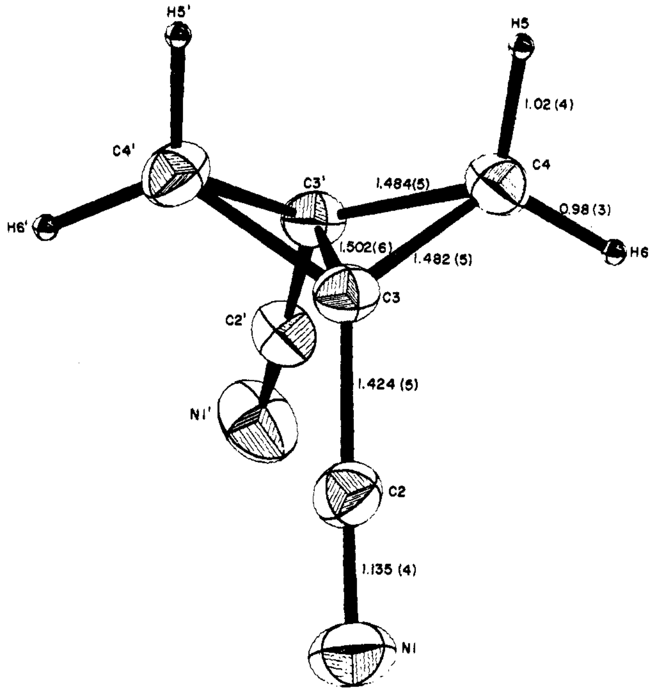

Figure 1.—Bond lengths for 1,3-dicyanobicyclo[1.1.0]butane in angstroms.

TABLE III
INTRAMOLECULAR ANGLES BETWEEN ATOMS OF 1,3-DICYANOBICYCLO[1.1.0]BUTANE

N-1-C-2-C-3	178.8 (3)
C-2-C-3-C-4	127.1 (3)
C-2-C-3-C-3′	124.6 (3)
C-2-C-3-C-4′	127.8 (3)
C-3-C-4-H-5	115.9 (14)
C-3-C-4-H-6	112.3 (12)
C-3-C-4-C-3′	60.9 (2)
C-4-C-3-C-3′	59.6 (2)
C-3-C-3′-C-4	59.5 (2)
C-4-C-3-C-4′	100.6 (3)
C-3-C-4′-H-5′	116.4 (14)
C-3-C-4′-H-6′	117.7 (12)
H-5-C-4-H-6	113.7 (15)

by the two three-membered carbon rings. The X-ray diffraction results of 126.4 ± 0.4° is larger than the values previously found, which ranged from 120.2° to 126°.[1-6] Perhaps the substitution of a nitrile group for hydrogen affects this dihedral angle.

In a survey of previous information on the structure of bicyclobutane, the largest discrepancy occurs in the C–C–H angle corresponding to C_3'–C_3–C_2 of dinitrile bicyclobutane where C_2 is substituted for H. The C–C–C angle found in this paper is 124.6 ± 0.2°, which is in moderate agreement with the microwave spectra[2,3] result of 130° 22′, the nmr spectra[5,6] result of 128.0°, and the electron diffraction result[4] of 125.5°. In contrast, the infrared work[1] placed this angle (CCH) as 163 ± 3°. They do state that the moments of inertia are rather insensitive to this angle.

There are no anomalous intermolecular contacts in this structure. Two interesting intramolecular contacts are the H_5–H_5' distance of 2.42 (5) Å and the C_2–C_2' distance of 3.118 (5) Å. The hydrogen atom repulsions appear to be of little importance because twice the van der Waals radius of hydrogen is about 2.4 Å. However, the C_2–C_2' repulsions may affect the geometry of the bicyclobutane moiety of this compound.

Two review articles on bicyclobutane describe the chemistry of these compounds in detail.[8,9] A model for the electronic structure has been proposed,[10] but, at the time of these calculations, only an inexact knowledge of the structure of bicyclobutane was known. More recently, calculations of the valence electron density distribution[11] and the first excited state charge density[12] have been made for bicyclobutane.

Registry No.—1,3-Dicyanobicyclo[1.1.0]butane, 27184-67-4.

