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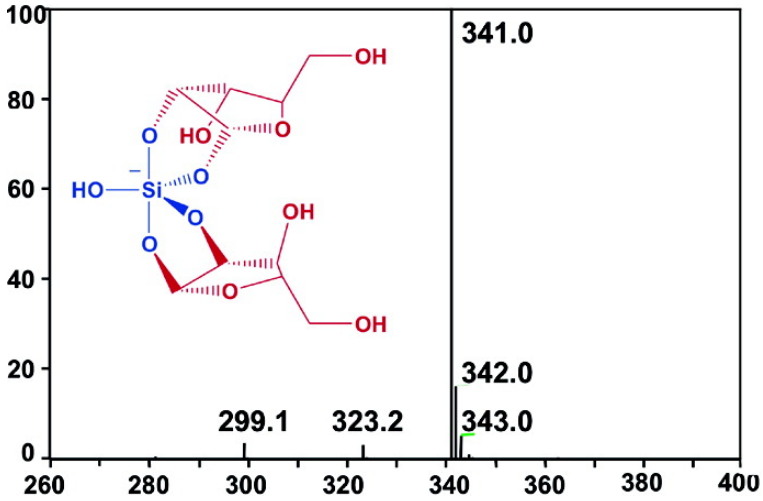

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Silicate Complexes of Sugars in Aqueous Solution

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Abstract: Certain sugars react readily with basic silicic acid to form soluble 2/1 (sugar/silicic acid) silicate complexes. Failure of monohydroxy compounds to give soluble products under these conditions indicates that the sugar silicates are chelates: five-membered diolato rings. Only furanose forms react. Pyranose sugars are stable under these conditions. Because all glycosides fail to react with silicic acid under these conditions, reaction appears to involve the anomeric position (C1 in aldoses, C2 in ketoses), which has a more acidic hydroxy group. Reaction is completed only when the anomeric hydroxy group is cis to an adjacent hydroxy group. The appropriate furanose form must have sufficient natural abundance and solubility to provide an observable product, as measured by ^{29}Si and ^{13}C NMR spectroscopy. These structural and practical constraints rationalize the successful reaction of the monosaccharides ribose, xylose, lyxose, talose, psicose, fructose, sorbose, and tagatose and the disaccharides lactulose, maltulose, and palatinose. Glucose, mannose, galactose, and sucrose, among others, failed to form complexes. This high selectivity for formation of sugar silicates may have ramifications in prebiotic chemistry.

Introduction

Silicon is the second most abundant element in the earth's lithosphere, after oxygen, and is found largely in the form of solid silicates and aluminosilicates. Nonetheless, and despite being located just below carbon in the periodic table, silicon has been found to have very little involvement in life processes.[1,2] Carbohydrates are the most abundant organic material in the biosphere, largely as cellulose, so that there ought to be considerable opportunity for silicates and carbohydrates to interact. What biochemistry there is of silicon, however, is related primarily to silica uptake by marine organisms and some plants. Considerable progress has been made in understanding proteins that control the biological production of silica nanostructures.[3] The critical connection between silicates and carbohydrates, however, has not been fully established.

Important experiments have been performed on certain sugar derivatives, such as the glycitols (polyhydroxy compounds, in which the sugar aldehyde function is reduced to the alcohol) and glyconic acids (in which the aldehyde function is oxidized to the carboxylic acid group). Kinrade and co-workers found that aqueous silicate solutions react with straight-chain polyhydroxy compounds (glycitols such as xylitol, threitol, and sorbitol).[4] Their evidence was based entirely on ^{13}C and ^{29}Si NMR experiments. In these strongly basic solutions, they found ^{29}Si signals that corresponded to pentacoordination and hexacoordination, depending on the pH. They observed several peaks within the coordination ranges, indicating that several high-coordination forms existed with sugars attached to silicon presumably via oxygen chelates. The same group found NMR evidence for similar complexes between sugars and glyconic acids under less basic conditions.[5] Klüfers and co-workers suggested that the connection between the glycitols and silicic acid takes the form of a five-membered diolato ring.[6] They later supported the suggestion with X-ray structures of the mannitolato, xylitolato, and threitolato complexes.[7] These are 3/1 complexes with hexacoordinate silicon. The glycitol hydroxy groups that are not covalently bonded to silicon provide important hydrogen-bonding interactions. The authors observed that the diolato ring forms with five-membered (furanoid) rather than six-membered (pyranoid) rings. The necessary O−C−C−O dihedral angle within the sugar derivative must be close to 0° to form the silicon-diolato chelate ring, an angle more easily achieved by furanoid than pyranoid rings.[7] There has been a report of the reaction of silicic acid with ribose.[8]

To date, all reported observations except for that with ribose have been made on either the polyhydroxy compounds (glycitols) or the monocarboxylic acids (glyconic acids).[4−8] Far more important would be the possible reactions of carbohydrates

† Northwestern University.
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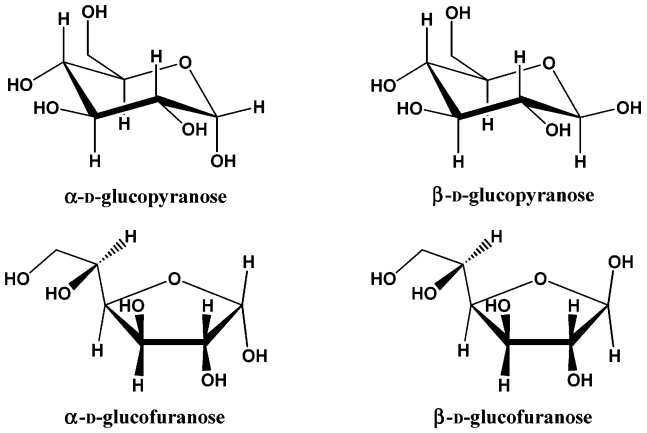
(1) Bond, R.; McAuliffe J. C. *Curr. Chem.* **2003**, *56*, 7−11.
(2) Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*; Wiley: New York, 2000.
(3) Cha, J.; Shimizu, K.; Zhou, Y.; Christiansen, S. C.; Chmelka, B. F.; Stucky, G. D.; Morse, D. E. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 361−365. Kröger, N.; Lorenz, S.; Brunner, E.; Sumper, M. *Science* **2002**, *298*, 584−586.
(4) Kinrade, S. D.; Del Nin, J. W.; Schach, A. S.; Sloan, T. A.; Wilson, K. L.; Knight, C. T. G. *Science* **1999**, *285*, 1542−1545.
(5) Kinrade, S. D.; Hamilton, R. J.; Schach, A. S.; Knight, C. T. B. *J. Chem. Soc., Dalton Trans.* **2001**, 961−963.
(6) Benner, K.; Klüfers, P.; Schuhmacher, J. *Z. Inorg. Allg. Chem.* **1999**, *625*, 541−543.
(7) Benner, K.; Klüfers, P.; Vogt, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 1058−1062.
(8) Kinrade, S. D.; Deguns, E. W.; Gillson, A.-M. E.; Knight, C. T. G. *J. Chem. Soc., Dalton Trans.* **2003**, 3713−3716.

Scheme 1



themselves. Whereas glycitols and glyconic acids exist primarily as open-chain compounds, carbohydrates exist predominantly as rings with either five members (aldofuranoses, ketofuranoses) or six members (aldopyranoses, ketopyranoses). We report herein evidence for widespread reactions of aldoses and ketoses with silicic acid.

Results

The experiment involved dissolution of the sugar in D_2O and addition of an aqueous sodium silicate solution of precisely defined stoichiometry. The pH of these solutions was 11.7.[9] We examined all four aldopentoses (ribose, arabinose, xylose, and lyxose), seven of the eight aldohexoses (allose, altrose, glucose, mannose, gulose, galactose, and talose), all four ketohexoses (psicose, fructose, sorbose, and tagatose), several disaccharides (sucrose, lactulose, maltulose, palatinose, and turanose), 2-deoxyribose, fucose (6-deoxygalactose), the 1-*O*-methylglycosides of fructose, ribose, and xylose, and some nonsugar model compounds. The purpose of this survey was to determine the structural and stereochemical basis for reaction of sugars with silicic acid.

Sugars usually are complex mixtures of five-membered and six-membered rings, in which the C1 stereochemistry can be either α or β. Scheme 1 illustrates the four forms for D-glucose, which in general will be abbreviated αP, βP, αF, and βF. These forms are in slow equilibrium with each other and with the open-chain form in aqueous solution. The percentages have been measured for neutral pH and are collected in Table 1.[10] In all cases but one, the open-chain form is present at less than 1% and is ignored.

The sugar silicate solutions were characterized initially by ^{29}Si NMR spectroscopy. Although previous workers used silicic acid containing enriched ^{29}Si, we used natural abundance materials to examine a large number of substrates. As a result, overnight runs were required for acquisition of data. When reaction occurred to form a soluble product, one or more new peaks were observed in the ^{29}Si NMR spectrum. Table 2 contains the ^{29}Si resonances observed in reactions with various sugars, as well as for control samples. Omissions from the table imply that no signals were observed. By way of example, Figure 1a provides the ^{29}Si spectrum of D-ribose silicate, Figure 2a provides that of D-fructose silicate, Figure 3 provides that of several disaccharide silicates, and Figure 4 provides that of 1,4-anhydroerythritol silicate.

The ^{1}H spectra generally were broad and uninformative. The ^{13}C spectra, however, were extremely useful in understanding the stability of the solutions and the sites of coordination. For most systems, they were recorded under three conditions: (1) at ambient pH (simple dissolution in D_2O) in the absence of silicic acid, (2) at pH ca. 12 in the absence of silicic acid (in D_2O with the pH adjusted), and (3) dissolved in silicic acid at pH 11.7. Comparison of the first two solutions provides the effect of pH alone. Comparison of the last two solutions provides the effect of coordination with silicic acid alone. Individual ^{13}C resonance positions are given in the Experimental Section for solutions containing silicic acid. Figure 5 contains all three spectra for D-ribose, Figure 6 contains those for D-talose, Figure

Table 1. Percentage of Ring-Size and Anomeric Sugar Isomers

	αP	βP	αF	βF
ribose[a]	21.5	58.5	6.5	13.5
arabinose[a]	60	35.5	2.5	2
xylose[a]	36.5	63	<1	<1
lyxose[a]	70	28	1.5	0.5
allose[a]	14	77.5	3.5	5
altrose[a]	27	43	17	13
glucose[a]	38.0	62.0	b	0.1
mannose[a]	64.9	34.2	0.6	0.3
gulose[a]	16	81	b	3
galactose[a]	30	64	2.5	3.5
talose[a]	42	29	16	13
psicose[a]	22	24	39	15
fructose[a]	2.5	65	6.5	25
sorbose[a]	93	2	4	1
tagatose[a]	71	18	2.5	7.5
erythrose[c,d]	b	b	25.5	62.6
lactulose[e,f]	b	61.5	7.6	29.3
maltulose[e,f]	b	64.0	12.1	22.4
palatinose[g]	b	b	28.6	71.4
sucrose	b	b	b	100
turanose[h]	<4	39	20	41

[a] Reference 10. [b] This form is impossible, inaccessible, or undetected. [c] Snyder, J. R.; Johnston, E. R.; Serianni, A. S. *J. Am. Chem. Soc.* **1989**, *111*, 2681−2687. [d] The open-chain form also is present. [e] The keto form also is present at equilibrium. [f] Pfeffer, P. E.; Hicks, K. B. *Carbohydr. Res.* **1982**, *102*, 11−22. [g] Jarrell, H. C.; Conway, T. F.; Moyna, P.; Smith, I. C. P. *Carbohydr. Res.* **1979**, *76*, 45−57. [h] Angyal, S. J. *Adv. Carbohydr. Chem. Biochem.* **1984**, *42*, 15−68.

