g of uranyl sulfate and 0.45 g of oxalic acid in 100 ml of water was prepared.

This solution was irradiated for 20 min under the same conditions as the samples and was then titrated with potassium permanganate.

The titrations of both photolyzed and unphotolyzed solutions of actinometer were run as follows. A 1-ml sample of the actinometer solution was diluted with an equal volume of 10% H_2SO_4, and then heated to 60° on the steam bath. The heated solution was titrated with permanganate solution (0.034 M) until an approximate end point was reached. Subsequent samples were treated in the same way, with the exception that about 90% of the required amount of permanganate was added to the sample while cold, and the sample was allowed to stand until it became colorless. The sample was then heated to 60° and the titration continued to the end point. Three to five samples of blanks and photolyzed solutions were titrated and the average difference in the volume of permanganate needed for the blanks and the photolyzed solutions (V) was used in the calculations (eq 1); V = difference in volume of permanganate

$$I = \frac{2.5[\mathrm{KMnO_4}]V6.023}{0.57t} \times 10^{23} \qquad (1)$$

(in liters), I = high-intensity quanta per unit time, t = time of irradiation. Intensities using this method usually ranged between 3 and 4 × 10^{16} quanta/sec. It was not observed until the uranyl oxalate actinometer had been in use for some time that the potassium chromate filter solution transmitted light at wavelengths greater than 4000 Å, a region in which the actinometer was active. Since our samples absorbed only in the 3130-Å region, the light intensity reaching the samples was less than that calculated from photolysis of the actinometer. A correction was made by running simultaneous uranyl oxalate and benzophenone–benzhydrol actinometers[44] and obtaining the ratio of light intensities measured by each. The latter actinometer did not absorb at wavelengths longer than 4000 Å. The light intensity measured by the benzophenone–benzhydrol actinometer was found to be 0.56 that of the intensity measured by uranyl oxalate.[46] The error in determining the absolute light intensities is estimated to be about 50%.

Analyses and Quantum Yield Determinations. Solutions of acetone and olefin were routinely photolyzed to low conversions (3–10% of product, based on olefin) to minimize the extent of conversion to the other olefin isomer.

The samples were analyzed by vapor phase chromatography and concentrations of products in the 0.001–0.005 M range were easily detected. The chromatographic conditions under which the various analyses were performed varied little between runs and are outlined below.

The acetone–MB photoreactions were analyzed on a 10 ft 5% Carbowax 20M column at 100°, with a helium flow of 25 cc/min. Retention times under these conditions were 2 min for **6**, 4 min for **5** and **7**, and 5 min for **4**. The identical retention times of **5** and **7** and the tendency of **6** and **7** to decompose on the vpc column led to problems in analysis. Both **6** and **7** were quantitatively destroyed in the photolysis solution by stirring the sample with approximately 10 μl of 0.01 M HCl directly after the irradiation was stopped. In those cases where the isomerization of 1-methoxy-1-butene was studied, a 10 ft 25% $\beta\beta\beta$ column (Chrom P) at 70° was used.

Peak areas were obtained by multiplying the height of the peak times the width at half-height. This method was found to be as reliable as the use of the Disc integrator on the recorder and was in general much easier to use.

The absolute quantum yields were measured as follows. After each photolysis, 5 μl of tetrachloroethylene was added to each milliliter of solution as an internal standard. Peak areas were then obtained relative to the area of the tetrachloroethylene peak. Absolute yields were obtained by analyzing solutions containing known amounts of **4** and **5** in addition to 5 μl of tetrachloroethylene. The concentrations of **4** and **5** in the photolyzed solutions could then be calculated and the quantum yields were obtained from eq 1.

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(46) Unpublished results, David Weiss, Columbia University.

Mechanism of Permanganate Oxidation of Tertiary Hydrogen to Hydroxyl[1a]

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Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. *Received June 25, 1969*

Abstract: The kinetics and stereochemistry of oxidation of tertiary benzylic hydrogen to hydroxyl by potassium permanganate were studied in concentrated aqueous base. The reaction is first order in both permanganate and organic compound, and it requires about 2.4 equiv of permanganate per mol of organic. At 25.0° and 2.5 M base, the second-order rate constants for γ-phenyl-, γ-phenyl-γ-d-, γ-(p-nitrophenyl)-, and γ-tolylvaleric acids are 3.8, 0.33, 1.4, and 3.5 × 10^{-3} M^{-1} sec^{-1}; 30–40% retention of configuration was observed. A mechanism which involves hydrogen atom abstraction by permanganate accommodates the experimental facts.

The oxidation of tertiary hydrogen to hydroxyl by permanganate in aqueous base is a reaction of considerable synthetic and mechanistic interest.[2] The reaction, at least in its first step, involves conversion of ⋗C–H to ⋗C–OH and provides a potentially useful method of chemically activating a saturated carbon. Although aspects have been investigated previously, the mechanism of the reaction has never been clearly ascertained.

Kenyon and Symons[3] observed some time ago that certain optically active carboxylic acids, *e.g.*, 4-methylhexanoic acid, could be oxidized to optically active lactones. These authors suggested that the reaction proceeded with carboxylate participation, and they assumed that inversion of configuration occurred at the reaction center. Subsequently, however, Eastman and Quinn[4] showed that the epimeric dihydro-α-terpineols

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(1) (a) Presented in part at the 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968; (b) Alfred P. Sloan Foundation Fellow.

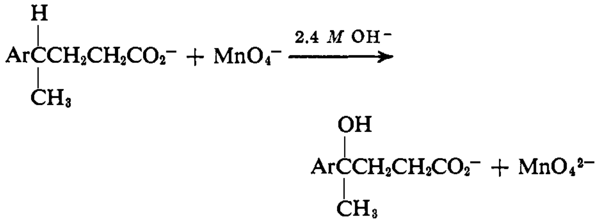
(2) For general reviews of the field see (a) R. Stewart in "Oxidation in Organic Chemistry," Part A, K. B. Wiberg, Ed., Academic Press, New York, N. Y., 1965, Chapter I; (b) J. W. Ladbury and C. F. Cullis, *Chem. Rev.*, **58**, 403 (1958).

