[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE JOHNS HOPKINS UNIVERSITY AND MIDDLEBURY COLLEGE]

THE OXIDATION OF TETRONIC ACIDS. I. STRUCTURAL CRITERIA FOR THE FORMATION OF 1,2-DIKETONES

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No satisfactory mechanism has been devised for the production of 2,3-butanedione by the acid oxidation of 3-methyltetronic acid (I). Wolff proposed (1) an intermediate 3-hydroxytetronic acid (II) whose hydroxylic hydrogen atom was assumed to rearrange to the 5-position with simultaneous loss of carbon dioxide. This hypothesis was based upon his observation that 3-bromo-3-methyltetronic acid (III) was slowly hydrolyzed by base to form a solution from which 2,3-butanedione and carbon dioxide were liberated on acidification. To date no further work has appeared on this remarkable reaction.

In order to explore the limits of the oxidation reaction, and at the same time to gain information regarding its nature, we have prepared and studied various types of tetronic acids from which α-diketones might arise. These fall into three structural classes. In class (a) are acids carrying only 5-substituents, while in (b) the substitution is entirely on the 3-carbon atom, and in (c) both 3- and 5-substitution are present. These compounds and the results of their oxidation are shown in Fig. 2 where, for the sake of uniformity, non-enolic structures are used.

It is apparent that the formation of α-diketones is not a general reaction, but is dependent upon certain structural features in the parent tetronic acid. The first and most important of these is the presence of methylene hydrogen to permit enolization. Second, if the 3-carbon is monosubstituted, α-diketones are produced regardless of substitution on the 5-carbon atom. On the other hand, if the 3-carbon is unsubstituted, the 5-carbon must carry one and only one substituent group. Significant differences also appear with respect to the natu e of the diketones produced. Thus, if the tetronic acid carries one 3-substituent, then regardless of 5-substitution, the over-all oxidation process results in decarboxylation with *reduction* of the 5- and *oxidation* of the 3-carbon atoms.[3] However, in the case of monosubstitution on the 5-carbon, this rule is exactly reversed. These cases, and also that of tetronic acid itself, will be considered later in this paper.

It is necessary at this point to consider the possibility of α-diketones arising from the oxidation of the hydrolysis products of tetronic acids. Previous work (1, 2) has shown that ketols result from hydrolysis of tetronic acids, and in both the earlier oxidation by Wolff (1) and the present investigation, ketols accom panied α-diketones. Moreover, it has been established that ketols are capable

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[2] From the M. S. thesis of Mrs. Helen R. Patterson, Middlebury College, 1946.

[3] The rule has been substantiated for a 3,5-disubstituted tetronic acid containing dissimilar groups. This will appear in a later communication.

of acid-catalyzed isomerizations (3), and of oxidation by air (4) to the corresponding α-diketones. Of special significance in this context is the report (5) that α-hydroxybutyraldehyde isomerizes in hot acid solution to 3-hydroxy-2-butanone, with simultaneous formation of 2,3-butanedione and polymeric products.

We thus turned our attention to the acid hydrolysis of several tetronic acids. The experiments were conducted under nitrogen to protect the products, and the amounts of carbon dioxide evolved furnished a guide to the completion of the hydrolysis. From 3-ethyltetronic acid [Class (b)(I)], 1-hydroxy-2-pentanone was obtained, and oxidation of this ketol under the normal conditions failed to furnish any 2,3-pentandione. The products were carbon dioxide, formic acid, and butyric acid.

Surprising results attended our studies of 3,5-dimethyltetronic acid [Class (c)(I)], and 5-methyltetronic acid [Class (a) (I)]. The former, on hydrolysis, slowly formed the expected 2-hydroxy-3-pentanone, but oxidation of this ketol did not produce 2,3-pentanedione. Similarly, no 2,3-butanedione was formed on oxidation of the hydrolysis product of 5-methyltetronic acid. Yet in both instances, traces of the respective α-diketones were formed during the hydrolysis. The oxidation products were not further studied, but they undoubtedly contained degraded acids because some carbon dioxide was evolved during each oxidation. The possibility that the diketones did actually form but were further oxidized is remote for two reasons. First, the diketones are readily produced from the parent tetronic acids under the same experimental conditions. Second, carbon dioxide should not result from the oxidation of either 2,3-pentanedione or 2-3-butanedione. It may be that isomerization to primary ketols is the explanation for the formation of carbon dioxide,[4] but in any event, this does not affect the main argument.

