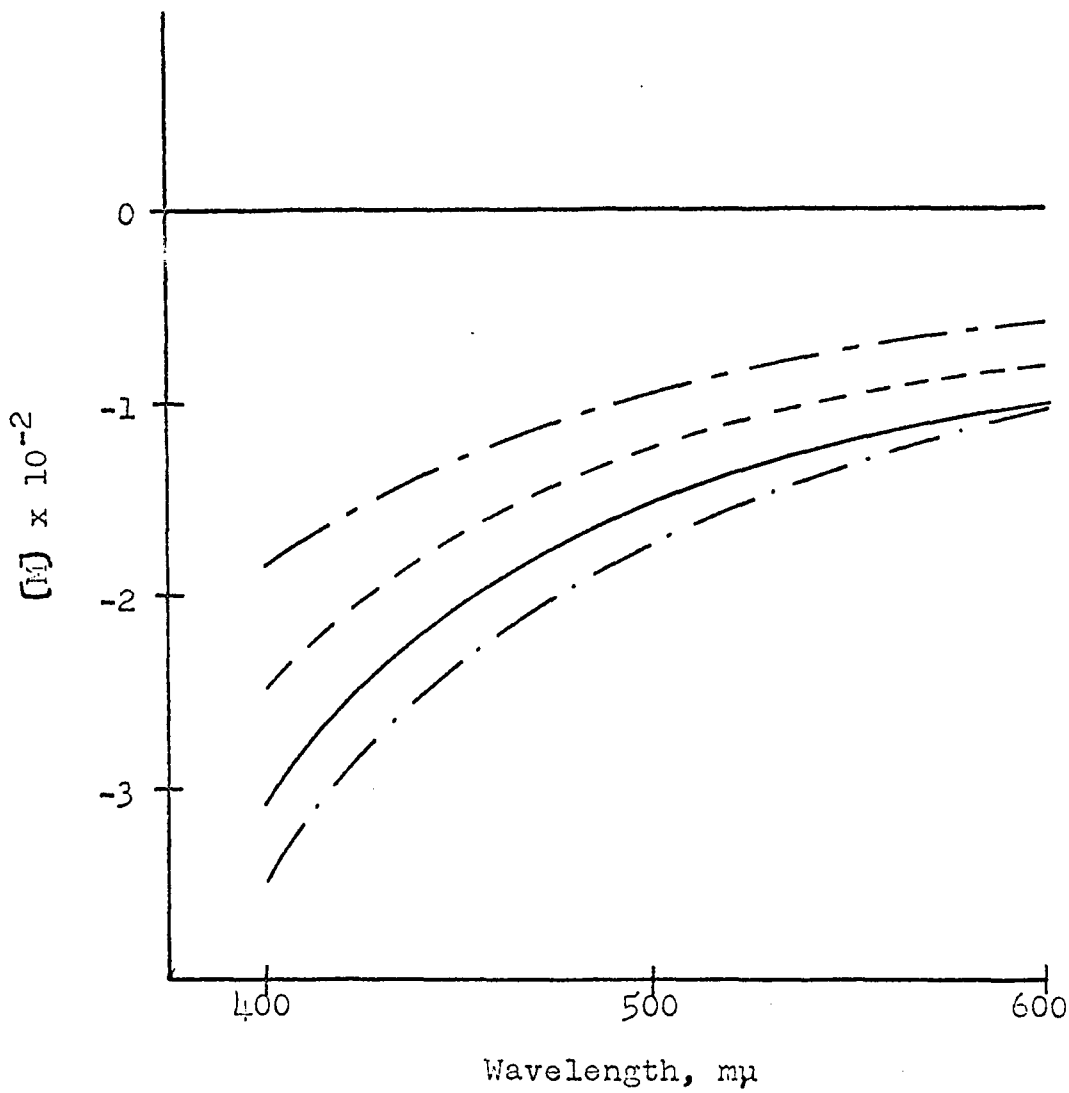


Fig. 42. RD Curves of L-Erythrose Osotriazole (XXIII-L). The curves were obtained from the Rudolph instrument using pyridine (—— · ——), methanol (————), acetic acid (— — —) and water (—— - ——). (Tables IXa, Xa, XIa, & XIIa)

OPTICAL ROTATORY DISPERSION DATA

TABLE VIII

OPTICAL ROTATORY DISPERSION DATA

Osotriazole of:	D-Erythrose (XXIII)		D-Erythrose (XXIII)		D-Xylose (XXII)		L-Arabinose (XXI-L)		D-Galactose (XX)	
Molecular Weight:	205		205		235		235		265	
Concentration: (g/100ml)	0.0187		0.028		0.025		0.023		0.0267	
Solvent:	Methanol		Methanol		Methanol		Methanol		Methanol	
Path Length:	0.1 dcm.		0.1 dcm.		0.1 dcm.		0.1 dcm.		0.1 dcm.	
Instrument:	Bellingham-Stanley		Cary 60		Bellingham-Stanley		Cary 60		Bellingham-Stanley	
	λ(mμ)	[M]	λ(mμ)	[M]	λ(mμ)	[M]	λ(mμ)	[M]	λ(mμ)	[M]
	300	+560	350	+457	325	-1297	300	-870	400	-510
	279	+1300	300	+2811	305	-2012	279	-2080	290	-1200
	273	0	283	+3760	286	-3046	264	-5550	276	-2020
	256	-3900	250	0	266	0	248	0	-260	-4220
	242	-1870	240	-703	242	+2870	232	+2080	245	0
	229	-3740	234	0	221	+790	217	0	238	+510
	219	-560	215	+2811	215	+846			228	0
	211	-4100	210	+465					221	+850
	209	-3360								

TABLE VIII Cont.

