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A Study of the Iron-Tartrate-Alkali System and its Complexing Reaction with Cellulose-Related Polyhydroxy Compounds

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A STUDY OF THE IRON-TARTRATE-ALKALI SYSTEM AND ITS COMPLEXING REACTION WITH CELLULOSE-RELATED POLYHYDROXY COMPOUNDS

A thesis submitted by

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SUMMARY

The behavior of the iron-tartrate-alkali cellulose solvent (FeTNa) was investigated with respect to its composition and its ability to form new complexes with cellulose-related, polyhydroxy compounds.

A program of continuous variations was applied to the mixture of ferric nitrate and sodium tartrate in a solution of 2.0M excess sodium hydroxide. Using optical rotation at 546 mμ and optical absorbance at 440 mμ, the optimum combining iron-to-tartrate mole ratio was found to be one to four and one-half at a total concentration (iron plus tartrate) of 0.40 mole per liter. A solution of FeTNa, which was prepared at this mole ratio and at a concentration of 0.50M with respect to iron, failed to dissolve a sample of acetate-grade cotton linters.

A sample of FeTNa was prepared with a mole ratio of iron-to-tartrate of one to three and at a 0.50M concentration of iron, also in a 2.0M sodium hydroxide solution. This was found to be stable for several months before discoloration took place. This solution easily dissolved a sample of the cotton linters to form a clear, very viscous solution which was 1% (w/v) in cellulose concentration. This complex solvent corresponded very closely to the FeTNa solvent which is described in the literature. The preparation of this solvent required care in the handling of the ingredients and was successful only if minimum volumes of water were employed in the mixing and transfer operations.

This 1:3 FeTNa solvent was employed in continuous-variations programs with model compounds to evaluate the effect of the location and spacing of the models' hydroxyl groups upon the co-ordination reaction (new complex formation) between the model compound and FeTNa. These tests indicated that FeTNa (1:3 mole ratio) was able to form new complexes with glycol pairs of hydroxyl groups on certain model compounds; the methoxyl group was capable of blocking this reaction. Not

only was the glycol pair required on the model but, in addition, other oxygen atoms were needed, atoms whose electronegativity apparently served to confer water solubility upon the new complex. Model compounds which contained both a glycol group and extra oxygen atoms complexed well with FeTNa. Compounds which contained the glycol pair of hydroxyl groups but no extra oxygen atoms, or those which possessed many oxygen atoms but no glycol pairing of hydroxyls, reacted only to a small extent with the 1:3 FeTNa. Those models which contained neither a glycol group nor more than two oxygen atoms did not react at all. The models tested were methyl α-D-glucopyranoside; methyl β-D-glucopyranoside; glycerol; propane-1,3-diol; methanol; sodium succinate; butane-2,3-diol; butane-1,4-diol; ethylene glycol; methyl 2,3,4,6-tetra-O-methyl-β-D-glucopyranoside; methyl cellosolve; trans-cyclohexane-1,2-diol; cis-cyclohexane-1,2-diol; methyl 4,6-di-O-methyl-β-D-glucopyranoside; methyl 3-O-methyl-(α,β)-D-glucopyranoside; mannitol; and sorbitol. Optical rotation at 546 mμ was employed at a constant total concentration of 0.50 molar with respect to the iron and the model.

These results indicated that the probable mechanism for the ability of the 1:3 mole ratio iron-tartrate system to dissolve cellulose depends upon the difference between this 1:3 ratio in which the solvent is prepared and the 1:4.5 ratio which is the optimum. This ligand deficiency in the FeTNa of 1:3 mole ratio is filled by the glycol pair of hydroxyl groups on carbon atoms two and three on the glucopyranoside repeating unit of cellulose and a new complex is formed; the energy of this new chelate formation loosens the physical structure of the cellulose fiber and carries it into solution. It is this ligand deficiency which gives rise to the ability of an iron-tartrate system of 1:3 mole ratio to dissolve cellulose.

INTRODUCTION

Prior to about 1950, a researcher had but two choices of methods for the study of the hydrodynamic behavior of the cellulose polymer in solution. The first involved the preparation of a derivative of cellulose by a "polymer-homologous" reaction and the subsequent dissolution of this derivative in a suitable organic solvent. The second method required the use of one of the two copper-based complex solutions which were able to dissolve cellulose directly; these were cuprammonium hydroxide and cupriethylenediamine hydroxide.

Each of these methods had its disadvantages. No reaction for the formation of a cellulose derivative is entirely without degrading action on the polymer; even the preparation of the commonly used trinitrate derivative involves a small but nevertheless real reduction in degree of polymerization (DP). Moreover, the measured hydrodynamic behavior will be that of the derivative polymer and may be only indirectly related to the original cellulose. A further complication is the variable degrees of substitution (DS) which are encountered in the preparation of cellulose derivatives; each different DS represents, in effect, a different polymer species and will behave differently in solution.

The value of the copper-based, direct cellulose solvents is reduced primarily by the degradation of the cellulose which occurs in the alkaline solution, principally from the action of atmospheric oxygen. The reduction in DP of cellulose dissolved in cuprammonium is severe enough to require the rigid exclusion of air during the handling of the solution. Cupriethylenediamine is not quite so harsh. The solution of cellulose may be exposed to the atmosphere for brief periods provided that the air is excluded for the major portion of the handling and processing time. Another disadvantage of the copper complexes is their

intense blue color which makes the use of optical, physical measurements quite difficult. Furthermore, the difficulty in the preparation of these solvents may cause trouble in reproducing the required component compositions among different batches.

In an attempt to find some other solvent which would be able to dissolve all samples of cellulose directly and yet avoid these problems, Jayme and his students at Darmstadt experimented with other metallic ions in complex solutions (1, 2). The studies consisted mainly of the substitution of other metals for the copper in the well-known copper-based solvents. These new solutions were then tested for any ability to dissolve cellulose. One of these, the cadmium-ethylenediamine complex, proved to be quite successful. This material appeared to have little sensitivity to atmospheric oxygen; it was subsequently studied quite extensively by Henley (3).

There was, however, another complex solution investigated which did not resemble the metal-amine or metal-ammonia complexes but still was able to dissolve cellulose. This was the complex formed between the ferric ion and tartaric acid; this formation took place in an excess of sodium hydroxide solution. The green solution, abbreviated FeTNa (or EWNN in German), appeared to be fairly insensitive to the effects of atmospheric oxygen upon the dissolved cellulose. It also possessed some other properties which indicated the possibility of this material becoming a useful tool for the study of wood pulps and other cellulosic materials.

THE IRON-TARTRATE CELLULOSE SOLVENT AND ITS PROPERTIES

In the mid 1950's, work on the iron-tartrate-alkali cellulose solvent began to appear (4-8). These investigations and many later ones generally took the

form of a determination of the composition of the complex solution which would dissolve cellulosic materials and the properties of the cellulose solutions which resulted.

THE IRON-TARTRATE SYSTEM

As reported by Jayme (1, 9), the green-colored complex solution of iron(III) and tartrate has a structure in which three tartrate anions are associated with one central metal ion. The three tartrate anions are linked to the iron through the oxygen atoms of the tartrate hydroxyl groups. In a strongly alkaline solution, one of the hydroxyl groups on each tartrate loses a proton (10); the resulting diolate anion (of single negative charge) becomes the co-ordinating ligand. The carboxylate groups which remain on the tartrate anion confer water solubility upon the complex, which is itself uncharged. This proposed structure is based upon an earlier work of Franke (11) and is illustrated in Fig. 1. Although the two bonds to the iron are illustrated differently, they undoubtedly become equivalent in the actual complex. It is also likely that the oxygen atoms are arranged in a regular octahedron about the central iron atom.

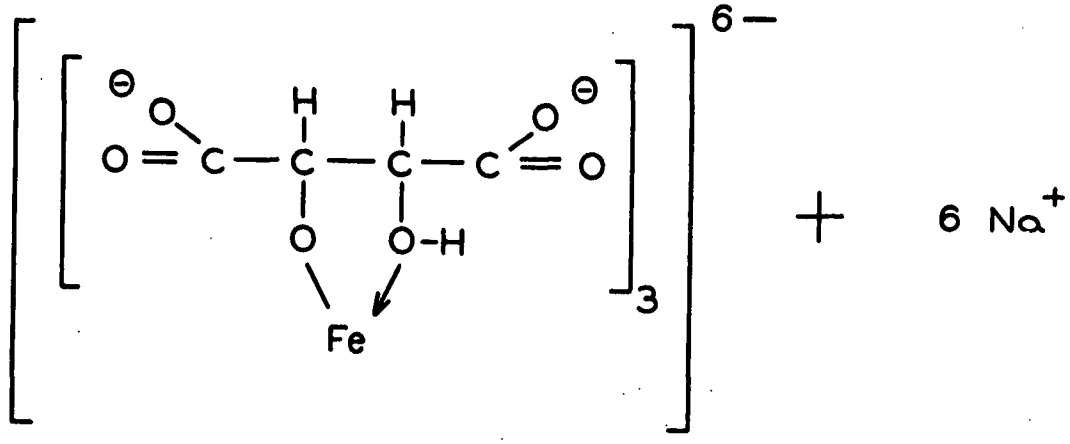

Figure 1. Iron-Tartrate Molecular Structure (1:3 Mole Ratio)

The reaction for the complex formation is listed as:

$$3\ Na_2C_4H_4O_6 + Fe(NO_3)_3 + 3\ NaOH \text{ ----- } Na_6[Fe(C_4H_3O_6)_3] + 3\ NaNO_3 + 3\ H_2O$$

When this complex is formed (dissolved in an excess of alkali which is two- to four-normal over that required for the complex formation), the dark-green cellulose solvent is produced.

Supporting evidence for this structure and composition of the complex seems to be lacking. Very little has been reported in the literature concerning tartrate complexes in general and iron-tartrate complexes specifically (12-14). One pattern does appear in those studies which have been done, however. That pattern is the importance of the conditions under which the complex is studied; these include the pH of the solution, total concentration of the complex, temperature, and the source of the tartrate ligand (free acid or tartrate salt). In addition, the carboxyl group is considered in some cases to be able to participate in the bonding with the ferric ion in the formation of a complex. Any study of the tartrate complexes also seems to be hampered by the difficulty encountered in the isolation of the complex itself; usually only the solution characteristics can be observed. This, of course, is not unique to the iron-tartrate complex but is encountered in the study of many co-ordination reactions.

Franke (11) proposed the 1:3 iron-tartrate structure as a result of the observation of the color changes which occur when different ratios of ferric ion and tartrate ion in solution are made alkaline. Since the color change between brown and yellow-green was sharp and distinctive at a molar ratio of 1:3 and since this color change was only slightly dependent upon the total iron concentration, the 1:3 iron-tartrate structure was assumed. Little further work has been done concerning the structure and composition of the iron-tartrate

complex under highly alkaline conditions. This complex is unstable when the solution is neutralized or diluted; hydrolysis to ferric oxide takes place. Very little else is known. It appears to be an assumption of Jayme that the 1:3 complex is the structure of the cellulose solvent which he has investigated.

METHOD OF PREPARATION OF FeTNa SOLVENT

The preparation of the cellulose solvent may be done by one of two techniques. The first is that proposed by Jayme and Lang (2) in which an insoluble, intermediate product is isolated and washed. This intermediate is presumably an insoluble complex of iron and tartrate formed in a molar ratio of 1:1. It is prepared by mixing equimolar amounts of ferric nitrate and sodium tartrate solutions and washing (in the dark) the precipitated brown solid. This solid is then reacted (also in the dark) with more sodium tartrate and a concentrated alkali solution to form the 1:3 molar ratio complex solution. A slight excess of tartrate may be added to improve the stability of the solution in storage.

A second method is used to prepare the green 1:3 ratio solvent directly (15). Ferric nitrate and the tartrate salt are mixed in the proper proportions; the light-protected mixture is stirred and cooled while alkali is added. This alkali is sufficient to prepare the complex and also to provide the required excess. The preparation is completed by bringing the volume to the proper level.

Solvents prepared by this second method suffer from a high ion concentration (the nitrate ions remain in solution) but the method is simpler in practice and does not have the varying content of iron which is observed when the method involving the isolation of the intermediate is employed (16). Apparently, the isolation and washing of the intermediate solid results in some losses in iron because of the solubility and hydrolysis of the complex. Both methods appear to

be capable of producing solutions which dissolve cellulose but the direct method seems to be favored because of the reproducibility of solvent composition (16).

SOLVENT PROPERTIES OF FeTNa COMPLEX

As a cellulose solvent, the iron-tartrate complex solution has exhibited some very desirable properties. Solutions of cellulose in FeTNa seem to be affected very little by atmospheric oxygen; degradation of the polymer is very slight and can usually be neglected. Elaborate precautions to exclude air are therefore unnecessary and measurements such as viscosity determinations can be obtained without undue haste (9, 17).

The technique of the preparation of cellulose solutions and the measurement of the viscosity has also been established (15, 16, 18, 19). The proper concentrations of the complex and the excess alkali have been determined for the best solvent properties. The intrinsic viscosity can be used to establish a molecular weight or a D.P. value for the cellulose sample. It also has been determined that by a change in any of three variables in the composition of the FeTNa solvent, the "dissolving power" or the ability of the complex to dissolve various cellulosic samples can be varied over a considerable range. These variables include the total concentration of complex (assuming a 1:3 mole ratio), the amount of tartrate used to prepare the FeTNa (above or below the amount corresponding to the 1:3 ratio), and the free (excess) alkali concentration (9). The proper choice of solvent composition allows cellulose materials of the highest D.P. values to be dissolved, for example, unbleached native cotton (1, 20). By the use of sedimentation-diffusion measurements, it has been determined that the cellulose dissolved in FeTNa is molecularly disperse to the same extent that it is in solutions of the copper-based solvents (21).

The variability of the solvent properties of FeTNa allows its use for various other purposes. In the study of fibers and their structure, FeTNa can be used to effect limited degrees of swelling. This swelling can be varied by changing the solvent composition until the fiber structure has been loosened by the desired amount; the swelling will then halt, which allows unhurried observations to be made (22).

Another use of this variable composition involves the separation of hemicelluloses from an isolated hemicellulose mixture. The hemicelluloses can be fractionated by precipitation on the basis of the configuration of the main-chain (or backbone) sugar ring. The mannans and xylans can be precipitated by FeTNa of a specified composition while the glucans and galactans remain in solution (23, 24). The separation is not particularly well defined but nevertheless it is apparently useful for certain purposes.

Cellulose itself may be fractionated by FeTNa on the basis of chain length (D.P.). From a solution of cellulose in FeTNa, fractions can be precipitated by the addition of a 1:3 glycerol-water mixture (9, 18, 20, 25). The white cellulose powder can be washed free of solvent by the glycerol-water mixture, which prevents contamination of the precipitate by iron oxide. Only the shortest cellulose chains escape precipitation by this method, which appears to be a very useful procedure for cellulose studies.

Quite recently, the iron-tartrate cellulose solvent has found use as a method or tool in studies of the behavior of pulps or other cellulosic materials, for example, the work of Malm and his co-workers (26, 27). Its acceptance as a cellulose solvent with many properties superior to the copper-based solvents appears to be established.

APPROACH TO THE STUDY

Most of the characteristics of FeTNa as a cellulose solvent seem to have been sufficiently elucidated. This study investigated other behavior of the system in order to establish the probable mechanism whereby the dissolving process is effected.

MECHANISM OF CELLULOSE SOLUTION

The investigation of the dissolving mechanism can be approached by an initial comparison with the reported behavior of the copper-based complex solvents to determine if a similar mechanism might also be operative in the case of the iron-tartrate system.

BEHAVIOR OF COPPER-BASED SOLVENTS

Most of the earlier results with the copper-based cellulose solvents have been reviewed by Heuser (28). The work of Reeves, however, forms the basis for the presently accepted mechanism by which these complexes are able to dissolve cellulose (29-39).

The complex of copper(II) and ammonia is in the form of a square-planar complex ion; four ammonia molecules occupy the four co-ordination sites of the divalent copper ion by taking positions at the corners of a plane square. This ion, soluble in an excess of ammonia, is prepared by the action of ammonia upon fresh copper oxide or by the reaction of atmospheric oxygen and ammonia with copper metal. This solution, cuprammonium hydroxide, is able to swell and disperse cellulose fibers with a facility which depends upon the composition of the solvent, the physical structure of the fiber, and the D.P. of the cellulose polymer.

Beginning in 1944, Reeves reported on studies of the reaction of cuprammonium solutions with compounds which were structurally related to the cellulose polymer; these were monomer sugar derivatives whose configurations were similar to the glucoside repeating unit of cellulose. Of special interest was the spatial relationship between hydroxyl groups on these "model compounds," hydroxyl groups which were able to form a new complex with the complex copper ion.

From the behavior of his many model compounds, Reeves was able to conclude that in order for the cuprammonium ion to enter into a new complex with two hydroxyl groups on the model, these hydroxyls had to be located on adjacent carbon atoms (i.e., a glycol grouping). Moreover, in a fixed-ring system (such as the furanoside or pyranoside series of glycosides), the glycol group had to possess such an orientation that the projected angle between the carbon-oxygen bonds of the group (measured with reference to the carbon-carbon bond) must be zero degrees (true cis) or, alternatively, at angles up to 60 degrees to enable the new complex to be formed. Angles of 120 or 180 degrees precluded complex formation. This orientation of the hydroxyl groups was determined mainly by the conformation of the glycopyranoside ring to be expected in solution which, in turn, depended upon the configuration of the groups on the ring.

In most cases, this spacing requirement described very well the behavior of substituted sugars or related polyhydroxy compounds with respect to the reaction or the lack of a reaction with a cuprammonium solution (29-34). Hydroxyl pairs whose oxygen atoms were situated at a distance apart which was greater than that permitted by the sixty-degree glycol pair showed little indication of new-complex formation. Using this knowledge of the steric requirements of the glycol-copper complex and the known configurations of other polyhydroxy ring compounds, Reeves was then able to predict the conformation in solution of many

of these other model compounds (33-38). Further studies indicated that equimolar quantities of glycol-containing compound and copper reacted to form the new complex. Also revealed was the probability that the singly charged diolate anion was the species which reacted in the one-to-one molar ratio with the copper (39).

This reaction between copper and glycol results in the displacement of ammonia from the original cuprammonium ion (28); one glycol pair is able to displace a pair of ammonia molecules and form a new chelate with copper through the hydroxyl oxygen atoms. The stability of this new complex ion is very much dependent upon the alkalinity of the solution.

The mechanism for the dissolution of cellulose can then be deduced from an extension of the reported behavior with the model compounds. Since cellulose does form a new complex with cuprammonium (34), one can assume that the glycol pair on carbon atoms two and three of the beta glucopyranoside repeating unit of cellulose is involved. The reaction of the copper with the glycol group frees two ammonia molecules and causes the copper ion, with the other two ammonia molecules still remaining, to become attached to the sugar ring of the pyranoside unit. A new chelate is formed by this action; the formation of the new chelate replaces two ammonia molecules with a single diol pair of hydroxyl groups. The energy, which is supplied to the lateral hydrogen bonds and serves to loosen the physical (crystalline) structure of cellulose, is provided by the increased stability of the ammonia-copper-glycol complex over that of the ammonia-copper complex alone. Recombination of the dispersed polymer chains is prevented by the bulky copper-ammonia group which projects from the side of the polymer. The hydrophilic nature of the new complex enables the cellulose to remain molecularly dispersed in the aqueous medium. This type of mechanism has been proposed also by Meyer from purely stereochemical considerations (40).

A mechanism similar to this appears to be operative in the case of cupri-ethylenediamine and cadoxene (cadmium ethylenediamine) solvents also. Both apparently prefer to complex with the glycol pair of hydroxyl groups on substituted sugar pyranoside rings rather than react with hydroxyl groups which are spaced further apart (41-43). With cellulose, then, the metal ion probably complexes at the side of the glucopyranoside unit (carbon atoms two and three) with the release of one ethylenediamine molecule; this release has been observed in the case of the copper-based solvent (42). This new complex involving the glycol pair does show one difference when compared to that of cuprammonium; no new chelate ring is formed by the reaction of copper with the glycol in the case of these ethylenediamine solvents. Instead, a ring involving oxygen atoms (from the glycol) replaces a ring involving nitrogen atoms (from the diamine). The thermodynamic driving force for this displacement complexing reaction appears to be the preference of the metal ion for the oxygen atoms over the nitrogen atoms. While this driving force would be expected to be less than that for cuprammonium, in which a new chelate ring is formed where there was none before the displacement, the ethylenediamine solvents nevertheless appear to be quite able to dissolve most samples of cellulosic materials.

POSSIBLE DISSOLVING MECHANISM OF THE IRON-TARTRATE SYSTEM

One difference becomes apparent immediately if the same type of displacement mechanism were to be considered for the case of the FeTNa complex and its cellulose-dissolving ability. According to the literature proposals, the tartrate ligand, co-ordinated to the central ferric ion, has as its electronegative electron-donor atoms the oxygen atoms of the hydroxyl group instead of the nitrogen atoms of the amine group as is the case with the copper-based solvents. If both the tartrate ligand and a ligand consisting of the glucopyranoside unit

of cellulose do co-ordinate through hydroxyl groups, and if the glycol pair of hydroxyls is involved in the glucopyranoside as it must be with the tartrate, then, the two ligands become essentially identical. If this is true, then there seems to be no reason for the glucopyranoside to displace the tartrate from the iron-tartrate complex, a process which would involve the sugar ring, the ferric ion, and the remaining tartrates in a new complex in a manner analogous to the copper solvents. This type of displacement, if it actually takes place, would provide the energy required to loosen the cellulose fiber structure and disperse the polymer molecules if and only if the displacement complex (tartrate-iron-glucopyranoside) were significantly more stable than the tartrate-iron complex alone. For the FeTNa, this does not appear to be possible because of the apparent identical nature of the two ligand groups.

The apparent identity of the glycol groups (the two which must compete for the ferric ion if a displacement does take place) is illustrated in Fig. 2. Both molecules are shown in the most probable conformations, with the hydroxyl groups on carbon atoms two and three illustrated for the glucopyranoside in the C-1 chair form. This figure shows the sixty-degree spacing between hydroxyl groups for both compounds. If this identity does in fact exist, and the assumptions mentioned are allowed, then a thermodynamic driving force to provide a displacement co-ordination reaction appears to be absent and the iron-tartrate-alkali complex would not be expected to dissolve cellulose as it does.

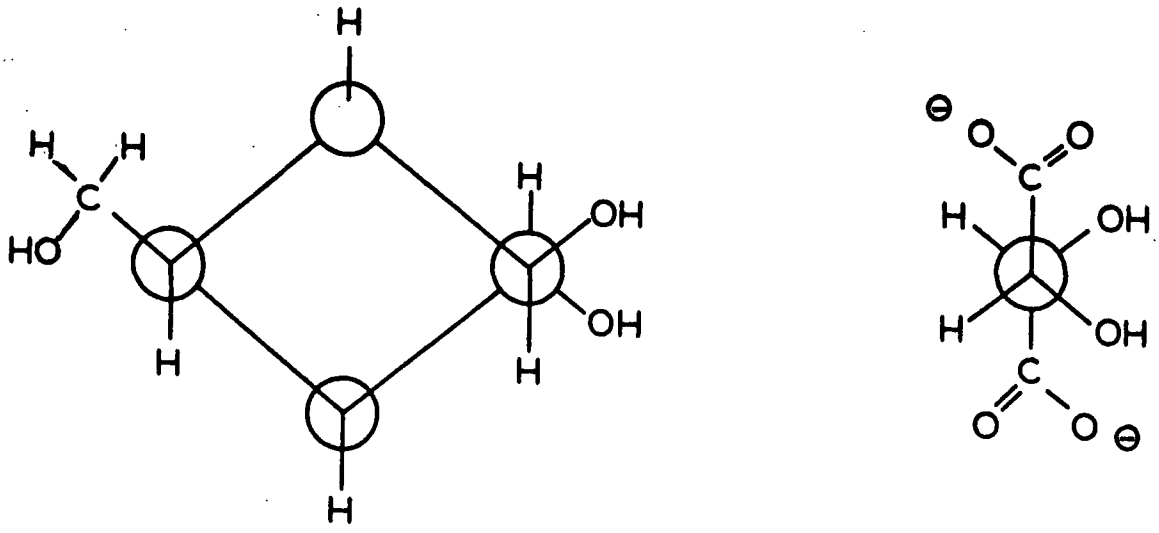

Figure 2. Most Stable Conformation of Glycol Groups in Competing Ligands

METHOD OF DETERMINATION OF ACTUAL FeTNa DISSOLVING MECHANISM

In order to ascertain the dissolving mechanism by which the iron-tartrate operates, one or more of the assumptions must be questioned and replaced, if possible, by experimental evidence. Assumptions to be questioned appear to be three in number: (1) the structure and composition of the iron-tartrate complex solvent system is that which is proposed by the literature; (2) the glycol pair of hydroxyl groups on the glucopyranoside ring of cellulose is involved in a new-complex formation; or (3) the glycol pair is involved and it is identical with the glycol pair of hydroxyl groups on the tartrate anion.

