489. *The Oxidation of Cyclohexanone and Related Compounds by Ferriin.*

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The kinetics and products of the oxidation of cyclohexanone by ferriin [tris-1,10-phenanthrolineiron(III)] have been studied, both in the presence and the absence of oxygen. Evidence from kinetic and tracer studies indicates that the initial rate-limiting step is an electron-transfer from the ketone molecule to the oxidant thereby generating the 2-oxocyclohexyl radical. The rates of oxidation of a variety of other compounds have been measured.

REACTIONS in which organic compounds are oxidised generally involve atom or group transfer processes, and when a transition-metal ion is the oxidant a preliminary step is often the formation of a complex between the reactants.[1] Redox processes involving the simple transfer of an electron between the reagents are well established in the inorganic field,[2] but are thought to occur in the oxidation of organic compounds only (*a*) when the organic product is a particularly stable free radical, *e.g.*, oxidation of quinols,[3] phenols, and aromatic amines,[4] and in some charge-transfer complexes;[5] (*b*) in anodic electrode processes, *e.g.*, Kolbé oxidation;[6] and (*c*) when the organic compound being oxidised is itself a free radical.[7]

Preliminary experiments indicated that the tris-1,10-phenanthrolineiron(III) complex ion (referred to subsequently as ferriin or Fe^{III}) oxidised cyclohexanone rapidly. Since the ligands are resistant to displacement and the ion is known to oxidise inorganic ions by an electron-transfer mechanism[8] this oxidation was selected for detailed study to see whether a similar mechanism is applicable. The series of 1,10-phenanthroline complexes has the additional advantage that their electronic and steric characteristics can be considerably modified by altering the ligand or the metal ion.[8,9]

[1] Littler and Waters, *J.*, 1960, 2767.

[2] Stranks, " Modern Coordination Chemistry," ed. Lewis and Wilkins, Interscience, New York, 1960, p. 186; Halpern, *Quart. Rev.*, 1961, **15**, 207; Halpern and Orgel, *Discuss. Faraday Soc.*, 1960, **29**, 7; Sacher and Laidler, *Trans. Faraday Soc.*, 1963, **59**, 396.

[3] Baxendale, Hardy, and Sutcliffe, *Trans. Faraday Soc.*, 1951, **47**, 963; Baxendale and Hardy, *Trans. Faraday Soc.*, 1954, **50**, 808; Marcus, *J. Chem. Phys.*, 1957, **26**, 872.

[4] Stone and Waters, *Proc. Chem. Soc.*, 1962, 253.

[5] Bose and Labes, *J. Amer. Chem. Soc.*, 1961, **83**, 4505.

[6] Kolthoff and Lingane, " Polarography," Interscience, New York, 1962.

[7] Kochi, *J. Amer. Chem. Soc.*, 1962, **84**, 3271; de la Mare, Kochi, and Rust, *J. Amer. Chem. Soc.*, 1963, **85**, 1437; Collinson, Dainton, Mile, Tazuke, and Smith, *Nature*, 1963, **198**, 26.

[8] Ford-Smith and Sutin, *J. Amer. Chem. Soc.*, 1961, **83**, 1830.

[9] Gordon, Williams, and Sutin, *J. Amer. Chem. Soc.*, 1961, **83**, 2061.
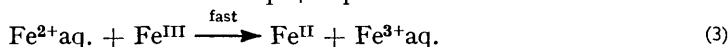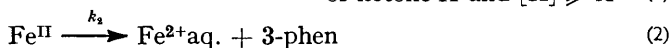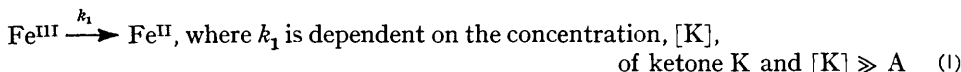
RESULTS AND DISCUSSION

The Oxidation of Cyclohexanone under Nitrogen (Table 1).—In this reaction ferriin is reduced to ferroin, and under the conditions of these experiments both species are unstable. Ferroin [10] is slowly hydrolysed to free Fe^{2+}aq. and 1,10-phenanthroline; and

TABLE 1.

Oxidation of cyclohexanone under nitrogen (see ref. 27).

(*a*) $[H_2SO_4] = 1.50M$, 25°.

