

Chapter 2

The Role of Silicates in the Synthesis of Sugars Under Prebiotic Conditions

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2.1 Sugars and Life

Before life, there must have been the molecules of life—amino acids for proteins, heterocyclic bases such as adenine for nucleic acids, and sugars for polysaccharides. In 1953, Miller demonstrated that amino acids could be produced from mixtures of water, carbon monoxide, ammonia, and hydrogen with the help of an electric spark [1]. Oró and Kimball were able to prepare the nucleotide base adenine from hydrogen cyanide and ammonia [2]. Many advances on these experiments have been made in the subsequent decades. In 1967 Gabel and Ponnampuruma reported experiments indicating that simple sugars could be prepared from formaldehyde, based on the Butlerov reaction [3]. Breslow in 1959 already had provided an aldol mechanism for this reaction [4]. Reid and Orgel, however, in a companion paper to that of Gabel and Ponnampuruma, concluded that the Butlerov reaction was impractical because the sugars decompose and “some method of stabilizing the sugars is essential” [5]. The authors respectively used aluminosilicates and a mixture of carbonate and hydroxyapatite, but obtained yields under 5 % of unstable sugars.

2.2 The Formose Reaction

The Butlerov reaction (Fig. 2.1) had come to be known as the formose reaction, as it converts formaldehyde to sugars (-oses). Our expansion of the Breslow mechanism is as follows.

Formaldehyde (C1) alone is incapable of undergoing an aldol reaction, since it lacks an acidic proton alpha to the carbonyl group. The two-carbon sugar glycolaldehyde (C2) is the smallest such system with an active hydrogen, so Breslow hypothesized it must be present in catalytic amounts. The product of the aldol condensation

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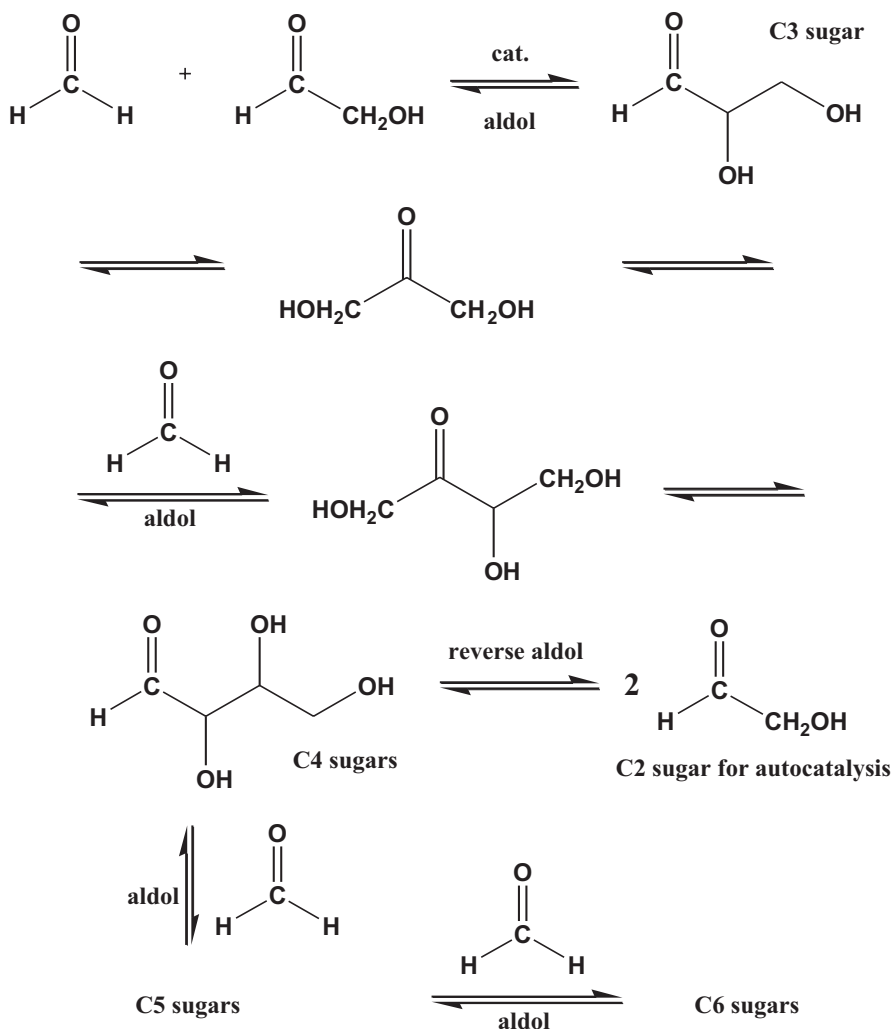