Table 2. ^{29}Si Resonance Positions (δ) for Solutions of Sugars Dissolved in Highly Basic Silicic Acid

sodium silicate	−71.9, −80.0, −88.1, −97.0, −106.0 (broad)
D-ribose	−99.0, −99.4, −99.5
D-xylose[a]	−98.3, −98.5, −98.8
D-lyxose[a]	−99.8, −100.1
D-talose	−100.9 (br)
D-psicose	−100.0, −100.4, −139.8, −140.4, −141.0
D-fructose	−100.3, −100.6, −100.9, −101.2, −101.6
L-sorbose	−98.7, −99.3, −99.6
D-tagatose	−137.5, −138.3, −138.8, −139.1
lactulose	−98.1, −99.0, −99.4
maltulose	−100.3, −100.9, −101.2, −101.5
palatinose	−100.8 (broad), 101.4 (broad)
1,4-anhydroerythritol[a]	−97.5, −98.3, −98.5

[a] These solutions also contained resonances from unreacted sodium silicate.

(9) This solution provides the lowest pH (11.7) at which reactions occur successfully with sugars. Although gelling occurs sometimes (but not always, as with sucrose), high-resolution spectra of the materials in solution still may be obtained. Solution normally used by other workers[4−8] has considerably higher basicity (pH 12.7−13.4).

(10) Collins, P. M.; Ferrier, R. J. *Monosaccharides*; Wiley: Chichester, 1995; p 41. Lichtenhaler, F. W.; Ronninger, S. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1489−1497.

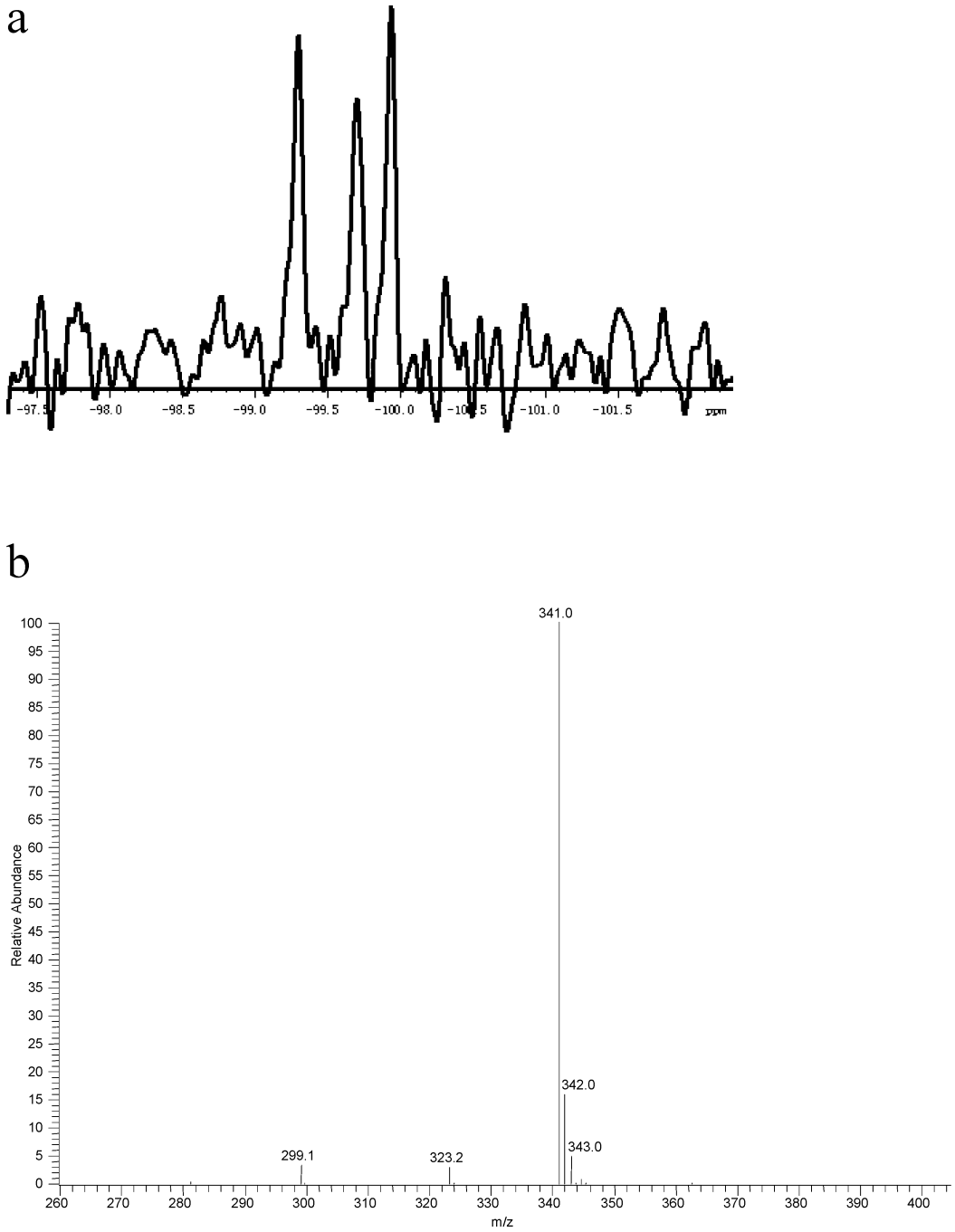


Figure 1. (a) The 79 MHz ^{29}Si NMR spectrum of D-ribose silicate. (b) The ESI-MS of D-ribose silicate.

7 contains those for D-fructose, and Figure 8 contains those for D-palatinose.

The solutions that produced new, observable ^{29}Si resonances were considered to contain stable sugar silicates, so they also were examined by electrospray mass spectrometry. Figure 1b illustrates the spectrum for D-ribose, and Figure 2b illustrates that for D-fructose.

Discussion

Coordination Number of Silicon. The coordination number may be discerned from the resonance position in the ^{29}Si spectrum. For materials containing a single silicon atom bonded only to oxygen, resonances of tetracoordinated Si (**1**) start around δ −70 and continue to lower frequency (depending on O substitution), those of pentacoordinated (**2**) start around δ −100, and those of hexacoordinated (**3**) start around δ −140.

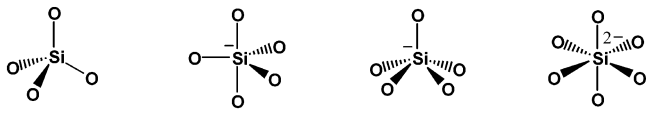


Table 2 shows that almost all of the sugar silicates fall into the range for pentacoordinated silicate. Geometries of either the trigonal bipyramid (**2a**) or the tetragonal pyramid (**2b**) are implied. No resonances of tetracoordinated silicate were observed, except for unreacted silicic acid in the cases of xylose

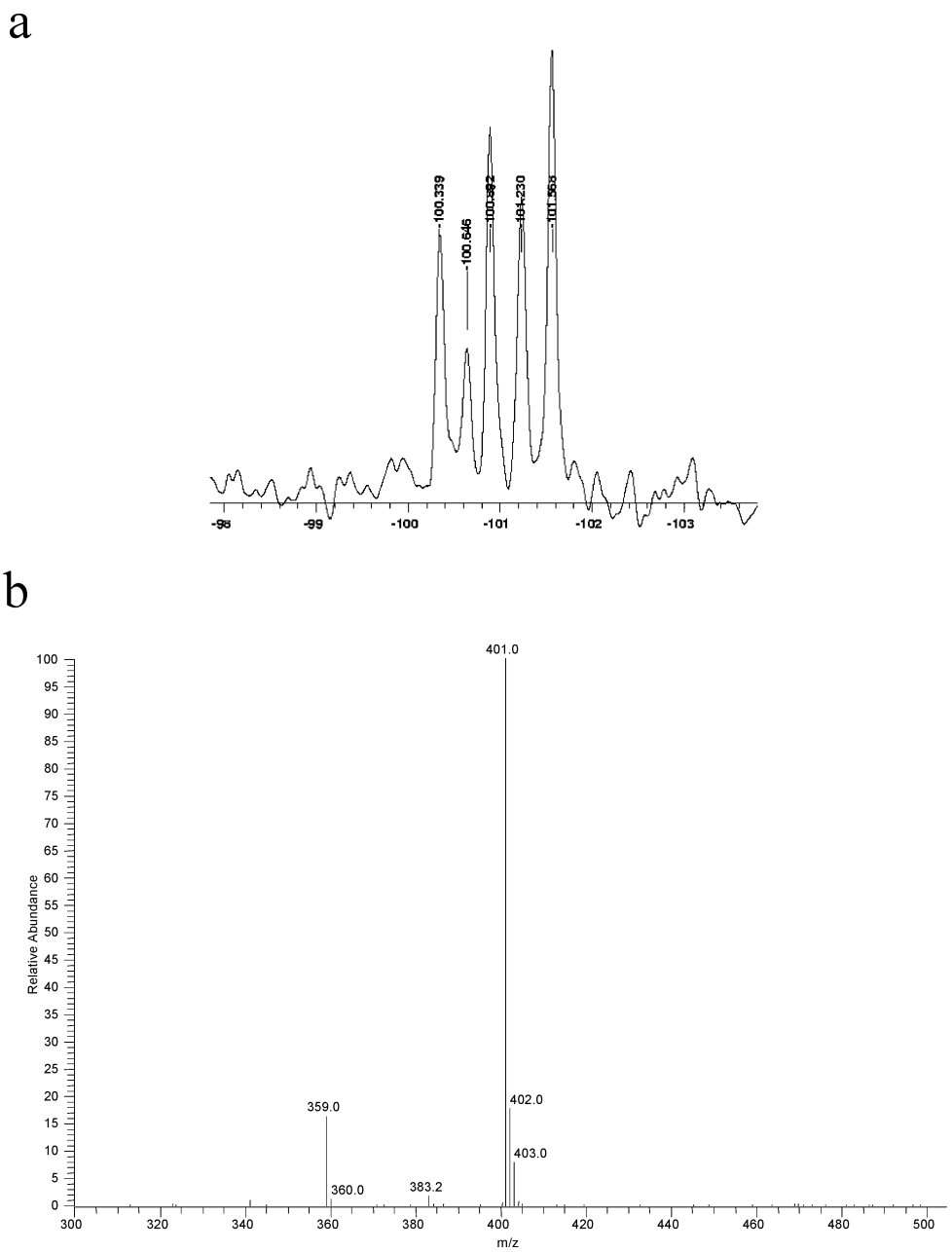


Figure 2. (a) The 79 MHz ^{29}Si NMR spectrum of D-fructose silicate. (b) The ESI-MS of D-fructose silicate.

and lyxose. The low-frequency resonances of the ketohexoses psicose and tagatose suggest hexacoordination in these cases.

