[CONTRIBUTION FROM THE LABORATORY OF APPLIED ORGANIC CHEMISTRY, TOKYO UNIVERSITY]

Electrolytic Oxidation of Salts of Aliphatic Acids by the Hofer–Moest Reaction. I. Formation of Methanol from Sodium Acetate

BY TAISEKI KUNUGI

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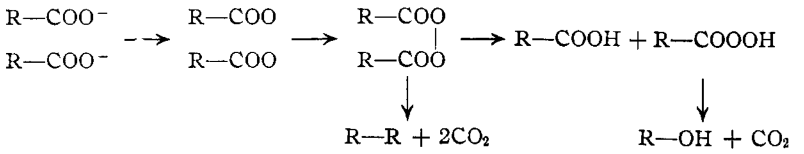
The formation of methanol during the electrolysis of aqueous sodium acetate has been investigated; the influences of time, concentration, current density, temperature, anodic material and added salts on the course of this reaction have been explored. A method is presented for the analysis of the mixtures of methanol and formaldehyde formed during the electrolysis, as well as a method for the analysis of the residual acetate.

Two types of reaction occur at a smooth platinum anode when the solution of a salt of an aliphatic acid is electrolyzed. One is the well known Kolbe reaction, giving a paraffin, while the other gives an alcohol and is known as the Hofer–Moest reaction.[1] The mechanism proposed by Fichter[2] for these reactions is



$$\begin{matrix} R{-}COO^- & & R{-}COO & & R{-}COO & & \\ & \dashrightarrow & & \longrightarrow & | & \longrightarrow & R{-}COOH + R{-}COOOH \\ R{-}COO^- & & R{-}COO & & R{-}COO & & \\ & & & & \downarrow & & \downarrow \\ & & & & R{-}R + 2CO_2 & & R{-}OH + CO_2 \end{matrix}$$

It is assumed that the formation of a paraffin from the peroxide is favored in an acid solution whereas the peroxide is hydrolyzed in an alkaline solution, giving a peracid which decomposes to an alcohol.

In addition to ethane and methanol, the electrolysis of sodium acetate is known to give methyl acetate, methane, ethylene and formic acid. Under the conditions imposed in this study, the amounts of these substances are negligible and have therefore been ignored. On the other hand, formaldehyde is formed by the oxidation of methanol and an analysis of the products must take into account the formaldehyde which is produced.

Unlike the Kolbe reaction, the Hofer–Moest reaction has not been carefully studied. The present investigation is an attempt to define the best conditions for the production of methanol by the electrolysis of aqueous sodium acetate. Factors which are herein examined include current density, concentration of acetate, temperature, kind of anode, *p*H of solution, kind and concentration of admixed inorganic salt. The anode potential is also a factor in these reactions and anode potential values are reported in this paper. However, Glasstone and Hickling[3] have demonstrated that the anode potential is a secondary factor and no attempt has been made in this investigation to relate the methanol yield to the anode potential.

Experimental

Determination of Residual Sodium Acetate.—Enough 4 *N* HCl was added to 5 ml. of the electrolysis solution to decompose the carbonate and bicarbonate. The solution was then neutralized by 2 *N* NaOH (free of carbonate), using phenolphthalein. The methanol and formaldehyde were vaporized, the solution again neutralized by 2 *N* NaOH (phenolphthalein), then diluted to 50 ml. with distilled water and titrated with 0.3 *N* HCl, using Tropaeolin OO as the indicator.

Determination of Formaldehyde.—To 2 ml. of the electrolysis solution was added 10 ml. of 0.1 *N* iodine solution, followed by 2 *N* NaOH to a light yellow color. After 15 minutes, the solution was acidified with 2 *N* HCl and titrated with 0.1 *N* $Na_2S_2O_3$.

A methanol-free formaldehyde solution was analyzed both by the above method and by chromic acid oxidation followed by titration of the excess chromic acid with 0.1 *N* Mohr solution. 1.00 ml. of 0.1000 *N* $Na_2S_2O_3$ was equivalent to 1.014 ml. of 0.1000 *N* Mohr solution.

