Poly(*N*-Bromobenzene-1,3-disulfonamide) and *N*,*N*,*N*′,*N*′-Tetrabromobenzene-1,3-disulfonamide as a Mild and Efficient Catalyst for Chemoselective Thioacetalization of Carbonyl Functions and Transthioacetalization Reactions

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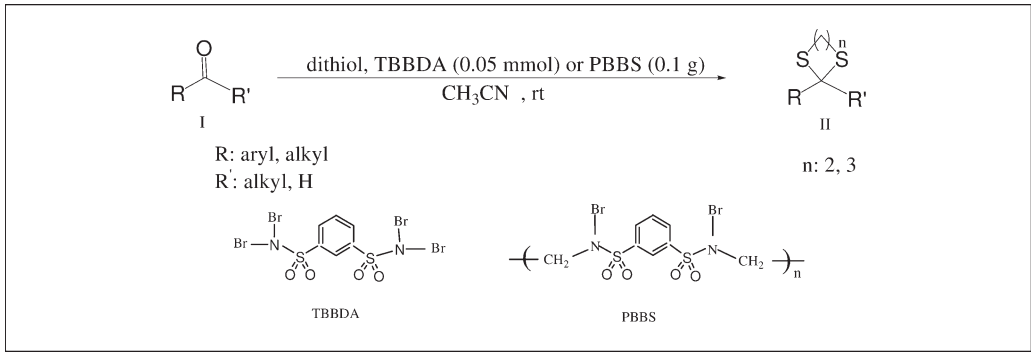

Poly(*N*-bromobenzene-1,3-disulfonamide) and *N*,*N*,*N*′,*N*′-tetrabromobenzene-1,3-disulfonamide are effective catalysts for chemoselective dithioacetalization of aldehydes in the presence of ketones under neutral conditions.

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INTRODUCTION

The protection of carbonyl functionality as a dithioacetal [1] is important in the total synthesis of complex natural and non-natural products [2]. Thioacetals are quit stable toward a wide variety of reagents [3] and are also useful in organic synthesis as acyl carbanion equivalents [3] in C—C bond-forming reaction.

Transthioacetalization of acetals and acylals has also been used as an alternative method for the preparation of thioacetals [4]. They are usually prepared by the condensation of carbonyl compounds with thiols or dithiols using a strong protic acid such as HCl [5] or Lewis acids such as $BF_3.OEt_2$ [6] or $ZnCl_2$ [7] as catalysts. Other Lewis acids viz. $AlCl_3$ [8], $LnCl_3$ [9], $TiCl_4$ [10], WCl_6 [3], $InCl_3$ [11], $Sc(OTf)_3$ [12], $Bi(NO_3)_3$ [13], $VO(OTf)_2$ [14], $CoCl_2$ [15], $BiCl_3$ and $Bi(SO_4)$ [13], $SiCl_4$ [16], $Al(HSO_4)$ [17], P2O5/SiO_2 [18], and [bmim]HSO_4 [19]. A number of milder procedures employing lithium salts [20], $NiCl_2$ [21], trichloroisocyanoric acid [22], NBS [23], I_2 [24], microwave [25], and silica functionalized sulfonic acid [26] have also been reported for this purpose. Unfortunately, many of these protocols suffer from the drawbacks such as a requirement for stoichiometric amounts of catalysts, low yields of the products, long reaction times, the use of expensive reagents and/or chlorinated organic solvents, harsh reaction conditions, difficulties in work-up, and in some instances strong acidic reagents.

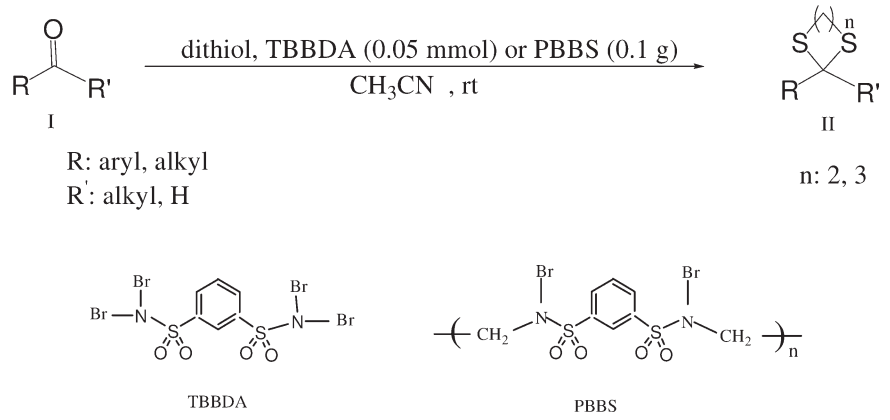
N-Halo compounds are versatile reagents and have been employed as potentially reactive intermediates that are widely used in organic synthesis. *N*-halo reagents are easy to handle with all of the halogen being consumed, and not half, as in the case of elemental halogens. Some specific features of *N*-halo reagents such as the high activity of the *N*-X bond and the various modes of splitting of this bond determine their wide application in organic synthesis [26,27].

