*Carbohydrate Research*, 76 (1979) 121–130


# THE BEHAVIOR OF INOSOSES IN NEUTRAL AND BASIC AQUEOUS SOLUTION*

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(Received March 23rd, 1979; accepted for publication, May 29th, 1979)

## ABSTRACT

N.m.r. spectra ($^1H$ and $^{13}C$) have shown that, of three inososes studied, the 2,3,4,6/5-isomer exists in solution as the keto form, and the 2,4,6/3,5-isomer is partially, and the 2,3,5/4,6-isomer is almost fully, hydrated. In alkaline solution, each of the inososes rapidly loses a molecule of water, to give *trans*-2,3,4,5-tetrahydroxy-2-cyclohexen-1-one. On acetylation in the presence of a base, this compound gives tetraacetoxybenzenes; hydrogenation yields several cyclohexanepentols.

## INTRODUCTION

The inososes (pentahydroxycyclohexanones) are reactive compounds and useful intermediates, but, beyond a few of their obvious reactions (acetylation, reduction, formation of the phenylhydrazone)[1], their chemistry has not been extensively explored. They are stable in acid solution, but very sensitive to alkalinity. The literature on the behavior of inososes in alkaline solution is confusing, but the most characteristic property is their strong reducing power therein. In such a medium, a peak in the u.v. spectrum of inososes is displaced to ~305 nm, and the extinction is considerably increased[2]. These properties have been explained by postulating that the inososes isomerize into enediols in alkaline solution. From an alkaline solution of 2,3,4,6/5-inosose (**1**) ("*epi*-inosose"), von Euler and Glaser[3] isolated, initially as the lead salt, an acidic substance that showed the typical properties of compounds containing the keto-enediol group, -CO-C(OH)=C(OH)- (named "*aci*-reductones" by von Euler, and "enediolic acids" by Fatiadi and Isbell[4]). It was assumed that ring-opening had occurred, to give an aliphatic keto-enediol, but the possibility of a ring-structure for the product was not excluded. Despite this work, it has generally been assumed that, in alkaline solutions of inososes, the enediol tautomer is present[2,5],

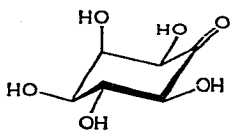
*Cyclitols: Part XXXVII. For Part XXXVI, see *Aust. J. Chem.*, 28 (1975) 1279–1289.

yet no-one has reported the recovery of an inosose from its alkaline solution. Fatiadi[6] studied the changes occurring in alkaline solution, but he attributed the strong u.v. absorption at 305 nm to the formation of DL-*xylo*-pentahydroxy-2-cyclohexen-1-one (an enol form of a diketocyclitol).

It was observed[7] that a freshly prepared, aqueous solution of 2D-2,3,5/4,6-inosose ("*dextro*-inosose") shows absorption at 258 nm, attributed to the carbonyl group, which disappears after 48 h. The explanation proposed — that the inosose dimerizes in dilute solution — appears unlikely, because hydroxyketones that readily dimerize, *e.g.*, 1,3-dihydroxy-2-propanone, are converted into monomers in aqueous solution. Apart from this instance, it has not been suggested that inososes would undergo any reaction in neutral, aqueous solution.

*Inososes in Neutral, Aqueous Solution*

The $^1$H-n.m.r. spectrum of 2,4,6/3,5-inosose (**3**) ("*scyllo*-inosose") shows a two-proton signal at $\delta$ 4.38, at lower field than those of protons in inositols; this signal was, therefore, assigned to H-2 and H-6, the protons attached to the carbon atoms adjacent to the ketone group. It was then noticed that the triplet at $\delta$ 3.39,



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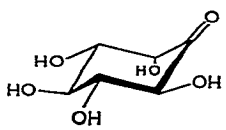

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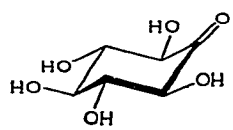

