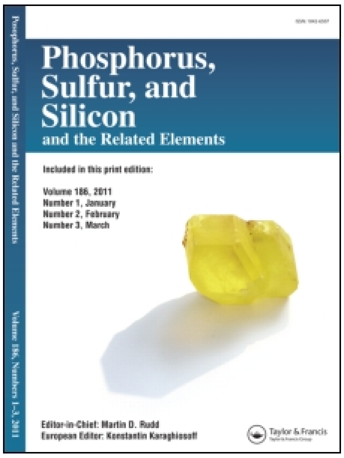

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2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO), N-Bromosuccinimide (NBS) and Bromine as Efficient Catalysts for Dithioacetalization and Oxathioacetalization of Carbonyl Compounds and Transdithioacetalization Reactions

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2,4,4,6-TETRABROMO-2,5-CYCLOHEXADIENONE (TABCO), N-BROMOSUCCINIMIDE (NBS) AND BROMINE AS EFFICIENT CATALYSTS FOR DITHIOACETALIZATION AND OXATHIOACETALIZATION OF CARBONYL COMPOUNDS AND TRANSDITHIOACETALIZATION REACTIONS

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The use of 2,4,4,6-tetrabromo-2,5-cyclohexadienone (TABCO), N-bromosuccinimide (NBS), and bromine as efficient catalysts for conversion of carbonyl compounds to their cyclic and acyclic dithioacetals and 1,3-oxathiolanes under mild reaction conditions are described. These catalysts are also used for efficient transdithioacetalization of acetals, diacetals, ketals, acylals, enamines, hydrazones, and oximes with high yields in the presence of thiols.

Keywords: 1,3-Oxathiolane; 2,4,4,6-tetrabromo-2,5-cyclohexadienone (TABCO); bromine; carbonyl compound; dithioacetalization; N-bromosuccinimide (NBS); thiol; transdithioacetalization

INTRODUCTION

The protection of organic compounds is an important goal in multistep organic synthesis.[1] Due to the resistance of thioacetals toward hydrolytic cleavage under ordinary acidic and basic conditions, the protection of carbonyl groups as their cyclic and acyclic dithioacetals has attracted organic chemists.[2] Cyclic S,S-acetals for example, 1,3-dithianes

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*Present address: Bu-Ali Sina University, Hamedan, Iran.

This article is dedicated to Professor Ahmad Banihashemi on the occasion of his 70th birthday.

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and 1,3-dithiolanes, also have found wide synthetic uses as precursors of acyl anion equivalents and as masked methylene group in organic synthesis.[3–7]

Dithioacetals can be prepared by condensation of carbonyl compounds and thiols or dithiols in the presence of protic acids, Lewis acids, and some silicon reagents.[3–36] Some of the reported methods suffer from: 1) long reaction times, 2) stoichiometric use of expensive reagents, and 3) low selectivity when applied to the mixture of aldehydes and ketones.

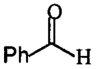
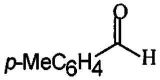
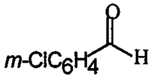
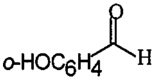
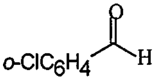
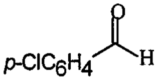
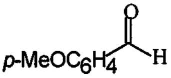
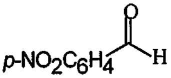
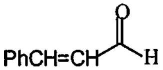
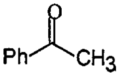
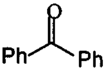
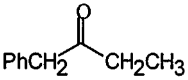
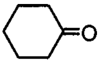
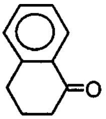
Recently, transdithioacetalization of acetals has gained favor as alternative method for the preparation of dithioacetals, in which catalysts such as $BF_3.OEt_2$,[37] $Bu^i{}_2AlS(CH_2)_2SAlBu^i{}_2$,[38] and $CoCl_2$, Me_3SiCl[39] have been employed. This interesting transformation was later extended to transdithioacetalization of ketals, oxathioacetals and oxathioketals by Envirocat EPZ10^{R},[40] and also to ketals, oximes, enamines and tosylhydrazones using natural kaolinitic clay.[41] However, since most of these catalysts work under reflux conditions and some of them are not easily available,[40,41] introducing of cheap, easily available, selective, and efficient catalysts is always welcome by synthetic organic chemists.

