

Permanganate Ion Oxidations. 13. Soluble Manganese(IV) Species in the Oxidation of 2,4(1*H*,3*H*)-Pyrimidinediones (Uracils)^{1,2}

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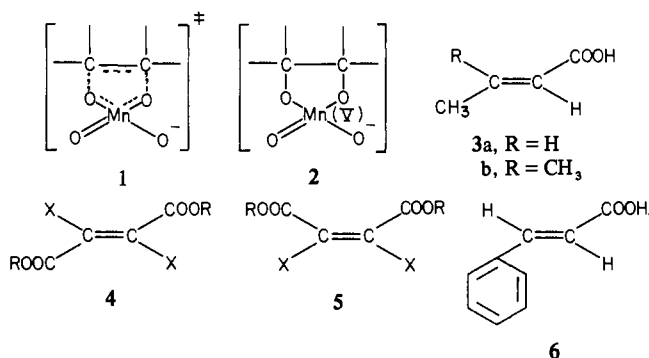
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Abstract: The permanganate ion oxidation of 2,4(1*H*,3*H*)-pyrimidinediones [uracil (**7**) and 5-methyl- (**8**), 6-methyl- (**9**), 5-fluoro- (**10**), 5-chloro- (**11**), 5-bromo- (**12**), 5-iodo- (**13**), 5-acetyl- (**14**), and 5-nitrouracil (**15**)] is first order in each reactant. After the initial oxidation step, a soluble manganese(IV) species is formed at a rate comparable to the rate of disappearance of permanganate ion. The relative rates of oxidation for **7/8/9/10/11/12/13/14/15** are 1:8:0.04:37:6:7:8:1.3:1.3. Relatively small ΔH^\ddagger values and large negative ΔS^\ddagger values are obtained. The initial oxidation step probably involves a concerted [3 + 2] cycloaddition of permanganate ion across the 5,6 double bond of the uracil. The spectra of the Mn(IV) species from uracils are compared with the spectra from (*E*)-2-butenoic acid (**3a**), 3-methyl-2-butenoic acid (**3b**), and (*E*)-3-phenylpropenoic acid (**6**), and with previous reports of cyclic hypomanganate ester [manganese(V)] intermediates.

Introduction

Although permanganate ion has been extensively used as an oxidizing agent for well over a century, there are still unanswered questions concerning the mechanisms of many of the oxidation processes.⁴⁻⁷ Recent reports^{6,8-20} have focused on the possible intermediacy of cyclic five-membered activated complexes (**1**) and of cyclic hypomanganate [manganese(V)] esters (**2**) during the oxidation of carbon-carbon double bonds.

It is generally accepted that aqueous solutions of permanganate ion react rapidly with carbon-carbon double bonds^{4,5,21,22} to form



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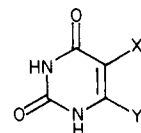
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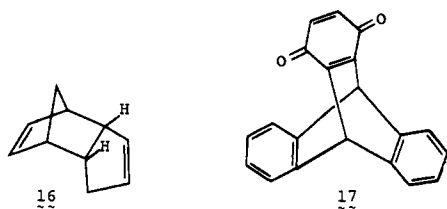
transient manganese and/or organomanganese intermediates which are subsequently transformed to glycols, carbonyl compounds, α -hydroxycarbonyl compounds, or carboxylic acids. Intermediate manganese species have been postulated for the permanganate ion oxidation of (*E*)-2-butenoic acid (**3a**) in neutral and alkaline solutions,^{7,15,21} of derivatives of (*E*)- and (*Z*)-2-butene-1,4-dioic acids (**4** and **5**) in acidic media,^{8,9,11} of (*E*)-3-phenylpropenoic acid (**6**) in acidic media,^{10,16,17} of derivatives of 2,4(1*H*,3*H*)-pyrimidinedione (**7-8-15**) in neutral media,^{6,12-14} and



- 7**, X = Y = H
8, X = CH₃; Y = H
9, X = H; Y = CH₃
10, X = F; Y = H
11, X = Cl; Y = H
12, X = Br; Y = H
13, X = I; Y = H
14, X = CH₃CO; Y = H
15, X = NO₂; Y = H

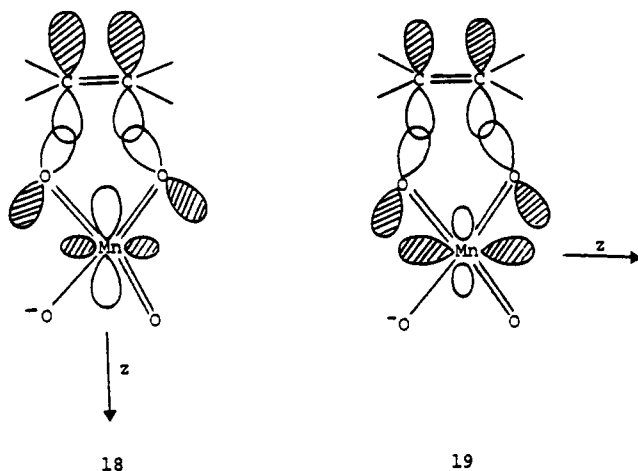
of *endo*-dicyclopentadiene (**16**) in methylene chloride.¹⁸ Intermediate manganese species appear to be involved in the permanganate ion oxidation of 9,10-dihydro-9,10-*o*-benzenoanthracene-1,4-dione (**17**).²⁰ However, in spite of these reports, it appears that the existence of the transient cyclic Mn(V) ester

