COMMUNICATION

An exceptionally simple and catalytic method for regeneration of carbonyl functionality from the corresponding 1,3-oxathiolanes

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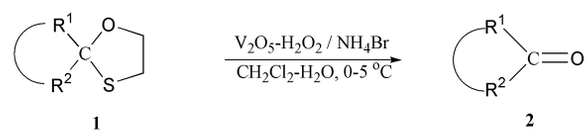
A wide variety of 1,3-oxathiolanes 1 can be chemoselectively deprotected to the corresponding carbonyl compounds 2 in good yields by employing V_2O_5–H_2O_2 catalyzed oxidation of ammonium bromide in a CH_2Cl_2–H_2O mixture at 0–5 °C. Some of the major advantages of this procedure are its mild conditions, and that it is highly selective and efficient, high yielding, and cost-effective. Furthermore, no brominations occur at the double bond or allylic position or α to the keto position or aromatic ring.

Introduction

The protection and deprotection strategy is a common tactic in multistep organic synthesis. Among the various functional groups, the protection of carbonyl groups as 1,3-oxathiolanes has attracted much considerable interest owing to their many important applications. They are usually used as acyl carbanion equivalents[1] for carbon–carbon bond forming reactions. The most remarkable application is the use of chiral 1,3-oxathiolanes for the synthesis of optically active tertiary alcohols bearing a carbonyl functionality at the α-position, first demonstrated[2] by Eliel and Lynch. Later on, these protected compounds were further utilized by Utimoto's group in organic synthesis.[3] In addition, the use of oxathioacetals is much more convenient than the corresponding *O*,*O*-acetals or *S*,*S*-acetals because they are comparatively more stable than *O*,*O*-acetals under acidic conditions and easier to remove than the corresponding *S*,*S*-acetals. Although a large number of methods have been developed for the deprotection of 1,3-dithiolanes[4] to the corresponding carbonyl compounds, only a few methods are known in the literature for the deprotection of 1,3-oxathiolanes.[5] The usual procedures for the deprotection of 1,3-oxathiolanes are as follows: i) by using isoamyl nitrite,[6a] and chloramine-T,[6b] ii) by employing TMSOTf alone,[7a] iii) by using TMSOTf in the presence of *p*-nitrobenzaldehyde,[7b,c] or polymer supported *p*-nitrobenzaldehyde,[7d] iv) by utilizing halonium ion sources in the presence of expensive silver salts[8a,b] or by using NBS in acetone.[8c] Unfortunately, some of these methods have serious drawbacks such as the removal of the by-product 1,3-oxathiolanes derived from *p*-nitrobenzaldehyde,[7b,c] or the use of an expensive polymer-supported reagent,[7d] and sometimes the failure to deprotect non-benzylic oxathioacetals[7a] and also their much longer reaction times.[7d] Other drawbacks related to halonium ion sources include the need for a large molar excess of reagents such as expensive silver salts[8a,b] and again much longer reaction times.[8c] Recently, a further method was reported[9] by Kirihara *et al.* using a catalytic amount of trichlorooxyvanadium, which requires drastic reaction conditions. Consequently, it seems to us that there is still a great need for better alternatives that might proceed under reaction conditions that are mild, clean, environmentally benign, efficient, site-selective, operationally simple, and economically much cheaper.

The discovery of vanadium bromoperoxidase (VBrPO),[10] a vanadium enzyme that catalyzes the oxidation of bromide by hydrogen peroxide,[11] as well as our ongoing research to develop a new methodology,[12] prompted us to use a V_2O_5–H_2O_2 catalyzed oxidation of ammonium bromide for the cleavage of various 1,3-oxathiolanes to the parent carbonyl compounds. In this communication, we would like to report a catalytic and environmentally favorable protocol for the deprotection of various oxathioacetals by employing V_2O_5, H_2O_2 and NH_4Br (Scheme 1). The catalyst V_2O_5 is used for oxidation of ammonium bromide by H_2O_2 and all these chemicals are environmentally acceptable.



