157. *The Mechanisms of Oxidation of Cyclohexanone under Acid Conditions. Part II.*[1] *One-electron Oxidants.*

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The initial rates of the oxidations of cyclohexanone by vanadium(V), cobalt(III), cerium (IV), and manganese(III) have been studied. Comparative reaction velocities have been measured for cyclohexanone and 2,2,6,6-tetradeuterocyclohexanone in water and in deuterium oxide. It is concluded that these one-equivalent oxidants attack the ketone rather than the enol form of the substrate.

IT has been assumed that oxidations of ketones always take place *via* the enolic tautomer.[2] This conclusion is based almost entirely on evidence that the oxidisable C–H bonds are the same ones as are also easily broken in enolisation. The considerations of the effects of isotopic substitution, both in the ketone and in the solvent, described by Best, Littler, and Waters in a preceding paper,[3] show that it is possible to distinguish between attack by the oxidant directly on the ketone and its attack on the enol even in those systems where the rate of oxidation is not limited by the rate of enolisation. The present paper describes how to apply measurements of solvent and substrate isotope effects to those systems in which the rate of oxidation is of the first order with respect to oxidant concentration. Comparative measurements of the rate of enolisation have also been made, in order to determine whether this is slower than the rate of oxidation, as the observation that an oxidation is faster than enolisation excludes the possibility of attack by oxidant on the enol.

The facts that the rates of these oxidations are of the first order in oxidant and that the enolisation rate of a ketone under the same conditions is independent of oxidant concentration make it necessary to devise a criterion for comparing reaction velocities which will not be invalidated by these differences. The rate of disappearance of ketone at the beginning of a reaction would be a suitable figure for comparison, but it is not independent of ketone concentration or acidity. If this initial rate is divided by the ketone concentration to give k_1, and then by the acidity to give k_2, constants are obtained which are identical with the first-order enolisation constant k_1 and the second-order, catalysed enolisation constant k_2 determined in the preceding paper,[1] if the reaction proceeds at the

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[1] Part I, preceding paper.

[2] Shorter and Hinshelwood, *J.*, 1950, 3276; Shorter, *J.*, 1950, 3425.

[3] Best, Littler, and Waters, *J.*, 1962, 822.

same rate as does enolisation. Values for k_2 have been calculated from the measured values of k', the first-order oxidation constant, by assuming that each mole of ketone consumes two equivalents of oxidant in the rapid initial steps of the reaction, *i.e.*, $n = 2$ (cf. the preceding paper). Since, throughout, the ketone has been used in large excess the subsequent stages of these reactions have no kinetic significance in relation to this work.

RESULTS

(1) The kinetics of the oxidation of cyclohexanone by vanadium(V) perchlorate have been investigated previously and were found to follow the equation[4] $d(V^V)/dt = k[H^+][\text{ketone}][V^V]$.

TABLE 1.

Oxidation by vanadium.

$[V^V] = 0{\cdot}0431$M. $[H^+] = 0{\cdot}38$M (H_2SO_4). [Salt] = 0·46M. 50°.

[Ketone] (M)	Type	Solvent	$10^4k'$ (sec.$^{-1}$)	$10^4k''$ (l. mole^{-1} sec.$^{-1}$)
0·203	H	H_2O	3·79	19·6
0·201 *	H	H_2O	3·73	18·5
0·139	H	D_2O	6·07	43·7
0·177	D	D_2O	1·89	10·7
0·177	D	H_2O	0·759	4·3

$k''_{D_2O}/k''_{H_2O} = 2{\cdot}4$. $k''_H/k''_D = 4{\cdot}2$.

From *, $k_1 = 4{\cdot}0 \times 10^{-5}$ (sec.$^{-1}$) and $k_2 = 10{\cdot}5 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$.

N.B.: In all Tables, k' = first-order rate constant (sec.$^{-1}$), k'' = second-order rate constant (l. mole^{-1} sec.$^{-1}$), D = 2,2,6,6-tetradeuterocyclohexanone, and k_1 and k_2 have the same significance as in Part I but are calculated from the initial rate of consumption of ketone.

