[Contribution from the Chemical Laboratory of Harvard University]

CERTAIN NEW OXIDATION REACTIONS OF ALDEHYDES

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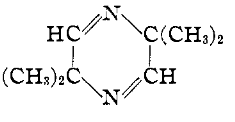
As a continuation of the quantitative study of the irreversible oxidation of organic compounds,[1] we have investigated the oxidation of aldehydes by reversible oxidizing reagents of known potential. In this work we employed the following oxidizing agents in dilute solution at 80°: potassium ferricyanide, potassium tungsticyanide, potassium molybdicyanide, potassium dichromate and ceric sulfate. The last two were used in molar sulfuric acid solution and the others in alkaline buffer solutions. The quantitative results showed that the reduction of these reagents by aliphatic aldehydes proceeded rapidly at certain acidities and that the results could be formulated in terms of "apparent oxidation potentials" as in previous papers from this Laboratory. An examination of the products of the reaction showed surprising complications, however. Instead of the expected oxidation to the corresponding acid, other reactions were apparently predominant in both the alkaline and the acid solutions. We have established that these reactions are the result of an oxidation in the α-position, which we have been able to study in some detail in the case of *iso*butyraldehyde. The difficulty of isolating products from dilute solutions containing inorganic reagents has prevented our obtaining equally satisfactory evidence with the other aldehydes. Therefore, this paper is concerned primarily with the behavior of *iso*butyraldehyde. The results of our quantitative study will be reported later.

The Formation of Dihydropyrazine and Piperazine Derivatives by the Action of Ferricyanide

*Iso*butyraldehyde is oxidized by potassium ferricyanide at 80°, if the solution is made slightly alkaline by the slow addition of potassium hydroxide. In dilute solution (about 0.14 *M* with respect to aldehyde) the chief product is 2,2,5,5-tetramethyldihydropyrazine (I); the yield is about 27%. No *iso*butyric acid is produced. In more concentrated solutions (about 0.28 *M*) 2,2,5,5-tetramethyl-3,6-dicyanopiperazine (II) is also formed. The combined yield of the piperazine and dihydropyrazine derivatives amounted to about 60% of the aldehyde employed, but the iso-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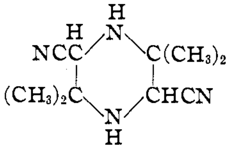
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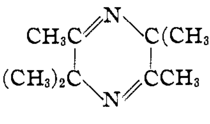
III

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[1] Conant and Pratt, This Journal, 48, 3178, 3220 (1926).

lation of the dihydropyrazine from the more concentrated runs is unsatisfactory since it is contaminated with some oily material.

In this strange reaction the nitrogen atoms of the heterocyclic compounds have been gained at the expense of the ferricyanide ion, since ferric hydroxide and formic acid are also formed. The maximum yield of the two compounds from 0.14 mole of aldehyde corresponds to a gain of 0.126 g. atom of nitrogen. This would be made available by the complete decomposition of 0.021 mole of ferricyanide (about 10% of the equivalent amount of the oxidizing agent). The amount of ferric hydroxide actually obtained corresponded to the decomposition of 0.0130 mole of ferricyanide or 65% of this amount. The major part of the ferricyanide ion was reduced to ferrocyanide, which was isolated from the reaction mixture as crystalline potassium ferrocyanide. An electrometric titration of the reaction mixture also showed that at least 65% of the oxidizing agent was reduced to ferrocyanide.

Further insight into the mechanism of the reaction was obtained by studying the action of potassium ferricyanide in alkaline solution at 80° on methyl *iso*propyl ketone. The product of the oxidation in this case is the known hexamethyldihydropyrazine (III);[2] the yield was about 25%. The constitution of the tetramethyldihydropyrazine (I) follows from the analysis, molecular weight and the transformation by reduction into a piperazine derivative which yielded a di-nitroso compound. The action of hydrocyanic acid on the dihydropyrazine yielded the dicyanopiperazine (II), whose structure was thus established.

The fact that methyl *iso*propyl ketone yields a dihydropyrazine when oxidized with alkaline ferricyanide throws much light on the mechanism of the reaction with *iso*butyraldehyde. The α-oxidation of the ketone is the normal course of the oxidation and it seems quite certain that the α-amino ketone, $CH_3COCNH_2(CH_3)_2$, is an intermediate product. This substance is known to undergo condensation to hexamethyldihydropyrazine in alkaline solution.[2] As a by-product of this condensation another volatile basic material (probably a pyrrole derivative) is formed. We have also found a small amount of other volatile basic material in our reaction mixture. Further evidence of the existence of an intermediate product is afforded by the fact that the formation of hexamethyldihydropyrazine proceeds slowly after oxidation is complete. Thus, a reaction mixture from which no more dihydropyrazine could be distilled yielded an appreciable quantity after standing overnight and again distilling. In view of this fact it seems possible that a new preparative method for certain α-amino ketones and aldehydes might be developed.

An examination of the structure of the dihydropyrazine resulting from *iso*butyraldehyde as well as the analogy with the reaction of methyl *iso*-

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[2] Gabriel, *Ber.*, **44**, 65 (1911).

propyl ketone shows that the fundamental mechanism is the oxidation of the α-carbon atom. It is the possibility of this reaction and not the presence of the aldehydic group which is responsible for the peculiar course of the reaction between *iso*butyraldehyde and ferricyanide. The mechanism by which the nitrogen is introduced into the organic molecule is obscure. It might involve the formation of the α-hydroxy aldehyde (or ketone) but this possibility appears to be eliminated by the fact that α-hydroxy-*iso*butyraldehyde yields no dihydropyrazine when heated with a mixture of ferri- and ferrocyanides in alkaline solution. Since the work reported below demonstrates that the α-oxidation of aldehydes in dilute solution is a regular reaction of these substances, we believe that the first step in the process is an oxidation (dehydrogenation) involving the elimination of the α-hydrogen atom. The first product is probably a highly reactive substance which combines with the complex cyanide forming the α-amino aldehyde (or ketone).