Oligomerization. Resonances of tetracoordinated silicates also provide information about the number of additional silicons bonded through oxygen to the resonating silicon. If there are no other silicon atoms, the structure is monomeric silicic acid, $Si(OH)_4$ (or derivatives with carbon attached, SiOC), and the resonance occurs in the previously quoted position, δ ca. −70. This structure is termed Q^0 and is illustrated by the peak at δ −71.9 (Table 2) for sodium silicate. If one oxygen is bonded to another Si (**Si**OSi), the structure is termed Q^1 and the resonance is shifted to lower frequency (more negative) by about 8 ppm, as illustrated by the peak at δ −80.0 for sodium silicate. Progressive substitution of Si leads to Q^2 [**Si**$(OSi)_2$], Q^3 [**Si**$(OSi)_3$], and Q^4 [**Si**$(OSi)_4$] structures, illustrated respectively by the peaks clustered at δ −88.1, −97.0, and −106.0 for sodium silicate. Although there are several ^{29}Si resonances for each sugar silicate, they are found invariably in the narrow range of δ −98.3 to −101.6 for pentacoordination. This range indicates that all of the molecules lack additional silicon atoms. One or more such silicon atoms would have produced multiple resonances, presumably every 8 ppm or so. The substitution patterns therefore can be designated as P^0, according to the notation of Kinrade et al.,[4] by which is meant structures **2** and **3** in which each O is attached to either H or C but not to Si. Thus, sodium silicate is oligomeric, but the sugar silicates are not.

Stability in Base. Birchall[11] has argued that silicic acid cannot have an important role with sugars because the medium must be highly basic and sugars are unstable in base. The stability of SiOC linkages, however, was established for polyols[4−7] although not for the parent sugars themselves, other than ribose.[8] Consequently, we sought evidence to demonstrate that decom-

(11) Birchall, J. D. *Chem. Soc. Rev.* **1995**, *24*, 351−357.

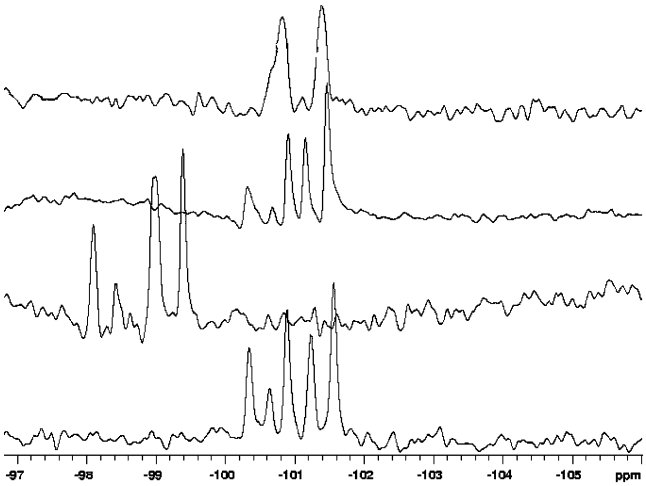


Figure 3. The 79 MHz ^{29}Si NMR spectrum of the silicates of palatinose, maltulose, lactulose, and D-fructose (from top to bottom).

position is not a factor in the study of sugars in silicic acid solution. The primary reactions of aldoses in base are anomerization and isomerization from the ring form to the open-chain aldehyde (or ketone), followed by enolization and C2 epimerization. A hydride shift can lead to ketoses from aldoses, and reverse aldol condensations can result in chain cleavage. Even C3 and C4 epimerization can occur by a sequence of reversible reactions.

For each sugar, we performed a control experiment, whereby the stability of the sugar was examined under conditions of basicity similar to that of the experiment in silicic acid (pH 11.7). In these experiments, no silicic acid was present. The resulting ^{13}C NMR spectra are presented in the middle of Figures 5−8. Various peaks broadened at pH 12, but upon neutralization to return to the starting conditions, the original spectra were obtained (bottom spectra) with no new resonances and all old resonances restored. Thus, the sugars are stable at pH 12 for the times involved in these experiments. No anomerization, epimerization, ketonization, fragmentation, or other decomposition occurred.

It is worthwhile to examine the ^{13}C spectrum of D-ribose in detail, in anticipation of assessing the changes that occur in the presence of silicic acid. The spectrum at neutral pH has already been fully analyzed.[12] At neutral pH (Figure 5, bottom),[13] resonances for the anomeric carbon, for example, are found in the region δ 95−105. The four resonances correspond from left to right to the βF, αF, βP, and αP forms (see Scheme 1 and Table 1). Other isolated peaks include those in the regions around δ 85 (C4 of αF and βF) and δ 78 (C2 of βF). When the pH was changed to ca. 12 (Figure 5, middle), all of the peaks from the pyranose forms remained sharp and at essentially unchanged positions. The peaks from the furanose forms, however, were altered profoundly. The peaks from C1 and C2 nearly disappeared. Sometimes broad peaks could be seen. The peaks for C3 (δ 72.79), C4 (δ 84.92), and C5 (δ 65.59) are present as single rather than double peaks, presumably overlapping for the α and β forms.

These observations have been explained in terms of the known rates for ring opening and closing.[14] Furanose ring-opening and -closing rates are much faster than pyranose rates. Whereas the pyranose rates do not fall in the range to which NMR is sensitive, furanose rates are sufficiently rapid to broaden

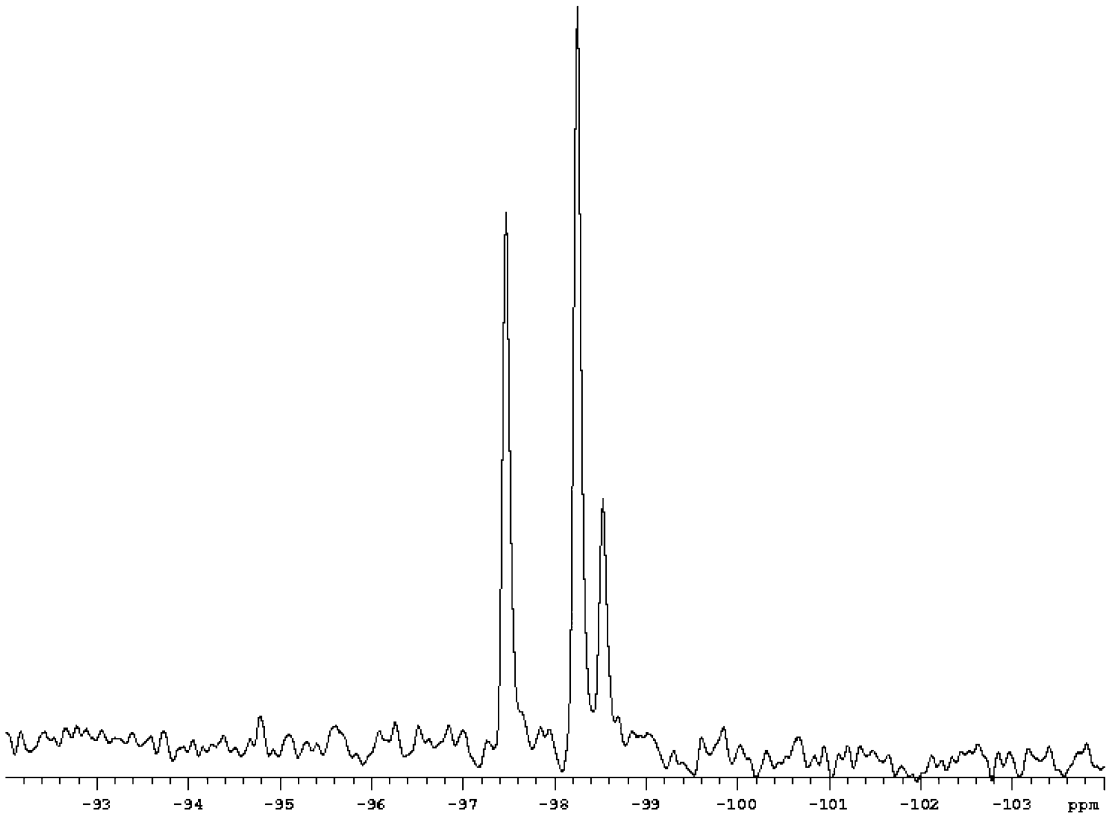


Figure 4. The 79 MHz ^{29}Si NMR spectrum of 1,4-anhydroerythritol silicate.

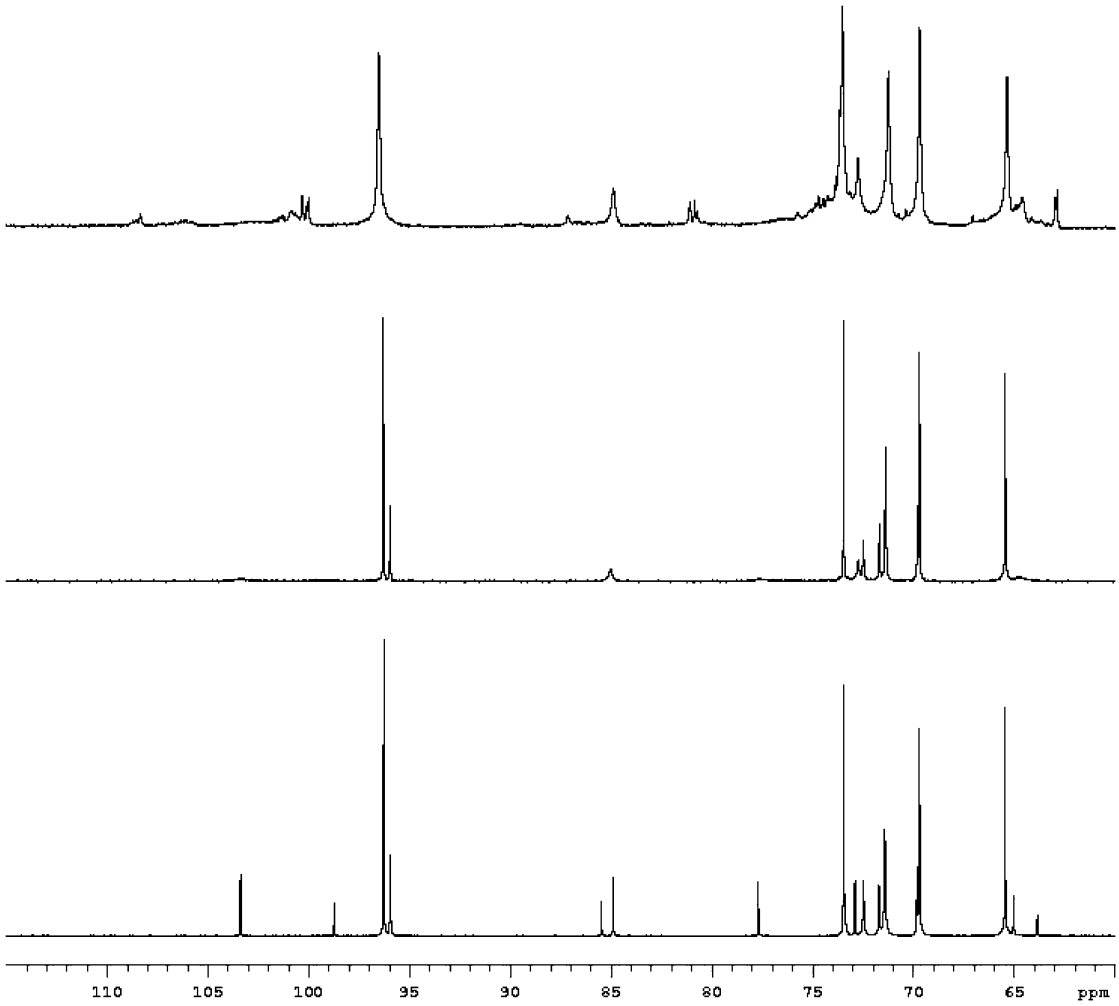
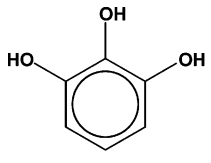


Figure 5. The 100 MHz ^{13}C NMR spectra of D-ribose (top) as the silicate, (middle) as the free sugar at pH ca. 12, and (bottom) as the free sugar at pH ca. 7.

the peaks at high pH. Such broadening does not occur when the anomeric carbon is substituted, preventing ring-chain isomerism. Neutralization of the solution regenerates all of the furanose peaks, unchanged. With some minor variations, this phenomenon is repeated in the spectra of all of the sugars studied, whereby some furanose peaks are broadened by the ring-opening/closing process. These observations will be relevant to our analysis of the spectra of sugar silicates, which are measured at the same basic pH.