If the composition of the FeTNa were not the 1:3 mole ratio as assumed, the dissolving of cellulose could probably be explained even if the new complex were to be formed at the glycol pair on the glucopyranoside repeating unit. A different composition might easily accommodate a new glycol pair in the structure and permit its co-ordination directly to the iron. If the 1:3 composition proves

to be correct, then one must examine the ligands involved, the tartrate anion and the glucopyranoside sugar unit, to verify the glycol group as the reacting ligand. This could be done by the determination of which hydroxyl groups on the glucopyranoside ring are involved in a new complex formation with the iron-tartrate system, if such a new complex does form.

In cellulose, not only are the hydroxyl groups at positions two and three potential complexing sites, but so also is the group at position six. If the six position were found to be involved in new-complex formation, then the driving force for the dissolving of cellulose might very well be stereochemical in nature. A spacing of oxygen atoms (in hydroxyl groups) further apart than that permitted by a glycol pairing might lead to an increase in stability of such a complex with iron over that of a ligand which has only the glycol pair. This increased distance between oxygen atoms could be provided by the glucopyranoside ring by offering the hydroxyl groups at carbon atoms three and six if the ring itself assumes some boat conformation, possibly the B-3 shape (34). Such a conformation might well be possible with the monomer units of cellulose when the polymer is dissolved in the iron-tartrate solvent. The new complex which might be formed would have two ring systems in which the ferric ion bridges across the pyranoside ring. The action of dissolution might then be a shedding by the FeTNa of one tartrate anion (whose hydroxyls are somewhat too close together for the best fit with the iron) and its replacement by a glucopyranoside unit of cellulose (whose hydroxyls may be fit into the optimum spacing by a slight rotation about the bond between carbon atoms five and six). In the B-3 conformation, the proximity of the hydroxyl groups on carbons three and six and the ability to vary the spacing between them can best be seen by an examination of molecular models. The increased stability of the new complex, in which the glucopyranoside unit is

involved, over the original FeTNa complex would then provide the required energy to disrupt the cellulose physical structure.

However, if the glycol pair on the glucopyranoside ring is found to participate in the new-complex formation (and the 1:3 composition of the iron-tartrate is verified), then one would seem forced to assume that the glycol groups on the two competing ligands are not identical. In conformation, they seem to be the same. Chemically, their behavior in complexing reactions may be changed by the groups and structure comprising the remainder of each molecule. The carboxylate group adjacent to each hydroxyl group on the tartrate anion might well modify the reactivity (by induction, possibly) to such an extent that the complex with iron would be significantly less stable with tartrate than it would be with the glucopyranoside glycol pair. Or the ring system of the glucopyranoside might provide such an increase in the conformational stability of its glycol pair that the new complex between iron and the sugar is favored over that of iron with the tartrate (in which some change of conformation is much more likely). This effect of the modification of the relative behavior of the glycol pairs of the two competing ligands appears to be the least likely explanation of the cellulose-dissolving ability of FeTNa. One would suspect that the energy released by the tartrate displacement would not be sufficient to loosen the physical structure of cellulose.

Initial efforts to establish the mechanism of the cellulose-dissolving action of FeTNa, then, should consist of two steps; the verification of the composition of the iron-tartrate system itself and the location of the positions on the glucopyranoside ring at which this system forms a new complex. That is the purpose of this study.

EXPERIMENTAL PROGRAM

Both segments of the experimental work utilized the method of continuous variations to examine the formation of complexes in solution (44, 45). This procedure was used to determine the combining mole ratio which comprises the iron-tartrate system and to ascertain the presence or absence of a complex formation between FeTNa and selected model compounds.

OPTIMUM MOLE RATIO OF THE IRON-TARTRATE SYSTEM

The composition of the FeTNa system was studied by the examination of ferric nitrate and sodium tartrate in a program of continuous variations. The physical properties used were the optical rotation at the green line of mercury (546 mμ) and the optical absorbance in the visible wavelength region. The result indicated the optimum combining ratio of the ferric and tartrate ions which forms the complex system.

LOCATION OF COMPLEXING POINTS ON THE GLUCOPYRANOSIDE RING

The identification of the hydroxyl groups on the glucopyranoside ring which participate in a chelation with the iron-tartrate system requires the use of substituted sugar derivatives. These derivatives have selected hydroxyl groups on the ring substituted with another chemical group, a substitution which blocks the action of the hydroxyls as efficient donor groups for co-ordination reactions. The methyl ether group is often used; it is stable under most conditions likely to be encountered in co-ordination reactions. It also has been used before as a blocking group in complexing reactions with the copper-based and cadmium-based cellulose solvents. Until it could be verified experimentally, the efficacy of the methyl ether as a blocking group was assumed for iron complexes also.

The location of the chelation points on the sugar ring was done by means of the synthesis of partially methylated glucopyranosides, each with two methoxyl groups. Since, in the cellulose monomer unit, positions one and four are blocked by the glucoside linkage between units, these positions must also be blocked in a model compound. Position one is blocked by a methyl group as the methyl glucopyranoside; position four is blocked by a methyl ether group. The remaining three hydroxyl groups which are available in cellulose must then be blocked in sequence. The three, doubly methylated glucopyranosides appropriate to do this are, therefore, the 2,4-dimethyl-, the 3,4-dimethyl-, and the 4,6-dimethyl-glucopyranosides. To conform to the anomer present in cellulose, the beta form is indicated. Of these three dimethyl glucopyranosides, only one should show strong indications of complex formation with the iron-tartrate solution; any tendency for the other models to complex should be weak or absent. The determination of which one of the three doubly methylated glucopyranosides does complex with FeTNa established the chelation points on the glucoside sugar ring.

The method of continuous variations was used to establish the presence or absence of a co-ordination reaction between the model compounds and the iron-tartrate system. In this use of the method, only a qualitative indication is required, although the determination of the mole ratio of the combining species would be desirable. Here, the danger of a negative (zero) continuous-variations result becomes quite evident. If the reaction between model compound and the FeTNa does proceed by a displacement co-ordination mechanism, then the replacement of one pair of hydroxyl groups (on the tartrate ligand) by another pair (on the model compound ligand) might well cause no change to occur in the physical property which is being measured. Hence, no reaction would be indicated whereas one actually did take place. A positive continuous-variations result, indicative

of a co-ordination reaction, is sufficient evidence in itself while a negative indication should be supported by some confirming evidence, if possible.

Besides the substituted glucopyranosides, other model compounds were tested for ability to complex with the iron-tartrate. These additional models were compounds which contain hydroxyl groups; their use is designed to provide further information about the suspected importance of the conformation of the diol groups on the ligand and the influence which this conformation may have on any new-complex formation with FeTNa. Some of these extra model compounds are structurally related to the glucopyranoside sugar unit or to the original tartrate anion. Other, additional model compounds were tested; they are included to verify the assumed use of the methyl ether group as a blocking unit for complexing reactions with iron. All of these additional models provide evidence of the importance of the spacing of diol groups on potential ligand compounds and the result of the influence of the remaining portion of the ligand molecule.

EXPERIMENTAL PROCEDURES AND TECHNIQUES

Unless otherwise specified, all chemicals used were reagent grade and were weighed with the accuracy indicated. Where noted, triply distilled water was prepared by a second distillation of ordinary distilled water from an alkaline potassium permanganate solution, followed by a third distillation in which the water had been acidified with a few drops of sulfuric acid; both distillations were from an all-glass distillation apparatus. Filtrations were done under reduced pressure (water aspirator), usually in Büchner funnels used in conjunction with round-bottomed flasks. Concentrations at reduced pressure were done in a rotary evaporator which was equipped with a condenser at its outlet; heat was supplied by a water bath whose temperature could be noted.

COMPOSITION OF FeTNa – OPTIMUM MOLE RATIO OF 1 TO 4.5 IRON-TO-TARTRATE

An apparatus was assembled which consisted of a 100 ml., three-necked, round-bottomed flask equipped with a glass-rod stirrer, a thermometer, and a bent tube which could be used to add liquids to the flask. This flask and the bent tube were coated with black paint to exclude light and were supported in a dish which could be filled with an ice-water bath. The thermometer and stirring rod were arranged so that the thermometer bulb was nearly in the center of the lower half of the flask while the bent glass-rod stirrer swept along the sides of the flask to insure good agitation.

CALCULATIONS

Calculations were made which would provide a series of solutions of varying mole ratios of ferric nitrate and tartaric acid in a total volume of 50 ml. A preliminary experiment with the apparatus established a total molarity (sum of

the two ingredients) of 0.40; this was the largest quantity which could be handled and transferred in the various operations without the volume becoming greater than required. The actual molarities are listed in Appendix I, which also shows the various mole ratios which were obtained in the series. The alkali to be added to form the complex was in the form of a 50% solution which had already been prepared (actual concentration: 0.50174 g. NaOH per gram of solution). The alkali requirement was calculated on the basis of two moles for every mole of tartaric acid (to convert it to the sodium salt), three moles for every mole of ferric nitrate (to form either ferric hydroxide or the complex ion, depending upon the tartrates available in the particular mixture), plus a sufficient excess in order to provide a 2.0 molar solution of free sodium hydroxide. While this calculation assumed that three moles of alkali were required to form each mole of complex, the largest amount of alkali was added to provide the excess and should have been sufficient to maintain a highly alkaline solution regardless of the actual consumption of alkali during the reaction. A later calculation was made for the preparation of the mixture which had the 1:4.5 mole ratio of iron to tartrate. This mixture was required after the results of the continuous-variations procedures had been examined for the other mixtures. It was prepared and examined after the work on the other mixtures in the series had been completed.

PROCEDURES

For each mixture in the continuous-variations series, the experimental procedure was essentially the same. Solid ferric nitrate monohydrate and solid tartaric acid were weighed into two plastic (polyethylene) beakers on an analytical balance to within 0.2 mg. of the calculated amount. The ferric nitrate was dissolved in 4 ml. of triply distilled water; the tartaric acid was added to this solution and transferred with a small amount of water. When the acid had

dissolved, the mixed solution was transferred to the black flask (with the ice bath in place) and stirred until the temperature was below 5°.

Into a plastic beaker was weighed the proper amount (to within 0.5 mg. of the calculated amount) of the 50% sodium hydroxide solution; the pickup of atmospheric moisture by this solution was quite small. While stirring the contents of the black flask, this alkali was added in small portions to the flask through the bent tube. The temperature was prevented from rising above 15° by the slow alkali addition and rapid stirring; the time required for each addition was usually one hour or more. The last of the alkali was rinsed into the reaction flask with a little water.

The completed solution was transferred from the black flask to a 50-ml. volumetric flask. The volume was brought to the mark by immersing the volumetric flask in a constant-temperature bath at 20.0 $\pm$ 0.1° until the contents had warmed to temperature, then adding water a few drops at a time. The solution was agitated thoroughly and poured into a plastic bottle; each solution was then stored in a constant-temperature room at 22-23°.

The appearance of the solutions immediately after their preparation showed differences in color among the various iron-tartrate mole ratios. At ratios of iron to tartrate higher than one-to-one (in the direction of increasing iron content), the solutions were all dark brown-black in color, a color so intense that most of these solutions appeared to be opaque. Each solution also contained some solid in a very gummy form; this was undoubtedly ferric hydroxide. The two solutions corresponding to mole ratios less than 1:1 but greater than 1:3 contained no solid but they were the same deep brown-black color (similar in appearance to strong coffee); under strong light they were seen to be somewhat transparent. The appearance of the solution of 1:3 mole ratio showed a startling

difference; it was a bright, brilliant green color and very clear and transparent; it had just a trace of a yellow cast. All other solutions of mole ratios down to the lowest (1:7) were this same brilliant yellow-green color and were all clear at the time they were brought to volume; no further differences could be detected in their appearance. The abrupt change in color from brown to green at an iron-tartrate mole ratio of one to three was striking and unmistakable.

After one hour, the solution of the 1:3 ratio began to discolor; it turned a pale brown. After several days, it was dark brown and had begun to precipitate some solid. All solutions above the 1:3 ratio, which were already brown in color, had also begun to precipitate solid at this time. Also starting to discolor were the mixtures of 1:4 and 1:5 iron-tartrate ratios; these were quite pale, however. By the end of one week of storage at 22-23°, all solutions except the 1:6 and 1:7 mixtures had successively turned brown and precipitated a brown solid. These last two mixtures remained clear and green. All mixtures were shaken frequently during their storage to aid in the formation and precipitation of the solid.

Also prepared at this time was a series of reference solutions of sodium tartrate (without iron) whose concentrations corresponded to the molarities of the tartrate in the iron-tartrate mixtures. A stock solution of sodium tartrate was prepared by adding sufficient alkali to a carefully weighed amount ($\pm$ 0.1 milligram) of tartaric acid to convert the acid to the sodium salt and to provide enough excess to make the solution 2.0 molar in sodium hydroxide. This solution was diluted with 2.0M sodium hydroxide (by buret) to prepare the series of proper concentrations. Each solution was poured into a plastic bottle and stored with the iron-tartrate mixtures at 22-23°.

After six weeks of storage with intermittent agitation, each solution was filtered through a Gooch crucible which had a glass-fiber disk supporting a dry, packed asbestos pad. With the exception of the three solutions highest in original iron content, the amount of precipitate removal was very small. Each filtrate was clear and green in color; the intensity of the color increased as the iron-tartrate mole ratio decreased. The color differences, after the filtration, were slight; except for the few solutions of the highest mole ratios, the colors appeared to be quite similar. All solutions were transparent after the filtration.

The optical rotation of each solution (iron-tartrate mixtures and the sodium tartrate solutions) was then measured. A Zeiss-Winkel polarimeter (reading to 1/100 degree) was used in conjunction with a two-decimeter, jacketed polarimeter tube and a circulating, constant-temperature bath ($\pm$ 0.02°). The mercury light source of the polarimeter was filtered to isolate the green line (546 mμ). The temperature in the circulating line was measured by means of calibrated thermometers in the inlet and outlet lines of the jacketed polarimeter tube; the average of the two was kept constant at 25.00 $\pm$ 0.02° for each measurement. The green mixtures proved to be quite transparent to the green light source although they were opaque to the mercury blue line. The values of the optical rotations are recorded in Appendix I; they are values for the two decimeter path length and are the averages of at least five readings for both rotation and zero point. The values for the tartrate rotations are also shown.

Each solution was filtered again through a packed, dry asbestos pad. The optical absorbance of each solution was then recorded in the wavelength range from 370 to 900 mμ using a Beckman DK-2 ratio-recording spectrophotometer. Pyrex cells (one centimeter path length) were used; the reference solvent was

2.0M sodium hydroxide. Although the temperature was not closely controlled (the instrument did not have a temperature jacket), the actual temperature in the sample cavity ranged only from 25.5 to 27.5°; this was made possible by holding the ambient temperature at 17 to 18°. The absorbance of a 0.40M solution of sodium tartrate (the stock solution) was found to be uniformly zero in this wavelength region.

The determination of the absorbance values was made difficult by the lack of any absorbance peaks in the machine tracings. All samples absorbed very little at wavelengths down to 500 mμ; at this point the absorbance began to increase rapidly until it soon left the chart scale (1.0 absorbance); however, the slope of each plot was different for each sample in this region. In spite of the steep slope, absorbance values were marked off for each mixture at a wavelength of 440 mμ; at this point all samples had absorbance values between zero and one. The recorded values of the absorbance are tabulated in Appendix I; they will be subject to the plotting error and the temperature variations which have been mentioned.

A final mixture was prepared after the examination of the rotation and the absorbance results. This was a solution whose mole ratio of iron to tartrate was one to four and one-half. This solution, prepared as were the others, was bright green upon completion of the alkali addition but after one day it too had turned brown and began to precipitate a very small amount of the brown solid. It was filtered after standing for one week; the optical rotation of this mixture and a corresponding tartrate solution were then recorded and included in the results. The absorbance was not measured because of the necessity for the remeasurement of all other samples in order to insure a common basis for comparison. The concentrations and the rotation values are included in Appendix I.

RESULTS

The continuous-variations values recorded in Appendix I are plotted in Fig. 3 to 5. Figure 3 is the plot of the actual two-decimeter rotation values of the iron-tartrate mixtures and the rotation values of the tartrate solutions as a function of concentration. Subtraction of the tartrate values from the mixture values (in a point-by-point difference) gives the continuous-variations deviations; these deviation values are plotted in Fig. 4 on a scale which is expanded from that of Fig. 3 by a factor of two. On this plot the various mole ratios which were employed in the series are indicated by the arrows; the peak deviation value shown is that for the solution of mole ratio of 1:4.5. Figure 5 is a plot of the absorbance values; since both components (ferric hydroxide and sodium tartrate) were nonabsorbing, the plot becomes a direct recording of continuous-variations deviations. The mole ratios are also indicated in this figure; the value of the solution of 1:4.5 ratio was not measured; the deviation peak is assumed to be at this point. It is to be noted that although the magnitude of the continuous-variations deviations curves may change with a change in the wavelength (for either rotation or absorbance), the shape of the curves and the peak deviations will be independent of the wavelength used for the measurements. Therefore, these two curves have been plotted to a similar scale.

As evidenced by the continuous-variations plots, the optimum combining mole ratio of the ferric ion and the tartrate ion is not <u>one</u> to <u>three</u> but rather <u>one</u> to <u>four</u> <u>and</u> <u>one-half</u>.

ADDITIONAL EXPERIMENTS WITH 1:4.5 FeTNa

A 500 ml., round-bottomed, three-necked flask was coated with black paint to exclude light. It was equipped with a stirrer, a dial thermometer, and a

