undergo the second (irreversible) change at room temperature. This latter fact may result from the large content of disulfide linkages in this protein, approximately 16 per molecule.[30] Thus it can be imagined that these restrain the altered polypeptide chains so that actual unfolding is prevented, thus facilitating the return of the chains to their native configuration when the force of repulsion is released. Ovalbumin, on the other hand, appears to undergo the initial transition much less readily than A; furthermore, possibly due to its very low content of disulfide linkages, perhaps one per molecule,[31] the expanded molecule is not stable but goes on, irreversibly, to the unfolded form. Clearly many other possibilities exist and this mechanism is highly speculative. It would appear to deserve further experimental test, however, and such studies are in progress in this Laboratory.

NOTE ADDED DECEMBER 7, 1953.—The very interesting studies of Kauzmann and co-workers on the effect of urea and of guanidine salts on the viscosity and optical rotation of serum albumin and other proteins have now appeared in print.[32] These studies represent a marked advance in our understanding of denaturation and in the case of A appear to be rather closely related to our own. Thus it appears probable that the marked effects they observe in urea below 40° represent the same change in configuration which takes place in acid. This conclusion is based on (1) the similar shifts in viscosity and rotation in the two cases (2) the reversibility in both cases and (3) the fact that unpublished studies in this Laboratory by flow birefringence indicate that there is no unfolding of A under the conditions they employ.

Another very interesting communication by Gutfreund and Sturtevant[33] concerning a reversible reaction of A in acid should be mentioned. These workers have observed a heat uptake, upon reducing the *p*H of A solutions from 4.5 to 3.4, which is measurably slow (half-time approximately 2.5 minutes) and which is almost certainly a reflection of the same process covered in the present paper. The half-time is compatible with our conclusion that the reaction is immeasurably fast since in our studies measurements were not made earlier than about twenty minutes after mixing.

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(30) J. T. Edsall, *Adv. Protein Chem.*, **3**, 464 (1947).

(31) H. L. Fevold, *ibid.*, **6**, 202 (1951).

(32) R. B. Simpson and W. Kauzmann, THIS JOURNAL, **75**, 5139 (1953); J. Schellman, R. B. Simpson and W. Kauzmann, *ibid.*, **75**, 5152 (1953); W. Kauzmann and R. B. Simpson, *ibid.*, **75**, 5154 (1953); H. K. Frensdorff, M. T. Watson and W. Kauzmann, *ibid.*, **75**, 5157 (1953).

(33) H. Gutfreund and J. M. Sturtevant, *ibid.*, **75**, 5447 (1953).

AMES, IOWA

[CONTRIBUTION FROM THE GENERAL ELECTRIC RESEARCH LABORATORY]

The Autoxidation of 2-Nitropropane in Basic Solution[1]

BY GLEN A. RUSSELL

RECEIVED OCTOBER 2, 1953

2-Nitropropane is oxidized by air to acetone and nitrite ion in an autocatalytic manner in the presence of an excess of aqueous base at room temperature. The reaction is catalyzed by the addition of ferric and other ions and completely inhibited by the addition of arsenic trioxide and other compounds. The observed autocatalysis, catalysis, inhibition and dependence of rate on the concentration of hydroxide ion has been explained on the basis of a free radical mechanism proceeding by an ion–radical chain and involving an intermediate hydroperoxide. An essential feature of the proposed oxidation chain is a one-electron transfer between a peroxy radical and the anion of 2-nitropropane to produce a peroxy anion and a free alkyl radical. It has been postulated that the hydroperoxide formed in this manner can either dissociate to alkoxy and hydroxyl radicals (autocatalysis), or react with the anion of 2-nitropropane *via* a S_N2 displacement on oxygen to produce the observed products of the reaction.

Introduction

The autoxidation of carbanions or organometallic compounds possessing considerable ionic character has received extensive investigation. It has been found that in ether solution triphenylmethylsodium reacts with oxygen to give mainly triphenylcarbinol with the formation of traces of triphenylmethyl peroxide but without the formation of isolable amounts of triphenylmethyl hydroperoxide.[2] Aliphatic Grignard reagents are known to react very readily with oxygen, with the formation of the corresponding alcohol as a major product,[3] except for triphenylmethylmagnesium bromide which has been reported to yield 57% of triphenylmethyl peroxide.[4] Small amounts of peroxidic materials have been detected in the air oxidations of cyclohexyl- and ethylmagnesium halides at low temperatures,[5a] and it has been postulated that the oxidations proceed *via* the formation of peroxidic intermediates.[5] Recently, it has been found that the slow addition of a dilute ethereal solution of an aliphatic Grignard reagent to a saturated ethereal solution of oxygen results in the formation of the hydroperoxide as the major product.[6] Phenylmagnesium bromide, when oxidized in ethyl ether, produces benzene, phenol, biphenyl and α-phenylethanol.[3a,5b,7] The formation of the latter compound suggests that the reaction involves free radicals which may attack the ethyl ether to produce acetaldehyde. It has been found that the yield of phenol can be improved by replacing the ethyl ether by benzene[8] or by phenetole,[7] or by coöxidizing an aromatic and aliphatic Grignard reagent.[3b,8] The reaction of a large number of organolithium compounds with oxygen has been investigated and found to yield the same products as the oxidations of the corresponding Grignard reagents.[9]

The autoxidations of triphenylmethide ion, Grignard reagents and organolithium compounds

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(1) Presented before the Organic Chemistry Division of the American Chemical Society at the Chicago Meeting, Sept. 6–11, 1953.

(2) W. E. Bachmann and F. Y. Wiselogle, THIS JOURNAL, **58**, 1943 (1936).

