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Complete List of Authors:	Hovey, Tanden; Regis University, Chemistry Mishra, Disha; Regis University, Chemistry Singh, Manveer; Regis University, Chemistry Anaya, Grecia; Regis University, Chemistry Owusu, Chantele ; Regis University, Chemistry Barvian, Nicole; Regis University, Chemistry Sorauf, Kellen; Regis University, Chemistry Patro, Dambarudhar; Khallikote University, Chemistry Panigrahi, Akhil; Khallikote University, Chemistry Mahapatro, Surendra; Regis University, Chemistry

PATHWAYS IN PERMANGANATE OXIDATION OF MANDELIC ACID: REACTIVITY AND SELECTIVITY OF INTERMEDIATE MANGANESE SPECIES.

Tanden A. Hovey[1], Disha Mishra[1,3], Manveer Singh[1], Grecia Anaya[1], Chantele Owusu[1], Nicole C. Barvian[1], Kellen J. Sorauf[1], Mata Dambarudhar Patro[2,4], Akhil K. Panigrahi[2] and Surendra N. Mahapatro[1*]

[1]Department of Chemistry, Regis University, Denver, CO 80221, USA.

[2]Department of Chemistry, Khallikote University, Berhampur, 760001, Odisha, India

[3]Participant, Regis University, Science Bridge program, Legacy High school, Broomfield, CO

[4]Visiting Professor from Khallikote University, India

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Abstract

We report a comprehensive kinetic and product study of the oxidation of mandelic acid (MA) by permanganate in the pH range 1-13, including a full accounting of total oxidizing equivalents (five and three- electron change in acid and basic medium respectively). In the entire pH range, the reaction shows a primary kinetic deuterium isotope effect ($k_H/k_D \geq$ 8-9), indicating rate-limiting hydride transfer. The deuterium label in α-deutero-mandelic acid is retained in benzaldehyde. Benzaldehyde (BZ) is formed in post rate limiting steps due to reactions involving manganese intermediates. In alkaline pH (≥13), in the presence of barium acetate, Mn(VI) is removed as insoluble blue barium manganate, the stoichiometry of the first-step of reduction was found to be: MA + 2Mn(VII) = PGA + 2Mn(VI). Manganate MnO_4^{2-}, is directly reduced to MnO_2 giving an additional mole of phenylglyoxylic acid (PGA). The experimentally observed ratio of benzaldehyde to phenylglyoxylic (BZ/PGA) provides a basis for discrimination between mechanistic choices that include direct reduction of Mn(V) to Mn(III) (in acid medium), disproportionation to Mn(IV) and Mn(VI) or oxidation to Mn(VI) by a second mol of permanganate. Interestingly, at pH 4, a stoichiometric, soluble Mn(IV) is observed for the first time for a hydroxy-acid oxidation, reminiscent of the *Guyard* reaction. Because of the widespread use of permanganate as an environmental green oxidant, results from mandelic acid oxidation have implications for the remediation of dissolved organic matter (DOM) including hydrocarbons and nitroaromatics in waste and ground water.

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Keywords

Permanganate, oxidations, hydroxy-acids, kinetics and mechanism, manganese intermediates, kinetic-deuterium isotope effect, contaminant abatement in waste or ground water

Synopsis

This study reports on the role of intermediates in permanganate oxidation of a model hydroxy-acid. It is significant in the context of waste water treatment for contaminant abatement and water quality.

Introduction:

Over the past 350 years, since the synthesis of potassium permanganate by John Rudolph Glauber, there has been remarkable achievements in the research and discovery of new facets of aqueous manganese redox chemistry.[1] Permanganate is a versatile oxidant with wide ranging applications in organic synthesis,[2-5] and analytical chemistry including permanganate chem-luminescence. [6] The current resurgence in permanganate chemistry is due to its wide spread use as an environmental green-oxidant for the remediation of dissolved organic matter (DOM) and emerging persistent organic contaminants (EOC) in waste and groundwater including hydrocarbons, nitroaromatics (TNT), bromophenols, antibiotics, chlorinated hydrocarbons (TCE and PCE),[7-13] and ground water arsenic.[14] Oxidation of cellulose results in carboxylated cellulose Nano-crystals.[15,16] Permanganate is also used as an ethylene scavenger in horticulture produce,[17] in the denim industry,[18] and as a probe for DNA-foot printing.[19-20]

Permanganate oxidations have been reviewed extensively.[21-29] Definitive work of Simandi,[30-34] Wiberg,[35-37] Freeman,[38-40] Parez-Benito,[41-45] Lee,[46-49] and Stewart,[50-52] have greatly contributed to our understanding of the mechanisms of oxidations of a diverse group of organic compounds. This includes aromatic hydrocarbons (C-H oxidation),[35,53,54] alcohols,[50,51] aldehydes,[37] alkenes ,[30, 38,39] oxalic acid,[55-59] amines,[52,60] sulfoxides,[61] and amino acids.[41-45]

Permanganate oxidations are inherently complex due to a number of intermediates resulting from initial two and one electron reductions of Mn(VII). Both Mn(V) and Mn(VI) have no known aqueous chemistry except in highly alkaline medium. Adding to the complexity, there are a number of pH dependent disproportionation/comproportionation reactions.[62-63] A soluble, tobacco colored manganese (IV) species has been observed in a large number of reactions in neutral pH (phosphate buffer) including oxidation of sulfite,[31] amino acids,[41-44] and thiosulfate,[64] alkenes .[34, 36, 39,47] A colloidal Mn(IV) has also been identified in permanganate oscillating reactions.[65-67] Manganese(III) is known to be stabilized by pyrophosphate, EDTA and citrate.[68-70].

Earlier published reports on the permanganate oxidation of hydroxy-acids (citric, tartaric and mandelic acid) by acid permanganate,[40,71-75] have been limited without any comprehensive product analysis and full accounting of oxidizing equivalents on the basis of 5-electron (acid) or 3- electron change in basic pH (≥ 7). The reported stoichiometry (eq 1) is not supported by quantitative product analysis (either for CO_2 or benzaldehyde; which was detected by its smell).[71]

$$5C_6H_5CH(OH)COOH + 2MnO_4^- + 6H^+ \longrightarrow 5\,C_6H_5CHO + 5CO_2 + 8H_2O + 2Mn^{2+} \quad (1)$$

Freeman and Scot[40] studied the oxidation of mandelic acid in the pH range of 7.3-12.7; benzaldehyde was reported as the sole product. In another study in acidic pH, Benerjee[72] reports 94 % yield of benzaldehyde in the presence of fluoride (0.02 M) and 1.0 M HClO4 without mentioning the experimental method to quantify benzaldehde.[40] The observed primary deuterium kinetic isotope effect (k_H/k_D) of 3.5 is in direct conflict with their observation of the formation of benzaldehyde as the only product. Phenylglyoxylic acid (PGA) is the expected and logical product of rate limiting C-H cleavage; there is no conceivable and rational

pathway which would lead to benzaldehyde from the decarboxylation of the carbocation (in eq 2 and 3)

$$C_6H_5CH(OH)COOH) + H^+ + MnO_4^- \longrightarrow C_6H_5C^+(OH)COOH + H_2MnO_4^- \qquad (2)$$

$$C_6H_5C^+(OH)COOH \longrightarrow C_6H_5CHO + CO_2 + H^+ \qquad (3)$$

The express purpose of the present investigation is to resolve this conflict and to provide a full accounting of oxidizing equivalents under pseudo first-order kinetic conditions (excess mandelic acid over permanganate). In addition, the oxidation of mandelic acid by permanganate provides an opportunity to study competing C-H versus C-C cleavage and to gain insight into the selectivity and reactivity of manganese intermediates in the oxidation.

We report a comprehensive study of the permanganate oxidation of mandelic acid in a wide pH range including kinetic deuterium isotope effect, reverse-phase HPLC product studies, determination of intermediate oxidation states by classical iodometry, and by tracing the deuterium label in the oxidative decarboxylation leaving benzaldehyde. In addition, we report for the first time, a soluble (presumably colloidal) Mn(IV) species both in acid medium (pH 4) and at pH 7. Using the rapid disproportionation of potassium manganate (K_2MnO_4) in acid medium, we have gained insight into the reactivity of Mn(V) in acidic and neutral pH. In addition, using periodate as a cooxidant, we have been able to turn over the Mn(V)-Mn(VII) cycle with significant increase in the yield of phenylglyoxylic acid.

EXPERIMENTAL SECTION

Materials and Methods

α-Deuteromandelic acid was synthesized by base catalyzed deuterium exchange of sodium mandelate in D_2O in a PARR pressure vessel maintained at 155°C for 15 days.[76-77] After completion, the reaction mixture was acidified and extracted with ethyl acetate, dried (anhydrous sodium sulfate). The isolated sample was further purified by recrystallization from ethyl acetate. The purity of α-deutero-mandelic acid was checked from ^{1}H-NMR (200 MHz; absence of the α-proton in the δ5.2-5.3 ppm region of ^{1}HNMR spectrum) and by EI-MS (molecular ion, m/z = 153, base peak m/z = 108). The deuterium content was determined by mass spectrometry and NMR ; ≥98 %. (Figures S1-3).

Given the recognized problems associated with colloidal MnO_2 and its ability to catalyze disproportionation reactions of manganate(VI)[62] and hypomanganate (V) (each leading to more MnO_2), extreme care was taken to avoid/destroy oxidizable organic matter in water.[78] Nano-pure water was distilled from a concentrated alkaline solution of potassium permanganate using an all-glass distillation setup.

The following materials from Sigma Aldrich were of the highest grade and were used without any further purification including DL-mandelic acid (m. p.118 ^{o}C), phenylglyoxylic acid (benzoyl formic acid), benzoic acid, and benzaldehyde (Sure /Seal^{TM}; ≥99%)). Solutions were freshly prepared in deoxygenated solutions for use as LC standards. Acetonitrile, glacial acetic and *Nano*-pure water were filtered through a 4-8 µm filter and then used for preparing the solvent mixture for LC analysis.

A molar absorptivity value of 2440 $M^{-1}cm^{-1}$ (526 nm) was used to calculate the initial concentration of permanganate.[78] A value of 1640 $M^{-1}cm^{-1}$ at 606 nm[47-48] was used for manganate in 0.1 M NaOH or KOH. Kinetic measurements and spectral scans were performed on a Beckman DU 640 UV-Vis spectrophotometer (Diode Array detection) or on a Shimadzu double- beam spectrophotometer using quartz cuvettes (10 mm path length) at 25.0 ± 0.5 °C (using a circulating VWR thermostatic water bath and cell holders). Linear regression analyses were performed in Excel.

The initial permanganate concentrations were 3×10^{-4} M in kinetic studies and 1.0×10^{-3} M in a total volume of 10 mL for product studies. Kinetic measurements were performed under pseudo-first-order conditions with a large excess of the reductant (20-125 times excess). Ionic strength was adjusted with $NaClO_4$ in some experiments. Pseudo-first-order rate constants were determined from the linear plots of log (or ln) A_t- A_∞ (at 526 nm), A_∞–A_t for Mn(VI) at 606 nm) and A_∞ –A_t versus time for the soluble (colloidal) manganese(IV) at 418 nm. The plots covered the reactions for well over three half-lives. The rate constants are the average of at least two measurements and are reproducible to within ±7%.

Product analysis was carried out using Agilent 1100 Series HPLC System and Agilent 1100 series G1315B Diode Array Detector (254 nm detection). The flow rate used was 1 mL/min and the column was maintained at 20 ^{o}C. The mobile phase solvent composition (v/v) was 74% water, 20% acetonitrile and 6% glacial acetic acid. The column was an Agilent Eclipse XDB-C18; 5 m 4.6 x 150 mm. The solvent composition provided a clean separation of all four components (mandelic acid, phenylglyoxylic acid, benzoic acid, and benzaldehyde). A typical HPLC separation for the four components is given in Figure 1. Product yields were estimated by comparing peak integral areas of individual standards with that of the products (Figures S5-7).

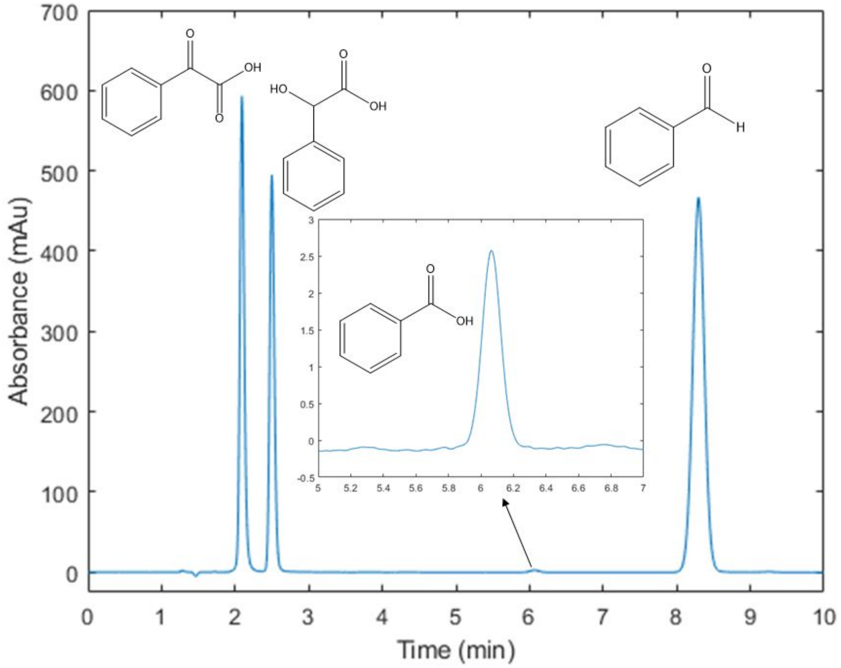


Figure 1. shows a typical HPLC elution of products of the reaction performed in pH 7.4 (phosphate buffer, 0.1 M)**.**

Competition experiment

A reaction mixture containing benzaldehyde (0.01 M), phenylglyoxylic acid (0.01 M) in acidic medium ($HClO_4$ = 0.1M) and permanganate (0.005 M)) was allowed to stand until the reaction was complete. LC analysis showed that 75 % of the phenylglyoxylic acid was oxidized to benzoic acid.