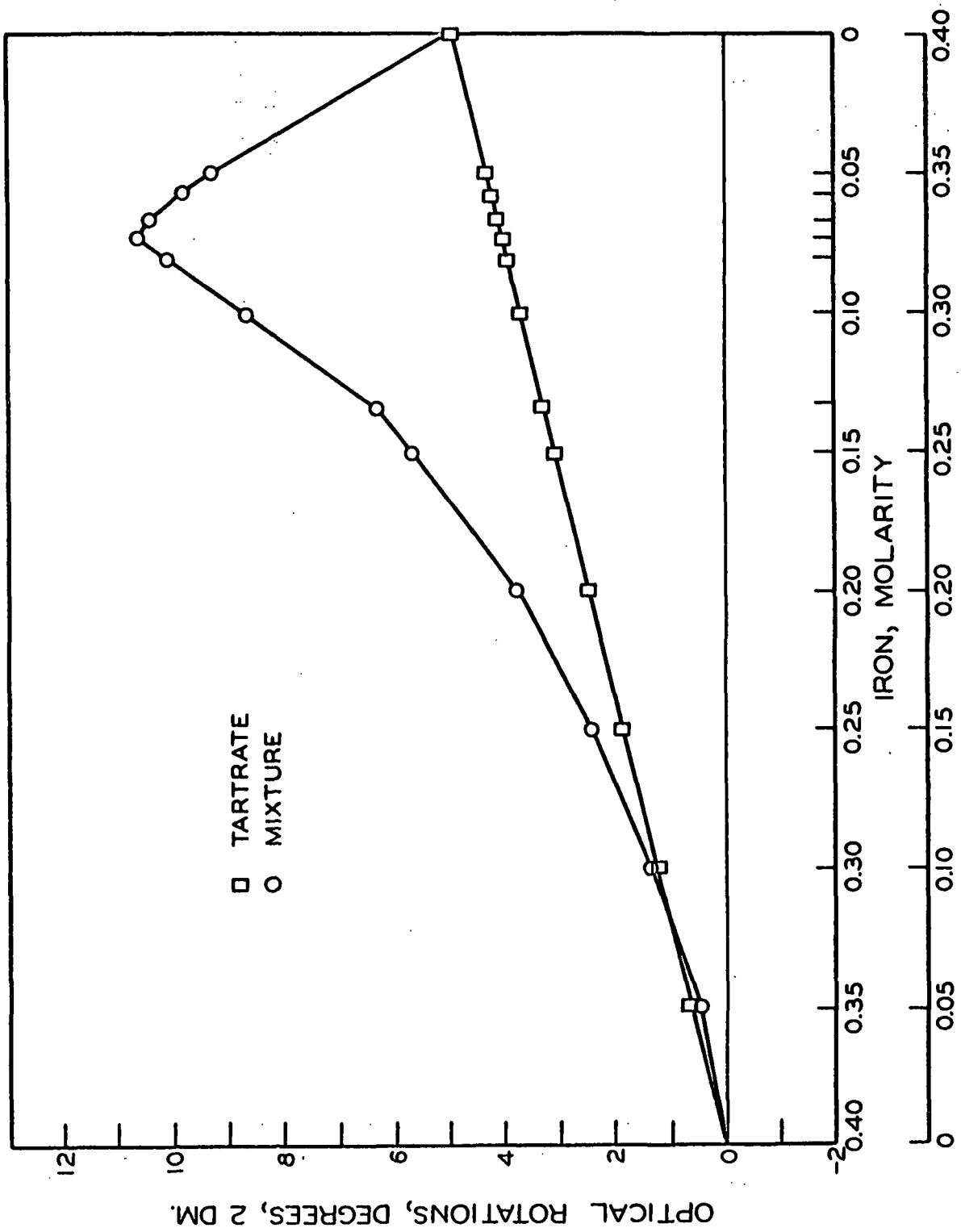

Figure 3. Optical Rotation: Ferric Nitrate – Sodium Tartrate

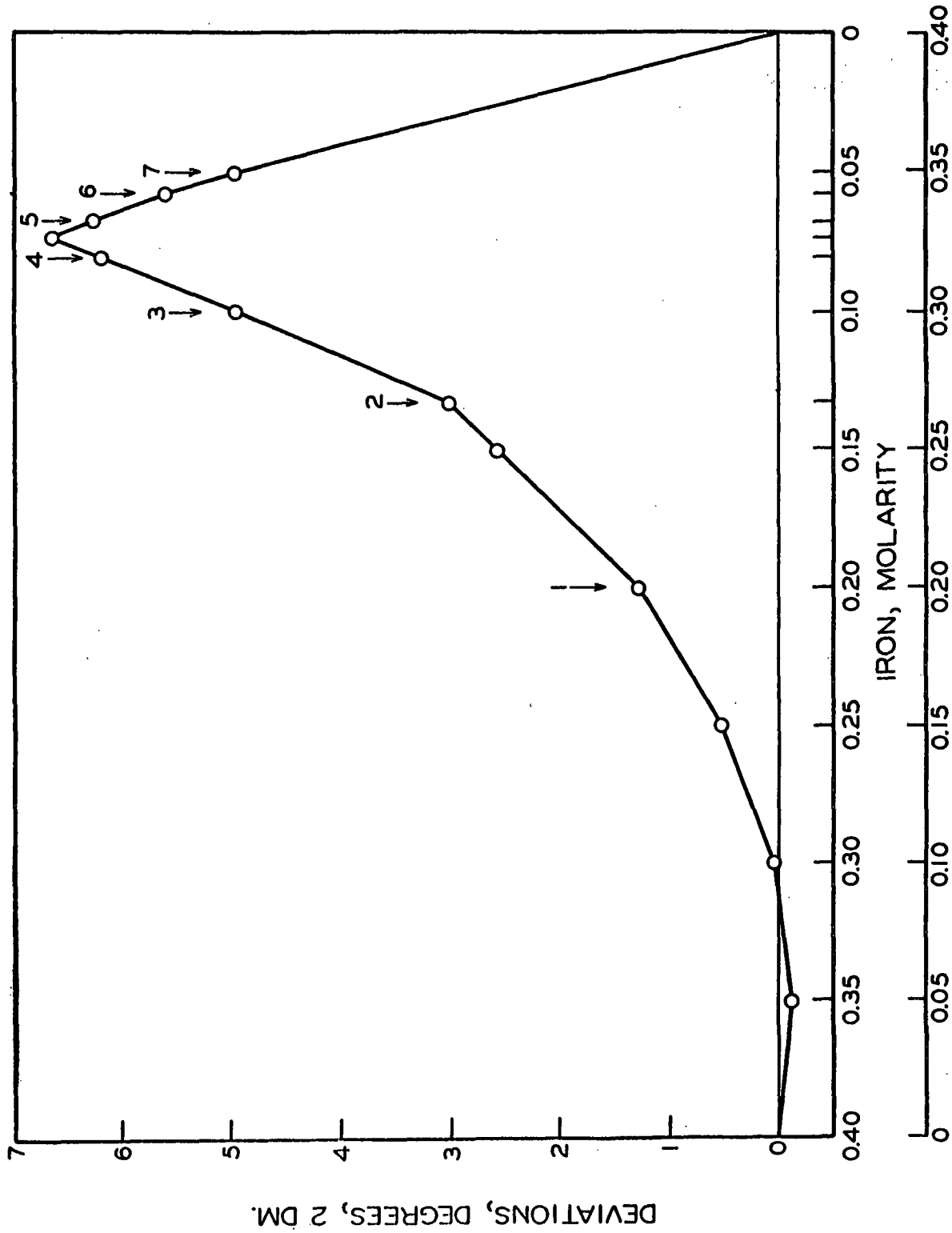

Figure 4. Deviations: Ferric Nitrate – Sodium Tartrate

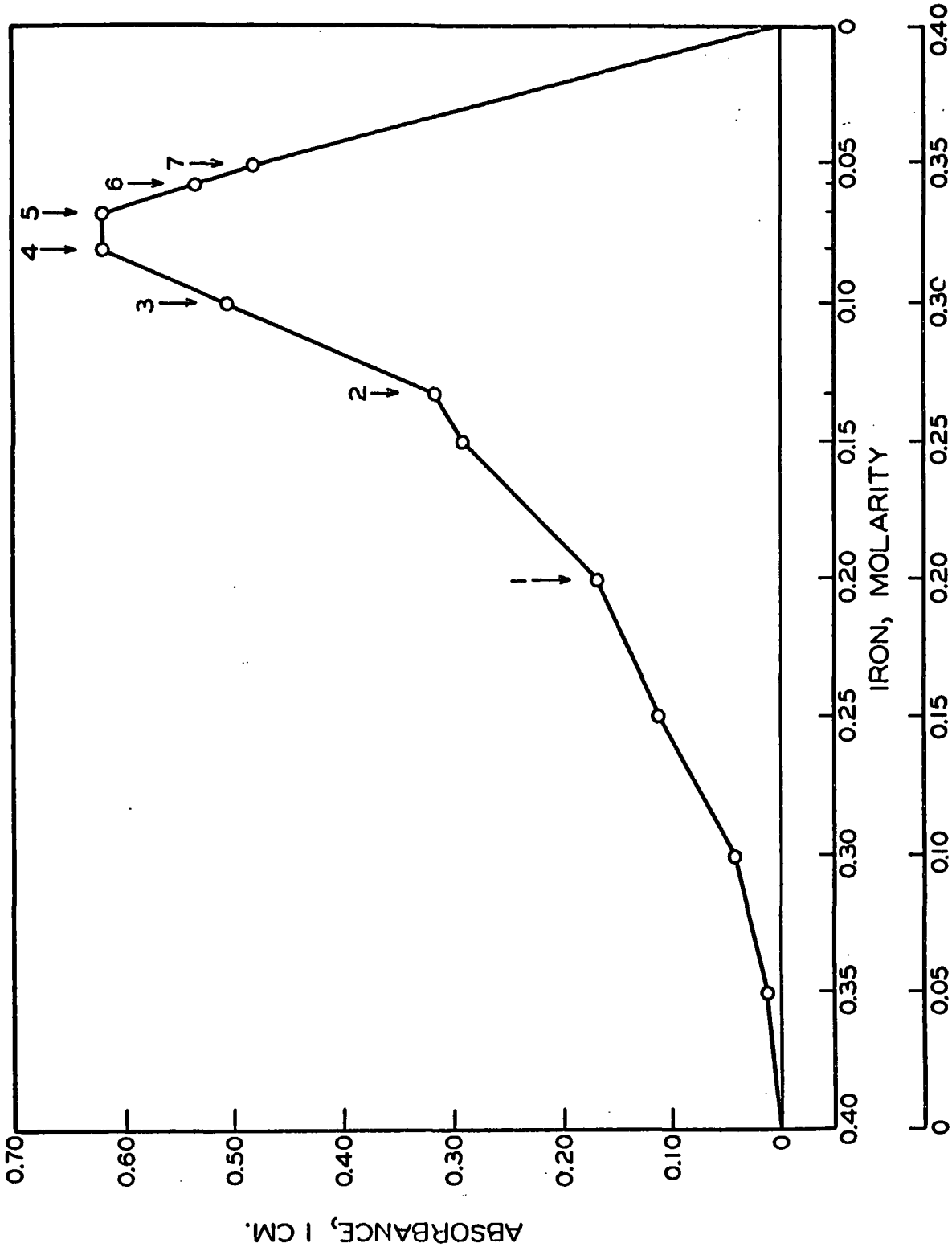

Figure 5. Absorbance: Ferric Nitrate – Sodium Tartrate

bent, black-coated tube and was supported in an enameled pan. Amounts of ingredients were calculated which would provide 250 ml. of a solution which was 0.50M with respect to iron and which had 4.5 moles of tartrate for each mole of iron. For each mole of tartrate were provided three moles of alkali, two for conversion of the acid to the sodium salt and one for the formation of the complex. Additional alkali was calculated to provide an excess corresponding to a 2.0M solution of sodium hydroxide. These calculations assumed that one mole of alkali would be required for each mole of tartrate which reacted to form the complex.

The proper amounts of ferric nitrate monohydrate (50.50 g.), tartaric acid (85.28), and solid sodium hydroxide (88.65 g.) were weighed into plastic weighing bottles. The tartaric acid was dissolved in a minimum amount (100 ml.) of warm water (40°); the ferric nitrate was added to this solution, which was stirred until both solids had all dissolved. This mixed solution (dark red-brown in color) was transferred to the black flask and cooled to 5° by means of an ice bath in the pan. The alkali had been dissolved in an equal weight of water and cooled; it was then added in small portions to the rapidly stirred contents of the flask. The addition was done over a period of 1.5 hours to prevent the heat which was evolved by the alkali addition from raising the temperature of the reaction mixture above 18°.

The completed solution, bright green and clear, was transferred to a round-bottomed flask. In spite of careful transfer operations, the volume was nearly twice the required 250 ml. This volume was decreased by reduced-pressure concentration; the maximum bath temperature which was reached was 60°. The solution, still a brilliant green color, was concentrated to 200 ml., transferred to a 250-ml. volumetric flask, and brought to volume with water. After thorough mixing, the slightly viscous solution was filtered through a dry, packed-asbestos

pad on a glass-fiber disk to remove any traces of debris, although there was little in the solution. The filtered solution was stored in a plastic bottle.

This complex solution failed to dissolve cellulose. One-half gram of air-dried, fluffed, acetate-grade cotton linters (Buckeye Cellulose Corp.) was weighed into a plastic bottle. The FeTNa complex just prepared was cooled to zero degrees; 50 ml. of the cold solution were pipetted into the bottle. This was shaken intermittently by hand for several hours while the fiber suspension was kept cold by immersing the bottle frequently in an ice bath. In spite of vigorous agitation, the fibers failed to dissolve; the small fibers became suspended in the green solution but very little swelling was evident, nor did the viscosity of the solution increase to any noticeable extent. Even after several days of intermittent agitation, during which time the suspension was kept in a refrigerator, little swelling was evidenced by the fibers; there was probably no dissolution at all. The appearance of this suspension was very similar to that of a second sample of linters in which 2.0M sodium hydroxide solution was used to suspend the fluffy fibers. Under these conditions, the iron-tartrate complex solution of 1:4.5 mole ratio does not dissolve this cellulose sample; this is in contrast to the behavior of the 1:3 FeTNa which is described later.

COMPLEXING OF MODEL COMPOUNDS WITH 1:3 MOLE RATIO FeTNa

The FeTNa complex which was selected to determine the complexing behavior of model compounds had the composition which corresponded to a one to three mole ratio of iron to tartrate; this complex was contained in a solution which was 2.0M in sodium hydroxide. This composition corresponds to that of the cellulose solvent which is described in the literature. All of the continuous-variations testing, with but one exception, employed FeTNa of this composition. The

selection of this composition was done because of the importance of the behavior of the model compounds with the FeTNa complex which is capable of cellulose dissolution.

PREPARATION OF 1:3 MOLE RATIO FeTNa COMPLEX

The preparation of the FeTNa complex (1:3) followed the direct procedure in which no intermediate was isolated (15); since the exact knowledge of the iron content was important to the subsequent continuous-variations calculations, any method of preparation by which this content became uncertain was to be avoided. An important modification from the literature description was the absence of any extra tartrate (for stabilization) in these preparations; the amount of tartrate added was exactly three times the amount of iron present on a molar basis.

The preparation employed the same apparatus as was used to prepare the 1:4.5 ratio complex. Initial attempts at the preparation employed the tartrate salts as the source of the tartrate anion; both potassium sodium tartrate and sodium tartrate were tried. Using the same procedure as described earlier, it was found to be impossible to prepare a complex solution which was 0.50M with respect to iron and still maintain the volume below the required limit. When concentration at reduced pressure was attempted to remove the excess water, the bright green solutions invariably began to turn pale brown, then deepen in color until they became an opaque brown-black liquid. This behavior was noticed even when mild bath temperatures (below 40°) were employed during the concentration. It also became apparent that once the discoloration started, it proceeded quickly to form the black solution even if the solution were quickly cooled in a cold bath. None of these discolored solutions was deemed to be useful.

By switching to tartaric acid as the tartrate source, this difficulty was obviated. More tartaric acid could be dissolved in less water than could the tartrate salts. Also, the ferric nitrate could be dissolved in this concentrated tartrate solution without the addition of any more water; this combined solution could then be transferred to the black reaction flask. Although the quantity of alkali required was increased (for the conversion of the acid to the sodium salt), this was more than offset by the reduced volume required for both tartrate and iron. By very careful transfer and washing operations, the volume could usually be kept below the required final volume and still maintain a quantitative preparative procedure. The success of this procedure with the tartaric acid depended upon the avoidance of the necessity for reduced-pressure concentration of the finished complex solution.

After many trials, a final procedure was adopted which proved to be successful in subsequent preparations. Tartaric acid (56.85 g.) was dissolved in 50 ml. of triply distilled water by heating the solution to 40°. Ferric nitrate nonohydrate (50.86 g.) was weighed into a plastic beaker and transferred to the warm tartrate solution with a few milliliters of water. When both solids had dissolved, the mixed solution was transferred to the black flask with a minimum of water. This solution was cooled to 5° with the ice bath. Sodium hydroxide (66.67 g.) had been dissolved in 60 ml. of water and cooled. This alkali solution was added in small portions to the rapidly stirred contents of the black flask through the bent tube. Over a period of about one hour, the temperature was held below 20° during the alkali addition. The clear, green solution was transferred carefully from the reaction flask to a 250-ml. volumetric flask and brought to 20° in a temperature bath. The volume was brought to the mark with small portions of water (usually only a few milliliters were required), with rapid agitation of the

flask between portions. The completed solution was filtered through a dry, packed asbestos pad and stored in a plastic bottle in a refrigerator. This solution, prepared by this procedure, was 0.50M in iron, 2.0M in excess (free) sodium hydroxide, and had an iron-tartrate mole ratio of one to three.

The success of this procedure required that transfers and washings be done with a minimum amount of water; preparations which exceeded the required volume were discarded. Using this technique, other solutions of FeTNa (0.50M in iron) were prepared which contained 2.0M, 1.0M, and 0.5M free sodium hydroxide. All of these solutions were apparently stable (the absence of any discoloration) when stored in a refrigerator. By careful concentration at reduced pressure (and with luck), a FeTNa solution was prepared which was 1.0M in iron and 2.0M in alkali. This was prepared in the usual fashion but was concentrated at reduced pressure at a bath temperature of 30° where the outlet condenser of the rotary evaporator was cooled with ice water. This solution was quite viscous and appeared to be at the upper limit of FeTNa concentration. When stored at room temperature, all of these FeTNa solutions began to discolor after several months; those which had the lowest concentration of free alkali were the first to turn brown. By keeping them cold, these complex solutions retained their clear, green color for periods of storage of at least one year.

DISSOLVING OF CELLULOSE

To verify the ability of this 1:3 mole ratio FeTNa to dissolve cellulose, 1.00 g. of the fluffed, acetate-grade cotton linters were weighed into each of two plastic bottles. Into one bottle was pipetted 50 ml. of 2.0M sodium hydroxide solution; the fibers were dispersed by shaking the bottle. This suspension was cooled in an ice bath; 50 ml. of the 1.0M FeTNa (2.0M alkali) were then added by

pipet. The slurry was shaken vigorously, then returned to the ice bath and shaken occasionally; all fibers appeared to have dissolved within one hour. The result was a clear, green, extremely viscous solution.

Into the second bottle, containing the linters, was pipetted 100 ml. of the 0.5M FeTNa (also 2.0M in alkali) which had been cooled in the ice bath. The suspension was agitated and returned to the ice bath. By shaking the suspension intermittently over a period of several hours, this sample of cellulose soon dissolved completely to yield a highly viscous solution which was identical in appearance to the first cellulose solution. Both solutions remained bright green over several months of storage in a refrigerator; in addition, little viscosity decrease was noticed for either sample during this time.

The FeTNa of 1:3 iron-tartrate mole ratio dissolved this cellulose sample easily, whereas, in contrast, FeTNa of a 1:4.5 mole ratio was unable to do so under identical conditions.

PREPARATION OF MODEL COMPOUNDS

The preparation of each model compound which was used in this segment of the study is described in detail in Appendix II. Sufficient amounts of each material were obtained to enable enough solution to be prepared so that the jacketed, two-decimeter polarimeter tube could be used for the continuous-variations measurements; the capacity of this tube was 12 ml. of solution. Two partly methylated glucosides were prepared; these were methyl 4,6-di-O-methyl-β-D-glucopyranoside and methyl 3-O-methyl-(α,β)-D-glucopyranoside. An attempted synthesis of methyl 3,4-di-O-methyl-β-D-glucopyranoside by the method of Mitra, Ball, and Long (46) was not successful; two separate attempts yielded only a small quantity of material whose physical constants failed to match literature

values. This material was not used in the continuous-variations testing program; the preparation therefore is not described in the appendix.

CONTINUOUS-VARIATIONS MEASUREMENTS

The technique of continuous variations requires the establishment of a constant total molarity to be used in the preparation of the mixtures. For this study, 0.50M was selected; this is the concentration of FeTNa which easily dissolves cellulose and which can be prepared without undue difficulty. As a solvent basis, 2.0M sodium hydroxide was selected.

For the preparation of the continuous-variations mixtures, an amount of model compound corresponding to a 0.50M solution was weighed (to within 0.1 mg. of the desired amount) into a 50-ml. volumetric flask. The sample was dissolved in 15 to 20 ml. of triply distilled water. The solution was then made alkaline by pipetting 25 ml. of 4.0M sodium hydroxide into the flask; after brief agitation, the volume was brought to the mark with water. This technique proved to be successful with all model compounds except methyl 2,3,4,6-tetra-O-methyl-β-D-glucopyranoside; when the aqueous solution of this model was made alkaline, the glucoside immediately separated as an oil from an aqueous phase. This material, evidently "salted out" of solution by the alkali, was recovered by extracting the alkaline suspension with diethyl ether, evaporating the ether from the separated solution, and seeding the sirup which resulted. The other model compounds remained in solution after the addition of the alkali although a very faint yellow cast was noticed with the glucosides and the substituted glucosides. Mannitol failed to dissolve completely in the water alone; however, it too dissolved completely when the alkali was added. These solutions of model compounds, 0.50M in model and 2.0M in sodium hydroxide, were all clear and transparent.

The mixtures of model compounds and FeTNa were prepared in glass vials. Into five vials respectively were added, by buret, 12.00, 9.00, 7.50, 6.00, and 3.00 ml. of FeTNa (0.50M in iron, 1:3 iron-tartrate mole ratio, and 2.0M in sodium hydroxide). To each of these vials were then added 3.00, 6.00, 7.50, 9.00, and 12.00 ml. of the model compound solution (0.50M with respect to the model and 2.0M in alkali). This technique gave mixtures of the following concentrations of FeTNa/model: 0.40/0.10, 0.30/0.20, 0.25/0.25, 0.20/0.30, and 0.10/0.40M. Also prepared at the same time was a series of mixtures of diluted FeTNa; this was done by using 2.0M sodium hydroxide in place of the alkaline solution of model compound in the preparation of the mixtures. This yielded a series of FeTNa solutions of molarities of 0.50, 0.40, 0.30, 0.25, 0.20, and 0.10. One additional mixture was prepared for model compounds which were optically active; this was a solution which was 0.25M with respect to the model. This was prepared by the dilution of 7.50 ml. of the 0.50M model-compound solution with 7.50 ml. of 2.0M sodium hydroxide solution. All mixtures were agitated thoroughly over a period of one-half hour.

The optical rotation of each mixture was then measured at 546 mμ and at 25.00 ± 0.02°; the apparatus was the same as that described for the first continuous-variations measurements with ferric nitrate and tartaric acid. The actual recorded rotation values for the two-decimeter path length are tabulated in Appendix III; these values represent the average of at least five readings. A fresh set of diluted FeTNa mixtures was not prepared for each model compound. Models were tested in groups (of about three) with the same batch of FeTNa; the same set of measurements for the rotation of FeTNa was applied to the plots for each model compound in the group. The values of the rotation for intermediate concentrations of optically active model compounds were calculated from the

rotation value recorded for the 0.50M concentration; the value at 0.25M concentration was measured to check the linearity of the rotation-concentration relationship. Attempts to provide correlating evidence by the use of spectrophotometric methods were abandoned after a few trials. The lack of temperature control (with the Beckman DK-2) and the absence of any significant absorbance peaks in the visible wavelength region resulted in very erratic continuous-variations plots when the respective values were subtracted. These plots provided very little useful information and are not included.

Departure from this procedure occurred with only one model compound tested; this was the methyl 2,3,4,6-tetra-O-methyl-β-D-glucopyranoside. A few experiments with the recovered material revealed that the glucoside would remain in solution in a medium which was 1.0M in sodium hydroxide. Since a solution of FeTNa had already been prepared which was only 1.0M in excess sodium hydroxide, this was used as a solvent basis for a set of continuous-variations mixtures with the fully methylated glucoside. When prepared (as described earlier), the 0.50M solution of the glucoside in 1.0M alkali was colorless and transparent. However, when the FeTNa solution was added to the glucoside solution to prepare the mixtures, the glucoside again separated immediately as an oil emulsion, the oil soon rose to the top of each sample vial and formed a layer. Since the purpose of this test with the fully methylated glucoside was the establishment of the efficacy of the methyl ether group as a blocking group for the complex formation with FeTNa, the "salting out" of the sugar by the addition of the iron-tartrate was considered to be evidence confirming this behavior. Had a new complex been formed, the glucoside probably would have been carried into solution, which it was not. Continuous-variations plots, however, were not possible with this model compound because of the cloudiness of the mixtures from the formation of the emulsion.

To insure that the mixtures of FeTNa and model compounds had reached equilibrium before the optical rotations were measured, two extra mixtures were prepared. These were a solution of 0.25/0.25M FeTNa(1:3)/methyl β-D-glucopyranoside and a solution of 0.10M FeTNa alone. Each was prepared by adding the ingredients (in solution form) by pipet to a plastic bottle, agitating the mixture briefly, then placing it in the jacketed polarimeter tube as quickly as possible. The first reading of optical rotation was made ten minutes after the mixing of each sample. Neither of these two samples showed any change in optical rotation (± 0.02° for the average of five readings) over a period of two hours; this indicated that the equilibrium between FeTNa (1:3) and the model compounds was rapid and was probably attained in less than ten minutes.

After the measurement of optical rotation, each continuous-variations sample was returned to its vial and stored in a constant-temperature room at 22-23°. Upon standing, differences in appearance became evident among the sets of mixtures of FeTNa with the different model compounds. Many sets remained clear and bright green in all concentrations; these showed no changes at all upon storage for periods of time as long as several months.

Other sets of mixtures, however, had started to discolor and turn brown within one day. The brown color appeared first in those mixtures which were most dilute in FeTNa (0.10M); after several weeks the solution next in the series (0.20M FeTNa) had started to discolor. These solutions were all allowed to stand for several months, after which it was noticed that the brown color had been caused by a solid which was forming in the solutions. This solid had apparently coagulated from a colloidal state which had been formed as a result of the dilution of the FeTNa (1:3) in the process of the preparation of the continuous-variations mixtures. By shaking the sample vials to hasten the coagulation and

to remove the precipitate from the glass walls, the supernatant liquid was revealed to be clear and green. The precipitate was a reddish brown color; it could be filtered from the mixture, after which the filtrate remained clear and green (without any discoloration) for periods of storage up to an additional year at least. This process of discoloration and subsequent precipitation of the solid was very distinctive; if a set of mixtures had failed to discolor after one day or so, it failed to discolor even after six months of additional storage.

Initially, this precipitate was assumed to be ferric hydroxide (or, more likely, hydrated ferric oxide). To verify this assumption, a sample of FeTNa (1:3 ratio) was diluted fivefold (to 0.10M iron) with 2.0M sodium hydroxide. This solution discolored after one day; it was then allowed to stand at 22-23° for six months with occasional agitation. The precipitate which had formed had, by this time, coagulated into small, reddish-brown platelets. These were filtered from the mixture in a fritted-glass funnel and washed with 500 ml. of 2.0M alkali followed by an additional washing with one liter of water. The solid did not peptize and pass through the filter during the washing as had other samples of the solid which had not been allowed to coagulate for as long a period of time. The solid was then dried over phosphorous pentoxide.

The amount of carbon in the precipitate was determined by the Van Slyke wet-combustion procedure (47) to see if any organic material was present. The actual weighing, burning, and calculation of the carbon content was done by J. K. Crossman, who was very familiar with the technique (48). A preliminary experiment indicated that the method was capable of correctly measuring the carbon content of a sample of sodium tartrate. The combustion results with the dilution precipitate of FeTNa indicated a carbon content of only 0.88% for an average of two samples. This result indicated that the precipitate was inorganic in nature and was undoubtedly ferric oxide which was contaminated with a trace of tartrate.

This precipitation behavior is undoubtedly the effect of the dilution of FeTNa by the model compound solutions during the preparation of the various mixtures. Dilution of FeTNa with alkali alone also causes the appearance of the precipitate. If the model is capable of complex formation with the iron-tartrate system, the ferric ion which is freed by the decomposition of the FeTNa as a result of the dilution is incorporated into the new complex and cannot form the insoluble ferric hydroxide. If the model will not complex with the iron, the concentration of the ferric ion exceeds that which is defined by the solubility product of ferric hydroxide because of the dilution; a colloidal suspension of ferric oxide is formed which eventually coagulates to form the solid precipitate.

This precipitation behavior of FeTNa of 1:3 mole ratio was used as supporting evidence for the failure of any particular model compound to complex with the iron. Since the lack of a continuous-variations deviation is not a conclusive result by itself, the appearance of the discoloration and the precipitate served to confirm the negative indication of complexing. In all cases with these model compounds, the negative (zero deviation) continuous-variations indications were accompanied by the precipitate formation. With those models which showed large deviations, precipitation of the iron did not take place.

These procedures and descriptions have applied to FeTNa of 1:3 iron-tartrate mole ratio. As a final experiment with continuous variations, FeTNa of 1:4.5 ratio was tested with methyl β-D-glucopyranoside as a model. The techniques and procedures were the same. The notable difference in behavior of this 1:4.5 ratio complex was the complete absence of any discoloration or precipitation when this FeTNa was diluted fivefold (from 0.50 to 0.10M) with 2.0M sodium hydroxide. Even after several months of storage at 22-23°, all mixtures in the series of diluted FeTNa samples remained as bright, clear, and green as did the mixtures of FeTNa with the glucoside.

RESULTS

The data from the optical rotation measurements (Appendix III) are plotted in the form of continuous-variations deviations curves. The method of plotting is illustrated in Fig. 6 and 7 for two representative model compounds; the first is a compound which has a negative rotation and which also shows a large deviation, while the second example is a positive-rotation compound which shows a very small deviation. The rotation of FeTNa, plotted as a function of the molarity of the iron, is added to the rotation of the model; this gives the sum line. This sum is subtracted from the measured rotation value of the corresponding mixture of FeTNa/Model to yield the deviation curve. The actual rotation values measured for a two-decimeter path length are shown in the plots; intermediate values for the model-compound rotations are calculated from the measured values of the 0.50M sample. Models which are optically inactive have continuous-variations plots in which the FeTNa rotation values become the sum line also; the deviations are then measured from the FeTNa line.

Figures 8 through 23 list the models and illustrate the deviations curves for the sixteen compounds which were tested; the scale is expanded by a factor of ten from that of the sample plots. Noted on each plot is the precipitation behavior of each model compound (the presence or absence of the formation of ferric oxide upon storage of the samples). These plots are quite curved in most cases and do not adequately demonstrate the maximum combining mole ratio of FeTNa (1:3) and model compound. However, the continuous-variations procedure was used only to determine the presence or absence of new-complex formation; the combining mole ratio is not required information.

