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An efficient deprotection of dithioacetals to carbonyls using Oxone–KBr in aqueous acetonitrile

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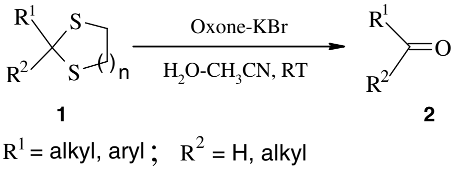
Abstract—A simple and efficient method has been developed for the chemoselective dethioacetalization of dithioacetals to aldehydes and ketones using Oxone–KBr in aqueous acetonitrile at room temperature.

Protection and deprotection of functional groups is a common tactic in multistep organic syntheses. As a carbonyl protecting group, the *S*,*S*-acetal function has found wide use in organic synthesis due to its easy access[1] and high stability towards both acidic and basic conditions. In addition, *S*,*S*-acetals are often used as acyl anion equivalents in C–C bond forming reactions.[2] A large number of efficient methods are available for deprotection of dithioacetals to carbonyls.[3,4] Some recently introduced methods include the use of reagents such as $ZrCr_2O_7$,[5] Dess–Martin periodinane,[6] $Bi(OTf)_3$,[7] TABCO–DMSO,[8] $NaNO_2$–CH_3COCl,[9] $FeCl_3$–KI,[10] benzyltriphenylphosphonium peroxymonosulfate,[11] TBHP[12] and silica chloride–DMSO.[13] However, many of these methods suffer from serious drawbacks such as the use of expensive catalysts,[6,7,11] toxic reagents[5,8,9,13] and in a few cases, more than stoichiometric amounts required of the reagents.[11,12] Hence, improved methods for dethioacetalization using cheap and less toxic reagents coupled with simple reaction conditions and easier work-up procedures are required.

In this letter, we report a very simple and efficient approach for the chemoselective dethioacetalization of dithioacetals using Oxone–KBr in aqueous acetonitrile (Scheme 1).



Scheme 1.

Oxone is a stable 2:1:1 ternary composite of K_2SO_4, $KHSO_4$ and $KHSO_5$ and its use in various oxidative[14] and deprotective transformations[15] is well documented. In fact, Oxone supported on alumina[15a] and an organic solvent soluble derivative of Oxone, benzyltriphenylphosphonium peroxymonosulfate,[11] (BTPP) in the presence of $AlCl_3$ have already been reported for demasking dithioacetals. As with TBHP,[12] the use of Oxone or BTPP for demasking of dithioacetals proceeds via conversion to the corresponding disulfoxide followed by attack of water to generate the carbonyl group. This necessitates either the use of a large excess (5 equiv) of Oxone[15a] or the initial preparation of expensive, benzyltriphenyl phosphonium peroxymonosulfate. To avoid these drawbacks and due to our continued interest in the chemistry of Oxone,[16a–c] we envisioned a simple approach for dethioacetalization using Oxone in combination with an alkali metal bromide. We earlier reported the combination of Oxone–KBr in aqueous acetonitrile medium for the bromination of activated arenes[16b] as well as in the synthesis of azo-bis-nitriles.[16c] From these experiences, we surmised that the Br^+ ion generated by the combination of Oxone–KBr would be attacked by the dithiane, making it a good leaving group with a subsequent attack by a water molecule leading to the carbonyl (Scheme 2). However, this concept was

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Keywords: Oxone; Dethioacetalization; Deprotection.

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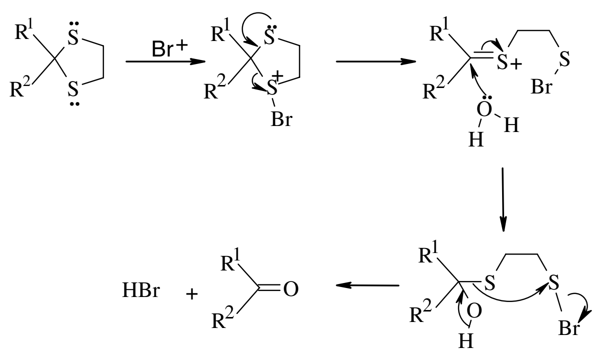
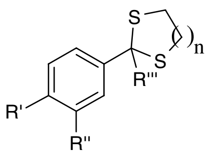
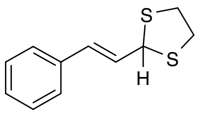
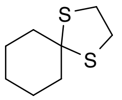
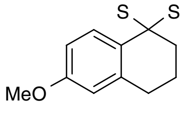
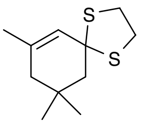


