as further substantiation of the dioxetane CL mechanism for *t*-MVP and 7,8-Diol.

The only experiment in which the CL yield of 7,8-Diol did not parallel that of *t*-MVP was in the low-temperature photosensitization reactions. At room temperature, CL from 7,8-Diol was directly proportional to the amount of $^1O_2$ produced during the irradiation period. At −78 °C, CL from 7,8-Diol shows rapid saturation with the time of irradiation. This inability to accumulate a chemiluminescent intermediate from 7,8-Diol at −78 °C during long intervals of irradiation could be due to (a) secondary photochemical reactions of $^1O_2$ with 7,8-Diol competing with the formation of a 9,10-dioxetane from 7,8-Diol or (b) low-temperature inhibition of dioxetane formation, possibly by steric hinderance. The absence of accumulation, upon low-temperature irradiation, of a chemiluminescent intermediate from *trans*-(methoxyvinyl)-2-methylpyrene implies that ortho-substituted vinylpyrenes may be better models to explain the anomalous behavior of 7,8-Diol at low temperature.

The absence of a product of $^1O_2$-induced CL of 7,8-Diol, isolable by HPLC and exhibiting a fluorescence identical with the CL, implies that the dialdehyde product is either unstable or reactive. However, the pyrene-1-carboxaldehyde product of *t*-MVP dioxetane decomposition is isolable and stable, and its fluorescence emission spectrum is identical with the *t*-MVP dioxetane emission.

Singlet oxygen induced CL from *t*-MVP has striking similarities with the CL from 7,8-Diol. These encompass (a) solvent effects on CL, (b) lifetimes of CL, (c) CL emission spectra, (d) activation energies, and (e) microsomal enzymatic CL. The differences in ϕ_{CL} can be attributable to the fact that *t*-MVP is much more reactive with $^1O_2$ and that an ene reaction is possible with 7,8-Diol but is not possible with *t*-MVP. The evidence we have presented demonstrates the dioxetane mechanism for the CL of *t*-MVP by isolation of pyrene-1-carboxaldehyde, the expected dioxetane decomposition product whose fluorescence spectrum was identical with the observed *t*-MVP CL dioxetane emission spectra and by the parallel effects of solvent on *t*-MVP dioxetane CL and the fluorescence quantum yields of pyrene-1-carboxaldehyde. Except for the isolation of the proposed dialdehyde product of 7,8-Diol CL, the CL lifetimes, solvent effects, activation energies, and spectra of 7,8-Diol dioxetane parallel that of *t*-MVP.

The factor ϕ_{FL} for a product excited state is probably lower than the photophysical fluorescence quantum yield of 6 (ϕ_{Fluor}). Excited states produced by photon absorption are governed by photoselection rules and initially have the conformation of the ground-state molecule in its ground-state solvent cage. Chemically produced excited-state products are not governed in their formation by photoselection rules, and their initial conformations relative to their solvent cages may be quite different. Therefore quenching of CL excited states may be significantly different from the quenching of photoexcited states. Lee and Seliger[20] measured ϕ_{CL}(luminol) = 0.0125, whereas photoexcited ϕ_{Fluor} of the aminophthalic acid product was 0.3. Whether this large difference is attributable to a difference between chemiexcited ϕ_{FL} and photoexcited ϕ_{Fluor} or to an effect on ϕ_{EX} cannot be determined. The result is that the components of the product $\phi_{\mathrm{EX}}\phi_{\mathrm{FL}}$ cannot readily be evaluated from substitution of independently measured values of ϕ_{Fluor} measured by photoexcitation. Therefore the derived values of ϕ_{EX} in Table III are minimum values.

From Table III for *t*-MVP, ϕ_{CL}(dioxetane) ≅ 0.03 which is more than a factor of 2 higher than for luminol. However $^1O_2$ reactions with *t*-MVP (Scheme III) result in both dioxetane (10% yield) and apparently endoperoxide (87% yield) with an overall ϕ_{CL}(*t*-MVP) of 0.003. This high ϕ_{CL} and the high specificity of this CL for $^1O_2$ make *t*-MVP an excellent probe for $^1O_2$,[37] since photon detection in the CL assay has a greater advantage in sensitivity than the use of non-CL chemical traps for $^1O_2$, similar to fluorescence assay techniques compared with a spectrophotometric assay, i.e., a factor of 10^5–10^6. It should be possible to detect $^1O_2$ or $^1O_2$ equivalents in cells using trace amounts of *t*-MVP or other second generation CL probes, where the presence of the probe may not interfere with normal physiological processes.

Registry No. **1**, 61443-57-0; **2**, 77267-10-8; **4** (R_1 = OMe; R_2 = H), 93265-41-9; **4** (R_1 = H; R_2 = OMe), 102699-15-0; 4 (R_1,R_2 = 1,3-dithian-2-yl), 102699-16-1; **4** (R_1 = OMe; R_2 = H) (2-methoxy), 102699-17-2; **4** (R_1 = Cl; R_2 = H), 102699-18-3; 4 (R_1 = Bu-*t*; R_2 = H), 102699-19-4; **4** (R_1 = R_2 = H), 17088-21-0; 4 (R_1 = H; R_2 = OMe) (2-methoxy), 102699-20-7; **6**, 3029-19-4; O_2, 7782-44-7; 2-(trimethylsilyl)-1,3-dithiane, 13411-42-2; (methoxymethyl)triphenylphosphonium chloride, 4009-98-7; neopentyltriphenylphosphonium iodide, 3740-00-9; 2-methylpyrene-1-carboxaldehyde, 102699-21-8; *N*,*N*,*N*′-trimethylethylenediamine, 142-25-6; naphthalene-1-carboxaldehyde, 66-77-3; (methoxyvinyl)naphthalene, 102699-14-9.