After examination of the results of the deviations plots and the precipitation behavior of the model compounds, these compounds were divided into three

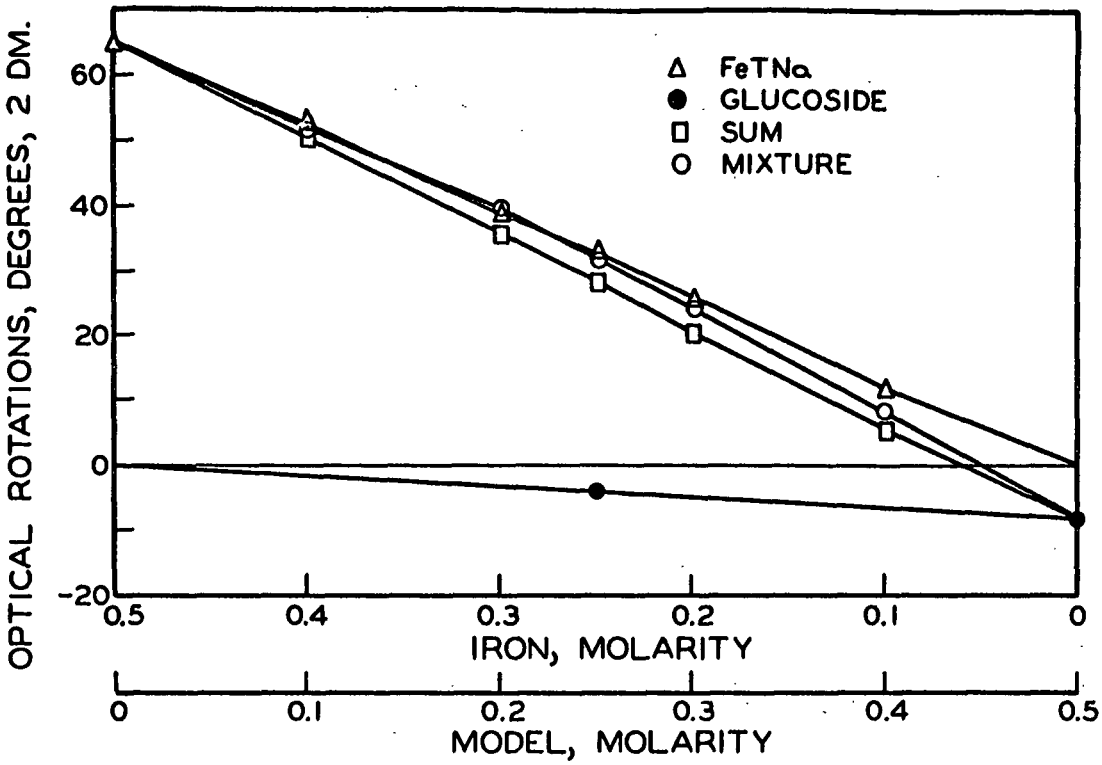

Figure 6. Optical Rotation: FeTNa (1:3) – Methyl 4,6-di-O-methyl-β-D-glucopyranoside

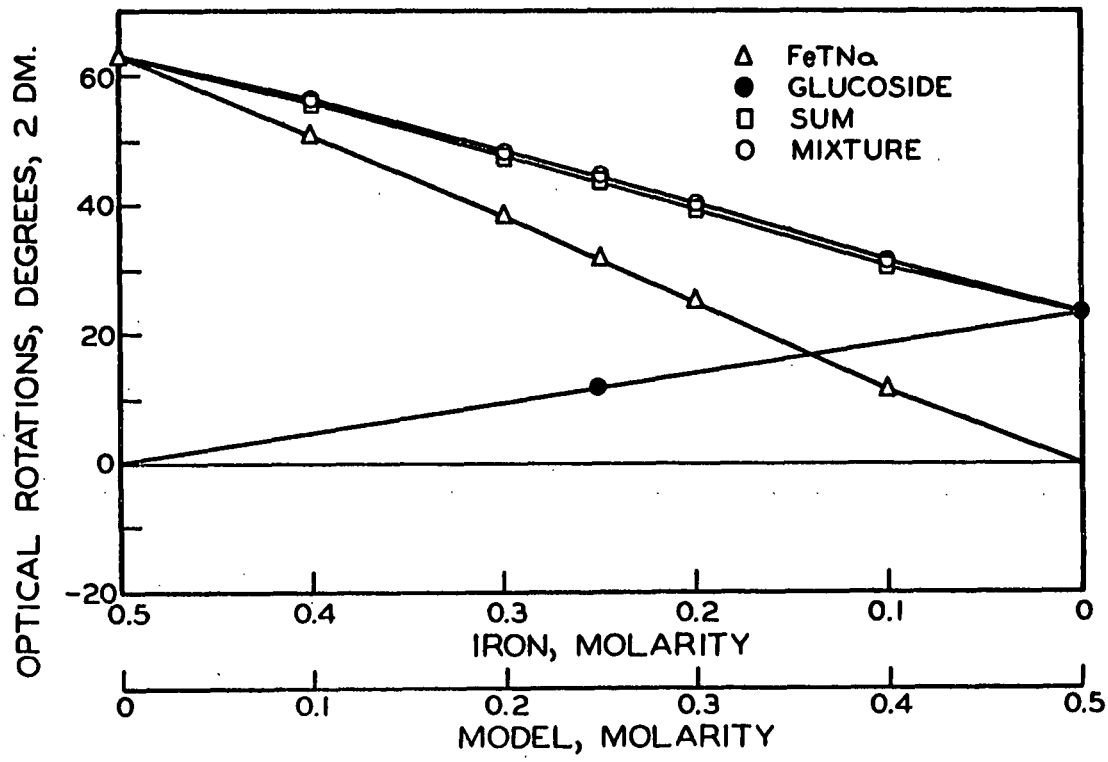

Figure 7. Optical Rotation: FeTNa (1:3) – Methyl 3-O-methyl-(α,β)-D-glucopyranoside

