monium chloride and 100 ml. of liquid ammonia. After evaporation of the ammonia, the sticky residue was filtered and washed with cold water. Crystallization from ethanol afforded 4.0 g. (67%) of 6-(2-phenyl-2-hydroxyethyl)-3-cyano-2(1)-pyridone (17), m.p. 195-196° (205-206° after recrystallization from ethanol).

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 70.47; H, 4.95; N, 11.47. Found: C, 70.50; H, 5.03; N, 11.65.

Acetylation was accomplished by dissolving 1.9 g. of 17 in 10 ml. of acetic anhydride and 1 drop of sulfuric acid. The mixture was warmed on the steam bath to effect solution and then allowed to stand at room temperature for 8 hr. A small amount of potassium carbonate was added, and the acetic anhydride and acetic acid were removed under reduced pressure. The residue was taken up in ethyl acetate, and the solution was filtered and evaporated. Recrystallization of the residue from ethanol afforded 1.75 g. (78%) of acetylation product 18, which momentarily melted and then resolidified at about 200° and then melted again at 308-310° dec. The first transition may have reflected loss of acetic acid or the occurrence of some other chemical transformation.

Anal. Calcd. for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.93. Found: C, 68.28; H, 4.95; N, 10.02.

C. Of Dianion 8 with Benzophenone to Form 19. This reaction was carried out as in part A of this section, using 0.05 mole of dianion 8, 9.1 g. (0.05 mole) of benzophenone, and 10 g. of ammonium chloride. Recrystallization of the product from ethanol afforded 15.8 g. (80%) of 4-(2,2-diphenyl-2-hydroxethyl)-6-phenyl-3-cyano-2(1)-pyridone (19), m.p. 240-242°. Further recrystallization raised the melting point to 250-251.5°.

Anal. Calcd. for $C_{26}H_{20}N_2O_2$: C, 79.57; H, 5.14; N, 7.14. Found: C, 79.87; H, 5.18; N, 7.14.

Dehydration was accomplished by dissolving 2.5 g. of 19 in 25 ml. of concentrated sulfuric acid at about 5°, and then pouring the solution over 100 g. of ice. The resulting solid was collected, washed with sodium carbonate solution, and water, and recrystallized from ethanol to afford 2.0 g. (91%) of 4-(2,2-diphenyl-vinyl)-6-phenyl-3-cyano-2(1)-pyridone (20), m.p.

272-274°. Further recrystallization raised the melting point to 275-276°.

Anal. Calcd. for $C_{26}H_{18}N_2O$: C, 83.40; H, 4.85; N, 7.48. Found: C, 83.47; H, 4.86; N, 7.60.

Conjugate Additions. A. Of Dianion 2 to Form 21. To a stirred solution of 0.05 mole of dianion 2 in 700 ml. of liquid ammonia was added 11.0 g. (0.105 mole) of chalcone. After 1 hr. the ammonia was evaporated, and the residue was dissolved in ether, ice, and water. The aqueous layer was separated and acidified with 6 M hydrochloric acid. The resulting precipitate was collected, washed with water, and recrystallized from ethanol to afford 14.9 g. (87%) of 6-(2,4-diphenyl-4-oxobutyl)-3-cyano-2(1)-pyridone (21), m.p. 216-222° (227-228° after recrystallization from ethanol).

Anal. Calcd. for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.04; H, 5.11; N, 8.34.

A sample of 21 was recovered unchanged after treatment with cold, concentrated sulfuric acid.

B. Of Dianion 8 to Form 22. This reaction was carried out as in part A of this section, using 0.05 mole of dianion 8. Recrystallization of the product from ethanol afforded 18.0 g. (86%) of 4-(2,4-diphenyl-4-oxobutyl)-6-phenyl-3-cyano-2(1)-pyridone (22), m.p. 252-255°; further recrystallization raised the melting point to 261.5-262°.

Anal. Calcd. for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.29; N, 6.69. Found: C, 80.58; H, 5.33; N, 6.50.

This product was unchanged by treatment with cold, concentrated sulfuric acid.

C. Of Dianion 25 to Form 26. This reaction was carried out as in part A of this section, using 0.05 mole of dianion 25. Recrystallization of the product from glacial acetic acid afforded 12.4 g. (65%) of 1,2,5,6,7,8-hexahydro-3-cyano-8-(1,3-diphenyl-3-oxo-propyl)-2-quinolone (26), m.p. 259-260° (lit.[6] m.p. 261-263°).

Independent synthesis of 26 was accomplished by addition of chalcone to the dianion of 2-formylcyclohexanone, followed by cyclization with cyanoacetamide. The identity of samples of 26 obtained by the two routes was established by mixture melting point and by infrared spectra.

The Kinetics of the Permanganate Oxidation of Acetone[1]

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The kinetics of the permanganate oxidation of acetone were examined in basic aqueous solution. The data suggest that the enolate ion is an intermediate, and that it is oxidized by permanganate via an electron transfer rather than addition to the double bond. The rates of oxidation of the possible intermediates, and the products of the oxidation were determined. The data indicate the nature of the reactions which occur.

One of the most common modes of oxidation of aliphatic aldehydes and ketones involves reaction at the α-position.[2] Our interest in the general subject of

(2) *Cf.* J. S. Littler, *J. Chem. Soc.*, 827, 832 (1962).

permanganate oxidation has led us to examine the details of α-oxidation by this reagent. In order to have a relatively simple case in which to study this type of oxidation, we have examined the oxidation of acetone.

