STUDIES ON THE LEAD-CATALYZED SYNTHESIS OF ALDOPENTOSES

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Abstract. The object of this work was to find an efficient means of synthesizing ribose in a manner that could be considered prebiotic. The starting point for synthesis was an aqueous solution of formaldehyde. Heretofore the most frequently used catalyst for this purpose has been calcium hydroxide. Unfortunately this system produces a wide array of products in addition to ribose which constitutes 1% or less of the final product. Attempts were made to find more mild conditions under which the formaldehyde could be reacted. Magnesium hydroxide suspensions were used for this purpose. Formaldehyde does not yield any sugars when incubated in magnesium hydroxide suspensions alone. However, if the magnesium hydroxide suspension was supplemented with doubly charged lead salts and catalytic amounts of any intermediate in the prebiotic pentose pathway, aldopentoses accounted for 30 per cent or more of the final product. The presence of lead in the incubation mixture also accelerated a number of other reactions including the interconversion of the four common aldopentoses, ribose, arabinose, lyxose and xylose.

1. Introduction

One of the favored hypotheses regarding the origin of life is that it started with RNA or RNA-like molecules. This hypothesis has become increasingly popular since the discoveries of Cech *et al*. (1981) and Altman (1989) that certain RNAs possess enzyme-like activity. The notion that RNA has the potential for acting as a catalyst has been reinforced by discoveries of additional so-called ribozymes.

Whereas the RNA-only hypothesis is very attractive, it is unclear if the first RNAs possessed precisely the same components as contemporary RNAs. In particular, the presence of ribose has been questioned because of the difficulty in finding a feasible prebiotic pathway for the synthesis of ribose (Schwartz and Graaf, 1993).

It is generally considered that the most likely prebiotic precursor for ribose synthesis is formaldehyde. Studies on the conversion of formaldehyde into sugars date back to Butlerow (1861). Since that time a wide variety of conditions have been used (Mizuno and Weiss, 1974); the process whereby formaldehyde is converted into sugars is usually referred to as the formose reaction. Favored conditions for the formose reaction most frequently employ calcium hydroxide as the catalyst. Within a matter of 15 to 20 min at temperatures between 45 and 65 °C a concentrated solution of formaldehyde is transformed into a broad array of products including ribose.

The first intermediate in the formose reaction is believed to be glycolaldehyde. In small amounts glycolaldehyde also catalyzes the reaction. If glycolaldehyde functions as an intermediate and a catalyst in the reaction there must be a mechanism

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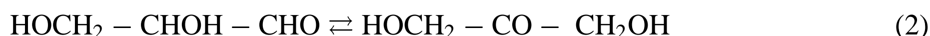
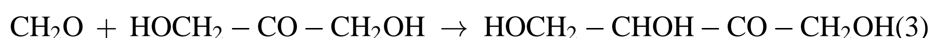
whereby each glycolaldehyde incorporated results in the generation of one or more glycolaldehydes. This consideration led Breslow (1959) to propose a cycle of reactions in which the glycolaldehyde consumed in the first step is regenerated in the fifth step:

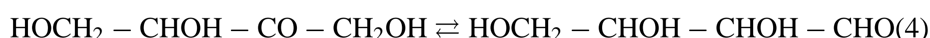
$$CH_20 + HOCH_2 - CHO \rightarrow HOCH_2 - CHOH - CHO \quad (1)$$



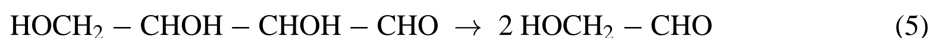
$$HOCH_2 - CHOH - CHO \rightleftarrows HOCH_2 - CO - CH_2OH \quad (2)$$



$$CH_2O + HOCH_2 - CO - CH_2OH \rightarrow HOCH_2 - CHOH - CO - CH_2OH \quad (3)$$



$$HOCH_2 - CHOH - CO - CH_2OH \rightleftarrows HOCH_2 - CHOH - CHOH - CHO \quad (4)$$



$$HOCH_2 - CHOH - CHOH - CHO \rightarrow 2\ HOCH_2 - CHO \quad (5)$$

Step one in the cycle involves an aldol condensation between formaldehyde and glycolaldehyde that results in glyceraldehyde. Step two involves the tautomerization of glyceraldehyde to dihydroxyacetone. Step three involves an aldol condensation of dihydroxyacetone with formaldehyde to form a ketotetrose. Step four involves tautomerization of the ketotetrose to an aldotetrose. Finally step five involves a reverse aldol condensation in which an aldotetrose breaks down into two glycolaldehydes. In support of this cycle of reactions it has been found that other intermediates of the cycle (glyceraldehyde, dihydroxyacetone or the aldotetrose erythrose) have comparable catalytic effects to glycolaldehyde. The cycle does not directly explain how ribose or other sugars are made. For ribose the most likely pathway would probably involve an aldol condensation between glycolaldehyde and glyceraldehyde. Reactions of this sort that tap intermediates in the cycle must be slower than the reactions within the cycle; otherwise the concentrations of glycolaldehyde and the other intermediates in the cycle would be reduced which would slow down the formose reaction or even bring it to a halt.