Structural Factors. Among the controls we studied for sugars were simple alcohols and phenols. In no case did a monohydroxylic alcohol or phenol (e.g., methanol and phenol) form a stable, soluble complex under our conditions. The result usually was formation of insoluble gels or precipitates and never a new, observable ^{29}Si resonance (silicic acid peaks remained). Aliphatic alcohols and polyols have been reported to form small amounts of tetracoordinated species with tetrabutylammonium silicate at pH 12−12.5.[15,16] Under our conditions, such materials do react but form insoluble gels that give no ^{29}Si resonances. Our objectives were to characterize major, soluble products. The reaction with aliphatic alcohols is further discussed in a later section.

In contrast, catechol (1,2-dihydroxybenzene) readily formed a soluble complex with silicic acid, with a ^{29}Si resonance at δ −144.3, as previously observed.[15] Substituted catechols such as 4-methylcatechol, pyrogallol (**4**), L-DOPA (**5**), and 3,3′,4,4′-tetrahydroxybiphenyl also gave such resonances, whose positions (respectively δ −144.1, −142.3, −143.1, and −143.0) are all indicative of hexacoordination (**3**).[17] We substantiated this



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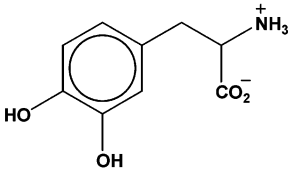

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conclusion by the observation of a parent peak for the catechol complex at *m*/*z* 353 in the electrospray mass spectrum, corre-

(12) King-Morris, M. J.; Serianni, A. S. *J. Am. Chem. Soc.* **1985**, *107*, 3501−3508. Bock, K.; Pedensen, C. *Adv. Carbohydr. Chem.* **1983**, *41*, 27−66.
(13) The solvent was D_2O, but H_2O also was present whenever silicic acid was included. Protons also derived from the HO groups from the sugar and in the control pH 12 solution from NaOH. Thus, the measured pH was a combination of pH and pD (pD = pH + 0.4) and should not be considered exact. Nonetheless, the small differences are not significant.
(14) Goux, W. J. *J. Am. Chem. Soc.* **1985**, *107*, 4320−4327.

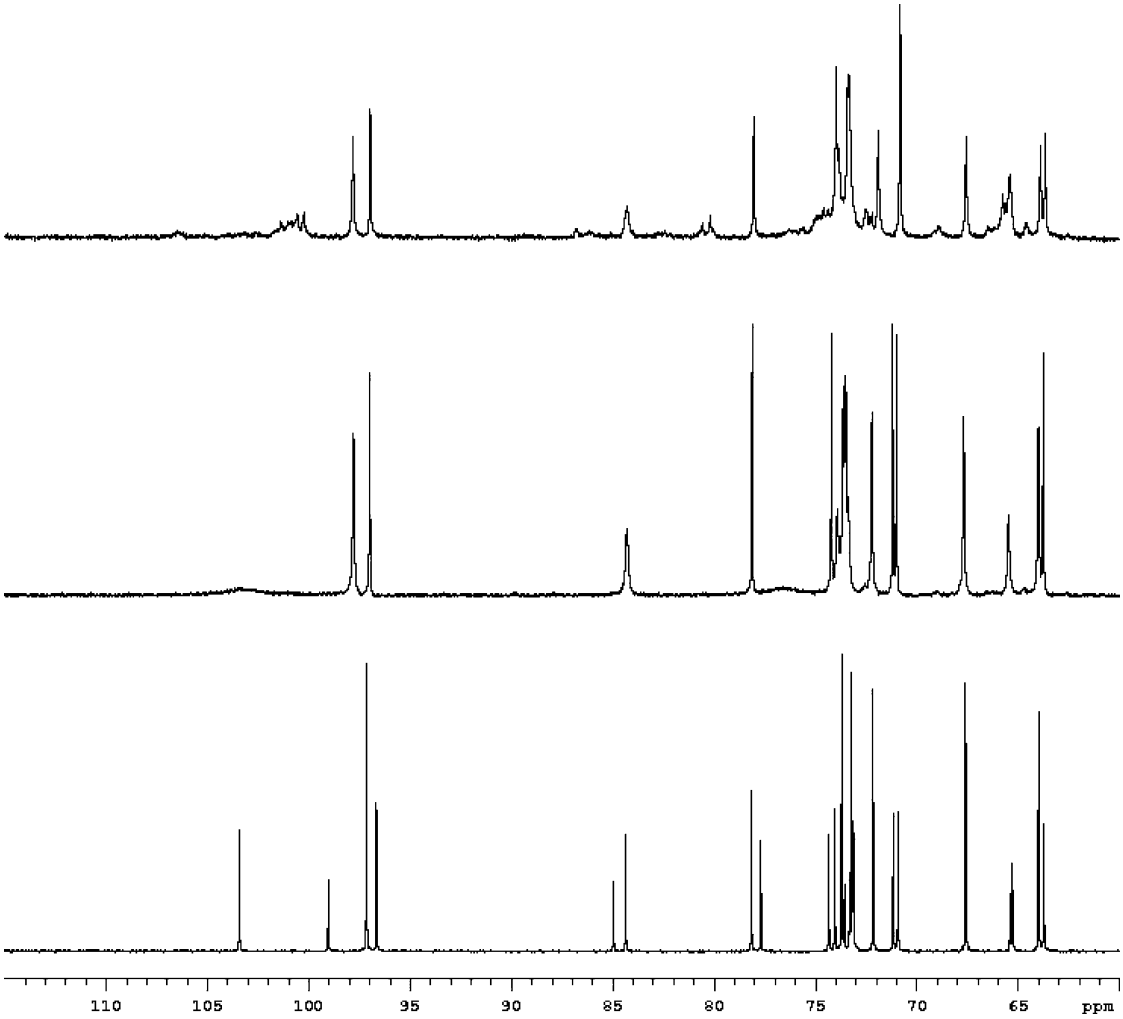
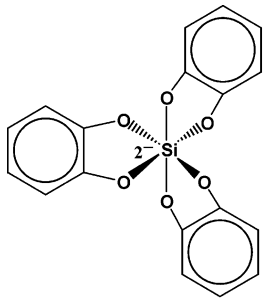


Figure 6. The 100 MHz ^{13}C NMR spectra of D-talose (top) as the silicate, (middle) as the free sugar at pH ca. 12, and (bottom) as the free sugar at pH ca. 7.

sponding to the doubly negatively charged 3/1 species (**6**) described previously.[18] Similar 3/1 structures were confirmed



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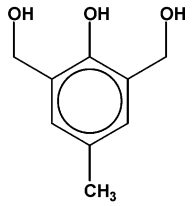

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by ES-MS for pyrogallol (*m*/*z* 401.2), L-DOPA (614.2), and 3,3′,4,4′-tetrahydroxybiphenyl (676.9). This experiment generates singly charged species in which the parent ion carries one proton more than the nominal structures. Consequently, these numbers are one unit greater than the calculated figures for the 3/1 structures (respectively, *m*/*z* 352.0, 400.0, 613.1, and 676.1). This is the first time mass spectrometry has been applied to this subject.

Simple aliphatic diols such as ethylene glycol failed to give stable, soluble complexes with silicic acid under our conditions. Several groups succeeded in preparing such complexes only at very high temperatures.[19] Mixed aliphatic/aromatic systems such as 2,6-bis(hydroxymethyl)-1,4-cresol (**7**) also failed to give stable, soluble complexes under our conditions. The flexibility of open-chain diols may be a deterrent.

Thus, both chelating and acidity factors seem to be operating. The ability to form two C−O bonds in the diolato chelate structure is clearly favorable in comparison with only a single C−O bond. The failure of aliphatic 1,2-diols to form stable silicates suggests that a pK_a factor also may be important. The pK_a of catechol at 9.3 is typically at least 6 orders of magnitude lower than those of aliphatic alcohols, which are in the range 15−19. At pH 12, phenols exist preponderately in the ionized form, whereas alcohols are largely un-ionized. The ionized form

(15) Kinrade, S.; Maa, K. J.; Schach, A. S.; Sloan, T. A.; Knight, C. T. G. *J. Chem. Soc., Dalton Trans.* **1999**, 3149−3150.
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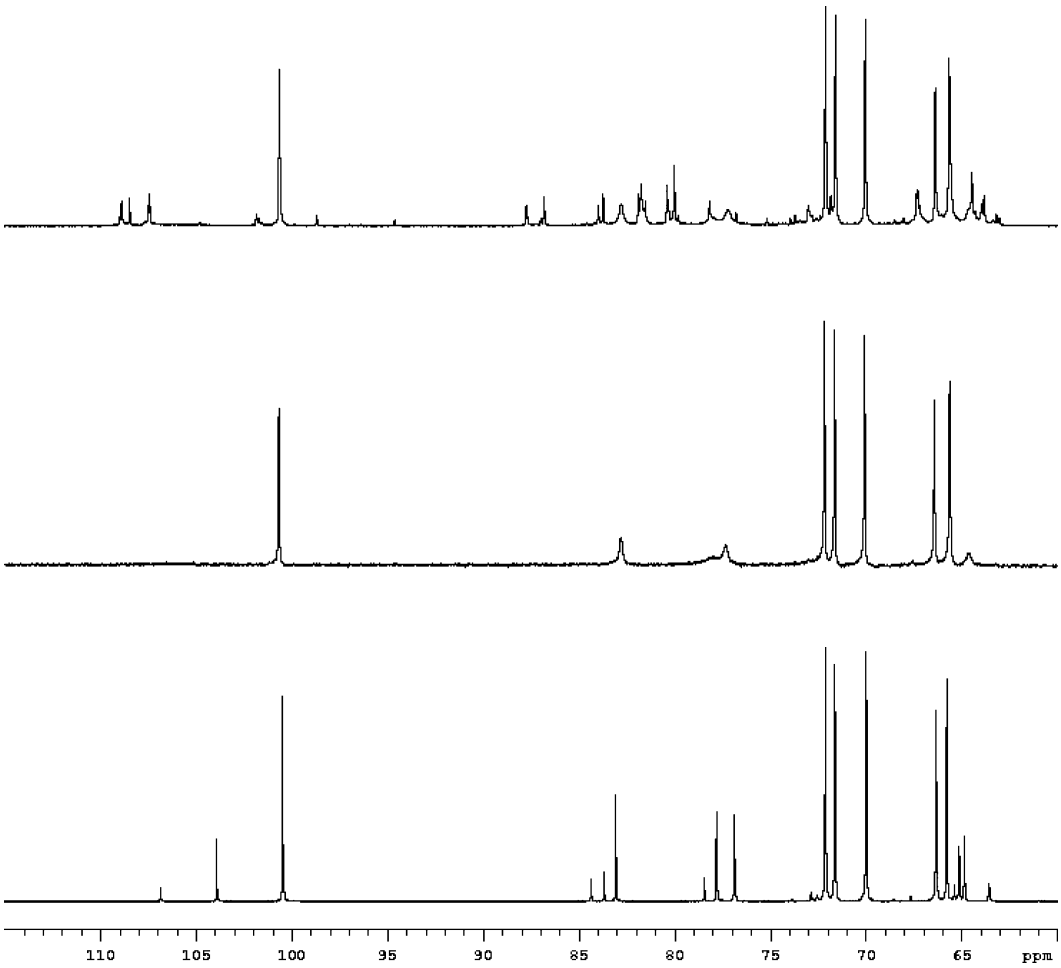

Figure 7. The 100 MHz ^{13}C NMR spectra of D-fructose (top) as the silicate, (middle) as the free sugar at pH ca. 12, and (bottom) as the free sugar at pH ca. 7.

is more nucleophilic and hence is more likely to react with silicic acid.

