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Catalytic Action of Iron and Manganese Ions in the Photochemically-Induced Oxidation of D-Fructose with Atmospheric Oxygen

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D-Fructose is susceptible to photochemically-induced oxidation by atmospheric oxygen in the presence of a catalytic amount of iron or manganese cations in a neutral to weakly basic pH range. Metal hydroxide does not precipitate from a solution in this pH range because of the high sequestering ability of D-fructose. Upon irradiation of Pyrex-filtered light, D-fructose degraded into D-erythrose and other fragments. This reaction is shown to proceed by coupling with an oxidation-reduction cycle involving a metal cation, i.e., the photooxidation of D-fructose by M(III) and the subsequent reoxidation of the resultant M(II) by atmospheric oxygen.

It is well recognized that trace amounts of transition metal cations like Cu(II), Mn(II), and Fe(III) often play key roles in many biological activities.¹⁾ Among them, the ability of saccharides to sequester metals in aqueous solutions has been drawing considerable interest because of their physiological and chemical importance and the possible applications of metal-saccharide systems to clinical use.²⁻⁴⁾ However, the photochemical properties of metal-saccharide systems are not yet well understood. Recent reports from our and other laboratories have shown that the photochemically-induced oxidation of monosaccharides by transition metals leads to a degradation of saccharides with selective C–C bond cleavage.⁵⁻⁸⁾ For instance, the photooxidation of D-fructose in an acidic $FeCl_3$ solution causes a C_2—C_3 bond cleavage of D-fructose via the formation of an Fe(III)–D-fructose complex to give D-erythrose in nearly 90% yield.⁷⁾ In a preceding letter, we showed that D-fructose and D-glucose are susceptible to photochemically-induced oxidation by atmospheric oxygen in the presence of a catalytic amount of transition-metal ions in the neutral pH range.⁹⁾ The catalytic action of transition metals for the oxidation and oxygenation of organic substrates with atmospheric oxygen is a subject of current interest.¹⁰⁾ Thus, the results of our research might have physiological and chemical importance. Therefore, we further extended our study to clarify the role of metal ions in this type of reaction. Here, we wish to report on more detailed aspect of the catalytic action of iron and manganese ions in the photochemically-induced oxidation of D-fructose in neutral to weakly basic solution.

Experimental

Materials. D-Erythrose and D-fructose were obtained from Aldrich Chem. Co. and Wako Pure Chem. Ind. Ltd., respectively. Other chemicals were also obtained commercially, and some of them were purified by conventional methods prior to use.

Photoirradiation. Sample solutions were freshly prepared using deionized water. The pH of solutions were adjusted to appropriate values by the addition of a concd NaOH solution. Photoirradiation was carried out at 20 °C by one of the following three methods.

1) 70 ml of a solution whose pH was initially adjusted to 9.6 was placed in a reaction vessel and internally irradiated by a 100 W high-pressure mercury lamp (Type UM-102, Ushio Electric Inc.) through a Pyrex-made water jacket. During irradiation, the solution was magnetically stirred and air was continuously bubbled from the bottom of the vessel. As the pH of the solution gradually decreased during photoirradiation, small amounts of concd NaOH solution were added every hour during irradiation to keep the solution within the pH range 6 to 9.6.

2) 500 ml of the solution was placed in a larger reaction vessel fitted with a pH electrode and irradiated using the same procedure described above. The pH of the solution was monitored by a TOA HM-20B pH meter and was kept constant during irradiation by a controlled addition of a 2 M¹¹⁾ NaOH solution with a HSM-10A pH stat (Toa Electronics Ltd.).

3) 3 ml of the solution in a quartz cell was degassed by three freeze-thaw cycles and then irradiated by light of a known wavelength and energy ($1—2.3\times10^{-2}$ W) in a JASCO CRM-FA spectro-irradiator with a 2 kW Xenon lamp.

