for fifteen minutes gave 40.7 cc. of gas (measured under standard conditions). This is equivalent to 1.43 so-called "active hydrogens."

With pentabromo-nitrobenzene, 0.2552 g. of the compound when heated with methylmagnesium iodide at 70° for one and one-half hours gave 10.95 cc. of gas[6] (measured under standard conditions). This is equivalent to 0.99 so-called "active hydrogens." By way of reference, mention should be made of an experiment with pentabromobenzene, C_6HBr_5. When 0.2763 g. of this compound was heated at 70° for one-half hour, 0.35 cc. of gas was evolved. This is equivalent to 0.027 so-called "active hydrogens," and is within experimental error.

The pentabromo-nitrobenzene was prepared by the following reactions. First, *p*-nitro-aniline was brominated to 2,6-dibromo-4-nitro-aniline.[7] This was then diazotized and the amino group replaced by hydrogen to give 3,5-dibromonitrobenzene,[7] which was then reduced to 3,5-dibromo-aniline.[8] Bromination of the 3,5-dibromoaniline gave the pentabromo-aniline,[9] from which the amino group was replaced by hydrogen by means of the diazo reaction to give pentabromobenzene.[10] The pentabromobenzene when nitrated gave the desired pentabromo-nitrobenzene, which melted at 230°. The melting point of our pentabromobenzene was 158–159°.

Summary

The interference of the nitro group in the Zerewitinoff method for the quantitative estimation of active hydrogen is an inherent property of the nitro group because gas is evolved from compounds such as tetranitromethane and pentabromo-nitrobenzene which contain no hydrogen.

AMES, IOWA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

THE IRREVERSIBLE OXIDATION OF ORGANIC COMPOUNDS. IV.[1] THE OXIDATION OF ALDEHYDES

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The first two papers of this series[2] were concerned with the rate of oxidation of phenols and enols by strictly reversible oxidizing agents such as potassium ferricyanide. It was found that the speed of these irreversible oxidations was a function of the oxidation potential of the reagent and that the results could be formulated in terms of "apparent oxidation potentials."

In attempting to extend our methods to the study of the oxidation of aldehydes, we encountered surprising complications. A qualitative study[1]

[6] Some halogen-nitro compounds like bromopicrin, when treated with methylmagnesium iodide evolve a mixture of gases, a part of which is methyl bromide.

[7] Meyer, Meyer and Taeger, *Ber.*, **53**, 2041 (1920).

[8] Holleman, *Rec. trav. chim.*, **25**, 194 (1906).

[9] Hantzsch and Smythe, *Ber.*, **33**, 520 (1900).

[10] Jacobson and Loeb, *ibid.*, **33**, 703 (1900).

[1] The third paper of this series was published in THIS JOURNAL, **50**, 2783 (1928), under the title "Certain New Oxidation Reactions of Aldehydes."

[2] Conant and Pratt, *ibid.*, **48**, 3178, 3220 (1926).

of the action of a number of reversible oxidizing agents on aldehydes showed that the oxidation products were rarely the expected acids. Instead, the products were usually the result of a process of alpha oxidation, particularly if the reaction was carried out in a very dilute solution. For example, if ceric sulfate in sulfuric acid is employed, *iso*butyraldehyde is oxidized to the α-hydroxy-aldehyde; the same aldehyde with potassium ferricyanide in alkaline solutions yields a dihydropyrazine, presumably through the intermediate formation of an α-amino aldehyde, some of the nitrogen of the complex cyanide being transferred to the organic molecule. In the concluding portion of this present paper we are able to present conclusive evidence that α-amino compounds are formed by the oxidizing action of alkaline ferricyanide at elevated temperatures.

In spite of the complexity of the situation as revealed by the qualitative results, a quantitative study of the rates of oxidation has yielded quite definite results of considerable interest. Our electrochemical method of studying the rate of oxidation has been applied to the oxidation at 80° of a variety of aldehydes in acid solution using ceric sulfate and in alkaline or neutral solution using molybdicyanide, tungsticyanide and ferricyanide. On the whole, the results obtained with acid solutions and with alkaline solutions are consistent with the qualitative information, which showed that the primary reaction was the same under both sets of conditions and involved two equivalents of oxidizing reagent. In the following presentation of the quantitative results which we have obtained in the course of the last three years, we shall purposely avoid a detailed mathematical treatment of the data. Considering the complexity of the reaction which we are measuring, we can only hope to outline a first approximation to the final quantitative formulation.

The Rate of Oxidation in Acid Solution.—Since the object of this entire investigation was to examine the relationship between the rate of oxidation and the oxidation–reduction potential of the reagent employed, only those reagents could be used which are strictly reversible[3] and whose oxidation–reduction potential can be measured. Furthermore, since our experimental method of determining the rate of the reaction consists in noting the change of potential of the oxidizing mixture, only those reversible systems could be employed with which electrode equilibrium is established rapidly.