The main problem with the formose reaction as a prebiotic route to ribose is that ribose only constitutes a small percentage of the product. In 1990 a ray of hope was cast on this problem by the finding (Muller *et al.*, 1990) that there are conditions under which ribose 2,4-bisphosphate is the major product. This occurs when the first condensation product in the formose reaction, glycolaldehyde, is phosphorylated on the C2 carbon and then incubated with formaldehyde. Unfortunately the conditions used for synthesis of ribose 2,4-bisphosphate and the conditions that would probably be necessary to convert it into a derivative more suitable for RNA synthesis do not seem very prebiotic. Despite this limitation it is encouraging to find that there is a way in which the formose reaction can be modified so that a ribose derivative is the major product.

Our investigations on ribose synthesis began with this as a starting point. We were driven by the belief that there must be a solution to the problem of synthesizing reasonable concentrations of ribose if indeed ribose was in the first nucleic acids.

Table I
Chromatographic properties of sugars and their precursors

Sugar	Abbreviation	R_F[a]	Spot color[b]	Spot intensity[b]
Arabinose	Ar	0.47	red	strong
Dihydroxyacetone	Di	0.64	greenish brown	strong
Erythrose	Er	0.58	brown	strong
Formaldehyde	Fa	Smear[d]	yellow	strong
Fructose	Fr	0.49	brown	very faint
Glyceraldehyde	Gc	Smear[d]	greenish brown	strong
Glycolaldehyde	Gk	–	–	–
Glucose	Gl	0.31	brown	medium
Lyxose	Ly	0.44	red	strong
Mannose	Ma	0.39	brown	medium
Ribose	Ri	0.54	red	strong
Xylose	Xy	0.39	red	strong

[a] On thin layer cellulose in 88% phenol.
[b] Using aniline hydrogen phthalate stain.
[c] Probably evaporated before staining.
[d] The average migration rate of the smears is considerably lower than expected suggesting a strong interaction of the compounds with the cellulose paper. Most of the remaining compounds form hemiacetals suggesting that the aldehyde group in glyceraldehyde and formaldehyde is more accessible for an interaction of this sort.

Moreover it seems likely that the solution must be a simple one to have occurred in the primitive earth environment. In this paper we present a progress report on our investigations which have led us to a scheme that we feel has prebiotic potential.

2. Experimental

(1) Source of supplies. Most chemicals were purchased from either the Sigma or the Aldrich chemical companies. The formaldehyde used in our studies was 37% certified ACS grade from Fisher Scientific. It was stored in 10% methanol in a brown bottle at 20 °C. Even six months after use it was free of visible polymer. The $\propto$-hydroyacetophenone was prepared as a 4% solution in ethanol and used at a final concentration of 0.05%.

(2) Chromatographic procedures. Thin layer paper for chromatography was a product of Macherey-Nagel. The specific paper used was cellulose MN300 UV_{254}. Although ultraviolet was not used for detection purposes in our work, we found the running characteristics and the resolution of spots was superior to the MN300 paper lacking the fluor. All papers were washed by running first in water and then blow dried. The paper we used comes in the form of 20 × 20 cm sheets with a plastic backing. These sheets were frequently cut into smaller strips but the longitudinal running direction was always 20 cm. Samples were

applied about 1.5 cm from one end of the paper with a 5λ capillary pipette. A single spot might contain from 1λ to 7λ; it was always applied in aliquots of 1λ or less. The running solvent consisted of 88% phenol and 12% water. Chromatography was done in a covered glass tank at 16 °C over a period of about 16 hr. This is the time it took for the solvent to climb to a height of about 17 cm. The run was stopped by removing the paper from the chromatography tank and blow dried. Residual phenol was removed by a rapid rinse in absolute ethanol followed by blow drying. The sheet was briefly immersed in stain (described below), then blotted and blow dried. The dried paper was placed in a 75 °C oven for 20 min. The R_F values and colors produced by the compounds in which we were interested are given in Table I. It was reassuring to be able to characterize most of the compounds of interest by both their R_F values and their color. When making mobility comparisons between samples it was noted that the same compound will usually run more slowly in the presence of other substances. In cases where this might cause some confusion internal markers were incorporated into the sample. The chromatographic stain was aniline hydrogen phthalate containing 0.46 mL of aniline, and 0.83 gm phthalic acid in 50 mL of water-saturated butanol. (Partridge, 1949)