1 **2**

R^1 = alkyl / aryl, R^2 = H / alkyl / aryl

Scheme 1

Results and discussion

A wide variety of structurally different 1,3-oxathiolanes **1a**–**1p** were prepared by treatment with the appropriate carbonyl compound and 2-mercaptoethanol in the presence of a catalytic amount of *n*-tetrabutylammonium tribromide (TBATB).[13] Next, we attempted to optimize the reaction conditions for cleavage of 1,3-oxathiolanes to obtain the desired parent carbonyl compounds. We found that a mixture of substrate–ammonium bromide–vanadium pentaoxide–hydrogen peroxide (1 : 1 : 0.1 : 10) in dichloromethane–water solvent (5 : 1, 6 ml $mmol^{-1}$ substrate) gave the best results. We also observed that the same reaction was completed within a much shorter period if the amount of V_2O_5 was increased from 0.1 to 0.25 equivalents and the amount of ammonium bromide from 1 to 3 equivalents. By following the above typical reaction procedure, the substrate 2-(*p*-methoxyphenyl)-1,3-oxathiolane (**1a**) reacted smoothly to provide the desired compound *p*-methoxybenzaldehyde (**2a**) in 85% yield. The compound **2a** was characterized by comparison of its IR and ^{1}H-NMR spectra with those of an authentic sample. Similarly, compounds **1b**–**1e** were smoothly converted to the desired carbonyl compounds **2b**–**2e** in good yields under identical reaction conditions. Likewise, 2-(*p*-nitrophenyl)-1,3-oxathiolane (**1f**) was also converted directly into the *p*-nitrobenzaldehyde (**2f**) within 2.5 h in 90% yield. It is important to highlight that the same compound **2f** was obtained from compound **1f** on treatment with NBS[8c] but only after 6 h, which shows that our protocol is much more effective in comparison to this earlier reported method. Subsequently, various protected compounds **1g**–**1p** were transformed into their corresponding carbonyl compounds **2g**–**2p** without any difficulty under identical reaction conditions. The results summarized in Table 1 clearly demonstrate that the method is equally efficient for a wide variety of oxathioacetals. It is noteworthy that no brominations (for entries **1i**–**1k**) take place at either the double bond or the allylic positions, a result that would be very difficult to achieve by using NBS. It is also important to mention that other protecting groups such as Bn, Ac, TBDMS (for entries **1b**, **1c** and **1h**) were unaffected under the experimental

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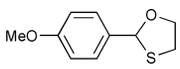
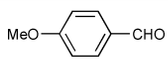
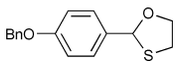
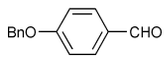
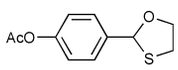
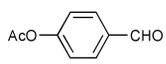
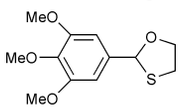
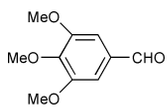
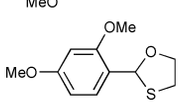
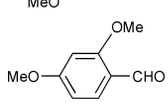
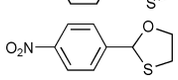
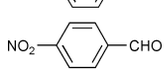
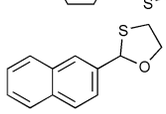
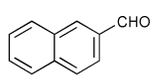
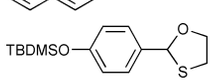
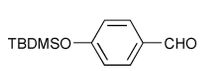
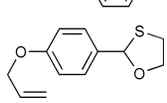
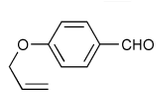
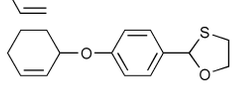
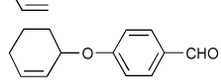
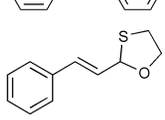
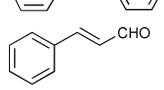
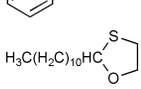
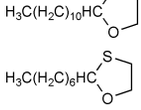
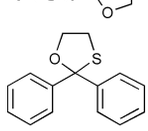
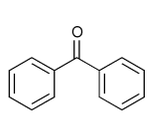
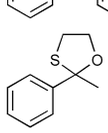
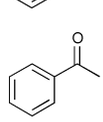
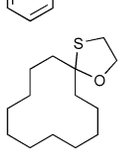
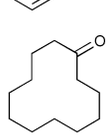
Table 1 Cleavage of various oxathioacetals **1** to the parent carbonyl compounds **2** by ammonium bromide in the presence of V_2O_5 and H_2O_2