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Buffered Permanganate Reactions. Effect of Calcium on the Rate of Disproportionation of Manganate(VI)

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Received January 13, 1972

The pronounced influence pH exerts on the kinetic course of many permanganate oxidations is well recognized.[1] This effect is rarely related to variations in oxidation potential, but can be usually explained by mechanistic factors, such as ionization of the substrate or protonation of permanganate, for example. Furthermore, permanganate oxidations tend to give rise to simultaneous operation of several mechanisms and, consequently, to the formation of multiple reaction products under unfavorable reaction conditions.

Control of pH by employment of suitable buffer systems is a common method for manipulation of yields and product ratios in the application of oxidations to organic synthesis. A typical example is the neutral oxidation of certain organic substrates in Mg^{2+}-ion buffered systems, in which the equilibrium concentration of OH^- ions in solution is limited by the solubility of magnesium hydroxide.[2]

$$Mg^{2+} + 2OH^- \longrightarrow Mg(OH)_2\ (s) \qquad (1)$$

Permanganate oxidations of organic compounds often proceed at faster rates in alkaline than in neutral solutions. In many such instances the observed rate enhancement is associated with an increasing degree of substrate ionization. The reaction pattern of alkaline permanganate oxidations is, however, usually highly complex in view of the different pathways by

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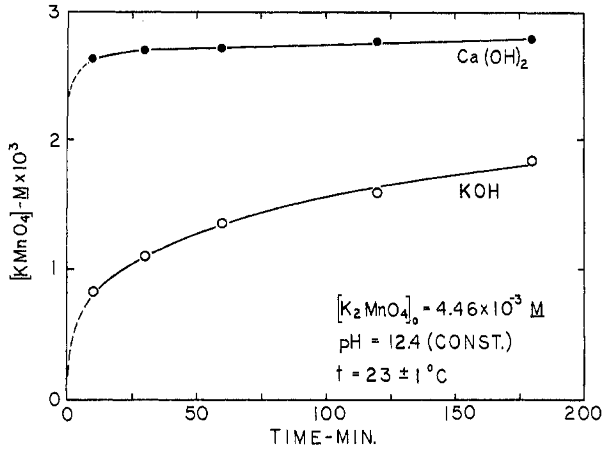

Figure 1.—Rate of potassium manganate(VI) disproportionation in the presence of calcium and potassium hydroxide at pH 12.4 and at 23 ± 1°.

which permanganate ion may be reduced to its final end products.

Organic substrates, which reduce alkaline permanganate directly beyond manganate(VI) (eq 2) have

$$MnO_4^- + e \longrightarrow MnO_4^{2-} \quad (2)$$

not been reported,[3] and permanganate is known[1] to oxidize a vast number of compounds at a rate much faster than does manganate(VI). Thus, the full utilization of permanganate, as usually represented by a 3-equiv net reduction (eq 3) depends to a large extent

$$MnO_4^- + 3e + 4H^+ \longrightarrow MnO_2 + 2H_2O \quad (3)$$

on the rate of disproportionation of manganate(VI) yielding permanganate and manganese dioxide (eq 4).

$$3MnO_4^{2-} + 2H_2O \rightleftharpoons 2MnO_4^- + MnO_2 + 4OH^- \quad (4)$$

There is sufficient evidence for this reaction to be reversible, but much uncertainty remains with regard to kinetic parameters and the magnitude of the equilibrium constant.[1] This inconsistency is believed to stem from differences in the reactivity of manganese dioxide, since the numerical position of the disproportionation equilibrium is strongly affected by the direction of its approach.

The rate of manganate(VI) disproportionation is most strongly influenced by the hydroxide ion concentration and by temperature, among other factors. The reaction is immeasurably fast in acid and extremely slow in 3 *N* base. Decomposition of manganate(VI) yielding hypomanganate or manganate(V) (eq 5) has

$$MnO_4^{2-} + OH^- \longrightarrow MnO_4^{3-} + OH\cdot \quad (5)$$

been observed to occur in 8 *N* KOH solution.[1] Thus, an experimental examination of manganate(VI) disproportionation (eq 4) is limited to a narrow range of hydroxide ion concentrations only. Decomposition of permanganate (eq 6) is an additional factor complicating the study of alkaline systems containing manganate species. The reaction is strongly catalyzed by hydroxyl ions and by manganese dioxide, which is almost always present in these solutions. Low permanganate yields, as have been observed in certain alkaline oxidations, are in great part attributed to this decomposition reaction.[4]

$$4MnO_4^- + 4OH^- \longrightarrow 4MnO_4^{2-} + O_2 \quad (6)$$

We have observed a significant acceleration of the rate of manganate(VI) disproportionation in the presence of calcium. As shown in Figure 1 near stoichiometric disproportionation of manganate(VI) occurs in less than 10 min in calcium hydroxide, as compared to an exceedingly slow approach to equilibrium in a KOH system under otherwise identical conditions. The rate acceleration was found to increase with increasing concentration of calcium and to reach a limiting value under conditions (pH 12.4) corresponding to saturation with respect to solid calcium hydroxide ($K_{sp} = 5.5 \times 10^{-6}$).

