5-Ethyl-2,8-dimethyl-10,10-diphenyl-5,10-dihydrophenazasiline. (*A*) *From N-ethyl-2,2'-dibromodi-p-tolylamine.* A solution of 5.75 g. (0.015 mole) of N-ethyl-2,2'-dibromodi-p-tolylamine in 50 ml. of ether, cooled in an ice bath, was treated with 0.03 mole of n-butyllithium. After stirring for 30 min., a solution of 3.80 g. (0.015 mole) of dichlorodiphenylsilane in 50 ml. of ether was added and the reaction mixture heated at reflux for 17 hr. Subsequently, 30 ml. of toluene was added and the ether distilled. After refluxing the resulting solution for 2 hr., Color Test I[11] was negative. The reaction mixture was hydrolyzed with 50 ml. of water and worked up in the usual manner. The reaction products were taken up in petroleum ether (b.p. 60–70°) to give 3.76 g. of yellow solid, m.p. 147–158°. This material was taken up again in petroleum ether, treated with charcoal, and concentrated to give 3.27 g. (54%) of colorless crystals, m.p. 159–162°. The analytical sample melted at 160.5–162°.

Anal. Calcd. for $C_{28}H_{27}NSi$: C, 82.91; H, 6.71; Si, 6.93. Found: C, 83.23, 83.00; H, 6.89, 6.86; Si, 7.15, 7.01.

(*B*) *From 5-ethyl-2,8-dibromo-10,10-diphenyl-5,10-dihydrophenazasiline.* An ethereal solution of 0.023 mole of n-butyllithium was added to 4.0 g. (0.0075 mole) of 5-ethyl-2,8-dibromo-10,10-diphenyl-5,10-dihydrophenazasiline in 100 ml. of ether, while cooling in an ice bath. The reaction mixture was allowed to warm to room temperature and stirred for 45 min. A solution of 3.15 g. (0.025 mole) of freshly distilled dimethyl sulfate in 25 ml. of ether was added, and after refluxing for 2 hr. Color Test I[11] was negative. Subsequently, the usual work-up and crystallization from petroleum ether (b.p. 60–70°) gave 2.54 g. of colorless solid, m.p. 150–160°. This material was recrystallized twice from petroleum ether to give 1.89 g. (62%) of colorless crystals, m.p. 158–160°. An additional recrystallization raised the melting point to 159–161°. The material was identified as 5-ethyl-2,8-dimethyl-10,10-diphenyl-5,10-dihydrophenazasiline by mixed melting point and by comparison of the infrared spectra.

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[CONTRIBUTION FROM THE NEW BEDFORD INSTITUTE OF TECHNOLOGY]

Chromatographic Adsorption. V. Isomer Distributions during Methyl Mannoside and during Methyl Arabinoside Formations by the Fischer Method Using a Cation Exchange Resin as Catalyst

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Methyl mannoside and methyl arabinoside formations by the Fischer method, using a strongly acidic ion-exchange resin as catalyst, were followed by chromatographing aliquots on a starch column with butanol-pyridine-water (10:3:3 by volume). D-Mannose disappeared at a first order rate to yield, initially at first order rates, the α- and β-methyl mannofuranosides and mannopyranosides and to reach a final equilibrium containing all four methyl mannosides after seventy-two hours. Arabinose behaved similarly to reach a final equilibrium mixture after twenty-four hours. The same final equilibrium mixtures could be formed from any of the methyl glycosides by similar treatment.

Although the Fischer method of glycoside formation has been known for a long time and a modification of this method using an ion-exchange resin as the acid catalyst for a shorter time,[1] only one quantitative study of the distribution of all four existing isomers during the course of the reaction has been attempted. This was done in paper III of this series[2] in which the isomer distribution during methyl galactoside formation was investigated using a Florex XXX adsorption column for the separations. Unfortunately only two fractions were obtained and the percentages of the four methyl galactosides had to be calculated from the optical rotations of these fractions. Since publication of this paper there has been considerable activity in the field of chromatographic and electrophoretic separations of methyl glycoside mixtures.[3–11] Most of these methods use cellulose partition columns with varied solvent combinations. The separation of the four methyl mannosides[10] has been accomplished completely enough for quantitative analysis using a cellulose powder column with butanol-pyridine-water (10:3:3 by volume) as developer. An improved separation of the methyl mannosides and also separation of the four methyl arabinosides has been obtained by

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replacing the cellulose powder column with a starch column.[11]

EXPERIMENTAL

Materials. The D-mannose and L-arabinose were Pfanstiehl C.P. materials of specific rotations +14.25° and +104°, respectively. The methyl α-D-mannopyranoside and methyl β-L-arabinopyranoside were crystalline materials of specific rotations +79.5° and +242°, respectively, all rotations being for the D line of sodium in water solution at 20°. The methanol was reagent grade and the strongly acidic ion exchange resin was Dowex-50 (X-8) 50–100 mesh, obtained from The Dow Chemical Company, Midland, Mich. This resin was obtained moist in the acid form and the water was replaced by methanol in six overnight treatments with fresh portions of the alcohol.