Tracing the deuterium label in the 2,4-dinitrophenylhydrazone derivative of benzaldehyde by mass spectrometry

Deutero (α-C-D) mandelic acid (1 mmol) was oxidized by acid permanganate (pH 1; 0.4 mmol) in a total volume of 50 mL. After completion of the reaction, 25 mL (0.2 mmol of permanganate) of the reaction mixture was treated with 100 mL of an acidic solution (1.0 M HCl or H_2SO_4) of 2% of 2,4 –dinitrophenyl hydrazine (Aldrich 97 %) and left overnight. The precipitated yellow solid was isolated by vacuum filtration, washed first with 2M HCl (to remove any unreacted 2,4-dinitrophenylhydrazine) and then with a solution of sodium bicarbonate (to remove 2,4-nitrophenylhydrazone derivative of phenylglyoxylic acid), and dried in a vacuum oven. The isolated yield of the 2,4-dinitophenylhydrazone of benzaldehyde derivative was 0.31 mmol (yield = 1.55 mol (0.31 mmol/0.2 mmol) of benzaldehyde per mol of permanganate). Mass spectra of the derivative showed that deuterium label in the mandelic acid is retained in the product, 2,4-dinitrophenylhydrazone derivative of benzaldehyde (m/z = 287; Figure S4A). A portion of reaction mixture was saved for ESI-mass spectra in the positive mode in the presence of oxalic acid. Figure S4B clearly shows deuterated- benzaldehyde [$C_6H_5CDOH^+$]; m/z = 108.

Determination of intermediate oxidation states

The average oxidation state of the intermediate manganese species (at pH 4, 7 and 13) was determined by first adding acidified (HCl) potassium or sodium iodide to 5 mL aliquots of reaction mixture and then titrating the liberated iodine (present in the soluble form as I_3^- in aqueous excess iodide) with a standard (1 mM) thiosulfate solution using starch as an indicator.[38, 39] In a typical titration, 5 mL aliquots of the reaction mixture (mandelate = 0.05 M and permanganate = 1×10^{-3} M; total volume = 50 mL) were acidified with 20 mL of 2.0 M HCl and treated with excess KI/NaI (ca. 0.2 g). The liberated iodine (present as I_3^-) was titrated against freshly prepared 1 mM -3.5 mM sodium thiosulfate in the presence of freshly prepared starch solution. The solution went from an intense blue to a colorless end point.

$$\mathrm{Mn(IV)} + 3\mathrm{I}^- = \mathrm{Mn(II)} + \mathrm{I}_3^- \quad (4)$$

In acid medium the stoichiometry for manganate-iodide reaction is:

$$\mathrm{Mn(VI)} + 6\mathrm{I}^- = \mathrm{Mn(II)} + 2\mathrm{I}_3^- \quad (5)$$

Synthesis of potassium manganate [K_2MnO_4]

Potassium manganate (K_2MnO_4) was prepared by reduction of permanganate by KOH using published methods.[79, 80]

$$2KMnO_4 + 2KOH \longrightarrow 2K_2MnO_4 + \tfrac{1}{2}O_2 + H_2O \qquad (6)$$

The concentration of Mn (VI) was determined by dissolving a weighed amount of K_2MnO_4 in 0.2 M NaOH or KOH solution (1mM) and using the molar absorptivity of 1640 M^{-1} cm^{-1} at 606 nm[39, 40] and also by iodometric titrations in acid medium. The Mn(VI) oxidation state ($3d^1$) was confirmed by EPR at 40-80 K in concentrated solution of KOH and LiCl.[81]

Results and Discussions

Spectral scans and manganese Intermediates.

Acid pH 1.

Successive spectral scans in the wavelength range (350-750 nm) were carried out using Beckman DU-7 rapid scanning UV-Vis and a Shimadzu double beam spectrophotometer at several pH values (1, 4, 7, and 13). At pH 1 spectral scans were carried out both in the presence and absence of pyrophosphate. Figure 2 shows spectral titrations at pH 1 leading to the smooth conversion to Mn(II). Also, it did not reveal the presence of any intermediate including Mn(III) which is known to be stabilized pyrophosphate.[68-70]

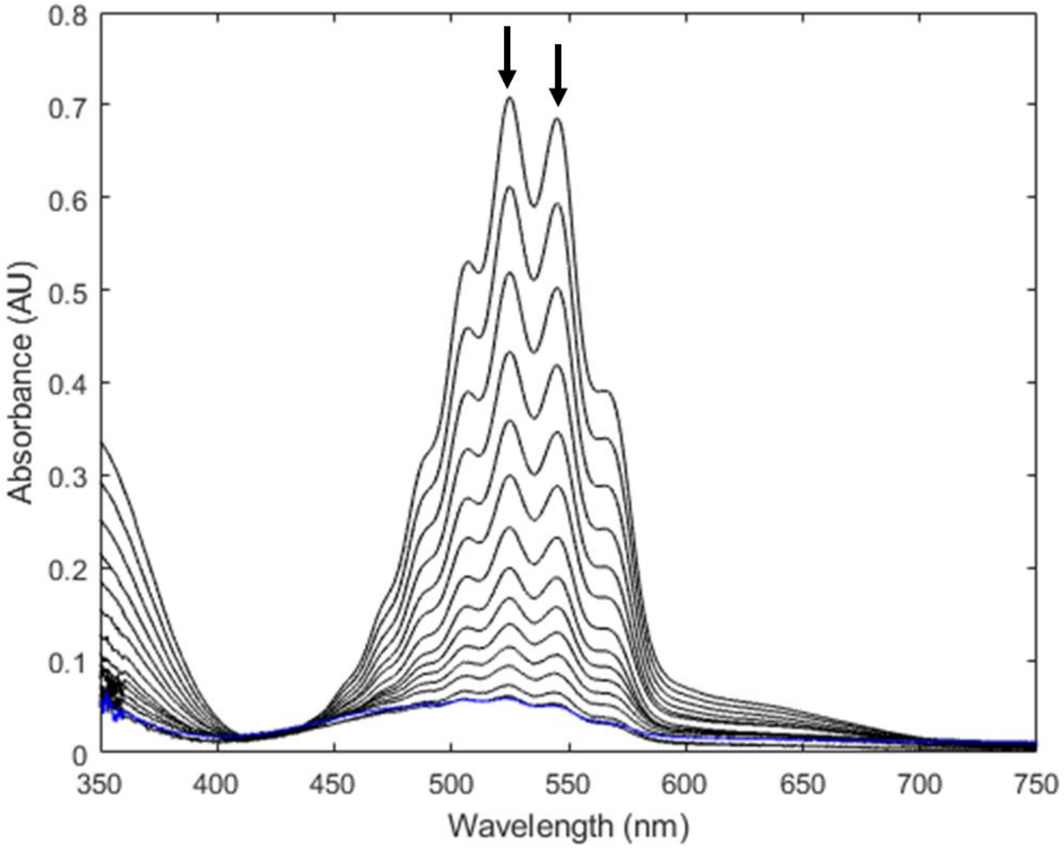


Figure 2. Spectral titrations at pH 1. Mandelic acid = 0.05 M. MnO_4^- = 3.0 x10^{-4} M. Sodium pyrophosphate = 0.1 M. 25 °C. Scan interval 180 seconds.

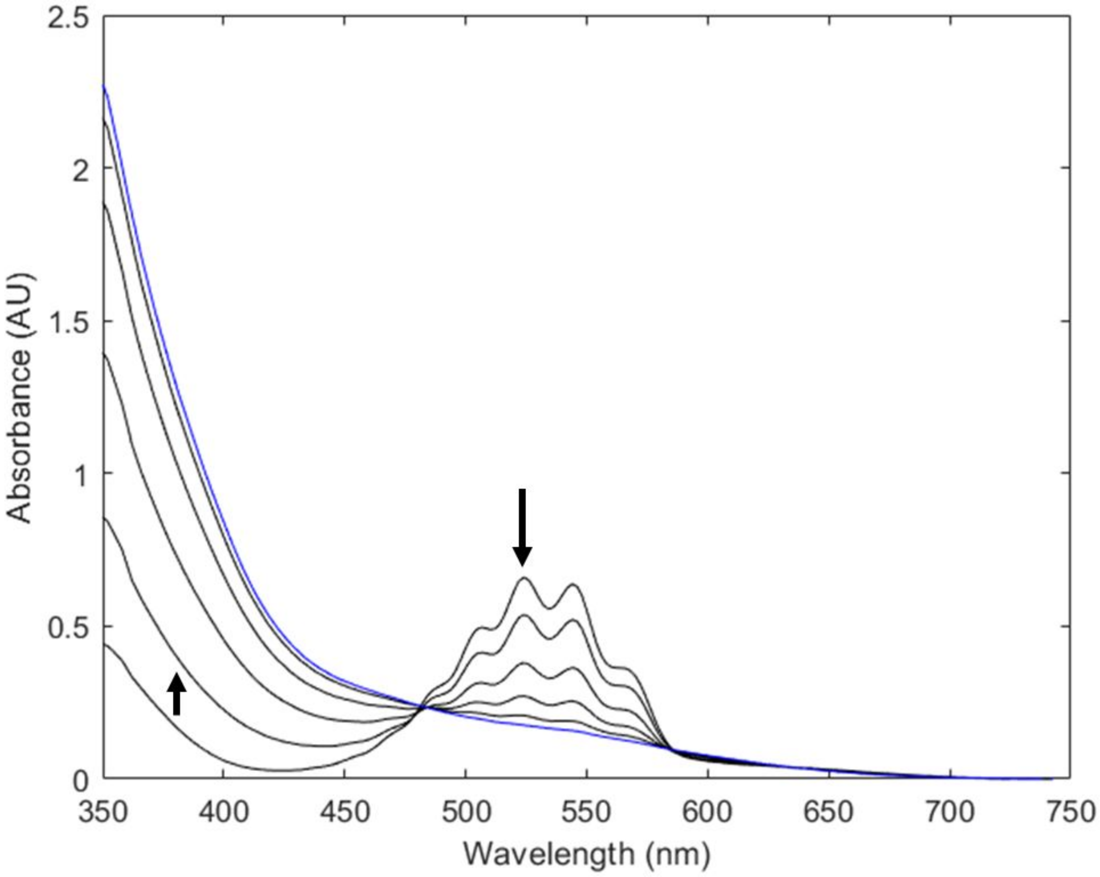


Figure 3. Spectral Scans at pH 4.2 (mandelic acid-mandelate buffer 0.1M). Conditions: Mandelic acid-mandelate ion = 0.1 M; pH 4; MnO_4^- = 3.0 X 10^{-4} M, 25 ^{o}C); successive 30 second spectral scans at pH 4.2.

Figure 3 is similar to the spectra observed by Freeman et al earlier in the oxidation of uracil, (*E*)-2-butenoic- and (E)-3-phenylpropenoic acid.[38] The spectral scans showed an isosbestic point at 468-469nm which implies one intermediate, presumably Mn(IV).

Figure S12 shows the spectrum of the yellow manganese species at the end of spectral scans in Figure 3.

The observed isosbestic point at 469-470 nm (Figure 4; phosphate buffer; pH 7) is consistent with a soluble (colloidal) Mn(IV) intermediate which has been reported earlier in the permanganate oxidation uracils,[38] unsaturated acids,[47] amino acids,[41-44] thiosulfate,[64] sulfite,[31, 32] and toluene.[54] The loss of isosbestic point was observed at longer time scans presumably due to conversion of soluble manganese(IV) to MnO_2 particles.

$$\text{Mn(IV) (soluble/colloidal)} \longrightarrow MnO_2 \qquad (7)$$

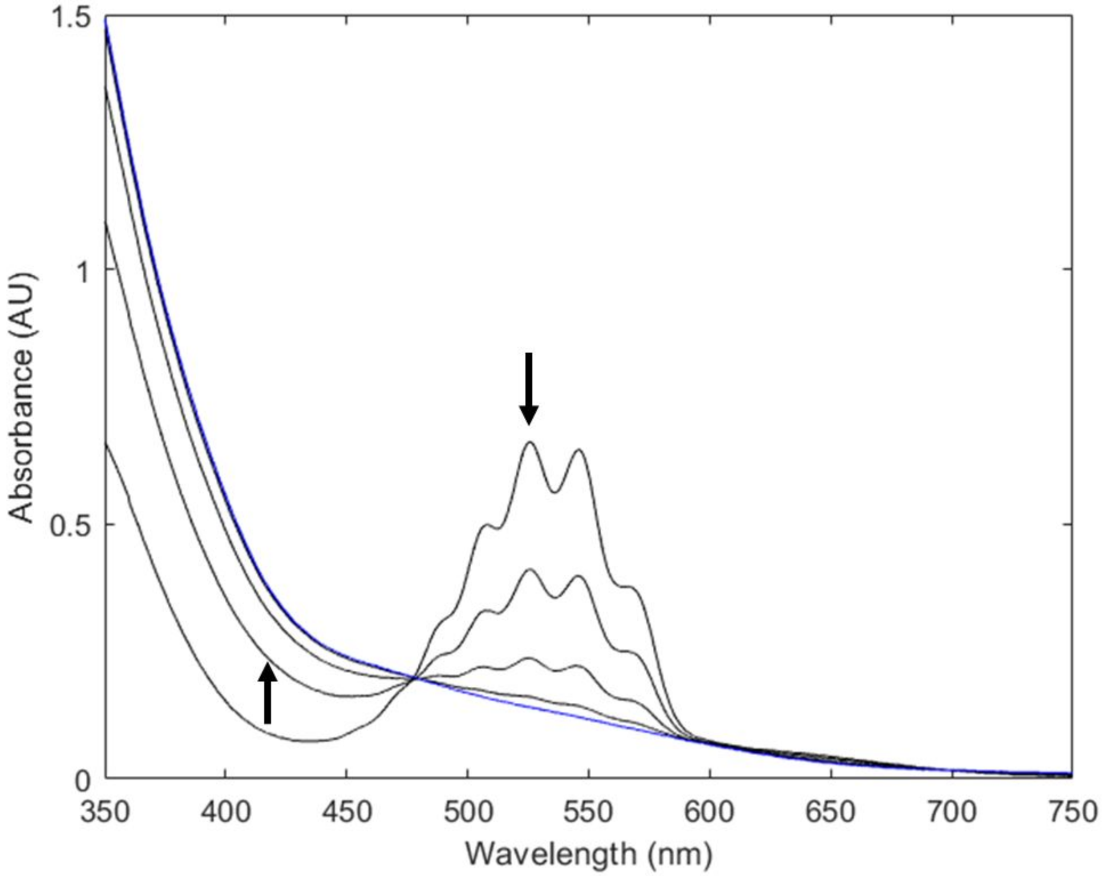


Figure 4. Successive spectral scans in the oxidation of mandelic acid at neutral pH 7. Conditions: neutral pH (6.8-7.4); phosphate buffer; 0.1 M. MA = 0.05 M. [MnO_4^-] = 3 x 10^{-4} M. 25 ± 0.5 ^{o}C. Scan interval 180 seconds.