Fig. 2.1 The formose reaction

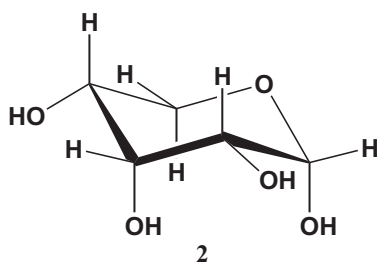
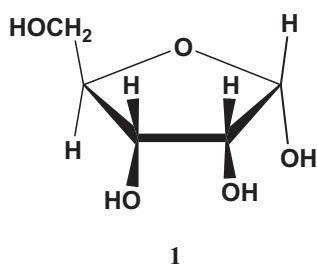
of C1 and C2 is glyceraldehyde (C3). Isomerization of glyceraldehyde to its ketose isomer and condensation of the ketose with a second molecule of C1 gives a four-carbon ketose, which can isomerize to the C4 aldose. Reverse aldol condensation of the C4 aldose delivers two molecules of the original catalyst, C2. Thus the reaction produces its own catalyst, i.e., it is autocatalytic. Following an induction period as the catalyst builds up, such a reaction continues exponentially. The C4 product also could add another molecule of formaldehyde to produce C5 products, which could condense again to form C6 products. Hence the products are multifarious and unstable, but are formed quickly and efficiently.

2.3 The Interaction(s) of Carbohydrates with Silicates

Our focus in this article is on carbohydrates, which constitute the most abundant organic materials in the biosphere, and in particular their interactions with silicates, the most abundant materials in the lithosphere. Although no naturally occurring organosilicon molecule has ever been isolated, such molecules are implied by the presence of silica as supporting tissue in sponges, diatoms, radiolarians, and some higher plants. Such biostructures imply a robust silicate biochemistry, which is largely unknown at present. Progress has been made primarily in understanding the proteins, called silicateins, which are responsible for biouptake of aqueous silicate and production of ordered silica nanostructures [6, 7].

The seminal experiments in identifying interactions between the organic world of carbohydrates and the inorganic world of silicates were reported by the groups of Kinrade and of Klüfers in 1999 [8, 9–11]. Kinrade [8] reported that aqueous sodium silicate reacts with certain glycitols (linear polyols with a single hydroxy group on each carbon, e.g., $\text{HOCH}_2\text{CHOHCHOHCH}_2\text{OH}$), as well as glyconic acids (open chain sugars in which the aldehyde has been oxidized to the carboxylic acid, e.g., $\text{HOCH}_2\text{CHOHCHOHCO}_2\text{H}$). They used ^{29}Si NMR spectroscopy to confirm that the glycitols and glyconic acids are complexed with pentavalent (negatively charged) silicon. Klüfers [10] inferred that the complexes between silicate and glycitols comprise five-membered diolato rings. They confirmed the five-membered structures with X-ray analysis of the glycitols of mannose, xylose, and threose, [11] which proved to form 3:1 hexacoordinated diolato complexes with silicate.