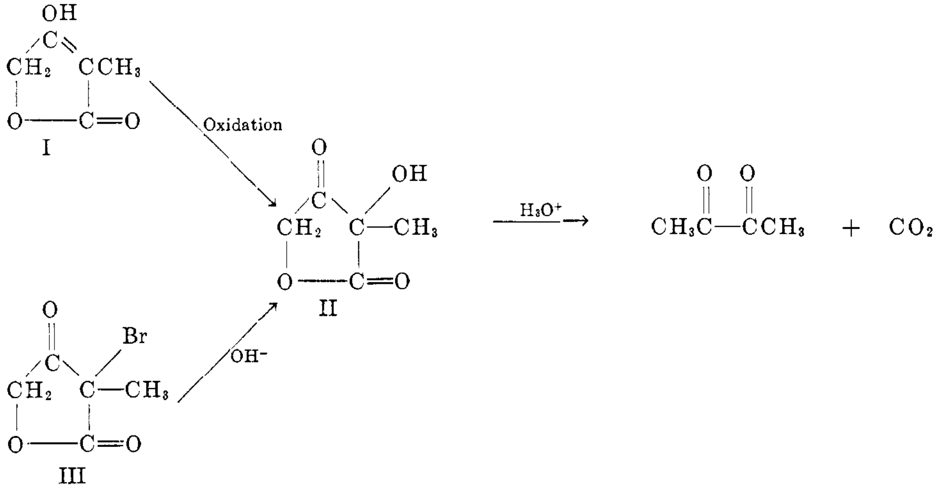

FIGURE 1. OXIDATION OF 3-METHYLTETRONIC ACID

The oxidation of tetronic acids, then, is attended with some hydrolysis. The

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[4] This point is under investigation in these laboratories.