The angle of chelation bite also is important, as the anion of 2,4-pentanedione failed to form an acac complex with silicic acid. It should be noted that resorcinol (1,3-dihydroxybenezene) also failed. Because its chelation bite is essentially impossible, resorcinol resembles a monophenol in reactivity. The strength of the Si−O bond also is critical, as the nitrogen and sulfur analogues of catechol (respectively, 1,2-phenylenediamine and benzenedithiol) failed to form stable, soluble complexes with silicic acid.

These experiments revealed a number of structural factors. (1) The Si−O bond is a necessary component of complexation, as analogous Si−N and Si−S bonds failed to form. (2) Chelation is necessary, as mono alcohols and phenols failed. (3) The angle of chelation bite is important, as acetylacetone chelation (flat six-membered rings) failed whereas 1,2-dihydroxyphenyl chelation (five-membered rings) succeeded. (4) The acidity of the hydroxy group is critical, as aromatic diols succeeded whereas aliphatic diols failed. Exceptions are discussed in a later section.

Positions of Complexation. The heuristic approach of the previous section led to the conclusion that 1,2-diols with relatively acidic hydroxy groups react with silicic acid to form five-membered ring chelates. The observation of new ^{29}Si resonances when sugars are dissolved in silicic acid indicated that chelates apparently are formed. Examination of the ^{13}C spectrum can provide detailed information concerning which hydroxy groups are involved. The needed comparison is of the spectra of the sugars in silicic acid (top spectra in Figures 5−8) with those at pH ca. 11.7 in the absence of silicic acid (middle spectra).

The ^{13}C resonance of **C**−OH should move in a reproducible fashion on complexation with silicon to form the entity **C**−OSi. The carbon attached to oxygen thus experiences a β effect of the silicon atom. Its adjacent carbon (**C**C−OSi) experiences a γ effect. Unfortunately, the electronic effects of silicon have not been well characterized in the literature,[20] and the effects of a silicon bearing three oxygen substituents have not been characterized at all. Replacement in simple hydrocarbons of a CH bond with $CSiMe_3$ causes an average β effect (**C**CSi) of 0.9 ppm (the positive sign indicates a shift to higher frequency) and an average γ effect (**C**CCSi) of 1.4 ppm.[20] The trimethylsilyl group also introduces a trio of methyl groups that are γ to the carbon atom being examined (**C**C$SiMe_3$). The normal carbon γ effect of −2.5 (multiplied by three) offsets the normal high

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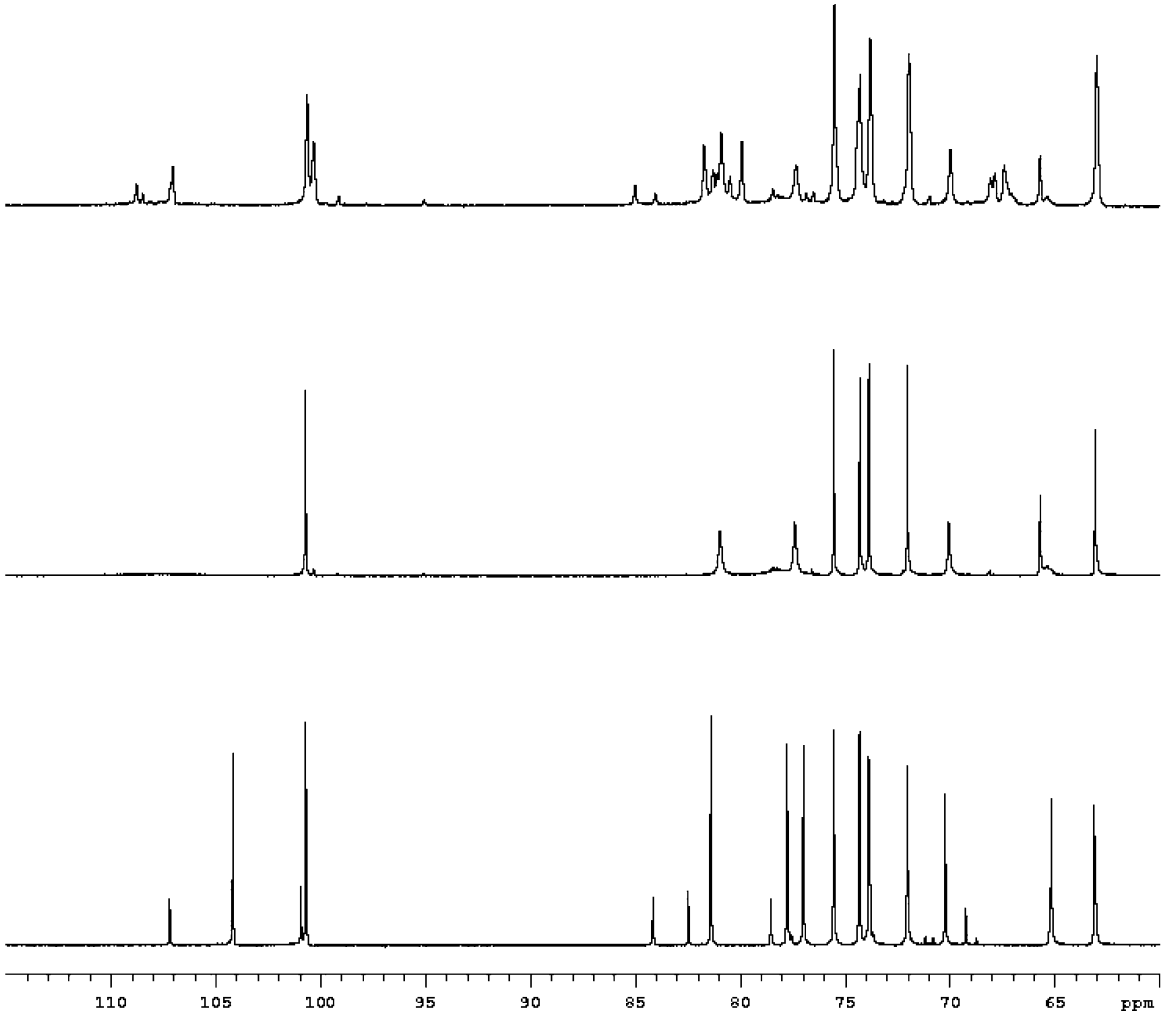


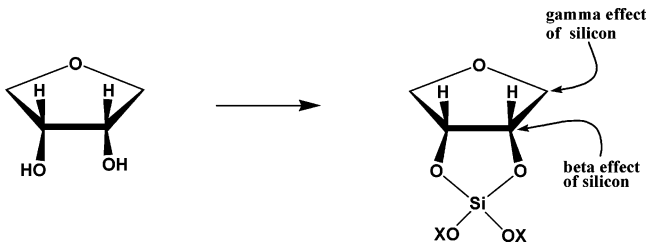
Figure 8. The 100 MHz ^{13}C NMR spectra of D-palatinose (top) as the silicate, (middle) as the free sugar at pH ca. 12, and (bottom) as the free sugar at pH ca. 7.

frequency shift, resulting in the low value of 0.9. Correction for the carbon γ effects results in a value of 8.4 for the β effect of silicon, in line with other β effects. The methyls also introduce an offsetting δ effect on the γ effect of silicon, but the usually negligible value of δ effects does not necessitate a correction.

There are three drawbacks to this calculation. (1) It involves a large correction for the γ effect of carbon. (2) The pathway does not contain the oxygen atom present in the sugars (**C**OSi, rather than **C**CSi for the β effect). (3) The sugars contain three γ oxygens rather than γ methyls, which may impart an important contribution. The second problem may be obviated by examining systems with oxygen along the pathway, of which a number exist.[20] The β effect in five such systems was found to average 1.3 ppm, or 8.8 ppm after correction for the γ effects of methyl, marginally larger than in the all-carbon system. The γ effect in these systems was measured to be 0.5. Thus, oxygen along the pathway plays no substantive role.

The assumptions in these calculations still are too uncertain to allow confidence in the results. Therefore, we sought a system in which we could measure the effects directly. There are few systems in which the desired structural change (**C**OH → **C**OSiO$_3$) is present, and none in which the three γ oxygens consist of two diolato oxygens and one adjacent hydroxyl oxygen. 1,4-Anhydroethritol (*cis*-3,4-dihydroxytetrahydrofuran) possesses the same ring structure as ribose but lacks 1-hydroxy

Scheme 2



and 4-hydroxymethyl groups. It has been found to complex with silicic acid.[8] Scheme 2 illustrates the structural changes that occur on complexation. Carbons 2 and 3 experience the β effect of silicon and three γ effects of oxygen. Carbons 1 and 4 experience the γ effect of silicon and three δ effects of oxygen. The ^{13}C spectrum in aqueous solution contains two peaks at δ 70.0 and 71.4. The resonance at higher frequency presumably is from C2 and C3 because of the electron-withdrawing effect of oxygen. On complexation, several new peaks appear (Figure 9, upper spectrum). The two peaks at low frequency are from unreacted material. There is a set of overlapping peaks at δ 75.4 and four peaks at δ 71.7−72.3. Thus, upon complexation, all shifts caused by β/γ silicon and γ/δ oxygens are to high frequency. We attribute the presence of multiple peaks to stereochemical variants that are discussed in a later section. To