In continuation of our recent works on dithioacetalization of carbonyl compounds and transdithioacetalization reactions,[34–36] we now introduce compounds that they potentially carry positive halonium ions and can be used as efficient catalysts for both dithioacetalization and transdithioacetalization reactions. The compounds we have used for this purpose are: 2,4,4,6-tetrabromo-2,5-cyclohexadienone (TABCO),[42–47] N-bromosuccinimide (NBS) and molecular bromine (Br_2). We have employed them as efficient and chemoselective catalysts for the conversion of aldehydes and ketones to their corresponding cyclic and acyclic dithioacetals and also 1,3-oxathiolanes under mild reaction conditions. The transdithioacetalization of acetals, diacetals, ketals, acylals, imines, enamines, and hydrazones in $CHCl_3$ at room temperature and oximes under reflux condition were also performed in the presence of these catalysts.

RESULTS AND DISCUSSION

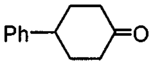
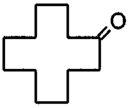
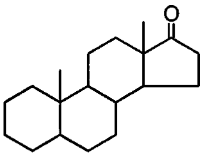
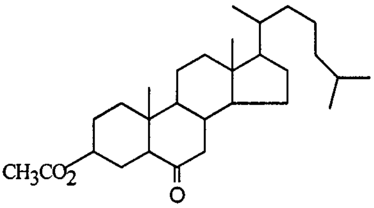
Various types of aromatic aldehydes with electron-donating and electron-withdrawing groups, cinnamaldehyde and aliphatic aldehydes were converted to their cyclic S,S-acetals with $HS(CH_2)_nSH$, $n = 2$, 3 in the presence of TABCO (Method A, Table I), NBS (Method B, Table II) or Br_2 (Method C, Table II) as catalysts, with excellent yields

TABLE I Dithioacetalization of Carbonyl Compounds with $HS(CH_2)_nSH$ Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO, Method A) in $CHCl_3$ at Room Temperature

Entry	Substrate	n	Sub/thiol/cat	Time (min)	Yield^a (%)
1		2	1/1.5/0.2	10	94
		3	1/1.5/0.3	3	95
2		2	1/1.5/0.2	8	95
		3	1/1.5/0.3	3	93
3		2	1/1.5/0.2	15	93
		3	1/1.5/0.3	3	92
4		2	1/1.5/0.3	8	91
		3	1/1.5/0.3	6	90
5		2	1/1.5/0.2	18	92
		3	1/1.5/0.2	15	92
6		2	1/1.5/0.2	20	94
		3	1/1.5/0.3	6	95
7		2	1/1.5/0.2	5	96
		3	1/1.5/0.2	4	96
8		2	1/1.5/0.2	25	92
		3	1/1.5/0.3	5	93
9		2	1/1.5/0.2	7	94
		3	1/1.5/0.3	3	95
10		2	1/2.0/0.3	45	89
		3	1/2.0/0.4	25	90
11		2	1/2.0/0.4	180	85
		3	1/2.0/0.4	150	84
12		2	1/2.0/0.4	100	89
		3	1/2.0/0.4	80	89
13		2	1/1.5/0.3	25	92
		3	1/1.5/0.3	15	93
14		2	1/1.5/0.3	80	90
		3	1/1.5/0.4	50	91

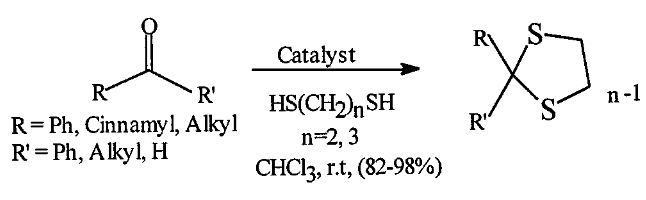
(Continued on next page)

TABLE I Dithioacetalization of Carbonyl Compounds with $HS(CH_2)_nSH$ Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO, Method A) in $CHCl_3$ at Room Temperature *(Continued)*

