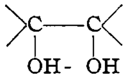
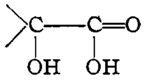
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BANTING INSTITUTE, UNIVERSITY OF TORONTO]

Oxidative Cleavage of α-Keto Acids and α-Keto Alcohols by Means of Lead Tetraacetate

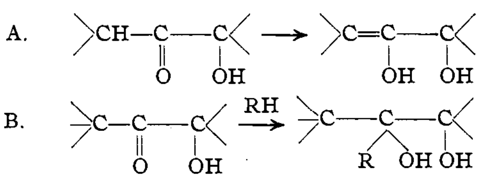
BY ERICH BAER

In 1930 and 1931 Criegee[1] reported the possibility of splitting glycols into aldehydes and ketones by oxidation with lead tetraacetate in absolutely dry solvents. The usefulness of this reaction has been considerably increased by the recent observation of Baer, *et al.*,[2] that, where the rate of reaction between glycol and oxidizing agent is sufficiently rapid, the same operation may be carried out successfully in water, or in organic solvents containing water. Nevertheless, the method was still confined to compounds which *already contained* a pair of adjacent hydroxyl groups as exemplified by glycols (I) or α-hydroxycarboxylic acids (II).


(I)


(II)

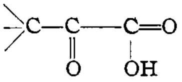
Very little has been published[3] however, concerning the extension of this technique to compounds which were not glycols, but whose structure would permit the formation of adjacent hydroxyl groups. Examples of such a type could be expected among compounds containing vicinal keto-hydroxyl groups which might be able to form the necessary hydroxyls either by enolization (reaction A) or, by addition to the keto group of water, alcohols (*e. g.*, methyl alcohol, ethyl alcohol, benzyl alcohol) or hydrocyanic acid, etc. (reaction B).

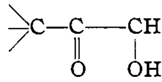


R = HO—, CH_3O—, C_2H_5O—, $C_6H_5CH_2O$—, CN—

An indication of the possibility of such oxidative cleavage is to be found in two papers by Baeyer[4] in which are described the conversion of keto-isocamphoronic acid into dimethyl tricarballylic acid, pinoyl-formic acid into pinic acid and homoterpenoyl-formic acid into homoterpenylic acid by oxidation with lead peroxide in the presence of acetic or sulfuric acid. These reactions are probably to be interpreted as oxidative cleavages induced by the intermediary formation of lead tetraacetate or plumbic disulfate.

From the great variety of compounds which could conceivably form two adjacent hydroxyl groups according to reaction A or B, a few representatives of the α-ketocarboxylic acids (III) and the α-keto alcohols (IV) (with aliphatic and aromatic substituents) have been chosen as experimental material.


(III)


(IV)

The substances examined were pyruvic acid, phenylpyruvic acid, trimethylpyruvic acid, and phenylglyoxylic acid; acetyl-methylcarbinol, benzoylcarbinol, benzoin and anisoin. Their ability to enter into cleavage reactions with lead tetraacetate has been studied, and the results of the investigation constitute the subject matter of this paper.

After it had been established that under certain conditions all these substances are split by lead tetraacetate, an attempt was made to obtain a more detailed understanding of the reaction. The main point at issue was whether a pair of adjacent hydroxyl groups is actually necessary for cleavage. Secondly, if so, which of the above-mentioned possibilities (A or B) describes their formation? Finally, does the cleavage of the resulting "pseudoglycol" follow the same mechanism which Criegee postulated for the splitting of α-glycols?

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(1) Criegee, *Ann.*, **481**, 275 (1930); *Ber.*, **64**, 260 (1931); *Angew. Chem.*, **50**, 153 (1937).

(2) E. Baer, J. Grosheintz and H. O. L. Fischer, THIS JOURNAL, **61**, 2607 (1939).

(3) The present investigation of the cleavage of α-keto alcohols was completed and nearly ready for publication when a paper entitled "Über durch Pervanadinsäure katalysierte Oxydationen" was published by W. Treibs (*Ber.*, **72**, 1194 (1939)) in which he mentioned, in support of his theory on the oxidation and cleavage of saturated cyclic ketones by H_2O_2, that he had succeeded in splitting an α-keto alcohol (benzoin) by lead tetraacetate into benzoic acid and benzaldehyde. However, he gave no experimental data in the above-mentioned paper. Apparently Treibs did not recognize the mechanism involved in the cleavage of α-keto alcohols and α-keto acids with lead tetraacetate, *viz.*, the necessity of forming a pair of new adjacent OH groups as the initial step in this reaction, when he asserts that α-keto acids are not cleavable by lead tetraacetate. Since considerable time has now elapsed and Treibs' experimental data have not yet appeared, it has been decided to publish the paper which was written at that time.

(4) A. Baeyer, *ibid.*, **29**, 1916, 1919, 2792 (1896).

The elucidation of the first two questions is closely connected and they have been investigated together. It is well-known that α-keto acids and α-keto alcohols may form enols or addition compounds, and therefore it seemed equally possible that the cleavage could occur through the enol forms or through the addition products of the keto forms.

To distinguish between these two possible reaction courses we were guided by the following considerations. If it can be shown that oxidative cleavage does not take place when conditions allow the formation of enol forms, but does occur as soon as substances capable of forming pseudoglycols by addition are supplied, the probability of the first alternative being correct may be considered very slight. The second alternative will be further supported if α-keto compounds which are unable to form enols because of their lack of an enolizable hydrogen atom adjacent to the keto group (*e. g.*, trimethylpyruvic acid, phenylglyoxylic acid) undergo an oxidative cleavage in the presence of glycol-forming substances, but not in their absence.

The experiments, therefore, were carried out so that in each case the α-keto acid or α-keto alcohol was dissolved in an indifferent solvent and brought into contact with lead tetraacetate in the absence of water or any other glycol-forming substance. If no significant amount of cleavage (*e. g.*, enol cleavage) or consumption of oxidizing agent had been detected after a definite time interval, then water, an alcohol, or hydrocyanic acid was added. The products of cleavage of the addition compound so formed were determined quantitatively where practicable or in other cases isolated as completely as possible and identified.

The investigation of the action of lead tetraacetate upon keto acids was particularly simple by reason of the ease with which one of the products of the reaction, carbon dioxide, could be determined quantitatively. For this operation, the keto acids were dissolved in glacial acetic acid, lead tetraacetate was added, and the carbon dioxide evolved was measured gravimetrically or volumetrically. All four of the keto acids examined yielded, with lead tetraacetate alone, only a trivial amount of carbon dioxide. The evolution of gas always came quickly to a complete standstill, and never amounted to more than 5–10% of the theoretical. It was probably caused by unavoidable traces of moisture in the solvents or the reagents, or adsorbed on the walls of the reaction vessel (see blank values in experiments II (1a, 2a, 3a); III (1a, 2a, 3a); IV (1a, 2a); V (1a). After a considerable time only a small amount of the keto acid and lead tetraacetate were used up. The addition of water, methanol, ethanol, benzyl alcohol, or hydrocyanic acid to the same mixture caused an almost instantaneous and complete cleavage of the α-keto acids. The cleavage reaction yielded 1 mole of carbon dioxide (Expt. II (1a, 2a, 3a); III (1a, 2a); IV (1a, 2a); V (1a)) for each mole of keto acid consumed and required 1 mole of lead tetraacetate (Expt. II (1c); III (1c); IV (1c); V (1c); VI (1b); VIII (1c); IX (1c)).