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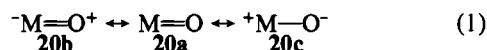


2 remains to be demonstrated.^{4-7,10}

Orbital symmetry treatment of reacting orbitals suggest that the permanganate ion oxidation of alkenes could involve a concerted electrocyclic process ([3 + 2], Hückel-type system, **18** or **19**).^{23,24} Bonding interactions are possible whether the d_z^2 orbital



is parallel or perpendicular to the double bond. Alternatively, the possibility that organometallic intermediates having metallic carbon σ bonds are involved in the oxidation of olefins by high-valent (d^0) transition-metal reagents has been suggested.^{25,26} Support for this hypothesis is obtained from ab initio calculations,^{27,28} dipole moment measurements,^{29,30} and photoelectron spectroscopy studies³¹ which suggest oxo transition-metal species such as permanganate ion, chromyl acetate, chromyl chloride, osmium tetraoxide, and selenium dioxide are better represented by the dipolar resonance structure **20c**. Thus, according to this

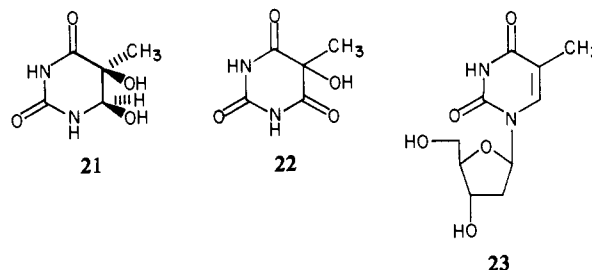


hypothesis, oxidations of olefins by high-valent (d^0) transition-metal reagents are initiated by attack of the organic reductant at the metal center.²³⁻²⁵

In order to obtain pertinent information concerning postulated intermediates and the activated complex in the permanganate ion oxidation of carbon-carbon double bonds, we have examined the kinetics and mechanisms of the oxidation of **3a**, **3b**, **6**, and the biologically important uracils (**7-15**) via spectrophotometric stopped-flow and chemical quenching techniques. These results are compared and contrasted with previous reports of Mn(V) intermediates,^{6,10,15-20} and other kinetic data for the permanganate ion oxidation of unsaturated systems.^{14,22,24}

The mild selective permanganate ion oxidation of specific bases in nucleic acids is useful in studies on the chemical structures of nucleic acids.³² Although overoxidation can occur under vigorous

conditions, permanganate ion oxidizes 5-methyl-2,4(1*H*,3*H*)-pyrimidinedione (5-methyluracil, thymine, **8**) to (*Z*)-5,6-dihydroxy-5,6-dihydrothymine [(*Z*)-thymine glycol, **21**] and 5-



hydroxy-5-methylbarbituric acid (**22**) as the primary oxidation products.³³⁻³⁵ Product **22**, which is favored at low pH values, is not formed from **21** but is formed directly from **8**.³⁴ Similar results have been obtained from the oxidation of uracil (**7**)³⁶ and thymidine (**23**).³⁷⁻³⁹ Thus, the permanganate ion oxidation of uracils bears a close similarity to the oxidation of olefins.⁴⁻⁷

Experimental Section

Solutions were prepared immediately before use in demineralized water which had been slowly distilled in an all-glass still from potassium permanganate. The appropriate amounts of KH_2PO_4 and Na_2HPO_4 to maintain the pH and ionic strength were dissolved in the standard (Titrisol) permanganate ion solution or in the reductant solution. Commercially available **3a**, **3b**, **6**, and 2,4(1*H*,3*H*)-pyrimidinediones **7-15** were recrystallized from water or aqueous ethanol. The pH values were determined on a Corning Digital 110 expanded-scale pH meter.

Spectra of the Mn(IV) species were determined on a Cary 14, a Cary 219, a Beckman ACTA III, or a Beckman MIV spectrophotometer by recording the absorbance vs. time curves at preselected wavelengths and/or by repetitive scanning of the ultraviolet-visible region.