In alkaline medium (≥ 13), spectral scans showed the formation of a green manganese intermediate which grows at 606 nm. The isosbestic point observed at 470 nm was lost due to precipitation of MnO_2 during the later stages of the reaction (Figure 5)

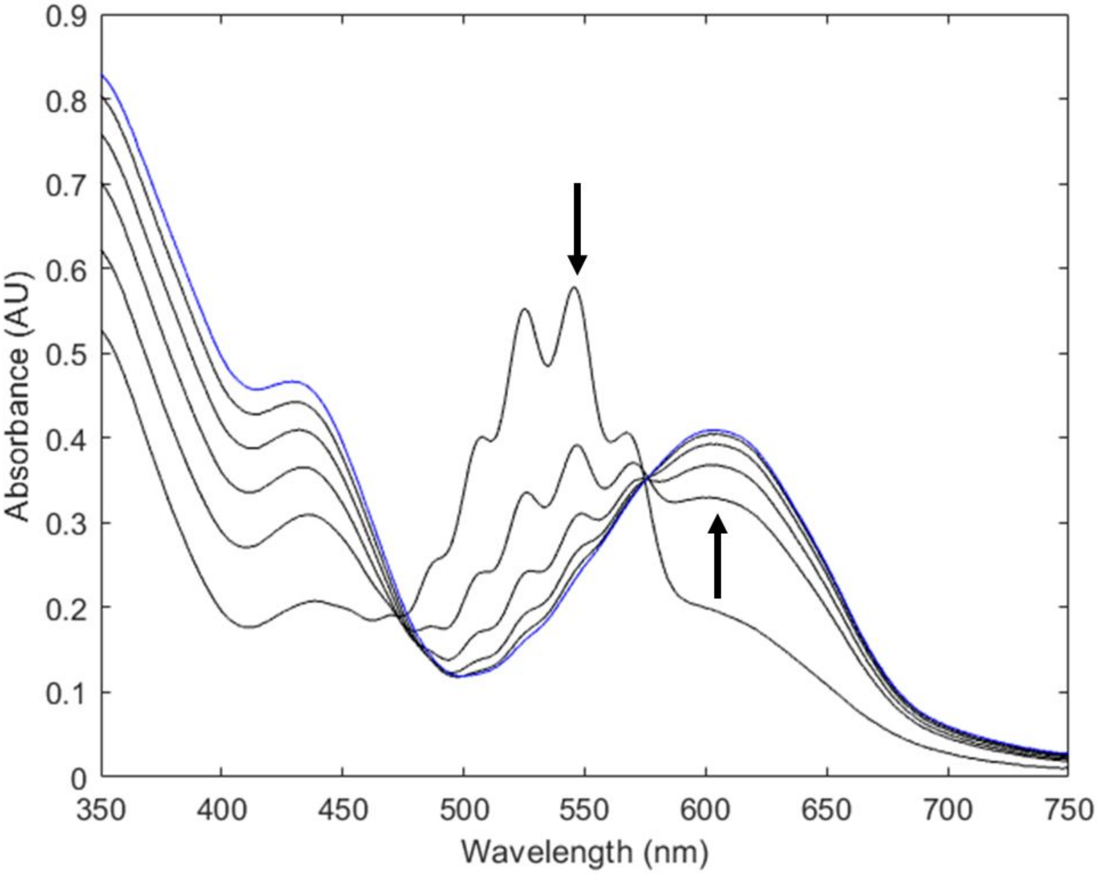


Figure 5. Successive spectral scans in the reaction of mandelic acid at pH 13. Conditions: [MA] = 0.05 M, MnO_4^- = 3.0×10^{-4} M, NaOH= 0.15; mandelic is titrated with an equivalent of NaOH to give 0.05 M mandelate ion. pH = 13; 25.0 ± 0.5 °C. Scan interval 180 seconds. Isosbestic points at 470 and 576 nm.

Kinetic studies and rate-laws

The kinetics of oxidation of mandelic acid by permanganate has been studied by Bakore et al.,[71] Banerji,[72] and Freeman.[40] At any given acidity, first order dependence each on permanganate, mandelic acid and H^+ has been established. In acid medium, the reaction shows an induction period followed by autocatalytic phase and is influenced by ionic strength, added Mn(II), and fluoride. We essentially confirmed the kinetic results reported in earlier studies.[40, 71-74] The effect of ionic strength was more pronounced at higher pH due to the dissociation of mandelic acid to mandelate anion ($pK_a = 3.85$).[82]

The rate expression at constant ionic strength in acid medium is given by:

$$-d[MnO_4^-]/dt = k_{obs}\,[\text{mandelic acid}]\,[MnO_4^-]\,[H^+] \qquad (8)$$

Autocatalysis could not be completely eliminated even at a tenfold higher concentration of added Mn(II) (MnO_4^- = 3×10^{-4}M and Mn(II) = 3.0×10^{-3} M). We did not see any evidence for a stable Mn(III) intermediate even in the presence of added pyrophosphate (3×10^{-3} M) which suggests that Mn(III) intermediate reacts with mandelic acid in an extremely fast step relative to ligand exchange with pyrophosphate. Kinetic traces in acid medium are given in Figures S17-18.

As this study was undertaken with the express purpose of gaining insight into the structure and reactivity of manganese intermediates and the selectivity (if any) for either C-H or C-C cleavage, we did not pursue the kinetics of oxidation of mandelic acid in acid medium any further.

We confirmed the rate law at pH 7-7.4

$$-d[MnO_4^-]/dt = k_{obs}\,[\text{mandelate anion}]\,[MnO_4^-], \qquad (9)$$

which is consistent with earlier observation of Freeman and Scott[40] who reported a zero-order dependence on hydroxide ions in the pH range 7.3-to 12.7.

In the alkaline pH (13 and above), first order dependence on $[OH^-]$, mandelate anion and MnO_4^- was observed.

$$-d[MnO_4^-]/dt = d[Mn(VI)]/dt = k_{obs}\,[\text{mandelate anion}]\,[OH^-]\,[MnO_4^-] \qquad (10)$$

Table 1. Second -order rate constants for mandelic acid oxidation at selected pH values

pH	Second order rate constants[a]; k_2 M^{-1} s^{-1} at 25.0±0.5°C
1.0	0.305[b]
4.3	0.174
7.4	0.023
10	0.030
13	0.060

[a] Rate constants are reproducible to ± 7%.

[b] Estimated from half -life of the autocatalytic reaction in acid medium

The effect of ionic strength was more significant at pH ≥13 than in any other pH region. A plot of log second-order constants versus square-root of ionic strength was linear ($R^2 = 0.983$; Figure S16)

Intermediate manganese species

pH 4

As the end of spectral scans in Figure 3; the solution turned tobacco-yellow. Kinetics showed that concomitant with the loss of 526 nm absorbance was the growth of an intermediate at 418 nm (Figure 6). After an initial slow induction period, first-order kinetics was observed at both wavelengths. The 418 nm intermediate decayed in a much slower phase extending over many hours (half-life ≈ 55 minutes) resulting in Mn(II) as the final product of permanganate reduction. (Figure S13).

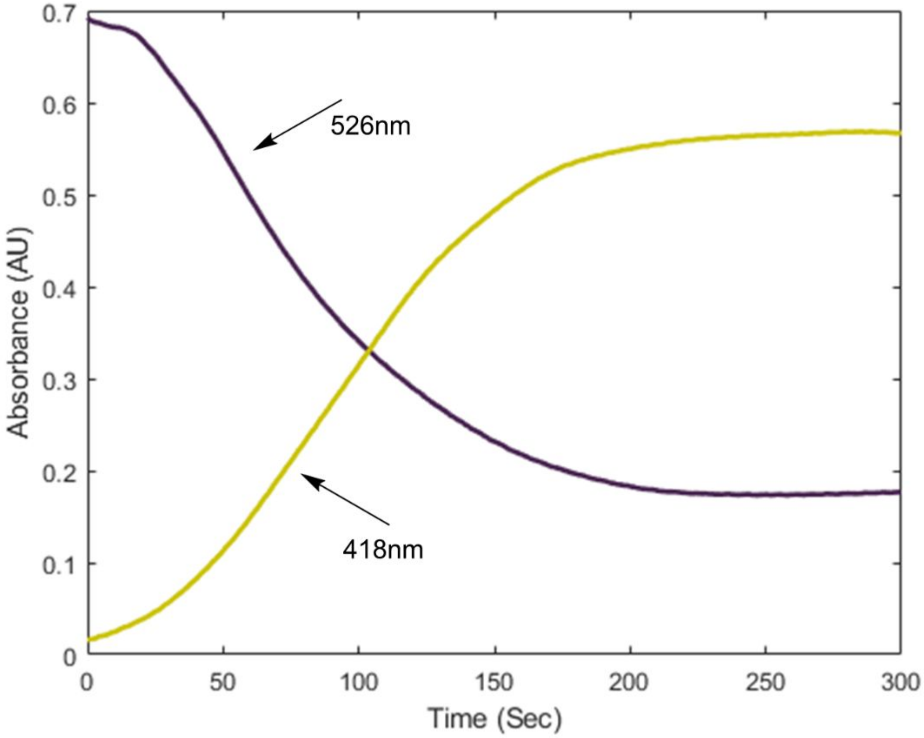


Figure 6. The growth of a soluble Mn(IV) species at pH 4 (mandelic acid -mandelate buffer; 0.1 M) at 25.0 °C. [MnO_4^{-}] = 3.0×10^{-4} M.

pH 7-7.4

A soluble Mn(IV) intermediate was also observed at 418 nm in pH 7 (phosphate buffer; Figure S8). At both wavelengths (418 nm and 526 nm) the first-order rate constants were nearly same within 7% of each other. A plot of A_{526} versus A_{418} was linear ($R^2 = 0.999$; Figure S14) indicating that there was no interference of any insoluble particles of MnO_2

Alkaline pH (13)

At pH ≥13, the reduction of permanganate is accompanied by changes in the visible spectrum (350-750 nm); the permanganate spectrum is replaced by the characteristic spectrum of Mn(VI), manganate with an absorption maximum of 606 nm without any evidence for manganese (V) at 657-660 nm (Figure 7)

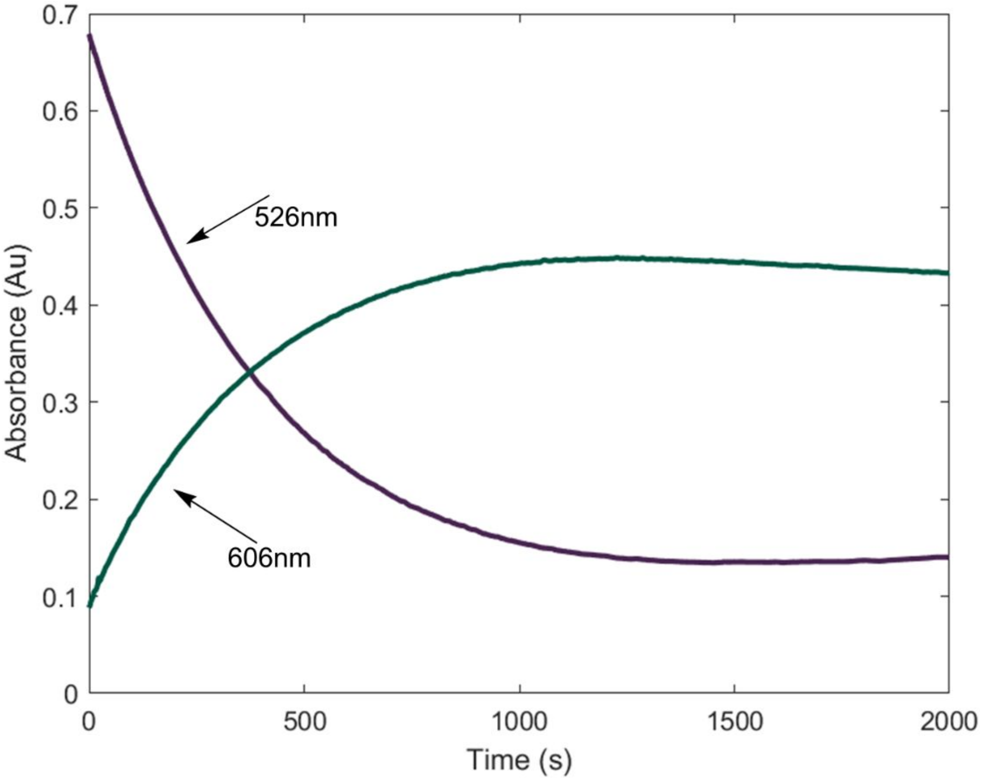


Figure 7. Growth of a Mn(VI) intermediate at 606 nm and decay of permanganate at 526 nm (pH 13 and above). $[MnO_4^-]$ = 3 x 10-4 M, [Mandelate] = 0.05 M; 22 25.0 ± 0.5 °C.

At 606 nm, using the maximum absorption value of 0.45 at the highest point of the growth curve in Figure 7 and literature molar absorptivity of 1630-1700 $M^{-1}cm^{-1}$ [48] for an initial permanganate concentration of 3.0 x 10^{-4} M, we calculate a manganate concentration of 2.65 x 10^{-4} M (86 % of initial Mn(VII)). Our results show a 1:1 stoichiometry of permanganate: manganate. The agreement between calculated values of pseudo-first-order rate constants (through three half-lives) for the growth of Mn(VI) and decay of Mn(VII) shows that precipitation of MnO_2 was minimal. We analyzed the products near or at the end of the stable plateau of the 606 nm growth curve (about 20 minutes) and after 24 hours when the reaction resulted in the precipitation of black/brown MnO_2.