Entry	Substrate	n	Sub/thiol/cat	Time (min)	Yield[a] (%)
15		2	1/1.5/0.3	90	90
		3	1/1.5/0.4	45	92
16		2	1/1.5/0.3	40	91
		3	1/1.5/0.4	30	90
17		2	1/2.0/0.4	180	87
		3	1/2.5/0.4	140	87
18		2	1/2.5/0.4	240	82
		3	1/2.5/0.5	200	75

[a] Isolated yield.

at room temperature. We have also investigated the protection of carbonyl groups of various aromatic, aliphatic and steroidal ketones in the presence of these catalysts at room temperature (Scheme 1).



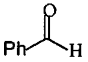
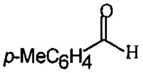
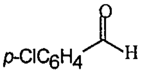
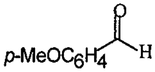
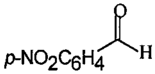
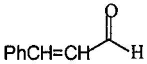
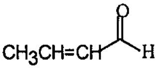
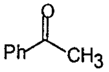
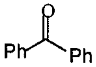
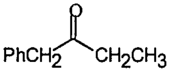
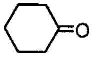
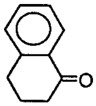
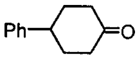
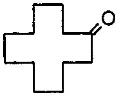
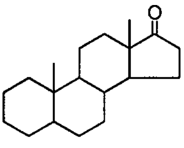
Catalyst :

Method A) TABCO
Method B) NBS
Method C) Br_2

SCHEME 1

We observed that dithioacetalization of ketones with these catalysts proceeded very smoothly and cleanly with excellent yields but with longer reaction times in comparison with aldehydes (Tables I and II).

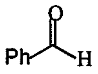
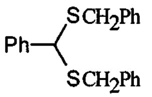
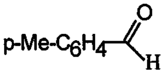
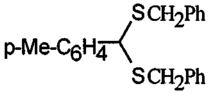
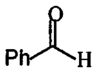
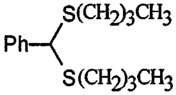
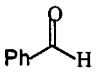
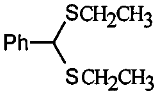
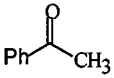
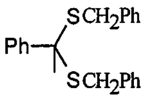
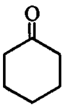
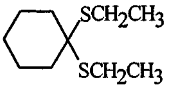
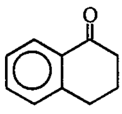
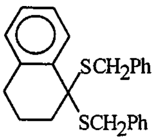
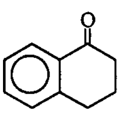
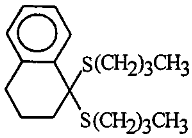
TABLE II Dithioacetalization of Carbonyl Compounds with $HS(CH_2)_nSH$ Catalyzed by N-Bromosuccinimide (NBS, Method B) Bromine (Br_2, Method C) in $CHCl_3$ at Room Temperature

Entry	Substrate	n	Sub/thiol/cat, method	Time (min)	Yield[a] (%)
1		2	1/1.5/0.2, B	5	96
		3	1/1.5/0.1, C	4	95
2		2	1/1.5/0.2, B	6	97
		3	1/1.5/0.1, C	3	96
3		2	1/1.5/0.2, B	9	95
		3	1/1.5/0.1, C	15	96
4		2	1/1.5/0.2, B	5	96
		3	1/1.5/0.1, C	4	96
5		2	1/1.5/0.2, B	15	94
		3	1/1.5/0.1, C	20	93
6		2	1/1.5/0.2, B	4	94
		3	1/1.5/0.1, C	4	90
7		2	1/1.5/0.2, B	5	94
		3	1/1.5/0.1, C	4	92
8		2	1/2.0/0.3, B	45	90
		3	1/2.0/0.2, C	50	91
9		2	1/2.5/0.4, B	170	87
		3	1/2.5/0.4, C	160	85
10		2	1/2.0/0.4, B	80	90
		3	1/2.0/0.3, C	90	89
11		2	1/1.5/0.3, B	15	92
		3	1/1.5/0.2, C	10	91
12		2	1/1.5/0.3, B	70	90
		3	1/1.5/0.2, C	80	86
13		2	1/2.0/0.4, B	80	90
		3	1/2.0/0.2, C	55	89
14		2	1/1.5/0.2, B	30	87
		3	1/1.5/0.2, C	35	85
15		2	1/2.5/0.4, B	170	83
		3	1/2.5/0.4, C	140	82

[a] Isolated yield.