Analyses of the Irradiated Solutions. Syrup obtained from the irradiated solution was analyzed by previously described methods; D-fructose by high-performance liquid chromatography and D-erythrose by gas-liquid chromatography after acetylation of the syrup.⁷⁾ D-Erythrose could also be isolated from the syrup by column chromatography with anion-exchange resins (Hitachi Gel #3019N, Hitachi Ltd.; 300×20 mm; CH_3OH). Formic acid in the solution was determined according to a method of Isbell et al.¹²⁾ The irradiated solution was treated with cation-exchange resins (Amberlite IR-120, H^+-form, Rohm & Haas) and then extracted three times with ether. The amount of ether-extractable acid, which was identified to be formic acid after converting to *p*-bromophenacyl formate (mp 99—101 °C; lit, 99—100 °C¹³⁾), was determined by titration with a 0.2 M NaOH solution.

Other Measurements. UV-visible spectra were recorded by a JASCO UVIDEC-505 spectrophotometer at 20 °C and electron-spin-resonance (ESR) spectra were measured at room temperature by a JEOL JES-FE3X spectrometer operated in the X band.

Titration of 30 ml metal–D-fructose solutions were carried out pH-metrically at 25 °C by the addition of 0.1 M NaOH at a rate of 0.5 ml min^{-1} under an anaerobic atmosphere or 0.13 ml min^{-1} under an aerobic atmosphere.

Results

Photoirradiation in the Presence of Metal Salts. Though addition of concd NaOH solutions to acidic $FeCl_3$, $MnCl_2$, or $CuCl_2$ solutions usually resulted in a formation of a colloidal precipitate of metal hydroxide, no precipitate was formed in the presence of a large excess of D-fructose. The solutions remained clear even in the weakly acidic to basic pH range, demonstrating the ability of D-fructose to sequester metal cations in aqueous media.

Seventy millilitre of a solution containing D-fructose (2.8×10^{-2} mol) and a catalytic amount of metal chloride (1.4×10^{-4} mol) was irradiated by Pyrex-filtered light (method 1, see Experimental section). The pH of the solution initially adjusted to 9.6 was kept within the range between 6 to 9.6 during irradiation. Though the formation of a brown colloidal precipitate was observed at the end of irradiation in the presence of $FeCl_3$ or $FeCl_2$, no precipitate was formed even after 24 h of irradiation in the presence of $MnCl_2$. Irradiation in the presence of $CuCl_2$ led to the deposition of metallic copper on the surface of the water jacket at an early stage of the reaction and no light was transmitted to the solution thereafter. Results are summarized in Table 1. Though D-erythrose was the main oxidation product, its yield markedly decreased in the case of $MnCl_2$. No reaction proceeded without photoirradiation or in the absence of any of the metal salts or oxygen.

Oxidation-reduction Cycle of Iron and Manganese Ions. We showed in a preceding letter that the irradiation of an $FeCl_3$–D-fructose solution at pH 9.6 under anaerobic conditions caused the reduction of Fe(III) into Fe(II) and a subsequent aeration of the irradiated solution led to the oxidation of Fe(II) to Fe(III) again.[9] Spectral changes shown in Fig. 1(a) confirm the photoreduction and subsequent oxidation of Fe(II) ion. Similar experiments were carried out for the $MnCl_2$–D-fructose system. A $MnCl_2$ (2×10^{-3} M)–D-fructose (0.4 M) solution was adjusted

Table 1. Photoirradiation in the Presence of Metal Chloride at 20 °C

Metal Chloride	Irradiation Time/h	D-Fructose Oxidized 10^{-3} mol	D-Erythrose Formed 10^{-3} mol
$FeCl_3$[a]	12	9.1	6.7 (74%)[b]
$FeCl_2$[a]	12	8.5	6.2 (73%)
$MnCl_2$[a]	24	15.4	8.7 (56%)
$CuCl_2$	6	0	0

A 70 ml of the D-Fructose(2.8×10^{-2} mol)–metal chloride (1.4×10^{-4} mol) solution was irradiated by the method 1.

a) Ref. 9, b) Conversion based on the D-fructose oxidized (mol%).