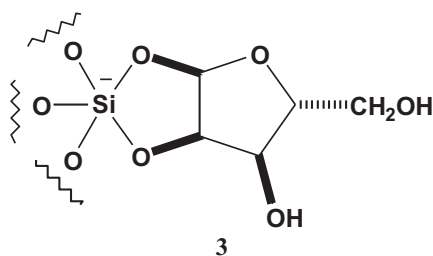
In contrast to glycitols and glyconic acids, sugars (glycoses) exist as cyclic structures. Thus the linear form, e.g., $\text{HOCH}_2\text{CHOHCHOHCHO}$, is converted to a ring form, which can have either five members (furanose) or six members (pyranose), as illustrated in **1** and **2** for ribose.



Four-carbon sugars can exist only as furanoses, and smaller sugars cannot exist in the cyclic forms. Sugars with five or more carbons exist in both furanose and pyranose forms. Like the glycitols and glyconic acids, sugars have strings of hydroxy groups, which conceivably could complex with silicate. Given the stereochemical restrictions that Kinrade and Klüfers had found for the glycitols and glyconic acids, it was

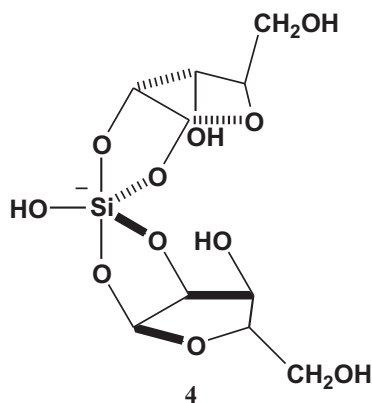
likely that sugars would have similar or stronger restrictions, as the rings in which they exist are conformationally more restricted. In an early report, Kinrade and co-workers [12] found that ribose forms a complex with silicate.

Lambert and co-workers reported the first comprehensive examination of sugar silicates in 2004 [13]. They examined all four aldopentoses, seven of the eight aldohexoses, all four ketohexoses, several disaccharides, and the 1-*O*-methyl glycosides of several sugars. Of these, the monosaccharides ribose, xylose, lyxose, talose, psicose, fructose, sorbose, and tagotose, and the disaccharides lactulose, maltulose, and palatinose successfully formed sugar silicate complexes, as signified by observation of ^{29}Si signals in the pentacoordinate region. Notable failures include the monosaccharides arabinose, glucose, mannose, and galactose, the disaccharides sucrose and turanose, and all the 1-*O*-methyl glycosides. For a positive result, three structural factors had to be operative: (1) The anomeric oxygen must be free, that is without *O*-methyl glycosidation. The anomeric hydroxy hydrogen is the most acidic in the molecule and probably initiates the reaction. (2) The carbon adjacent to the anomeric carbon must bear a hydroxy group *cis* to the anomeric hydroxyl. By a chelating effect, silicate complexes with two of the sugar hydroxyls, and *cis*-diols are the most amenable. (3) These elements must reside in a furanose, not a pyranose, ring. Apparently puckering of the six-membered ring sterically inhibits formation of the five-membered oxalato ring. The resulting complex would take the form **3** for D-ribose.



The common sugars glucose and mannose lack significant amounts of the key furanose form. All five disaccharides contain furanose rings, but in sucrose the two anomeric carbons are bonded through a glycosidic linkage, so the key anomeric hydroxyl is blocked. In tagotose the 2 hydroxyl is linked to the second sugar ring, so the molecule lacks a *cis* diol structure that includes a furanoid anomeric hydroxyl. Since such a structure is available in lactulose, maltulose, and palatinose, those three disaccharides form sugar silicates.

The final element of the structure of the complexes involved the question of stoichiometry, which for structure **3** could be a 1:1 combination of sugar and silicate in which the remaining three linkages to silicon are hydroxyls, or a 2:1 sugar/silicate combination in which one of the linkages is hydroxyl and the other two are a second sugar. Electrospray mass spectral examination of the complexes indicated that all are 2:1 complexes, such as **4** for ribose [13].