In a control experiment the 4 spots judged to be the four straight chain aldopentoses were run in a second dimension to insure their identity. After running in the phenol solvent the paper was thoroughly rinsed in ethanol and dried. Then the paper was turned at right angles and run in cyclohexanol-pyridine-water (80-46-39). The spots ran as expected in the second solvent with approximate R_F values of 0.35, 0.31, 0.29 and 0.25 respectively for ribose, lyxose, xylose and arabinose. Identification as well as homogeneity of spots was also tested in another way which proved to be more sensitive for detecting impurities. First bands of the sample were chromatographed using the standard phenol-water solvent. After removing the water and phenol, the paper was sprayed at the edges to determine the precise locations of the four pentoses. The unsprayed portions of the bands were cut from the paper, eluted and run as spots in the cyclohexanol-pyridine-water solvent. The original bands ran with the expected R_f values in the second solvent. Since the R_f values for the four straight chain aldopentoses are quite different for the two solvents we consider this an excellent identity test. It should be emphasized that we only see those compounds that stain with aniline hydrogen phthalate.

(3) Spot analysis. A 10λ sample from an incubation mixture was spotted on Whatman 3 mm paper, sprayed with the aniline hydrogen phthalate stain and dried at 75 °C. Spot analysis was very useful for quick monitoring of the course of a reaction. Formaldehyde gives a yellow color; the intermediates in the glycolaldehyde cycle and hexoses give greenish brown or brown colors; and the aldopentoses give a red color. A sample that contains a mixture of formaldehyde and other stainable components will always show a yellow color first even in cases where the final spot is brown or red. Thus we can determine

when and if all of the formaldehyde is consumed. In spot analysis from the formose reaction products we found that yellow color development sometimes precedes greenish brown or brown but never red. This indicates that very few aldopentoses are made until the formaldehyde supply has been exhausted. Estimates for amounts of each of the four pentoses were obtained by thin layer chromatography in parallel with standards containing known amounts of each pentose. The most accurate estimates required two chromatograms. In the first chromatogram a sample was run in parallel with a series of standards differing in aldopentose concentration in increments of 20%. In the second chromatogram the test sample was run in parallel between the two standards that came closest to matching the sample in color intensity in the first run. This method of estimation by visual comparison was reproducible to within 15%.

(4) Incubations. All incubations were done in stoppered 13 × 100 mm test tubes placed in thermostated water baths or ovens. The usual sample size was 0.5 mL. It contained freshly diluted formaldehyde, other specified carbohydrates and other specified inorganic catalysts as indicated. Samples were assayed after incubation for a specified time or during the incubation by removing small aliquots for spot analysis or chromatography.

3. Results and Discussion

The low yields of aldopentoses at the high pHs generated by calcium hydroxide (pH 11.5) led us to seek milder conditions for the synthesis of ribose from formaldehyde. Calcium hydroxide was abandoned and replaced by magnesium hydroxide which has a pH of 9.4. While magnesium hydroxide is a strong base like calcium hydroxide it is much less soluble; this accounts for the lower pH. In magnesium hydroxide suspensions the aldopentoses were much more stable; less than 10% loss was experienced in 12 hr at 67 °C with ribose. In a calcium hydroxide suspension the loss of ribose under these conditions was about 95%. Unfortunately some of the reactions of the glycolaldehyde cycle were much slower in magnesium hydroxide suspensions as evidenced by the fact that no aldopentoses were formed from formaldehyde alone and only matching amounts were formed in the presence of small amounts of glycolaldehyde. Clearly the latter compound was not operating catalytically as it had done in the calcium hydroxide suspensions.

4. Plumbous Ion Remedies the Rate Problem at Lower pHs

The frustrations of working at the lower pHs generated by magnesium hydroxide suspensions led us to look for additional catalytic agents. First we pursued reports that ∝-hydroxyacetophenone could catalyze sugar formation from formaldehyde and that it might even be superior to most other carbohydrate catalysts (Mizuno and