The ceric ion appears to be the only oxidizing agent which meets these specifications and which attacks aldehydes in acid solution at 80° at a measurable rate. The ferric ion and reagents of lower oxidizing potential are without effect; the action of the chromate ion is very slow and the system CrO_4^{--}–Cr^{+++} is not rapidly reversible. The action of potassium permanganate is too rapid and, as will be shown elsewhere, this reagent has

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[3] Conant, *Chem. Reviews*, **3,** 1 (1926).

peculiarities of its own. The thallic–thallous system has a potential of 1.20 volts at 80° in 1 N sulfuric acid as compared with 1.42 for the ceric–cerous system and 0.71 for the ferrous–ferric. It would thus seem at first sight that the thallic ion would be a reversible oxidizing agent suitable for our study, particularly as acetaldehyde reduces it at 80° in 1 N sulfuric acid. Investigation, however, proved that the system was not rapidly reversible. Thus, although the ferric–ferrous system is 500 millivolts lower in potential, it takes more than a minute for an excess of thallic sulfate to oxidize ferrous sulfate in dilute solution to a point where ferrous ions can no longer be detected with ferricyanide. Similarly the characteristic yellow color of ceric sulfate is not discharged by an excess of thallous sulfate even on long standing, although there is a difference of about 200 millivolts representing the driving force of the reaction. The thallous–thallic system is clearly not sufficiently mobile to be of service. We were, therefore, confined to the use of one reagent, ceric sulfate.

The results obtained with ceric sulfate are summarized in Tables I and II. The apparatus and procedure were identical with those used in our previous work. The essential experimental facts are given in the footnote to Table I. The fraction of ceric sulfate (S) reduced at a given time was calculated from the change in potential (ΔE) of the electrode immersed in the reaction mixture, an equimolecular mixture of cerous and ceric sulfate being used in every experiment. The validity of this

$$\Delta E = 0.000198\, T \log \frac{1+S}{1-S} \qquad (1)$$

calculation was tested by adding definite amounts of ferrous sulfate solution to an equimolecular mixture of cerous and ceric sulfates. Each increment of ferrous ion produced a practically instantaneous drop in potential which corresponded within the experimental error of 1 millivolt to the change of potential calculated from Equation 1.

TABLE I

RATE OF OXIDATION OF ALDEHYDES AND GLUCOSE AT 80° IN 1 N SULFURIC ACID WITH CERIC SULFATE ($E_0' = 1.424$, P_H, 0.37)

Concn. of reagent, moles, /liter $\times 10^3$	Subs. oxidized	Concn. moles /liter $\times 10^3$	Fraction (S) of reagent reduced in, minutes				$k \times 10^2$ Calcd. from S at, minutes				Average
			3	5	8	15	3	5	8	15	
2	Acetaldehyde	2	0.30	0.47	0.70	..	11.9	12.6	15.0	..	13.17
0.2	Acetaldehyde	0.2	.11	.21	.31	0.52	3.9	4.7	4.6	4.9	4.50
9.5	Acetaldehyde	9.5	.31	.53	.88	..	12.3	15.1	..	..	13.70
2	Propionaldehyde	2	.63	..	..	..	33.2	..	..	..	33.2
0.2	Propionaldehyde	0.2	.49	.76	..	..	22.4	28.5	..	..	25.4
2	*n*-Butyraldehyde	2	.50	.72	..	..	23.2	25.4	..	..	24.3
0.2	*n*-Butyraldehyde	0.2	.33	.54	..	..	13.4	15.5	..	..	14.5
2	*Iso*butyraldehyde	2	.83	..	..	..	59.0	..	..	..	59.0
2	Glucose	2	.24	.41	.61	.88	9.2	10.5	11.7	14.4	11.4
0.2	Glucose	0.2	..	..	.09	.18	..	..	1.2	1.3	1.25