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attributed to H-5 and H-3, integrated at more than 2 protons, and its central signal was higher than required by the 1 : 2 : 1 ratio of triplet signals. To explain this "anomaly", we propose that the inosose is in equilibrium with its hydrate, for which, all (or nearly all) of the $^1$H signals coincide at $\delta$ 3.39. To test this proposal, the spectrum of **3** in dimethyl sulfoxide was determined and it proved to be normal; on gradually adding deuterium oxide, there was initially no change, but, when the composition reached 60% of $D_2O$, the central signal of the triplet was found to be enlarged. Formation of the hydrate under these conditions is quite slow, and may be monitored by n.m.r. spectroscopy. When deuterium oxide was added to the solution in $Me_2SO$ to give a 3:2 mixture, ~8% of the hydrate was found soon after mixing at 25°; but, when compound **3** was dissolved in deuterium oxide, and then sufficient $Me_2SO$ was added to produce the same solvent mixture, the initial hydrate content was ~30%. Over several hours, the compositions of the two samples gradually approach each other. As expected, the composition varies with the temperature; in aqueous solution the proportion of the hydrate is ~40% at 25°, 20% at 40°, and 13% at 60°.

Final proof of the formation of the hydrate in solution was provided by the $^{13}$C-n.m.r. spectrum, which showed eight lines, instead of the expected four, including the signal of the carbon atom of the ketone group at $\delta$ 206.6, and of another quaternary carbon atom at $\delta$ 95.0; this was attributed to the $C(OH)_2$ group.

By contrast, the n.m.r. spectra of 2,3,4,6/5-inosose (**1**) do not indicate the

presence of a hydrate. The $^1$H-n.m.r. spectrum shows five signals, each integrating for one proton, three of them at a field lower than $\delta$ 4.0 (one equatorial proton and two adjacent to the ketone group). The $^{13}$C-n.m.r. spectrum shows six signals, one at very low field (ketone group), and none around $\delta$ 95 (hydrated ketone). If this compound were hydrated, one of the two hydroxyl groups on C-1 would be *syn*-axial to the hydroxyl group on C-3; this interaction seems to minimize the extent of hydration.

A third inosose, the 2L-2,3,5/4,6-isomer (**2**), is almost completely hydrated in aqueous solution. The 100-MHz, $^1$H-n.m.r. spectrum could not be interpreted, but all of the signals are at field higher than $\delta$ 3.8, showing the absence of a ketone group. In $Me_2SO$–$D_2O$, however, the ketone form is readily visible, H-2 and H-6 appearing at $\delta$ 4.03 and 4.53, respectively. In 9:1 $Me_2SO$–$D_2O$, there is ~50% of the ketone form present, but, in a 3:2 mixture, only 12%. On closer inspection, signals of the ketone form are also discernible in the spectrum recorded in $D_2O$, and these show the presence of ~4% of the ketone form. The $^{13}$C-n.m.r. spectrum shows six lines, including a signal at $\delta$ 95.3 (hydrate); only a very small carbonyl signal is detectable, at $\delta$ 208.4. It has been noted[7] that the enantiomer of this inosose reduces Benedict solution at a rate appreciably lower than that of 2,4,6/3,5-inosose.

In the hydrated form of inosose **2**, there is one *gauche* interaction (between hydroxyl groups) fewer than in that of the other two inososes studied; the hydrated form is, therefore, the more favored. Analysis showed that the inosose crystallizes as the hydrate. Two methyl ethers of **2** also crystallize as hydrates[8], whereas **1** and **3** crystallize in the anhydrous, *keto* form.

The n.m.r. spectrum of **2** did not change during two days, nor after the solution had been heated for 10 min at 75°; indeed, the compound does not seem to undergo any changes in aqueous solution. The rapidly changing u.v. absorption, described for its enantiomer by Magasanik and Chargaff[7], must, therefore, have been due to an impurity. It is most probable that this impurity was the keto-enediol **6** (see later) formed by the elimination of one molecule of water per molecule; this compound and the closely related DL-*xylo*-2,3,4,5,6-pentahydroxy-2-cyclohexen-1-one[4] (**8**) show u.v. absorption that is much stronger than that of inososes and that disappears rapidly in the presence of air and light. Inosose **2** seems to decompose readily; when, with the intention of converting it into the *keto* form, a sample was thoroughly dried by repeatedly evaporating benzene from it, the $^1$H-n.m.r. spectrum showed that it contained a considerable proportion of the keto-enediol **6**. The inosose was initially liberated from its phenylhydrazone by the classical method[9,10], also used by Magasanik and Chargaff[7], namely, treatment with benzaldehyde. When we employed the somewhat milder treatment with an acidic ion-exchange resin[11], we obtained a sample of the inosose that showed no u.v. absorption at 258 nm.

