lifetime of the living end will probably be different for PF_6^-, PF_5OH^-, and $(PF_5OHPF_5)^-$ or $^-PF_5O$ polymer since the rates of polymerization with a PF_6^- gegen ion are known to be faster than with $SbCl_6^-$, *e.g.*, and PF_6^- is known to hinder transfer reactions.[32]

The polymerization solutions of the three dextran-like polymers at −78° maintained the characteristic color of the oxonium ion which was immediately discharged on adding a terminating agent such as water or methanol. The polymers thus appear to be living[33] in that at least part remain indefinitely active at this temperature.

The most striking characteristic of this polymerization is, of course, its high stereoregularity. The band at 891 ± 7 cm^{-1} in the infrared region characteristic of a β-anomeric linkage[34] is absent and the high optical rotation characteristic of an α linkage is even more convincing evidence. Rotations of +195 to +208 compare favorably with the value of +215 at 25° (*c* 0.53, HCl_2CCCl_2H) for the methylated natural dextran containing 95% α-(1→6)-D-glucosidic linkages.[35] The small amount of α-(1→3)-D-glucosidic linkages presumably increases the dextrorotatory power of the methylated natural polymer as it does the unsubstituted dextran.[36] Additional evidence for exclusive α linkage was also obtained from the nmr of the perethylated dextran. No observable C_1 axial proton resonance, which would be present if β linkages were present, was observed δ 0.45 upfield[37] from the very intense C_1 equatorial hydrogen resonance at δ 4.97.[38] Of the carbon atoms adjacent to the trialkyloxonium ion, the C-1 atom is the most electropositive and would be the expected site of attack. Apparently not only is attack on C-6 essentially absent but randomization *via* carbonium ion formation during propagation also must be nearly negligible.

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Formation of Fructosazine

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Condensation of 2 moles of 2-amino-2-deoxy-D-glucose (D-glucosamine) or 2-amino-2-deoxy-D-mannose (D-mannosamine) in hot methanol gave, in each case, 2,5-bis(D-*arabino*-tetrahydroxybutyl)pyrazine (fructosazine). The yield of fructosazine derived from 2-amino-2-deoxy-D-mannose at 37° was about three times as large as that derived from 2-amino-2-deoxy-D-glucose. The presence of 2-amino-2-deoxy-D-mannose was observed together with fructosazine in a methanolic alkaline solution of 2-amino-2-deoxy-D-glucose.

The formation of fructosazine was studied at first with 2-amino-2-deoxy-D-glucose[1] (D-glucosamine), and with D-fructose and ammonia[2] in methanol. Stolte[3] identified this product as a pyrazine derivative, on the basis of the formation of pyrazine-2,5-dicarboxylic acid by oxidation of this product, and he named it as fructosazine having a formula of $C_{12}H_{20}N_2O_8$. Later Taha[4] carried out an experiment with 2-amino-2-deoxy-D-glucose and aqueous ammonia, and separated the fructosazine from the reaction mixture after 6 months by cellulose column chromatography in the yield of 4.6%, and Kuhn, Krüger, Haas, and Seeliger[5] synthesized fructosazine from 1-amino-1-deoxy-D-fructose in a yield of 26%.

It takes many days or sometimes even several months for the formation of fructosazine under the mild conditions which were employed by the previous investigators. We have found that fructosazine is formed during 4 hr by bubbling air into the methanolic solution of 2-amino-2-deoxy-D-glucose in the presence of a slight excess of sodium methoxide at 70°. Fructosazine prepared from 2-amino-2-deoxy-D-glucose under the new reaction conditions showed an infrared spectrum and physical constants identical with those of fructosazine prepared from 1-amino-1-deoxy-D-fructose. The compound was converted into pyrazine-2,5-dicarboxylic acid,[6] mp 253° dec, and its dimethyl ester, mp 169°. Identity of this ester was established by mixture melting point and comparison of the infrared spectrum with that of the authentic sample prepared[6] from 2-(D-*arabino*-tetrahydroxybutyl)quinoxaline.[7]

Fructosazine showed an absorption maximum at 274 mμ and spectroscopic determination of the compound was possible. Table I shows the yields of fructosazine as determined by spectroscopy at 40 and 70°. When the crude compound was purified by treatment with a cation ion-exchange resin, the yield was diminished,[8] and the eluate with 3 *N* hydrochloric acid produced

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TABLE I
YIELD OF FRUCTOSAZINE

Starting material	Wt, g	Reaction temp, C°	Total	Yield, %	After treatment with resin, g	Yield, %	Recovery from resin, g
2-Amino-2-deoxy-D-glucose–HCl	20	40	1.88 g	12.7	0.99 g	6.7	...
	20	70	3.66 g	24.8	1.61 g	10.8	2.01 g
2-Amino-2-deoxy-D-mannose–HCl	2	70	581.2 mg	39.4	277.8 mg	18.6	295.2 mg

a side product. The nature of this compound was not investigated.