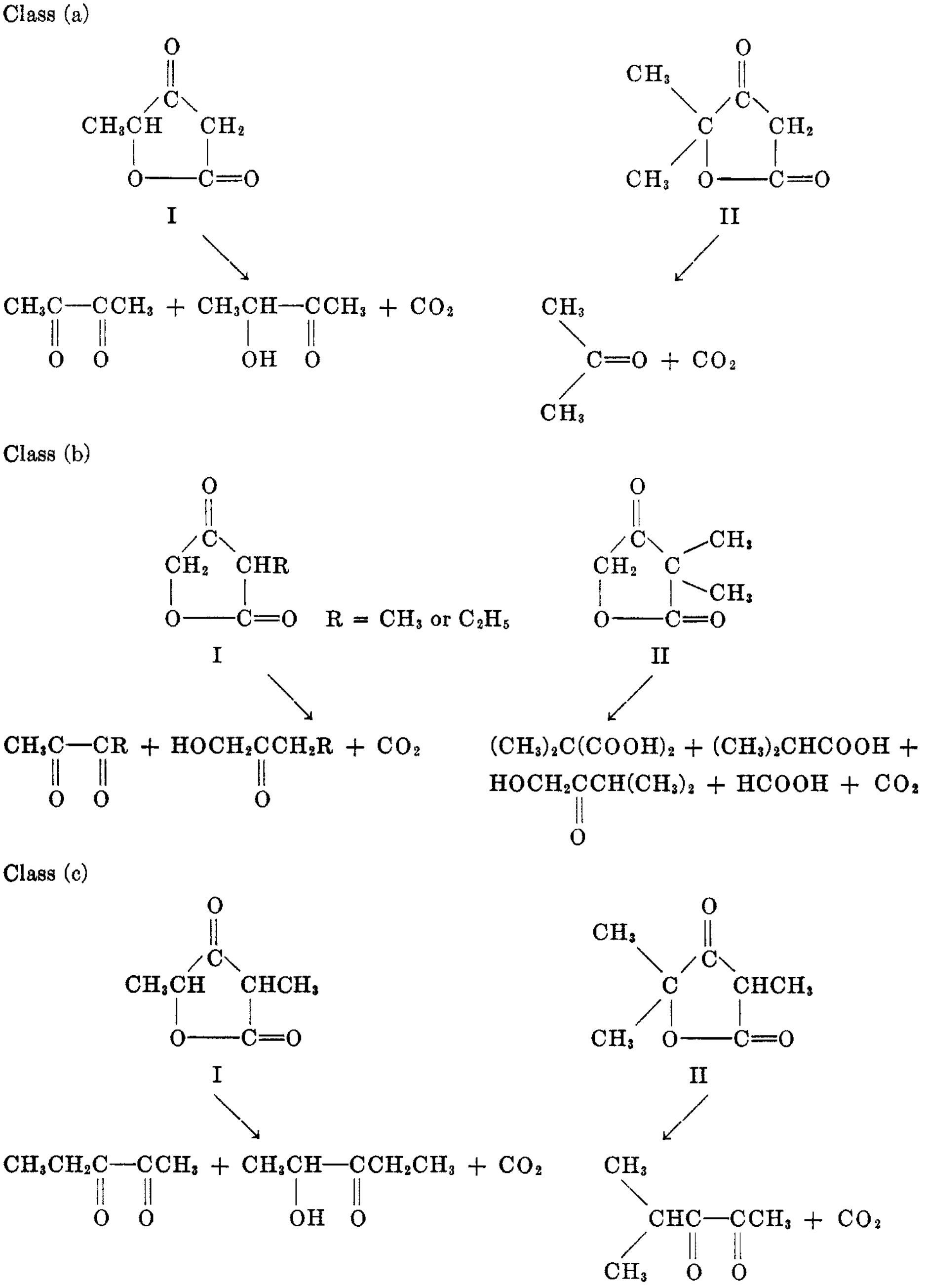

FIGURE 2. TETRONIC ACIDS: COURSE OF OXIDATION BY STRUCTURAL CLASSES

resulting ketols are oxidized, but do not form α-diketones. Thus the route whereby α-diketones are formed must involve oxidation of the tetronic acid *before* hydrolysis of the lactone ring occurs.

The question which next arises concerns the site of oxidation in the tetronic acid molecule. To answer this question we studied 3,3-dimethyltetronic acid[5] [Class (b)(II)], and 5,5-dimethyltetronic acid [Class (a)(II)]. These isomers are unique in that oxidation, before hydrolysis, must attack the 5-position of the former, and the 3-position of the latter. The products obtained from 3,3-dimethyltetronic acid were carbon dioxide, formic acid, isobutyric acid, 1-hydroxy-3-methyl-2-butanone (isolated as the phenylosazone), and dimethylmalonic acid. The formation of dimethylmalonic acid affords clear proof of oxidation at the 5-position. Although α-ketoisovaleraldehyde was anticipated, none was isolated. If any did form, it must have been further oxidized, presumably to formic and isobutyric acids. On the other hand, the *only* products isolated from the oxidation of 5,5-dimethyltetronic acid were carbon dioxide and acetone. This deep degradation of 5,5-dimethyltetronic acid is the more remarkable in view of the fact that 3,5,5-trimethyltetronic acid [Class (c)(II)], which must also undergo initial oxidation at the 3-position, readily forms carbon dioxide and 4-methyl-2,3-pentanedione. A further apparent exception is found in 5-methyltetronic acid [Class (a)(I)], and its isomer, 3-methyltetronic acid [Class (b)(I)], which was studied by Wolff (1). Both of these, on oxidation, yield carbon dioxide and 2,3-butanedione, but it may be noted that either or both of these isomers can be oxidized at the 3- or the 5-position. Similar considerations apply to the last pair of isomers, 3-ethyltetronic acid [Class (b)(I)], and 3,5-dimethyltetronic acid [Class (c)(I)], both of which, on oxidation, furnish carbon dioxide and 2,3-pentanedione.

There is thus a striking difference in oxidation behavior between tetronic acids substituted on the 3-position and those which are free of this substitution. This difference is not readily explained on the basis of classical organic structures, but it becomes comprehensible when the resonance possibilities of these molecules are considered. Determination of the dissociation constants (6), dipole moments (7), and Raman spectra (8) of tetronic acid, 3-hydroxytetronic acid, ascorbic acid, and other monosubstituted tetronic acids, show that these substances are abnormally strong acids due to greater resonance energy in their anionic forms. Moreover, in its undissociated state tetronic acid is represented by IV, with some contribution from the higher energy dipolar forms V and VI (7, 8).

Resonance between similar dipolar forms will likewise contribute to the stability of *enolic* 3-hydroxytetronic acids, *viz.*, IX, X, XI (where R is alkyl or hydrogen). Of the six acids studied only 5,5-dimethyltetronic acid [Class (a)(II)], and 5-methyltetronic acid [Class (a)(I)] are capable of being oxidized to this type of enolic resonating system, *i.e.* after C_3 is hydroxylated, and in the case of 5-methyltetronic acid this will be true only if the 3-position is attacked first. These stabilized structures would be expected to undergo further oxidation *before* decarboxylation occurs, and this must lead to deep degradation. Again, however, 5-methyltetronic acid can be oxidized at the 5-carbon, and this

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[5] The substance is not acidic, and should be named α,α-dimethyl-β-ketobutyrolactone. To conform with the older literature it is here called a tetronic acid.

would certainly result in the formation of carbon dioxide and 2,3-butanedione.[6] The fact that 2,3-butanedione is obtained from 5-methyltetronic acid strongly points to some oxidation of the 5-carbon.