(3) (a) M. T. Goebel and C. S. Marvel, *ibid.*, **55**, 1693 (1933); (b) M. S. Kharasch and W. B. Reynolds, *ibid.*, **65**, 501 (1943).

(4) J. Schmidlin, *Ber.*, **39**, 628, 4183 (1906).

(5) (a) H. Wuyts, *Compt. rend.*, **148**, 930 (1909); *Bull. soc. chim. Belg.*, **36**, 222 (1927); (b) C. W. Porter and C. Steele, THIS JOURNAL, **42**, 2650 (1920).

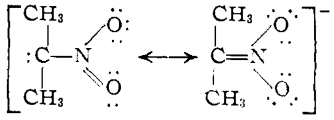
(6) C. Walling and S. A. Buckler, *ibid.*, **75**, 4372 (1953).

(7) H. Gilman and A. Wood, *ibid.*, **48**, 806 (1926).

(8) D. Ivanov, *Bull. soc. chim. France*, [4] **39**, 47 (1926).

(9) E. Müller and T. Töpel, *Ber.*, **72**, 273 (1939).

proceed so rapidly that only the stoichiometry and the products of the oxidation can be used to interpret the mechanism. In hopes of obtaining a more moderate reaction, the oxidation of the anion of 2-nitropropane, a resonance-stabilized anion possessing partial carbanion structure, was investigated in aqueous and alcoholic solution.



Results

Effect of Concentration of Base.—2-Nitropropane does not react with oxygen at room temperature in either aqueous or alcoholic solutions.

The sodium salt of 2-nitropropane readily absorbs *oxygen at room temperature in 0.5–6 M* aqueous sodium hydroxide, but only a very slow absorption of oxygen occurs in the absence of base or in the presence of very concentrated base (*ca.* 10 *M*). As shown in Fig. 1, the concentration of hydroxide ion affects the rate and general shape of the oxidation curve besides influencing the total amount of oxygen absorbed.

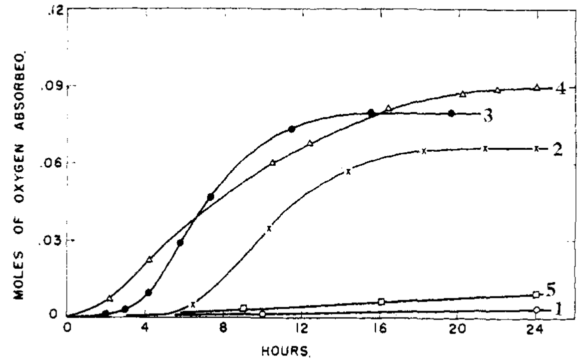
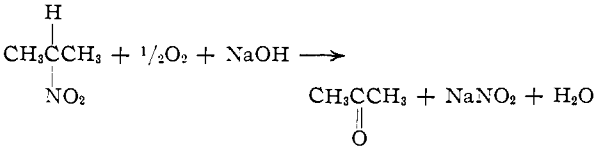


Fig. 1.—Oxidation of 0.1 mole of 2-nitropropane (1.0 *M*) at 25°: 1, 1.00 *M* aq. sodium hydroxide; 2, 1.55 *M;* 3, 2.00 *M;* 4, 4.65 *M;* 5, 10.0 *M.*

At concentrations of base of 1.5–5 *M*, more than one-half but less than one mole of oxygen is absorbed per mole of 2-nitropropane (1.0 *M*) at a rate which increases with time after an initial induction period (see Fig. 1). The initial portion of the oxidation curve does not represent inhibition of the oxidation by some impurity present in the 2-nitropropane, since once the rapid oxidation has commenced, the addition of fresh 2-nitropropane does not cause a retardation in the rate of oxidation as long as an excess of base is maintained. Furthermore, if the oxidation is halted after the rate of oxygen absorption has become rapid and the reaction mixture allowed to stand in an inert atmosphere at room tempearture, the ability of the solution to undergo rapid oxidation decreases with time and eventually approaches that of a freshly prepared 2-nitropropane solution.

The oxidation of 2-nitropropane dissolved in alcoholic lithium ethoxide[10] is affected by the quantity of base present in a quite different manner than are the oxidations in aqueous base. Thus, the lithium salt of 2-nitropropane is rapidly oxidized in alcoholic solution only in the presence of free 2-nitropropane. Furthermore, the 2-nitropropane not neutralized by the lithium ethoxide is not oxidized.

Products and Stoichiometry.—The products of the oxidation in aqueous or alcoholic solutions are acetone (up to 83%), nitrite ion (up to 97%) and small amounts of 2,3-dimethyl-2,3-dinitrobutane, nitrate ion and an organic acid fraction. Thus, the major reaction occurring is



$$\mathrm{CH_3\overset{H}{\underset{NO_2}{C}}CH_3 + {}^1/_2O_2 + NaOH \longrightarrow CH_3\underset{\overset{\|}{O}}{C}CH_3 + NaNO_2 + H_2O}$$

Because of the side reactions producing organic acids, more than one-half of a mole of oxygen is absorbed per mole of 2-nitropropane oxidized. The production of organic acids is more pronounced in aqueous than in alcoholic solutions, at elevated temperatures and at the higher concentrations of aqueous sodium hydroxide. The yield of acetone varies with these conditions in the reverse manner, as shown in Table I.