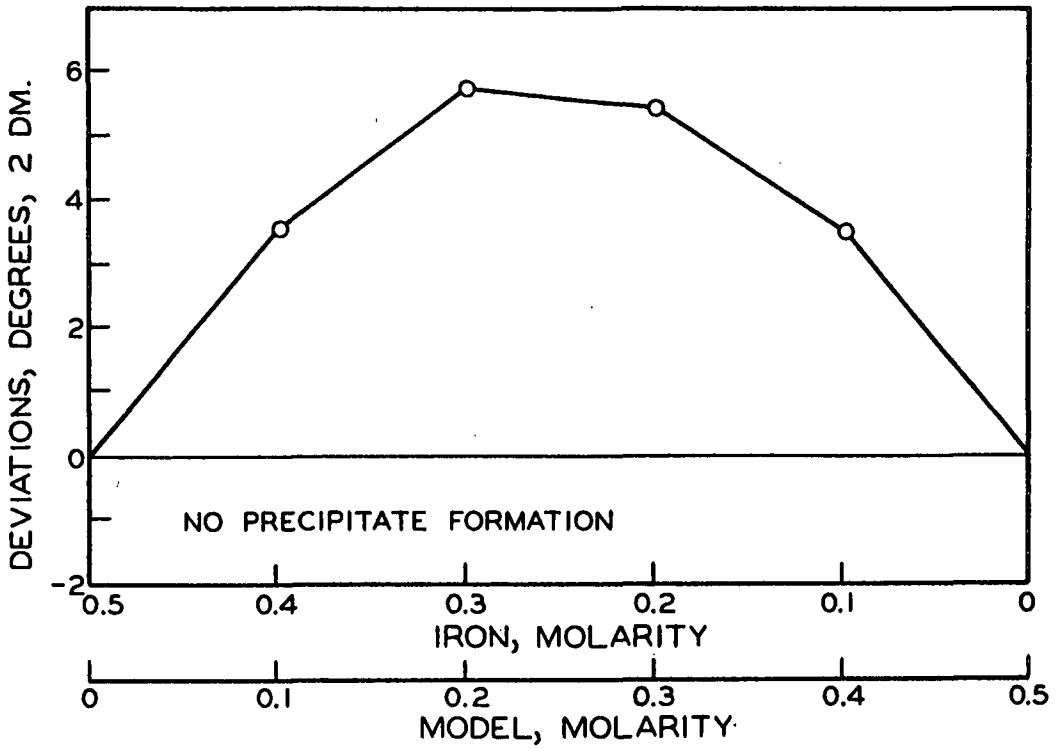

Figure 8. Deviations: FeTNa (1:3) – Methyl α-D-glucopyranoside

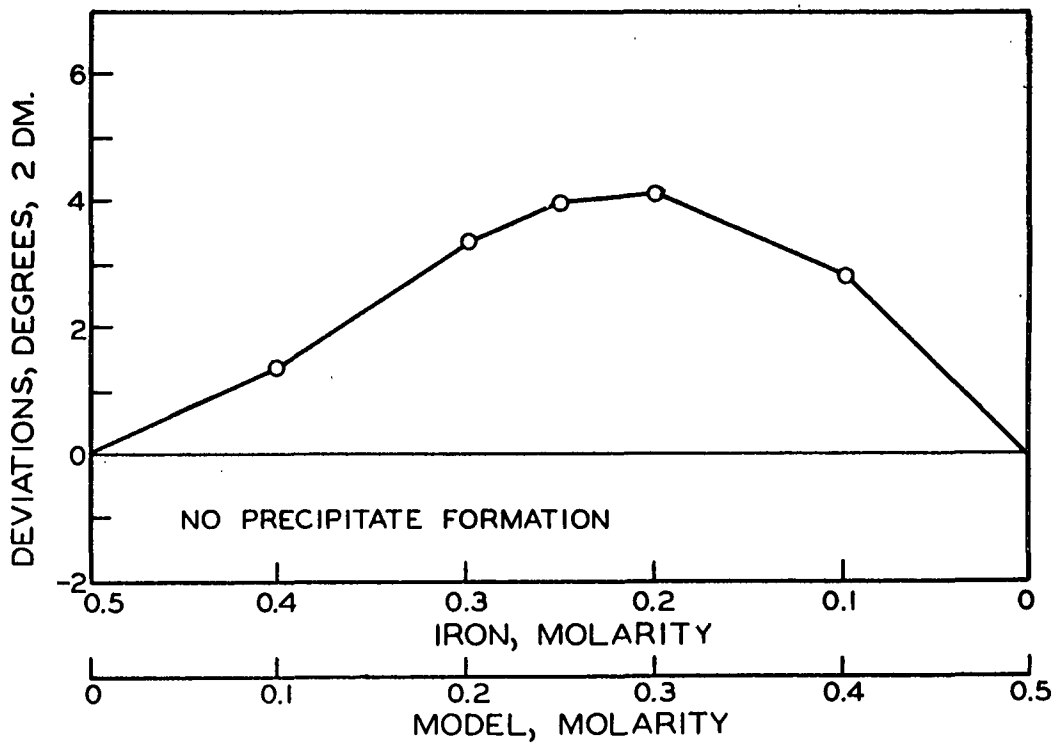

Figure 9. Deviations: FeTNa (1:3) – Methyl β-D-glucopyranoside

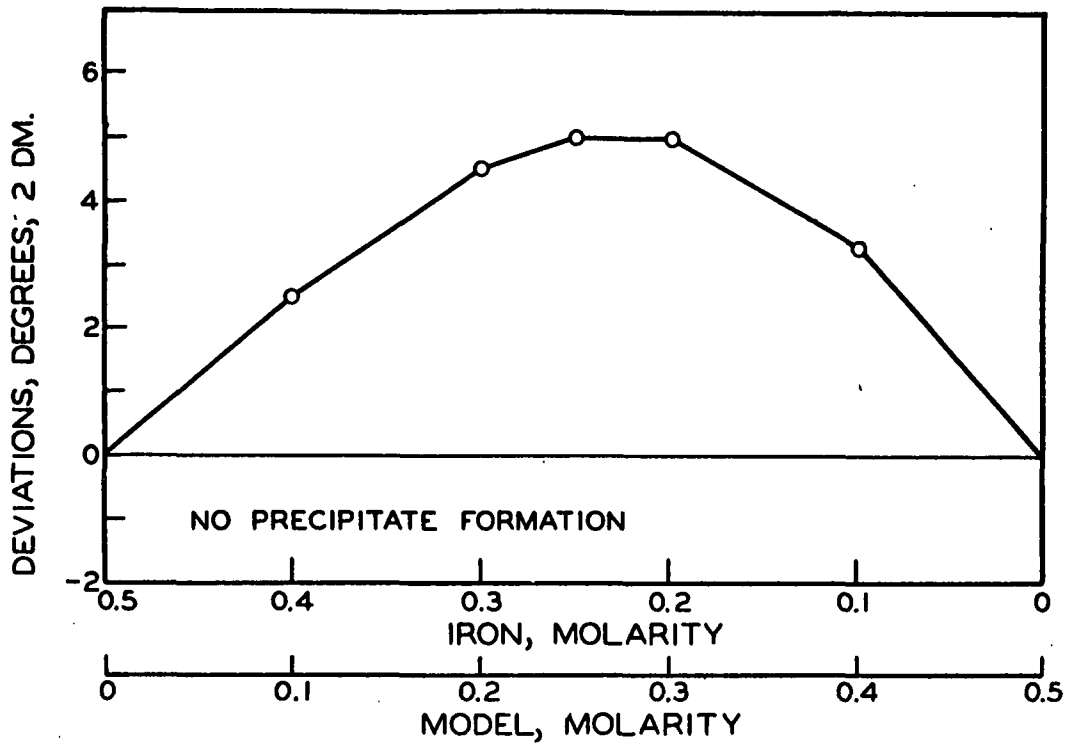

Figure 10. Deviations: FeTNa (1:3) – Glycerol

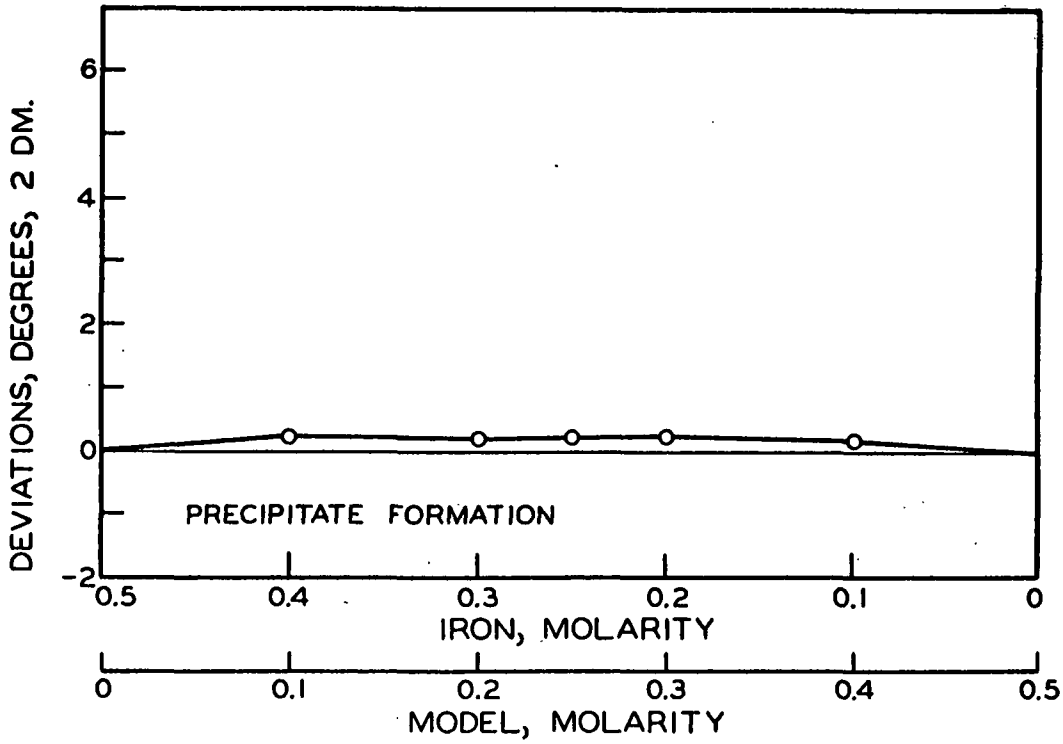

Figure 11. Deviations: FeTNa (1:3) – Propane-1,3-diol

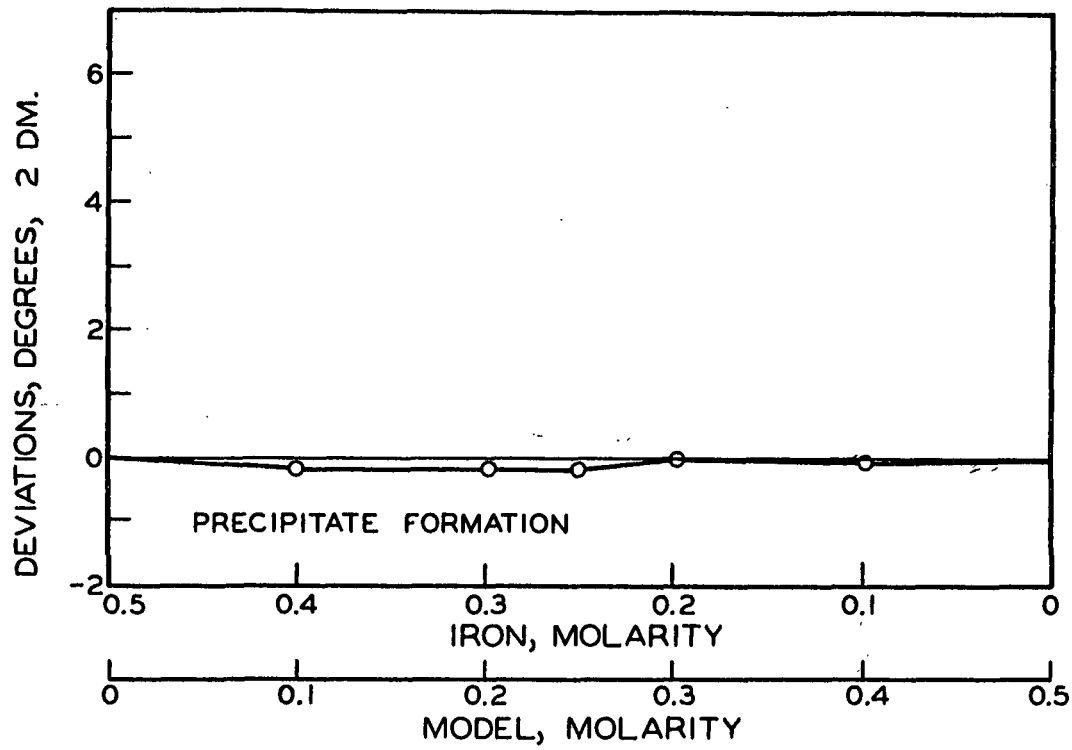

Figure 12. Deviations: FeTNa (1:3) – Methanol

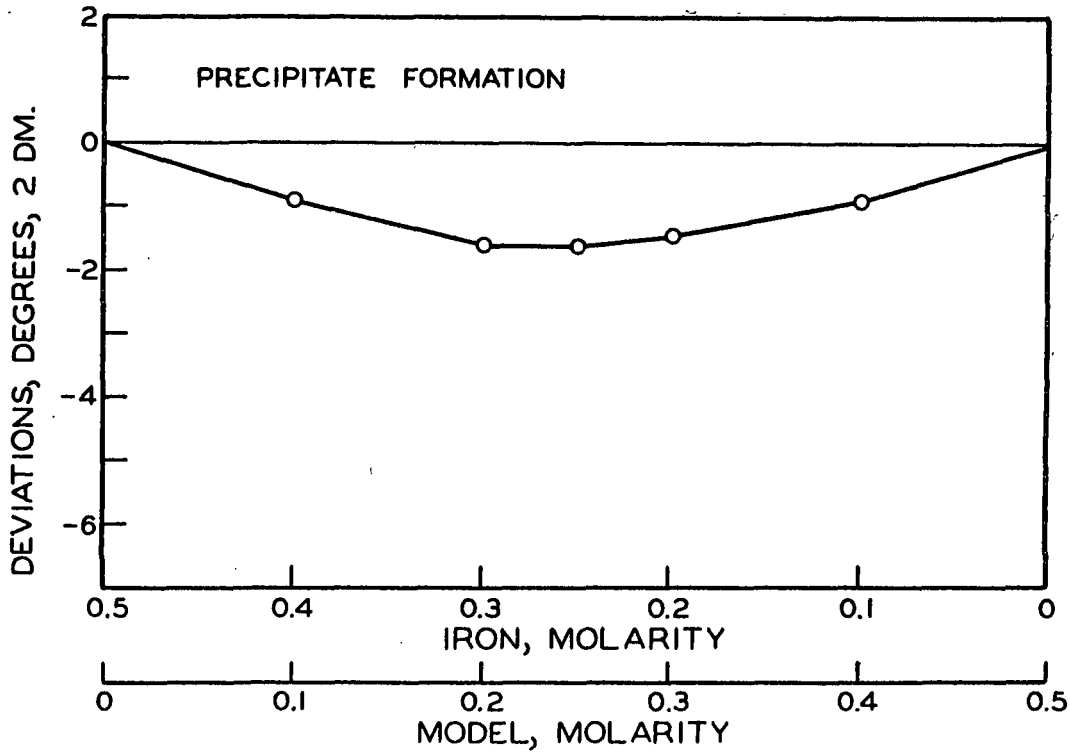

Figure 13. Deviations: FeTNa (1:3) – Sodium Succinate

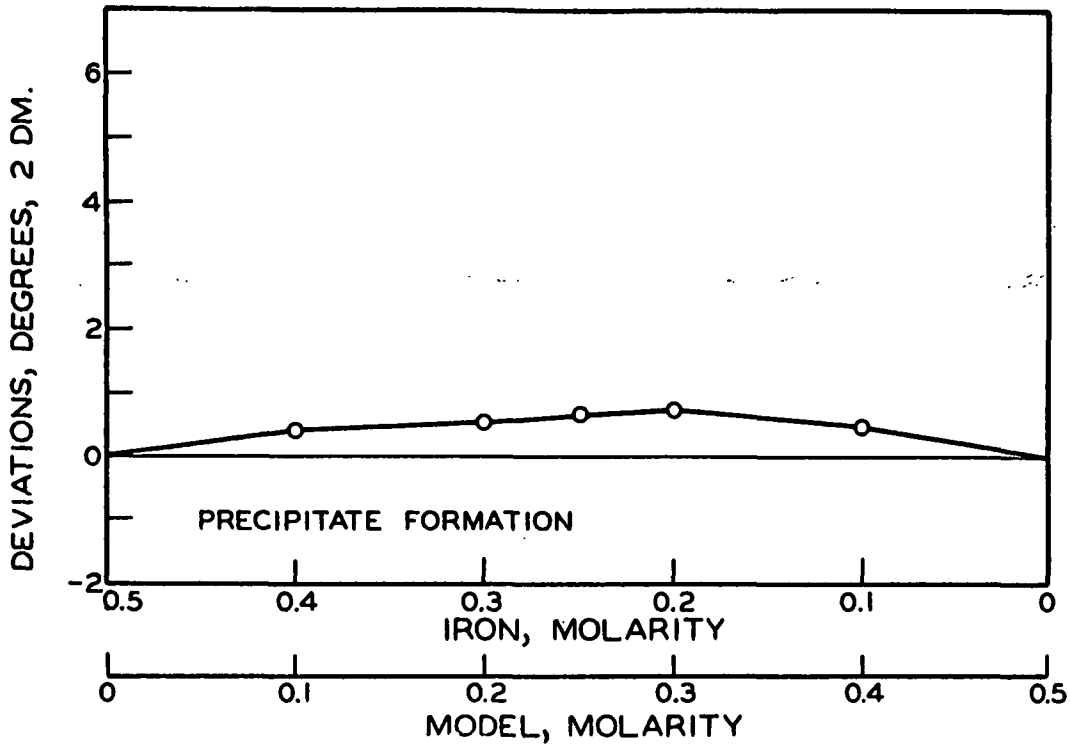

Figure 14. Deviations: FeTNa (1:3) – Butane-2,3-diol

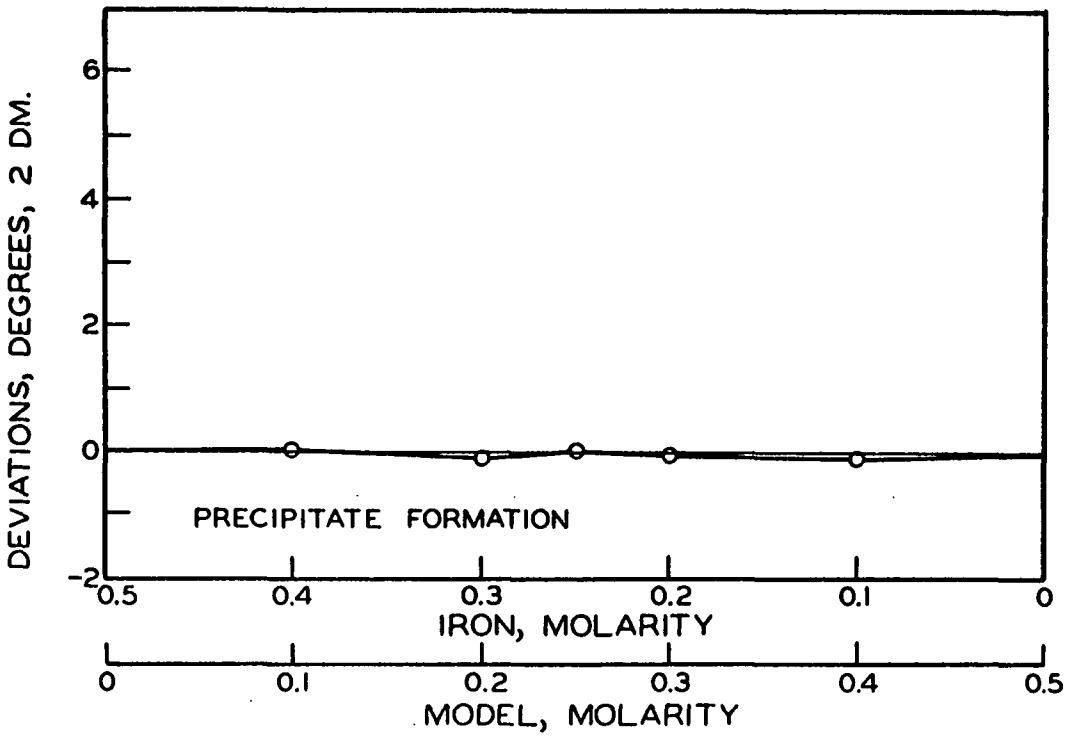

Figure 15. Deviations: FeTNa (1:3) – Butane-1,4-diol

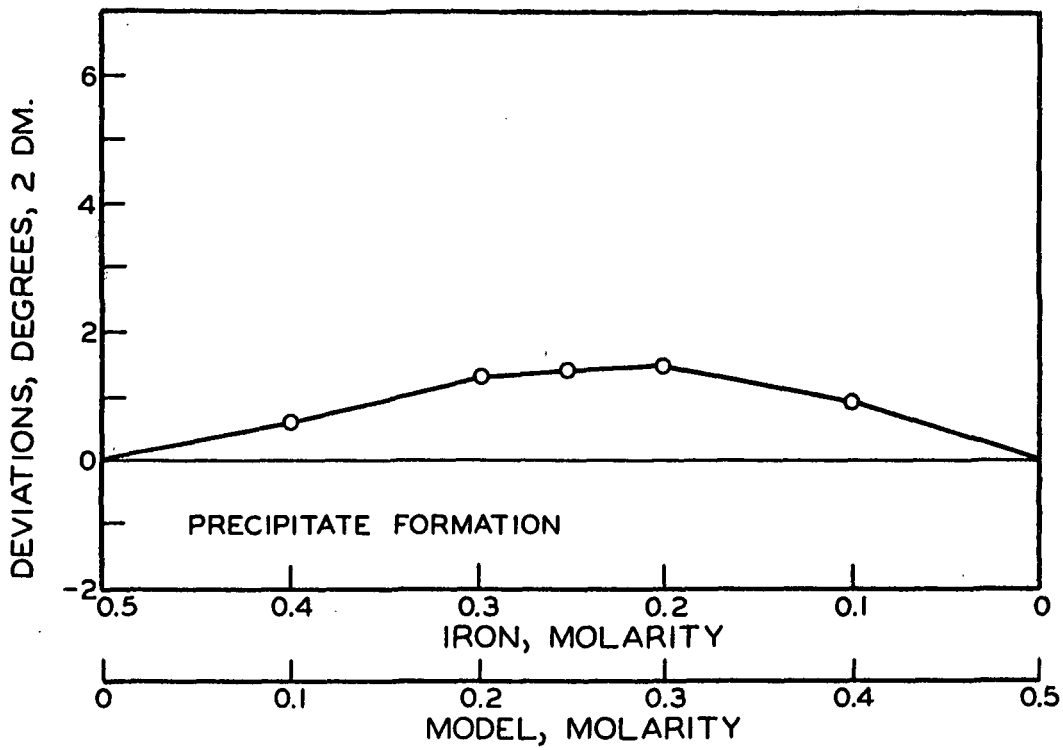

Figure 16. Deviations: FeTNa (1:3) – Ethylene Glycol

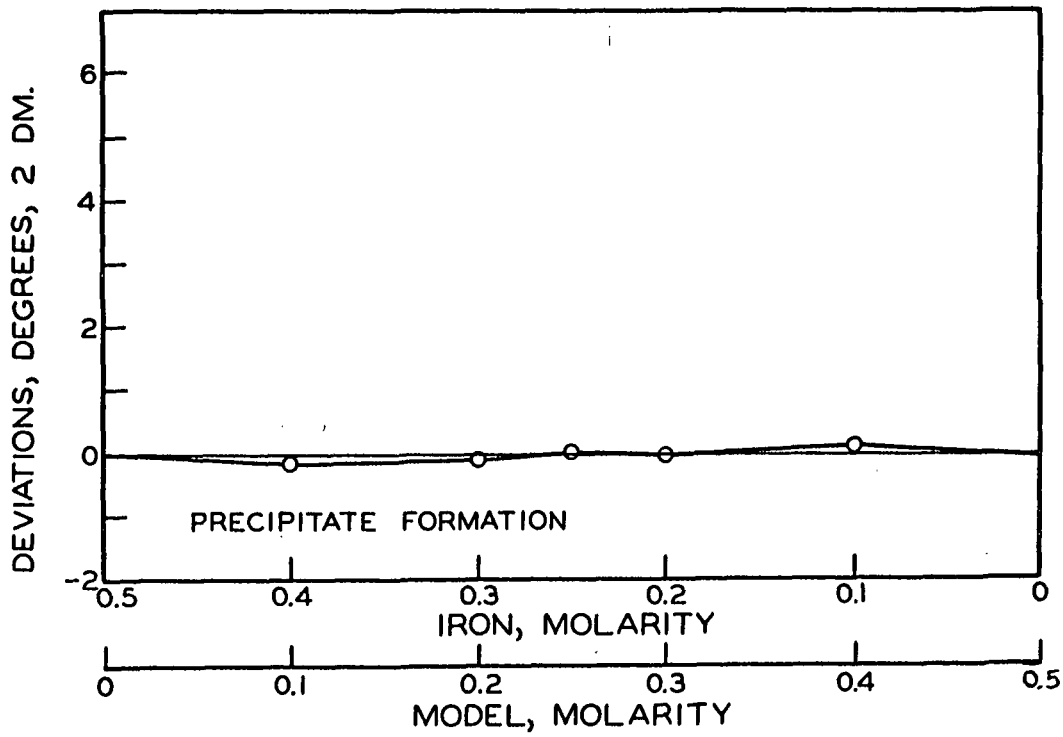

Figure 17. Deviations: FeTNa (1:3) – Methyl Cellosolve

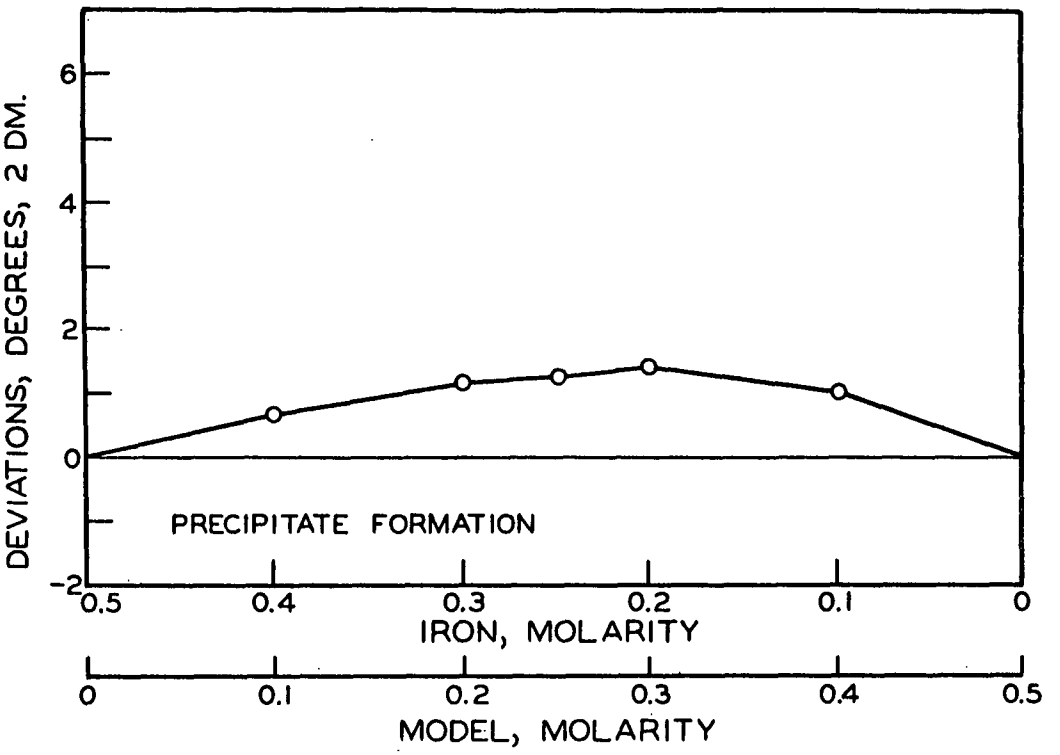

Figure 18. Deviations: FeTNa (1:3) – trans-Cyclohexane-1,2-diol

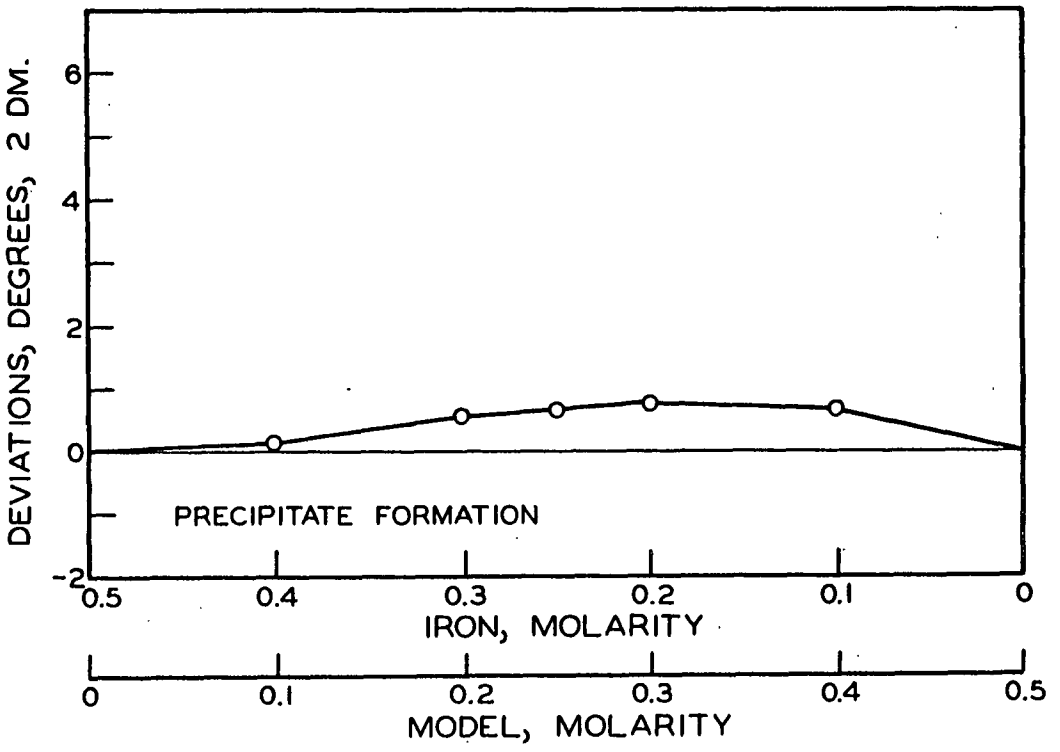

Figure 19. Deviations: FeTNa (1:3) – cis-Cyclohexane-1,2-diol

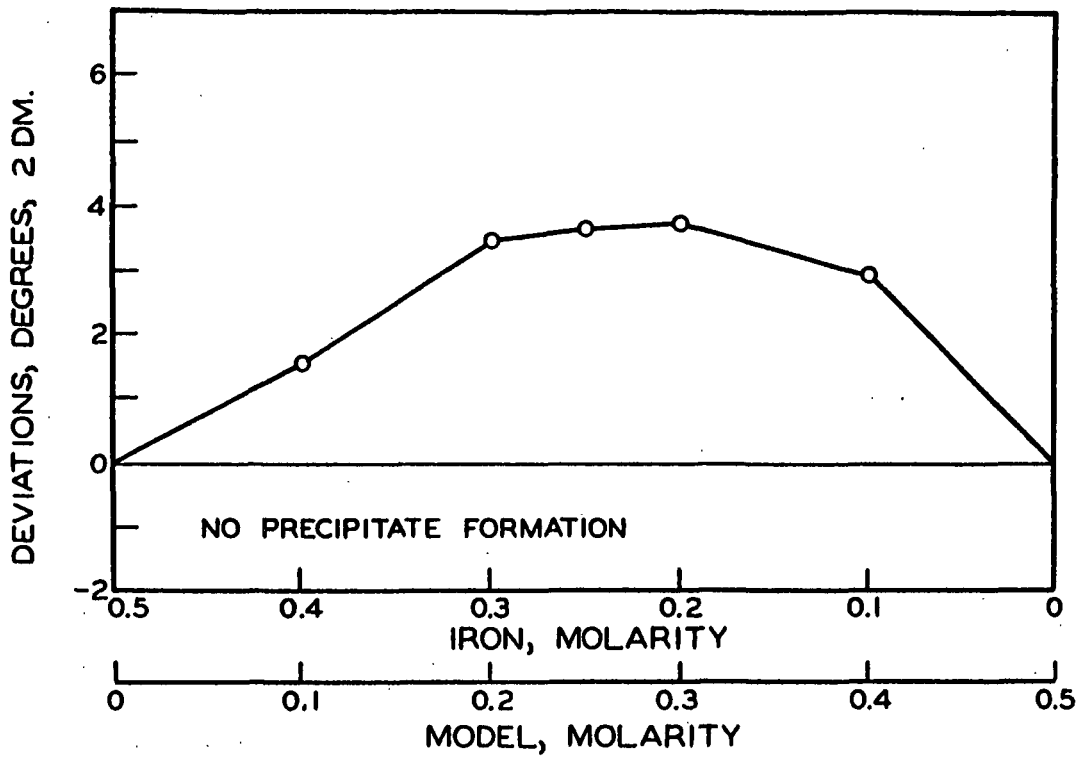

Figure 20. Deviations: FeTNa (1:3) – Methyl 4,6-di-O-methyl-β-D-glucopyranoside

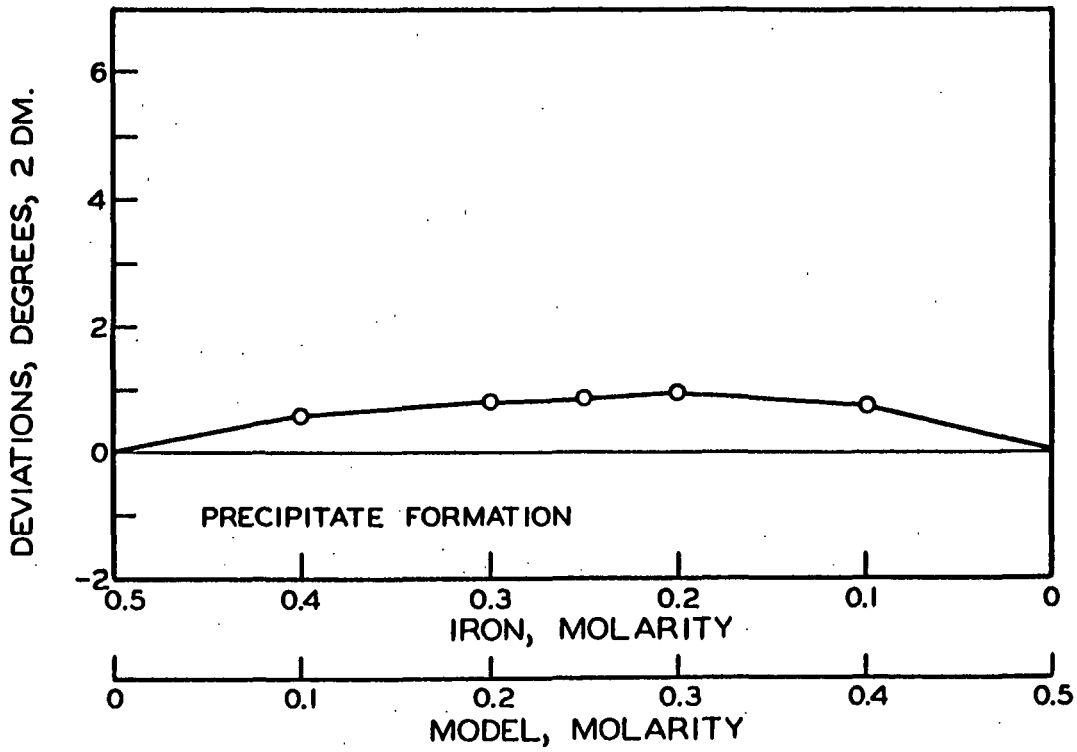

Figure 21. Deviations: FeTNa (1:3) – Methyl 3-O-methyl-(α,β)-D-glucopyranoside

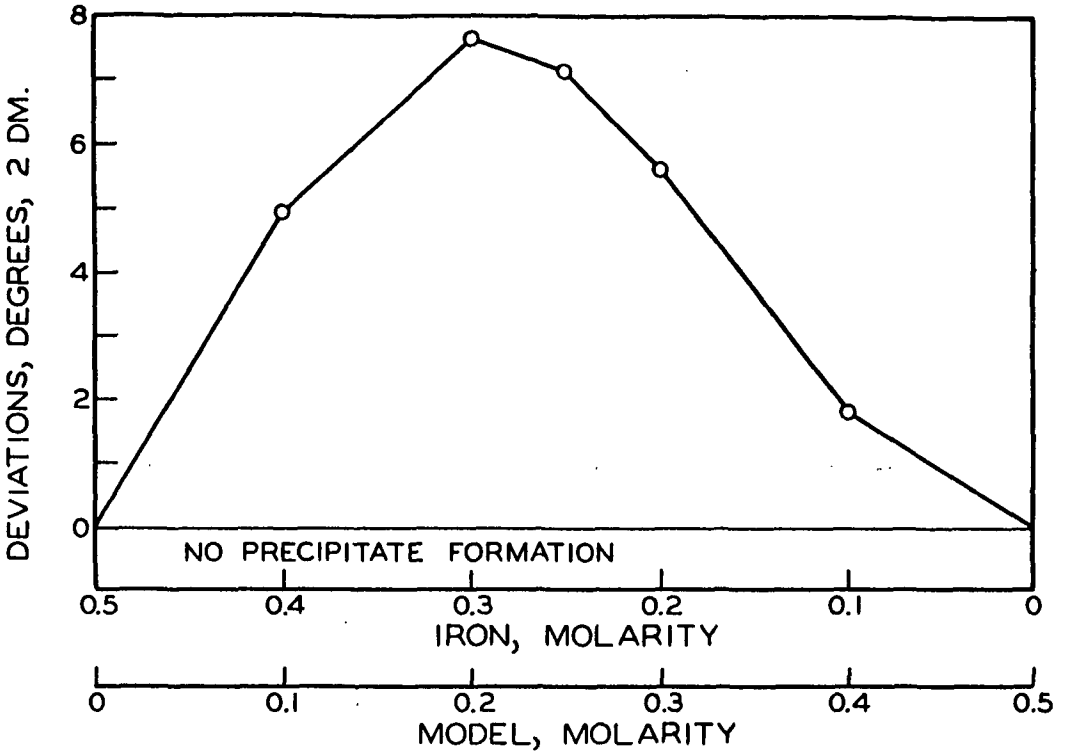

Figure 22. Deviations: FeTNa (1:3) – Mannitol

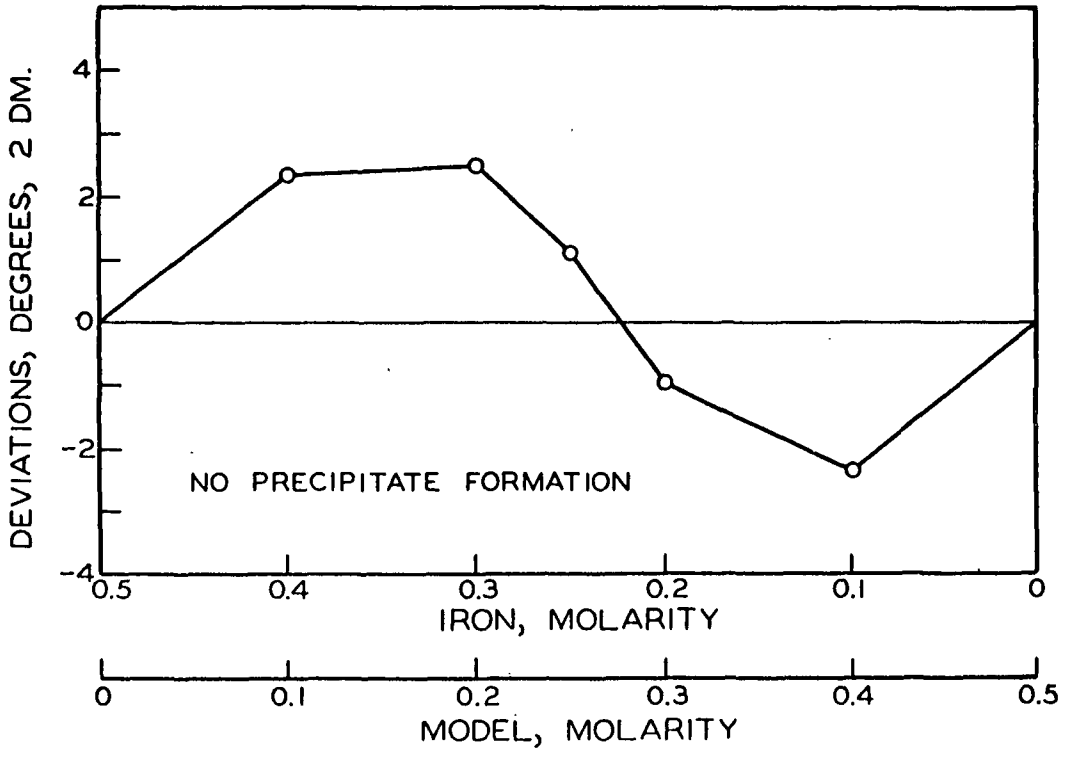

Figure 23. Deviations: FeTNa (1:3) – Sorbitol

groups on the basis of these results: (1) Models which precipitate ferric oxide and show a deviation curve which essentially is zero within experimental error; these include propane-1,3-diol, butane-1,4-diol, methanol, and methyl cellosolve; (2) Models which do precipitate ferric oxide but yet which show a small but significant continuous-variations deviation; these are methyl 3-O-methyl-(α,β)-D-glucopyranoside, ethylene glycol, butane-2,3-diol, cis- and trans-cyclohexane-1,2-diols, and sodium succinate; and (3) Models which do not precipitate the ferric oxide and also show large deviations curves, including methyl α- and β-D-glucopyranoside, glycerol, methyl 4,6-di-O-methyl-β-D-glucopyranoside, sorbitol, and mannitol. This grouping of model compound behavior will be discussed later in terms of model-compound structure and its influence upon new-complex formation with the FeTNa complex.

Figures 24 and 25 are the complete continuous-variations plots for the mixtures of FeTNa of 1:4.5 mole ratio with methyl β-D-glucopyranoside. These plots illustrate the nonlinearity of the rotation-concentration relationship which occurs with FeTNa of this composition.

SUPPLEMENTARY EXPERIMENTS

In addition to the two major segments of experimental work, several minor tests were performed in an attempt to further illuminate the behavior of FeTNa and its possible mechanism of cellulose dissolution. These results were incomplete and are described only briefly; they were concerned with attempted substitutions of other metallic ions for the ferric ion, and a substitution of some other ligand for the tartrate anion in mixtures which were analogous to the 1:3 mole ratio FeTNa cellulose solvent.

