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Preliminary communication

A diradical mechanism for the degradation of reducing sugars by oxygen*†

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For three quarters of a century, scientists in many disciplines have been concerned with the reactions of carbohydrates with oxygen. Nef[1] found that treatment of D-glucose, D-mannose, and D-fructose with oxygen in aqueous, alkaline solutions affords D-arabinonic acid and formic acid in high yields, with small proportions of D-erythronic, D-glyceric, and glycolic acids, and certain rearrangement products. He recognized that many reactions are involved in the degradations, and that most of the products are formed by oxidative cleavage of enediols derived from the sugars. Bamford and Collins[2] advanced the hypothesis that, in the degradation of D-glucose, oxygen adds to the 1,2-enolate anion, forming a hydroperoxide that decomposes to D-arabinonic acid and formic acid. To account quantitatively for the D-erythronic, D-glyceric, and glycolic acids found, Dubourg and Naffa[3] extended this hypothesis[2] to include peroxide degradation of enediols derived from fragments formed by cleavage of the carbon chain of the parent sugars. Subsequently, De Wilt and Kuster[4] developed an integral reaction scheme, including the formation and oxidation of all of the enediols that may be derived from the sugar. The scheme consists of a repeated set of reactions, each starting with an enolate anion. Although a substantial proportion of carbon dioxide was found, it was not included in the reaction scheme.

In this communication, a simplified mechanism for the interpretation of the reactions of reducing sugars with oxygen is presented. It accounts for all of the products formed in the oxidation of D-fructose, without recourse to all possible enediols. The results obtained by Dubourg and Naffa[3] for the oxidation of D-fructose at 25° are given in Table I. Repetition of the measurements in our laboratory confirmed the data within reasonable experimental error, except for the oxygen consumed and the carbon dioxide formed. Our values for these, which are somewhat higher than those of Dubourg and Naffa, are used in Table I.

The mechanism proposed by Dubourg and Naffa begins with heterolytic addition of oxygen to the 1,2-enediol anion, followed by formation of a dioxetane ring. However, addition of ordinary (triplet) oxygen to the enediol by this mechanism seems questionable, because triplet oxygen has little tendency to add heterolytically to a double bond. In view

*Dedicated to the memory of Professor Edward J. Bourne.

†Reactions of Carbohydrates with Hydroperoxides: Part VIII. For Part VII, see Ref. 6.

TABLE I

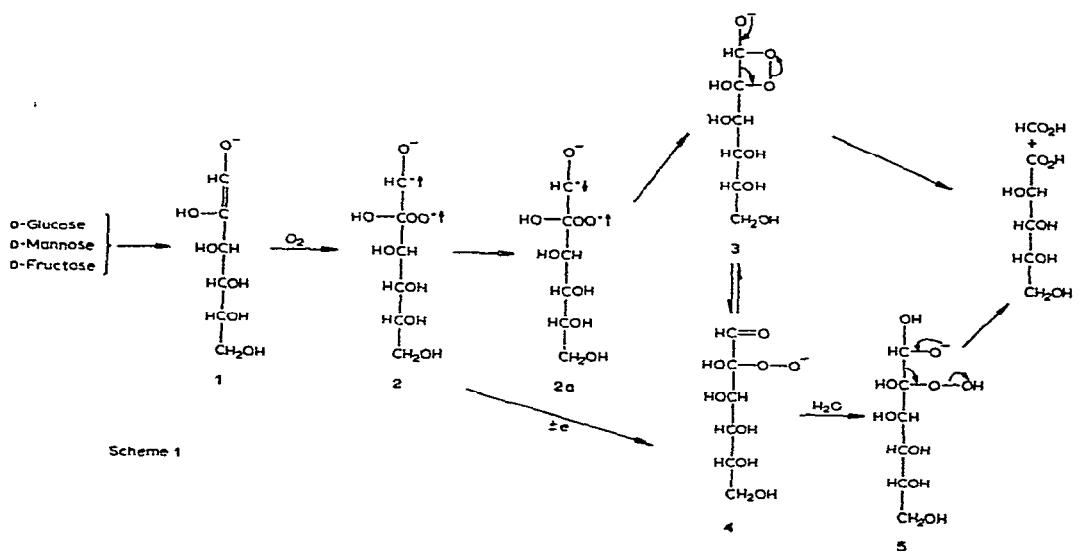
OXIDATION OF D-FRUCTOSE BY OXYGEN IN ALKALINE SOLUTION [a]

