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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 -H₂O₂ catalyzed oxidation of ammonium bromide in a CH₂Cl₂-H₂O 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 a to the keto position or aromatic ring.

Introduction

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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 equivalents¹ 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 demonstrated² 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-dithiolanes⁴ to the corresponding carbonyl compounds, only a few methods are known in the literature for the deprotection of 1,3oxathiolanes.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 1,3oxathiolanes 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 reported⁹ 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 -H₂O₂ 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.

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 substrateammonium 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 V₂O₅ 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 ¹H-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. 2-(p-nitrophenyl)-1,3-oxathiolane (1f) was also Likewise 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

Table 1	Cleavage of various	oxathioacetals 1	to the parent	carbonyl compou	nds 2 by ammoni	ium bromide in the pres	sence of V2O5 and H2O2
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Entry	Substrate (1)	Reaction time/h	Product (2) ^{<i>a</i>}	Yield ^b (%)
 a	MeO	0.75	MeO-CHO	85
b	BnO - C	1.25	BnO-CHO	88
c		1.0	АсО-СНО	84
d		1.25	MeO MeO	82
e	MeO OMe	1.25	MeOOMe	85
	MeO		МеО	
f		2.5		90
g	S S S S	0.75	СНО	90
h		0.75	твомосторосно	85
i		1.0	О-СНО	73
j		1.0	Сно	68
k	S O	1.0	СНО	70
1	H ₃ C(H ₂ C) ₁₀ HC	1.5	CH ₃ (CH ₂) ₁₀ CHO	76
m	H ₃ C(H ₂ C) ₆ HC	1.25	CH ₃ (CH ₂) ₆ CHO	86
n	s s	1.25		96
0	s s	1.5		90
р	s o	1.0		92
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^a Products were characterized by IR, ¹H-NMR and ¹³C-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 characterized¹⁴ by IR, ¹H-NMR and ¹³C-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 1,3oxathiolanes to the corresponding carbonyl compounds in presence of other protecting groups using V_2O_5 -H₂O₂ 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

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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% H₂O₂ 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 CH₂Cl₂ (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 $(1 \times 15 \text{ ml})$ and finally washed with brine solution $(1 \times 10 \text{ ml})$. The organic layer was dried over anhydrous Na2SO4 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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- 14 Spectroscopic data for compound 1j: ¹H-NMR (300 MHz, CDCl₃) δ 1.85–2.09 (m, 6H, cyclohexyl CH₂-), 3.16–3.32 (m, 2H, -SCH₂-), 3.87–3.95 (m, 1H, -OCH₂-), 4.48–4.54 (m, 1H, -OCH₂-), 4.79–4.91 (m, 1H, -OCH-), 5.83–5.99 (m, 3H, olefinic H, -O-CH-S), 6.89 (d, 2H, J = 8.5 Hz, ArH), 7.39 (d, 2H, J = 8.5 Hz). Anal. calcd. for C₁₅H₁₈O₂S: C 68.67, H 6.91. Found C 68.52, H 6.88%. Spectroscopic data for compound 1j: ¹H-NMR (400 MHz, CDCl₃) δ 1.63–2.18 (m, 6H, cyclohexyl CH₂-), 4.91 (s, 1H, -ArOCH-), 5.84–5.87 (m, 1H, olefinic H), 7.01 (d, 2H, J = 8.8 Hz, ArH), 7.82 (d, 2H, J = 9.0 Hz, ArH), 9.87 (s, 1H, -CHO); ¹³C-NMR (100 MHz, CDCl₃) δ 18.76, 24.95, 28.11, 71.10, 115.59 (2C), 125.16, 129.59, 131.99 (2C), 133.05, 163.09, 190.70. Anal. calcd. for C₁₃H₁₄O₂: C 77.20, H 6.98. Found C 77.01, H 6.94%.
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