Different structural features apply in the cases of 3-ethyltetronic acid [Class (b)(I)], 3,5-dimethyltetronic [Class (c)(I)], and 3,5,5-trimethyltetronic acid [Class (c)(II)]. In their undissociated forms, these acids will be represented by VII (where R′ is alkyl and R is alkyl or hydrogen), with some resonance between dipolar forms analogous to V and VI. However oxidation of these three acids at the 3-position must lead to VIII which is incapable of enolization and dipolar resonance. The stability of VIII will therefore be much less than that of VII,

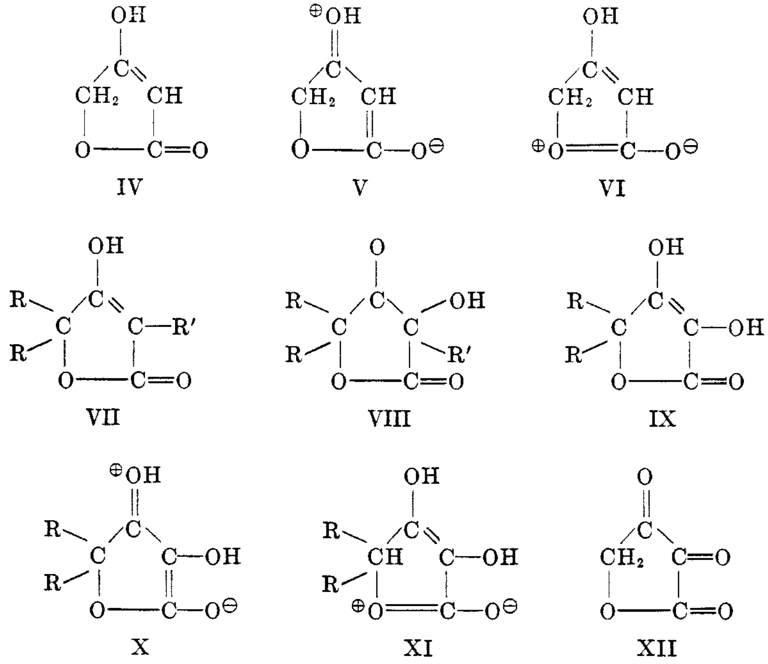

FIGURE 3. TETRONIC ACIDS: RESONANCE STRUCTURES

and decarboxylation will readily occur (compare Fig. 1) and, in fact, occurs in such a way that α-diketones are produced in accordance with the rule which was earlier described.

A somewhat similar situation appears to obtain in the case of 3-ketotetronic acid (XII) which has been prepared (9) by gentle oxidation of 3-hydroxytetronic acid (IX, where R is hydrogen). The ketotetronic acid is unstable and in aqueous solution decarboxylates to form pyruvic acid (9).[7]

[6] Compare the synthesis of α-ketoisovaleraldehyde in the experimental part.

[7] In the absence of any evidence to the contrary, the isolation of pyruvic acid instead of the expected β-hydroxypyruvic aldehyde, seems to us to be yet another example of the peculiar oxidation rule discussed earlier.

The original question as to how α-ketones are formed from 3-alkyl-3-hydroxytetronic acids has thus been accentuated rather than solved by this work. In carrying out the oxidations, however, it was apparent that the production of α-diketones was not a smooth process. As each drop of oxidant engaged the acidic solution of the tetronic acid, a vigorous surge of carbon dioxide occurred, *accompanied* by small amounts of the volatile diketone. Although measurements failed to establish a quantitative relationship between the yield of diketone and the amount of carbon dioxide evolved, obviously because of simultaneous ketol oxidation, however, the complete dependence of diketone formation upon carbon dioxide elimination strongly suggests an intimate relationship. This relationship will form the subject of a second communication.

EXPERIMENTAL

3-Ethyltetronic acid [*Class* (*b*)(*I*)]. Ethyl α-ethylacetoacetate was brominated in ice-water by the method of Conrad and Schmidt (10). The product, obtained in 73% yield, had b.p. 62–66° at 2 mm. It has been shown (11) that a mixture of α-and γ-bromoesters is always obtained under such conditions. Cyclization was accomplished by heating the ester,[8] to which one drop of concentrated hydrobromic acid had been added, at 100° for 12 hours. Cooling caused the dark liquid to solidify to a gray mass. This was broken up and collected; yield 51%. It was recrystallized from water; m.p. 127–128°. Reported m.p. 126.5° (12). The ferric chloride (enol) test was strong.