10^3[ketone] (M)	2·0	2·5	3·0	2·5
10^4[ferriin] (M)	2·5	2·5	2·5	5·0
*10^3k(sec.$^{-1}$)	0·585	0·70	0·835	0·71
k/[ketone] (l. mole^{-1} sec.$^{-1}$)	0·923	0·280	0·277	0·284

(*b*) [Ferriin] $= 2.0 \times 10^{-3}M$, [ketone] $= 0.01M$, 5°.

$[H_2SO_4]$ (M)	0·00	0·50	1·00	1·50
$[NaHSO_4]$ (M)	1·50	1·00	0·50	0·00
† $[H^+]$ (M)	0·299	0·735	1·166	1·649
10^3k (sec.$^{-1}$)	0·542	0·545	0·512	0·548

(*c*) [Ferriin] $= 2.5 \times 10^{-4}M$, [ketone] $= 2.5 \times 10^{-3}M$, $[H_2SO_4] = 1.50M$, 15°.

	No additive	[1,10-Phen] $= 3.0 \times 10^{-4}M$	$[Fe^{3+}$ aq.] $= 1.3 \times 10^{-4}M$
10^3k (sec.$^{-1}$)	0·320	0·333	0·320

(*d*) [Ferriin] $= 2.5 \times 10^{-4}M$, [ketone] $= 2.5 \times 10^{-3}M$, $[H_2SO_4] = 1.50M$.

Temperature (°K)	278	288	298	308
10^3k	0·16	0·32	0·71	1·41

(*e*) [Ferrin] $= 2.5 \times 10^{-4}M$, [ketone] $= 2.5 \times 10^{-3}M$, $[H_2SO_4] = 1.50M$, 15°.

10^3k_1 (sec.)	protio-ketone	0·334	0·280	0·320	$k_H/k_D = 2.2 \pm 0.2$
	deutero-ketone	0·145	0·150	0·122	

* {d[Fe^{III}]/dt}/[Fe^{III}]. † Calculated by using the value 0·077 for the dissociation constant of the bisulphate ion (see ref. 37).

ferriin [10,11] to a dinuclear complex [12] which does not oxidise cyclohexanone. The rate of hydrolysis of ferroin is comparable with its rate of formation in these reactions, and the hydrolysis product (Fe^{2+}aq.) reduces ferriin rapidly.[8] If A is the concentration of ferriin, and B of ferroin we have:

$$Fe^{III} \xrightarrow{k_1} Fe^{II}, \text{ where } k_1 \text{ is dependent on the concentration, [K],}$$

$$\text{of ketone K and } [K] \gg A \quad (1)$$

$$Fe^{II} \xrightarrow{k_2} Fe^{2+}aq. + 3\text{-phen} \quad (2)$$

$$Fe^{2+}aq. + Fe^{III} \xrightarrow{fast} Fe^{II} + Fe^{3+}aq. \quad (3)$$

giving $dA/dt = -k_1A - k_2B$ and $dB/dt = k_1A$. On solution this gives

$$A = 2k_1A_0 \left[\frac{-1}{\sqrt{(1 - 4k_2/k_1)}} \sinh \frac{k_1t}{2} \sqrt{(1 - 4k_2/k_1)} + \cosh \frac{k_1t}{2} \sqrt{(1 - 4k_2/k_1)} \right] \exp\left(\frac{-k_1t}{2}\right)$$

and

$$B = \frac{2A_0}{\sqrt{(1 - 4k_2/k_1)}} \left[\sinh \frac{k_1t}{2} \sqrt{(1 - 4k_2/k_1)} \right] \exp\left(\frac{-k_1t}{2}\right).$$

or if $k_1 = 4k_2$

$$A = A_0 \left(1 - \frac{k_1t}{2}\right) \exp\left(\frac{-k_1t}{2}\right), \text{ and } B = A_0 k_1t \exp\left(\frac{-k_1t}{2}\right).$$

Also

$$k_1t_{max.} = \frac{2}{\sqrt{(1 - 4k_2/k_1)}} \tanh^{-1} \sqrt{(1 - 4k_2/k_1}$$