Products	*Millimoles formed per millimole of D-fructose*	
	Experimental	*Calculated* [b]
D-Arabinonic acid	0.77	0.77
D-Erythronic acid	0.05	0.05
D-Glyceric acid	0.10	0.10
Glycolic acid	0.15	0.15
Formic acid	1.02	1.02
Carbon dioxide	0.13 [c]	0.15
Oxygen consumed	1.2 [c]	1.27
Carbon atoms accounted for	96.7%	97.0%

[a] Conditions: 760 mmHg; 25°; 1.5M potassium hydroxide; experimental data of Dubourg and Naffa[3]. [b] Calculated on the basis of Scheme 3. [c] Value determined by the author.

of the inherent properties of triplet oxygen[5], and the need to account for the carbon dioxide and hydrogen peroxide formed, a new mechanism is required.

Heretofore, insufficient attention has been given to the fact that triplet oxygen is a diradical with two unpaired electrons. According to the mechanism depicted in Scheme 1, it combines with an enediol (1), producing diradical 2. This diradical has two electrons in close proximity, which do not combine because they have parallel spins. Diradical 2, however, reacts rapidly with a substance having unpaired electrons of opposite spin. By a change in the spin of one of the unpaired electrons, the diradical may be converted into the dioxetane 3 of Dubourg and Naffa, or to the hydroperoxide 4. The change in the spin

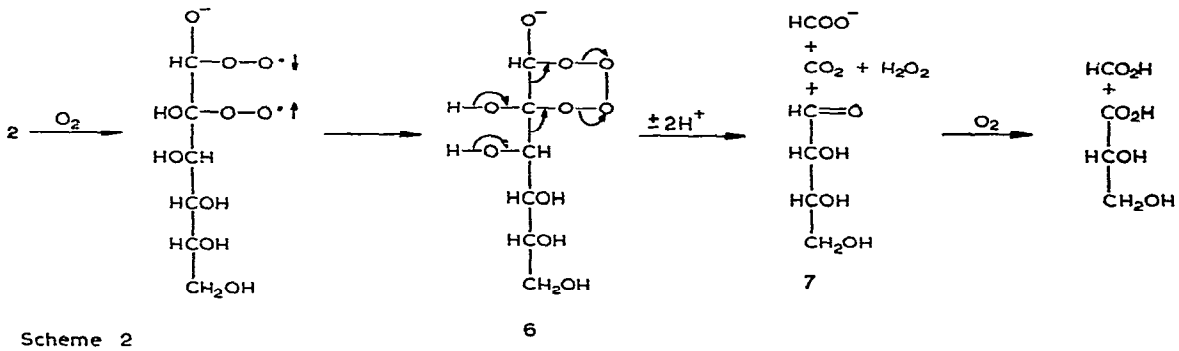


Scheme 1

of 2 to that of 2a may be accomplished by energy derived from the heat of reaction. The conversion 2 → 4 may involve a chemical reaction leading to the release of an electron at C-1, and addition of an electron to the peroxy group. The resulting intermediates, 3 or 4, may decompose with formation of formic acid and D-arabinonic acid.

Intermediate 4 is the same as the hydroperoxide adduct of D-*arabino*-hexosulose. Decomposition of hydroperoxide adducts of glycosuloses and α,β-dicarbonyl compounds, in general, may take place either by conversion into dioxetane derivatives, followed by intramolecular cleavage as depicted in 3, or by the process indicated by 4 and 5. Formation of a dioxetane intermediate may account for the rapid, ionic reaction noted[6] for the oxidative cleavage of glyoxal by alkaline hydrogen peroxide.