Determination of Methanol.—To 1 ml. of the electrolysis solution was added 25 ml. of a chromic acid solution (2.20 g. of $K_2Cr_2O_7$ in a small amount of water and enough 98% H_2SO_4 to give 500 ml. of solution). The mixture was heated for five minutes at 95–97°, cooled, diluted with 175 ml. of distilled water, and the residual chromic acid titrated with 0.1 *N* Mohr solution.[4]

The above analysis gives the sum of methanol and formaldehyde. The actual methanol content can be obtained by correcting for the formaldehyde found previously.

Apparatus.—In each experiment, 200 ml. of solution was used. The cell was a 250-ml. beaker, suspended in a water-bath for temperature control. The beaker was fitted with a rubber stopper, holding an air-tight stirrer, thermometer, reflux condenser, sampling hole and the electrodes; distance between electrodes, about 50 mm.; available area of stirrer, about 120 sq. mm.; speed of stirrer, 35–40 r.p.m.

Electrodes.—The cathode used in all experiments was a platinum spiral. Unless otherwise specified, the anode was a platinum spiral with an area of 6.64 sq. cm. Before electrolysis the anode was washed with concentrated hydrochloric acid, with concentrated nitric acid, with water, and finally heated to redness.

Chemicals.—The sodium acetate was recrystallized twice and heated to constant weight at 120°. The sodium perchlorate was the monohydrate prepared by Merck and Co. in Germany. The potassium bicarbonate was of 94.5% purity. The sodium carbonate was prepared by heating pure sodium bicarbonate for one hour at 270–300°. The disodium phosphate was recrystallized twice and then dried to constant weight at 100°.

Explanation of Tabulated Items. 1. **Total Methanol.**—The total methanol percentage yield is calculated as the ratio of the total weight of methanol produced (including the methanol equivalent to the formaldehyde formed by oxidation) to the theoretical weight of methanol corresponding to the weight of acetate actually consumed.

2. **Oxidation of Methanol.**—The percentage of methanol oxidized is calculated as the ratio of the formaldehyde produced (expressed as the equivalent weight of methanol) to the total weight of methanol produced (including the methanol equivalent of the formaldehyde).

3. **Current Efficiency of Methanol.**—The current efficiency of methanol production is calculated as the ratio of the total weight of methanol produced (including the methanol equivalent of the formaldehyde) to the theoretical weight of methanol. The theoretical weight of methanol is calculated on the assumption that the quantity of electricity involved, in coulombs, oxidizes two acetate ions/two electrons and that the oxidation of two acetate ions gives one methanol molecule.

4. **Current Efficiency of Ethane.**—This calculation is based on the assumption that any acetate which disappears

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(1) H. Hofer and M. Moest, *Ann.*, **323**, 284 (1902).

(2) Fr. Fichter, *Trans. Electrochem. Soc.*, **75**, 309 (1939).

(3) S. Glasstone and A. Hickling, *ibid.*, **75**, 341 (1939).

(4) F. G. Benedict and R. S. Norris, THIS JOURNAL, **20**, 293 (1898).

TABLE I

Temp., °C.	Time, hours	Current, amperes	Current density, amperes per sq. dm.	Terminal voltage	Molarity of sodium acetate		Total methanol, %	Oxidation of methanol, %	Current efficiency in %	
					Initial	Final			Ethane	Methanol
27–32	2.0	1.55	25	9.8–10.8	1.29	1.12	74	10	7	44
27–32	3.5	1.55	25	9.8–10.8	1.29	1.00	89	8	3	52
27–32	5.0	1.55	25	9.8–10.8	1.29	0.88	93	8	2	54
27–32	5.0	0.63	10	8.5–8.9	0.66	.29	53	18	30	66
27–32	5.0	1.55	25	9.8–10.8	.66	.26	81	49	5	46
27–32	5.0	2.48	40	19–22	.66	.23	66	34	7	24
27–33	3.5	1.55	25	9.4–9.8	3.16	2.61	40	15	33	43
27–33	5.0	1.55	25	9.5–10.2	1.89	1.20	58	11	21	56
27–33	5.0	1.55	25	9.8–10.8	1.29	0.88	93	8	2	54
27–33	5.0	1.55	25	17–19	0.50	.12	57	39	11	31
5–14	5.0	0.63	10	10–11	1.35	.93	29	13	53	41
27–32	5.0	.63	10	8.0–8.4	1.32	1.01	29	18	38	30
48–53	5.0	.63	10	6.2–7.0	1.35	1.16	40	20	20	27