RESULTS AND DISCUSSION

In this communication, we wish to report a mild and highly chemoselective procedure for the conversion of aldehydes in present of ketones into 1,3-dithiolanes and 1,3-dithianes using catalytic amount of poly(*N*-bromobenzene-1,3-disulfonamide) (PBBS) and *N*,*N*,*N*′,*N*′-tetrabromobenzene-1,3-disulfonamide (TBBDA) [28–35] under almost neutral reaction conditions (Scheme 1).

First we carried out the reaction of benzaldehyde, with 1,2-ethandithiol in presence of TBBDA (0.05 mmol) at room temperature using different solvents such

Scheme 1



as CH_2Cl_2, $CHCl_3$, CCl_4, CH_3CN, EtOH. The results are listed in Table 1.

It shows that CH_3CN is a better solvent (yield 96%) than other solvents tested. In addition, we also studied influence of the amount of TBBDA and PBBS on the reaction yields. We found that the good yield is obtained in 0.05 mmol of TBBDA and 0.1 g of PBBS. In the light of this, subsequent studies were carried out under the following optimized conditions, that is, with TBBDA (0.05 mmol) and PBBS (0.1 g) at room temperature in CH_3CN.

As shown in Table 2, various types of aromatic aldehydes with electron-donating and electron-withdrawing groups were cleanly and rapidly converted to the corresponding dithianes and dithiolanes in the presence of catalysts. However, aromatic and aliphatic ketones were slowly converted to their corresponding *S,S*-acetals (Table 2, entries 23–28). Transthioacetalization of *O,O*-acetals, *O,O*-ketals and acylals was also achieved efficiently with a catalytic amount of TBBDA and PBBS to afford the corresponding *S,S*-acetals in high yields (Table 2, entries 31–38).

We observed that the reaction with aldehydes takes place rapidly in the presence of TBBDA and PBBS when compared with ketones (Table 2). The difference in reactivity of the TBBDA and PBBS catalysts towards aldehydes and ketones gave us impetus to study chemoselective reactions. Towards this objective, we carried out initial experiments with equimolar mixtures of an aldehyde and a ketone (Scheme 2). When an equimolar (1 mmol) mixture of *p*-methoxybenzaldehyde and acetophenone was allowed to react with 1.1 mmol of 1,2-ethandithiol and catalytic amount of TBBDA and PBBS in acetonitrile at room temperature, a high yield (97%) of (**II**) was obtained and unchanged acetophenone was recovered (Scheme 2). So, the relatively slow reaction rate of ketones (Table 2) allows for chemoselective protection of acylal in the presence of ketone (Scheme 2).

Our preliminary examination shows that TBBDA or PBBS are reusable catalytic reagents. Thus, after the successful thioacetalization of *p*-chlorobenzaldehyde in first run, which gave the corresponding product in 98% isolated yield (Table 2, entry 7), the TBBDA catalyst was subjected to a second thioacetalization reaction from which it gave the product in 90% yield; the average chemical yield for five consecutive runs was 55%. In this curve (Scheme 3), we show the repetition is reduced gratuately. The data shows a good agreement with the function of $y = -10.6x+110.8$ with a regression coefficient of $R^2 = 0.978$.

To compare PBBS and TBBDA with previously published methods for the thioacetalization of carbonyl compounds with benzaldehyde, *p*-chlorobenzaldehyde and *p*-methoxybenzaldehyde we carried out the following studies, as shown in Table 3. This clearly demonstrates that PBBS and TBBDA are good catalysts for the thioacetalization of carbonyl compounds.

Table 1

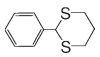
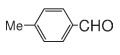
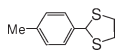
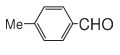
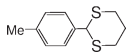
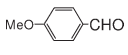
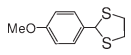
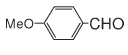
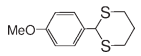
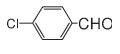
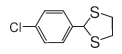
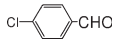
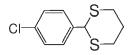
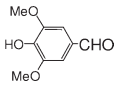
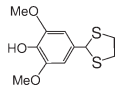
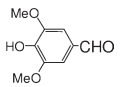
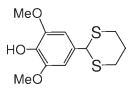
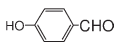
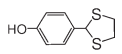
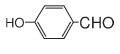
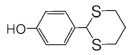
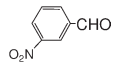
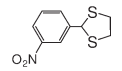
Solvent effect on the reaction of benzaldehyde and 1,2-ethandithiol by TBBDA in room temperature.[a]

Entry	Solvent	Time (min)	Yield (%)[b]
1	CH_2C1_2	40	90
2	$CHC1_3$	60	80
3	CCl_4	90	85
4	CH_3CN	35	96
5	EtOH	35	90

[a] 0.05 mmol.
[b] Isolated yield.

