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SEMIDIONE RADICAL ION FORMATION IN MONOSACCHARIDE OXIDATION. AN ELECTRON SPIN RESONANCE STUDY

Paul R. West*, G. Wayne Schnarr and Lucien Sitwell,

Department of Chemistry, University of Victoria,
P.O. Box 1700, Victoria, B.C. Canada, V8W 2Y2.

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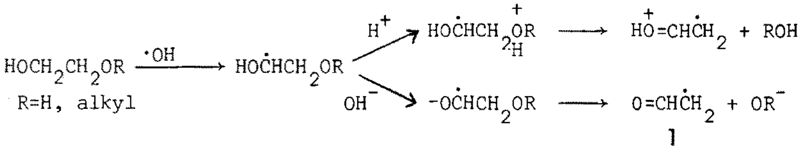
In the free radical oxidation of aqueous glycols and glycol ethers, abstraction of hydrogen from carbon atoms bearing hydroxyl groups is followed by acid[1] and base[2] catalysed fragmentation producing 2-alkanoyl radicals **1**, equation 1.



(1)

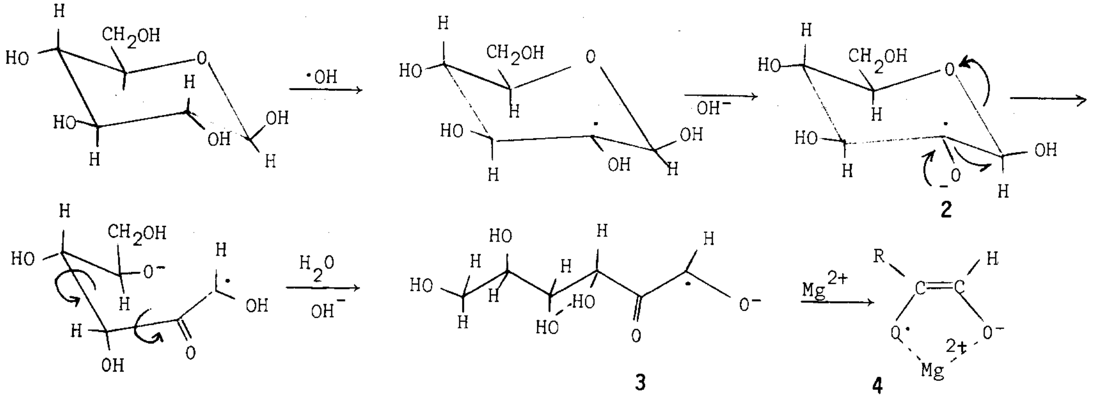
E.s.r. observations[3a] and product studies[3b] have confirmed the acid-catalysed pathway in the oxidation of carbohydrates.

We now report a study of the oxidation of sugars (hexoses) in neutral and basic solution initiated by the titanium III reduction of aqueous hydrogen peroxide.[4] A three stream high velocity flow system has been used in conjunction with an e.s.r. spectrometer to observe the steady-state radical population during the reaction of 0.01 M[Ti^{III}(EDTA)] with 0.1 M [H_2O_2] and a third solution of glucose, galactose, fructose or mannose (0.1 M). Observations are made 20-50 msec after mixing is completed.

In experiments at pH 4.5 each sugar gave a different, complex spectrum of the cyclic abstraction radicals (totally symmetric about $g = 2.0032$). Approximate analysis based on the epimeric differences among galactose, glucose and mannose indicated the expected attack at every carbon in the aldohexoses.[5]

At pH $\geq$ 7 an intense new doublet of doublets appeared at low field in the spectra of glucose, mannose and fructose. It was assigned to the *cis* C-1, C-2 semidione **3** [a_{CHO^-} 8.9 G, a_{CHOH} 4.7 G, g = 2.0049] that can be formed by fragmentation of the deprotonated C-2 abstraction radical **2** as shown for β-D-glucose in Scheme I. Comparable reactivity of both anomers is likely. Clearly deprotonation of the C-2 radical formed by attack on the free aldehyde form of the sugar (<1%) provides an alternative minor route to the semidione radical ions.

Scheme I.



Loss of vicinal hydroxy groups from ketyl **2** and other abstraction radicals will yield neutral 2-alkanoyl radicals. However, such species are rapidly reduced by Ti III (EDTA) to diamagnetic enolates[4a], equation 2, greatly simplifying the spectra. Apart from semidione signals only diminishing weak background signals of abstraction radicals were detected above pH 7.5.

$$R\dot{C}H\overset{O}{\overset{\|}{C}}R' + \text{Ti III(EDTA)} \longrightarrow RCH{=}\overset{O^-}{\overset{|}{C}}R' + \text{Ti IV(EDTA)} \qquad (2)$$