Table 1 shows the effect of isotopic replacement on the reaction rate. The equivalent enolisation constant k_2 is $10{\cdot}5 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ at 50°. This is rather lower than the value determined from the mercury(II) oxidation at 25°.[1] The reaction is known[4] to result in oxidation at the α-position.

(2) Cobalt(III) has been used by D. G. Hoare of this Laboratory to oxidise diethyl ketone. The reaction was found to be of first order in ketone, independent of acidity in sulphuric acid at constant bisulphate concentration, and inversely dependent on acidity in perchloric acid.[5] Section (*a*) of Table 2 confirms the finding that the initial reaction is of the first order for cyclohexanone also. The effect of isotopic substitution is shown in section (*b*) for sulphuric acid solution, and in section (*c*) for perchloric acid solution. A similar inverse acid-dependence and a solvent isotope effect of $k_{D_2O}/k_{H_2O} \approx 0{\cdot}5$ are observed in cobalt(II)–cobalt(III) isotopic exchange.[6] The equivalent enolisation constant k_2 is 280×10^{-5} l. mole^{-1} sec.$^{-1}$ in sulphuric acid at 25°, and $9{\cdot}6 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ in perchloric acid at 0·5°. The former is very much greater than k_2 for the mercury(II) oxidation at 25° ($15{\cdot}9 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ and the latter is almost three times as great as the enolisation rate at 10° ($8{\cdot}5 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$).[1]

(3) Ceric sulphate shows an acid dependence [Table 3, section (*a*)] of the form $k = a + b[H^+]$. Section (*b*) shows that the initial reaction is of the first order in ketone; section (*c*) shows the effect of bisulphate ion;[5] and section (*d*) shows the effect of isotopic substitution.

The equivalent enolisation constant k_2 is 17×10^{-5} l. mole^{-1} sec.$^{-1}$ at 25° and $6{\cdot}0 \times 10^{-5}$ at 10°. Ceric perchlorate has been used by Venkatakrishnan and Santappa[7] to oxidise acetone, and a value of $k_2 = 3 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ at 30° can be obtained from the figures that these authors give for oxidation of a 0·1285M-ketone solution. This is to be compared with a value of $4{\cdot}8 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ at 25° from the work of Dawson and Ark[8] (if we assume that the product is monoiodoacetone). Venkatakrishnan and Santappa, however, show that ceric perchlorate and acetone from a complex with a stability constant of 4, which subsequently decomposes to give oxidation products. Other workers[3] have shown that oxidation commences at the position α to the carbonyl group.

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[4] Littler and Waters, *J.*, 1959, 3014.

[5] Hoare and Waters, unpublished work.

[6] Bonner and Hunt, *J. Amer. Chem. Soc.*, 1960, **82**, 3826.

[7] Venkatakrishnan and Santappa, *Z. phys. Chem.* (*Frankfurt*), 1958, **16**, 73.

[8] Dawson and Ark, *J.*, 1911, **99**, 1740.

TABLE 2.

Oxidation by cobalt.

(*a*) $[\mathrm{Co^{III}}] = 9·5 \times 10^{-4}$M. $[\mathrm{H^+}] = 0·21$M (H_2SO_4). [Salt] = 0·25M. 25°.

10^3 [Ketone] (M)	1·89	3·78	5·67	7·56	9·45
$10^4k'$ (sec.$^{-1}$)	23·1	38·5	53·7	78·5	1·0
$10^4k''$ (l. mole^{-1} sec.$^{-1}$)	1·22	1·02	0·95	1·04	1·66

Mean value for $k'' = 1·08$ l. mole^{-1} sec.$^{-1}$.

(*b*) $[\mathrm{Co^{III}}] = 9·5 \times 10^{4}$M. $[\mathrm{H^+}] = 0·21$M (H_2SO_4). [Salt] = 0·25M. 25°.

10^3 [Ketone] (M)	Type	Solvent	$10^4k'$ (sec.$^{-1}$)	k'' (l. mole^{-1} sec.$^{-1}$)
1·84	D	H_2O (90%)	25·3	1·375
1·89	H	D_2O (85%)	25·1	1·33
1·89 •	H	H_2O (100%)	23·1	1·22
1·84	D	D_2O (95%)	26·7	1·45

$k''_{D_2O}/k''_{H_2O} = 1·07$. $k''_{H}/k''_{D} = 0·9$.

