Solvent-free oxidative deprotection of 1,3-dithianes and 1,3-dithiolanes using poly(*N,N′*-dibromo-*N*-ethyl-benzene-1,3-disulfonamide), *N,N,N′,N′*-tetrabromobenzene-1,3-disulfonamide and NBS

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Abstract

A simple and efficient deprotection of 1,3-dithianes and 1,3-dithiolanes of aromatic, aliphatic and α,β-unsaturated aldehydes and ketones in the solvent-free to the corresponding parent carbonyl compounds in excellent yields using poly(*N,N′*-dibromo-*N*-ethyl-benzene-1,3-disulfonamide) [PBBS], *N,N,N′,N′*-tetrabromobenzene-1,3-disulfonamide [TBBDA] and NBS at room temperature.

Keywords: PBBS, TBBDA, NBS, solvent-free, deprotection, 1,3-dithianes, 1,3-dithiolanes, room temperature

Introduction

Cyclic S,S-acetals, such as 1,3-dithianes and 1,3-dithiolanes are useful carbonyl protective groups against addition of nucleophiles including organometallic reagents.[1]

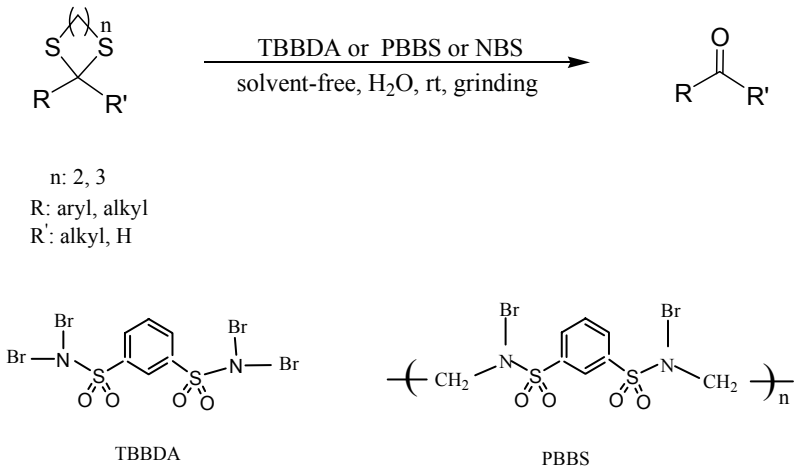
Thioacetals are often used as protecting groups for carbonyl compounds, particularly in multistep natural product synthesis,[2,3] due to their stability towards both acidic and basic conditions. The regeneration of parent carbonyl compounds is not always a facile and straightforward process and therefore development of dethioacetalization protocols has engaged the attention of organic chemists over the years.[4,5] Therefore, many of methods should be available for the deprotection of thioacetales. Among the various reagents employed for this purpose are dimethylsulfoxide in the presence of iodine[6] or t-butyl chloride,[7] *N*-halosuccinimide,[8] dinitrogen tetroxide complexes of iron(III) and copper(II) nitrates,[9] DDQ,[10] tellurium tetrachloride,[11] dimethylsulfoxide,[12] *N*-fluoro-2,4,6-trimethylpyridinium triflate-water,[13] photosensitized oxygenation reactions,[14] trichloroisocyanuric acid,[15] SiO_2Cl/DMSO,[16] *N,N′*-diiodo- *N,N′*-1,2-ethanediyl-bis(*p*-toluenesulphonamide),[17] zirconium sulfonyl phosphonate,[18] *m*-$ClC_6H_4CO_3H$/CF_3CO_2H,[19] SeO_2,[20] $HgCl_2$,[21] ammonium persulfate/K10/MW,[22] $Hg(NO_3)_2.3H_2O$,[23] $CeCl_3.7H_2O$-NaI,[24] *N*-benzyl-DABCO-tribromide,[25] electrophilic halogen,[26]

