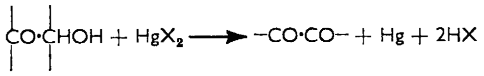
Kinetics and Mechanism of the Oxidation of Acyloins by Mercuric Halides

By Saul Patai and Izhak Shenfeld

The oxidation of acyloins in aqueous or dry pyridine by mercuric halides yields the corresponding diketones and metallic mercury. With benzoin and anisoin the reactions were of the first order, depending on the concentration of the substrate only, but being enhanced by the presence of water (up to 40% v/v) in the solvent. The reaction was followed by measuring volumetrically the amount of mercury deposited. The mechanism of the oxidation is discussed.

DURING an investigation of organic reactions in melts and solids [1] the oxidation of neat acyloins by a variety of mercuric salts was investigated.[2] The oxidation of benzoin in alcoholic solutions by mercuric acetate [3] and of a cyclic acyloin by mercuric perchlorate [4] has been investigated, and in the second reaction precipitation of metallic mercury was observed. In most oxidations by mercuric salts, involving a variety of substrates and solvents, the reaction proceeds as a rule to the mercurous stage only.[3-5] We found that both in the heterogeneous oxidation of acyloins in melts [2] and in the homogeneous oxidation involving the same reactants but in pyridine solvent containing various amounts of water, the reaction gave metallic mercury quantitatively, according to the stoicheiometric equation:



$$\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{O}\cdot\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{HOH} + \mathrm{HgX_2} \longrightarrow -\mathrm{CO}\cdot\mathrm{CO}- + \mathrm{Hg} + 2\mathrm{HX}$$

EXPERIMENTAL

Materials.—Analytical grade mercuric chloride and bromide were used. Commercial pyridine was distilled from KOH, the fraction boiling at 111—112° (at 700 mm.) being used for qualitative experiments. For kinetic runs chromatographic grade pyridine was dried over KOH, distilled and used so, or diluted with distilled water.

All substrates were purified until their physical properties agreed well with those in the literature. Benzoin,[6] furoin,

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[1] Y. Halpern, M. Michman, and S. Patai, *J. Chem. Soc.*, (*B*), 1966, 149.

[2] O. Goldberg, M. Michman, and S. Patai, *Israel J. Chem.*, 1966, in press.

[3] S. Rao and T. R. Seshadsi, *Proc. Indian Acad. Sci.*, 1940, **11***A*, 23.

[4] J. S. Littler, *J. Chem. Soc.*, 1962, 827.

[5] R. Stewart, "Oxidation Mechanisms," W. A. Benjamin Inc., New York, 1964, p. 81.

[6] For references, see R. Adams, ed., "Organic Reactions," John Wiley & Sons, New York, 1948, Vol. IV, p. 300.

butyroin,[7] methyl mandelate,[8] and diphenylmethanol[9] were prepared according to known procedures. Anisoin, pyridoin, acetoin, deoxybenzoin, 1,2-diphenylethane-1,2-diol, 1- and 2-phenylethanol, and L-ascorbic acid were commercial products.

Disproportionation of Mercurous Chloride in Dry or Aqueous Pyridine.—Mercurous chloride becomes black immediately on contact with pyridine. When stirred in cold dry or aqueous pyridine, or more quickly when refluxed in these solvents, it is quantitatively disproportionated to mercuric chloride and mercury. The latter was isolated in 94% yield.

Qualitative experiments.—About 0·01 mole of the substrate to be oxidised and 0·012 mole of $HgCl_2$ were refluxed for 6—25 hr. in 80% pyridine, usually under nitrogen or argon. In all cases when oxidation occurred, the reaction mixture became dark and metallic mercury precipitated. The mercury, collected and weighed, gave as a measure for the yield of oxidation: with acetoin, 40% after 12 hr. (black mixture); with butyroin, 2—3% after 6 hr.; with deoxybenzoin, 2·4% after 25 hr.; with methyl mandelate, 1% after 20 hr.; no precipitation of mercury occurred with 1- and 2-phenylethanol, diphenylmethanol, or 1,2-diphenylethane-1,2-diol.