3,3-Dimethyltetronic acid. [*Class* (*b*) (*II*)]. Ethyl α,α-dimethyl-γ-acetoxyacetoacetate was prepared by the method of Conrad and Gast (13). In agreement with these authors and contrary to Koelsch (14), some cyclization occurred spontaneously over a two-month period, but it was difficult to separate the liquid tetronic acid thus formed from the acetoxyester. It was therefore treated as follows. The acetoxyester (100 g., 0.46 mole) was added dropwise to 400 g. of rapidly stirred concentrated sulfuric acid. The temperature was maintained below 8° during the addition. After being kept in a closed container at refrigerator temperature for 48 hours, the solution was poured onto 1 kg. of chopped ice, and the whole allowed to reach room temperature. After standing for a further two hours, the mixture was exhaustively extracted with chloroform. The chloroform solution was washed free of sulfuric acid with water, and without drying, the solvent was distilled through a short column. Yield, 89.4%, b.p. 207–212° at 760 mm. Conrad and Gast (13) report b.p. 208–212°. The enol test (ferric chloride) was negative. The *oxime* had m.p. 132–134°; reported value (13), 134°.

Anal. Calc'd for $C_6H_9NO_3$: N, 9.79. Found: N, 9.62, 9.96.

3,5-Dimethyltetronic acid [*Class* (*c*) (*I*)]. Ethyl α-propionylpropionate was prepared by the method of McElvain (15). After bromination (10), it was dried and distilled. Yield of bromoester, 56%, b.p. 52.5–62° at 0.5–1.0 mm. Previous work by Hantzsch and Wohlbruck (16) had shown that this bromoester, on heating[9] above 100°, formed *either* α-propionylacrylic acid or 3,5-dimethyltetronic acid. We therefore carried out this thermal reaction in such a way that the by-products could be isolated. The brominated ethyl α-propionylpropionate was heated in a small distillation flask whose side-arm led to the bottom of a test tube containing 5 ml. of water. This test tube was connected in series to two other test tubes which were placed in ice-salt mixture. At 110° (internal temperature), the bromoester began to boil, and at 122° globules of liquid, immiscible with water, collected in

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[8] 3-Ethyltetronic acid forms spontaneously from the bromoester on keeping for about three years.

[9] 3,5-Dimethyltetronic acid forms spontaneously from the bromoester on keeping for about one year.

the first test tube. When the internal temperature reached 160° the reaction was complete. The dark brown residue in the distillation flask was poured into ice-water, and the resultant semisolid mass was collected. The yield of dry solid was 76%. The liquid from the first test tube was separated from the water and dried. It had b.p. 37.5–39° and was shown to be ethyl bromide. No other products were obtained. The reaction, then, is a typical cyclization to a tetronic acid, and this view is substantiated by the strongly enolic nature (ferric chloride test) of the solid product.

Recrystallization of the solid product from water furnished fine white crystals, m.p. 121–122.5°. Hantzsch and Wohlbruck (16) reported m.p. 106–108°, while Emmerling and Kristeller (17) gave m.p. 124°.

Methyltetronic acid [*Class* (*a*) (*I*)]. This was prepared according to the directions of Benary (18), and had the reported m.p. 117–119°.

5,5-Dimethyltetronic acid [*Class* (*a*) (*II*)]. The procedure of Benary (19) was used, and after recrystallization of the solid product from benzene it had m.p. 144–146° instead of the reported (19) m.p. 142–143°. Zeisel determination showed the absence of ethoxyl groups,[10] and the enol (ferric chloride) test was strong.

Anal.[11] Calc'd for $C_6H_8O_3$: C, 56.2; H, 6.25.
Found: C, 56.3; H, 6.20.

It was found that the yield of product could be augmented to 50% by distilling the oily mother-liquor under nitrogen at 4 mm. pressure. The lower fraction, boiling at 67–84°, consisted mostly of ethyl malonate, but the fraction boiling at 84–150° contained some 5,5-dimethyltetronic acid which separated on chilling.

3,5,5-Trimethyltetronic acid [*Class* (*c*) (*II*)]. Ethyl isobutyrylacetate was prepared by the procedure of Kroeker and McElvain (20) and alkylated with methyl iodide and sodium ethoxide by the modification of Schroeter (21). Ethyl α-isobutyrylpropionate was obtained in 91.5% yield; b.p. 92° at 16 mm. Bromination was accomplished by the dropwise addition of bromine (1 mole) in an equal volume of carbon tetrachloride to a rapidly stirred solution of the ester (1 mole) in two volumes of carbon tetrachloride, with the internal temperature maintained below 5°. To complete the rearrangement to the γ-bromoester, the bromination mixture was allowed to stand overnight in the cold-room (22). The mixture was then washed with ice-water and dried. After removal of the solvent the residual brown oil was distilled under nitrogen. Yield, 95%; b.p. 88–90° at 4 mm.; a pale straw-colored[12] oil.

