Selective Deprotection of Thioacetals by MnO₂, BaMnO₄ and KMnO₄ in the Presence of Anhydrous AlCl₃ and FeCl₃ in Dry CH₃CN

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Abstract: Dried manganese dioxide (MnO₂), potassium permanganate (KMnO₄) and barium manganate (BaMnO₄) in the presence of anhydrous aluminum and ferric chlorides performed efficient deprotection of S,S-acetals, 1,3-dithiolanes and 1,3-dithianes, in dry CH₃CN at room temperature. Thioacetals derived from enolizable carbonyl compounds remained almost intact.

INTRODUCTION

Protection of carbonyl groups as their open chain and cyclic thioacetals is an important task in the synthesis of organic molecules. Thioacetals are stable towards ordinary acidic and basic conditions and can act as acyl synthetic equivalent groups. Many procedures are available in the literature for this purpose and along this line, we have recently introduced new efficient methods for this synthetically important transformation.

Deprotection of thioacetals to their carbonyl compounds is not an easy process and straightforward. Therefore, there is a great demand, in this area of chemistry, for the introduction of mild, efficient, and selective practical methods. Clay supported ammonium, ferric or cupric nitrates, zirconium sulfonyl phosphonate, oxides of nitrogen, air / bismuth (III) nitrate, Fe(phen)3(PF6)3, DDQ, SeO₂ / AcOH, hv / pyrylium / O₂, N-fluoro-2,4,6-trimethylpyridinium triflate-water system, methylene green/visible hn, SbCl₅ / N₂, GaCl₃ / H₂O or GaCl₃ / MeOH / O₂, (CF₃CO₂)₂Iph, m-CIC₆H₄CO₂H / CF₃CO₂H, NaNO₃ / aqueous solution (NO⁺, H₂ONO⁺, ClONO) or t-butyl hypochlorite (Cl⁻) in anhydrous CCl₄, t-butyl bromide (iodide) / DMSO, DMSO / HCl / H₂O, TMSI (Br) / DMSO, LiN(i-C₃H₇)₂ / THF, HgO / 35% aqueous HBF₄, benzeneseleninic anhydride, periodic acid, isoamyl nitrite, O-mesitylenesulfonyl hydroxylamine, Et₃O⁺BF₄⁻, MeI in moist acetone or in 96% methanol, ceric ammonium nitrate (CAN) in aqueous CH₃CN, HgO-BF₃ / H₂O-THF, N-chloro-p-toluenesulphonamide (chloroamine-T), 1-chlorobenzotriazole, N-halosuccinimide, and CuCl₂ / CuO and hypervalent (tert-butylperoxy) iodane / CH₃CN-H₂O has been documented in the last two decades.

In spite of extensive studies on the chemistry of MnO₂ and KMnO₄, a strong competitor of MnO₂, dethioacetalization of S, S-acetals, 1,3-dithiolanes and 1,3-dithianes has not been studied by these reagents yet. In this report we have presented new efficient and non-hydrolytic methods for the deprotection of thioacetals.
thioacetals derived from aldehydes and non-enolizable ketones using dry MnO$_2$, BaMnO$_4$ and KMnO$_4$ as nucleophiles in the presence of unhydrous AlCl$_3$ and FeCl$_3$ in dry CH$_3$CN. A mechanism has also been proposed for the reactions.