The compounds other than carbon dioxide resulting from the cleavage of the α-keto acids were determined by repeating the experiments as before, but using larger quantities so that the products could be isolated. According to the nature of the glycol-forming substance supplied the oxidative cleavage yielded either the free acid (Expt. III (1b); IV (1b); V (1b), its ester (Expt. II (3b); III (3); IV (2b)), or the nitrile of the original keto acid (Expt. IV (3)). These were in most cases easily isolated in good yield. However, the figures given in the experimental part obviously represent the lower limits of the actual quantities formed, because of some unavoidable losses in the isolation processes.

The presence of acetic acid arising from lead tetraacetate during the reaction made it difficult to detect the acetic acid or trimethylacetic acid expected as cleavage products of pyruvic acid and trimethylpyruvic acid, respectively. In these two cases the oxidative cleavage was carried out in benzene and in the presence of benzyl alcohol, so that instead of the free acids, their benzyl esters, which are easily isolated, resulted. These compounds as well as the silver salts, obtained by treatment of their saponification products with silver nitrate, served to identify the cleavage products as acetic or trimethylacetic acid, respectively.

The only exception to the normal course of the keto acid cleavage so far observed occurred in the case of phenylpyruvic acid. The cleavage product of this compound, to be analogous to those of the other keto acids, should have been phenylacetic acid. However, the cleavage required 2 moles of lead tetraacetate, and no crystalline product could be isolated. Since saponification gave mandelic acid, the original cleavage product was probably acetylmandelic acid. To explain its formation we may assume that the lead tetraacetate simultaneously effected the oxidative cleavage and an acetylation of the —CH_2— group, situated as it is between two strongly negative substituents. Similar acetylations caused by lead tetraacetate are already known, *e. g.*, that of acetoacetic ester.[5] Phenylpyruvic acid was the only keto acid of this type investigated. However, it may be expected that the cleavage of other acids of the same type will also yield derivatives of hydroxy acids. Since the hydroxy acids which would be obtained by saponification can easily be converted into aldehydes by a further oxidative reaction with lead tetraacetate, it is possible to obtain from this type of α-keto acids, aldehydes with two carbon atoms less (Equation C).

$$\text{(C)}\quad RCH_2COCOOH \xrightarrow[+\ \text{saponification}]{2Pb(OAc)_4} RCHOHCOOH \xrightarrow{Pb(OAc)_4} RCHO$$

The investigation of the α-keto alcohols was carried out as outlined above. Here, as before, the effect of lead tetraacetate on the keto compounds was first examined in dry solvents and in the absence of any glycol-forming substances. Contrary to the experience with keto acids, a slow consumption of oxidizing agent was observed. After the lead tetraacetate had completely disappeared, attempts to recognize the product of the reaction led to the isolation of the direct oxidation products of the keto alcohols—their diketones—which were obtained in good yields, but no more than traces of cleavage could be detected (see Expt. X (a, b, c)).

However, when the experiments were conducted so that the lead tetraacetate was added to the solutions of the α-keto alcohols in the presence of hydroxyl-forming substances (*e. g.*, water or alcohol) then the oxidative cleavage occurred at once and the two cleavage products, 1 mole of acid or its ester and 1 mole of aldehyde or ketone, could be isolated either as such or in the form of derivatives (see Expts. VI, VII, VIII, IX).

In the case of α-keto alcohols the oxidative cleavage and the direct oxidation tend to occur simultaneously. In the presence of glycol-forming substances the cleavage reaction predominates; in the absence of such substances the direct oxidation becomes the main reaction but proceeds far more slowly than does the above cleavage reaction.

The results of the experiments may be summarized thus. In the *absence* of hydroxyl-forming substances α-keto acids are not attacked by lead tetraacetate, while α-keto alcohols are oxidized slowly to their corresponding diketones. In the *presence* of hydroxyl-forming substances α-keto acids and α-keto alcohols undergo rapid oxidative cleavage.

These observations can probably be best interpreted as follows.

For the occurrence of oxidative cleavage of α-keto acids and α-keto alcohols the initial formation of a pair of adjacent hydroxyl groups is necessary. These glycols (or pseudoglycols) are formed by the addition of water, alcohols, or hydrocyanic acid to the keto group according to reaction B.

The oxidative cleavage of the keto compounds takes place, therefore, through their pseudoglycol forms and not, or only to an insignificant extent, through their enol form.

Further support for this view is the fact that trimethylpyruvic acid and phenylglyoxylic acid, which, by reason of their lack of enolizable hydrogen atoms cannot form an enol, are split by lead tetraacetate only in the presence of glycol-forming substances.

From the fact that the oxidative cleavage of α-keto acids and α-keto alcohols takes place only after the formation of a glycol, and from the nature of the resulting products, it may be assumed that the actual cleavage reaction is brought about by the same mechanism as the typical glycol cleavage produced by the action of lead tetraacetate. The fact that the cleavage products of pseudoglycols are in part different from those of true glycols does not invalidate the assumption as to the parallelism of the two reaction mechanisms, but is a natural consequence of the varying degrees of oxidation of the starting materials.

If one attempts to apply Criegee, Kraft, and Rank's[6] proposed reaction mechanism to formulate the course of the cleavage reaction following the initial formation of the two adjacent hydroxyl groups (D, 2; E, 2), a combination of the pseudoglycols with tetravalent lead must be assumed. According to Criegee these lead compounds induce the formation of biradicals which then

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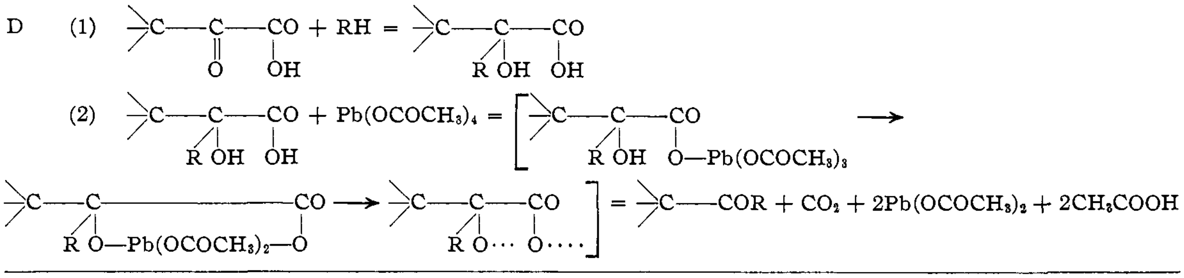
[5] O. Dimroth and R. Schweizer, *Ber.*, **56**, 1380 (1923).

[6] R. Criegee, L. Kraft and B. Rank, *Ann.*, **507**, 159 (1933).