Such structures can exist as several stereoisomers. The illustrated structure for ribose silicate has the two ribose rings *syn* to each other and pointing away from the remaining silicate hydroxyl. The two groups could be *syn* to each and pointing towards the silicate hydroxyl, or they could be *anti* to each other with one pointing towards and the other away from the silicate hydroxyl. There also could be regioisomers, as the two sugar rings could be arranged with a different relationship of the C1 and C2 bonds, for example. The ^{29}Si spectra of sugar silicates exhibit multiple peaks (usually three to five), representing the multiple isomers. Unfortunately, these solutions never yielded crystalline materials from which X-ray structures could be obtained. In 2005, Klüfers et al. obtained such structures in nonaqueous media, although with phenyl in place of the silicate hydroxyl, confirming all aspects of the structures, including furanose rings, *cis*-diol coordination, and 2:1 stoichiometry [14]. These experiments by Kinrade, Lambert, and Klüfers established a rich link between carbohydrates and silicates.

These reactions take place in highly basic medium, typically pH 10.5. Sugars are famously unstable in base, isomerizing from aldehydes to ketones, undergoing aldol condensations, and breaking apart in reverse aldols. The silicate complexes, however, are reasonably stable for hours to days under these highly basic conditions, without isomerization or decomposition. Silicate formation, moreover, is almost instantaneous even at room temperature. This distinction between sugars and sugar silicates under basic conditions has ramifications in the field of prebiotic chemistry. On the one hand, silicate formation could be a mechanism for sequestering sugars under extreme conditions, for example as found on comets lacking an atmosphere. The higher stability and lower volatility of sugar silicates could allow them to abide in space until they arrive at a planet with an atmosphere. Such conjectures are highly speculative. On the other hand, silicate formation could provide the stabilization mechanism that Reid and Orgel stated was necessary before the formose reaction could be considered practical for the prebiotic synthesis of oligosaccharides (“some method of stabilizing the sugars is essential”) [4].

Lambert and co-workers reported the realization of this possibility in what they termed the bottom-up synthesis of sugar silicates (in distinction to the direct reaction between, or top-down synthesis of, sugars with silicate) [15]. They compared various formose reactions either with sodium hydroxide as catalyst (classic formose conditions) or with sodium silicate as catalyst. They found that formaldehyde (C1) alone produces low yields under both conditions, as it lacks the α hydrogen to initiate the condensation. They studied the reactions of glycolaldehyde (C2) and glyceraldehyde (C3), either alone or mixed with the other or with C1. These sugars exist in the straight chain and other forms, but they do not have enough carbons to form a furanose ring. In the case of C3 alone, the reaction occurs with either catalyst to form C6 oligomers within seconds at room temperature. Under standard formose conditions, however, the oligomers decompose quickly, so that within 12 h little sugar product remains. When the same reaction is carried out with C3 in the presence of sodium silicate as catalyst, solely C6 products are formed, remaining almost unchanged for 12 h or more. Similar results occur with C2 alone. The reaction of C2 and C3 together is more complex, because it can proceed from simple dimerization to give C4 and C6, but also by the cross reaction to give C5. It appears that C5 products are the most abundant, and, again, the products are unstable in the presence of sodium hydroxide but robust when the catalyst is sodium silicate.

The possibility that silicate mediation can stabilize the products of the formose reaction may revive its role as the mode for prebiotic synthesis of sugars. Silicate minerals are widely available, although the basic conditions are less available in Nature. On earth, such conditions occur naturally under conditions of extreme evaporation and concentration, as occurs in the Dead Sea, the Great Salt Lake, and the lakes of the Atacama Desert of Chile [16]. A similar rationale had been proposed with borate minerals [17, 18]. Although borates may be kinetically more effective than silicates, their much lower availability makes them a less likely stabilizing agent under prebiotic conditions [19]. Moreover, Grew et al. have pointed out that the development of borate minerals in the Earth's crust may have occurred too late to be useful for prebiotic processes: "concentrations of B either on land or in the sea sufficient to play a role in ribose stabilization are thus unlikely" [20].

