

50 *The Action of Hydrogen Peroxide on Symmetrical Triketones.***13. The Action of Hydrogen Peroxide on Symmetrical Triketones.**

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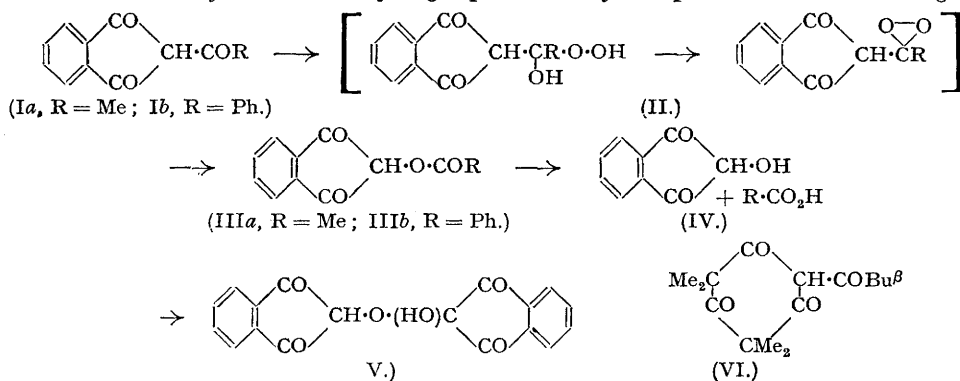
The oxidation of 1 : 3-diketo-2-acylindane and triacylmethane derivatives with hydrogen peroxide in acid, alkaline, and neutral media has been investigated.

IN the course of investigations on leptospermone (Briggs, Hassall, and Short, *J.*, 1945, 706) it was shown that oxidation of this tetramethylphloroglucinol derivative (VI) with hydrogen peroxide resulted in specific attack on the acyl side chain with the formation of an ester. In view of the interest attached to compounds of natural occurrence and physiological activity containing the symmetrical triketone structure present in leptospermone (*Aspidium filix mas* derivatives : Boehm, *Annalen*, 1901, **318**, 230; diketoacylindanes : Kilgore, Ford, and Wolfe, *Ind. Eng. Chem.*, 1942, **34**, 494; protokosin : Hems and Todd, *J.*, 1937, 562; humulone and lupulone : Wollmer, *Ber.*, 1916, **49**, 780) and the possible application of this method of oxidation in further degradative studies on such structures, the reaction has been further investigated using diketoacylindane and triacylmethane derivatives as representative types.

In the concentrated sulphuric acid (Baeyer and Villiger, *Ber.*, 1900, **33**, 124; Ruzicka and Stoll, *Helv. Chim. Acta*, 1928, **11**, 1159) or alkaline (Dakin, *Amer. Chem. J.*, 1909, **42**, 474) solutions which have been applied in similar hydrogen peroxide oxidations, 1 : 3-diketo-2-acetyl- and 2-benzoyl-indane are degraded to phthalic acid and acetic and benzoic acids respectively. Perbenzoic acid (Burchhardt and Reichstein, *Helv. Chim. Acta*, 1942, **25**, 1434) and peracetic acid (Wacek and Bezdard, *Ber.*, 1941, **74**, 845) had no action on the ketones. In ethereal solution hydrogen peroxide converted diketobenzoylindane into a compound  $C_{16}H_{10}O_4$ , which was identified as 1 : 3-diketo-2-benzoyloxyindane (IIIb), since on alkaline hydrolysis it gave 2-hydroxy-1 : 3-diketoindane (IV) and benzoic acid. The product (IV) was characterised by precipitation as hydrindantin (V) (Ruhemann, *J.*, 1911, **99**, 792) on treatment with aqueous triketoindane hydrate. Similar reactions occur with the product  $C_{11}H_8O_4$  (IIIa) obtained on oxidation of 1 : 3-diketo-2-acetylindane under neutral conditions. In alkaline and sulphuric acid media (IIIa) and (IIIb) decompose to phthalic acid and the corresponding carboxylic acid. Since the diketoacylindanes are themselves stable to acid and alkaline hydrolysis (Schwerin, *Ber.*, 1894, **27**, 104), their oxidation to simple acids apparently proceeds through the ester intermediates.

Oxidation of triacylmethane derivatives with hydrogen peroxide did not follow the same course as that of diketoacylindanes. Under neutral conditions tribenzoylmethane was unattacked, but on long standing dibenzoylacetylmethane decomposed slightly to unstable amorphous peroxides. In alkaline solution degradation to the corresponding simple carboxylic acids occurred. In acid conditions hydrolysis rather than oxidation took place.