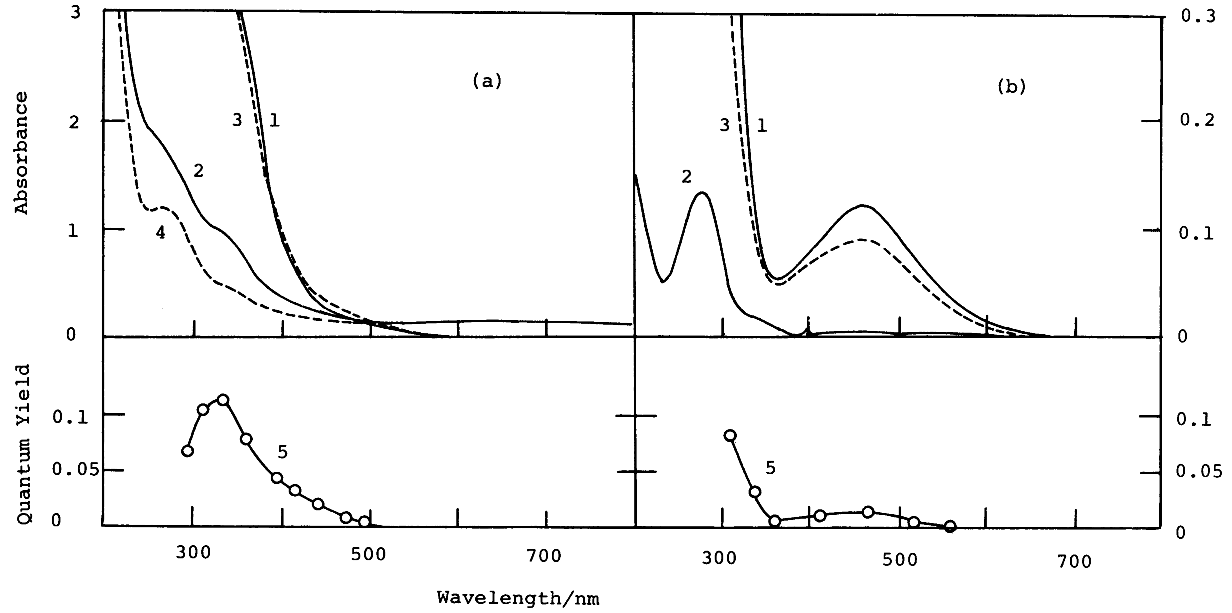


Fig. 1. Absorption and Action Spectra of (a) $FeCl_3$ (2×10^{-3} M)- and (b) $MnCl_2$ (2×10^{-3} M)–D-Fructose (4×10^{-1} M) Sloutions at pH 9.6 and 20 °C.

Initial solution(1) was irradiated for 30 min under anaerobic conditions(2), and then the solution was aerated(3). Spectrum (4)represents the $FeCl_2$(2×10^{-3} M)–D-fructose (4×10^{-1} M) solution at pH 9.6 prepared under anaerobic conditions, and curves(5) shows the quantum yields of the reduction of M(III) at different wavelengths.

to pH 9.6 by the addition of concd NaOH under an aerobic atmosphere. The colorless solution became slightly reddish and the d-d transition-band characteristics for the high-spin Mn(III) state were observed at 400—500 nm (Fig. 1(b)).[14] No signal was observed in the ESR spectrum of the solution, further supporting the formation of Mn(III) species.[15] Photoirradiation after deaerating the solution gave a clear colorless solution, showing practically no absorption in the visible region. The ESR spectrum of the irradiated solution showed a sextet signal, confirming the formation of a high-spin octahedral Mn(II) complex.[15] The aeration of the irradiated solution again made the solution faintly reddish and the ESR signal disappeared. Thus, it was shown that a photochemically-induced reduction of Mn(III) to Mn(II) and subsequent oxidation to Mn(III) by atmospheric oxygen does take place in the presence of a large excess of D-fructose in a weakly basic pH range without forming any precipitate. The action spectrum of the reduction of Mn(III) obtained by method 3 is also shown in Fig. 1(b).