Table 2

Thioacetalization of carbonyl compounds and transthioacetalization catalyzed by TBBDA and PBBS in CH_3CN at ambient conditions.

			TBBDA		PBBS	
Entry	Substrate	Product	Time(min)[h]	Yield (%)[a]	Time (min)[h]	Yield (%)
1			(35)	96	(40)	92
2			(35)	90	(40)	90
3			(40)	92	(40)	90
4			(45)	90	(45)	88
5			(15)	97	(30)	95
6			(20)	97	(35)	92
7			(20)	98	(20)	98
8			(25)	98	(30)	96
9			[1]	95	[1.2]	92
10			[1.2]	90	[1.3]	86
11			(25)	94	(30)	94
12			(30)	90	(40)	90
13			(45)	90	(50)	85

(*Continued*)

Table 2
(*Continued*)

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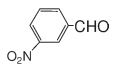
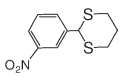
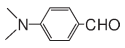
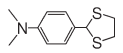
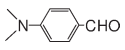
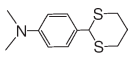
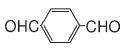
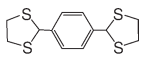
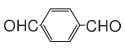
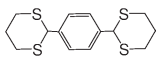
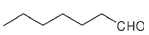
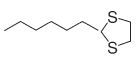
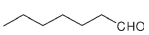
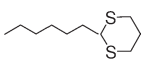
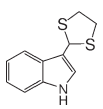
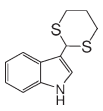
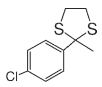
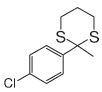
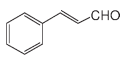
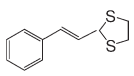
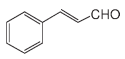
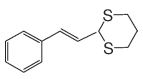
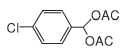
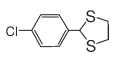
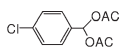
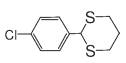
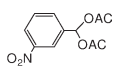
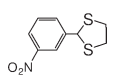
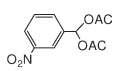
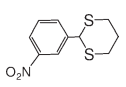
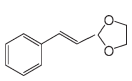
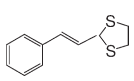
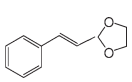
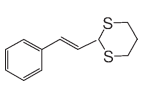
14			(55)	88	[1.1]	82
15			(50)	90	[1]	88
16			(55)	90	[1.1]	85
17			(5)	98	(5)	98
I8			(5)	97	(5)	96
19			[1.6]	86	[2]	85
20			[2]	80	[2.5]	75
21			[1.3]	88	[1.5]	80
22			[1.5]	82	[1.7]	80
23			[7]	40	[7]	40
24			[8]	35	[8.5]	35
25			[4.5]	65	[5]	65
26			[5]	60	[5.2]	60

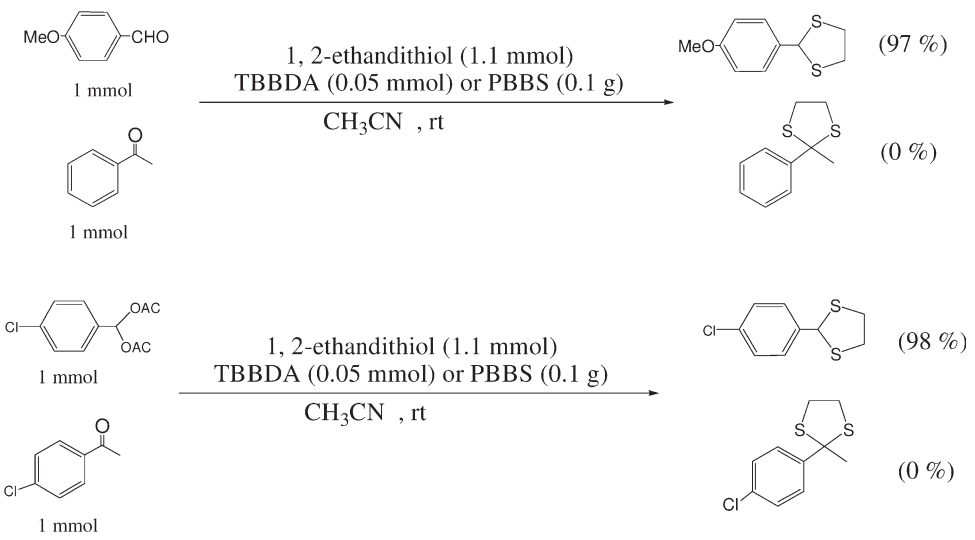
(*Continued*)