The rate of oxidation of acetone was determined spectrophotometrically using a tenfold range of acetone concentration, a tenfold range of permanganate concentration, and an eightfold range of base concentration. The data are presented in Table I. Only the

Table I. Rate Data for the Oxidation of Acetone at $25.0°^a$

[Acetone] $\times$ $10^4 M$	[OH$^-$], M	[MnO$_4^-$] $\times$ $10^4 M$	$m_i \times 10^3$ sec.$^{-1}$	$m_i/$ [acetone], M^{-1} sec.$^{-1}$
20.3	0.050	4.03	11 ± 1	5.2
40.5	0.050	4.03	20 ± 1	4.9
81.0	0.050	4.03	39 ± 1	4.8
121.5	0.050	4.03	58 ± 1	4.8
162.0	0.050	4.03	77 ± 2	4.8
202.5	0.050	4.03	96 ± 3	4.7
40.5	0.100	4.03	43 ± 1	10.6
40.5	0.200	4.03	89 ± 6	22.
40.5	0.300	4.03	130 ± 11	32.
40.5	0.400	4.03	170 ± 4	42.
40.5	0.050	2.01	20 ± 1	4.9
40.5	0.050	6.04	17 ± 1	4.2
40.5	0.050	10.07	15 ± 2	3.7
40.5	0.050	15.10	16 ± 1	4.0
40.5	0.050	20.13	12 ± 2	3.0
121.5	0.050	2.01	51 ± 1	4.2
121.5	0.050	6.04	58 ± 2	4.8
121.5	0.050	10.07	49 ± 1	4.0
121.5	0.050	15.10	45 ± 2	3.7
121.5	0.050	20.13	44 ± 1	3.6

^{a} $\mu = 0.4\ M$, $\lambda = 510\ m\mu$.

values of m_i, the initial slope from a first-order plot, are given because of the later intervention of subsequent fast oxidation steps. The constancy of the values of $m_i/$[acetone] at constant hydroxyl ion and permanganate concentrations indicates a first-order dependence on acetone concentration. A plot of $m_i/$[acetone] against the hydroxyl ion concentration (Figure 1) gives a straight line passing through the origin, indicating a first-order dependence on hydroxyl ion concentrations. At constant acetone and hydroxyl ion concentrations, the rate constants decrease somewhat with increasing permanganate concentrations. However, to a first approximation there is a first-order dependence on permanganate, giving the rate law

$$\frac{d[Mn^{VII}]}{dt} = -k[\text{acetone}][HO^-][MnO_4^-]$$

The observed third-order rate constant was 107 l.^{2} mole^{-2} sec.$^{-1}$ at 25° when [MnO$_4^-$] = 4 × 10^{-4} M.

The data suggest a scheme in which the enolate ion is formed in an equilibrium step and is oxidized by permanganate in the rate-determining step. The steps would then be
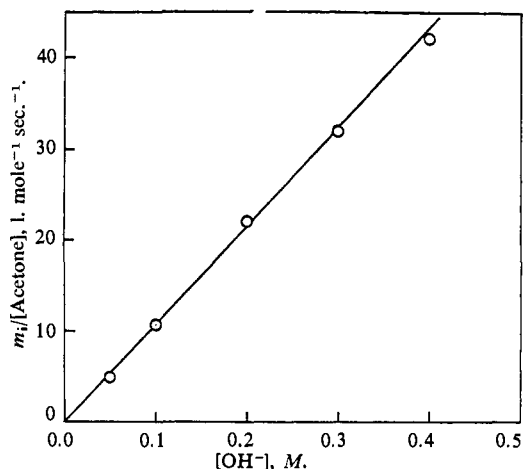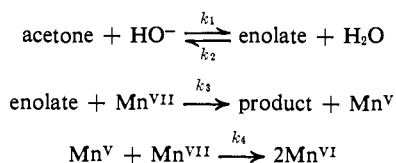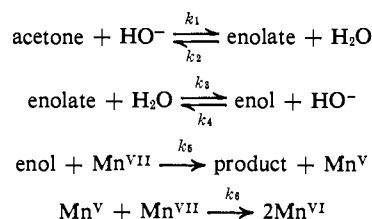
$$\text{acetone} + HO^- \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{enolate} + H_2O$$

$$\text{enolate} + Mn^{VII} \overset{k_3}{\longrightarrow} \text{product} + Mn^V$$

$$Mn^V + Mn^{VII} \overset{k_4}{\longrightarrow} 2Mn^{VI}$$

Figure 1. Effect of hydroxyl ion concentration on the rate of permanganate oxidation of acetone. The conditions are: [permanganate] = 0.0004 M, μ = 0.4 M, λ = 510 mμ, T = 25.0°.

The last step will be assumed to be faster than the others. Assuming a steady, state concentration for the enolate, the rate law becomes

$$\frac{-d[Mn^{VII}]}{dt} = \frac{2k_1k_3[Mn^{VII}][\text{acetone}][HO^-]}{k_2[H_2O] + k_3[Mn^{VII}]}$$

The value of k_1 has been determined[3] and was found to be 0.174 l. mole^{-1} sec.$^{-1}$ at 25°. If $k_3[Mn^{VII}] \ll k_2[H_2O]$, the $k_{obsd} = 2k_1k_3/k_2[H_2O]$. Using 55 M as the concentration of water, $k_3/k_2 = 1.7 \times 10^4$. From this value it can be seen that, as the concentration of permanganate increases, $k_3[Mn^{VII}] \approx k_2[H_2O]$, and this will quantitatively account for the decrease in observed rate constants with increasing permanganate oxidation.

In the above analysis, it was assumed that permanganate reacted with the enolate ion. Another possibility is that it reacts with the enol which is in equilibrium with the enolate ion. The steps would then be

$$\text{acetone} + HO^- \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{enolate} + H_2O$$

$$\text{enolate} + H_2O \underset{k_4}{\overset{k_3}{\rightleftharpoons}} \text{enol} + HO^-$$

$$\text{enol} + Mn^{VII} \overset{k_5}{\longrightarrow} \text{product} + Mn^V$$

$$Mn^V + Mn^{VII} \overset{k_6}{\longrightarrow} 2Mn^{VI}$$

Applying the steady-state approximation, the rate law for this sequence of steps becomes

$$\frac{-d[Mn^{VII}]}{dt} = \frac{2k_1k_3k_5[\text{acetone}][HO^-][Mn^{VII}]}{k_2k_4[HO^-] + (k_2 + k_3)k_5[Mn^{VII}]}$$

If the equilibrium between enol and enolate ion were to be maintained, $k_4[HO^-] > k_5[Mn^{VII}]$. Under these conditions, the rate expression reduces to

$$\frac{-d[Mn^{VII}]}{dt} = \frac{k_1k_3k_5[\text{acetone}][HO^-][Mn^{VII}]}{k_2k_4[HO^-]} =$$

$$\frac{k_1k_3k_5}{k_2k_4}[\text{acetone}][Mn^{VII}]$$

Here, no base dependence would be noted. On the other hand, if $k_5[Mn^{VII}]$ were greater than $k_4[HO^-]$,