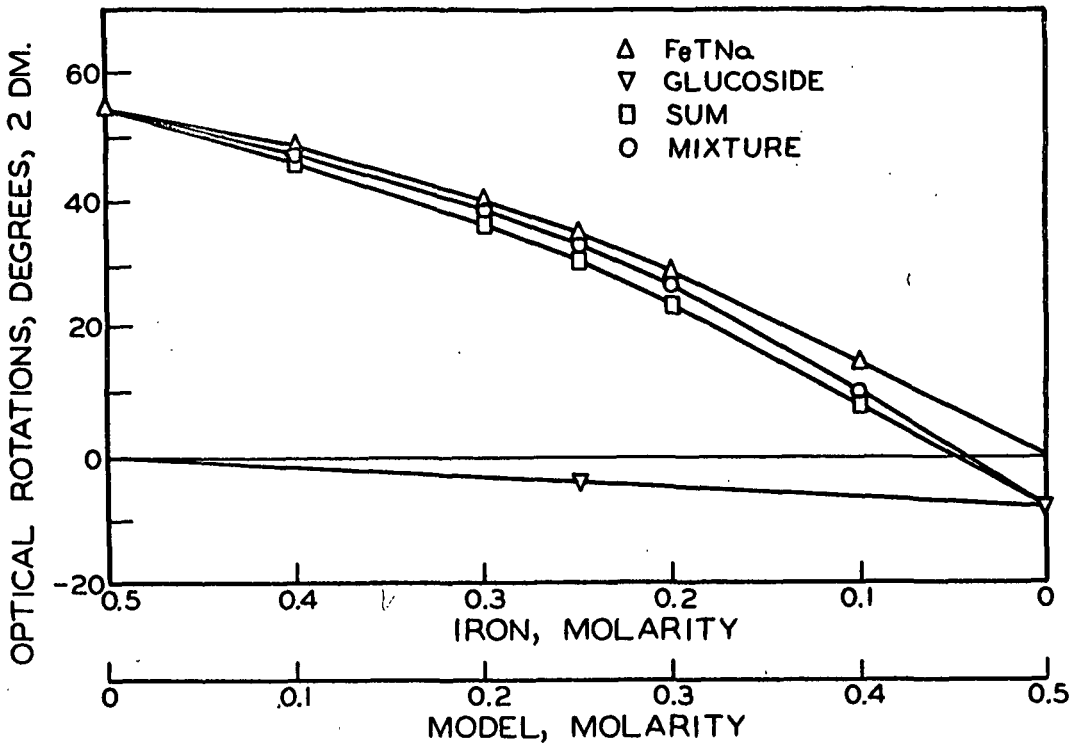

Figure 24. Optical Rotation: FeTNa (1:4.5) – Methyl β-D-glucopyranoside

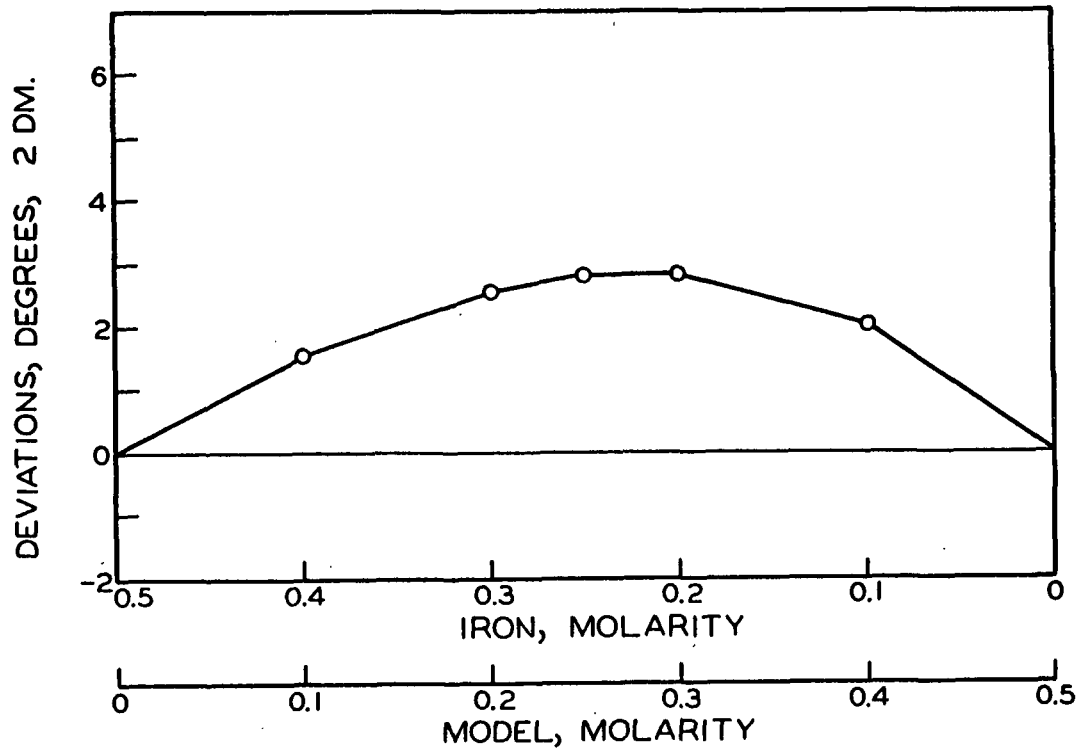

Figure 25. Deviations: FeTNa (1:4.5) – Methyl β-D-glucopyranoside

OTHER METALLIC IONS

Using a 1:3 mole ratio of metal to tartrate, mixtures of aluminum tartrate and chromium tartrate were prepared in which the concentration of the metal ion was 0.50M; this was done by the substitution of aluminum nitrate or chromium nitrate for the iron in the usual FeTNa preparation procedure. The aluminum-tartrate mixture was clear and colorless, as was the aluminum nitrate solution alone; no change in color was apparent. However, the observed optical rotation of this solution (546 mμ, 25°, 2 dm.) was 29° whereas an equivalent solution of sodium tartrate alone had a rotation of only 18°. This mixture might have resulted in the formation of a complex between the aluminum and the tartrate. When this solution was used in an attempt to dissolve acetate-grade cotton linters, the fibers remained intact without any trace of any dissolution.

The chromium nitrate – tartaric acid mixture was a deep blue-green, almost black, opaque solution. Its optical rotation could not be measured; since there was no color change from the color of the chromium nitrate solution alone, there is some doubt whether a complex had formed. Any possibility that this mixture might be able to dissolve cellulose was dispelled when a suspension of the cotton linters in the cold chromium-tartrate mixture was filtered after several days of intermittent agitation; the pad of linters was recovered in nearly quantitative yield. There appears to be little similarity between the behavior of these two metal-tartrate mixtures and the FeTNa complex.

OTHER COMPOUNDS AS LIGANDS

With the continuous-variations evidence which showed glycerol to be capable of new-complex formation with FeTNa (1:3 ratio), an attempt was made to substitute glycerol for the tartrate in the formation of a complex analogous to FeTNa.

Using a mole ratio of 1:3 iron-glycerol, the usual preparative procedure produced not a clear, green solution as with the tartrate but instead produced the dark brown-black, opaque mixture which is characteristic of decomposed FeTNa. Small clumps of solid were noticed along the edges of the container after storage of the mixture for a few weeks; this and the brown color indicated that the iron probably had not complexed with the glycerol but instead was present as colloidal ferric oxide. This mixture was discarded. No further attempts were made with any other compounds as substitute ligands for the tartrate anion.

FeTNa (1:3) WITH MESO-TARTARIC ACID

The use of meso-tartaric acid in the formation of the FeTNa complex was investigated to determine the effect, if any, which the difference in configuration between the meso form and the L(+) form had upon the formation or characteristics of the resultant complex. With the meso form, both the carboxylate group pair and the hydroxyl group pair may assume trans or opposed conformations with the tartrate anion in solution; this is in contrast to the probable conformation of the L(+) form which has been illustrated earlier in Fig. 2.

With the apparatus used in the preparation of the first continuous-variations mixtures, a control sample was prepared which was 0.50M in iron and had a mole ratio of 1:3 iron-L(+) tartrate; the procedure was identical to the usual FeTNa preparation except that only 50 ml. of solution were prepared. This solution was a brilliant, clear green color; its observed optical rotation (546 mμ, 25°, 2 dm.) was +62.46°.

A second sample was prepared in which meso-tartaric acid hydrate (Aldrich Chemical Co., Milwaukee, Wis.) was substituted for the L(+) form; the iron-tartrate mole ratio was still 1:3. This preparation, when completed, was also green but

decidedly more yellow in appearance and less saturated in color when compared with the control sample. It also appeared to be slightly cloudy immediately upon completion of the preparation, whereas the control sample was clear. The optical rotation of the meso-formed FeTNa was zero.

Both samples were stored in a constant-temperature room at 22-23°. After eight weeks, the control sample was still clear and green while the meso-FeTNa had begun to discolor and form a very small amount of brown solid. More ferric oxide continued to form with continued storage time until, after six months, the meso-FeTNa was quite brownish in color and had accumulated a significant quantity of solid. The control sample of L(+)-FeTNa remained clear and brilliant green. Although no other tests were performed on either sample, the decrease in stability of the meso-formed FeTNa with respect to the control solution was very apparent and distinctive.

DISCUSSION AND INTERPRETATION

The discussion of the experimental results is grouped into two categories: (1) information about the complex of iron and tartrate, and (2) the reaction of 1:3 mole ratio FeTNa with the model compounds which were tested. This observed behavior is extended and interpreted in consideration of a possible mechanism whereby the 1:3 FeTNa solvent is able to dissolve cellulose.

THE IRON-TARTRATE COMPLEX SYSTEM

Examination of the continuous-variations plots for the mixtures of ferric nitrate and tartaric acid (Fig. 3-5) summarizes the available experimental information for the formation of the iron-tartrate system.

COMPOSITION

The maximum deviation of the continuous-variations relationship occurs at a ratio of one ferric ion in combination with four and one-half tartrate ions; this clearly established the optimum mole ratio for the formation of the iron-tartrate complex as 1:4.5. This ratio represents an optimum value, that is, the number of tartrate anions which are capable of association (presumably by complex formation) with the ferric ion provided that an ample supply of the tartrate is present. At this ratio, the maximum amount of complex is formed; less complex is formed at higher or lower mole ratios because of a deficiency of either one of the components in the mixture.

The continuous-variations plots show no sharp discontinuities at concentrations which would correspond to compositions of an iron-tartrate complex other than the 1:4.5 ratio. However, these plots are concave upward; the normal curvature for plots which describe the formation of a single complex species (of a

given mole ratio) is concave downward. This normal (or usual) curvature results from the formation of a complex whose stability constant is not high but rather may be fairly low. Complexes with very high stability constants and which consist of a single species in solution exhibit a continuous-variations deviation plot which consists of two straight lines meeting at a peak corresponding to the combining ratio. Complexes with lower stability constants have a rounded peak and show curvature which is concave downward. At the optimum mole ratio, not all of the components combine to form the complex; the concentrations of the components which remain in solution are determined by the value of this stability constant. At low values, a reduced amount of the complex is present and the deviation peak which is recorded by continuous variations will be lowered. With mixtures of components at mole ratios other than the optimum value, one component is present in excess amount; this excess drives the equilibrium toward the formation of more complex. The result of this is the formation of a greater amount of complex relative to the amount of limiting component which was added originally. This causes the curved, concave-downward, deviations plots.

The opposite curvature exhibited by the iron-tartrate system is probably caused by the existence of several species of complex in solution as well as by the removal of the iron as precipitation and subsequent filtration. These several species, in equilibrium with each other and with the components, may change their relative amounts as the proportions of iron and tartrate are varied in the continuous-variations procedure. These different species undoubtedly have different physical properties. The measured rotation or absorbance will be the weighted average of these several values and the amounts of each species. Hence, a curvature of the continuous-variations deviation plot in a direction opposite to that which would be predicted could easily be caused by a mixture of species; each species need not appear as a separate peak in the deviations plot.

The removal of the iron from the equilibrium system adds to the curvature of the plot since the iron actually remaining in the system is no longer the amount which was added. The amount added is indicated on the abscissa; the curvature is then enhanced (or even entirely caused) by this "apparent plotting error." This error decreases as the amount of iron which is removed decreases. The position of the deviation peak will not be affected, however, by this precipitation.

STRUCTURE

Establishment of the optimum combining mole ratio as 1:4.5 iron-tartrate does not infer that the 1:3 structure proposed in the literature (Fig. 1) is nonexistent; this combination of a central ferric ion and three tartrate anions may very well be present in any iron-tartrate mixture. This study has shown, however, that other structures (and compositions) must be considered in the evaluation of such mixtures. Moreover, such other structures need not be limited to those which include only a single ferric ion; this indication stems from the nonintegral combining ratio of iron to tartrate. A structure containing two ferric ions linked in some fashion by the tartrate ligands is entirely possible.

The experimental evidence also does not deny the possibility of the existence of iron-tartrate structures whose compositions include more tartrate ligands per ferric ion than the optimum amount. Since the ferric ion usually has a co-ordination number of six, as many as six tartrates might be incorporated into a complex structure (although this seems to be unlikely). Nor does the evidence deny the existence of structures with mole ratios below 1:3 iron-tartrate. The evidence does show that several structures are probably present at the same time in the alkaline iron-tartrate mixture.

This study has not provided sufficient experimental information to enable the various structures of iron-tartrate to be defined. One must conclude, however, that the combination of the ferric ion and the tartrate ion forms a complicated system which cannot be described in simple terms or by a single structure.

REACTION OF 1:3 RATIO FeTNa WITH MODEL COMPOUNDS

The behavior of the model compounds in mixtures with FeTNa of 1:3 mole ratio has already been described in terms of the continuous-variations deviation curves and the formation of the ferric oxide precipitate. This behavior can now be interpreted in terms of the molecular structure of the models and the possible effect which this structure has upon the formation of a new complex between FeTNa of 1:3 mole ratio and the individual model compound.

COMPLEX BLOCKING BY THE METHYL ETHER GROUP

The efficiency of the methyl ether group in blocking a complex formation when it is substituted for a hydroxyl group can be ascertained from the behavior of four model compounds: methyl 2,3,4,6-tetra-O-methyl-β-D-glucopyranoside, methyl cellosolve, ethylene glycol, and methanol. The "salting out" of the fully methylated glucoside by the addition of the FeTNa has already been interpreted as the failure of a pair of methoxyl groups to co-ordinate with iron in spite of the presence of an oxygen atom in each group (in the form of an ether linkage).

A comparison of Fig. 12, 16, and 17 establishes the behavior of a methoxyl-hydroxyl pair with respect to its co-ordination ability. If this chemical pair were no different from a glycol pair of hydroxyl groups, then the co-ordination tendency of the methyl cellosolve would have been identical with that of ethylene glycol. Since the co-ordination tendency of the cellosolve is essentially zero

and is much less than that of ethylene glycol, the methoxyl group must have blocked whatever co-ordination ability was present in the glycol pair.

The plot for methanol, which also indicates zero deviation and no new-complex formation, illustrates the inability of a single hydroxyl group on a simple alcohol to participate in the complex formation. Its behavior matches that of the methyl cellosolve.

COMPLEX FORMATION ON THE GLUCOPYRANOSIDE RING

The identification of the hydroxyl groups on the glucopyranoside ring which participate in complex formation with the 1:3 FeTNa is done from an examination of the deviations plots of four model compounds: methyl α-D-glucopyranoside, methyl β-D-glucopyranoside, methyl 4,6-di-O-methyl-β-D-glucopyranoside, and methyl 3-O-methyl-(α,β)-D-glucopyranoside (Fig. 8, 9, 20, 21). With the confirmation of the methoxyl group as a blocker, these model compounds clearly establish the formation of a new complex between the glucopyranoside and 1:3 iron-tartrate. These results also indicate the glycol pair of hydroxyl groups on the sugar ring as the chemical grouping which is included in the new complex with iron.

Comparison of the deviation curves of methyl β-D-glucopyranoside and methyl 4,6-di-O-methyl-β-D-glucopyranoside shows that the ability of the unsubstituted glucoside to complex with the 1:3 FeTNa is altered very little by the isolation of the glycol pair of hydroxyl groups on carbon atoms two and three as a result of the blocking of the remaining groups. Since simple alcohols do not complex, this glycol pair must be the location on the sugar ring at which the new chelate is formed. Assuming that the glucopyranoside ring still prefers the C-1 chair conformation, this glycol group has the orientation illustrated in Fig. 2 and

would seem to be identical to the orientation of the glycol pair of hydroxyls on the tartrate anion.

When the deviation curves of methyl α-D-glucopyranoside and methyl 3-O-methyl-(α,β)-D-glucopyranoside are compared, a sharp decrease in the tendency of the substituted glucoside to complex with the 1:3 FeTNa becomes evident. This is a result of the absence of any glycol pairing of hydroxyl groups because of the methoxyl group in position three. This particular location of the blocking group serves to interrupt the pairing of hydroxyl groups on the glucopyranoside ring into glycol groups. The slight complexing tendency which remains with this model compound is evidence of a very small ability of the 1:3 FeTNa to complex with pairs of hydroxyl groups which are spaced further apart than that which is permitted by a glycol pairing. This complexing may take place either at positions two and four on the ring or at positions four and six with this particular model compound.

The behavior of the glucoside substituted at position three serves as confirming evidence for the observed indication of new-complex formation between 1:3 FeTNa and the glycol pair of hydroxyl groups on the sugar ring. The unsubstituted glucopyranosides (both alpha and beta anomers) probably are capable of forming the new complex involving hydroxyl groups at either positions two and three or positions three and four.

REACTION OF OTHER GLYCOL GROUPS WITH 1:3 FeTNa

One other significant behavior pattern becomes apparent when the results with the other model compounds are examined. These models contain two or more hydroxyl groups on either a ring system or on a straight carbon chain; many of these also have the hydroxyl groups arranged in glycol pairs. Of these models

which do possess the glycol group, only those which contain additional oxygen atoms in their structure are able to complex with 1:3 FeTNa to an extent which is sufficient to prevent the precipitation of ferric oxide. This pattern can be observed by a comparison of the deviation curves for all model compounds except the sodium succinate (Fig. 8-12, 14-23).

Glycerol, both alpha- and beta-glucopyranosides, the 4,6-dimethyl-glucopyranoside, and the two polyhydric alcohols sorbitol and mannitol all contain both a glycol pair and extra oxygen atoms; they all complex very well with 1:3 FeTNa and also keep the iron in solution. Butane-2,3-diol, ethylene glycol, and the cis- and trans-cyclohexane-1,2-diols contain a glycol group but they have no additional oxygen atoms; they show a small (but significant) deviation curve indicating a slight tendency to complex, but ferric oxide is also precipitated.

The necessity for additional oxygen atoms (besides those in the glycol pair) seems to be related to the solubility effect of these electronegative groups in an aqueous medium. This hypothesis is obtained from an extension of the behavior of "inner complexes" described by Quagliano (49). These inner complexes are completely chelated structures; they are commonly formed by the co-ordination of a bidentate, singly charged ligand with a metallic ion whose co-ordination number is twice its ionic charge. This reaction neutralizes the charges on both metal and ligand, which results in the insolubility of the chelate structure in the aqueous medium in which it is formed. However, if the chelating ligand contains hydrophilic groups in addition to the group participating in the chelation, the resulting complex remains water soluble and does not precipitate, separate as an oil, or become organic extractible.

The application of this behavior of hydrophilic groups can be used to explain the need for additional oxygen atoms on the model (in addition to the glycol pair)

in the reaction between the models and 1:3 FeTNa. This may be illustrated in a simplified manner by the simultaneous equilibria diagrammed in Fig. 26.

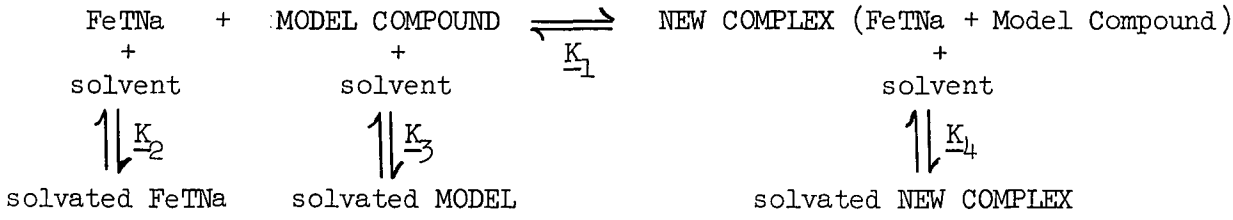

Figure 26. Possible Equilibria in New-Complex Formation

The probable importance of the solvation energies of the species involved in the formation of a new complex between FeTNa (1:3) and the model compound are considered in this diagram, where $\underline{K}_1$, $\underline{K}_2$, $\underline{K}_3$, and $\underline{K}_4$ represent the equilibrium constants which are involved. While $\underline{K}_2$ will be expected to be large (independently of the choice of a model compound), the value of $\underline{K}_4$ might change markedly when the various model compounds are compared. If the glycol-containing model has no extra electronegative oxygen atoms, the solvation of the new complex might be difficult and the entire simultaneous equilibria might be shifted in the direction of the solvated ingredients; that is, the value of $\underline{K}_4$ is low in comparison with $\underline{K}_2$. With models which contain extra oxygen atoms, solvation of the new complex is facilitated, $\underline{K}_4$ becomes large, and the equilibrium is shifted in the direction of formation of the new complex. The continuous-variations deviation then is large and the precipitation of ferric oxide is prevented. The extra oxygen atoms in methoxyl groups, in additional hydroxyl groups, and even the glucopyranoside ring oxygen may well serve as hydrophilic groups and aid in the formation of the new complex.

The test with sodium succinate indicates the moderate tendency for carboxylate groups to participate in complex formation with FeTNa; this compound is

structurally related to the tartrate anion but does not have the hydroxyl groups of the latter. Mannitol and sorbitol show startling differences in deviation plots; this is the result of only a slight difference in configuration between the two compounds and seems to illustrate the very great dependence of complex formation upon the configuration of the ligand. A comparison of the deviation plots of three other models, butane-2,3-diol, propane-1,3-diol, and butane-1,4-diol, reveals the dependence of complex formation upon hydroxyl-group spacing; even though all three compounds have only a small tendency to complex (because of the solubility problem), a steady decrease (to a zero value) can be noticed in the deviation curves as the spacing of the hydroxyl groups increases in distance.

The indication of complex formation between FeTNa of 1:4.5 mole ratio and methyl β-D-glucopyranoside is probably the result of the mutual dilution which is required by the continuous-variations procedure (Fig. 24, 25). This was the only model compound which was tested with FeTNa of the 1:4.5 mole ratio.

PROBABLE MECHANISM FOR DISSOLVING OF CELLULOSE BY FeTNa

With the information provided by the experimental results, an estimate can be made concerning the mechanism of the cellulose-dissolving process of 1:3 FeTNa.

As demonstrated by this study, the key factor in the mechanism of cellulose dissolution by FeTNa is not a significant difference in the competing ligands (as with the copper-based solvents). Instead, the key is the ability of the iron-tartrate complex to be prepared in a composition which is deficient in the amount of ligand but yet which remains reasonably stable. During the dissolving process, this deficiency is partly satisfied by the glycol groups on the cellulose

polymer, a process which incorporates the cellulose into the iron-tartrate complex. The energy which is released by this new-complex formation is sufficient to loosen the physical structure of the cellulose fiber and the polymer chains pass into solution.

The iron-tartrate complex solvent is prepared in a proportion of ingredients corresponding to three moles of tartrate anion for every ferric ion. At this composition, the ferric ion is complexed with fewer than the optimum number of tartrate anions. The ferric ion is present in excess; it may be in the form of some complex with a portion of the tartrates present, it may be complexed with tartrate anions and water molecules, or it may be present simply as a metastable, colloidal form of ferric hydroxide (ferric oxide). The discoloration and precipitation of the 1:3 FeTNa solution with extended storage times is probably a flocculation or aggregation of the colloidal, excess iron.

When a sample of cellulose is placed in this 1:3 ratio complex mixture, the glycol pair of hydroxyl groups at carbon atoms two and three of the glucopyranoside repeating unit become involved in the formation of a new complex with the iron-tartrate structure(s). This glycol pair serves to supply the extra ligand required to satisfy a "glycol deficiency" of the 1:3 ratio complex; this "glycol-" or "ligand deficiency" is the difference between the 1:3 ratio which is used in the solvent preparation and the 1:4.5 ratio which is the optimum combining ratio of iron with tartrate. A new chelate is formed between iron and the glycol pair on the cellulose repeating unit; this new chelate is not required to displace any tartrate ligands already present before the chelate can be formed. Instead, only molecules of water or possibly hydroxyl ions need to be displaced from the original iron-tartrate structure. The absence of any requirement for a tartrate displacement and the actual formation of a new chelate give rise to a very strong

thermodynamic driving force for the complexing of cellulose to the 1:3 FeTNa, hence, the great dissolving power of the solvent. The over-all mole ratio of the complex structure between iron and the combination of tartrate and cellulose-glycol probably will not approach the 1 to 4.5 value unless large amounts of cellulose are present. It may be pointed out, also, that the continuous-variations deviations curves (with most model compounds) reach their maximum value at a mole ratio (iron to model) of 1:1.5; this corresponds to this ligand deficiency which has been noted. If the glycol deficiency (or ligand deficiency) of the solvent is altered during its preparation, the cellulose-involving, new-complex-forming driving force, and therefore the dissolving power, is also changed; this allows the limited fiber-swelling studies to be performed.