We also studied the possibility of dithioacetalization of carbonyl compounds to their corresponding acyclic dithioacetals with benzylthiol, 1-butanethiol, and ethylthiol catalyzed by all these catalysts. The reactions were occurred at room temperature and acyclic dithioacetals were obtained in excellent yields (Table III).

TABLE III Dithioacetalization of Carbonyl Compounds with Benzylthiol, 1-Butylthiol and Ethylthiol Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO, Method A), N-Bromosuccinimide (NBS, Method B) and Bromine (Br_2, Method C) in $CHCl_3$ at Room Temperature

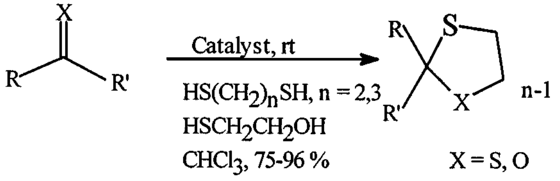
Entry	Substrate	Product	Thiol	Subs/thiol/ cat, method	Time (min)	Yield[a] (%)
1			$PhCH_2SH$	1/2.5/0.2, A	5	95
				1/2.5/0.1, B	4	97
				1/2.5/0.2, C	5	96
2			$PhCH_2SH$	1/2.5/0.2, A	5	95
				1/2.5/0.1, B	4	98
				1/2.5/0.2, C	5	96
3			$CH_3(CH_2)_3SH$	1/2.5/0.2, A	5	95
				1/2.5/0.1, B	5	95
				1/2.5/0.2, C	5	96
4			CH_3CH_2SH	1/2.5/0.2, A	6	95
				1/2.5/0.1, B	5	97
				1/2.5/0.2, C	6	96
5			$PhCH_2SH$	1/3.0/0.3, A	45	92
				1/3.0/0.2, B	40	93
				1/3.0/0.3, C	45	91
6			CH_3CH_2SH	1/3.0/0.3, A	12	91
				1/3.0/0.2, B	15	92
				1/3.0/0.3, C	20	91
7			$PhCH_2SH$	1/3.0/0.4, A	75	90
				1/3.0/0.2, B	65	91
				1/3.0/0.3, C	80	92
8			$CH_3(CH_2)_3SH$	1/3.0/0.4, A	75	92
				1/3.0/0.2, B	60	92
				1/3.0/0.3, C	70	91

[a] Isolated yield.

In order to show the ability of TABCO, NBS, and Br_2 to act as selective catalysts, we studied dithioacetalization of aldehydes and ketones with 1,3-propanedithiol in binary mixtures. By these methods, benzaldehyde was protected in the presence of 4-nitrobenzaldehyde with the ratio of 95:5. 4-Methylbenzaldehyde was protected in the presence of benzaldehyde with the ratio of 85:15. Benzaldehyde in the presence of acetophenone was exclusively protected. Acetophenone was quantitatively converted to its S,S-acetal whereas, benzophenone remained almost intact. The results of these selective protections are shown in Table IV.

1,3-Oxathiolanes are considerably more stable than the corresponding O,O-acetals, and ketals under acidic conditions and in comparison with S,S-acetals and ketals are more easily deprotected.[1] To extend the synthetic applications of the reaction, we studied 1,3-oxathioacetalization of different carbonyl groups with 2-mercaptoethanol catalyzed by TABCO. 1,3-Oxathiolanes were obtained from the reaction of aldehydes and ketones with 2-mercaptoethanol at room temperature in high yields when TABCO was used as a catalyst in $CHCl_3$ (Table V). Similarly, NBS and Br_2 showed to be efficient catalysts for this transformation at room temperature.