(3) (a) J. Kenyon and M. C. R. Symons, *J. Chem. Soc.*, 2129 (1953); (b) J. Kenyon and M. C. R. Symons, *ibid.*, 3580 (1953).

could be oxidized to their corresponding diols with *retention* of configuration. The apparent discrepancy was resolved by Wiberg and Fox,[5] who showed that the oxidation of 4-methylhexanoic acid in fact proceeds with retention of configuration. On the basis of the stereochemistry and ^{18}O-tracer experiments, Wiberg and Fox proposed a mechanism for oxidation by permanganate similar to that proposed previously for chromate oxidations.[6]

There have been only limited kinetic studies undertaken of aqueous basic permanganate oxidations. Both Symons[7,8] and Heckner, Landsberg, and Dalchau[9] found apparent fractional order in organic substrate indicating, possibly, a prior reaction of permanganate with solvent water to produce hydroxyl radicals followed by their subsequent reactions with organic compounds. Wiberg and Fox were able to carry out preliminary kinetic studies which indicated rate constants of *ca.* 10^{-3} M^{-1} $\sec^{-1}$.

Because of our interest in reactions of C–H bonds, and because of the remaining uncertainties in the elucidation of the mechanism of oxidation of tertiary hydrogens, we have undertaken a detailed study of the reaction. In this paper we report the results of our studies of the kinetics and products of eq 1. The sub-



$$\mathrm{Ar}\overset{\mathrm{H}}{\underset{\mathrm{CH_3}}{\mathrm{C}}}\mathrm{CH_2CH_2CO_2^-} + \mathrm{MnO_4^-} \xrightarrow{2.4\ M\ \mathrm{OH^-}} \mathrm{Ar}\overset{\mathrm{OH}}{\underset{\mathrm{CH_3}}{\mathrm{C}}}\mathrm{CH_2CH_2CO_2^-} + \mathrm{MnO_4^{2-}} \quad (1)$$

Ar = C_6H_5 and substituted phenyl

strate chosen, γ-phenylvaleric acid, is soluble in the medium; it contains a tertiary benzylic hydrogen; it can be easily modified with ring substituents; and the γ-deuterio compound is easily prepared. The parent compound has been reported to be oxidized in good yield.[3a] The reaction was carried out under conditions where the products, kinetics (including substituent and isotope effects), stoichiometry, and stereochemistry could be studied. The conditions were chosen so that permanganate would not oxidize the solvent, and the reduction product, manganate, was stable. The results indicate that the reaction can be explained in terms of a relatively straightforward mechanism which may provide a general model for oxidations of saturated carbon–hydrogen bonds by permanganate.

Experimental Section[10]

γ-Phenylvaleric Acid. As described previously,[11] (±)- and (−)-γ-phenylvaleric acid were prepared from γ-valerolactone.

γ-Valerolactone-γ-*d*. This compound (>95% by nmr) was prepared by reduction of ethyl levulinate by sodium borodeuteride (96+ %, Metal Hydrides, Inc.) in isopropyl alcohol. No γ-proton could be detected by nmr.

γ-Phenylvaleric acid-γ-*d* was prepared from γ-valerolactone-γ-*d*. No γ proton was detectable by nmr; mass spectral analysis of the molecular ion indicated 96.3% deuterium. The S-benzylisothiouronium salts of undeuterated and deuterated acids had mp 141.5–142.0° and 140.0–140.6°, respectively (lit.[3a] 134°), and mmp 142.5–143.0°.

Anal. Calcd for $C_{19}H_{23}DO_2N_2S$: C, 66.05; H, 7.29; N, 8.11. Found: C, 65.82; H, 7.04; N, 8.27.

γ-(*p*-Nitrophenyl)valeric Acid. γ-Phenylvaleric acid was treated with concentrated nitric acid at room temperature for 24 hr. The reaction was worked up by addition to ice and water. The resulting yellow solid was washed with water, triturated with benzene, recrystallized from water-methanol (light green solid, mp 119–123°), and fractionally sublimed (85–90° (0.1 Torr)) to give colorless γ-(*p*-nitrophenyl)valeric acid, mp 122–123°, lit.[12] 125°; nmr (acetone-d_6), δ 1.32 (d, 3, J = 7 Hz, methyl), 2.1 (m, 4, methylene), 3.0 (q, 1, J = 7 Hz, benzyl), 7.5 (d, 2, aromatic *meta* to NO_2), 8.2 (d, 2, aromatic *ortho* to NO_2), and 11.6 (s, 1, acid).

γ-Tolylvaleric Acids. A mixture of tolylvaleric acids was prepared from toluene and γ-valerolactone.[11] The products were distilled on a microcolumn (113.5–114.5° (0.07 Torr)). The nmr spectrum (CCl_4) showed two sets of doublets (J = 7 Hz) centered at δ 1.18 and 1.23 (total three protons), a complex multiplet at δ 2.0 (4 protons), broad singlet at δ 2.3 (3 protons) apparently two signals separated by ≤1 Hz, two sets of quartets, J = 7 Hz, at δ 2.45–3.25 (total 1 proton), a complex aromatic region at δ 6.8–7.2 containing a singlet peak at δ 7.0 (total 4 protons), and a singlet at δ 12.2 (1 acid proton). This spectrum is that of a mixture of at least two isomers, 64–36% based on areas of the methyl signals. The acids were converted to their methyl esters and subjected to vpc analysis. This gave two peaks which were isolated by preparative vpc. The nmr of the major component indicated that it itself was a mixture of isomers. A fairly detailed analysis (including decoupling experiments) of all of the spectra indicated that the mixture consisted of 36% *ortho*, 36% *para*, and 28% *meta* isomers of γ-tolylvaleric acid. A 50–50 mixture of the *ortho* and *para* isomers was used in kinetic experiments.

γ-Phenyl-γ-valerolactone. A solution of phenylmagnesium bromide (0.25 mol) in 160 ml of ether was added to a cooled (0°) mixture of ethyl levulinate (0.2 mol) in 200 ml of ether over 1 hr. The mixture was allowed to stand an additional hour, then worked up by addition of ice and ammonium chloride. The ester was hydrolyzed by refluxing with ethanolic aqueous sodium hydroxide for 1 hr. After extraction with ether followed by drying, the product was distilled to give colorless γ-phenyl-γ-valerolactone, bp 106–108° (0.6 Torr), lit.[13] 134–139° (7 Torr); ir (film) 1775 cm^{-1}; nmr (CCl_4) δ 1.66 (s, 3, methyl), 2.4 (m, 4, methylene), 7.3 (s, 5, aromatic). The lactone was then further purified by preparative vpc (Ucon HB 5100 on 60–80 Chromosorb W, 6 ft × $^1/_2$ in., 202°, retention time 22 min).

