Kinetic Features of the Oxidation of Aldehydes, Ketones, and Nitroparaffins with Alkaline Ferricyanide.

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Reaction orders have been determined for the oxidation of three aldehydes, four ketones, and two nitroparaffins by alkaline ferricyanide. Oxidation occurs only after these substances have been converted into the anions of their enolic or aci-forms. The reacting systems do not catalyse vinyl polymerisation and it is concluded that the oxidisable anions form complexes with $[Fe(CN)_6]^{3-}$ and are then attacked by more ferricyanide.

Since the system * Red. + $\{Fe(CN)_6\}^{3-} \rightleftharpoons$ Ox. + $\{Fe(CN)_6\}^{4-}$ involves one-electron transfer, free radicals are probable intermediates in oxidations of organic compounds by potassium ferricyanide, but there is very little experimental evidence that this is indeed the case. Oxidation of phenol by alkaline ferricyanide has been explained on this basis and a coloured free radical has been produced in this way from 2 : 4 : 6-tri-*tert.*-butylphenol (Cook and Woodworth, *J. Amer. Chem. Soc.*, 1953, **75**, 6242). Again, production of the dimer $(Me_2C{\cdot}NO_2)_2$, though only in 6—15% yield, in the oxidation of 2-nitropropane has been ascribed to the formation of a transient radical intermediate (Schlechter and Kaplan, *ibid.*, p. 3980). To obtain more definite information concerning the possible

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* Red. = a reducing agent and Ox. = an oxidising agent, and braces are used to delineate complex ions so as to avoid confusion with the more usual square brackets, which in this paper are required later to denote concentrations.

participation of organic free radicals in oxidations of simple organic compounds by aqueous alkaline ferricyanide we have carried out a kinetic investigation of its oxidising actions on propanal, butanal, and *iso*butanal, on dimethyl, diethyl, di*iso*propyl, and ethyl methyl ketones, and also on nitroethane and 2-nitropropane. From its outcome we have been forced to conclude that though the oxidation proceeds in several consecutive stages the expected *free* radicals of the above-named substances have no independent existence under our experimental conditions. We have found, significantly, that the diagnostic test of catalysis of vinyl polymerisation, which can be exhibited by oxidations of these same compounds with manganic pyrophosphate (Drummond and Waters, *J.*, 1953, 2836). is negative with all the ferricyanide oxidations which we have as yet examined under a nitrogen atmosphere, and the rate of reduction of $\{Fe(CN)_6\}^{3-}$ is not changed by the addition of vinyl cyanide to the reacting mixtures. However, if samples of the butanals which have been distilled in air, and therefore probably contain small amounts of peroxides, are used then some polymerisation of vinyl cyanide does occur at the outset of the reaction, but if, with these aldehydes, the vinyl cyanide is added after enough time has been allowed to permit the alkaline ferricyanide–ferrocyanide mixture to destroy any initial peroxide then there is no polymerisation. The absence of polymerisation cannot therefore be due merely to the use of an alkaline medium.

Very few quantitative studies of oxidations of organic compounds by alkaline ferricyanide have hitherto been made. The ferricyanide method of glucose estimation (Hagedorn and Jensen, *Biochem. Z.*, 1923, **135**, 46), later developed by Hawkins and Van Slyke (*J. Biol. Chem.*, 1929, **81**, 459) and by Hawkins (*ibid.*, 1929, **84**, 69, 78), does not give stoicheiometric end-points and requires careful control of pH, temperature, and reaction time. The volumetric procedure (Lang, *Z. anorg. Chem.*, 1924, **138**, 271) depending on the precipitation of a complex zinc ferrocyanide to complete the reaction

$$2\{Fe(CN)_6\}^{3-} + 2I^- \longrightarrow 2\{Fe(CN)_6\}^{4-} + I_2$$

gave results of poor reproducibility in our hands, probably because atmospheric oxidations could not altogether be prevented. Potentiometric measurements of the change with time of the [Ferricyanide]/[Ferrocyanide] ratio, used by Conant, Aston, and Tongberg (*J. Amer. Chem. Soc.*, 1930, **52**, 407) in an earlier survey of this subject, proved to be more reliable provided that only the initial stages of oxidations were followed and that care was taken both to work in a nitrogen atmosphere and to prevent the occurrence of any of the photochemical reactions of ferri- or ferro-cyanides.

