

# 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 peroxidic antimicrobial agents stimulated initial interest in this class of compounds.<sup>1–5</sup> Apart from their biological activities,<sup>6,7</sup> *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.<sup>4,7,8</sup> *gem*-Dihydroperoxides can also be employed as oxidizing agents under various conditions to perform transformations such as epoxidation<sup>1–5</sup> and sulfoxidation.<sup>2–5,9</sup> In addition, in situ decomposition of *gem*-dihydroperoxides can generate singlet oxygen as the active oxidant<sup>8,10</sup> in olefin oxidation, for example.<sup>11</sup> The ability of *gem*-dihydroperoxides to generate radicals allows them to be furthermore exploited as radical initiators,<sup>2–5</sup> for example methyl ethyl ketone peroxide is used in the manufacturing

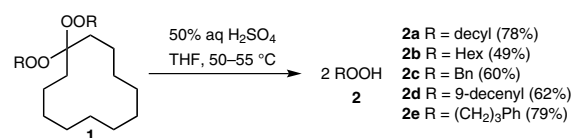
of acrylic resins, reinforced plastics, and unsaturated polyester resins.<sup>6</sup>

Itoh and co-workers established two catalyst-free preparative protocols for *gem*-dihydroperoxides, of which the one employs hydrogen peroxide<sup>12</sup> as terminal oxidant and the other molecular oxygen.<sup>13,14</sup> The latter is achieved in combination with a photosensitizer (anthracene<sup>13</sup> or anthraquinone<sup>14</sup>) and exposure of the reaction mixture to light.

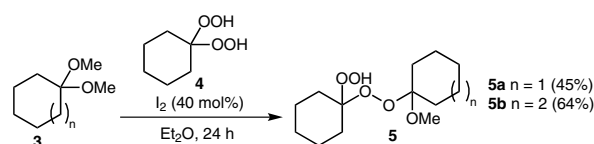
Reaction times can generally be reduced upon introduction of a catalyst, amongst which molecular iodine<sup>15</sup> as well as numerous transition-metal Lewis acids have proven effective.<sup>4,5,8,16,17</sup> Brønsted acids are comparably active as either homogeneous (sulfuric acid<sup>3</sup>) or heterogeneous catalysts, for example silica-sulfuric acid<sup>2</sup> or triflic acid-functionalized silica-coated ferromagnetic nanoparticles.<sup>18</sup>

### Abstracts

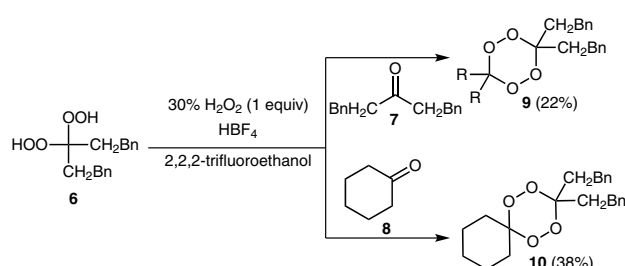
(A) Dussault and co-workers<sup>19</sup> prepared primary and secondary alkyl hydroperoxides in moderate to high yields (48–79%) via double alkylation of 1,1-dihydroperoxides, followed by acid-catalyzed hydrolysis of the resulting strained cyclic alkylated *gem*-bishydroperoxides (bisperoxyacetals).



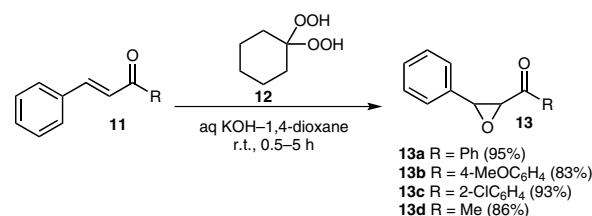
(B) 1-Hydroxy-1'-alkoxyperoxides were prepared by Terent'ev et al.<sup>6</sup> in moderate yield (40–64%) through iodine-catalyzed cross-coupling of *gem*-bishydroperoxides and acetals. This cross-coupling is also effective upon substitution of the acetal with an enol ether.



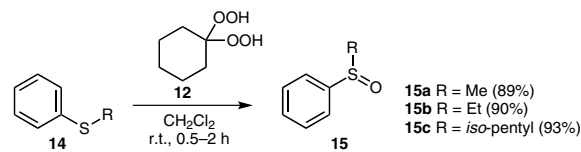
(C) Symmetrical and asymmetrical tetraoxanes can be prepared from *gem*-dihydroperoxides. The combination of a *gem*-dihydroperoxide and its carbonyl analogue in the presence of fluoroboric acid and hydrogen peroxide favors formation of symmetrical tetraoxanes.<sup>20</sup> Similarly, asymmetrical tetraoxanes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



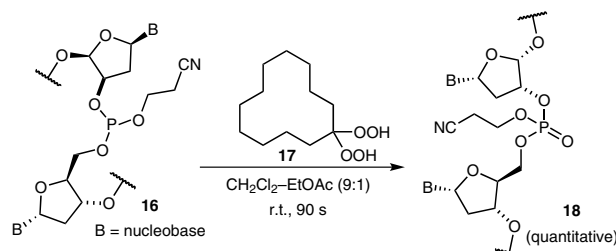
(D) Jakka et al.<sup>1</sup> reported the epoxidation of various  $\alpha,\beta$ -unsaturated ketones utilizing cyclohexylidene-bis(hydroperoxide) as a stoichiometric oxidant under Weitz–Scheffer reaction conditions (aqueous, alkaline).



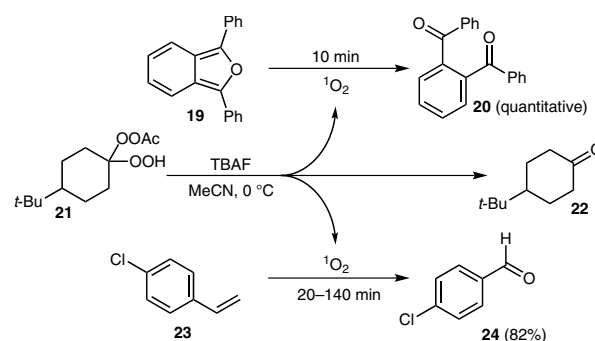
(E) Sulfoxidation of thiophenol ethers can be achieved under neutral conditions at ambient temperature, producing sulfoxides in high yields (79–93%) in less than two hours.<sup>9</sup>



(F) Subsequent to observing the oxidation of triphenylphosphine to triphenylphosphine oxide in the presence of 1,1-dihydroperoxy-cyclododecane, Sekine and co-workers<sup>21</sup> 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.<sup>22</sup> If this degradation is performed in the presence of an organic substrate, an oxidative transformation of the substrate is observed.<sup>10</sup> This protocol also allows for oxidative cleavage of olefinic substrates to yield aldehydes or ketones in moderate to high yields (35–82%).<sup>11</sup>



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