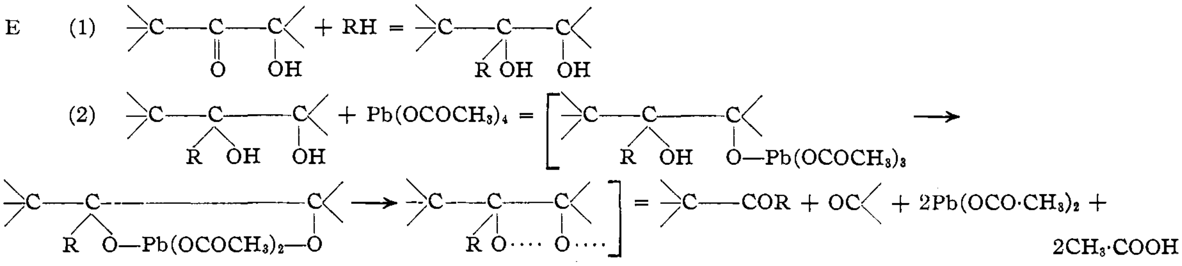
D



$$\text{(1)}\ \rangle C-\underset{\overset{\|}{O}}{C}-\underset{OH}{C}O + RH = \rangle C-\underset{R\ OH}{C}-\underset{OH}{C}O$$

$$\text{(2)}\ \rangle C-\underset{R\ OH}{C}-\underset{OH}{C}O + Pb(OCOCH_3)_4 = \left[\rangle C-\underset{R\ OH}{C}-\underset{O-Pb(OCOCH_3)_3}{C}O \longrightarrow \rangle C-\underset{R\ O-Pb(OCOCH_3)_2-O}{C}\text{———}CO \longrightarrow \rangle C-\underset{R\ O\cdots}{C}-\underset{O\cdots}{C}O\right] = \rangle C-COR + CO_2 + 2Pb(OCOCH_3)_2 + 2CH_3COOH$$

E

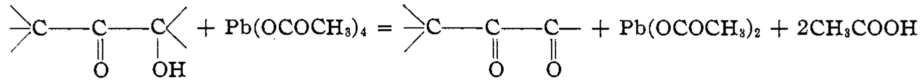


$$\text{(1)}\ \rangle C-\underset{\overset{\|}{O}}{C}-\underset{OH}{C}\langle + RH = \rangle C-\underset{R\ OH}{C}-\underset{OH}{C}\langle$$

$$\text{(2)}\ \rangle C-\underset{R\ OH}{C}-\underset{OH}{C}\langle + Pb(OCOCH_3)_4 = \left[\rangle C-\underset{R\ OH}{C}-\underset{O-Pb(OCOCH_3)_3}{C}\langle \longrightarrow \rangle C-\underset{R\ O-Pb(OCOCH_3)_2-O}{C}\text{———}C\langle \longrightarrow \rangle C-\underset{R\ O\cdots}{C}-\underset{O\cdots}{C}\langle\right] = \rangle C-COR + OC\langle + 2Pb(OCO\cdot CH_3)_2 + 2CH_3\cdot COOH$$

R = HO—, CH_3O—, C_2H_5O—, $C_6H_5CH_2O$—, CN—

F



$$\rangle C-\underset{\overset{\|}{O}}{C}-\underset{OH}{C}\langle + Pb(OCOCH_3)_4 = \rangle C-\underset{\overset{\|}{O}}{C}-\underset{\overset{\|}{O}}{C}- + Pb(OCOCH_3)_2 + 2CH_3COOH$$

decompose spontaneously into the end-products. The lead compounds assumed as intermediate stages are probably short-lived and have not yet been isolated. Their detection not only would have constituted a support for Criegee's scheme, but would have demonstrated also the close relationship between the two reactions. A substance which precipitated when lead tetraacetate was added to a solution of phenylglyoxylic acid in dry acetic acid, and which at first was suspected of being such an intermediate compound, was found later to be the plumbous salt of the starting material (Expt. IV (1)).

Even though the proof is lacking that the oxidative cleavage of pseudoglycols by lead tetraacetate proceeds through intermediate compounds similar to those postulated by Criegee for the cleavage of true glycols, the equations D and E include the assumed intermediary compounds which are placed in brackets.

The possible application of the use of lead tetraacetate to split α-keto acids and α-keto alcohols may simplify the solution of a number of problems concerning chemical constitution or tautomerism just as Criegee's glycol cleavage has proved very valuable for solving similar problems. An example of such an application where the use of lead tetraacetate would constitute a considerable simplification, is that of the tautomeric reactions of 1,2-ketols investigated by v. Auwers, Ludewig, Müller, Pötz and Noll.[7] In this case, the presence of substance I or II even in a mixture should be easy to detect and to determine on the basis of the cleavage products obtained by oxidation with lead tetraacetate in the presence of water as shown in equations G and H.

$$\text{(G)}\quad \underset{\text{(I)}}{C_6H_5COCH(OH)CH_3} \xrightarrow{Pb(OCOCH_3)_4,\ H_2O} C_6H_5COOH + CH_3CHO$$

$$\text{(H)}\quad \underset{\text{(II)}}{C_6H_5CH(OH)COCH_3} \xrightarrow{Pb(OCOCH_3)_4,\ H_2O} C_6H_5CHO + CH_3COOH$$

Another use of this reaction with lead tetraacetate is the detection of compounds which it is seldom possible to isolate. For example, the formation of addition products of water or alcohols with the keto group of α-keto alcohols and α-keto acids, which can be considered as hydrates or semiacetals, is often problematical. However if a mixture containing such components be subjected to an oxidative cleavage, the nature of the decomposition products will show whether or not formation of addition products has occurred.

A further practical application is the quantitative determination of α-keto acids by measurement of the carbon dioxide evolved during oxidative cleavage with lead tetraacetate.

The same reaction may be used to differentiate α-keto acids qualitatively from β-, γ-, etc., keto

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[7] Von Auwers, H. Ludewig and A. Müller, *Ann.*, **526**, 143 (1936); v. Auwers, H. Pötz and W. Noll, *ibid.*, **535**, 219 (1938).

acids since in such an analogous series only the alpha-keto acids evolve carbon dioxide. To carry out this operation the acid is dissolved in as little water, or water-containing acetic acid, as possible and lead tetraacetate added. The evolution of carbon dioxide indicates the presence of an alpha-keto acid.

The investigation is being extended to other classes of compounds which should be capable of cleavage by application of the same principle.

Experimental

α-Keto Acids

I. Methods of Following Oxidative Cleavage

The cleavage reactions to be described give rise to carbonic acid and an organic acid or an acid derivative. The reactions may, therefore, be followed quantitatively by determining the carbon dioxide evolved, and qualitatively by identifying the second acid (or its derivative). The procedures used are described in detail below.