The dicyanopiperazine (II) is probably formed by the interaction of the dihydropyrazine and the hydrocyanic acid set free by the decomposition of a portion of the complex ion.

The oxidation of acetaldehyde by alkaline potassium ferricyanide at 80° yields no acetic acid, no volatile basic products and only a trace of ferric hydroxide. The reduction of the ferricyanide to ferrocyanide was evident both from the electrometric measurements and by the isolation of large amounts of potassium ferrocyanide. After concentration and precipitation of the inorganic salt by alcohol, a gummy material was left. It corresponded, however, to only 10% of the aldehyde employed. No satisfactory evidence as to its nature has yet been obtained and beyond the significant fact that no acetic acid is formed in the reaction, we are not able to make any statements in regard to the course of the reaction between ferricyanide and acetaldehyde. The reaction of ferricyanide with other aliphatic aldehydes has not yet been investigated.

The α-Oxidation of Aldehydes in Acid Solution

In order to determine whether or not α-oxidation of aldehydes is a general reaction, we examined the action of a number of oxidizing agents in acid solution. Again, our most satisfactory results were obtained with *iso*butyraldehyde, though the facts given below prove beyond doubt that α-oxidation also takes place to some extent under certain conditions with *n*-butyraldehyde and acetaldehyde.

Potassium dichromate oxidizes a dilute solution of *iso*butyraldehyde in molar sulfuric acid at 80°, with the formation of acetone, carbon dioxide and *iso*butyric acid. In a solution 0.14 *M* with respect to both aldehyde and reagent the yield of acetone was 37%. In more concentrated solutions (0.28 *M* to 0.56 *M*) less carbon dioxide (29 to 35%) and more *iso*butyric acid was obtained. The formation of acetone and carbon dioxide must be the result of the oxidation of *iso*butyraldehyde in the α-position. *Iso*butyric acid under the same conditions is not oxidized by dichromate but both α-hydroxy-*iso*butyric aldehyde and acid yield acetone.

The oxidation of *n*-butyraldehyde by dichromate in molar sulfuric acid at 80° yields considerable amounts of carbon dioxide. This must be the result of oxidation of the carbon chain, presumably in the α-position. The reaction was studied by determining both the evolution of carbon dioxide and the number of equivalents of oxidizing agent required for complete oxidation. In a 0.07 *M* solution the amount of α-oxidation was 25% as determined by the carbon dioxide; 3.6 hydrogen equivalents of dichromate were consumed per mole of aldehyde. The number of equivalents increased to 4.1 in a 0.035 *M* solution and 4.4 in a 0.018 *M* solution. The oxidation to *n*-butyric acid corresponds to two equivalents, to carbon dioxide and propionic acid to eight equivalents. Thus, on the basis of the amount of oxidizing agent used up, the process of α-oxidation comprised about 40% in the very dilute solutions. The amount of carbon dioxide did not increase above 25% but this is undoubtedly due to the difficulty of driving off and determining very small amounts of carbon dioxide in the more dilute solutions.

Ceric sulfate in molar sulfuric acid at 80° is rapidly reduced by *iso*butyraldehyde and in this case it was possible to obtain evidence of the formation of α-hydroxy-*iso*butyraldehyde in addition to acetone. Unfortunately the isolation of the hydroxy aldehyde from very dilute solutions is difficult and it was not possible to obtain the pure substance or a definite derivative. However, we developed a procedure for estimating the amount of this aldehyde in a dilute water solution which also contained acetone and *iso*butyraldehyde. The details of the procedure are given in the experimental portion of this paper. The method was carefully tested with known solutions of the three compounds. It depends on the different degree of volatility with steam of the three and on a rather specific reaction of the hydroxy aldehyde. This compound does not give the usual iodoform test but does give iodoform if the solution is warmed with an excess of sodium hydroxide.

Only about 20% of *iso*butyric acid was formed in the ceric sulfate oxidations. In addition to the α-hydroxy aldehyde, the acetone and the acid, one other product was shown to be present in small amounts. This was a crystalline solid melting at 166–169° and volatile with steam. Only about 0.01 g. per gram of aldehyde was obtained. The elucidation of its structure awaits further work.

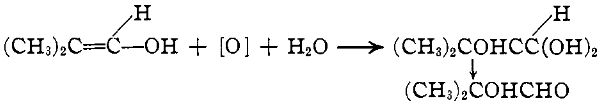
A few experiments were performed with potassium permanganate. A 0.5 *M* solution of this reagent was very slowly dropped into a 0.1 *M* solution of *iso*butyraldehyde in molar sulfuric acid at 80–90°. Distillation of the reaction mixture yielded a distillate which contained acetone and gave the characteristic tests for α-hydroxy-*iso*butyraldehyde. The amount of *iso*butyric acid was estimated by the Du Claux method; it amounted to only 40% of the theoretical quantity. *Iso*butyric acid itself is not attacked by permanganate under the same conditions.

Acetaldehyde is oxidized in the α-position, yielding carbon dioxide, if potassium permanganate in molar sulfuric acid in *very dilute* solution is employed. The temperature was 80–90°. One hundred cc. each of 0.25 M solution of the reagent and 0.25 M solution of the aldehyde were slowly dropped into 200 cc. of molar sulfuric acid which was rapidly stirred. If no excess of permanganate is allowed to accumulate, the amount of carbon dioxide evolved may correspond to as much as 20% α-oxidation. The yield of acetic acid (determined by the Du Claux method) drops accordingly. If the aldehyde and permanganate are mixed at once, the formation of acetic acid is practically quantitative.[3]

Cobaltic sulfate in 8 N sulfuric acid at 0° oxidizes *iso*butyraldehyde. The presence of both acetone and hydroxy aldehyde was shown by tests performed with the distillate; *iso*butyric acid is also formed; no estimation of the relative amounts of products was found possible. Palladium black and chloranil (tetrachloroquinone) slowly oxidize *iso*butyraldehyde and the presence of α-hydroxy aldehyde in the product was shown by tests performed on the distillate.