**RESULTS AND DISCUSSION**

Recently we have found that a mixture of MnO$_2$ and AlCl$_3$ is an effective reagent for selective oxidative deprotection of benzylic trimethylsilyl- and tert-butyldimethylsilyl ethers$^{43}$. Also we have shown that various types of trimethylsilyl ethers and tert-butyldimethylsilyl ethers deprotected and oxidized by potassium permanganate (KMnO$_4$) and barium manganate (BaMnO$_4$) in the presence of Lewis acids in dry non-aqueous media$^{44}$. In continuation of our studies for dethioacetalization of acyclic and cyclic dithioacetals in non-aqueous media, we decided to study the reactions of these manganese-based oxidants for this purpose. First we started to explore the behavior of MnO$_2$ in the presence of different hydrated and unhydrous metal salts such as ZnCl$_2$, MnCl$_2$.4H$_2$O, CdCl$_2$.2H$_2$O, ZrOCl$_2$.8H$_2$O, FeCl$_3$, AlCl$_3$, PbCl$_2$, CuSO$_4$.5H$_2$O in aprotic organic solvents for the deprotection of 2-(4-Me-Phenyl)-1,3-dithiane as a model compound. Our observations showed that only anhydrous AlCl$_3$ and FeCl$_3$ were effective catalysts for the promotion of this reaction in dry CH$_3$CN. Addition of AlCl$_3$ or FeCl$_3$ in dry CH$_3$CN in the absence of MnO$_2$ did not effect any changes upon dethioacetalization of thioacetals after two days. Manganese dioxide was also ineffective reagent for this purpose in the absence of AlCl$_3$ and FeCl$_3$. We have also found that the order of the addition of MnO$_2$ and the Lewis acids to the reaction mixture was very crucial. Lewis acids (1.5-2mmol) should be added first to the reaction mixture and the mixture should be stirred for a few minutes before the addition of MnO$_2$ (6-7mmol) to the reaction mixture. The reactions proceeded smoothly and the desired carbonyl compounds were isolated in 82-96% yields (Scheme 1, Table 1).

![Scheme 1](image)

Table 1: Deprotection of thioacetals by MnO$_2$, KMnO$_4$ and BaMnO$_4$ catalyzed with AlCl$_3$ in CH$_3$CN at room temperature

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Time(min)</th>
<th>ratio of oxidants$^a$</th>
<th>Yield%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MnO$_2$, KMnO$_4$, BaMnO$_4$</td>
<td>MnO$_2$, KMnO$_4$, BaMnO$_4$</td>
<td>MnO$_2$, KMnO$_4$, BaMnO$_4$</td>
</tr>
<tr>
<td>1</td>
<td><img src="image" alt="Substrate 1" /></td>
<td>90, 45, 60</td>
<td>6, 3, 4</td>
<td>95, 94, 93</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Substrate 2" /></td>
<td>90, 50, 60</td>
<td>6, 3, 4</td>
<td>96, 95, 95</td>
</tr>
</tbody>
</table>
By this method only benzylic dithioacetals of aldehydes and non-enolizable ketones were converted to their carbonyl compounds. Dithioacetals derived from enolizable ketones were isolated intact from the reaction mixtures (Scheme 2, Table 2).

Scheme 2.

Table 2: The results of deprotection of thioacetals of enolizable ketones by MnO₂, KMnO₄ and BaMnO₄ in CH₃CN at room temperature in the presence of AlCl₃

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Time(min)</th>
<th>ratio of oxidants a</th>
<th>Yield%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>120, 120, 120</td>
<td>7, 4, 5</td>
<td>NR, NR, NR</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>120, 120, 120</td>
<td>7, 4, 5</td>
<td>NR, NR, NR</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>120, 120, 120</td>
<td>7, 4, 5</td>
<td>NR, NR, NR</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>120, 120, 120</td>
<td>7, 4, 5</td>
<td>NR, NR, NR</td>
</tr>
</tbody>
</table>
In order to explain this observation, we have proposed the possibility of formation of a complex between dithioacetals and the Lewis acids in the reaction mixture. These complex does not carry a carbonyl group anymore and therefore, the reaction dose not proceed further (Scheme 3).

\[
\begin{align*}
\text{R}^1 = &\text{aryl, R}^2 = \text{H, Me, Ph, n = 0, 1} \\
\text{Scheme 3.}
\end{align*}
\]