From *, $k_1 = 58 \times 10^{-5}$ sec.$^{-1}$, and $k_2 = 280 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$.

(*c*) $[\mathrm{Co^{III}}] = 3·02 \times 10^{-3}$M. $[\mathrm{H^+}] = 0·33$M ($HClO_4$). [Salt] = 0·33M. 0·5°.

[Ketone] (M)	Type	Solvent	$10^4k'$ (sec.$^{-1}$)	$10^4k''$ (l. mole^{-1} sec.$^{-1}$)	
0·198	H	D_2O	11·3	57	} 72
0·192	H	D_2O	16·7	87	
0·187 •	H	H_2O	39·8	159	

$k''_{H_2O}/k''_{D_2O} = 2·2$.

From *, $k_1 = 3·18 \times 10^{-5}$ sec.$^{-1}$, and $k_2 = 9·6 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$.

TABLE 3.

Oxidations by ceric sulphate.

(*a*) $[\mathrm{Ce^{IV}}] = 3·695 \times 10^{-3}$M. [Ketone] = *ca.* 0·035M. [Salt] = 2·24M. 15·2°.

$[\mathrm{H^+}]$ (M)	0·115	0·328	0·540	0·753	0·965	1·178	1·604	1·815
$10^4k'$ (sec.$^{-1}$)	2·45	3·0	3·45	4·25	4·48	5·04	6·4	6·8
$10^4k'$ (calc.)	2·32	2·97	3·52	4·07	4·62	5·17	6·27	6·82

Calc. from $k' = 2·12 \times 10^{-4} + 2·59 \times 10^{-4}\,[\mathrm{H^+}]$ (sec.$^{-1}$).

(*b*) $[\mathrm{Ce^{IV}}] = 3·69 \times 10^{-3}$M. [Salt] = 0·115M. $[\mathrm{H^+}] = 0·115$M. 10·2°.

[Ketone] (M)	0·049	0·098	0·147	0·168
$10^4k'$ (sec.$^{-1}$)	1·96	3·86	6·1	7·7
$10^4k''$ (l. mole^{-1} sec.$^{-1}$)	40·0	39·4	41·5	41·5

Mean value of $k'' = 40·6 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$.

(*c*) $[\mathrm{Ce^{IV}}] = 3·69 \times 10^{-3}$M. $[\mathrm{H^+}] = 0·115$M. [Ketone] = 0·098M. 10·2°.

[Salt] (M)	0·115	1·17	2·02
$10^4k'$ (sec.$^{-1}$)	3·85	3·63	4·18

Hence $k_1 = 0·675 \times 10^{-5}$ sec.$^{-1}$ and $k_2 = 6·0 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$.

(*d*) $[\mathrm{H^+}] = 0·12$M. [Salt] = 0·12M. $[\mathrm{Ce^{IV}}] = 3·88 \times 10^{-3}$M.

Temp.	[Ketone] (M)	Type	Solvent	$10^4k'$	$10^4k''$		
50°	0·193	H	H_2O	62·1	320		$k_{H.H_2O}/k_{D.D_2O} = 4$
50	0·183	D	D_2O	14·6	80		
25	0·184	H	H_2O	18	98	104 •	$k_{D_2O}/k_{H_2O} = 1·3$
25	0·190	H	H_2O	19·9	105		
25	0·195	H	H_2O	21·4	110		
25	0·193	H	D_2O	24·3	126	136	
25	0·191	H	D_2O	28·1	147		
10·8	0·185	H	H_2O	8·80	47·6		$k_H/k_D = 6·0$
10·8	0·0876	H	H_2O	4·24	48·4		
10·8	0·167	D	H_2O	1·20	7·18		
10·8	0·0793	D	H_2O	0·705–	8·88		

• Hence $k_1 = 2·04 \times 10^{-5}$ sec.$^{-1}$ and $k_2 = 17 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ at 25°.

TABLE 4.

Oxidation by manganic sulphate.

(*a*) [Ketone] = 0·0406M. $[H^+]$ = 4·83M. [Salt] = 4·89M. 25°.