[10] Dickens, Basolo, and Neumann, *J. Amer. Chem. Soc.*, 1957, **79**, 1286; Basolo, Hayes, and Neumann, *J. Amer. Chem. Soc.*, 1954, **76**, 3807.
[11] Lee, Kolthoff, and Leussing, *J. Amer. Chem. Soc.*, 1948, **70**, 2348.
[12] Harvey and Manning, *J. Amer. Chem. Soc.*, 1952, **74**, 4744; Anderegg, *Helv. Chim. Acta*, 1962, **45**, 1643.

where $t_{max.}$ is the time at which the maximum concentration ($B_{max.}$) of B occurs, and after which the equations no longer hold, since A = 0. It can also be shown that the error involved in treating the decay of A or the increase of B as if they were simple first-order processes is negligible near the time origin, when k_1 is large relative to k_2, and is greater, at any later time, for A than for B. The experimentally determined k_1 (7×10^{-4} sec.$^{-1}$) and k_2 ($7 \cdot 22 \times 10^{-5}$ sec.$^{-1}$) for a particular experiment, when substituted into the above equations, give rise to a value of $t_{max.}$ in agreement with that observed (3900 sec.), and a value of $B_{max.}/A_0$ of $0 \cdot 829$, in agreement with the observed ratio of $0 \cdot 806$, showing that the extent of conversion of ferriin into ferroin in steps 1 and 2 is 97%, *i.e.*, essentially complete. Since the acidity of the reaction mixture is such that no Fe^{II} can be reformed from Fe^{2+}aq. and 1,10-phenanthroline [11,13] the reduction of Fe^{III} must occur without loss of the ligands. Any reversible dissociation process is also precluded by the inability of free 1,10-phenanthroline or Fe^{3+}aq. to influence the rate of the reaction, which is only dependent on the concentrations of ketone and oxidant.

The observed isotope effect ($k_H/k_D = 2 \cdot 2$ at 15°) is too low to be consistent with an enolisation process ($k_H/k_D = 5 \cdot 15$ at 25°, determined on the same specimens of ketone [14]). In addition the rate of consumption of ketone (assuming a stoicheiometry of $2Fe^{III}$ + ketone $\longrightarrow$ products) was found, at low acidity and 5°, to be $5 \cdot 4 \times 10^{-7}$ moles l.$^{-1}$ sec.$^{-1}$ [Table 1(*b*)]. This is too fast for a preliminary enolisation step to be possible, since in solutions of the same ketone concentration and acidity, the enolisation rate, from iodination, is known to be 9×10^{-7} moles l.$^{-1}$ sec.$^{-1}$ at 25°,[14] and therefore no more than $2 \cdot 25 \times 10^{-7}$ moles l.$^{-1}$ sec.$^{-1}$ at 5°.

The product from the initial step of the oxidation is a free radical which can initiate polymerisation of acrylonitrile, react with oxygen, and be further oxidised to 2-hydroxy-cyclohexanone since this is the least oxidised product. This radical must therefore be the 2-oxocyclohexyl radical, which is also produced by the attack of other one-equivalent oxidants on cyclohexanone.[15] A mixture of the reagents in the proportion 1 of ketone : 2 of Fe^{III} gave the most satisfactory second-order plots, in agreement with the resistance of 2-hydroxycyclohexanone to further attack (Table 3).

The experiments with tritium as tracer show that the first step in the reaction does not involve tritium transfer to the ligand. Although the activity transferred in the first experiment from α-tritiocyclohexanone was comparable with that expected if tritium transfer to the ligand was occurring (reaction 4), this transfer of activity was due in fact to a small percentage (*ca.* 3%) of the labelled 2-oxocyclohexyl radicals adding on to the ligand, *i.e.*, reaction (8) in competition with reaction (6) (cf. ref. 9). When this alkylation reaction (8) was eliminated by increasing the effectiveness of reaction (7) by introducing Fe^{3+}aq. at the start, the activity transferred was less than 0·1% of that expected if reaction (4) occurs. The data are most easily explained if a simple electron transfer takes place (reaction 5). This is consistent with the rather low enthalpy (12 kcal./mole) and unfavourable entropy of activation (−21 e.u.), as compared with, say, the oxidation of cyclohexanone by vanadium(v),[16] which has an almost identical free energy $\Delta G°$ [$\Delta H^{\ddagger} = 18 \cdot 8$ kcal./mole and $\Delta S^{\ddagger} = -13$ e.u. for oxidation by vanadium(v); [17] $k_H/k_D = 5 \cdot 2$ at 15°]. The α-proton of the ketone must then be lost to the solvent, as indicated, to give the stabilised 2-oxocyclohexyl radical; a low isotope effect is not surprising since the degree of interaction between the virtually instantaneous single electron transfer and the slower heterolytic C–H bond fission, with which it is concerted, may well be small. A similar low isotope effect ($k_H/k_D = 1 \cdot 9$ at 25°) has been observed in the oxidation of cyclo-hexanone by cerium(iv) perchlorate,[17] and no isotope effect at all was observed in oxid-

