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## **Selective Deprotection of Thioacetals by MnO<sub>2</sub>, BaMnO<sub>4</sub> and KMnO<sub>4</sub> in the Presence of Anhydrous AlCl<sub>3</sub> and FeCl<sub>3</sub> in Dry CH<sub>3</sub>CN**

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**Abstract:** Dried manganese dioxide (MnO<sub>2</sub>), potassium permanganate (KMnO<sub>4</sub>) and barium manganate (BaMnO<sub>4</sub>) 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 CH<sub>3</sub>CN 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<sup>1</sup>. 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<sup>2-5</sup>.

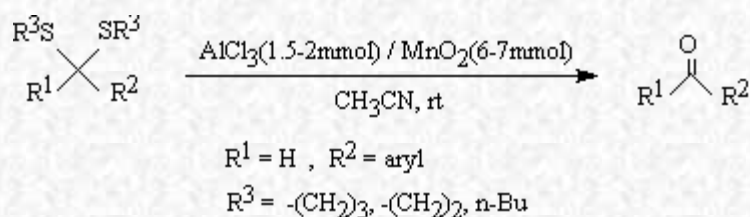
Deprotection of thioacetals to their carbonyl compounds is not an easy process and straightforward<sup>6</sup>. Therefore, there is a great demand, in this area of chemistry, for the introduction of mild, efficient, and selective practical methods. Clay supported ammonium<sup>7</sup>, ferric or cupric nitrates<sup>8</sup>, zirconium sulfonyl phosphonate<sup>9</sup>, oxides of nitrogen<sup>10</sup>, air / bismuth (III) nitrate<sup>11</sup>, Fe(phen)<sub>3</sub>(PF<sub>6</sub>)<sub>3</sub><sup>12</sup>, DDQ<sup>13</sup>, SeO<sub>2</sub> / AcOH<sup>14</sup>, hv / pyrylium / O<sub>2</sub><sup>15</sup>, N-fluoro-2,4,6-trimethylpyridinium triflate-water system<sup>16</sup>, methylene green/visible hn<sup>17</sup>, SbCl<sub>5</sub><sup>18</sup> / N<sub>2</sub>, GaCl<sub>3</sub> / H<sub>2</sub>O or GaCl<sub>3</sub> / MeOH / O<sub>2</sub><sup>19</sup>, (CF<sub>3</sub>CO<sub>2</sub>)<sub>2</sub>Iph<sup>20</sup>, m-ClC<sub>6</sub>H<sub>4</sub>CO<sub>3</sub>H / CF<sub>3</sub>CO<sub>2</sub>H<sup>21</sup>, NaNO<sub>3</sub> / aqueous solution (NO<sup>+</sup>, H<sub>2</sub>ONO<sup>+</sup>, ClNO) or t-butyl hypochlorite (Cl<sup>+</sup>) in anhydrous CCl<sub>4</sub><sup>22</sup>, t-butyl bromide (iodide) / DMSO<sup>23</sup>, DMSO / HCl / H<sub>2</sub>O<sup>24</sup>, TMSI (Br) / DMSO<sup>25</sup>, LiN(i-C<sub>3</sub>H<sub>7</sub>)<sub>2</sub> / THF<sup>26</sup>, HgO / 35% aqueous HBF<sub>4</sub><sup>27</sup>, benzeneseleninic anhydride<sup>28</sup>, periodic acid<sup>29</sup>, isoamyl nitrite<sup>30</sup>, O-mesitylenesulfonyl hydroxylamine<sup>31</sup>, Et<sub>3</sub>O<sup>+</sup>BF<sub>4</sub><sup>-32</sup>, MeI in moist acetone<sup>33</sup> or in 96% methanol<sup>34</sup>, ceric ammonium nitrate (CAN) in aqueous CH<sub>3</sub>CN<sup>35</sup>, HgO-BF<sub>3</sub> / H<sub>2</sub>O-THF<sup>6</sup>, N-chloro-p-toluenesulphonamide (chloroamine-T)<sup>36</sup>, 1-chlorobenzotriazole<sup>37</sup>, N-halosuccinimide<sup>38</sup>, and CuCl<sub>2</sub> / CuO<sup>39</sup> and hypervalent (tert-butylperoxy) iodane<sup>40</sup> / CH<sub>3</sub>CN-H<sub>2</sub>O has been documented in the last two decades.

