SbCl₃-Catalyzed conversion of ketones and aldehydes into gem-dihydroperoxides (DHPs) with 30% H₂O₂

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ABSTRACT

A simple and efficient conversion of ketones and aldehydes into corresponding gem-dihydroperoxides (DHPs) has been developed by SbCl₃-catalyzed oxidation with 30% H₂O₂ at room temperature. The reactions proceeded smoothly under mild conditions at room temperature. Simple experimental procedure, use of inexpensive and non-toxic catalyst, high yields and low reaction times are the main merits of the present method.

Keywords

Gem-dihydroperoxide; antimony trichloride; SbCl₃; catalyst; ketone; aldehyde; hydrogen peroxide

Academic Discipline And Sub-Disciplines

Chemistry; Synthetic Organic chemistry

SUBJECT CLASSIFICATION

Oxidative Organic transformation

Council for Innovative Research

Peer Review Research Publishing System

Journal: Journal of Advances in Chemistry

Vol. 11, No. 5
editorjaconline@gmail.com
www.cirjac.com
1. INTRODUCTION

In recent years, gem-dihydroperoxides (DHPs) as stable derivatives of ketones and aldehydes [1], have emerged as widely used effective and high-potent oxidants in various transformations including the oxidation of various compounds [2] such as sulfides [3], enantioselective oxidation of 2-substituted 1,4-naphthoquinones [4], and as initiators in polymerization reactions [5]. Also, owing to their important role as useful intermediates in the synthesis of various peroxides including tetraoxanes [6], and their analogues such as silatetroxanes [7], spirobisperoxyketals [8], and tetroxycycloalkanes [9], and epoxidation of α,β-unsaturated ketones [10], much research has been directed towards gem-dihydroperoxides in the last few years [11]. It is interesting to note that, gem-dihydroperoxides are closely relevant to peroxidic antimalarial drugs [6a,11]. They possess the gem-peroxy linkage as a salient structural feature [11e,12] in common with many well-known antimalarial cyclic organic peroxides [1,6a,13].

In literature, different protocols are reported on the synthesis of gem-dihydroperoxides most of which suffer from significant drawbacks such as the use of strong acidic media, use of concentrated H2O2, and low yields of the products [1]. Most of the methods documented in literature utilize a Brønsted or Lewis acid e.g., HCO2H [9,11b,14]; NaH2SO4·3H2O [15]; H2SO4 [16]; F3CCOOH [17]; H2WO4 [13c,16]; F3BOEt2 [13d,17]; bismuth (III) triflate [17b], and phosphomolybdic acid [17c] to promote the conversion of ketones, ketals or enol ethers into corresponding DHPs on treatment with aqueous H2O2. In addition, various other catalysts such as ceric ammonium nitrate (CAN) [13f], methyltrioxorhenium (prepared from Re2O8) [6a], and iodine [13g] have been reported to promote such conversions. However, these methods are not mild enough to offer general applicability and impose limitations such as long yields, long reaction times, use of harmful catalyst and high concentration of H2O2, and incapability with sensitive functional groups. Thus, there is still necessity to develop efficient and benign approaches for the synthesis of DHPs. Dussault et al. [13h] has reported a remarkably mild and highly efficient protocol for Re2O8-catalyzed conversion of ketones, aldehydes or acetals into 1,1-dihydroperoxides by H2O2 with a major improvement. In this paper we report the application of antimony trichloride (SbCl3) as an efficient and non-toxic catalyst to activate the mild conversion of ketones and aldehydes into respective DHPs. SbCl3 is a commercially available ionic salt which is soluble in water and many other organic solvents and has been widely used as catalyst in synthetic organic chemistry [18].

2. EXPERIMENTAL

2.1 Material and instruments

Solvents and chemicals were obtained from Aldrich and Merck chemical companies and used without purification. Melting points were determined in open capillary tubes in a Stuart SMP3 apparatus and uncorrected. 1H and 13C NMR spectra were recorded on 90 MHz (22.5) JEOL FX90Q, 200 (50) MHz Varian and 400 (100) MHz BRUKER spectrometers in CDCl3 and DMSO-d6 solution using Me4Si as an internal standard. IR spectra were recorded on a Perkin Elmer GX FT IR spectrometer (KBr pellets).