OPTICAL ROTATORY DISPERSION DATA

Osotriazole of:	D-Galactose (XX)	D-Galactose Tetraacetate (XLVI)	L-Sorbose (XIX-L)	D-Glucose (XI)
Molecular Weight:	265	433	265	265
Concentration: (g/100ml)	0.045	0.085	0.0045	0.003
Solvent:	Methanol	Methanol	Methanol	Methanol
Path Length:	0.1 dcm.	0.1 dcm.	0.1 dcm.	0.1 dcm.
Instrument:	Cary 60	Cary 60	Cary 60	Cary 60

λ(mμ)	[M]	λ(mμ)	[M]	λ(mμ)	[M]	λ(mμ)	[M]
350	-284	350	-589	350	-599	310	-1128
290	-1012	325	-892	325	-917	300	-2820
284	-1154	285	-2117	285	-3108	286	-7360
256	0	274	0	271	0	268	0
234	+1036	270	+1650	245	+3768	245	+12140
227	0	264	+1303	240	+2828	240	+11600
220	-1508	236	+5781	235	+3676	235	+12260
		221	0	225	+1884	215	0
		220	-1139				

SOLVENT STUDY ROTATORY DISPERSION DATA

TABLE IXa

R.D. Data for D-Erythrose Osotriazole (XXIII), D-Xylose Osotriazole (XXII) and L-Arabinose Osotriazole (XXI-L) in Pyridine

Osotriazole of:	D-Erythrose (XXIII)	D-Xylose (XXII)	L-Arabinose (XXI-L)
Molecular Weight:	205	235	235
Concentration: (g/100ml)	0.5265	.0.4000	0.4005
Path Length:	0.1 dcm.	0.1 dcm.	0.1 dcm.
Temperature:	22.7°	22.7°	22.7°
λ(mμ)	(+) [M]	(-) [M]	(-) [M]
600	105	135	76
589	109	147	76
580	117	159	82
575*	118	162	82
570	121	165	82
560	129	170	88
550	132	182	94
540	140	200	100
530	148	212	100
525*	150	218	100
520	152	224	100
510	164	240	106
500	171	247	106
490	179	270	117

TABLE IXa Cont.

Osotriazole of:	D-Erythrose (XXIII)	D-Xylose (XXII)	L-Arabinose (XXI-L)
λ(mμ)	(+) [M]	(-) [M]	(-) [M]
480	195	282	117
475*	200	290	123
470	207	300	123
460	218	329	129
450	234	353	135

*Not included in Drude equation solvent study

TABLE IXb

R.D. Data for D-Galactose Osotriazole (XX), L-Sorbose Osotriazole (XIX-L) and D-Glucose Osotriazole (XI) in Pyridine

Osotriazole of:	D-Galactose (XX)	L-Sorbose (XIX-L)	D-Glucose (XI)
Molecular Weight:	265	265	265
Concentration: (g/100ml)	0.363	0.4005	0.3876
Path Length:	0.1 dcm.	0.1 dcm.	0.1 dcm.
Temperature:	22°	22.9°	23°

λ (mμ)	(-) [M]	(-) [M]	(-) [M]
600	73	126	205
589	88	133	219
580	95	139	232
575*	97	143	239
570	102	146	246
560	110	153	260
550	117	159	273
540	124	172	280
530	131	179	287
525*	135	185	295
520	139	193	301
510	146	199	321
500	153	212	341
490	161	225	362

TABLE IXb Cont.

Osotriazole of:	D-Galactose (XX)	L-Sorbose (XIX-L)	D-Glucose (XI)
λ (mμ)	(-) [M]	(-) [M]	(-) [M]
480	175	238	390
475*	180	245	400
470	183	251	410
460	190	271	437
450	204	292	472

*Not included in Drude equation solvent study

TABLE Xa

R.D. Data for D-Erythrose Osotriazole (XXIII), D-Xylose Osotriazole (XXII) and L-Arabinose Osotriazole (XXI-L) in Methanol

Osotriazole of:	D-Erythrose (XXIII)	D-Xylose (XXII)	L-Arabinose (XXI-L)
Molecular Weight:	205	235	235
Concentration: (g/100ml)	0.280	0.445	0.493
Path Length:	0.1 dcm.	0.1 dcm.	0.1 dcm.
Temperature:	22°	26°	26°

λ (mμ)	(+) [M]	(-) [M]	(-) [M]
600	110	106	86
589	117	106	86
580	117	106	86
575*	117	106	86
570	117	106	86
560	132	111	86
550	132	116	114
540	132	127	114
530	139	137	114
525*	139	148	124
520	139	148	124
510	146	158	124
500	154	180	133
490	161	190	143

TABLE Xa Cont.

Osotriazole of:	D-Erythrose (XXIII)	D-Xylose (XXII)	L-Arabinose (XXI-L)
λ(mμ)	(+) [M]	(-) [M]	(-) [M]
480	168	195	152
475*	175	211	153
470	183	211	157
460	190	222	167
450	205	242	172

*Not included in Drude equation solvent study

TABLE Xb

R.D. Data for D-Galactose Osotriazole (XX), L-Sorbose Osotriazole (XIX-L) and D-Glucose Osotriazole (XI) in Methanol

Osotriazole of:	D-Galactose (XX)	L-Sorbose (XIX-L)	D-Glucose (XI)
Molecular Weight:	265	265	265
Concentration: (g/100ml)	0.519	0.562	0.493
Path Length:	0.1 dcm.	0.1 dcm.	0.1 dcm.
Temperature:	28°	28°	28°

λ (mμ)	(-) [M]	(-) [M]	(-) [M]
600	92	99	140
589	102	99	140
580	102	108	150
575*	112	108	151
570	112	108	140
560	112	108	140
550	112	113	161
540	112	113	161
530	112	118	161
525*	112	118	161
520	117	118	172
510	138	122	193
500	142	132	215
490	142	141	225

TABLE Xb Cont.

Osotriazole of:	D-Galactose (XX)	L-Sorbose (XIX-L)	D-Glucose (XI)
λ(mμ)	(-) [M]	(-) [M]	(-) [M]
480	168	151	226
475*	174	160	231
470	163	165	236
460	168	174	258
450	174	188	290

*Not included in Drude equation solvent study

TABLE XIa

R.D. Data for D-Erythrose Osotriazole (XXIII), D-Xylose Osotriazole (XXII) and L-Arabinose Osotriazole (XXI-L) in Acetic Acid

Osotriazole of:	D-Erythrose (XXIII)	D-Xylose (XXII)	L-Arabinose (XXI-L)
Molecular Weight:	205	235	235
Concentration: (g/100ml)	0.661	0.450	0.475
Path Length:	0.1 dcm.	0.1 dcm.	0.1 dcm.
Temperature:	24°	22.2°	22.2°

λ(mμ)	(+) [M]	(-) [M]	(-) [M]
600	81	110	25
589	84	115	25
580	90	120	30
575*	90	125	30
570	93	130	30
560	93	136	35
550	99	141	39
540	99	146	50
530	102	151	50
525*	102	155	50
520	105	157	54
510	115	162	54
500	121	172	69
490	133	193	79

TABLE XIa Cont.

