Preliminary communication

Oxidation of 2-deoxy-D-arabino-hexose ("2-deoxy-D-glucose") by alkaline hydrogen peroxide* †

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In prior publications, we have shown that, under alkaline conditions, hydrogen peroxide rapidly combines with carbohydrates having a free, or potentially free, carbonyl group, and that the resulting adduct decomposes in a manner characteristic of the structure involved. Adducts from α -hydroxy carbonyl compounds, in general, decompose with formation of a lower aldehyde and a carboxylic acid¹. By repetition of the process, aldoses², ketoses³, uronic acids⁴, and related compounds⁵⁻⁸ are degraded stepwise to formic acid, oxalic acid, and carbon dioxide.

Cleavage of the hydroperoxide adducts of the foregoing compounds is relatively rapid, and obscures slower reactions that are important for compounds lacking an α -hydroxyl group. Inasmuch as 2-deoxyaldoses lack this important feature, we undertook a study of the reactions of 2-deoxy-D-arabino-hexose ("2-deoxy-D-glucose", 1) with alkaline hydrogen peroxide. The reactions were found to be much more complicated than those of a normal aldose. Detailed study showed two successive processes, namely, (1) a primary process (see Scheme 1), presumably beginning with nucleophilic addition of hydrogen peroxide to the carbonyl form of the sugar, and (2) a secondary process, exemplified by the oxidation of D-arabinitol (7) (see Scheme 2), that, under more-severe conditions leads to complete degradation of the primary oxidation-products. The primary process, by way of a Bayer-Villiger type of reaction⁹, gives 2-deoxy-D-arabino-hexonic acid (5), D-arabinitol (7), 2-deoxy-D-arabino-hexono-1,4-lactone (9), and a small proportion of formic acid, whereas the secondary process affords formic acid in high yield.

It was found that the secondary process is accelerated by an increase in temperature and inhibited by magnesium ion. These results appeared to indicate that the secondary process depends on a reaction involving hydroxyl radicals. Study of the decomposition of hydrogen peroxide in the presence of potassium hydroxide by the method of continuous variation showed that the decomposition is accelerated by hydroperoxide anion, and that the reaction provides an abundant source of hydroxyl radical.

^{*}Reactions of Carbohydrates with Hydroperoxides, XII. For Part IX, see ref. 8.

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Sum		3	H ₂ O ₂	→	2 °OH	+	02	+	2 H ₂ O
(4)	OOH-	+	ЮН	->	H ₂ O	+.	*O ₂ -		
(3)	H ₂ O ₂	+	°02-	→	юн	÷	OH-	+	0,
(2)	H ₂ O ₂	. +	OOH-	·> ·	'OH	+	H ₂ O	+	'0 ₂ -
(1)	H ₂ O ₂ :	÷	OH-	→.	OOH-	+	H ₂ O	··	

In view of this observation, it seemed probable that the secondary process involves oxidation of the substrate and of its primary oxidation products by hydroxyl radical formed from hydrogen peroxide and hydroperoxide anion. The overall process is highly exothermic, and, unless care is taken, the temperature rises, enhancing the secondary process at the expense of the primary.



It is noteworthy that treatment of 1 with alkaline hydrogen peroxide affords not only D-arabinitol (7) and 2-deoxy-D-arabino-hexonic acid (5), but also 2-deoxy-D-arabinohexono-1,4-lactone (9). These products were separated from the reaction mixture under conditions whereby conversion of 5 into 9 could not have occurred. Consequently, it may be concluded that acyclic hydroperoxide 2 exists in equilibrium with furanoid form 8, and that this is converted, without ring-opening, into 2-deoxy-D-arabino-hexono-1,4lactone (9), as indicated in Scheme 1.

The experiments on which the foregoing is based were conducted in the following way. Samples of 1 were treated with hydrogen peroxide and potassium hydroxide in various proportions at $0-40^{\circ}$ in the presence and absence of magnesium hydroxide. After times ranging from one hour to many days, the excess of hydrogen peroxide was decomposed by addition of activated carbon. The mixture was filtered, and aliquots of the filtrate were used for determining specific rotation, chromatographic behavior, formic acid, and organic peroxide. The rest of the solution was passed successively through a cation- and an anion-exchange resin. The salt-free effluent, hereafter called the neutral fraction, was evaporated to dryness. Paper chromatography revealed four principal constituents and a small proportion, apparently polymeric, that remained at the origin. In a typical experiment, conducted in the presence of magnesium hydroxide, three compounds were separated by preparative chromatography, and crystallized: lactone 9 (30 mol%), unreacted or regenerated 1 (25%), and 7 (7.3%). The fourth substance appeared to be an organic peroxide of unknown structure. Lactone 9 was also prepared by extraction of the

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neutral fraction with acetone; on concentration, the extract afforded 2-deoxy-D-arabinohexono-1,4-lactone, m.p. 97°, $[\alpha]_D^{25}$ +67.8° (c 4, H₂O); lit.¹⁰ m.p. 95–97°, $[\alpha]_D$ +68° (c 2, H₂O).

Treatment of a portion of the lactone with an equivalent amount of 11thium hydroxide, and concentration of the solution, afforded crystalline lithium 2-deoxy-Darabino-hexonate, a new salt; $[\alpha]_D^{25} + 4.3^\circ$ (c 4, H₂O).

Anal. Calc for C₆H₁₁LiO₆: C, 38.73; H, 5.96; Li, 3.73. Found: C, 38.93; H, 6.18; Li, 3.65.

Lithium 2-deoxy-D-arabino-hexonate was also prepared from the acidic material retained on the anion-exchange resin.

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