NOTE.—In each experiment 100 cc. of 1 N sulfuric acid was placed in the cell and such amounts of ceric and cerous sulfate added (as 0.2 M solutions) as necessary to make an equimolecular mixture with the concentration of *ceric* ion given in Col. 1. The ceric sulfate was prepared by electrolytic oxidation of cerous sulfate and the concentration was determined by electrometric titration with ferrous ammonium sulfate. The temperature was 80 ± 0.5°. The aldehyde was added in a 0.2 M water solution in such amounts as to give the concentration noted in Col. 3; the time was recorded with a stop-watch. The potentials of the bright platinum electrodes (two were employed) were measured against a saturated calomel electrode at the same temperature. The potential of this calomel at 80° against a hydrogen electrode in 0.2 N hydrochloric acid at the same temperature was 0.253 which, corrected for vapor pressure, gives a value of 0.263 for 1 atm. of hydrogen. We have arbitrarily assumed the hydrogen-ion activity of hydrochloric acid to be independent of the temperature; therefore, the activity in 0.2 N hydrochloric acid is 0.76. Using this value and the measurement just mentioned, we assign the value of +0.210 volt to the calomel saturated electrode at 80° on the hydrogen scale. Using this value and measuring the hydrogen electrode in 1 N sulfuric acid at 80°, we find a P_H value of 0.37. The ceric–cerous electrode against the saturated calomel was found to be 1.214 at 80°, thus giving a value of 1.424 for E_0' at 80°. This was the initial potential (±3 millivolts) in all the experiments listed above.

The values of the velocity constant given in Table I were calculated from the usual monomolecular Equation 2, the time being in minutes.

$$k = \frac{2.3}{t} \log \frac{1}{1 - S} \tag{2}$$

It is evident from an inspection of Table I that, in the case of the aldehydes, changing the concentration of the reactants affects the rate only slightly, which fact points to a rate-controlling step which is monomolecular. In the case of glucose the effect of dilution, however, is almost as much as would be predicted if a bimolecular process were involved. Since this work has been primarily concerned with aldehydes, we will leave to another paper a further consideration of the peculiarities of the glucose reaction. The data given in Table II show that lowering the temperature 20° decreases the rate of the reaction 3- to 4-fold.

TABLE II

RATE OF OXIDATION OF ALDEHYDES AND GLUCOSE AT 60° IN 1 N SULFURIC ACID WITH CERIC SULFATE

Concn. of reagents $\times 10^3$	Subs. oxidized	Concn. moles /liter $\times 10^3$	Fraction (S) of reagent reduced in, minutes				$k \times 10^2$ Calcd. from S at, minutes				Average
			3	5	8	15	3	5	8	15	
2	Acetaldehyde	2	0.07	0.11	0.19	0.33	2.4	2.3	2.6	2.7	2.5
2	Propionaldehyde	2	.28	.45	.59	.83	11.0	12.0	11.1	11.8	11.5
2	*n*-Butyraldehyde	2	.16	.28	.43	.67	5.8	6.6	7.0	7.6	6.9
2	*Iso*butyraldehyde	2	.28	.44	.63	..	10.9	11.6	12.4	..	11.6
2	Glucose	2	..	..	..	.22	..	..	..	2.6	2.6

The potential of the ceric–cerous electrode at 60° was 1.200 against the saturated calomel at the same temperature.

The Rate of Oxidation in Alkaline Solution.—The only oxidizing agents which we have been able to employ in neutral or alkaline solution are the complex cyanides of iron, tungsten and molybdenum which were used in our previous papers. Such reagents as Tollens' solution and Fehling's solution are not reversible oxidizing agents and none of the quinones or dyes which have been investigated are sufficiently powerful oxidizing agents to attack aldehydes in dilute solution even at 80°.

The data in Table III show the effect of dilution on the rate of the reaction. In the case of the aldehydes (Section A), the reaction is clearly of the second order and the values of k_2 have been calculated from Equation 3. With glucose and the naphthols (which are included for purposes

$$k_2 = \frac{1}{tC} \times \frac{S}{1 - S} \tag{3}$$

of comparison) the rate of the reaction is more nearly independent of the dilution and the values of k given are those calculated by means of the first-order equation.

TABLE III

EFFECT OF DILUTION ON THE RATE OF OXIDATION OF CERTAIN SUBSTANCES AT 80°. REAGENT, POTASSIUM FERRICYANIDE

P_H	Concn. of reagent, moles per liter × 10^3	Subs. oxidized	Concn., moles per liter × 10^3	Fraction (S) of reagent reduced in, minutes			k_2 calcd. from S at minutes		
				5	15	30	5	15	30
		(A) Aldehydes (Second-order reaction)							
10.75	1.83	Acetaldehyde	1.83	0.10	0.30	0.51	12	16	19
10.75	9.17	Acetaldehyde	9.15	.32	.70	> .9	10	17	...
8.6	1.91	Propionaldehyde	1.91	.21	.52	.70	28	38	41
8.6	9.55	Propionaldehyde	9.55	.68	.89	..	44	56	...
9.0	1.91	*n*-Butyraldehyde	1.91	.35	.68	.83	58	73	84
9.0	9.17	*n*-Butyraldehyde	9.55	.76	.9	> .9	69	...	...
7.5	1.91	*Iso*butyraldehyde	1.91	< .1	.21	.38	..	9.4	10
7.5	9.17	*Iso*butyraldehyde	9.55	.16	.47	.76	4.1	6.5	11
9.0	1.91	Acrolein	1.91	.08	.32	.51	9	16	18
9.0	9.17	Acrolein	9.55	.32	.71	> .9	10	18	...
.	.	(B) Sugar and naphthols (Essentially first-order reaction)							
9.0	2	*d*-Glucose	2	0.05	..	0.39			
9.0	10	*d*-Glucose	10	.09	..	.47			
9.0	2	*d*-Fructose	10	.08	..	.65	1.7	3.5	...
9.0	10	*d*-Fructose	10	.12	..	.64	2.5	3.4	...
5.3	1.93	α-Naphthol	1.93	.16	.33	.46	3.5	2.8	2.1
5.3	9.6	α-Naphthol	9.6	.30	.53	.64	7.2	5.0	3.4
7.5	1.93	β-Naphthol	1.93	.06	.13	.25	1.2	.92	.96
7.5	9.6	β-Naphthol	9.6	.14	.35	.49	3.0	2.9	2.2