The plot of log A_{526nm} versus A_{606nm} is linear (R^2 = 0.999; Figure S15), which suggests that during the accumulation of the Mn(VI) species, there was no incursion of the second slow step of the reaction, the conversion of Mn(VI) to Mn(IV).

Dependence on pH

First-order rate constants for the growth of 418 nm and 606 nm intermediates are listed in Table 2.

Table 2. Rate constants for the first-order growth of intermediates in the oxidation of mandelic acid/mandelate at 25.0 ± 0.5 °C. In replicate measurements rate constants are reproducible to ± 7%.

pH	MA, M	First-order Growth (s^{-1}) at 418 nm	First-order Growth (s^{-1}) at 606 nm	First-order Rate Constant -decay (s^{-1}) at 526 nm
4.0-4.2	0.1	0.0172		0.0179
7.0-7.4	0.05	1.14×10^{-3}		1.30×10^{-3}
13	0.05		3.20×10^{-3}	2.81×10^{-3}

Iodometric determination of average oxidation state of manganese species

The iodometric titration curves (Figures S9-11) show stabilization of the thiosulfate titers indicating formation of relatively stable intermediate manganese species. Table 3 summarizes the average oxidation states of intermediate manganese species at or near the stable plateau of the absorbance curves at 418 and 606 nm (Figures 6,7 and S8). For example, at pH 13, at the stable plateau in Figure 8 for an initial concentration of 5×10^{-6} moles of initial permanganate, we estimated 4.6×10^{-6} moles of Mn(VI) (92 %), thus establishing a 1:1 stoichiometry for Mn(VII) to Mn(VI) at pH 13. This checks remarkably well with the concentration of Mn(VI) determined from absorbance measurements at the height of the 606 nm growth curve. Unlike the Mn(IV) species at pH 7, the pH 4 species decayed in a much slower step extending over several hours (half-life ≈ 55 minutes) (Figure S13).

The average oxidation state of 418 and 606 nm intermediates obtained from iodometric titration curves (Figures S9-11 are shown in Table 3)**.**

Table 3. Average oxidation state of intermediate manganese species near and toward the stable plateau of the absorbance curves in **Figures 5,7, and Figure S9-11**

pH	MA (M)	Oxidation state	time elapsed (sec)
4.0-4.2	0.1-0.5	3.8-4.2	150-300
7.0-7.4	0.05	3.8-4.1	1500-3000
13.0-13.5	0.05	5.8-6.1	750-1500

Product studies

Reverse phase HPLC was used to quantify both primary products (phenylglyoxylic acid; PGA) and benzaldehyde; BZ) and secondary oxidation product (benzoic acid; BA). The product yields (per mol of permanganate,) were estimated from the standard curves for each product (linear with regression coefficients $R^2 = 0.999$) (See Figures S5-7).

Product yields in permanganate oxidation of mandelic acid at several pH values are given in Table 4. The total expected yields are close to the theoretical values of 2.5 mol of 2-electron products/per mol of Mn(VII) in acid medium; this is based on a 5-electron reduction to Mn(II). In basic medium (pH 7 and above), the theoretical yield is 1.5 moles of two electron oxidation products /mol of Mn(VII), consistent with the three-electron reduction to Mn(IV).

In addition to the primary products, phenylglyoxylic acid (PGA) and benzaldehyde(BZ), we observed small but significant amounts of benzoic acid (BA) in acid medium. In a formal sense, benzoic acid is a four-electron oxidation product which could arise from oxidative decarboxylation of phenylglyoxylic acid or from the oxidation of benzaldehyde. To the best of our knowledge, there is no direct pathway to benzoic acid. The only precedent we are aware of is in the three-electron oxidation of mandelic acid to the benzoyl radical in chromic acid oxidation.[77]

When considering the total oxidizing equivalents, the yield of benzoic acid was multiplied by factor of two. At pH 1, the data in Table 4 shows that for a net 5-electron change, approximately 70 to 80 % of the total available oxidizing equivalents (2.5) are accounted for in the three products. After taking account in the yield of benzoic acid, the products ratio, BZ/PGA, pointed to possible stoichiometry under conditions of product analysis (fifty-fold excess of mandelic acid over permanganate).

Table 4. Products in the permanganate oxidation of mandelic acid[a]

			Product Yield mol/mol of $KMnO_4$ **[a]**						
Entry #	pH	MA (M)	$C_6H_5COCOOH$ **PGA**	C_6H_5COOH **BA**[**b**]	C_6H_5CHO **BZ**	Total	% of total oxidizing equivalents (**TOE**)	[f]BZ/PGA	Comments
1	1	0.05	0.14	0.30	1.27	2.01 (2.5)[**c**]	80	1.7	
2	1	0.5	0.30	0.28	0.86	1.72 (2.5)	69	1.0	
3	1	0.05	0.11	0.33	1.21	1.98 (2.5)	79	1.6	
4	0.3 [H^+] = 0.5 M	0.1	0.19	0.31	0.93	1.74 (2.5)	70	1.1	[g]MnO_4^- = 0.002 M
5	0 [H^+]= 1.0 M	0.1	0.19	0.32	0.85	1.68 (2.5)	67	1.0	[g]MnO_4^- = 0.002 M
6	4.2	0.1	0.34	0.12	2.0	2.58 (2.5)	103	3.4	
7	7.0-7.4	0.05	0.5 0.51	0.05 0.05	1.0 0.83	1.60 (1.5)[**d**] 1.43 (1.5)	107 95	2.2 1.8	
8	13	0.05	0.36[**e**]	-	-	0.36 (0.5)	72		Removed as insoluble $BaMnO_4$
9	13	0.05	1.20 1.25	- -	0.013 0.005	1.21 (1.5)[**d**] 1.25 (1.5)[**d**]	81 83		

[a] [MA] = 0.05 M; [MnO_4^-] = 1.0 x 10^{-3} M, Reactions carried in a total volume of 10 mL.

[b] Total yield = PGA + 2BA + BD

[c] 2.5 moles of 2-electron oxidation product based on 5-oxidizing equivalents in acidic medium

[d]1.5 moles of 2-electron oxidizing products based on 3-oxidizing equivalents at pH ≥ 7

[e]Barium acetate captures Mn(VI) as barium manganate.

[f]For entry #1

$[PGA]_T$ = [PGA] + 2[BA] ex. (0.14 + 2x0.30) = 0.74

[BZ]/$[PGA]_T$ ex. 1.27/0.74 = 1.7

For entry # 7 at pH 7.4, we assign the benzoic acid to benzaldehyde. At neutral PH benzaldehyde is 80-90 times more reactive than phenylglyoxylic acid.

$[BZ]_T$ = BZ + 2BA ex. (1.0 + 2x0.05) = 1.1

$[BZ]_T$/[PGA] ex. 1.1/0.5 = 2.2

[g] Mn(VII) = 0.002 M

pH 7-7.4

The spectrophotometric scans in Figure 4, the growth curve at 418 nm (Figure S8) and the iodometric titration curve (Figure S10), taken together, point to a stoichiometric soluble Mn(IV) species; Mn(VII): Mn(IV)); 1:1. We analyzed for the two primary products at the end of the stable plateau in Figure S8 by filtering off the solid MnO_2 using a micron filter or immersing it boiling water which induces conversion of soluble Mn(IV) to insoluble MnO_2. The data in Table 4 show that benzaldehyde and phenylglyoxylic acid are formed in nearly a 2:1 ratio. Based on a 3-electron reduction of Mn(VII), the higher than 100 % oxidizing equivalent suggests that the soluble Mn(IV) or MnO_2 particles still have some oxidizing ability.

pH ≥ 13

The spectrophotometric titration in Figure 5, growth of the intermediate (at 606 nm) (Figure 7) and the iodometric titrations (Figure S9), all show that there is a stoichiometric manganese(VI) intermediate. At the height point of the 606 nm growth curve and the relatively stable plateau, we analyzed the product after trapping most of the Mn(VI) as the highly insoluble barium manganate.[83] Under these conditions, phenylglyoxylic acid (0.35 mol /mol of Mn(VII) was observed as the only product (expected theoretical 0.5 mol of PGA/mol of permanganate). In the presence of barium acetate, we have accounted for 70 % of expected Mn(VI), confirming the stoichiometry for the first step of the reaction.

$2Mn(VII) + C_6H_5C(OH)COO^- = 2Mn(VI) + C_6H_5COCOO^-$ (11)

Table 5. Relative reactivity of mandelic acid and related compounds in permanganate oxidation.[a]

Substrate		k_2, $M^{-1}s^{-1}$		
	pH	1	7	13
Mandelic Acid		0.30	0.026	0.060
Phenylglyoxylic Acid		22.0	0.003	0.002
Benzaldehyde		6.00	0.27 (0.35)[b]	2.73

[a] $[MnO_4^-] = 3 \times 10^{-4}$ M, and T = 25 ± 0.5 °C

[b] K. B. Wiberg and R. Stewart. The Mechanisms of Permanganate Oxidation. I. The Oxidation of Some Aromatic Aldehydes. *J. Am. Chem. Soc.* **1955**, 77, 7, 1786–1795.

Reference # 37

Second-order constants for mandelic acid, benzaldehyde and phenylglyoxylic acid are given in Table 5. In acid medium (pH 1), phenylglyoxylic acid is about seventy times more reactive than mandelic acid, while in alkaline medium, benzaldehyde is forty times more reactive than mandelic acid. This should be reflected in the products in acid medium (5-equivalent change); we have quantified benzoic acid in small but significant amount in the 1-7. Table 4 (entry # 1) shows that the yield of benzoic acid is 0.3 mol/mol of permanganate. As benzaldehyde is a 4-electron oxidation product, the total yield of PGA is in fact 0.74 (0.30 x 2 + 0.14 = 0.74) which accounts for 74 % of PGA based on one mole of PGA per mol of permanganate.

Kinetic deuterium isotope effect

In the entire pH range (1-13) of this study, a substantial primary kinetic isotope effect ($k_H/k_D \approx$ 8-9) was observed in the reaction of α-deuterated (C-D) mandelic acid), indicating that the C-H bond is cleaved in the rate-determining step (Table 6).

Table 6. Deuterium isotope effect in the permanganate oxidation of mandelic acid**[a]**.

pH	MA, M	$10^4 k_H$ s^{-1}	$10^4 k_D$ s^{-1}	k_H/k_D
1	0.02**[b]**	18	2.0	9.0
7	0.02	5.0	0.60	8.3
13	0.02	10	1.2	8.3
13	0.05	27	3.0	9.0

[a]Conditions: T = 25.0 ± 0.5 ^oC, $[MnO_4^-]$ = 3.0×10^{-4} M

[b]Sodium pyrophosphate = 0.05

Mechanism

Any mechanism for mandelic acid oxidation by permanganate must explain the following experimental facts:

(1). In the entire pH range of this study (1-13), the observed primary kinetic isotope effect (k_H/K_D) ≈9) points to rate-determining C-H cleavage involving hydride transfer to the oxo-manganese bond resulting in a reactive Mn(V) transient and one mole of phenylglyoxylic acid.

$$C_6H_5CH(OH)COO^-H^+ + Mn(VII) = C_6H_5COCOO^-H^+ + Mn(V) \quad (12)$$

(2). The proposed mechanism should be consistent with the observed stoichiometry, specifically, the ratio of benzaldehyde (BZ) to phenylglyoxylic acid (PGA), and accounting of the 5- and 3-oxidizing equivalents in acid and basic (pH ≥ 7) medium respectively.

(3). The proposed mechanism should consider the known disproportionation and comproportionation reactions of Mn(VI), Mn(V), and Mn(III) as a function of pH.

Stoichiometry: Acid pH (≤1)

The product analysis data in Table 4 at pH ≤ 1, is consistent with the stoichiometry shown in eq. 17. We did not find any evidence for Mn(III) accumulation even in the presence of added pyrophosphate.[68-70] The proposed reaction sequence (eqs 13-17) shows the 5-electron reduction of Mn(VII) via two successive 2-electron steps leading to Mn(III). The disproportionation of Mn(III), if any could be a minor component (eq 16).

$$2\mathrm{Mn(VII)} + 2\mathrm{C_6H_5CH(OH)COOH} \longrightarrow 2\mathrm{Mn(V)} + 2\mathrm{C_6H_5COCOOH} \quad (13)$$

$$2\mathrm{Mn(V)} + 2\mathrm{C_6H_5CH(OH)COOH} \longrightarrow 2\mathrm{Mn(III)} + 2\mathrm{C_6H_5CHO} + 2\mathrm{CO_2} \quad (14)$$

$$2\mathrm{Mn(III)} + \mathrm{C_6H_5CH(OH)COOH} \longrightarrow 2\mathrm{Mn(II)} + \mathrm{C_6H_5CHO} + \mathrm{CO_2} \quad (15)$$

$$2\mathrm{Mn(III)} \longrightarrow \mathrm{Mn(IV)\ and\ Mn(II)} \quad (16)$$

$$5\mathrm{C_6H_5CH(OH)COOH} + 2\mathrm{MnO_4^-} + 6\mathrm{H^+} \longrightarrow 2\mathrm{C_6H_5COCOOH} + 3\mathrm{C_6H_5CHO} + 3\mathrm{CO_2} + 8\mathrm{H_2O} + 2\mathrm{Mn^{2+}} \quad (17)$$

The reaction stoichiometry (eq 17) is validated by the observed BZ/PGA ratio in the range of 1.0 -1.7 (expected 1.5; data shown in Table 4; entry # 1-5)

pH 4

Interestingly, at pH 4-4.3 (mandelic acid - mandelate buffer; 0.1-0.5M), the oxidation of the mandelate ion shows an intermediate at 418 nm; iodometric titrations suggest an average oxidation state + 4; the 418 nm intermediate decays in a longer time scale extending over hours (Figure S13). The loss of Mn(VII) at 526 nm and growth of Mn(IV) at 418 nm occurred with nearly identical first-order rate constants (Table 2). Product analysis showed nearly four moles of benzaldehyde per mole of phenylglyoxylic acid (BZ/PGA ≈ 4).