(3) R. P. Bell and H. C. Longuet-Higgins, *J. Chem. Soc.*, 639 (1946).

the rate expression would become

$$\frac{-d[Mn^{VII}]}{dt} = \frac{k_1k_3k_5[\text{acetone}][HO^-][Mn^{VII}]}{(k_2 + k_3)(k_5[Mn^{VII}])} =$$

$$\frac{k_1k_3}{k_2 + k_3}[\text{acetone}][HO^-]$$

and the reaction rate would be independent of permanganate concentration. It can be seen that such a mechanism cannot account for good first-order dependence on both [HO⁻] and [Mn^{VII}] under any set of conditions. It seems reasonable to conclude that the enol cannot be the species which reacts with permanganate.

If the equilibrium constant for enolate formation in alkaline solution were known, k_2 could be calculated and subsequently k_3, the rate constant for the reaction of the enolate ion with permanganate. The amount of enol present in 1.7 M neutral acetone solution at 25° has been found to be 2.5 × 10⁻⁴%.[4] The pK_a of the enol is not known, but it may be estimated to be about 14. The value will be lower than that for saturated alcohols (p$K_a \sim 16$) because the hydroxyl group is attached to an sp² carbon orbital rather than to sp³. On the other hand, it would be expected to be greater than that for phenol (p$K_a = 11$). These data place the pK_a of acetone at about 20.

Using a linear, free-energy relationship between rates and equilibrium constants for enolization, Bell[5] has estimated the pK_a for acetone to be 20. The agreement between the values obtained in these two different ways gives confidence in the value. Using this equilibrium constant, k_3 must be on the order of 5 × 10⁷ l. mole⁻¹ sec.⁻¹.

We have attempted to learn something about the nature of the subsequent oxidation steps by determining the products of oxidation and by measuring the rates of oxidation of possible intermediates. A reasonable sequence of steps would be Scheme I.

Scheme I
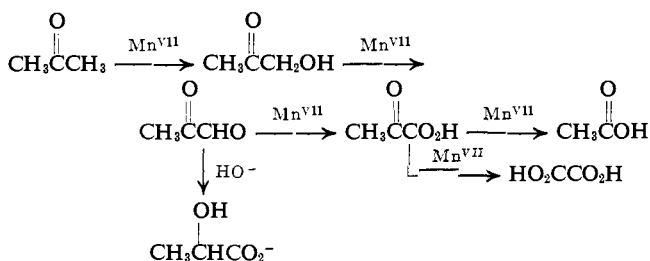
The oxidation of pyruvic acid by permanganate is known to give acetic and oxalic acids in a ratio which appears to be dependent on the base concentration.[6] Pyruvaldehyde is known to undergo a facile, base-catalyzed rearrangement to lactic acid, which, as indicated later, is only slowly oxidized under the reaction conditions. The aldehyde exists in aqueous solution largely as the hydrate. Therefore, in analogy with the bromination of 1,1-dibromoacetone, the site of oxidation would probably be at the methylenediol group leading to pyruvic acid as the principal product. The

first two steps, formation of acetol and pyruvaldehyde, have been generally assumed.

Solutions of acetone-C¹⁴ and permanganate in aqueous base were mixed (final concentrations, 0.0054 M acetone, 0.0054 M permanganate, and 0.1 M hydroxyl ion) and allowed to react for 20.8 sec. at 25° before quenching with bisulfite solution. Under these conditions, 13% of the acetone reacted, and some permanganate still remained. The products were identified by isotope dilution analysis giving the data summarized in Table II.

Table II. Product Yields from Acetone-2-C¹⁴ Oxidation

Product	Mole %[a]
Acetol	4
Pyruvaldehyde	0
Lactic acid	6[b]
Pyruvic acid	27
Oxalic acid	19
Acetic acid	47

[a] Based on the amount of acetone which had reacted. [b] Possibly somewhat high due to contamination with acetic acid.

The product study indicates that the above scheme is at least approximately correct. All of the expected compounds were observed with the exception of pyruvaldehyde. The formation of pyruvic acid suggests that pyruvaldehyde was formed as an intermediate, and as shown later, it is the most rapidly oxidized of all the intermediates and presumably would be present in a very low steady-state concentration. The lactic acid which was found probably arises from pyruvaldehyde by a base-catalyzed rearrangement either during the reaction or during work-up. The results obtained in the present work differ considerably from those obtained by Evans and Sefton (80% oxalic acid and 20% acetic acid). However, these workers used higher acetone and permanganate concentrations and used reaction times long enough to effect complete reduction of permanganate. These differences in procedure probably account for the difference in products.

The kinetics of the oxidation of acetol, pyruvaldehyde, pyruvate ion, and lactate ion were investigated. The oxidation of acetol was studied over a fivefold range of acetol concentration, an eightfold range of hydroxyl ion concentration, and a tenfold range of permanganate concentration, giving the data summarized in Table III. Again, the initial rates of reaction were measured because of the relatively high rates of oxidation of the products first formed.

It may be seen from the last seven entries in Table III that the rate of reaction shows a first-order dependence on the permanganate concentration. The kinetic dependence on hydroxyl ion and on acetol is shown in Figures 2 and 3. There is a first-order dependence on the concentration of acetol, but there are both zero-order and first-order terms describing the effect of hydroxyl ion on the rate of reaction. The rate law is then

$$\frac{-d[Mn^{VII}]}{dt} =$$

$$k_a[\text{acetol}][Mn^{VII}] + k_b[\text{acetol}][Mn^{VII}][HO^-]$$

where $k_a = 50$ l. mole⁻¹ sec.⁻¹ and $k_b = 1200$ l.[2]

