Pergamon

Tetrahedron Letters 43 (2002) 6031–6033

TETRAHEDRON LETTERS

A convenient oxidative demasking of 1,3-dithiolanes and dithianes to carbonyl compounds with TBHP

Nivrutti B. Barhate, Popat D. Shinde, Vishal A. Mahajan and Radhika D. Wakharkar*

Division of Organic Chemistry: Technology National Chemical Laboratory, Pune 411 008, India

Received 24 April 2002; revised 5 June 2002; accepted 24 June 2002

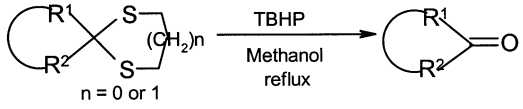
Abstract—Regeneration of carbonyl compounds from their 1,3-dithiolanes and dithianes was achieved using *tert*-butyl hydroperoxide (TBHP, aq. 70%) in high yields. Thus, an efficient, economic and experimentally simple protocol for dethioacetalization has been demonstrated.

The protection of functional groups and their regeneration constitute important and essential processes in the synthesis of polyfunctional molecules and complex natural products. The carbonyl group, among various functional groups, can be protected as an acetal, oxime, hydrazone, cyclic thioacetal etc. Cyclic thioacetals have been widely used as carbonyl protecting groups mainly because 1,3-dithianes played an important role in the development of the synthon concept and their role in umpolung is well established. Dithianes can be efficiently used as acyl carbanion equivalents for carbon–carbon bond forming reactions. Moreover, *S*,*S*-acetals are much more stable than *O*,*O*-acetals and *O*,*S*-acetals (1,3-oxathiolanes) under various reaction conditions required for synthetic organic transformations.

A large number of methods have been developed for the protection (and deprotection) of carbonyl compounds as 1,3-dithianes and dithiolanes.[1] However, selective removal often requires trial and error. Considerable effort has been expended in the development of methods for the demasking of 1,3-dithianes and dithiolanes and the search for a new reagent/catalyst is still actively pursued. Chemical procedures are widely used, as they are more accessible for synthetic chemists than other methods involving photolytic or electrolytic processes. However, some chemical procedures require heavy metals salts[1–3] such as mercury, silver, thallium, cadmium and selenium salts which are inherently toxic and/or expensive. Alternative methods reported include the use of a catalytic amount of *p*-toluenesulfonic acid,[4] iron(III) nitrate and montmorillonite K10,[5] ferric nitrate and silica gel,[6] TFA/H_2O,[7] Amberlyst 15,[8] bis(trifluoroacetoxy) iodobenzene,[9] $ZnBr_2$,[10] organic ammonium tribromides[11] and alkylative methods using methyl iodide.[12–14]

Recently we demonstrated the remarkable practical utility of *tert*-butyl hydroperoxide (TBHP, aq. 70%) for halogenation of arenes, alkenes and alkynes,[15,16] regeneration of carbonyl compounds from their corresponding oximes, phenylhydrazones and tosylhydrazones[17] and oxidation of benzylic alcohols.[18] In view of the oxidative properties of this reagent and its wide spectrum of use, we employed TBHP in methanol for dethioacetalization reactions.

When acetophenone dithioacetal in methanol was stirred with TBHP (2 equiv.) under reflux for 6 h, smooth formation of acetophenone (Scheme 1; Table 1, entry **1**) was observed in 90% yield. Methanol was found to be the best solvent as in other solvents, such as carbon tetrachloride and dichloromethane, the reaction was sluggish and did not go to completion. Dithioacetals under these conditions are expected to undergo oxidative cleavage by formation of disulfoxides that eventually promote hydrolytic cleavage to the corresponding ketone which explains the requirement for 2 equiv. of TBHP for completion of the reaction.



