oxide prior to ignition. The average deviation of the percentages found from those calculated was ±0.15; the maximum in any case did not exceed 0.3 except for the following salts: ethylamine, % H, calcd. 4.6, found 4.2; *m*-amylamine, % H, calcd. 6.2, found 5.8; *l*-aspartic acid, % H, calcd. 3.3, found 3.7; *dl*-leucine, % C, calcd. 39.4, found 38.9; guanidine, % H, calcd. 3.5, found 3.1.

Determination of Solubilities.—The saturated solutions were approached from the supersaturated side by placing samples saturated at 40–50° and containing an excess of the solid phase in a thermostat at 25.0 ± 0.5° and allowing forty-eight or more hours, with shaking, for the attainment of equilibrium.[12] 10.00-ml. aliquots were withdrawn, evaporated to dryness at 80° and the residues weighed. The solubilities of the various diliturates, in water at 25°, are given in Tables I and II and those of dilituric acid, in a number of different solvents at 25°, in the text. The over-all accuracy (*i. e.*, reproducibility) of the solubility data in these tabulations is ±4%.

Recovery of Glycine from its Diliturate.—To 8.4 g. of glycine diliturate in 100 ml. of hot water was added 3 ml. of 15 *N* ammonium hydroxide. The solution was cooled to room temperature, the precipitate removed and the filtrate evaporated to 20 ml. Upon adding 100 ml. of ethanol to the concentrate, glycine began to precipitate. After cooling to 5° the pure white product was recovered and dried *in vacuo*. The weight was 2.30 g. or 89% of the theoretical amount.

Summary

A number of salts of dilituric acid (5-nitrobarbituric acid) have been prepared and a study of their properties has shown that dilituric acid is a satisfactory reagent for the isolation and determination of many organic and inorganic bases.

PASADENA, CALIF. RECEIVED NOVEMBER 3, 1939

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[12] Preliminary experiments with a monovalent salt, soluble in water at 25° to the extent of 50 millimoles per liter, gave identical results, within the limits of experimental error (±2%), when the saturated solution was approached from both sides.

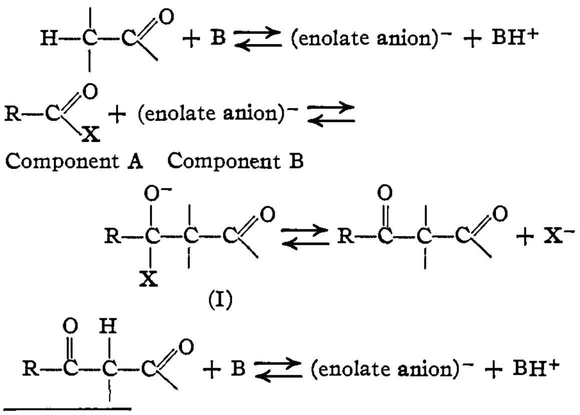
[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF DUKE UNIVERSITY]

Condensations Brought about by Bases. IX. The Relationship between the Claisen and Perkin Types of Condensations[1,2]

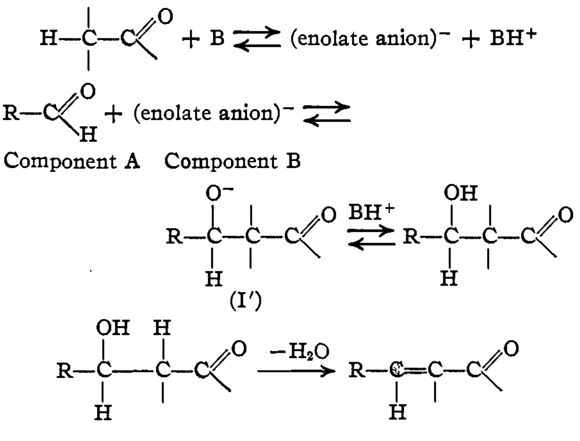
BY CHARLES R. HAUSER AND DAVID S. BRESLOW

The mechanisms for the Claisen[3] (acetoacetic ester) and Perkin[4] types of condensations in the presence of a base B have been represented by the following ionic equations.

Claisen Type

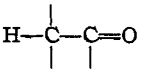


Perkin Type



The purpose of this paper is to compare these two types of condensation and to discuss certain experiments in which it is possible for either or both types to occur.