Osotriazole of:	D-Erythrose (XXIII)	D-Xylose (XXII)	L-Arabinose (XXI-L)
λ(mμ)	(+) [M]	(-) [M]	(-) [M]
480	140	198	79
475*	140	204	85
470	149	209	89
460	161	219	94
450	171	235	114

*Not included in Drude equation solvent study

TABLE XIb

R.D. Data for D-Galactose Osotriazole (XX), L-Sorbose Osotriazole (XIX-L) and D-Glucose Osotriazole (XI) in Acetic Acid

Osotriazole of:	D-Galactose (XX)	L-Sorbose (XIX-L)	D-Glucose (XI)
Molecular Weight:	265	265	265
Concentration: (g/100ml)	0.510	0.486	0.149
Path Length:	0.1 dcm.	0.1 dcm.	0.1 dcm.
Temperature:	22.2°	22.2°	22.2°
λ(mμ)	(-) [M]	(-) [M]	(-) [M]
600	73	98	124
589	88	120	124
580	104	120	124
575*	107	125	124
570	109	125	124
560	135	125	124
550	135	130	160
540	135	130	160
530	135	136	160
525*	135	138	175
520	135	141	178
510	140	147	213
500	145	152	213
490	151	158	213

TABLE XIb Cont.

Osotriazole of:	D-Galactose (XX)	L-Sorbose (XIX-L)	D-Glucose (XI)
λ(mμ)	(-) [M]	(-) [M]	(-) [M]
480	156	179	249
475*	158	185	258
470	161	190	267
460	182	196	302
450	203	206	302

*Not included in Drude equation solvent study

TABLE XIIa

R.D. Data for D-Erythrose Osotriazole (XXIII), D-Xylose Osotriazole (XXII) and L-Arabinose Osotriazole (XXI-L) in Water

Osotriazole of:	D-Erythrose (XXIII)	D-Xylose (XXII)	L-Arabinose (XXI-L)
Molecular Weight:	205	235	235
Concentration: (g/100ml)	0.395	0.4775	0.4625
Path Length:	0.1 dcm.	0.1 dcm.	0.1 dcm.
Temperature:	23.2°	23°	23°

λ(mμ)	(+) [M]	(-) [M]	(-) [M]
600	62	74	41
589	67	74	51
580	72	93	56
575*	78	93	61
570	78	93	71
560	78	98	71
550	78	98	76
540	78	98	76
530	78	98	76
525*	83	98	76
520	83	98	81
510	83	103	86
500	93	103	91
490	104	103	97

TABLE XIIa Cont.

Osotriazole of:	D-Erythrose (XXIII)	D-Xylose (XXII)	L-Arabinose (XXI-L)
λ(mμ)	(+) [M]	(-) [M]	(-) [M]
480	109	113	107
475*	115	118	107
470	119	118	112
460	130	128	117
450	140	137	127

*Not included in Drude equation solvent study

TABLE XIIb

R.D. Data for D-Galactose Osotriazole (XX), L-Sorbose Osotriazole (XIX-L) and D-Glucose Osotriazole (XI) in Water

Osotriazole of:	D-Galactose (XX)	L-Sorbose (XIX-L)	D-Glucose (XI)
Molecular Weight:	265	265	265
Concentration: (g/100ml)	0.386	0.3765	0.0072
Path Length:	0.1 dcm.	0.1 dcm.	0.1 dcm.
Temperature:	23°	23.5°	22°

λ(mμ)	(-) [M]	(-) [M]	(-) [M]
600	82	84	184
589	82	84	221
580	89	92	184
575*	89	92	184
570	89	92	184
560	96	92	184
550	103	106	188
540	110	106	221
530	110	106	221
525*	110	106	221
520	110	113	221
510	117	127	221
500	117	127	221
490	117	127	221

TABLE XIIb Cont.

Osotriazole of:	D-Galactose (XX)	L-Sorbose (XIX-L)	D-Glucose (XI)
λ(mμ)	(-) [M]	(-) [M]	(-) [M]
480	117	127	221
475*	117	141	221
470	124	141	294
460	130	141	294
450	130	141	298

*Not included in Drude equation solvent study

TABLE XIII

R. D. Data for D-Galactose Osotriazole Tetraacetate (XLVI) in Methanol, Pyridine and Acetic Acid

Osotriazole of:	D-Galactose Tetraacetate (XLVI)	D-Galactose Tetraacetate (XLVI)	D-Galactose Tetraacetate (XLVI)
Molecular Weight:	433	433	433
Concentration: (g/100 ml)	0.339	0.6103	0.670
Solvent:	Methanol	Pyridine	Acetic Acid
Path Length:	0.1 dcm.	0.1 dcm.	0.1 dcm.
Temperature:	24°	23.5°	24°
λ (mu)	(-) [M]	(-) [M]	(-) [M]
600	102	106	129
589	102	121	136
580	102	121	142
575*	102	128	155
570	115	142	155
560	128	156	174
550	153	156	168
540	166	163	174
530	166	174	177
525*	166	185	187
520	166	192	187
510	166	213	194
500	179	213	207
490	179	241	220

TABLE XIII Cont.