In each experiment 100 cc. of buffer solution was placed in the cell and after it had come to temperature equilibrium in the thermostat, 2 cc. each of a solution of oxidized and reduced forms of reagent were added; the resulting concentrations were those in Col. 2. After waiting for ten minutes (to allow for temperature readjustment), a 0.2 molar solution of the aldehyde was added in such amount that the concentration of the cell was that given in Col. 4. The naphthols were added as solids.

As in the case of the oxidation of phenols and enols, the rate of oxidation of aldehydes by the complex cyanides is a function of the alkalinity of the solution. The more alkaline the solution the more rapid the reaction. In this connection it must be remembered that the potential of the complex cyanides (unlike the quinones) is practically constant from *P*H values 3–12. We have determined the *P*H at which each aldehyde is just appreciably oxidized by (a) ferricyanide, (b) tungsticyanide, (c) molybdicyanide. The data are summarized in Table IV.

TABLE IV

THE RATE OF OXIDATION OF CERTAIN ALDEHYDES AT 80 ± 0.2° IN DIFFERENT BUFFER SOLUTIONS 0.002 *M* WITH RESPECT TO SUBSTANCE AND REAGENT. *F* = POTASSIUM FERRICYANIDE; *M* = POTASSIUM MOLYBDICYANIDE; *T* = POTASSIUM TUNGSTICYANIDE

Substance	Reagent	*P*H of soln.	E_0' of reagent	Fraction reacted (*S*) in minutes		Reaction constant (first-order reaction) $k \times 10^2$ calcd. at			App. oxid. potential
				5	30	5 min.	30 min.	Average	
Formaldehyde	F	10.9	0.296	< 0.1	< 0.1	..	..	...	...
	M	10.9	.647	.12	.68	2.6	3.8	3.2	0.593
	M	10.4	.647	< .1	.13	..	0.9	0.9	.648
Acetaldehyde	F	10.9	.292	.16	.73	3.5	4.4	4.0	.228
	F	10.4	.302	.06	.26	1.2	1.0	1.1	.298
	T	10.4	.408	.40	> .9	10.2	..	10.2	.301
	T	9.0	.432	.10	.39	2.1	1.7	1.9	.402
	M	7.5	.669	.12	.69	2.6	3.9	3.2	.615
	M	6.8	.650	< .1	.12	..	0.43	0.43	.717
Propionaldehyde	F	9.0	.322	.47	.87	12.7	6.8	10.2	.214
	F	8.2	.324	< .05	.40	..	1.7	1.7	.300
	T	8.2	.431	.59	> .9	17.8	..	17.8	.299
	T	7.5	.424	.17	.74	3.7	4.5	4.1	.359
	M	6.1	.670	.19	> .9	4.2	..	4.2	.604
	M	5.4	.680	< .05	.13	..	0.5	0.5	.712
*Iso*butyraldehyde	F	8.2	.321	.09	.72	1.9	4.2	3.2	.268
	F	7.5	.310	< .1	.38	1.7	1.6	1.7	.286
	T	6.8	.424	.08	.53	1.7	2.5	2.1	.390
	T	6.1	.433	< .05	.23	..	0.87	0.87	.440
	M	6.1	.674	.1	> .9	2.1	..	2.1	(.602)
	M	5.4	.681	< .05	.13	..	0.5	0.5	.703
n-Butyraldehyde	F	8.2	.325	< .05	.18	..	.73	0.73	.301
	F	9.0	.319	.35	.83	8.6	5.9	7.2	.228
	T	7.5	.423	.13	.71	2.8	4.1	3.5	.366
	T	8.2	.431	.56	> .9	16.4	..	16.4	.303
	M	6.1	.673	.21	> .9	4.7	..	4.7	.602
	M	5.4	.681	< .1	< .1	..	..	...	...
Acrolein	F	9.0	.319	.08	.51	1.7	2.4	2.1	
	F	8.6	.320	< .1	.32	..	1.3	1.3	
	M	6.1	.668	.07	..	1.5	..	1.5	
	M	5.4	.668	< .1	< .1	..	..	...	