The oxidation state of manganese in the reaction was determined, as previously described,^{4,10} by quenching the reaction with excess NaI and titrating the iodine released against standard thiosulfate solution.⁴⁰

The kinetics were determined with a specially designed stopped-flow reactor in a Beckman DU spectrometer^{21,41,42} and/or on a Durrum Model D-110 stopped-flow spectrophotometer. The Beckman DU spectrometer was connected via an energy-recording adapter to a Rikadenki Mark II strip-chart recorder equipped with a 60-Hz filter box. The temperature was maintained with a Forma Model 2095-2 refrigerated and heated bath circulator.

Kinetic experiments were performed under pseudo-first-order conditions with a large excess of reductant. The rates were determined by monitoring the disappearance of permanganate ion (510, 515, 522, 524, 525, or 584 nm) or by observing the rate of formation of the Mn(IV) species (405, 415, 420, 425, 435, or 439 nm). The pseudo-first-order rate constants (k_p) were calculated by the computer programs LSKINI⁴³ and/or LORAK.^{15,44} The observed initial and final absorbance values were compared with those calculated by LSKINI. The rate constants are the average of two or more experiments and were calculated on a PDP-10 computer. In general, rate constants obtained by observing the rate of formation of the Mn(IV) species were comparable to those calculated from the rate of disappearance of permanganate ion.

Results

Kinetic Data. Figure 1 shows the disappearance of permanganate ion at 520 nm and the formation of a Mn(IV) species at 420 nm.^{17,19,40} Kinetic data for the permanganate ion oxidation

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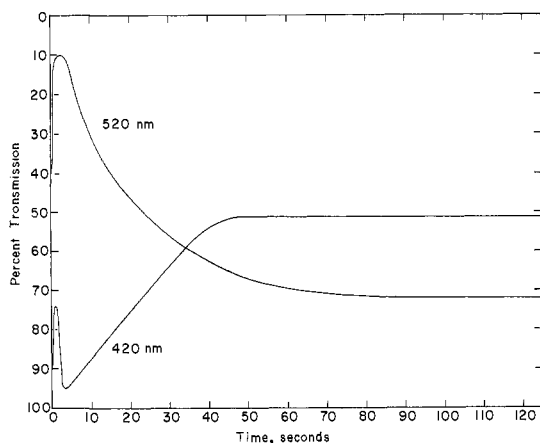


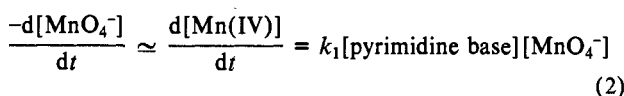
Figure 1. Disappearance of permanganate ion at 520 nm and formation of a Mn(IV) species at 420 nm: 25.0 °C, $\mu = 0.20$, pH 6.73 (phosphate buffers), $[\text{MnO}_4^-] = 4.00 \times 10^{-4}$ M, $[\text{thymine (8)}] = 4.00 \times 10^{-3}$ M.

Table I. Permanganate Ion Oxidation of Thymine (8)^a

λ , nm	$10^3 \times$ [thymine], M	$10^4 \times$ [MnO ₄ ⁻], M	$10^2 \times$ k_{ψ} , ^b s ⁻¹	k_1 , ^c M ⁻¹ s ⁻¹
524	4.00	4.00	6.21	15.6
524	3.00	4.00	4.82	16.1
524	2.00	4.00	3.15	15.7
524	1.00	4.00	1.59	15.9
425	4.00	4.00	6.73	16.8 ^d
425	3.00	4.00	5.01	16.7 ^d
425	2.00	4.00	3.88	14.4 ^d
425	1.00	4.00	1.47	14.7 ^d
524	4.00	2.00	6.79	17.0
524	4.00	3.00	6.35	15.9
524	4.00	4.00	6.41	16.0
524	4.00	8.00	5.86	14.6
524	4.00	10.00	6.03	15.1
405	4.00	4.00	6.71	16.8 ^d
415	4.00	4.00	6.60	16.5 ^d
420	4.00	4.00	6.58	16.4 ^d
439	4.00	4.00	6.60	16.5 ^d
510	4.00	4.00	6.56	16.4
584	4.00	4.00	6.06	15.1

^a Temperature 25.0 °C, $\mu = 0.20$, pH 6.73 with KH₂PO₄-Na₂HPO₄ buffers. ^b Pseudo-first-order rate constant from disappearance of permanganate ion. ^c Second-order rate constant $= k_{\psi}/[\text{8}]$. ^d Obtained from the rate of formation of Mn(IV).

of thymine (8) are summarized in Table I. The consistent values of the second-order rate constant ($k_1 = k_{\psi}/[\text{8}]$) at constant permanganate ion concentration imply a first-order dependence on permanganate ion and on thymine (8), respectively. Plots of the pseudo-first-order rate constants (k_{ψ}) vs. uracil 7 or 8 concentration give straight lines which pass through the origins. The slopes of these plots are in agreement with the k_1 values calculated by observing the disappearance of permanganate ion or the appearance of Mn(IV). Additional support for the first-order dependence on oxidant concentration is also shown in Table I by the constancy of k_{ψ} during changing permanganate ion concentration. The kinetic data are consistent with an overall second-order reaction (eq 2).