[13] Kolthoff, Leussing, and Lee, *J. Amer. Chem. Soc.*, 1950, **72**, 2173; Irving and Mellor, *J.*, 1955, 3457.
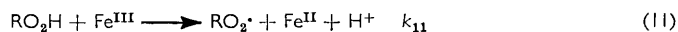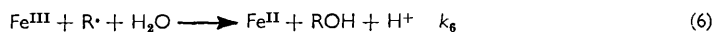[14] Green, Kemp, Littler, and Waters, *J.*, 1964, in the press.
[15] Robertson and Waters, *J.*, 1948, 1574; Drummond and Waters, *J.*, 1955, 497.
[16] Littler and Waters, *J.*, 1959, 3014.
[17] T. J. Kemp, D.Phil. Thesis, Oxford, 1963.

(or at some other position on the ligand) (4)

$$R\cdot + Fe^{III} (phen)_3 + H_2O \longrightarrow ROH + Fe^{II} (phen)_3 + H^+ \qquad (6)$$

$$R\cdot + Fe^{3+} aq + H_2O \longrightarrow ROH + Fe^{2+} aq + H^+ \qquad (7)$$

(8)

ations of ketones by cobalt(III).[18] These reagents also attack the ketonic form of the substrate and may act by an electron-transfer mechanism analogous to that suggested here.

The Oxidation of Cyclohexanone under Oxygen (Table 2).—Oxygen has a profound

TABLE 2.

Ærobic oxidation of cyclohexanone.

(a) $[H_2SO_4] = 1.50M$, 25°.

10^3[ketone] (M)	0.625	1.25	2.00	2.50	3.00	5.0
10^4[ferriin] (M)	2.5	2.5	2.5	2.5	2.5	5.0
$10^3 k$ (sec.$^{-1}$)	0.866	1.57	2.95	3.38	4.35	6.44
k/[ketone] (l. mole^{-1} sec.$^{-1}$)	1.38	1.25	1.48	1.35	1.45	1.29

(b) [Ferriin] $= 2.5 \times 10^{-4}$M, [ketone] $= 2.5 \times 10^{-3}$M, 25°.

$[H_2SO_4]$ (M)	0.00	0.50	1.00	1.50
$[NaHSO_4]$ (M)	1.50	1.00	0.50	0.00
$[H^+]$ (M)	0.299	0.735	1.17	1.65
$10^3 k$ (sec.$^{-1}$)	4.09	3.94	3.77	3.38

(c) [Ferriin] $= 2.5 \times 10^{-4}$M, [ketone] $= 2.5 \times 10^{-3}$M, $[H_2SO_4] = 1.50$M.

Temp. (°K)	278	288	298	308
$10^3 k$ (sec.$^{-1}$)	0.495	1.26	4.05	10.0

(d) [Ferriin] $= 2.5 \times 10^{-4}$M, $[H_2SO_4] = 1.50$M, 25°.

10^3[ketone] (M)	2.0	2.5	3.0
$10^3 k$ (sec.$^{-1}$) { ketone	2.95	3.55, 3.54	4.35, 4.53, 4.47
{ deutero-ketone	0.462	0.55, 0.62	6.82, 7.03, 7.05
k_H/k_D	6.4	6.1	6.4

[18] Littler, *J.*, 1962, 832; Hoare and Waters, *J.*, 1962, 971.

