[Contribution from the Chemical Laboratory of the Ohio State University]

THE DEHYDRATION OF 3-HYDROXY-3,4,4-TRIMETHYLPEN-TANOIC ACID¹

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The dehydration of neopentyl type alcohols frequently results in molecular rearrangement. In general, if the hydroxyl group involved is primary or secondary, rearrangement is largely complete, but if tertiary, only partial (1). In connection with some other research, we were interested to know what effect the presence of a carboxyl function in the *beta* position to the hydroxyl group might have on rearrangement.

Previous workers (2) have reported that several β -hydroxy esters involving cyclic compounds did not rearrange even though the hydroxyl was of the pinacolyl type. However, no study of simple acyclic β -hydroxy esters having this feature has been reported. In this paper we show that no rearrangement occurs on the dehydration of 3-hydroxy-3,4,4-trimethylpentanoic acid, I, or its methyl and ethyl esters.

This acid has been prepared previously by two workers (3, 4). They were unable to achieve the expected dehydration using such reagents as concentrated sulfuric acid (3), anhydrous formic acid, phosphorus pentoxide in benzene, and zinc chloride in acetic acid (4). The only product obtained was a saturated crystalline lactone to which they assigned the structure of β -t-butyl- γ -butyrolactone, II. We obtained the same lactone by treating the ethyl ester of I with phosphorus oxychloride (5).



We have obtained unsaturated acids from I or its esters by three methods: (A) treatment of the methyl ester with thionyl chloride and pyridine in ether, followed by hydrolysis (6); (B) heating the ethyl ester with iodine, followed by hydrolysis (7); and (C) heating I with acetic anhydride. In all cases the product formed a mixture of the same solid and liquid unsaturated acids. Both acids yielded the lactone, II, on treatment with sulfuric acid; both formed pinacolone on fusion with sodium hydroxide (8); and on hydrogenation both yielded the known 3,4,4-trimethylpentanoic acid, IV (9). From this we conclude that the solid and liquid acids are the geometrical isomers of β -t-butylcrotonic acid, III. The solid isomer agrees in melting point with an unsaturated acid of the same structure synthesized by Wouseng (4) from pinacolone. That one acid might,

¹The material in this paper was taken from the Ph.D. Dissertation of R. R., The Ohio State University, June 1943.

be 2-*t*-butyl-3-butenoic acid, V, is considered unlikely (10), and, for our purpose. unimportant, since the hydrogenation experiment establishes the carbon skeleton.



Several attempts were made to dehydrate the methyl or ethyl ester of I by heating over a small amount of iodine (7). Erratic results were obtained. In one instance, heating of the ethyl ester at 160–180° under slightly diminished pressure caused no appreciable dehydration. In another experiment at atmospheric pressure, the ester had been refluxing for some time without dehydration when reaction started suddenly and proceeded rapidly. In another experiment with the methyl ester, cleavage apparently took place, for a lachyrmatory liquid, probably iodopinacolone, was obtained. Because of the thermal stability of the methyl ester of I, an attempt was made to dehydrate it by passing the vapors over alumina at 300–325° (11). However, cleavage took place, a 58% yield of pinacolone being obtained. A similar cleavage of β -hydroxy esters has previously been brought about with strong alkali (12).

In the hope of establishing conclusively the formula of the lactone, IV, several experiments were carried out. The lactone proved extraordinarily resistant to reduction, both catalytic (Raney nickel) and chemical (hydrogen iodide). On oxidation it was either completely broken down (potassium permanganate or 50% nitric acid) or untouched (chromic acid). In this connection it should be mentioned that trimethylacetic acid was oxidized by potassium permanganate. The lactone was easily hydrolyzed with alkali but acidification in the cold immediately returned the lactone. We were also unable to prepare the corresponding γ -hydroxy ester (13).

On treatment with phenylmagnesium bromide a compound, $C_{20}H_{24}O$, was obtained in 72% yield. The analysis and method of preparation suggest the formula of 2,2-diphenyl-4-*t*-butyltetrahydrofurane, VI. From these experiments it would appear that the structure of IV might best be established conclusively by synthesis.

HYDROXYTRIMETHYLPENTANOIC ACID

EXPERIMENTAL²

Methyl 3-hydroxy-3,4,4-trimethylpentanoate. In the best of several experiments, 100 cc. of a thoroughly dried solution of 100 g. of pinacolone and 154 g. of methyl bromoacetate in benzene was added to 65 g. of freshly sandpapered zinc foil (14) and a few crystals of iodine in a three-necked 3-liter flask fitted with ground-in reflux condenser, stirrer, and dropping-funnel. After the reaction had begun, the remainder of the solution was added to maintain gentle reflux. After working up the product in the usual way 115 g. (66%) of the methyl ester, b.p. 88-90° at 14 mm., was obtained. The methyl ester and the ethyl ester, b.p. 104-107° at 18 mm., were obtained in about 53% yield when all of the reactants were placed together at once. After alkaline hydrolysis and crystallization from petroleum ether the hydroxy acid, I, was obtained as colorless crystals, m.p. 75-76°.

Dehydration Experiments

With $POCl_s$. A solution of 15 g. each of ethyl ester and phosphorus oxychloride in dry benzene was refluxed for three hours, cooled, and poured on ice. After washing the benzene layer well with bicarbonate, the solvent was removed, and the residue vacuum distilled to yield 10 g. (94%) of the lactone, II, b.p. 117° at 22 mm., m.p. 99–100°.