After prolonged reaction some breakdown of both $Fe(CN)_6$ ions occurs and the oxidations do not appear to cease at any definite stage. Several equivalents of ferricyanide can eventually be consumed per mole of organic substance and, in particular, the oxidation of a normal aliphatic aldehyde does not yield merely the corresponding fatty acid. The complicated nature of this oxidation and the fact that aldehydes and ketones behave similarly was first stressed by Conant and Aston (*ibid.*, 1928, **50**, 2783) who from the oxidations of *iso*butanal and methyl *iso*propyl ketone with hot alkaline ferricyanide isolated dihydropyrazine derivatives and suggested that the attack started at the α-CH group of the system $R_2CH{\cdot}CO{\cdot}R'$.

Conant, Aston, and Tongberg (*loc. cit.*), who examined aldehyde oxidation more quantitatively, found that the more alkaline the solution the more rapid was the reaction, and, in accordance with Conant's contemporary views (Conant, *Chem. Reviews*, 1926, **3**, 1; Conant and Pratt, *J. Amer. Chem. Soc.*, 1926, **48**, 3178, 3220) concerning "apparent oxidation potentials," they considered that the initial stage of the oxidation of an organic substance by an electron-abstracting agent might be fast, reversible, and pH dependent; *i.e.*:

$$R\text{-}H - e \rightleftharpoons R\cdot + H^+ \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (1)$$

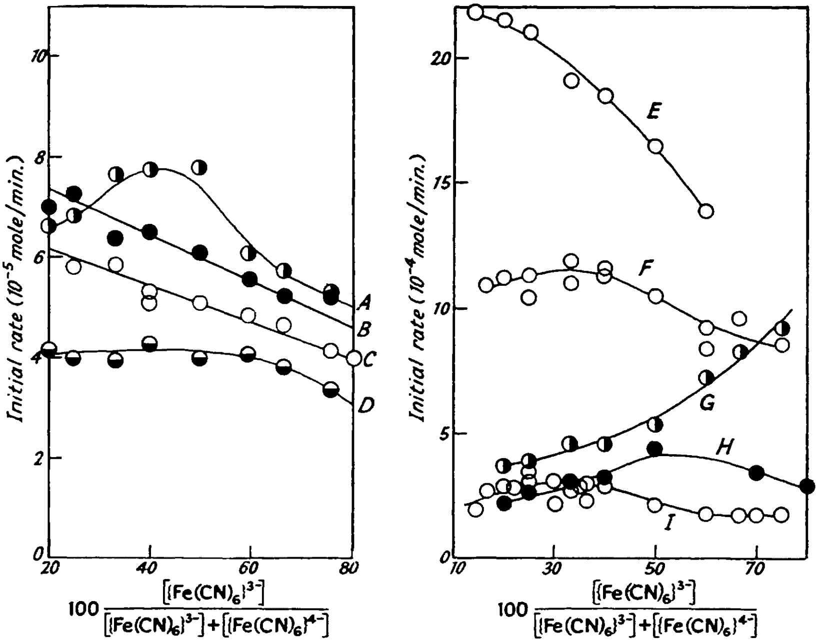
Consequently oxidation of a substance R–H would not be expected to set in until the redox potential of the equilibrium (1) fell below that of the pH-independent ferricyanide–ferrocyanide system. Though Conant, Aston, and Tongberg attempted to find reaction orders they invariably worked with mixtures initially containing equivalent amounts of ferri- and ferro-cyanide, for then, since $\Delta\pi = (\boldsymbol{R}T/\boldsymbol{F})\log(1 + s)/(1 - s)$, the potential drop

($\Delta\pi$) varies linearly with s (the fraction of ferricyanide reduced) for an appreciable portion of the reaction and the potential measurements can very simply be converted into reaction velocity constants. Had they worked with varying initial [Ferricyanide]/[Ferrocyanide] ratios they would have discovered that ferrocyanide anions do not retard the oxidations of aldehydes or ketones, as would be the case if the reaction process had a reversible first stage (1), or better (2):

$$\text{R-H} + \{\text{Fe(CN)}_6\}^{3-} \rightleftharpoons \text{R}\cdot + \text{H}^+ + \text{Fe(CN)}_6^{4-} \quad . \quad . \quad . \quad . \quad . \quad (2)$$

With all our substrates the initial rate of reaction is somewhat dependent upon the [Ferricyanide]/[Ferrocyanide] ratio, as Fig. 1 shows, but the change is usually quite small and may be due to salt effects or complex formation.

FIGS. 1*a and b*. *Variation of the initial oxidation rate with the ratio* $\dfrac{[\{\text{Fe(CN)}_6\}^{3-}]}{[\{\text{Fe(CN)}_6\}^{3-}] + [\{\text{Fe(CN)}_6\}^{4-}]}$



For all Figs: *A*, Propanal. *B*, Di*iso*propyl ketone. *C*, Diethyl ketone. *D*, Ethyl methyl ketone. *E*, Acetone. *F*, *n*-Butanal. *G*, 2-Nitropropane. *H*, *iso*Butanal. *I*, Nitroethane.

