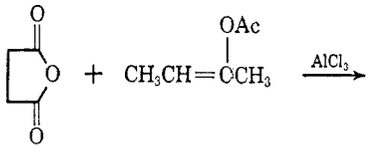
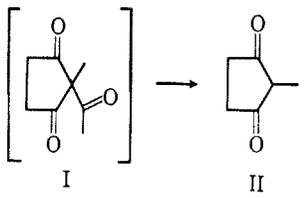
More recently Bucourt, *et al.*,[3] have reported a more direct approach through the cyclization of diethyl propionylsuccinate.

In this paper we wish to report a convenient, one-step preparation of II in good yield from available starting materials. When succinic anhydride is allowed to react with 2-buten-2-ol acetate (the major enol acetate of methyl ethyl ketone) in the presence of aluminum chloride, a crystalline product (II) is obtained directly after quenching the reaction in cold water. Recrystallization from water provides high quality product in yields of 80–85% of theory.





I II

The analogous reaction of isopropenyl acetate with succinic anhydride has been reported earlier by Merényi and Nilsson[4] to give 2-acetylcyclopentane-1,3-dione. In our reaction, no sign of the corresponding 2-methyl-2-acetylcyclopentane-1,3-dione intermediate (I) could be detected. Direct hydrolysis of the reaction mixture under mild conditions gave product II directly.

Nitrobenzene is the solvent of choice. From a perusal of the variables, optimal yields are obtained with 3.5 moles of aluminum chloride and 1.5 moles of 2-buten-2-ol acetate per mole of succinic anhydride. The reaction is carried out in two stages; the first stage of the condensation is run at low temperature to avoid loss of enol acetate by O → C acyl migration. Ultimately more forcing conditions are required to complete the over-all reaction, as evidenced by measurement of the hydrogen chloride evolved.

### Experimental Section[5]

**2-Methylcyclopentane-1,3-dione (II).**—To a 2-l., three-necked flask protected from moisture by an atmosphere of dry nitrogen and fitted with a stirrer, condenser, and thermometer, there was added 1.0 l. of azeotropically dried nitrobenzene. Anhydrous aluminum chloride (466 g, 3.5 moles) and succinic anhydride (100 g, 1.0 mole) were added with stirring, the temperature being allowed to rise from 45 to 80°. The solution was heated at 110° for 20 min to form the complex and then cooled to room temperature. 2-Buten-2-ol acetate[6] (171 g, 1.5 moles) was added over 15 min while the temperature was maintained near 25° with cooling. After aging for 30 min, the reaction was reheated and aged at 110° for 2 hr. The reaction was cooled to room temperature and quenched by addition to 1.0 l. of water maintained at 5–10°. The addition was carried out with vigorous stirring over a 60-min period. The crude product crystallized from the heterogeneous system and was aged for 3 hr at 5°. The brown product was collected by filtration and washed with two 60-ml portions of nitrobenzene to displace the mother liquors. The residual nitrobenzene was removed by washing the cake with petroleum ether (bp 30–60°). The dried crude product weighed 126 g: $\lambda_{max}^{0.1\ N\ HCl}$ 252 mμ (ε 12,670).

**Purification.**—The crude was dissolved in 3400 ml of hot water (90°) and stirred for 30 min with 13 g of Nuchar C-190N.[7] The clarified filtrate was concentrated *in vacuo* to about 350 ml and aged with agitation at 5° for 1 hr. After filtering and washing with a small quantity of cold water, the product was air dried: 81.2 g; mp 212–214°; $\lambda_{max}^{0.1\ N\ HCl}$ 252 mμ (ε 18,000) (lit.[3] mp 210–212°).

*Anal.* Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.02; H, 6.92.

From the recrystallization mother liquor there was obtained upon further concentration 2.8 g, mp 207–211°. The aqueous portion of the crude mother liquor was extracted continuously with methyl isobutyl ketone to provide an additional 7.8 g: mp 207–210°; $\lambda_{max}^{0.1\ N\ HCl}$ 252 mμ (ε 17,900). The over-all yield amounted to 82%. The product was identical in all respects with that obtained by known methods.[1,3]

**Registry No.**—II, 765-69-5.

(7) Trade name for activated carbon available from Industrial Chemical Sales Division of the West Virginia Pulp and Paper Co., New York, N. Y.

(3) R. Bucourt, A. Pierdet, G. Costerousse, and E. Toromanoff, *Bull. Soc. Chim. France*, 645 (1965).

(4) F. Merényi and M. Nilsson, *Acta Chem. Scand.*, **17**, 1801 (1963); **18**, 1368 (1964).

(5) Melting points are uncorrected. We are indebted to A. Kalowsky for ultraviolet spectra and to R. N. Boos and associates for elemental analyses.