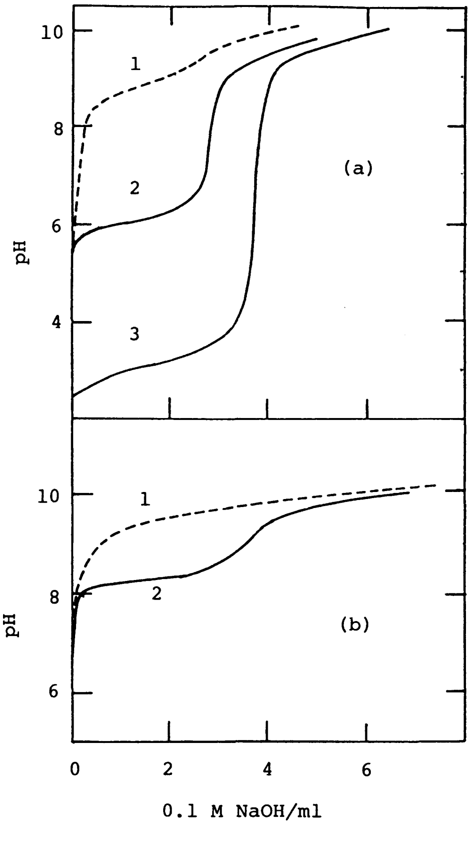


Fig. 2. Titration Curves of Metal Chloride(4×10^{-3} M)–D-fructose(8×10^{-1} M) Solutions(30 ml) by 0.1 M NaOH at 25 °C.
(a): 1. FeCl$_2$ under anaerobic, 2. FeCl$_2$ under aerobic, and 3. FeCl$_3$ under aerobic atmosphere. (b): 1. MnCl$_2$ under anaerobic, and 2. MnCl$_2$ under aerobic atmosphere.

To study the oxidation process of Fe(II) and Mn(II) further, FeCl$_3$–, FeCl$_2$–, and MnCl$_2$–D-fructose solutions were titrated using a 0.1 M NaOH solution under anaerobic or aerobic atmosphere (Fig. 2). When FeCl$_2$ was titrated in an oxygenated solution, Fe(II) was oxidized to Fe(III) at around pH 6. However, the oxidation of Mn(II) was observed only above pH 8 under similar conditions.

Effect of pH on the Reaction. Since the pH of a solution is an essential factor for the photochemically-induced oxidation of monosaccharide in the presence of transition-metal ions, the effect of pH on the reaction was further studied for FeCl$_3$–D-fructose systems. For this purpose, 500 ml of the FeCl$_3$(1×10^{-3} mol)–D-fructose(2×10^{-1} mol) solution was irradiated for 120 h with a controlled addition of a small amount of 2 M NaOH in order to maintain the pH of the solution more strictly (method 2). Without the addition of 2 M NaOH, the pH of the solution (initially adjusted to 9.6) decreased to about 3 after 12 h of irradiation. The irradiation of a solution whose pH was below 6.8 resulted in the formation of a colloidal precipitate within 24 h. The amounts of 2 M NaOH required to maintain the initial pH of the solution during irradiation are shown in Fig. 3 and the irradiation results are summarized in Table 2. A considerable amount of 2 M NaOH was consumed to maintain the pH of the solution and the yield of D-erythrose in the oxidation products markedly decreased, especially when irradiated at a higher pH. This suggested the formation of acids as oxidation products. Formic acid was detected from the ether-extract of the irradiated solution.

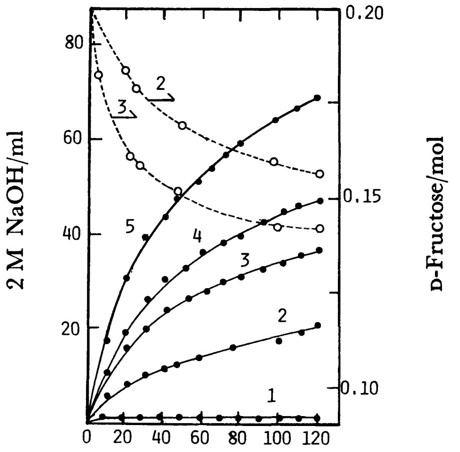


Fig. 3. Time Cource of the Photooxidation of D-Fructose (2×10^{-1} mol/500 ml) by Method 2 in the Presence of FeCl$_3$ (1×10^{-3} mol) at 1. pH 6.8, 2. pH 7.2, 3. pH 7.8, 4. pH 8.4 and 5. pH 9.0.
(—●—): 2 M NaOH required to maintain the initial pH, and (—○—): D-fructose.