We also clarified a puzzling reaction reported for 2D-2,3,5/4,6-inosose. Magasanik and Chargaff[7] reduced this compound with sodium amalgam; instead of the expected mixture of *myo*- and *chiro*-inositol, they obtained a new compound, isolated as its acetate, m.p. 175–176°, in 27% yield. A molecular-weight determination (730)

suggested that this compound was derived from a dimer of the inosose. It is, however, difficult to envisage how the inosose could dimerize in dilute aqueous solution; the nature of this compound has remained a puzzle.

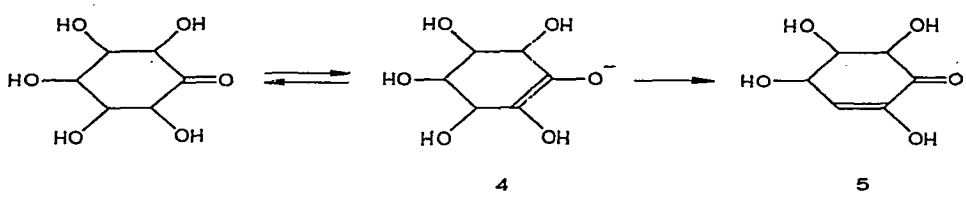
We repeated the reduction with the L-enantiomer of the inosose, and found that five compounds were formed; namely, *muco*-, *myo*-, *scyllo*-, and *chiro*-inositol, and an unidentified compound in the ratios of ~48:13:2:23:14. Now, the hexa-acetate of *muco*-inositol melts at 177–178°, and *muco*-inositol could have been formed by epimerization at C-6 of the inosose should the solution have become alkaline during reduction; if this is the compound that Magasanik and Chargaff[7] isolated, their determination of the molecular weight must have been in error. Owing to the great sensitivity of the inosose to alkalinity, we cannot be certain that the course of their reaction was the same as that of ours; they did not[7] control the pH closely ("the solution was kept neutral by the addition of N acetic acid"), nor did we.

To show that inososes epimerize in mildly alkaline solution, a sample of 2,3,5/4,6-inosose was dissolved in 0.15M sodium carbonate solution and made neutral after 15 min; its n.m.r. spectrum was recorded and found to be complex. Besides signals of the starting material, the doublet at $\delta$ 4.38 and the triplet at $\delta$ 3.39 of 2,4,6/3,5-inosose were readily recognized. The inosose that would give *muco*-inositol on reduction, namely, 2,3,5,6/4-inosose, is unknown, and therefore its signals could not be identified in the spectrum.

*Inososes in Alkaline Solution*

When an inosose is dissolved in a solution of sodium hydroxide, as described by von Euler and Glaser[3], and the solution is made neutral ten minutes later, it gives a precipitate with lead acetate. If the inosose is dissolved in a solution of barium hydroxide, a precipitate is rapidly formed. When these insoluble salts are decomposed with acid, essentially a single compound is obtained, as judged by its $^1$H-n.m.r. spectrum. The spectrum in $D_2O$ shows the presence of four hydrogen atoms in a $CH_2$-CH-CH arrangement, whereas, the acyclic, reductone structure suggested by von Euler and Glaser[3] would have five hydrogen atoms attached to carbon. That the compound still contained a six-membered carbon ring was shown by acetylation with acetic anhydride and sodium acetate, which gave tetraacetoxybenzenes. The large coupling-constant (8.7 Hz) between the two single hydrogen atoms shows that they are *trans* to each other. The unusually large, geminal coupling-constant (16.2 Hz) is typical of a methylene group adjacent to a double bond[12]. Taking the acidic nature of the compound into consideration also, it is DL-*trans*-2,3,4,5-tetrahydroxy-2-cyclohexen-1-one (**7**) or one of its tautomeric forms (*e.g.*, **6**). von Euler and Glaser's analysis[3] corresponds to the monohydrate of this formula. The fully hydroxylated analog (**8**) of this compound, which shows similar properties, was prepared by Fatiadi and Isbell[4].