Two mechanisms (Baeyer and Villiger, *Ber.*, 1899, **32**, 3625; Wacek and Eppinger, *Ber.*, 1940, **73**, 644) have been suggested for the oxidation of ketones to esters. The first, which involves the rearrangement of an intermediate peroxide, appears to be more satisfactory. It is supported by experiments on the oxidation of cyclohexanone (Stoll and Scherrer, *Helv. Chim. Acta*, 1930, **13**, 142) and by the direct conversion of fluorenone mono-peroxide to the lactone of 2-hydroxydiphenyl-2'-carboxylic acid (Wittig and Pieper, *Ber.*, 1940, **73**, 295). Indirect evidence for the formation of an intermediate hydroxy-hydroperoxide (II) has been provided (Barnes and Lewis, *J. Amer. Chem. Soc.*, 1936, **58**, 947). The complete course of reaction between the diketoacylindanes and hydrogen peroxide may be represented in the following way :



## EXPERIMENTAL.

*Action of Hydrogen Peroxide.*—(1) On 1:3-diketo-2-acetylindane. The triketone was prepared by Kilgore's, Ford, and Wolfe's modification (*loc. cit.*) of Schwerin's method (*Ber.*, 1894, **27**, 104). There was a small increase in yield when the sodium methoxide recommended was replaced by sodamide.

In alkaline solution. In a typical experiment the ketone (1.0 g.) was dissolved in a slight excess of 0.5N-sodium hydroxide, and after addition of excess of a solution of pure hydrogen peroxide (0.75 g. of 50% aqueous solution), it was left at 0° for 8 days. The reaction mixture yielded on acidification a precipitate of unchanged ketone (0.1 g.) and phthalic acid (0.75 g.), m. p. and mixed m. p. 203° (decomp.). Ether extraction gave a trace of phthalic acid and acetic acid (0.15 g.); *p*-phenylphenacyl ester, m. p. and mixed m. p. 115°.

In acid solution. 1:3-Diketo-2-acetylindane (1.0 g.), dissolved in sulphuric acid (10 c.c. of 80% solution), was treated at 0° with aqueous hydrogen peroxide (0.75 g. of 50% solution). After the initial reaction had subsided the mixture was left at room temperature for 24 hours, and then poured on ice. Phthalic and acetic acids were obtained in quantitative yield.

In neutral solution. The ketone was dissolved in the minimum of absolute ether, treated with excess of ethereal hydrogen peroxide [5 c.c. of 20% solution; prepared by concentrating a dried ethereal extract of freshly distilled and concentrated hydrogen peroxide (approximately 25%)], and left for 21 days at room temperature. The reaction mixture, on evaporation and treatment with water, yielded a light yellow solid, which was separated by extraction with chloroform into insoluble phthalic acid (0.02 g.) and a mixture of unchanged ketone (0.22 g.) and white leaflets (0.70 g.), m. p. 96°, which were separated by crystallisation from ethyl acetate–light petrol (b. p. 40–70°) [Found, for the leaflets: C, 64.5, 64.4; H, 4.1, 4.1; *M* (cryoscopic in benzene), 192.  $C_{11}H_8O_4$  requires C, 64.7; H, 3.9%; *M*, 204]. In alcoholic solution this product, 1:3-diketo-2-acetoxyindane (IIIa), has no action on ferric chloride or acidified potassium iodide but gives a series of colour reactions. It dissolves very slightly in water to give a yellow solution, but gives colourless solutions in non-polar solvents. In 2N-sodium hydroxide it gives a yellow solution which rapidly changes to a deep ultramarine-blue. On acidification in the absence of oxygen this passes reversibly from blue (pH 11.0) through red (pH 6.0) to light yellow (pH 4.0). Both the red and the blue solution are rapidly decolorised through atmospheric oxidation. An alcoholic solution develops a strong purple stain on the human skin after several hours.

(2) On 1:3-diketo-2-acetoxyindane. The indane (0.10 g.), when dissolved in 2N-sodium hydroxide to give a blue solution or in the form of its yellow solution in 2N-sodium carbonate, reacted vigorously with excess of hydrogen peroxide. Acidification of the mixture gave phthalic acid in quantitative yield. Similarly in sulphuric acid solution (80%) quantitative oxidation to phthalic and acetic acids occurred.

