before. After removing the liquid ammonia the product was extracted with chloroform and distilled giving the hepta-*O*-methyl derivative V as a colorless liquid, 1.94 g., b.p. (bath temp.) 185–190° (0.003 mm.), $n^{27}D$ 1.4411, $[\alpha]^{26}D$ +16.9° (pure liquid), +9.7° in methanol (*c* 7). The substance was insoluble in water.

Anal. Calcd. for $C_{18}H_{38}O_{10}$: C, 52.2; H, 9.25; OCH_3, 52.4. Found: C, 52.3; H, 9.25; OCH_3,[14] 50.1.

Hydrolysis of the Heptamethyl Ether V.—A suspension of the methyl ether (V, 1 g.) in *N* sulfuric acid (30 ml.) was refluxed for 3 hr. when the clear solution had become optically inactive. The solution was distilled at atmospheric pressure and the first 5 ml. of distillate was treated with *p*-nitrophenylhydrazine[10] whereby there was produced rapidly methoxyacetaldehyde *p*-nitrophenylhydrazone,[15] m.p. and mixed m.p. 116° (after recrystallization from ethanol–water (2:3)).

The aqueous, acidic distillation residue after removal of the methoxyacetaldehyde–water azeotrope, was saturated with ammonium sulfate and extracted with ether. The dried (Na_2SO_4), combined extracts were evaporated and the sirupy product distilled giving: fraction 1, 1,3-di-*O*-methyl-glycerol (0.102 g.), b.p. (bath temp.) 1 atm., 180–190°, $n^{31}D$ 1.4165. Fraction 2, a mixture of 1,3-di-*O*-methyl-glycerol and 1,4-di-*O*-methyl-erythritol (0.067 g.), b.p. (bath temp.) 145–150° (30 mm.), $n^{31}D$ 1.4223. Fraction 3, 1,4-di-*O*-methyl-erythritol (0.044 g.), b.p. (bath temp.), 180–190° (30 mm.), $n^{27}D$ 1.4385, R_f (butan-1-ol–ethanol–water (4:1:5) 0.65.

Treatment of fraction 1 (52 mg.) in pyridine (3 ml.) with *p*-nitrobenzoyl chloride (150 mg.) as previously described[10] afforded 1,3-di-*O*-methylglycerol *p*-nitrobenzoate, m.p. and mixed m.p. 41.5,[10] after recrystallization from light petroleum ether.

Fraction 3 (40 mg.) was treated in pyridine (3 ml.) with *p*-toluenesulfonyl chloride (150 mg.) for 1 day at room temperature and for 10 min. at 80–85°. The reaction mixture was cooled, poured into ice-water and the crystals of 1,4-di-*O*-methyl-2,3-di-*O*-tosyl-erythritol so formed were filtered, washed with water and recrystallized from ethanol, m.p. and mixed m.p. 140°.

Anal. Calcd. for $C_{20}H_{26}O_8S_2$: C, 52.4; H, 5.7; S, 13.9. Found: C, 52.2; H, 5.8; S, 13.9.

ST. PAUL, MINN.

(14) G. Gran, *Svensk Papperstidn.*, **56**, 179 (1953).

(15) N. L. Drake, H. M. Duvall, T. L. Jacobs, H. T. Thompson and H. M. Sonnichsen, THIS JOURNAL, **60**, 73 (1938).

[CONTRIBUTION FROM DIVISION OF CHEMISTRY, NATIONAL BUREAU OF STANDARDS]

Branched-chain Higher Sugars. I. A 9-Aldo-4-*C*-formyl-nonose Derivative[1,2]

BY ROBERT SCHAFFER AND HORACE S. ISBELL

RECEIVED SEPTEMBER 19, 1958

Two molecules of 5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose in alkaline solution combine to form a branched-chain decose derivative (I) by an aldol condensation. An explanation is offered for the occurrence of this condensation, which is not a typical carbohydrate reaction. A proof of the complete structure and configuration of I is presented and the compound is named 9-aldo-4-*C*-formyl-1,2:8,9-di-*O*-isopropylidene-L-*xylo*-L-*ido*-nono-1,4:9,6-difurano-4(1),7-α-pyranose.

Introduction

In a Communication to the Editor,[3] the authors pointed out that branched-chain aldoses containing 8 to 14 carbon atoms can be obtained in reasonably good yield by aldol condensation of suitable sugar derivatives. The present paper describes work establishing the structure of the branched-chain decose derivative I obtained from 5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose (II)[4,5] by treatment with alkali.

The aldol condensation occurs with two-carbon and three-carbon hydroxy-aldehydes, hydroxy-ketones and *O*-substituted hydroxy-aldehydes.[6] Although, prior to the present work, a variety of sugars had been synthesized by aldol condensations, the only products reported from tetroses or higher sugars are a heptulose[7] and a dodecitol.[8] (The latter was separated from an electrolyzed alkaline hexose mixture and its synthesis may be considered to have included an aldol condensation.)