effect on the kinetics of this oxidation, though it is still of first order in both ketone and ferriin. A reaction scheme which can account for the observations is

$$Fe^{III} + K \longrightarrow Fe^{II} + R\cdot + H^+ \qquad k_5 \qquad (5)$$

$$Fe^{III} + R\cdot + H_2O \longrightarrow Fe^{II} + ROH + H^+ \qquad k_6 \qquad (6)$$

$$R\cdot + O_2 \longrightarrow RO_2\cdot \qquad k_9 \qquad (9)$$

$$RO_2\cdot + K \longrightarrow RO_2H + R\cdot \qquad k_{10} \qquad (10)$$

$$RO_2H + Fe^{III} \longrightarrow RO_2\cdot + Fe^{II} + H^+ \qquad k_{11} \qquad (11)$$

$$RO_2\cdot + X \longrightarrow products \qquad k_{12} \qquad (12)$$

Equations (5) and (6) are the same as for reactions under nitrogen, equations (10) and (11) have been previously postulated in oxidation and autoxidation reactions,[15] reaction (11) is analogous to the reaction of ferriin with hydrogen peroxide,[19] and is necessary to account for the accelerated removal of Fe^{III}. Equation (12) represents a variety of reactions which remove the peroxy-radical $RO_2\cdot$. An important case is where $X = Fe^{III}$. Such a reaction is necessary to avoid uncontrolled chain branching *via* reactions 9, 10, and 11, and to compete with reaction 10 so that the effect of isotopic substitution on k_{10}, in which the α-hydrogen atom of the ketone is removed, will be observable. If it is assumed that the concentrations of $R\cdot$, $RO_2\cdot$, and RO_2H are small and constant it can be shown that oxygen accelerates the reduction of ferriin, provided that either $2k_{10}[K] > k_{12}[X]$ or $X \equiv Fe^{III}$; and that one molecule of ketone is oxidised for each two molecules of Fe^{III} reduced, as observed, provided that $k_6[Fe^{III}] > k_9[O_2]$ or that $X \equiv Fe^{III}$. Also k_{11} does not enter the rate equations, so that even though it may be acid-dependent, the overall process is not. The small observed change of rate with acidity can be attributed to specific salt effects,[10,20] as Fe^{III} is sufficiently large and highly charged for ion-pairing to become important. This scheme is also consistent with the observed activation parameters $\Delta H^\ddagger = 16.5$ kcal./mol.; $\Delta S^\ddagger = -2.1$ e.u. and primary isotope effect $k_H/k_D = 6.3$, though these are composite quantities. The products observed are also similar to those observed in previous work on the autoxidation of cyclohexanone.[15,21]

Other Oxidations (Table 3).—It is clear that the relative ease of oxidation of various

TABLE 3.

Comparative oxidations.

[Ferriin] $= 2.5 \times 10^{-4}$M, [H_2SO_4] $= 1.50$M, 25°.

Substrate	[Substrate]M	k' (sec.$^{-1}$)	k'/[Substrate]
Cyclohexane-1,2-dione	0.00438	4.21×10^{-2}	9.61
Phenol	0.00866	1.64×10^{-3}	4.48×10^{-1}
Cyclohexanone	0.00250	7.00×10^{-4}	2.80×10^{-1}
Cyclohexenone	0.01	2.37×10^{-3}	2.37×10^{-1}
2-Hydroxycyclohexanone $\{$	0.00256	1.80×10^{-4}	7.0×10^{-2}
	0.0025	1.65×10^{-4}	6.6×10^{-2} *
Pyruvic acid	0.072	4.78×10^{-4}	6.6×10^{-3}
Biacetyl	0.010	2.1×10^{-4}	2.1×10^{-3}
Acetoin	0.10	1.2×10^{-4}	1.2×10^{-3}
Oxalic acid	0.187	2.3×10^{-4}	1.2×10^{-3}
Ethyl acetoacetate	0.05	3.4×10^{-5}	6.8×10^{-4}
Cyclohexanol	0.10	6.6×10^{-5}	6.6×10^{-4}
Malonic acid	0.10	2.6×10^{-5}	2.6×10^{-4}
Pinacol	0.10	1.2×10^{-5}	1.2×10^{-4}
Mandelic acid	0.10	1.0×10^{-5}	1.0×10^{-4}
Acetaldehyde	0.10	8.1×10^{-6}	8.1×10^{-5}

* All reactions were conducted under nitrogen except this one. Values of k' (the first-order rate constant) lower than 10^{-4} are approximate, because of the decomposition of the ferrin or the ferroin.