(4) G. Schwarzenbach and C. Wittwer, *Helv. Chim. Acta*, **30**, 669 (1947).
(5) R. P. Bell, *Trans. Faraday Soc.*, **39**, 253 (1943).
(6) W. L. Evans and E. J. Witzeman, *J. Am. Chem. Soc.*, **34**, 1099 (1912); W. L. Evans and L. B. Sefton, *ibid.*, **44**, 2276 (1922).
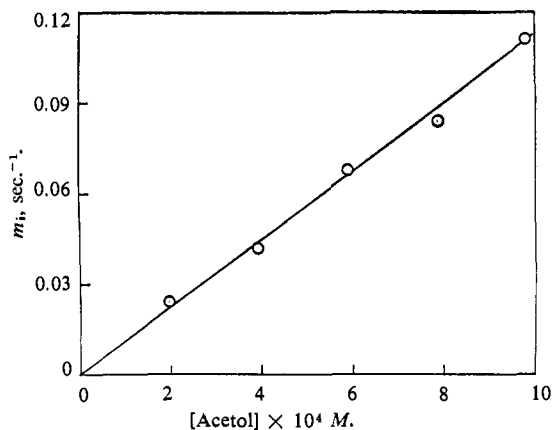
Figure 2. Effect of acetol concentration on the rate of permanganate oxidation of acetol. The conditions are: [permanganate] = 0.0004 M, [HO⁻] = 0.05 M, T = 25.0°.
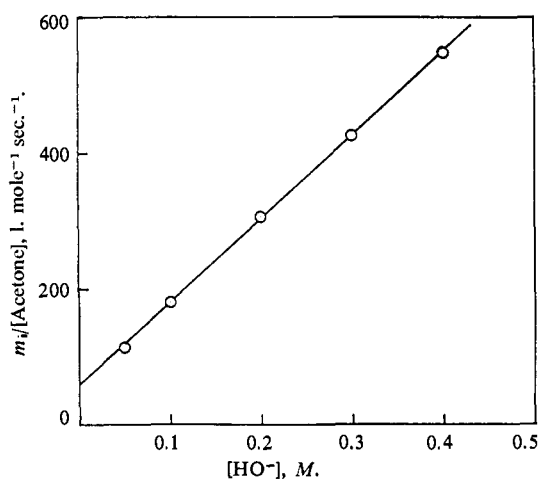

Figure 3. Effect of hydroxyl ion concentration on the rate of permanganate oxidation of acetol. The conditions are: [permanganate] = 0.0004 M, [acetol] = 0.0006 M, μ = 0.4 M, T = 25.0°.
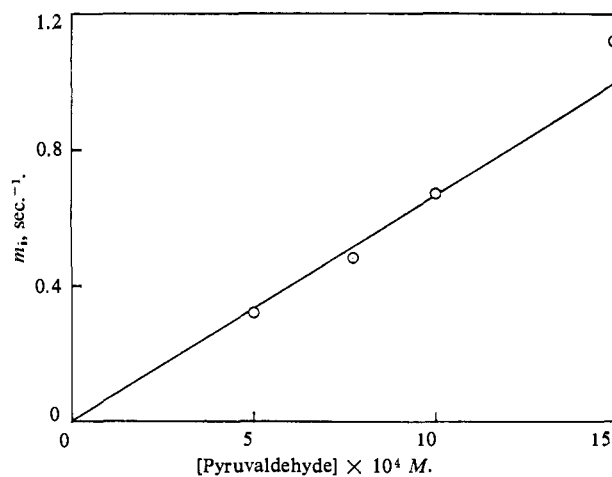

Figure 4. Effect of pyruvaldehyde concentration on the rate of permanganate oxidation of pyruvaldehyde. The conditions are: [permanganate] = 0.0004 M, [HO⁻] = 0.1 M, 25°.
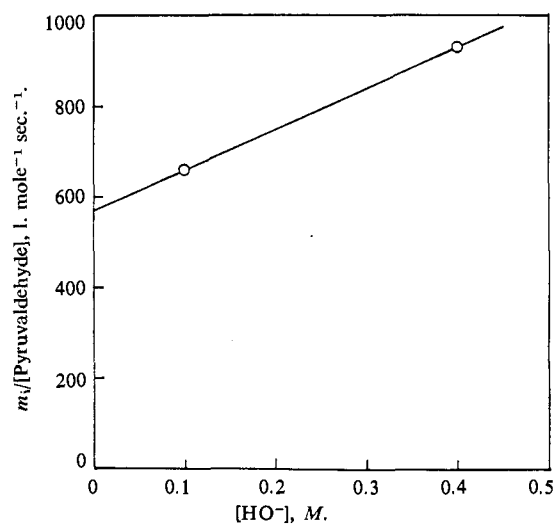

Figure 5. Effect of hydroxyl ion concentration on the rate of permanganate oxidation of pyruvaldehyde. The conditions are: [permanganate] = 0.0004 M, [pyruvaldehyde] = 0.001 M, μ = 0.4 M, T = 25.0°.

mole⁻² sec.⁻¹. With 0.1 M hydroxyl ion, reaction a accounts for about one-third of the initial oxidation rate.

Table III. Rate Data for the Oxidation of Acetol at 25.0°[a]

[Acetol] $\times$ 10^4 M	[OH⁻], M	[MnO₄⁻] $\times$ 10^4 M	$m_i \times 10^3$ sec.⁻¹	$m_i/$[acetol], M^{-1} sec.⁻¹
1.96	0.050	3.93	24 ± 1	120
3.93	0.050	3.93	42 ± 1	107
5.89	0.050	3.93	68 ± 1	115
7.85	0.050	3.93	84 ± 7	107
9.82	0.050	3.93	106 ± 11	108
5.89	0.100	4.03	105 ± 1	178
5.89	0.200	4.03	184 ± 12	312
5.89	0.300	4.03	253 ± 17	429
5.89	0.400	4.03	325 ± 3	552
5.89	0.050	2.01	67 ± 3	104
5.89	0.050	3.02	70 ± 2	119
5.89	0.050	6.04	60 ± 4	102
5.89	0.050	8.05	68 ± 5	115
5.89	0.050	10.07	57 ± 5	97
5.89	0.050	15.10	53 ± 2	90
5.89	0.050	20.13	61 ± 2	103

[a] μ = 0.4 M, λ = 510 mμ.

The oxidation of pyruvaldehyde was studied over a fourfold range of hydroxyl ion concentration and a five-fold range of permanganate concentration, giving the data summarized in Table IV. The value of m_i for 15 $\times$ 10⁻⁴ M pyruvaldehyde is probably high since the first point was obtained at 0.2 sec., which in this case corresponds to 20% reaction.