Anal. Calc'd for $C_9H_{15}BrO_3$: Br, 31.84. Found: Br, 31.75.

It was *cyclized* according to the following procedure. The bromoester (1 mole) was slowly added to an aqueous solution of barium hydroxide (1.5 formula-weights), and the mixture was shaken for one hour to effect a clear solution. It was then allowed to stand at room temperature for seven days, during which a small amount of flocculent material separated. The mixture was then concentrated under a vacuum to about one-third of its original volume, with the internal temperature maintained below 40°. On cooling to 0° crystals formed. Addition of cold, dilute hydrochloric acid (1:3) dissolved the crystals at *p*H 6. The *p*H was slowly taken to about 1, during which much powdery white material separated. This was collected and the filtrate was extracted with ether. After removal of the ether an oil remained which slowly solidified. This was added to the main batch and the whole was recrystallized from water. Stout needles, some reaching two inches in length, were obtained in 58% yield; m.p. 135–139°. Recrystallization from benzene formed short white needles, m.p. 137–139°. The enol test (ferric chloride) was strong.

Anal.[13] Calc'd for $C_7H_{10}O_3$: C, 59.12; H, 7.09.
Found: C, 58.93; H, 7.01.

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[10] We wish to thank Mr. B. E. Harrell for this determination.

[11] We wish to thank Mr. John F. Yost for this microanalysis.

[12] At temperatures much above 100° the product darkens with elimination of hydrogen bromide.

[13] We wish to thank Mr. T. E. Gompf for this microanalysis.

α-Ketoisovaleraldehyde. The original method of Conrad and Gast (13) involved: (a) bromination of 3,3-dimethyltetronic acid to form 5-bromo-3,3-dimethyltetronic acid, (b) cold hydrolysis of the bromo compound to give 5-hydroxy-3,3-dimethyltetronic acid, and (c) thermal decarboxylation of the hydroxytetronic acid and sublimation of the resultant 3-methyl-2-ketobutyraldehyde. In the present study it was found advantageous to prepare the ketoaldehyde directly by steam-distillation of 5-bromo-3,3-dimethyltetronic acid. Delicate long white needles, relatively insoluble in cold water, were obtained in 22% yield (based on the 3,3-dimethyltetronic acid); m.p. 95–96°, without recrystallization. Conrad and Gast (13) reported 95°, and Dakin and Dudley (23), who prepared the compound by a totally different route, give 95–96°. The reported (13) m.p. of the *phenylosazone* is 115°. When treated with excess phenylhydrazine in acetic acid, our product formed the orange-colored derivative, m.p. 113–114°.

1-Hydroxy-2-pentanone. The general method of Bunnett and Cason (24) was used for the preparation of 1-chloro-2-pentanone from di-*n*-propylcadmium and chloroacetyl chloride. The chloroketone, obtained in 20% yield, had b.p. 47° at 5 mm. Fourneau and Maréchal (25) report 59° at 17 mm. Alcoholysis of the chloroketone was accomplished by Nef's method (26), the ketol being isolated after refluxing the chloroketone in an absolute methanol-sodium formate mixture for 41 hours. The product, obtained in 15% yield, had b.p. 152° at 760 mm. It formed the known (27) 2,4-dinitrophenylosazone when treated with excess reagent. After recrystallization from toluene the orange-red osazone had m.p. 234° with decomposition.

Oxidation and hydrolysis experiments. In the oxidation and hydrolysis experiments in which the evolved carbon dioxide was determined, the following apparatus was used. A three-necked 100-ml. reaction flask was equipped with a condenser for downward distillation, a dropping-funnel, and an inlet tube that reached to the bottom of the flask. The condenser led to a receiver which was connected to a trap cooled in Dry Ice. The trap, in turn, was connected to a sulfuric-acid bubbler. The bubbler was necessary to remove the last traces of the volatile diketones. Attached to the bubbler was a drying-tube filled with Anhydrone, and to this was attached an Ascarite tube. A weighed sample of the tetronic acid was placed in the reaction flask together with dilute sulfuric acid and nitrogen or air (freed from carbon dioxide), was passed through the system until the Ascarite tube maintained a constant weight. The contents of the flask were then brought to the boiling point, and a solution of chromic oxide in water was added dropwise. This method permitted the diketones to distill as formed, and minimized further oxidation. The Ascarite tube was weighed periodically, and when the carbon dioxide evolution became negligible, the reactions were considered complete. For the hydrolysis experiments a vertical condenser was used instead of the downward one, but the rest of the apparatus remained unchanged.