The aldol condensation involves two molecules, one in the aldehyde form and the other in the enol form. Presence of both forms is necessary for the reaction to take place. Under the conditions used in aldol condensations, tetroses and higher reducing sugars establish equilibrium states consisting of furanose and pyranose modifications, together with small proportions of the open-chain aldehyde and enol forms. However, the enol form of the sugar is very reactive and undergoes isomerization and degradation reactions in competition with the aldol condensation. On account of this complication and the low concentration of the aldehyde form, reducing sugars in general do not undergo noticeable aldol formation. With substances in which ring closure and isomerization reactions are blocked by substituent groups, the tendency for aldol condensation should be greatly enhanced by the resulting presence of more of the free aldehyde and enediol forms in the reaction mixture. With substance II, used in the present study, the fused-ring structure prevents the aldehyde group at carbon 5 from forming either a pyranose or a furanose ring, and it restricts enolization to the formation of the 4,5-enediol. Hence, it is not surprising that, on treatment with aqueous calcium hydroxide, this compound undergoes aldol condensation to give a product shown to be the branched-chain decose derivative I.

The structure of I was assigned on the basis of the following evidence: (a) The analysis corresponds to the formula $(C_8H_{12}O_5)_n$ and the molecular weight corresponds to the formula $C_{16}H_{24}O_{10}$. This formula is twice that of the monomeric form of the parent substance II. Hence it appears that the

(1) This work was sponsored by the Division of Research, Atomic Energy Commission.

(2) Presented before the Division of Carbohydrate Chemistry at the 132nd Meeting of the American Chemical Society at New York, N. Y., September 11, 1957.

(3) R. Schaffer and H. S. Isbell, THIS JOURNAL, **80**, 756 (1958).

(4) K. Iwadare, *Bull. Chem. Soc. Japan*, **16**, 40 (1941).

(5) R. Schaffer and H. S. Isbell, THIS JOURNAL, **79**, 3864 (1957).

(6) J. C. Sowden, in "The Carbohydrates," W. W. Pigman, ed., Academic Press, Inc., New York, N. Y., 1957, pp. 113–114.

(7) L. Hough and J. K. N. Jones, *Nature*, **167**, 180 (1951).

(8) M. L. Wolfrom, W. W. Binkley, C. C. Spencer and B. W. Lew, THIS JOURNAL, **73**, 3357 (1951).

compound is formed by self-combination of two molecules of II.

(b) The substance does not react with sodium metaperiodate. Therefore, the compound does not have two or more contiguous hydroxyl groups and excludes the possibility that the substance is an acyloin condensation product.

(c) The substance reacts in alkaline solution with one mole of iodine per $C_{16}H_{24}O_{10}$ to give a monobasic acid that was isolated as a crystalline sodium salt III. Thus, it has one aldose reducing group. This excludes the possibility of a dimer of an epimer of II.

(d) The infrared absorption spectrum of the solid substance does not show the presence of a free carbonyl group; hence, the reducing aldose group must be present as a cyclic hemiacetal in the crystalline compound.

(e) Removal of the two isopropylidene groups of III by acid hydrolysis gives a product (V) which reacts with two moles of iodine per mole, as required for a monobasic acid having two aldehyde groups. Thus the parent substance I must be a derivative of a branched-chain trialdehyde.

(f) Prolonged acetylation of I with acetic anhydride and pyridine yields a triacetate IX. This establishes the presence of three free hydroxyl groups. Reduction of I with sodium borohydride gives X, a substance that on acetylation yields a tetraacetate XI. In view of the lack of absorption bands in the infrared spectrum of I, corresponding to the presence of a carbonyl group, and from the fact that I yields only a triacetate (whereas its reduction product X yields a tetraacetate), it follows that I has two alcoholic hydroxyl groups and a third in a hemiacetal ring structure.

(g) An aldol condensation of two molecules of II gives a structure consistent with the foregoing properties. Construction of a molecular model for I shows that the only way in which the aldehyde group attached to carbon 4 could form a ring is with the hydroxyl group of carbon 7 to give a pyranose. Hence compound I must have a 4(1),7-pyranose ring. The preceding observations establish the general structure of I. Other evidence is required for the assignment of configuration.

In the aldol condensation, two molecules of II so combine that carbon atoms 1 through 4 and 4(1) of I are derived from carbon atoms 1 to 5 of the molecule of II reacting in the enol form; and carbon atoms 9 to 5 of I are derived from carbon atoms 1 to 5 of a molecule of II reacting in the carbonyl form. The furanose ring in both molecules of II would be expected to remain intact, and no change in the configurations of carbon atoms 1 to 3 of the reacting species seems probable. Hence, the location of the two dioxolane rings in the product, and the configurations of carbon atoms 1 to 3 and 7 to 9 are predictable. In the condensation, one molecule of II is turned through 180°, causing an apparent change in configuration, and the resulting compound must have, at carbon atoms 1 to 3 and 7 to 9, the configurations shown in I. The configurations at carbon atoms 4 and 6 cannot be predicted because the asymmetry at these locations has been disturbed. The configurations for these atoms and carbon atom 5 must be assigned by other means.

Substance I shows a preferential hydrolysis of one of its isopropylidene groups in dilute acid at room temperature; the resulting monoisopropylidene derivative XIII was obtained in crystalline form. The location of the more acid-sensitive isopropylidene group of I was ascertained by treating the hydrolytic product XIII with excess periodate under such conditions that the remaining isopropylidene group was not hydrolyzed. The oxidation product thus obtained was reduced with sodium borohydride, and the isopropylidene group of the reduced product was removed by acid hydrolysis. The sugar in the hydrolyzate was separated by paper chromatography, and identified as xylose. From the considerations given above for the configurations within the furanose rings of I, it is clear that the fragment is D-xylose. This fragment could arise only from XIII, by oxidation to II, reduction of II to 1,2-*O*-isopropylidene-D-xylose, and hydrolysis to D-xylose. The degradation of XIII to D-xylose discloses that the configurations of carbon atoms 6 to 9 are the same as they were in II.

