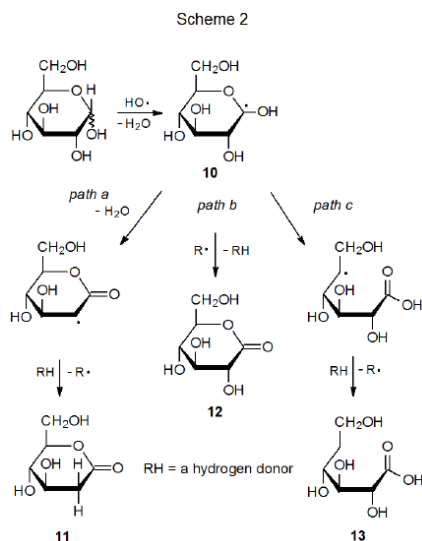


IV. Reactions of First-Formed Radicals

A. Reactions in Neutral Solution

In discussing the various products arising from reaction in neutral solution of first-formed radicals (typically reactions in which the hydroxyl radical is generated by γ -radiolysis), it is convenient to distinguish between products with a molecular weight less than or equal to that of the substrate and those with a higher molecular weight. Because first-formed radicals can undergo dimerization, disproportionation, elimination, and rearrangement, the number of possible reaction products is staggering; nevertheless, many of them have been identified.^{1,2,24,25}

Product yields for reactions begun by γ -radiolysis of water can be expressed in terms of G-values; that is, the molecules or radicals formed per 100 eV of energy absorbed. A G-value also can be used as a measure of substrate reacted. In the reaction of D-glucose shown in Scheme 2 the G-value for consumption of starting material is 5.6.² The values for formation of products **11-13** are 0.95, 0.15, and <0.08, respectively. The G-values cited for D-glucose and compounds **11-13** were determined in the presence of N_2O to maximize the formation of the hydroxyl radical.

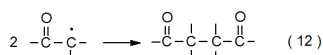


1. Low-Molecular-Weight Products

Although many low-molecular-weight products are formed in detectable amounts from reactions of simple sugars, the yields of most are quite low. Many of these compounds are produced by reactions of the first-formed radicals; for example, the major, low-molecular-weight product (**11**) from reaction of D-glucose is believed to arise by loss of the elements of water from the first-formed radical **10** (Scheme 2, path a).² Another reaction of **10** that forms a low-molecular-weight product is loss of a hydrogen atom to give D-glucono-1,5-lactone (**12**) (Scheme 2, path b), and a third reaction is opening of the pyranoid ring in **10** by fragmentation of the bond between C-5 and the ring oxygen atom to give, after hydrogen-atom abstraction, a carboxylic acid (**13**) (Scheme 2, path c).² All of the reactions of the radical **10** shown in Scheme 2 are driven, at least in part, by the stability gained from forming a C=O double bond.

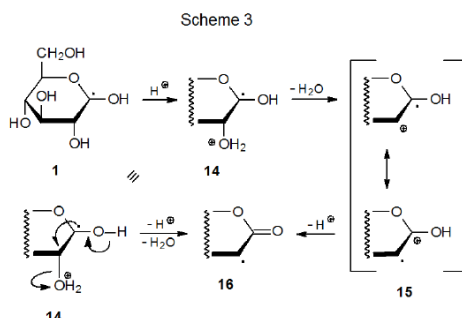
2. High-Molecular-Weight Products

The products **11-13** (□ Scheme 2) and the other low molecular-weight products (more than twenty identified) account for less than half of the D-glucose consumed during γ -radiolysis because most products formed have high molecular weights. Little is known about either the structure of the high-molecular-weight materials or the mechanism of their formation. One proposal is that dimerization of radicals that have lost the elements of water may be the first step in formation of some high-molecular-weight products (eq 12).²

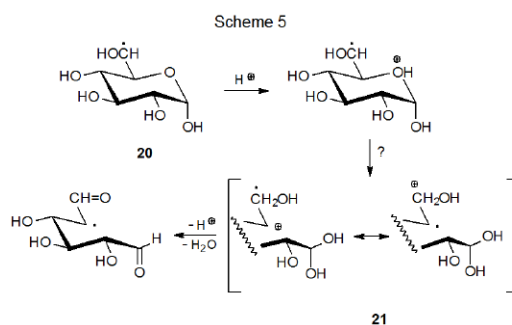
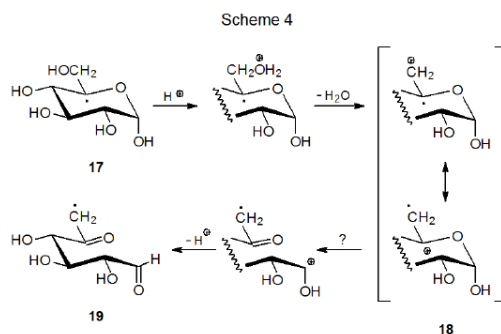


