# A novel method for the deprotection of *S*,*S*-acetals using air and a catalytic amount of bismuth(III) nitrate[†]

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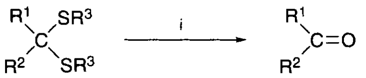
***S*,*S*-Acetals are smoothly deprotected with air in the presence of a catalytic amount of bismuth(III) nitrate pentahydrate under ambient conditions to regenerate the original carbonyl compounds in good to excellent yields.**

The *S*,*S*-acetal function finds wide use in organic synthesis as a carbonyl protecting group due to its easy access[1] as well as high stability under both acidic and basic conditions. In addition, this function is often employed as the acyl anion equivalent.[2] However, the use of *S*,*S*-acetals is occasionally hampered by the lack of efficient procedures for regenerating the original carbonyl functionalities. In spite of a plethora of the existing methodologies for the deprotection of *S*,*S*-acetals,[3] there still exists an incessant demand for better ones, which feature simpler manipulation, milder conditions and use of cheaper and less toxic reagents, preferably in catalytic amounts.[§] We now report a novel deprotection of *S*,*S*-acetals, which considerably meets these requirements.

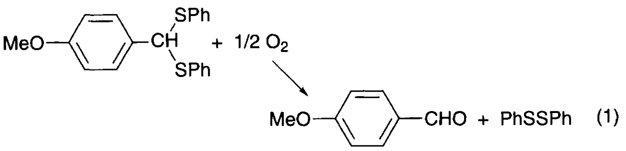
Most of the known deprotection methods of *S*,*S*-acetals require the use of a stoichiometric or an excess amount of demasking reagent, which includes heavy metal salts such as mercury(II), silver(I) and copper(II) salts as well as oxidizing agents such as molecular halogens, *N*-halosuccinimides and MCPBA. However, the present method is based on the combined use of molecular oxygen and a catalytic amount of bismuth(III) nitrate. To the best of our knowledge, the literature to date contains no precedent for such an economical and environmentally conscious deprotection of *S*,*S*- acetals. In contrast to the mercuric reagents most commonly employed in the laboratory, bismuth(III) salts are of quite low toxicity; a variety of bismuth(III) carboxylate-based preparations have been administered orally for treatment of intestinal disorders.

The general experimental procedure for the deprotection is as follows: To a solution of *S*,*S*-acetal (0.5 mmol) in dry benzene or dichloromethane (10 cm$^3$) was added finely powdered bismuth(III) nitrate pentahydrate $Bi(NO_3)_3 \cdot 5H_2O$ (2–20 mol%) followed by water (1 mmol). When needed, bismuth(III) chloride (5 mol%) was also added. The mixture was magnetically stirred in a stoppered flask for an appropriate time at ambient temperature, while the progress of the reaction was intermittently monitored by GLC. The stopper was loosened at intervals in order to admit fresh air into the reaction vessel. After the reaction, the mixture was worked up as usual, and the yield of carbonyl compound was determined by isolation or GLC. The results are summarized in Table 1.

Both cyclic and acyclic *S*,*S*-acetals derived from aldehydes and ketones were smoothly deprotected in air to regenerate the parent carbonyl compounds in good to excellent yields. Under an argon atmosphere, however, the reaction scarcely proceeded (run 3). These findings suggest that oxidation by molecular oxygen is involved as a key step in the deprotection. This idea is supported by the formation of the disulfide as another major product (run 10). In order to know the stoichiometry of the reaction, 4-methoxybenzaldehyde *S*,*S*-diphenyl acetal was deprotected under an oxygen atmosphere and the consumption of oxygen was measured volumerically. About 0.5 equiv. of molecular oxygen was consumed to produce a quantitative amount of diphenyl disulfide and 4-methoxybenzaldehyde [eqn. (1)].



**Scheme 1** *Reagents and conditions*: i, *S*,*S*-acetal (0.5 mmol), $Bi(NO_3)_3 \cdot 5H_2O$ (2–20 mol%), $H_2O$ (2.0 equiv.), PhH (10 cm$^3$), room temp., air



When the reaction was sluggish, it was considerably facilitated by the additional presence of a second bismuth(III) salt, *i.e.* bismuth(III) chloride, as an auxiliary additive (runs 2, 9 and 16). Bismuth(III) sulfate also proved to be effective. Without bismuth(III) nitrate, however, *S*,*S*-acetals remained intact even in the presence of the second bismuth salt.

Benzene was the best choice of solvent, followed by toluene and acetonitrile. Dichloromethane was also acceptable, although the use of a larger amount of bismuth(III) nitrate (10 mol%) together with bismuth(III) chloride (5 mol%) as an additive was necessary (run 2). In THF and methanol, however, the reaction hardly proceeded.

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**Table 1** Deprotection of *S*,*S*-acetals using a catalytic amount of $Bi(NO_3)_3 \cdot 5H_2O$

| Run | R$^1$ | R$^2$ | R$^3$ | $Bi(NO_3)_3 \cdot 5H_2O$/ mol% | $BiCl_3$/ mol% | React. time/h | Yield[a] (%) |
|---|---|---|---|---|---|---|---|
| 1 | *p*-$MeOC_6H_4$ | H | $(CH_2)_2$ | 2 | — | 5 | 88[b] |
| 2 | *p*-$MeOC_6H_4$ | H | $(CH_2)_2$ | 10 | 5 | 2 | 89[b,c] |
| 3 | Ph | H | $(CH_2)_2$ | 2 | — | 6 | 72 |
| 4 | Ph | H | $(CH_2)_2$ | 2 | — | 6 | 8[d] |
| 5 | *p*-$ClC_6H_4$ | H | $(CH_2)_2$ | 5 | — | 9 | 81[b] |
| 6 | *p*-$MeOC_6H_4$ | H | $(CH_2)_3$ | 2 | — | 4.5 | 91[b] |
| 7 | Ph | H | $(CH_2)_3$ | 2 | — | 4 | 91 |
| 8 | $Me(CH_2)_6$ | H | $(CH_2)_3$ | 20 | — | 6 | 75 |
| 9 | $Me(CH_2)_6$ | H | $(CH_2)_3$ | 20 | 5 | 2 | 79 |
| 10 | *p*-$MeOC_6H_4$ | H | Ph | 10 | — | 12 | 98[b,e] |
| 11 | *p*-$MeOC_6H_4$ | H | Et | 10 | — | 10 | 91[b] |
| 12 | $Me(CH_2)_6$ | H | Et | 20 | — | 6 | 96 |
| 13 | $Me(CH_2)_5$ | Me | $(CH_2)_3$ | 10 | — | 3 | 92 |
| 14 | $Me(CH_2)_4$ | Et | $(CH_2)_3$ | 10 | — | 5 | 98 |
| 15 | Ph | Me | $(CH_2)_3$ | 10 | — | 10 | 76 |
| 16 | Ph | Me | $(CH_2)_3$ | 10 | 5 | 2 | 76 |

[a] GC yield unless otherwise noted. [b] Isolated yield. [c] In $CH_2Cl_2$. [d] Under argon. The substrate was recovered mostly intact. [e] Diphenyl disulfide was obtained in 83% yield.

## Footnotes

† Part of this work was presented at the 1995 International Chemical Congress of Pacific Basin Societies (PACIFICHEM '95) in Honolulu, Hawaii, December 1995.

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§ Excepting the photo- and electro-chemical methods which employ physical means and special equipments, only two examples of catalytic deprotection of *S*,*S*-acetals have been known to date.[4,5]

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