Pyruvic acid appears to be the primary acid produced, although the formation of lactic acid cannot be excluded. From the data of Table I, it is clear that very nearly one equivalent of acid is produced for every mole of 2-nitropropane not oxidized to acetone, and that the organic acids produced do not contain nitrogen. This removes the possibility that a degradative oxidation producing carbonate, formate or acetate ions occurs. Pyruvic acid can be detected as a reaction product, and it seems likely that the major portion of the organic acid fraction isolated consisted of the condensation products of pyruvic acid, which are readily formed in basic solution and which are not easily identified. The organic acids may be produced from the acetone formed or directly from 2-nitropropane or its anion. When acetone was added at the start of an oxidation (expt. 9, Table I), the amount of oxygen absorbed and the amount of organic acids produced increased (compare with expt. 4), but the data are not sufficiently consistent to state whether or not all of the acids are produced by the oxidation of acetone.

Relatively high yields of 2,3-dimethyl-2,3-dinitrobutane are obtained in the sluggish oxidation of 2-nitropropane which occurs in the presence of an equivalent amount or deficiency of aqueous sodium hydroxide. Increasing the concentration of hydroxide ion causes a drastic reduction in the amount of 2,3-dimethyl-2,3-dinitrobutane produced, as shown in Table II.

Catalysis and Inhibition.—The effects of various organic and inorganic substances on the oxidation of 2-nitropropane were studied. The products of the oxidation (acetone, nitrite ion, etc.) have no catalytic effect. As summarized in Fig. 2, ferric chloride (one mole %) catalyzes the reaction, as do ferrous chloride, chromic chloride and sodium sulfide.

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[10] It is advantageous to use the lithium salt of 2-nitropropane to obtain a homogeneous alcoholic solution.

TABLE I

OXIDATION OF 2-NITROPROPANE IN BASIC SOLUTION AT 25°[a]

Expt.	Reactants[b] 2-Nitropropane	Reactants[b] NaOH	O_2 absorbed	Time, hr.	Acetone	Sodium nitrite	Organic[c] acids	Sodium nitrate	$C_6H_{12}(NO_2)_2$
1	0.104	0.104	0.0139	56	.....	....	...	....	0.00089
2	.109	.155	.0684	16	0.0902	0.103	0.020	0.0023	.00081
3	.110	.180	.0770	16	.0899	.106	.020	.0028	.00044
4	.110	.201	.0778	14	.0871	.106	.022	.0029	.00027
5	.110	.363	.0861	17	.0705	.107	.036	.0010	.00003
6	.109	.465	.0938	16	.0628	.105	.046	.0011	<.00001
7	.111	1.00	.0490	144	.....	....	...	....	<.00001
8[d]	.109	0.202	.0730	17	.0758	.0982	.033	.0019	.00079
9[e]	.110	.200	.0806	17	.0809[f]	.104	.035	.0016	.00043
10[g]	.220[h]	.102	.0596	21	.0886	.0922	.005	.0048	.00079

[a] All quantities in moles unless otherwise specified. [b] Diluted to 100 ml. [c] Equivalents. [d] 35°. [e] 0.0676 mole of acetone added. [f] 0.1485 mole of acetone in product. [g] Lithium salts in absolute ethanol. [h] The reaction ceased when the base had been consumed. The amount of unreacted 2-nitropropane was about 0.12 mole.

TABLE II

OXIDATION OF 1 *M* 2-NITROPROPANE AT 25°

Sodium hydroxide concn., moles $l.^{-1}$	$\frac{\text{Moles of } (CH_3)_2C(NO_2)\text{—}C(NO_2)(CH_3)_2}{\text{Moles of } O_2 \text{ absorbed}}$
1.0	0.064
1.5	.012
2.0	.004
3.6	.0004
4.6	<.0001
10	<.0001

Arsenic trioxide (one mole %) inhibits the oxidation, and no absorption of oxygen was noted for periods up to eight hours (the longest experiment). Manganese dioxide, manganous sulfate and ammonium ceric nitrate are also efficient inhibitors, while permanganate ion is a powerful inhibitor after obvious reduction by the basic 2-nitropropane solution.

The addition of small amounts of persulfate, dichromate, sulfite, hydrosulfite, thiosulfate, iodide, cupric or cuprous ions, nitric oxide, hydrogen peroxide, acrylonitrile, *p*-thiocresol or benzaldehyde have no effect on the reaction. Sodium sulfite in the presence of cupric ions also has no effect, and a mixture of potassium dichromate and arsenic trioxide shows only the inhibitory effect of the arsenic trioxide. Picric acid, quinone and *p*-nitrosodimethylaniline, inhibitors for many free-radical reactions, are poor inhibitors for this oxidation, possibly because of their reactivity toward the basic 2-nitropropane solution. Radiation from a tungsten filament has no catalytic effect and the oxidation is not catalyzed by electrolysis.

Oxidation of Other Resonance-stabilized Carbanions.—The sodium salt of 1-nitropropane absorbs oxygen in an autocatalytic manner in aqueous sodium hydroxide solution at 25°. The major products of the reaction are nitrite ion and an organic acid fraction. Nitrocyclohexane reacts more slowly than 1- or 2-nitropropane without pronounced autocatalysis to give nitrite ion, organic acids and small quantities of cyclohexanone and 1,1′-dinitrodicyclohexane. The sodium salt of phenylnitromethane in aqueous sodium hydroxide shows no reactivity toward oxygen at 25° even in the presence of ferric salts. Acetone, ethyl acetoacetate and diethyl malonate are inactive toward oxygen under conditions where 1- or 2-nitropropane is readily autoxidized.