(6) Available from Eastman Chemical Products, Inc., Kingsport, Tenn.

## Oxidation of β-Lactone Dimer of Dimethylketene

R. DONALD CLARK

*Research Laboratories, Tennessee Eastman Company, Division of Eastman Kodak Company, Kingsport, Tennessee*

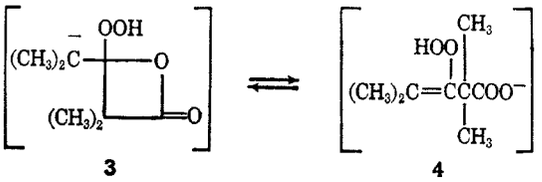
*Received October 31, 1966*

The oxidation of 3-hydroxy-2,2,4-trimethyl-3-pentenoic acid β-lactone (**1**) with hydrogen peroxide in slightly basic aqueous media yields as final products isopropyl isobutyrate and carbon dioxide. There was evidence of the intermediate formation of sodium isopropyl dimethylmalonate (**2**).

The results may be interpreted as a nucleophilic attack of the hydroperoxide anion on **1**, resulting in a ring opening which gives the intermediate sodium 2,2,4-trimethyl-3-oxoperoxyvalerate which undergoes an intramolecular Baeyer–Villiger rearrangement (Scheme I). The ring intermediate is favored by the presence of *gem*-dimethyl groups.

This route is proposed because the lactone ring of **1** is easily opened by nucleophilic reagents[1,2] of which the hydroperoxide anion is an example. The alternative mechanism of hydrolysis followed by an intermolecular Baeyer–Villiger reaction was rejected because lactone **1** is relatively stable to hydrolysis under the conditions of the reaction in the absence of hydrogen peroxide.

In another alternative mechanism, the initial attack of the hydroperoxide anion at the isopropylidene double bond of **1** is followed by rearrangement of the intermediate (**3** or **4**) to half-ester **2**. The intermediates **3**

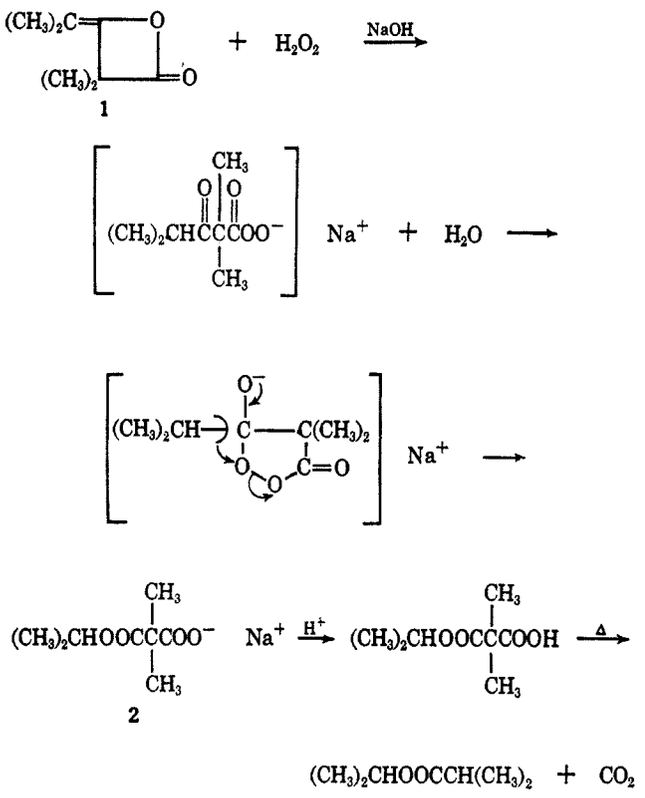


**3** **4**

(1) R. H. Hasek, R. D. Clark, E. U. Elam, and J. C. Martin, *J. Org. Chem.*, **27**, 60 (1962).

(2) "2,2,4-Trimethyl-3-hydroxy-3-pentenoic Acid, β-Lactone," Eastman Chemical Products, Inc., Kingsport, Tenn., 1961, Technical Data Sheet No. X-129.

SCHEME I



and **4** were considered less plausible than those proposed because the nucleophilic attack on **1** has been found to occur consistently at the carbonyl carbon atom[1,2] in contrast to that on saturated β-lactones. Furthermore, **3** is also an intermediate in the formation of the epoxide, which was not found and which would not be expected to rearrange to **2**. It is also reasonable to expect that the rearrangement of **4** would involve the same intermediates as for the proposed mechanism.