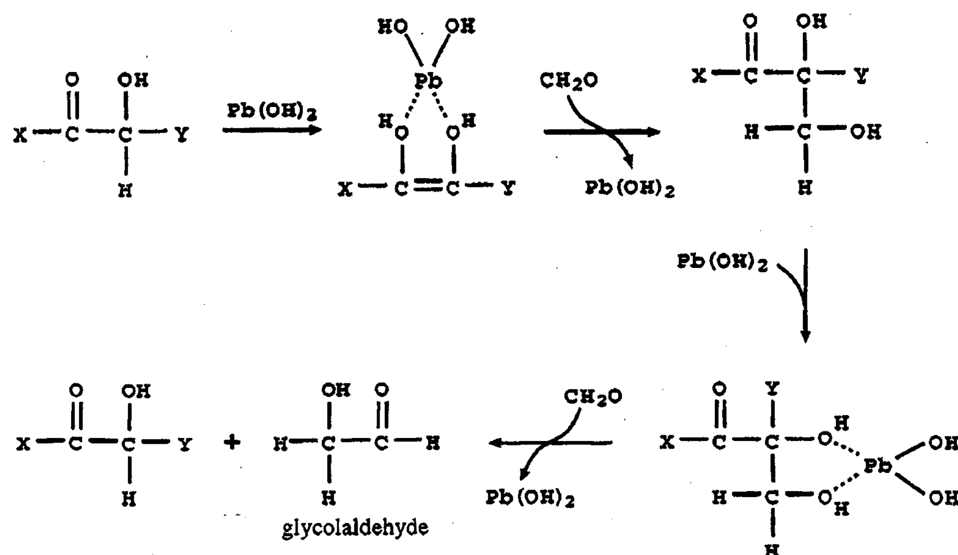


Figure 1. Proposed mechanism whereby ∝-hydroxyacetophenone in connection with lead hydroxide catalyzes the synthesis of glycolaldehyde from formaldehyde. The organic catalyst is drawn in a general form. In ∝-hydroxyacetophenone x = benzene and y = hydrogen.

Weiss, 1974). When ∝-hydroxyacetophenone was added to a magnesium hydroxide suspension it stimulated sugar synthesis but the yields were small and positive results required prolonged incubations of ten hours or more at elevated temperatures. Despite the limitations experienced in working with ∝-hydroxyacetophenone these were the first positive results we had observed at the lower pHs so we sought a means for potentiating the action of ∝-hydroxyacetophenone. A very encouraging observation had been made by Langenbeck (1954) in the 1950s that lead hydroxide in conjunction with benzoin catalyzes the formation of glycolaldehyde from formaldehyde. When we added lead hydroxide together with ∝-hydroxyacetophenone there was a pronounced stimulation effect. In short order we found conditions under which this new concoction increased the yields of aldopentoses from formaldehyde by 20-fold over that found in the absence of lead. We could now convert formaldehyde into the four aldopentoses with an efficiency of 20–30%. Actually we used lead nitrate in which the lead is present as the doubly charged plumbous ion; this converts to the anionic form of lead hydroxide at the pH that prevails in a magnesium hydroxide suspension.

The stimulatory action of plumbous ion has not been duplicated with any other metallic cations despite an extensive search. So far we have obtained negative results with Mn^{2+}, Fe^{2+}, Zn^{2+}, Co^{2+}, Sn^{2+}, Tl^{2+}, Mg^{2+} and Ca^{2+}. We speculate that this special property of plumbous ion is due to an extraordinary affinity for cis hydroxyls. A mechanism for its action based on Langenbeck's proposed mechanism for the catalysis of glycolaldehyde synthesis by benzoin and lead is

shown in Figure 1. In this mechanism lead hydroxide stabilizes the enediol form of $\propto$-hydroxyacetophenone. In this form one of the carbons of the enediol-lead complex attacks a formaldehyde carbon. Following the formation of a formaldehyde adduct the lead shifts to another location resulting in reaction with a second formaldehyde molecule. Overall this leads to the formation of one glycolaldehyde from two formaldehyde molecules and the return of $\propto$-hydroxyacetophenone to its original form. Even though this mechanism was designed to explain how $\propto$-hydroxyacetophenone catalyzes the formose reaction, it should be apparent that the constellation of key atoms in the organic catalyst are found in most sugars. In fact we have observed that $\propto$-hydroxyacetophenone can be replaced by any of the glycolaldehyde cycle intermediates. At incubation times of 10 hr. or more lead by itself catalyzes the conversion of formaldehyde into sugars.

In view of the seemingly unique role of lead in our experiments we have pondered the legitimacy of lead as a prebiotic catalyst. Obviously lead is less abundant than many other metals that are considered to be likely prebiotic catalysts. Nevertheless lead is the most abundant element in the solar spectrum for elements above atomic number 56 and it might be even more abundant than this in the Earth's crust. Indeed lead is a component of numerous minerals, for example, galena (PbS), boulangerite ($Pb_5Sb_4S_{11}$), bournonite ($PbCuSbS_3$), cerussite ($PbCO_3$), anglesite ($PbSO_4$), pyromorphite ($Pb_5(PO_4)_3Cl$), mimetite ($Pb_5(AsO_4)_3Cl$), and vanadite $Pb_5(VO_4)_3Cl$. So whereas lead is not as abundant as metals like Mg^{2+}, Ca^{2+} and Fe^{2+}, it should be found in numerous locales.

We scanned the literature to see if lead had been used in any other prebiotic studies. Sawai described lead-catalyzed non-template assisted oligomerization of adenosine 5'-phosphorimidazolide (Sawai, 1976). Following this Orgel and his colleagues observed that plumbous ion catalyzes polyA and polyG synthesis on complementary polynucleotide templates (Lohrmann and Orgel, 1980; Sleeper and Orgel 1979). Possibly these observations were more significant than at first believed. There is also an extensive literature on the Pb^{2+} -catalyzed hydrolysis of RNA (Farkas, 1968).

