

SYNLETT Spotlight 474

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

gem-Bishydroperoxides

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Johannes grew up in the diamond city Kimberley, South Africa. He pursued his interest in science by obtaining a B.Sc. degree in chemistry and biology in 2004 from the University of the Free State. His fondness for organic chemistry led him to procure a M.Sc. degree from the same institution in 2008. He is currently completing a Ph.D. degree under the supervision of Professor B. C. B. Bezuidenhoudt at the University of the Free State.

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Introduction

The relevance of *gem*-dihydroperoxides to peroxidic anti-malarial agents stimulated initial interest in this class of compounds.^{1–5} Apart from their biological activities,^{6,7} *gem*-dihydroperoxides have been established as important building blocks in synthetic chemistry, for example the preparation of organic peroxides, trioxanes, tetraoxanes, spirobisperoxyketals, and dicarboxylic diesters.^{4,7,8} *gem*-Dihydroperoxides can also be employed as oxidizing agents under various conditions to perform transformations such as epoxidation^{1–5} and sulfoxidation.^{2–5,9} In addition, in situ decomposition of *gem*-dihydroperoxides can generate singlet oxygen as the active oxidant^{8,10} in olefin oxidation, for example.¹¹ The ability of *gem*-dihydroperoxides to generate radicals allows them to be furthermore exploited as radical initiators,^{2–5} for example methyl ethyl ketone peroxide is used in the manufacturing

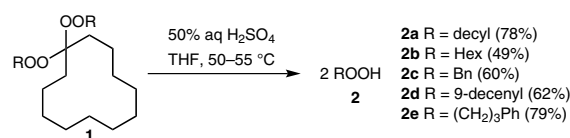
of acrylic resins, reinforced plastics, and unsaturated polyester resins.⁶

Itoh and co-workers established two catalyst-free preparative protocols for *gem*-dihydroperoxides, of which the one employs hydrogen peroxide¹² as terminal oxidant and the other molecular oxygen.^{13,14} The latter is achieved in combination with a photosensitizer (anthracene¹³ or anthraquinone¹⁴) and exposure of the reaction mixture to light.

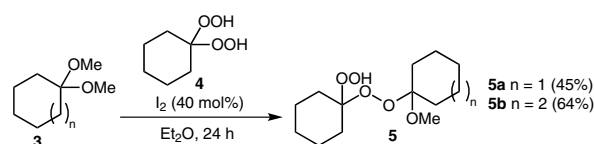
Reaction times can generally be reduced upon introduction of a catalyst, amongst which molecular iodine¹⁵ as well as numerous transition-metal Lewis acids have proven effective.^{4,5,8,16,17} Brønsted acids are comparably active as either homogeneous (sulfuric acid³) or heterogeneous catalysts, for example silica-sulfuric acid² or triflic acid-functionalized silica-coated ferromagnetic nanoparticles.¹⁸

Abstracts

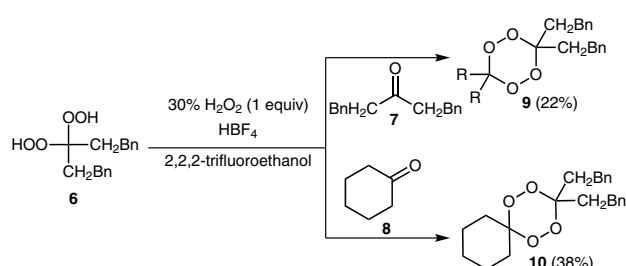
(A) Dussault and co-workers¹⁹ prepared primary and secondary alkyl hydroperoxides in moderate to high yields (48–79%) via double alkylation of 1,1-dihydroperoxides, followed by acid-catalyzed hydrolysis of the resulting strained cyclic alkylated *gem*-bishydroperoxides (bisperoxyacetals).



(B) 1-Hydroxy-1'-alkoxyperoxides were prepared by Terent'ev et al.⁶ in moderate yield (40–64%) through iodine-catalyzed cross-coupling of *gem*-bishydroperoxides and acetals. This cross-coupling is also effective upon substitution of the acetal with an enol ether.



(C) Symmetrical and asymmetrical tetraoxanes can be prepared from *gem*-dihydroperoxides. The combination of a *gem*-dihydroperoxide and its carbonyl analogue in the presence of fluoroboric acid and hydrogen peroxide favors formation of symmetrical tetraoxanes.²⁰ Similarly, asymmetrical tetraoxanes are obtained when two non-identical carbonyl compounds are introduced.⁷



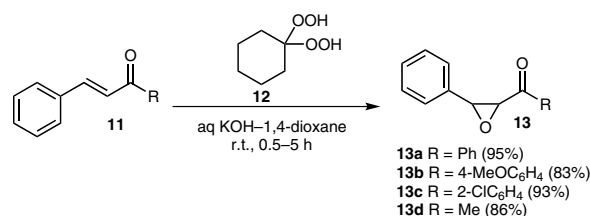
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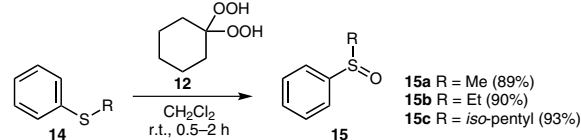
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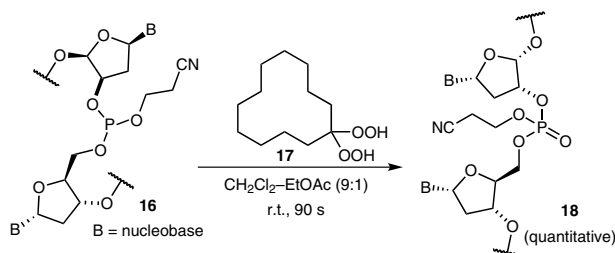
(D) Jakka et al.¹ reported the epoxidation of various α,β -unsaturated ketones utilizing cyclohexylidene-bis(hydroperoxide) as a stoichiometric oxidant under Weitz–Scheffer reaction conditions (aqueous, alkaline).



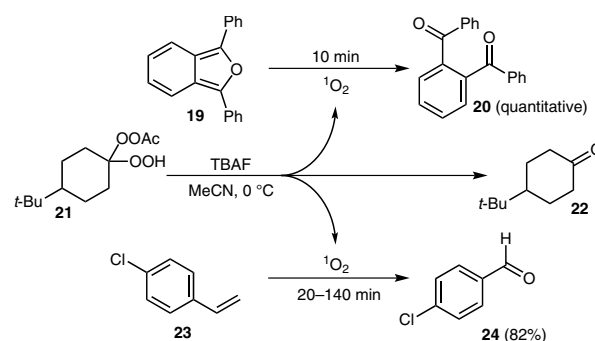
(E) Sulfoxidation of thiophenol ethers can be achieved under neutral conditions at ambient temperature, producing sulfoxides in high yields (79–93%) in less than two hours.⁹



(F) Subsequent to observing the oxidation of triphenylphosphine to triphenylphosphine oxide in the presence of 1,1-dihydroperoxy-cyclododecane, Sekine and co-workers²¹ prepared oligodeoxyribonucleotides in a similar fashion via the oxidation of phosphite intermediates to their respective phosphate analogues.



(G) Dussault and co-workers reported the liberation of singlet oxygen when monoactivated *gem*-dihydroperoxide derivatives were exposed to anhydrous alkaline conditions.²² If this degradation is performed in the presence of an organic substrate, an oxidative transformation of the substrate is observed.¹⁰ This protocol also allows for oxidative cleavage of olefinic substrates to yield aldehydes or ketones in moderate to high yields (35–82%).¹¹



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