2-Amino-2-deoxy-D-mannose also gave fructosazine under the same conditions. Identity of the fructosazine obtained from 2-amino-2-deoxy-D-mannose and from 2-amino-2-deoxy-D-glucose was established by comparison of infrared spectra and physical constants. The fructosazine obtained from 2-amino-2-deoxy-D-mannose and 2-amino-2-deoxy-D-glucose gave the same pyrazine-2,5-dicarboxylic acid and its corresponding dimethyl ester.

The yield of crude fructosazine produced from 2-amino-2-deoxy-D-mannose was 39.4% as determined by spectroscopy at the reaction temperature of 70°, while that from 2-amino-2-deoxy-D-glucose was 24.8% as shown in Table I. The yields of the purified fructosazine after treatment with ion-exchange resin were 18.6% from 2-amino-2-deoxy-D-mannose and 10.8% from 2-amino-2-deoxy-D-glucose, respectively. The difference of the yields was more prominent in the reaction at 37°, where the yield of purified fructosazine produced from 2-amino-2-deoxy-D-mannose (17%) was three times as large as that from 2-amino-2-deoxy-D-glucose (5.5%).

It was reported previously that 2-acetamido-2-deoxy-D-glucose (*N*-acetyl-D-glucosamine) is epimerized to 2-acetamido-2-deoxy-D-mannose[9] (*N*-acetyl-D-mannosamine) and 2-acetamido-2-deoxy-D-galactose (*N*-acetyl-D-galactosamine) to 2-acetamido-2-deoxy-D-talose[10] (*N*-acetyl-D-talosamine) in aqueous alkaline solution. No case of the corresponding epimerization has been reported with free amino sugars. We confirmed the formation of 2-amino-2-deoxy-D-mannose in addition to the formation of fructosazine. Evidence of the epimerization of 2-amino-2-deoxy-D-glucose to 2-amino-2-deoxy-D-mannose was obtained by the paper chromatographic detection[11] of 2-amino-2-deoxy-D-mannose in the methanolic solution of 2-amino-2-deoxy-D-glucose, from which fructosazine formed had been separated.

Similar experiments of the epimerization of free amino sugars and their condensation to fructosazine and its analogs are being studied in aqueous solution and the results will be reported elsewhere.

Experimental Section[12]

Fructosazine from 2-Amino-2-deoxy-D-glucose.—Twenty grams of 2-amino-2-deoxy-D-glucose hydrochloride was suspended in 100 ml of hot methanol containing 2.4 g of metallic sodium, and, after shaking the mixture, the sodium chloride deposited was filtered off. The filtrate was warmed to 70° in a water bath under reflux, and air was bubbled into the solution for 4 hr. After refrigeration overnight, crude fructosazine precipitated and was collected by filtration, yield 3.0 g (21%). The precipitate was dissolved in 300 ml of water and passed through an Amberlite IR-20 (H^+) column (3 × 70 cm). The eluate and washings with water were combined and neutralized with Dowex 1X8 (HCO_3^-), 200–400 mesh, and the resin was removed by filtration. After treatment with charcoal, the filtrate was concentrated *in vacuo* to a syrup. This syrup was dissolved in 50 ml of methanol, and the mixture was kept in a refrigerator overnight to give a crystalline product, yield 1.2 g. Recrystallization was carried out from water and methanol: mp 237° dec; $[\alpha]^{20}D$ −84.1° (*c* 1.0, water); ν_{max}^{Nujol} 1350, 1100, 1040, 945, 900, and 860 (C=CH) cm^{-1}; $\lambda_{max}^{H_2O}$ 274 mμ.

Anal. Calcd for $C_{12}H_{20}N_2O_8$: C, 45.00; H, 6.29; N, 8.75. Found: C, 44.96; H, 6.34; N, 8.73.

The infrared spectrum was identical with that of the fructosazine prepared from 1-amino-1-deoxy-D-fructose;[5] the latter spectrum was kindly provided by Dr. R. Kuhn.

2,5-Bis(D-*arabino*-tetraacetoxybutyl)pyrazine.—The octaacetate was obtained from 1 g of fructosazine according to the method previously reported by Taha:[4] yield 650 mg (32.6%); mp 174°; $[\alpha]^{11}D$ −7.2° (*c* 1.0, chloroform); ν_{max}^{Nujol} 1730 (C=O), 1230, and 855 (C=CH) cm^{-1}.

Anal. Calcd for $C_{28}H_{36}N_2O_{16}$: C, 51.22; H, 5.53; N, 4.27. Found: C, 51.49; H, 5.96; N, 4.22.