For all except Fig. 1, graphs refer to results obtained with equimolar amounts of ferricyanide and ferrocyanide as oxidant.

Except in the case of *n*-butanal, the initial rate of oxidation is proportional to the hydroxyl-ion concentration of the solution (see Fig. 2), whilst in most cases the reaction order with respect to the organic substrate is also unity (see Fig. 3). The reaction order with respect to ferricyanide however is variable. The reaction is of zero order for *iso*butanal, of first order at low concentrations but tending to zero at high concentrations with *n*-butanal and diethyl ketone, and of first order with propanal, ethyl methyl ketone, di*iso*propyl ketone, and 2-nitropropane; with acetone and nitroethane it is of first order at low concentrations of ferricyanide but becomes of second order at higher concentrations (see Fig. 4). Consequently we are dealing with an oxidation in which no single reaction is regularly the rate-controlling process.

The alkali-dependence of the reaction indicates that the oxidised substances are not the aldehydes, ketones, or nitroparaffins themselves but the anions of their enolic or aci-forms. Enolisation prior to oxidation is thought to be necessary for the very similar

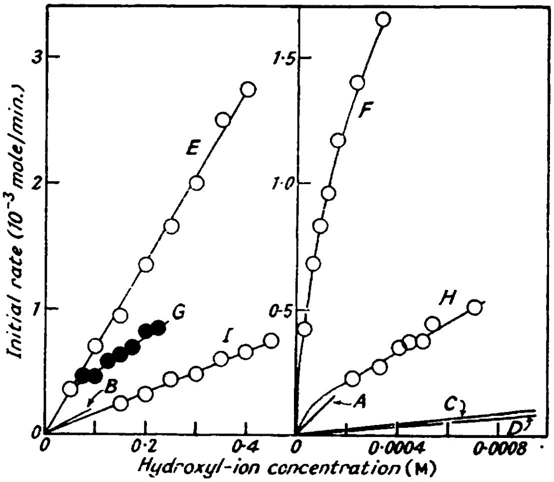


FIG. 2. *Variation of initial oxidation rate with hydroxyl-ion concentration.*

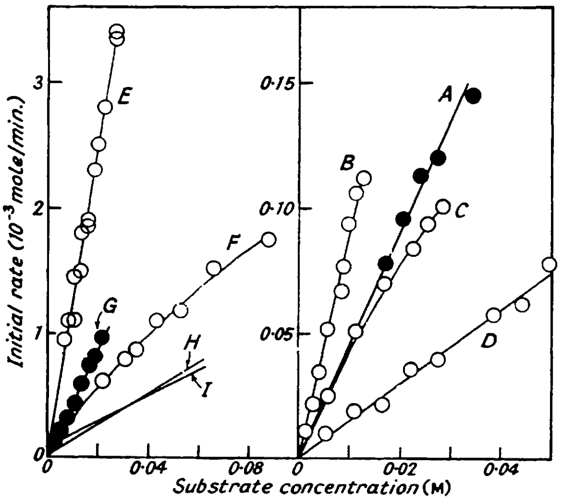
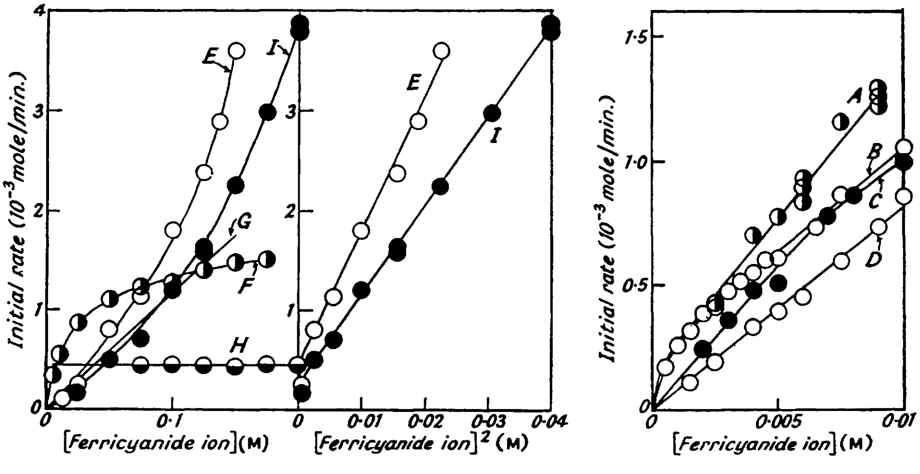
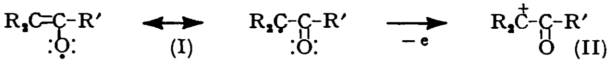