Caution: Although we did not encounter any problem with these reactions, peroxidic compounds are potentially explosive and should be handled with precautions; all reactions should be carried out behind a safety shield inside a fume hood and transition metal salts or heating should be avoided.

2.2 General procedure for conversion of ketones and aldehydes into corresponding gem-dihydroperoxides

A mixture of carbonyl substrate 1 (1 mmol), 30% aqueous H2O2 (2 mL) and SbCl3 (0.02 g, 0.1 mmol) in MeCN (3 mL) was stirred at room temperature for an appropriate time (Table 3). After completion of the reaction as monitored by TLC, the reaction mixture 1 was stirred at room temperature for an appropriate time (Table 3). After completion of the reaction as monitored by TLC, the reaction mixture was purified by silica-packed column chromatography (hexane-EtOAc). The products were characterized on the basis of their physical properties and spectral (1H, 13C NMR and IR) analysis and compared with those reported in the literature [13,18,19,20]. The characteristic data of the new products 2s and 2q along with some representative products are given below.

2.2.1-Dihydroperoxyundecane (2k) 1H NMR (200 MHz, CDCl3): δ 9.51 (bs, 2H, OOH), 1.76-1.60 (m, 2H), 1.38 (s, 3H), 1.32-1.19 (bs, 14H), 0.82 (t, J= 7 Hz, 3H); 13C NMR (50 MHz, CDCl3): 112.3, 33.4, 32.0, 29.4, 29.1, 28.4, 23.6, 22.5, 17.6, 13.8, 13.5.

2.2.2- (4-Methylphenyl)-1,1-dihydroperoxyethane (2m) 1H NMR (200 MHz, CDCl3): δ 9.71 (bs, 2H, OOH), 7.30 (d, J = 8 Hz, 2H), 7.15 (d, J = 8 Hz, 2H), 6.28 (s, 1H), 2.32 (s, 3H); 13C NMR (50 MHz, CDCl3): 139.5, 129.4, 129.0, 126.7, 109.8, 21.1.

2.2.3- (1-Naphthalen-1-yl)-1,1-dihydroperoxyethane (2p) Colorless oil; IR (KBr pellet): 3324, 3052, 2922, 2853, 1594, 1573, 1508, 1461, 1356, 1279, 1240, 1192, 1128, 941, 863, 802, 775, 591 cm−1; 1H-NMR (CDCl3, 90 MHz): δ 8.83-8.75 (bs, 2H, OOH), 8.10-7.20 (m, 7H, Ar-H), 2.65 (s, 3H, CH3); 13C-NMR (CDCl3, 22.5 MHz): δ 136.0, 134.4, 131.1, 129.9, 127.8, 126.5, 125.0, 123.0, 107.0, 20.5.

2.2.4-dihydroxyperoxy-1-phenylpropane (2q) White solid, m.p: 98-100 °C. (KBr pellet): 3424, 3244,1626, 1374, 873, 825, 665 cm−1; 1H NMR (400 MHz, CDCl3): δ 9.95 (bs, 2H, OOH), 6.8-7.3 (m, 5H, Ar), 2.2 (s, 2H, CH2), 1.54 (s, 3H, CH3); 13C NMR (100 MHz, DMSO): δ 108.4, 110.0, 126.3, 128.5, 128.7, 141.9; Anal. Calcd for C13H14O4: C, 58.69; H, 6.52. Found: C, 58.61; H, 6.45.
1,1,2,2-tetrahydroperoxy-1,2-diphenylethane (2s)\textsuperscript{new}: White solid, m.p: 50-52 °C. (KBr pellet): 3436, 3072, 3013, 2888, 1687, 1602, 1583, 1454, 1424, 1326, 1292, 1179, 1128, 934, 809 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 9.56 (bs, 4H, OOH), 7.4-7.9 (m, 10H, Ar); \textsuperscript{13}C NMR (100 MHz, DMSO) \(\delta\) 129.0, 129.7, 131.2, 133.3, 167.7; Anal. Calcd for C\textsubscript{14}H\textsubscript{14}O\textsubscript{8}: C, 54.19; H, 4.51. Found: C, 53.97; H, 4.35.

