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PERMANGANATE ION OXIDATION OF THYMINE: SPECTROPHOTOMETRIC DETECTION OF A STABLE ORGANOMANGANESE INTERMEDIATE[1]

Fillmore Freeman*, Charles Orise Fuselier, and Elaine Marie Karchefski
Department of Chemistry, University of California, Irvine, California 92664

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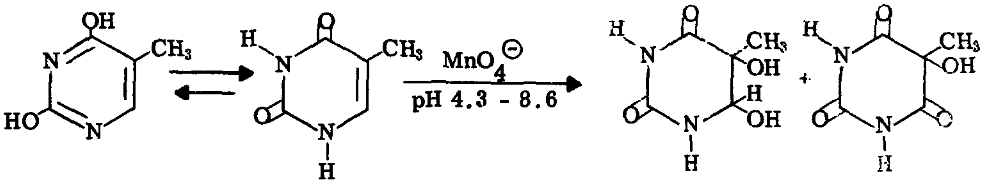
Permanganate ion quantitatively oxidizes 5-methyl-2,4(1H,3H)-pyrimidinedione [thymine, (1)] in phosphate buffered solutions to varying proportions of cis-5,6-dihydroxy-5,6-dihydrothymine (2) and 5-hydroxy-5-methylbarbituric acid (3).[2] The ratio 2:3 is pH dependent, and 2 predominates in alkaline media. The stability of 2 under the reaction conditions suggests that it is not a precursor of 3,[2-4] and it is possible that 2 and 3 are formed from a common intermediate which has several possible modes of reaction.[5]

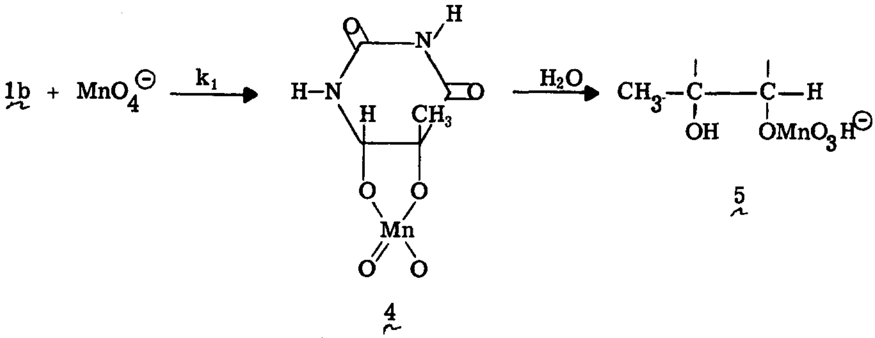


1a 1b 2 3

(1)

Thus, in analogy with the permanganate ion oxidation of olefins, 4, [cis-5,6-dihydroxy-5-methylhydrouracilato(2-)-$\underline{O}^5$,$\underline{O}^6$] dioxomanganate(1-), is probably one of the more plausible of several possible organomanganese intermediates for the mild permanganate ion oxidation of 1.

The kinetics of the permanganate ion oxidation of 1 have been examined in order to better understand the mechanisms of the mild and selective permanganate ion oxidation of nucleic acid derivatives and to obtain information concerning transient organomanganese



(2)

ester intermediates. The kinetics were studied via spectrophotometric stopped-flow techniques under pseudo-first order conditions by monitoring the disappearance of permanganate ion at 510, 515, 522, 524, and 584 nm, and by observing the formation of the postulated intermediate (4) at 405, 415, 420, 425, 435, and 439 nm.[6] The initial (A_0) and final (A_∞) absorbances and the pseudo-first order rate constant (k_ψ) were calculated by a computer program, LSG.[7]

The permanganate ion oxidation of 1 is first order in oxidant and first order in reductant ($k_1 = 16.1\ M^{-1}\ sec^{-1}$). The rate constants obtained by observing the rate of disappearance of permanganate ion at 510, 515, 522, 524, and 584 nm are comparable, within experimental error, to the rate constants obtained by monitoring the rate of formation of an intermediate at 405, 415, 420, 425, 435, and 439 nm. These data are consistent with the formation of 4 or another organomanganese species and imply that the same reaction is being observed at all eleven wavelengths.

The kinetic data argue against an oxidation process involving two successive first order or pseudo-first order steps whereby the organomanganese intermediate is oxidized by permanganate ion to a manganese(VI) intermediate since the rate constants are calculated over approximately 90% reaction with small standard deviations and curves of transmittance with time have relatively stable infinity values. Moreover, no evidence was obtained for the disappearance of the intermediate at the eleven wavelengths studied. Thus, it appears that

1b is possibly being oxidized to uniquely stable **4** which is in accord with the stereochemistry of *cis*-diol formation (**2**).[2,3,5]

Studies of the acidic and basic equilibria of **1** suggest that it exists in the lactam form (**1b**) in the neutral pH region.[8-10] Consequently, oxidation of the carbon-carbon double bond in **1b** by permanganate ion is consistent with a 1,3-cycloaddition process in which manganese(VII) is reduced to tetrahedral manganese(V). The activated complex is probably "Huckel-like" in which all overlapping pairs of reacting orbitals are bonding.[11] This electrocyclic process is consistent with the observed activation parameters ($\Delta H^{\ddagger} = 6.74$ and 6.66 kcal/mole and $-\Delta S^{\ddagger} = 30.4$ and 30.8 eu at 415 and 524 nm, respectively).

Although structure **4** cannot be definitely assigned to the observed organomanganese intermediate, it is of interest to note that its ultraviolet spectrum ($\lambda_{max} = 303, \varepsilon \cong 3962$) in phosphate buffered solution (pH = 6.73) resembles the hypomanganate ion ($MnO_4^{\equiv}$) ultraviolet spectrum ($\lambda_{max} = 323, \varepsilon \cong 4000$).[12,13] Thus, it is seen that the spectrum of the observed organomanganese intermediate could be consistent with some type of manganese(V) oxyanion. Studies are in progress to further characterize the organomanganese intermediates from **1** and other 2,4(1H,3H)-pyrimidinediones.

Although other reasonable mechanisms are possible, **4** or another manganese(V) oxyanion could lead to **5** which can be hydrolyzed to **2** or oxidized to **3**.

Although transient organomanganese intermediates have been proposed for the permanganate ion oxidation of carbon-carbon double bonds, this is one of the few examples of the direct spectrophotometric observation of these postulated intermediates.[14-16] Wiberg, Deutsch and Roček,[14] and Lee and Brownridge[15,16] have recently reported spectrometric evidence for formation of transient manganese(V) and manganese(VI) ester intermediates in the permanganate ion oxidation of the carbon-carbon double bonds in crotonate anion[14] and cinnamic acid.[15,16] We have also observed intermediate organomanganese species in the permanganate ion oxidation of thiophenearcrylic acid.[17]

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