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Permanganate Ion Oxidations. 17. Kinetics and Mechanism of the Oxidation of (*E*)-3-(2-Thienyl)-2-propenoates and (*E*)-3-(3-Thienyl)-2-propenoates in Phosphate-Buffered Solutions[1]

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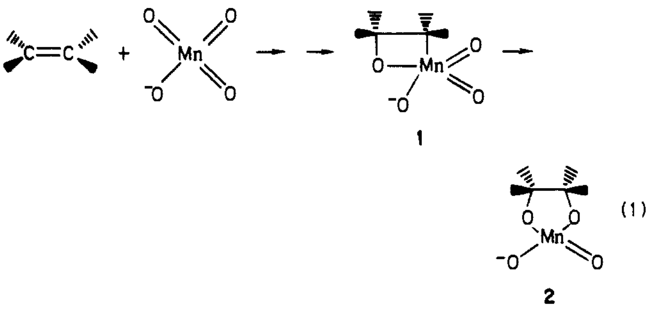
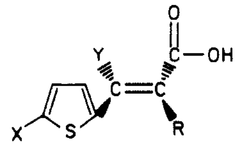
Contribution from the Department of Chemistry, University of California—Irvine, Irvine, California 92717. *Received December 2, 1985*

Abstract: The kinetics and mechanism of the permanganate ion oxidation of (*E*)-3-(2-thienyl)-2-propenoates and (*E*)-3-(3-thienyl)-2-propenoates have been studied at 418, 526, 584, and 660 nm in phosphate-buffered solutions (pH 6.83 ± 0.03). The reaction is first order in permanganate ion and first order in substrate. A rate-determining step leading to the formation of a metallacyclooxetane or a cyclic manganate(V) diester is supported by low enthalpies of activation, large negative entropies of activation, small substituent effects, steric effects, and an inverse secondary deuterium kinetic isotope effect. The ambiphilic nature of permanganate ion is considered.

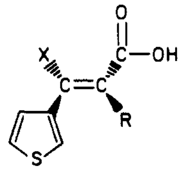
Recently, there has been considerable discussion concerning the oxidation state of the manganese species observed during the permanganate ion oxidation of carbon–carbon double bonds.[1,3-29] Although it was thought that the observed manganese species was the long-sought elusive cyclic manganate(V) intermediate (**2**), it is now generally agreed that the inorganic product is soluble (colloidal) manganese dioxide.[1,6-8,17] There also appears to be inconsistencies concerning the effects of substituents on the rate of permanganate ion oxidation of carbon–carbon double bonds.[1,23,28,30]



Despite the fact that the permanganate ion oxidation of both aliphatic and aromatic carbon–carbon double bonds has been extensively studied, relatively little work has been carried out with heterocycle-substituted unsaturated systems. Thus, we have investigated the permanganate ion oxidation of the anions of 3-(2-thienyl)-2-propenoic acids (**3–12**) and of 3-(3-thienyl)-2-propenoic acids (**13–15**) in order to assess the influence of the thiophene ring, to compare the effects of benzene and thiophene nuclei, to apply linear free energy relationships to the thiophene ring[31-37] and to the carbon–carbon double bond, and to determine whether the heterocycle would play a role in stabilizing the proposed transient manganate(V) intermediate (**2**).



	X	Y	R
3	H	H	H
4	H	D	H
5	H	H	CH_3
6	H	CH_3	H
7	H	H	C_6H_5
8	H	H	CN
9	Br	H	H
10	CH_3	H	H
11	H (3-methyl-2-thienyl)	H	H
12	NO_2	H	H



	X	R
13	H	H
14	H	CH_3
15	H	CN

Experimental Section

Melting points were determined in open capillary tubes with a Thomas–Hoover apparatus and are uncorrected. Elemental analyses were performed by Robertson Laboratory, Inc., Florham Park, NJ.

IR spectra were obtained with a Perkin-Elmer 283 spectrophotometer, calibrated with the 1601-cm^{-1} absorption of polystyrene, in CCl_4, as neat films, or as KBr disks.

High-resolution mass spectra were obtained with a VG 7070E-HF mass spectrometer (70 eV). Medium-resolution mass spectra were obtained with a Finnigan 9610 GC-EI-CI mass spectrometer with a Nova 3 data system operating at an ionization potential of 70 or 100 eV. Chemical ionization mass spectra were obtained by using 2-methylpropane as the reactant gas.

^1H NMR spectra were recorded at 80 MHz (Varian FT-80A) and at 250 MHz (Bruker WM-250) with the solvent(s) noted. Chemical shifts (δ) are reported downfield from internal Me_4Si (~0.5% for Fourier transform) at δ 0.00. Apparent coupling constants (J) are reported in hertz (Hz). Because of the data digitization with the FT instrument, J values are ±0.40 Hz maximum but normally are accurate to ±0.20 Hz. ^{13}C NMR data were obtained with a Bruker WM-250 spectrometer. The NMR of previously prepared substrates agreed with literature values.

Solutions were prepared immediately before use in water which had been deionized and then slowly distilled from an all-glass Corning mega-pure apparatus. Appropriate quantities of KH_2PO_4 and Na_2HPO_4 to maintain pH and ionic strength were dissolved in the substrate solution. Ionic strength was also adjusted by adding KCl to the permanganate solution when necessary. Standard (Titrisol) potassium permanganate solutions were used. The pH values were determined on an Altex *ϕ60* pH meter in the substrate solution before reaction and in the product mixture after oxidation.