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oxone/KBr,[27] HBr/H_2O_2,[28] benzyltriphenylphosphonium tribromide,[29] $NaClO_2$ and NaH_2PO_4 in aqueous methanol.[30]

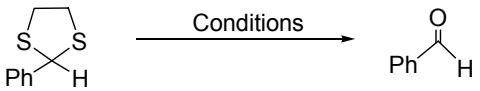
Results and Discussion

Many of the existing methods involve the use of toxic metal ions, long reaction times, environmentally hazardous reagents and solvents. Therefore, we studied the use of poly(*N,N′*-dibromo-*N*-ethyl-benzene-1,3-disulfonamide) [PBBS], *N,N,N′,N′*-tetrabromobenzene-1,3-disulfonamide [TBBDA][31-36] and NBS for the deprotection of thioacetals at room temperature (Scheme 1).



Scheme 1. Deprotection of thioacetales with TBBDA, PBBS and NBS.

Initially, we decided to explore the role of our reagents in CH_3CN as solvent system for the deprotection of 2-(phenyl)-1,3-dithiane used as a model compound (Scheme 2). In the absence of reagent, no dethioacetalization of the model compound was observed, even after prolonged reaction time. Since deprotection of the model compound failed in the absence of reagent, the effect of reagents was also investigated in various conditions, and the results are presented in Table 1.



Scheme 2. Deprotection of 2-(phenyl)-1,3-dithiane used as a model compound.

Table 1. Optimization of reaction condition in room temperature

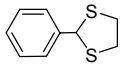
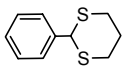
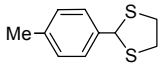
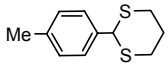
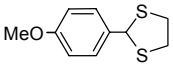
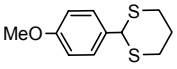
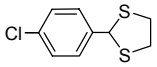
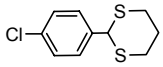
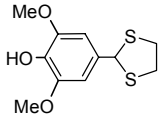
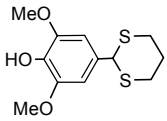
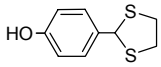
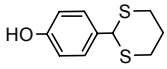
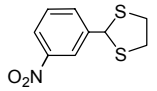
Entry	Condition	Time	Yield %
1	MeCN/ no reagent	12 h	0
2	MeCN/ (0.1 g) TBBDA	1 h	90
3	CH_2Cl_2/ (0.1 g) TBBDA	2 h	85
4	$CHCl_3$/ (0.1 g) TBBDA	2 h	80
5	EtOH/ (0.1 g) TBBDA	2.5 h	82
6	MeCN/(2-3 drop H_2O)/ (0.1 g) TBBDA	20 min.	90
7	Solvent-free / (2-3 drop H_2O)/ (0.1 g) TBBDA/ grinding	5 min.	92
8	Solvent-free / (2-3 drop H_2O)/ (0.05 g) TBBDA/ grinding	5 min.	80
9	Solvent-free / (2-3 drop H_2O)/ (0.15 g) TBBDA/ grinding	2 min.	98
10	Solvent-free / (2-3 drop H_2O)/ (0.2 g) TBBDA/ grinding	2-3 min.	98
11	Solvent-free / (2-3 drop H_2O)/ (0.1 g) PBBS/ grinding	5 min.	90
12	Solvent-free / (2-3 drop H_2O)/ (0.2 g) PBBS/ grinding	3 min.	96
13	Solvent-free / (2-3 drop H_2O)/ (0.3 g) PBBS/ grinding	3 min.	96
14	Solvent-free / (2-3 drop H_2O)/ (0.5 g) NBS/ grinding	5 min.	80
15	Solvent-free / (2-3 drop H_2O)/ (0.1 g) NBS/ grinding	5 min.	82
16	Solvent-free / (2-3 drop H_2O)/ (0.15 g) NBS/ grinding	3 min.	90
17	Solvent-free / (2-3 drop H_2O)/ (0.2 g) NBS/ grinding	3 min.	90