Strong base therefore causes $\beta$-elimination from the enediol form (**4**) of the inosose, giving an unsaturated ketone (**5**) which then rearranges to one of the keto-enediols (**6** or **7**). It is not possible to distinguish these two tautomeric forms; they



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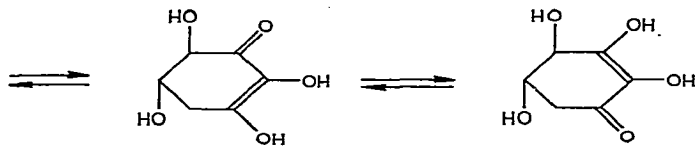

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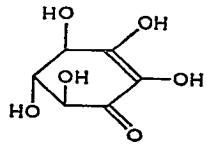
are certainly in equilibrium with each other and with various diketo forms. The same compound is also formed when the inosose is dissolved in an aqueous solution of sodium carbonate, but the reaction is then slower, requiring several hours for completion.

The same keto-enediol is formed from 2,4,6/3,5-, 2,3,4,6/5-, and 2,3,5/4,6-inosose. The reason for this unexpected observation is that repeated keto-enol equilibria cause epimerization on every carbon atom of the keto-enediol molecule, resulting ultimately in the more stable isomer in which the hydroxyl groups on C-4 and C-5 are *trans*. This is readily observed when the reaction of an inosose with sodium carbonate is conducted in $D_2O$, and the reaction is monitored by $^1$H-n.m.r. spectroscopy: gradually all of the signals disappear from the spectrum, owing to exchange with deuterium. The last signal to disappear (after ~24 h) is the doublet of H-4 of the keto-enediol. Another evidence of this extensive epimerization is the reaction of 2L-2,3,5/4,6-inosose with bases, which gives an optically inactive product.

The product formed by acetylation of the keto-enediol in the presence of sodium acetate was crystalline, but proved to be a mixture. By chromatography, 1,2,3,4- and 1,2,3,5-tetraacetoxybenzene were isolated in the ratio of ~1:2. The former tetraacetate is the product of acetylation, followed by $\beta$-elimination, from either structure **6** or **7** of the keto-enediol. The 1,2,3,5-isomer must be derived from another form, *e.g.*, **5**, of the keto-enediol. It may be recalled that acetylation of inososes under the same conditions gives only the 1,2,3,5-isomer, by two successive $\beta$-eliminations[13]; our keto-enediol was, however, not contaminated by an inosose, as judged by its n.m.r. spectrum.

Further evidence for the structure and configuration of the keto-dienol (**6**) was sought by hydrogenation, cyclohexanepentols being the reaction products expected. Fatiadi and Isbell[4] obtained *scyllo*- and *myo*-inositol from the hydrogenation of the fully hydroxylated, keto-enediol **8** over Raney nickel; in these isomers, the secondary hydroxyl groups newly created adjacent to the pre-existing ones appear in *trans*



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orientation. Should the stereochemical outcome of the hydrogenation be the same for the present keto-enediol, it would be expected that four cyclohexanepentols would be formed, namely, the 1,3,4/2,5-, 1,2,4/3,5-, 1,2,3,5/4-, and 1,3,5/2,4-isomers. When the hydrogenation was conducted with a platinum oxide catalyst, g.l.c.[14] of the acetates showed the presence of 12 products, four of which had retention times characteristic of cyclohexanepentol acetates. The other products had shorter retention-times, and appear to be cyclohexane-tetrols and -triols; hydrogenolysis had, therefore, occurred during the treatment with hydrogen over platinum. There were no inositols amongst the reaction products. Because of the complexity of the mixture, none of the products was isolated, but the cyclohexanepentols were identified, by comparison with authentic samples, by g.l.c.[14], paper chromatography[15], and paper electrophoresis in borate buffer[16] and in calcium acetate solution[17], as 1,2,3,5/4- (28%), 1,2,4/3,5- (14%), 1,3,5/2,4- (3%), and 1,3,4/2,5-cyclohexanepentol (3%); that is, the expected products were formed.

When the hydrogenation was conducted with Raney nickel catalyst, there was considerably less hydrogenolysis. The four cyclohexanepentols were obtained essentially free from other compounds, the 1,2,3,5/4-isomer being the main product (40%). After acetylation, prolonged standing under ethanol produced crystals, identified as the pentaacetate of the 1,3,5/2,4-isomer; after concentration, the mother liquors deposited a mixture of the pentaacetates of the 1,2,3,5/4- and 1,2,4/3,5-isomers.