Reactions in Other Solvents.—Benzoin (0·01 mole) and mercuric chloride (0·022 mole) in 80% acetic acid (150 ml.) after refluxing for 5 hr. gave only a slight precipitate of Hg_2Cl_2. The same amounts of reactants in 50 ml. of dry ethanol refluxed for 20 hr. gave 25% of the theoretical amount of Hg_2Cl_2. L-Ascorbic acid gave 70% yield of mercury after heating with mercuric chloride in 80% pyridine for 5 min. at 80°. The product of oxidation, presumably dehydroascorbic acid, could not be isolated from the basic solution, owing to difficulties described previously.[10]

Preparative Experiments.—(*a*) Mercuric chloride (0·012 mole) and benzoin (0·01 mole) in 40 ml. of dry pyridine, refluxed for 5 hr., gave 70% yield of mercury and about 60% of impure (m. p. 85°) benzil which could be purified only with difficulty, giving about 30—35% of the pure product, m. p. 94° (lit.,[11] 94—95°).

(*b*) Mercuric chloride (0·055 mole) and benzoin (0·05 mole) in 200 ml. of 80% pyridine, refluxed for 6 hr., gave 98·5% yield of mercury. After removal of the mercury, the solvent was evaporated and the residue dissolved in carbon tetrachloride, filtered, and washed with 5% aqueous hydrochloric acid. The solution was dried and evaporated and the residue after one crystallisation from ethanol gave yellow needles of pure benzil (m. p. 94—95°, 85% yield).

(*c*) α-Pyridoin (0·015 mole) and mercuric chloride (0·015 mole) in 150 ml. of 80% pyridine gave, after 10 minutes' heating at 80°, 85% yield of mercury. Worked up as under (*b*) the pyridil was obtained after crystallisation from CCl_4 in 70% yield, m. p. 154—155° (lit.,[12] 155°).

(*d*) Furoin (0·01 mole) and mercuric chloride (0·012 mole) in 50 ml. of 80% pyridine, refluxed for 4 hr. and worked up as under (*b*) but using chloroform instead of carbon tetrachloride, gave 70% yield of mercury and after crystallisation from ethanol, 50% yield of furil, m. p. 165° (lit.,[13] 165°).

Apparatus for Kinetic Runs.—From a 250 ml. Pyrex pear-shaped separating funnel the tap was removed and a U-tube attached. The free upper end of the U was fused to the reaction vessel (see Figure 1). Both branches of the U were made from the same constant-bore capillary tubing (i.d. *ca.* 1·6 mm.), branch *A* being calibrated in mm. A rubber bulb was attached by rubber tubing to end *B*. The whole was submerged in a water thermostat at 80° ± 0·02°.

The vessel was charged with metallic mercury until this filled the curve of the U-tube, then flushed by nitrogen or argon, and two solutions, one containing the substrate and the other the mercuric salt, both at thermostat temperature, were added simultaneously. The vessel was shaken cautiously, and a slight current of the inert gas maintained. The addition of the mixtures had to bring the mercury level within the calibrated range of arm *A*. Mercury started to precipitate after a period; sometimes when falling into the capillary it was broken into drops, but by agitation of the mercury column by use of the rubber bulb the mercury was coagulated into an unbroken column.

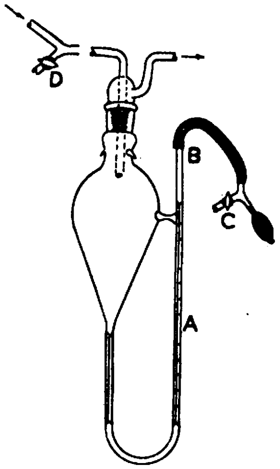

FIGURE 1 Reaction vessel

The height of the mercury in *A* was determined immediately after mixing the reactant ($h = 0$) and h_t (height of the mercury column at time t) was measured every 10—20 min. at the start of the reaction and at longer intervals later. Before each measurement, taps *C* and *D* were opened to equalise pressure.