The nmr spectrum was determined in deuteriochloroform at 60 Mc with Varian Model A-60 spectrometer and tetramethylsilane (τ 10.00) was used as the internal reference standard: τ 1.47 (singlet, two protons, C-3 of pyrazine ring), 3.77 (doublet, two protons, C-1′),[13] 4.27 (quartet, two protons, C-2′), 4.63 (multiplet, two protons, C-3′), 5.75 (multiplet, four protons, C-4′), 7.78, 7.89, 7.95, 8.10 (singlets, 24 protons, 1′-OAc, 2′-OAc, 3′-OAc, 4′-OAc[13]).

Pyrazine-2,5-dicarboxylic Acid.—Five grams of fructosazine was dissolved in 300 ml of hot water and to the solution was added 2.5 g of potassium hydroxide. Oxidation of fructosazine was carried out according to the method of Mager and Berends[6] by adding potassium permanganate in small portions. After the oxidation, the precipitate was filtered off, the filtrate and washings were combined, and this solution was concentrated *in vacuo* to about 70 ml. Fifty milliliters of Amberlite IR-120 (H^+) was added to this solution and the mixture was allowed to cool. After decantation of a part of the supernatant, the fine precipitate was collected by filtration, and recrystallization was carried out from 2 *N* aqueous ammonia and concentrated hydrochloric acid according to the method of Schut, Mager, and Berends[14] to give pyrazine-2,5-dicarboxylic acid, yield 1.5 g (50%), mp 253° dec.

Anal. Calcd for $C_6H_4N_2O_4 0.25H_2O$: C, 41.75; H, 2.63; N, 16.23. Found: C, 41.92; H, 2.86; N, 16.50.

2,5-Dimethoxycarbonylpyrazine (Pyrazine-2,5-dicarboxylic Acid Dimethyl Ester).—Five-hundred milligrams of pyrazine-2,5-dicarboxylic acid was boiled with 15 ml of methanolic hydrogen chloride according to the method of Mager and Berends[6] under reflux for 1 hr. After cooling the reaction mixture, the crystal produced were collected, yield 560 mg (96%). Recrystallization from methanol gave 550 mg of the pure product: mp 169°; ν_{max}^{Nujol} 1720 (C=O), 1285, 1150, 1030 (C—O—C), 965, 830 (C=CH), and 765 cm^{-1}.

Anal. Calcd for $C_8H_8N_2O_4$: C, 48.98; H, 4.11; N, 14.28. Found: C, 49.59; H, 4.26; N, 14.30.

Fructosazine from 2-Amino-2-deoxy-D-mannose.—Twenty grams of 2-amino-2-deoxy-D-mannose hydrochloride was suspended in 150 ml of hot methanol containing 2.4 g of metallic sodium, and, after shaking, the sodium chloride deposited was

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removed by filtration. After allowing the solution to stand for 3 days at 37°, the precipitate was filtered and then dissolved in 300 ml of water. This solution was passed through an Amberlite IR-120 (H^+) column (3 × 70 cm), and the effluent was treated with Dowex 1X8 (HCO_3^-), 200–400 mesh. The resin was filtered off and the neutral filtrate was concentrated *in vacuo* to a syrup and methanol was added to give 2.48 g of crystals, yield 17%, $[\alpha]^{20}D$ −87.6°. Under the same conditions and by the same treatment, fructosazine was obtained in the yield of only 5.5% from 2-amino-2-deoxy-D-glucose hydrochloride. This fructosazine, after two recrystallizations from water and methanol, had mp 235° dec, $[\alpha]^{20}D$ −83.4° (*c* 1.0, water).

Anal. Calcd for $C_{12}H_{20}N_2O_8$: C, 45.00; H, 6.29; N, 8.75. Found: C, 45.29; H, 6.54; N, 8.77.

Fructosazine prepared from 2-amino-2-deoxy-D-mannose, showed an infrared spectrum identical with that of fructosazine from 2-amino-2-deoxy-D-glucose and from 1-amino-1-deoxy-D-fructose.

From the fructosazine prepared from 2-amino-2-deoxy-D-mannose, the following compounds were prepared.

2,5-Bis(D-*arabino*-tetraacetoxybutyl)pyrazine had mp 173°, $[\alpha]^{11}D$ −7.1° (*c* 1.0, chloroform). Pyrazine-2,5-dicarboxylic acid had mp 251° dec. 2,5-Dimethoxycarbonylpyrazine showed mp 169°.

Analyses, infrared spectra, and mixture melting points showed that they were identical with the compounds prepared from 2-amino-2-deoxy-D-glucose.