Materials. Purified water was prepared by distilling deionized water from dilute alkaline permanganate. **Potassium permanganate** stock solutions were prepared by weighing out appropriate amounts of potassium permanganate (B and A, reagent) and diluting to the desired volume with purified water. The solutions were heated to boiling, cooled, filtered through sintered glass, and stored in dark bottles. **Potassium hydroxide** stock solutions were prepared by diluting 600 g of potassium hydroxide (B and A, reagent) to 1 l. with purified water. Base concentration did not change with time. **Incubated permanganate** solutions were prepared by mixing 20 ml of permanganate stock solution (*ca.* 0.3 *M*), 5 ml of purified water, and 10 ml of potassium hydroxide solution (8.88 *M*) in a gs 125-ml Erlenmeyer flask. The solution was maintained at 25.0° for at least 24 hr, then filtered through sintered glass. Por-

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(4) R. H. Eastman and R. A. Quinn, *J. Amer. Chem. Soc.*, **82**, 4249 (1960). Also see H. Kwart and G. D. Null, *ibid.*, **82**, 2348 (1960).

(5) K. B. Wiberg and A. S. Fox, *ibid.*, **85**, 3487 (1963).

(6) K. B. Wiberg and G. Foster, *ibid.*, **83**, 423 (1961).

(7) M. C. R. Symons, *J. Chem. Soc.*, 3956 (1953); M. C. R. Symons, *ibid.*, 3676 (1954).

(8) K. A. K. Lott and M. C. R. Symons, *Discussions Faraday Soc.*, 205 (1960).

(9) K. H. Heckner, R. Landsberg, and S. Dalchau, *Ber. Bunsenges. Phys. Chem.*, **72**, 649 (1968).

(10) Melting and boiling points are uncorrected. Ir spectra were recorded with a Perkin-Elmer 237B grating spectrophotometer. Nmr spectra were recorded on a Varian A-60 or HA-100 spectrometer. Chemical shifts are expressed in ppm (δ) downfield from internal tetramethylsilane: s = singlet, d = doublet, m = multiplet, etc. Optical rotations were taken neat with a Zeiss polarimeter in an end-filled 0.5-dm tube (0.25-ml capacity) and are an average of at least six readings. Vpc experiments were carried out with a Varian-Aerograph A-90-P3 chromatograph (60 ml/min). Microanalyses were carried out by E. Meier and J. Consul, Stanford Microanalytical Laboratory. Mass spectra were recorded on a CEC Model 21-103C mass spectrometer, heated inlet, 70 eV. We thank Dr. Alan Duffield for these.

(11) J. I. Brauman and A. J. Pandell, *J. Amer. Chem. Soc.*, **89**, 5421 (1967).

(12) J. Colonge and E. Fichet, *Bull. Soc. Chim. Fr.*, 412 (1955).

(13) J. A. Reid and E. E. Turner, *J. Chem. Soc.*, 3219 (1951).

tions were used for reaction. Solutions prepared in this way were *ca.* 0.1 M in permanganate and 2.54 M in base. **Barium nitrate** (B and A, reagent) solutions were made up to *ca.* 0.12 M. **Sodium cyanide** (B and A reagent) solutions were prepared fresh for each kinetic run at *ca.* 0.08 M. Exact concentrations were determined by titration with standard silver nitrate. **Silver nitrate** (B and A reagent or Tritisol, E. Merck AG) solutions were *ca.* 0.005 M. Those made from B and A reagent were standardized against sodium chloride (B and A reagent).[14] Tritisol solutions were prestandardized.

Kinetic Methods. Cyanide Method. The disappearance of permanganate was followed with a volumetric method based on the rapid oxidation of cyanide to cyanate by permanganate in basic solution:[15] $2MnO_4^- + CN^- + 2OH^- \rightarrow CNO^- + 2MnO_4^{2-} + H_2O$. The rate of oxidation of cyanide by permanganate is about 80 times faster[15] than the rate of oxidation of cyanide by manganate(VI) and this, coupled with the insolubility of barium manganate[16] ($K_{sp} \cong 10^{-10}$), permits permanganate determination[17] in the presence of manganate(VI).

A 2-ml portion of reaction mixture was added to a solution of 10 ml of 2 M potassium hydroxide solution, 5 ml of 0.12 M barium nitrate solution, and 5 ml of sodium cyanide solution. The manganate(VI) originally present and that formed by the reduction of permanganate by cyanide were precipitated as insoluble barium manganate. The mixture was allowed to stand at room temperature for at least 30 min and was then filtered through S and S No. 589 White Ribbon filter paper which was previously washed with 1 M carbonate-free base to prevent peptization of the barium manganate. The precipitate and flask were washed with 1 M carbonate-free base. A few drops of 10% potassium iodide solution (Baker Analyzed reagent) were added to the filtrate, and the solution was titrated with standardized 0.005 M silver nitrate solution. A 5-ml sample of the sodium cyanide solution was similarly titrated with silver nitrate solution. The stoichiometry for the titration is given by $Ag^+ + 2CN^- \rightarrow Ag(CN)_2^-$. The end point was taken as the first sign of turbidity and was reproducible to ±0.05 ml.

Knowing the molarity of the silver nitrate solution (M), the volume of silver nitrate solution needed to titrate the 5 ml of sodium cyanide solution (V'), and the volume of silver nitrate solution to titrate the excess cyanide (V), one can calculate the permanganate concentration from the equation $[MnO_4^-] = 2M(V' - V)/\text{ml}$, since 2 ml of permanganate solution was quenched. An error of ±0.05 ml in V and V' results in a maximum error of ± 0.001 M in the permanganate concentration. The initial permanganate concentrations were usually in the range of 0.1 M, and ± 0.001 M is a ±1% error. As the permanganate concentration decreases the percentage error increases and, therefore, the method becomes less reliable with increasing time. For example, if the permanganate concentration is 0.014 M, the error is ±7%.

The accuracy of the method was checked with permanganate solutions of known concentration and found to be better than 5%. The difference was always in the direction of the experimentally determined value lower than the known value. The permanganate solutions were prepared from weighed samples of reagent grade potassium permanganate and, thus, subject to some error.