[19] Baxendale, *Chem. Soc. Special Publ. No.* 1, 1954, 40.
[20] Schilt, *J. Amer. Chem. Soc.*, 1963, **85**, 904.
[21] Pritzkow, *Ber.*, 1954, **87**, 1668; Mellor, D.Phil. Thesis, Oxford, 1962.

simple compounds is very different from that observed when other one-equivalent oxidants are used. Compounds containing ketone groups are considerably more easily oxidised than those with hydroxyl groups, and compounds which are easily oxidised by, for example, vanadium(v) [22] *via* a chelate complex are much more resistant to oxidation by Fe^{III}, compared with compounds that can only act as monodentate ligands. This may be the result of the increased stability of chelate complexes, and so also, of transition states derived from them. It seems probable, therefore, that this Table gives a true measure of the ease of oxidation of these compounds to free radicals by electron abstraction by ions with which they cannot complex.

EXPERIMENTAL

Materials.—Ferroin perchlorate was prepared from AnalaR 1,10-phenanthroline, and oxidised by technical lead dioxide (AnalaR lead dioxide is ineffective [23]) in dilute sulphuric acid at 0—5°. Perchloric acid was added slowly to precipitate crystalline ferriin perchlorate.[8] When required for kinetic purposes, it was recrystallised from water at 0° by the addition of dilute perchloric acid. The fine, almost black crystals obtained were dried *in vacuo* and stored in the dark.[24]

[2,4,6-$^3H_1$]Cyclohexanone was prepared by hydrogenation of phenol,[25] which had been tritiated by acid-catalysed exchange with tritiated water.[26] It was exchanged under alkaline conditions with a large volume of water,[14,27] and the resulting 4-tritiocyclohexanone was isolated and purified *via* the bisulphite compound.

2-Hydroxycyclohexanone, m. p. 98°, was recrystallised from ethyl acetate, giving a highly crystalline form, not previously recorded, having infrared absorptions at 1690 cm.$^{-1}$ (carbonyl) and 3350—2650 cm.$^{-1}$, very broad (hydrogen bonded −OH), m. p. on rapid heating 167—172°. A sample of this material, after sublimation (140°/10 mm.) had m. p. 101—104°, and its infrared spectrum showed no carbonyl absorption, while the OH absorption centred on 3330 cm.$^{-1}$ was much sharper. Evidently this material is the hemiketal form.[28] The recrystallised material was used for the kinetic studies.

Other substrates listed in Table 3 were recrystallised or distilled before use.

Analysis.—Ferriin could not be estimated iodimetrically, as the amount of iodine liberated from an acidified iodide solution was always less than expected. Instead it was reduced by a known amount of ferrous ammonium sulphate; the resulting ferroin was precipitated as its perchlorate, and the filtrate was titrated with ceric sulphate, a known amount of ferroin being used as indicator. By carrying this out on a small scale, with an Agla micrometer syringe as a burette, it was found that the recrystallised anhydrous ferriin perchlorate was $100 \pm 0.5\%$ pure. The anhydrous material appeared to absorb a little water ($\sim$1 mole) on being kept in air.[29]

Kinetic Methods.—As solutions of ferriin are unstable, a weighed portion of solid was added as the final component of each reaction mixture. The reaction was followed spectrophoto-metrically, usually by use of the increase of the ferroin absorption at 510 mμ,[30] but sometimes the decrease of the ferriin absorption at 607 mμ,[8] for which Beer's law also holds. A Unicam S.P. 500 with a thermostatted cell block was used,[25] and the cell compartment was flushed with dry carbon dioxide when it was necessary to exclude air. Solutions were deoxygenated by passing oxygen-free nitrogen through them for 20 min. As it was impossible to determine directly the optical density at infinite time because of hydrolysis, a sample of each reaction mixture was withdrawn, completely reduced with solid ferrous sulphate, kept on ice, and used as soon as possible for the measurement of the optical density. This value was used to determine the first-order rate constant. The aerobic reactions gave good first-order graphs for the first two half-lives; anaerobic reactions were less satisfactory as hydrolysis was more