The kinetic dependence on the concentrations of reactants is indicated in Figures 4 and 5. There is a good first-order dependence on pyruvaldehyde, and also a first-order dependence on permanganate. The hydroxyl ion dependence shows both zero-order and first-order terms with the former being the more important. The rate law then appears to be

$$\frac{-d[Mn^{VII}]}{dt} = k_a[\text{pyruvaldehyde}][Mn^{VII}] +$$

$$k_b[\text{pyruvaldehyde}][Mn^{VII}][OH^-]$$

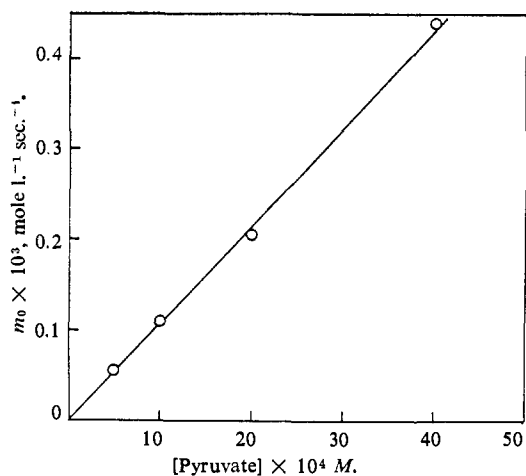where k_a = 560 l. mole⁻¹ sec.⁻¹ and k_b is 930 l.² mole⁻² sec.⁻¹.

Figure 6. Effect of pyruvate concentration on the rate of permanganate oxidation of pyruvate. The conditions were: [permanganate] $= 0.0004\ M$, $[HO^-] = 0.1\ M$, $T = 25.0°C$.
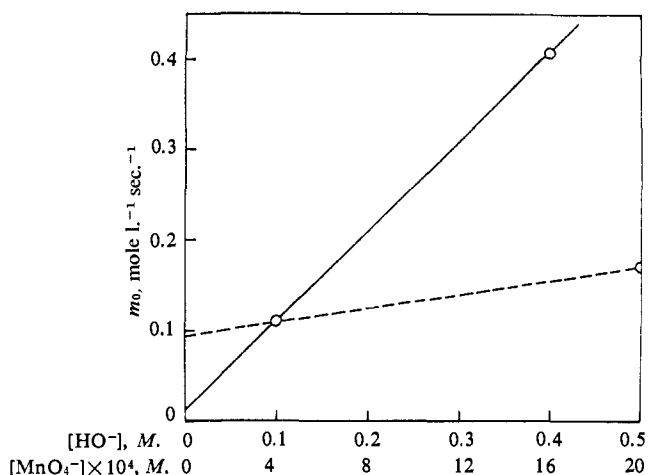

Figure 7. Effect of hydroxyl ion (solid line) and permanganate (broken line) concentrations on the rate of permanganate oxidation of pyruvate. The conditions were: [pyruvate] $= 0.001\ M$, $T = 25.0°$.

The oxidation of pyruvate was studied over a fourfold range of hydroxyl ion concentration, a fivefold range of permanganate concentration, and an eightfold range of pyruvate concentration, giving the data summarized in Table V. The kinetic dependence on the concentrations is shown in Figures 6 and 7.

Table IV. Rate Data for the Oxidation of Pyruvaldehyde at 25.0°[a]

[Pyruvaldehyde] $\times$ $10^4\ M$	[OH$^-$], M	[MnO$_4^-$] $\times$ $10^4\ M$	$m_i \times 10^2$ sec.$^{-1}$	$m_i/$ [Pyruvaldehyde], l. mole^{-1} sec.$^{-1}$
5.00	0.100	4.00	32 ± 1	640
7.62	0.100	4.00	49 ± 1	644
10.13	0.100	4.00	67 ± 1	662
10.02	0.400	4.00	93 ± 4	929
10.02	0.100	20.0	56 ± 1	559
14.98	0.100	4.00	112 ± 1	748

[a] $\mu = 0.40\ M$, $\lambda = 510\ m\mu$.

Table V. Rate Data for the Oxidation of Pyruvate Ion at 25.0°

[Pyruvate] $\times$ $10^4\ M$	[OH$^-$], M	[MnO$_4^-$] $\times$ $10^4\ M$	$m_0 \times 10^{3a}$ mole l.$^{-1}$ sec.$^{-1}$
5.00	0.100	4.00	0.056
10.01	0.100	4.00	0.110
10.08	0.400	4.00	0.408
10.08	0.100	20.0	0.170
20.01	0.100	4.00	0.204
40.03	0.100	4.00	0.440

[a] Initial zero-order rate constants.

There is a first-order dependence on the concentrations of pyruvate ion and hydroxyl ion, and there appears to be one part of the reaction which is dependent on the permanganate concentration and another part which is independent. The data suggest the rate law

$$\frac{-d[MnO_4^-]}{dt} = k_a[\text{pyruvate}][Mn^{VII}][HO^-] +$$
$$k_b[\text{pyruvate}][HO^-]$$

where $k_a = 400\ \text{l.}^2\ \text{mole}^{-2}\ \text{sec.}^{-1}$ and $k_b = 0.9\ \text{l. mole}^{-1}\ \text{sec.}^{-1}$. However, more work would be required before this rate law could be firmly established.

The data for the oxidation of lactate ion was limited to two substrate concentrations (50 and 100 $\times$ $10^{-4}\ M$) with 0.1 M hydroxyl ion and 4 $\times$ $10^{-4}\ M$ permanganate. The values of m_i were 0.0108 and 0.0192 sec.$^{-1}$, respectively, indicating a first-order dependence on substrate concentration. If the rate of reaction is assumed to have a first-order dependence on lactate and permanganate, $k = 2\ \text{l. mole}^{-1}\ \text{sec.}^{-1}$ with 0.1 M base.

Table VI gives a comparison of the relative rates of oxidation of acetone and some of its derivatives.