Spectroscopic Method. This method is not of general utility and was only used once to determine initial rates. Two milliliters of reaction mixture was diluted to 500 ml in a volumetric flask with purified water, and the absorbance of the resulting solution was determined at 510 mμ on a Bausch and Lomb Spectronic 505 spectrophotometer. The ϵ (510 mμ) for potassium permanganate was determined to be 1870 on this instrument. The method is based on the assumption that the manganate(VI) would not disproportionate rapidly at high dilution and, thus, not interfere with the permanganate determination. This method worked only during the initial part of reaction when the manganate concentration was low. In solutions prepared at longer reaction times, the disproportionation occurred rapidly enough to interfere seriously with the permanganate determination, as evidenced by the absorbance at 510 mμ increasing with successive measurements on the same sample.

Vpc Method. This method was used to follow the disappearance of γ-phenylvaleric acid. The method consisted of quenching 5 ml of reaction mixture by running it into an acidic sodium sulfite solution (10 ml). The manganese species present were reduced to Mn(II) and the organic material formed an insoluble oil. The organic material was extracted with three 35-ml portions of ether, and the ether layers were dried with sodium sulfate. The ether was evaporated, and the resulting oil was treated with excess oxalyl chloride and heated to ensure complete reaction (30 min). The excess oxalyl chloride was taken off on a rotary evaporator, and 1 ml of absolute methanol was added. Two milliliters of standard solution of n-hexadecane (0.1505 M, n-decane solvent) was added to the methanolic solution of the methyl ester. A few milliliters of ether were added to make the mixture homogeneous. The total volume at this point was about 10 ml. A sample was analyzed by vpc (column 20% silicone GE-SF-96 on 60–80 firebrick, 5 ft × $^1/_4$ in., $T = 175°$, retention time of methyl γ-phenylvalerate = 12.2 min, retention time of n-hexadecane = 27.2 min), and the areas of n-hexadecane and methyl γ-phenylvalerate were determined. Vpc analysis of a standard solution of known weights of methyl γ-phenylvalerate and n-hexadecane indicated that the ratio of the area of the hydrocarbon to that of the ester for equimolar amounts was 1.27:1.

Kinetic runs were carried out at 25.0 ± 0.1° by adding measured amounts of substrate (0.5–1 g) to 30 ml of incubated permanganate solution. Samples were withdrawn at intervals and analyzed as above.

Stereochemical Studies. To 100 ml of alkaline potassium permanganate solution ($[MnO_4^-]_0 = 0.108$ M, $[OH^-]_0 = 2.54$ M) incubated for 72 hr at 25.0° was added 0.91 g (5.12 mmol) of (−)-γ-phenylvaleric acid ($[\alpha]^{25}\text{D}$ −4.52°, neat), 20.4% optically pure.[18] The solution was kept at 25.0° for 5 hr after which barium nitrate was added and the mixture was worked up in the usual way. After the ether extracts (3 × 80 ml) were dried with sodium sulfate for 9 days, they were extracted with three 80-ml portions of saturated sodium bicarbonate solution. The ether layer was dried with sodium sulfate and the solvent was evaporated leaving 0.55 g (3.12 mmol, 58%) of (−)-γ-phenyl-γ-valerolactone, $[\alpha]^{22}\text{D}$ −2.78° (neat), 5.52% optically pure.[3b] An infrared spectrum was identical with that of pure lactone.

The bicarbonate layer from above was made acidic and was extracted with two 100-ml portions of ether. The ether layers were dried with sodium sulfate and the solvent was evaporated leaving 0.31 g of material. An infrared spectrum indicated a mixture of lactone and starting material. It was estimated from the carbonyl region that the mixture consisted of about one-third lactone and two-thirds starting material. Therefore, the total yield of lactone was about 0.65 g (3.7 mmol, 68%). The mixture had a rotation of $\alpha^{24}\text{D}$ −1.94° (l = 0.5, neat).

Reaction conditions and optical purities for a number of runs are summarized in Tables I and II. Control experiments showed that the starting material and product did not racemize when subjected to the reaction conditions nor did the γ-deuterio compound exchange deuterium.

Table I. Reaction Conditions for Oxidations of (−)-γ-Phenylvaleric Acid at 25.0°

Run	$[(-)$-acid$]_0$, M	$[MnO_4^-]_0$,[a] M	$[OH^-]_0$, M
1	0.0512	0.108	2.54
2[b]	0.0710	0.16	1.30
3[c]	0.0504	0.387[d]	1.30
4	0.0333	0.345[d]	0.58
5[e]	0.158	1.192[d,f]	0.88[g]

[a] All solutions were incubated. [b] A total of 1.28 g of material was isolated and consisted of about 66% lactone, 32% starting material, and 2% benzoic acid by weight from vpc analysis of the methylated mixture. [c] A 95% yield of lactone based on γ-phenylvaleric acid was obtained. [d] Sodium permanganate (Fisher Scientific Co.). [e] 0.40 M in sodium nitrate. [f] Determined volumetrically with sodium oxalate. [g] Sodium hydroxide.

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[14] W. C. Pierce, E. L. Haenisch, and D. T. Sawyer, "Quantitative Analysis," John Wiley & Sons, Inc., New York, N. Y., 1958, p 324.

[15] R. Stewart and R. Van der Linden, *Can. J. Chem.*, **38**, 2237 (1960).

[16] H. I. Schlesinger and H. B. Siems, *J. Amer. Chem. Soc.*, **46**, 1965 (1924).

[17] A. Y. Drummond and W. A. Waters, *J. Chem. Soc.*, 435 (1953).

[18] P. A. Levene and R. E. Marker, *J. Biol. Chem.*, **110**, 329 (1935).