Methyl glycoside formation. D-Mannose (100 g.) or L-arabinose (83 g.) was introduced into a 1-l. ground joint three-neck flask fitted with a Teflon[12] stirring paddle and two reflux condensers. Methanol (500 ml.) was added and the flask heated to reflux with agitation at 500 r.p.m. Dowex-50 damp with methanol (50 g.) was then added and 1-ml. samples were withdrawn at intervals and mixed with 1 ml. of pyridine in numbered vials. The pyridine ensured stoppage of the reaction even if particles of ion exchange resin were accidentally withdrawn by the pipet. Complete solution of the sugar occurs in 10–15 min. and the quantities chosen are such that approximately 1*M* sugar solutions are produced. Equilibrium among the various isomers was reached in 72 hr. with the mannosides and 24 hr. with the arabinosides. The reaction mixtures were filtered from the ion exchange resin, concentrated under vacuum, and, after removal of any crystalline material, chromatographed on a 4.5 × 48 in. starch column using butanol-pyridine-water (10:3:3, by volume) in order to obtain the pure methyl glycosides in quantity. After removal from the reaction mixture and mixing with pyridine, 200λ of each sample, containing approximately 20 mg. of carbohydrate, was chromatographed into 10 ml. fractions on a 1 × 30 in. starch column with butanol-pyridine-water (10:3:3 by volume) as described in a previous publication.[11] Anthrone in 90% (vol.) sulfuric acid was found to give a deeper color with methyl arabinoside mixtures and the same depth of color with methyl mannoside mixtures as was obtained previously[9] with 95% sulfuric acid. With 90% sulfuric acid the absorption maximum occurred in both cases at 620 mμ and Beer's law was found to hold very closely.

Methyl glycoside interconversions. Methyl α-D-mannopyranoside (10.8 g.) was refluxed 72 hr. with 5 g. of Dowex-50 in 50 ml. of methanol to produce an equilibrium mixture of the same composition as obtained from D-mannose. Methyl β-L-arabinoside (18.2 g.) was refluxed 24 hr. with 10 g. of Dowex-50 in 100 ml. of methanol to produce an equilibrium mixture of the same composition as obtained from L-arabinose. A mixture (9.1 g.) of methyl β-L-arabinofuranoside (3%), methyl β-L-arabinopyranoside (25%), and methyl α-L-arabinopyranoside (72%) was refluxed 24 hr. with 5 g. of Dowex-50 in 50 ml. of methanol to produce the above mentioned equilibrium mixture.

DISCUSSION

Fig. 1, giving the overall analysis of the reaction mixture of D-mannose with methyl alcohol, shows the disappearance of mannose at a first order rate of 1.10[13] and the initial rapid formation of α- and β-mannofuranosides and their subsequent change to pyranosides, principally α-mannopyranoside. That β-mannopyranoside is formed from the furanosides is evident upon comparing the decrease of D-mannose and the increase of β-mannopyranoside over the range of four to six hours, remembering that the majority of the mannose is forming other isomers and that β-mannopyranoside is forming α-mannopyranoside. That *both* pyranosides are formed initially from mannose appears likely because of the absence in their curves of an initial point of inflection which would be expected if their formation depended upon a prior formation of furanosides. If the composition of the methyl mannoside mixture (excluding mannose) is plotted on a