In spite of extensive studies on the chemistry of MnO<sub>2</sub> and KMnO<sub>4</sub><sup>41</sup> and the less studied BaMnO<sub>4</sub><sup>42</sup>, a strong competitor of MnO<sub>2</sub>, 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 derived from aldehydes and non-enolizable ketones using dry  $\text{MnO}_2$ ,  $\text{BaMnO}_4$  and  $\text{KMnO}_4$  as nucleophiles in the presence of anhydrous  $\text{AlCl}_3$  and  $\text{FeCl}_3$  in dry  $\text{CH}_3\text{CN}$ . A mechanism has also been proposed for the reactions.

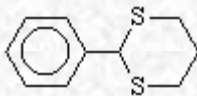
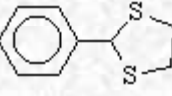
## RESULTS AND DISCUSSION

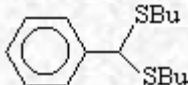
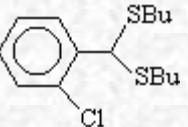
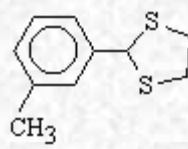
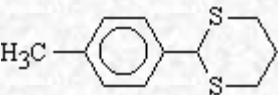
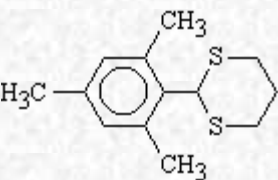
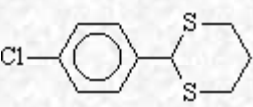
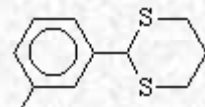
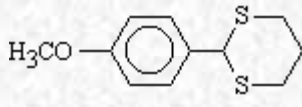
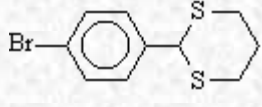
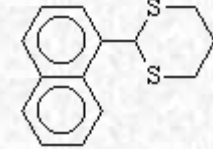
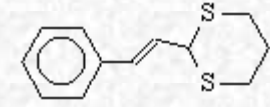
Recently we have found that a mixture of  $\text{MnO}_2$  and  $\text{AlCl}_3$  is an effective reagent for selective oxidative deprotection of benzylic trimethylsilyl- and *tert*-butyldimethylsilyl ethers<sup>43</sup>. Also we have shown that various types of trimethylsilyl ethers and *tert*-butyldimethylsilyl ethers deprotected and oxidized by potassium permanganate ( $\text{KMnO}_4$ ) and barium manganate ( $\text{BaMnO}_4$ ) in the presence of Lewis acids in dry non-aqueous media<sup>44</sup>. 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  $\text{MnO}_2$  in the presence of different hydrated and anhydrous metal salts such as  $\text{ZnCl}_2$ ,  $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ ,  $\text{CdCl}_2 \cdot 2\text{H}_2\text{O}$ ,  $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ ,  $\text{FeCl}_3$ ,  $\text{AlCl}_3$ ,  $\text{PbCl}_2$ ,  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  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  $\text{AlCl}_3$  and  $\text{FeCl}_3$  were effective catalysts for the promotion of this reaction in dry  $\text{CH}_3\text{CN}$ . Addition of  $\text{AlCl}_3$  or  $\text{FeCl}_3$  in dry  $\text{CH}_3\text{CN}$  in the absence of  $\text{MnO}_2$  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  $\text{AlCl}_3$  and  $\text{FeCl}_3$ . We have also found that the order of the addition of  $\text{MnO}_2$  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  $\text{MnO}_2$  (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.**

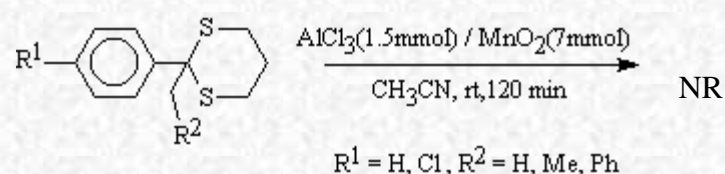
**Table 1:** Deprotection of thioacetals by  $\text{MnO}_2$ ,  $\text{KMnO}_4$  and  $\text{BaMnO}_4$  catalyzed with  $\text{AlCl}_3$  in  $\text{CH}_3\text{CN}$  at room temperature

Entry	Substrate	Time(min)	ratio of oxidants <sup>a</sup>		
			$\text{MnO}_2$ , $\text{KMnO}_4$ , $\text{BaMnO}_4$	$\text{MnO}_2$ , $\text{KMnO}_4$ , $\text{BaMnO}_4$	$\text{MnO}_2$ , $\text{KMnO}_4$ , $\text{BaMnO}_4$
1		90, 45, 60	6, 3, 4	95, 94, 93	
2		90, 50, 60	6, 3, 4	96, 95, 95	