Table II. Rotations and Optical Purities for Oxidations of (−)-γ-Phenylvaleric Acid

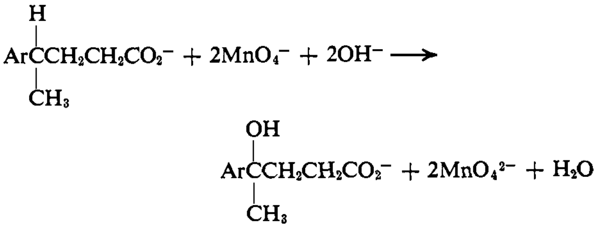
Run	[α] of starting acid (neat), deg	OP of starting acid, %[a]	[α] of γ-phenyl-γ-valerolactone (neat), deg	OP of lactone, %[b]	Stereochemical integrity, %
1	$[\alpha]^{25}D$ −4.52	20.4	$[\alpha]^{22}D$ −2.78	5.52	27
2[c]	$[\alpha]^{20}D$ −2.95	13.3	$[\alpha]^{23}D$ −2.25	4.47	34
3	$[\alpha]^{20}D$ −3.91	17.7	$[\alpha]^{26}D$ −3.05	6.08	34
4	$[\alpha]^{22}D$ −1.42	6.43	$[\alpha]^{24}D$ −1.28	2.59	40
5	$[\alpha]^{21}D$ −3.01	13.6	$[\alpha]^{26}D$ −0.13	0.25	2

[a] Based on $[\alpha]^{20}D$ −22.1° for pure acid.[18] [b] Based on $[\alpha]^{20}D$ −50.36° for pure lactone.[3b] [c] The lactone was isolated as in run 1. Its rotation was substantially the same after purification by preparative vpc and distillation, indicating that the method of isolation gave essentially pure material.

Results

When permanganate solutions prepared with purified water were examined as a function of time with no organic material present, the permanganate concentration diminished over a period of about 6 hr to *ca.* 75% of its initial value (0.16 *M*), then remained constant at *ca.* 0.12 *M* for at least 15 hr. This result suggests that previous kinetic results which show components of the oxidation which are zero order in organic may be artifacts. Only incubated solutions were used in our experiments, and it is unquestionably clear that under our conditions *organic substrate is required for permanganate decomposition.*[19] Further, it is clear from the kinetic data that the reaction is second order overall, first order each in permanganate and organic. The precise values of the rate constants depend on the method of treatment of data, but k_2 is *ca.* $4 \times 10^{-3}\ M^{-1}\ \text{sec}^{-1}$ for γ-phenylvaleric acid at 25°.

The balanced reaction, eq 2, is a formal two-electron oxidation and thus requires 2 mol of permanganate per mol of organic substrate. However, when equivalent amounts of permanganate and organic were allowed to react, only *ca.* 70% of oxidized product could be isolated. The material balance was composed of starting material and a few per cent of benzoic acid. Only when an excess of permanganate was employed could essentially complete conversion be obtained. The peculiar stoichiometry is further emphasized by the observation that a second-order plot of permanganate disappearance (assuming 2:1 stoichiometry) gives a rate constant greater than that from a corresponding plot of organic substrate disappearance. The discrepancy in rates and stoichiometry arises from oxidation of some of the starting material to benzoic acid. If this side oxidation reaction proceeds completely to benzoic acid and carbon dioxide it requires 24 mol of permanganate. Thus, production of 2% of benzoic acid would account for the loss of some 24% of the permanganate. Since 1–2% benzoic acid could be observed, it seems clear that this can account for the stoichiometry. *Examination of a large number of experiments indicates a stoichiometry of 2.4 mol of permanganate per mol of organic.* Similar stoichiometry was observed for all substrates.



$$\text{ArC(H)(CH}_3\text{)CH}_2\text{CH}_2\text{CO}_2^- + 2\text{MnO}_4^- + 2\text{OH}^- \longrightarrow \text{ArC(OH)(CH}_3\text{)CH}_2\text{CH}_2\text{CO}_2^- + 2\text{MnO}_4^{2-} + \text{H}_2\text{O} \quad (2)$$

The oxidation to benzoic acid can occur by (a) oxidation of product, (b) oxidation of starting material at a site other than the γ position, or (c) reaction at the γ position followed by oxidation of an intermediate. Possibility a is excluded by kinetic experiments. The product, γ-phenyl-γ-valerolactone, is oxidized in a process which is first order in lactone and zero order in permanganate with $k_1 = 3 \times 10^{-7}\ \text{sec}^{-1}$. Hence, the oxidation of the product does not contribute appreciably to loss of permanganate, but since the value was known, the kinetic scheme was modified to include this step (this necessitated using numerical integration by digital computer). Possibility b can be eliminated as follows. The side oxidation reaction causes the permanganate to disappear at *ca.* $^1/_5$ the rate of the main reaction. This follows directly from the stoichiometry (or yield) data. Thus, if attack were occurring elsewhere in the molecule and if the normal reaction at the γ position could be suppressed, the rate would still be 20% of normal and none of the normal hydroxy acid product would be produced. In fact, substitution of D for H at the γ position results in a rate decrease of 91% ($k_H/k_D \approx 11.5$) while the yield of hydroxy acid remains essentially the same. Therefore, the side reaction must have the same rate-determining step as the main reaction, leaving possibility c, oxidation of an intermediate species. This requires that the yield remain constant throughout the reaction, which it does.

It is now possible to deal with the kinetic data.[21] When the data were treated in the conventional way,[22] good second-order plots were obtained (Figure 1). However, in order to take account of the small amount of permanganate disappearance due to product oxidation, the phenomenological scheme 3 was used, the appropriate differential equations being integrated numerically.[23] The value of k_2 was chosen so as to minimize the sum of the squares of the differences between calculated and measured concentrations. With this technique, concentrations of both permanganate and organic could be fit to 70–90% reaction. Changes

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[19] Our findings concerning the stability of basic permanganate solutions are substantiated by the work of Vepřek-Šiška and Ettel[20] who have demonstrated that the decomposition of permanganate to manganate(VI) and oxygen in basic solution is a trace-catalyzed reaction depending on minute quantities of nickel and cobalt ions present as impurities in the solution.

[20] J. Vepřek-Šiška and V. Ettel, *J. Inorg. Nucl. Chem.*, **31**, 789 (1969); J. Vepřek-Šiška, V. Ettel, and A. Regner, *ibid.*, **26**, 1476 (1966); *Collect. Czech. Chem. Commun.*, 31, 1237 (1966).

[21] For details see A. J. Pandell, Ph.D. Dissertation, Stanford University, 1968.

[22] S. W. Benson, "The Foundations of Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p 18.

[23] D. F. DeTar and C. E. DeTar, *J. Phys. Chem.*, 70, 3842 (1966); D. F. DeTar, *J. Chem. Educ.*, **44**, 191 (1967). The method involves computation of trapezoidal areas evaluated at small time intervals. No variation in computed concentrations was observed when the interval was varied from 1 to 9 sec. See ref 21 for details.