Table VI. Rates of Oxidation of Acetone and Its Oxidation Products for 25° and 0.10 M Hydroxide[a]

Compd.	k (4 $\times$ $10^{-4}\ M$ MnO$_4^-$), l. mole^{-1} sec.$^{-1}$	k (54 $\times$ $10^{-4}\ M$ MnO$_4^-$), l. mole^{-1} sec.$^{-1}$
Acetone	10.6	4.5
Acetol	178	178
Pyruvaldehyde	650	650
Pyruvate	275	57
Lactate	2	2

[a] Rate of disappearance of permanganate.

The rate constants are given in terms of the rate of disappearance of permanganate. It is possible to compare the results of the product study with these rate constants via numerical integration. In Table VII are presented the results based on the scheme given previously (Scheme I). The only assumption made was that the part of the reaction of pyruvate ion which was dependent on both permanganate and hydroxyl ion concentrations would give acetate ion, and that the part which was independent of permanganate would give oxalate ion. This appeared reasonable since a reaction which does not involve permanganate in the rate-determining step probably involves enolization as the slow step. Oxidation of the enol would give oxa-

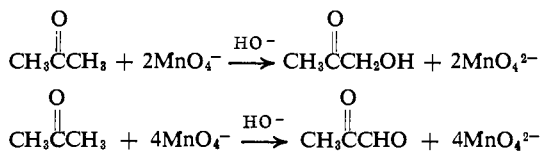**Table VII.** Comparison of Observed and Calculated Product Distribution[a]

Compd.	Found, %	By numerical integration, % Scheme I	By numerical integration, % Scheme II
Acetol	4	18	6
Pyruvaldehyde	0 (6)[b]	6	5
Pyruvic acid	27	39	41
Acetic acid	47	25	35
Oxalic acid	19	12	14

[a] Results for numerical integration through 21 sec. [b] 6% of lactic acid, which may have been derived from pyruvaldehyde during work-up, was found.

late ion. The reaction which is dependent on the concentrations of both permanganate and hydroxyl ion has a counterpart in the oxidation of benzaldehyde which does lead to a carboxylic acid.[7]
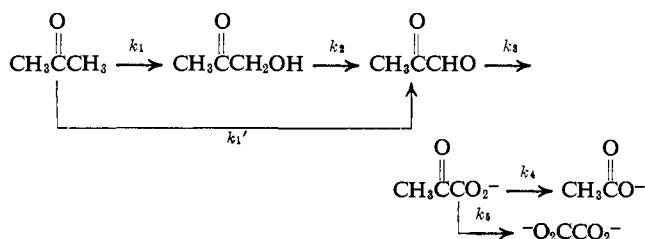
The principal point of disagreement between observed and calculated values lies in the amount of acetol which is calculated. It seems reasonable to attribute at least part of the 6% lactic acid formed to rearrangement of pyruvaldehyde during work-up. The ratio of acetic acid to oxalic acid is about right, and although the amount of pyruvic acid which is calculated is somewhat high, this value is quite sensitive to all of the rate constants.

Since four times as much acetol was predicted than was found, and since the amount of acetol is not strongly affected by rate constants other than those for its formation and disappearance, both of which are known quite well, it appears probable that some of the acetone goes directly to pyruvaldehyde, bypassing acetol. Thus there may be two simultaneous processes.

$$CH_3\overset{O}{\overset{\|}{C}}CH_3 + 2MnO_4^- \xrightarrow{HO^-} CH_3\overset{O}{\overset{\|}{C}}CH_2OH + 2MnO_4^{2-}$$

$$CH_3\overset{O}{\overset{\|}{C}}CH_3 + 4MnO_4^- \xrightarrow{HO^-} CH_3\overset{O}{\overset{\|}{C}}CHO + 4MnO_4^{2-}$$

The over-all scheme would then be

Scheme II

As a trial, the rate constants for the disappearance of acetone were taken as $k_1 = 0.6$ and $k_1' = 0.85$, making the rate constant for the disappearance of permanganate 4.6 ($2k_1 + 4k_1'$). The other rate constants were the same as used previously. Numerical integration now gave the values given in Table VII under Scheme II. These data fairly satisfactorily reproduce the observed values. We do not pretend to have determined how the observed rate constant for the disappearance of permanganate in the oxidation of acetone should be split between the k_1 and k_1'. However, it seems fairly clear that both processes are involved

(7) K. B. Wiberg and R. Stewart, *J. Am. Chem. Soc.*, **77**, 1786 (1955).

and that the two rate constants have comparable magnitudes.

Having achieved an over-all view of the process, we may try to infer the details of the individual steps. We have studied the rates of permanganate oxidation for a variety of alkenes in aqueous solution, and have found the rate constants to vary over the small range of 100–500 l. mole^{-1} sec.$^{-1}$ at 25° with electron-releasing groups giving a slight rate retardation.[8] The observation that the rate constant for the enolate–permanganate reaction is on the order of 5×10^7 l. mole^{-1} sec.$^{-1}$ indicates that this sort of process is unlikely, and suggests that an electron-transfer reaction is more probable. Reactions of this type are among the few which proceed with rate constants on this order of magnitude. Thus, the probable course of the reaction is
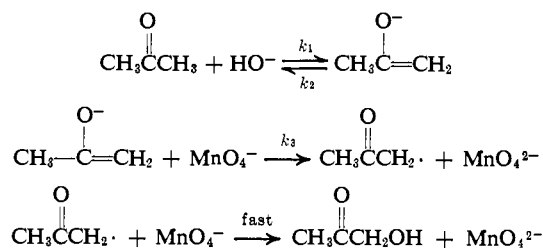
The radical formed in the first oxidation step would be expected to react rapidly with permanganate, leading to acetol formation by a process which cannot be specified in detail.

This scheme may easily account for the direct formation of pyruvaldehyde from acetone. The last step given above may proceed in part as follows.
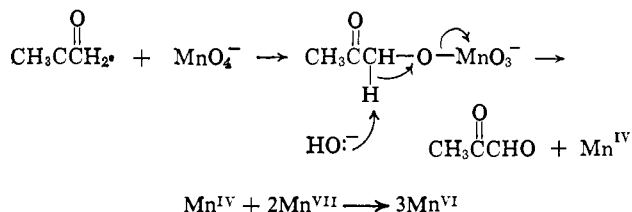
It is possible that this process may compete with direct hydrolysis of the manganate intermediate which would lead to acetol.

