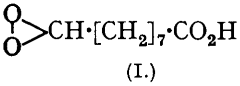
39. *Peroxides derived from η-Aldehydo-octoic Acid and Nonaldehyde : Bis-α-hydroxy-ω-carboxyoctyl Peroxide and Bis-α-hydroxynonyl Peroxide.*

By George King.

Bis-α-hydroxy-ω-carboxyoctyl peroxide (II) and bis-α-hydroxynonyl peroxide (III) have been synthesised from η-aldehydo-octoic acid and nonaldehyde respectively. Although these peroxides are well-defined crystalline substances, the latter is particularly unstable, even in the solid form, and both tend to dissociate in solution to some extent into the free aldehydes and hydrogen peroxide. Their general reactions and peroxidising properties have been studied.

A peroxide derived from η-aldehydo-octoic acid (azelaic semialdehyde) was first reported by Harries (*Ber.*, 1909, **42**, 455), who obtained it as one of the hydrolytic products of oleic acid ozonide, and assigned to it the structure (I). It was subsequently shown by Rieche and Sauthoff (*Sitzungsber. physik.-med. Soz. Erlangen*, 1929/30, **61**, 369) to belong to the class of bis-α-hydroxyalkyl peroxides, and to have the structure (II).



$\left.\begin{array}{l}O\\|\\O\end{array}\right>CH\cdot[CH_2]_7\cdot CO_2H$

(I.)

$$HO_2C\cdot[CH_2]_7\cdot CH(OH)\cdot O\cdot O\cdot CH(OH)\cdot[CH_2]_7\cdot CO_2H$$

(II.)

(III.) $$CH_3\cdot[CH_2]_7\cdot CH(OH)\cdot O\cdot O\cdot CH(OH)\cdot[CH_2]_7\cdot CH_3$$

Bis-α-hydroxynonyl peroxide (III) affords another example of this type of compound, whose general properties have been described by Rieche (" Alkylperoxyde und Ozonide," 1931; *Ber.*, 1931, **64**, 2328). According to Rieche, both these peroxides occur among the products of cleavage of oleic acid ozonide as a result of secondary reactions involving the equilibrium

$$R\cdot CH(OH)\cdot O\cdot OH + R\cdot CHO \rightleftharpoons R\cdot CH(OH)\cdot O\cdot O\cdot CH(OH)\cdot R$$

rather than by the direct union of hydrogen peroxide and aldehydes arising during the decomposition. Although peroxides of type (III) can usually be synthesised readily from hydrogen peroxide and the corresponding aldehydes (Rieche, *loc. cit.*; Wieland and Wingler, *Annalen*, 1923, **431**, 301), Rieche was unable to obtain (II) in a similar manner from azelaic semialdehyde, doubtless because the latter itself had not at that time been isolated in even a reasonably pure state (King, J., 1938, 1826).

The author has found that η-aldehydo-octoic acid reacts smoothly and normally with hydrogen peroxide, affording bis-α-hydroxy-ω-carboxyoctyl peroxide in good yield, and advantage has been taken of this to investigate its properties, as well as those of the corresponding peroxide derived from nonaldehyde. Both peroxides are well-defined crystalline substances, the former being distinctly the more stable, but experimental evidence suggests that in most media they undergo reversible dissociation into the free aldehydes and hydrogen peroxide, dissociation being promoted by rise of temperature, thus:

$$R\cdot CH(OH)\cdot O\cdot O\cdot CH(OH)\cdot R \rightleftharpoons 2R\cdot CHO + H_2O_2$$

EXPERIMENTAL.

Bis-α-hydroxy-ω-carboxyoctyl Peroxide (II).—η-Aldehydo-octoic acid (2·7 g., m. p. 38·5°), prepared from 9 : 10-dihydroxystearic acid (King, *loc. cit.*, p. 1827), in glacial acetic acid (20 ml.) was treated with hydrogen peroxide (1·0 ml. of 90—100 vol.) at room temperature; after 48 hours an equal bulk of water was added, and the whole cooled in ice-water. The product was collected, washed with 50% acetic acid and water (yield, 2·2 g., m. p. 112°), and recrystallised from acetone and alcohol, bis-α-hydroxy-ω-carboxyoctyl peroxide separating in small, somewhat elongated, hexagonal plates, m. p. 112·5° (decomp.) (Harries, *loc. cit.*, gave m. p. *ca.* 98°) [Found: C, 57·2; H, 9·0; equiv., 189; *M* (in dioxan), 343, 441. Calc. for $C_{18}H_{34}O_8$: C, 57·3; H, 9·0%; equiv. (dibasic), 189; *M*, 378]. The m. p. fell to 106° after the peroxide had been kept for 5 months over sulphuric acid in a desiccator.