Solvent:	Methanol	Pyridine	Acetic Acid
λ(mμ)	(-) [M]	(-) [M]	(-) [M]
480	179	263	226
475*	192	270	233
470	204	298	245
460	217	312	252
450	230	333	278

*Not included in Drude equation solvent study

NUCLEAR MAGNETIC RESONANCE DATA

TABLE XIV

N.M.R. Spectral Data of the Aldo Sugar Family Osotriazole Derivatives in Pyridine

D-Glucose Osotriazole (XI)

Protons	Chemical Shift τ	Integral Protons	Mult.[a]	Coupling Constant c.p.s.
C-1	1.65	1	s	
C-3	3.94	1	d	$J_{3,4}=2.0$
C-4	5.38	1	m	
C-5		1	m	
C-6	5.31	2	m	

L-Sorbose Osotriazole (XIX-L)

Protons	Chemical Shift τ	Integral Protons	Mult.[a]	Coupling Constant c.p.s.
C-1	1.67	1	s	
C-3	4.16	1	d	$J_{3,4}=5.0$
C-4	5.34	1	m	
C-5		1	m	
C-6	5.61	2	m	

D-Galactose Osotriazole (XX)

Protons	Chemical Shift τ	Integral Protons	Mult.[a]	Coupling Constant c.p.s.
C-1	1.73	1	s	
C-3	4.27	1	d	$J_{3,4}=7.5$
C-4	5.30	1	m	
C-5		1	m	
C-6	5.70	2	m	

L-Arabinose Osotriazole (XXI-L)

Protons	Chemical Shift τ	Integral Protons	Mult.[a]	Coupling Constant c.p.s.
C-1	1.65	1	s	
C-3	4.33	1	d	$J_{3,4}=6.0$
C-4	5.28	1	x	$J_{3,4}=6.0$ $J_{4,5}=4.6$
C-5	5.62	2	t	$J_{5,6}=4.8$ $J_{5,6}=6.0$

[a]Mult., Multiplicity; d, doublet; m, multiplet; q, quartet; s, singlet; t, triplet; x, sextet.

TABLE XIV Cont.

N.M.R. Spectral Data of the Aldo Sugar Family Osotriazole Derivatives in Pyridine

D-Xylose Osotriazole (XXII)

Protons	Chemical Shift τ	Integral Protons	Mult.[a]	Coupling Constant c.p.s.
C-1	1.68	1	s	
C-3	4.32	1	d	$J_{3,4}=3.6$
C-4	5.40	1	x	$J_{3,4}=3.6$ $J_{4,5}=3.6$
C-5	5.72	2	m	$J_{4,5}=4.5$ $J_{4,5}=6.6$

D-Erythrose Osotriazole (XXIII)

Chemical Shift τ	Integral Protons	Mult.[a]	Coupling Constant c.p.s.
2.19	1	s	
4.95	1	d	$J_{3,4}=5.5$
6.08	2	d	$J_{3,4}=5.5$

Glyceral Osotriazole (XXIV)

Protons	Chemical Shift τ	Integral Protons	Mult.[a]	Coupling Constant c.p.s.
C-1	1.89	1	s	
C-3	4.90	2	s	

Glyoxal Osotriazole (XXV)

Chemical Shift τ	Integral Protons	Mult.[a]	Coupling Constant c.p.s.
2.09	2	s	

[a]Mult., Multiplicity; d, doublet; m, multiplet; q, quartet; s, singlet; t, triplet; x, sextet.

INFRARED SPECTRA

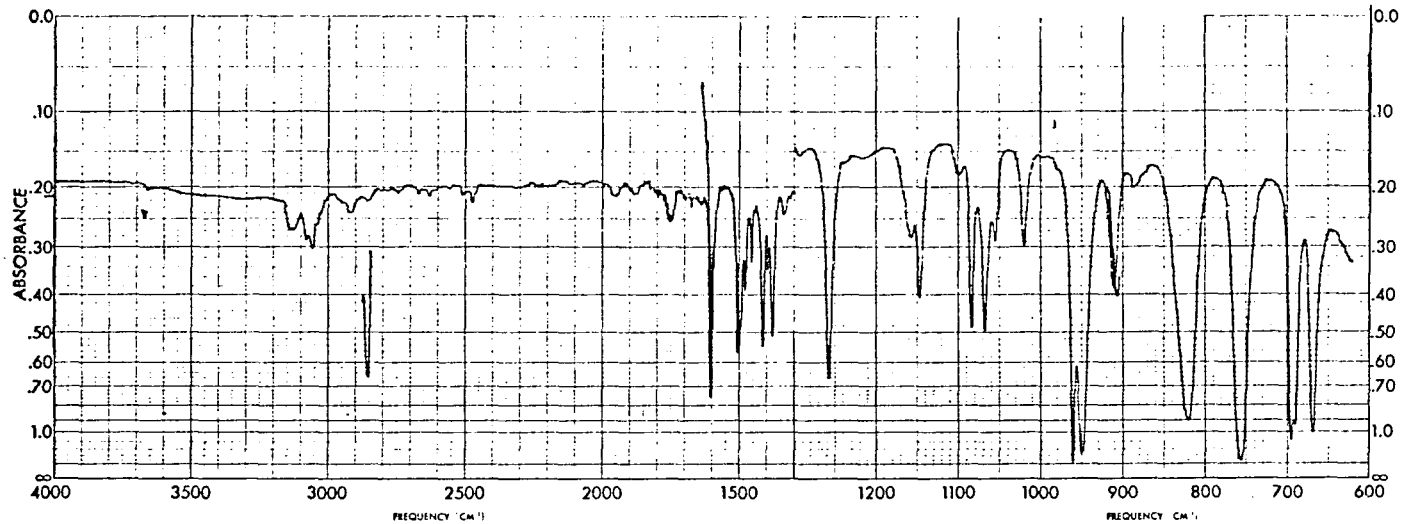


Fig. 43. Infrared Spectrum of 2-Phenyl-2,1,3-Triazole (XXV). (film)