Calibration.—The vertical displacement of mercury in the measuring arm was calibrated by adding weighed amounts of mercury to the vessel and measuring the height differences. Addition of 0·538 g. of mercury caused a vertical displacement of 1 cm. in the measuring arm (*i.e.*, a total of 2 cm. in both arms). The accuracy is about ±0·3 mm. (0·016 g. of mercury). Hence, when starting with 0·015 mole of each reactants, when 100% reaction would give 3·009 g. of mercury, the error caused by readings of level was about ±0·5%.

Derivation of Rate Equation.—The first-order rate coefficients were determined as follows:

$$kt = \ln \frac{a}{a-x} = \ln \frac{h_\infty - h_0}{h_\infty - h_t} = F \text{ (Figure 2)}$$

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[7] J. M. Snell and S. M. McElvin, *Org. Synth.*, Coll. Vol. 2, 1943, p. 114.

[8] S. F. Acree, *Ber.*, 1904, **37**, 2767.

[9] F. Y. Wiselogle and H. Sonneborn, *Org. Synth.*, Coll. Vol. 1, 1941, p. 90.

[10] J. Kenyon and N. Munro, *J. Chem. Soc.*, 1948, 158.

[11] H. T. Clarke and E. E. Dreger, *Org. Synth.*, Coll. Vol. 1, 1941, p. 88.

[12] W. Mathes, W. Sauermilch, and T. Klein, *Ber.*, 1951, **84**, 452.

[13] W. W. Hartman and J. B. Dickey, *J. Amer. Chem. Soc.*, 1933, **55**, 1228.

h_∞ could be calculated from the amount of mercury expected, and was in several cases, especially in comparatively fast runs, also obtained experimentally in good agreement with the calculated value.

RESULTS

(1) Oxidation of aliphatic acyloins as well as of methyl mandelate and of deoxybenzoin by mercuric chloride in 80% pyridine–water at reflux is slow and gives only low yields. Primary and secondary alcohols not containing an α-keto-group *e.g.*, diphenylmethanol, 1- and 2-phenylethanol, and 1,2-diphenylethane-1,2-diol do not react at all.

Sample run (no. 10 of Table 2): benzoin (0·075M) $+HgCl_2$ (0·075M) in 60% pyridine, 200 ml. of solution at 80°

t (min.)*	h_t(cm.)	$\ln\left(\frac{h_\infty}{h_\infty - h_t}\right)$	10^5k (sec.$^{-1}$)†
0	0·00	0·000	—
4	0·20	0·016	15·30
7	0·35	0·028	15·35
17	0·85	0·072	16·20
29	1·30	0·115	15·20
33	1·40	0·125	14·50
35	1·50	0·135	14·75
43	1·70	0·154	13·70
57	2·15	0·210	14·10
63	2·35	0·236	14·35
78	2·70	0·285	14·00
96	3·15	0·359	14·30
105	3·30	0·385	14·05
114	3·50	0·426	14·30
122	3·65	0·458	14·40
135	3·90	0·517	14·65
146	4·05	0·558	14·65
160	4·20	0·602	14·40
168	4·35	0·651	14·85
183	4·50	0·707	14·80
204	4·70	0·793	14·90
215	4·80	0·845	15·05
234	4·90	0·903	14·80
257	5·00	0·969	14·40
274	5·10	1·045	14·60
309	5·20	1·146	14·20
∞	5·60 (calc.)	—	—

* The value of t was corrected, by subtracting the induction period of 6 min. from the actual readings (see Figure 2).

† k (average of all values given in the Table: $14{\cdot}63 \times 10^{-5}$ sec.$^{-1}$. k, calculated from the slope of line of $\ln\left(\frac{h_\infty}{h_\infty - h_t}\right)$ against t in Figure 2: $14{\cdot}90 \times 10^{-5}$ sec.$^{-1}$.

TABLE 1

Overall first-order rate coefficients of the oxidation of benzoin and anisoin at 80° in 80% pyridine–water

Run	Acyloin (mole l.$^{-1}$)*	Oxidant (mole l.$^{-1}$)*	10^5k (sec.$^{-1}$)
1	Benzoin (0·150)	$HgCl_2$(0·150)	9·27
2	Benzoin(0·150)	$HgCl_2$(0·075)	9·55
3	Benzoin(0·075)	$HgCl_2$(0·150)	8·78
4	Benzoin(0·100)	$HgBr_2$(0·100)	9·48
5	Benzoin(0·100)	$HgBr_2$(0·133)	8·86
6	Anisoin(0·100)	$HgCl_2$(0·100)	1·34

* Concentration at 25° c.