The peroxide was very sparingly soluble in light petroleum, chloroform, and benzene, and sparingly in ether, acetone, and alcohol in the cold. It dissolved appreciably in boiling water, but with some decomposition. The peroxide gave colours with Schiff's reagent and with titanium sulphate solution only after being boiled for a few minutes with water and then cooled, suggesting dissociation into η-aldehydo-octoic acid and hydrogen peroxide. It liberated iodine rapidly from a warm solution of potassium iodide, but very slowly in the cold, and reduced Fehling's solution appreciably on boiling.

Action of Water and Aqueous Sodium Hydroxide on Bis-α-hydroxy-ω-carboxyoctyl Peroxide.—(*a*) The peroxide (0·5 g.), after being refluxed with water (25 ml.) for 8—9 hours, gave negative tests with titanium sulphate and potassium iodide: the cooled solution, treated with *p*-nitrophenylhydrazine in dilute acetic acid, deposited the *p*-nitrophenylhydrazone of η-aldehydo-octoic acid (0·42 g.; *ca.* 50%), which crystallised from alcohol and acetone in short orange rods or prisms, m. p. and mixed m. p. 144°. (A comparable solution of hydrogen peroxide required boiling for 7 hours to destroy all peroxide reactions.)

(*b*) A solution of the peroxide in cold 2N-sodium hydroxide gave an immediate yellow colour with titanium sulphate solution. On warming, some evolution of oxygen occurred and the solution then no longer gave peroxide reactions. After several minutes' boiling, acidification with 2N-sulphuric acid, and extraction with ether, a pale yellow, viscous oil was obtained, apparently identical in properties with the polymerised product resulting from the action of alkali on the semialdehyde itself (King, *loc. cit.*, p. 1828).

Further Properties of the Peroxide.—With semicarbazide hydrochloride and sodium acetate in warm aqueous alcohol, bis-α-hydroxy-ω-carboxyoctyl peroxide afforded the semicarbazone of η-aldehydo-octoic acid, m. p. and mixed m. p. 166·5° (Found: C, 52·3; H, 8·6; N, 18·0; equiv., 229. Calc. for $C_{10}H_{19}O_3N_3$: C, 52·4; H, 8·3; N, 18·3%; equiv., 229). Presumably, hydrogen peroxide was eliminated during this condensation, since the aqueous-alcoholic mother-liquor liberated iodine freely from potassium iodide.

Similarly, with Brady's reagent in warm 90% alcohol, the 2 : 4-dinitrophenylhydrazone of the semialdehyde readily separated, m. p. 120·5° after repeated crystallisation from alcohol, not depressed by an authentic specimen.

Further evidence of the ease with which the peroxide dissociates into the semialdehyde and hydrogen peroxide in various solvents was afforded by the immediate yellow colour obtained on adding titanium sulphate solution to a cold saturated solution in dioxan, a strong positive Schiff's reaction in the same solvent, and the rapid consumption of permanganate, with effervescence, in the presence of sulphuric acid. Similar results were obtained in cold alcoholic solution, and it was noteworthy that the peroxide dissolved more freely in alcohol containing dilute sulphuric acid than in alcohol alone.

Estimation of "Active Oxygen" by Lea's Method.—Bis-α-hydroxy-ω-carboxyoctyl peroxide (0·0341 g.) was treated in a Pyrex tube with potassium iodide (1·0 g.) and glacial acetic acid–chloroform (20 ml. of 2 : 1 by vol.), with the precautions described by Lea (D.S.I.R. Food Investigation Special Report No. 46, "Rancidity in Edible Fats," 1938, p. 107). After heating, pouring into water (30 ml.), and rinsing out, the liberated iodine required 16·35 ml. of N/100-sodium thiosulphate, allowance having been made for a blank (Calc.: 18·05 ml., assuming 1 atom of active O per mol.). The percentage of active oxygen found was therefore 3·84 (*i.e.*, 90·8% of the theoretical).

Oxidation of η-Aldehydo-octoic Acid by Labile Peroxides in Ether.—The occurrence of bis-α-hydroxy-ω-carboxyoctyl peroxide among the products of oxidation of the 9 : 10-dihydroxystearic acids with periodic acid has been observed by the author on several occasions. Its formation was ultimately traced to the oxidation of η-aldehydo-octoic acid by "labile peroxides" in the rather large bulk of ether used for extraction. These peroxides are readily detected by the yellow colour imparted to a few drops of titanium sulphate solution when shaken with several ml. of the ether, and can be removed by fractionation of the ether through a long column, the peroxides being less volatile. According to H. King (J., 1929, 738), old specimens of ether may contain the equivalent of 2—10 g. of hydrogen peroxide per l., mainly in the form of hydroxyethyl hydrogen peroxide, $CH_3\cdot CH(OH)\cdot O\cdot OH$.