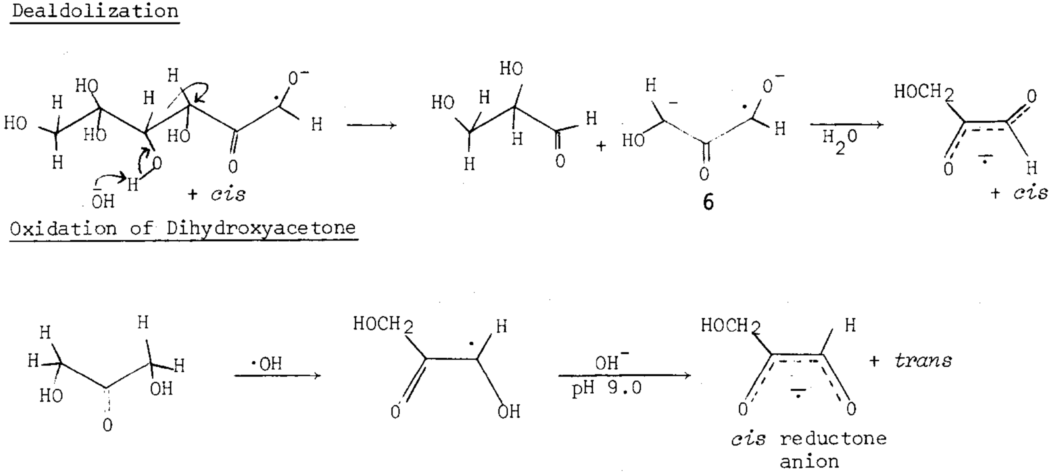
In the pyranose form, fructose can produce **3** by ring opening of the hemiketal during fragmentation of the corresponding C-1 abstraction radical. In the spectrum of galactose at pH 7.5 the new semidione signal has a_{CHO^-} 8.7 G, but a lower CHOH splitting of 2.3 G (g = 2.0049). Since galactose is epimeric at C-4 relative to glucose, we infer hydrogen bonding affects the conformational equilibrium for rotation about the C2, C3 bond with altered β hydrogen hyperfine splitting[6] in the diastereomeric radical ion.

To confirm the semidione assignment, glucose, mannose and fructose were reacted in the presence of 0.1-0.3 M $MgSO_4$[7], drastically reducing the signal from **3** with appearance of the Mg^{2+} chelate **4**; a_{CHOH} 6.6, a_{CHO^-} 9.4 G, g = 2.00465 (Scheme I). Now in each spectrum a less intense signal of the trans C1, C2 semidione **5** was clearly revealed (a_{CHO^-} 8.3 G, a_{CHOH} 4.7 G, g = 2.0051). In the absence of magnesium ions we estimated that the cis:trans ratio was at least 4:1 for glucose and mannose, though somewhat lower for fructose (2.5:1).

At pH 7.5 the spectrum of semidione **3** was also observed with the Fenton reagent (Fe II (EDTA)-H_2O_2-glucose) with the expected reduced intensity and higher line width. As anticipated, oxidation of methyl-α-D-glucoside at pH 7-9 gave no detectable semidione signals. However, attack at the glycosidic O-methyl group does produce a radical of the ether type $\cdot CH_2OR$ that is *not* subject to base catalysed fragmentation. Signals from this species dominate the spectrum at pH 9.0 (a_{CH_2OR} 18.0 G, a_{OCHOCH_2} 1.4 G, g = 2.0032).

Above pH 8.0 in addition to **3** and **5**, reductone anions $HOCH_2C(O^\cdot)=C(O^-)H$ appeared in the four reducing sugar spectra in cis:trans ratio 1:5. The assignment was based on superimposability with spectra from the oxidation of 1,3-dihydroxy acetone at pH 9.0 where the identical radical ions are formed though now in cis:trans ratio 3:1,[8] Scheme II.

Scheme II.



Parameters of the reductone anions in both experiments were *cis:* a_{CH_2OH} 6.4 G, a_{CHO^-} 8.9 G, g = 2.0049 and *trans:* a_{CH_2OH} 6.4 G, a_{CHO^-} 8.5 G, g = 2.0050.[9,10] Note that reaction in the presence of 0.1 M $MgSO_4$ sharply diminished the *cis* isomer and the reductone magnesium chelate appeared (a_{CH_2OH} 7.5 G, a_{CHO^-} 9.4 G, g = 2.00465).[6]

Base-catalysed dealdolization of the sugar semidiones **3** and **5** leads directly to reductone anions, Scheme II. Though the shift in the dominant steady-state isomer from *cis* in the sugar semidione to *trans* in the reductone anion could reflect rotational equilibration of a dianion intermediate such as **6**, reactivity differences between **3** and **5** are also possible. Nonequilibrium conformations existing immediately following ring opening may also react. Note that for the aldohexoses at pH 9.0, sugar semidiones and the reductone anions are observed at ca. equal intensity while the reductone semidione is only 20 percent of the fructose semidione signal under identical experimental conditions.

In further control experiments, deliberate addition of the sugar substrates to either the hydrogen peroxide or Ti III (EDTA) solution 30 minutes before the flow experiment produced no change in the relative intensities in the spectra recorded at pH 9.0. As well, the reductone and sugar semidione species are both observed at pH 9.0 on varying the initial hydrogen peroxide concentration from 0.2 to 0.02 molar.

Acknowledgement

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(10) Spectral parameters are quoted to ± 0.05 G on hyperfine splitting, and ± 0.0001 on g values relative to Fremy's salt. For signals from isomeric radical ions recorded in the same spectra Δg and Δa_H values are known with greater precision.