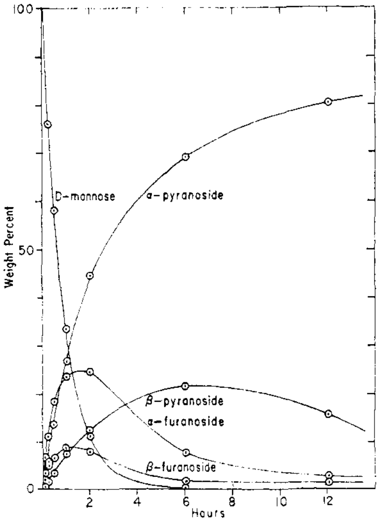

Fig. 1. Formation of methyl-D-mannosides

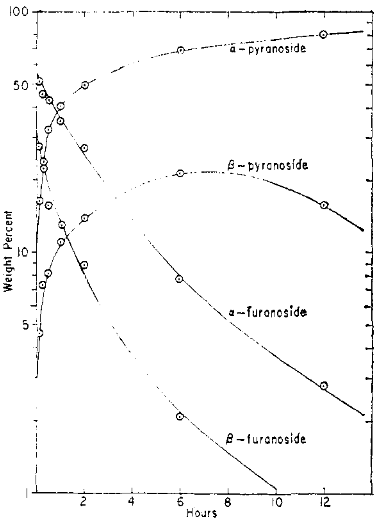

Fig. 2. Composition of methyl mannoside mixture

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[12] A Teflon paddle produces a minimum of mechanical destruction of the resin with resultant clogging of the filter by fine resin particles. In this connection the recently developed Dowex-50W may be superior to the older Dowex-50 in that it is advertised as having greater mechanical strength as well as throwing less color.

[13] All rate constants given in this paper are first order, calculated with time in hours and Briggsian logarithms.

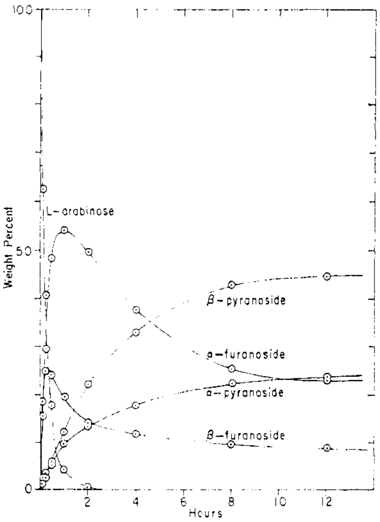

Fig. 3. Formation of methyl-L-arabinosides

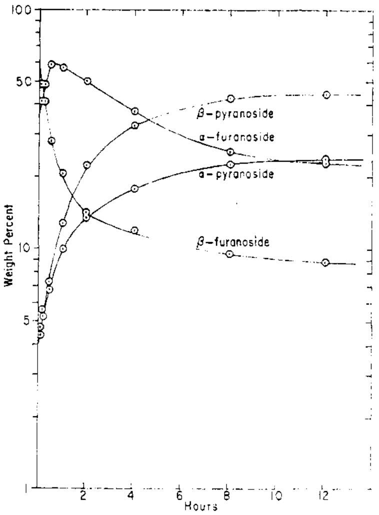

Fig. 4. Composition of methyl arabinoside mixture

logarithmic scale (Fig. 2) and the various curves extrapolated back to zero time, it appears that the various methyl mannosides are produced from mannose in the proportion of about 55% α-mannofuranoside, 31% β-mannofuranoside, 11% α-mannopyranoside, and 3% β-mannopyranoside, making the rate constants 0.61, 0.34, 0.12, and 0.03, respectively. The final equilibrium mixture, reached after a reflux period of seventy-two hours contains 89% α-mannopyranoside, 7% β-mannopyranoside, and 2% each of the mannofuranosides. This same equilibrium mixture was also reached upon refluxing α-mannopyranoside with Dowex-50 in methyl alcohol for the same length of time.

Figs. 3 and 4 for reaction of L-arabinose are comparable to Figs. 1 and 2 for D-mannose. L-Arabinose was found to disappear at a first order rate of 3.6 and in this case also it is evident, from the absence of initial points of inflection in their curves, that both α- and β-pyranosides are formed directly from arabinose as well as from the furanosides. The initial composition of the methyl arabinoside mixture, obtained by extrapolation of the log curves as in the case of the methyl mannosides, is estimated to be 36% α-arabinofuranoside, 56% β-arabinofuranoside, and 4% of each of the pyranosides, making the rate constants 1.3, 2.0, 0.15, and 0.15, respectively. The final equilibrium mixture, reached after twenty-four hours, contains 24% α-arabinopyranoside, 45% β-arabinopyranoside, 23% α-arabinofuranoside, and 8% β-arabinofuranoside. Methyl β-L-arabinopyranoside produced this same equilibrium mixture when refluxed for the same length of time with Dowex-50 methyl alcohol. Methyl α-L-arabinopyranoside apparently also yields the same equilibrium mixture upon similar treatment.

It can be concluded that in both of the methyl glycoside formations studied all of the four possible methyl glycosides are formed directly from the initial sugar and that all of the methyl glycosides formed are readily inter-convertible in acidic boiling methyl alcohol. A true equilibrium mixture is finally reached and the same mixture is produced whether starting with the reducing sugar or with any of the methyl glycosides.

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