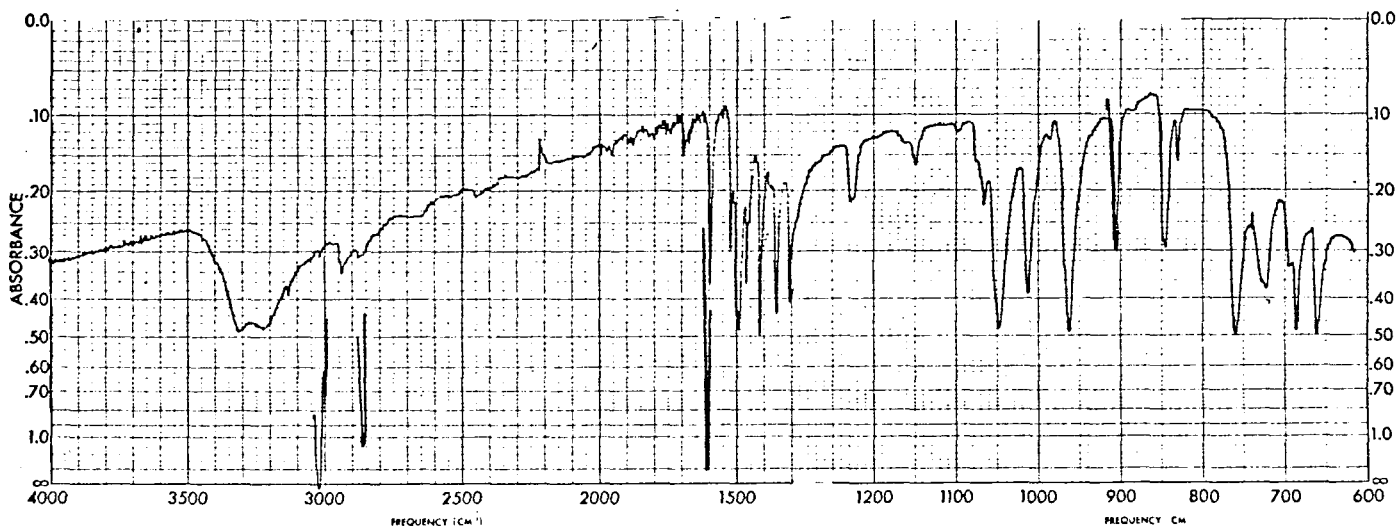


Fig. 44. Infrared Spectrum of 2-Phenyl-4-methanol-2,1,3-Triazole (XXIV). (double mull)

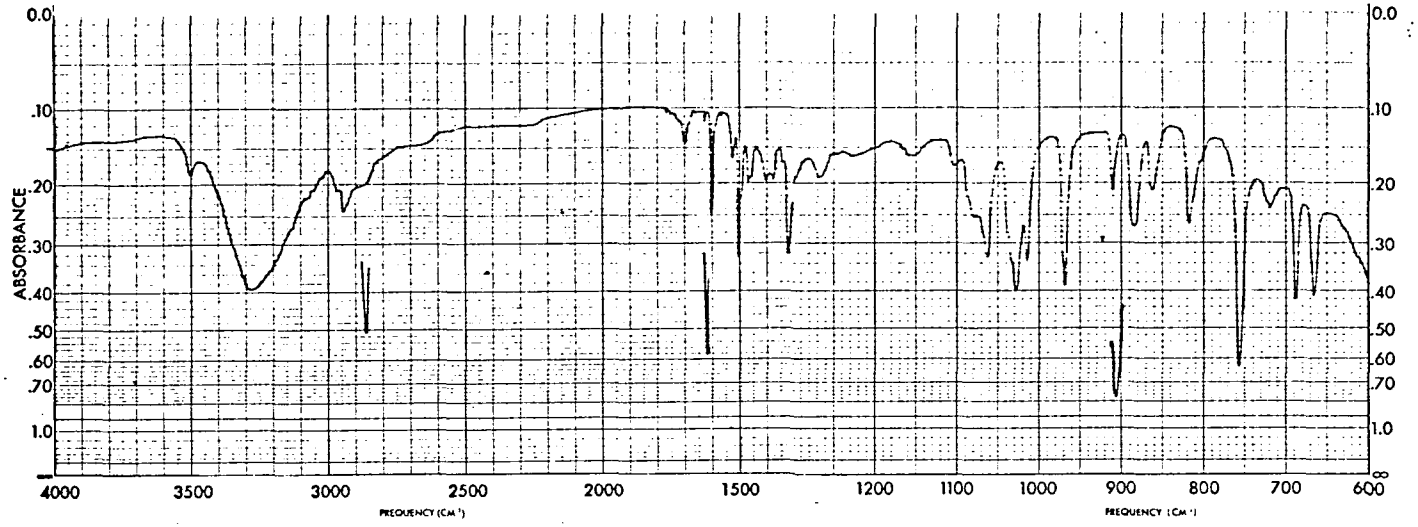


Fig. 45. Infrared Spectrum of 2-Phenyl-4-(D-Glyceraldehyde-dihydroxy-ethyl)-2,1,3-Triazole (XXIII). (double mull)

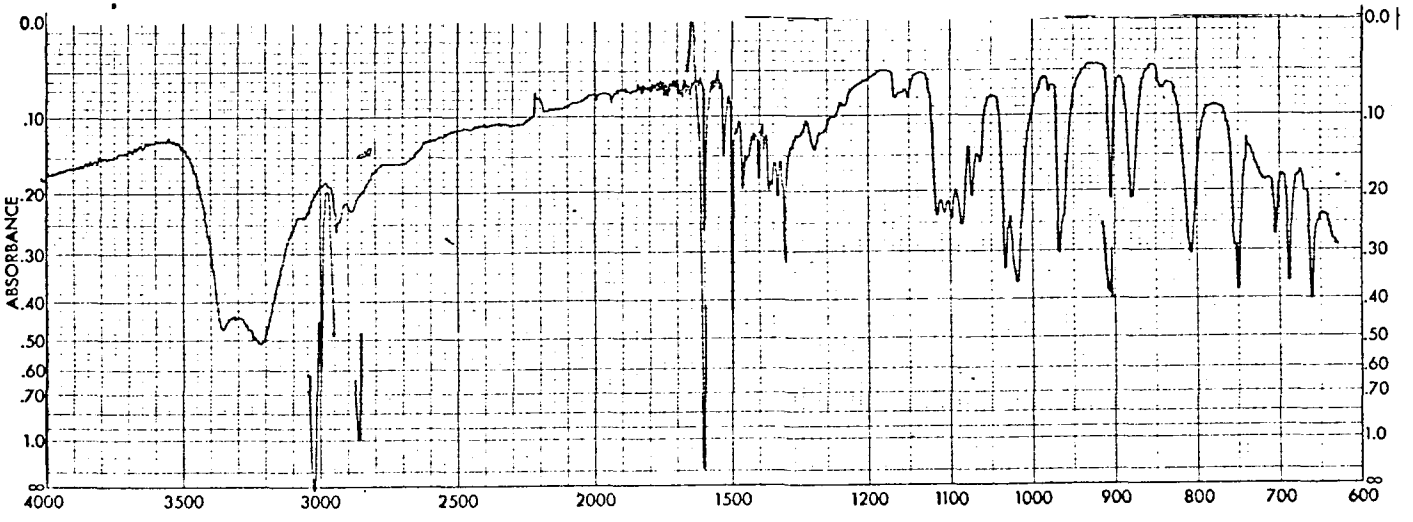


Fig. 46. Infrared Spectrum of 2-Phenyl-4-(L-Erythrose-trihydroxypropyl)-2,1,3-Triazole (XXI-L). (double mull)