A scheme analogous to that for acetone might be expected for the hydroxide-dependent oxidation path of acetol and pyruvaldehyde. In both cases, enolization should proceed preferentially toward the hydroxy group(s) in analogy with the halogenation of acetone. It is more difficult to explain the hydroxide independent part of the oxidation of these substrates. The reaction path must be one which is not favored in the case of acetone. In view of the limited data which are available, it does not seem appropriate to attempt to delineate possible mechanisms for the hydroxide-independent path. The same is true for the oxidation of pyruvate. Here it is especially important to determine which product(s) arise from each of the two kinetically distinguishable paths. Another question which remains to be answered concerns whether or not a four-electron oxidation, similar to that proposed for part of the reaction of acetone, may occur with acetol or pyruvaldehyde.

(8) These results will be presented in a subsequent manuscript.

Experimental Section

Materials. Acetone was purified by the Livingston[9] modification of the Shipsey-Werner method. Acetone-2-C[14] was obtained from the New England Nuclear Corp. and was diluted with approximately ten times its volume of unlabeled acetone and 8 ml. of water. The concentration of acetone was determined gravimetrically using 2,4-dinitrophenylhydrazine, and the activity was determined using the derivative.

Acetol was prepared by a literature procedure.[10] Pyruvaldehyde was obtained as a 30% aqueous solution from the Carbide and Carbon Chemical Corp. and was purified by distillation (b.p. 100–102°). The pyruvaldehyde concentration was determined gravimetrically using 2,4-dinitrophenylhydrazine. Lactic acid was purified as the cupric lactate dihydrate and was recovered by removal of copper using a Dowex 50W-4X ion-exchange column in the same fashion as used by Hughes, Ostwald, and Tolbert[11] for zinc lactate.

Pyruvic acid was obtained from Aldrich Chemical Co. and was converted to the sodium salt by neutralization and precipitation by ethanol. Sodium acetate was reagent grade.

Kinetic Method. The rate of disappearance of permanganate was followed spectrophotometrically at 510 mμ. Since the half-life for most reactions was short, a stopped flow reactor was used. The spectrometer (Beckman DU) was coupled to a strip chart recorder (0.2 sec. for full-scale deflection) *via* an energy-recording adapter. A photomultiplier tube was used as the sensing element and in order to decrease noise and decrease the spectrometer response time the standard load resistor was replaced by a 1-megohm resistor.

The kinetics were studied under pseudo-first-order conditions, and the rate constant was estimated by taking the initial slope of a plot of ln $(A - A_\infty)$ against time. The curves had a significant curvature resulting from the further oxidation of the products of the initial reaction. The curvature was minimized by using a considerable excess of the substrate, and it was not difficult to obtain the initial slope. The rate constants given in the tables are the average of two or more determinations, and the deviations are the average deviations for the set of runs. The deviations are reasonably small, suggesting that it is possible to estimate the slopes with reasonable accuracy. In all cases, the ionic strength was maintained by the addition of sodium chloride.

Product Study. Two solutions, one containing permanganate and the other containing acetone-C[14] and hydroxide ion, were mixed in a flow reactor. The final concentrations of permanganate, acetone, and hydroxide ion were 0.0054, 0.0054, and 0.1 M, respectively. The residence time in the reactor was 20.8 sec. at 25°, and the solution was quenched with aqueous bisulfite as it left the reactor. Because of interference in the separation method, two separate determinations were necessary with some products analyzed in one and some in the other.

(9) R. Livingston, *J. Am. Chem. Soc.*, 69, 1220 (1947).
(10) P. A. Levine and A. Walti, "Organic Syntheses," Coll. Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 5.
(11) D. M. Hughes, R. Ostwald, and B. M. Tolbert, *J. Am. Chem. Soc.*, 74, 2434 (1952).

The determination of acetone, acetol, pyruvic acid, and lactic acid was made as follows. To the quenched solution derived from 5 mmoles each of permanganate and acetone-C[14] were added known amounts of acetone (5 mmoles), sodium pyruvate (5 mmoles), acetol (5 mmoles), and lactic acid (25 mmoles). Enough 50% sulfuric acid was added to turn the mixture clear and it was then allowed to stand for 10 min. A freshly prepared solution of 4 g. (20 mmoles) of 2,4-dinitrophenylhydrazine in 20 ml. of 50% sulfuric acid was added, causing an immediate formation of a yellow precipitate. In order to avoid oxidation of the acetol derivative, the solution was filtered after 5 min. After standing for 10 hr., it was again filtered.

The filtrate was made slightly basic with potassium hydroxide pellets and then concentrated to 350 ml. using an air stream and a temperature of ~80°. The solution was acidified and continuously extracted with ether for 48 hr. Besides ether, the distilling flask contained 5 g. of barium carbonate and 10 ml. of water. After the extraction was finished, the ether was removed by means of a rotary evaporator and the aqueous barium carbonate slurry was filtered and washed with 20 ml. of water. Most of the water was evaporated using a stream of air. The remaining syrup was triturated with 30 ml. of acetone and the residue was dissolved in 30 ml. of water containing a few drops of concentrated hydrochloric acid. To this solution was added 30 ml. of 95% ethanol and 3 g. of phenacyl bromide. The mixture was heated on a steam bath for 45 min. and then allowed to stand for 8 hr. At the end of this time crystals of phenacyl lactate had formed. The lactate was recrystallized three times from aqueous ethanol and dried under vacuum at 60° over phosphorus pentoxide for 12 hr., m.p. 213–215°.

The combined mixture of 2,4-dinitrophenylhydrazones obtained above was digested on a steam bath with a saturated solution of sodium bicarbonate. The resulting mixture was filtered; the filtrate was acidified with 50% sulfuric acid giving the 2,4-DNP of pyruvic acid. It was purified by recrystallization from ethanol.

The base-insoluble 2,4-DNP's were dissolved in 400 ml. of benzene and chromatographed over alumina. After eluting with 400 ml. of benzene, all of the acetone 2,4-DNP was off the column and the bands of the acetol and pyruvaldehyde derivatives had developed. These bands were eluted from the column with chloroform.