The over-all structure of the complex consisting of the iron, the tartrate, and the glucopyranoside repeating unit of cellulose cannot be determined from this study. To do this requires first a knowledge of the structure(s) present in the FeTNa solvent. The nature of those structures is not known.

SUGGESTIONS FOR FUTURE WORK

Further studies of the iron-tartrate cellulose solvent should be concerned initially with an examination of the ferric ion – tartrate ion system. The equilibrium relationships and probable structures involved in the equilibrium should be delineated, if possible. As a first step, the apparent molecular weight of the complex mixture should be determined, possibly by means of a sedimentation-diffusion ultracentrifuge technique.

Examination of the type of bonding involved between ferric ion and tartrate ligand could take the form of magnetic susceptibility measurements to differentiate between a single unpaired electron ("inner-orbital" bonding, $3d^2\ 4s\ 4p^3$) and five unpaired electrons ("outer-orbital" bonding, $4s\ 4p^3\ 4d^2$) (50).

The role of the hydroxyl ion in the equilibrium should also be clarified, since this ion undoubtedly does participate in the equilibrium system. Also desirable would be a clarification of the mechanism whereby the glycol pair of hydroxyl groups (such as those on the glucopyranoside repeating unit of cellulose) can be incorporated into the structure of the FeTNa complex.

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APPENDIX I

CONTINUOUS-VARIATIONS DATA SHEET: FERRIC NITRATE – SODIUM TARTRATE

TABLE I

OPTICAL ROTATION: DEGREES, TWO DECIMETERS

Molarity, iron/tartrate	Mole Ratio, iron/tartrate	Mixture Rotation	Tartrate Rotation	Deviation
0.35/0.05		0.52	0.64	-0.12
0.30/0.10		1.35	1.31	+0.04
0.25/0.15		2.42	1.90	+0.52
0.20/0.20	1:1	3.79	2.51	+1.28
0.15/0.25		5.70	3.11	+2.59
0.133/0.266	1:2	6.34	3.32	+3.02
0.10/0.30	1:3	8.67	3.70	+4.97
0.08/0.32	1:4	10.15	3.94	+6.21
0.07272/0.32727	1:4.5	10.63	3.98	+6.65
0.06667/0.33333	1:5	10.42	4.14	+6.28
0.05714/0.34286	1:6	9.86	4.23	+5.63
0.05/0.35	1:7	9.30	4.30	+5.00
0.40			4.89	

TABLE II

ABSORBANCE: ONE CENTIMETER

Molarity, iron/tartrate	Mole Ratio, iron/tartrate	Mixture Absorbance
0.35/0.05		0.012
0.30/0.10		0.043
0.25/0.15		0.112
0.20/0.20	1:1	0.169
0.15/0.25		0.290
0.133/0.266	1:2	0.316
0.10/0.30	1:3	0.505
0.08/0.32	1:4	0.620
0.07272/0.32727	1:4.5	--
0.06667/0.33333	1:5	0.619
0.05714/0.34286	1:6	0.534
0.05/0.35	1:7	0.482
0.40		0

APPENDIX II

PREPARATION OF MODEL COMPOUNDS

This section describes the synthesis and/or purification of the various model compounds which were used in the continuous-variations procedures with FeTNa. Each of the syntheses differed in some manner from the procedures which were reported in the literature and is therefore described in some detail. All reported melting points are on the basis of a capillary melting-point apparatus which had been calibrated against a series of known-melting standards. The specific optical rotations, where reported, are at the wavelength of the sodium D line as measured by a Zeiss-Winkel polarimeter. The temperatures and concentrations were as close to the reported literature values as was possible. Low-pressure distillations were done in a Nester and Faust semimicro spinning-band fractionating column which was six millimeters in bore and eighteen inches in length and was equipped with a stainless-steel mesh band. The infrared spectra were all done by Lowell Sell of the Institute's analytical department. It is to be noted that very high purity is not required for the continuous-variations procedures and therefore extensive purifications and characterizations were not attempted.

METHYL α-D-GLUCOPYRANOSIDE

Commercially available methyl α-D-glucopyranoside (Eastman Kodak) was used without any purification. Paper chromatography showed this material to have glucose present as an impurity in an amount estimated to be much less than one per cent. The melting point was 167-169°C.; literature value: 167°C. (51).

METHYL β-D-GLUCOPYRANOSIDE

The Koenigs-Knorr reaction for the synthesis of glycosides was selected for the preparation of methyl β-D-glucopyranoside; this type of preparation is described by Wolfrom and Thompson (52). The preparation of the O-acetylglucosyl bromide was done by a procedure modified from that of Barczai-Martos and Körösy (53). The Koenigs-Knorr procedure itself was adapted from the work of Reynolds and Evans (54). Deacetylation of the resulting tetraacetate was accomplished by a catalyzed transesterification using sodium methylate in methanol (55). The modifications in the published procedures were dictated by the experience obtained from many trials in which enough material was produced to be used as a starting material for further syntheses.

2,3,4,6-TETRA-O-ACETYL-α-D-GLUCOPYRANOSYL BROMIDE

Experimental

An apparatus was assembled consisting of a two-liter, three-necked flask equipped with a thermometer, a Teflon stirring paddle, and a dropping funnel. This was supported inside an enameled pan in which an ice bath could be installed with the cold water being circulated over the flask by means of a pump.

Without the ice bath, 400 ml. of acetic anhydride and 2.5 ml. of 70% perchloric acid were mixed in the flask. To the rapidly stirred solution were added 100 g. of anhydrous D-glucose in small portions over a period of 30-40 minutes; the temperature remained between 30 and 40°C. This was followed by the addition of 30 g. of amorphous, red phosphorus.

The ice bath was installed and the reaction mixture was cooled. Into the dropping funnel were placed 65 ml. of bromine. This was dripped into the rapidly

stirred reaction mixture over a period of 30-40 minutes while the temperature remained between 12 and 14°C. The dropping funnel was then used to add 39 ml. of water, also over a period of 30-49 minutes and at the same temperature as the bromine. The ice bath was then removed and the mixture was stirred at room temperature for two hours.

At the end of this time, 300 ml. of chloroform and 800 ml. of ice water were added to the flask and the mixture was stirred vigorously for a few minutes. The excess phosphorus was removed by filtering both layers through a Celite pad. The aqueous phase was separated, extracted with chloroform (3 x 150 ml.), and discarded. The combined chloroform solution was washed with 500 ml. each of water, a saturated solution of sodium bicarbonate, a dilute bicarbonate solution, and water again; these aqueous washes were back-extracted with chloroform.

The combined chloroform solution was dried over calcium chloride with a small amount of bicarbonate added. After decolorizing the solution with carbon (Nuchar), the chloroform was removed by reduced-pressure concentration at a low bath temperature of 56 to 60°C. The thick sirup which resulted was crystallized from 250 ml. of anhydrous diethyl ether, washed with 2:1 petroleum ether (30-60°C.): diethyl ether, and dried in a vacuum at room temperature. The yields for the several preparations ranged from 63 to 82%. The melting points of this essentially crude product were from 75 to 87°; literature value: 87°C. (53), 87.5-88.5°C. (56), or 88-89°C. (57). This material was used as the starting material for the next stage.

METHYL 2,3,4,6-TETRA-O-ACETYL-β-D-GLUCOPYRANOSIDE

Experimental

A three-liter, three-necked flask was coated with black paint to exclude light. This was fitted with a Drierite outlet tube, a dropping funnel, and a

Teflon stirrer. Silver oxide was prepared by mixing a solution of 200 g. of silver nitrate in 2 l. of hot water with a solution of 46 g. of sodium hydroxide in 1.5 l. of water, washing the precipitated solid with 5 l. of hot water and 500 ml. of absolute ethanol, and drying the powder under a vacuum (58). Alcohol-free chloroform was prepared by shaking one liter of CP chloroform with 12% sulfuric acid, then neutralizing the chloroform with a saturated sodium bicarbonate solution. After washing with water (3 x 1 l.), the chloroform was dried over calcium chloride, dried over phosphorus pentoxide, and finally distilled from phosphorus pentoxide at atmospheric pressure (54).

Into the opaque flask were placed 125 g. of the silver oxide, 500 g. of 20 mesh Drierite (previously heated at 250°C. for six hours), 500 ml. of the purified chloroform, 100 ml. of absolute methanol, and 25 g. of iodine. The flask was sealed and stirred for one hour to remove any moisture. A solution of 200 g. of the 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide in 750 ml. of purified chloroform was dripped slowly into the flask over a period of two hours. The contents were then stirred rapidly in the sealed flask over a period of 24 hours at room temperature.

All solids were filtered from the mixture. The chloroform solution was dried over Drierite and concentrated at reduced pressure. The crude sirup crystallized; this was purified by recrystallization from 500 ml. of absolute ethanol and a wash with 2:1 (v/v) water:ethanol. The yields varied from 76 to 84%, while the melting points of the several runs ranged from 101.5-104 to 102.5-104.5°C.; literature value: 104-105°C. (59, 60). The specific rotations in chloroform were also recorded, these ranged from -16.7 to -18.0° (t=25°, c=2.2); literature values: -18.3° (59) or -18.2° (60). This material was deacetylated in the next step of the synthesis to yield the desired glucoside.

METHYL β-D-GLUCOPYRANOSIDE

Experimental

Into 1835 ml. of absolute methanol were dissolved 100 g. of methyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside by heating the mixture gently over steam. To this solution, after cooling, were added 62 ml. of a stock solution of sodium methylate which contained 1.0372 g. of sodium per 1000 ml. of alcohol (1/400 of the theoretical amount of sodium). The reaction solution was allowed to stand at room temperature for two days with occasional agitation.

The volatile materials were then removed by concentration of the solution at reduced pressure. The resulting sirup was dissolved in 300 ml. of cold water and deionized with 40 ml. of MB-3 mixed-bed ion-exchange resin. The water was removed by evaporation at reduced pressure; this resulted in a crystalline solid. The product was recrystallized from 300 ml. of absolute ethanol. All of the material from the several runs, plus a second crop, was collected and combined. The yield for the combined material was 93.8% based upon the hemihydrate of the glucoside. The melting point was 104-108°C.; the specific rotation in water was -32.9° (t=26°, c=2.4); the literature values for the melting point range from 104° to 109-111°C. (61), the value for the specific rotation is -32.5° (61).

This combined crop was spotted on chromatographic paper and developed in 4:1:5 butanol:acetic acid:water (by volume). The spots were located with the silver nitrate sequence of reagents (silver nitrate – sodium hydroxide – sodium thiosulfate). By comparison of this chromatogram with the series of reference chromatograms of J. K. Crossman (48), it was decided that the only impurity present was glucose in an amount no greater than 0.4%. No further purification was attempted. This material was used both as a model compound and as a starting material for further syntheses.

GLYCEROL

Reagent-grade glycerol (J. T. Baker) was used as a model compound without any further purification.

PROPANE-1,3-DIOL

Propane-1,3-diol was purchased from Eastman Kodak as reagent-grade material and was not purified.

METHANOL

Specially purified methanol was obtained from W. H. Trice. This material had been refluxed and redistilled from a mixture of zinc powder and potassium hydroxide. The ultraviolet spectrum showed the final product to have a purity which exceeded that of spectral-grade material (62).

SODIUM SUCCINATE

Reagent-grade succinic acid (Merck) was converted to the sodium salt by the addition (by pipet) of the calculated amount of extra 4.0M sodium hydroxide to the aqueous solution of the acid during the preparation of the alkaline solution for the continuous-variations measurements. The sodium succinate was not isolated and redissolved.

BUTANE-2,3-DIOL

Practical-grade butane-2,3-diol (Eastman Kodak) was distilled in the spinning-band fractionating column. At a pressure of 10 mm., the fraction boiling at 79-79.5°C. (vapor temperature) was collected after discarding a generous forerun.

BUTANE-1,4-DIOL

Practical-grade butane-1,4-diol (Eastman Kodak) was fractionated in the spinning-band column. After discarding the forerun, the fraction boiling at 112.5-113°C. at 7 mm. of pressure was collected.

ETHYLENE GLYCOL

Reagent-grade ethylene glycol (Baker) was used directly in the continuous-variations mixtures without any extra purification.

METHYL 2,3,4,6-TETRA-O-METHYL-β-D-GLUCOPYRANOSIDE

For the preparation of the fully methylated glucoside, the modification of the Purdie's reagents suggested by Walker, Gee, and McCready was selected (63). This method uses N,N-dimethylformamide as a solvent for the reaction, which permits essentially complete methylation to be accomplished in a single application. Beginning with glucose, a major portion of the product is the beta glucopyranoside form; oxidation of the reducing sugar is prevented from being extensive by the rapid glycosidation which occurs during the reaction.

EXPERIMENTAL

Silver oxide was prepared as described previously for the Koenigs-Knorr procedure. Dimethylformamide (reagent grade) was dried over Drierite, then filtered before use.

A three-liter, three-necked flask (opaqued with black paint) was fitted with a Teflon stirrer and a Drierite outlet tube and supported in a pan. In 500 ml. of the dry dimethylformamide were dissolved 20 g. of anhydrous D-glucose by warming the flask with hot water in the pan. After one hour, the solution was cooled

and 103 ml. of methyl iodide were added. The addition of 261 g. of fresh silver oxide was done in small portions over a period of 25 minutes while the flask was being cooled with cold water in the pan. The flask was then stoppered and the rapid stirring was continued at room temperature.

After 18 hours of stirring, the silver oxide was filtered off and washed with dimethylformamide and chloroform. Since the addition of the chloroform had caused a precipitate to appear in the filtrate, this was filtered again. After concentration of the solution at reduced pressure (using an all-glass apparatus), the sirup which resulted was taken up in chloroform; this solution was again filtered after cooling it to zero degrees. The chloroform solution was washed with water (3 x 300 ml.) and dried over sodium sulfate.

The chloroform was removed by concentration at reduced pressure. The last of the dimethylformamide was removed by two codistillations with water at reduced pressure. The resulting dark sirup was then purified by fractional distillation in the spinning-band column. After removal of the transfer solvent (chloroform), three fractions were removed under the following conditions:

Fraction	Volume, ml.	Pressure, mm. Hg	Vapor Temp., °C.	Bath Temp., °C.
1	1.7	0.25	66-69	123-128
2	3.5	0.25	69	129-132
3	2.8	0.20-0.25	68-69	130-131

Fraction No. 2 crystallized in the receiver; these seeds were used to solidify the other fractions. Fraction No. 2 was characterized by an infrared spectrum as well as melting point and optical rotation. The spectrum indicated complete methylation by the absence of the hydroxyl stretching frequency absorbance band.

The melting point was 37-38°C., the specific rotation in water was -9.92° (t=25°, c=4.0); literature values: 40-41° and -17.3°, respectively (64). Although the measured values were low, the beta anomer of the fully methylated glucopyranoside was indicated, with the major impurity probably being the alpha form. Fractions No. 2 and 3 were combined for use as a model compound.

METHYL CELLOSOLVE

Technical-grade methyl cellosolve (Schaar) was purified by low-pressure distillation in the spinning-band fractionating column. After discarding a large forerun, the fraction boiling at 34-34.5° at 18 mm. of pressure was collected and used as a model compound.

TRANS-CYCLOHEXANE-1,2-DIOL

A sample of trans-cyclohexane-1,2-diol was obtained from H. Hintz. This material had been purchased (K & K Lab.) and recrystallized by him from ethyl acetate. The melting point was 102.5-104°C.; literature value: 101.5-103°C. (65).

CIS-CYCLOHEXANE-1,2-DIOL

The synthesis of cis-cyclohexane-1,2-diol was adapted from a procedure of Clarke and Owen (66), which was used successfully by H. Hintz (67). The reaction employed is the neutral permanganate oxidation of cyclohexene to put the cis glycol pair of hydroxyl groups on the carbon ring.

EXPERIMENTAL

Into 600 ml. of absolute ethanol were dissolved 26 g. of cyclohexene in a two-liter, three-necked flask equipped with a Teflon stirrer, a dropping funnel,

and a thermometer. Also prepared was a solution of 40 g. of potassium permanganate and 30 g. of magnesium sulfate in 800 ml. of water. After cooling the alcoholic solution to -20°C. with an acetone-dry ice bath, the permanganate solution was dripped slowly into the rapidly stirred reaction mixture over a period of two hours; the temperature was maintained below -13°C. during this time.

The mixture was allowed to warm to room temperature. The solids were filtered from the mixture on Celite and washed with hot water. The solvents were removed from the filtrate by reduced-pressure concentration. The sirup which resulted was divided between chloroform and salt-saturated water; the chloroform was then separated and dried with magnesium sulfate.

After the removal of the chloroform at reduced pressure, the sirup crystallized. This solid was dissolved in a large amount (55 ml.) of ethyl acetate, decolorized with Nuchar carbon, and recrystallized. The result was small platelets which melted at 98.5-99°C.; literature value: 98°C. (66). The yield was 15%.

METHYL 4,6-DI-O-METHYL-β-D-GLUCOPYRANOSIDE

The sequence of steps described by Bollenback (68) was used for the unequivocal synthesis of methyl 4,6-di-O-methyl-β-D-glucopyranoside. This sequence consisted of five steps: methyl β-D-glucopyranoside ---→ methyl 4,6-O-benzylidene-β-D-glucopyranoside ---→ methyl 2,3-di-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside ---→ methyl 2,3-di-O-benzyl-β-D-glucopyranoside ---→ methyl 2,3-di-O-benzyl-4,6-di-O-methyl-β-D-glucopyranoside ---→ methyl 4,6-di-O-methyl-β-D-glucopyranoside. Procedures were selected from the literature for the experimental conditions for each step; a small quantity of material was then processed to indicate any possible difficulties and to enable the procedures to be changed

without the danger of the complete loss of product at a late stage. None of the literature descriptions was employed without modification.

The preparation of the methyl 4,6-O-benzylidene-β-D-glucopyranoside was done by the condensation of benzaldehyde with the beta glucoside with zinc chloride as a catalyst. This was patterned after the method of Richtmeyer (69). This material was then reacted with benzyl chloride in the presence of alkali to yield the benzyl ether derivative, methyl 2,3-di-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside (70). The removal of the benzylidene group without the simultaneous hydrolysis of the methyl aglucone was done under conditions of mild acid hydrolysis (69, 71, 72); this resulted in methyl 2,3-di-O-benzyl-β-D-glucopyranoside. The subsequent methylation of the open hydroxyl groups to give methyl 2,3-di-O-benzyl-4,6-di-O-methyl-β-D-glucopyranoside was done by the modification of the Purdie's reagents as used before for the fully methylated glucoside (63). The last step, the removal of the benzyl ether groups, was done by a chemical hydrogenolysis with sodium and alcohol, a procedure which does not disturb the methyl ether groups (70, 71). The product of this sequence, methyl 4,6-di-O-methyl-β-D-glucopyranoside, was then used as the model compound.

METHYL 4,6-O-BENZYLIDENE-β-D-GLUCOPYRANOSIDE

EXPERIMENTAL

Zinc chloride was fused in a muffle furnace at 350°C.; 67 g. of the melt were poured into a dry, one-liter bottle containing about one pound of 4-mm. glass beads. The solidified material was ground by rotating the sealed bottle for several days. To this were added 600 ml. of filtered, chlorine-free benzaldehyde. The bottle was again sealed and shaken on a reciprocating shaker until the beads had ground the zinc chloride to a smooth suspension.

This suspension was shaken with 80 g. of dried methyl β-D-glucopyranoside (prepared as described earlier) for 33 hours at room temperature, then it was allowed to stand for an additional 15 hours. The reaction mixture was poured in a fine stream into a rapidly stirred, ice-cold solution of 660 g. of sodium bisulfite in 6 l. of water. A fine, white solid precipitated in an aqueous solution. This solid was filtered off and washed by stirring it with cold water (3 l.), 10% sodium bisulfite solution (1 l.); cold water (1 l.), 10% bisulfite solution (1 l.), and washed again with cold water in a filter funnel. The final washes were with a cold, saturated sodium bicarbonate solution and cold water. The solid cake was rinsed in a filter funnel with 30-60°C. petroleum ether and dried in a vacuum oven at 40-45°C. The yield was 76%.

This crude product had no odor of benzaldehyde; it was not recrystallized but rather it was used as a starting material for the next stage of the synthesis. The melting point was 191-193°C.; literature value: 199-201°C. (73).

METHYL 2,3-DI-O-BENZYL-4,6-O-BENZYLIDENE-β-D-GLUCOPYRANOSIDE

EXPERIMENTAL

Into a one-liter resin kettle (fluted sides) were placed 150 g. of powdered, dried potassium hydroxide and 86 g. of methyl 3,6-O-benzylidene-β-D-glucopyranoside. The kettle was equipped with a mercury-seal stirrer and a Drierite outlet tube. To this solid mixture were added 1170 ml. of benzyl chloride. The solids were suspended by rapid stirring while the mixture was heated by means of a boiling water bath. The temperature was maintained at about 98°C. for the next five hours while the thick mixture was stirred rapidly.

After cooling the mixture, the paste was dissolved in one liter of water. The solution was concentrated at reduced pressure to remove the extra benzyl chloride by steam distillation. Additional water was added at several times during the concentration process until no more benzyl chloride was being removed. The solid which had formed was washed with water, then dissolved in chloroform. The chloroform solution was washed repeatedly with water; these water washes were combined and back-extracted with chloroform. The combined chloroform solution was dried with magnesium sulfate and concentrated at reduced pressure; a pale-yellow solid was the result.

The crude product was recrystallized initially from 800 ml. of absolute ethanol. Because of a low temperature coefficient, five crops of crystals were obtained which differed very little in melting points; these ranged from 118-119.5°C. down to 116-117°C.; literature value is 119-120°C. (74). The yield of the combined crops was 69%. This combined material was used as a starting material for the next step.

METHYL 2,3-DI-O-BENZYL-β-D-GLUCOPYRANOSIDE

EXPERIMENTAL

Into a five-liter flask was placed a solution of 98 g. of methyl 2,3-di-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside in 2000 ml. of filtered acetone. The addition of 800 ml. of water precipitated the solid; this was redissolved by heating the flask with steam and adding 400 ml. of additional acetone. The addition of 120 ml. of normal hydrochloric acid was followed by the gentle boiling of the clear solution under reflux for 3 hours, 15 minutes.

The warm solution was dumped into 500 ml. of water containing 30 g. of dispersed barium carbonate. The neutralized solution was reheated and filtered

while hot to remove the excess barium. Upon cooling, the needlelike solid which had precipitated was filtered off and the filtrate was concentrated at reduced pressure. More needles appeared. All of these crystals were redissolved in chloroform; this solution was washed with water. The water washes were combined and back-extracted with chloroform. All chloroform layers were dried with sodium sulfate and concentrated at reduced pressure. The resulting white sirup crystallized spontaneously.

Recrystallization was done from 400 ml. of absolute ethanol, which resulted in three crops of acceptable material and a residue. The three crops all melted at 121-123°C.; literature value: 122-123°C. (74). The total yield was 96%. These three crops were the next stage starting material.

METHYL 2,3-DI-O-BENZYL-4,6-DI-O-METHYL-β-D-GLUCOPYRANOSIDE

EXPERIMENTAL

Silver oxide was prepared as described for the Koenigs-Knorr reaction. Reagent-grade dimethylformamide was stored over Drierite until required, then filtered.

Methyl 2,3-di-O-benzyl-β-D-glucopyranoside (76 g.) was dissolved in 1000 ml. of the dried dimethylformamide in an opaque, three-necked, three-liter flask equipped with a Teflon stirrer and a Drierite outlet tube. To this solution were added 200 ml. of methyl iodide. While stirring this mixture, 260 g. of fresh silver oxide were added in small portions over a period of two hours while cooling the flask in a pan of cold water. The flask was stoppered and the mixture was stirred rapidly at room temperature for 70 hours.

The solid silver oxide was filtered from the mixture on Celite and washed with chloroform. The solid which precipitated in the filtrate was filtered off; the filtrate was transferred to an all-glass distillation apparatus and concentrated at reduced pressure. The sirup which resulted was dissolved in n-butanol and again concentrated to remove more of the dimethylformamide. The resulting sirup was dissolved in chloroform; this solution was washed with water, dried with magnesium sulfate, and concentrated at reduced pressure.