B. Acid-Catalyzed Reactions

Under strongly acidic conditions ($\text{pH} = 1$) four of the first-formed radicals generated from D-glucose eliminate the elements of water to give in each case a carbonyl-conjugated radical.^{6,26} A proposed mechanism for this reaction, shown in Scheme 3, involves protonation of the hydroxyl group adjacent to a radical center in the first-formed radical **1** to produce an intermediate (**14**) with an excellent leaving group that departs to form a radical cation (**15**). This radical cation then deprotonates to give the carbonyl-conjugated radical **16**. Another mechanistic possibility for forming **16** is a concerted reaction beginning with the protonated radical **14** (Scheme 3). Forming carbonyl-conjugated radicals by acid-catalyzed reaction also has been studied in noncarbohydrate systems.^{5,27,28}

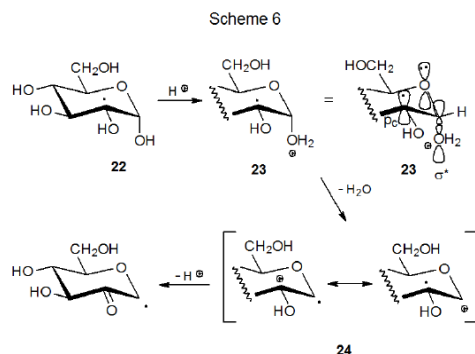


The acid-catalyzed reactions of three first-formed radicals produced from D-glucose deserve further comment. Two of these radicals, **17** (Scheme 4) and **20** (Scheme 5), do not undergo the carbonyl-group-forming reaction characteristic of the other first-formed radicals (Scheme 3).⁶ Although **17** could start along this pathway by producing the radical cation **18**, deprotonation of **18** to give a carbon-centered radical with an adjacent carbonyl group cannot take place. Formation of a carbonyl-conjugated radical from **18** would require opening of the pyranoid ring (Scheme 4). Evidence against such reaction is that **17** is less reactive than other first-formed radicals, and when it does react, no carbonyl-conjugated radical can be detected. The first-formed radical **20** also must undergo ring opening if a carbonyl-conjugated radical is to be produced; in fact, ring opening in this case is necessary to form the radical-cation **21** (Scheme 5). The radical **20**, which is the least reactive of the first-formed radicals derived from D-glucose, also gives no indication of forming a carbonyl-conjugated radical.⁶



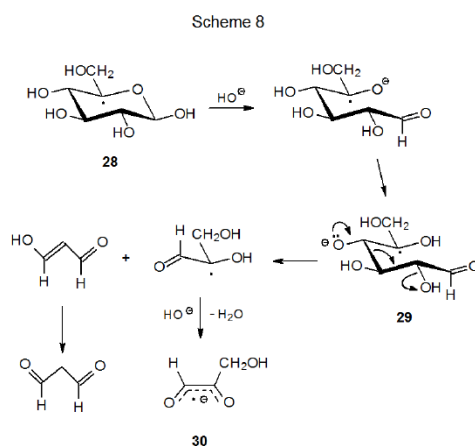
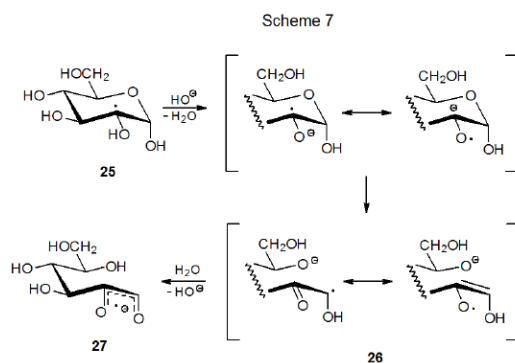
The radical **22** is the third, first-formed radical produced from D-glucose that deserves further comment. This radical is noteworthy because it is the most reactive of the first-formed radicals. Protonation of **22** gives the intermediate **23** in which the leaving group

has an axial orientation and, therefore, the *p*-type orbitals on C-2 and the ring oxygen atom in **23** begin stabilizing the radical cation **24** as it starts to develop (Scheme 6).⁶



C. Base -Catalyzed Reaction

Proton abstraction from O-2 in the first-formed radical **25** begins a process that generates the ring-open radical anion **26** (Scheme 7). (Since an α -hydroxy radical is far more acidic than its parent alcohol,² the proton attached to O-2 should be removed much more readily than any other proton in **25**.) The radical anion **26** rapidly undergoes a proton transfer to produce the semidione **27**, one of two semidiones formed from base-catalyzed reaction of a first-formed, D-glucopyranosyl radical.^{11,29} The second of these two (**30**) is proposed to arise from the radical **28** according to the mechanism outlined in Scheme 8.¹¹ (Semidiones **27** and **30** are readily detected because for each of them the negative charge slows the rates of dimerization and reduction and thus leads to more prominent ESR spectra.¹¹)



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