We continued this study by investigating the possibility of using these catalysts for transdithioacetalization reaction of different protected compounds of carbonyl groups (Scheme 2). These reactions are especially interesting since *O*,*O*-acetals are generally more reactive than their corresponding carbonyl compounds in the dithioacetalization reactions and give efficiently the desired product at short reaction time with excellent yield. Various types of diethyl acetals and ketals were converted to their cyclic 1,3-dithioacetals (Table VI, entries 1–7, 11, 14, 15, 17, 18) and also to their acyclic dithioacetals (Table VI, entries 13,



R = Ph, Cinnamyl, Alkyl
R' = Ph, Alkyl, H
X = $(OEt)_2$, $-O(CH_2)_nO-$[n = 2, 3], $-(OCH_2)_2C(CH_2O)_2-$
NOH, NHNPh, NR'', $(OAc)_2$ [R' = H]
Catalyst = TABCO, NBS, Br_2

SCHEME 2

TABLE IV Selective Dithioacetalization of Carbonyl Compounds with $HS(CH_2)_3SH$ Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO, Method A), N-Bromosuccinimide (NBS, Method B) and Bromine (Br_2, Method C) in $CHCl_3$ at Room Temperature

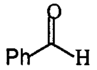
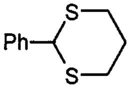
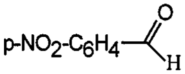
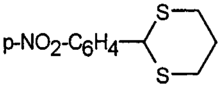
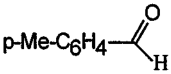
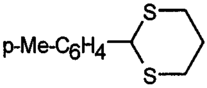
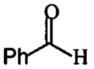
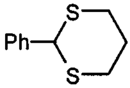
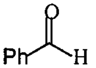
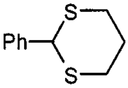
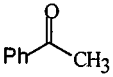
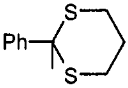
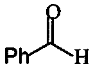
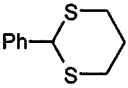
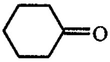
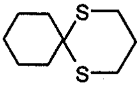
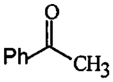
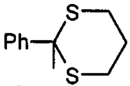
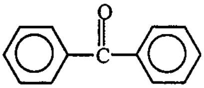
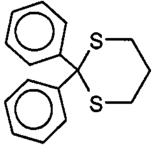
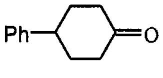
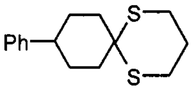
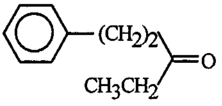
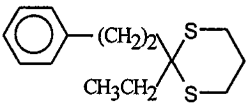
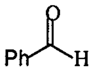
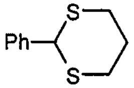
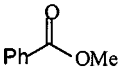
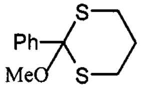
Entry	Substrate 1 Substrate 2	Product 1 Product 2	Sub 1/sub 2/thiol/ cat, method	Time (min)	Yield[a] (%)
1			1/1/1.5/0.2, A	5	95
					5
2			1/1/1.5/0.2, A	3	85
					15
3			1/1/1.5/0.2, A	5	100
					0
4			1/1/1.5/0.1, B	5	100
					0
5			1/1/2.0/0.2, B	40	100
					0

TABLE IV Selective Dithioacetalization of Carbonyl Compounds with $HS(CH_2)_3SH$ Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO, Method A), N-Bromosuccinimide (NBS, Method B) and Bromine (Br_2, Method C) in $CHCl_3$ at Room Temperature *(Continued)*

Entry	Substrate 1 Substrate 2	Product 1 Product 2	Sub 1/sub 2/thiol/ cat, method	Time (min)	Yield[a] (%)
6			1/1/2.0/0.3, C	50	100
					0
7			1/1/1.5/0.2, C	5	100
					0