The stoichiometry ratio of BZ/PGA = 4 could be explained if one considers that the incipient Mn(V), presumably complexed with mandelic acid (present in large excess), is oxidized to Mn(VI) by a second molecule of permanganate (eq 18-21). Both Mn(VI) and Mn(IV) selectively cleave the C-C bond.

$$\text{Mn(VII)} + C_6H_5CH(OH)COOH \longrightarrow \text{Mn(V)} + C_6H_5COCOOH \quad (18)$$

$$\text{Mn(V)} + \text{Mn(VII)} \longrightarrow 2\ \text{Mn(VI)} \quad (19)$$

$$2\text{Mn(VI)} + 2C_6H_5CH(OH)COOH \longrightarrow 2\text{Mn(IV)} + 2C_6H_5CHO + 2CO_2 + 4H^+ \quad (20)$$

$$2\text{Mn(IV)} + 2C_6H_5CH(OH)COOH \longrightarrow 2\text{Mn(II)} + 2C_6H_5CHO + 2CO_2 + 4H^+ \quad (21)$$

$$5C_6H_5CH(OH)COOH + 2MnO_4^- + 6H^+ \longrightarrow C_6H_5COCOOH + 4C_6H_5CHO + 4CO_2 + 8H_2O + 2Mn^{2+} \quad (22)$$

Alternatively, a mechanism involving disproportionation of Mn(V) (eq 24), would lead to a different stoichiometry (BZ/PGA= 1.5). The experimentally observed ratio of BZ/PGA = 3.4 points to minimal contribution from Mn(V) disproportionation (if any).

$$2\text{Mn(VII)} + 2C_6H_5CH(OH)COOH \longrightarrow 2\text{Mn(V)} + 2C_6H_5COCOOH \quad (23)$$

$$2\text{Mn(V)} \longrightarrow \text{Mn(VI)} + \text{Mn(IV)} \quad (24)$$

$$\text{Mn(VI)} + C_6H_5CH(OH)COOH \longrightarrow C_6H_5CHO + \text{Mn(IV)} \quad (25)$$

$$2\text{Mn(IV)} + 2C_6H_5CH(OH)COOH \longrightarrow 2\ C_6H_5CHO + \text{Mn(II)} \quad (26)$$

$$5C_6H_5CH(OH)COOH + 2MnO_4^- + 6H^+ \longrightarrow 2C_6H_5COCOOH + 3C_6H_5CHO + 3CO_2 + 8H_2O + + 2Mn^{2+} \quad (27)$$

We observed significantly higher deuterium isotope effects (k_H/k_D = 8-9) in the entire pH range of this study than the results of prior studies using MnO_4^- in acid medium by Banerji (k_H/k_D =3.76)[72] and by Freeman[40] at pH 13.6 (k_H/k_D = 2.79-5.45). Surprisingly, phenylglyoxylic acid (PGA), the expected product of C-H cleavage was not even suspected and searched for. *If the carbocation in eq 3 were to lose CO_2 to give benzaldehyde, it would lead to the loss of the deuterium label in the benzaldehyde.*

We tested the mechanism (eq 2 and 3) by isolating benzaldehyde as the 2,4-dinitophenylhydrazone derivative. Interestingly, the deuterium level remained intact in the 2,4-DNPH derivative (m/z = 287). We, therefore, conclude that benzaldehyde could not be a product of decarboxylation of the carbocation. Under the reaction conditions, phenylglyoxylic acid is not decarboxylated to benzaldehyde.

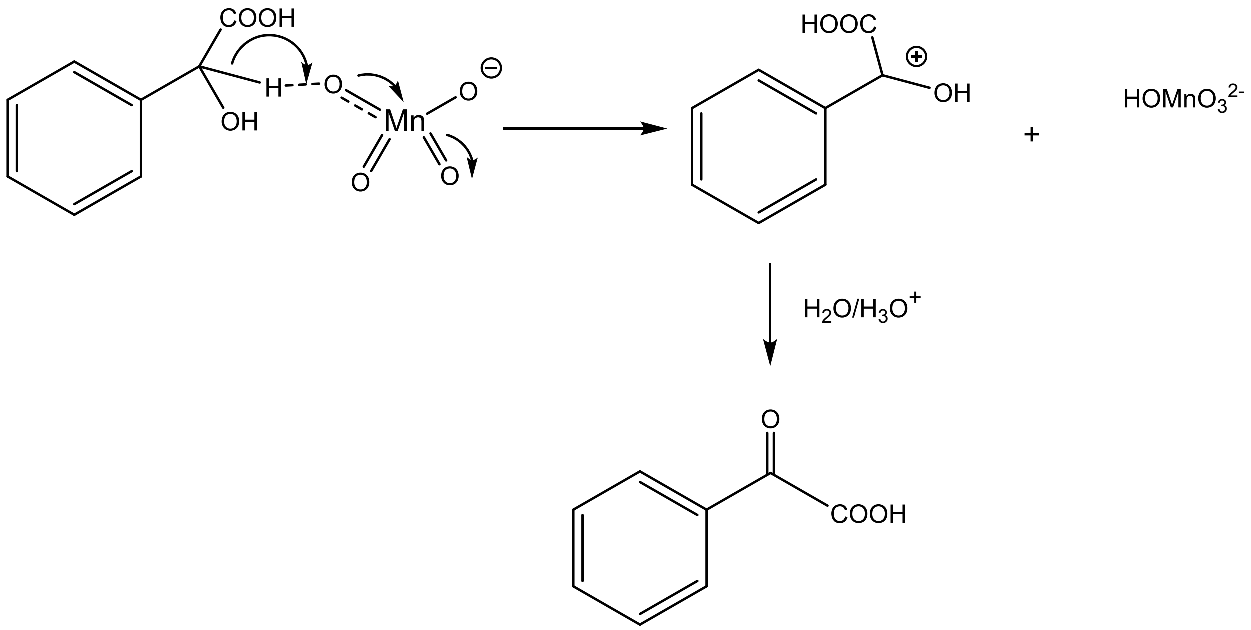
The magnitude of the observed primary kinetic isotope effect (8-9; Table 5) suggests that the rate -limiting step in the entire pH range of this study involves hydride transfer. It is worth comparing the second-order rate constants observed at pH 7 (in phosphate buffer) for toluene with mandelic acid. Our observed second-order rate constant of 2.44 x 10^{-2} M^{-1} s^{-1} (pH 7 and at 25 ^{o}C) is about 30 times higher than the rate constant for toluene (7.4 x 10^{-4} M^{-1} s^{-1} at 293 K) at pH 7.[54] Hydride abstraction in permanganate oxidations has been invoked in the oxidation of alkoxide[50, 51] and formate.[84] The magnitude of the kinetic isotope effect (KIE) observed in the present work is in accord with the analysis of Westheimer.[85]

Additional evidence for the solvent stabilized carbocation comes from the observed substituent effect; *4*-methoxy-mandelic acid reacts approximately 50 times faster than mandelic acid while *4*-nitro-mandelic acid reacts slower than mandelic acid.[40] The activation enthalpy is highly negative (-30 eu) which points to an ordered transition state relative the starting ground state involving mandelic acid, MnO_4^- and H^+. Using literature reported values of pK_a of $HMnO_4$ (-2.25),[86] one could conclude that $HMnO_4$ is not likely to be present significant concentrations at moderate acidities (0.1 M-to 1.0 M $HClO_4$). It is reasonable to assume that a proton is required to stabilize the transition state (TS). With increase in the pH, regardless of the nature of electron transfer (outer-sphere or inner-sphere), the TS must carry the burden of increasing negative charges, -2 (MnO_4^- + mandelate anion) and -3 (mandelate anion + MnO_4^- + OH^-) at pH 7 and 13 respectively, consistent with the observed significant ionic strength effect at pH ≥13 (Table S2-3 and Figure S16).

The rate-limiting step: mechanism of hydride transfer

To account for the observed substantial primary isotope effect of 9.7 at 293 K, Mayer and Gardner have proposed hydride (H^-) transfer from toluene to a permanganate oxygen.[54] More recently, using density functional theory (DFT) at B3LYP level, Blotvogel et al have reached the same conclusion regarding C-H activation involving the methyl group of hexamethylphosphoramide (HMPA).[53] Wiberg and Stewart have also proposed rate-limiting hydride transfer from formate ion to permanganate.[84] Hydride transfer to permanganate could occur by either outer-sphere or inner-sphere mechanisms. In formate oxidation, permanganate serves as nucleophile to initiate a bond to the formyl carbon atom .[84] In the chromic acid oxidation of mandelic acid, hydride transfer is shown to occur in a cyclic transition state involving the ester derived from mandelic acid and chromic acid.[77]

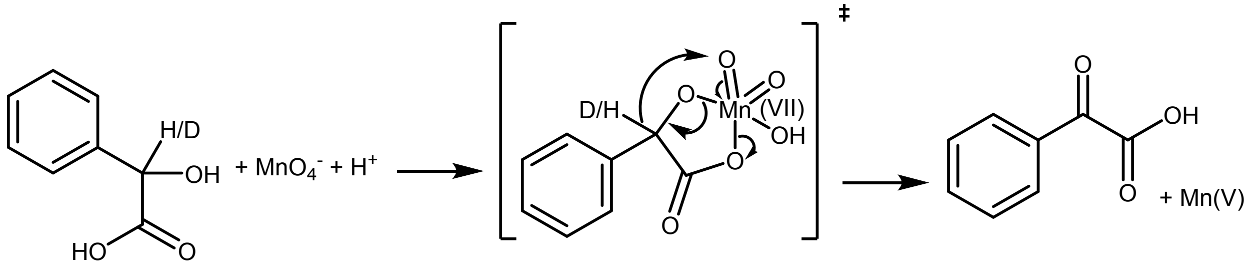
Scheme 2 shows a possible outer-sphere mechanism in which the C-H hydrogen is orientated toward the O=Mn (oxo) bond; the hydride (two electrons and a hydrogen) is presumably transferred to an unoccupied molecular orbital of the Mn-oxo bond.[86(a), 87] The only concern with outer-sphere hydride transfer is that a free hydride would react with water to give molecular hydrogen.[88] It is relevant to note the organic textbook[89] examples of hydride transfer include the 150 years old Cannizzaro reaction (disproportionation of benzaldehyde with no α- hydrogen) in strong alkali and sodium borohydride reduction of carbonyl group (in aldehydes, ketones and esters); borohydride reduction is carried out in protic solvents such as methanol and ethanol.



Scheme 2. Outer-sphere mechanism: rate-limiting hydride transfer

Alternatively, an inner-sphere mechanism would require a transition state that brings the reactants together. As mandelic acid is oxidized 30-400 times faster than toluene (at pH 7 and 1 respectively), it is reasonable to assume that both the -OH and -COOH groups expand the coordination sphere of the manganese in the transition state (TS). In Scheme 3, we envision a transition state in which the coordination around manganese expands to nearly square pyramidal geometry. It is relevant to point out that in the analogous chromic acid co-oxidation of alcohols with oxalic acid[90] chromate esters with expanded structures (to square pyramidal TS) are routinely postulated. Also seen in the picolinic acid-catalyzed oxidation of alcohols[91] and oxidation of hydroxy acids (second order region).[92,93]

Scheme 3. Potential inner-sphere mechanism



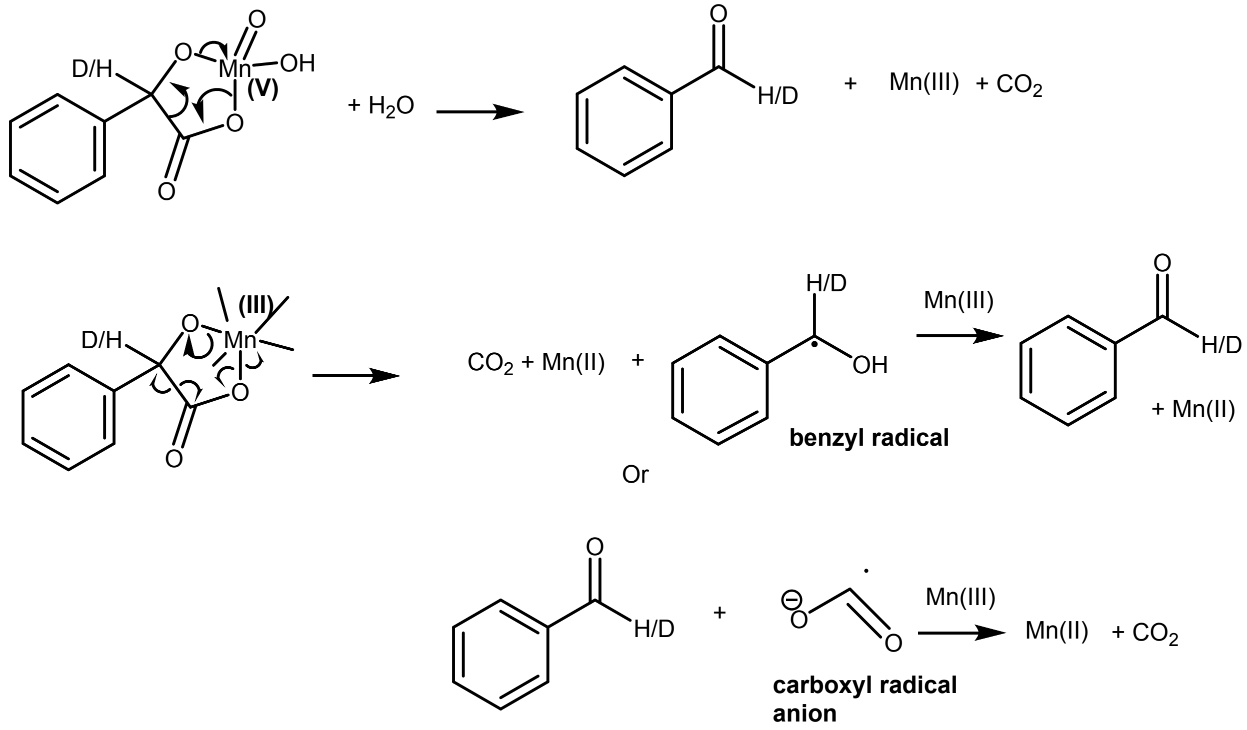
Both Cr(VI) and Mn(VII) are *d*^{o} systems. The very small size of Mn^{7+} ion in permanganate could be the principal reason for its reluctance to bind with other ligands; Mn_2O_7, (anhydride of $HMnO_4$) is a molecular compound with two tetrahedral manganese centers.[94]

Admittedly, at this time, the inner-sphere mechanism (shown in Schemes 3) is speculative; we do not have any experimental evidence for the transition state(s) including the intermediate complex that shows an expansion of the coordination sphere of tetrahedral permanganate. Unequivocal mechanistic conclusions would require ^{18}O-labeling experiments (MnO_4^{18} and H_2O^{16} and MnO_4^{16}/H_2O^{18}) and computational mapping of the potential energy surface (PES) and of the reaction pathway for the initial interaction of permanganate with mandelic acid/mandelate anion. Both of these experimental approaches are beyond the scope of the current work.