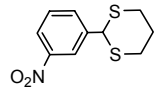
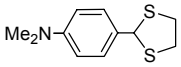
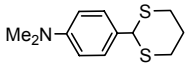
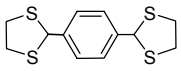
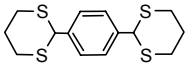
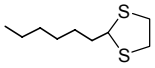
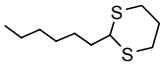
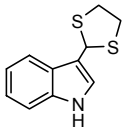
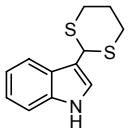
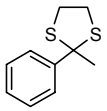
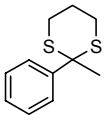
In the solvent system, the best results were achieved using acetonitrile. In recent years, there has been an increasing interest in reactions that proceed in the absent of solvents due to the reduced pollution, low cost, simplicity in process and handling. Therefore, we decided to test this reaction solvent-free and in various ratio of reagents. We found that the reaction was rapid and gave excellent yields of the products when catalyzed by *N,N,N′,N′*-tetrabromobenzene-1,3-disulfonamide [TBBDA] (2 min., 98%, entry 9), by poly(*N,N′*-dibromo-*N*-ethyl-benzene-1,3-disulfonamide) [PBBS] (3 min., 96%, entry 12) and by NBS (3 min., 90%, entry 16).

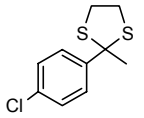
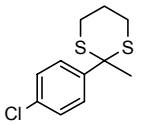
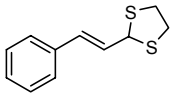
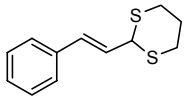
To test the generality and versatility of this procedure in the deprotection of thioacetales and thioketales, we examined a number of 1,3-dithianes and 1,3-dithiolanes of aromatic, aliphatic and α,β-unsaturated aldehydes and ketones using the optimized conditions (Table 2).

As shown in Table 2, various types of 1,3-dithianes and 1,3-dithiolanes (aromatic, aliphatic and α,β-unsaturated) with electron-donating and electron-withdrawing groups were cleanly and rapidly converted to the corresponding parent carbonyl compounds in the solvent-free conditions using poly(*N,N′*-dibromo-*N*-ethyl-benzene-1,3-disulfonamide) [PBBS], *N,N,N′,N′*-tetrabromobenzene-1,3-disulfonamide [TBBDA] and NBS at room temperature. The cleavages were completed within 2-6 minutes in good to excellent yields and without any over oxidation

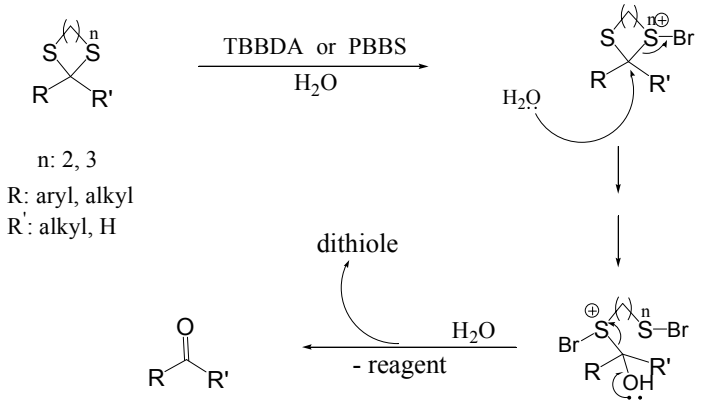
Table 2. Deprotection of thioacetals to the corresponding parent carbonyl compounds using TBBDA, PBBS and NBS in solvent-free