The benzene was removed from the acetone 2,4-DNP and it was recrystallized twice from 95% ethanol. After drying at 60° under vacuum it melted at 127–128°. The chloroform was removed from the acetol 2,4-DNP and it was recrystallized three times from 60% aqueous ethanol. After drying as above it had a melting point of 132–134°.

The determination of acetone, oxalic acid, and acetic acid and acetol plus pyruvaldehyde proceeded as follows. To the quenched reaction mixture from a run identical with that above was added acetone (5 mmoles) potassium oxalate (12.5 mmoles), sodium acetate (25 mmoles), and acetol (5 mmoles). The solution was acidified with 50% sulfuric acid, and a solution of 5.8 g. of 2,4-dinitrophenylhydrazine in 30 ml. of 50% sulfuric acid was added. The solution was heated at 90° for 8 hr. in order to completely convert the acetol 2,4-DNP to pyruvaldehyde di-2,4-DNP.

The hot mixture was filtered and the residue, crude pyruvaldehyde 2,4-DNP was washed with 95% ethanol. The aqueous filtrate on cooling deposited impure yellow crystals of acetone 2,4-DNP. The filtrate which contained acetate ion was processed to give phenacyl acetate in the same way that the lactate containing filtrate was processed to give phenacyl lactate (see above).

To the aqueous solution remaining after the ether extraction was added an excess of barium chloride which precipitated barium sulfate and barium oxalate. The barium oxalate was separated from the sulfate by repeated extraction with hot water.

The products were purified as follows. The pyruvaldehyde di-2,4-DNP was recrystallized twice from nitrobenzene and dried at 60° under vacuum over phosphorus pentoxide for 12 hr., m.p. 295–299°.

The acetone 2,4-DNP was dissolved in benzene and chromatographed over alumina. It was then recrystallized twice from 95% ethanol and dried as above,

m.p. 123–125°. The phenacyl acetate was recrystallized four times from aqueous ethanol and dried at 25°, m.p. 39–40°. The barium oxalate precipitate was dissolved in 20 ml. of 2 M hydrochloric acid and barium ion precipitated with 50% sulfuric acid. The mixture was filtered and brought to pH 2 with potassium hydroxide pellets. Most of the water was removed by heating the solution in a stream of air, and then the residue was triturated with acetone, the acetone solution was filtered and concentrated to 1 ml., from which oxalic acid crystallized. The oxalic acid was sublimed under reduced pressure.

The analyses for C^{14} content were performed by the New England Nuclear Corp. using a liquid scintillation counter and an independent efficiency determination for each sample. The amount of each product was calculated from the observed activity of the product, the activity of the starting acetone, and the amounts of material used.

Kinetics of Reactions of Piperidine with Ethers of 2,4-Dinitrophenol in 10% Dioxane–90% Water. Dependence of Base Catalysis on the Group Displaced[1]

## J. F. Bunnett and Claude Bernasconi

Contribution from the Department of Chemistry, Brown University, Providence, Rhode Island. Received July 6, 1965

Rates of reactions of several 2,4-dinitrophenyl ethers with piperidine, to form 2,4-dinitrophenylpiperidine, have been measured as a function of sodium hydroxide concentration. The sensitivity of these reactions to base catalysis varies with the leaving group. When the leaving group is 2,4-dinitrophenoxy or p-nitrophenoxy, catalysis by NaOH is weak. When it is methoxy, catalysis is strong. When catalysis is strong, the second-order rate coefficient (k_A) is curvilinearly related to base concentration; the plot (Figure 1) for 2,4-dinitrophenyl phenyl ether is a good example of this effect. The reaction of 2,4-dinitrophenyl phenyl ether with piperidine is subject to general base catalysis by piperidine, and the plot of k_A vs. piperidine concentration is curvilinear. The solvent deuterium isotope effect on this reaction, as catalyzed by NaOH, changes in direction as the alkali concentration is varied. All these observations are compatible with the intermediate complex mechanism, as sketched in eq. 1, and many of them fulfill specific expectations from it. They constitute important additional evidence for this mechanism. The reaction of 2,4-dinitrophenyl phenyl sulfide with piperidine, under the conditions of our experiments, was only moderately accelerated by sodium hydroxide. Incidentally, our measurements furnished rate coefficients (k_{OH}) for reactions of the several substrates with NaOH to form 2,4-dinitrophenol.

Primary and secondary amines react with many 1-substituted-2,4-dinitrobenzenes to form 2,4-dinitrophenylamines. Some of these reactions are strongly accelerated by bases, but others are insensitive to base catalysis.[2]

In previous papers,[5,6] the susceptibility of such a reaction to catalysis by bases has been associated with the frequency of reversion of intermediate complex I to reactants. The second step of the intermediate complex mechanism of substitution is judged to be

$$(1)$$
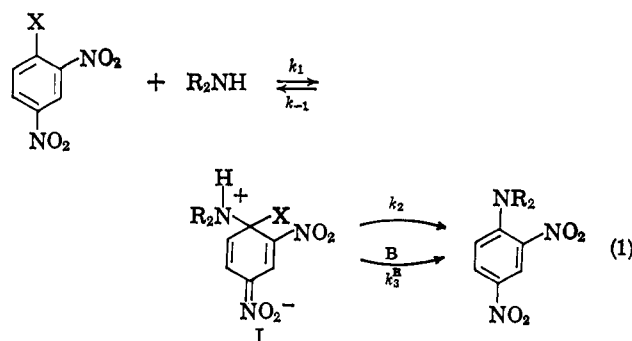
(2) The mild augmentations of second-order rate coefficients for such reactions caused by addition of relatively large amounts of amines and other compounds[3] are of uncertain character,[4] and are not designated as "base catalysis" in the present discussion.

(3) S. D. Ross, *Progr. Phys. Org. Chem.,* 1, 31 (1963).

(4) J. F. Bunnett and R. H. Garst, *J. Am. Chem. Soc.,* 87, 3875 (1965).

(5) J. F. Bunnett and J. J. Randall, *ibid.,* 80, 6020 (1958).

(6) J. F. Bunnett and R. H. Garst, *ibid.,* 87, 3879 (1965).