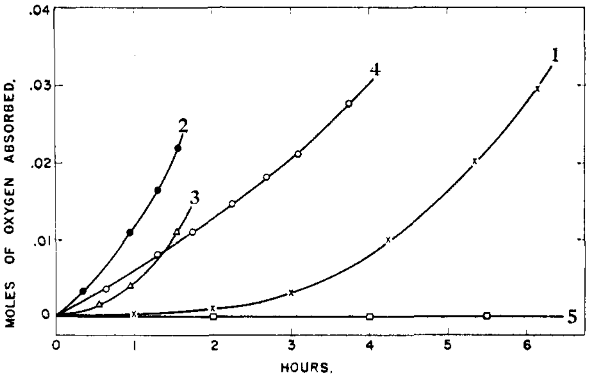


Fig. 2.—Oxidation of 0.1 mole of 2-nitropropane (1.0 *M*) at 25° in the presence of 2.0 *M* sodium hydroxide: 1, autoxidation; 2, Fe^{III} (0.01 *M*); 3, Fe^{II} (0.01 *M*); 4, Na_2S (0.01 *M*); 5, As_2O_3, $KMnO_4$, MnO_2 or $MnSO_4$ (0.01 *M*).

Discussion

While it has been suggested that the reaction of Grignard reagents[5b] and organolithium compounds[9] with oxygen may proceed *via* an ionic mechanism according to equations 1 and 2

$$R^-M^+ + O_2 \longrightarrow ROO^-M^+ \quad (1)$$

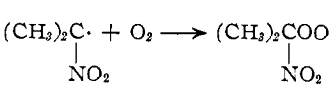
$$ROO^-M^+ + R^-M^+ \longrightarrow 2RO^-M^+ \quad (2)$$

the isolation of α-phenylethanol from the oxidations of phenylmagnesium bromide[3b,5b,7] and phenyllithium[9] in ethyl ether suggests a free radical mechanism. The oxidation of the anion of 2-nitropropane clearly cannot occur *via* reaction 1, since this step does not account for the induction periods or the autocatalysis observed.[11]

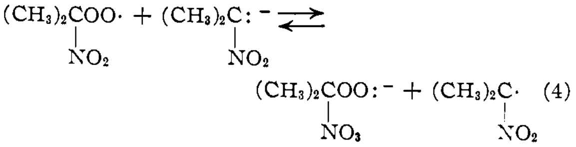
The autocatalysis and the ability of traces of many substances to catalyze or inhibit the oxidation of 2-nitropropane demonstrate a free radical mech-

[11] Reaction 1 involves the pairing of the odd electrons of oyxgen—a process which requires an energy of activation of 38 kcal. mole^{-1} for isolated oxygen molecules (G. Herzberg, "Spectra of Diatomic Molecules," 2nd. Ed., D. Van Nostrand Co., Inc., New York, 1950, p. 346). Although this energy of activation is not independent of the environment of the oxygen molecule, it is not surprising that oxygen fails to react readily with the anions derived from 2-nitropropane, acetone, diethyl malonate or ethyl acetoacetate.

anism. The following chain reaction is suggested.[12]

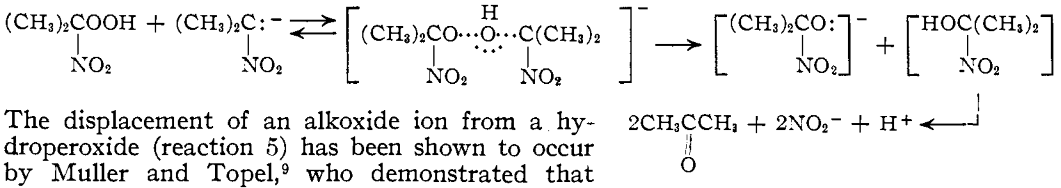


$$(CH_3)_2\underset{NO_2}{C}\cdot + O_2 \longrightarrow (CH_3)_2\underset{NO_2}{C}OO\cdot \qquad (3)$$



$$(CH_3)_2\underset{NO_2}{C}OO\cdot + (CH_3)_2\underset{NO_2}{C}:^- \rightleftarrows (CH_3)_2\underset{NO_3}{C}OO:^- + (CH_3)_2\underset{NO_2}{C}\cdot \qquad (4)$$

By itself, the above reaction sequence predicts that one mole of oxygen should be absorbed per mole of 2-nitropropane and that the product of the reaction should be a hydroperoxide. The observations that only one-half of a mole of oxygen is absorbed per mole of 2-nitropropane oxidized, and that the major products of the oxidation are acetone and nitrite ion, can be reconciled with the suggested free radical chain oxidation, however, if reaction 5 is assumed to occur readily[13]

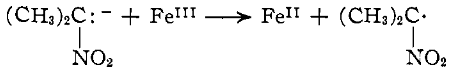


$$(CH_3)_2\underset{NO_2}{C}OOH + (CH_3)_2\underset{NO_2}{C}:^- \rightleftarrows \left[(CH_3)_2\underset{NO_2}{C}O\cdots\overset{H}{O}\cdots\underset{NO_2}{C}(CH_3)_2\right]^- \longrightarrow \left[(CH_3)_2\underset{NO_2}{C}O:\right]^- + \left[HO\underset{NO_2}{C}(CH_3)_2\right] \longrightarrow 2CH_3\underset{O}{\overset{\|}{C}}CH_3 + 2NO_2^- + H^+ \qquad (5)$$

The displacement of an alkoxide ion from a hydroperoxide (reaction 5) has been shown to occur by Muller and Topel,[9] who demonstrated that phenyllithium and the lithium salt of 1,2,3,4-tetrahydro-1-naphthyl hydroperoxide react quantitatively at low temperatures to give the corresponding alkoxides.[14] There is no independent evidence that a highly resonance-stabilized anion, such as the anion of 2-nitropropane, will react with a hydroperoxide in this manner.[15]

The concept of a free radical oxidation mechanism involving an intermediate hydroperoxide may be used to explain the autocatalysis, catalysis, inhibition and the effect of the sodium hydroxide–2-nitropropane ratio on the oxidation. Thus, autocatalysis can result from a homolytic scission of the hydroperoxide yielding alkoxy and hydroxyl radicals which can enter into an electron transfer reaction with the anion of 2-nitropropane as in reaction a (ref. 13) and thereby generate new oxidation chains. The induction periods observed for the oxidation may represent periods during which the hydroperoxide concentration is increasing, perhaps by a very slow ionic reaction of oxygen with the anion of 2-nitropropane, to a point where its autocatalytic ability is observable.