Scheme 2.

associated with the serious drawback of probable ring bromination[16b,17] in the case of activated arenes as well as the formation of α-bromoketones.[18] To overcome this problem, we planned to avoid the presence of excess Br$^+$ in the system by slow addition of a solution of Oxone in water to the reaction mixture containing KBr. Thus the Br$^+$ ion formed would participate chemoselectively in the dethioacetalization reaction.

To check the feasibility of this procedure, the dithioacetal of anisaldehyde was selected as a model compound. Thus, to an equimolar (10 mmol, each) mixture of the dithioacetal of anisaldehyde and KBr in aqueous acetonitrile (3:1, v/v, 7 mL), was added dropwise with stirring, a solution of Oxone (10 mmol) in water (18 mL) and the stirring was continued until completion of the reaction (TLC). Work-up of the reaction mixture furnished anisaldehyde as the sole product[19] (89%), there was no formation of either the ring bromination product or the over-oxidation product. To determine the functional group compatibility and to investigate the chemoselectivity in this deprotection, a series of dithioacetals derived from substituted aromatic, conjugated as well as aliphatic aldehydes were successfully dethioacetalized employing the present reaction conditions. The interesting points to note are the non formation

Table 1. Deprotection of dithioacetals using Oxone–KBr in aqueous acetonitrile

Entry	Substrate	*n*	Time (min)	Yield[a,b] (%)
1				
	(a) $R' = R'' = R''' = H$	2	20	91
	(b) $R' = Me$, $R'' = R''' = H$	2	20	89
	(c) $R' = OMe$, $R'' = R''' = H$	1	25	89
	(d) $R' = CH(Me)_2$, $R'' = R''' = H$	1	20	92
	(e) $R' = NO_2$, $R'' = R''' = H$	1	25	79
	(f) $R' = N(Me)_2$, $R'' = R''' = H$	1	20	82
	(g) $R' = OH$, $R'' = R''' = H$	1	15	80
	(h) $R' = OH$, $R'' = OMe$, $R''' = H$	1	20	78
	(i) $R' = R'' = H$, $R''' = Me$	1	15	93
	(j) $R' = R''' = Me$, $R'' = H$	1	20	87
	(k) $R' = OMe$, $R'' = H$, $R''' = Me$	1	15	84
2		—	15	78
3		—	120	81
4		—	120	65
5		—	60	72

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[a] All products are known compounds and were characterized by ^{1}H NMR spectroscopy.

[b] Yields refer to pure isolated products.

of, (i) ring brominated products in the case of aldehydes containing ring activating groups (Table 1, entries: 1b–d,f–h); (ii) dibrominated product in the case of a conjugated aldehyde (entry 2), and (iii) over-oxidation products. The results of the present study are summarized in Table 1.

The non formation of ring brominated products and over-oxidation products has also been reported by Khan et al.[20] in their Br^+ mediated protocol to effect chemoselective dethioacetalization. We next turned our attention towards the dethioacetalization of dithioacetals of ketones. The results obtained during studies with three representative compounds, viz. cyclohexanone, (entry 3) *p*-methoxy acetophenone (entry 1k) and 6-methoxytetralone (entry 4) showed neither the formation of, (i) α-brominated cyclohexanone nor (ii) the ring brominated derivatives with *p*-methoxy acetophenone or 6-methoxytetralone.

We have developed a very simple and efficient protocol for chemoselective dethioacetalization using Oxone–KBr in water acetonitrile at room temperature. The protocol avoids the use of Oxone in large excess and also avoids the initial conversion of Oxone to BTPP to effect dethioacetalization. These studies have revealed that the present protocol can be used for the chemoselective dethioacetalization to carbonyls.