Entry	Substrate	TBBDA		PBBS		NBS	
		Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)
1		(2)	98	(3)	96	(3)	90
2		(2)	98	(3.5)	96	(3.5)	90
3		(2)	96	(3)	92	(3)	85
4		(2)	96	(3)	90	(3)	85
5		(2)	98	(3)	90	(4)	90
6		(2.5)	97	(3.5)	90	(4.5)	88
7		(3)	95	(3.5)	92	(4)	90
8		(3)	92	(4)	90	(4.5)	90
9		(4)	96	(4)	92	(4)	80
10		(4)	96	(4)	85	(4)	75
11		(3)	90	(4)	80	(5)	80
12		(3.5)	92	(4)	80	(5)	80
13		(2)	98	(2)	90	(3)	85

14		(2)	95	(3)	85	(3)	85
15		(3)	92	(3)	85	(4)	90
16		(3.5)	90	(3)	85	(4	90
17		(4)	94	(4.5)	90	(6)	90
18		(4)	95	(5)	90	(6	90
19		(5)	96	(5)	96	(5)	92
20		(4)	95	(5)	90	(6)	90
21		(4)	96	(5)	90	(5)	87
22		(4.5)	96	(5)	85	(5)	85
23		(4)	90	(4)	90	(4.5)	90
24		(4)	90	(5)	90	(5.5)	86
24		(3)	98	(3)	96	(3)	90
26		(3)	98	(4)	92	(4)	90

27		(3.5)	96		(4)	94	(4.5)	92
28		(4)	96		(5)	90	(5)	90
29		(3)	92		(5)	90	(6)	80
30		(3)	90		(5)	86	(6)	82

Since PBBS, TBBDA and NBS contain bromine atoms which are attached to the nitrogen atoms; it is very probable that they release Br^+ *in situ* which can act as electrophilic species and oxidant in the reaction medium. Therefore, we propose the following mechanism for this conversion (Scheme 3).



Scheme 3. Proposed mechanism for this reaction.

In summary, in this study we have introduced a new and useful solvent-free application of TBBDA, PBBS and NBS as efficient reagents for the dethioacetalization of aldehydes and ketones under mild reaction conditions at room temperature. The method has the advantages of very short reaction time (2-5 min.), no side products, good yield and solid state reaction.

Experimental Section

General procedure for deprotection of 1,3-dithianes and 1,3-dithiolanes using TBBDA and PBBS solvent-free. Substrate (1 mmol), [TBBDA (0.15 g) or PBBS (0.2 g) or NBS (0.15 g)]

and a few drops of water were added to a mortar and the mixture was pulverized with a pestle. A spontaneous reaction took place [2-5 min., Table 2, monitored by TLC (9:1, hexane/acetone)]. After completion of the reaction, CH_2Cl_2 (10 ml) was added, and insoluble reagent was removed by filteration. The filtrate was evaporated under reduced pressure and the resulting crude material was purified by chromatography on silic-gel column (eluent: CH_2Cl_2) to give pure carbonyl compounds.