Fate of Mn(V) in acid medium (≤ 1)

Two-electron reduction of permanganate results in tetrahedral hypomanganate, Mn(V), present as either $HO\text{-}MnO_3^{2-}$ or as cyclic or acyclic hypomanganate esters. Both cyclic and acyclic hypomanganate esters have been invoked in the oxidation of alkenes (simple and substituted alkenes; crotonic, cinnamic acid, allyl alcohol, and acrylonitrile among others).[30, 34, 36, 39] In acid medium, Mn(V) cleaves the C-C bond leading to benzaldehyde and a Mn(III) species which is a one-electron oxidant. Mn(III) complexes are octahedral, both mono-oxalate and *bis*-oxalate Mn(III) complexes are observable intermediates in $KMnO_4$/oxalic acid/H_2SO_4.[95,96] It is for these reasons we assume that the Mn(III) species has at least one mandelic ligated to the Mn(III) center and remaining ligands presumably water. Manganese, Mn(III) is a known powerful one-electron oxidant (redox potential of 1.52 V vs NHE)[97]. The benzyl and or carboxylate radical anion (Scheme 4) are key intermediates in the reaction steps involving Mn(III).

Scheme 4



Definitive evidence for the existence of the carboxylate anion radical is known in the literature on the chromic acid oxidation oxalic acid.[98, 99] The COOH radical is more stable than the *t*-butyl[100] and methyl radical[101] and is directly observed in the gas phase.[102] Carbon dioxide has been used to scavenge solvated electrons in radiation chemistry.[103]The carboxyl radical is involved in the oxidation of oxalic acid by Mn(III) and Ce(IV) and is stable enough to react with dioxygen eventually leading to large amounts of hydrogen peroxide.[104, 105]

At pH 4 the observed (1:1) (Mn(VII) : Mn(IV) stoichiometry rules out the origin of Mn(IV) through Mn(III) disproportionation route (eq 16). Both Mn (III) and Mn(IV) are known transients in oxalic acid as part of the Guyard reaction involving the interaction of Mn(II) with Mn(VII)[55-59, 106] (eq 28)

$$2\mathrm{Mn(III)} \longrightarrow \mathrm{Mn(II)} + \mathrm{Mn(IV)} \qquad (16)$$

$$2\mathrm{MnO_4^-} + 3\mathrm{Mn^{2+}} + 2\mathrm{H_2O} \longrightarrow 5\mathrm{MnO_2} + 4\mathrm{H^+} \qquad (28)$$

The near stoichiometric Mn(IV) intermediate suggests that it is directly formed from a higher oxidation state presumably Mn(VI).

Oxidation at neutral (pH 6.8-7.4)

The formation of a stoichiometric soluble Mn(IV) intermediate (Figure S8), benzaldehyde to phenylglyoxylic acid ratio (BZ/PGA = 2; Table 4) and the observed primary kinetic isotope effect (Table 5) are all consistent with the observed stoichiometry at neutral pH (6.8-7.4).

$$2MnO_4^- + 3C_6H_5CH(OH)COO^- \longrightarrow C_6H_5COCOO^- + 2C_6H_5CHO + 2MnO_2 + 2CO_2 + 4OH^- \quad (29)$$

We have accounted for 100% of the products based on a net three-electron reduction of permanganate to Mn(IV). Data in Table 4 also indicates some over oxidation above and beyond the stoichiometry (see above), which could be due to some residual oxidizing activity of hydrated manganese dioxide, H_2MnO_3.[107]

Oxidation in alkaline medium (pH ≥13)

When a permanganate solution is mixed with hydroxide, it is reduced to manganate; it is a unique reaction with hydroxide as the reducing agent presumably involving the hydroxyl radical.[79, 108]

$$4MnO_4^- + 4OH^- \longrightarrow 4\,MnO_4^{2-} + 2H_2O + O_2 \quad (30)$$

$$MnO_4^- + OH^- \longrightarrow MnO_4^{2-} + OH^{\cdot} \quad (31)$$

The standard synthetic method for potassium manganate involves heating of potassium permanganate with a highly concentrated solution of KOH[79-81] to 110-120°C for hours.

At ambient temperature at pH 13, in the absence of mandelic acid, the permanganate-hydroxide reaction is extremely slow. In the presence of mandelic acid at pH 13, the loss of permanganate (526 nm) and growth of 606 nm (green color) occur at a much faster rate relative to the control reaction without mandelate. By the time both the 526 and 418 nm curves have plateaued (essentially complete), in the control reaction at pH 13 (without mandelate), the percentage conversion to manganate is less than 5%.

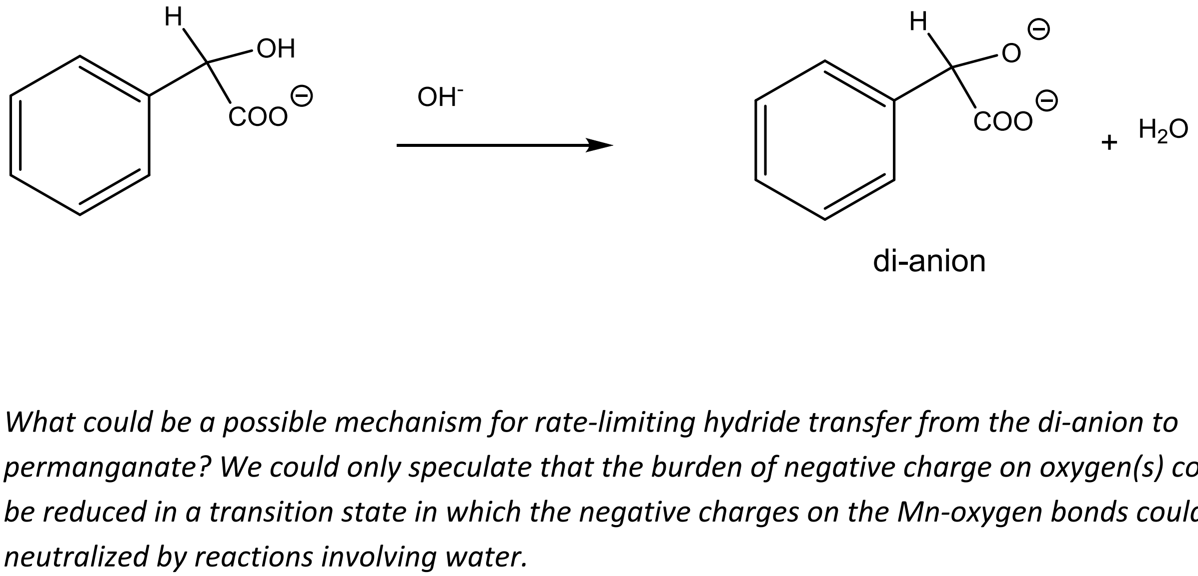
At pH 13 or above the oxidation of mandelic acid, $C_6H_5CH(OH)COO^-$, shows a stoichiometric green intermediate, (MnO_4^{2-} shows a λ_{max} at 606 nm). At the stable plateau of the 526 and 606 nm curves (≈20 minutes); Figure 7), we quenched the reaction mixture with barium acetate which removed the Mn(VI) as the insoluble teal-blue barium manganate.[83] After filtering off the precipitate, using a 2-micron filter, the solution was analyzed by HPLC. The stoichiometry (eq 32) was confirmed for the first step of the mandelate anion with permanganate in alkaline medium (Table 4, entry #8).

$$2MnO_4^- + C_6H_5CH(OH)COO^- + 2OH^- \longrightarrow 2MnO_4^{2-} + C_6H_5COCOO^- + 2H_2O \qquad (32)$$

$$MnO_4^{2-} + C_6H_5CH(OH)COO^- \longrightarrow C_6H_5COCOO^- + MnO_2 + 2OH^- \qquad (33)$$

Before precipitation as MnO_2, the manganese (IV) may be in the form a hydrated species, H_2MnO_3 or $HMnO_3^-$. We analyzed the products either after placing the reaction mixture in boiling water or leaving it overnight for 12-24 hours. The yield of phenylglyoxylic acid (PGA) increased to 1.2 mol of PGA/mol of permanganate. Based on 1.5 moles of 2-electron oxidation products (theoretical), we have accounted for nearly 80% of oxidizing equivalents. It is relevant to note that phenylglyoxylic acid is synthesized by permanganate in alkaline medium.[2] The first-order dependence on permanganate, hydroxide and mandelate anion requires bringing together three negative charges into an activated complex or transition state. It is facilitated at higher ionic strength (plot of square root of ionic strength is linear; Figure S16 and Table S3). To account for the first-order dependence on OH^-, initial deprotonation of the hydroxyl group was suggested.[40]

Scheme 5



What could be a possible mechanism for rate-limiting hydride transfer from the di-anion to permanganate? We could only speculate that the burden of negative charge on oxygen(s) could be reduced in a transition state in which the negative charges on the Mn-oxygen bonds could be neutralized by reactions involving water.

Oxidation by potassium manganate

Potassium manganate was further characterized by EPR at the University of Denver.

The Mn(VI) oxidation state was confirmed by EPR at 40-80 K in concentrated solution of KOH and LiCl. High concentrations of LiCl were added to the solution to make a glassy sample when rapidly cooled. Continuous wave spectra are observable up to higher than 80 K in glassy alkaline LiCl. EPR spectra of MnO_4^{2-} in glassy alkaline LiCl at X-band at 80 K exhibit $g_1 = 1.978 \pm 0.001$, $g_2 = 1.968 \pm 0.001$, $g_3 = 1.956 \pm 0.001$ and $A_1 = 182 \pm 9$, $A_2 = 275 \pm 15$, and $A_3 = 400 \pm 15$ MHz

Figure 8 shows CW spectra at 80 K of MnO_4^{2-} in alkaline LiCl glass. The magnetic fields that correspond to the average g values at the two frequencies are aligned.

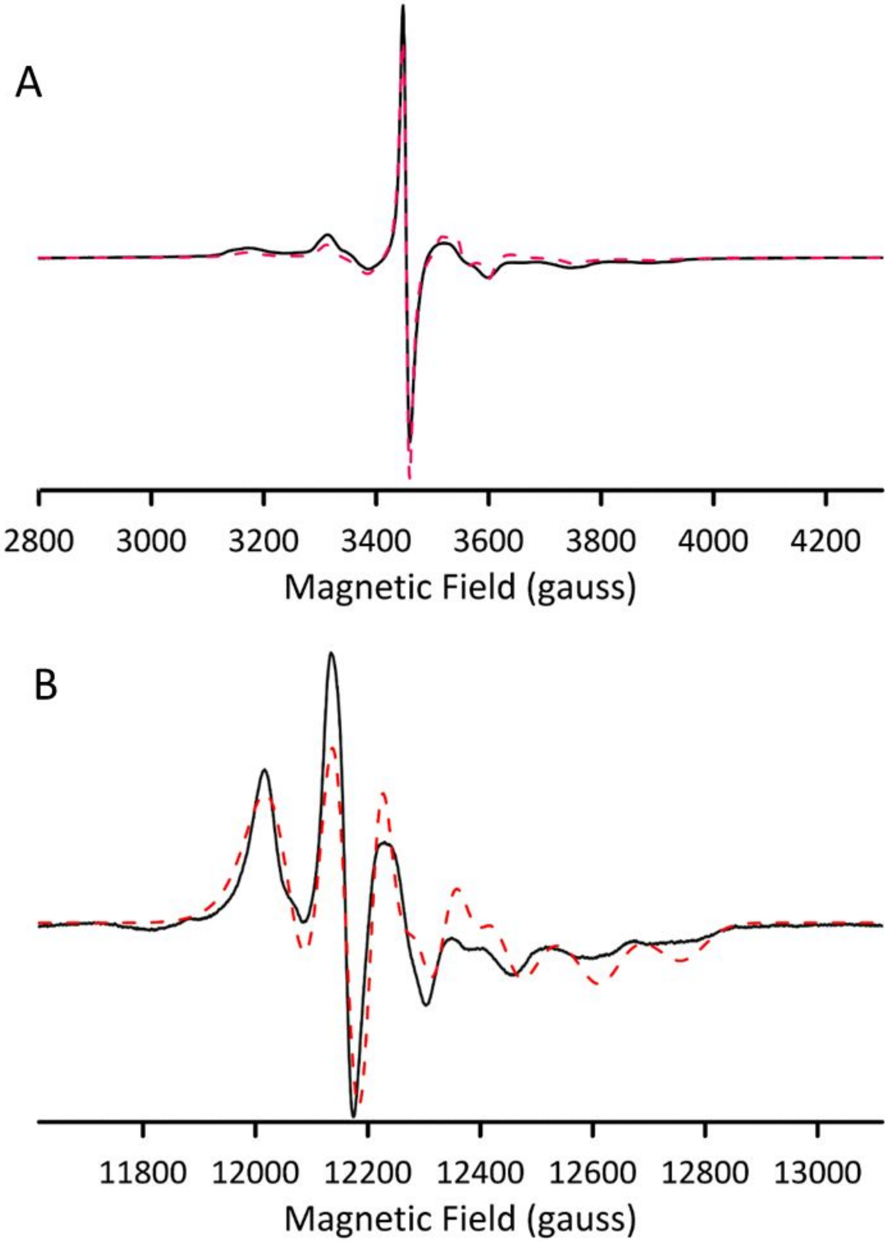


Figure 8. Figure reproduced with permission from ref 81. A) X-band spectrum (black line) obtained with frequency of 9.6830 GHz. The simulated spectrum was obtained with anisotropic peak-to-peak linewidths along axes 1, 2, and 3 of 7.0, 6.0, and 6.5 G and A-strain along axes 1, 2, and 3 of -16, 24.3, and 16.5 G. B) Q-band spectrum (black line) obtained with a frequency of 33.94 GHz. The simulated spectrum was obtained with anisotropic peak-to-peak linewidths along axes 1, 2, and 3 of 34, 50, and 60 G and A-strain along axes 1, 2, and 3 of -14, -61, and 15 G. Simulations of the EPR spectra of MnO_4^{2-} are described in ref 81.