(2) The kinetics of the reactions with benzoin and with anisoin are of first order in the substrate and zero order in the oxidant. (3) In identical experimental conditions (80% pyridine, 80°) the first-order rate coefficient with anisoin is only one tenth that for reaction with benzoin. With α-pyridoin the reaction is practically instantaneous and nearly quantitative (85% reaction in about 1 min.), and similarly with L-ascorbic acid (70% reaction in 5 min.). (4) Mercuric chloride and bromide give nearly identical reaction rates with benzoin (cf. Table 1, runs no. 1, 2, and 3 on one hand with 4 and 5 on the other). (5) The first-order rate coefficients obtained with benzoin are linearly proportional to the concentration of water in solvents containing between 100 and 60% pyridine. At higher water concentrations no experiments could be carried out, since although mercuric halides are soluble both in pyridine and in water, in mixtures containing more than 40% water precipitation of a solid (probably the pyridine–mercuric halide complex) occurred when the boiling solution was cooled to the reaction temperature. The rates followed the equation

$$\frac{d[\text{Benzoin}]}{dt} = (k_1 + k_2[H_2O])[\text{Benzoin}] \qquad (1)$$

where k_1 is the rate coefficient in dry pyridine and k_2 is the rate coefficient for the water-promoted reaction. (6) An induction period was observed; this is very short in the faster runs and becomes more pronounced in the slower ones (Figure 2). (7) Initially added hydrochloric acid had a pronounced inhibiting effect on the reaction in 90·5% pyridine (run 11, Table 2). When the amount of HCl added was one and a half times the equivalent amount of $HgCl_2$ used, the observed rate coefficient was $1{\cdot}39 \times 10^{-5}$ sec.$^{-1}$, in contrast to $5{\cdot}31 \times 10^{-5}$ sec.$^{-1}$ under the same conditions in the absence of initially added acid. On the other hand, in 70% pyridine, addition of HCl to the reaction mixture did not inhibit the reaction at all, but gave a very slight acceleration.

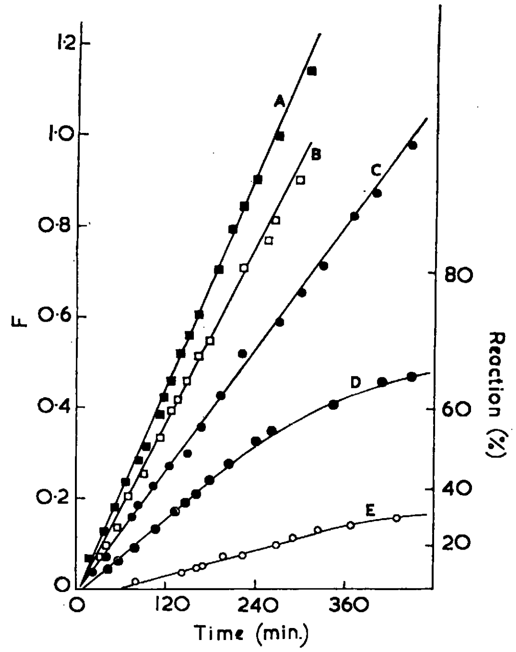


FIGURE 2 Kinetic curves showing the oxidation of benzoin by mercuric chloride at 80° in various solvents: *A*, 100% pyridine (run no. 7); *B*, 90% pyridine + 10% water (run no. 8); *C*, 80% pyridine + 20% water (run no. 1); *D*, 70% pyridine + 30% water (run no. 9); *E*, 60% pyridine + 40% water (run no. 10). (For clarity, only some of the experimental points are drawn)

$$F = \ln\frac{h_\infty - h_\infty}{h_\infty - h_t}$$

TABLE 2

Effect of additives (water and HCl) on the rates of oxidation of benzoin by mercuric chloride in pyridine at 80°