References

1. Grobel, B.-T.; Seebach, D. *Synthesis* **1977**, 356; and references cited therein.
2. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, Wiley: New York, 1991.
3. Komatsu, N.; Uda, M.; Suzuki, H. *Synlett* **1995**, 984.
4. Greene, T. W.; Wuts, P. G. M. *In Protective Groups in Organic Synthesis*, 3rd Ed.; John Wiley and Sons: New York, 1999, pp 333-344.
5. Hajipour, A. R.; Mallakpour, S. E.; Baltork, I. M.; Adibi, H. *Molecules* **2002**, *7*, 674; and references cited therein.
6. Chattopadhyaya, J. B.; Ramarao, A. V. *Tetrahedron Lett*. **1973**, *58*, 3735.
7. Olah, G. A.; Mehrotra, A. K.; Narang, S. C. *Synthesis* **1982**, 151.
8. Corey, E. J.; Erickson, B. W. *J. Org. Chem*. **1971**, *36*, 3553.
9. Firouzabadi, H.; Iranpoor, N.; Zolfigol, M. A. *Bull. Chem. Soc. Jpn*. **1998**, *71*, 2169.
10. Mathew, L.; Sankararaman, S. *J. Org. Chem*. **1993**, *58*, 7576.
11. Tani, H.; Inamasu, T.; Masumoto, K.; Tamura, R.; Shimizu, H.; Suzuki, H. *Phosphoruse, Sulfur, Silicon, Relat. Elem*. **1992**, *67*, 261.
12. Rao, C. S.; Chandrasekharam, M.; Ila, H.; Junjappa, H. *Tetrahedron Lett*. **1992**, *33*, 8163.
13. Kiselyov, A. S.; Strekowski, L. *Tetrahedron* **1993**, *49*, 2151.
14. Kamata, M.; Sato, M.; Hasegawa, E. *Tetrahedron Lett*. **1992**, *33*, 5085.
15. Firouzabadi, H.; Iranpoor, N.; Hazarkhani, H. *Phosphorus, Sulfur, Silicon, Relat. Elem*. **2002**, *177*, 2571.
16. Firouzabadi, H.; Iranpoor, N.; Hazarkhani, H.; Karimi, B. *J. Org. Chem*. **2002**, *67*, 2572.
17. Ghorbani-Vaghei, R.; Zolfigol, M. A. *J. Chin. Chem. Soc*. **2005**, *52*, 327.
18. Curini, M.; Marcotullio, M. C.; Pisani, E.; Rosati, O. *Synlett* **1997**, 769.
19. Cossy, J. *Synthesis* **1987**, 1113.
20. Haroutounian, S. A. *Synthesis* **1995**, 39.
21. Corey, E. J.; Bock, M. G. *Tetrahedron Lett*. **1975**, *16*, 2643.
22. Nemai, C. G.; Mrityunjoy, D.; *Synlett* **2004**, 659.
23. Habibi, M. H.; Tangestaninejad, S.; Montazerzohori, M.; Mohamadpoor-Baltork, I. *Molecules* **2003**, *8*, 663.

24. Yadav, J. S.; Reddy, B. V. S.; Raghavendra, S.; Satyanarayana, M. *Tetrahedron Lett*. **2002**, *43*, 4679.
25. Moghadam, F. M.; Boeini, H. Z.; Zargarani, D.; Bardajee, G. R. *Synth. Commun.* **2006**, *36*, 1093.
26. Shaterian, H.; Hadadzadeh, H. *Phosphorus, Sulfur and Silicon* **2006**, *181*, 1059.
27. Desai, U. V.; Pore, D. M.; Tamhankar, B. V.; Jadhav, S. A.; Wadgaonkar, P. P. *Tetrahedron Lett.* **2006**, *47*, 8559.
28. Ganguly, N. C.; Datta, M. *J. Chem. Reas.* **2005**, 218
29. Hajipour, A. R.; Pourmousavi, S. A.; Ruoho, A. E. J. *Sulfur. Chem.* **2004**, *25*, 401.
30. Ichige, T.; Miyake, A.; Kanoh, M.; Nakata, M. *Synlett* **2004**, 1686.
31. Ghorbani-Vaghei, R.; Zolfigol, M, A.; Chegeny, M.; Veisi, H. *Tetrahedron Lett.* **2006**, *47*, 4505.
32. Ghorbani-Vaghei, R.; Jalili, H. *Synthesis* **2005**, *7*, 1099.
33. Ghorbani-Vaghei, R.; Shahbazee, E. J. *Braz. Chem. Soc.* **2005**, *16*, 647.
34. Zolfigol, M, A.; Ghorbani-Vaghei, R.; Mallakpour, S; Chehardoli, G; Ghorbani Choghamani, A; Yazdi Hosain, A. *Synthesis* **2006**, *10*, 1631.
35. Ghorbani- Vaghei, R.; Jalili, H; Shahbazee, E; Veisi, H. J. *Chin. Chem. Soc*. **2006**, *53*, 2.
36. Ghorbani-Vaghei, R.; Shahbazee, E; Veisi, H. *Mendeleev Commun.* **2005**, 207.

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