Substituent Effects. The inductive, polar, and resonance effects of substituents at the 5- or 6-position of 7 are shown in Table II. One of the most striking differences (~ 195) in rates is between 8 and 6-methyluracil (9). It is also of interest to note that 5-fluorouracil (10) is the most reactive of the nine pyrimidine bases and 5-acetyl- (14) and 5-nitrouracil (15) react at rates comparable to that for 7.

Table II. Summary of Kinetic Results for the Permanganate Ion Oxidation of Uracils^a

uracil	k_1 , ^b M ⁻¹ s		
	425 nm ^c	524 nm ^d	rel rates
uracil (7)	1.96 ^e	1.93	1.00
5-methyluracil (thymine) (8)	16.5 ^e	16.1	8.34
6-methyluracil (9)	0.093	0.083	0.04
5-fluorouracil (10)	77.4	70.6	36.6
5-chlorouracil (11)	11.3	11.0	5.70
5-bromouracil (12)		13.7	7.10
5-iodouracil (13)	16.2	16.1	8.34
5-acetyluracil (14)	2.78	2.59	1.34
5-nitrouracil (15)		2.62	1.34

^a 0.05 M KH₂PO₄-Na₂HPO₄ buffers, $\mu = 0.20$, 25.0 °C, $[\text{uracil}] = 4.00 \times 10^{-3}$ M, $[\text{MnO}_4^-] = 4.00 \times 10^{-4}$ M. ^b Second-order rate constant $= k_{\psi}/[\text{uracil}]$. ^c Obtained from rate of formation of Mn(IV). ^d Obtained from rate of disappearance of permanganate ion. ^e Wavelength (λ) 415 nm.

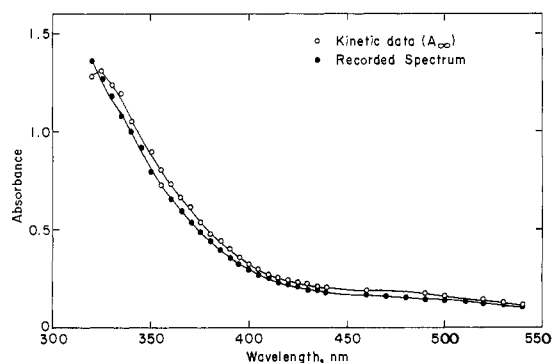


Figure 2. Comparison of the observed (solid circles) and calculated (open circles, 34 wavelengths) absorption spectra of Mn(IV) from the permanganate ion oxidation of thymine (8). Sample cell: $[\text{8}] = 4.00 \times 10^{-3}$ M, $[\text{MnO}_4^-] = 4.00 \times 10^{-4}$ M, pH 6.71 (0.05 M KH₂PO₄-Na₂HPO₄ buffers), 25.0 °C, $\mu = 0.20$. Reference cell: $[\text{8}] = 3.6 \times 10^{-3}$ M, pH 6.71 (0.05 M phosphate buffers).

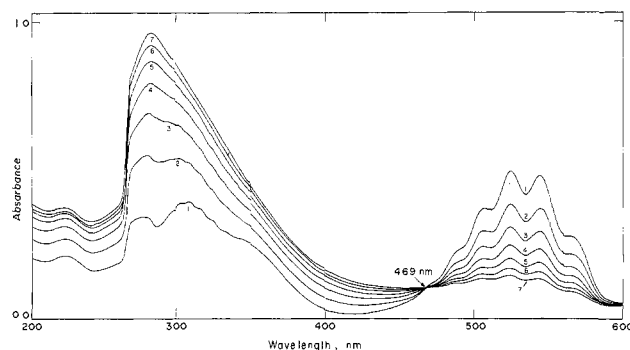


Figure 3. Successive UV-vis spectra for the reaction of 4.00×10^{-3} M 6-methyluracil (9) with 4.00×10^{-4} M MnO₄⁻ in a phosphate-buffered aqueous solution of pH 6.7 at 25.0 °C in 0.5-cm cells. The reference cell contained 3.6×10^{-3} M 9 in the same buffer.

Thermodynamic Parameters. The activation parameters were determined for eight pyrimidine bases at 15.0 and 25.0 °C. Table III shows the relatively low enthalpies of activation (ΔH^\ddagger) and the large negative entropies of activation (ΔS^\ddagger).

Ionic Strength. It is seen in Table IV that the second-order rate constant for the permanganate ion oxidation of thymine (8) does not change appreciably over a tenfold change in ionic strength. Qualitatively, this is consistent with the Debye-Hückel theory which relates the activity coefficient of an ion and the ionic strength in dilute solutions. According to this theory, if one of the reactants is a neutral molecule (8, eq 2), there should be no effect of the ionic strength.