Although an exhaustive interpretation of the role of calcium in the disproportionation of manganate(VI) requires further experimental exploration, the author tends to favor a mechanism involving the precipitation of highly reactive tetravalent species of manganese by Ca^{2+} ions. Some of the following observations related to the chemistry of this system are in support of this interpretation. (1) Attainment of the disproportion equilibrium is extremely slow when approached by reaction of inactive or precipitated forms of manganese dioxide with permanganate in basic solution. This indicates that only highly reactive species of manganese(IV) are capable of participating in the backward reaction. (2) Colloidal forms of hydrous manganese dioxide exhibit a strong sorption tendency for calcium ions with subsequent sol destabilization being observed.[5,6] Whether Ca^{2+}-ion interaction with tetravalent manganese operates *via* the mechanism of sorption and counterion destabilization or by the formation of an inactive calcium manganate(IV) is not presently understood. Apart from certain mechanistic implications, the calcium ion induced acceleration of the disproportionation of manganate(VI) is felt to be of immediate importance to synthetic applications of permanganate reactions, because of an associated net gain in permanganate yields. This effect has been experimentally verified in the oxidation of cyanide with permanganate.

In the range pH 12–14, cyanide is quantitatively oxidized to cyanate[7,8] (eq 7) with a concurrent 1-equiv

$$2MnO_4^- + CN^- + 2OH^- \longrightarrow 2MnO_4^{2-} + CNO^- + H_2O \quad (7)$$

net reduction of permanganate yielding manganate(VI). The reaction is quantitative in this pH range only and exhibits a nonstoichiometric pattern with a variety of reaction products being formed at lower pH regimes.

A rapid and 3-equiv net reduction of permanganate was realized when conducting the reaction under conditions of saturation with respect to calcium hydroxide (eq 8). This result was found to be independent of an

$$2MnO_4^- + 3CN^- + H_2O \xrightarrow[\text{pH 12.4}]{Ca(OH)_2} 3CNO^- + 2MnO_2 + 2OH^- \quad (8)$$

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excess of calcium hydroxide, which tends to rule out the possibility of heterogeneous catalysis. While this favorable yield shift was demonstrated for cyanide oxidation only, a dependence of this effect on the nature of the substrate seems highly unlikely considering that manganate(VII) is usually the primary oxidant[1,3] in alkaline aqueous systems. In light of these evidences it becomes apparent that the reaction is of considerable interest to the field of organic synthesis.

It should further be noted that the observed effect is probably limited to calcium among the alkaline earth metals, because the higher members of this group (Sr^{2+}, Ba^{2+}) tend to form insoluble salts with the transient manganate(VI) ion.

Since the observed phenomena discussed in this paper promise to lead to more and deeper insights into the chemistry of oxyanions of manganese, the author hopes to encourage further investigations of these reactions.

Experimental Section

Potassium Manganate(VI).—Pure crystalline potassium manganate(VI) was prepared according to the method described by Scholder and Waterstradt[9] as follows. Powdered reagent grade potassium permanganate (20 g) was slowly added to a 1000-ml round flask containing a cold solution of 250 g of KOH in 250 ml of distilled water. The solution was heated to boiling for 20 min under a reflux condenser, which was attached to an absorption tube containing "Ascarite" to prevent back-diffusion of carbon dioxide. After cooling to ambient temperature and crystallization, the reaction product was separated by filtration through a Gooch filtering crucible of medium pore size. The following solutions were employed for further purification of the raw product: I, 50 ml of 40% KOH (filtered); II, 50 ml of CH_3OH and 5 g of KOH (filtered); III, 100 ml of CH_3OH and 3 g of KOH (filtered); IV, 50 ml of CH_3OH and 0.5 g of KOH (filtered); V, 100 ml of ethyl ether (water free). Solutions II–V were precooled to −15°. The crystals were first washed with 50 ml of I at room temperature, then with 50 ml of II, and finally with 40 ml of III, both at −15°. Further removal of adhering KOH was accomplished by resuspension and shaking of the crystals in 50 ml of III, followed by filtration and successive washing with 50 ml of IV, and four times each with 25 ml of ether (V). The temperature was kept below −10° during each of the latter operations. The crystals were then vacuum dried over P_2O_5 for a minimum period of 3 hr.

