**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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**Introduction**

The relevance of *gem*-dihydroperoxides to peroxodic anti-malarial agents stimulated initial interest in this class of compounds. Apart from their biological activities, *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. Dihydroperoxides can also be employed as oxidizing agents under various conditions to perform transformations such as epoxidation and sulfonation. In addition, in situ decomposition of *gem*-dihydroperoxides can generate singlet oxygen as the active oxidant in olefin oxidation, for example. The ability of *gem*-dihydroperoxides to generate radicals allows them to be furthermore exploited as radical initiators, for example methyl ethyl ketone peroxide is used in the manufacturing of acrylic resins, reinforced plastics, and unsaturated polyester resins.

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

Reaction times can generally be reduced upon introduction of a catalyst, amongst which molecular iodine as well as numerous transition-metal Lewis acids have proven effective. Bronsted acids are comparably active as either homogeneous (sulfuric acid) or heterogeneous catalysts, for example silica-sulfuric acid or triflic acid-functionalized silica-coated ferromagnetic nanoparticles.

**Abstracts**

(A) Dussault and co-workers 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. 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. Similarly, asymmetrical tetraoxanes are obtained when two non-identical carbonyl compounds are introduced.
(D) Jakka et al.\(^1\) reported the epoxidation of various \(\alpha,\beta\)-unsaturated ketones utilizing cyclohexyldiene-bishydroperoxide as a stoichiometric oxidant under Weitz–Scheffer reaction conditions (aqueous, alkaline).

![Epoxidation Reaction](image)

(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.\(^9\)

![Sulfoxidation Reaction](image)

(F) Subsequent to observing the oxidation of triphenylphosphine to triphenylphosphine oxide in the presence of 1,1-dihydroperoxy-cyclohexodecane, Sekine and co-workers\(^2\) prepared oligodeoxyribonucleotides in a similar fashion via the oxidation of phosphate intermediates to their respective phosphate analogues.

![Nucleotide Oxidation](image)

(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.\(^16\) This protocol also allows for oxidative cleavage of olefinic substrates to yield aldehydes or ketones in moderate to high yields (35–82\%).\(^11\)

References