Spectra of Manganese(IV) and Manganese(V) Species. Figure 2 shows a comparison of the recorded and calculated (from 34 wavelengths) spectra from the permanganate ion oxidation of

Table III. Activation Parameters for the Permanganate Ion Oxidation of Substituted Uracils^a

uracil	ΔG^\ddagger , kcal/mol		ΔH^\ddagger , kcal/mol		$-\Delta S^\ddagger$, kcal/mol	
	425 nm	524 nm	425 nm	524 nm	425 nm	524 nm
uracil (7)	17.0 ^b	17.1	6.60 ± 0.8 ^b	5.3 ± 0.8	45 ± 3 ^b	40 ± 3
5-methyluracil (thymine (8))	15.8 ^b	15.8	6.7 ± 0.7 ^b	6.9 ± 0.7	31 ± 2 ^b	30 ± 1
5-fluorouracil (10)	14.9	15.0	7.1 ± 0.4	7.9 ± 0.6	26 ± 1	23 ± 2
5-chlorouracil (11)		16.0		7.4 ± 0.6		29 ± 2
5-bromouracil (12)		15.9		7.5 ± 0.6		28 ± 2
5-iodouracil (13)	15.8	15.8	7.2 ± 0.9	7.3 ± 0.6	29 ± 4	29 ± 2
5-acetyluracil (14)		16.9		7.7 ± 0.7		31 ± 3

^a Determined at 15.0 and 25.0 °C by observing the formation of Mn(IV) at 425 nm or the disappearance of permanganate ion at 524 nm. ^b Wavelength (λ) 415 nm.

 Table IV. Effect of Ionic Strength on the Permanganate Ion Oxidation of Thymine (8)^a

μ^b	pH ^c	pH ^d	k_1^e , M ⁻¹ s
0.0	6.0	8.25	14.9
0.1	6.79	6.86	15.9
0.2	6.73	6.78	15.7
0.8	6.50	6.58	17.0, 17.5 ^f
1.0	6.47	6.56	17.3, 17.3 ^f

^a [8] = 4.00 × 10⁻³ M, [MnO₄⁻] = 4.00 × 10⁻⁴ M, 25.0 °C, 524 nm. ^b Ionic strength varied by adjusting concentrations of KH₂PO₄ and Na₂HPO₄ buffers while maintaining the ratio [KH₂PO₄]/[Na₂HPO₄] constant. ^c pH of permanganate ion solution containing buffers. Changes in pH could be the result of secondary salt effects. ^d pH of reaction medium after reaction. ^e Second-order rate constant = $k_1 = k_{\psi}/[8]$. ^f Obtained from rate of formation of Mn(IV) at 425 nm.

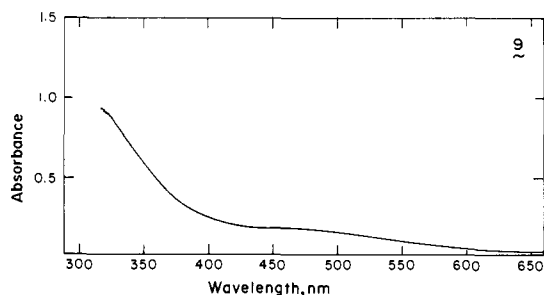


Figure 4. Spectrum of Mn(IV) from the permanganate ion oxidation of 9. Experimental conditions are the same as those for Figure 3.

thymine (8). Figure 3 shows the successive UV-vis spectra for the reaction of 9 and permanganate ion in a phosphate-buffered aqueous solution of pH 6.7. The isobestic point at 469 nm, which implies that one reactant (MnO₄⁻) and one product [Mn(IV)] are absorbing in the visible region, does not necessarily exclude formation of undetectable 2. Figure 4 shows the Mn(IV) spectrum approximately 20 h after the oxidation of 9. Similar Mn(IV) spectra were obtained for the other uracils (7, 10–14). The time required for precipitation of the Mn(IV) species from different reductants varied from several minutes to many hours.

Figure 5 presents the ultraviolet and visible spectrum of inorganic hypomanganate [Mn(V)] ion.

Table V shows some of the approximate absorption maxima of proposed Mn(V) intermediates and Mn(IV) species.

Average Oxidation State of Manganese. Table VI shows the average oxidation state of manganese from the oxidation of 7–10. It is seen that in all four cases the average oxidation state of manganese is +3.50 ± 0.13, which is inconsistent with a Mn(V) species. It is assumed that addition of a reductant to an intermediate such as 2 will not cause it to undergo an internal oxidative decomposition.

Discussion

Neglecting mixed tautomers, the tautomerism of uracil (7) is shown by structures 7a (amido form, lactam) and 7b (2,4-di-

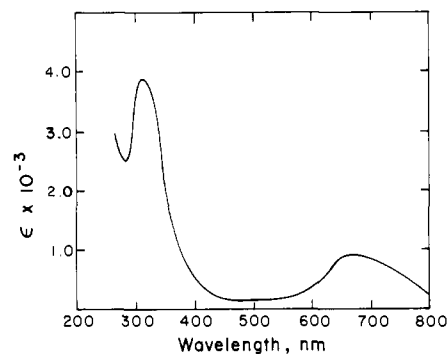


Figure 5. Ultraviolet-visible spectrum of inorganic hypomanganate ion.