(1). **Quantitative Determination of Carbon Dioxide (Gravimetric).**[8]—The quantitative determination of carbon dioxide evolved during the oxidative cleavage was carried out by passing a slow current of dry, carbon dioxide-free air through the reaction flask to sweep the evolved gas into an absorption vessel. By means of gentle suction, air was drawn through a train assembled as follows: (1) a potassium hydroxide solution and calcium chloride tube; (2) the reaction vessel (a 125-cc. Erlenmeyer flask, with 3-holed rubber stopper, carrying a dropping funnel and the inlet and outlet tubes); (3) a U-tube filled with calcium chloride and kept at $-10°$; (4) a weighed absorption vessel for the quantitative determination of carbon dioxide. A weighed amount of the substance was placed in the dry reaction flask and absolutely water-free acetic acid and lead tetraacetate were added through the dropping funnel. The mixture was warmed to 50° while a slow stream of air was drawn through the apparatus. Since, for the establishing of the pseudoglycol theory, it was just as essential to prove the non-evolution of carbon dioxide in the absence of hydroxyl-forming substances as it was to determine the quantity of carbon dioxide produced in their presence, such a blank experiment always preceded the actual test run. The increase in weight of the carbon dioxide absorption vessel was measured after thirty minutes. The amount of carbon dioxide found in the absence of hydroxyl-forming substances was in all cases only a small per cent. of the total and was probably due to unremovable minute traces of moisture in the apparatus, in the substance, or in the solvent. After the apparatus was reassembled, water (or anhydrous hydroxyl-forming substances under investigation) was allowed to flow into the decomposition flask which was warmed to 50° while air was drawn through the apparatus until the weight of the carbon dioxide absorber remained fairly constant (forty to sixty minutes).

(2) **Identification of the Second Acid.**—It is impossible to describe a general procedure for the isolation and identification of the second product of the oxidative cleavage reactions. These will be dealt with under the individual headings which follow.

II. The Oxidative Cleavage of Pyruvic Acid in the Presence of Hydroxyl-forming Compounds

(1) **Water as the Hydroxyl-forming Component.**—(a) **Quantitative determination of carbon dioxide:** 0.3517 gram of water-free pyruvic acid (distilled several times) dissolved in 10 cc. absolutely dry acetic acid yielded, after addition of 2.8 g. of finely pulverized dry lead tetraacetate 11.8 mg. of carbon dioxide. Upon adding 10 cc. of water, oxidative cleavage occurred immediately as indicated by the visible evolution of carbon dioxide. The reaction was completed in a few minutes. After thirty minutes the increase in weight of the carbon dioxide apparatus was 169.8 mg. Calcd. amount carbon dioxide: 175.8 mg. Found: 181.6 mg., 103.2%.

(b) The second cleavage product, according to theory, would be acetic acid, which naturally cannot be detected in the presence of the large amount of acetic acid present as solvent.

(c) **Determination of Lead Tetraacetate Required for the Cleavage of 1 Mole of Pyruvic Acid.**—A mixture of 10 cc. of 0.1 *M* pyruvic acid (in glacial acetic acid), 30 cc. of 0.05 *M* lead tetraacetate (in glacial acetic acid) and 5 cc. of water or 5 cc. of methyl alcohol was kept at 50° for one hour. The decrease of lead tetraacetate was determined by back-titrating the excess of oxidizing agent with 0.1 *N* thiosulfate after addition of 75 cc. of a solution of potassium iodide and sodium acetate (20 g. of potassium iodide and 500 g. of sodium acetate made up to 1 liter); 21.5 cc. of 0.05 *M* lead tetraacetate solution was used up in the presence of water and 20.5 cc. in the presence of methyl alcohol, which is equivalent to 1.07 mole and 1.02 mole of lead tetraacetate, respectively, per 1 mole of keto acid oxidized.

(2) **Methyl Alcohol as the Hydroxyl-forming Component.**—(a) The oxidative cleavage of pyruvic acid in the presence of methyl alcohol was carried out in the same way as described in (II, 1a). 0.3651 gram of keto acid yielded 9.9 mg. of carbon dioxide; after addition of 10 cc. of water-free methyl alcohol a further 175.4 mg. of carbon dioxide was produced; total carbon dioxide, 185.3 mg. (101.5% of the theoretical).

(b) The isolation of the second product, methyl acetate, from a large excess of free acetic acid and methyl alcohol was not tried because of the obvious experimental difficulties.

(3) **Benzyl Alcohol as the Hydroxyl-forming Component.**—(a) The same method was used for the cleavage of pyruvic acid in the presence of benzyl alcohol: 0.3268 g. of pyruvic acid yielded 14.2 mg. of carbon dioxide. After addition of 0.8 g. of absolutely dry benzyl alcohol, a further 143.2 mg. of carbon dioxide was liberated in one hour; total, 157.4 mg. of carbon dioxide (96% of the theoretical).

(b) The isolation of the second product, benzyl acetate, was possible because of its high boiling point. By using

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(8) If a Warburg apparatus is available the reaction may be followed by a volumetric measurement of the evolved carbon dioxide. The gas is liberated almost instantly. This volumetric procedure has the advantage that only very small quantities (about 0.5 mg.) of reactants are required; moreover, the time necessary for the determination is only a small fraction of that necessary for the gravimetric procedure.

anhydrous benzene as the solvent, it was possible to prove that the acid required by theory (acetic acid) is indeed the acid obtained by the oxidative cleavage of pyruvic acid.

To a solution of 1.76 g. (1/50 mole) of absolutely dry pyruvic acid[9] and 2.16 g. (1/50 mole) of absolutely dry benzyl alcohol in 50 cc. of water-free benzene[10] was added 9.3 g. (1/50 mole + 5%) of lead tetraacetate. The temperature of the solution rose from 24 to 40°, carbon dioxide was evolved and lead acetate precipitated. After one hour the lead tetraacetate was almost used up, carbon dioxide evolution had stopped and the mixture had returned to its initial temperature. After standing overnight the solution was decanted from the lead salt; the salt was washed with benzene and the combined benzene solutions were concentrated. The concentrate was diluted with ether, allowed to stand for a while, then filtered and concentrated again. The residue was fractionally distilled first *in vacuo* and then under normal pressure. The last distillation yielded two fractions: (1) b. p., 170–179°, *ca.* 0.3 g; (2) b. p., 202–212°, *ca.* 1.4 g., $n^{21}\text{D}$ 1.5150. Fraction (1) was identified as benzaldehyde by its b. p., odor and the m. p. of the *p*-nitrophenylhydrazone (192°). Fraction (2) judging by its b. p., refractive index and saponification number was fairly pure benzyl acetate. The corrected yield (1.2 g.) of benzyl acetate corresponds to 40% of the theoretical. Final proof of the identity of the acid formed from pyruvic acid in the oxidation was obtained by saponifying the benzyl ester (fraction 2) with aqueous alcoholic potassium hydroxide solution. After evaporation of the solvent the residue was acidified with sulfuric acid and the volatile acid was distilled over with the water. Water was added to the residue and the distillation was repeated until the distillate was no longer acid. The combined distillates were neutralized with barium hydroxide, concentrated *in vacuo* to a small volume and by addition of a concentrated silver nitrate solution, the silver salt of the acid was precipitated. The silver salt, recrystallized from water and dried in high vacuum, was found to contain 64.3% silver; calculated for silver acetate 64.6% silver. From 1.40 g. of fraction (2) was obtained 1.24 g. of silver acetate. In order to ascertain that the benzyl acetate (fraction 2) obtained in experiment II 3(b) was actually the product of the reaction between pyruvic acid, benzyl alcohol and lead tetraacetate, and not formed by the action of lead tetraacetate on benzyl alcohol, the experiment was repeated without pyruvic acid. After standing for forty-eight hours at room temperature, the mixture was worked up as described previously. After concentration of the solution by distilling off the ether and benzene, the residue obtained was separated into three fractions by distillation *in vacuo:* (1) b. p. (7 mm.) 62–64°, 0.45 g. (chiefly benzaldehyde, identified as *p*-nitrophenylhydrazone, m. p. 192–193°; (2) b. p. (7 mm.) 85–100°, 0.65 g. (chiefly unchanged benzyl alcohol containing a small amount of a benzyl ester); (3) a higher boiling residue which was not examined further.