By reaction of XIII with only two moles of periodate per mole, partially degraded products are obtained. After extraction of these with ethyl acetate and acid hydrolysis of the extracted material to remove the isopropylidene group, glucuronic acid was separated by paper chromatography. (Cleavage of the 3,4- and 4,4(1)-carbon bonds of XIII by periodate gives 1,2-*O*-isopropylidene-D-glucofuranuronic acid, and hydrolysis of the latter by acid yields D-glucuronic acid.) The production of this acid confirms the configurations of the carbon atoms which had been revealed by the separation of D-xylose. Furthermore, it establishes both the configuration at carbon atom 5, and the location of the branch at carbon atom 4. Hence, it may be concluded that the substance is a 9-aldo-4-*C*-formyl-nonose derivative with an L-*xylo*-L-*altro* or an L-*xylo*-L-*ido* configuration. A decision between the two possibilities can be reached by a consideration of steric factors and of the relative positions of the glycosidic hydroxyl group at 4(1) and the hydroxyl groups at carbon atoms 3 and 5.

In both configurations, the 1,4-furanose ring is rigidly attached at carbon 4 to the pyranose ring by a spirane type of linkage, and the 9,6-furanose ring is fused to the pyranose ring at carbon atoms 6 and 7. Fusion to the 9,6-furanose ring imposes a B3 or 3B conformation[9] upon the pyranose ring. Molecular models in both configurations show that three, *cis*, axial substituents (other than hydrogen) are present on the pyranose ring in the 3B conformation. These are formed by the 1,4-furanose and 9,6-furanose rings. In the B3 conformation, only two, *trans*, axial substituents are present: one from the 1,4-furanose ring and the other from the hydroxyl group at carbon atom 5. In view of the instability of pyranose structures having three large axial groups on the same side of the ring, in

(9) R. E. Reeves, THIS JOURNAL, 71, 215 (1949).

all probability substance I has the B3 conformation. The conformations are represented in Fig. 1.

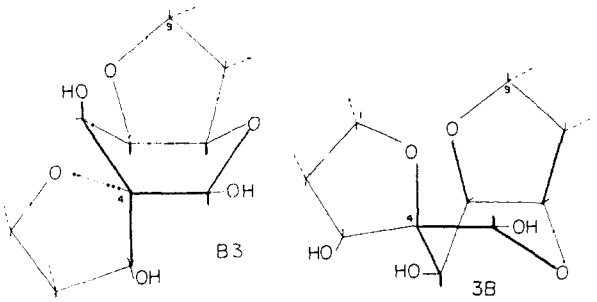


Fig. 1.—Partial structures of I in the L-*xylo*-L-*ido* configuration, illustrating the B3 and 3B conformations (with the axial bonds on the pyranose ring shown by heavy lines). For the two conformations of the L-*xylo*-L-*altro* configuration, the 1,4-furanose ring only is pivoted at carbon 4 through an angle of 180° to the plane of carbon atoms 4(1), 4 and 5. (Completed structures require isopropylidene groups on oxygen atoms at the dashed positions.)

With this conformation, the hydroxyl at carbon 5 in each of the two possible compounds is remote from the hydroxyl groups of carbon 3 and carbon 4(1); in the compound having the L-*xylo*-L-*altro* configuration, the hydroxyl at carbon 3 and the anomeric carbon at 4(1) are *cis* with respect to the 1,4-furanose ring; and in the compound having the L-*xylo*-L-*ido* configuration they are *trans*. One would anticipate that, if compound I had the L-*xylo*-L-*altro* configuration, it would give acetal, ketal or carbonate derivatives linking carbons 3 and 4(1). Attempts to prepare these derivatives were not successful. Also, with the L-*xylo*-L-*altro* configuration, the glycosidic hydroxyl group of the anomer with an equatorial glycosidic hydroxyl is in position to form the intramolecular hydrogen bond with the hydroxyl group of carbon atom 3. This structure should give the infrared absorption characteristic of an intramolecular hydrogen bond. No absorption of this character was found either for the crystalline substance or the amorphous, equilibrated material. Absence of evidence for a *cis* relationship of the hydroxyl group at carbon 3 and the anomeric carbon atom suggests that compound I has the L-*xylo*-L-*ido* configuration.

The stereochemistry of the aldol condensation would also favor formation of a compound with the configuration given in I. The main, directing influences in the enolic intermediate would be the presence of (a) the *cis*, fused, 5-membered rings, (b) the *endo* methyl group from the dioxolane ring, and (c) the hydroxyl group at carbon 3. The combined effect of (a) and (b) is to oppose condensation at carbon 4 from the *endo* side. The effect of (c) would hinder an *exo* condensation. The combined steric effects of (a) and (b), however, should predominate. The product would then have the 4(1)-aldehyde group on the *endo* side and, consequently, the L-*xylo*-L-*ido* configuration.