### Experimental Section

**Reaction of Hydrogen Peroxide with 3-Hydroxy-2,2,4-trimethyl-3-pentenoic Acid β-Lactone (1).**—Into a 4-l. beaker outfitted with a stirrer, a thermometer, and electrodes for a pH meter were placed 600 ml of water and 180 g of a 30% solution of hydrogen peroxide. The mixture was stirred and maintained at pH 8 to 9 during the gradual concurrent addition of 200 g of 3-hydroxy-2,2,4-trimethyl-3-pentenoic acid β-lactone[1] and 1400 ml of 1 *N* sodium hydroxide. The temperature was kept at 30 to 40° by cooling the mixture with ice during the addition period of 1 hr. After the addition step the mixture was stirred for 15 min. A sample of the mixture was titrated with potassium permanganate and then with potassium iodide. A trace of hydrogen peroxide was found, but the presence of a peroxy acid was not indicated.

The mixture was acidified to pH 1.0 with 20% hydrochloric acid, and the product was extracted with four 200-ml portions of pentane. The extract was washed with three 50-ml portions of water and then evaporated *in vacuo* at room temperature to a small volume in a rotary flash evaporator. The yield of isopropyl hydrogen dimethylmalonate was 176 g (72%). *Anal.* Calcd for $C_8H_{14}O_4$: neut equiv, 174. Found: neut equiv, 186. Infrared absorption was at 5.9 μ (broad).

An attempt was made to distil the product *in vacuo* but decomposition began at about 50°. Therefore, the product was destructively distilled at atmospheric pressure, and a gas, noncondensable in Dry Ice, was evolved. The gas was passed into a solution of calcium hydroxide. A precipitate formed which redissolved upon continued bubbling of the gas through the mixture. The distillate was redistilled to yield 108 g of isopropyl isobutyrate (82% from **2**), bp 118–120°.[3] The infrared spectrum of this product was identical with that of an authentic sample of isopropyl isobutyrate.

**Hydrolytic Stability of 1.**—A mixture of 20.0 g (0.14 mole) of **1** and 100 ml of water was stirred vigorously and maintained at 30° for 30 min. During this time the pH of the mixture was maintained at 8.0 by gradual addition of 0.1 *N* sodium hydroxide. The amount of base consumed was 3.5 ml (0.35 mequiv), corresponding to 0.25% hydrolysis.

**Registry No.**—**1**, 3173-79-3; isopropyl hydrogen dimethylmalonate, 7695-26-3.

(3) S. Young and E. C. Fortey, *J. Chem. Soc.*, **81**, 785 (1902).

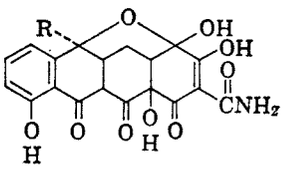
## Chemistry of Tetracyclines. I. Mercuric Acetate Oxidation of Tetracycline

J. S. PAUL SCHWARZ, HAROLD E. APPLEGATE, JACQUELINE L. BOUCHARD, AND FRANK L. WEISENBORN

*The Squibb Institute for Medical Research, New Brunswick, New Jersey*

*Received March 24, 1966*

Blackwood and Stephens[1] have reported the oxidation of tetracycline hydrochloride with N-chlorosuccinimide in water to the hemiketal (I), and Esse and co-workers[2] have reported the oxidation of 6-demethyltetracycline with chloric acid in acetic acid to the analogous hemiketal (II).



I, R = $CH_3$
II, R = H

In an attempt to accomplish the same transformation, we have treated tetracycline base (IV) in acetic acid with mercuric acetate. Crystallization of the product produced instead the dimethylamine salt of quinone VII as the only isolable product, the free quinone VII being isolated on acidic work-up of the reaction. The structure of VII was indicated by infrared bands in the hydroxyl (2.95 μ) and carbonyl (γ-lactone, 5.62 μ) regions and by ultraviolet absorption maxima (Table I) characteristic for quinone [299 mμ (ε 18,900), 422 mμ (ε 490)] and 8-hydroxy-1-tetralone [340 mμ (ε 5500)] chromophores. When VII was reductively acetylated, pentaacetate VIII was produced. As expected, for this structure, the 10-acetoxyl and the two pairs of symmetrically oriented acetoxyls on ring A gave rise to a three-proton singlet and two six-proton singlets in the appropriate region of the nmr spectrum.

The sequence of events leading from tetracycline (IV) to quinone VII is believed to be that depicted in Scheme I. Since tetracycline is stable at room temperature in glacial acetic acid with or without added

(1) R. K. Blackwood and C. R. Stephens, *Can. J. Chem.*, **43**, 1382 (1965); *J. Am. Chem. Soc.*, **86**, 2736 (1964).

(2) R. C. Esse, J. A. Lowery, C. R. Tamorria, and G. M. Sieger, *ibid.*, **86**, 3874 (1964).