$[Mn^{III}]$ (M)	0·015	0·025	0·038
$10^4k'$ (sec.$^{-1}$)	7·65	7·5	7·45 *

From *, $k_1 = 35{\cdot}1 \times 10^{-5}$ sec.$^{-1}$ and $k_2 = 7{\cdot}3 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$.

(*b*) [Ketone] = 0·0406M. [Salt] = $[H^+]$ + 0·34M. $[Mn^{III}]$ = 0·02M. 25°.

$[H^+]$ (M)	4·83	3·92	3·01	2·55	2·10	1·65	1·19
$10^4k'$ (sec.$^{-1}$)	7·95	7·12	7·02	7·5	8·35	9·3	$MnO_2\downarrow$

(*c*) [Ketone] = 0·0406M. $[Mn^{III}]$ = 0·02M. 25°.

$[H^+]$ (M)	4·86	4·38	3·93	3·47	3·02	2·56
[Salt] (M)	4·90	4·87	4·84	4·81	4·78	4·75
$10^4k'$ (sec.$^{-1}$)	7·95	8·18	8·25	7·95	8·07	8·55

(*d*) [Ketone] = 0·0390M. $[H^+]$ = 3·62M. [Salt] = 4·78M. $[Mn^{III}]$ = 0·347M. 25°.
$10^4k'$ (sec.$^{-1}$) = 5·6. Hence $k_1 = 249 \times 10^{-5}$ sec.$^{-1}$ and $k_2 = 69 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$.

(*e*) $[H^+]$ = 4·31M. [Salt] = 4·35M. $[Mn^{III}]$ = 0·014M. 10·8°.

[Ketone] (M)	Type	$10^4k'$ (sec.$^{-1}$)	$10^4k''$	
0·039	H	1·30	33·3	Mean 31·3 × 10^{-4}
0·059	H	2·01	34·1	
0·078	H	2·31	29·6	
0·098	H	3·07	31·3	
0·088	D	0·687	7·7	Mean 7·65 × 10^{-4}
0·067	D	0·51	7·6	

k_H/k_D = 4·1.

(4) Manganese(III), in the form of manganic pyrophosphate, has been found to oxidise cyclohexanone at a rate approaching a limit equal to the rate of iodination under identical conditions (*n* is assumed to be unity for both reactions).[9] However, the nature of the pyrophosphate complex is uncertain and so further experiments have been carried out with manganic sulphate. Table 4, section (*a*), shows that the initial reaction is of the first order in manganese(III); section (*b*) shows that the dependence on sulphuric acid is complex; but section (*c*) shows that at constant bisulphate concentration the reaction is largely independent of acidity. The maximum value of k_2 observed [section (*d*)] is 69×10^{-5} l. mole^{-1} sec.$^{-1}$ at 25°. Section (*e*) shows the effect of isotopic substitution, and also that the reaction is of the first order in cyclohexanone. Drummond and Waters [9] showed that the first product of oxidation of cyclohexanone by manganic pyrophosphate is the acyloin; this is in agreement with our detection of diketone and adipic acid among the products of its oxidation by manganic sulphate.

DISCUSSION

The conclusions of Best, Littler, and Waters [3] can be generalised as:

(i) The solvent isotope effect:

For ketone attack $k_{D_2O}/k_{H_2O} = ca.\ (2{\cdot}5)^x$ (*A*)

For enol attack $k_{D_2O}/k_{H_2O} = ca.\ (2{\cdot}5)^{x+1}$ (*B*)

when $-d[\text{Oxidant}]/dt = k[H^+]^x$.

(ii) The primary isotope effect k_H/k_D is significant only when the ketone is attacked directly, since it may also reflect the rate-controlling influence of the enolisation equilibrium:

$$R{\cdot}CO{\cdot}CD_2R' + H_3O^+ \rightleftharpoons R{\cdot}\overset{OH}{C}{=}CD{\cdot}R' + H_3O^+$$

$K_H/K_D \approx 5$ at 50°

Oxidation by vanadium(V) is always slower than enolisation, but the solvent isotope effect fits equation *A* above ($x = 1$), and not *B*, so it must involve attack on the ketone.