[22] Jones and Waters, *J.*, 1963, 352, and earlier Papers.
[23] Salt and Tomlinson, *Chem. and Ind.*, 1961, 549.
[24] Dwyer and McKenzie, *J. Proc. Roy. Soc. New South Wales*, 1947, **81**, 93; Sutin and Gordon, *J. Amer. Chem. Soc.*, 1961, **83**, 70; Glikman and Podlinyaeva, *Ukrain. khim. Zhur.*, 1955, **21**, 211.
[25] Weissman and Schoenheimer, *J. Biol. Chem.*, 1941, **140**, 779.
[26] Koizumi, *Bull. Chem. Soc. Japan*, 1939, **14**, 353.
[27] Best, Littler, and Waters, *J.*, 1962, 822.
[28] Sheehan, O'Neill, and White, *J. Amer. Chem. Soc.*, 1950, **72**, 3376.
[29] Schilt and Taylor, *J. Inorg. and Nuclear Chem.*, 1959, **9**, 211.
[30] Moss, Mellor, and Frederick-Smith, *Ind. Eng. Chem. Analyt. Edn.*, 1942, **14**, 931.

important towards the end of the reaction, and traces of residual oxygen caused an acceleration at the beginning. Even in the most unfavourable cases, however, it was possible to find an intermediate straight portion of the graph which was sufficiently long to give self-consistent and reproducible results.

Product Studies.—(a) *Ketone oxidation products.* In order to minimise the quantity of complex used in product studies, lead dioxide was added to the mixture of ferroin and cyclo-hexanone in sulphuric acid in order to generate and regenerate ferriin *in situ*. The lead dioxide itself causes negligible oxidation of cyclohexanone. For example, dilute sulphuric acid (100 ml.), lead dioxide (2 g.), and ferroin perchlorate (0·1 g.) were cooled to 0—5°, and cyclo-hexanone (2·0 ml.) was added. After the suspension had been stirred for 20 min. at this temperature, it was filtered through a sintered-glass funnel, which was then washed with a little water. The combined filtrate and washings were continuously extracted with ether for 24 hr., the extract was dried, and the ether was removed, leaving a yellow oil. A portion of the ethereal extract was esterified (ethanol–sulphuric acid) and the product was distilled *in vacuo*. The ethereal extract was examined by thin-film chromatography on Kieselgel G (Merck), a 50% v/v mixture of ethyl acetate and light petroleum (b. p. 60—80°) being used as solvent.[21] The plates were developed by spraying them with Brady's reagent. The ethereal extract and the ester mixture were also analysed by vapour-phase chromatography on a column of 10% Apiezon L + 3% glycerol triphosphate, supported on Embacel, at 122°. The following products were obtained, the R_F and retention times being given in parentheses: cyclohexanone (0·9—0·92, 0·9 min.), cyclohexane-1,2-dione [31] (0·5—0·58, 3·6 min.), 2-hydroxycyclohexanone (0·35—0·4), diethyl adipate (18·5 min.); and, from ærobic oxidation only: cyclohexane-1,4-dione (0·17), 4-hydroxycyclohexanone (0·10), and ω-hexanolactone [32] (8·2 min.; ethyl ω-hydroxyhexanoate [33] 12·8 min.). All R_F values and retention times were confirmed by comparison with authentic samples, except for cyclohexane-1,4-dione (lit. value 0·16) [21] and 4-hydroxycyclohexanone (lit. value 0·09).[21] Authentic 2-hydroxycyclohexanone appeared to disproportionate to a mixture of cyclohexanone and cyclohexane-1,2-dione under the v.p.c. conditions. The hydroxycyclohexanones were the most prominent products of experiments of short duration. Prolonged oxidation (2½ hr. at 15°) yielded an extract which contained crystalline material. This was washed with chloroform, sublimed (180°, 1 mm.), and washed again. Its infrared spectrum was identical with that of pure adipic acid, and the m. p. and mixed m. p. (150—151°) confirmed its identity.