Oxidation of mandelic acid with manganate (MnO_4^{2-}) in acid medium and neutral pH; disproportionation of manganate

When an alkaline potassium manganate solution (0.1M NaOH) is mixed with an acid solution of mandelic acid (0.1 M mandelic acid and $HClO_4$ = 0.2 M), there was an instantaneous disproportionation to Mn(V) and Mn(VII) which was evident in the burst of purple color due to permanganate. Second order rate constants for the disproportionation reaction (eq 34) have been estimated at pH 1 (1.0×10^7 $M^{-1}sec^{-1}$)[63] and at pH 7-9.3 (150 M^{-1} s^{-1} to 3.4×10^4 $M^{-1}S^{-1}$).[33]

$$2\text{Mn(VI)} \longrightarrow \text{Mn(V)} + \text{Mn(VII)} \qquad (34)$$

The reactive and nascent Mn(V) is expected to cleave the C-C bond giving benzaldehyde. Mn(II)) following (Scheme4).

Product analysis under the condition of disproportionation of Mn(VI), showed 100% accounting of the oxidizing equivalents based on initial concentration of manganate (0.001M) and reduction to Mn(II) in acid medium. If Mn(VI) was allowed to disproportionate in phosphate buffer (pH 7.4), the data in Table 7 shows 100 % accounting of the oxidizing equivalents products based on a 3-electron reduction to Mn(IV).

Table 7. Products in the manganate (MnO_4^{2-}) oxidation of mandelic acid[a]

Product Yield mol/mol of K_2MnO_4 **a** (potassium manganate)									
Entry #	pH	MA (M)	$C_6H_5COCOOH$ **PGA**	C_6H_5COOH **BA**	C_6H_5CHO **BZ**	Total**b**	% of total oxidizing equivalents (**TOE**)[b]	(BZ/PGA)[e]	Comments
1	1.3	0.05	0.163	0.156	1.10	1.60 (2.0)**c**	80	2.3	
2	7.0-7.2	0.05	0.320	-	0.57	0.89 (1.0)**d**	89	1.8	
3	13	0.05	0.936	-	0.050	0.985 (1.0)**d**	98	-	20 min boiled
4	13	0.05	0.972	-	0.017	0.989 (1.0)**d**	99	-	24 hrs. at RT

[a] [MA] = 0.05 M; $[MnO_4]^{2-}$ = 1.0 x 10^{-3} M; Reactions carried in a total volume of 20 mL.

[b] Total yield = PGA + 2 BA + BD

[c] 2.0 moles 2-electron-oxidation products based on 4-oxidizing equivalents in acid medium, manganate is eventually converted to Mn(II).

[d] 1.0 moles of 2-electron oxidizing products based on 2 -oxidizing equivalents in basic medium; Mn(VI) is converted to $MnO_{2.}$

[e] (BZ/PGA) = BZ/(PGA+2BA)

A typical calculation for entry # 1

$[PGA]_T$ = (0.163 + 2x 0.156) = 0.475.

$[BZ]/[PGA]_T$ = 1.1/0.475 = 2.3

To a 10 mL solution of mandelic acid (0.1 M in 0.2M in $HClO_4$), 10 mL of potassium manganate (0.002 M) in 0.1 M NaOH was added.   During the time of mixing 2-5 seconds, it rapidly disproportionated resulting in a burst purple color. The resulting solution was acidic (0.1 M $HClO_4$)

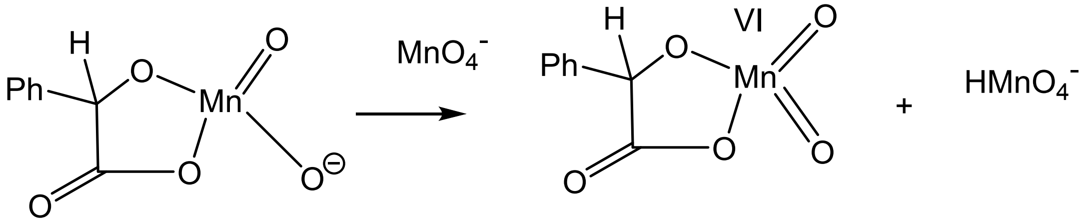
2Mn(VI) = Mn(V) + Mn(VII)

Fate of Mn(V) (pH ≥ 4-13)

Manganese(V) is the logical product of hydride transfer (C-H bond) to permanganate. Hypomanganate and manganate esters have been routinely postulated as intermediates in the reaction pathway involving alkenes (cinnamic and crotonic acid) even in highly acidic medium[34]. At one time, the 415-420 nm intermediate in acid medium was thought to be the elusive hypomanganate ester.[34] Based on the oxidation state determination by iodometry, the 415 nm intermediate is associated with a soluble/ colloidal Mn(IV) species.[31,32]

Several pathways are available for Mn(V)- two electron reduction to Mn(III), disproportionation to Mn(IV) and Mn(VI) and or oxidation to Mn(VI) by a second mol of permanganate (comproportionation reaction; Scheme 6). Comproportionation should be the more favorable of these due to the low concentration of Mn(V) relative to the initial concentration of permanganate.

Scheme 6. **Comproportionation of Mn(V) with Mn(VII)**



Reliable determination of second-order rate constants for Mn(VI) disproportionation is experimentally feasible both at 526 nm (permanganate) and 610 nm (manganate) by stopped-flow methods, while there is no direct method to determine Mn(V) disproportionation in acidic medium. The disproportionation of Mn(VI) to Mn(V) and Mn(VII) is instantaneous at pH 1 (k_2 = 1.0 x 10^7 M^{-1} s^{-1} [63]. The disproportionation of manganate, Mn(V) is thought to occur via dimeric intermediates such as $[Mn_2O_7]$[109] or via the hypomanganate esters of diols.[109]

The rate of disproportionation of Mn(V) at pH 7 has been estimated (10^{12} M^{-1} s^{-1} from data obtained in highly alkaline pH)[110-112] which is higher than oxidation of hypomanganate by permanganate (4.6 x 10^{4} M^{-1} s^{-1}) or the oxidation of hypomanganate by periodate (3.3 x 10^5 M^{-1} s^{-1}). Our product studies using periodate/permanganate suggest that periodate oxidation of Mn(V) must be competitive with disproportionation by at least one order of magnitude. Insight into the role of these intermediates comes indirectly from the use of probes such as formate, ethanol/methanol, As(III), sulfoxides[113], bisulfite[114], TEMPO radical,[115] among others. Simandi et al have reported selective oxidations by short-lived manganese(V).[116, 117] Taking advantage of the extremely fast reaction between periodate[110-112] and Mn(V), we hoped to intervene in the mandelic acid-permanganate reaction at the Mn(V) stage by deoxidizing the Mn(V) back to permanganate. In principle, this should lead to the recycling of the first step of the reaction over and over again and should manifest in large increase in the amount of phenylglyoxylic acid relative to the control without any periodate. Using a ten-fold excess of periodate over permanganate (periodate = 0.01M; permanganate = 0.001M), we carried out product analysis in pH 7 (phosphate buffer). Product analysis data in Table 8 shows a remarkable increase in the yield of PGA relative to benzaldehyde.

Table 8. Products in the permanganate oxidation of mandelic acid under conditions of Mn(V)-Mn(VII) turnover in the presence of periodate[**a**].

Product Yield mol/mol of $KMnO_4$ [a]									
Entry #	pH	MA (M)	$C_6H_5COCOOH$ **PGA**	C_6H_5COOH **BA**[b]	C_6H_5CHO **BZ**	Total	% of total oxidizing equivalents (**TOE**) [b]	PGA/BZ[d]	Comments
1	7	0.05	0.50 0.51	0.05 0.05	1.0 0.82	1.60 (1.5)[c] 1.43 (1.5)	107 95	0.45 0.55	Control without periodate
2	7	0.05	3.70	0.239	0.620	4.8(1.5)	320	3.36	Periodate = 0.01 M $[MnO_4^-]$ = 0.001 M
3	7	0.05	3.82	0.156	0.646	4.78 (1.5)	318	3.98	Periodate = 0.005 M $[MnO_4^-]$ = 0.0005 M

[a] [MA] = 0.05 M; $[MnO_4^-] = 1.0 \times 10^{-3}$ M, Reactions carried in a total volume of 10 mL. The control reaction of periodate with mandelic acid at pH 7 over a period of seven days showed negligible amounts of both PGA and benzaldehyde and no benzoic acid.

[b] Total yield = PGA + 2BA + BD

[c] 1.5 moles of 2-electron oxidizing products based on 3-oxidizing equivalents at pH 7.

[D] At pH 7 benzoic acid is derived from oxidation of benzaldehyde

$[BZ]_T$ = BZ + 2BA ex. (1.0 + 2x0.05) = 1.1

$[PGA]/[BZ]_T$ ex. 0.5/1.1 = 0.45

At pH 7, the control reaction (in the absence of periodate), the yield of is 0.5 mol of PGA per mol of permanganate. In the presence of 10-fold excess of periodate ($MnO_4^- = 0.001$ M) the PGA yield increases to 3.7 mol PGA /mol of permanganate, which is 7.4 times more PGA relative to control. These results unequivocally demonstrate that the Mn(V) resulting from hydride transfer is re-oxidized to Mn(VII); in essence our results show a catalytic turn-over in the presence of a cooxidant.

$$\mathrm{Mn(VII)} + C_6H_5CH(OH)COOH \longrightarrow \mathrm{Mn(V)} + C_6H_5COCOOH \qquad (18)$$

$$H_3IO_6^{2-} + HMnO_4^{2-} \longrightarrow IO_3^- + MnO_4^- + H_2O + 2OH^- \qquad (36)$$

Our results show that Mn(V) capture by periodate is highly competitive with its disproportionation or its oxidation to Mn(VI) by a second mol of permanganate.

In addition, we have used the stoichiometric product ratio of BZ/PGA for discriminating the Mn(V)-disproportionation versus oxidation to Mn(VI) by permanganate.

Disproportionation of Mn(V)

$$2\,\mathrm{Mn(VII)} + 2\mathrm{MA} \longrightarrow 2\mathrm{Mn(V)} + 2\mathrm{PGA}$$

$$2\mathrm{Mn(V)} \longrightarrow \mathrm{Mn(IV)} + \mathrm{Mn(VI)}$$

$$\mathrm{Mn(VI)} + \mathrm{MA} \longrightarrow \mathrm{Mn(IV)} + \mathrm{BZ} + CO_2$$

Net stoichiometry: $2\mathrm{Mn(VII)} + 3\mathrm{MA} \longrightarrow 2\mathrm{Mn(IV)} + 2\mathrm{PGA} + \mathrm{BZ} + CO_2$
(BZ/PGA = 0.5)

Oxidation of Mn(V) to Mn(VI) by permanganate

$$\mathrm{Mn(VII)}\text{-} + \mathrm{MA} \longrightarrow \mathrm{Mn(V)} + \mathrm{PGA}$$

$$\mathrm{Mn(V)} + \mathrm{Mn(VII)} \longrightarrow 2\,\mathrm{Mn(VI)}$$

$$2\mathrm{Mn(VI)} + 2\,\mathrm{MA} \longrightarrow 2\,\mathrm{Mn(IV)} + 2\mathrm{BZ} + 2\mathrm{CO2}$$

Net stoichiometry: $2\mathrm{Mn(VI)} + 3\mathrm{MA} \longrightarrow 2\mathrm{Mn(IV)} + \mathrm{PGA} + 2\mathrm{BZ} + 2CO_2$
(BZ/PGA = 2)

The product analysis data for pH 7 clearly shows that the BZ/PGA ratio is 2 (instead of 0.5) consistent with Scheme 7 (comproportionation of Mn(V) with Mn(VII)).