The crude silver salt obtained from fraction 2 weighed 0.18 g., (which would correspond to 0.16 g. of benzyl acetate, *ca.* 5% of the theoretical). The silver content of this salt revealed it to be slightly impure silver acetate. The above blank showed, therefore, that in twice the time allowed in the experiment with pyruvic acid, the benzyl alcohol and lead tetraacetate did not yield at most more than 5% of benzyl acetate.

Therefore, in the main experiment the benzyl acetate obtained can only be a product of the reaction between pyruvic acid, benzyl alcohol and lead tetraacetate, thus proving that the reaction product of oxidative cleavage of pyruvic acid is acetic acid.

III. Oxidative Cleavage of Trimethylpyruvic Acid

(1) Oxidation in the Presence of Water. (a) Quantitative Determination of Carbon Dioxide.—The determination was carried out in the same way as described for pyruvic acid: 530.0 mg. of keto acid yielded 5.6 mg. of carbon dioxide in water-free medium (room temperature); addition of 10 cc. of water gave a further 168.9 mg. of carbon dioxide (temperature of reaction flask 40–45°). The total amount of carbon dioxide obtained was 174.5 mg. (97.5% of the theoretical).

(b) Isolation and Identification of the Second Cleavage Product.—1.30 grams (0.01 mole) of trimethylpyruvic acid was dissolved in 35 cc. of distilled water at 40° and 4.43 g. (0.01 mole) of finely pulverized lead tetraacetate was added in three portions with shaking. The oxidation took place immediately and was accompanied by a strong evolution of carbon dioxide. After thirty minutes 5 cc. of 5 *N* sulfuric acid was added and the solution extracted with ether in a continuous extractor for twenty-four hours. The ether extract, dried with sodium sulfate, was concentrated and the residue separated by fractional distillation under normal pressure into three fractions: (1) boiling up to 100°, (2) from 100–120° (1.89 g., mainly acetic acid), and (3) 120–160° (1.5 g.). Fraction 3 was separated again by fractional distillation into three fractions with b. p. ranges 118–125°, 126–148°, 148–165°. The last two fractions were only slightly soluble in water and possessed an odor similar to that of butyric acid. For the further purification and identification of the acid, an aqueous solution of the combined last two fractions, neutralized with barium hydroxide and concentrated to a small volume, was mixed with a concentrated aqueous solution of silver nitrate and the precipitated mixture of silver salts (acetate and silver trimethylacetate) separated by recrystallization from hot water. The silver trimethylacetate thus obtained was almost pure. Silver determination: calcd., for silver salt of trimethylacetic acid, Ag, 51.6. Calcd. for silver salt of acetic acid, Ag, 64.6. Found: Ag, 53.7.

(c) Lead Tetraacetate Required for Cleavage.—The determination was carried out as described in II (1c): 10 cc. of 0.1 *M* trimethylacetic acid required 19.2 cc. of 0.05 *M* lead tetraacetate in the presence of water and 20.1 cc. in the presence of methyl alcohol which is equivalent to 0.96 and 1.00 mole of lead tetraacetate, respectively, for the cleavage of 1 mole of trimethylacetic acid.

(2) Oxidation in the Presence of Methyl Alcohol.—(a) Quantitative Determination of Carbon Dioxide: 496.7 mg. of keto acid yielded 5.9 mg. of carbon dioxide in dry acetic acid; addition of 10 cc. of absolutely dry methyl alcohol gave a further 174.10 mg. of carbon dioxide (tem-

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[9] Dehydrated by shaking for a long time with Drierite and centrifuged just before using.

[10] Dried with metallic sodium.

perature of reaction flask, 45–50°); total amount of carbon dioxide obtained, 180.0 mg. (107% of the theoretical.)

(3) **Isolation and Identification of the Cleavage Product of Trimethylpyruvic Acid in the Presence of Benzyl Alcohol. (Benzyl Trimethylacetate as Intermediate Compound.)**—To a solution of 1.30 g. (0.01 mole) of keto acid and 1.08 g. (0.01 mole) of absolutely dry benzyl alcohol in 20 cc. water-free benzene was added 4.43 g. (0.01 mole) of lead tetraacetate. The temperature of the solution rose in a short time from 24 to 37° with strong evolution of carbon dioxide. After the solution had cooled to its initial temperature and the evolution of carbon dioxide had stopped, the lead diacetate was centrifuged off, washed several times with benzene and ether and the wash solutions added to the supernatant. By carefully distilling off the ether and benzene and distillation of the residue *in vacuo*, 1.26 g. of a clear liquid boiling from 84–91° (at 7 mm.) was obtained. According to the saponification data, it contained 56% of benzyl trimethylacetate (0.374 g. of esterified trimethylacetic acid, 37% of the theoretical). The remainder apparently consisted of unesterified benzyl alcohol. The preparation of the silver salt of trimethylacetic acid from benzyl trimethylacetate was carried out as described for the preparation of silver acetate from benzyl acetate. The silver salt (crude product) obtained by this method contained 52.7% silver. Calculated for silver salt of trimethyl acetic acid, 51.6% of silver.

IV. Oxidative Cleavage of Phenylglyoxylic Acid

(1) **Oxidation in the Presence of Water.—(a) Quantitative Determination of Carbon Dioxide.**—0.4667 gram of absolutely dry phenylglyoxylic acid was dissolved in 10 cc. of absolutely dry acetic acid and a suspension of 4 g. of finely pulverized lead tetraacetate in 15 cc. of acetic acid was added. A bulky white, crystalline precipitate formed.[11] During the blank run the carbon dioxide liberated equalled 9.2 mg. After the addition of 15 cc. of water the precipitate dissolved again and an additional 120.8 mg. of carbon dioxide was obtained: total, 130.0 mg. (95% of the theoretical).

(b) Identification of the Second Cleavage Product.—To a solution of 1.5 g. of phenylglyoxylic acid in 50 cc. of 30% acetic acid was added a suspension of 4.48 g. of finely pulverized lead tetraacetate in 40 cc. of glacial acetic acid. The oxidative cleavage proceeded quickly and with slight warming. After the lead tetraacetate was used up the lead was precipitated by addition of the calculated amount of sulfuric acid. Concentration of the solution *in vacuo*, extraction of the residue with boiling ether and evaporation of the extract yielded 1.18 g. (96.7% of the theoretical) of pure benzoic acid, m. p. 122.5° (recrystallized from water); mixed m. p. with pure benzoic acid, 122.5°.

