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THE SELECTIVE BOND CLEAVAGE OF ALDOHEXOSES BY THE IRON(III) CHLORIDE-CATALYZED PHOTOREACTION

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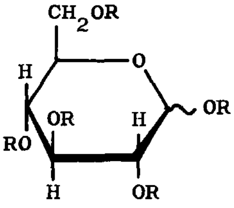
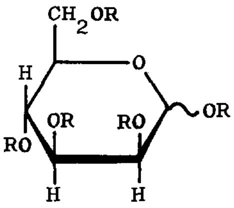
Photoreaction of D-glucose, D-mannose, and D-galactose in pyridine in the presence of iron(III) chloride induced a selective bond cleavage at C1-C2 position, and produced corresponding 4-O-formyl-D-aldopentopyranoses.

In our previous papers, we reported on the catalytic effects of titanium(IV) chloride1) and iron(III) chloride2) for the photoreaction of ketones and olefins, respectively. Some time ago, we reported that the irradiation of D-glucose, D-mannose, and D-galactose in methanol in the presence of titanium(IV) chloride induced a selective cleavage of the C5-C6 bond of the sugar molecules, and produced pentodialdose derivatives.3) In the present paper we will describe the effect of iron(III) chloride for the photoreaction of the aldohexoses, which induced a selective cleavage at the C1-C2 bond, producing aldopentose derivatives.

A pyridine solution (150 ml) of D-glucose (1a, 1.50 g, 8.3 mmol) and iron(III) chloride (8.3 mmol) was irradiated with a high-pressure mercury lamp in a Pyrex tube for 30 h while oxygen gas was bubbled through. Acetic anhydride (15 ml) was added to the solution and the solution was stirred for 12 h at room temperature. The solution was concentrated, washed with cold aqueous hydrochloric acid, and extracted with dichloromethane. The distillation of the product gave two fractions. The higher-boiling fraction, bp 160 °C/0.35 mmHg, which crystallized on standing was identified as D-glucose pentaacetate 1b by comparing with the authentic sample prepared by the known method.4) The lower-boiling fraction (Fraction A), bp 148-150 °C/0.35 mmHg, indicated two peaks on a gas chromatogram, and was shown to be an anomeric mixture of 1,2,3-tri-O-acetyl-4-O-formyl-D-arabinopyranose 4a in view of the following facts. The yields of 4a and 1b were 38% and 41%, respectively.



1



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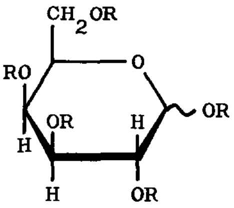
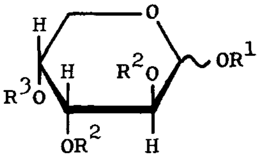


3

a: R = H, b: R = CH_3CO



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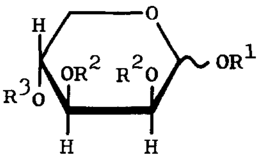
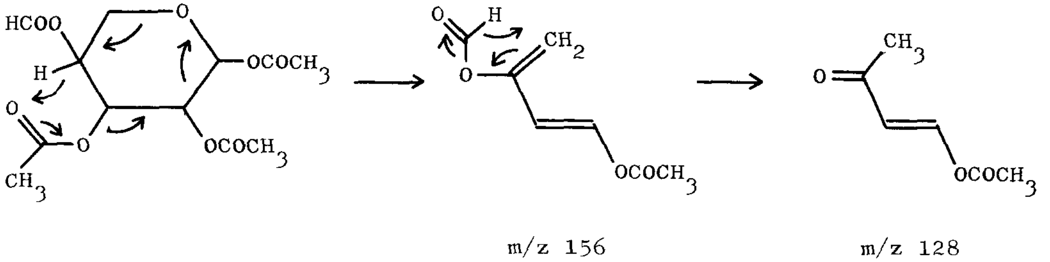