(b) *Products from attack on the complex.* After removal of the excess of lead compounds from a reaction conducted as above, the mixture was boiled to hydrolyse all complexes. It was then brought to pH 5 with sodium acetate and the completely re-formed ferroin was extracted with dichloromethane. The extract was reduced to a small volume, and the ferroin precipitated by addition of ether. This process was repeated, and then an aqueous solution of the complex was continuously extracted with ether for 24 hr. The complex was precipitated from water with sodium perchlorate, washed with ether, redissolved in water, and reprecipitated. This process was designed to remove all traces of oxidation products arising from the ketone. When the original mixture had a large ketone : ferroin ratio (*e.g.*, 100 : 1) and the reaction had been carried on for a long time, the recovered complex was not crystalline, and had $\lambda_{max.}$ = 515 mμ (cf. pure ferroin $\lambda_{max.}$ = 510 mμ; *tris*-5-methyl-1,10-phenanthroline ion $\lambda_{max.}$ = 515 mμ [8,33]). The recovered complex also had an infrared spectrum (mull in hexa-chlorobutadiene) showing absorptions due to a carbonyl group (1700 cm.⁻¹), a hydroxyl group (3600 cm.⁻¹), and methylene groups (2900 and 1460 cm.⁻¹), which are absent from the spectrum of ferroin.[32] The complex was destroyed by prolonged alkaline hydrolysis, and the free ligand was extracted continuously with dichloromethane, and examined by thin-film chromatography, 50% v/v methanol–ethyl acetate being used as solvent. The spots were detected by fluorescence under a u.v. lamp, or by developing with a spray of aqueous ferrous ammonium sulphate. Pure 1,10-phenanthroline had an R_F value of 0·4, and there was also present a considerable amount of a second 1,10-phenanthroline, R_F 0·17.

(c) *Tracer studies.* From the mixture resulting from the reaction of 2-tritiocyclohexanone [14] (16 μc; 1 ml.), lead dioxide (2 g.), and ferroin (0·1 g.) in 2N-sulphuric acid (100 ml.) in a blackened flask under nitrogen for 6½ hr. at room temperature, the ferroin was extracted

[31] *Org. Synth.*, 1952, **32**, 35.
[32] Stoll and Rouvé, *Helv. Chim. Acta*, 1935, **18**, 1087.
[33] Robinson and Smith, *J.*, 1937, 371.

and purified as described above. A sample was combusted in oxygen following Dobbs's method,[34] and the resulting radioactive water was absorbed in Hayes's solution [34] (2,5-diphenyl-oxazole, 1,4-di-(5-phenyl-2-oxazolyl)benzene, and naphthalene in dioxan), and the activity was measured using an I.D.L. Coincidence Scintillation Counter 2022, by comparison with a standardised sample of tritiated naphthalene. The observed transfer of activity was 1·4%. After allowance had been made for (*a*) the incompleteness of the oxidation (86% complete if no loss of oxidant), (*b*) the hydrolysis of the oxidant during the reaction (about 25%, calculated from the known hydrolysis rate of ferriin), (*c*) the primary isotope effect (calculated from the measured k_H/k_D, using Swain's relationship [35]), and (*d*) the probable loss of some of the tritium from the ligand [second step of reaction (4)] during subsequent oxidations at the same site on the same ligand, and by assuming $k_H/k_T \simeq 6$,[36] a value of about 2% was calculated on the assumption that the first step of the oxidation involved hydrogen transfer from the ketone to the ligands (reaction 4). However a repeat experiment with 0·60 g. of 4-tritiocyclohexanone (15·3 μc./g.) gave 4·1% transfer of activity, corresponding to the addition of between 2 and 3 2-oxocyclohexyl radicals to each ferroin molecule, or substitution of the ligands by about 3% of the radicals. The lower transfer with α-tritio-ketone may well be due to losses of tritium by enolisation during the separation process. A further experiment was then carried out with a much higher ratio of complex to ketone, so that corrections (*a*), (*b*), and (*d*) above are negligible. An excess of ferric (Fe³⁺aq.) ion was also used to promote reaction (7) in preference to reactions (6) and (8) above. 2-Tritiocyclohexanone (43 μc; 2 ml.) was oxidised with 0·75 g. of ferroin sulphate and lead dioxide for 3 hr. at room temperature. The ligand was isolated and recrystall-ised from water. It was then found, by thin-layer chromatography, to be free from substituted material, and its radioactivity was found to correspond to $5·3 \times 10^{-3}\%$ transfer. The calculated transfer, assuming that reaction (4) occurs, is 7%.

[34] Dobbs, *Analyt. Chem.*, 1963, **35**, 783; Hayes, *Intern. J. Appl. Rad. and Isotopes*, 1956, **1**, 46.
[35] Swain, Stivers, Reuwer, and Schaad, *J. Amer. Chem. Soc.*, 1958, **80**, 5885.
[36] Melander., *Chem. Soc. Special Publn.*, 1962, No. 16, 77.
[37] Ashurst and Higginson, *J.*, 1956, 343.