(c) Lead Tetraacetate Required for Cleavage.—The determination was carried out as described in II (1c). Ten cc. of 0.1 *M* phenylglyoxylic acid required 19.7 cc. of 0.05 *M* lead tetraacetate in the presence of water and 19.0 cc. in the presence of methyl alcohol, which is equivalent to 0.99 and 0.95 mole of lead tetraacetate, respectively, per mole of keto acid oxidized.

(2) **Oxidation in the Presence of Ethyl Alcohol.—(a) Quantitative Determination of Carbon Dioxide.**—0.5448 gram of phenylglyoxylic acid dissolved in 10 cc. of acetic acid yielded 7.8 mg. of carbon dioxide during the blank run. Addition of 5 cc. of ethyl alcohol liberated an additional 146.4 mg. of carbon dioxide; total, 154.2 mg. of carbon dioxide (96.5% of the theoretical).

(b) Isolation of Ethyl Benzoate from Cleavage in the Presence of Ethyl Alcohol.—To a solution of 1.5 g. of phenylglyoxylic acid and 10 cc. of absolutely dry ethyl alcohol in 30 cc. of absolutely dry benzene was added a solution of 4.43 g. of lead tetraacetate in 60 cc. of benzene and the mixture was kept at 45°[12] (carbon dioxide evolution). After one hour the lead acetate precipitate was centrifuged off and washed with ether. The combined benzene and ether solutions were extracted with 10% sodium bicarbonate solution to remove acetic acid, dried with solid potassium carbonate and concentrated. The residue, distilled *in vacuo*, yielded 1.2 g. (80% of the theoretical) of benzoic acid ethyl ester b. p. (756 mm.) 211–212°, $n^{26}\text{D}$ 1.5038.

(3) **Isolation of the Cleavage Product in the Presence of Hydrogen Cyanide.**—To a solution of 1.5 g. of phenylglyoxylic acid in 25 cc. of absolutely dry benzene was added a suspension of 4.43 g. of lead tetraacetate in 40 cc. of dry benzene and the mixture kept at 40–45°. The bright orange color which appeared immediately disappeared in a few minutes and the lead salt of the α-keto acid began to precipitate from the colorless solution. After forty-five minutes the solution was cooled in ice water, and about 5 cc. of anhydrous hydrogen cyanide was added, whereupon the lead salt of the α-keto acid redissolved quickly with simultaneous evolution of carbon dioxide and precipitation of lead acetate. The clear benzene solution was decanted and concentrated, using a fractionating column. In order to remove traces of lead salt the residue was dissolved in dry ether, filtered and again concentrated. The concentrate was distilled *in vacuo* and yielded 0.65 g. of phenylglyoxylic *nitrile* (50% of the theoretical), b. p. (9 mm.) 82°; b. p. (758 mm.) 208–210°; $n^{26}\text{D}$ 1.5303.

V. Oxidative Cleavage of Phenylpyruvic Acid

(1) **Oxidation in the Presence of Water. (a) Quantitative Determination of Carbon Dioxide.**[13]—0.492 gram of dry phenylpyruvic acid dissolved in 10 cc. of absolutely dry acetic acid yielded, after addition of 2.8 g. of finely pulverized lead tetraacetate, 13.2 mg. of carbon dioxide in the blank run. After addition of 10 cc. of water, a further 112.8 mg. of carbon dioxide was produced; total, 126.0 mg. of carbon dioxide (95% of the theoretical).

(b) The Identification of the Second Cleavage Product.—To 1.64 g. (0.01 mole) of phenylpyruvic acid dissolved in 30 cc. of glacial acetic acid was added 50 cc. of water and immediately afterward 9.3 g. (0.021 mole) of finely pulverized lead tetraacetate. The temperature of the solution rose very quickly from 27 to 39°. After ten minutes an additional 40 cc. of water was added and the mixture kept at room temperature for one hour. The lead

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[11] The lead content of this precipitate (41%) agrees with that of plumbous phenylglyoxylate.

[12] The yield of benzoic acid ester does not differ when one adds the lead tetraacetate to the phenylglyoxylic acid in benzene first and the ethyl alcohol after thirty minutes.

[13] The experiment was carried out at room temperature except at the end when the reaction flask was warmed to 50°.

was removed by addition of 21 cc. of 2 *N* sulfuric acid and the precipitate extracted several times with alcohol and ether. The supernatant liquid combined with the alcohol and ether washings was evaporated to dryness *in vacuo*. Since attempts to isolate phenylacetic acid failed, it was obvious that secondary reactions had occurred (see theoretical part). The residue was dissolved in a mixture of 25 cc. of alcohol and 25 cc. of 2 *N* sodium hydroxide and warmed for one hour on the water-bath. After addition of 25 cc. of 2 *N* sulfuric acid the solution was evaporated again to dryness and the residue (I) exhaustively extracted with boiling ether. From the ether extract was obtained 500 mg. of fairly pure mandelic acid. Dissolving of residue (I) in a few cc. of dilute hydrochloric acid, evaporation to dryness and extraction with ether yielded a further 220 mg. of crude mandelic acid: total yield 0.77 g. of mandelic acid (50.6% of the theoretical); m. p. 118.5° after recrystallizing twice from chloroform. A mixed m. p. with mandelic acid showed no depression. The acid was readily soluble in water, gave an intense yellow color with ferric chloride and was oxidized to benzaldehyde by lead tetraacetate. The synthetically obtained mandelic acid by acetylation with acetic anhydride yielded acetylmandelic acid with the correct m. p., 54°.

(c) Lead Tetraacetate Required for Cleavage.—The determination was carried out as described in II (1c). Ten cc. of 0.1 *M* phenylpyruvic acid required 39.0 cc. of 0.05 *M* lead tetraacetate in the presence of water and 37.8 cc. in the presence of methyl alcohol which is equivalent to 1.95 and 1.90 moles of lead tetraacetate, respectively, for the cleavage of 1 mole of keto acid. The second mole of lead tetraacetate probably was used in the acetylation of the —CH_2— group.

α-Keto Alcohols

Oxidative Cleavage of α-Keto Alcohols by Lead Tetraacetate in the Presence of Hydroxyl-forming Compounds.—The oxidative cleavage of α-keto alcohols by lead tetraacetate in the presence of hydroxyl-forming compounds leads to the formation of two products, one an acid, the other an aldehyde (or ketone, if the carbinol is tertiary in type). Both products of the cleavage of four α-keto alcohols have been identified (with one exception) as described below. The exception was in the case of acetylmethylcarbinol where the acid expected is acetic acid.

VI. Oxidative Cleavage of Acetylmethylcarbinol in the Presence of Water

(a) Identification of Acetaldehyde.—To 0.88 g. (0.1 mole) of freshly distilled acetylmethylcarbinol (b. p. 143.5–145°) dissolved in 20 cc. of 90% acetic acid was added 4.45 g. of lead tetraacetate. The solution became slightly warm. In order to avoid loss of acetaldehyde the process of oxidation was carried out in a closed vessel which was cooled occasionally. After twenty minutes the solution was cooled in ice and 50 cc. of water and 0.54 cc. of concentrated sulfuric acid were added. The lead sulfate was removed by centrifuging and the supernatant liquid added to a solution of lukewarm dilute hydrochloric acid containing 2.1 g. of 2,4-dinitrophenylhydrazine. The preparation was kept in ice for thirty minutes to ensure complete precipitation. After filtering with suction, the precipitate was washed with dilute hydrochloric acid and dried *in vacuo* over phosphorus pentoxide and potassium hydroxide; 2.13 g. (95% of the theoretical) of acetaldehyde 2,4-dinitrophenylhydrazone was obtained which melted at 162° after recrystallization from alcohol.