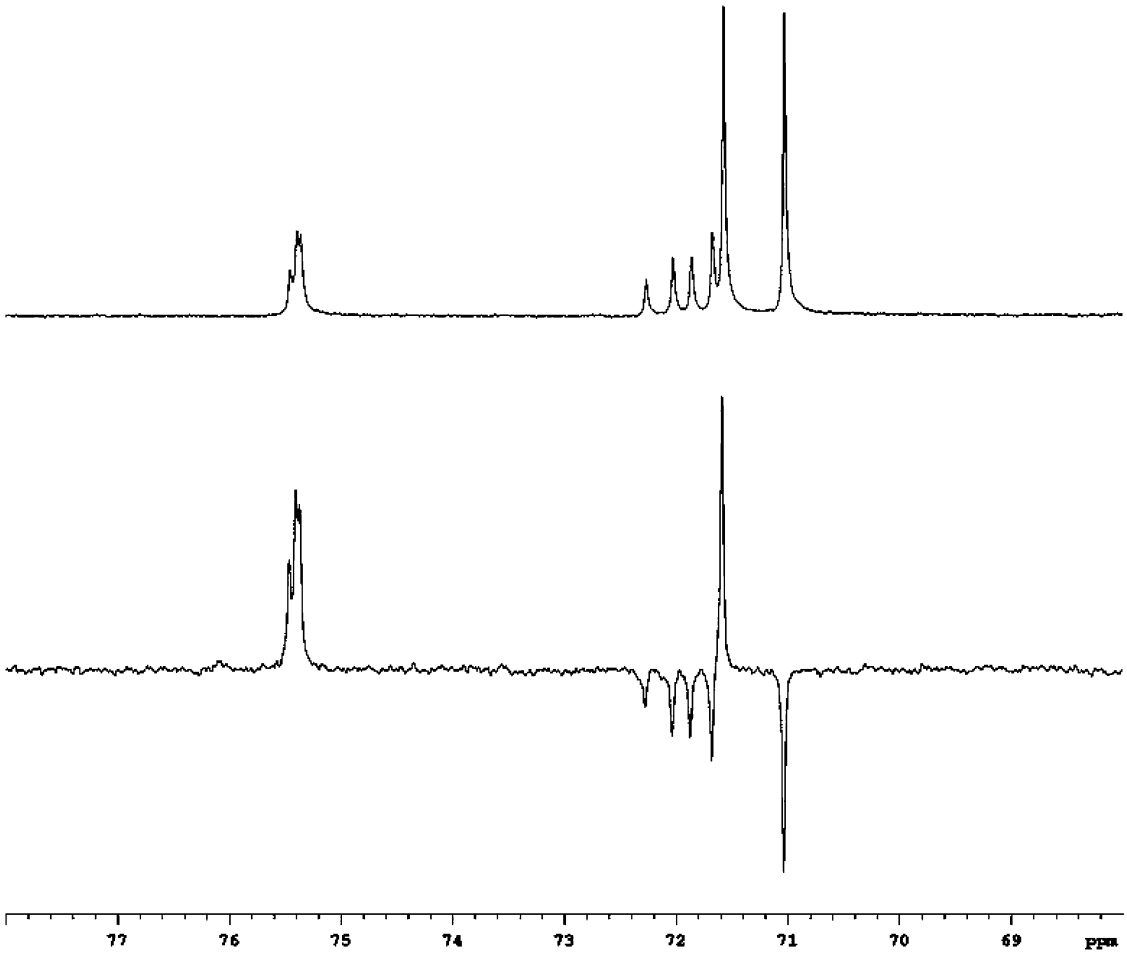


Figure 9. (Upper) The 125 MHz ^{13}C spectrum of 1,4-anhydroerythritol silicates. (Lower) The DEPT spectrum of the same material, in which CH peaks are positive and CH_2 peaks are negative.

assign the peaks in the complexed spectrum, we carried out a DEPT experiment, given in the lower portion of Figure 9 (CH_2 groups give negative peaks, and CH groups give positive peaks). The DEPT experiment confirms that the higher frequency peak of the starting material is from C2 and C3 and proves that the higher frequency peaks in the silicate complex also are from these carbons. This assignment is unambiguous and is the reverse of that in a previous report based on 1D decoupling experiments.[8] The β effect of silicon in this context is found to be 3.9 ppm and the γ effect 0.8, in line with the earlier models but far more reliable. The fact that the β effect is larger than the γ effect has important ramifications on the conclusions of previous workers,[8] altering their position of complexation.

We now can proceed with examination of the ^{13}C spectra of the sugars. According to the results just discussed, the position at which complexation occurs will experience a β effect of about 4 ppm. Shifts of the more distant carbons will be less than a ppm.

In the presence of silicic acid, the C1 resonances for the pyranose forms of ribose (Figure 5, top) are found essentially unchanged at δ 96.30 and 96.62 (originally, δ 96.14 and 96.45). Consequently, no reaction has occurred at the site. A new cluster of peaks is found at δ 100−101, which we attribute to the αF isomer, because its position originally was at δ 98.73. Two broad peaks occur in the region δ 106−108, which we attribute to the βF isomer, whose original position was δ 103.38. These shifts (β effects of 2−5 ppm) indicate coordination of C1 with silicon in the furanose isomer only. Multiple C1 ^{13}C peaks correspond to the multiple peaks observed in the ^{29}Si spectrum. We discuss the structural significance of the multiplicity in a later section. Suffice it to say that there are multiple forms of the silicate complexes present for each isomer. We can conclude that one site of attachment of the sugar with Si is at C1 of the furanose forms.

It is likely that reaction at C1 is related to its higher acidity. Whereas the pK_a of typical alcohol hydrogens is in the region 15−19 (which includes methanol, ethanol, and *tert*-butyl alcohol), and the presence of an adjacent hydroxy group lowers the pK_a by about one unit, the pK_a of the anomeric hydroxyl group is usually about 12. In general, the anomeric hydroxyl is the most acidic site for both pentoses and hexoses.[21] Moreover, the anomeric hydroxyls of furanoses are kinetically more acidic than those of pyranoses.[22] This difference may contribute to the absence of complexation by all pyranoses (six members) and the failure of some furanoses (five members) to complex. The acidity of the anomeric hydroxy groups is reflected in the ^{13}C chemical shifts of the anomeric carbons. For example, in fructose the α and β furanose forms produce C2 chemical shifts

(21) Christensen, J. J.; Rytting, J. H.; Izatt, R. M. *J. Chem. Soc. B* **1970**, 1646−1648.
(22) Gillet, B.; Nicole, D. J.; Delpuech, J. J. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1329−1335.

at δ 103.9 and 106.9, whereas the β pyranose form produces a chemical shift at 100.5 (C2 is anomeric in ketoses). The significant difference is reproduced in many other sugars and is related to the differences in acidity. The pK_a values for ribose, lyxose, and xylose, which successfully formed complexes with silicic acid, are close to 12.1.[23] Arabinose and 2-deoxyribose, which did not form complexes, are less acidic, with respective pK_a's of 12.34 and 12.61.[23] Thus, it is possible that in some cases lower acidity of the anomeric hydroxyl is a deterrent to reaction with silicic acid, both for furanoses and pyranoses. Other factors, such as stereochemistry, are assessed in a later section.

The pyranose peaks for all of the other carbon atoms of ribose also remained essentially unchanged. The resonance positions at pH ca. 7 for furanose C2 are δ 77.60 for βF and δ 73.36 for αF. The former peak disappears on introduction of silicic acid and is replaced by a cluster of peaks at δ 80−81 (a β effect of 2.4−3.4 ppm), which we attribute to the complexed βF isomer. New peaks in the δ 74−75 region are likely to come from the complexed αF isomer. Changes in the C2 resonance position thus suggest that complexation also is occurring at C2. The resonances for the C3 and C5 carbons are relatively unchanged, although peak overlap, particularly for C3, makes conclusions uncertain. The peaks at δ 63.85 (C5, αF) and 65.02 (C5, βF) are replaced by peaks at δ 62.9 and 64.6, respectively, again as clusters. There is no hydroxy group on C4 in ribose. The approximate constancy of the C3 and C5 resonance positions suggests that these hydroxy groups are not involved in complexation.

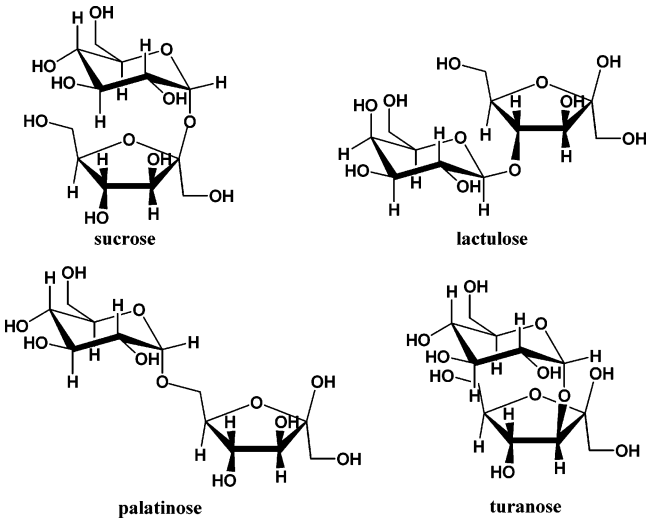
The conclusion based on the movement of ^{13}C peaks is that chelation occurs at C1 and C2 in ribose. Similar conclusions are obtained by analysis of the remaining aldose spectra. For xylose and talose (Figure 6), the pyranose resonances remain unchanged, the C1 and C2 peaks shift, and the other peaks remain unchanged. Talose has relatively high proportions of furanose rings. Although the C1 and C2 resonances clearly move, it is possible in this case that the C6 resonances also move, indicating a possible alternative site of coordination.

In the case of fructose, a ketose, it is the C2 position that is anomeric, and the C2 resonances clearly move on treatment with silicic acid (Figure 7), as do the C1 and C3 resonances. The C4 and C6 resonances appear to remain unchanged (C5 does not bear a hydroxy group). We conclude from the ^{13}C spectra that silicon attachment occurs in ketoses at the anomeric C2 and the two adjacent carbons C1 and C3.

Previous workers[4−7] observed complexation of glycitols and glyconic acids, which have no analogue of the anomeric hydroxyl. These materials exist in conformationally flexible open-chain forms. Kinrade et al.[4] suggested and Benner et al.[6,7] confirmed through X-ray crystallography the important hydrogen-bonding role of nonchelating hydroxy groups in complexes of the glycitols (polyhydroxy derivatives). The rings in the sugars generally make the nonchelating hydroxy groups sterically unavailable for this supporting role. Sugars thus have more stringent structural requirements than glycitols for complexation.

Blocking the Anomeric Carbon. Analysis of ^{13}C chemical shifts indicates that C1 and C2 appear to be the points of attachment for chelation of aldoses. What then happens if one of these positions is blocked? One simple test is to convert the reducing sugars to their methyl glycoside derivatives. These nonreducing sugars prohibit interconversion of the anomeric center but also prevent any new reaction from occurring there. We prepared the 1-*O*-methyl derivatives of ribose and xylose and the 2-*O*-methyl derivative of fructose (ROH → ROCH$_3$), all sugars that gave silicates according to the appearance of new ^{29}Si peaks and changes in the ^{13}C chemical shifts. The three glycosides showed no reaction on dissolution in basic silicic acid according to these NMR criteria. Thus, it appears that it is necessary that the anomeric carbon have a free hydroxy group for reaction to occur with silicic acid.

Scheme 3



Nucleosides provide another useful test of the effect of C1 substitution. We examined guanosine and adenosine under the usual conditions and found no reaction. No new ^{29}Si peaks appeared, and the ^{13}C peaks underwent no significant shifts relative to each other. In these molecules, the C1 carbon is blocked by the presence of the base, similar to the *O*-methyl glycosides above. Previous authors reported that these molecules underwent reaction.[8] The ^{29}Si spectra in their Figure 4, however, contain almost entirely peaks only from silicic acid, which appear (Table 2) as multiplets at δ ca. −100 (dotted line in their figure), the expected location for the product peaks. These reactions were carried out at higher pH than we used, and it is possible that decomposition occurred.

One subtle fact needs to be emphasized. Ribose and other reacting aldoses produce clearly observable C1 resonances in silicic acid (top spectra in Figures 5−7). As already remarked, at pH ca. 12 in the absence of silicic acid, these sugars exhibit severely broadened C1 furanose resonances, or none at all, because of rapid ring-chain isomerization (middle spectra in Figures 5−7). The presence of silicon at C1 prevents this process, as with glycosides and nucleosides, so that C1 resonances are sharper (top spectra in Figures 5−7). Thus, the observation of well-defined C1 resonances in silicic acid at pH 11.7 is ipso facto evidence for reaction at C1, although reaction elsewhere is not excluded.