Hydrolysis of 3-ethyltetronic acid. The acid, 12.56 g. (0.098 mole), was boiled in *N* sulfuric acid under nitrogen for 35 hours. By this time the yield of carbon dioxide was 97%. The vertical condenser was replaced by one for downward distillation, and the colorless ketol was distilled from the brown hydrolysis residue. The distillate was exhaustively extracted with ether and the extract was dried over sodium sulfate. Evaporation of the ether left a colorless oil which strongly reduced Fehling's solution in the cold and which, when treated with excess 2,4-dinitrophenylhydrazine reagent, yielded the same osazone that was obtained from synthetic 1-hydroxy-2-pentanone; m.p. and mixture m.p. 234° with decomposition.

The pale yellow *monophenylhydrazone* was prepared from the hydrolysis product and from the synthetic ketol. After recrystallization from aqueous ethanol the m.p. and mixture m.p. was 70°. This derivative is relatively unstable, and in impure condition it rapidly changes to tar.

Anal. Calc'd for $C_{11}H_{16}N_{20}$: N, 14.50. Found: N, 14.40.

Oxidation of 1-hydroxy-2-pentanone. At 0° an aqueous solution of 15.4 g. (0.154 mole) of chromic oxide was added dropwise and under nitrogen to 7.8 g. (0.072 mole) of the ketol dissolved in 200 ml. of water and 22.5 g. (0.23 mole) of sulfuric acid. After the addition, which required two hours, the reactants were allowed to remain at room temperature for nine hours. At this time the yield of carbon dioxide was 65%. The volatile products were distilled from the reaction mixture. The total yield of carbon dioxide was 68.5%, and some unoxidized ketol was recovered from the Dry-Ice trap. The acidic distillate was made basic with solid sodium bicarbonate, and distilled. The distillate from this operation was strongly reducing, and the preparation of derivatives showed it to contain 1-hydroxy-2-pentanone.

The basic residue, after concentration to small bulk, was acidified with hydrochloric acid and exhaustively extracted with ether. The ether extract was dried over calcium chloride, and distilled. Two fractions were obtained, one boiling about 100° and the other from 140–159°. The higher-boiling fraction was shown to be butyric acid, since its *p*-toluide had m.p. 72°, either alone or admixed with the *p*-toluide of butyric acid. The lower-boiling acid strongly reduced mercuric ion and potassium permanganate solution. It was proved to be formic acid by preparing its *p*-bromophenacyl derivative which had m.p. 139° (28).

Oxidation of 3,5-dimethyltetronic acid. An aqueous solution of 9.6 g. (0.096 mole) of chromic oxide was added dropwise to a boiling solution of 8.0 g. (0.063 mole) of 3,5-dimethyltetronic acid in 64 g. of dilute (1:3) sulfuric acid. Carbon dioxide elimination was vigorous and the yellow diketone slowly distilled from the reaction mixture. The yield of carbon dioxide was not determined in this experiment. Isolation of the diketone was accomplished by the tedious method of von Pechmann (29). The yield of 2,3-pentanedione was 28.4%; b.p. 105–111° [reported b.p. 104–111° (29)]. Treatment with excess hydroxylamine reagent formed the known (30) dioxime, m.p. 172–172.5°. It has been shown (30) that α-diketones form only disemicarbazones; the one from 2,3-pentanedione has m.p. 251–252° (30). Our product had m.p. 254–255°.

Hydrolysis of 3,5-dimethyltetronic acid. Under nitrogen, 1.20 g. (0.0094 mole) of the acid was boiled in 15 ml. of dilute (1:3) sulfuric acid for 100 hours. The yield of carbon dioxide was 90%. A trace of yellow oil resembling 2,3-pentanedione in its color and odor, was found in the Dry-Ice trap. The colorless distillate strongly reduced Fehling's solution, and with excess phenylhydrazine reagent formed an orange derivative, m.p. 163° [the phenylosazone of 2,3-pentanedione has m.p. 166–167° (4)]. After acidification with sulfuric acid, the distillate was oxidized. The yield of carbon dioxide was 10%, but no yellow diketone was obtained.

A similar hydrolysis, but carried out under purified air, formed carbon dioxide in 100% yield after boiling for about 35 hours. More diketone was obtained during this hydrolysis than in the previous one. Oxidation of the distillate failed to form any diketone, but carbon dioxide was obtained in 54% yield on boiling the oxidation mixture for 17 hours.