It is evident from the above equations that in both the Claisen and Perkin reactions component B is the enolate anion of a compound of the type


$\mathrm{H{-}\overset{|}{\underset{|}{C}}{-}\underset{|}{C}{=}O}$ (ester, anhydride, aldehyde, ketone, etc.). Component A, however, is different in the two condensations. In the Claisen reaction

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[1] Paper VIII, THIS JOURNAL, **62**, 62 (1940).

[2] This paper was presented before the Division of Organic Chemistry at the Baltimore meeting of the American Chemical Society, April, 1939.

[3] Two types of reaction are known as Claisen condensations, the acetoacetic ester type and the condensation of a ketone with benzaldehyde by means of alkali. In the present paper the Claisen condensation refers only to the acetoacetic ester type. See (a) Hauser and Renfrow, THIS JOURNAL, **59**, 1823 (1937); (b) Hauser, *ibid.*, **60**, 1957 (1938).

[4] See Hauser and Breslow, *ibid.*, **61**, 793 (1939).

component A is a compound of the type $R{-}C{\overset{\displaystyle /\!\!/ O}{\underset{\displaystyle \diagdown X}{}}}$ (ester, anhydride, acid chloride, etc.), where X is an atom or group that is released as an anion during reaction; whereas in the Perkin reaction component A is an aldehyde, which contains the hydrogen atom in place of X.

A further inspection of the above equations shows that the first two steps of the Claisen and Perkin reactions are analogous. In both types of condensation a compound of the type $H{-}\overset{|}{\underset{|}{C}}{-}\underset{|}{C}{=}O$ is converted by a base into its enolate anion (component B) which condenses with the carbonyl group of component A, giving the anions (I) and (I′) with the negative charge on the oxygen atom, but here the analogy ends. The anion (I) formed in the second step of the Claisen reaction releases X as an anion, forming the β-keto compound (which may or may not be converted into its enolate anion), whereas in the Perkin reaction this is not possible, as there is no X present in the aldehyde; instead, the corresponding anion (I′) takes up a proton from the medium to give the "aldol," which may eliminate water to form an unsaturated compound.

Certain experiments in which it is possible for both the Claisen and Perkin types of condensation to occur now will be considered. Whenever the Perkin reaction is carried out using the enolate of an ester or anhydride as component B, the Claisen type of condensation also is possible, since the ester or anhydride may serve as component A for the latter type of condensation. Thus the fact, noted by Perkin,[5] that carbon dioxide and a ketone are formed when an anhydride is heated with its sodium salt, is best explained on the basis that the anhydride undergoes self-condensation (Claisen type) to give an acetoacetic ester type of intermediate; it is well known that acetoacetic acid gives carbon dioxide and acetone on heating. In this Laboratory we have observed that phenylacetic anhydride[6] (in which the hydrogen on the α-carbon is reactive), when heated with sodium acetate, gives dibenzyl ketone. The latter is formed presumably by the decomposition of an acetoacetic ester type of intermediate. Actually, however, when benzaldehyde is present, an ester or anhydride undergoes very little self-condensation (Claisen type) on treatment with a base, the main reaction being the Perkin condensation giving cinnamic acid or one of its derivatives. Thus, for example, benzaldehyde with acetic anhydride and a base (sodium acetate or a tertiary amine) gives mainly cinnamic acid, and with ethyl acetate and a base (sodium ethoxide or sodium triphenylmethyl), mainly ethyl cinnamate.

It is rather striking that while ethyl acetate when treated with sodium triphenylmethyl is converted to acetoacetic ester within a few minutes,[7] a mixture of ethyl acetate and benzaldehyde when treated with this base gives mainly ethyl cinnamate; if the latter reaction is stopped within one minute the intermediate "aldol," ethyl β-phenyl-β-hydroxypropionate, is obtained in fair yield (20%).[4] Thus, although the Claisen type of condensation occurs very rapidly in the presence of the strong base, sodium triphenylmethyl, the Perkin type of reaction occurs even more rapidly. This is what might be expected, however, since the carbonyl group of benzaldehyde is more active than that of the ester[8] (or anhydride); moreover, when equimolar quantities of ethyl acetate, benzaldehyde and sodium triphenylmethyl are used, most of the ester is probably rapidly converted into its enolate, which cannot serve as component A in the condensation.

The reaction in which component B is a compound of the type $H{-}\overset{\displaystyle R}{\underset{\displaystyle R}{C}}{-}\underset{|}{C}{=}O$, such as ethyl isobutyrate, is of especial interest. Scheibler reported[9] that ethyl isobutyrate condenses with benzaldehyde in the presence of sodium ethoxide to give the "aldol," ethyl β-phenyl-β-hydroxypi-

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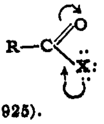
(5) Perkin, *J. Chem. Soc.*, **49**, 322 (1886).