Table 2. Effect of pH on the Photochemically-Induced Oxidation of D-Fructose in the Presence of $FeCl_3$ at 20 °C

pH	D-Fructose oxidized 10^{-3} mol	D-Erythrose[a] /10^{-3} mol	NaOH consumed /10^{-3} mol	Formic Acid /10^{-3} mol
6.8	49	27 (55%)	5	5
7.2	44	18 (41%)	42	12
7.8	54	18 (33%)	74	19
8.4	80	12 (15%)	99	31
9.0	92	6 (7%)	133	38

A 500 ml of the D-fructose(0.2 mol)–$FeCl_3$(1×10^{-3} mol) solution was irradiated by the method 2 (see Experimental) for 120 h.

a) Conversions based on the D-frucotse oxidized are given in parentheses(mol%).

Discussion

Catalytic Action of Iron and Manganese Ions. Titration curves in Fig. 2 show that Fe(III) exists as $[Fe^{III}(OR^-)_3]$ at neutral to weakly basic pH in the presence of a large excess of D-fructose, where OR^- represents OH^- or a dissociated form of D-fructose. Fe(II) is supposed to exist as Fe^{2+} or to some extent as $[Fe^{II}(OR^-)]^+$ at around pH 9. These results are essentially the same as those in the absence of D-fructose ($pK_a=6$ for $[Fe^{III}(OH^-)_2]^+ + OH^- \rightleftarrows [Fe^{III}(OH^-)_3]$, and $pK_a=9.2$ for $Fe^{2+} + OH^- \rightleftarrows [Fe^{II}(OH^-)]^+$).[16,17] However, no precipitate was formed in this pH range in the presence of D-fructose, and both Fe(III) and Fe(II) remained in the solution.

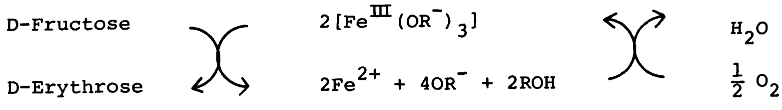
The oxidation of Fe(II) by atmospheric oxygen in the presence of D-fructose was shown to take place at an appreciable rate above pH 6 in the dark (Fig. 2). This result is consistent with the fact that the oxidation-reduction potential of Fe(III)/Fe(II) decreased at a higher pH of the solution. Several studies have shown that the rate of oxidation of Fe(II) strongly depends on the hydroxide ion concentration. The half-lives of Fe^{2+} in an air-saturated solution at pH 8 is estimated to be 45 s.[17,18] This oxidation process can be written as follows at a neutral pH,

$$2Fe^{2+} + 1/2O_2 + 6HOR \longrightarrow 2[Fe^{III}(OR^-)_3] + 4H^+ + H_2O,$$

where ROH represents H_2O or D-fructose. Therefore, the pH of the solution decreases upon the oxidation of Fe(II).

When D-fructose is degraded by a photochemically-induced oxidation with Fe(III) in a acidic medium under either an aerobic or an anaerobic atmosphere, 2 mol of Fe(III) is required to oxidize 1 mol of D-fructose into D-erythrose.[7] The irradiation of D-fructose solutions at a neutral pH in the presence of a small amount of $FeCl_3$ also caused the degradation of D-fructose, mostly into D-erythrose. However, the amount of D-fructose oxidized or D-erythrose formed is much more than that of Fe(III) (Table 1). The reaction requires the presence of oxygen, a small amount of iron ions, and irradiation with light. Irradiation in the absence of oxygen caused only a reduction of Fe(III) into Fe(II) without a detectable decrease in D-fructose. This was because the amount of iron ion in a solution was quite small compared to that of D-fructose. Therefore, the reaction was concluded to involve a photochemically-induced oxidation with atmospheric oxygen by coupling with the oxidation-reduction cycle of iron ions (Scheme 1). Little difference was observed for reactions in the presence of different iron species at the beginning ($FeCl_3$ and $FeCl_2$). Also Fe(II) was shown to be oxidized to Fe(III) by atmospheric oxygen at an appreciable rate at neutral pH. These facts further support the mechanism shown above, and the results shown in Fig. 1(a) also confirm that the oxidation-reduction cycle of iron is operative and repeatable. The photochemical process of the reaction was the reduction of Fe(III) into Fe(II) with a concomitant oxidation of D-fructose to D-erythrose. The highest quantum yield of the process was observed at 300—350 nm, showing that the exitation of the ligand-to-metal charge transfer (LMCT) band of Fe(III) was the key step of the process.[19] The results are substantially the same as those of reactions in acidic media.[7]

It was noted in relation to the results shown in



Scheme 1.