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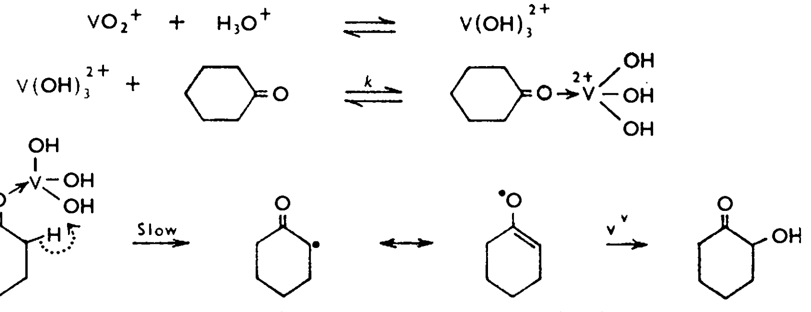
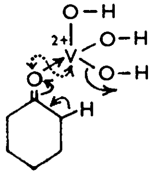
[9] Drummond and Waters, *J.*, 1955, 497.

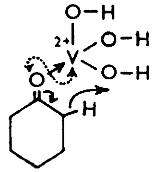
The primary isotope effect shows that the α-C–H bond is broken in the rate-determining step of the oxidation. The following mechanism is consistent with these observations and with the observed kinetics:



This slow step can equally be written as a proton or hydride-ion transfer:



or



whereas abstraction of an acyclic hydrogen atom cannot be written in such alternative ways. Such a cyclic hydrogen transfer would be expected to be favoured energetically over an acyclic mechanism.

Oxidation by cobalt(III) is much faster than enolisation, and also the solvent isotope effect fits equation *A* both in sulphuric acid ($x = 0$) and in perchloric acid ($x = -1$). No primary isotope effect is observed, however, which implies either that the α-C–H bond is not broken, or that if it is broken this stage of the reaction is not rate-determining. The latter situation could occur if the formation of a cobalt–ketone complex is slower than its decomposition by oxidation, and the former if the slow step is an electron-transfer, $Co^{III} + [C_2H]_5C{:}O \longrightarrow Co^{II} + [CH_2]_5C^{+}\text{–}O\cdot$. There is evidence that $Co(H_2O)_6^{3+}$ may be fairly inert to substitution.[10] In either case the active oxidant appears to be $Co(H_2O)_5OH^{2+}$ in perchloric acid, and a sulphate complex in sulphuric acid.

Oxidation by ceric sulphate has been observed to be faster than enolisation. The solvent isotope effect observed can be accounted for by equation *A* above if 20% of the reaction in water goes through the protonated transition state ($x = 1$) and the remaining 80% by the unprotonated route ($x = 0$). The primary isotope effect shows that the C–H bond is broken in the rate-determining step of the oxidation. The data of Venkatakrishnan and Santappa [7] show that a ceric–acetone complex is formed immediately the solutions are mixed, and that the oxidation proceeds through this complex. If it were formed from the enol, as they suggest, the enolisation rate would limit the rate for formation of the complex, and the complex concentration should increase slowly, with a half-life of about 24 min. at 25°. Hence it must be concluded that the complex is formed from the ketone, and that in this system also the oxidation involves direct attack on the ketone. It therefore appears that the style of mechanism written above for oxidation by vanadium(V) is equally applicable to oxidation by cerium(IV) where the oxidant species are $Ce(SO_4)_3^{2-}$, $Ce(SO_4)_2SO_4H^-$, and Ce^{4+} (or $CeOH^{3+}$). *K* is sufficiently large to be kinetically detectable in perchlorate solutions but not in sulphate solutions.

Manganese(III), in the form of a sulphate complex, can also oxidise cyclohexanone at a rate greater than that of enolisation, and the primary isotope effect observed (4·0) is considerably smaller than would be expected if it were due to the enolisation

[10] Friedman, Taube, and Hunt, *J. Chem. Phys.*, 1950, **18**, 759.

pre-equilibrium ($k_H/k_D \approx 8{\cdot}0$ at 10°). It is therefore clear that oxidation by manganic sulphate involves direct attack on the ketone, and that the α-C–H bond is broken in the rate-determining step. A mechanism analogous to that written above for oxidation by vanadium is consistent with these facts and with the observed kinetics.