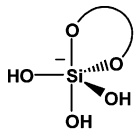
Another approach to probing the location of bonding between silicon and specific sugar positions is to examine disaccharides, which have specific connections between the two rings (Scheme 3; only the β forms are shown). Sucrose, for example, is composed of glucose and fructose rings that are connected through their respective anomeric carbons. We found that

(23) Bethell, G. S.; Ferrier, R. J. *J. Carbohydr. Res.* **1973**, *31*, 69−80.

sucrose failed to react with silicic acid, consistent with a sugar lacking an open hydroxy group on an anomeric carbon. The disaccharide lactulose (see Scheme 3) is composed of a galactose ring connected via its anomeric carbon with C4 of a fructose ring. The galactose anomeric hydroxyl is blocked by the fructose ring, but the fructose anomeric hydroxyl is free. As Figure 3 shows, lactulose gives four peaks in the ^{29}Si spectrum with a pattern very similar to that of fructose, although shifted to higher frequency. The 4 position of the fructose ring is blocked by attachment to galactose and could not be used for reaction with silicic acid. Therefore, this position is not essential for complexation. Palatinose is composed of a glucose ring attached via its anomeric carbon with C6 of a fructose ring. It too reacts with silicic acid (Figures 3 and 8). These observations with lactulose and palatinose confirm that reaction at C4 and C6 of fructose is not important (C5 lacks a hydroxy group), focusing attention on C1 and C3 (C2 is the anomeric carbon and is necessary for reaction). Maltulose (not shown in Scheme 3) is composed of a glucose ring attached via its anomeric carbon to C4 of fructose, and it too reacts with silicic acid (Figure 3). Finally, turanose (Scheme 3) fails to react or decomposes on exposure to silicic acid, as no new ^{29}Si resonances appear. It contains a glucose ring connected via its anomeric carbon to C3 of a fructose ring. This latter position must then be unblocked for reaction to occur with silicic acid.

Experiments with glycosides and nucleosides thus confirm that the anomeric carbon (C1 of aldoses, C2 of ketoses) must have an available hydroxy group for reaction to occur with silicic acid. Blocking C4 or C6 of fructose does not prevent reaction, indicating that these positions are not involved. Blocking C3 of fructose prevents reaction, so this position adjacent to the anomeric carbon also is necessary for reaction. The role of C1 in ketoses is not clear.

Complexation Ratio from Mass Spectrometry. The ^{13}C spectra gave strong evidence for the location on the sugar for complexation with silicic acid, but they provided no information concerning the stoichiometry. The ^{29}Si spectra indicated (in most cases) pentacoordination without oligomerization. We therefore need to specify how many of the five coordination sites are occupied by sugar oxygens. The most likely alternatives are 1/1 complexation, as in **8**, and 2/1 complexation, as in **9**. In



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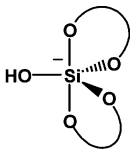

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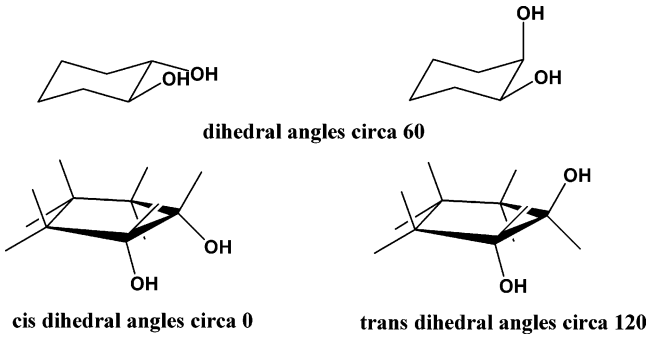
pentacoordination, 3/1 complexation is not possible unless the third sugar molecule is monocoordinated. This arrangement is highly improbable, given the failure of monoalcohols and even monophenols to form soluble silicate complexes. A 3/1 complex, of course, is possible for the hexacoordinated species, analogous to **6**.

We carried out electrospray mass spectrometric experiments directly on the newly prepared silicic acid solutions. Figure 1b shows the results for ribose. A strong peak at *m*/*z* 341.1 in a very simple spectrum clearly indicates a 2/1 (sugar to silicic acid) complex. The aldopentoses xylose (*m*/*z* 341.1) and lyxose (*m*/*z* 341.1) also gave parent peaks clearly indicative of 2/1

Scheme 4



complexes, despite the weakness of the ^{29}Si spectra. Fructose produced the simple spectrum illustrated in Figure 2b, with a strong parent peak at *m*/*z* 401.3 indicative again of a 2/1 complex. The ketohexose sorbose also gave a parent peak at *m*/*z* 401.0 consistent with a 2/1 complex. We were unable to obtain mass spectra of the other two ketohexoses, psicose and tagatose, because of gelling of the solution. These were the two cases that produced hexacoordinate species either in part or entirely according to their ^{29}Si spectra. The disaccharide palatinose also gave a parent peak (*m*/*z* 724.2) indicative of a 2/1 complex. We conclude that, in the preponderance of cases, 2/1 complexes of the type **9** formed. Kinrade et al. have come to this same conclusion for ribose by the difficult process of comparing intensities of ^{13}C and ^{29}Si peaks. They preferred structures, however, with higher levels of oligomerization at this ratio (4/2 or 8/4, their Species 2 and 3). We have found no evidence for either 4/2 or 8/4 structures in the mass spectra, but rather only monomeric 2/1 complexes.

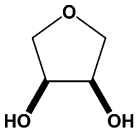
Role of the Diol Dihedral Angle. It has already been established that all pyranose rings fail to react with silicic acid, whereas many furanose rings react readily. There may be a small acidity factor that favors the five-membered ring, but it probably is more important that the HO−C−C−OH dihedral angle in six-membered rings is ill-suited to complex with silicic acid. The resulting diolato ring contains five members, fused to a five-membered ring for furanoses or to a six-membered ring for pyranoses. Cis, vicinal substituents in the five-membered diolato ring have very small dihedral angles, approaching 0°. The HO−C−C−OH group in the sugar becomes O−C−C−O in the diolato ring, with necessarily a very small dihedral angle. The HO−C−C−OH dihedral angle present in a six-membered ring (ca. 60° for axial−equatorial or equatorial−equatorial relationships) is much too large to work. The small HO−C−C−OH dihedral angles already present in the furanose rings (ca. 0° for cis relationships) are ideally suited for formation of the nearly flat diolato ring. Even in furanose rings, the trans relationship (ca. 120°) present in half the forms is unsuitable. Thus, for every sugar, only one of the four isomers is suitable for forming a complex with silicic acid (Scheme 4). If the natural percentage of this one form is very small, it is possible that we would not observe complex formation by ^{29}Si, because we are examining ^{29}Si at natural abundance.

These structural constraints explain many of our negative results. For example, the favorable furanose form of glucose is the βF (in which the 1 and 2 hydroxyls are cis), but it is absent (Table 1). The same form also is absent for gulose and is present at the level of only 0.3% for mannose. The favorable form is present at 6.5% for ribose and at decent levels for all four

ketohexoses, which must have contributed to the positive results for these systems.

Substrate Availability. The extent of formation of complexes between silicic acid and sugars, aliphatic alcohols and diols, phenols, and catechols has been rationalized by four factors: (1) chelate formation, (2) HO acidity, (3) diol stereochemistry, and (4) substrate availability. The first three already have been discussed thoroughly. They do not, however, explain several observations, so that exceptions must be possible. Harris,[16] Kinrade,[15] and their respective co-workers found that methanol reacts with an ammonium silicate to form $CH_3OSi(OH)_3$. Methanol provides neither chelation nor heightened acidity. Harris's conditions, however, involved 45% v/v methanol. In all cases, reaction was only partial, and the equilibrium constant $[Si(OH)_4 + CH_3OH \rightleftharpoons CH_3OSi(OH)_3 + H_2O]$ was always on the side of silicic acid ($K = 0.46-0.80$). Thus, even with an overwhelming excess of alcohol, conversion is low. The poor properties of methanol are overcome by higher substrate availability (the concentration is raised to 45%). Higher availability is possible because of the high solubility of methanol in water. Thus, complexation can occur in the absence of one or more of the three principal factors, compensated by the fourth factor of higher product availability. Sugars and catechols, however, still react more completely.

We have already discussed 1,4-anhydroerythitol (**10**) as a model for sugars. Lacking an anomeric carbon, it still has a



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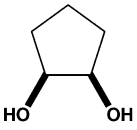

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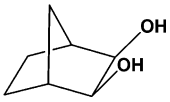

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five-membered ring, analogous to furanoses, and a pair of cis hydroxy groups. This molecule forms complexes with silicic acid, producing the ^{29}Si spectrum in Figure 4, previously observed by Kinrade et al.[8] Unlike almost all of the sugars for which we observed complexation, **10** is not converted entirely to the complex. Like methanol, **10** reacts only partially, as seen in the ^{13}C spectra in Figure 9. The major difference between **10** and reducing sugars or catechols is the absence of a hydroxy group with heightened acidity. As with methanol, a critical factor is the high solubility of **10** in water. Thus, greater substrate availability compensates for the poorer acidity. In addition, the absence of substituents on the 2 and 5 carbons may provide better steric accessibility of the 3 and 4 hydroxy groups. Even with higher solubility and possibly better steric accessibility, **10** still reacts less fully with silicic acid than do catechol and reducing sugars such as ribose.

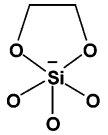
As a test of the hypothesis of substrate availability, we examined *cis*-1,2-dihydroxycyclopentane (**11**) and *cis*-2,3-dihydroxynorbornane (**12**). These molecules resemble **10** by having cis diols attached to a five-membered ring. Neither substrate, however, formed an observable stable, soluble complex with silicic acid. Although **11** and **12** are stereochemically able to form the ring, we believe that their low solubility in water (poor substrate availability) prevents sufficient sugar silicate to be formed and detected under our conditions. We also examined the trans form of **10**, 1,4-anhydrothreitol, and failed to observe any sugar silicate. Despite high product availability, the trans diol stereochemistry does not permit complexation.

Substrate availability also is an important factor in the formation of sugar silicates, as outlined in the previous section. The one anomer with a furanose ring and a cis stereochemistry (Scheme 1) must be present in sufficient amount to provide an observable product. Thus, glucose and mannose have very small amounts of the favorable anomer, and we observe no product with these substrates. Only sugars with an abundance of that anomer gave positive results. Xylose and lyxose provide an interesting borderline behavior. Both of these substrates did produce an observable ^{29}Si result (Table 2). The peaks, however, were weak, and in only these two cases (of all of the successful cases listed in Table 2) we also observed resonances from unreacted silicic acid. In this aspect, these two substrates resemble methanol and 1,4-dihydroerythritol (**10**), whose solutions also contained resonances of unreacted silicic acid. Xylose and lyxose suffer from lack of sufficient available substrate. Keep in mind that the sugar isomers do not interconvert over the time scale of the experiments.

Insufficient substrate availability can inhibit complex formation, because of either low solubility (**11** and **12**) or low anomer abundance (glucose, mannose, and, to a lesser extent, xylose and lyxose). The high substrate availability of methanol and 1,4-anhydroerythritol (**10**) can compensate for the absence of diol structure or heightened HO acidity. The existence of sugar silicates from methanol and **10** implies that it is possible that complexation can occur with compounds that do not include the anomeric carbon, as was already observed also with polyhydroxy compounds.[4-7] For example, glycosides in which the anomeric position is blocked might form a chelate at the 2 and 3 positions, given cis stereochemistry. Such complexation, however, is less favorable and would have to be augmented by higher substrate availability. When both 1,2 and 2,3 positions offer synperiplanar arrangements and are available, complexation will always favor 1,2 reaction in aldoses because of the heightened acidity of the anomeric OH. Nonetheless, 2,3 reaction is a viable option, although we have not observed it under our conditions.