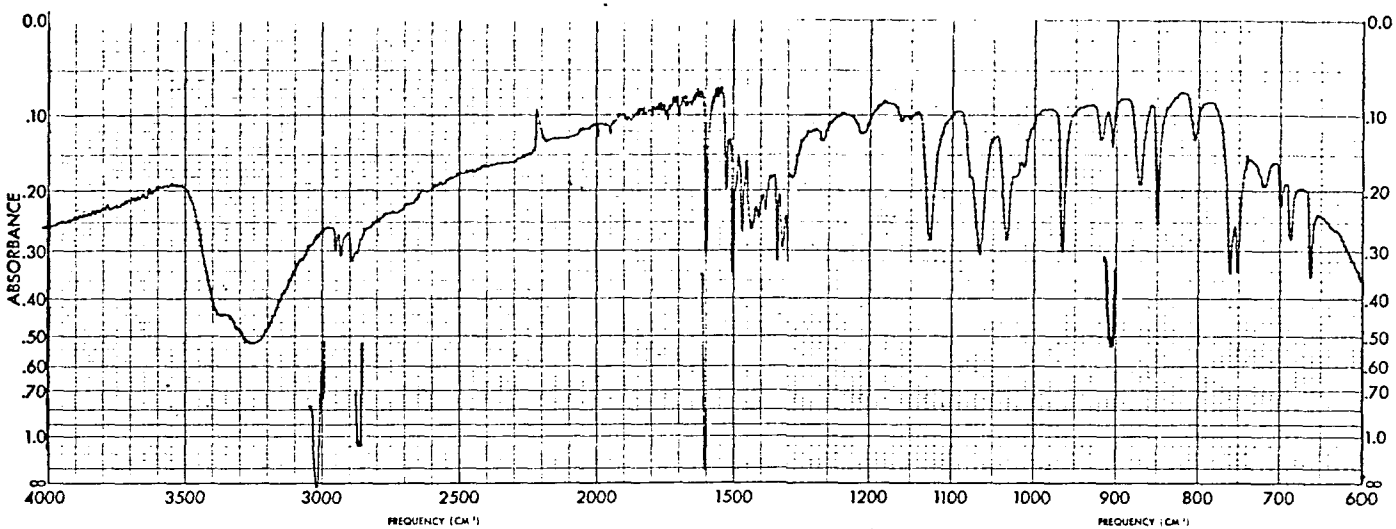


Fig. 47. Infrared Spectrum of 2-Phenyl-4-(D-Threose-trihydroxypropyl)-2,1,3-Triazole (XXII). (double mull)

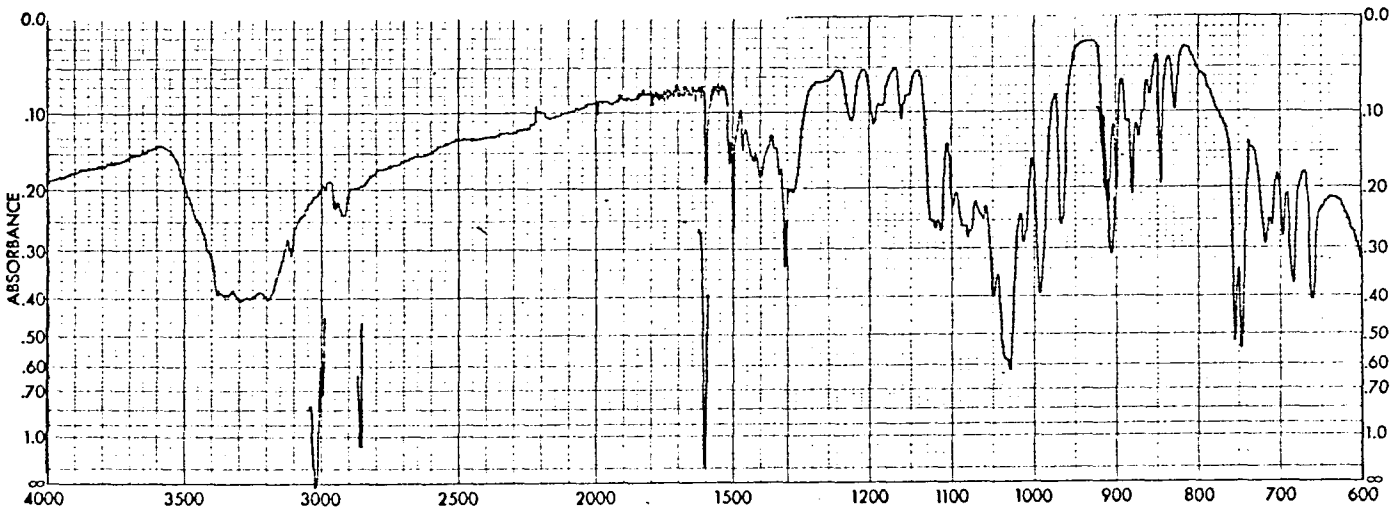


Fig. 48. Infrared Spectrum of 2-Phenyl-4-(D-Lyxose-tetrahydroxybutyl)-2,1,3-Triazole (XX). (double mull)