Substrates were recrystallized from aqueous ethanol before they were used. Liquid reagents were fractionally distilled under reduced pressure, and solvents were purified according to standard procedures.

The kinetics were determined on a Durrum Model D-110 stopped-flow spectrometer which was connected to a Tracor-Northern 1710 Multichannel Analyzer. The data were transferred to an IBM PC for analysis and printing. 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 substrate. The rates were determined by monitoring the disappearance of permanganate ion at 526, 584, and 660

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nm or by observing the rate of formation of soluble (colloidal) manganese dioxide at 418 nm. The pseudo-first-order rate constants (k_ψ) were calculated from plots of -ln ($A_t - A_\infty$) or -ln ($A_\infty - A_t$) on a first-order kinetics program. All rate constants are the average of two or more experiments.

Spectra of manganese dioxide were obtained on a Beckman ACTA III or a Cary 219 spectrophotometer by recording the absorbance vs. time curves at preselected wavelengths and/or by repetitive scanning of the ultraviolet–visible region.

(*E*)-3-(2-Thienyl)-2-propenoic acid (3) was recrystallized from aqueous ethanol, mp 145–146 °C [lit.[38,39] mp 146–147 °C].

(*E*)-3-Deuterio-3-(2-thienyl)-2-propenoic acid (4): Dideuterio(2-thienyl)methanol, which was prepared by the $LiAlD_4$ reduction of ethyl (2-thienyl)methanoate, was oxidized with pyridinium chlorochromate (PCC) to 1-deuterio-2-thiophenecarboxaldehyde:[40–42] NMR ($CDCl_3$) δ 6.2 (s, 1 H), 7.07–7.42 (m, 3 ThH).

Condensation of 1-deuterio-2-thiophenecarboxaldehyde with 1,3-propanedioic acid[38,39,43–45] gave (*E*)-3-deuterio-3-(2-thienyl)-2-propenoic acid (**4**), mp 145–145.7 °C. ^{1}H NMR showed the absence of hydrogen at C-3. EIMS, *m/z* calcd for $C_7DH_5O_2S$ 155.0151; obsd 155.0141.

(*E*)-2-Methyl-3-(2-thienyl)-2-propenoic acid (5) was prepared by condensation of 2-methyl-1,3-propanedioic acid and 2-thiophenecarboxyaldehyde,[38,43] mp 145.2–147.2 °C [lit.[44] mp 139.5–140 °C]; EIMS, *m/z* calcd for $C_8H_8O_2S$ 168.0040; obsd 168.0040.

(*E*)-3-Methyl-3-(2-thienyl)-2-propenoic acid (6) was prepared from hydrolysis of ethyl 3-methyl-(2-thienyl)-2-propenoate,[44] mp 114–114.8 °C [lit.[44] mp 112.5–113 °C]. EIMS, *m/z* calcd for $C_8H_8O_2S$ 168.0245; obsd 168.0254.

(*E*)-2-Phenyl-3-(2-thienyl)-2-propenoic acid (7) was prepared from 2-thiophenecarboxaldehyde and 2-phenylethanoic acid,[46] mp 187–187.5 °C [lit.[46] mp 190–192 °C]. EIMS, *m/z* calcd for $C_{13}H_{10}O_2S$ 230.0401; obsd 230.0405.

(*E*)-2-Cyano-3-(2-thienyl)-2-propenoic Acid (8). In a 50-mL round-bottomed flask equipped with a Dean-Stark water separator which in turn was attached to a reflux condenser were added 11.5 g (10.3 mmol) of freshly distilled 2-thiophenecarboxaldehyde, 7.87 g (9.35 mmol) of 2-cyanoethanoic acid, 0.38 g (5 mmol) of ammonium acetate, and 30 mL of benzene.[41] The mixture was refluxed until the theoretical amount of water (1.85 mL) was collected (4 h) and then refluxed for an additional 1 h. The mixture was allowed to cool to 22–24 °C and filtered, and the solid was washed with two 5-mL portions of cold water. The crude solid was recrystallized from aqueous ethanol to give 12.8 g (76% yield) of **8**, mp 232–234.5 °C. EIMS, *m/z* calcd for $C_8H_5NO_2S$ 179.0041; obsd 179.0020. CIMS, *m/z* $[MH]^+$ 180 (100%); ($[MH]^+$ + 1) 181 (11.74%); ($[MH]^+$ + 2) 182 (6.6%). Anal. ($C_8H_5NO_2S$) C, H, N, S.

(*E*)-3-(5-Bromo-2-thienyl)-2-propenoic acid (9) was prepared as previously described,[38,39,45,47] mp 210–212 °C [lit.[44] mp 209–210 °C]. EIMS, *m/z* calcd for $C_7BrH_5O_2S$ 233.9173; obsd 233.9149.

(*E*)-3-(5-Methyl-2-thienyl)-2-propenoic acid (10) was prepared from 5-methyl-2-thiophenecarboxaldehyde and 1,3-propanedioic acid,[38,39,45,47] mp 164–166 °C [lit. mp 165–166 °C]. EIMS, *m/z* calcd for $C_8H_8O_2S$ 168.0245; obsd 168.0257.

(*E*)-3-(3-Methyl-2-thienyl)-2-propenoic acid (11) was prepared from 3-methyl-2-thiophenecarboxaldehyde and 1,3-propanedioic acid,[38,39,43–45] mp 170–171.5 °C [lit.[44] mp 171.5–172 °C]. EIMS, *m/z* calcd for $C_8H_8O_2S$ 168.0245; obsd 168.0254.