Mechanism of the Reaction

The most obvious explanation of our somewhat unexpected results would be that the enolic form of the aldehyde was oxidized by the addition of two hydroxyl groups.



$$(\mathrm{CH_3})_2\mathrm{C{=}}\overset{\mathrm{H}}{\mathrm{C}}\mathrm{{-}OH} + [\mathrm{O}] + \mathrm{H_2O} \longrightarrow \begin{array}{c}(\mathrm{CH_3})_2\mathrm{COHC}\overset{\mathrm{H}}{\mathrm{C}}(\mathrm{OH})_2\\ \downarrow \\ (\mathrm{CH_3})_2\mathrm{COHCHO}\end{array}$$

Such an explanation seems to us improbable, however, for several reasons. In the first place, it gives no clue to the striking effect of dilution which so materially increases the amount of α-oxidation with acid oxidizing agents. In the second place, such reagents as ceric sulfate, cobaltic sulfate, palladium and chloranil and ferricyanide do not usually add oxygen to an ethylene linkage as demanded by this mechanism. A third argument against the above mechanism is the fact that the amount of enol present in a strongly acid solution must be very small and yet our results show that α-oxidation proceeds in molar sulfuric acid. The oxidation of the enolic form of acetaldehyde has been carefully studied by Evans and Adkins.[3,4] Using a solution 0.1 M in respect to both potassium permanganate and acetaldehyde, they found that at 25° or at 75° only acetic acid was formed if no alkali were added. With increasing amounts of potassium hydroxide the yield of acetic acid diminished and carbon dioxide and oxalic acid were formed. Obviously these investigators were studying the real oxidation of the enolic form of acetaldehyde. Such an

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[3] Compare Evans and Adkins, THIS JOURNAL, **41**, 1385 (1919).

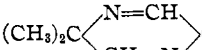
[4] See also Denis, *Am. Chem. J.*, **38**, 569 (1917).

oxidation is an α-oxidation but would appear to be different from the α-oxidation we have studied by using *very dilute* solutions of permanganate and aldehyde in sulfuric acid.

If the oxidation of the enolic form according to the equation written above is eliminated, it is necessary to construct some other hypothesis. Since the quantitative results are important in this connection, we will postpone a further consideration of the mechanism until the next paper.

We are indebted to Mr. Carl O. Tongberg for his assistance during part of the experimental work.

Experimental Part

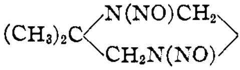


$(CH_3)_2C\left\langle\begin{matrix}N{=}CH\\CH{=}N\end{matrix}\right\rangle C(CH_3)_2$

2,2,5,5-Tetramethyldihydropyrazine, $(CH_3)_2C\left\langle\begin{matrix}N{=}CH\\CH{=}N\end{matrix}\right\rangle C(CH_3)_2$.—One hundred and fifteen grams of potassium ferricyanide (0.35 mole) was dissolved in one liter of water in a flask fitted with a mechanical stirrer, a reflux condenser and dropping funnel. The flask and contents were heated in a bath at 80° and 10.0 g. of redistilled *iso*butyraldehyde (0.14 mole) were run in; 320 cc. of 1.0 *N* sodium hydroxide was then dropped in over forty-five minutes with stirring. After all of the sodium hydroxide had been introduced, the mixture was allowed to stand for fifteen minutes at 80°, filtered from a red sediment of iron oxide (which weighed 1.11 g. after ignition) and then distilled slowly under ordinary pressure until 1000 cc. of distillate had been collected. The 1000 cc. of distillate was then distilled through a long spiral column until the refractive index of the distillate fell to that of water. The distillate was then continuously extracted for six hours, using 50 to 100 cc. of ether. After drying the ether was distilled from the extract until no more ether passed over. On cooling the residue crystallized. Most of the remaining ether was removed by applying suction to the flask for two or three minutes after cooling. The crystals after drying between filter paper melted at 76–81°. The yield was 2.62 g. (27.5% of the theoretical). The compound was purified by sublimation in vacuum and by drying over dehydrite. It melted at 83–84° and distilled at 160° without decomposition. It is very soluble in water, forming a weakly basic solution which turns methyl orange but not phenolphthalein. A dilute solution gives a yellow precipitate with bromine water and a white precipitate on adding an equal volume of saturated mercuric chloride solution. The application of the bromine test to a fresh reaction mixture showed that the dihydropyrazine was present immediately after the oxidation was complete.

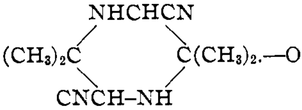
No detectable amount of dihydropyrazine was formed when α-hydroxy-*iso*butyraldehyde was substituted for *iso*butyraldehyde.

Anal. Calcd. for $C_8H_{14}N_2$: C, 69.6; H, 10.1; N, 20.3. Found: C, 69.5; 69.2; H, 10.4, 10.2; N (Kjeldahl), 20.2. *Equiv. Weight* by titration with standard HCl (methyl orange end-point), calcd., 69.0. Found: 68.2. *Mol. wt.* in benzene (freezing point): Sample, 0.1240; benzene, 17.37 g.; $\Delta t = 0.257°, 0.263°$. Calcd. for $C_8H_{14}N_2$: 138. Found: 141, 136.



Dinitroso-2,2,5,5-tetramethylpiperazine, $(CH_3)_2C\left\langle\begin{matrix}N(NO)CH_2\\CH_2N(NO)\end{matrix}\right\rangle C(CH_3)_2$.—The tetramethyldihydropyrazine was reduced to the corresponding piperazine by means of sodium and alcohol. The piperazine was distilled with steam from the diluted reaction mixture and the distillate treated with hydrochloric acid and potassium nitrite. The dinitroso compound separated as a white crystalline precipitate; 3 g. of the dihydropyrazine yielded 1.8 g. of crude product, m. p. 208–210°. It was recrystallized from 5% acetic acid and melted at the same point.