2,5-Dimethoxycarbonylpyrazine *via* **2-(D-*arabino*-tetrahydroxybutyl)quinoxaline.**—1-Deoxy-1-*p*-toluidino-D-fructose was prepared[15] from D-glucose and *p*-toluidine, and, from this material, 2-(D-*arabino*-tetrahydroxybutyl)quinoxaline was prepared.[7] Pyrazine-2,3,5-tricarboxylic acid was prepared[6] from 2-(D-*arabino* tetrahydroxybutyl)quinoxaline. 2,5-Dimethoxycarbonylpyrazine was prepared[6] by decarboxylation and esterification with methanolic hydrogen chloride from pyrazine-2,3,5-tricarboxylic acid, mp 169°, over-all yield 210 mg (0.8%).

Anal. Calcd for $C_8H_8N_2O_4$: C, 48.98; H, 4.11; N, 14.28. Found: C, 48.69; H, 4.35; N, 14.27.

No depression in the melting point was observed when this material was mixed with a sample of 2,5-dimethoxycarbonylpyrazine derived from fructosazines prepared from both 2-amino-2-deoxy-D-glucose and 2-amino-2-deoxy-D-mannose, and they showed identical infrared spectra.

Paper Chromatographic Identification[11] of 2-Amino-2-deoxy-D-mannose in the Reaction Mixture from 2-Amino-2-deoxy-D-glucose.—In the experiment for the formation of fructosazine from 2-amino-2-deoxy-D-glucose in methanol at 70°, the methanolic mother liquor, after removing the precipitated fructosazine, was concentrated *in vacuo* at 0°, and the residue was diluted with water. This solution was passed through a column of Dowex 50X8 (H^+), 200–400 mesh. This column was eluted with 0.22 *N* hydrochloric acid, and the Elson–Morgan reaction-positive fraction was collected and concentrated *in vacuo*, and methanol was added to give crystals. These crystals were chromatographed on Toyo Roshi No. 50 filter paper previously soaked in 0.1 *M* barium chloride, in butanol–pyridine–water (6:4:3, v/v). Besides a spot corresponding to 2-amino-2-deoxy-D-glucose hydrochloride (R_f 0.31), another spot (R_f 0.37) which had the same mobility as 2-amino-2-deoxy-D-mannose hydrochloride (R_f 0.37) was detected.

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Electrolytic Oxidation of Cyclobutane-1,3-dicarboxylic Acids. An Electrochemical Synthesis of 2,4-Dicarbomethoxybicyclobutane[1]

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Anodic oxidation of *trans,trans,trans*-1,3-dicarboxy-2,4-dicarbomethoxycyclobutane in the Kolbe manner gives 2,4-dicarbomethoxybicyclobutane. In contrast, electrolysis of α-truxillic acid under similar conditions results in ring contraction and formation of the lactone of *cis,cis*-1-carboxy-2-α-hydroxybenzyl-3-phenylcyclopropane as the major product. A cationic mechanism is invoked to explain the difference in behavior exhibited by these cyclobutane-1,3-dicarboxylic acids.

As part of a continuing program directed toward the synthesis of tetrahedrane (I) the feasibility of employing the Kolbe electrochemical synthesis[3] for the formation of highly strained small-ring systems including bicyclobutanes has been investigated. Electrolytic studies were conducted on α-truxillic acid (II) (Scheme I) and *trans,trans,trans*-1,3-dicarboxy-2,4-dicarbomethoxycyclobutane (III) in order to determine the potential value of electrode reactions for 1,3-bond formation in cyclobutyl systems. *trans,trans,trans*-1,2,3,4-Tetracarboxycyclobutane (IV) (the obvious direct Kolbe precursor for I) was excluded as a substrate in these preliminary studies since olefin formation and rearrangement may be anticipated as possible complicating factors when vicinal carboxyl groups are present.[4]

Electrolysis of α-truxillic acid (II) in methanol (2 × 3 cm platinum electrodes; 80 v, 0.8 amp) until the solution was basic afforded at least eight products as established by thin layer chromatography. Of these, only the major product VII, mp 131–133°, was isolated by column chromatography in quantities sufficient for characterization. The hydrocarbon fraction constituted <1% of the material eluted and, therefore, it must be concluded that, under the conditions employed, anodic bisdecarboxylation with concomitant cyclization, does not occur in this case. The γ-lactone V, if formed, was not isolated either.

The structure of VII, obtained from II by electrolysis, was established by direct comparison with an authentic sample of this lactone synthesized independently according to the method of Stoermer and Schenck by deamination of γ-truxillamic acid (VI).[5] The isomeric lactone VIII (mp 120–121°) may be prepared from β-truxillamic acid (IX) by the same procedure. Paudler, Herbener, and Zeiler[6a] recently published their data on the electrochemistry of cyclobutane-1,2-dicarboxylic acids including β-truxinic acid (X). It is noteworthy

(1) For a preliminary report of this work, see A. F. Vellturo and G. W. Griffin, *J. Am. Chem. Soc.*, **87**, 3021 (1965).

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