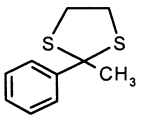
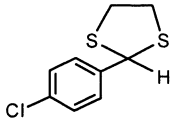
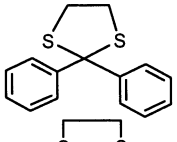
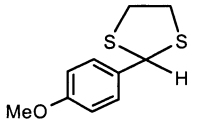
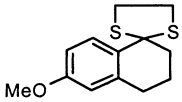
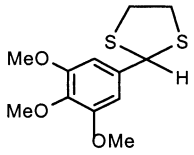
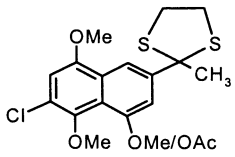
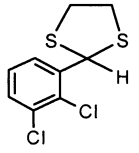
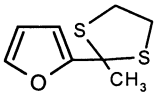
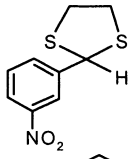
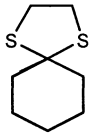
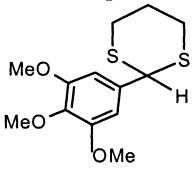
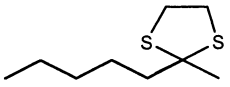
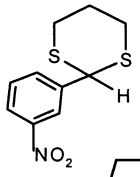
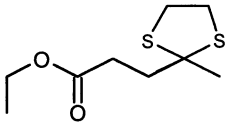
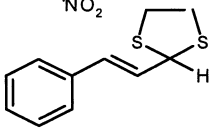
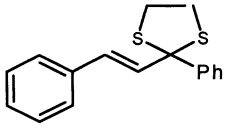
Scheme 1.

Keywords: demasking; 1,3-dithiolanes; dithianes; carbonyl; TBHP.

* Corresponding author. Fax: +91-20-5893614; e-mail: rdw@dalton.ncl.res.in

0040-4039/02/$ - see front matter
PII: S0040-4039(02)01210-8

Table 1. Dethioacetalization of various 1,3-dithiolanes and 1,3-dithianes using TBHP (aq. 70%) in methanol

Entry	Substrate	% Yield[a]	Entry	Substrate	% Yield[a]
1.		90	10.		78
2.		92	11.		70
3.		95	12.		75
4.		93	13.		80
5.		85	14.		77
6.		90	15.		76
7.		85	16.		80
8.		92	17.		83
9.		88			

a : *the figures indicate yield of product after isolation and the products were characterized by spectroscopic methods as well as by direct comparison with authentic samples.*

To study the scope of this transformation different dithioacetals were treated with TBHP in methanol.

The results summarized in Table 1 clearly demonstrate the efficiency of TBHP for cleavage of dithioacetals. 1,3-Dithiolanes of aryl ketones (entries **1**, **2**, **4** and **5**), tetralone (entry **3**), aliphatic ketones (entries **7** and **8**), a cyclic aliphatic ketone (entry **6**), an α,β-unsaturated ketone (entry **9**) and substituted benzaldehydes (entries **10**–**16**) were successfully converted to the corresponding carbonyl compounds in good to excellent yields.

It is noteworthy that the conversion was effective even in the presence of a carboxylic ester (entry **8**). As exemplified by benzaldehydes **10**–**16** and compounds **3** and **4**, substituents and their position on the aromatic ring did not alter the efficacy of the cleavage. The yields of dithiolane deprotection of benzaldehydes were on the low side probably due to over-oxidation of the aldehyde. It is significant that cinnamaldehyde dithiolane and chalcone dithiolane were smoothly cleaved to cinnamaldehyde and chalcone wherein no epoxidation was observed. The corresponding 1,3-dithianes of 3,4,5-

trimethoxybenzaldehyde and 3-nitrobenzaldehyde (entries **15** and **16**) on treatment with TBHP in methanol also furnished the cleavage products in good yields, indicating the generality of the reagent for dithiolanes as well as dithianes.

The dithioacetals were prepared by reported procedures.[19] In a typical procedure the dithioacetal (10 mmol) was dissolved in methanol (10 ml) and TBHP (20 mmol, 2 equiv.) was added to the reaction mixture which was refluxed until completion of reaction. After completion (4–6 h as monitored by TLC), methanol was removed under reduced pressure. The residue was taken up in ethyl acetate, washed with water, dried over sodium sulfate and concentrated to afford the crude product which was purified by column chromatography (silica gel; petroleum ether: EtOAc) to furnish the pure product in yields as shown in Table 1. All compounds in Table 1 were characterized by direct comparison with authentic samples as well as IR and NMR spectroscopy.