Table V. Approximate Absorption Maxima of Proposed Mn(V) Intermediates and Mn(IV) Species

olefin	approx λ_{\max} , nm	olefin	approx λ_{\max} , nm
3 ^{15,a}	290	11 ^c	308
6 ^{16,17,b}	415	12 ^c	309
7 ^c	285	13 ^c	306
8 ^c	296	14 ^c	287
9 ^c	286	16 ^{18b,d}	275
10 ^c	298	Mn(IV) ^{5,40,e}	290

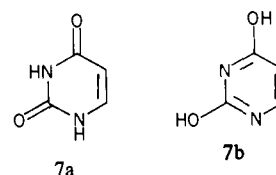
^a 0.2 M sodium hydroxide. ^b 0.99 M perchloric acid. ^c This work: 0.05 M KH₂PO₄ and Na₂HPO₄ buffers, pH 6.71, μ = 0.20, 25.0 °C. ^d Permanganate ion solubilized in CH₂Cl₂ by use of an equimolar amount of triethylbenzylammonium chloride. ^e Irradiation of KMnO₄ in aqueous solutions by γ^{60} CO rays.

Table VI. Average Oxidation State of Manganese^a

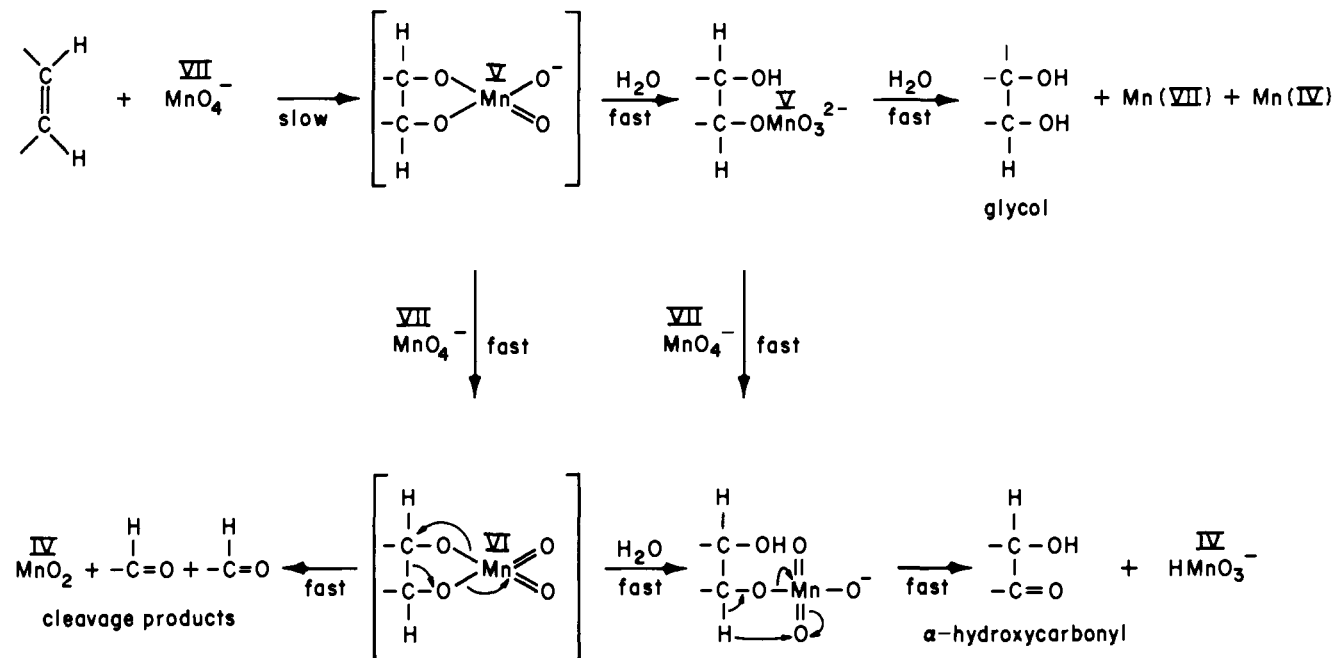
pyrimidine base	oxidation state	time elapsed, min
uracil (7)	3.60	4.0
	3.57	5.0
	3.47	6.0
	3.43	15.0
thymine (8)	3.39	1.0
	3.40	1.5
	3.40	2.0
	3.35	5.0
6-methyluracil (9)	3.75	110.0 ^b
	3.77	120.0
	3.70	120.0 ^c
5-fluorouracil (10)	3.33	1.0