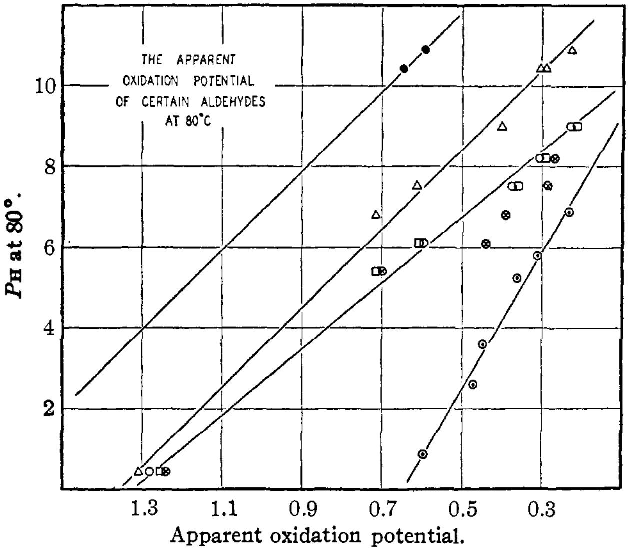
NOTE.—The experiments recorded in the above table were all performed in duplicate. The results agreed within 20% (expressed as fraction reacted in a given time). To save space only one determination has been recorded and the 15-minute values of S and k_S have been omitted, but were included in the average value of k_S used in calculating the apparent oxidation potential. With most of the compounds many experiments in other buffer solutions were carried out, in which the rates were too fast or too slow to give significant values for k_S. All these results were consistent with our electrochemical formulation. The following experimental details are to be noted in connection with the above data. The hydrogen electrode (corrected for vapor pressure) in 0.2 N hydrochloric acid was taken as the standard of potential at 80°. It was arbitrarily assumed that the activity of the hydrogen ion at this temperature in this solution was 0.76 (the value at 25°). On this basis the hydrogen electrode in 0.2 N hydrochloric acid was given the value of -0.053 at 80°. The particular saturated calomel electrode used as a working standard at 80° had a value of $+0.225$ on this basis; this value was repeatedly checked. The normal potentials of the reagents were determined at 80° against this calomel electrode. The P_H of the buffer solutions at 80° was determined directly with the hydrogen electrode. All the buffer solutions were 0.2 molar with respect to the buffering ion and were made up to an ionic strength of 0.6 with appropriate amounts of sodium chloride. The materials used in preparing the various solutions were as follows: P_H 5.3, sodium acetate and acetic acid (molybdicyanide potentials showed an abnormally large "drift" in acetate buffers and they were not employed with this reagent); P_H 5.4, 6.1, 6.8, potassium dihydrogen phosphate and sodium hydroxide; P_H 8.2, 8.6, 9.0; P_H 10.4, 10.75, 10.9, secondary and tertiary sodium phosphates.

The most convenient method of summarizing the behavior of aldehydes toward reversible oxidizing agents is by formulating the results in terms of "apparent oxidation potentials." This method has been developed and used in previous papers. In this instance it is more difficult to apply because the rate of oxidation in alkaline solution is so dependent on the dilution. In spite of this complication a fairly satisfactory picture of the process may be developed by confining the attention to one concentration (0.002 M) and in the case of the results with both ceric sulfate and the complex cyanides calculating the rate constant from the monomolecular formula. The apparent oxidation potential is then defined as the potential of the reagent which will just bring about the oxidation at the rate $k = 0.01$ at 80° and the P_H specified. The rate constants given in Table IV are the *first order constants.* Since it rarely happens that $k = 0.01$ in any actual experiment, an interpolation between two values is necessary (or sometimes an extrapolation). In a few cases it was possible to measure the rate of oxidation of a given aldehyde with two reagents in the same buffer. The results of these experiments show that consistent values of the apparent oxidation potential are obtained by using Equation 4, which is of the usual form but contains the quite empirical factor 0.003 T (instead of the usual 0.002 T or 0.001 T).

$$\text{Apparent oxidation potential} = E_0' \text{ (of reagent)} + 0.003\,T \log \frac{0.01}{k} \qquad (4)$$

The values of the apparent oxidation potential given in Table IV and plotted in Fig. 1 were thus calculated using the average value of *k*. The success of the empirical equation in representing the data is shown by the calculation of apparent oxidation potential of acetaldehyde at *P*H = 10.4, propionaldehyde *P*H = 8.2, and *n*-butyraldehyde at *P*H = 8.2. The two values in each case calculated from the results with two reagents agree within a few millivolts.