Catalysis of the oxidation by the addition of ferric chloride can presumably occur *via* reaction 6[16]



$$(CH_3)_2\underset{NO_2}{C}:^- + Fe^{III} \longrightarrow Fe^{II} + (CH_3)_2\underset{NO_2}{C}\cdot \qquad (6)$$

Chromic salts may catalyze the reaction similarly, and ferrous salts may act as catalysts *via* oxidation

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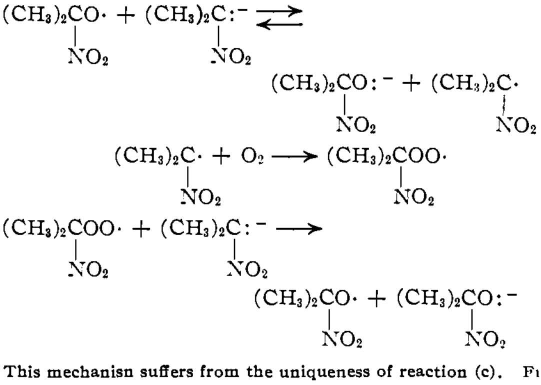
[12] Evidence for the existence of the 2-nitroisopropyl radical has been presented previously. It has been postulated as an intermediate in the formation of 2,3-dimethyl-2,3-dinitrobutane in the electrolysis of aqueous basic 2-nitropropane (R. Pearson and W. V. Evans, *Trans. Electrochem. Soc.*, **84**, 173 (1943)) and more recently in the oxidative dimerization of the anion of 2-nitropropane by oxidizng agents such as sodium persulfate and potassium ferricyanide (H. Shechter and R. B. Kaplan, THIS JOURNAL, **75**, 3980 (1953)). The reaction of this radical with oxygen in the presence of basic solutions of 2-nitropropane to produce acetone and nitrite ions evidently has not been appreciated previously. The formation of large amounts of acetone in the electrolysis and in the reaction of oxidative coupling agents with basic 2-nitropropane solutions may thus involve autoxidation although the decomposition of the 2-nitroisopropyl radical to yield acetone and nitric oxide previously has been favored.

[13] A reaction path involving a free radical chain oxidation that could yield acetone and nitrite ion directly is



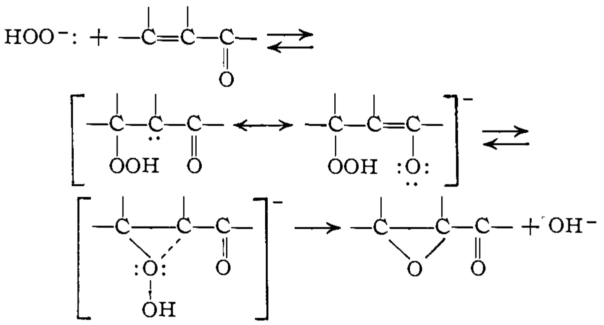
$$(CH_3)_2\underset{NO_2}{C}O\cdot + (CH_3)_2\underset{NO_2}{C}:^- \rightleftarrows (CH_3)_2\underset{NO_2}{C}O:^- + (CH_3)_2\underset{NO_2}{C}\cdot \qquad (a)$$

$$(CH_3)_2\underset{NO_2}{C}\cdot + O_2 \longrightarrow (CH_3)_2\underset{NO_2}{C}OO\cdot \qquad (b)$$

$$(CH_3)_2\underset{NO_2}{C}OO\cdot + (CH_3)_2\underset{NO_2}{C}:^- \longrightarrow (CH_3)_2\underset{NO_2}{C}O\cdot + (CH_3)_2\underset{NO_2}{C}O:^- \qquad (c)$$

This mechanism suffers from the uniqueness of reaction (c). Furthermore, the isolation of hydroperoxides from the oxidation of certain Grignard reagents under special conditions (ref. 6) is compatible with reactions 3–5 but not with reactions a–c.

[14] The epoxidation of α,β-ethylenic ketones and their vinylogs by basic hydrogen peroxide (E. Weitz, *Ann.*, **418**, 29 (1919); E. Weitz and A. Scheffer, *Ber.*, **54B**, 2327 (1921)) probably proceeds *via* a somewhat similar displacement on an oxygen atom.



The attempted preparation of unsaturated amides from certain α,β-ethylenic nitriles by basic hydrogen peroxide has similarly led to the formation of glycidamides (J. V. Murray and J. B. Cloke, THIS JOURNAL, **56**, 2749 (1934)).

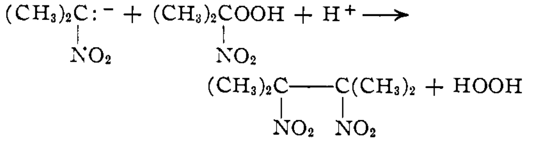
[15] At room temperature the potassium salts of *t*-butyl hydroperoxide and 2-nitropropane do not react in aqueous solution. Sodium peroxide also does not react with 2-nitropropane in basic solution to produce acetone and nitrite ion. It is thought that these results do not remove reaction 5 as a possibility since the hydroperoxides involved are quite different.