With this configuration, the 4(1),7-pyranose ring has the D-*talo* structure. Inasmuch as the pyranose entity has the D-configuration, and the mutarotation of I consists of a decrease in dextrorotation, the substance is related to α-D-talo-

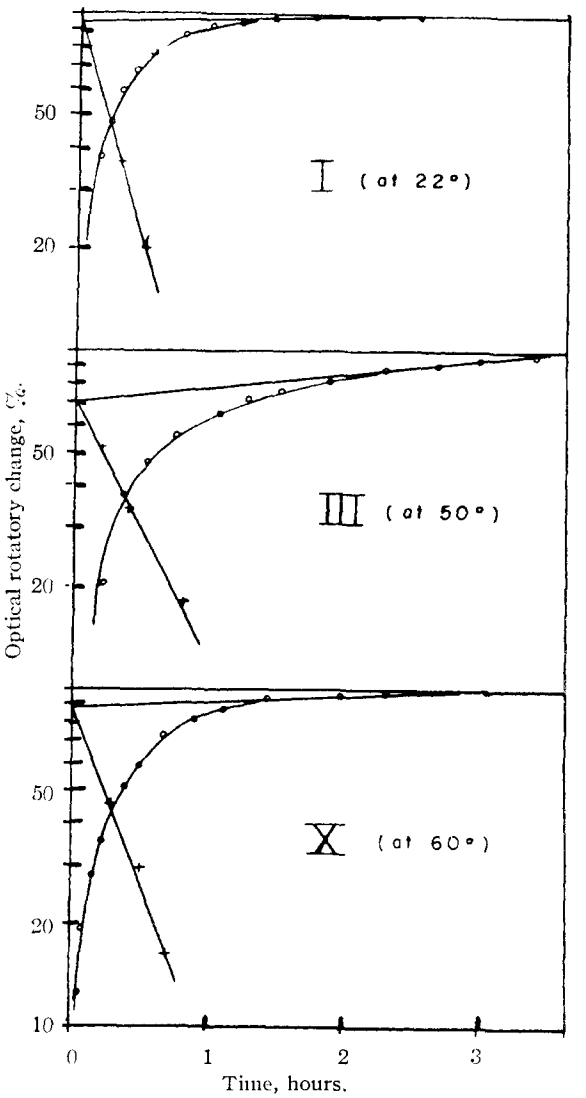


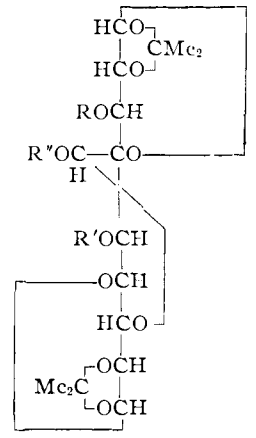
Fig. 2.—Semi-log graphs of changes in optical rotation of I, III and X upon acid hydrolysis showing for each system the experimental data (dots on the curved line), an extrapolation of the straight-line portion of the experimental curve to zero time, and the graphically obtained straight line (with crosses) representing the change in optical rotation for the faster hydrolysis step. The percentages plotted are based on these changes in specific rotations: I, +55.6° to +74.1°; III, −41° to +60°; and X, −2° to +52°.

pyranose. Present nomenclature rules[10] are not adequate for naming compound I. It will be designated provisionally as 9-aldo-4-*C*-formyl-1,2:8,9-di-*O*-isopropylidene-L-*xylo*-L-*ido*-nono-1,4:9,6-difurano-4(1),7-α-pyranose.

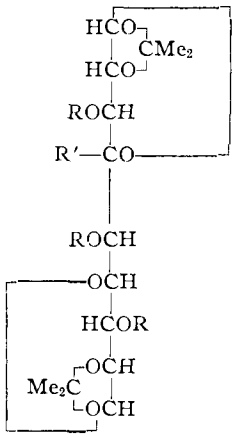
The pronounced susceptibility to hydrolysis of the 1,2-*O*-isopropylidene group of compound I by acid is noteworthy, because the two isopropylidene groups present in the substance are similar in that they are fused at the anomeric and adjacent carbon atoms, to furanose rings. The faster hydrolysis of the 1,2-*O*-isopropylidene group cannot be related to the uncommon linkage of its fused furanose ring to a tertiary carbon atom because, under similar hydrolytic conditions, neither the

(10) *Chem. Eng. News*, **31**, 1776 (1953).

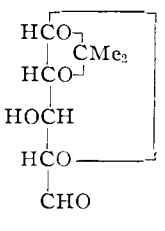
corresponding acid IV nor the corresponding reduced product X show this sensitivity (Fig. 2). The difference in behavior between compound I and compounds IV and X may arise from the presence of the additional ring (the pyranose ring) in I. It is of interest to note that, although compound I exhibits mutarotation, its oxidation by hypoiodite is unusually slow, and no reaction products with phenylhydrazine, (2,4-dinitrophenyl)-hydrazine or hydroxylamine could be separated. Thus, the pyranose structure is extraordinarily stable and there is little tendency toward formation of the open-chain aldehyde.