The general consistency of the results is also shown by Fig. 1. The results at *P*H 0.37 were calculated from the data in Table I using Equation 4; they are as follows: acetaldehyde, apparent oxidation potential = 1.307; propionaldehyde, 1.252; *n*-butyraldehyde, 1.278; *iso*butyraldehyde, 1.236. It should be noted that formaldehyde is not appreciably attacked by ceric sulfate, a fact which fits perfectly with the results at *P*H 11. For the purposes of comparison the results with α-naphthol and β-naphthol are included. Some of these are new measurements (Table VI) and some from a previous paper. The best straight line has been drawn through the formaldehyde, acetaldehyde and the *n*-butyraldehyde points; *n*-propionaldehyde is indistinguishable from *n*-butyraldehyde. The *iso*butyraldehyde values are the most irregular. It is quite clear that the data obtained in acid solution with ceric sulfate are part of the general picture. The position of the points in alkaline and



●, Formaldehyde; □, propionaldehyde; ⊗, isobutyraldehyde; △, acetaldehyde; ○, *n*-butyraldehyde; ⊙, β-naphthol at 60° (from previous work).

Fig. 1.—The apparent oxidation potential of certain aldehydes at 80°.

neutral solution would have led to the prediction of the apparent oxidation potential at *P*H = 0.37 within at least 100 millivolts.

TABLE V

RATE OF OXIDATION OF FORMALDEHYDE AND ACETALDEHYDE AT 60 ± 0.2° IN DIFFERENT BUFFER SOLUTIONS 0.002 *M* WITH RESPECT TO THE SUBSTANCE AND REAGENT. F = POTASSIUM FERRICYANIDE; M = POTASSIUM MOLYBDICYANIDE

Substance	Reagent	*P*H of soln.	E_0' of reagent	Fraction reacted (S) in minutes 5	30	Reaction constant (first order) $k \times 10^2$, in minutes 5	30
Formaldehyde	F	12.0	0.345	< 0.1	< 0.1	..	..
	M	12.0	.646	.4	$>$ .9	10	..
	M	11.2	.666	$<$ .1	.12	..	0.43
Acetaldehyde	F	11.2	.348	$<$ .1	.14	..	0.51
	F	12.0	.347	.28	.89	6.5	7.4
	M	9.2	.663	.34	$>$ .9	8.3	..
	M	8.4	.665	$<$ .1	.24	..	0.88

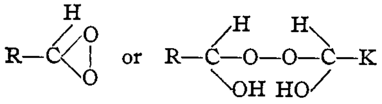
TABLE VI

DETERMINATION OF APPARENT OXIDATION POTENTIAL OF α- AND β-NAPHTHOLS AT 80 ± 0.2° IN DIFFERENT BUFFER SOLUTIONS 0.002 *M* WITH RESPECT TO SUBSTANCE AND REAGENT. F = POTASSIUM FERRICYANIDE

Substance	Reagent	*P*H of soln.	E_0' of reagent	Fraction reacted (S) in 5 min.	30 min.	Reaction constant $k \times 10^2$ 5 min.	30 min.	App. oxid. potential, volt
α-Naphthol	F	8.2	0.324	0.9	0.9	..	..	...
	F	6.12	.322	.71	.9	25	..	0.231
	F	5.36	.325	.25	.60	5.7	3.1	.281
	F	5.26	.330	.16	.46	3.5	2.1	.299
β-Naphthol	F	8.2	.324	.45	.78	12.0	5.0	.261
	F	7.5	.313	.06	.25	1.2	.96	.312

Discussion of Results

While Equation 4 and Fig. 1 are a satisfactory empirical formulation of the results, interpretation of them in terms of a simple mechanism does not seem possible. The slope of the *P*H–apparent oxidation potential line corresponds approximately to 0.003 T. This is in marked contrast to the oxidations of enols and phenols, where in almost every case the slope is 0.0002 T, the apparent oxidation potential curve paralleling the line for the hydrogen electrode. The contrast between the behavior of aldehydes and the naphthols is clear from Fig. 1. Since the rate of the oxidation of aldehydes by reversible reagents (at 80° in dilute solutions) seems to be a regular function of the potential of the reagent and the *P*H of the solution, this reaction must be classified with those oxidations which may be formulated on an electrochemical basis. For the reasons given elsewhere[3] it seems that in all such processes there is a reversible step followed by a slow irreversible rate-controlling reaction. We are inclined to believe that the reversible step in the case at hand involves the formation of a peroxide of the types



or a free radical from the hydrated form of the aldehyde. The abnormal slope of the apparent oxidation potential–*P*H curve might be due to hydroxyl-ion catalysis of the irreversible step. The apparent second order reaction with the complex cyanides may be due to the interaction of the first product and the cyanide with the formation of the dihydropyrazine. We have not been able, however, to devise a combination of any such mechanisms which will lead to the quantitative relationships actually found. Considering the complexities revealed by the qualitative study of the reactions, it is perhaps not surprising that the quantitative results defy analysis.