[16] Although ferric salts are both catalysts for the autoxidation of basic 2-nitropropane and coupling agents for the oxidative dimerization,[12] potassium persulfate, an excellent agent for oxidative coupling, did not show any catalytic ability for autoxidation under the conditions employed. A possible explanation for this discrepancy is that small amounts of the material, whose effect on the oxidation was to be tested, were added to the basic 2-nitropropane solution several minutes before agitation in an oxygen atmosphere was commenced. Thus, the persulfate which very rapidly effects dimerization,[12] may have been completely consumed before the autoxidation was started. Alternately, dimerization by potassium persulfate may not involve a one-electron transfer.

to the ferric state or by their ability to decompose hydroperoxides in a manner that produces free radicals.[17] Sodium sulfide, which is itself readily oxidized in basic solution, may function as a catalyst because its oxidation involves free radical intermediates.

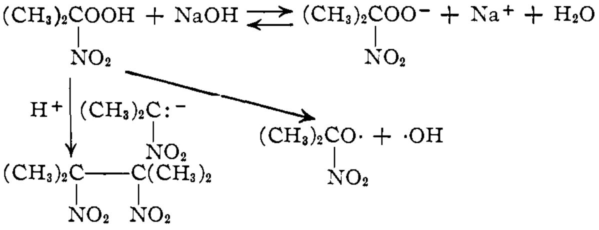
The strong inhibitory effect of arsenic trioxide is not surprising on the basis of a hydroperoxide catalyst, since analytical methods have been developed for the analysis of peroxides based on their quantitative reduction by arsenic trioxide.[18] Manganese dioxide, manganous salts and the reduction products of potassium permanganate (alkaline potassium permanganate readily oxidizes secondary nitro compounds to the corresponding ketones[19]), all inhibitors, may also destroy unstable hydroperoxides. It is not understood why a mixture of cupric and sulfite ions, a known generator of inorganic free radicals,[20] does not catalyze the oxidation nor why ammonium ceric nitrate functions as an inhibitor. A mixture of potassium dichromate and arsenic trioxide, which has been postulated to generate free radicals in basic solution,[21] perhaps failed to catalyze the reaction because of the superior inhibitory power of arsenic trioxide.

The sluggish oxidation of 2-nitropropane in the absence of an excess of aqueous sodium hydroxide and the production of relatively large amounts of 2,3-dimethyl-2,3-dinitrobutane under these conditions[22] may have a common interpretation. The 2,3-dimethyl-2,3-dinitrobutane may be formed by the coupling of 2-nitroisopropyl radicals, but, if this is the case, it is not apparent why the yield should be so dependent on the concentration of hydroxide ion (Table II). An alternate explanation is that the 2,3-dimethyl-2,3-dinitrobutane is formed at the expense of the intermediate hydroperoxide. Reaction 7 fulfills this requirement although it suffers from the fact that both reacting centers are tertiary carbon atoms.[23]



$$(CH_3)_2\underset{NO_2}{C}{:}^- + (CH_3)_2\underset{NO_2}{C}OOH + H^+ \longrightarrow (CH_3)_2\underset{NO_2}{C}-\underset{NO_2}{C}(CH_3)_2 + HOOH \quad (7)$$

Thus, the effect of the concentration of base on the oxidation of 2-nitropropane can be explained as



$$(CH_3)_2\underset{NO_2}{C}OOH + NaOH \rightleftarrows (CH_3)_2\underset{NO_2}{C}OO^- + Na^+ + H_2O$$

$$(CH_3)_2\underset{NO_2}{C}OO^- \longrightarrow (CH_3)_2\underset{NO_2}{C}O\cdot + \cdot OH$$

$$(CH_3)_2\underset{NO_2}{C}OOH \xrightarrow{H^+ \;|\; (CH_3)_2\underset{NO_2}{C}{:}^-} (CH_3)_2\underset{NO_2}{C}-\underset{NO_2}{C}(CH_3)_2$$

At low hydroxide ion concentrations, autocatalysis is absent because the hydroperoxide is converted to 2,3-dimethyl-2,3-dinitrobutane. At intermediate hydroxide ion concentrations, the concentration of free hydroperoxide is large enough that a pronounced autocatalysis is caused by its dissociation into free radicals; while at very high concentrations of sodium hydroxide, autocatalysis is not observed because the hydroperoxide may be stabilized against free radical decomposition by conversion to its salt or perhaps destroyed by the concentrated sodium hydroxide solution.

The results obtained in alcoholic solution are now explainable. Thus, autocatalysis does not occur for oxidations of 2-nitropropane attempted in the presence of an excess of lithium ethoxide because the free hydroperoxide cannot exist in the presence of even a small quantity of a base as strong as lithium ethoxide. In the presence of an excess of 2-nitropropane, the free hydroperoxide can exist because of the acidic nature of the solvent and autocatalysis results. The acidity of the solvent (ethanolic 2-nitropropane) evidently is not great enough to allow reaction 7 to compete favorably with the dissociation of the hydroperoxide into free radicals.

The essential features of the mechanism proposed for the oxidation of 2-nitropropane in basic solution are thought to be generally applicable to the oxidation of carbanions in aqueous solution or in the presence of other ionizing solvents. The extension of this mechanism to the oxidation of Grignard reagents, organolithium compounds, and the like in non-ionizing solvents may or may not be in order. It does seem obvious that free radicals are involved in the oxidation of aryl Grignard reagents, as evidenced in the production α-arylethanols in ethyl ether solution.[3b,5b,7] However, it is not apparent whether the free radicals which attack the ethyl ether to produce acetaldehyde *via* hydrogen atom abstraction are involved in an oxidation chain or whether they result as a side reaction of the Grignard reagent, etc., with the hydroperoxide formed by a non-radical reaction. The recent report of the formation of free-radicals in the reaction of di-*t*-butyl peroxide with Grignard reagents[24] suggests that the oxidation of Grignard reagents, etc., *via* a free radical mechanism should be self-initiating and autocatalytic.