during the electrolysis gives either methanol or ethane. The current efficiency of ethane is therefore the ratio of the difference between the weight of acetate consumed and the weight of acetate converted to methanol (including the methanol equivalent of the formaldehyde) to the theoretical weight of acetate converted by the number of coulombs of electricity involved in the electrolysis.

Data Not Included in Tables. Table II.—Initial concentration of sodium acetate, 1.20 to 1.35 *M*; current, 1.54 amperes; current density, 25 amperes/sq. dm.; temperature, 24–27°; time, 5.0 hours.

Table III.—Temperature, 25–30°; current density, 25 amperes/sq. dm.; time, 5.0 hours for platinum or platinized platinum and 3.0 hours for other anodes; solution A, mixture of 0.76 *M* sodium acetate and 0.77 *M* acetic acid; solution B, 1.56 *M* sodium acetate; solution C, mixture of 1.55 *M* sodium acetate and 0.39 *M* potassium bicarbonate; platinum anode, area of 6.60 sq. cm.; platinized platinum anode, above anode electroplated with platinum black; graphite anode, area of 6.00 sq. cm., crumbled during electrolysis; nickel anode, 9.26 sq. cm. plate, considerably corroded; iron anode, 5.85 sq. cm. plate, considerably corroded; lead peroxide anode, 4.50 sq. cm. compact cylinder, changed from black to greenish-black with solution A, apparently unchanged by B and C.

Discussion of Results

A summary of the time, current density, concentration and temperature studies is presented in Table I. There are no significant differences between the two- and five-hour periods of electrolysis, indicating only that there is no marked change in the course of the electrolysis with time if the concentration of the acetate is not materially changed. The production of methanol is highest at a current density of 25 amperes/sq. dm., while the formation of ethane is favored by lower current densities. Unfortunately, however, the oxidation of methanol is also highest at 25 amperes/sq. dm. A high acetate concentration promotes the formation of ethane while a concentration of about one to one and one-half molar appears to be most favorable for the production of methanol. The temperature data seem to indicate an increase in methanol formation and a decrease in ethane formation with a rise in temperature. The current efficiency of methanol formation, however, decreases as the temperature rises.

The influence of added inorganic salts is summarized in Table II. The formation of methanol is adversely affected by the presence of sodium sulfate and disodium phosphate. On the other hand, methanol formation is stimulated by the addition of sodium perchlorate, sodium carbonate or potassium bicarbonate. Sodium perchlorate appears to be most effective at high concentrations, while potassium bicarbonate is more effective at lower concentrations. It is interesting to observe

TABLE II

Terminal voltage	Added salt in moles/mole of sodium acetate		Total methanol, %	Oxidation of methanol, %	Current efficiency in %	
					Ethane	Methanol
12.3–12.6	None		61	17	12	38
11.5–11.8	Na_2SO_4	0.10	53	12	18	37
10.1–10.4	Na_2SO_4	.50	49	28	19	36
11.5–11.9	$NaClO_4$	.10	64	26	13	43
10.5–10.7	$NaClO_4$	.25	68	22	11	48
9.6– 9.8	$NaClO_4$	.50	74	16	9	48
12.1–12.3	$KHCO_3$	.10	74	22	8	40
11.3–11.5	$KHCO_3$	.25	85	14	4	41
10.2–10.5	$KHCO_3$	.50	62	22	9	32
9.8–10.1	$KHCO_3$	.75	58	26	11	29
9.3– 9.7	$KHCO_3$	1.00	45	42	16	26
12.0–12.2	Na_2CO_3	0.10	90	30	3	43
11.0–11.2	Na_2CO_3	.25	79	66	2	16
10.1–10.4	Na_2CO_3	.50	65	100	2	7
13.4–14.7	Na_2HPO_4	.10	54	22	18	41
13.8–14.0	Na_2HPO_4	.25	46	20	21	35