Following our finding that many sugars and glycolaldehyde cycle intermediates can replace $\propto$-hydroxyacetophenone we have used dihydroxyacetone (DHA) routinely as the catalyst in most of our experiments. The use of DHA is arbitrary as glycolaldehyde or other cycle intermediates work just as well. Our standard system for the synthesis of the aldopentoses now contains 50 mg of magnesium hydroxide, 0.4 mg of DHA, 7 mg of lead nitrate and variable amounts of formaldehyde in 0.5 mL. The concentrations of each of these components has been studied as has the temperature and time of reaction. Reactions as usual were monitored by the spot test and thin layer chromatography using aniline hydrogen phthalate stain (see Experimental Details). The study of the time course for the reaction under optimal conditions at 75 °C is shown in Figure 2. At this temperature and 2.8% formaldehyde the reaction is complete in about 150 min. At 90 min ribose and arabinose are beginning to appear. In the lower part of the chromatogram the region con-

Table II
Approximate time for optimum yield of aldopentoses as a function of temperature

Time (hr)	Temperature (°C)
150	35
46	45
21	55
4.5	67
3.0	75
0.4	90

taining lyxose and xylose is partially obscured by a broad brown smear probably due to hexoses. This smear is not present in samples incubated for 150 min or longer. There is remarkably little in the pattern above the aldopentoses which is the region where C3 and C4 glycolaldehyde cycle intermediates would be expected to appear. Except for glycolaldehyde, which is not visible when following our staining procedure, this negative result indicates that most of the glycolaldehyde cycle intermediates must be present at quite low concentrations in the lead-magnesium hydroxide system. More studies on the course of the reaction are needed.

The formose reaction was examined over a broad range of temperatures from 35 to 90 °C. Over this range of temperatures the rate of the reaction appears to double for every 7.5 °C rise in temperature (Table II). Preliminary indications are that the optimum temperature for aldopentose synthesis is somewhere between 55 and 75 °C. Most of our experiments have been done at 67 °C. Over the formaldehyde concentration range of 0.9 to 4.5% there is a steady rise in the time required to achieve optimum levels of aldopentoses.

The chromatogram in Figure 2 was overexposed so that all of the stainable reaction products could be seen. At a shorter exposure time one gets a better idea of the relative rate of appearance of the four aldopentoses (Figure 3). Invariably ribose is the first aldopentose to appear. This is followed by arabinose and finally by the other two aldopentoses. Lyxose is usually present in the smallest amounts. In time the amount of arabinose exceeds the amount of ribose. The possible significance of these kinetic observations is discussed in the next section.

4.1. Plumbous Ion Catalyzes the Interconversion of the Aldopentoses

In magnesium hydroxide without lead we observed that arabinose and ribose slowly interconvert. As this reaction progresses for several days it approaches a point where the arabinose is favored over the ribose by a ratio of about 3:1. We suspect that this reflects the equilibrium between the two sugars. Not observed in magnesium hydroxide suspensions was any conversion of ribose or arabinose into the other two aldopentoses.