Stable magnesium complexes have been obtained from the enediol forms of some keto sugars[18]. It appeared of interest to prepare such complexes from inososes, but all our attempts led only to salts of the keto-enediol. The question was then raised whether the anion (4) of the enediol has any finite existence: does it immediately suffer $\beta$-elimination or has it a lifetime sufficiently long for it to undergo other reactions? In the latter case, it would revert to the inosose, and, if the reaction were carried out in deuterium oxide, the inosose would become labelled with deuterium.

The $^1$H-n.m.r. spectra of inososes and their reaction products are poorly resolved in alkaline solution, and do not provide a means of monitoring the reaction. It was found, however, that, after 15 min in 0.2M sodium carbonate solution, some 2,3,4,6/5-inosose is still present in solution, and it can be recovered, after acidification, by crystallization. When this process was performed in deuterium oxide, the n.m.r. spectrum of the recovered inosose disclosed that about 3/4 of the hydrogen on C-2 and 1/3 of the hydrogen on C-6 had been replaced by deuterium. The enediol therefore persists in solution for a brief period, but, apparently, complex-formation with

magnesium does not stabilize it sufficiently to prevent elimination leading to the keto-enediol **6**.

## EXPERIMENTAL

*General methods.* — Solutions were evaporated under diminished pressure at temperatures not exceeding 50°. $^1$H-N.m.r. spectra were recorded with a Japan Electron Optics JNM-4H-100S spectrometer (in Sydney) and with a Cameca spectrometer at 250 MHz (in Grenoble); the $^{13}$C-n.m.r. spectra, with a Brucker WP-60 instrument (in Sydney), and with the Cameca (in Grenoble). $^1$H Chemical shifts were measured from internal $Me_4Si$ ($\delta$ 0.00) in chloroform solutions, and from internal *tert*-butanol ($\delta$ 1.23) in aqueous solutions; for $^{13}$C-n.m.r. spectra, 1,4-dioxane ($\delta$ 67.4) was used as the internal reference. In order to observe the carbonyl and hydrated carbonyl carbon atoms, a repetition rate of 5–8 sec was used. Mass spectra were measured on an A.E.I. MS 30 double-beam spectrometer. Gas–liquid chromatography was conducted in Sydney, in a custom-built instrument, in 120-cm columns, with nitrogen as the carrier gas and a hydrogen flame-ionization detector; a column of 1.5% of LAC-1R-296 on Chromosorb W at 215° (column *A*) or of 3.0% of SP-2401 on Chromosorb W at 232° (column *B*) was used.

*The inososes.* — 2,4,6/3,5-Pentahydroxycyclohexanone[9] and DL-2,3,4,6/5-pentahydroxycyclohexanone[10] were prepared by methods previously reported.

A generous supply of the phenylhydrazone of 2L-2,3,5/4,6-pentahydroxycyclohexanone[8] was donated by Dr. Laurens Anderson; it was purified by recrystallization from ethanol (100 parts). The inosose was liberated either by treatment with benzaldehyde[9,10] in water, or Amberlite IR-120($H^+$) ion-exchange resin[11] in aqueous ethanol (owing to the low solubility of the phenylhydrazone in water). The sample obtained by the former method showed weak and transient u.v. absorption[7], but that prepared by the latter showed none. Analyses of samples dried to constant weight in a desiccator at room temperature showed that the inosose crystallizes as its hydrate, m.p. 138–141° (dec.). Magasanik and Chargaff[7] recorded m.p. 138–139° for its enantiomer, and obtained an analysis corresponding to that calculated for a hemihydrate, but did not indicate how their compound was dried.

*Anal.* Calc. for $C_6H_{12}O_7$: C, 36.74; H, 6.17. Found: C, 36.98, 36.37; H, 6.34, 5.79.