3		100, 60, 70	7, 3, 4	89, 91, 90
4		150, 100, 120	7, 4, 5	88, 90, 91
5		60, 30, 45	6, 3, 4	93, 95, 92
6		60, 30, 40	6, 3, 4	92, 96, 95
7		60, 45, 45	6, 3, 4	90, 92, 91
8		120, 95, 100	7, 4, 5	92, 90, 91
9		60, 45, 55	6, 3, 4	91, 91, 90
10		50, 40, 50	6, 3, 4	90, 92, 90
11		100, 80, 95	7, 4, 5	91, 90, 92
12		70, 35, 50	6, 3, 4	92, 94, 95
13		70, 45, 65	6, 3, 4	85, 84, 83

14		75 , 45 , 60	6 , 3 , 4	82 , 84 , 85
15		75 , 50 , 60	6 , 3 , 4	91 , 92 , 90

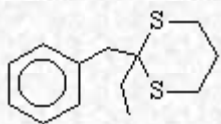
By this method only benzylic dithioacetals of aldehydes and non-enolizable ketones were converted to their carbonyl compounds. Dithioacetals derived from enolizable ketones were isolated intact from the reaction mixtures (Scheme2, Table 2).



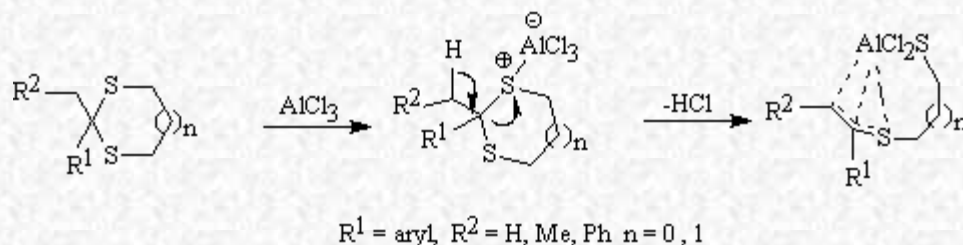
**Scheme 2.**

**Table 2:** The results of deprotection of thioacetals of enolizable ketones by  $\text{MnO}_2$ ,  $\text{KMnO}_4$  and  $\text{BaMnO}_4$  in  $\text{CH}_3\text{CN}$  at room temperature in the presence of  $\text{AlCl}_3$

Entry	Substrate	Time(min)	ratio of oxidants <sup>a</sup>			Yield%
			$\text{MnO}_2$ , $\text{KMnO}_4$ , $\text{BaMnO}_4$	$\text{MnO}_2$ , $\text{KMnO}_4$ , $\text{BaMnO}_4$	$\text{MnO}_2$ , $\text{KMnO}_4$ , $\text{BaMnO}_4$	
1		120, 120 , 120	7 , 4 , 5	NR , NR, NR		
2		120, 120 , 120	7 , 4 , 5	NR , NR, NR		
3		120, 120 , 120	7 , 4 , 5	NR , NR, NR		
4		120 , 120 , 120	7 , 4 , 5	NR , NR, NR		