^a [Pyrimidine base] = 4.00 × 10⁻³ M; [MnO₄⁻] = 8.00 × 10⁻⁴ M; 25.0 °C; phosphate buffers (pH 6.70). ^b [MnO₄⁻] = 4.00 × 10⁻⁴ M. ^c [MnO₄⁻] = 4.00 × 10⁻⁵ M.

hydroxypyrimidine, lactim). Uracil 7 and its derivatives exist in neutral solution in the lactam form.^{45–54}



Scheme I



The kinetic data ($-d[\text{MnO}_4^-]/dt$) are consistent with the permanganate ion oxidation of the 5,6 double bond in 2,4-(1*H*,3*H*)-pyrimidinediones to form a cyclic five-membered activated complex which could resemble **1**.^{4,23,24} Activated complex **1** could then lead to the undetectable cyclic hypomanganate ester **2** which is rapidly hydrolyzed or oxidized. The substituent effects (Table II), thermodynamic parameters (Table III), and salt effects (Table IV) are consistent with a concerted [3 + 2] cycloaddition of permanganate ion to the 5,6-double bond in the lactam form of uracils.^{23,24} However, these data do not exclude an initial fast step involving a charge-transfer complex and/or an organomanganese intermediate having a Mn-C σ bond.²⁵

With the exception of **9** and **10**, the permanganate ion oxidation of uracils is not strongly influenced by substituent effects (Table II). The permanganate ion oxidation of alkenoic acids or **6** in neutral and alkaline solutions is also remarkably insensitive to electronic effects.^{15,21} Moreover, in aqueous perchloric acid, the rate of oxidation of (*E*)-3-phenylpropenoic acids gives a Hammett ρ value -1.1 .^{16,17} The oxidation of stilbenes in aqueous dioxane solution⁵⁵ gives a ρ value of 0.65. In aqueous acid media, the rates of oxidation of substituted maleic acids **5** appear to be more influenced by steric factors than by electronic effects,⁹ and the permanganate ion oxidation of acyclic olefins in acetic anhydride is also rather insensitive to the extent of alkyl substitution at the double bond.^{56,57}

Although **9** is oxidized slower than the other uracils, it also ultimately leads to a soluble Mn(IV) species (cf. Figures 2-4).

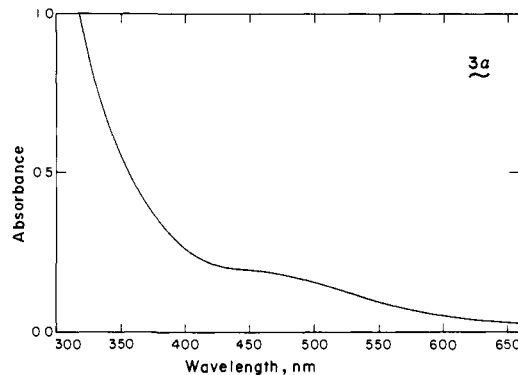


Figure 6. Spectrum of Mn(IV) species from the permanganate ion oxidation of (*E*)-2-butenic acid (**3a**).

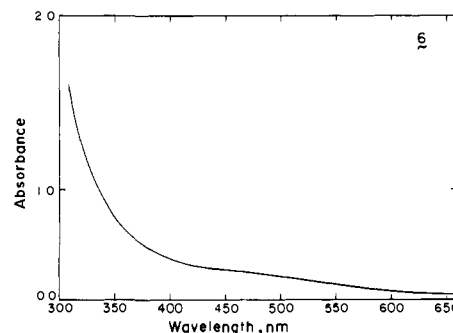


Figure 7. Spectrum of Mn(IV) species from the permanganate ion oxidation of (*E*)-3-phenylpropenoic acid (**6**).

The rate-accelerating effect of fluorine on **10** is also of interest since the initially formed diol can easily lose hydrogen fluoride. Although a change in mechanism is possible when a potential leaving group is substituted at the double bond, **10** also leads to the same soluble Mn(IV) species.

In order to ascertain whether the soluble Mn(IV) species is a result of the oxidation of uracils or a consequence of the buffer and pH chosen, **3a**, **3b**, and **6** were oxidized for comparison purposes. Figures 6 and 7 and the spectrum from **3b** show the similarity among these and the Mn(IV) species from uracils. Moreover, all of the Mn(IV) spectra in this study are remarkably similar to the spectra reported for the permanganate ion oxidation of **3a** in neutral and alkaline solutions¹⁵ and for the triethyl-

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benzylammonium permanganate oxidation of **16** in methylene chloride.^{18b}

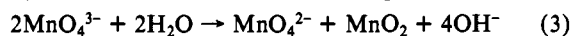
The above data suggest that the observed manganese species formed during the permanganate ion oxidation of **3a**, **3b**, **6**, and **7-15** is probably a soluble $\text{Mn}^{\text{IV}}[\text{H}_2\text{MnO}_3]$ species which slowly precipitates.⁶³ It also appears that the previously reported intermediates detected in the permanganate ion oxidation of **3a**, **4-6**, **16**, and (*Z*)-2-butene-1,4-diol⁶⁴ are also $\text{Mn}(\text{IV})$ compounds.¹⁰