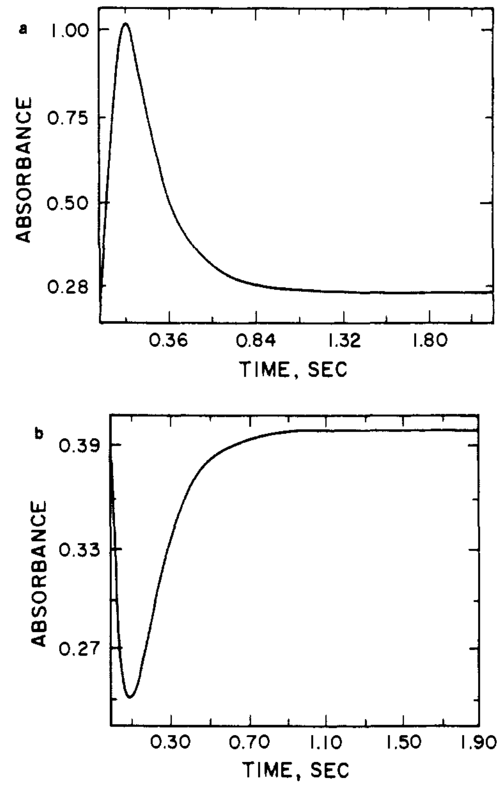

Figure 1. (a) Typical curve for the disappearance of permanganate ion at 526 nm at 25.0 °C. [MnO_4^-] = 4.00 × 10^{-4} M; [(*E*)-3-(2-thienyl)-2-propenoate] = 4.00 × 10^{-3} M; [KH_2PO_4] = [Na_2HPO_4] = 0.2 M; pH 6.86; μ = 0.80. (b) Typical curve for the formation of soluble (colloidal) manganese dioxide at 418 nm during the permanganate ion oxidation of (*E*)-3-(2-thienyl)-2-propenoate (**3**). Experimental conditions are the same as in part b.

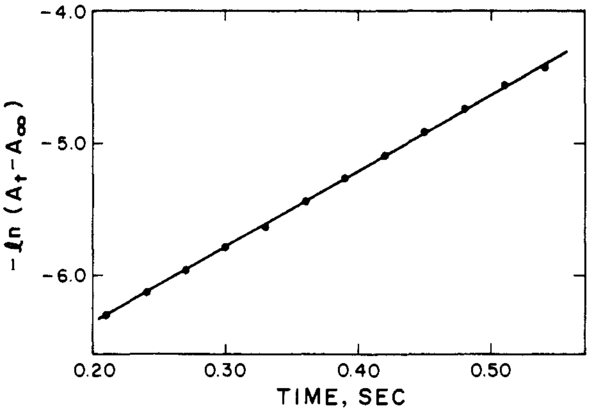

Figure 2. Typical pseudo-first-order plot for the rate of disappearance of permanganate ion at 526 nm. Temperature = 25.0 °C; [**3**] = 4.00 × 10^{-3} M; [MnO_4^-] = 4.00 × 10^{-4} M; [KH_2PO_4] = [Na_2HPO_4] = 0.20 M; pH 6.83; μ = 0.80.

(*E*)-3-(5-Nitro-2-thienyl)-2-propenoic acid (12)[38,39,48,49] was prepared from 5-nitro-2-thiophenecarboxaldehyde, which was obtained from the hydrolysis of 5-nitro-2-thiophenemethanediol diacetate,[48,49] and 1,3-propanedioic acid,[38,39] mp 254–255 °C [lit.[39] mp 255–256 °C]. EIMS calcd for $C_7H_5O_4NS$ 198.9939; obsd 198.9925.

(*E*)-3-(3-Thienyl)-2-propenoic acid (13) was prepared from 3-thiophenecarboxaldehyde and 1,3-propanedioic acid,[38,39] mp 151–152 °C [lit.[46] mp 153–153.5 °C]. EIMS, *m/z* calcd for $C_7H_6O_2S$ 154.0088; obsd 154.0077.

(*E*)-2-Methyl-3-(3-thienyl)-2-propenoic Acid (14). To a 150-mL round-bottomed flask fitted with a reflux condenser were added 8.72 g (74 mmol) of 2-methyl-1,3-propanedioic acid, 6.3 mL (85.9 mmol) of piperidine, and 46 mL (594.6 mmol) of azabenzene. After being refluxed for 24 h, the product mixture was cooled and poured into a mixture of 92 mL of concentrated hydrochloric acid and 100 g of ice. The mixture was filtered, and the filtrate was washed (2×) with 30 mL of ether. The ether solution was extracted (2×) with 30 mL of 10% $NaHCO_3$ solution. The precipitate was triturated with 100 mL of 10% $NaHCO_3$ solution, 40 mL of ether was added, and the layers were separated. The ether layer was extracted (2×) with 20 mL of 10% $NaHCO_3$ solution. The

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Table I. Kinetic Data for the Permanganate Ion Oxidation of (*E*)-3-(2-Thienyl)-2-propenoate (**3**) and (*E*)-3-(3-Thienyl)-2-propenoate (**13**)[a]

concn of **3** or **13** × 10^3 M	$[MnO_4^-]$, × 10^4 M	k,[b] M^{-1} s^{-1}
3		
4.00	0.40	1219 ± 80
4.00	1.60	1267 ± 3
4.00	2.00	1267 ± 6
4.00	2.80	1306 ± 13
1.30	4.00	1520 ± 6
1.60	4.00	1499 ± 3
2.20	4.00	1491 ± 15
2.70	4.00	1442 ± 6
4.00[c]	4.00	1341 ± 10
4.00[d]	4.00	1418 ± 15
4.00[e]	4.00	1461 ± 75
13		
4.00[f]	4.00	1071 ± 2

[a] Temperature = 25.0 °C; $[KH_2PO_4]$ = $[Na_2HPO_4]$ = 0.20 M; pH 6.83 ± 0.03; $\mu = 0.80$; $\lambda = 526$ nm. [b] Second-order rate constant = k = $k_\psi/[\mathbf{3}]$ or $k_\psi/[\mathbf{13}]$. [c] At 418 nm $k = 1408 \pm 4$ M^{-1} s^{-1}. [d] At 584 nm. [e] At 660 nm. [f] At 418 nm $k = 1098 \pm 2$ M^{-1} s^{-1}.