In one experiment, dihydroxystearic acid (3·11 g.), m. p. 132°, was oxidised with periodic acid in the manner previously described by the author (*loc. cit.*), and the products were extracted with ether (330 ml.) containing labile peroxides equivalent to 0·26 g. of hydrogen peroxide (estimated by the method of H. King, *loc. cit.*). After distillation of the solvent and removal of nonaldehyde by steam-distillation, the remaining aqueous liquid (*ca.* 100 ml.) was cooled, depositing crude bis-α-hydroxy-ω-carboxyoctyl peroxide (1·36 g., m. p. 99—101°). After being washed with ether and crystallised successively from alcohol and acetone, this melted at 112°, undepressed by an authentic specimen. The aqueous mother-liquor contained η-aldehydo-octoic acid (0·24 g.), recovered in the form of its 2 : 4-dinitrophenylhydrazone, m. p. 122°.

Bis-α-hydroxynonyl Peroxide (III).—Hydrogen peroxide (1·7 ml. of " 90—100 " vol.) was added to nonaldehyde (3·8 g.), prepared from dihydroxystearic acid (King, *loc. cit.*), in glacial acetic acid (25 ml.). Crystals began to separate almost immediately. After 24 hours at room temperature, an equal bulk of water was added, and the whole cooled in ice. The product (3·1 g., m. p. 73°) was crystallised twice from absolute alcohol, giving pure bis-α-hydroxynonyl peroxide in colourless, elongated, hexagonal plates, m. p. 78° (Harries and Franck, *Annalen*, 1910, **374**, 365, gave m. p. 72°) [Found : C, 67·9; H, 12·1; *M* (in dioxan), 306. Calc. for $C_{18}H_{38}O_4$: C, 67·9; H, 12·0%; *M*, 318]. This was very sparingly soluble in water and cold light petroleum, somewhat sparingly in alcohol, but readily in ether at room temperature. The peroxide was unstable even in the solid form, had a distinct odour of nonaldehyde, and lost all its peroxidising properties when kept over sulphuric acid in a desiccator for 14 days, becoming at the same time semi-liquid. Shaken with water and titanium sulphate solution, it gave no appreciable colour for some minutes, but a deep yellow colour developed at once on warming. Similarly, iodine was liberated slowly from aqueous potassium iodide in the cold, but rapidly on warming. A cold aqueous suspension slowly gave a magenta colour with Schiff's reagent. When boiled with water, the peroxide decomposed rapidly into nonaldehyde and hydrogen peroxide. Heated above its m. p., especially at 120—150°, it decomposed with effervescence, leaving a mixture of nonaldehyde and nonoic acid.

Estimation of " Active Oxygen " in Bis-α-hydroxynonyl Peroxide.—By Lea's method, 0·0348 g. of the peroxide liberated iodine equivalent to 21·5 ml. of N/100-sodium thiosulphate (Calc. : 21·85 ml.). The percentage of active oxygen found was therefore 4·94 (Calc., assuming one atom of active O per mol., 5·03%), *i.e.*, 98·2% of the theoretical.

Distillation of Bis-α-hydroxynonyl Peroxide with Aqueous Sulphuric Acid (cf. H. King, *loc. cit.*, p. 745).—The peroxide (0·40 g.) was distilled with 2N-sulphuric acid (25 ml.) and water (35 ml.) from a long-necked distilling flask for 20 mins., at the end of which time no further nonaldehyde came over. The clear residual liquid, after being cooled, required 22·7 ml. of N/10-potassium permanganate (Calc. : 25·16 ml., assuming complete decomposition of the peroxide into 2 mols. of nonaldehyde and 1 mol. of hydrogen peroxide), *i.e.*, the hydrogen peroxide obtained represented 90·2% of the theoretical. The aqueous distillate, containing nonaldehyde in suspension, was shaken with Brady's reagent (1 g. of 2 : 4-dinitrophenylhydrazine in 250 ml. of 2N-hydrochloric acid), giving nonaldehyde 2 : 4-dinitrophenylhydrazone (0·758 g., m. p. 104—105·5°. Calc. : 0·810 g.). This crystallised from alcohol in broad yellow needles, m. p. and mixed m. p. 106·5°.

The author gratefully acknowledges his indebtedness to Dr. G. W. Ellis, O.B.E., for numerous helpful suggestions, and to the Chemical Society for a grant.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, LONDON, W. 2.

[*Received, November 10th,* 1941.]