(b) Lead Tetraacetate Required for Cleavage.—The equivalent was determined as described in II (1c). The oxidative cleavage of 1 mole acetylmethylcarbinol required 1 mole of lead tetraacetate in the presence of water.

VII. Oxidative Cleavage of Benzoylcarbinol with Lead Tetraacetate

(1) In the Presence of Water. (a) Isolation of Benzoic Acid.—1.36 g. (0.01 mole) of benzoylcarbinol was dissolved in 25 cc. of 90% acetic acid and 4.84 g. (0.011 mole) of finely powdered lead tetraacetate added. The mixture was kept for twenty minutes at 50–55° with frequent shaking. After the cleavage was completed, the lead was precipitated as lead sulfate by addition of the calculated amount of concentrated sulfuric acid and removed by centrifuging. The acetic acid solution, evaporated *in vacuo*, yielded a residue out of which the benzoic acid was extracted with ether. On evaporation of the ether 0.96 g. (78.6% of the theoretical) of almost pure benzoic acid remained; m. p. after recrystallization from water was 122°. The mixed m. p. with benzoic acid showed no depression.

(b) The cleavage of the carbinol and isolation of aldehyde was carried out by procedures similar to those described for acetyl-methyl-carbinol. 1.36 g. (0.01 mole) of benzoylcarbinol yielded 1.75 g. (83% of the theoretical) of formaldehyde 2,4-dinitrophenylhydrazone which when purified by recrystallization from alcohol or petroleum ether had m. p. 154.5°.

(2) In the Presence of Ethyl Alcohol. Isolation of Ethyl Benzoate.—To a solution of 1.36 g. (0.01 mole) of absolutely dry benzoylcarbinol in a mixture of 25 cc. of absolute glacial acetic acid[14] and 5 cc. absolute ethyl alcohol 4.84 g. (0.011 mole) of finely powdered lead tetraacetate was added. The solution was heated to 50–55° and kept at this temperature for thirty minutes with frequent shaking. The preparation was diluted with 60 cc. of distilled water and the ethyl benzoate formed was extracted with ether under reflux. The ether extract was shaken with saturated sodium bicarbonate solution to remove free acid and was carefully concentrated. Distillation of the residue yielded 0.90 g. (60% of the theoretical) of benzoic acid ethyl ester, b. p. (747 mm.) 211–212°.

VIII. Oxidative Cleavage of Benzoin with Lead Tetraacetate

(1) In the Presence of Water. (a) Isolation of Benzoic Acid.—The cleavage of benzoin and isolation of the cleavage product, benzoic acid, were carried through in the same way as described for the cleavage of benzoylcarbinol (VII, 1a). However, before evaporation, the ether extract was shaken with saturated sodium sulfite solution for three hours to remove the benzaldehyde. From 2.12 g. (0.01 mole) of benzoin 0.9 g. (74% of the theoretical) of pure benzoic acid of m. p. 122.5° was obtained.

(b) Identification of Benzaldehyde as *p*-Nitrophenylhydrazone.—2.12 g. (0.01 mole) of benzoin was oxidized

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[14] Glacial acetic acid and ethyl alcohol were dried by shaking for several days with Drierite and centrifuged before using.

with 4.5 g. of lead tetraacetate in 25 cc. of glacial acetic acid (VII, 1a). After removal of lead as sulfate, 2 g. of *p*-nitrophenylhydrazine was added and the solution warmed to 50°. After thirty minutes the preparation was diluted with a four-fold volume of water and kept at 0° for an hour. The crude hydrazone after recrystallization from ethyl alcohol yielded 1.8 g. (75% of the theoretical) of benzaldehyde-*p*-nitrophenylhydrazone with m. p. 192°.

(c) **Lead Tetraacetate Required for Cleavage.**—The equivalent was determined as described in II (1c) except that, due to the insolubility of benzoin in acetic acid, a 0.05 *M* solution was used. The mixture was kept at 50° for two and one-half hours. The oxidative cleavage of 1 mole of benzoin required 1.01 mole of lead tetraacetate in the presence of water and 1.01 mole in the presence of methyl alcohol.

(2) **In the Presence of Ethyl Alcohol. Isolation of Ethyl Benzoate.**—The cleavage of benzoin with lead tetraacetate in the presence of ethyl alcohol was carried out as described for benzoylcarbinol. After dilution with water the mixture was extracted with ether. The ether layer was shaken with saturated sodium bicarbonate solution to remove acids and with concentrated sodium bisulfite to remove benzaldehyde. After evaporation of the ether, the residue was distilled *in vacuo* and redistilled at atmospheric pressure.

From 2.12 g. (0.01 mole) of benzoin 1.26 g. (84% of the theoretical) of benzoic acid ethyl ester was obtained, b. p. (756 mm.) 212°. Hydrolysis of the ethyl ester yielded benzoic acid, m. p. 122.5°.

IX. Oxidative Cleavage of Anisoin by Lead Tetraacetate

(1) **In the Presence of Water.** (a) **Isolation of Anisic Acid.**—The cleavage of anisoin with lead tetraacetate was carried out by the same procedure as described for benzoylcarbinol. However, in this case, the anisic acid was separated from the ether extract by shaking with an aqueous solution of sodium bicarbonate. Acidification of the bicarbonate extract yielded anisic acid. From 2.72 g. (0.01 mole) of anisoin, 1.1 g. (76.8% of the theoretical) of anisic acid, m. p. 185° (recrystallized from water), was obtained.

(b) **Isolation of Anisaldehyde as *p*-Nitrophenylhydrazone.**—The ether extract (IX, 1a) freed of the anisic acid by the sodium bicarbonate solution was concentrated by distilling off the ether under ordinary pressure. The residue contained crystals which were isolated by taking up the residue in ethyl alcohol and filtering. The alcohol-insoluble material, yellow-green in color, weighed 0.15 g. (5% of the starting material), had a m. p. 133° and proved to be anisil.[15]

The alcoholic solution which contained the anisaldehyde was added to a warm solution of *p*-nitrophenylhydrazine in dilute hydrochloric acid; yield 2.12 g. (83% of the theoretical)[16] of *p*-nitrophenylhydrazone of anisaldehyde; m. p. after recrystallization from ethyl alcohol, 162°.

(c) **Lead Tetraacetate Required for Cleavage.**—The equivalent was determined as described in II (1c). The mixture was kept at 50° for four hours. The oxidative cleavage of 1 mole of anisoin required 0.93 mole of lead tetraacetate in the presence of water and 0.97 mole in the presence of methyl alcohol.