Table 2
(*Continued*)

Entry	Substrate	Product	TBBDA		PBBS	
			Time(min)[h]	Yield (%)[a]	Time (min)[h]	Yield (%)
27			[4]	65	[4.5]	65
28			[5]	62	[5]	60
29			[1.2]	92	[1.5]	90
30			[1.2]	90	[1.3]	89
31			[1.5]	92	[1.6]	90
32			[2]	86	[2]	85
33			[2]	90	[2]	90
34			[2.2]	87	[2.2]	86
35			[1.5]	92	[1.7]	85
36			[2]	90	[2.5]	88
37			[6]	75	[6.5]	75
38			[7]	70	[8]	70

[a] Products were characterized from their physical properties, comparison with authentic samples and by spectroscopic methods (^{1}H NMR and IR).

Scheme 2



CONCLUSION

In summary, in this study we have introduced a new and useful catalytic application of TBBDA and PBBS as efficient catalysts for the thioacetalization of aldehydes, *O,O*-acetals, *O,O*-ketals and acylals under mild reaction conditions. The method is highly chemoselective for protection of aldehydes in the presence of ketones. Moreover, the method has advantages in terms of high yields of products, short reaction times, operational simplicity and easy work up of products.

EXPERIMENTAL

General procedure for thioacetalization and transthioacetalization of acetals and acylals catalyzed by TBBDA and PBBS in CH_3CN. To a stirred solution of substrate 1–18 (1mmol) and TBBDA (0.05 mmol) or PBBS (0.1 g) in CH_3CN (2 mL) was added 1,2-ethandithiol or 1,3-propandithiole (1.1 mmol) at room temperature. The mixture was stirred for an appropriate time (Table 2). After completion of reaction as indicated by TLC, the organic solvent was concentrated in vacuum and then CH_2Cl_2 (10 mL) was added, and the catalyst was removed by filtration. Evaporation of the solvent under reduced pressure gave the products. Further purification was achieved by recrystalization from ethanol (90%).

Scheme 3

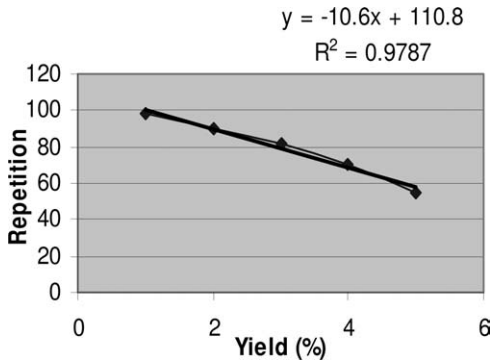


Table 3

Reaction times and yield for previously published methods.

Substrate	Conditions	Reaction time (min)	Yield (%)
Benzaldehyde	NBS, 1,2 propandithiol, CH_2C1_2, rt	40	80[23]
Benzaldehyde	$NiCl_2$, 1,2 propandithiol, CH_2CI_2- MeOH, rt	165	96[21]
Benzaldehyde	$CoCl_2$, 1,2 propandithiol, CH_3CN, rt	300	89[15]
Benzaldehyde	Trichloroisocyanoric acid, 1,2 propandithiol, $CHCl_3$, rt	60	95[22]
p-(Cl)-benzaldehyde	$CoCl_2$,1,3 propandithiol, CH_3CN, rt	30	88[15]
p-(Cl)-benzaldehyde	NBS, 1,3 propandithiol, CH_2C1_2, rt	30	78[23]
p-(Cl)-benzaldehyde	$Sc(OTf)_3$, 1,3 propandithiol, CH_2C1_2, rt	40	90[12]
p-(Cl)-benzaldehyde	Trichloroisocyanoric acid, 1,2 propandithiol, $CHC1_3$, rt	120	94[22]
p-(MeO)-benzaldehyde	NBS, 1,3 propandithiol, CH_2Cl_2 rt	30	70[23]
p- (MeO)-benzaldehyde	$NiCl_2$, 1,3 propandithiol, CH_2C1_2-MeOH, rt	75	89[21]
p-(MeO)-benzaldehyde	$CoCl_2$ 1,3 propandithiol, CH_3CN, rt	30	92[15]

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