Also, we find unequivocal evidence for the comproportionation pathway in the definitive and seminal work of Gardner and Mayer on the oxidation of toluene by permanganate at neutral pH.[54] Hydride transfer from toluene results in a carbocation that is stabilized by a molecule of water.

$$C_6H_5CH_3 + MnO_4^- \longrightarrow [C_6H_5CH_2OH_2^+] + HOMnO_3^{2-} \quad (37)$$

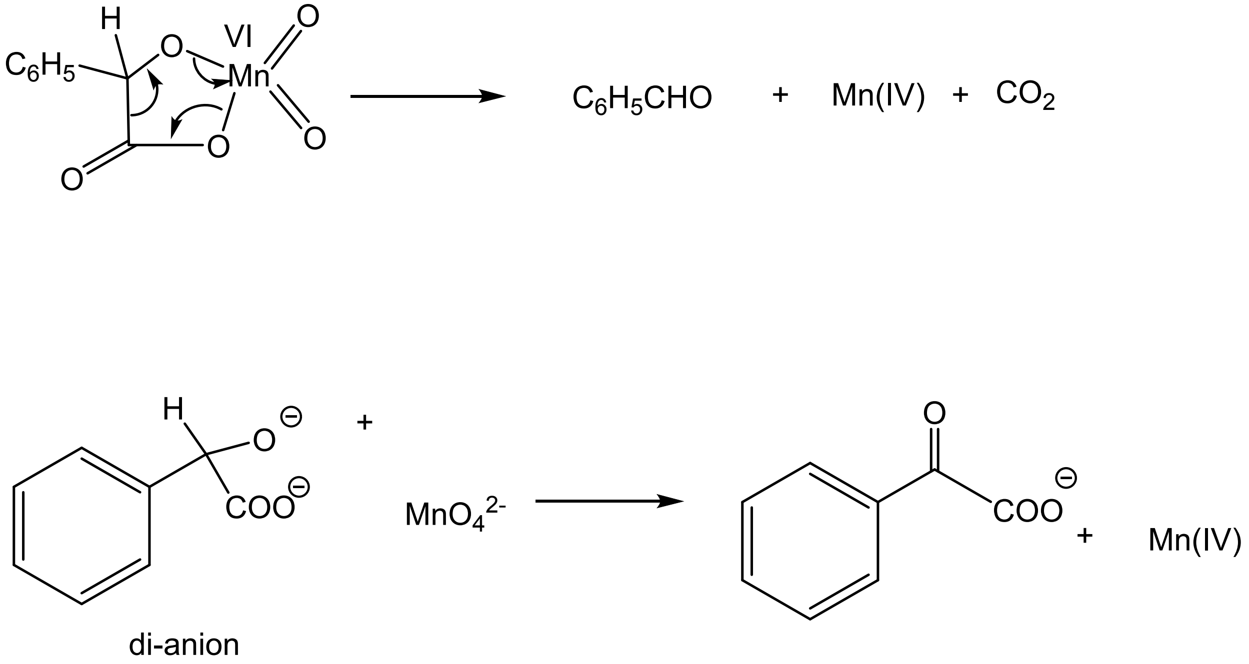
$$C_6H_5CH_3 + 2Mn(VII) \longrightarrow C_6H_5COOH + 2Mn(IV) \quad (38)$$

At first, we were intrigued by the finding that that benzoic acid is formed in near stoichiometric yield (85% of the total oxidizing equivalents at neutral pH). Mayer's finding is consistent with the century old paradigm: hydrocarbon oxidation occurs in the linear sequence, hydrocarbon to primary alcohol to aldehyde and finally to carboxylic acid. Gardner and Mayer did not address the fate of Mn(V) and the pathway leading to Mn(IV) as the final production of reduction of permanganate. Hydride transfer from benzyl alcohol to hypomanganate or hydride transfer within the hypomanganate ester (of benzyl alcohol) can be safely ruled out as it would lead to Mn(III) without the benefit of ligand stabilization. If formed, Mn(III) can potentially undergo disproportionation to Mn(II) and Mn(IV) which is not supported by the observed stoichiometry (eq 38)[54]. On the other hand, Mn(V) disproportionation would lead to a different stoichiometric outcome- one mol of benzyl alcohol plus one mol of benzaldehyde. One is left with the only viable option that Mn(V) is oxidized to Mn(VI) using a second mol of permanganate. The two moles of Mn(VI) are responsible for the oxidation of the benzyl alcohol to benzoic acid in extremely fast steps..

Mn(VI) reactivity: an interesting dichotomy.

It is intriguing that in acidic and neutral pH, Mn(VI) cleaves the C-C bond, while in alkaline pH it gives phenylglyoxylic acid. It is most likely that decarboxylation in neutral pH is facilitated in a cyclic intermediate or transition state (Scheme 7) which requires concerted bond formation and cleavage. In alkaline pH, such a cyclic intermediate is not favored; outer-sphere hydride transfer to MnO_4^{2-} leads to MnO_2 and phenylglyoxylic acid.

Scheme 7.

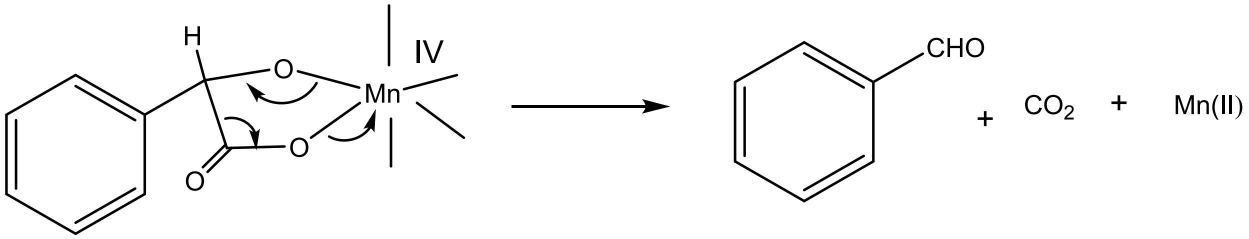


Role of soluble manganese(IV)

Manganese(IV), MnO_2 is the ultimate product of three-electron reduction of permanganate in alkaline medium. At neutral pH, the oxidation of a wide range of inorganic and organic substrates by permanganate in aqueous medium (pH ≤ 7) (and in methylene chloride by tetra-butyl ammonium permanganate) result in soluble brown-yellow species that have been assigned the oxidation state of + 4 based on characteristic optical spectrum (the absorbing species follows Rayleigh Law ($A \alpha \lambda^{-4}$)[54, 118] and by classical iodometric titrations.[38,39,54] The soluble (colloidal) Mn(IV) species on standing for extended hours or on heating, is converted to molecular manganese dioxide (MnO_2). Plots of log lambda (350 to 750) vs log A resulted in scatter with no meaningful correlation ($R^2<0.9$). The manganese species at pH 7 at the height of the curve (Figure S8) has a tobacco yellow color and is most likely a mixture of soluble Mn(IV) and hydrated MnO_2. On standing for several hours, it turns cloudy; a brown precipitate of MnO_2 or hydrated species (H_2MNO_3) is formed which could be retained by a micron-filter before HPLC analysis. Manganese(IV) intermediates could arise via multiple pathways that include disproportionation of Mn(III), Mn(V) and Mn(VI) in acidic medium,[22] and via the Guyard reaction.[106] Perez-Benito have studied the nature of soluble(colloidal) Mn(IV) in the oxidation of diverse group of organic/inorganic compounds by permanganate by using combination of UV-Vis. and nephelometric methods.[118] In the oxalate-permanganate reaction, reduction of Mn(IV) to Mn(II) involves at least one molecule of bound oxalic acid.**[57,59]** Water-soluble di-nuclear –µ-oxo bridged Mn(IV) compound, $[K_4\ Mn_2O_2\ (C_2O_4)_4.\ 4H_2O]$ has been isolated.[119]

Scheme 8 shows a simple mechanism of reduction of mandelic acid bound Mn(IV)complex. Octahedral soluble Mn(IV) had been reported using sorbitol[120] and biguanide ligands.[121]
The soluble Mn(IV) observed in our work may involve at least one mandelic acid in octahedral environments in aqueous solution.

Scheme 8. Oxidation of mandelic acid by soluble Mn(IV) in acid pH

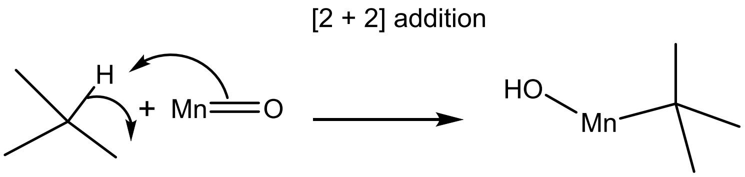


Role of radical intermediates

Hydrogen atom transfer (from C-H bonds) or oxidative decarboxylation by Mn(III) intermediate species could lead to potential radical intermediates. In the oxidation of toluene by *tetra*-n-butyl permanganate in neat toluene, a significantly smaller isotope effect ≈ 2.5, was observed by Mayer.[54] Hydrogen transfer leads to a benzyl radical.

$$Ph\text{-}CH_3 + MnO_4^- \longrightarrow PhCH_2^{\bullet} + HOMnO_3^- \qquad (39)$$

Lee et al.[48,49] favored a free radical mechanism which involves an organo-manganese intermediate resulting from [2+2] addition the C-H bond of mandelic acid across the Mn=O in alkaline medium by permanganate in 1.0 M KOH or by potassium manganate in KOH (4-10 M). The resulting C-Mn bond suffers hemolytic cleavage to give radical intermediates. Organo-metallic intermediates have been inferred in hydrocarbon oxidations by high-valent group 6 oxides. [122, 123]



(40)

Our attempts to trap potential radicals $C_6H_5CO\cdot$, $\cdot COO^-$, $C_6H_5C\cdot(OH)(COOH)$ by using vinyl polymerization of acrylonitrile/ acrylamide were unsuccessful due the rapid reaction of acrylamide and acrylonitrile with permanganate.[124, 36(b)] Unequivocal evidence for radical involvement will require EPR spin-trap measurements. These studies are beyond the scope of the present work.

Summary conclusions

The rate-limiting step in the entire pH range of this study involves C-H cleavage leading to phenylglyoxylic acid (PGA) and a reactive Mn(V) species, presumably complexed with mandelic acid. In acid medium, the manganese (V) species is selective for C-C cleavage leading to benzaldehyde. We did not see any evidence for the stabilization of Mn(III) by pyrophosphate. The stoichiometry in the acid medium can be represented as:

$5MA + 2Mn(VII) = 2PGA + 3BZ + 3CO_2 + 2Mn(II)$

Benzaldehyde is formed in post rate-limiting steps involving manganese intermediates; the deuterium label in α-detuero-mandelic acid is retained in benzaldehyde.

Our work resolves the apparent conflict of the observed kinetic deuterium isotope effect with the major product of oxidation benzaldehyde in acid medium. In acid medium (pH = 1), PGA effectively competes for the available permanganate; this competition is reflected in the small but significant amounts of benzoic acid.

At pH 4-4.5, a soluble brown-yellow Mn(IV) species is rapidly formed and decays in a slow step, reminiscent of the Guyard reaction (oxalic acid/MnO_4^-/H_2SO_4). At neutral pH (7-7.4), the growth of a yellow soluble (colloidal) manganese (IV) species is observed at 418 nm with a stoichiometry of

$3MA + 2Mn(VII) = PGA + 2BZ + 2CO_2 + 2Mn(IV)$ (soluble/colloidal).

In alkaline (pH ≥13), permanganate is rapidly reduced to a green manganese(VI) intermediate (610 nm). Using the capture of Mn(VI) as the insoluble barium manganate, the stoichiometry for the first step can be represented as: 2Mn(VII) + MA = 2Mn(VI) + PGA.

At neutral pH, using the experimentally determined stoichiometric ratio of benzaldehyde to phenylglyoxylic acid (BZ/PGA), we have shown that the oxidation of hypomanganate (Mn(V)) by permanganate is the preferred pathway relative to its disproportionation.

In addition, the periodate/permanganate system, has allowed us to intervene in the reaction at the Mn(V) stage, resulting in a turnover of the Mn(V) to Mn(VII). This leads to a significant increase in the yields of phenylglyoxylic acid (PGA) at the expense of benzaldehyde(BZ); it provides unequivocal support for the first step-rate-limiting hydride-transfer from mandelic acid to permanganate.

Environmental implications

Permanganate is used as the first line of treatment for dissolved organic matter and emerging contaminants in waste and ground water. Even though the redox reaction is initiated by permanganate, the better part of the oxidation is carried out manganese intermediates, especially by Mn(V) and Mn(VI). Mandelic acid serves as a model substrate for both C-H hydroxylation and C-C cleavage (oxidative decarboxylation) reactions. Both Mn(V) and Mn(VI) could potentially undergo disproportionation/comproportionation reactions. Manganese(III) derived from two-electron reduction of Mn(V) could be potentially stabilized by citrate and humic acid. The current investigation has given insight into the reactivity and selectivity of these manganese intermediates.

AUTHOR INFORMATION:

Corresponding Author

Surendra Mahapatro- Department of Chemistry, Regis University, Denver, Colorado, 80221 USA.

https://orcid.org/0000-0002-6480-0248

Email: smahapat@regis.edu

Authors

Tanden Hovey - Department of Chemistry, Regis University, Denver, Colorado, 80221 USA.

https://orcid.org/0000-0001-8676-1270

Email: thovey@regis.edu

Disha Mishra

https://orcid.org/0009-0001-2491-2085

mishradish1@gmail.com

Manveer Singh -- Department of Chemistry, Regis University, Denver, Colorado, 80221 USA.

ORCID ID: 0009-0006-9864-4059

Email: msingh004@regis.edu

Chantele Owusu- Department of Chemistry, Regis University, Denver, Colorado, 80221 USA.

Email: cowusu001@regis.edu

ORCID ID: 0009-0003-6806-0122.

Grecia Anaya - Department of Chemistry, Regis University, Denver, Colorado, 80221 USA.

Email: ganaya@regis.edu

ORCID ID: 0009-0006-0272-0097

Dr. Kellen Sorauf, Data Science, Anderson College of Business and Computing

ORCID ID is 0009-0007-9697-7631

Email: ksorauf@regis.edu

Dr. Mata Dambarudhar Patro. Department of Chemistry, Khallikote University, Berhampur, 760001, Odisha, India

ORCID ID is 0009-0007-9697-7631

Email: mdpatro1951@gmail.com

Dr. Akhil Krishna Panigrahi. Department of Chemistry, Khallikote University, Berhampur, 760001, Odisha, India

E-mail: akhiljyoti44@gmail.com

ttps://orcid.org/0009-0009-7973-9564

E-mail: akhiljyoti44@gmail.com

Nicole Barvian Department of Chemistry, Regis University, Denver, Colorado, 80221 USA.

ORCID ID 0009-0005-0176-3039

nbarvian@att.net <nbarvian@att.net>

Author contributions

Undergraduate student (T. A. H., M. S., C. O., G. A. and N. C. B.) involvement extended from year to year with each student performing a part of the research. The entire project was planned and supervised by S. N. M. The feasibility of the project was examined by N. C. B. including preliminary kinetic studies and HPLC product analysis. Preliminary results were reported by N. C. B. at the NCUR conference at Cal Tech in 1991. EPR, HPLC product analysis, kinetic measurements, spectral scans, and oxidation state determination were carried out by T. A. H. Kinetics studies, spectral scans, and synthesis of manganate were carried out C. O., M. S. and G. A. The synthesis of deuterated mandelic acid, kinetic deuterium isotope effect, mass spectra of deuterated benzaldehyde and its derivative, and determination of oxidation states were carried out by M. D. P. and A. K. P. The work of D. M. was supervised by K. J. S.; working together, they contributed to HPLC method development, kinetic analysis, reproduction of earlier experiments. All contributed to manuscript writing at different stages of development including a comprehensive literature review.

Conflict of Interest

The authors declare no competing financial interest

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