(6) Actually, in this experiment sodium phenylacetate and acetic anhydride were used, but under the experimental conditions phenylacetic anhydride and sodium acetate were formed by double decomposition. See Breslow and Hauser, THIS JOURNAL, **61**, 786 (1939).

(7) Hudson, Dick and Hauser, *ibid.*, **60**, 1960 (1938).

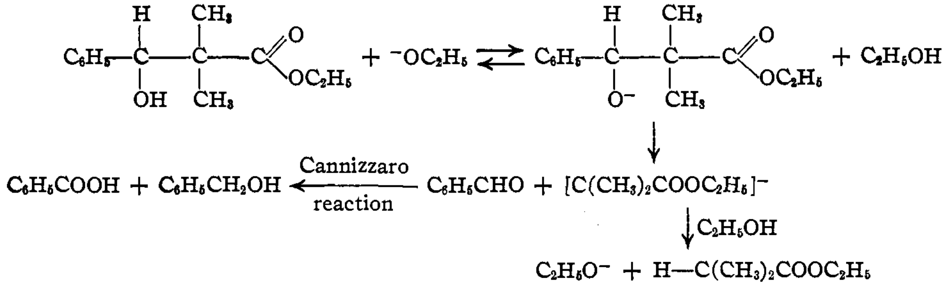
(8) The relative order of activity of the carbonyl group has been indicated by the reaction with the Grignard reagent; the following order is found

$$R{-}C{\overset{/\!\!/ O}{\underset{\diagdown H}{}}} > R{-}C{\overset{/\!\!/ O}{\underset{\diagdown Cl}{}}} > R{-}C{\overset{/\!\!/ O}{\underset{\diagdown OC_2H_5}{}}}$$

(See Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, p. 418). This order may be explained on the basis of the tendency for the T effect; the positive charge on the carbon atom that would result from the change $\overset{\curvearrowright}{C{=}O}$ is partially neutralized in the last two compounds, thus,  $R{-}C{\overset{/\!\!/ O}{\underset{\diagdown \ddot{X}:}{}}}$.

(9) Scheibler and Friese, *Ann.*, **448**, 158 (1925).

valate, but Müller, Gawlick and Kreutzmann[10] were unable to confirm this result. In agreement with Müller and co-workers, we have obtained the Cannizzaro reaction products, benzyl alcohol and benzoic acid, when benzaldehyde and ethyl isobutyrate were allowed to stand with sodium ethoxide and we were unable to isolate any of the hydroxy-ester reported by Scheibler. We have shown further that when this ester, ethyl β-phenyl-β-hydroxypivalate, is allowed to stand with sodium ethoxide, it is decomposed practically completely giving benzaldehyde (most of which undergoes the Cannizzaro reaction forming benzoic acid and benzyl alcohol) and ethyl isobutyrate. This reaction may be illustrated by the following ionic equations in which the enolate anion is represented by a non-committal formula.



$$C_6H_5\text{—}\underset{OH}{\overset{H}{C}}\text{—}\underset{CH_3}{\overset{CH_3}{C}}\text{—}C{\overset{O}{\underset{OC_2H_5}{\lessgtr}}} + {}^-OC_2H_5 \rightleftarrows C_6H_5\text{—}\underset{O^-}{\overset{H}{C}}\text{—}\underset{CH_3}{\overset{CH_3}{C}}\text{—}C{\overset{O}{\underset{OC_2H_5}{\lessgtr}}} + C_2H_5OH$$

$$C_6H_5COOH + C_6H_5CH_2OH \xleftarrow[\text{reaction}]{\text{Cannizzaro}} C_6H_5CHO + [C(CH_3)_2COOC_2H_5]^-$$

$$\downarrow C_2H_5OH$$

$$C_2H_5O^- + H\text{—}C(CH_3)_2COOC_2H_5$$

Müller and co-workers reported that ethyl isobutyrate does not condense with benzaldehyde even in the presence of the stronger base, sodium triphenylmethyl. Recently, however, we have shown[4] that condensation does occur in the presence of this base, and that the "aldol," ethyl β-phenyl-β-hydroxypivalate, can be isolated if the reaction is stopped by acidification within a short time (twenty minutes). We have now shown that this hydroxy ester on standing with sodium triphenylmethyl is partly decomposed, as is illustrated above with the ethoxyl anion from sodium ethoxide, into benzaldehyde (most of which undergoes the irreversible Cannizzaro reaction) and, presumably, the enolate of ethyl isobutyrate. This enolate then condenses with ethyl isobutyrate (formed from some of the enolate and triphenylmethane) to give ethyl isobutyryl-isobutyrate, which seemed to be present in small amounts among the reaction products.