4-Cyanopheny-1,1-dihydroperoxymethane (2w): White solid; mp 107-110 °C; IR (KBr): 3414, 2916, 2235, 1611, 1405, 1333, 1243, 1199, 1122, 1083, 977, 824 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (200 MHz, CDCl\textsubscript{3}): \(\delta\) 10.08 (s, 2H, OOH), 8.04-7.78 (m, 4H, Ar), 7.24 (s, 1H, CH); \textsuperscript{13}C NMR (50 MHz, CDCl\textsubscript{3}): \(\delta\) 139.3, 129.4, 128.0, 126.1, 117.0, 112.1.

3. RESULTS AND DISCUSSION

In continuation of our efforts to develop new approaches for synthesis of DHPs [19] and their application in various organic transformations [21], herein, we report SbCl\textsubscript{3} as an efficient and hitherto unreported catalyst in promoting the synthesis of gem-DHPs from ketones and aldehydes using aqueous H\textsubscript{2}O\textsubscript{2} (30%) at room temperature.

To establish the optimum reaction conditions, different solvents such as Et\textsubscript{2}O, EtOAc, CH\textsubscript{2}Cl\textsubscript{2}, CHCl\textsubscript{3}, CCl\textsubscript{4}, CH\textsubscript{3}CN, and different catalyst loadings were examined in conversion of cyclohexanone into respective gem-dihydroperoxides with aqueous H\textsubscript{2}O\textsubscript{2} (30%) at room temperature as model reaction (Table 1). As seen in Table 1, the reaction worked out best in terms of yield (98%) and reaction time (10 min) when CH\textsubscript{3}CN was used as the solvent of choice and 10 mol\% catalyst loading (entry 7). Further increasing the amount of catalyst showed no improving effect on the yield.

Using these optimized reaction conditions (10 mol\% catalyst, room temperature, solvent CH\textsubscript{3}CN), the scope and efficiency of the reaction were explored for the synthesis of gem-dihydroperoxides 2a-z through SbCl\textsubscript{3}-catalyzed reaction of ketones and aldehydes 1a-z (Scheme 1), and the results are summarized in Table 3.
As shown in Table 3, generally, the aliphatic ketones $1a-k$ react more readily than the aromatic ketones $1l-s$ to afford the corresponding gem-DHPs in higher yields. It was observed that, under the same reaction condition no conversion to gem-DHP was observed for benzophenone as it remained almost intact after 10 hours (entry r). This can be likely due to the strong resonance stabilization and steric effects caused by phenyl groups. Moreover, as previously known by Žmitek [20] and Rieche [22], we noticed that, simple aliphatic aldehydes such as octanal $1y$ and dihydrocinnamaldehyde $1z$, react differently to provide 1,1-hydroxyhydroperoxides instead of giving their corresponding gem-dihydroperoxides (entries y and z); that is the addition of only one molecule of hydrogen peroxide to the carbonyl group has occurred.

Table 3. Synthesis of gem-dihydroperoxides with SbCl$_3$ (cat.) /30% aq. H$_2$O$_2$^a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ketone or aldehyde 1</th>
<th>Product 2</th>
<th>Time (min)</th>
<th>Yield (%)^b</th>
<th>Mp (°C)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
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<td>15</td>
<td>97</td>
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<td>93</td>
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</table>
Conditions: carbonyl 1 (1 mmol), 30% aq. $H_2O_2$ (2 mL), $CH_3CN$ (3 mL), $SbCl_3$ (0.1 mmol), room temperature.

Isolated Yield.

A simple and reasonable mechanism to explain the conversion of ketones and aldehydes 1 into respective gem-DHPs 2 is given in Scheme 2. As shown in this Scheme, the initial step likely involves the nucleophilic addition of hydrogen peroxide on $SbCl_3$-activated carbonyl compound 1 to produce the hydroxy-hydroperoxy intermediate (I). Subsequently, dehydrative substitution of hydroxyl group in the intermediate (I) occurs through nucleophilic attack by hydrogen peroxide under the activation by $SbCl_3$ to furnish the product 2.

![Scheme 2](image)

**CONCLUSIONS**

In summary, a new efficient homogeneous catalyst $SbCl_3$ has been explored for promotion of the synthesis of gem-dihydroperoxides from aliphatic and aromatic ketones and aldehydes using aqueous $H_2O_2$ (30%) in acetonitrile at room temperature. The attractive features of this new approach are: the readily available and non-toxic catalyst, high yields of the products, mild reaction conditions and the operational simplicity.

**ACKNOWLEDGEMENT**

The authors are thankful to Bu-Al Sina University Research Council for the financial support.

**REFERENCES**