(2) **In the Presence of Ethyl Alcohol. Isolation of the Anisic Acid Ethyl Ester.**—The cleavage of anisoin in the presence of ethyl alcohol was carried out exactly as described for benzoin (VIII, 2). The residue obtained by evaporation of the ether extract contained a crystalline substance which was separated by taking up in alcohol and filtering. The isolated substance (0.45 g., 16.5% of the starting material) had a m. p. 133° and was found to be anisil. The alcoholic filtrate and wash solution were combined and concentrated and the residue distilled *in vacuo;* 2.72 g. (0.01 mole) of anisoin yielded 1.02 g. (68% of the theoretical) of anisic acid ethyl ester, b. p. (8 mm.) 125–130°; b. p. (750 mm.) 267–269°. The ester after saponification with alkali and acidification yielded anisic acid (m. p. 182°).

X. Oxidation of α-Keto Alcohols with Lead Tetraacetate in Absence of Hydroxyl-forming Compounds.[17]

(a) **Diacetyl from Acetylmethylcarbinol.**—0.88 gram (0.01 mole) of freshly distilled acetylmethylcarbinol and 4.43 g. (0.01 mole) of lead tetraacetate in 30 cc. of absolutely water-free benzene was kept at 50° for four hours. After cooling the solution to room temperature the lead salt was separated by centrifuging and washed several times with benzene. The combined benzene solutions were heated with a mixture of 30 cc. of 20% hydroxylamine chlorohydrate, 30 cc. of 20% sodium acetate and 30 cc. of 10% nickel chloride at 80° for one hour with frequent shaking. By distilling off the benzene, 0.60 g. of nickel dimethylglyoxime was obtained which corresponded to 0.358 g. of diacetyl (41.6% of the theoretical).

(b) **Benzil from Benzoin.**—To a solution of 2.12 g. (0.01 mole) of benzoin (dried in high vacuum) in 25 cc. of absolutely dry acetic acid was added 4.43 g. (0.01 mole) of finely pulverized lead tetraacetate and the mixture kept at 50° for twenty-four hours with occasional shaking and exclusion of moisture. The solution was evaporated to dryness *in vacuo* at about 40–45° bath temperature and the residue completely extracted with ether. After shaking the ether extract with saturated sodium bicarbonate solution and evaporating to dryness, 1.75 g. of benzil (83.4% of the theoretical) with m. p. 94–95° (recrystallized from carbon tetrachloride and ethyl alcohol) was obtained.

(c) **Anisil from Anisoin.**—The oxidation of anisoin to anisil was carried out exactly as described for benzoin: 2.72 g. (0.01 mole) of anisoin yielded 2.0 g. (74% of the theoretical) of anisil with m. p. 133° and 0.30 g. (20% of the theoretical) of anisic acid,[18] m. p. 184.5° (recrystallized from water).

Acknowledgment.—Grateful acknowledgment is made to Dr. C. C. Lucas for assistance in preparing this manuscript in English as well as to H. N. MacFarland for preparing some of the keto acids used in this investigation.

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(15) This substance, which is here a by-product, becomes the main product when working in the absence of hydroxyl-forming compounds (see Xc).

(16) After deduction of the anisoin used up in the formation of anisil.

(17) In this and the following experiments, the solvents used must be absolutely dry to avoid oxidative cleavage.

(18) Obtained by acidification of the sodium bicarbonate extract of the ether solution.

Summary

1. Under certain conditions lead tetraacetate effects quantitative oxidative cleavage of α-keto acids and α-keto alcohols. The reaction seems to be one of general application.

2. This reaction occurs only after formation of a vicinal hydroxyl pair and therefore has to be considered as a glycol cleavage.

3. The formation of the "pseudoglycols" takes place by addition to the keto group. Water, alcohols (*e. g.*, methyl, ethyl and benzyl alcohols) and hydrocyanic acid were found capable of such an addition.

4. In the absence of substances forming pseudoglycols by addition no reaction takes place between lead tetraacetate and α-keto acids, whereas α-keto alcohols are oxidized in good yield to their diketones.

5. The nature of the cleavage products is determined by the glycol-forming substance added.

6. In the presence of water, alcohols or hydrocyanic acid the products are as follows: (a) from 1 mole of α-keto acid and 1 mole of lead tetraacetate are obtained 1 mole of carbon dioxide and 1 mole of acid (or ester or keto nitrile). (b) From 1 mole of α-keto alcohol and 1 mole of lead tetraacetate are obtained 1 mole of acid (or its ester) and 1 mole of aldehyde (or ketone).

7. The present use of lead tetraacetate to detect vicinal hydroxyl groups in compounds of unknown constitution may be extended to the detection of the α-keto acid and α-keto alcohol groups, if one compares the reaction of the substance with lead tetraacetate in dry solvents with the behavior in the presence of compounds capable of forming pseudoglycols, as explained above.

8. The method of oxidative cleavage may be employed not only to determine α-keto acids quantitatively by the carbon dioxide evolved but also to distinguish them qualitatively from other keto acids (β, γ, · · ·, etc.).

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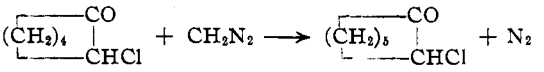
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

The Ring Enlargement of Two Cyclic Alpha-Chloroketones

BY THOMAS R. STEADMAN[1]

A study of the reaction of diazomethane with cyclic α-chloroketones was undertaken in these laboratories in order that further light might be shed on the process of ring enlargement of cyclic systems. Giraitis and Bullock[2] have reported briefly on work similar in character to that described in the present paper. The present investigation has been confined to experiments based on Meerwein's mode of operation,[3,4] involving the introduction of nitrosomethylurethan at a suitable rate into a solution of the ketone in methanol containing a small amount of sodium carbonate. This is quite different from the method employed by Giraitis and Bullock,[2] who used diazomethane in ethereal solution.

The principal reactions in the case of α-chlorocyclohexanone may be represented by the following equations, although the actual intermediate may not be diazomethane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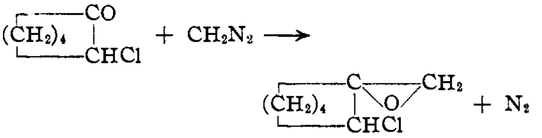
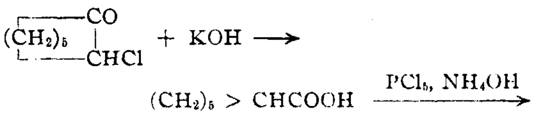

II

It is important to note that when the ring was enlarged, the methylene group entered the ring in such a manner that the chlorine atom remained alpha to the carbonyl group. This was shown by the fact that when the chloroketone was treated with alcoholic sodium hydroxide, cyclohexane carboxylic acid was obtained and identified by conversion to the amide:


III

This degradation was first recognized by Favorskii and Boshowski.[5]

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[1] This investigation was begun by the author at the suggestion and under the direction of the late Prof. E. P. Kohler.

[2] Giraitis and Bullock, THIS JOURNAL, **59**, 951 (1937).

[3] Meerwein, *Chem. Zentr.*, **104**, II, 1758 (1933); German Patent 579,309.

[4] Kohler, Tishler, Potter and Thompson, THIS JOURNAL, **61**, 1057 (1939).

[5] Favorskii and Boshowski, *J. Russ. Phys.-Chem. Soc.*, **50**, 582 588 (1917); *C. A.*, **18**, 1476 (1924).