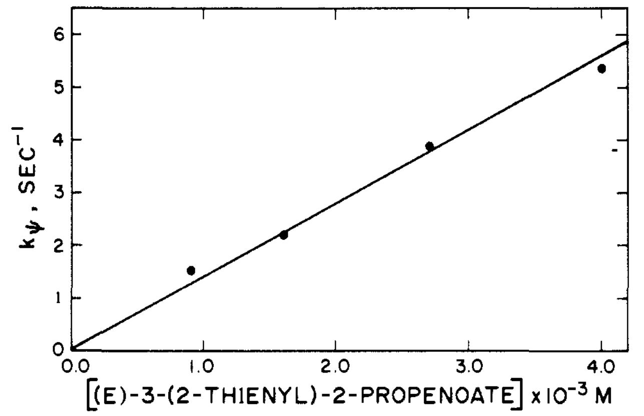


Figure 3. Effects of (*E*)-3-(2-thienyl)-2-propenoate (**3**) concentration on the pseudo-first-order rate constants (k_ψ) for the permanganate ion oxidation in 0.20 M KH_2PO_4–Na_2HPO_4 (pH 6.80, $\mu = 0.80$) at 25.0 °C.

combined $NaHCO_3$ extracts were combined and acidified to pH 2 with dilute HCl. Recrystallization of the solid from aqueous ethanol gave 4.2 g (52.5%) of 2-methyl-3-(3-thienyl)-2-propenoic acid (**14**), mp 131–133 °C. EIMS, *m/z* calcd for $C_8H_8O_2S$ 168.0245; obsd 168.0253.

(*E*)-2-Cyano-3-(3-thienyl)-2-propenoic acid (15) was prepared from 3-thiophenecarboxaldehyde and cyanoethanoic acid via the procedure described above.[41] Recrystallization from aqueous ethanol gave **15**, mp 210–211 °C. EIMS, *m/z* calculated for $C_8H_5NO_2S$ 179.0041; obsd 179.0030.

Results

Order of Reaction. The kinetics of the permanganate ion oxidation of the anions of 3-(2-thienyl)-2-propenoic acids (**3–12**) and 3-(3-thienyl)-2-propenoic acids (**13–15**) were determined under pseudo-first-order conditions in phosphate-buffered solutions. The rate of disappearance of permanganate ion was monitored at 526, 584, or 660 nm (Figure 1a) and the rate of formation of soluble (colloidal) manganese dioxide was observed at 418 nm (Figure 1b). A first-order dependence on the concentration of permanganate ion is suggested by the linearity of the pseudo-first-order plots (Figure 2) and by the consistent value of the pseudo-first-order rate constant (k_ψ) at 526 nm when the concentrations of (*E*)-3-(2-thienyl)-2-propenoate anion (**3**) and buffers were held constant and the concentration of permanganate ion was varied (Table I). The consistent values of the second-order rate constant at different concentrations of **3** and constant buffer and permanganate ion concentrations are in accord with a first-order dependence on the concentration of (*E*)-3-(2-thienyl)-2-propenoate (**3**). A plot of k_ψ vs. [anion of **3**] gives a straight line which passes through the origin with slope = k, which is indicative of a first-order dependence on the concentration of anion **3** (Figure 3). Moreover, a plot of ln k_ψ vs. ln [anion of **3**] is linear with a slope of 1.

$$-d[MnO_4^-]/dt = [(E)\text{-3-(2-thienyl)-2-propenoate}][MnO_4^-] \quad (2)$$

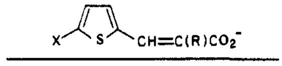
Buffer Concentration and Ionic Strength. Table II shows the effects of buffer concentration and ionic strength on the rate of

Table II. Effects of Buffer Concentration and Ionic Strength on the Rate of Permanganate Ion Oxidation of (*E*)-3-(2-Thienyl)-2-propenoate (**3**)[a]

$[KH_2PO_4]$,[b] M	pH[c]	μ[d]	k,[e] M^{-1} s^{-1}
0.025	6.68	0.10	887 ± 8
0.05	6.75	0.20	902
0.10	6.79	0.40	1023 ± 13
0.15	6.81	0.60	1268
0.15	6.63	0.80	1379 ± 65
0.15	6.53	1.00	1526
0.20	6.75	0.80	1418 ± 15
0.05	6.25[d]	1.20	1505 ± 3
0.10	6.33[d]	1.20	1506 ± 6
0.20	6.45[d]	1.20	1490 ± 4
0.30	6.80	1.20	1436 ± 26
0.05	6.24[d]	1.30	1559 ± 3
0.30	6.80[d]	1.30	1436 ± 26

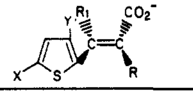
[a] $[MnO_4^-] = 4.00 \times 10^{-4}$ M; [**3**] = 4.00×10^{-3} M; 25.0 °C; $\lambda = 526$ nm. [b] $[KH_2PO_4]$ = $[Na_2HPO_4]$. [c] pH of reaction medium after reaction. [d] Ionic strength adjusted with KCl when necessary. [e] Second-order rate constant = k = $k_\psi/[\mathbf{3}]$.