TABLE III

Current, amperes	Terminal voltage	Solution	Anode	Total methanol, %	Oxidation of methanol, %	Current efficiency in %	
						Ethane	Methanol
1.54	17–18	A	Pt	20	13	49	24
1.54	13.3–13.5	B	Pt	57	21	17	47
1.54	11.0–11.3	C	Pt	69	22	11	47
1.54	14.8–15.1	A	Pt platinized	17	43	17	7
1.54	11.7–11.9	B	Pt platinized	55	16	6	11
1.54	9.8–10.1	C	Pt platinized	47	55	10	18
1.54	14.7–15.0	A[a]	Pt platinized	25	45	5	4
1.54	11.2–11.3	B[a]	Pt platinized	39	23	7	9
1.54	10.6–10.8	C[a]	Pt platinized	45	43	13	21
1.50	14.2–15.2	A	Graphite	47	4	12	22
1.50	9.7–10.8	B	Graphite	69	6	11	48
1.50	8.6–8.9	C	Graphite	64	18	12	41
2.30	17–18	A	Nickel	40	60	2	2
2.30	11.0–11.4	B	Nickel	17	24	1	2
2.30	9.3–9.5	C	Nickel	32	65	3	3
1.46	14.4–14.7	A	Iron	33	56	3	3
1.46	10.6–10.9	B	Iron	34	0	2	2
1.46	7.5–7.7	C	Iron	38	13	2	2
1.13	11.2–11.5	A	Lead peroxide	19	61	6	3
1.13	8.0–8.3	B	Lead peroxide	24	68	4	3
1.13	6.8–7.0	C	Lead peroxide	38	89	4	5

[a] Solution contains sodium fluoride, 0.125 *M*. See Glasstone[5] for discussion of effect of sodium fluoride.

that the degree of oxidation of methanol to formaldehyde is increased by sodium carbonate, reaching one hundred per cent. oxidation at a carbonate concentration of one-half molar.

The influence of the anodic material on the course of the electrolysis is summarized in Table III. Platinum and graphite give the best results for both methanol and ethane, while nickel, iron, lead peroxide and platinized platinum are not suitable for the production of methanol. Graphite appears to be superior to platinum if methanol is the desired product, since there is less loss of methanol by oxidation. Platinized platinum is inferior to platinum; the addition of sodium fluoride did not improve the efficiency as was observed by Glasstone.[5]

(5) S. Glasstone and A. Hickling, *J. Chem. Soc.*, 1878 (1934).

HONGO, TOKYO, JAPAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Kinetic Study of the Reversible Acid Denaturation of Ferrihemoglobin[1]

BY JACINTO STEINHARDT AND ETHEL M. ZAISER

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The denaturation of horse ferrihemoglobin, like that of carbonylhemoglobin, involves the liberation of 36 acid-binding groups, half of the total available for combining with acid, in the same *p*H range in the denatured protein. Detailed equilibrium and rate measurements show that, unlike the case of carbonylhemoglobin, the denaturation of ferrihemoglobin is fully reversible, whether measured by changes in spectroscopic absorption, loss of solubility or acid-binding capacity. From the rates of denaturation and the equilibrium points the magnitudes of the rate constants for both denaturation and regeneration processes have been obtained as a function of *p*H. The rate of liberation of basic groups is faster than the rate of denaturation measured by the other, more conventional, methods. It is shown that hydrogen-ion does not act as a perfect catalyst but must combine with protein in the process of denaturation. A partial physical model is proposed, which accounts for the effects observed.