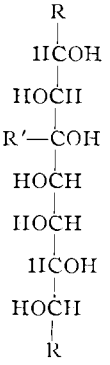
I, R, R′, R″ = H
VIII, R = H
R′, R″ = Ac
IX, R, R′, R″ = Ac

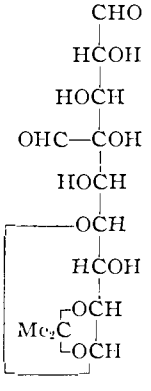


III, R = H
R′ = COONa
IV, R = H
R′ = COOH
X, R = H
R′ = CH_2OH
XI, R = Ac
R′ = CH_2OAc



II





V,[a] R = CHO
R′ = COOH
VI, R, R′ = COOH
XII,[a] R, R′ = CHO

XIII[a]

[a] These substances exist in hemiacetal ring forms.

Acetylation of I takes place at two distinct rates (determined by observations of the change in optical rotation during acetylation). By interrupting the acetylation after a reaction time corresponding approximately to completion of the faster change, a diacetylated product VIII is obtained in good yield. Acetate VIII is inert to oxidation by bromine in an acetate-buffered solution; hence, its anomeric hydroxyl group is acetylated. The location of the unsubstituted hydroxyl group has not been ascertained; however, examination of the molecular model of compound I in the proposed configuration and conformation shows that the hydroxyl group at carbon atom 3 would be somewhat shielded from reaction by the hydrogen atoms of carbons 5 and 6. This would diminish its rate of acetylation, and the diacetylated product may then be the 4(1)5-di-*O*-acetyl derivative of I.

Although compound III would be expected to give a trisubstituted derivative on reaction with methanesulfonyl chloride, the product isolated, VII, contains only two mesyl groups. Resistance to the introduction of the third mesyl group might be due to intermediate formation of a mixed anhydride derived from the salt III and the methanesulfonyl chloride. Further work is needed, however, to establish the structure of the di-*O*-mesyl derivative and, consequently, a definitive structure for it has not been shown.

Experimental

Preparation of 9-Aldo-4-*C*-formyl-1,2:8,9-di-*O*-isopropylidene-L-*xylo*-L-*ido*-nono-1,4:9,6-difurano-4(1),7-α-pyranose (I).—Six grams of finely powdered, crystalline II (prepared by the method given in reference 5) was dissolved in 0.5 l. of 0.05 *N* calcium hydroxide (prepared at 8°). After 1 day at 22°, the mixture was cooled to 0°, passed through a column containing 50 ml. each of ice-cold cation-[11] and anion-exchange[12] resins, and then through a carbon-coated filter. Dilute sodium hydroxide was added to a *p*H of 6. Upon concentration of the solution under reduced pressure, the product crystallized. Recrystallization from ethanol gave 1.8 g. (30% yield) of I, m.p. 235° with gradual decomposition, $[\alpha]^{20}D$ +62° (initial) changing in 1 hr. to +55.6° (*c* 1, water). In formamide, the molecular weight determined by freezing point depression was 374. The calculated value is 376. The product reacted only very slowly with hot Fehling solution, and did not react in 24 hr. with sodium metaperiodate.

Anal. Calcd. for $C_{16}H_{24}O_{10}$: C, 51.1; H, 6.4. Found: C, 50.7; H, 6.3.

A quantitative hypoiodite oxidation,[13] modified by employing a 40-min. time for addition of alkali and triiodide, and allowing an additional 20 min. before titration of excess oxidant, showed 0.93 mole of iodine consumed per mole of I.

A crystalline product was not obtained upon reaction of compound I with phenylhydrazine. With (2,4-dinitrophenyl)-hydrazine and with hydroxylamine, only unreacted I was isolated.

Compound I in acetone containing sulfuric acid yielded after 20 hr. mainly recovered I and a sirupy mother liquor. With benzaldehyde plus sulfuric acid or zinc chloride, and with paraldehyde plus sulfuric acid, only sirupy products were obtained. In an anhydrous pyridine solution, compound I reacts with phosgene; however, the product reacts readily with water to give I, which was recovered nearly quantitatively. Infrared absorption measurements were made with crystalline I and with amorphous I in potassium chloride pellets.[14] No absorption characteristic of intramolecular hydrogen bonding was detected.

Acid Hydrolysis of I.—A solution of 0.235 g. of I in 25 ml. of 0.25 *N* sulfuric acid at 22° exhibited a change in optical rotation that occurred with a half-time of 13 min. Examination of aliquots of the hydrolysis mixture, by testing periodically by periodate oxidation (4–4.5 moles of periodate

(11) Amberlite 1R-120H, Rohm and Haas Co., Philadelphia, Pa.

(12) Duolite A-4, Chemical Process Co., Redwood City, Calif.

(13) G. M. Kline and S. F. Acree, *J. Research Natl. Bur. Standards*, **5**, 1063 (1930).

(14) The infrared spectra of the compounds considered in this paper will be presented in a forthcoming publication. Measurements in the 2–15 μ region were made with a Beckman IR4 spectrometer using crystalline samples pressed into pellets of potassium chloride or iodide. For the spectrum of the α- and β-forms of I, an equilibrium solution of I in water containing potassium chloride was freeze-dried, and the dried residue pressed into a pellet.

consumed per mole after 2 to 3 hr. of hydrolysis), showed that the change is due to hydrolysis of one isopropylidene group. The partially hydrolyzed product was separated and found to be XIII. Complete hydrolysis of I at 22° requires many days. At 90°, complete hydrolysis takes less than 2 hr. The specific rotation for the hydrolyzed product, assumed to be 9-aldo-4-*C*-formyl-L-*xylo*-L-*ido*-nonose (XII), is $[\alpha]^{20}D$ +56°. Figure 2 shows the changes in optical rotation occurring during the hydrolysis.