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References and notes

1. Komatsu, N.; Uda, M.; Suzuki, H. *Synlett* **1995**, 984–996, and references cited therein.
2. Page, P. C. B.; Niel, M. B. V.; Prodger, J. C. *Tetrahedron* **1989**, *45*, 7643–7677.
3. Greene, T. W.; Wuts, P. G. *Protecting Groups in Organic Synthesis*, 2nd ed.; John Wiley and Sons: New York, 2000.
4. Banerjee, A. K.; Laya, M. S. *Russ. Chem. Rev.* **2000**, *69*, 947–955.
5. Firouzabadi, H.; Iranpoor, N.; Hassani, H.; Sabhani, S. *Synth. Commun.* **2004**, *34*, 1967–1972.
6. Langille, N. F.; Dakin, L. A.; Panek, J. S. *Org. Lett.* **2003**, *5*, 575–578.
7. Kamal, A.; Reddy, P. S. M. M.; Rajeshwar Reddy, D. *Tetrahedron Lett.* **2003**, *44*, 2857–2860.
8. Firouzabadi, H.; Iranpoor, N.; Shaterian, H. R. *Tetrahedron Lett.* **2003**, *44*, 4769–4773.
9. Khan, Abu. T.; Mandal, E.; Sahu, P. R. *Synlett* **2003**, 377–381.
10. Chavan, S. P.; Soni, P. B.; Kale, R. R.; Pasupathy, K. *Synth. Commun.* **2003**, *33*, 879–883.
11. Hajipour, A. R.; Mallakpour, S. E.; Bartork, I. M.; Adibi, H. *Molecules* **2002**, *7*, 674–680.
12. Wakharkar, R. D.; Mahajan, V. A.; Shinde, P. D.; Barhate, N. B. *Tetrahedron Lett.* **2002**, *43*, 6031–6033.
13. Firouzabadi, H.; Iranpoor, N.; Hazarkhani, H.; Karimi, B. *J. Org. Chem.* **2002**, *67*, 2572–2576.
14. (a) Webb, K. S.; Ruszkay, S. J. *Tetrahedron* **1998**, *54*, 401–410; (b) Varma, R. S.; Dahiya, R. K. *Molecules* **1998**, 282–285; (c) Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Synlett* **1999**, *6*, 777–779.
15. (a) Ceccherelli, P.; Curini, M.; Marcrotullio, M. C.; Epifano, F.; Rosati, O. *Synlett* **1996**, 767–768; (b) Marcotullio, M. C. *Recent Trends in Organic Synthesis* **2003**, *10*, 21–45.
16. (a) Kulkarni, P. P.; Kadam, A. J.; Desai, U. V.; Mane, R. B.; Wadgaonkar, P. P. *J. Chem. Res. (S)* **2000**, 184–185; (b) Tamhankar, B. V.; Desai, U. V.; Mane, R. B.; Wadgaonkar, P. P.; Bedekar, A. V. *Synth. Commun.* **2001**, *31*, 2021–2027; (c) Tamhankar, B. V.; Desai, U. V.; Mane, R. B.; Kulkarni, P. P.; Wadgaonkar, P. P. *Synth. Commun.* **2002**, *32*, 3643–3646.
17. Narender, N.; Srinivasu, M.; Prasad, R.; Kulkarni, S. J.; Raghavan, K. V. *Synth. Commun.* **2002**, *32*, 2313–2318.
18. Kim, E.-H.; Koo, B.-S.; Song, C.-E.; Lee, K.-J. *Synth. Commun.* **2001**, *31*, 3627–3632.
19. *Typical procedure*: To a well stirred solution of the dithioacetal (10 mmol) and KBr (10 mmol) in aqueous acetonitrile (3:1, v/v, 7 mL) was added dropwise a solution of Oxone (10 mmol) in water (18 mL). Stirring was continued at room temperature until completion of the reaction (TLC). The reaction mixture was extracted with ether (30 mL) and the ether extract washed with water, dried (Na_2SO_4) and evaporated. The residue obtained was chromatographed over silica gel. Elution with petroleum ether–ethyl acetate (9:1, v/v) furnished pure aldehyde/ketone which was characterized by ^1H NMR spectroscopy.
20. (a) Khan, A. T.; Mondal, E.; Sahu, P. R.; Bose, G. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1026–1028; (b) Khan, A. T.; Mondal, E.; Sahu, P. R.; Bose, G. *Chem. Lett.* **2001**, 1158–1159.