Table 2 that the irradiation of a solution whose pH was below 6.8 resulted in the formation of a colloidal precipitate. In this pH range, Fe(III) was supposed to exist in part as $[Fe^{III}(OR^-)_2]^+$ in the solution, and the relative instability of this species toward hydrolysis compared to that of $[Fe^{III}(OR^-)_3]$ may have been responsible for the precipitate formation.

It was also shown that manganese ions underwent a photoreduction from Mn(III) to Mn(II) and a subsequent reoxidation to Mn(III) due to atmospheric oxygen in the presence of a large excess of D-fructose at a weakly basic pH without the formation of any precipitate. Mn(III) and other higher oxidation states of manganese ion were interpreted to be involved in biological electron-transfer reactions.[20] However, relatively few Mn(III) complexes are known to be stable and soluble in aqueous solutions due to their high affinity toward hydroxide ions.[21,22] D-Fructose showed a good sequestering ability toward Mn(III), and Mn(III) species were formed with an appreciable rate above pH 8 under an aerobic atmosphere and remained in solution. The action spectrum of the reduction of Mn(III) at 260—650 nm showed that light of shorter wavelengths was more effective though a small maximum was observed at a region corresponding to the d-d transition band of Mn(III) (Fig. 1(b)). As the LMCT band of the Mn(III) species has been reported to be at 200—220 nm with a large extinction coefficient,[14] the excitation of the LMCT band is suggested to be most effective for the reduction of Mn(III), being consistent with that of Fe(III).

Effect of PH on the Catalytic Action of $FeCl_3$. The photooxidation of D-fructose by Fe(III) in an acidic media shows a high selectivity and gives D-erythrose in a nearly 90% yield via the formation of a D-fructose–Fe(III) complex.[7] As the reoxidation of Fe(II) does not proceed at an appreciable rate in an acidic solution, the pH of a solution should be kept above 6 for the oxidation-reduction cycle of iron ions to operate. However, the selectivity of the reaction to yield D-erythrose markedly decreased at a higher pH (Table 2). Though the yield of D-erythrose still complised more than a half of D-fructose oxidized at pH 6.8, the formation of formic acid and other acid products predominated in a more basic pH range. Aldonic acids, formic acid, and other acid products along with carbon dioxide were the common oxidation products of aldoses and ketoses with oxygen in highly alkaline solutions or with hydrogen peroxide.[23,24] Hydroxyl radical is thought to be involved in these reactions. The autoxidation of cellulose in alkaline conditions is known to be more extensive in the presence of transition-metal cations, and the photoirradiation of a cellulose-transition metal system leads to the formation of radical species.[25,26] Therefore, a free-radical process might be involved in the formation of acid products rather than a direct electron transfer from D-fructose to the Fe(III) via a complex formation. And this process becomes more dominant at a higher pH.

Thus, a catalytic amount of transition-metal cations in neutral to weakly basic solutions is shown to cause the photochemically-induced degradation of D-fructose in the presence of atmospheric oxygen. Cox et al. have noted that the presence of Fe(II) in freshly opened ampoules of "Imferon" (the ferric-dextran preparation frequently used for the treatment of iron-defficient anemia) is responsible for the hypotensive side effect of this preparation and that an exposure to the atmosphere abolishes this side effect.[27] This observation may be understood from the results presented here, i.e., the reduction of Fe(III) during the storage and reoxidation of Fe(II) by atmospheric oxygen in the presence of dextran. Furthermore, the results might have a wide variety of biological and physiological importance,[28] since saccharides and transition-metal cations are widely distributed in nature.

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