Table III. Activation Parameters for the Permanganate Ion Oxidation Substituted 2-Propenoates[a]



X	R	ΔG^*, kJ mol^{-1}	ΔH^*, kJ mol^{-1}	$-\Delta S^*$, J k^{-1} mol^{-1}
H	H	55.3	12.7	143
H	CH_3	60.0	14.1	153.9
H	CN	60.8	13.0	160.3
3-(3-thienyl)- 2-propenoate		55.7	12.7	144.2

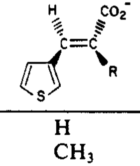
Table IV. Substituent Effects on the Permanganate Ion Oxidation of (*E*)-3-(2-Thienyl)-2-propenoates[a]



X	Y	R	R_1	k,[b] M^{-1} s^{-1} 418 nm	k,[b] M^{-1} s^{-1} 526 nm
H	H	H	H		1341 ± 10
H	H	CH_3	H	196 ± 1	188 ± 1
H	H	H	CH_3	450 ± 7	402 ± 6
H	H	C_6H_5	H		42 ± 4
H	H	CN	H	154 ± 3	133 ± 2
Br[c–e]	H	H	H	986 ± 46	1084 ± 12
CH_3	H	H	H	1399 ± 1	1473
H	CH_3	H	H		1436 ± 10
NO_2	H	H	H		1810 ± 14

[a] Temperature = 25.0 °C; $[KH_2PO_4]$ = $[Na_2HPO_4]$ = 0.20 M; μ = 0.80; pH 6.83 ± 0.03; $[MnO_4^-] = 4.00 \times 10^{-4}$ M; [anion] = 4.00×10^{-3} M. [b] Second-order rate constant = k = k_ψ/[anion]. [c] $[MnO_4^-] = 8.00 \times 10^{-5}$ M; [anion] = 7.00×10^{-4} M. [d] At 584 nm $k = 1067 \pm 62$ M^{-1} s^{-1}. [e] At 660 nm $k = 1134$ M^{-1} s^{-1}.

Table V. Substituent Effects on the Permanganate Ion Oxidation of (*E*)-3-(3-Thienyl)-2-propenoates[a]



R	k,[b] M^{-1} s^{-1} 418 nm	k,[b] M^{-1} s^{-1} 526 nm
H	1098 ± 2	1071 ± 2
CH_3	194 ± 5	287 ± 4
CN	524 ± 2	514 ± 1

[a] Temperature = 25.0 °C; $[KH_2PO_4]$ = $[Na_2HPO_4]$ = 0.20 M; pH 6.82 ± 0.02; $\mu = 0.80$; $[MnO_4^-] = 4.00 \times 10^{-3}$ M. [b] Second-order rate constant = k = k_ψ/[anion].

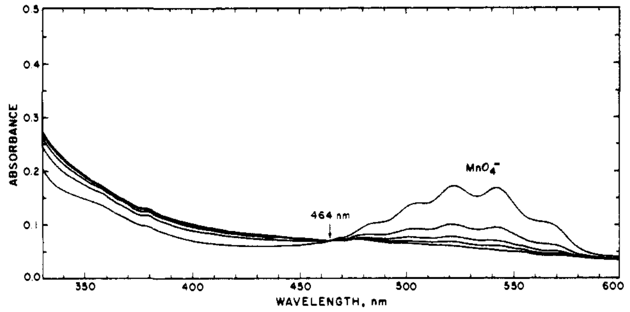


Figure 4. Sequential scans (scan rate = 10 nm s^{-1}) for the reaction of 8.00×10^{-5} M (*E*)-2-methyl-3-(2-thienyl)-2-propenoate (**5**) and 8.00×10^{-5} M $KMnO_4$ in 0.20 M KH_2PO_4–Na_2HPO_4 (pH 6.83, $\mu = 0.80$). The reference cell contained 0.20 M KH_2PO_4–Na_2HPO_4.

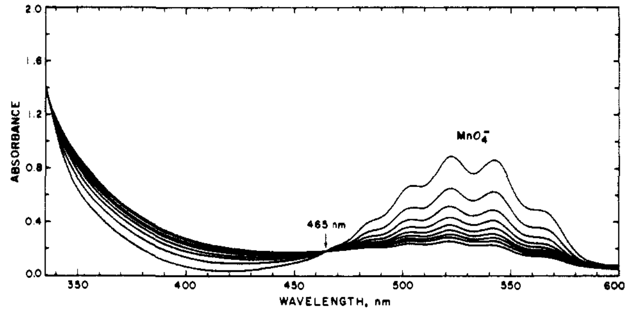


Figure 5. Sequential scans (scan rate = 10 nm s^{-1}) for the permanganate ion (4.00×10^{-5} M) oxidation of (*E*)-2-phenyl-3-(2-thienyl)-2-propenoate (**7**, 4.00×10^{-4} M) in 0.20 M KH_2PO_4–Na_2HPO_4 (pH 6.83, $\mu = 0.80$). The reference cell contained 0.20 *m* KH_2PO_4–Na_2HPO_4.

permanganate ion oxidation of (*E*)-3-(2-thienyl)-2-propenoate (**3**). The plot of log *k* vs. square root of ionic strength is linear.