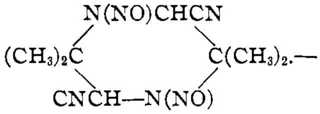
Anal. Calcd. for $C_8H_{16}N_4O_2$: C, 48.0; H, 8.11; N, 28.0. Found: C, 47.9; H, 8.1; N, 28.1.

2,2,5,5-Tetramethyl-3,6-dicyanopiperazine, 

—One hundred and eighty-five grams of potassium ferricyanide (0.56 mole) dissolved in 400 cc. of water, 10 g. of *iso*butyraldehyde (0.14 mole) and a solution of 14.3 g. of sodium hydroxide in 100 cc. of water were employed and the procedure was identical with that described in the preparation of the dihydropyrazine; the sodium hydroxide was added during thirty minutes, and the reaction mixture was then stirred for one hour longer at 80–85°. A small amount of oil formed on the surface of the reaction mixture. This on cooling solidified to crystals. The whole reaction mixture was continuously extracted for ten hours with 50–100 cc. of ether. The ether extract was mixed with a considerable quantity of white solid which was filtered off and dried between filter paper, m. p. 189–192°; yield, 2.0 g. The product after being twice recrystallized from benzene melted at 193–194.5°. The reaction mixture, after the ether extraction, was filtered from the fine red precipitate of ferric hydroxide, which when dried and ignited weighed 1.04 g. (0.0065 mole of Fe_2O_3, corresponding to 0.0130 mole of ferricyanide). The ether extract, after filtering off the solid already mentioned, was dried and distilled and the residue fractionated; the bulk of the product boiled at 170°; yield, 2.3 g. This fraction crystallized, but the crystals of the tetramethyldihydropyrazine were mixed with some thick oily materials.

Anal. Calcd. for $C_{10}H_{16}N_4$: C, 62.4; H, 8.4; N, 29.2. Found: C, 62.5; H, 8.6; N, 29.5. *Mol. wt.* Calcd. for $C_{10}H_{16}N_4$: 192. Found: (1) in acetone boiling-point method: 0.3360 g. (second increment) 14.2 g. of acetone; Δt, 0.211°, mol. wt., 187. (2) By the micro method in camphor: 206, 225.

The compound was also prepared by heating a 1% aqueous solution of 2,2,5,5-tetramethyldihydropyrazine at 100°, passing in hydrocyanic acid gas and allowing the mixture to stand for one hour at 70–90°. The dicyano compound separated as a white solid, the yield was 1.4 g. (theoretical). The identity of the material with that formed by the interaction of ferricyanide and *iso*butyraldehyde was established by a mixed melting point.

Dinitroso-2,2,5,5-tetramethyl-3,6-dicyanopiperazine, 

— A solution of 1.0 g. of recrystallized 2,2,5,5-tetramethyl-3,6-dicyanopiperazine in 50 cc. of glacial acetic acid was treated with 1.2 g. (12% excess of theoretical for dinitroso derivative) of *n*-butyl nitrite at room temperature. After standing overnight the crystals which had separated were filtered off, washed with acetic acid and dried between filter paper, m. p. (with violet decomposition), 178° (placed in baths below this temperature and slowly heated, the decomposition point is always 178°, if placed in baths somewhat above 178°, some time elapses before the decomposition takes place), yield, 1.04 g., 80% of the theoretical. Recrystallization from benzene did not raise the melting point.

Anal. Calcd. for $C_{10}H_{14}N_6O_2$: C, 48.0; H, 5.64; N, 33.6. Found: C, 48.0; H, 5.9; N, 35.3.

Investigation of Acidic Products Formed by the Interaction of Ferricyanide and *Iso*butyraldehyde

(a) **Experiments with Buffer Solutions.**—3.29 g. of potassium ferricyanide and 4.22 g. of potassium ferrocyanide were dissolved in one liter of the borate buffer which was made by adding a solution of 326 cc. of 0.2 *M* sodium hydroxide to 1000 cc. of 0.2 *M* boric acid 0.2 *M* in potassium chloride. The mixture was heated to 80° and 0.724 grams (0.01 *M*) of freshly distilled *iso*butyraldehyde in 50 cc. of water was added with vigorous mechanical stirring. The oxidation proceeds fairly rapidly in this buffer at 80° as was shown by the change of potential of a platinum electrode in a number of similar experiments. The mixture was stirred for twenty minutes at 80° and then a further 3.29 g. of potassium ferricyanide was added and the mixture stirred for five hours at 80°. At the end of this time the mixture was cooled and 10 cc. of 35% sodium hydroxide added to neutralize all of the boric acid; the solution was evaporated under reduced pressure to a small volume, acidified with sulfuric acid, then continuously extracted for six hours with ether. The ether solutions thus obtained contained boric acid and had an odor of hydrocyanic acid. The ether was distilled off and the residue dissolved in water. An aliquot portion of the aqueous solution thus obtained was titrated with standard sodium hydroxide, using a quinhydrone electrode. The electrometric end-point showed that the amount of acid present corresponded to only 0.0030 mole in the original reaction mixture (compared with 0.010 mole of aldehyde employed). The potential of the mid-point corresponded to a K_A of 1.42×10^{-4} for the acid (K_A for formic acid $= 2.14 \times 10^{-4}$; for *iso*butyric acid, 1.48×10^{-5}). Parallel experiments in which *iso*butyric acid was added to the buffer solution showed that our procedure extracted at least 95% of the material from a 0.01 *M* solution. It was also established that a titration using the quinhydrone electrode was satisfactory in the presence of boric acid and small amounts of hydrocyanic acid and that the value of K_A for the acid present could be determined with an accuracy of 30–40%.