Experimental

Preparation and Purification of Materials.—Benzaldehyde and ethyl isobutyrate were purified as previously described.[4,8]

Ethyl β-phenyl-β-hydroxypivalate was prepared according to the method of Blaise and Herman.[11] The zinc complex was hydrolyzed with cold 20% sulfuric acid until an extraction with dilute sodium carbonate gave no precipitate. The ester was collected at 153–158° at 11 mm. and recrystallized by dissolving it in an equal volume of petroleum ether (30–60°) and chilling the resulting solution for several days; m. p. 38.5–39°.

Sodium ethoxide was prepared from a weighed amount of sodium wire and excess absolute alcohol. The last traces of alcohol were removed by heating the sodium ethoxide for a half-hour at 150° at 20 mm., the flask being flushed out with nitrogen.

Sodium triphenylmethyl was prepared from Eastman Kodak Co. triphenylchloromethane according to the method previously described.[3a]

Attempted Condensation of Benzaldehyde with Ethyl Isobutyrate in the Presence of Sodium Ethoxide.—Sodium ethoxide (prepared from 4.6 g. of sodium) was covered with 100 cc. of dry ether and 17.4 g. (0.15 mole) of ethyl isobutyrate and 15.9 (0.15 mole) of benzaldehyde was added. The mixture was stirred mechanically. Heat was evolved, the ether refluxing, and the mixture turned a dark brown. After standing at room temperature for a week, the mixture was acidified with 30 cc. of glacial acetic acid, extracted with sodium carbonate until alkaline and dried over Drierite. The alkaline solution was acidified and the precipitate that formed recrystallized from hot water; in this way 1.0 g. of benzoic acid, m. p. 120–121°, was obtained. The ether was distilled off from the dried ethereal solution and the deep red residue distilled up to 120° at atmospheric pressure to remove ethyl isobutyrate. The residue was then collected up to 120° at 12 mm. A small residue was left behind, which started decomposing at 120° and gave only a small amount of dark red distillate up to 160°, showing the absence of ethyl phenylhydroxypivalate (b. p. 155–156° at 11 mm.[11]). The fraction boiling up to 120° at 12 mm. presumably consisted mostly of benzyl alcohol. This fraction yielded 7.2 g. of benzyl 3,5-dinitrobenzoate, m. p. 111–112°.[12] This is equivalent to 2.6 g. of benzyl alcohol.

The experiment was also run in the absence of any solvent, the mixture being allowed to stand for twenty-four hours before acidification. Essentially the same results were obtained.

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[10] Müller, Gawlick and Kreutzmann, *Ann.*, **515**, 97 (1934).

[11] Blaise and Herman, *Ann. chim. phys.*, [8] **23**, 532 (1911).

[12] This is the melting point recorded in the literature for this compound. See Shriner and Fuson, "Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1935, p. 87.

Decomposition of Ethyl β-Phenyl-β-hydroxypivalate with Sodium Ethoxide.—Sodium ethoxide (prepared from 2.3 g. of sodium) was covered with 500 cc. of dry ether and 22.2 g. (0.10 mole) of ethyl phenylhydroxypivalate added. The mixture was shaken mechanically for several hours. No heat was evolved but the mixture turned a dark red-brown. It was allowed to stand for sixteen days with occasional shaking. The mixture, which still contained a precipitate, was acidified with 20 cc. of glacial acetic acid in 75 cc. of ether, extracted with dilute sodium carbonate until alkaline and dried over Drierite. The alkaline solution, on acidification and subsequent recrystallization of the precipitate from hot water, yielded 1.1 g. of benzoic acid, m. p. 120–121°.

The ether was distilled off from the dried solution through a long Widmer column and the residue was transferred to a 125 cc. Claisen flask, using as little ether as possible. The ether was carefully distilled off and the residue distilled at atmospheric pressure. The fraction boiling at 105–115° was collected (3.0 g.), most of it coming over at 108–112°. It was identified as ethyl isobutyrate (b. p. 111°) by converting it to isobutyramide, m. p. 127.5–128.5°.[13] The residue from the atmospheric distillation was distilled at 11 mm. The first fraction (5.6 g.) was collected at 75–96°. The second fraction (0.5 g.) boiled at 101–130°, and the third (1.1 g.) at 130–165°. A deep red residue was left weighing 3.0 g.