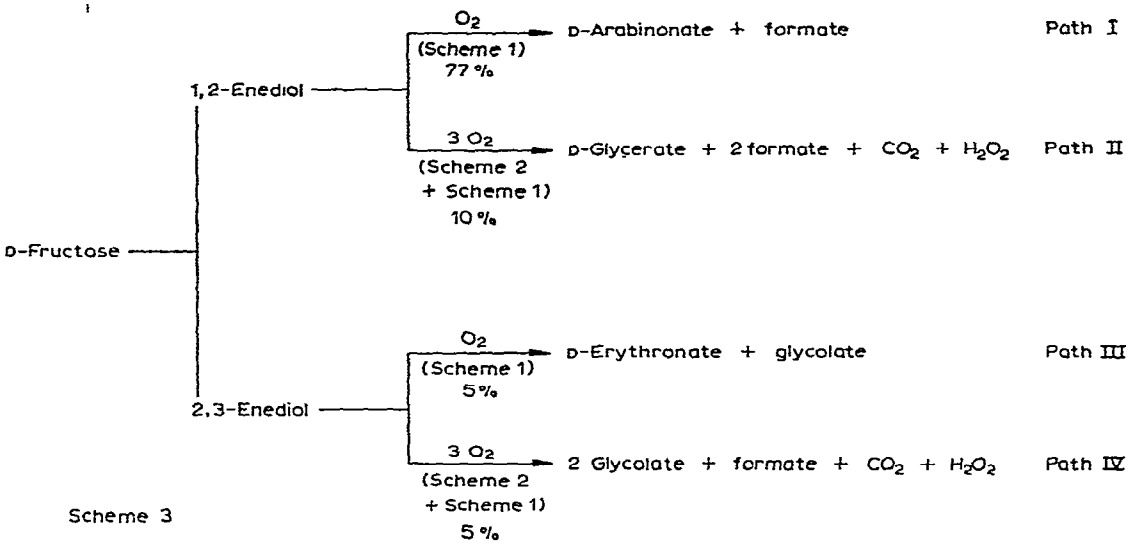
The mechanism of Scheme 2 begins with the addition of triplet oxygen to diradical 2 of Scheme 1. The coupling takes place between molecules having antiparallel spins for their unpaired electrons. The adduct, now having unpaired electrons with antiparallel spins, condenses (presumably in the transition state) to give the tetraoxane derivative 6, which decomposes with formation of one mole each of formate ion, carbon dioxide, D-erythrose (7), and hydrogen peroxide. By enolization and reaction with oxygen, 7 would be converted, as in Scheme 1, into formic acid and D-glyceric acid. The fate of the hydrogen peroxide is unknown; it may react with carbonyl compounds in the environment, or it may become involved in free-radical reactions initiated by traces of iron or other catalysts.



Scheme 2

Presumably, all of the enediols postulated by De Wilt and Kuster may be formed, directly or indirectly, from the sugar, and may react with oxygen in essentially the same manner as the 1,2-enediol. However, in the oxidation of D-fructose at 25°, all of the products formed may be accounted for, in the proportions found, by reactions starting with the 1,2- and 2,3-enediols. Certain products arise from *specific* enediols by the reactions of Schemes 1 and 2. The yields of these products reveal the contributions of the several reaction paths to the degradation process. Thus, as depicted in Scheme 3 for the data of Table I, the 1,2-enediol of D-fructose yielded 77% of D-arabinonic acid by path I, and 10% of D-glyceric acid by path II; the 2,3-enediol yielded 5% of D-erythronic acid by path III. The three paths account for 92% of the sugar oxidized, in the proportions found. The amounts of glycolic acid and formic acid are greater than those calculated for the three paths, and the excess corresponds to the proportion that would be formed by oxidation of 5% of the sugar by path IV. The calculated values given in Table I are based

on degradation of the sugar by the four reaction paths in the proportions cited. The results are in good agreement with the experimental values. Thus, the reaction products from D-fructose under the described conditions are explicable on the basis of the proposed reaction mechanisms, which involve only the 1,2- and the 2,3-enediols. The measurements account for 97% of the sugar oxidized. Presumably, 3% of the D-fructose was converted into saccharinic acids and other products by the Nef–Isbell series of reactions[7,8].



Scheme 3

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