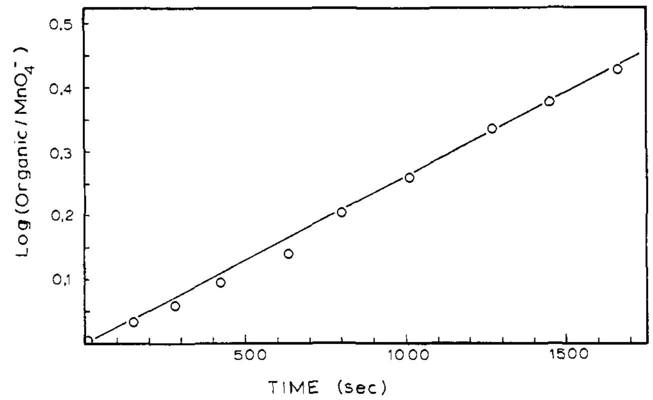


Figure 1. Second-order plot of permanganate disappearance. The organic (γ-phenylvaleric acid) concentration is calculated using the permanganate concentration and assuming 2.4:1 stoichiometry: $[Org] = [Org]_0-([MnO_4^-]_0 - [MnO_4^-])/2.4$.

of 10% from the optimal value of k_2 gave noticeably worse fitting of the data. A typical plot is shown in Figure 2. The rate constants obtained in this way are similar to those obtained by the conventional treatment, which is consistent with the observation that the product oxidation is a relatively minor perturbation.

$$R_3CH + 2.4MnO_4^- \xrightarrow{k_2} R_3COH + 2.4MnO_4^{2-}$$

$$R_3COH \xrightarrow{k_1(3 \times 10^{-7})} X$$

$$X + 22MnO_4^- \xrightarrow{\text{fast}} PhCO_2H + 4CO_2 + 22MnO_4^{2-} \quad (3)$$

Kinetic data for a series of substrates are shown in Table III. It should be recognized that if a simple treatment of data had been used, the values of these numbers would not be significantly different, and the relative values would be essentially identical. The kinetics are cleanly second order, and the rate constant is independent of initial organic concentration. The rate constants are only slightly sensitive to base concentration, decreasing by about 16% when the base concentration was lowered to 1.3 *M*.

Table III. Rates of Oxidation[a] of γ-Phenylvaleric Acids at 25.0°

Compound	k_2, M^{-1} sec^{-1}
γ-Phenylvaleric acid	3.8×10^{-3}
γ-(*p*-Nitrophenyl)valeric acid	1.4×10^{-3}
γ-Tolylvaleric acid[b]	3.5×10^{-3}
γ-Phenylvaleric acid-γ-*d*	$0.33^c \times 10^{-3}$

[a] 2.5 *M* OH⁻; error in $k_2 = \pm 5\%$. [b] 50–50 mixture of *ortho*- and *para*-substituted compounds. [c] $k_H/k_D = 11.5 \pm 1.2$.

The rate constants in Table III show little sensitivity due to the substituent. It is for this reason that the mixture of ring-methylated compounds gives clean kinetics. Thus, the *o*- and *p*-methyl compounds react at essentially the same rate.

The isotope effect is difficult to determine accurately ($k_H/k_D = 11.5 \pm 1.2$) owing to complications of further oxidation. The deuterium compound reacts so slowly that product oxidation begins to compete appreciably. Nevertheless, the effect is undoubtedly large.

The stereochemistry of the reaction can be ascertained from the data in Table II. Since (*R*)-(−)-γ-phenylvaleric acid[24] gives (*S*)-(−)-γ-phenyl-γ-valerolactone,[25] the oxidation must have proceeded with retention of configuration (eq 4). The extent of net re-

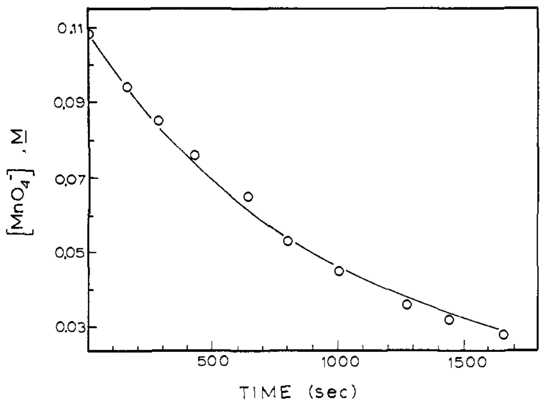
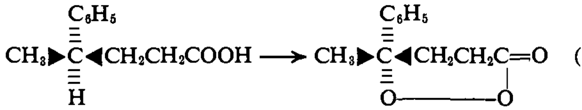


Figure 2. Experimental, ○, and calculated, —, concentrations of permanganate as a function of time. Same data as Figure 1.



$$\underset{(R)\text{-}(-)}{CH_3\blacktriangleright\overset{C_6H_5}{\underset{H}{C}}\blacktriangleleft CH_2CH_2COOH} \longrightarrow \underset{(S)\text{-}(-)}{CH_3\blacktriangleright\overset{C_6H_5}{\underset{O\text{———}}{C}}\blacktriangleleft \underset{O}{CH_2CH_2C{=}O}} \quad (4)$$

tention is in the range 30–40%. The data in Tables I and II indicate that the stereochemistry is independent of permanganate concentration (if it is maintained in the range of *ca.* 0.1 *M*) and somewhat dependent on base concentration. At very high permanganate concentration, the stereochemistry is very sensitive, dropping to only 2% retention.

Discussion

The results obtained in this work have definite implications regarding the mechanism of permanganate oxidation of tertiary hydrogens. It is evident that the data are inconsistent with a mechanism involving hydroxyl radicals or any other solvent oxidation. The pertinent observations to be accommodated by a mechanism are: (a) a rate law of the form rate = k_2[γ-phenylvaleric acid][MnO_4^-]; (b) an isotope effect $k_H/k_D = 11.5$; (c) a very small substituent effect; (d) 30–40% net retention of configuration; (e) stoichiometry of 2.4:1 which, in conjunction with isotope effect and other data, requires the presence of an intermediate that is oxidized to benzoic acid and carbon dioxide; and (f) similar stoichiometry for all substrates.