Configuration of Carbon Atoms 6–9 (Degradation of I to Xylose).—A sample of I was hydrolyzed for 2 hr. at 22° in 0.25 *N* sulfuric acid, oxidized with excess sodium metaperiodate, deionized, reduced with excess sodium borohydride, and then hydrolyzed with 0.1 *N* sulfuric acid at reflux temperature, again deionized, and finally chromatographed on paper. Xylose was detected by means of an aniline hydrogen phthalate spray on chromatograms developed with butanol–ethanol–water (4:1:5) and butanol–acetic acid–water (4:1:5).

Configuration of Carbon Atoms 5–9 (Degradation of I to Glucuronic Acid).—Another partially hydrolyzed sample of I, after deionization, was allowed to react to completion with 2 moles of periodate per mole of sample, and then neutralized with dilute sodium hydroxide. After evaporation to dryness, trituration with ethanol, and filtration, the residue was dissolved in water and treated with cation-exchange[11] resin. The acidic solution was extracted with ethyl acetate and the extracts were concentrated. A solution of the concentrate in water was refluxed for 1 hr. with a little cation-exchange resin.[11] Paper chromatography of an aliquot of this hydrolyzate (with the solvents and spray noted above) showed the two spots corresponding to glucuronic acid and glucuronolactone.

Preparation of 9-Aldo-4-*C*-formyl-8,9-*O*-isopropylidene-L-*xylo*-L-*ido*-nono-9,6-furanose (XIII).—One gram of I in 100 ml. of 0.25 *N* sulfuric acid was kept at 22° for 2 hr., treated with 50 ml. of anion-exchange resin,[12] and concentrated under reduced pressure to a sirup. Crystalline XIII was obtained from a solution of the sirup in a little 2-propanol and water; yield 70%, m.p. 136° with evolution of gas, on immersion in bath at 136°; m.p. about 190° on gradual heating; $[\alpha]^{22}D$ +46° → +80° in 6 hr. (*c* 1, water). Before analysis, the sample was heated for 2 hr. at 110° *in vacuo* over phosphorus pentoxide.

Anal. Calcd. for $C_{13}H_{20}O_{10}$: C, 46.4; H, 6.0. Found: C, 46.4; H, 6.1.

Preparation of Sodium 9-Aldo-1,2:8,9-di-*O*-isopropylidene-L-*xylo*-L-*ido*-nono-1,4:9,6-difurano-4-*C*-carboxylate Hydrate (III).—One gram of I in 100 ml. of water was treated dropwise, over a 2-hr. interval, with 70 ml. of a solution 0.1 *N* in iodine and 0.25 *N* in potassium iodide, and with 110 ml. of 0.1 *N* sodium hydroxide. After an additional 1-hr. period, the solution was cooled to 0° and passed through a column containing 40 ml. of ice-cold cation-exchange[11] resin, and the effluent was run into a stirred slurry of 3 g. of silver carbonate in water. This mixture was filtered, and passed, ice-cold, through an additional 20 ml. of cation-exchange[11] resin. The effluent was neutralized with dilute sodium hydroxide, and concentrated. Compound III crystallized from a concentrated solution in aqueous ethanol; yield 1.1 g., $[\alpha]^{20}D$ −20.3° (*c* 2, water).

Anal. Calcd. for $C_{16}H_{23}O_{11}Na \cdot 2.5H_2O$: C, 41.8; H, 6.1; Na, 5.0. Found: C, 42.3; H, 6.0; Na, 4.9.

A solution of 0.0005 mole of III in 10 ml. of 0.25 *N* sulfuric acid ($[\alpha]^{22}D$ initial, −45°) exhibits a very slow change in optical rotation at room temperature, and at 50° a more rapid change. Graphic analysis of the optical rotatory data taken at 50° (Fig. 2) shows a fast reaction involving a large change in optical rotation with an approximate half-time of 27 min., and then a second but smaller change, which ceases after a total of 7 to 8 hr. At 100°, a solution of similar composition proceeds to the same final $[\alpha]^{20}D$ of +84° in 20 min. The value +84° was calculated for the presumed product, 9-aldo-L-*xylo*-L-*ido*-nonose-4-*C*-carboxylic acid (V). A solution of this dialdehyde-acid (prepared by refluxing, for 20 min., a solution of 0.121 g. of III in 5 ml. of 0.3 *N* sulfuric acid) was treated with 0.6 g. of barium carbonate, filtered and the filtrate concentrated twice under reduced pressure with added water. The sirupy concentrate, in water, consumed 0.000505 mole of iodine or 96% of the amount required for 0.000263 mole of dialdehyde. Presumably, the ten-carbon, tricarboxylic acid VI was formed, but this has not been isolated in a crystalline state.