In considering Fig. 1 as a description of the oxidation of aldehydes at 80° in dilute solution, several points must be kept in mind. The curves refer to one concentration (0.002 M); in more concentrated solution the apparent oxidation potential would be lowered, in more dilute solutions raised, at least in the alkaline solutions. Judging from the results of Table III, the effect would be about 100 millivolts for each 10-fold change. The acid points would also be changed by change in concentration, since it is clear from Table I that there is a change of rate with change of concentration, though it is less than when ferricyanide is used. The effect of change in temperature is complicated because of the change of the *P*H value, the potential of the reagent and the rate of the oxidation. At temperatures near 80° the increase in the apparent oxidation potential of 80 to 100 millivolts for a 20° lowering of temperature would be expected from the data in Tables II and V. At 25° the aldehydes are only attacked by molybdicyanide in extremely alkaline solution.

The process or processes which are involved in the reaction which we have attempted to formulate in Fig. 1 involve the oxidation of the aldehyde in the α-position. The so-called "normal" oxidation of aldehydes to acids is another story. In this connection the action of two common reagents—Fehling's solution and Tollens' solution—is of interest. In neither of these reagents is there a mobile equilibrium between the oxidized and reduced form. According to our views, their action would therefore not be expected to fit into the electrochemical picture. That this is the case is shown by the fact that rough estimations of the rate of reduction of Fehling's solution at 80° gives the order: acetaldehyde > α- and β-naphthol > formaldehyde. Tollens' reagent at room temperature gives the order, formaldehyde > acetaldehyde > α-naphthol > β-

naphthol. Ammoniacal silver nitrate at 80° shows the following: formaldehyde and the naphthols instantaneous action, acetaldehyde much slower. The predicted speed of oxidation by reversible reagents from Fig. 1 is α-naphthol > β-naphthol > acetaldehyde > formaldehyde; this does not correspond with that found with any of the reagents just mentioned. It seems probable that in the case of the oxidation of aldehydes with the complex metal positive ions, an addition compound is first formed. The formation of such a compound and its rate of decomposition would not be expected to be a function of the oxidation–reduction potential of the reagent. It might further be noted that it is extremely probable that the chief product of the oxidation of aldehydes by cupric and silver hydroxide and their complexes is in every case the corresponding acid.

Further Evidence Concerning the Nature of the Product.—Except in a few cases, the process of α-oxidation does not stop with the formation of the hydroxy-aldehyde but proceeds further. This was made evident by the results published in the last paper. We have obtained further evidence on this point by determining the number of equivalents of ferricyanide or of ceric sulfate which are required for complete oxidation of a few aldehydes and sugars. The general procedure was to add an excess of reagent together with its reduced form and follow the change of potential with time. The rate of change of potential, which was at first rapid, gradually decreased until after two or three hours there was no appreciable change; this was taken as the end of the reaction. The total change of potential is a measure of the amount of oxidizing agent which has been reduced. A few typical results obtained using ceric sulfate are given in Table VII. A test of the method is given by the results with oxalic acid in which two equivalents must almost necessarily be involved.

TABLE VII

DETERMINATION OF THE NUMBER OF EQUIVALENTS INVOLVED IN THE OXIDATION OF CERTAIN COMPOUNDS BY CERIC SULFATE IN 1 *N* SULFURIC ACID AT 80°. TYPICAL RESULTS

Substance	Time, min.	ΔE, mv.	S	Equivalents
Oxalic acid,	0	0	0	
concn., 0.008	1	74	0.84	
mole per liter	14	74	.84	2.1
*Iso*butyraldehyde,	0	0	0	
concn., 0.001	65	56	.72	
mole per liter	88	60	.76	
	100	61	.77	
	126	64	.78	1.6

Where the number of equivalents is large the results are less certain and may be in error in the case of glucose, for example, by one or two equivalents. The following results have been obtained, all at 80°.