Rate-Determining Step. Kinetic and product studies carried out by other workers appear to be in conflict regarding the rate-determining step (rds) in permanganate oxidations.[2b] Some evidence has been obtained suggesting hydroxyl radical intermediates, while other evidence opposes this. However, both our work and the

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(24) For a review of the absolute configuration of γ-phenylvaleric acid see ref 11.

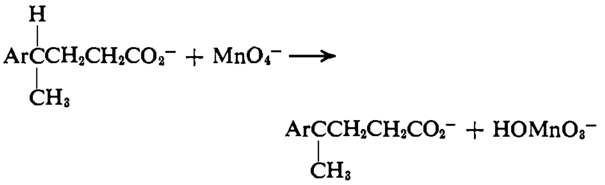
(25) The absolute configuration of γ-phenyl-γ-valerolactone has been related to (*S*)-(−)-3-phenylbutane-1,3-diol: Y. Senda and S. Mitsui, *Nippon Kagaku Zasshi*, **86**, 229 (1965); *Chem. Abstr.*, **63**, 4134*e* (1965). The conclusion stated by the abstracter concerning the absolute configuration of (+)-γ-phenyl-γ-valerolactone is incorrect. The original paper (in Japanese) indicates quite clearly that the (+)-lactone belongs to the (*R*) series and *not* the (*S*) series as stated in *Chemical Abstracts*. In addition, some previous work reported by Mitsui, *et al.*, concerning the hydrogenolysis of γ-hydroxy-γ-phenylvaleric acid and derivatives is corrected in this paper. The diol has been related to both (*R*)-(−)-atrolactic acid and (*S*)-(−)-2-phenylbutanol.[26]

(26) S. Mitsui, S. Imaizumi, Y. Senda, and K. Konno, *Chem. Ind.* (London), 233 (1964).

recent work of Vepřek-Šiška and Ettel[20] vitiate previous kinetic evidence for hydroxyl radical intermediates. Vepřek-Šiška and Ettel showed that the decomposition of permanganate in strongly basic solution is actually a transition metal catalyzed reaction. It now appears that even at high base concentrations (6 *M*) and temperatures (80°), permanganate does not *directly* oxidize the solvent, water, at an appreciable rate. Under our conditions (25°, 2.5 *M* base) we observe no solvent oxidation, and the kinetics are inconsistent with oxidation by hydroxyl radicals. The selectivity which we observe is also not consistent with hydroxyl radical intermediates. It is important to note that our solutions were extensively incubated and subsequently treated in a manner so as to eliminate trace impurities.

The rate law and the large isotope effect indicate that the rds involves reaction of permanganate and organic with cleavage of the C–H bond. Both the large isotope effect and the stereochemical and isotopic stability of the starting material show that this step is not reversible. Given that the rds involves C–H cleavage, what is the extent of ionic character? The fact that the starting material is stable has been used as an argument that proton removal to give a carbanion is not involved. This argument assumes tacitly that reprotonation of the carbanion would be fast, and is thus not compelling. However, the small substituent effect suggests strongly that there is little or no charge at the transition state. If the transition state involved only a small amount of bond breaking, the substituent effect would be difficult to interpret, but the large isotope effect shows bond breaking is extensive, and thus the reaction appears to have substantial radical character. Typical "polar" hydrogen atom abstractions from toluene[27] have ρ of -0.6 to -1.5; carbonium ion reactions generally have ρ between -4 and -5.[28] Although Stewart found a better fit with σ^+ than with σ in permanganate oxidation of benzylamines,[29] the rate differences (p-CH_3O ≈ twice p-NO_2) are so small that we feel both his and our data are accommodated best by a radical process.[30,31]

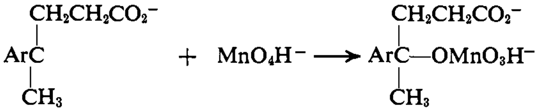
The isotope and substituent effects and the similar stoichiometry of the various substrates indicate that the side reaction reduction of permanganate has the same rds as the main reaction, and that the excess reduction occurs at some later stage. The implication of all of these results is that the rds is a hydrogen atom abstraction to form protonated manganate and a free radical (eq 5).



$$\mathrm{Ar}\overset{\displaystyle \mathrm{H}}{\underset{\displaystyle \mathrm{CH_3}}{\mathrm{C}}}\mathrm{CH_2CH_2CO_2^-} + \mathrm{MnO_4^-} \longrightarrow \mathrm{Ar}\underset{\displaystyle \mathrm{CH_3}}{\mathrm{C}}\mathrm{CH_2CH_2CO_2^-} + \mathrm{HOMnO_3^-} \qquad (5)$$

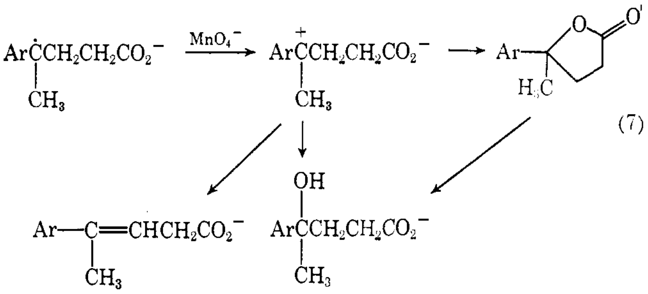
Subsequent Steps.

An extensive component of the reaction occurs with retention of configuration. The simplest way in which to account for this is by combination of the radicals produced in eq 5 prior to complete racemization of the organic radical (eq 6). The product of the combination is formally a Mn(V) ester of the hydroxy acid. Cage recombination of radicals is well known,[32] and is not unexpected in this case, since the Mn(VI) formed initially is an odd-electron species with one d electron. The extent of optical retention is also reasonable, particularly considering that the radicals are formed with no neutral molecules separating them.[33]



$$\mathrm{Ar}\overset{\displaystyle \mathrm{CH_2CH_2CO_2^-}}{\underset{\displaystyle \mathrm{CH_3}}{\mathrm{C}}} + \mathrm{MnO_4H^-} \longrightarrow \mathrm{Ar}\overset{\displaystyle \mathrm{CH_2CH_2CO_2^-}}{\underset{\displaystyle \mathrm{CH_3}}{\mathrm{C}}}\mathrm{—OMnO_3H^-} \qquad (6)$$

Some of the radical pairs may escape from the cage without recombining. The organic radical, now racemic, would then be oxidized by permanganate in a one-electron process to a carbonium ion which might then react with its carboxylate group to form lactone, or with solvent to form hydroxy acid or olefin (eq 7). The olefin which would be rapidly oxidized would comprise about 2% of the reaction mixture and account for the excess reduction of permanganate.