Activation Parameters. Table III shows the values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for the permanganate ion oxidation of several thienyl-substituted 2-propenoates.

Substituent Effects. Tables IV and V show the effects of substituents on the rate of permanganate ion oxidation of carbon–carbon double bonds in (*E*)-3-(2-thienyl)-2-propenoates and (*E*)-3-(3-thienyl)-2-propenoates.

Inverse Secondary Deuterium Kinetic Isotope Effects. A $k_H/k_D = 0.95$ was obtained from the permanganate ion oxidation of (*E*)-(2-thienyl)-2-propenoate (**3**, $k = 1395$ M^{-1} s^{-1}) and (*E*)-3-deuterio-3-(2-thienyl)-2-propenoate (**4**, $k = 1454$ M^{-1} s^{-1}) in 0.20 M KH_2PO_4–Na_2HPO_4 buffers (pH 6.80, $\mu = 0.80$).

Spectra of Manganese Product. Figures 4 and 5 show successive ultraviolet–visible spectra for the permanganate ion oxidation of 2-methyl-3-(2-thienyl)-2-propenoate (**5**, isosbestic point 464 nm) and 2-phenyl-3-(2-thienyl)-2-propenoate (**7** isosbestic point 465 nm). The spectra of both product mixtures are consistent with soluble (colloidal) manganese dioxide.[1,6-8,15,18,24]

Discussion

The kinetic data described above are in agreement with a bimolecular activated complex involving substrate and permanganate ion (eq 2). No direct evidence was observed for metallocyclooxetane **1** and the manganate(V) ester **2**, although they may be transitory intermediates during the oxidation process.[1,6-8,15,17a,22b,50-53] Typical ultraviolet–visible changes for the permanganate ion oxidation of double bonds (Figures 4 and 5) show excellent isosbestic points, which suggests a clean reaction with no buildup of an intermediate. However, if the manganate(V) diester **2** is formed, it has a short lifetime and is very rapidly converted to soluble (colloidal) manganese dioxide.

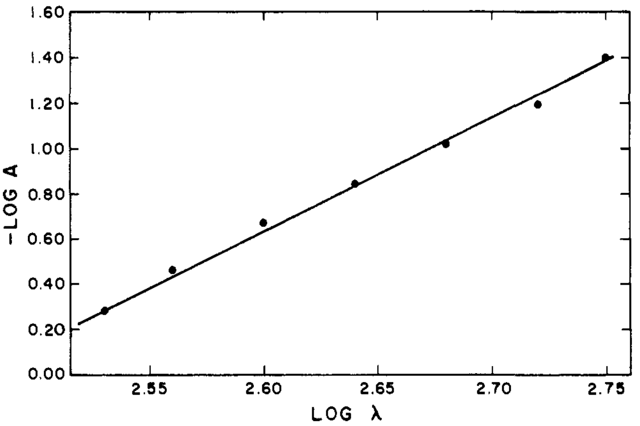


Figure 6. –log absorbance vs. log λ for the manganese species (MnO_2) obtained from the permanganate ion oxidation of (*E*)-3-(2-thienyl)-2-propenoate (**3**) in 0.20 M KH_2PO_4–Na_2HPO_4 (pH 6.83, $\mu = 0.80$) at 25.0 °C. Slope = 4.87 (correlation coefficient = 0.998).

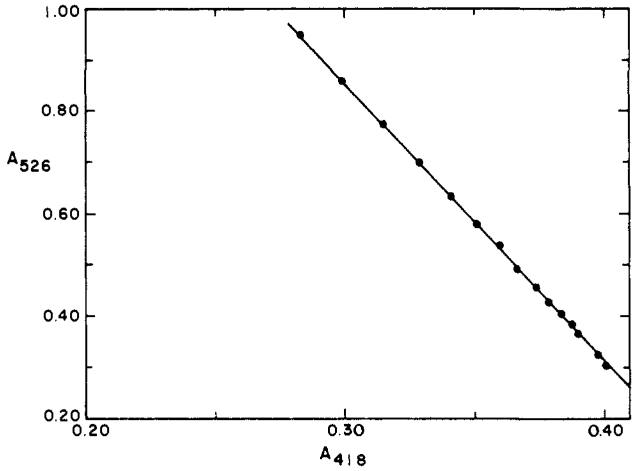


Figure 7. Absorbance at 526 nm vs. absorbance at 418 nm from the permanganate ion oxidation of (*E*)-3-(2-thienyl)-2-propenoate (**3**) in 0.20 M KH_2PO_4–Na_2HPO_4 ($\mu = 0.80$:; slope = –5.47; correlation coefficient = 0.999.

The colloidal nature of manganese dioxide is supported by a linear –log absorbance vs. log λ plot (Rayleigh's law, Figure 6).[1,6-9,15,18,24] Thus, the initially formed manganese dioxide would be expected to exist in solution in a mixture of colloidal particles. However, since colloidal manganese dioxide can adsorb phosphate ions on its surface,[54,55] the flocculation process is slowed owing to the high density of negative electrostatic charge on the surface of the colloidal particles.[24,56] Since the ratio of buffer concentration to the concentration of manganese dioxide is large, essentially all of the manganese dioxide formed during the reaction is initially solubilized. Thus, excellent linear plots of –log absorbance vs. wavelength (Figure 6) and of A_{526} vs. A_{418} are obtained (Figure 7).[56]

The kinetic data above are consistent with formation of a metallacyclooxetane (**1**,**16**) or a cyclic manganate(V) diester (**2**, **17**) in the rate-determining step (eq 1).[57,58] The inverse secondary