Run	Benzoin* (mole l.$^{-1}$)*	$HgCl_2$ (mole l.$^{-1}$)	Additive*	$10^5 k_{exp.}$ (sec.$^{-1}$)	$10^5 k_2$† (sec.$^{-1}$ mole^{-1})
7	0·100	0·100	none	1·92	—
8	0·100	0·100	H_2O, 5·55 mole l.$^{-1}$(10%)	5·31	0·61
1, 2, 3	(aver.)		H_2O, 11·10 mole l.$^{-1}$(20%)	9·20	0·65
9	0·075	0·075	H_2O, 16·65 mole l.$^{-1}$(30%)	12·60	0·64
10	0·075	0·075	H_2O, 22·20 mole l.$^{-1}$(40%)	14·90	0·67
11	0·100	0·100	H_2O, 5·27 mole l.$^{-1}$ (9·5%) +HCl, 0·3 mole l.$^{-1}$	1·39	—
12	0·075	0·075	H_2O, 16·65 mole l.$^{-1}$(30%) +HCl, 0·225 mole l.$^{-1}$	13·50	—

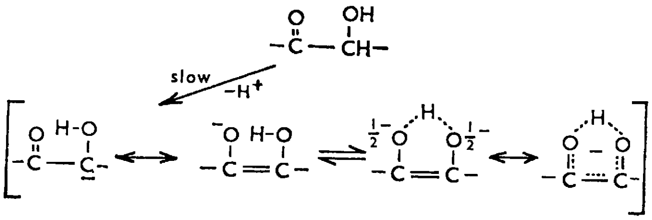
* Concentration at 25° c.

† Calculated from the equation $k_{exp.} = k_1 + k_2 (H_2O]$ using the value $k_1 = 1{\cdot}92 \times 10^{-5}$ sec.$^{-1}$ (run No. 7) in all calculations.

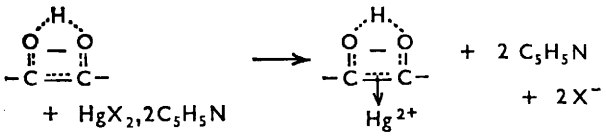
DISCUSSION

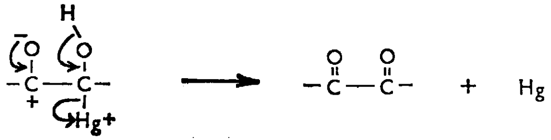
The experimental results allow us to obtain a fairly good picture of the oxidation. The first-order dependence of the rates on the acyloin concentration and the zero-order found in the oxidant indicate that the rate-determining step involves a unimolecular change of substrate. The most obvious hypothesis is a rate-determinating enolisation of the substrate, and fast attack of the mercuric salt on the enediol. Various additional experimental results support this: the rate is lowered by an electron-donating substituent (with anisoin it is much slower than with benzoin). Moreover, high mobility of the α-hydrogen atom involved in the enolisation is an essential feature; for instance, oxidation is much slower with aliphatic acyloins where, in the absence of the electron-attracting aromatic nucleus, the mobility of the α-hydrogen atom is smaller. Non-enolisable systems like primary and secondary alcohols or the diol, hydrobenzoin, did not react, while deoxybenzoin or methyl mandelate with a much lower tendency for enolisation, reacted very slowly. On the other hand, pyridoin which is known from spectroscopy and other data to exist in CCl_4 solution almost completely in the *trans*-enediol form, owing to intramolecular hydrogen bonding with the ring nitrogen atom,[14] gave in our conditions an almost instantaneous reaction. Similarly, L-ascorbic acid, which has an enediol group, gave a very fast reaction with mercuric chloride, showing that the enediol group is oxidised easily even in the absence of flanking aromatic groups.