The fact that the acid which was extracted was formic acid was further established by evaporating the solution and testing the salt for reducing properties. It reduced mercuric oxide and silver nitrate on heating. As a further confirmation that *iso*butyric acid was not obtained, the oxidation of *iso*butyraldehyde by ferricyanide was carried out as above, using a phosphate buffer of $P_{\text{H}} = 10.4$, 0.2 *M* in phosphate ion, in which the oxidation proceeds more rapidly. The ether extraction of the solution after concentration and acidification yielded only about 30% of the theoretical quantity of acid. This acid on conversion into sodium salt gave no crystalline *p*-toluide when heated with hydrochloric acid and *p*-toluidine; a blank with *iso*butyric acid showed this to be a sensitive test for this acid.

(b) **Oxidation Using Minimum Quantities of Sodium Hydroxide.**—One hundred and thirteen grams (0.343 mole) of potassium ferricyanide was dissolved in one liter of water in a 2-liter, round-bottomed flask fitted with a condenser, a stirrer, two bright platinum wire electrodes, a buret dropping funnel and a saturated potassium chloride bridge leading to a calomel electrode. The whole was heated to 80° by immersion in a bath at 80°. The electromotive force of the system was read on a potentiometer. 10.3 g. (0.143 mole) of *iso*butyraldehyde dissolved in 150 cc. of water was added from the dropping funnel. 1 *N* sodium hydroxide was added from the buret until the potential had fallen to a value which then remained constant, indicating that the reaction was complete; a total of 313 cc. of sodium hydroxide was added. The solution was removed from the bath and after cooling was found to be neutral to phenolphthalein and basic to methyl orange. Titration of a sample showed that 100 cc. of 1 *N* acid would be required to neutralize the entire batch to the methyl orange end-point; therefore 0.313 mole of sodium hydroxide was neutralized in the course of the reaction, calculated from the phenolphthalein end-point and 0.213 calculated from the methyl orange end-point. These amounts correspond to 2.19 and 1.5 moles per mole of aldehyde, respectively. On the basis of the reaction $2K_2Fe(CN)_6 + 2KOH \longrightarrow 2K_4Fe(CN)_6 + H_2O + O$, it is seen that if one molecule of the aldehyde takes up one atom of oxygen to yield a neutral substance, two equivalents of hydroxyl ion are used up. The formic acid which was found to be produced to the extent of about 0.3 mole per mole of aldehyde by the decomposition of ferricyanide would be half taken care of by the potassium ions of the potassium ferricyanide; 0.15 mole of free acid would thus be produced and about 0.3 mole of the weakly basic dihydropyrazine. The dihydropyrazine is sufficiently basic to turn methyl orange but not phenolphthalein; the discrepancy between these two end-points is thus accounted for as well as the slight excess over two moles of alkali required for the complete neutralization to phenolphthalein.

Determination of the Amount of Potassium Ferrocyanide Formed by the Reduction of Potassium Ferricyanide at 80° by *Iso*butyraldehyde.—A solution of 5 cc. of 0.05 *M* potassium ferricyanide in 60 cc. of 0.2 *N* potassium sulfate was heated in a thermostat at 80° in a cell equipped with two bright platinum electrodes, a mechanical stirrer and a saturated potassium chloride bridge connecting it with a saturated calomel electrode. One cc. of a 0.125 *M* solution of *iso*butyraldehyde was run in, followed by the slow addition of 5 cc. of 0.517 *N* sodium hydroxide over five minutes. Rapid reduction took place, the potential falling from 0.256 volt to −0.022 volt after all the alkali had been added. A blank was run at 80° using potassium *ferrocyanide* instead of ferricyanide without adding *iso*butyraldehyde, but 5 cc. of 0.056 *N* sodium hydroxide was added. The excess alkali in both experiments was neutralized by the addition of the calculated amount of sulfuric acid and 7 cc. of 2 N acetic acid was added to each cell after cooling to room temperature. The amount of ferrocyanide was determined by electrometric titration with 0.01 N potassium dichromate,[5] the experiment with the pure ferrocyanide serving to standardize the procedure. In two experiments 14.9 and 15.8 cc. of 0.01 N dichromate were required as compared to 25 cc. calculated from the ferricyanide used and 22.5 cc. by standardization using ferrocyanide in the blank run. The yield of ferrocyanide was thus 63–70% of the theoretical.

Oxidation of Methyl *Iso*propyl Ketone with Potassium Ferricyanide.—A solution of 115 g. of potassium ferricyanide in one liter of water in a flask fitted with a reflux condenser, mechanical stirrer and dropping funnel was heated in a bath at 80°, 11.4 g. of methyl *iso*propyl ketone added and 320 cc. of 1.0 N sodium hydroxide dropped in slowly over twenty-five minutes with vigorous mechanical stirring. The reaction mixture was allowed to stand for about thirty minutes at 80° after the alkali had been added and then slowly distilled until one liter had passed over. The clear distillate was redistilled slowly through a long spiral column. A crystalline solid separated in the receiver; it weighed 2.9 g. and melted at 85–87°. On again distilling the solution from which the the solid separated, more solid was obtained in the new distillate. The residue from the original reaction mixture also yielded a further quantity when after four days' standing 200 cc. was distilled from it. In this case the solid separated from the distillate without redistillation, which indicates that the four days' interval had caused the formation of the compound from some intermediate (presumably the α-amino ketone). In all 6.0 g. of hexamethyldihydropyrazine hexahydrate, m. p. 85–87°, was obtained, 33% of the theoretical amount. The identity of the compound[2] was established by the melting point of the hydrate (87–89° after steam distillation; Gabriel gives 88–89°) and anhydrous material (m. p. 65–63°; Gabriel gives 69–69.5°) and by analysis.