Oxidation of 3-ethyltetronic acid. The acid (8.8 g., 0.063 mole) was oxidized with 10.6 g. (0.106 mole) of chromic oxide and 60 ml. of dilute (1:3) sulfuric acid. Carbon dioxide was obtained in 64% yield. The yellow diketone was separated from the strongly reducing distillate, and transformed into the dioxime which did not depress the m.p. of the dioxime of 2,3-pentanedione. Based on the weight of dioxime obtained, the yield of diketone was 43%. In several oxidations it was shown that no quantitative relationship existed between the amount of carbon dioxide evolved and the yield of diketone.

Oxidation of 5-methyltetronic acid. The acid, 3.36 g. (0.03 mole), was treated with excess oxidant and it yielded 78% carbon dioxide. The distillate was yellow, neutral to bicarbonate solution, and it strongly reduced Fehling's solution. It gave a positive iodoform test. The yellow oil was separated and when treated with excess 2,4-dinitrophenylhydrazine reagent it formed an orange derivative, m.p. 317°. The 2,4-dinitrophenylosazone of 2,3-butanedione is reported (31) to melt at 314–315°. The disemicarbazone (30) has m.p. 278–279°; our product had m.p. 277°.

Hydrolysis of 5-methyltetronic acid. A 66.5% yield of carbon dioxide was obtained on boiling 2.7 g. (0.024 mole) of this acid in dilute sulfuric acid under nitrogen for 40 hours. Some yellow diketone had also formed. The water-white distillate was separated from the traces of yellow oil, acidified and treated with excess oxidant. On boiling for several hours, the yield of carbon dioxide was 21%, but no diketone was obtained.

Oxidation of 5,5-dimethyltetronic acid. A 3.03-g. sample (0.024 mole) was treated with excess oxidant. A colorless distillate was obtained, and the yield of carbon dioxide was 90%. The distillate was neutral to bicarbonate solution, and it failed to reduce either Fehling's solution or Tollens' reagent. It gave a positive iodoform test, and when treated with 2,4-dinitrophenylhydrazine it formed the known 2,4-dinitrophenylhydrazone of acetone, m.p. alone or admixed with authentic material, 126° (28). A recovery of 0.1 g. of unoxidized tetronic acid was obtained by extracting the oxidation residue with ether.

Oxidation of 3,5,5-trimethyltetronic acid. Oxidation of 4.02 g. (0.028 mole), with excess oxidant produced carbon dioxide in 90% yield. The distillate contained 1.5 ml. of a deep yellow oil; yield of diketone about 50%. The literature (32) gives m.p. 117° for the phenylosazone of 4-methyl-2,3-pentanedione, and m.p. 155° (33) for its dioxime. With excess phenylhydrazine our product formed a derivative, m.p. 114°, and with excess hydroxylamine solution, a compound m.p. 155°. Tetronic acid, 0.2 g., was recovered.

Oxidation of 3,3-dimethyltetronic acid. A 3.28-g. sample (0.027 mole), was oxidized in the usual manner. The yield of carbon dioxide was 140%. The distillate was acidic, colorless, and strongly reduced Fehling's solution. When treated with excess phenylhydrazine in acetic acid, a portion of the distillate yielded an orange-colored derivative, m.p. 115°. When mixed with the phenylosazone of α-ketoisobutyraldehyde (m.p. 113–114°) the mixture m.p. was 113–114°. Since α-ketoisovaleraldehyde is a white solid, volatile with steam and relatively insoluble in water, the distillate must have contained 1-hydroxy-3-methyl-2-butanone.

The distillate was made basic with solid sodium bicarbonate and evaporated to dryness. The residual salt reduced both acidic and basic potassium permanganate solution, showing the presence of formate ion. Ether extraction of a portion of the acidified residual salt furnished a few drops of liquid possessing the characteristic odor of isobutyric acid. A further portion of salt was refluxed with thionyl chloride and then treated with *p*-toluidine. The derivative that formed had m.p. 103° in accord with the reported m.p. (28) of the *p*-toliude of isobutyric acid.

Ether extraction of the oxidation residue furnished a small amount of crystalline material. After recrystallization from ether-ligroin it was obtained as long white needles, m.p. 193–194°, with vigorous decomposition. The substance was acidic and, as its analysis showed, was dimethylmalonic acid (34).

Anal.[14] Calc'd for $C_5H_8O_4$: C, 45.45; H, 6.06.
Found: C, 45.40, 45.32; H, 6.21, 6.08.

SUMMARY

Oxidation studies have been carried out on six tetronic acids, and structural criteria for the production of α-diketones have been established. It has been shown that the diketones result from oxidation of appropriate tetronic acids before hydrolysis of the lactone ring occurs. Those tetronic acids that are not oxidized to α-diketones have been discussed, and an explanation for their behavior has been advanced.

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