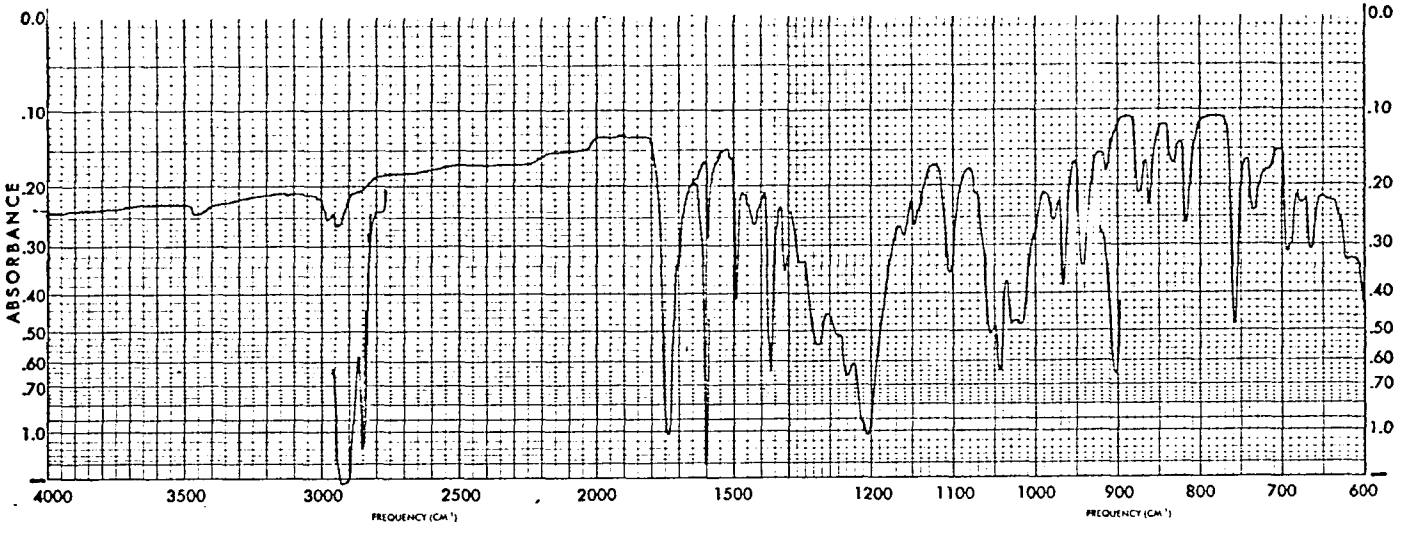


Fig. 49. Infrared Spectrum of 2-Phenyl-4-(D-Lyxose-tetraacetoxybutyl)-2,1,3-Triazole (XLVI). (double mull)

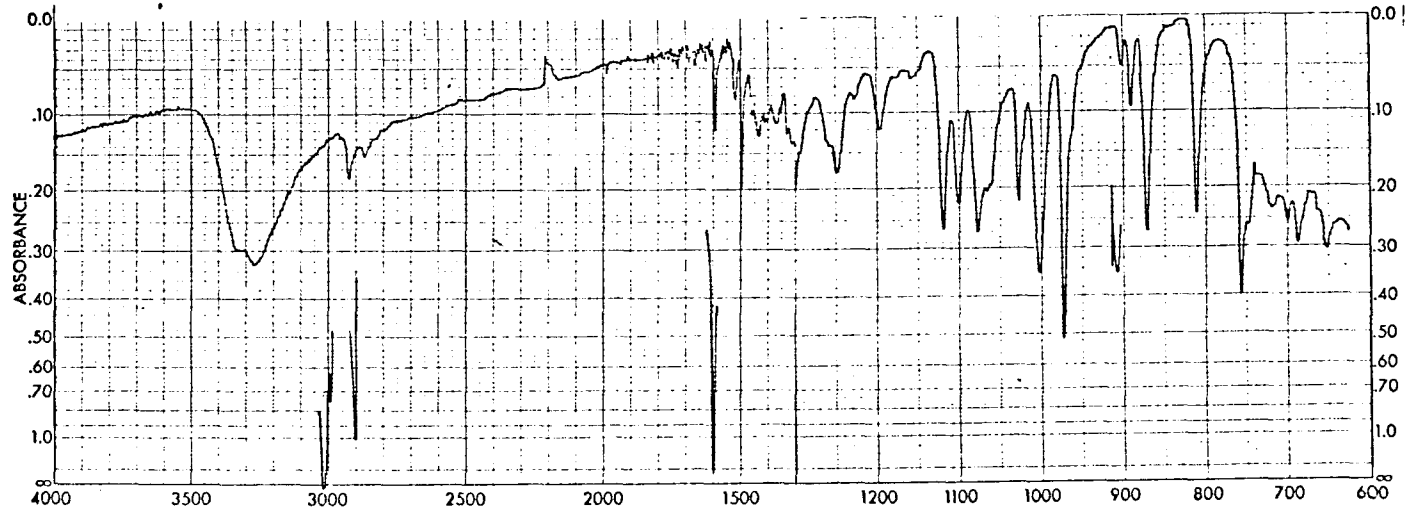


Fig. 50. Infrared Spectrum of 2-Phenyl-4-(L-Xylose-tetrahydroxybutyl)-2,1,3-Triazole (XLX-L). (double mull)