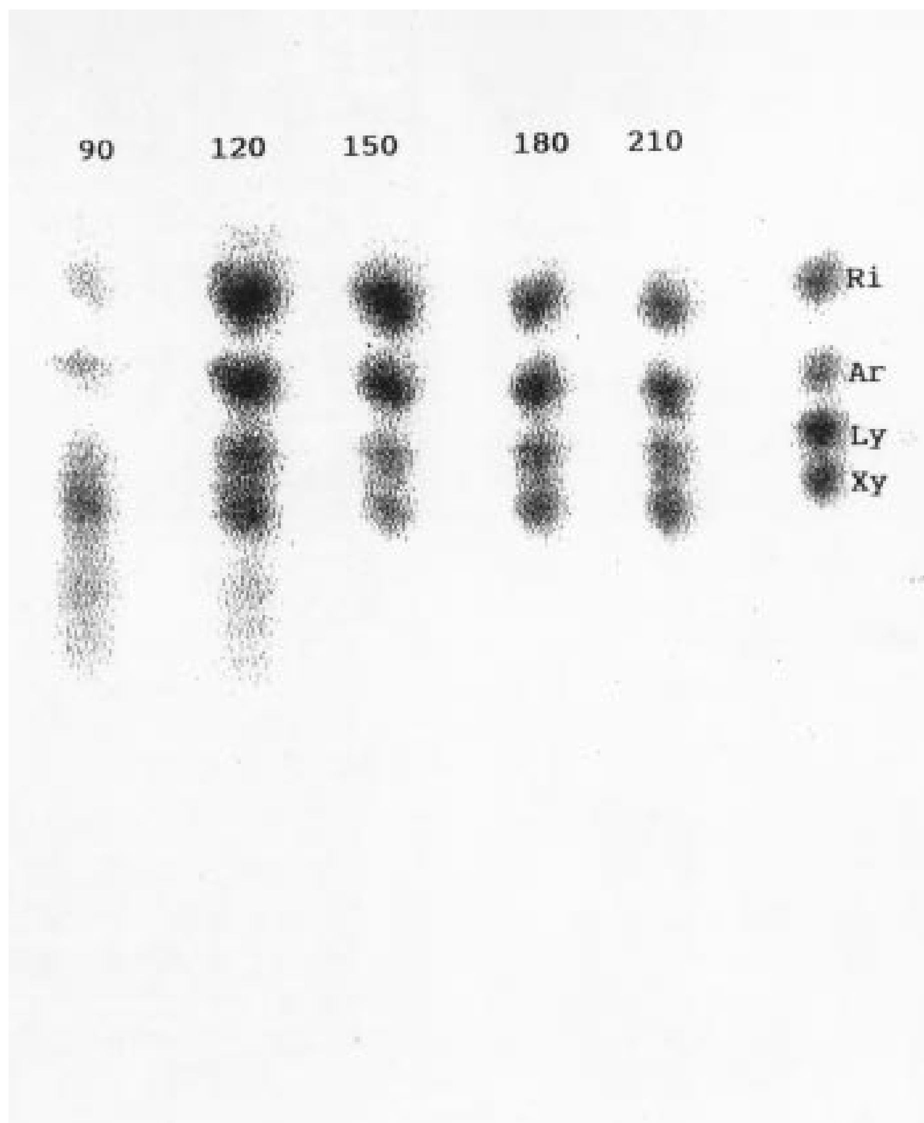


Figure 2. A time study for the standard incubation mixture containing 2.8% formaldehyde. In addition to formaldehyde the reaction mixture contained 50 mg magnesium hydroxide, 0.4 mg of DHA and 7 mg of lead nitrate in 0.5 mL. Reaction was carried out at 75 °C for the specified time (in minutes). Then an aliquot (from left to right 5.5λ, 7.0λ, 5.2λ, 5.1λ, and 5.0λ) was plated on thin layer cellulose for chromatography. Chromatography and staining procedures are described in Experimental Details The photograph was intentionally overexposed to permit viewing of even the faintest bands. A standard solution containing equimolar amounts of the four aldopentoses is shown at the far right.

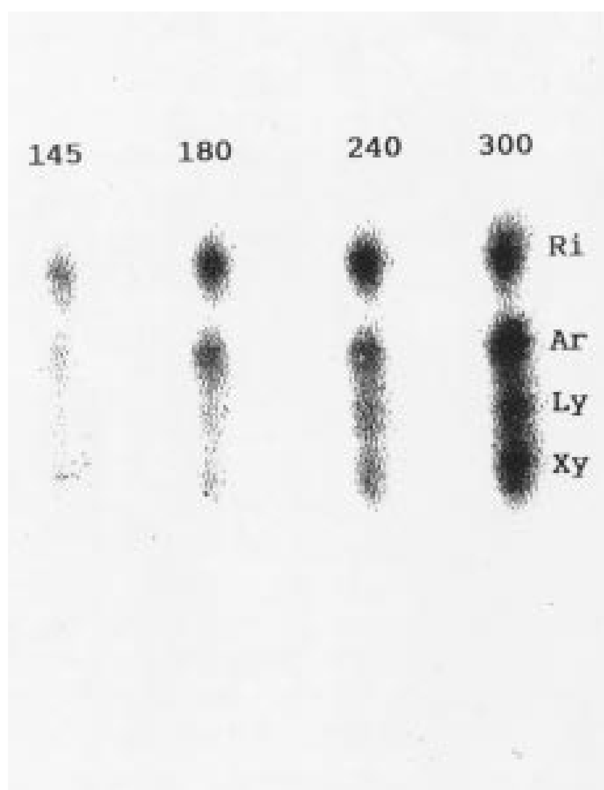


Figure 3. A time course for the standard incubation mixture containing 2.8% formaldehyde. In addition to formaldehyde the reaction mixture contained 50 mg magnesium hydroxide, 0.4 mg of DHA and 7 mg of lead nitrate in 0.5 mL. Reaction was carried out at 67 °C for the times specified. Then a 5λ aliquot was plated on thin layer cellulose. The remaining conditions were the same as in Figure 2 except that the photography of the originally stained chromatogram was lightly exposed to accentuate the differences in the relative amounts of the four aldopentoses at different stages after initiating the incubation. At 145 min as the aldopentoses are just beginning to show up, it can be seen that ribose dominates the pattern. At 180 min both ribose and arabinose are well represented. At 240 and 300 min the other two aldopentoses are more apparent.