The Oxidation of Acetaldehyde by Potassium Ferricyanide at 80° in Alkaline Solution.—A solution of 180 g. (0.546 mole) of potassium ferricyanide in one liter of water in the same apparatus that was used in oxidizing *iso*-butyraldehyde under these same conditions was heated to 80° and a solution of 10.75 g. (0.245 mole) of acetaldehyde in 100 cc. of water was added. 1 N sodium hydroxide was then added slowly until the potential of two bright platinum electrodes in the solution against a

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[5] The point of inflection in the e.m.f.-cc. curve at the end-point during the titration of potassium ferrocyanide in acid solution with potassium dichromate at these concentrations is not as sharp as one would expect. The titration curves show certain abnormalities and deviate from the theoretical logarithmic curve, but experiments showed that the comparative results are quite accurate.

saturated calomel half-cell had fallen to a steady value, indicating that the reaction was complete; 598 cc. of 1 *N* sodium hydroxide was required. The solution after cooling was alkaline; 74 cc. of 1 *N* sulfuric acid was required to neutralize this solution. Thus 524 cc. of 1 *N* sodium hydroxide had been used up, which corresponds to 2.14 equivalents of alkali per mole and demonstrates that practically no acidic substance was produced during the oxidation of acetaldehyde. That reduction of the ferricyanide had taken place was shown by the fall in potential of the system from 0.345 volt to −0.0301 volt. Only a trace of iron oxide was precipitated.

A run exactly the same as the one above was evaporated in vacuum in a bath at 50–55° to a volume of 300 cc., the distillate being collected in an ice-cooled receiver. An equal volume of alcohol was added to the residue. The salts thus precipitated were filtered off. This material was apparently mostly potassium ferrocyanide, giving a blue precipitate with ferric chloride. The mother liquor from the alcohol precipitated was evaporated in a vacuum below 40° to a volume of 80 cc. and 150 cc. of alcohol was added to precipitate the rest of the salts. Very little material was thrown out by this procedure. The solution after filtering was evaporated almost to dryness in a vacuum. A thick sirup was left behind; weight, 2 g. Analysis by the Kjeldahl method showed that this material contained 5.6% of nitrogen. The distillates were examined for possible oxidation products of acetaldehyde but nothing was found.

The Products of Oxidation of *Iso*butyraldehyde by Potassium Dichromate in Dilute Acid Solution at 80°.—A solution of 27.2 g. (0.555 equivalent) of potassium dichromate and 30 cc. (1.08 equivalents) of concentrated sulfuric acid was placed in a 2-liter flask fitted with a reflux condenser, dropping funnel and mechanical stirrer. The flask and contents were heated in a bath at 80°. With vigorous stirring, 10.0 g. (0.139 mole) of *iso*butyraldehyde was rapidly run in. The mixture was kept at 80° for three hours. The solution was then cooled. Its volume was 1040 cc. Titration of a sample with 0.05 *M* ferrous ammonium sulfate in acid solution, using potassium ferricyanide as outside indicator, showed that this solution was 0.072 *N* in dichromate. On refluxing a sample and again titrating, it was found that no more dichromate was used up. Thus 1 mole of *iso*butyraldehyde had used up 3.43 equivalents of potassium dichromate. From the solution 865 cc. was distilled at ordinary pressures. The first fractions had a distinct odor of acetone. By titration 0.0573 mole of *iso*butyric acid was found in the distillate. The distillate was neutralized and distilled slowly, using a long column. Three grams of material distilled over at 56.5° and the thermometer then rose rapidly to 99°. The first fraction on redistillation yielded 2 g. of a liquid, b.p. 56.5–60°, which was identified as acetone by the formation of dibenzalacetone.

The solution from which the acetone was distilled was concentrated to

20 cc., acidified with 15 cc. of 6 N sulfuric acid and extracted with ether. After drying with potassium sulfate the ether was distilled from the extract through a long column and the liquid residue fractionated: Fraction 1, 90–151°, water + *iso*butyric acid, 1.5 g.; Fraction 2, 151–153°, *iso*butyric acid, 2.02 g.

A similar experiment in which α-hydroxy-*iso*butyric acid was substituted for the *iso*butyraldehyde also yielded acetone.

Quantitative Study of the α-Oxidation of *Iso*butyraldehyde and *n*-Butyraldehyde in Different Concentrations. (a) **Apparatus.**—A 500-cc. round-bottomed, three-necked flask was fitted with a mechanical stirrer with a mercury seal, a reflux condenser connected to two U-tubes containing sulfuric acid and glass beads and provided with a tube going to the bottom of the flask, which served as a nitrogen inlet. A dropping funnel fitted with a pressure equalizer, in the form of a by-pass connected to the nitrogen stream, was fitted directly into this inlet tube. Nitrogen could be let through the by-pass so that it swept out the funnel and passed through the solution in the flask. The nitrogen was purified by passing through two towers of soda lime.

(b) **Procedure.**—A solution of potassium dichromate and sulfuric acid in 250 cc. of water was made in the flask and refluxed for one-half hour, keeping a current of nitrogen passing through the flask. The flask was then placed in a bath held at 80° and a weighed potash bulb similar to that used in combustions was connected to the other end of the two U-tubes containing sulfuric acid and glass beads. With rapid mechanical stirring the *iso*butyraldehyde either as pure liquid or solution was introduced and the reaction allowed to run at 80°. The solution was then refluxed for one-half to one hour to drive out all of the carbon dioxide. A slow current of carbon dioxide-free nitrogen was passed through the flask during the entire process. The bulbs were then disconnected and weighed with the usual precautions. The reaction mixture was then washed from the flask into a 500-cc. graduated cylinder, thoroughly mixed by blowing air through and its volume read to 2 cc. A buret was then filled with the solution and a titration made against a standard ferrous ammonium sulfate solution which was approximately 0.1 N, using dilute potassium ferricyanide as outside indicator. The volume in which the titration was carried out varied from 100–300 cc.; five cc. of concentrated hydrochloric acid per 100 cc. was always added. In the more concentrated solutions a portion of the reaction mixture was diluted before titration, so that the concentration of dichromate was about 0.1 N.