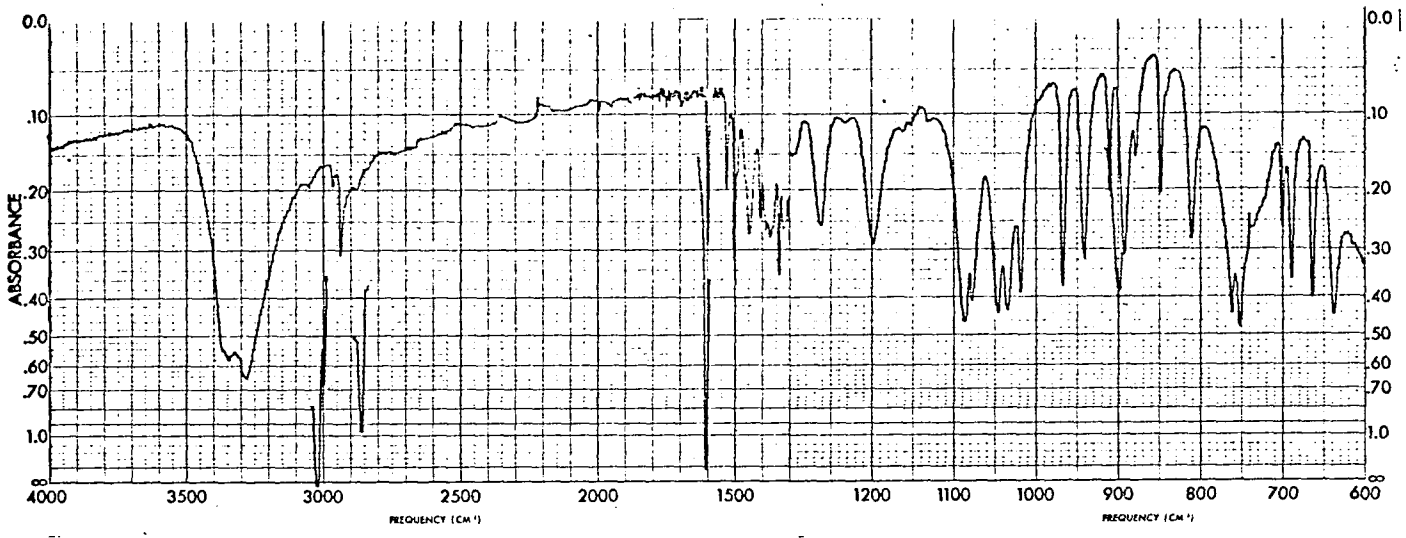


Fig. 51. Infrared Spectrum of 2-Phenyl-4-(D-Arabinose-tetrahydroxy-butyl)-2,1,3-Triazole (XI). (double mull)

BIBLIOGRAPHY

BIBLIOGRAPHY

1. J. H. van't Hoff, "Die Lagerung der Atome in Raume," Vieweg-Verlag, Brunswick, Germany, 1893, p. 119; P. A. Guye & M. Gautier, Compt. rend., 119, 740, 953 (1894).

2. C. S. Hudson, J. Am. Chem. Soc., 31, 66 (1909).

3. C. S. Hudson, J. Am. Chem. Soc., 32, 338 (1910).

4. P. Crabbé, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry", Holden-Day, San Francisco, 1965, p. 267.

5. C. S. Hudson, J. Am. Chem. Soc., 40, 813 (1918).

6. P. A. Levene, J. Biol. Chem., 23, 145 (1915).

7. C. S. Hudson, J. Am. Chem. Soc., 39, 462 (1917).

8. N. K. Richtmyer, Advances in Carbohydrate Chem., 6, 175 (1951).

9. N. K. Richtmyer and C. S. Hudson, J. Am. Chem. Soc., 64, 1612 (1942).

10. H. El Khadem, J. Org. Chem., 28, 2478 (1963).

11. J. A. Mills, Australian J. Chem., 17, 277 (1964).

12. E. L. Eliel, N. L. Allinger, S. J. Angyal and G. A. Morrison, Conformational Analysis, John Wiley & Sons Inc., New York, 1965, p. 391.

13. H. El Khadem, Advan. Carbohydrate Chem., 20, 169 (1965).

14. H. El Khadem, Tetrahedron Letters, No. 27, 1887 (1963).

15. J. H. Brewster, J. Am. Chem. Soc., 81, 5475, 5483 (1959).

16. D. A. Whiffen, Chem. Ind. (London), 964 (1956).

17. C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, New York, 1960, p. 236.

18. B. Sjoberg, Abstracts of Papers, Tronde Nord. Kemistmotet, Stockholm, August 1959.

19. C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, New York, 1960, p. 176.

20. H. Ohle, Ber., 67, 155 (1934).

21. R. M. Hann and C. S. Hudson, J. Am. Chem. Soc., 56, 957 (1934).

22. R. M. Hann and C. S. Hudson, J. Am. Chem. Soc., 66, 735 (1944).

23. A. Jonas and H. von Pechmann, Ann., 262, 294 (1891).

24. H. El Khadem, N. F. Iskander, and S. E. Zayan, Z. allgem. Chem., 320, 261 (1963).

25. H. El Khadem, N. F. Iskander and S. E. Zayan, Z. allgem. Chem., 325, 72 (1963).

26. H. El Khadem and Z. M. El-Shafei, J. Chem. Soc., 1655 (1959).

27. H. El Khadem, Ph.D., Dissertation, London, 129 (1952).

28. H. El Khadem and Z. M. El-Shafei, J. Chem. Soc., 3117 (1958).

29. E. Weygand, H. Gusebach, K. D. Kirchner, and M. Haselhirst, Chem. Ber., 88, 487 (1955).

30. G. Henseke and H. Winter, Chem. Ber., 93, 45 (1960).

31. C. Neuberg, Ber., 32, 3384 (1899).

32. R. L. Richtmyer, "Methods In Carbohydrate Chemistry", 2, 127 (1963).

33. E. Fischer, Ber., 20, 821 (1887).

34. L. F. Fieser and M. Fieser, "Organic Chemistry," D. C. Heath & Co., Boston, Mass., 1944, p. 351.

35. O. L. Chapman, Tetrahedrom Letters No. 23, 2599 (1966).

36. V. C. Barry and P. W. D. Mitchell, J. Chem. Soc., 4020 (1954).

37. C. Djerassi and W. Klyne, J. Chem. Soc., 4929 (1962).

38. C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, New York, 1960, p. 16.

39. H. Tichy, "Advances in Organic Chemistry," 5, R. A. Raphael, E. C. Taylor, and H. W. Wynberg, Interscience, New York, 1965, p. 235.

40. C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, New York, 1960, p. 150-177.

41. H. Freedman, J. Am. Chem. Soc. 83, 2900 (1961).

42. M. Karplus, J. Am. Chem. Soc., 85, 2871 (1963).

43. E. L. Eliel, N. L. Allinger, S. J. Angyal and G. A. Morrison, Conformational Analysis, John Wiley & Sons Inc., New York, 1965, p.111.

44. M. L. Wolfrom, G. Fraenkel, D. R. Lineback, and F. Komitsky, Jr., J. Org. Chem., 29, 457 (1964).

45. D. Horton and M. J. Miller, J. Org. Chem., 30, 2457 (1965).

46. G. T. Satsaronis, Prakt. Akad. Athenon, 31, 330 (1956).

47. J. L. Ricksomer and G. Sumrell, J. Org. Chem., 13, 807 (1948).

48. R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed., John Wiley & Sons, Inc., New York, 1956, p. 301.

49. W. T. Haskins, R. M. Hann and C. S. Hudson, J. Am. Chem. Soc., 67, 939 (1945).

50. W. T. Haskins, R. M. Hann and C. S. Hudson, J. Am. Chem. Soc., 68, 1766 (1946).

51. E. Fischer, and O. Pilotz, Ber., 24, 52 (1888).

52. E. Fischer, Ber., 19, 1921 (1886).