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(17) M. S. Kharasch, F. S. Arimoto and W. Nudenberg, *J. Org. Chem.*, **16**, 1556 (1951); W. S. Wise and G. H. Twigg, *J. Chem. Soc.*, 2172 (1953).

(18) S. Siggia, *Ind. Eng. Chem., Anal. Ed.*, **19**, 872 (1947); D. C. Walker and H. S. Conway, *Anal. Chem.*, **25**, 923 (1953).

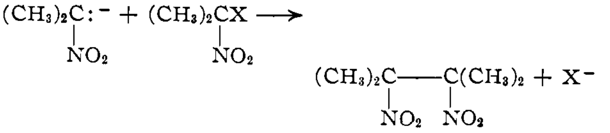
(19) S. S. Nametkin and E. I. Pozdynakova, *J. Russ. Phys. Chem. Soc.*, **45**, 1420 (1913); S. S. Nametkin and A. M. Khukhrikova, *ibid.*, **47**, 425 (1915).

(20) F. Haber and R. Willstätter, *Ber.*, **64**, 2844 (1931).

(21) I. M. Kolthoff and E. J. Meehan, *J. Polymer Sci.*, **9**, 327 (1952).

(22) The oxidation of 2-nitropropane in the presence of a deficiency of aqueous bases has been suggested as a method of preparing 2,3-dimethyl-2,3-dinitrobutane (C. S. Coe, E. C. Attanè and T. F. Doumani, U. S. Patent 2,465,974 (1949)).

(23) Reaction 7 appears more reasonable in view of the reaction of the 2-halo-2-nitropropanes with the anion of 2-nitropropane. H. B. Hass and E. F. Riley (*Chem. Rev.*, **32**, 373 (1943)) have reported 50 and 75% yields of 2,3-dimethyl-2,3-dinitrobutane from 2-chloro- and 2-bromo-2-nitropropane, respectively.



$$(CH_3)_2\underset{NO_2}{C}{:}^- + (CH_3)_2\underset{NO_2}{C}X \longrightarrow (CH_3)_2\underset{NO_2}{C}-\underset{NO_2}{C}(CH_3)_2 + X^-$$

(24) R. T. Morrison, C. Meltzer, S. Radel and L. Simet, Abstracts of Papers, 124th Meeting of the American Chemical Society, Chicago, Illinois, September 6–11, 1953, p. 34-O.

Experimental

Oxidation Procedure.—2-Nitropropane was dissolved in the desired amount of aqueous sodium hydroxide at 10–20° in a nitrogen atmosphere. The solution was diluted to 100 ml. and transferred to a 250-ml. erlenmeyer flask whose neck had been extended by a 25-cm. length of 16-mm. tubing. The flask was connected by rubber tubing to a manometer and gas buret with suitable attachments for evacuation of the system and for the admission of oxygen. The flask was evacuated and filled with oxygen several times, after which it was placed on a pivoted rack in a water-bath. The flask was usually shaken at a rate of 100 strokes/min. with a movement of 8 cm./stroke. Increasing the shaking rate did not affect the rate of oxidation. The oxygen absorption was followed either by the gas buret or by the use of a wet test meter until the oxygen absorption had become negligible. When the wet test meter was used, correction was made for the vapor pressure of water.

Analytical Procedures.—The oxidized aqueous solutions were first filtered. The precipitates proved to be pure 2,3-dimethyl-2,3-dinitrobutane; m.p. 211–212°, lit.[25] m.p. 213–214°.

Anal. Calcd. for $C_6H_{12}N_2O_4$: C, 40.8; H, 6.9; N, 15.9. Found: C, 41.0; H, 6.8; N, 16.2.

The filtrates were evaporated to dryness at room temperature in a 500-ml. Kjeldahl flask with a 40-cm. neck and the distillates collected in Dry Ice traps. Extraction of the solid residues with ether indicated the absence of non-volatile, non-ionic products. The residues were diluted to a known volume with water, and aliquots of this solution, analyzed for sodium hydroxide, sodium nitrite and sodium nitrate. The equivalents of organic acids formed were taken as the differences between the amounts of sodium hydroxide used and the amounts of sodium hydroxide, sodium nitrite and sodium nitrate found at the end of the oxidations.

Nitrate ion was determined gravimetrically as nitron nitrate[26] after destruction of the nitrite ion by hydrazine sulfate. Nitrate and nitrite ion were determined as nitron nitrate after oxidation of the nitrite ion by acidified potassium permanganate and destruction of the excess permanganate by hydrogen peroxide. The difference in the two nitrate ion determinations was taken as the nitrite ion concentration.

Rectification of the aqueous distillates from the vacuum evaporation indicated that only acetone and water were present. The dilute acetone solutions were concentrated by rectification through a 30-cm. by 10-mm. column packed with stainless steel helices until pure water distilled. The distillates were then analyzed for acetone by a volumetric procedure based on reaction with hydroxylamine hydrochloride in an alcohol–pyridine solution.[27]