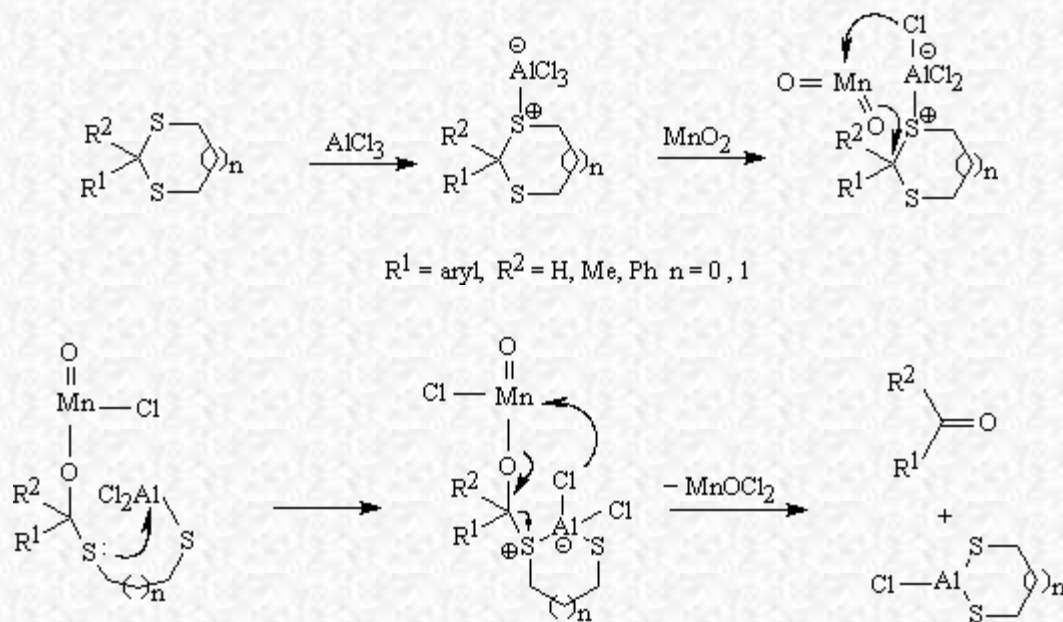


In order to explain this observation, we have proposed the possibility of formation of a complex between dithioacetals and the Lewis acids in the reaction mixture. These complex does not carry a carbonyl group anymore and therefore, the reaction dose not proceed further (Scheme 3).



**Scheme 3.**

In order to avoid a question about the presence of a trace of water in  $\text{MnO}_2$  powder, that may act as a nucleophile for the cleavage of C-S bonds, anhydrous  $\text{MnO}_2$  was prepared<sup>45</sup> by the decomposition of manganese (II) carbonate ( $\text{MnCO}_3$ ) at 220-280° C and  $\text{AlCl}_3$  sublimed freshly for this purpose. Non-aqueous reaction conditions suggest a non-solvolytic reaction occur in which oxygen of  $\text{MnO}_2$  acts as a nucleophilic species in this reaction. A mechanism is suggested in which the role of  $\text{MnO}_2$ , 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<sup>28</sup>.

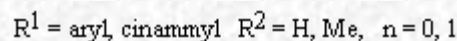
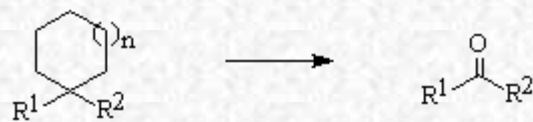


**Scheme 4.**

### Mechanism

These observations prompted us also to study dethioacetalization of S, S- acetals, 1,3- dithiolanes, and 1,3-dithianes by  $\text{KMnO}_4$ , and  $\text{BaMnO}_4$  in the presence of unhydrous  $\text{AlCl}_3$  and  $\text{FeCl}_3$  in dry  $\text{CH}_3\text{CN}$ . Both reagents were quite inactive in the absence of the Lewis acids for this purpose. The color of  $\text{KMnO}_4$  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;  $\text{KMnO}_4 > \text{BaMnO}_4 > \text{MnO}_2$  (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).



**Scheme 5.**

**Table 3:** Comparison of the reported methods with  $\text{AlCl}_3 / \text{MnO}_2$  method

R1	R2	n	Methods					
			Yields% (min)					
			I <sup>a</sup>	II <sup>18</sup>	III <sup>13</sup>	IV <sup>14</sup>	V <sup>9</sup>	VI <sup>24</sup>
Ph	H	1	96(90)	—	—	96(50)	95(60)	—
Ph	H	2	95(90)	—	70(60)	—	95(60)	97(5)
Ph	Me	2	—	—	75(30)	98(25)	95(30)	—
Ph	Ph	2	91(75)	—	82(120)	—	—	—
4-Me-C <sub>6</sub> H <sub>4</sub>	H	2	92(60)	90(10)	88(180)	—	—	—
4-Cl-C <sub>6</sub> H <sub>4</sub>	H	2	92(120)	—	87(120)	—	—	—
Cinammyl	H	2	85(70)	86(10)	—	—	—	—
4-MeO-C <sub>6</sub> H <sub>4</sub>	H	2	90(50)	76(10)	97(180)	—	—	—

a )  $\text{AlCl}_3 / \text{MnO}_2$  in  $\text{CH}_3\text{CN}$ .

## Conclusion

In this study, we have introduced new applications of  $\text{KMnO}_4$ ,  $\text{BaMnO}_4$  and  $\text{MnO}_2$  as effective reagents for non-hydrolytic deprotection of non-enolizable benzylic thioacetals in the presence of  $\text{AlCl}_3$ . Reactions were proceeded with lower equivalent amounts of  $\text{KMnO}_4$ ,  $\text{BaMnO}_4$  at room temperature in  $\text{CH}_3\text{CN}$  in comparison with  $\text{MnO}_2$  (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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