In the presence of the lead-containing system we found that when any one of the aldopentoses was incubated (in the absence of formaldehyde or DHA catalyst) it converts readily into a mixture containing all four aldopentoses (Figure 4). In the incubation of ribose (column 4 of Figure 4) it should be noted that there is more arabinose than ribose and lyxose is underrepresented. A kinetic study shows that arabinose is the first interconversion product observed when starting with ribose; xylose and lyxose follow. This result is remarkably similar to what is observed routinely when we start with formaldehyde and incubate for up to 5 hr at 67 °C. Reconsideration of the results of Figure 3 in the light of these interconversion results is consistent with the notion that ribose is the main if not the only sugar

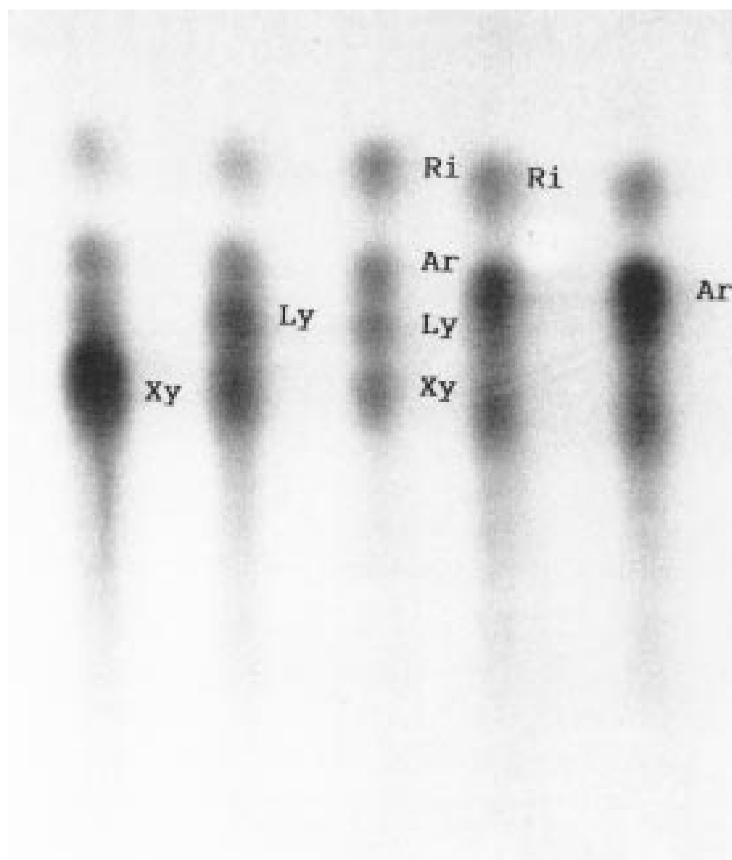


Figure 4. Interconversion of the aldopentoses. Four separate incubations were carried out in parallel. Each one initially contained only one of the four aldopentoses as indicated by the labeling of all except the 3rd column which was a standard containing equal amounts of the four aldopentoses. The incubations were done under standard conditions except that each mixture contained one aldopentose but no formaldehyde. The incubations were done at 67 °C for 7 hr. Further processing of the chromatograms is described in Experimental Details. Of the four chromatographic profiles the one that contained only ribose at the start resembles most closely the pattern seen in a conventional synthesis reaction where one starts with formaldehyde.

synthesized directly, the other sugars arising as interconversion products. Further work is necessary to reach a firm conclusion on this issue.

Interconversion of aldopentoses that differ in configuration at C2, like arabinose and ribose, is a well-known phenomenon that is believed to involve an enediol intermediate. In some of the results shown in Figure 4 the observed interconversions must involve changes in the configuration at C3. There are numerous possibilities for how this might be occurring in the presence of lead, but no concrete evidence for the precise mechanism.