5

a: R^1, R^2 = CH_3CO; R^3 = CHO, b: R^1 = CH_3; R^2, R^3 = CH_3CO,
c: R^1, R^2, R^3 = H

When the Fraction A was treated with titanium(IV) chloride in methanol followed by acetylation with acetic anhydride-pyridine, an oil was obtained which showed three peaks on a gas chromatogram. The product was assigned as a mixture of methyl glycosides of D-arabinose triacetate (4b, and its furanoside form), because the same mixture was obtained by treating D-arabinose (4c) with titanium(IV) chloride in methanol followed by acetylation. The identity of the products was verified by ^{1}H-NMR, GC, and GC-MS analyses. The two components in the Fraction A indicated similar mass spectrum on a GC-MS analysis, thus showing that both components have the same ring system. The ^{1}H-NMR spectrum of the Fraction A showed signals at δ 1.97-2.15 (9H) for acetyl, δ 7.9 and 8.1 (1H) for formyl, δ 5.60 and 6.25 (1H) for C1-H, δ 5.0-5.5 (3H) for protons at C2-C4, and δ 3.8-4.1 (2H) for C5-methylene. The signal of the C5-methylene consisted of a pair of quartets with chemical shifts and coupling constants very close to those reported for α- and β-D-arabinopyranose tetraacetate.5) The position of the formate group was assigned at C4 in view of the mass fragmentation peaks at m/z 156 and 128, which could be ascribed to the ions depicted in the Scheme 1, referring to the general fragmentation pattern of acylated



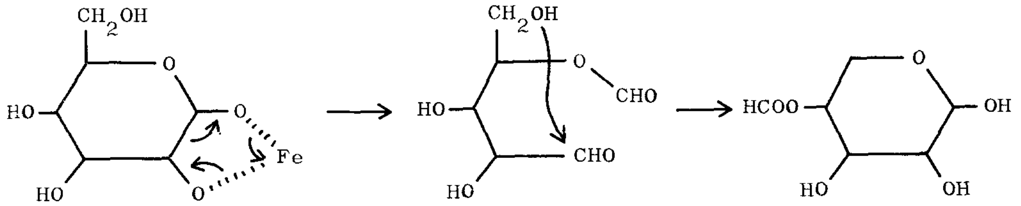
Scheme 1

pyranoses proposed by Biemann and his group.6)

Although D-mannose (2a) afforded the same product 4a under the same irradiation conditions, despite a lower yield of 17%, D-galactose (3a) gave an anomeric mixture of 1,2,3-tri-O-acetyl-4-O-formyl-D-lyxopyranose (5a) in 35% yield under the same conditions. In both cases the starting materials were recovered as pentaacetate 2b and 3b in 74% and 36% yields, respectively. The structure 5a was confirmed by ^{13}C- and ^{1}H-NMR, and by deriving the product into a mixture of D-lyxoside derivatives (5b, and its furanoside equivalents), which was identical with that obtained from D-lyxose (5c) in the same way as described for arabinose. The ^{1}H-NMR signal of the C5-methylene portion of 5a was very similar to that of D-lyxopyranose tetraacetate.5) Both 4a and 5a showed similar ^{1}H-NMR spectra with minor differences in coupling pattern.

All the photoreactions were quite clean, and the amounts of other products were negligible on a GC analysis. Both photoirradiation and the presence of iron(III) chloride were necessary for this reaction. However, the presence of oxygen was not requisite, although it enhanced the reactivity.

We schemed the present reaction as involving an electron transfer within an iron chelate formed from the 1,2-diol system at the C1 and C2 positions of the pyranoses, followed by recyclization of the fission products as shown in the Scheme 2. In support of this, methyl D-glucopyranoside and 1,2-O-isopropylidene-α-D-glucofuranose lacking this system did not undergo the present



Scheme 2

reaction, and the starting materials were recovered as acetates after the acetylation. It should be noted that iron(III) chloride induced the C1-C2 bond cleavage, while titanium(IV) chloride induced the C5-C6 bond cleavage upon irradiation. The present reaction is reminiscent of the oxidation by lead(IV) acetate which cleaves the C1-C2 bond of the hexoses most efficiently.7) However, the two reactions differ in that (1) the photoassisted oxidation by iron(III) chloride is quite selective, no further cleavage at the other bonds being observed, in contrast to the reaction by lead(IV) acetate or sodium periodate, which induces further bond cleavage producing lower sugars as byproducts,7) and (2) the present reaction proceeds through a pyranose form, in contrast to the oxidation by lead(IV) acetate which proceeds through a furanose form, producing 3-O-formyl pentoses.7) The presence of molecular oxygen is subsidiary, presumably serving only to oxidize the resulted iron(II) to iron(III).

Recently, Shiraishi and his group reported the iron(III) chloride-catalyzed photoreaction of D-fructose, D-glucose, and D-mannose in water.8) They speculated that the reaction proceeded through a formation of an iron chelate. Under their conditions, however, the reaction proceeded beyond the initial stage of C1-C2 bond fission, producing D-erythrose as major product, and in some cases, accompanied by D-arabinose.

The present reaction is characteristic in that the reaction stops at the first stage of the bond cleavage, producing pentoses in which only C4-OH is protected by formyl group. It is hoped that the further manipulation of the products could lead to a development of a novel synthon for introducing chiral centers into target molecules.

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