Equilibrium[2] and kinetic[3] measurements have shown that exposure of horse carbonylhemoglobin to dilute acid solutions (*p*H < 4) initiates a time-dependent reaction which liberates 36 acid-binding groups. Half of these groups appear to have *pK* near 4.4 and half *pK* near 6.1. Indications that the rates of liberation of these groups at any *p*H were identical with rates of loss of characteristic absorption at 5380 Å., and loss of solubility at the isoelectric point, made it appear probable that the liberation of these groups was concurrent with denaturation, as usually defined. The liberation appears to occur essentially as an all-or-nothing phenomenon, *i.e.*, no liberated groups are found in undenatured molecules; and denatured molecules always have the full complement of 36.[3]

The apparent first-order kinetics of the denaturation process (measured in any of the three ways) evidently concealed a more complex process. The rate of denaturation proved very sensitive to traces of oxygen—so sensitive, that reproducible data were obtained only if certain minimal amounts of air were deliberately added. Since ferrihemoglobin is formed rapidly when oxygen is present, and is denatured more rapidly than COHb itself, the transformation to denatured protein occurred at least in part through the intermediate formation of ferrihemoglobin. It seemed more promising, therefore, to investigate the connection between the appearance of 36 acid-binding groups and denaturation on the oxidized form of hemoglobin, in order to minimize the complication of successive or parallel reactions. The choice of ferrihemoglobin soon presented an additional attraction in that its denaturation by acid, unlike that of COHb, was found to be completely rather than partially reversible.[4] With COHb only the rates measured by the three methods could be compared. With ferrihemoglobin equilibria could be compared also. A direct comparison of equilibrium and kinetic constants may thus be made.

This paper therefore presents measurements on ferrihemoglobin similar to those already reported for COHb.[2,3] Direct measurement of the kinetics of the regeneration process, and examination of the identity of the regenerated material with relation to the native protein are given in a paper to follow.

Experimental

Except for the work with titration curves, which was straightforward,[3] working with ferrihemoglobin rather than COHemoglobin required overcoming three main difficulties: (a) close similarity of the spectra of both native and denatured forms over the greater part of the visible spectrum; (b) a marked dependence of absorption on *p*H in both native and denatured forms; and (c) practically complete and rapid reversal of denaturation, on returning solutions to a higher *p*H, in order to precipitate denatured protein.

The first of these difficulties was circumvented by measuring the change in absorption at either 4060 Å. (Soret band) or at 6300 Å., where there are major differences in absorption between native and denatured protein. The larger changes occur at the former wave length, and all the measurements reported here were made at 4060 Å. Calculations based on results obtained at 6300 Å., however, lead to the same conclusions.

The second difficulty was dealt with by taking into account the effect of *p*H on absorption, in calculating concentrations. This effect, over most of the visible region of the native ferrihemoglobin spectrum, is shown in Fig. 1.[5]

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[1] A preliminary account of this work was presented at the Meeting of the American Chemical Society at New York, N. Y., in September, 1951.

[2] J. Steinhardt and E. M. Zaiser, *J. Biol. Chem.*, **190**, 197 (1951).

[3] E. M. Zaiser and J. Steinhardt, THIS JOURNAL, **73**, 5568 (1951).

[4] *Cf.* H. F. Holden, *Australian J. Exptl. Biol. Med. Sci.*, **14**, 291 (1936).

[5] All extinction coefficients (ϵ) are expressed as log I_0/I for a 1-cm. thickness of solution containing 1 mmole of heme iron per liter. It will be observed that there is no measurable change with *p*H in this part of the spectrum of native ferrihemoglobin over most of the *p*H range of the kinetic experiments (3.5–4.2); or of denatured ferrihemoglobin at *p*H more acid than 3.5. The data differ in several important respects from those given for hog hemoglobin by W. M. Urbain and D. A. Greenwood (*Food Research*, **5**, 617 (1940)).