In order to avoid a question about the presence of a trace of water in MnO\(_2\) powder, that may act as a nucleophile for the cleavage of C-S bonds, unhydrous MnO\(_2\) was prepared\(^{45}\) by the decomposition of manganese (II) carbonate (MnCO\(_3\)) at 220-280\(^\circ\)C and AlCl\(_3\) sublimed freshly for this purpose. Non-aqueous reaction conditions suggest a non-solvolytic reaction occur in which oxygen of MnO\(_2\) acts as a nucleophilic species in this reaction. A mechanism is suggested in which the role of MnO\(_2\), as a nucleophile, has been clarified (Scheme 4). A similar conclusion and mechanism has also been proposed for deprotection of S,S-thioacetals by Barton and Ley using seleninic anhydride\(^{28}\).

\[
\begin{align*}
\text{R}^1 = &\text{aryl, R}^2 = \text{H, Me, Ph, n = 0, 1} \\
\text{Scheme 4.}
\end{align*}
\]

**Mechanism**

These observations prompted us also to study dethioacetalization of S, S- acetals, 1,3- dithiolanes, and 1,3-dithianes by KMnO\(_4\), and BaMnO\(_4\) in the presence of unhydrous AlCl\(_3\) and FeCl\(_3\) in dry CH\(_3\)CN. Both reagents were quite inactive in the absence of the Lewis acids for this purpose. The color of KMnO\(_4\) was changed from purple to dark...
brown but the formation of the carbonyl compounds was not observed at all. The formation of sulfoxides or sulfones was the most probable products formed in the reaction mixture in the absence of Lewis acids. When substituted groups on the aromatic rings bearing a lone-pair of electrons a complex formation between the Lewis acid and the substrates is very probable. This demands a higher molar ratios of the Lewis acids to be used for the reaction to proceed to completion. Our studies show that the rate of the reactions follows the sequence; KMnO4 > BaMnO4 > MnO2 (Table 1). Over-oxidation of the products has not been observed in reactions we have studied. In order to show the usefulness of the procedure, we have compared the results obtained with our presented method with some of those reported in the literature (Scheme 5, Table 3).

Table 3: Comparison of the reported methods with AlCl3 / MnO2 method

<table>
<thead>
<tr>
<th>R1</th>
<th>R2</th>
<th>n</th>
<th>Ia</th>
<th>II18</th>
<th>III13</th>
<th>IV14</th>
<th>V9</th>
<th>VI24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph</td>
<td>H</td>
<td>1</td>
<td>96(90)</td>
<td>96(50)</td>
<td></td>
<td>95(60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph</td>
<td>H</td>
<td>2</td>
<td>95(90)</td>
<td>70(60)</td>
<td>95(60)</td>
<td>97(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph</td>
<td>Me</td>
<td>2</td>
<td></td>
<td>75(30)</td>
<td>98(25)</td>
<td>95(30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph</td>
<td>Ph</td>
<td>2</td>
<td>91(75)</td>
<td>82(120)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-Me-C6H4</td>
<td>H</td>
<td>2</td>
<td>92(60)</td>
<td>90(10)</td>
<td>88(180)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-Cl-C6H4</td>
<td>H</td>
<td>2</td>
<td>92(120)</td>
<td>87(120)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cinammyl</td>
<td>H</td>
<td>2</td>
<td>85(70)</td>
<td>86(10)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4-MeO-C6H4</td>
<td>H</td>
<td>2</td>
<td>90(50)</td>
<td>76(10)</td>
<td>97(180)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a ) AlCl3 / MnO2 in CH3CN.

Conclusion
In this study, we have introduced new applications of KMnO₄, BaMnO₄ and MnO₂ as effective reagents for non-hydrolytic deprotection of non-enolizable benzylic thioacetals in the presence of AlCl₃. Reactions were proceeded with lower equivalent amounts of KMnO₄, BaMnO₄ at room temperature in CH₃CN in comparison with MnO₂ (Scheme 3, Table 2). The presence of Lewis acids in the reaction mixtures was essential and the sequence of the addition of the Lewis acids was also important. Work-up of the reaction mixture was easy and not time-consuming and the yields of the products were excellent.

Acknowledgements

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References


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