Synthesis and Reactions of β-Hydroxyhydroperoxides

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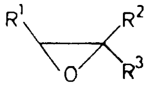
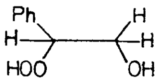
Summary Acid-catalysed reaction of epoxides with 98% H_2O_2 yields β-hydroxyhydroperoxides, which react with trifluoroacetic anhydride or dicyclohexylcarbodi-imide to give carbonyl compounds.

β-Hydroxyhydroperoxides[1,2] and dioxetans[3] have been invoked as intermediates in biological oxygenations. β-Hydroxyhydroperoxides have been prepared only with great difficulty from olefins either by *X*-ray irradiation[1] or by a sequential reaction with HOBr, conc. H_2O_2, and moist Ag_2O.[4] Synthetic routes to dioxetans include addition of singlet oxygen to electron-rich olefins[5] and base elimination of hydrogen halides from β-hydroxyhydroperoxides.[6] As alternative routes to both these potentially important oxygen-containing species, we have explored the possibility that acid- or base-catalysed opening of epoxides with 98% H_2O_2 would provide β-hydroxyhydroperoxides. We have not so far succeeded in the conversion of the latter into dioxetans, however. Definite proof for the occurrence of β-hydroxyhydroperoxides in biological processes has hitherto been lacking, owing to difficulties in their isolation since they may be present in minute quantities. We hope to examine their possible biological occurrence by using

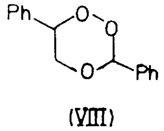


(I) $R^1 = Ph, R^2 = R^3 = H$
(II) $R^1 = R^2 = R^3 = Me$
(III) $R^1 = PhCH_2CH_2, R^2 = R^3 = Me$
(IV) $R^1 = R^2 = Ph, R^3 = H$



(V)

(VI) $R^1 = R^2 = R^3 = Me$
(VII) $R^1 = PhCH_2CH_2, R^2 = R^3 = Me$



(VIII)

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† In partial fulfilment of M.S. degree.

labelled substrates and isolating the minute quantities of the hydroxyhydroperoxides by dilution with compounds made by the method described here.

Four epoxides (I)—(IV), chosen for their structural differences, were allowed to react with a five-fold excess of 98% H_2O_2 in ether solutions at 0—5 °C, in the presence of catalytic amounts of $HClO_4$. After 2 h the β-hydroxyhydroperoxides (V)—(VII)‡ were isolated in yields of 60, 55, and 95%, respectively. Under these conditions, benzaldehyde was the only product isolated from the reaction of stilbene oxide (IV). Although an unsymmetric epoxide may be opened in two ways, only one product is formed in each case, as shown by n.m.r. spectroscopy. The formation of (V)—(VII) is consistent with an S_N1 reaction in which the hydroperoxy group is placed on the most stable carbonium ion of the intermediate. In the case of stilbene oxide, the hydroxyhydroperoxide formed probably undergoes acid-catalysed elimination of water, formation of two molecules of benzaldehyde apparently forcing the reaction in this direction.

Base-catalysed reactions of the epoxides with 98% H_2O_2 did not yield any isolable quantities of hydroxyhydroperoxides under various conditions of solvent, temperature (0—45 °C), and reaction time (up to 24 h). Starting materials were isolated unchanged, steric effects or lack of sufficient nucleophilicity of OOH^- probably being responsible for the failure.

When the hydroxyhydroperoxide (V) was treated with either dicyclohexylcarbodi-imide or trifluoroacetic anhydride and pyridine, benzaldehyde was the sole product. A stable 1,2,4-trioxan (VIII) was isolated when (V) was allowed to react with benzaldehyde.‡

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‡ Compounds (V)—(VIII) gave satisfactory elemental analysis for C and H, and the n.m.r. spectral parameters are consistent with the structures assigned.

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