FIG. 3. *Variation of initial oxidation rate with substrate concentration.*

FIGS. 4*a and b. Variation of initial oxidation rate with ferricyanide-ion concentration.*



oxidations of ketones with ceric sulphate (Hinshelwood and Shorter, *J.*, 1950, 3276; Shorter, *J.*, 1950, 3425) and for oxidations of both aldehydes and ketones with manganic pyrophosphate (Drummond and Waters, *J.*, 1950, 3425; 1955, in the press), but was rejected by Conant and Aston (*loc. cit.*) because *inter alia* one-electron abstracting agents do not readily attack olefinic bonds. It may be pointed out however that electron abstraction from the anion of an enol will give a mesomeric radical (I), and thus requires a lower energy increment than electron abstraction from a C–H bond or from the oxygen atom of a simple alkoxide anion. Further electron loss from (I) leads to oxidation at the α-carbon atom of :CH·CO· and not at the ·CHO group of an aldehyde :



$$R_2C{=}\underset{\overset{|}{:\ddot{O}:^{-}}}{C}-R' \longleftrightarrow R_2\dot{C}-\underset{\overset{\|}{:O:}}{C}-R' \;(\mathrm{I}) \xrightarrow{-e} R_2\overset{+}{C}-\underset{\overset{\|}{O}}{C}-R' \;(\mathrm{II})$$

In accordance with this view we have found that benzaldehyde, which cannot enolise, is not oxidised by alkaline ferricyanide and that the oxidation of furfuraldehyde is extremely slow. Formaldehyde too is much less easily oxidised than its homologues (Conant and Aston, *loc. cit.*).

Since no *free* organic radical appears to be formed we suggest that the ferricyanide anion must form a complex with the enolic anion of the substrate and this complex, which could equally well be described as a complex of the mesomeric structure (I) with a ferrocyanide anion, must then be attacked by a second ferricyanide ion (5) or perhaps by a similar complex (6); *i.e.* :

$$\mathrm{R{-}H} + \mathrm{OH^-} \rightleftharpoons \mathrm{R^-} + \mathrm{H_2O} \text{ (enolisation, reversible)} \quad . \quad . \quad . \quad . \quad (3)$$

$$\mathrm{R^-} + \{\mathrm{Fe(CN)_6}\}^{3-} \longrightarrow \text{Complex (X) (possibly reversible)} \quad . \quad . \quad . \quad . \quad (4)$$

$$\mathrm{X} + \{\mathrm{Fe(CN)_6}\}^{3-} \longrightarrow \text{Product} + 2\{\mathrm{Fe(CN)_6}\}^{4-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$2\mathrm{X} \longrightarrow \text{Dimer} + 2\{\mathrm{Fe(CN)_6}\}^{4-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

If the reversible enolisation (3) is much faster than the forward, rate-determining reaction (4), then the total reaction should be of first order with respect to [Substrate], [OH⁻], and [Ferricyanide], but if the enolisation is slower than (4) then the oxidation should be of zero order with respect to [Ferricyanide]. The latter circumstances evidently hold for *iso*butanal, whilst for *n*-butanal reactions (3) and (4) may have comparable speeds. The rates of (OH^-)-catalysed enolisations of acetone (Bell and Longuet-Higgins, *J.*, 1946, 636) and nitroethane (Maron and La Mer, *J. Amer. Chem. Soc.*, 1938, **60**, 2588) have been measured; at comparable concentrations both are much faster than their rates of oxidation as determined by us.

Apparently reactions (5) and perhaps (6) are much faster than (4); although they are bimolecular reactions between similarly charged ions they are probably highly exothermic. However with acetone, and perhaps with nitroethane, reaction (4) may reach an equilibrium so that (5) becomes rate-determining. It may well be that in all these oxidations the reaction orders of the rate-determining processes depend upon the concentration range examined, but for practical reasons we have been unable to vary our conditions very widely. For instance, since aldehydes are much more rapidly oxidised than ketones it has been necessary to work in carbonate buffers, in which slow enolisation is to be expected. Concentrations of substrates are limited on the one hand by their solubility in water and on the other by the need to ensure that only the first stage of the oxidative degradation is being examined.

EXPERIMENTAL

The organic substances were freshly distilled in nitrogen before use; with the aldehydes frequent fractionation was necessary. Solutions were prepared by weight in distilled water that had been flushed thoroughly with oxygen-free nitrogen, and a slow stream of nitrogen was led over the liquid whenever a flask of any solution was unstoppered.