*Characterisation of 2-hydroxy-1:3-diketointhane.* When air was blown through the acidified solution obtained on alkaline hydrolysis of 1:3-diketo-2-acetoxyindane (0.20 g.), a white solid (0.18 g.), m. p. 236° (decomp.), was precipitated. This was identified as hydrindantin hydrate (Ruhemann, *loc. cit.*) (Found: C, 60.5; H, 3.9. Calc. for  $C_{18}H_{10}O_6 \cdot 2H_2O$ : C, 60.3; H, 3.9%) by m. p. and mixed m. p. The same product was formed on acidification of the alkaline hydrolysis solution of 1:3-diketo-2-acetoxyindane with an alcoholic solution of 1:2:3-triketointhane hydrate.

(3) On 1:3-diketo-2-benzoylindane. The indane (prepared after the manner of Schwerin, *loc. cit.*) in 2N-sodium hydroxide solution reacted with excess of hydrogen peroxide more slowly than did the acetyl derivative to give, together with a trace of unchanged ketone, phthalic and benzoic acids, which were separated and identified by mixed m. p. determination. In sulphuric acid quantitative yields of these acids were also obtained.

A solution of 1:3-diketo-2-benzoylindane (1.0 g.) in the minimum of absolute ether, on treatment with a large excess of ethereal hydrogen peroxide (7 g. of 20% solution) during 20 days, gave on evaporation a light yellow solid from which phthalic acid (0.1 g.), benzoic acid (0.05 g.), and a white solid (0.70 g.), m. p. 136.5–137°, were obtained. This solid crystallised as prisms from ethyl acetate–light petrol (b. p. 40–60°) [Found: C, 72.2; H, 3.9; *M* (cryoscopic in benzene), 258.  $C_{16}H_{10}O_4$  requires C, 72.2; H, 3.8%; *M*, 266]. This product, 1:3-diketo-2-benzoyloxyindane (IIIb), gives similar colour reactions to the acetyl analogue. In 2N-sodium hydroxide the first-formed yellow solution changes more slowly than (IIIa) to deep ultramarine-blue. Alkaline hydrolysis of (IIIb) under hydrogen gave benzoic acid and 2-hydroxy-1:3-diketointhane, characterised, as previously, through conversion into hydrindantin.

(4) On tribenzoylmethane. Tribenzoylmethane (0.50 g.), prepared from dibenzoylmethane (*Org. Synth.*, Coll. Vol. I, 1941, 205) by the procedure of Birckenbach *et al.* (*Ber.*, 1932, **65**, 1071), was dissolved in 2N-sodium hydroxide solution and treated with excess of hydrogen peroxide (1.0 g. of 50% solution) overnight at room temperature. Concentration and acidification of the colourless solution yielded benzoic acid (0.47 g.), m. p. 122°. In sulphuric acid (10 c.c.) at 0°, hydrogen peroxide (1 c.c. of 50% solution) also converted the triketone (0.5 g.) into benzoic acid. Under neutral conditions (nitrobenzene solution or ethereal suspension) hydrogen peroxide had no action on the ketone over a period of 28 days.

(5) On dibenzoylacetylmethane. The methane (Claisen and Falk, *Annalen*, 1896, **291**, 25) in alkaline solution was degraded completely by hydrogen peroxide at room temperature in 3 days. Benzoic acid was isolated from the acidified solution in quantitative yield. In sulphuric acid solution (15 c.c.) at 0°, dibenzoylacetylmethane (0.5 g.) was hydrolysed to dibenzoylmethane (0.40 g.), m. p. and mixed m. p. 77°, in the absence of hydrogen peroxide.

Treatment of the keto-form of dibenzoylacetylmethane (1.0 g.) in ether with ethereal hydrogen peroxide (2 c.c. of 10% solution) at room temperature for 7 days yielded, besides unchanged material (0.3 g.), benzoic acid (0.2 g.) and a crude peroxide (m. p. 80–90°) which sublimed at 70–80°/0.01–0.02 mm. and readily liberated iodine from acidified potassium iodide. No pure material was isolated from the crude product.

The enolic form of dibenzoylacetylmethane (0.5 g.), m. p. 85° (107°; Claisen and Falk, *loc. cit.*), on

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standing in ethereal hydrogen peroxide for 30 days, yielded unchanged product (0.45 g.) and a trace (0.02 g.) of an amorphous peroxide.

The analyses were by Messrs. C. L. Carter and J. A. Mills.

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