Gel Formation. Spectral characterization as described thus far was carried out immediately after mixing of the reagents, so that even the long-term NMR experiments were completed in a few hours. Most of the sugar silicates formed a white gel after standing 10−12 h, and almost all did so after a month. Only sucrose and the glycitols (inositols) were stable indefinitely in silicic acid solution. Although sugars appear to be incorporated into the gels, we have no structural information on them. This study is concerned only with the soluble silicate products.

Analogues to Sugar Silicates. Whereas complexation of sugars with silicates was unknown prior to this study, at least two analogous structures are quite common, the isopropylidene acetals and the borates (compare structures **13**−**15**). The acetals



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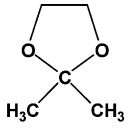

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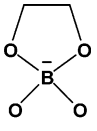

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have been found to form with almost all pentoses and hexoses.[24] Even double acetals form in many cases. Acetal formation occurs not only when the two hydroxy groups are cis to each other, but even in some trans cases. The anomeric hydroxyl plays no special role, and the acetals form with a much wider variety of sugars, including glucose.

The borate anion has long been known to form complexes with sugars.[25] The reaction is more general than the silicate reaction, as it occurs under acidic as well as basic conditions, and it occurs with most 1,2- and 1,3-diols, including glucose. Furanoses, however, are more reactive, and the anomeric hydroxyl plays an important role (the ^{13}C spectra of furanose borates and silicates are remarkably similar for a given sugar).[26]

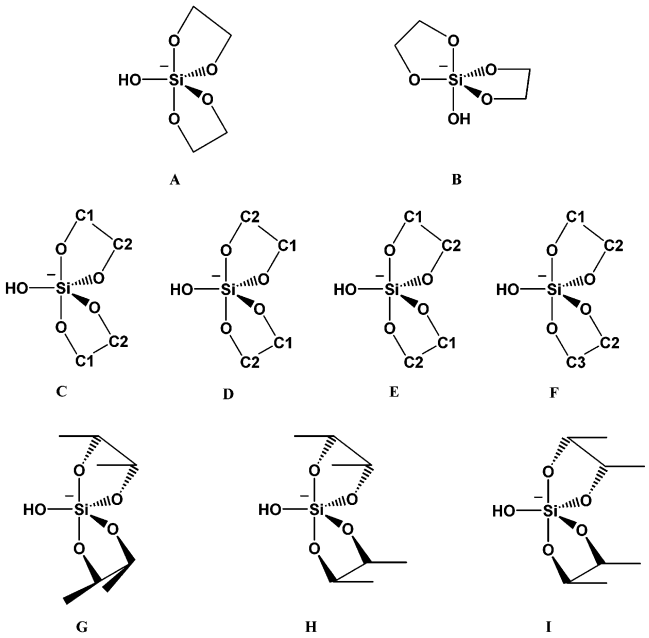
Despite similarities, the differences are important, in particular the high selectivity of the silicate reaction. Whereas acetal and borate formation is quite general with sugars, silicate formation is rather specific. We attribute the selectivity to the ability of silicon to hypercoordinate. The maximum coordination for both carbon and boron is four, as they reside in the second row of the periodic table. Silicon, from the third row, can hypercoordinate. The resulting complexes have 90° angles (see **8** and **9**). Angles in the borates and acetals are closer to tetrahedral. The smaller angle required in the hypercoordinate sugar silicates apparently imposes a stronger restriction on the acceptable HO−C−C−OH dihedral angles (probably demanding angles closer to 0°), so that many sugars fail to have the structural requirements.

Stereoisomers. The sugar silicates typically exhibit 3−5 resonances in the ^{29}Si NMR spectra (Figures 1−4). The presence of several peaks is mirrored in the ^{13}C spectra, particularly in the resonances of the anomeric carbons on dissolution in silicic acid (top spectra in Figures 5−8), and in 1,4-anhydroerythritol (Figure 9). The narrow range of the ^{29}Si resonances, as already noted, indicates that all of the species are monomeric in silicon. The multiple peaks of the sugar silicates are quite different from the multiplicity of silicic acid itself, which extends over a range from δ −70 to −106 (Table 2) as the result of oligomerization with the presence of multiple silicon atoms in the molecules.

We believe that the multiple peaks for the sugar silicates result from stereoisomerism deriving from the 2/1 stoichiometry, as depicted in Scheme 5. The mass spectral experiments indicated that the sugar silicates contain two sugar molecules for each silicic acid. We have depicted the result diagrammatically as structure **9**. This structure is redrawn in Scheme 5 as structure **A**, in which the five-membered diolato rings are shown. The two carbons of the diolato rings are part of the sugar ring, not shown. Structures **9** and **A** incorporate both rings through one axial (or apical) and one equatorial bond. Structure **B** depicts an alternative 2/1 complex in which one diolato ring is axial/equatorial but the other is diequatorial (diaxial, of course, is impossible). We do not, however, believe that such a species contributes to the spectral mutliplicities. It requires an angle of approximately 120° within the five-membered ring, which would be prohibitively strained. The arrangement of **A** is generally more stable.

Even within the axial/equatorial structure are there opportunities for stereochemical multiplicity, as was also recognized by

Scheme 5



Kinrade et al.[8] Structures **C**−**E** illustrate different stereoisomeric modes to place the sugar bonds. In structure **C**, both connections to C1 of the sugar occur at the axial positions to Si, whereas both connections to C2 occur at the equatorial positions. In structure **D**, the roles are reversed, and both C1 connections are equatorial and both C2 connections are axial. Finally, in structure **E**, there is one axial connection to C1 and one axial connection to C2. Thus, there are three distinct stereo modes for constructing a 2/1 complex. In the case of the ketoses, there can be both C1−C2 and C2−C3 ring fusions, which would result in additional isomers, such as **F**. If the complexes are square pyramids (**2b**) rather than trigonal bipyramids (**2a**), an analogous set of cis/trans isomers exist.

The three peaks for ribose (an aldose) and the five peaks for fructose (a ketose) thus can be explained by such stereoisomerism. The symmetrical molecule **10**, however, cannot exhibit this kind of stereoisomerism, because the two points of attachment are identical. There are further modes of stereoisomerism, however, illustrated by structures **G**−**I**. In these structures, the beginnings of the sugar furanose rings have been indicated by a pair of bonds on the atoms held in common to the diolato and furanose rings. In structure **G**, both furanose rings are directed syn to the remaining hydroxy group. In structure **I**, both furanose rings are anti to the hydroxy group. In structure **H**, one furanose ring is syn and one is anti. Each of the structures **C**−**E** can exist as each of the structures **G**−**H**, so that there are a total of nine possible aldose stereoisomers and more for the ketoses. The three observed ^{29}Si peaks for ribose may represent more than three species, if there is peak overlap. The three peaks observed for 1,4-anhydroerythritol (**10**, Figure 4) can be explained entirely by the syn/anti isomerism of structures **G**−**I**. The X-ray structure of **10** complexed with silicic acid proved to have the syn,syn structure **G**.[27]

Conclusions

Certain sugars form complexes with silicic acid under highly basic conditions. The resulting silicate has a 2/1 sugar/silicic

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acid stoichiometry, in which each sugar is attached via a pair of hydroxy groups to form a chelating diolato five-membered ring. Only furanose forms offer a sufficiently small HO−C−C−OH dihedral angle to allow formation of the nearly planar five-membered ring. Pyranose rings remain unchanged under the conditions of reaction. Reaction occurs with the anomeric carbon (C1 for aldoses, C2 for ketoses), whose hydroxy group hence must be free (no glycosidic linkage). The hydroxy groups on the anomeric carbon and its adjacent carbon must be cis for reaction to proceed to the chelate. The furanose ring with the appropriate stereochemistry must be present in at least ca. 1% to be observable with natural abundance ^{29}Si, and the compound must be sufficiently soluble. Most sugars that meet these criteria form sugar silicates that may be observed by ^{29}Si and ^{13}C NMR spectroscopy and mass spectrometry, including the aldoses ribose, xylose, lyxose, and talose, the ketoses psicose, fructose, sorbose, and tagatose, and the disaccharides lactulose, maltulose, and palatinose. Noteworthy failures to form complexes were glucose, mannose, galactose, and sucrose, which do not meet these requirements.

Ribose was the only aldose that formed a truly significant amount of the silicate (the ^{29}Si peaks for lyxose and xylose were much weaker), possibly relating to the 6.5% abundance of the α-furanose form able to form the complex. It is possible that selection and stabilization of ribose silicates played a role in the emergence of ribose as the key sugar in nucleotide biochemical activity. Borate minerals have been suggested as stabilizing agents for ribose in a prebiotic soup.[29] The more widespread silicate minerals may have performed a similar role more effectively. Formation of stable, solid silicates would reduce volatility and provide sequestering that might allow sugars to survive interplanetary transport on meteors. The role of sugar silicates in prebiotic evolution needs to be examined.

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Experimental Section

General Methods. Sodium silicate solution (14% NaOH, 27% SiO_2, Aldrich) was used as received. NMR spectra were recorded on either a Varian Unity Plus 400 (400 MHz, ^{1}H; 100 MHz, ^{13}C; 79 MHz, ^{29}Si) or a Varian Unity Plus 500 (500 MHz, ^{1}H; 125 MHz, ^{13}C) spectrometer. Chemical shifts for ^{1}H and ^{13}C spectra were referenced against external trimethylsilylpropionic acid sodium salt (TSP) and are reported relative to TSP; ^{29}Si was referenced with respect to external tetramethylsilane (1 M in C_6D_6) and is reported relative to tetramethylsilane. Electrospray mass spectrometry was performed with a Thermo Finnegan model LCQ Advantage mass spectrometer. We mixed 6 M sodium silicate solution with 4 M sugar solution in D_2O to form a final solution 3.3 M in sugar and 1.1 M in silicate.

1-*O*-Methyl glycosides were prepared by literature procedures.[28]

1,4-Anhydrothreitol. 3,4-Epoxytetrahydrofuran (0.5 g, 5.8 mmol) was dissolved in 15 mL of 3 M sulfuric acid. The mixture was heated to reflux for 24 h and then was allowed to cool to room temperature. Solid Na_2CO_3 was added to the solution until the pH reached 8−9. The mixture was then evaporated to dryness under vacuum at room temperature. The residue was extracted with tetrahydrofuran (3 × 10 mL). After filtration, all organic portions were combined and dried ($MgSO_4$) overnight. The solvent was evaporated, and 1,4-anhydrothreitol was obtained as a colorless oil (0.43 g, 72%): ^{1}H NMR (D_2O) δ 4.26 (d, 2H), 3.91 (m, 2H), 3.65 (m, 2H); ^{13}C NMR (D_2O) δ 78.72, 75.38.

Synthesis of Hypervalent Silicates. In a typical experiment, the sugar (2.8 mmol) in 0.7 mL of D_2O was added to commercial sodium silicate solution (0.15 mL, 0.9 mmol). The mixture was shaken vigorously and sonicated for a few seconds to ensure thorough mixing. Mass and NMR spectra were taken immediately. Specific results are compiled in the Supporting Information.

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Supporting Information Available: Additional experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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