It is apparent therefore that the enol form does not provide the easiest route for one-electron oxidation of a ketone. This is in agreement with the resistance of olefins to attack by one-electron oxidants. Attack on either ketone or enol would give the same mesomeric free radical; even if these reactions proceed at a comparable rate the much lower (*ca.* 10^{-4}—10^{-5}) concentration of enol than of ketone would ensure that attack on the ketone predominates. The oxygen atom of an enol molecule is less nucleophilic than that of a corresponding ketone molecule, and therefore a substrate–oxidant complex could more easily be formed from the ketonic form. Obviously these arguments do not apply to neutral or alkaline solution where attack on the strongly nucleophilic enolate anion provides an easy route for oxidation by both one- and two-equivalent steps.

EXPERIMENTAL

Kinetic Measurements.—All reactions except that in Table 4 (*d*) were carried out in a total volume of 1 ml. of solution in 2 mm. quartz Unicam cells. Reagents were measured by means of an "Agla" micrometer syringe, or (in the case of the corrosive oxidants) by a glass micropipette. The reactions were followed by the changes in the visible or ultraviolet spectra of the oxidants: For vanadium, increase of VO_2^+ absorption at 750 mμ; [11] cobalt, decrease of Co^{3+} absorption at 260 mμ; [12] cerium, decrease of $Ce(SO_4)^{2-}$ absorption at 380 mμ; [13] manganic, decrease of Mn^{3+} absorption at 510 mμ.[14] A Unicam SP 500 spectrophotometer was used throughout, with an Adkins thermostat-controlled cell-holder for temperatures above ambient, and below ambient a water-cooled cell with a thermostat-controlled water supply and a current of dry air to prevent condensation of moisture. All temperatures were held constant to ±0·2°. The reaction in Table 4 (*d*) was carried out in a total volume of 25 ml. Samples (1·0 ml.) were quenched in aqueous sodium iodide, and the iodine formed was titrated with thiosulphate.

Oxidant Solutions.—In order to avoid the difficulty of making up oxidant solutions in deuterium oxide the stock solution of oxidant usually contained sufficient acid to catalyse the reaction, and was of such a strength as to give a reasonable change of optical density in the course of the reaction when 0·05 ml. of oxidant solution was used in each 1 ml. of reaction mixture. Cerium and vanadium solutions were prepared as described previously.[15] Mr. D. G. Hoare kindly supplied cobaltic solutions which had been prepared by electrolytic oxidation. Manganic sulphate was prepared by adding potassium permanganate to a suspension of manganous sulphate in excess in 6M-sulphuric acid.[14] The visible spectrum of the resulting solution agreed with that reported for manganese(III) and had no trace of the manganese(VII) peaks; [14] the solutions were somewhat unstable and slowly deposited a brown material; they were standardised iodometrically.

Other Materials.—Preparation of cyclohexanone and 2,2,6,6-tetradeuterocyclohexanone has been described.[8] Deuterium oxide was 99·7% pure (from Norske Hydro), and in reactions in which it was used as the solvent it was 95% pure, unless otherwise stated.

Product Study.—The solution remaining after completion of experiment (*d*) of Table 4 was extracted three times with ether. The ethereal solution was dried and evaporated. From 20 mg. of cyclohexanone 12 mg. of a white crystals, insoluble in chloroform, were obtained having m. p. 158° and mixed m. p. 160° with adipic acid. The chloroform washings were warmed with hydroxylamine hydrochloride and sodium acetate; the resulting solution gave a pink colour when tested with nickel nitrate, demonstrating the presence of an α-diketone.

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[11] La Salle and Cobble, *J. Phys. Chem.*, 1955, **59**, 519.

[12] Hargreaves and Sutcliffe, *Trans. Faraday Soc.*, 1955, **51**, 786.

[13] Hargreaves and Sutcliffe, *Trans. Faraday Soc.*, 1955, **51**, 1105.

[14] Drummond and Waters, *J.*, 1953, 435; Selim and Lingane, *Analyt. Chim. Acta*, 1959, **21**, 536; Ubbelohde, *J.*, 1935, 1605.

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