Entry	Substrate (**1**)	Reaction time/h	Product (**2**)[a]	Yield[b] (%)
a		0.75		85
b		1.25		88
c		1.0		84
d		1.25		82
e		1.25		85
f		2.5		90
g		0.75		90
h		0.75		85
i		1.0		73
j		1.0		68
k		1.0		70
l		1.5	$CH_3(CH_2)_{10}CHO$	76
m		1.25	$CH_3(CH_2)_6CHO$	86
n		1.25		96
o		1.5		90
p		1.0		92

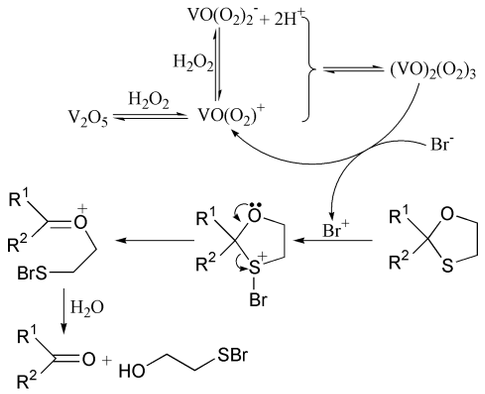
[a] Products were characterized by IR, ^{1}H-NMR and ^{13}C-NMR, by comparison with the spectra of authentic samples, as well as by elemental analyses. [b] Isolated yield.

conditions. All the deprotected compounds were fully characterized[14] by IR, ^{1}H-NMR and ^{13}C-NMR, by comparison with the spectra of authentic samples, as well as by elemental analyses.

The deprotection of various 1,3-oxathiolanes into the corresponding carbonyl compounds can be explained as follows. Vanadium pentaoxide reacts with hydrogen peroxide to generate reactive peroxovanadate(v) intermediates,[15] which oxidize Br^- to Br^+. The reactive bromonium ion can undergo further oxidation to Br_2 or Br_3^-, which might exist in solution. Then the reactive species Br^+ reacts with sulfur to form a bromosulfonium complex, which is finally hydrolyzed by water to yield the parent carbonyl compounds, as depicted in Scheme 2.

Conclusions

In summary, we have demonstrated a useful and catalytic method for the chemoselective deprotection of various 1,3-oxathiolanes to the corresponding carbonyl compounds in presence of other protecting groups using V_2O_5–H_2O_2 oxidation of ammonium bromide under very mild reaction conditions. In addition, all of these reagents are environmentally acceptable and easy to handle; maintaining the stoichiometric ratio while carrying out the reaction is also possible. It is noteworthy that no brominations take place at the double bond, allylic positions, aromatic ring or α to the keto position. Due to its operational simplicity, generality and efficacy, this method is expected to have a wide applicability for the cleavage of various



Scheme 2

oxathioacetals. Other alkali bromides can also be used for similar reactions, and such experiments are currently under investigation and will be reported in due course.

Experimental

To a suspension of V_2O_5 (0.018 g, 0.1 mmol) in water (1.0 ml) was added 30% H_2O_2 solution (1.2 ml, 10 mmol) at ice-bath temperature with continued stirring. After 25 min, the colour of the solution changed into a clear brown–red, and then ammonium bromide (0.098 g, 1 mmol) was added. The substrate 2-(*p*-nitrophenyl)-1,3-oxathiolane (**1f**) (0.211 g, 1 mmol) was added after 10 min in solution in CH_2Cl_2 (5 ml) with further stirring. The reaction was complete within 1 h and 55 min of stirring as monitored by TLC. The reaction mixture was then extracted with CH_2Cl_2 (2 × 15 ml), washed with water (1 × 15 ml) and finally washed with brine solution (1 × 10 ml). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Evaporation of the solvent gave the crude residue, which was finally purified by column chromatography on silica gel (eluent: hexane–EtOAc, 9 : 1). The product **2f** was obtained as a light yellow solid 0.136 g (90%), mp 105–106 °C (lit.[16] mp 104–106 °C).

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