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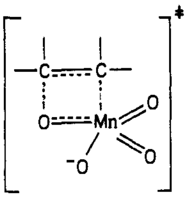
(56) The slowed flocculation process essentially extends the solubility lifetime of manganese dioxide–phosphate ion species. Other factors, including the size of flocculated manganese dioxide, and the orientation of the particles or the angle of incident radiation, are also important. In some experiments, kinetic data could not be obtained at 418 nm as a result of the flocculation process.

deuterium kinetic isotope effect ($k_H/k_D = 0.95$) from the oxidation of **3** and **4** indicates a change in hybridization from sp^2 at C-3 in the ground state to sp^3 in the activated complex.[13-15,18,30,59,60] A cycloaddition mechanism between permanganate ion and the carbon–carbon double bond is also supported by the large negative values for the entropy of activation (Table III).[20,26,28,30,53,61,62]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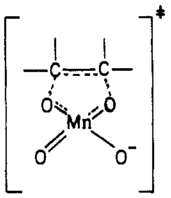
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(*E*)-3-(2-Thienyl)-2-propenoate (**3**, 1341 M^{-1} s^{-1}) and (*E*)-3-(3-thienyl)-2-propenoate (**13**, 1071 M^{-1} s^{-1}), which react with permanganate ion at essentially the same rates (Table III and IV), are oxidized faster than (*E*)-2-butenoate (**18**, 286 M^{-1} s^{-1})[1,8] and (*E*)-3-phenyl-2-propenoate (**19**, 590 M^{-1} s^{-1}).[1,8,61] If the attack of permanganate ion on the carbon–carbon double bonds in **13**, **15**, **18**, and **19** were electrophilic in nature, **13** and **15** would be expected to react fastest owing to the strong resonance donor ability of the thiophene ring system which overrides its inductive withdrawal effect.[63]

Substitution of methyl for hydrogen at C-2 in **3** to give **5** and in **13** to give **14** slows the rate of oxidation owing to steric effects (eclipsing of the cis substituents in the activated complex). Substitution of a larger phenyl group for methyl in **5** to give **7** also slows the rates of oxidation. Thus, steric factors are important in the permanganate ion oxidation of carbon–carbon double bonds.[1]

Replacement of hydrogen by cyano at C-2 in **3** to give **8** and in **13** to give **15** also slows the rates of oxidation because of steric factors and electron-withdrawal effects (Tables III and IV). These data are consistent with an electrophilic attack by permanganate ion on the carbon–carbon double bond.

The relatively small substituent effects observed with ring-substituted 3-(2-thienyl)-2-propenoates (Table IV) may suggest a cycloadditions mechanism between oxidant and substrate. Resonance stabilization of the ground state by electron-attracting substituents would increase the activation energy and lead to reduced rates of oxidation. Permanganate ion reacting as an ambiphile may also account for the small substituent effects.[1,8,64-66] Thus, the transmission effects in the thiophene system are similar to those observed in the permanganate ion oxidation of phenyl-substituted α,β-unsaturated carboxylate ions.[8,13-15,31,65]

Acknowledgment. We thank Professor Robert Taft for helpful discussions, Monica C. Keindl for expert technical assistance, the Alexander von Humboldt Foundation for partial support of this work, and the National Science Foundation for the purchase of the stopped-flow spectrometer (CHE 77-07970) and for financial assistance toward the purchase of the NMR spectrometers. Fillmore Freeman thanks the Fulbright Commission and the Alexander von Humboldt Foundation for fellowships.

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(57) Formation of π and/or σ complexes may precede the formation of intermediate **1** or **2**. Although formation of metallacycle **1** is consistent with the observed steric factors,[26,28] it does not account for the amount of oxygen transfer in the oxidation of alkenes[53] and alkynes.[58]

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(62) The rate-determining step may be preceded by rapid reversible formation of a π complex. Rearrangement of this complex to the product-determining cyclic manganate(V) diester is consistent with oxygen-18 and stereochemical studies in other unsaturated systems.

(63) On the other hand, phenyl, 2-thienyl, and 3-thienyl conjugation are expected to stabilize the ground state of the substrates and raise the energies of activation.

(64) The limited solubility of substrates precluded a more extensive study of substituent effects on the thiophene ring system. A concave upward LFER plot is expected if permanganate ion is ambiphilic.

(65) Small ρ values have been reported for the permanganate ion oxidation of several unsaturated systems.

(66) Since the reaction rates are determined by the difference in energy between the ground state and transition state, there may not be any merit in specifying the first step of a multistep reaction as being electrophilic or nucleophilic.

6-Polysubstituted α-Cyclodextrins. Application of Körner's Absolute Method of Isomer Determination

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Abstract: A rigioisomeric mixture of C-6 polysulfonated α-cyclodextrins was prepared by the reaction of α-cyclodextrin with mesitylenesulfonyl chloride in pyridine. All regioisomers in di-, tri-, and tetrasubstituted cyclodextrins were separated by reversed-phase column chromatography and assigned as to their regiochemistries by Körner's method.

In the past decade, specific preparation of primary di- (or poly-) substituted β-cyclodextrins has been studied in order to construct refined and sophisticated models of enzymes.[1] Transannular disulfonate capping methods have been developed to activate 6A,6B-, 6A,6C-, or 6A,6D-primary hydroxyls of β-cyclodextrin.[2] For α-cyclodextrin, sulfonation on three (6A,6C,6E) primary hydroxyls[3] and transannular sulfonation on two primary hydroxyls[4] were reported, but the position of the substituent was left unclear

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[‡] Kyushu University.

[§] Fukuoka University.

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