Hence we believe that the enediol or enediolate forms are responsible for the ease of oxidation by mercuric salts, and their formation is the rate-determining step. The presence of the double bond between the two carbon atoms involved in the reaction seems essential. It may be that this double bond is the actual site of the electrophilic attack by mercuric ions. Moreover, the enediol group is strongly acidic, and the ease of formation (especially in a basic solvent) of an exceptionally symmetrical and stable enediolate anion will make this a feasible reaction route:



The electrophilic attack by the mercuric halide–pyridine complex $HgX_2,2C_5H_5N$ [15-17] on the enolic double bond is probably analogous to the electrophilic aromatic mercuration [4,18] during which the more nucleophilic hydrogen-bonded cyclic enediolate entity displaces the pyridine molecules from the mercuric complex. The reaction will then proceed probably through a short-lived sigma-complex intermediate, which by elimination of H^+ and of Hg° is converted into the stable diketone.





The overall reaction as described is a two-electron (" heterolytic ") oxidation of an α-hydroxyketo-group by a mercuric salt, to form an α-diketone. In these oxidations, as a rule, mercurous salts precipitate [4,19-22] as determined by the fast equilibrium: [20]

$$Hg^\circ + Hg^{2+} \rightleftharpoons Hg_2{}^{2+}$$

When in aqueous solutions, precipitation of mercurous salts displaces the equilibrium to the right-hand side. In our reaction conditions, however, metallic mercury precipitates, owing to the strong complexing of the mercuric ions by pyridine, displacing the equilibrium to the left-hand side and enabling the formation and precipitation of free mercury.[20] The governing role of the stability of pyridine–mercuric complexes is well demonstrated by the fast disproportionation of mercurous chloride in dry or aqueous pyridine to give Hg° and Hg^{2+} (see Experimental section).

We believe that the induction periods observed are due

[14] For references see E. H. Rodd, " Chemistry of Carbon Compounds," Elsevier Publishing Co., New York, 1957, Vol. IVA, pp. 555—556.

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[19] G. H. Linhart and E. Q. Adams, *J. Amer. Chem. Soc.*, 1917, **39**, 948.

[20] A. M. Armstrong and J. Halpren, *Canad. J. Chem.*, 1957, **35**, 1020.

[21] R. L. Wolfgang and R. W. Dodson, *J. Phys. Chem.*, 1952, **56**, 872.

[22] J. G. Korinek and J. Halpren, *J. Phys. Chem.*, 1956, **60**, 285; *Canad. J. Chem.*, 1956, **34**, 1372.

either to physical effects, *e.g.*, to delayed nucleation of the mercury and/or to a small amount of residual dissolved oxygen. In the faster runs, precipitation of mercury is measurable after 6—10 min., and in the slower ones after up to 1 hr. Since the reaction curves conformed well to first-order kinetics, the induction period did not interfere with the kinetic calculations.

Medium Effects.—At least two effects may act additively enhancing the reaction rates on addition of water to pyridine: (*a*) The more water the solvent contains, the higher its dielectric constant, tending to stabilise charged intermediates; and (*b*) the presence of water produces hydroxyl ions in the medium, according to the equilibrium:

$$C_5H_5N + H_2O \rightleftharpoons C_5H_5\overset{+}{N}H + \overset{-}{O}H$$

Hence, the enolisation, which in the absence of water is catalysed only by pyridine molecules, will in the presence of water be enhanced by the more nucleophilic hydroxyl ions. There is no simple way to determine the relative importance of the role of the nucleophilic species present in solution (water, pyridine, and hydroxyl) and the linear dependency of the overall rate coefficients on the concentration of water may be fortuitous.

Figure 2 shows that the plot of $-\log (h_\infty - h_t)/(h_\infty - h_0)$ against time is straight for further in the reaction when more water is present. We interpret this as due to the better buffering ability of aqueous than dry pyridine; the acid formed during oxidation will inhibit the enolisation less, the more water is present. In dry pyridine the inhibition is conspicuous already after 25—30% reaction, while in 60% pyridine–water the curve is linear almost to completion.

In order to test this assumption we made experiments with initially added hydrochloric acid (runs 11, 12; Table 2). Indeed, in 90·5% pyridine (run 11) the measured rate coefficient was less than one-third that in the parallel run without acid (run 8), though in 70% pyridine the addition of hydrochloric acid had practically no effect, even giving a slight acceleration (which could be ascribed to a salt effect) but certainly no inhibition (runs 12 and 9; Table 2).

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