*2,4,6/3,5-Pentahydroxycyclohexanone.* $^1$H-N.m.r. data ($D_2O$): $\delta$ 4.38 (d, $J_{2,3}$ 9.6 Hz, H-2,6), 3.79 (t, $J_{4,5}$ 9.0 Hz, H-4), and 3.39 (t, H-3,5 and protons of the hydrate), at 25°, in the ratios of ~4:2:11. In 4:1 $Me_2SO$–$D_2O$: $\delta$ 4.18, 3.57, and 3.14, respectively, in the ratios of 2:1:2. $^{13}$C-N.m.r. data ($D_2O$) (*k* = keto form, *h* = hydrate): $\delta$ 206.6 (C-1*k*), 95.0 (C-1*h*), 76.9 (C-2,6*k*), 75.2 (*h*), 74.7 (C-3,5*k*), 74.6 (C-4*h*?), 74.0 (*h*), and 73.9 (C-4*k*).

*2,3,4,6/5-Pentahydroxycyclohexanone.* $^1$H-N.m.r. data ($D_2O$): $\delta$ 4.59 (dd, $J_{2,3}$ 3.2, $J_{2,6}$ 1.3 Hz, H-2), 4.26 (dd, $J_{5,6}$ 9.2 Hz, H-6), 4.25 (dd, $J_{3,4}$ 2.5 Hz, H-3)

3.99 (dd, $J_{4,5}$ 9.5 Hz, H-4), and 3.71 (t, H-5). $^{13}$C-N.m.r. data ($D_2O$): $\delta$ 208.1 (C-1), 76.9 (C-6), 75.3 (C-2), 74.9, 74.3, and 71.4.

*2L-2,3,5/4,6-Pentahydroxycyclohexanone.* $^1$H-N.m.r. data ($D_2O$): $\delta$ 3.79 (m), 3.70 (m), 3.60 (s), 3.55–3.30 (m), and very small signals of the keto form at 4.29 (d) and 4.10 (t). In 4:1 $Me_2SO$–$D_2O$, there are signals of the keto form at $\delta$ 4.53 (d, $J_{5,6}$ 9.5 Hz, H-6), 4.03 (d, $J_{2,3}$ 2.8 Hz, H-2) and 3.85 (t, $J$ 8.8 Hz, H-4?). $^{13}$C-N.m.r. data ($D_2O$): $\delta$ 95.3 (C-1), 75.2, 74.3, 73.8, 73.4, and 71.5.

*Reduction of 2L-2,3,5/4,6-inososе with sodium amalgam.* — The inosose (100 mg) was reduced by following Magasanik and Chargaff's method[7] as closely as possible. The crude acetylation product was taken up in chloroform, and analyzed by g.l.c. (column *B*): *chiro*-inositol ($R_t$ 9.1 min), *myo*-inositol (11.3), an unknown compound (13.4), and *muco*-inositol (14.6) were found. On this column, the acetate of *scyllo*-inositol coincides with that of *muco*-inositol; its presence was shown by the use of column *A*. From an ethanolic solution of the product, a solid separated that was shown to be a mixture of the acetates of *scyllo*-, *muco*-, and *chiro*-inositols. The presence of *muco*-inositol was confirmed by paper electrophoresis in calcium acetate solution[17].

DL-trans-*2,3,4,5-Tetrahydroxy-2-cyclohexen-1-one* (7). — 2,3,4,6/5-Inosose (0.5 g) was dissolved in water (12.5 mL) at 31° under nitrogen, and a solution (made at 100° and then cooled) of barium hydroxide (4.0 g) in water (25 mL) was added with vigorous stirring. A yellow precipitate formed immediately. After 30 min, the solid was separated by centrifugation, washed three times with water, and dried under diminished pressure. The solid (970 mg) contained 42.9% of barium. It was suspended in water (50 mL), and M sulfuric acid was added until the pH reached 6.5. Barium sulfate was removed by centrifugation, and the supernatant liquor and washings were combined, and evaporated by freeze-drying. The residual, amorphous powder (0.64 g) contained traces of barium, and resisted attempts at crystallization; $^1$H-n.m.r. data ($D_2O$): $\delta$ 4.11 (d, $J_{4,5}$ 8.7 Hz, H-4), 3.88 (td, $J_{5,6e}$ 5.2, $J_{5,6a}$ 9.0 Hz, H-5), 2.70 (dd, $J_{6a,6e}$ −16.2 Hz, H-6*e*), and 2.46 (dd, H-6*a*); mass-spectral data: *m/e* 160 ($M^+$), 142 ($M^+ - H_2O$), 101, and 89 (source temperature 160°; with the source at 170°, molecular ion was not observed). Paper chromatography in 4:1 acetone–water: $R_F$ 0.16; the inosose has $R_F$ 0.36.