Differential spectrophotometric analysis at 526 and 603 mμ of a solution of a weighed amount of the product in 2 *N* KOH revealed a purity of 100 ± 0.2% as K_2MnO_4 with no detectable trace of permanganate present. The assay of K_2MnO_4 prepared by this method is usually in the order of 99.8%.

Disproportionation of K_2MnO_4 in Aqueous KOH.—A quantity of 0.44 g of K_2MnO_4 was dissolved under magnetic stirring in 500 ml of 0.025 *N* KOH, which was preadjusted to pH 12.4 employing a pH meter. Control of pH throughout the duration of the experiment was accomplished by addition of small increments of 0.5 *N* nitric acid delivered from a microburette and by simultaneous pH monitoring. The solution was kept agitated with a magnetic stirrer. The temperature was maintained at 23 ± 1°.

The reaction was arrested by addition of 5 ml of a saturated solution of $Ba(OH)_2$ to 20-ml aliquots followed by rapid mixing for 10 min in order to facilitate the agglomeration of manganese(IV) and barium manganate. After filtration of this mixture through a fine Gooch crucible, the concentration of permanganate in the filtrate was determined by spectrophotometric analysis[7] at 526 mμ, with appropriate volume corrections taken into account.

Disproportionation of K_2MnO_4 in Aqueous $Ca(OH)_2$.—The disproportionation reaction in systems saturated with calcium hydroxide was conducted under conditions identical with those described for aqueous KOH with the following exceptions.

K_2MnO_4 was dissolved in 500 ml of distilled water containing 1 g of $Ca(OH)_2$. The pH of this solution remained at a constant value of 12.4 without necessitating adjustments throughout the duration of the experiment.

Oxidation of Cyanide.—The alkaline oxidation of cyanide with permanganate was investigated under a variety of experimental conditions and over a wide range of reactant concentrations.[10] A description of the experimental details of those studies relevant to this paper is given below.

Standardized solutions of KCN and $KMnO_4$ were employed. The reaction was initiated by addition of permanganate solution to solutions saturated with $Ca(OH)_2$ and containing KCN under conditions of rapid mixing and at room temperature. Initial concentrations varied for cyanide and permanganate between 10^{-3} and 10^{-2} *M* and between 3×10^{-4} and 3×10^{-3} *M*, respectively. An excess of each individual reactant was applied in some of the cases. The stoichiometric relationship postulated for the reaction in the presence of calcium hydroxide was established during advanced stages and after completion of the reaction, usually no later than 30 min after initiation. Quenching of the reaction, *i.e.* reduction of excess permanganate to manganese dioxide, was accomplished by dropwise addition of hydrogen peroxide or manganese nitrate. Manganese dioxide was separated by filtration through membrane filters (220 mμ); its removal by this method was readily accomplished by virtue of its precipitation in the presence of calcium ions. The concentration of cyanide was determined argentometrically by the Liebig method,[8] whereas permanganate was measured spectrophotometrically[7] in those cases in which an excess of the oxidant had been applied.

Registry No.—K_2MnO_4, 10294-64-1; KOH, 1310-58-3; $Ca(OH)_2$, 1305-62-0; KCN, 151-50-8.

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Conversion of Hetacillin into Cephalexin

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Received March 8, 1972

In 1963 Morin and collaborators[1] showed that thermal treatment of esters of penicillin V sulfoxide in acidic media gave rise to the corresponding esters of 7-phenoxyacetamido-3-methyl-3-cephem-4-carboxylic acid.[2] Later, when cephalexin[3] was shown to be of commercial importance, Chauvette and coworkers[4] reported the synthesis of cephalexin in a multistep sequence from penicillin V sulfoxide ester. We wish to report the synthesis of cephalexin from commercial hetacillin[5] by a four-step series of reactions. Hetacillin (**1**) was nitrosated[6,7] to block its secondary amino function and subsequently oxidized to the sulfoxide **3** with sodium metaperiodate.[8] The sulfoxide **3** was thermally rearranged as the free acid in the presence of *p*-toluenesulfonic acid to the cephalosporin derivative **4**, de-

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