Although the spectra of $\text{Mn}(\text{IV})$ from the permanganate ion oxidation of **3a**, **3b**, **6**, and the uracils show some resemblance to the spectrum of $\text{Mn}(\text{V})$ (Figure 5),^{58,62} the oxidation state data

(63) Although the composition of the soluble $\text{Mn}(\text{IV})$ species cannot be formulated at this time, we regard it as H_2MnO_3 . Other possibilities include phosphate complexes.

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in Table VI argue strongly against a pentavalent manganese species. However, it is not unreasonable to expect formation of a transient, undetectable hypomanganate ester (**2**) as an intermediate in these reactions. A mechanism which regards $\text{Mn}(\text{V})$ and $\text{Mn}(\text{VI})$ as short-lived intermediates (eq 3 and 4) and can



account for the variety of products obtained from the permanganate ion oxidation of carbon-carbon double bonds is shown in Scheme I. The fate of the hypomanganate ester (**2**) and the product distribution are determined by the reaction conditions.

Acknowledgment. I express my thanks to Professor Manfred Eigen, at the Max Planck Institut für Biophysikalische Chemie, Göttingen, for his hospitality during the preparation of this manuscript.

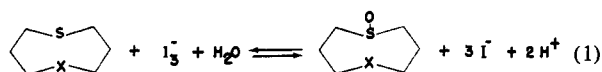
Intramolecular Catalysis of Organic Oxidation and Reduction Reactions: Rapid and Microscopically Reversible Thioether-Sulfoxide Interconversions in Dilute Acid

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Abstract: We recently reported that the aqueous HI reduction of 1,5-dithiacyclooctane 1-oxide was accelerated by about 10^6 compared to common sulfoxides. We have now observed a rate acceleration of about the same magnitude in the reverse reaction: the I_2 oxidation of the corresponding thioether. The acceleration and insensitivity of the rate to pH and buffers are attributed to intramolecular catalysis by the transannular thioether group. Similarly, 5-methyl-1-thia-5-azacyclooctane 1-oxide and its thioether are rapidly and easily interconverted. Although different rate laws are observed in the two systems, these anchimerically assisted processes allow either the oxidation or the reduction to occur rapidly and completely in *dilute acid*. The direction of the reaction is reversed quantitatively in the same solution by a slight change of pH. These unique reversible redox systems are simple models which satisfy the criteria of speed and reversibility required by biochemical electron- and proton-transfer reactions.

We recently reported that the HI reduction of certain mesocyclic sulfoxides proceeds 10^6 times faster than the reduction of Me_2SO and attributed the acceleration to intramolecular catalysis.^{1,2} We now report an acceleration of a similar magnitude in the reverse reactions: the oxidation of mesocyclic thioethers 1,5-dithiacyclooctane (A) and 5-methyl-1-thia-5-azacyclooctane (G) by aqueous I_2 . *Of paramount importance is the fact that the position of the redox equilibria (eq 1) can be shifted rapidly*



A ; X = S

G ; X = NCH₃

E ; X = S

M ; X = NCH₃

and essentially quantitatively to either side by a change of less than 2 pH units. For example, under the proper conditions, the oxidation of A with I_2 at pH 3.5 is 95% complete in 2 min; the reaction can be completely reversed in the same solution in less than 5 s when the pH is lowered to 1.5. The cycle can be repeated. Further oxidation of E to 1,5-dithiacyclooctane 1,5-dioxide occurs

at least 10^6 times slower than the rate of formation of E from A. This difference in rate illustrates the enormous catalytic effect of the transannular thioether group relative to a transannular sulfoxide group. The tertiary amine group is an equally effective catalyst in promoting the rapid and reversible interconversion of G and its sulfoxide M. These redox systems are unique in their speed and simplicity and in the extent of their reversibility by addition of acid or base. We are not aware of any redox reactions of organic molecules which are as rapid and which can be reversed as completely in the same solution by changing either the pH or the concentration of any of the reagents.

Experimental Section

Materials and Solvents. 1,5-Dithiacyclooctane (A) and 5-methyl-1-thia-5-azacyclooctane (G) and their sulfoxides were synthesized as described elsewhere.^{1,3}

Solutions of buffer were prepared with use of analytical reagent grade salts. The pH values of the buffers and of the HClO_4 solutions were checked before the reaction. The solutions were diluted with conductivity water which had been boiled and cooled under N_2 .

Spectrophotometric Kinetic Measurements. Equal volumes of separate solutions of the sulfide in water and the buffered triiodide solutions were thermostated and simultaneously injected into a thermostated 1-cm

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