Addressing a different issue, Vázquez-Mayagoitia et al. carried out *ab initio* calculations at the B3LYP level on silicate complexes of the C5 sugars arabinose, lyxose, ribose, and xylose [21]. They studied five different stereochemical versions for each sugar, such as **4**. They found that the ribose silicates were more stable than the other sugar silicates, "to the extent that the least stable of these is even more stable than the most stable stereoisomer of the other 2:1 sugar-silicate complexes." They suggested that formose reactions in the presence of sodium silicate should form ribose products preferentially over the other C5 sugars.

2.4 Summary

In summary, polyhydroxy compounds readily form complexes with sodium silicate at room temperature. Stereochemical requirements limit the reaction to sugars that exist in the furanoid form, have an unsubstituted anomeric hydroxy group, and

have a *syn* hydroxyl adjacent to the anomeric hydroxyl. Ribose is one such sugar with the appropriate stereochemistry. Once in the silicate form, sugars are far more stable under basic conditions. This observation suggests a sequestering mechanism for sugars under extreme conditions. It also suggests a mechanism for stabilizing sugars as they are formed during the formose reaction. This aldol reaction of small sugars had been discarded as a process for the prebiotic synthesis of sugars because of their rapid decomposition. Indeed, glyceraldehyde (C3) dimerizes to a stable solution of C6 sugar silicates in the presence of sodium silicate but dimerizes to an unstable solution in the presence of sodium hydroxide. Similarly in the presence of sodium silicate, glycolaldehyde (C2) leads to a stable solution of C4, and a mixture of C2 and C3 leads to a stable solution containing C5 as the primary product. Based on calculations ribose forms the most stable sugar silicate. Stabilization also could be realized with borate salts, but their role in the prebiotic environment has been questioned on geochemical grounds.

References

1. Miller SL (1953) *Science* 117:528
2. Oró J, Kimball AP (1961) *Arch Biochem Biophys* 94:217–227
3. Gabel NW, Ponnampertuma C (1967) *Nature* 216:453–455
4. Breslow R (1959) *Tetrahedron Lett* 1:22
5. Reid C, Orgel LE (1967) *Nature* 216:455
6. Cha J, Shimizu K, Zhou Y, Christiansen SC, Chmelka BF, Stucky GD, Morse DE (1999) *Proc Natl Acad Sci USA* 96:361–365
7. Kröger N, Lorenz S, Brunner E, Sumper M (2002) *Science* 298:584–586
8. Kinrade SD, Del Nin JW, Schach AS, Sloan TA, Wilson KL, Knight CTG (1999) *Science* 285:1542–1545
9. Kinrade SD, Hamilton RJ, Schach AS, Knight CTB (2001) *J Chem Soc Dalton Trans* 961–963
10. Benner K, Klüfers P, Schuhmacher J (1999) *Z Anorg Allg Chem* 625:541–543
11. Benner K, Klüfers P, Vogt M (2003) *Angew Chem Int Ed* 42:1058–1062
12. Kinrade SD, Deguns EW, Gillson A-ME, Knight CTG (2003) *J Chem Soc Dalton Trans* 3713–3716
13. Lambert JB, Lu G, Singer SR, Kolb VM (2004) *J Am Chem Soc* 126:9611–9625
14. Kästle X, Klüfers P, Kopp F, Schuhmacher J, Vogt M (2005) *Chem Eur J* 11:6326–6346
15. Lambert JB, Gurusamy-Thangavelu SA, Ma K (2010) *Science* 327:984–986
16. Stumm W, Morgan JJ (1996) *Aquatic Chemistry* 3rd edn. Wiley-Interscience, New York
17. Ricardo A, Carrigan MA, Olcott AN, Benner SA (2004) *Science* 303:196
18. Kim H-J, Benner SA (2010) *Science* 329:902–a
19. Lambert JB, Gurusamy-Thangavelu SA, Ma K (2010) *Science* 329:902–b
20. Grew ES, Bada JL, Hazen RM (2011) *Orig Life Evol Biosph* 41:307–316
21. Vázquez-Mayagoitia Á, Horton SR, Sumpter BG Šponer J, Šponer JE, Feuntes-Cabrera M (2011) *Astrobiology* 11:115–121

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