In all cases the completeness of the reaction was tested by subsequently refluxing the solution for two hours and titrating again. If there was no appreciable amount of dichromate used up the reaction was assumed to be complete.

The results are summarized in Table I; the per cent. α-oxidation is calculated directly from the amount of carbon dioxide and also from the number of equivalents of dichromate used up per mole, assuming for *iso*butyraldehyde the reaction

$$(CH_3)_2CHCHO + 3O \longrightarrow (CH_3)_2CO + CO_2 + H_2O$$

and for *n*-butyraldehyde

$$CH_3CH_2CH_2CHO + 4O \longrightarrow CH_3CH_2COOH + CO_2 + H_2O$$

TABLE I

THE AMOUNT OF α-OXIDATION IN THE REACTION OF BUTYRIC ALDEHYDES WITH POTASSIUM DICHROMATE AT 80° AT VARIOUS TEMPERATURES[a]

				Concentration					α-Oxidation	
Expt.	Concd. H_2SO_4, cc.	K_2CrO_7, g.	Aldehyde, g.	H_2SO_4 normal	K_2CrO_7, normal	Aldehyde, molal	Eqts. per mole	CO_2 per mole	From CO_2, %	From no. of equivalents, %
				(A) *Iso*butyraldehyde						
A1	30	27.3	10	4.3	2.23	0.555	3.20	0.286	28.6	30.0
A2	30	2.56	0.619*	0.43	0.208	.0344	3.70	.308	30.8	42.5
				(B) *n*-Butyraldehyde						
B1	7.5	6.82	1.244	1.08	.556	.0691	3.62	.2455	24.5	27.0
B2	5.0	3.413	0.631*	0.72	.278	.0351	4.19	.216	21.6	36.5
B3	2.5	1.706	.310*	.36	.139	.0173	4.42	.257	25.7	40.2
B4	2.5	1.706	.32	.36	.139	.0178	4.32	.283	28.3	38.7

[a] The sulfuric acid and potassium dichromate were dissolved in 250 cc. of water except when a star indicates that the aldehyde was added as a solution in 25 cc. of water. In these cases 225 cc. of water was used. In Experiment B1, the remainder of the reaction mixture was distilled in steam till no more acid came over. The distillate was diluted to 500 cc. Titration showed it to be 0.1702 *N* in acid. Allowing for the reaction mixture used in titration of dichromate, from this result we calculate that 0.666 moles of acid are yielded per mole of aldehyde.

Action of Potassium Dichromate on *n*-Butyric Acid and *Iso*butyric Acid in Acid Solution at 80° in the Presence of Chromic Sulfate.—To a solution of 100 cc. of water, 3 cc. of concentrated sulfuric acid, 2.73 g. of potassium dichromate, and 9.27 g. of chrome alum (potassium chromium sulfate) was added 1.22 g. of *iso*butyric acid in one experiment and 1.22 g. of *n*-butyric acid in another. The mixtures were refluxed for four hours and the solution titrated for dichromate with ferrous ammonium sulfate as has been already described for the aldehyde oxidations. It was found that in both cases no detectable amount of potassium dichromate had been reduced.

The Oxidation of *Iso*butyraldehyde by Ceric Sulfate at 80°.—A mixture of 300 cc. of 0.6 *M* sulfuric acid and 3.0 g. (0.042 mole) of *iso*butyraldehyde was heated to 80° in a flask equipped with a stirrer, dropping funnel, reflux condenser and nitrogen-inlet tube. A total of 300 cc. of 0.156 *N* ceric sulfate solution (containing 10 cc. of sulfuric acid) was dropped in slowly during two hours; the reduction of the ceric salt was evident by the decolorization. The reaction mixture was neutralized with 60 g. of sodium bicarbonate and slowly distilled through a long spiral column. Fractions of 3 to 10 cc. each were collected and tested with (a) Schiff's reagent (decolorized fuchsine), (b) Tollens reagent, (c) by adding a few drops of a saturated solution of *p*-nitrophenylhydrazine hydrochloride, (d) by adding a few drops of iodine solution followed by enough 10% sodium hydroxide to decolorize, (e) by boiling for thirty seconds with 3 drops of 10% sodium hydroxide and then applying test d. Distillation of a number of dilute solutions of acetone, *iso*butyraldehyde, and α-hydroxy-*iso*butyraldehyde (prepared by hydrolysis of α-bromo-*iso*butyraldehyde) showed that it was possible to identify these compounds in the presence of each other by means of this fractionation and these tests. The distillation of 37 cc. from 500 cc. of a 1 per cent. *iso*butyraldehyde solution is sufficient to remove so much aldehyde that subsequent fractions give no test with Schiff's reagent, whereas with the hydroxy aldehyde, the aldehyde continues to come over and give this test from even a 0.2% solution after 100 cc. have been distilled. The iodoform test (d) is specific for acetone and the same test after heating with sodium hydroxide (e) is specific for the hydroxy aldehyde in the absence of acetone. The acetone comes over completely in the first tenth; test (e) is then specific. The formation of an amorphous yellow precipitate with *p*-nitrophenylhydrazine (test c) and the Tollens test (test b) also persisted much longer when a solution of the hydroxy aldehyde was distilled. These several confirmatory tests were always available and exactly the same procedure was used in testing a reaction mixture that was used in the blank runs.

It was found that after one-tenth of the reaction mixture had been distilled tests a, b, c and e were still given strongly by the distillate. This proves the presence of hydroxy-*iso*butyraldehyde. By comparing the tests with those given by corresponding distillates from a solution of known concentration of hydroxy aldehyde, it was estimated that the reaction mixture contained 0.5 g. of α-hydroxy-*iso*butyraldehyde. The first fractions of the distillate gave the iodoform test in the cold, proving the presence of acetone.