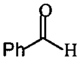
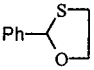
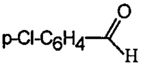
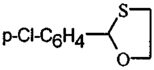
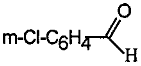
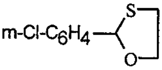
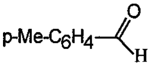
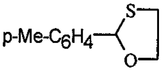
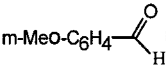
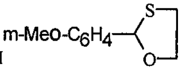
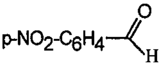
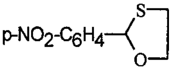
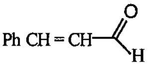
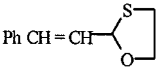
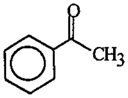
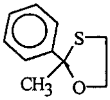
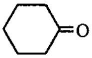
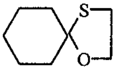
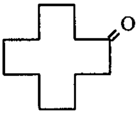
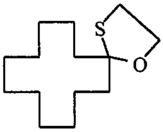
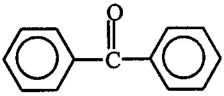
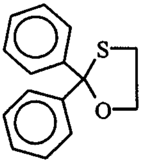
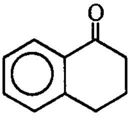
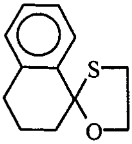
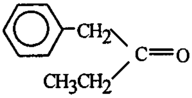
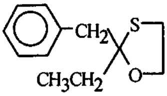
[a]Yield based on GC and NMR analysis.

16, 19) in short reaction times in the presence of catalytic amounts of TABCO in high to excellent yields. Similarly, NBS and Br_2 showed to be efficient catalysts for this transformation at room temperature. By the use of these catalysts, the sterically hindered benzophenone diethylacetal was also converted to its corresponding 2,2-diphenyl-1,3-dithiolane in good yield at room temperature (Table VI, entry 17). We also have performed the conversion of acetals and ketals to their corresponding 1,3-oxathiolanes with 2-mercaptoethanol in excellent yields in the presence of TABCO, NBS and Br_2 at room temperature. This transformation was performed in the presence of 0.1 mmol of either catalyst for acetals (Table VI, entries 8–10) and 0.3 mmol of the catalyst for ketals at room temperature (Table VI, entry 12).

Transdithioacetalization of 1,3-dioxanes (Table VII, entries 1–5 and 15–18) and 1,3-dioxolanes (Table VII, entries 6–14) with $HS(CH_2)_3SH$ were also studied in the presence of these catalysts. The results obtained using TABCO as catalyst in these reactions are represented in the Table VII. The reactions proceeded well at room temperature and the corresponding 1,3-dithianes were obtained in high to excellent yields.

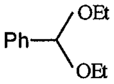
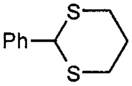
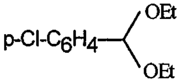
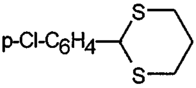
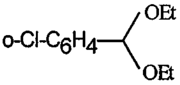
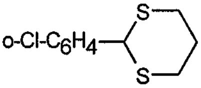
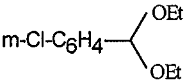
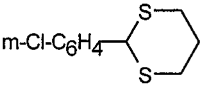
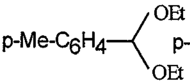
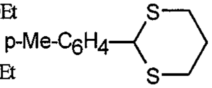
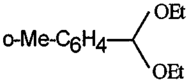
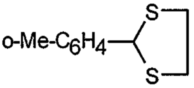
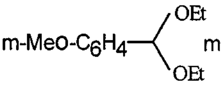
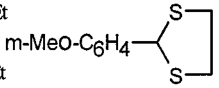
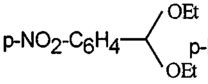
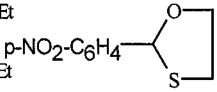
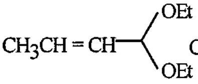
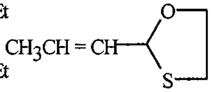
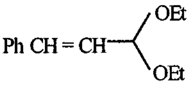
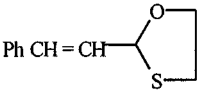
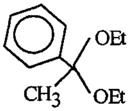
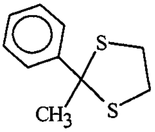
Diacetals of [2,2-bis(hydroxymethyl)-1,3-propanediol] are stable crystalline derivatives of aldehydes and ketones which their handling is