Preparation of 9-Aldo-1,2:8,9-di-*O*-isopropylidene-di-*O*-mesyl-L-*xylo*-L-*ido*-nono-1,4:9,6-difurano-4-*C*-carboxylic Acid (VII).—One gram of III was freed of water of crystallization by heating for 1.5 hr. at 110° *in vacuo* over phosphorus pentoxide. An ice-cold, stirred solution of the dried salt in 60 ml. of anhydrous pyridine was treated with 2 ml. of methanesulfonyl chloride. After 20 hr. at room temperature, 3 ml. of water was added dropwise, the mixture filtered, and the filtrate neutralized with aqueous sodium hydroxide and concentrated under reduced pressure to about 5 ml. The concentrate was diluted with water to 25 ml., and dilute sulfuric acid was added to a *p*H of 1.9. The acidified solution was extracted with chloroform, and then readjusted to a *p*H of 1.9, re-extracted, and the combined extracts concentrated. Compound VII crystallized from a solution of the concentrate in ethyl acetate; yield 0.93 g., m.p. 197–199°, $[\alpha]^{20}D$ −62.5° (*c* 1, ethyl acetate), neut. equiv. 548 (calcd. 548). Compound VII reacts instantly as an acid to litmus paper.

Anal. Calcd. for $C_{18}H_{28}O_{15}S_2$: S, 11.7. Found: S, 11.8.

Preparation of 4(1),5-Di-*O*-acetyl-9-aldo-1,2:8,9-di-*O*-isopropylidene-L-*xylo*-L-*ido*-nono-1,4:9,6-difurano-4(1),7-α-pyranose (VIII).—A mixture of 0.2 g. of I in 6 ml. of pyridine and 4 ml. of acetic anhydride, after 30 min. at room temperature, was poured into 100 ml. of ice-water and freeze-dried. A solution of the residue in a few drops of ethanol plus water gave 0.12 g. of crystalline product. Recrystallization from ethanol plus pentane gave VIII combined with 1 mole of ethanol of crystallization per mole; m.p. 105° on rapid heating, or m.p. 155–175° on slow heating, $[\alpha]^{20}D$ +138° (*c* 0.75, ethanol).

Anal. Calcd. for $C_{20}H_{28}O_{12} \cdot C_2H_5OH$: C, 52.2; H, 6.8. Found: C, 52.4; H, 6.5.

Quantitative acetyl analysis[15] (4 hr. of refluxing of 0.1 g. of VIII in 10 ml. of 0.2 *N* sulfuric acid) showed 2.0 equivalents of acetic acid per mole; VIII was recovered unchanged after an attempted oxidation (24 hr.) with bromine in an aqueous ethanol solution containing sodium acetate and acetic acid.

Preparation of 3,4(1),5-Tri-*O*-acetyl-9-aldo-1,2:8,9-di-*O*-isopropylidene-L-*xylo*-L-*ido*-nono-1,4:9,6-difurano-4(1),7-α-pyranose (IX).—A solution of 0.2 g. of I in 6 ml. of pyridine and 3.6 ml. of acetic anhydride, after overnight reaction, was cooled to 0° and poured into 200 ml. of ice-water. The triacetate crystallized quickly from the stirred aqueous mixture. The crude product (weighing 0.253 g.) was recrystallized from ethanol; m.p. 222.5–223.5°, $[\alpha]^{20}D$ +145° (*c* 0.5, ethanol).

Anal. Calcd. for $C_{22}H_{30}O_{13}$: C, 52.6; H, 6.0. Found: C, 52.3; H, 6.2; quant. acetyl analysis[15] showed 2.9 acetyl groups per molecule.

Preparation of 9-Aldo-4-*C*-(hydroxymethyl)-1,2:8,9-di-*O*-isopropylidene-L-*xylo*-L-*ido*-nono-1,4:9,6-difuranose (X).—A stirred ice-cold solution of 0.5 g. of I in 50 ml. of water was treated with 0.5 g. of sodium borohydride. One hr. later, 15 ml. of ice-cold cation-exchange resin[11] was added. After stirring for 0.5 hr., the mixture was filtered and the filtrate concentrated *in vacuo*. The concentrate was dissolved in methanol and reconcentrated several times with added methanol to remove the methyl borate. The residue finally was dissolved in a small volume of ethanol, from which X crystallized; yield 0.43 g., m.p. 170–172°, $[\alpha]^{20}D$ +5.8° (*c* 1.3, ethanol).

Anal. Calcd. for $C_{16}H_{26}O_{10}$: C, 50.8; H, 6.9. Found: C, 50.9; H, 6.9.

A graph of optical rotatory changes accompanying acid hydrolysis of a solution of 0.107 g. of X in 10 ml. of 0.25 *N* sulfuric acid at 60° is shown in Fig. 2. The half-time for hydrolysis of one isopropylidene group is 18 min.

Preparation of 3,4(1),5,7-Tetra-*O*-acetyl-9-aldo-4-*C*-(hydroxymethyl)-1,2:8,9-di-*O*-isopropylidene-L-*xylo*-L-*ido*-nono-1,4:9,6-difuranose (XI).—A mixture of 0.3 g. of X in 7 ml. of pyridine and 5 ml. of acetic anhydride was kept for 4 days at room temperature. It then was poured into 100 ml. of ice-water, and, after stirring for an hour, freeze-dried. The dried residue, dissolved in a little methanol, crystallized in quantitative yield on addition of water; m.p. 119–121°, $[\alpha]^{20}D$ +8.8° (*c* 0.4, methanol).

(15) D. H. Brauns, THIS JOURNAL, **47**, 1294 (1925).

Anal. Calcd. for $C_{24}H_{34}O_{14}$: C, 52.8; H, 6.2. Found: C, 53.0; H, 6.3; quant. acetyl analysis showed 3.9 eq. of acetic acid per mole of XI.