The amount of *iso*butyric acid formed was estimated by acidifying with sulfuric acid the residue from the distillation just described and again distilling. The first 4 cc. was 0.025 N in acid as determined by titration; after 400 cc. had been collected the distillate was running only 0.0025 N in acid. The total acid distilled over up to this point was 0.00329 mole or only 14% of the aldehyde employed. In another similar experiment an estimate of the *iso*butyric acid was made by the method of Duclaux.[6] According to this author the ratio of acidity in the first three 10cc. portions is 1:0.83:0.64 and 25% of the acid distils in the first 10 cc. The corresponding numbers found on distilling the acidified reaction mix-

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[6] Duclaux, This Journal, **39**, 731, 746 (1917).

ture were 1: 0.82: 0.60. Assuming that 25% of the acid was distilled in the first 10 cc., the total *iso*butyric acid in the reaction mixture was found to be only 22% of the theoretical based on the aldehyde employed.

Oxidation of *Iso*butyraldehyde with Permanganate in Dilute Sulfuric Acid.—The experiments were carried out by dropping a dilute solution of the permanganate into a well-stirred solution of the aldehyde in molar sulfuric acid. In a typical experiment 0.025 mole of aldehyde in 200 cc. of molar sulfuric acid was treated with 0.008 mole of potassium permanganate in 100 cc. of water at 25°. On distilling through a fractionating column the fractions of the distillate gave strong positive tests for acetone and α-hydroxy-*iso*butyraldehyde. The method of testing was the same as that described above. The same result was obtained at 80°.

Oxidation of Acetaldehyde with Potassium Permanganate in Acid Solution.—The amount of carbon dioxide formed in the oxidation of acetaldehyde was determined in the same manner as that described above in the experiments with *iso*butyraldehyde and dichromate. The method was tested by the liberation of carbon dioxide from bicarbonate; the recovery of carbon dioxide was 80%. The temperature was 85–95°. Both the aldehyde and the permanganate in dilute solutions were slowly dropped into 200 cc. of molar sulfuric acid which was stirred. The maximum yield of carbon dioxide was obtained by operating in such a way that no excess of permanganate was ever present as determined by the color. One hundred cc. of 0.25 M permanganate and 100 cc. of 0.25 M acetaldehyde solution were employed. The extent of α-oxidation as measured by the carbon dioxide evolution varied from 3.2 to 22%. The amount of acetic acid formed was estimated by distilling over one-tenth and titrating the distillate. A blank run with 0.020 mole of acetic acid and the same volume of sulfuric acid and water showed that 6.2% of the acid distilled in the first tenth. Using this factor, the amount of acetic acid was found in a series of runs to vary from 0.022 mole to 0.017. The highest amount corresponded to the lowest yield of carbon dioxide and *vice versa.*

Oxidations of *Iso*butyraldehyde with Other Reagents.—*Iso*butyraldehyde (0.025 mole) in 670 cc. of 8 N sulfuric acid containing 0.055 mole of cobaltic sulfate (prepared by electrolytic oxidation) was allowed to stand at 0° for one hour and overnight at room temperature. The reduction of the cobaltic salt was evident at 0° by the color change. The material was distilled in the usual way and the fractions of the distillate were tested. Strong tests for acetone and α-hydroxy-*iso*butyraldehyde were obtained. The first tenth of the distillate was titrated and the total *iso*butyric acid calculated from a factor obtained in a blank run using the same sulfuric acid and pure *iso*butyric acid. The yield of *iso*butyric acid was estimated as 25% but there was some unchanged aldehyde so that not much significance can be attached to this figure.

A suspension of 0.020 mole of chloranil and 0.5 g. of palladium black in 400 cc. of water was heated to boiling in nitrogen and 0.011 mole of *iso*butyraldehyde in 100 cc. of water slowly added. The reaction took one hour. After cooling and filtering, the solution was distilled in the usual way. The distillate gave a strong test for α-hydroxy-*iso*butyraldehyde but contained no acetone.

Summary

1. The oxidation of *iso*butyraldehyde by ferricyanide in alkaline solution at 80° yields 2,2,5,5-tetramethyldihydropyrazine and 2,2,5,5-tetramethyl-3,6-dicyanopiperazine and no *iso*butyric acid. From methyl *iso*propyl ketone under the same conditions hexamethyldihydropyrazine is formed. The reaction involves the oxidation of the α-carbon atom and the gain of nitrogen from a fraction of the complex cyanide.

2. The oxidation of *iso*butyraldehyde with ceric sulfate at 80° in acid solution yields acetone and α-hydroxy-*iso*butyraldehyde as well as *iso*butyric acid. The same products are formed in acid solution by potassium permanganate and cobaltic sulfate. Chloranil and palladium yield α-hydroxy-*iso*butyraldehyde.

3. Potassium dichromate in acid solution at 80° oxidizes *iso*butyraldehyde in the α-position, yielding acetone to the extent of 40% in very dilute solutions. The process of α-oxidation is favored by dilution. *n*-Butyraldehyde is also oxidized in the α-position, as shown by the formation of carbon dioxide.

4. Potassium permanganate oxidizes acetaldehyde in acid solution at 80°, yielding carbon dioxide as well as acetic acid if precautions are taken to keep the reactants in *very dilute* solution with an excess of aldehyde.

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[CONTRIBUTION FROM THE ROCKEFELLER PHYSICAL AND BAKER CHEMICAL LABORATORIES OF CORNELL UNIVERSITY]

THE ABSORPTION SPECTRA OF SOME PHTHALEINS AND SULFONEPHTHALEINS OF PHENOL AND ORTHO-CRESOL[1]

BY R. C. GIBBS AND C. V. SHAPIRO[2]

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In continuation of our previous investigations[3] on the absorption spectra of compounds of the triphenylmethane series, data are now presented for some phthalein and sulfonephthalein derivatives of phenol and *o*-cresol.

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[3] Orndorff, Gibbs and co-workers, THIS JOURNAL, **47**, 2767 (1925); **48**, 1327, 1994 (1926); **49**, 1541, 1545, 1588 (1927); **50**, 819, 1755 (1928).