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**

Compiled by Johannes H. van Tonder

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. Bezuidenhout at the University of the Free State.

Faculty of Natural and Agricultural Sciences, Department of Chemistry, University of the Free State, Bloemfontein 9300, South Africa
E-mail: vtonderjh@gmail.com

**Introduction**

The relevance of *gem*-dihydroperoxides to peroxodic antimalarial 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, spirobisperoxyketalts, and dicarboxylic diesters.4,7,8 *gem*-Dihydroperoxides can also be employed as oxidizing agents under various conditions to perform transformations such as epoxidation1–5 and sulfoxidation.2–5,9 In addition, in situ decomposition of *gem*-dihydroperoxides can generate singlet oxygen as the active oxidant8,10 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 (bisperoxyacetics).

(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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(D) Jakka et al. reported the epoxidation of various α,β-unsaturated ketones utilizing cyclohexylidene-bishydroperoxide 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-cycloododecane, Sekine and co-workers prepared oligodeoxyribonucleotides in a similar fashion via the oxidation of phosphate 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.18 This protocol also allows for oxidative cleavage of olefinic substrates to yield aldehydes or ketones in moderate to high yields (35–82%).11

References