With iodine. (a) A mixture of 177 g. of ethyl ester and a few crystals of iodine was heated in a salt-bath at 180-200° for one hour. After cooling, the material was taken into benzene and washed with bisulfite. On vacuum distillation 153 g. of product, b.p. 85-98° at 13 mm., was obtained. This was fractionated at 13 mm. in a modified Claisen flask to yield the following fractions: A, 40 g., 78-83°; B, 6 g., 83-87°; C, 81 g., 87-95°; and D, 21 g., 95-100°. Saponification of D yielded mainly starting acid, I. Saponification of 16 g. of C yielded 12 g. (85%) of crystalline unsaturated acid which, when crystallized from ethanol, melted at 84.5-85.0°, corr.

Anal. Calc'd for C₈H₁₄O₂: C, 67.6; H, 9.9.

Found: C, 67.1, 67.1; H, 9.8, 9.9.

The amide melted at 141-142° corr.

Anal. Calc'd for C₈H₁₅NO: C, 68.0; H, 10.7; N, 10.0.

Found: C, 67.9, 67.8; H, 10.7, 10.7; N, 10.0, 10.1.

The unsaturated acid (4 g.) obtained from 5 g. of fraction A was liquid but gave in small yield an amide, m.p. $140-141^{\circ}$, which proved identical with the amide prepared from the acid obtained from fraction C.

(b) A mixture of 200 g. of the methyl ester of I and a few crystals of iodine was refluxed into a two-foot fractionating column packed with glass helices. A reaction set in but soon stopped. On further addition of more iodine the reaction proceeded a while and then ceased. Two more additions of 5 g. of iodine were made. No water appeared at the top of the column but a heavy water-insoluble liquid distilled. This liquid smelled like pinacolone but boiled higher and was lachrymatory. The experiment was discontinued as an undesired reaction was obviously taking place.

With thionyl chloride. To an ice-cold solution of 87 g. of the methyl ester of I in 190 cc. of dry ether and 110 cc. of dry pyridine was slowly added with stirring 65 g. of pure thionyl chloride. After three hours stirring at room temperature, this mixture was poured into water. The product was distilled to give 70 g. (90%) of unsaturated ester, b.p. 82–95° at 21 mm. Hydrolysis of portions of this ester mixture gave acid fractions similar to those previously described under the iodine dehydration products of the ethyl ester of I.

With acetic anhydride. After heating a solution of 21 g. of I in 125 cc. of acetic anhydride on the steam-bath for 8 hours, it was poured into water to effect hydrolysis of the excess acetic anhydride. On vacuum distillation of the organic acid 14.5 g. (78%) of solid unsaturated acid, m.p. 85-86°, was obtained.

²Microanalyses by Mr. J. E. Varner.

Proof of Structure of Unsaturated Acids

Hydrogenation. The catalytic reduction of 7.17 g. of pure solid unsaturated acid over 0.1 g. of Adams platinic oxide catalyst was complete in a short while. The liquid saturated acid, b.p. 97-98° at 4 mm., n_{\pm}^{n} 1.4320, was isolated in 83% yield. The amide formed from this acid melted alone and mixed with an authentic sample of amide, kindly supplied by Dr. Stevens (9), at 166-167° corr. A similar reduction of the liquid unsaturated acid produced an 83% yield of the same saturated acid.

Cleavage. A mixture of 2 g. each of solid unsaturated acid, m.p. 85-86°, and sodium hydroxide was placed in a small distilling flask. On heating to 225° in a salt-bath a liquid distilled and was caught in a solution of 2,4-dinitrophenylhydrazine in alcohol. After adding a small amount of concentrated hydrochloric acid, the solution was refluxed. On cooling, 1 g. (42%) of the 2,4-dinitrophenylhydrazone of pinacolone, m.p. and mixed m.p. 124-125°, was obtained. The liquid unsaturated acid gave approximately the same result on similar treatment.

Preparation and Properties of Lactone, IV

Preparation. The lactone was most easily prepared by refluxing the hydroxy acid, I, its methyl or ethyl esters, or the solid or liquid unsaturated acids, III, with 50% sulfuric acid. The lactone was then extracted with benzene and purified by distillation under reduced pressure, (b.p. 117° at 22 mm.), and by crystallization from high-boiling petroleum ether (m.p. 99-100°). The preparation using phosphorus oxychloride has been described under the dehydration experiments.

Properties. The lactone, IV, was recovered unchanged from reduction experiments involving refluxing in acetic acid with hydriodic acid and red phosphorus, heating in a sealed tube with 47% hydriodic acid and red phosphorus at 200°, and shaking at 200° over Raney nickel under 140 atmospheres pressure of hydrogen for 10 hours. Reduction proceeded over a copper-chromium oxide catalyst at 250° but no acidic fraction was formed (15). Oxidation with potassium dichromate in sulfuric acid did not proceed at all, and with alkaline permanganate or with nitric acid oxidation was general. An unsuccessful attempt was made to prepare the γ -hydroxy ethyl ester by the method of Meincke and McElvain (13). In another unsuccessful attempt to make the methyl ester, an alkaline solution of the saponified lactone was acidified at 0° and the supposed hydroxy acid extracted with ether and immediately treated with diazomethane. However, the diazomethane did not react and only the original lactone was obtained. A solution of 14.2 g. of IV in 150 cc. of ether was added to 200 cc. of 1.5 M phenylmagnesium bromide and refluxed for 2 hours. After hydrolysis, the material from the ether layer was crystallized from petroleum ether (Skellysolve C) to yield 20 g. (72%) of a substance, m.p. 79.5-80.0°.

Anal. Calc'd for C₂₀H₂₄O: C, 85.7; H, 8.6. Found: C, 86.2, 86.0; H, 8.5, 8.4.

The dehydration of 3-hydroxy-3,4,4-trimethylpentanoic acid and its esters has been shown to proceed without molecular rearrangement.

SUMMARY

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