Early reaction velocity measurements were made by adding aliquot portions of reacting mixtures at suitable time intervals to 2N-sulphuric acid to arrest reaction and then titrating the unused ferricyanide by Lang's method (*loc. cit.*). Trouble due to change of end-point with time was experienced with the aldehydes; on the average however the results accorded with the potentiometric measurements sufficiently well to establish that the potential changes of the reacting solutions were indeed due to the reduction of ferricyanide.

Potentiometric measurements were carried out in a wide-mouthed blackened bottle immersed in a thermostat at 25° ± 0·2°. The stopper of the bottle carried a bright platinum electrode, a saturated calomel electrode, a glass stirrer and its bearing, an inlet tube for oxygen-free nitrogen, and a stoppered hole through which known volumes of reagents could be added. Measurements were made with a Tinsley potentiometer (Model No. 3184) and, except in the first 2 min., equilibrium between the solution and the electrodes was rapidly attained. Potentials were measured to 0·2 mv at intervals of 3 min. and plotted against time for 20—30 min. Reaction velocities were computed from these potential–time lines by Conant and Aston's method (*loc. cit.*), reference being made to the appropriate part of an experimentally determined potential curve for ferrocyanide–ferricyanide mixtures of comparable strength.

With the aldehydes in particular, the use of nitrogen was essential. In the presence of air the oxidations appeared to be preceded by an induction period before they set in, in most cases, at the same rate as in de-aerated solutions. This effect, we think, may be due to the presence, or formation, of peroxide which re-oxidises some ferrocyanide to ferricyanide and sometimes caused a slight initial potential increase. In a nitrogen atmosphere the potential drop indicative of oxidation of the organic substance starts immediately and continues at a steady rate until about 0·1 equiv. of the less concentrated reagent has been consumed.

Further to obviate photochemical decompositions (compare Asperger, *Trans. Faraday Soc.*, 1952, **48**, 617, and earlier papers) weighed quantities of pure potassium ferrocyanide and potassium ferricyanide were first dissolved in a known volume of distilled water in a dark bottle under nitrogen. Aliquots of this solution, of the alkaline buffer, and of an aqueous solution of the substrate at the same temperature were mixed, with stirring in a stream of nitrogen, in the reaction vessel, timing of the reaction being made from the instant of last addition. For oxidations of aldehydes carbonate–bicarbonate buffers (*ca.* 0·1M) in the pH range 9—11 were used; with ketones and nitroparaffins, sodium hydroxide solutions had to be used together with much more dilute solutions of the reactants. Values of [OH$^-$] were calculated from pH's measured with a Doran pH meter and an "alkacid" glass electrode, with correspondingly prepared reaction mixtures containing no organic substrate.

Some of our detailed findings are tabulated; see also the Figures.

pH *values for convenient study of the kinetics of oxidation.*

Acetone	13—13·5	Ethyl methyl ketone	10—11
Diethyl ketone	10—11	Di*iso*propyl ketone	12—13
Propanol	9—10	*n*-Butanal	10—10·5
*iso*Butanal	10—11	2-Nitropropane	12·5—13·5
Nitroethane	12·5—13·5		

Extent of possible oxidation : equivalents of ferricyanide consumed per equivalent of substrate after 3 *weeks' reaction at* 25°.

Acetone	13·2	Ethyl methyl ketone	11·0	Diethyl ketone	13·7
Di*iso*propyl ketone	10·7	Propanal	8·0	*n*-Butanal	11·9
*iso*Butanal	12·4	Nitroethane	11·8	2-Nitropropane	20·2

Tests for Free-radical Formation.—With all the substances named, tests for the catalysis of vinyl polymerisation were carried out in evacuated Thunberg tubes (Drummond and Waters, *loc. cit.*); all were negative. With *n*-butanal it was shown that neither vinyl cyanide nor methyl methacrylate affected the oxidation rate. Excess of vinyl acetate, if mixed with the alkaline ferricyanide for 40 min. before addition of the aldehyde, completely stopped its oxidation. Diminutions of rate were also observed with additions of nitrosobenzene (to 50%), ethyl acetate, and vinyl propionate (to 75%), and the reacting solutions then noticeably changed colour when kept. The vinyl esters are not hydrolysed under these conditions since this would have led to acetaldehyde formation and enhanced reduction of the ferricyanide. Since the additions of the above substances to already reacting mixtures caused no immediate change in the rate of potential variation the effects described above may be due to complex formation with the ferricyanide or ferrocyanide (cf. *J.*, 1953, 1041).

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