A solution of 7.04 g. of acetone, 2.00 g. of sodium hydroxide, 10.0 g. of sodium nitrite (containing 1% of sodium nitrate) and 1.66 g. of sodium nitrate in 100 ml. of water was analyzed by the above procedures. The aqueous distillate was found to contain 6.97 g. of acetone (1% low) after concentration. The residue was diluted to 100 ml. with water, and upon titration with hydrochloric acid to the phenolphthalein end-point was found to contain 1.99 g. of sodium hydroxide (0.5% low). One ml. of the solution was treated with 2 ml. of a saturated potassium permanganate solution and 1 ml. of glacial acetic acid and warmed to 60° for five minutes. The excess potassium permanganate was destroyed by the dropwise addition of 30% hydrogen peroxide, the solution boiled for several minutes and cooled to 60°, and 10 ml. of a nitron acetate solution (10 g. of nitron in 100 ml. 5% acetic acid) was added. The nitron nitrate was allowed to crystallize overnight in the dark, and then was filtered and vacuum dried. To 0.6 g. of hydrazine sulfate in 15 ml. of water at 50°, 5 ml. of the stock solution was added slowly with stirring. The solution was gently boiled for two minutes, cooled to 60° and 1 ml. of glacial acetic acid and 10 ml. of nitron reagent added. The results of the two nitrate ion determinations indicated the presence of 10.05 g. of sodium nitrite (0.6% high) and 1.76 g. of sodium nitrate (theoretical).

Identity of the Organic Acid Fraction.—After neutralization of the excess sodium hydroxide by hydrochloric acid and evaporation of the solution to dryness, the sodium salts of the organic acids produced in the oxidation of 2-nitropropane were extracted with ethyl alcohol. Acidification with sulfuric acid followed by distillation resulted in extensive decomposition. When the sodium salts were treated with semicarbazide hydrochloride and acetic acid in aqueous solution, small amounts of the semicarbazone of pyruvic acid (m.p. 211–212°; mixed m.p. with an authentic sample, 211–212°) were formed, together with higher-melting products. Prepared solutions of pyruvic acid and sodium hydroxide indicated that pyruvic acid was unstable under the reaction conditions and that high-melting products could be formed from reaction with semicarbazide. Acidification of the sodium salts of the organic acids with sulfuric acid to a *p*H of 3, followed by extraction with ether, yielded an organic acid fraction whose infrared absorption spectrum was practically identical with that of the acid fraction obtained by the action of an excess of sodium hydroxide on pyruvic acid.

Oxidation of Other Anions.—1-Nitropropane (0.102 mole) absorbed 0.118 mole of oxygen in 24 hours at 25° in an autocatalytic manner in the presence of 0.322 mole of sodium hydroxide (100 ml. of aqueous solution). In 15 hours 90% of the total oxygen had been absorbed. The oxidation product was evaporated to dryness at room temperature. Distillation indicated that only water was present in the volatile fraction. Extraction of the residue with ether gave 1 ml. of unidentified oil. By analysis, the residue was found to contain 0.095 mole of nitrate and nitrite ion. Titration indicated the presence of only 0.094 mole of sodium hydroxide and it thus appears that 0.133 equivalent of organic acid was produced. Treatment with barium hydroxide indicated the presence of only 0.002 mole of carbonate ion. Since the presence of nitrite ion made preparation of derivatives difficult, an aliquot of the residue was neutralized to the phenolphthalein end-point with hydrochloric acid, dried and extracted with 600 ml. of warm absolute ethyl alcohol. Evaporation of the alcohol gave 9.1 g. (cor.) of a solid residue which still contained some nitrite ion. Attempts to prepare derivatives of organic acids present in this residue (as sodium salts) failed.

The oxidation of nitrocyclohexane (0.091 mole) in the presence of 0.204 mole of sodium hydroxide (100 ml. of aqueous solution) was sluggish and lacked sharp autocatalysis. The oxidation was halted after 25 hours at room temperature, during which time 0.046 mole of oxygen had been absorbed. Filtration gave 0.41 g. of water-insoluble material from which 0.24 g. of recrystallized 1,1′-dinitrodicyclohexane (m.p. 218–219°) was obtained. Extraction with ether indicated the presence of unreacted nitrocyclohexane.

In the presence of 0.001 mole of ferric sulfate, 0.095 mole of nitrocyclohexane absorbed 0.091 mole of oxygen in 40 hours at room temperature in the presence of 0.409 mole of sodium hydroxide (100 ml. of aqueous solution). The oxidized solution was extracted with 600 ml. of ether. Distillation of the ether extract gave *ca.* 1 g. of material that was found to contain 0.0103 mole of carbinyl compounds by reaction with hydroxylamine hydrochloride in the presence of pyridine. Upon concentration and cooling, a small amount (< 0.2 g.) of cyclohexanone oxime (m.p. 89–90°) was obtained from the solution used for analysis. From the residue of the distillation of the ethereal extract, 0.2 g. of 1,1′-dinitrodicyclohexane (m.p. 218–219°) was obtained by recrystallization. Analysis of the water soluble products of the oxidation indicated the presence of 0.0865 mole of nitrite ion, the absence of nitrate ion and the presence of 0.067 equivalent of organic acids. When the aqueous solution was acidified with hydrochloric acid and evaporated to dryness, a dark oil soluble in ethyl alcohol was formed. This oil could not be crystallized and attempts to prepare derivatives of organic acids present in this oil failed.

When 11.8 g. of phenylnitromethane (b.p. 106–108° at 8.5 mm.), in the presence of 0.375 mole of sodium hydroxide (100 ml. of aqueous solution), was shaken in an oxygen atmosphere at 25°, no oxygen absorption was noted for 16 hours. Under similar conditions, no oxygen absorption was noted for 5 hours in the presence of 0.01 *M* ferric sulfate.

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(25) J. Schmidt, *Ber.*, **36**, 1775 (1903).

(26) See J. W. Baker and D. M. Easty, *J. Chem. Soc.*, 1193 (1952), for an excellent description of this procedure.

(27) W. M. D. Bryant and D. M. Smith, THIS JOURNAL, **57**, 57 (1935).