This sirup was dissolved in a little (200 ml.) absolute ethanol for crystallization; the small amount of solid which resulted when the solution was cooled for several days was filtered off and washed. The melting point and specific rotation in chloroform, 103-112°C. and -19.3°, respectively, indicated that this material was not the desired product. The mother liquor was concentrated at reduced pressure to remove the last traces of solvents. When it was dried in a vacuum desiccator, the residue crystallized into a very pale, yellow solid. The yield of this solid residue was 96%; its melting point and specific rotation in chloroform were 39.5-40.5°C. and +28.1° (t=26°, c=2.1), respectively. The literature values are 40-41°C. and +32.0° (74). An infrared spectrum of a melt of this residue revealed no indications of the presence of hydroxyl groups. This solid residue of crude material was used as the starting material for the next step of the synthesis. The crystals which had been separated initially were discarded.

METHYL 4,6-DI-O-METHYL-β-D-GLUCOPYRANOSIDE

EXPERIMENTAL

The methyl 2,3-di-O-benzyl-4,6-di-O-methyl-β-D-glucopyranoside (65 g.) was dissolved in 500 ml. of 97% (v/v) ethanol in a beaker; this solution was cooled

in an ice bath. Metallic sodium was cut into chunks and added at intervals to the cooled, stirred solution until a total of 75 g. had been added. The stirring and cooling were continued for an additional five hours while a total of 1000 ml. of additional 97% ethanol was added in small portions. The mixture was then stirred overnight while it was allowed to warm to room temperature.

The solution was clarified by the addition of 500 ml. of water. Dry ice was then added to precipitate the sodium as the bicarbonate. The solid which resulted was filtered off and washed with hot absolute ethanol; the filtrate was filtered again to remove the rest of the solid. The yellow filtrate was concentrated at reduced pressure to a sirup. This sirup was redissolved in absolute ethanol and refiltered; this solution was diluted with water and deionized with MB-3 mixed-bed ion-exchange resin. Reconcentration to a sirup and weighing the residue indicated a yield of 135%.

A second treatment in a similar fashion reduced the yield of sirup to 125%; a third treatment resulted in a 102% yield. The fourth and last treatment gave a yield of 99.5% of a sirup whose specific rotation in chloroform was -18.8°. This sirup was dried under a vacuum and cycled between zero degrees and room temperature until it crystallized. Examination of this solid by thin-layer chromatography (Silica-Gel G base developed in 8:2:1 ethyl acetate:pyridine:water and sprayed with a mixture of concentrated sulfuric acid and 70% nitric acid) revealed the presence of three impurities in the crude product.

Of the several crystallizing solvents tried, ethyl acetate was the most successful (mixed solvents precipitated a gum instead of crystals) even though the solubility of the product was appreciable in the cold solvent. From this recrystallization, a first crop was removed in 6% yield from 55 ml. of solution;

this material had a melting point of 77-78°C. and was chromatographically pure by the thin-layer chromatographic technique. A second, third, and fourth crop were removed, combined, and then recrystallized from ethyl acetate. This material, in 36% yield, had a melting point of 75-76.5°C. and a specific rotation in chloroform of -29.9° (t=18°, c=1.7); literature values: 77-79°C. and -28.8°, respectively (73). Examination of this solid by infrared showed the presence of two hydroxyl groups (strong bands at 3350 and 3500 $cm.^{-1}$) with one band barely resolved as a doublet. No indications of any benzene rings were apparent. Thin-layer chromatography showed the slightest trace of a single impurity. This material was then assumed to be the desired methyl 4,6-di-O-methyl-β-D-glucopyranoside and was used as a model compound.

METHYL 3-O-METHYL-(α,β)-D-GLUCOPYRANOSIDE

The preparation of the pure alpha or beta anomer of methyl 3-O-methyl-D-glucopyranoside is not usually attempted with 3-O-methyl-D-glucose as an intermediate (75); the anomers are difficult to separate and only the alpha form has been isolated as a solid (76). However, the mixture of anomers was perfectly acceptable for this study; this could be prepared by a Fisher glycosidation of 3-O-methyl-D-glucose. The result would be a sirup.

The actual preparation of the 3-O-methyl-D-glucose was modified from the results of Glen (77); this material was then formed into the methyl glycopyranoside by treatment with methanol with a cation-exchange resin as a catalyst (78). The sequence of steps began with glucose: D-glucose ---→ 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose ---→ 1,2:5,6-di-O-isopropylidene-3-O-methyl-α-D-glucofuranose ---→ 3-O-methyl-D-glucose ---→ methyl 3-O-methyl-(α,β)-D-glucopyranoside. The di-isopropylidene derivative was formed by the condensation of glucose

with acetone in the presence of zinc chloride and phosphoric acid; this forms the furanose ring. The free hydroxyl group was then methylated by means of dimethyl sulfate and alkali in acetone to give the 1,2:5,6-di-O-isopropylidene-3-O-methyl-α-D-glucofuranose. The 3-O-methyl-D-glucose was formed by the acid hydrolysis of the isopropylidene groups with acidic IR-120 cation-exchange resin. The methyl glucopyranoside mixture was then formed by the reaction of methanol with the 3-O-methyl glucose at the boiling point in the presence of IR-120 resin. The reducing sugars were removed from the product by a treatment with hot alkali. The resulting sirup was used as the model compound.

1,2:5,6-DI-O-ISOPROPYLIDENE-α-D-GLUCOFURANOSE

Experimental

Zinc chloride was fused in a muffle furnace at 350°C.; 213 g. of the melt were poured into a two-liter bottle containing about one pound of 4-mm. glass beads. To this were added 1000 ml. of absolute acetone (prepared by refluxing CP acetone over potassium permanganate, then distilling it and drying the liquid over Drierite). The zinc chloride was ground up by shaking the bottle on a reciprocating shaker. Anhydrous D-glucose (250 g.) and 7.6 ml. of 85% phosphoric acid were transferred to the bottle with an additional 700 ml. of absolute acetone. This mixture was rotated in the sealed bottle for 40 hours, then stirred rapidly with a Teflon stirrer for an additional 23 hours.

The undissolved glucose was filtered from the mixture (along with the beads) and washed with acetone. To this filtrate was added a concentrated solution of alkali consisting of 155 g. of sodium hydroxide in 150 ml. of water. The zinc oxide which formed was filtered off; the filtrate was then concentrated at reduced pressure. The resulting solid was dissolved in chloroform; this solution was

washed with water, dried with magnesium sulfate, and decolorized with Nuchar. The yellow solution was again concentrated at reduced pressure; this resulted in a white solid with a pale-yellow cast in a yield of 83%. Recrystallization was done from 1100 ml. of cyclohexane to which a small amount (150 ml.) of chloroform had been added. The recrystallized yield was 49%; the melting point was 110-110.5°C.; literature value: 110-111°C. (79). This material was methylated in the next step of the synthesis.

1,2:5,6-DI-O-ISOPROPYLIDENE-3-O-METHYL-α-D-GLUCOFURANOSE

Experimental

The 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (192 g.) was dissolved in 220 ml. of acetone in a three-necked flask equipped with a reflux condenser, a thermometer, and a Teflon stirrer. With a water bath and a hotplate, the temperature of the solution was raised to 45°C. At that time, 86 g. of sodium hydroxide (pulverized, then dried in a vacuum oven) were added to the flask.

Practical-grade dimethyl sulfate (120 ml.) was added from a dropping funnel to the rapidly stirred reaction mixture over a period of 2 hours, 50 minutes. Then, the temperature was raised to 64°C. for an additional hour, and finally the mixture was stirred and heated at 79°C. for the last three hours. Water was added to the cooled solution until all of the solid had dissolved. This aqueous solution was extracted several times with chloroform; these extracts were washed with water, dried with magnesium sulfate, and concentrated to a sirup at reduced pressure.

An attempted removal of any acetone condensation products (such as mesityl oxide) by subjecting the sirup to a high vacuum and steam heat failed to remove

any fluid. Since this sirup was present in 140% yield, the condensation of acetone had evidently involved the acetone groups on the sugar ring of the isopropylidene derivative. This sirup was used directly for the next step of the synthesis; no crystallization was attempted.

3-O-METHYL-D-GLUCOSE

Experimental

The sirup of 1,2:5,6-di-O-isopropylidene-3-O-methyl-α-D-glucofuranose was rinsed into a three-necked flask with 250 ml. of hot water; this formed a suspension in the water. The flask was equipped with a Teflon stirrer, a reflux condenser, and a thermometer. The temperature of the suspension was raised to 96°C. by means of a hotplate and a water bath. To this hot suspension were added 100 g. of moist IR-120 cation-exchange resin. The mixture boiled at a temperature of 90°C. for one hour, after which the temperature of the contents of the flask remained at 96°C. with no evidence of boiling. The hydrolysis was continued for five hours at 96°C.

The cooled solution was filtered; the filtrate was separated into an aqueous layer and an oily layer of acetone condensation products. The remainder of the oil was removed from the water solution by extraction with petroleum ether (60-110°C.). The aqueous phase was decolorized with Nuchar and concentrated at reduced pressure to a sirup. The last of the water was removed by reduced-pressure codistillation with isopropanol; a white solid was the result.

Recrystallization was done from a large quantity of methanol (1400 ml.); three crops of approximately equal purity were removed in a total yield (for the last two steps of the synthesis) of 58%. The melting points were 168-169°C. for

the first crop and 166-167°C. for the third crop; literature value: 166-168°C. (77). This material was dried and used for the next synthetic step.

METHYL 3-O-METHYL-(α,β)-D-GLUCOPYRANOSIDE

Experimental

Regenerated IR-120 cation-exchange resin was equilibrated with methanol by washing the solid thoroughly with methanol, soaking it for ten days, and washing it again. The resin was then dried over calcium chloride.

The 3-O-methyl-D-glucose (73.5 g.) was rinsed into a three-necked flask with 230 ml. of absolute methanol. The flask was equipped with a reflux condenser, a Teflon stirrer, and was supported in an oil bath with a hotplate for heating. The suspension was heated until it boiled; 25 g. of the methanol-equilibrated IR-120 resin were added and the entire mixture was stirred. After 50 minutes, all of the sugar had dissolved to form a clear solution; this gentle refluxing at the boiling point was then continued for a total time of 47 hours.

The resin was filtered from the cooled solution; the filtrate was concentrated at reduced pressure to yield a sirup in theoretical yield. This sirup was dissolved in 80 ml. of hot water; 80 ml. of two normal sodium hydroxide were added and the amber-colored solution was stirred at 83°C. for 20 minutes. The alkali and saccharinic acids were removed by treatment with successive batches of MB-3 mixed-bed ion-exchange resin (500 ml. and 100 ml.). The clear solution was then concentrated at reduced pressure to a clear glass; the yield was 90%.

This glass was spotted on chromatographic paper and developed in 8:2:1 ethyl acetate:pyridine:water. Spraying with p-anisidine·HCl and the silver nitrate sequence of reagents located the spot for the mixed glucosides only by

the absence of any background color; neither reagent reacted with the product itself. No impurities were detected in the glass even though a slight trace of glucose was located in the 3-O-methyl-D-glucose used as a starting material for the last step. This clear, almost colorless glass was assumed to be the desired mixture of alpha and beta anomers of methyl 3-O-methyl-(α,β)-D-glucopyranoside and was used as a model compound without any further purification.

MANNITOL

Mannitol (Eastman Kodak) was dried in a vacuum oven at 40°C. and was used as a model compound without any further purification.

SORBITOL

Sorbitol from the Atlas Powder Co. (of unknown grade) was dried in a vacuum oven at 40°C. and was used directly as a model compound without any purification. An attempted recrystallization from ethanol resulted in a gummy solid instead of useful crystals or powder.

APPENDIX III

CONTINUOUS-VARIATIONS DATA SHEET

Optical Rotation: (degrees, two decimeters)

TABLE III

FeTNa (1:3) – MODEL COMPOUNDS

1. Methyl α-D-glucopyranoside

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	61.66				
0.40/0.10	49.64	7.14	60.36	56.78	+3.58
0.30/0.20	37.12	14.30	57.18	51.42	+5.76
0.25/0.25	--	--	54.58	--	--
0.20/0.30	24.37	21.64	51.45	46.01	+5.44
0.10/0.40	11.19	28.73	43.44	39.92	+3.52
0.50		36.12			

2. Methyl β-D-glucopyranoside

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.69				
0.40/0.10	50.54	-1.60	50.33	48.94	+1.39
0.30/0.20	38.05	-3.19	38.22	34.86	+3.36
0.25/0.25	31.59	-3.99	31.60	27.60	+4.00
0.20/0.30	25.08	-4.79	24.44	20.29	+4.15
0.10/0.40	11.66	-6.38	8.13	5.28	+2.85
0.50		-7.98			

3. Glycerol

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.69				
0.40/0.10	50.54		53.05	50.54	+2.51
0.30/0.20	38.05		42.60	38.05	+4.55
0.25/0.25	31.59		36.66	31.59	+5.07
0.20/0.30	25.08		30.13	25.08	+5.05
0.10/0.40	11.66		14.97	11.66	+3.31

TABLE III (Continued)

4. Propane-1,3-diol

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.69				
0.40/0.10	50.54		50.81	50.54	+0.27
0.30/0.20	38.05		38.25	38.05	+0.20
0.25/0.25	31.59		31.83	31.59	+0.24
0.20/0.30	25.08		25.34	25.08	+0.26
0.10/0.40	11.66		11.85	11.66	+0.19

5. Methanol

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.83				
0.40/0.10	50.53		50.36	50.53	-0.17
0.30/0.20	37.99		37.87	37.99	-0.12
0.25/0.25	31.51		31.37	31.51	-0.14
0.20/0.30	24.82		24.84	24.82	+0.02
0.10/0.40	11.49		11.43	11.49	-0.06

6. Sodium succinate

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.83				
0.40/0.10	50.53		49.63	50.53	-0.90
0.30/0.20	37.99		36.40	37.99	-1.59
0.25/0.25	31.51		29.91	31.51	-1.60
0.20/0.30	24.82		23.37	24.82	-1.45
0.10/0.40	11.49		10.59	11.49	-0.90

7. Butane-2,3-diol

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.69				
0.40/0.10	50.54		50.96	50.54	+0.42
0.30/0.20	38.05		38.61	38.05	+0.56
0.25/0.25	31.59		32.26	31.59	+0.67
0.20/0.30	25.08		25.83	25.08	+0.75
0.10/0.40	11.66		12.16	11.66	+0.50

TABLE III (Continued)

8. Butane-1,4-diol

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.69				
0.40/0.10	50.54		50.61	50.54	+0.07
0.30/0.20	38.05		38.00	38.05	-0.05
0.25/0.25	31.59		31.62	31.59	+0.03
0.20/0.30	25.08		25.07	25.08	-0.01
0.10/0.40	11.66		11.61	11.66	-0.05

9. Ethylene glycol

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.69				
0.40/0.10	50.54		51.18	50.54	+0.64
0.30/0.20	38.05		39.40	38.05	+1.35
0.25/0.25	31.59		33.04	31.59	+1.45
0.20/0.30	25.08		26.63	25.08	+1.55
0.10/0.40	11.66		12.63	11.66	+0.97

10. Methyl cellosolve

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.58				
0.40/0.10	50.39		50.27	50.39	-0.12
0.30/0.20	37.71		37.66	37.71	-0.05
0.25/0.25	31.25		31.26	31.25	+0.01
0.20/0.30	24.67		24.67	24.67	0
0.10/0.40	11.28		11.44	11.28	+0.16

11. trans-Cyclohexane-1,2-diol

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.69				
0.40/0.10	50.54		51.20	50.54	+0.66
0.30/0.20	38.05		39.18	38.05	+1.13
0.25/0.25	31.59		32.87	31.59	+1.28
0.20/0.30	25.08		26.50	25.08	+1.42
0.10/0.40	11.66		12.70	11.66	+1.04

TABLE III (Continued)

12. cis-Cyclohexane-1,2-diol

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.58				
0.40/0.10	50.39		50.55	50.39	+0.16
0.30/0.20	37.71		38.30	37.71	+0.59
0.25/0.25	31.25		31.94	31.25	+0.69
0.20/0.30	24.67		25.44	24.67	+0.77
0.10/0.40	11.28		11.98	11.28	+0.70

13. Methyl 4,6-di-O-methyl-β-D-glucopyranoside

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	64.34				
0.40/0.10	51.76	-1.60	51.72	50.16	+1.56
0.30/0.20	38.77	-3.20	39.06	35.57	+3.49
0.25/0.25	32.21	-4.00	31.87	28.21	+3.66
0.20/0.30	25.46	-4.80	24.39	20.66	+3.73
0.10/0.40	11.65	-6.40	8.20	5.25	+2.95
0.50		-8.00			

14. Methyl 3-O-methyl-(α,β)-D-glucopyranoside

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	62.83				
0.40/0.10	50.53	4.79	55.89	55.32	+0.57
0.30/0.20	37.99	9.58	48.36	47.57	+0.79
0.25/0.25	31.51	11.98	44.34	43.49	+0.85
0.20/0.30	24.82	14.38	40.13	39.20	+0.93
0.10/0.40	11.49	19.17	31.37	30.66	+0.71
0.50		23.73			

15. Mannitol

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	64.34				
0.40/0.10	51.76	-0.24	56.44	51.52	+4.92
0.30/0.20	38.77	-0.49	45.96	38.28	+7.68
0.25/0.25	32.21	-0.61	38.75	31.60	+7.15
0.20/0.30	25.46	-0.73	30.35	24.73	+5.62
0.10/0.40	11.65	-0.98	12.52	10.67	+1.85
0.50		-1.22			

TABLE III (Continued)

16. Sorbitol

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	64.34				
0.40/0.10	51.76	-0.16	53.97	51.60	+2.37
0.30/0.20	38.77	-0.32	40.97	38.45	+2.52
0.25/0.25	32.21	-0.40	32.98	31.81	+1.17
0.20/0.30	25.46	-0.48	24.06	24.98	-0.92
0.10/0.40	11.65	-0.64	8.66	11.01	-2.35
0.50		-0.80			

TABLE IV

FeTNa (1:4.5) – METHYL β-D-GLUCOPYRANOSIDE

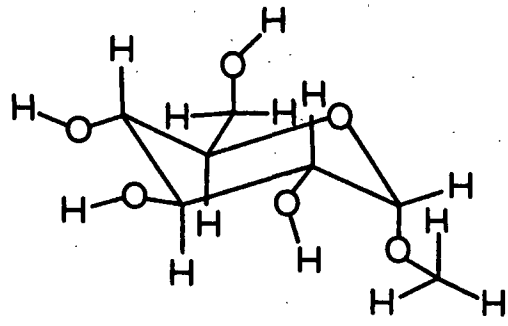
1. Methyl β-D-glucopyranoside

Molarity, FeTNa/model	FeTNa Rotation	Model Rotation	Mixture Rotation	Sum	Deviation
0.50	54.86				
0.40/0.10	48.18	-1.60	48.13	46.58	+1.55
0.30/0.20	39.82	-3.19	39.20	36.63	+2.57
0.25/0.25	34.60	-3.99	33.43	30.61	+2.82
0.20/0.30	28.75	-4.78	26.79	23.97	+2.82
0.10/0.40	14.68	-6.38	10.35	8.30	+2.05
0.50		-7.97			

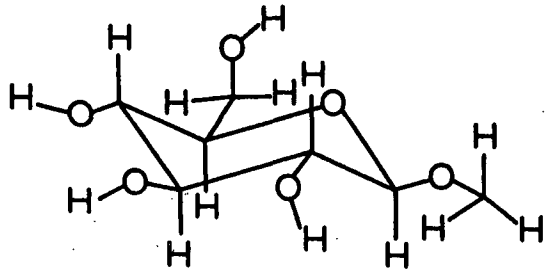
APPENDIX IV

STRUCTURE OF MODEL COMPOUNDS

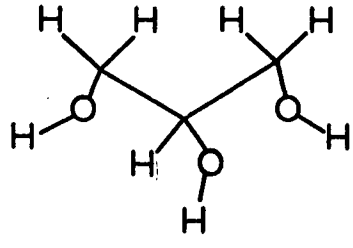
METHYL α-D-GLUCOPYRANOSIDE



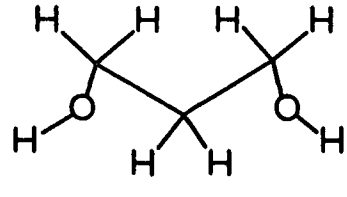
METHYL β-D-GLUCOPYRANOSIDE



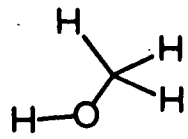
GLYCEROL



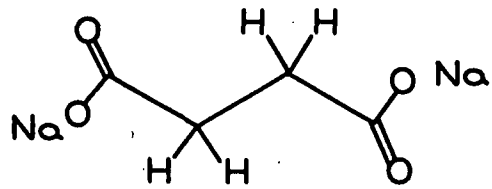
PROPANE-1,3-DIOL



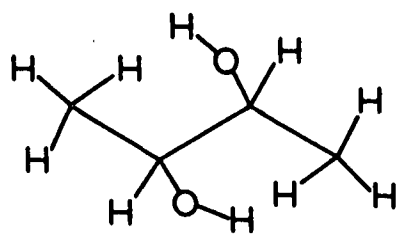
METHANOL



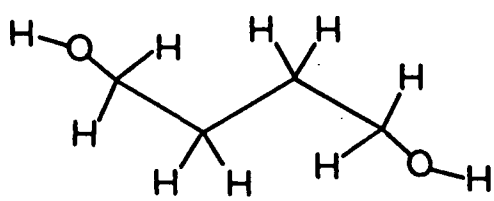
SODIUM SUCCINATE



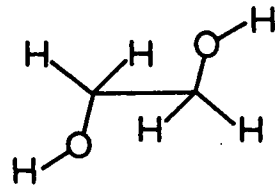
BUTANE-2,3-DIOL



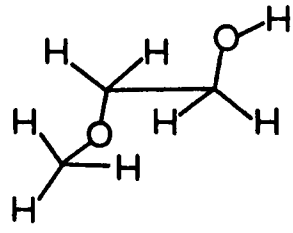
BUTANE-1,4-DIOL



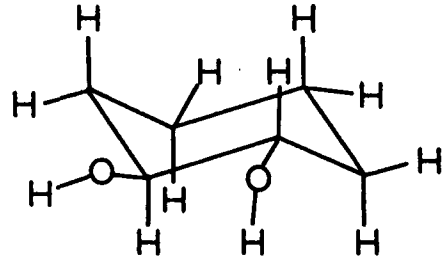
ETHYLENE GLYCOL



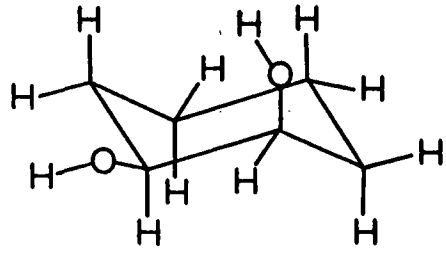
METHYL CELLOSOLVE



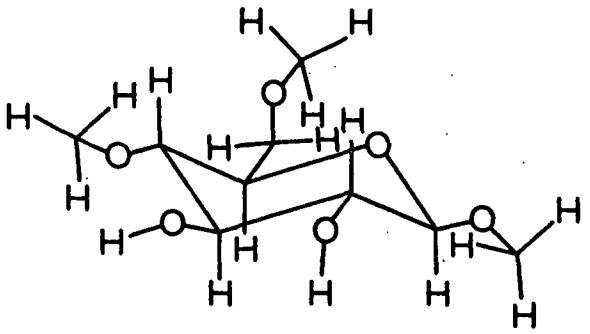
<u>TRANS</u>-CYCLOHEXANE-1,2-DIOL



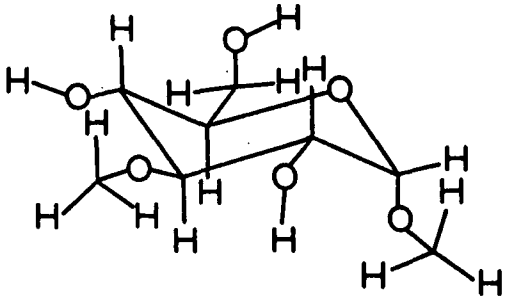
<u>CIS</u>-CYCLOHEXANE-1,2-DIOL



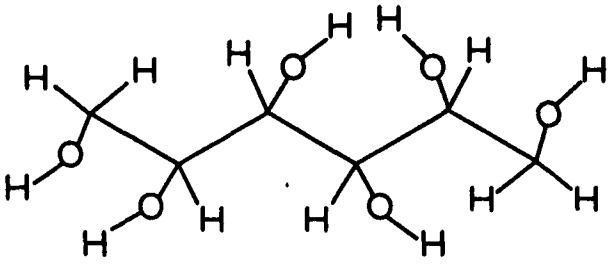
METHYL 4,6-DI-O-METHYL-β-D-GLUCOPYRANOSIDE



METHYL 3-O-METHYL-α-D-GLUCOPYRANOSIDE



MANNITOL



SORBITOL