The first fraction was treated with a saturated solution of sodium bisulfite. No precipitate was formed, showing the absence of any benzaldehyde. The mixture was extracted with ether, the ether evaporated and the residue refluxed with 25 cc. of 25% sodium hydroxide solution for six hours in order to hydrolyze any ethyl benzoate present.[14] The mixture was extracted with ether and the alkaline solution acidified. The precipitate formed was recrystallized from hot water, 0.24 g. of benzoic acid, m. p. 121–122°, being obtained. The ether solution was dried, the ether distilled off and the residue distilled at atmospheric pressure; 3.4 g. boiling at 203–204° was obtained. It was identified as benzyl alcohol by its 3,5-dinitrobenzoate, m. p. 110–111°.

The second fraction (mid-fraction) was discarded. The third fraction, which was an oily solid at room temperature, was water-insoluble. This was presumably recovered ethyl phenylhydroxypivalate, but it would not yield a crystalline solid even after several recrystallizations from 30–60° ligroin. A previous duplicate run yielded no recovered ester.

The yield of ethyl isobutyrate was 3.0 g. (25.9%). The yield of benzaldehyde, based on benzoic acid, benzyl alcohol and the benzoic acid formed by the hydrolysis of the small amount of ethyl benzoate in fraction one, was 4.5 g. (42.5%).

Decomposition of Ethyl β-Phenyl-β-hydroxypivalate with Sodium Triphenylmethyl.—Sodium triphenylmethyl was prepared from 41.8 g. (0.15 mole) of triphenylchloromethane dissolved in a liter of ether and 1000 g. of 1% sodium amalgam. The resulting solution was analyzed according to the method of Hudson, Dick and Hauser.[7] To the solution, containing 0.10 mole of sodium triphenylmethyl, was added an equivalent amount (22.2 g., 0.10 mole) of ethyl phenylhydroxypivalate. No appreciable amount of heat was evolved, but the resulting solution was colored a much lighter red than the original. A copious precipitate formed on standing. After standing sixteen days at room temperature, the mixture was acidified with 20 cc. of glacial acetic acid in 75 cc. of ether, extracted with sodium carbonate until alkaline and dried over Drierite. The carbonate extract on acidification gave a precipitate which, after recrystallization from hot water, yielded 0.14 g. of benzoic acid, m. p. 121–122°.

The dried ethereal solution was distilled from a water-bath through a short Widmer column. After the ether had been removed, the liquid remaining in the flask was heated to 120° at atmospheric pressure, but no distillate was obtained; evidently no appreciable amount of ethyl isobutyrate (b. p. 111°) was present in the reaction mixture. The residue was distilled at 12 mm. collecting everything up to 190°. A large residue remained, consisting at least partly of triphenylmethane. The distillate was then redistilled at 10 mm. Two fractions were collected, the first boiling up to 120° (3.9 g.) and the second at 140–165° (5.4 g.). The second fraction was chilled for several days with 5 cc. of petroleum ether (30–60°), the petroleum ether decanted off and the resulting precipitate dried *in vacuo*. In this manner 4.4 g. of ethyl phenylhydroxypivalate, m. p. 38.5–39.5°, was recovered unchanged.

The first fraction (3.9 g.) boiling up to 120° at 10 mm. consisted of a mixture of benzaldehyde, benzyl alcohol and apparently ethyl isobutyryl-isobutyrate. The benzaldehyde was first removed as the sodium bisulfite addition complex (0.05 g.). The mixture was then heated with alkali in an attempt to hydrolyze the ethyl isobutyrylisobutyrate, but no di-isopropyl ketone could be isolated; however the alkaline solution on acidification gave a strong odor of isobutyric acid. It should be mentioned that hydrolysis of this β-keto ester usually gives a poor yield of di-isopropyl ketone. The organic liquid left after the attempted hydrolysis consisted mostly of benzyl alcohol, which was identified as the 3,5-dinitrobenzoate, 2.1 g. of the latter being obtained.

Summary

1. The mechanisms for the Claisen and Perkin types of condensation are compared and reactions in which both types of condensation are possible are discussed.

2. It has been shown that in the presence of sodium ethoxide ethyl isobutyrate does not condense with benzaldehyde. The condensation product that would be formed, ethyl β-phenyl-β-hydroxypivalate, is decomposed by sodium ethoxide to give benzaldehyde and ethyl isobutyrate.