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WASHINGTON, D. C.

[CONTRIBUTION FROM THE ROHM & HAAS CO., REDSTONE ARSENAL RESEARCH DIVISION]

Amino-derivatives of 1,2-Dichlorohexafluorocyclopentene-1[1]

BY CHARLES O. PARKER

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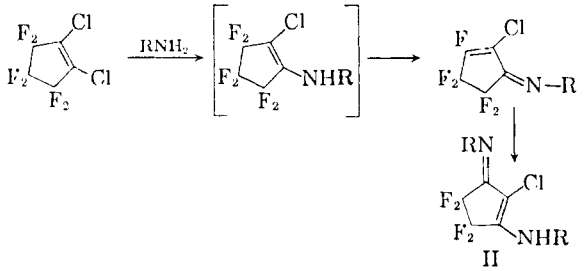
1,2-Dichlorohexafluorocyclopentene-1 reacted with secondary aliphatic amines and with sodium azide to give products monosubstituted in the 1-position. With ammonia and primary aliphatic amines, derivatives of 1-amino-2-chloro-3-iminotetrafluorocyclopentene-1 were formed. The latter series of products exhibited amphoteric properties, forming either cationic or anionic salts. The anions underwent alkylation on nitrogen. Both series of amino derivatives were susceptible to acid hydrolysis giving derivatives of 1-amino-2-chloro-3-ketotetrafluorocyclopentene-1.

It is the purpose of this paper to describe the rather facile reactions by which 1,2-dichlorohexafluorocyclopentene-1 (I) is converted into amino derivatives, to describe the chemical and physical properties of these previously unreported compounds and to relate these data to the structural assignments which have been made.

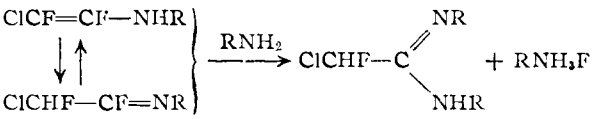
The amino-imines II formed by reaction of I with ammonia and primary aliphatic amines were found to be stable compounds having symmetrical structures. The four fluorine atoms were equivalent and the alkyl hydrogen atoms were equivalent, measured when the compounds were in solution. Further discussion of this feature may be found in the section on n.m.r. spectra. The positions of the ultraviolet absorption maxima of the amino-imines confirmed the presence of conjugated unsaturation in these molecules. These data can be correlated with only one structural arrangement of the amino groups, *i.e.*, the 1,3-positions which flank the remaining chlorine atom. One can construct a fully credible sequence of steps which leads to such a structure. As indicated below this sequence might proceed *via* β-elimination of fluoride ion from the hypothetical monosubstituted product.



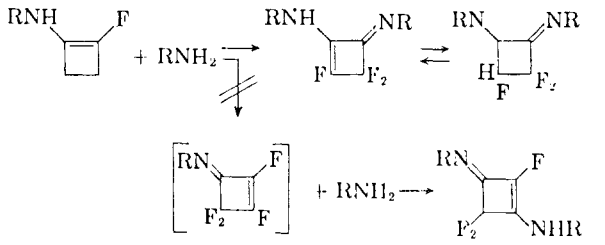
II

It is evident that structure II by either gain or loss of a proton is converted into ions either of which possesses unique symmetry of structure and charge distribution (see below).

Chlorofluoroölefins and perfluoroölefins (ethylenes) and perfluorocyclobutene also have been reported to form amino-imines by reaction with primary amines.[2] The ethylenes and cyclobutene both have been shown to react with nucleophilic reagents by an addition–elimination process.[2–5] The ethylenic adducts, after loss of hydrogen fluoride, cannot undergo a second stage β-elimination of fluoride ion and consequently attack of a second molecule of amine results in the formation of amidines (1,1-amino-imines). The cyclobutene-



imine intermediates supposedly have a choice between β-elimination of fluoride ion or the postulated second mole addition of amine analogous to the addition of alcohols.[6] If the formation of 1,2-amino-imines is correct as proposed by K. E. Rapp, *et al.*, it would seem that the explanation must involve a much lesser mobility of the double bond in the cyclobutene ring.



A few reactions of 1,2-dichlorohexafluorocyclopentene-1 (I) with nucleophilic reagents were investigated previously. The results were never published but manufacturers of I at one time cited this work in advertising the chemistry of I.[7] Since it is now evident that some of Latif's work was interpreted incorrectly, a brief account of the

(1) This research was carried out under Army Ordnance Contract DA-01-021-ORD-5135.

(2) K. E. Rapp, J. T. Barr, C. T. Bahner, J. D. Gibson and R. H. Lafferty, Jr., THIS JOURNAL, **72**, 3646 (1950).

(3) W. T. Miller, Jr., E. F. Fager and P. H. Griswold, *ibid.*, **70**, 431 (1948).

(4) K. E. Rapp, J. T. Barr, R. L. Pruett, C. T. Bahner, J. D. Gibson and R. H. Lafferty, Jr., *ibid.*, **74**, 749 (1952).

(5) W. T. Miller, Jr., and A. H. Fainberg, *ibid.*, **79**, 4164 (1957).

(6) J. D. Park, M. L. Sharrah and J. R. Lacher, *ibid.*, **71**, 2337 (1949).

(7) Hooker Electrochemical Co.