In summary, we have devised a simple and convenient method for the demasking of 1,3-dithiolanes and dithianes under neutral conditions in good to excellent yield. The advantages of this protocol are that it provides an economically viable, non-hazardous and efficient methodology using a readily available reagent. Application of commercially available TBHP (aq. 70%) offers experimentally simple conditions wherein no special precautions (inert atmosphere etc.) are necessary. On environmental grounds the use of methanol as the solvent provides an added advantage as it is preferred over chlorinated solvents such as dichloromethane and carbon tetrachloride, which are conventionally used for heterogeneous catalysis. The deprotection conditions being neutral and chemoselective are general for 1,3-dithiane and thiolanes of cyclic, acyclic and aliphatic aromatic, aldehydes and ketones as demonstrated in this communication.

Acknowledgements

N.B.B., P.D.S. and V.A.M. are thankful to the CSIR for their research fellowships.

References

1. Greene, T. W.; Wuts, P. G. M. *Protecting Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, 1999; pp. 329–344.
2. Smith, M. B. *Organic Synthesis*; McGraw-Hill: New York, 1994; Chapter 7.
3. Kocienski, P. J. *Protecting Groups*; Thieme: Stuttgart, 1994.
4. (a) Saleur, D.; Bouillon, J.-P.; Portella, C. *Tetrahedron Lett*. **1999**, *40*, 1885–1886; (b) Veyrat, M.; Fantin, L.; Desmoulins, S.; Petitjean, A.; Mazzanti, M.; Ramasseul, R.; Marchon, J. C.; Bau, R. *Bull. Soc. Chim. Fr*. **1997**, *134*, 703–711; (c) Alonso, E.; Ramon, D. J.; Yus, M. *An. Quim. Int. Ed*. **1998**, *94*, 56–61.
5. Hirano, M.; Ukawa, K.; Yakabe, S.; Clark, J. H.; Morimoto, T. *Synthesis* **1997**, 858–860.
6. Hirano, M.; Ukawa, K.; Yakabe, H.; Morimoto, T. *Org. Prep. Proceed. Int*. **1997**, *29*, 480–484.
7. Armstrong, A.; Jones, L. H.; Barsanti, P. A. *Tetrahedron Lett*. **1998**, *39*, 3337–3340.
8. Ballini, R.; Petrini, M. *Synthesis* **1990**, 336.
9. (a) Stork, G.; Zhao, K. *Tetrahedron. Lett*. **1989**, *30*, 287; (b) Liu, H. J.; Wiszniewski, V. *Tetrahedron Lett*. **1988**, *29*, 5471.
10. Vakalopoulos, A.; Hoffmann, H. M. R. *Org. Lett*. **2001**, *3*, 2185–2188.
11. Mondal, E.; Sahu, P. R.; Bose, G.; Khan, T. *Tetrahedron Lett* **2002**, *43*, 2843 and references cited therein.
12. Saleur, D.; Bouillon, J.-P.; Portella, C. *Tetrahedron Lett*. **2000**, *41*, 321–324.
13. Bouillon, J.-P.; Saleur, D.; Portella, C. *Synthesis* **2000**, 843–849.
14. Kolb, H. C.; Ley, S. V.; Slawin, A. M. Z.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2735.
15. Barhate, N. B.; Gajare, A. S.; Wakharkar, R. D.; Bedekar, A. V. *Tetrahedron Lett*. **1998**, *39*, 6349.
16. Barhate, N. B.; Gajare, A. S.; Wakharkar, R. D.; Bedekar, A. V. *Tetrahedron* **1999**, *55*, 11127.
17. Barhate, N. B.; Gajare, A. S.; Sudalai, A.; Wakharkar, R. D. *Tetrahedron Lett*. **1997**, *38*, 653.
18. Barhate, N. B.; Sasidharan, M.; Sudalai, A.; Wakharkar, R. D. *Tetrahedron Lett*. **1996**, *37*, 2067.
19. Vogel's *Textbook of Practical Organic Chemistry*, 5th ed.; Longman: Harlow, 1989; p. 787.