3. Although ethyl isobutyrate condenses with benzaldehyde in the presence of sodium triphenyl-

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[13] Shriner and Fuson, ref. 12, p. 131.

[14] Claisen reported the presence of methyl benzoate when benzaldehyde was treated with sodium methoxide. See Claisen, *Ber.*, **20**, 646 (1887).

methyl to give ethyl β-phenyl-β-hydroxypivalate, the latter on standing in the presence of this base is again decomposed.

4. The mechanisms of the above decompositions are discussed.

DURHAM, NORTH CAROLINA RECEIVED NOVEMBER 9, 1939

[CONTRIBUTION FROM THE UNITED STATES DEPARTMENT OF AGRICULTURE, BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE]

The Constituents of Certain Species of Helenium. III. The Ester Nature of Tenulin

BY E. P. CLARK

A description of tenulin and some of its derivatives was given in the second paper of this series.[1] No attempt was made to interpret the reactions reported, but as work on the material has progressed facts have emerged that warrant comment.

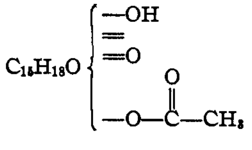
From the data already recorded the following conclusions may be drawn: Tenulin has a double bond, as two atoms of bromine *add* to form a dibromotenulin and hydrogenation with Adams catalyst yields a dihydro compound. Dihydrotenulin, as well as its isomer, dihydroisotenulin, readily forms phenylhydrazones, whereas the unhydrogenated materials do not. It is inferred, therefore, that both tenulin and isotenulin have a carbonyl group, which is sterically hindered by the presence of the double bond. Although tenulin does not give ordinary reactions for hydroxyl groups, the fact that heating it to 300° for a very short time produces an anhydro derivative is a reasonable indication that a sterically hindered hydroxyl group is present.

The work reported at this time shows that tenulin has also another hydroxyl group esterified as an acetate. This information was obtained in experiments having two different lines of approach. First it has been found that alkaline hydrogen peroxide oxidizes both tenulin and isotenulin to a monocarboxylic acid, $C_{15}H_{20}O_7$, which has been named "tenulinic acid." If potassium permanganate is used as the oxidizing agent, another acid, which crystallizes as $C_{17}H_{22}O_8 \cdot {}^1/_2H_2O$, is obtained. The difference between these two acids, aside from the water of crystallization, is C_2H_2O, which should result from the hydrolysis of an acetyl compound. Furthermore, tenulinic acid may be acetylated readily to give a quantitative yield of the second acid, and on hydrolysis it gives back tenulinic acid. The acid obtained by permanganate oxidation of both tenulin and isotenulin is therefore acetyltenulinic acid. The correctness of the formulas of the two acids was checked by the analysis of the acids themselves as well as by the analysis of their methyl esters.

The second approach was to apply hydrolytic reactions to isotenulin. When isotenulin is dissolved in concentrated sulfuric acid and heated for a short time, a substance, $C_{15}H_{20}O_4$, m. p. 255°, is obtained. This has the composition that would result from the hydrolytic loss of an acetyl group from isotenulin. At the same time exactly one mole of acetic acid is formed. The compound $C_{15}H_{20}O_4$, m. p. 255°, is identical with the by-product obtained by the action of 0.1 *N* sodium hydroxide or by prolonged action of 5% sodium carbonate solution on tenulin,[1] and this fact explains its formation as a by-product in the more drastic methods of preparing isotenulin. Further proof that the $C_{15}H_{20}O_4$ compound is deacetylated isotenulin is furnished by its ready reacetylation to isotenulin.

The same hydrolytic action takes place when concentrated sulfuric acid reacts on dihydroisotenulin. The deacetylated product $C_{15}H_{22}O_4$ melts at 203°. Alkali does not have the deep-seated action on dihydroisotenulin that it does on tenulin, and the hydrolysis may be brought about with little loss when aqueous alkali is employed. Both 10 and 50% potassium hydroxide solutions were used, and in each case the desacetyldihydroisotenulin, m. p. 203°, was obtained.

These facts constitute sufficient evidence of the presence of an acetoxy group in tenulin. It thus follows that tenulin may be represented as



$$C_{15}H_{18}O\left\{\begin{array}{l} -OH \\ = \\ =O \\ -O-\overset{\displaystyle O}{\overset{\|}{C}}-CH_3 \end{array}\right.$$

In further consideration of the acetyl group at-

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(1) Clark, THIS JOURNAL, 61, 1836 (1939).