An amorphous powder having the same n.m.r. spectrum was obtained from 2,4,6/3,5-inosose and from 2L-2,3,5/4,6-inosose; the latter sample had no optical activity. In aqueous solution, the compound is readily oxidized, giving a colored precipitate.

*Acetylation.* — A solution of the keto-dienol (0.5 g) and sodium acetate (0.25 g) in acetic anhydride (4 mL) was heated for 10 min on a steam-bath. After being cooled, the solution was poured onto ice–water, and extracted with chloroform, and the extract was dried ($Na_2SO_4$), and evaporated. The residue was crystallized from ethanol, to give a mixture of tetraacetoxybenzenes (421 mg), m.p. 125–128°; mass spectral data: *m/e* 310 ($M^+$), 268 ($M^+$ — Ac), 226 ($M^+$ — 2 Ac), 184 ($M^+$ — 3 Ac),

and 142 ($M^+$ — 4 Ac); g.l.c. (column *B*) showed two peaks, at 15.5 (1,2,3,5-) and 14.2 min (1,2,3,4-tetraacetoxybenzene).

The crystals and mother liquor were combined, and chromatographed on a column of silica gel (type H) with 6:1 chloroform–ethyl acetate. First to emerge was 1,2,3,5-tetraacetoxybenzene, m.p. 105° (after crystallization from ethanol), identical by mixed m.p. and g.l.c. with an authentic sample[13]; $^1$H-n.m.r. data ($CDCl_3$): $\delta$ 6.98 (s, aromatic H) and 2.26 (s, Ac).

The second component, crystallized from ethanol, was 1,2,3,4-tetraacetoxybenzene, m.p. 140° (lit.[19] m.p. 142°); $^1$H-n.m.r. data ($CDCl_3$): $\delta$ 7.12 (s, aromatic H) and 2.26 (s, Ac).

*Hydrogenation.* — (*i*) The keto-dienol (0.3 g) was hydrogenated in ethanol (60 mL) over Adams's platinum oxide catalyst (75 mg) for 24 h at 10 atm pressure. Filtration and evaporation yielded an amorphous powder (248 mg). After acetylation, g.l.c. (column *A*) showed peaks at 2.6, 3.3, 4.2, 5.3, 6.4, 7.6, 9.3, 12.3 (3%), 13.9 (14%), 17.5 (28%), and 21.5 min (3%). The last four peaks coincided (co-chromatography) with those of the peracetates of 1,3,4/2,5-, 1,2,4/3,5-, 1,2,3,5/4-, and 1,3,5/2,4-cyclohexanepentols, respectively.

(*ii*) Hydrogenation over Raney nickel W-2 at 8 atm pressure in 1:1 ethanol–water for 24 h gave a mixture consisting mainly of cyclohexanepentols. After acetylation, the mixture was stored under ethanol, from which, after a prolonged time, crystals of penta-*O*-acetyl-1,3,5/2,4-cyclohexanepentol, m.p. 188°, separated. After concentration, and further storage, more solid separated; this was shown, by g.l.c., to be the pentaacetate of 1,2,3,5/4-cyclohexanepentol contaminated with that of the 1,2,4/3,5-isomer.

*Exchange with deuterium.* — 2,3,4,6/5-Inosose (100 mg) was dissolved in deuterium oxide (1 mL), and a solution of sodium carbonate (35 mg) in deuterium oxide (0.5 mL) was added. After 15 min, the solution was made neutral with acetic acid, concentrated to ~0.5 mL, and stored at 0°; crystals of 2,3,4,6/5-inosose (50 mg) separated. In its $^1$H-n.m.r. spectrum, the signal of H-2 at $\delta$ 4.59 integrated to only ~0.25 H. The signal of H-6, which overlapped that of H-3, could not be evaluated; however, the signal of H-5 at $\delta$ 3.71 appeared as a triplet (molecules containing H-6) and a doublet (molecules containing D-6), and their ratio was ~2:1.

ACKNOWLEDGMENTS

We thank Dr. Laurens Anderson (Madison, Wisc.) for a generous gift of 2L-2,3,5/4,6-pentahydroxycyclohexanone phenylhydrazone. This research was supported by a research contract with Société L'Air Liquide, Paris.

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