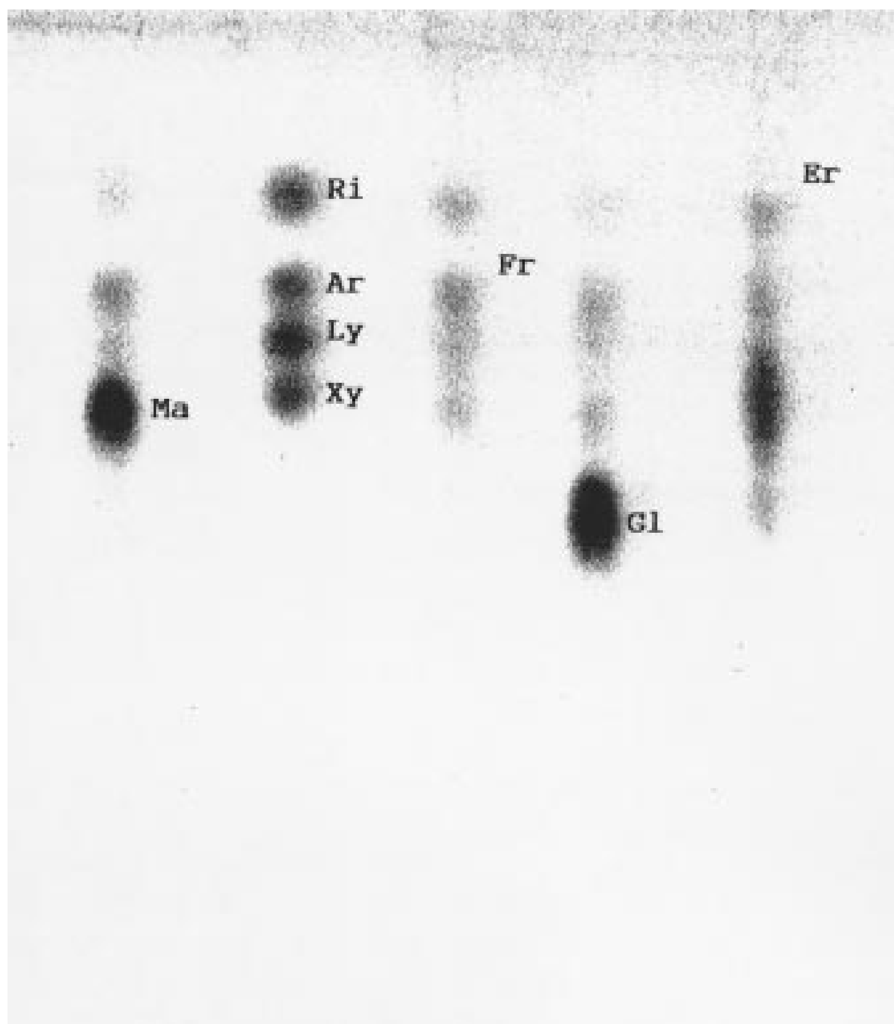


Figure 5. Synthesis of aldopentoses from mannose, fructose, glucose and erythrose. Incubation of each of these sugars was done as in Figure 4 except that the incubation time was 5 hr. After incubation greenish brown spots indicate the locations of the remaining mannose (Ma) and glucose (Gl). No fructose (Fr) is visible as a residue in the middle column 3 where one starts with fructose but fructose stains very poorly. The label Fr is placed next to column 3 where fructose would be expected to run. In column 5, the product of the incubation mixture initially containing erythrose, there is no greenish brown spot in the region where erythrose would be expected to run (Er). Rather there is a greenish brown smear in the region of xylose and glucose which probably comprises a mixture of hexoses. The remaining spots in all of the columns are red as would be expected for aldopentoses. In the aldopentose products derived from mannose the arabinose spot is strongest. The lyxose and ribose spots are very faint and any xylose that may be present is obscured by the strong overlapping mannose spot. In the middle (3rd) column all aldopentoses are visible; lyxose is the faintest and the other three are approximately equal in intensity. In the fourth column (glucose products) lyxose is very faint. The most visible spots are arabinose and xylose. In the 5th column containing the products derived from erythrose the ribose and arabinose spots are clearly visible. Because of the greenish-brown smear the lyxose and xylose spots are beyond detection.

5. Plumbous Ion Catalyzes Aldopentose Synthesis from Tetroses and Hexoses

In addition to the interconversions of aldopentoses that are catalyzed by lead we were quite surprised to see that small amounts of the aldopentoses were produced when the tetrose erythrose or the hexoses, mannose, glucose or fructose were incubated under the same conditions (Figure 5). Once again we could speculate on how this occurs in the complete absence of formaldehyde, but suffice it to say that in this case carbon-carbon cleavages would be required in places where we would not have expected them to occur. This observation could be of some importance because it reveals yet another possible route whereby existing carbohydrates in the prebiotic world could be converted to ribose. It should be emphasized that these observations on the conversion of tetroses and hexoses are very preliminary and that no attempt has been made to optimize conditions for these conversions.

6. A Significant Quantity of the Formaldehyde is Not Accounted for In Our Experiments

Under the most favorable conditions found thus far about 30% of the starting formaldehyde is converted into one of the four aldopentoses. This leaves 70% of the formaldehyde to be accounted for. Can the remaining formaldehyde be undergoing alternative reactions or does a fraction of the aldopentoses undergo further reactions after formation? The Cannizzaro reaction in which aldehydes disproportionate into acids and alcohols is a nagging concern when working with aldehydes under high pH conditions. This reaction could be a problem at the level of formaldehyde or at the level of the aldopentoses. Incubation of pure aldopentoses under the same conditions of temperature and time used for the formaldehyde conversions results in a loss of about 50% of the sugars. About a third of this ‘lost’ sugar is released into solution from the magnesium-lead hydroxide suspension when the insoluble mineral is extracted with a 0.1 m EDTA solution. This suggests that an aggregated complex of sugar and plumbous ion accounts for some of the ‘missing’ sugar. We are exploring the possibility that by working at even lower pHs we may be able to increase the yields of ribose.

Another possibility for improving the recoveries of ribose might be to trap the ribose soon after its formation. If ribose is the primary product in the lead-catalyzed synthesis as we suspect, this strategy could be quite effective in optimizing yields of ribonucleosides.

In conclusion it is clear that while we have not solved all of the problems associated with the prebiotic synthesis of ribose, there are now reasons for optimism.

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