Substance and reagent	No. of equivalents
Acetaldehyde with ferricyanide (*P*H 10.8)	1.9
Acetaldehyde with ceric sulfate (*P*H 0.37)	2.5
Propionaldehyde with ferricyanide (*P*H 10.8)	2.6
n-Butyraldehyde with ferricyanide (*P*H 10.9)	at least 5
n-Butyraldehyde with ceric sulfate (*P*H 0.37)	4
*Iso*butyraldehyde with ferricyanide (*P*H 10.9)	2
*Iso*butyraldehyde with ceric sulfate (*P*H 0.37)	1.6–3.0
d-Glucose with ferricyanide (*P*H 10.4)	12.2
d-Glucose with ceric sulfate (*P*H 0.37)	8.8
d-Fructose with ferricyanide (*P*H 10.4)	11.2
d-Arabinose with ferricyanide (*P*H 10.4)	7.5

The oxidation of *d*-glucose by both ferricyanide and ceric sulfate is probably complete, since a determination of the amount of carbon dioxide evolved using ceric sulfate showed 6 moles per mole of sugar; the value of the number of equivalents obtained with this reagent is therefore probably below the true value.

In the previous paper the formation of dihydropyrazine derivatives by the action of potassium ferricyanide on aldehydes and ketones was explained by the assumption that the α-amino compound was first formed and then underwent condensation. We have been able now to demonstrate the correctness of this mechanism, at least in the case of ketones. Gabriel[4] has shown that α-aminophenyl *iso*propyl ketone, unlike most α-amino ketones, does not condense to a dihydropyrazine. We therefore oxidized phenyl *iso*propyl ketone with ferricyanide according to our usual procedure and obtained the α-amino compound. The yield was small and all attempts to change the conditions to obtain a better yield failed. The method therefore does not appear very suitable for the preparation of this compound. The experimental details are given below.

A solution of 58 g. of potassium ferricyanide in 500 cc. of water was heated to 85–95° and 10.4 g. of phenyl *iso*propyl ketone and 200 cc. of 2 *N* sodium hydroxide was added. The hydroxide was added gradually and finally 25 cc. of 5 *N* sodium hydroxide was introduced. The characteristic red precipitate of ferric hydroxide formed rapidly. After thirty minutes the solution was cooled, filtered and extracted with chloroform. The basic material was extracted from the chloroform with dilute hydrochloric acid, then liberated by the addition of alkali and extracted with chloroform. On distillation 0.5 g. of α-aminophenyl *iso*propyl ketone was obtained (b. p. 247–257°, hydrochloride m. p. 187–188° after recrystallization from acetoacetic ester).

Evidence of the formation of α-aminomethyl *iso*propyl ketone was also obtained in some experiments conducted with methyl *iso*propyl ketone. The reaction mixture, obtained in the usual way, was filtered from the iron oxide, acidified with acetic acid and evaporated at 40° under diminished pressure to a small volume. The solution was then made strongly alkaline and stirred with benzene sulfone chloride for four hours. On working up the reaction mixture in the usual way, 1 g. of a white crystalline solid was obtained which was evidently the benzenesulfone derivative of the α-amino

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[4] Gabriel, *Ber.*, **44**, 60 (1911).

ketone. It melted at 93.5–94.5° after recrystallization from hot water. It was soluble in alkali but insoluble in acid; it contained nitrogen and sulfur.

Anal. Calcd. for $C_{11}H_{15}NSO_3$: C, 54.7; H, 6.3. Found: C, 53.9; H, 6.6. Mol. wt. in camphor (micro method): 255. Calcd.: 241.

In connection with the quantitative results reported in the first portion of this paper, it should be mentioned that a study was made of the action of molybdicyanide on *iso*butyraldehyde at 80° in a phosphate buffer. No evidence of the formation of acetone could be obtained. The distillate gave the test for the α-hydroxy*iso*butyraldehyde (see experimental portion of previous paper) but only in the first 30 cc. The amount of this found is therefore slight. The reaction mixture, also, did not give the characteristic precipitate of the dihydropyrazine perbromide when treated with bromine. However, after making alkaline, heating and reacidifying, the addition of bromine yielded a precipitate of what appeared to be the perbromide of the dihydropyrazine. It thus appears that with molybdicyanide as with ferricyanide the oxidation product is the α-amino aldehyde.

Summary

1. The rate of oxidation of a number of aldehydes at 80° in 1 *N* sulfuric acid by ceric sulfate has been measured.
2. The rate of oxidation of certain aldehydes at 80° in alkaline and neutral buffer solutions by ferricyanide, tungsticyanide and molybdicyanide has been determined.
3. A comparison of the results obtained at the different acidities shows that the reaction between aldehydes and reversible oxidizing agents can be formulated in electrochemical terms. The equations necessary to describe the change of rate with change in acidity (P_H) and change of potential of the reagent, however, contain factors which do not correspond to any simple mechanism.
4. The action of Fehling's solution, ammoniacal silver nitrate and Tollens' reagent are quantitatively different from the action of the reversible reagents.
5. α-Aminophenyl *iso*propyl ketone has been isolated from the products obtained by the oxidation of phenyl *iso*propyl ketone by ferricyanide.

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