(7)

The Mn(V) ester can undergo hydrolysis with C–O or Mn–O cleavage. The experimental evidence suggests that C–O cleavage is not important. C–O cleavage would give rise to a carbonium ion and extensive racemization. In addition, should carbonium ions intervene in this pathway, it is to be expected that some olefin would also be formed. The p-nitro compound should be particularly unreactive toward C–O cleavage since a large negative ρ is expected for such a reaction. If olefin is arising in this way, then the p-nitro compound should give considerably less olefin than the other compounds do. However, the p-nitro compound has about the same stoichiometry as the unsubstituted compound. Thus, we conclude that the Mn(V) ester hydrolyzes with Mn–O cleavage to give the hydroxy acid plus Mn(V). Mn(V) is relatively stable in strongly alkaline (8 *M*) solution, and its oxidation by permanganate is extremely rapid at room temperature.[34] Thus, it is quite reasonable to hypothesize its existence in this scheme. The mechanism outlined above for the entire reaction is shown in Figure 3.

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[27] G. A. Russell, *J. Amer. Chem. Soc.*, **78**, 1047 (1956); R. E. Pearson and J. C. Martin, *ibid.*, 85, 354 (1963).

[28] Y. Okamoto and H. C. Brown, *J. Org. Chem.*, **22**, 485 (1957); Y. Okamoto and H. C. Brown, *J. Amer. Chem. Soc.*, **79**, 1909 (1957); H. C. Brown and Y. Okamoto, *ibid.*, **79**, 1913 (1957).

[29] M. M. Wei and R. Stewart, *ibid.*, **88**, 1974 (1966).

[30] For a discussion of polar effects in radical reactions see W. A. Pryor, "Free Radicals," McGraw-Hill Book Co., New York, N. Y., 1966, p 170; also G. A. Russell, *J. Org. Chem.*, **23**, 1407 (1958).

[31] For an example in chromate oxidations, thought to proceed by a radical process, see K. B. Wiberg and R. J. Evans, *Tetrahedron*, **8**, 313 (1960).

[32] C. Walling, "Free Radicals in Solution," John Wiley & Sons, Inc., New York, N. Y., 1957, pp 76–79.

[33] D. F. DeTar and C. Weis, *J. Amer. Chem. Soc.*, **79**, 3045 (1957).

[34] (a) A. Carrington and M. C. R. Symons, *J. Chem. Soc.*, 3373 (1956); (b) J. S. F. Pode and W. A. Waters, *ibid.*, 717 (1956); in addition, Mn(V) in strongly alkaline solution does not oxidize unsaturated carboxylic acids and only slowly oxidizes alcohols and carbonyl compounds.

If the proposed mechanism is correct, one can estimate the limits of contributions from the various paths. Thus, if all carbonium ion forms olefin, then only 2–4% occurs by path b and the 60–70% racemization occurs prior to cage recombination. Alternatively, the recombination may occur with no racemization and thus 60–70% of the reaction would proceed through a carbonium ion, path b. The ^{18}O-labeling studies of Wiberg and Fox[5] were carried out under different conditions and with different substrates, but they do suggest that a considerable portion of reaction may occur through the carbonium ion pathway.

The product probably undergoes a slow, base-catalyzed elimination followed by rapid oxidation. This is not an important contributor to the reaction.

Alternatives. There are other pathways which may be important. It is possible that the initial step involves an insertion process, producing a Mn(V) ester directly. However, it would then be necessary to invoke homolytic cleavage of the ester to a radical and Mn(VI) to explain the data. This seems unlikely to us, and Wiberg has indicated other objections to insertion reactions as well.[5,35]

It is possible that the radicals which escape from the cage could react with Mn(VI) in solution to give Mn(V) ester. This would suggest that yields should improve at high Mn(VI) concentrations if no other side reactions intervene. It is also possible that the Mn(V) ester could be oxidized by MnO_4^- to a species which would produce radicals or carbonium ions faster than hydrolysis takes place. At high MnO_4^- concentration, we observe a marked decrease in the stereochemical integrity of the reaction, consistent with this.

The mechanism proposed here is similar to that previously proposed for chromate oxidations,[35] and it contains many features of mechanisms proposed for permanganate oxidations.[2,5] Although our choice of reaction conditions and substrates has allowed the study of an extremely clean system, under other conditions the reaction can become more complicated. Nevertheless its inherent simplicity and analogy with other reactions make this mechanistic model attractive as a working hypothesis for a general mechanism for reaction of permanganate with saturated C–H bonds.

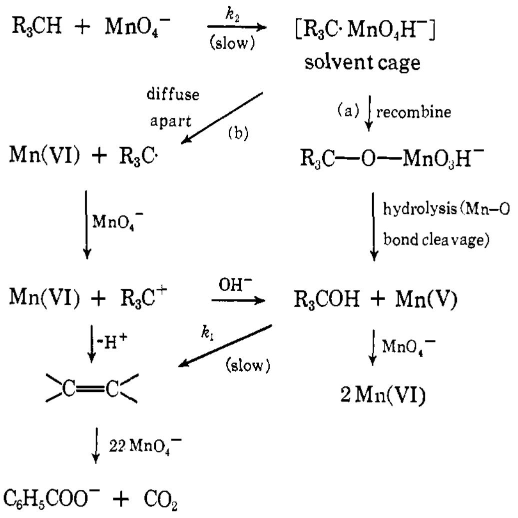

Figure 3. Mechanism of permanganate oxidation of γ-phenylvaleric acid. At 25.0°, $k_2 = 3.8 \times 10^{-3}\ M^{-1}\ \text{sec}^{-1}$; $k_1 = 3 \times 10^{-7}\ \text{sec}^{-1}$.

Acknowledgment. We thank Dr. Arlette Solladié-Cavallo for helpful discussions, and we acknowledge with thanks a grant from the Chevron Research Company.

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(35) In chromate oxidations: K. B. Wiberg, in ref 2a, Chapter II.