TABLE V Preparation of 1,3-Oxathiolanes from Carbonyl Compounds with 2-Mercaptoethanol Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO) in $CHCl_3$ at Room Temperature

Entry	Substrate	Product	Sub/thiol/cat	Time (min)	Yield[a] (%)
1			1/1.5/0.2	8	89
2			1/1.5/0.2	10	87
3			1/1.5/0.2	12	86
4			1/1.5/0.2	5	88
5			1/1.5/0.2	5	89
6			1/1.5/0.2	15	86
7			1/1.5/0.2	5	87
8			1/2.0/0.4	20	85
9			1/1.5/0.2	25	84
10			1/2.0/0.4	30	82
11			1/2.5/0.5	160	77
12			1/2.0/0.4	70	85
13			1/2.0/0.4	80	83

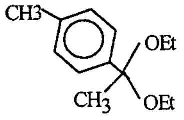
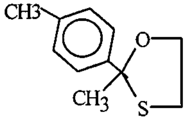
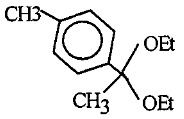
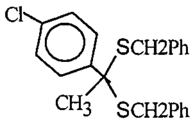
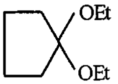
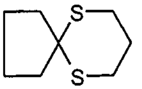
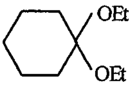
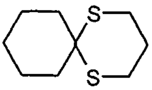
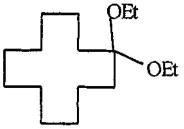
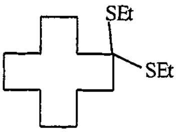
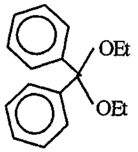
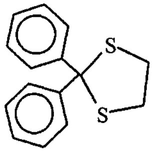
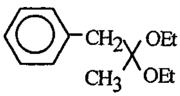
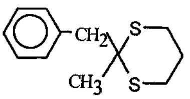
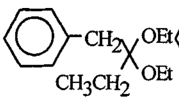
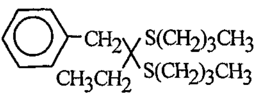
[a]Isolated yield.

TABLE VI Transdithioacetalization of Diethyl Acetals and Ketals with Thiols, Dithiols, and 2-Mercaptoethanol Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO) in $CHCl_3$ at Room Temperature

Entry	Substrate	Product	Thiol	Sub/thiol/ cat	Time (min)	Yield[a] (%)
1			$HS(CH_2)_3SH$	1/1.5/0.1	10	91
2			$HS(CH_2)_3SH$	1/1.5/0.1	25	90
3			$HS(CH_2)_3SH$	1/1.5/0.1	15	91
4			$HS(CH_2)_3SH$	1/1.5/0.1	10	93
5			$HS(CH_2)_3SH$	1/1.5/0.1	5	94
6			$HS(CH_2)_2SH$	1/1.5/0.1	12	90
7			$HS(CH_2)_2SH$	1/1.5/0.1	15	91
8			$HS(CH_2)_2OH$	1/1.5/0.1	35	90
9			$HS(CH_2)_2OH$	1/1.5/0.1	10	90
10			$HS(CH_2)_2OH$	1/1.5/0.1	15	90
11			$HS(CH_2)_2SH$	1/2.0/0.3	40	88

(Continued on next page)

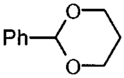
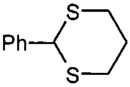
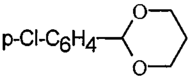
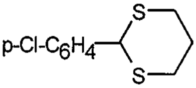
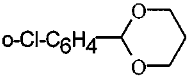
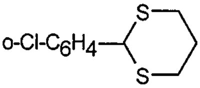
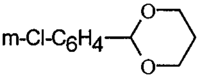
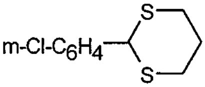
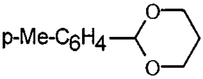
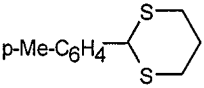
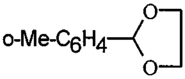
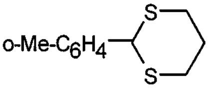
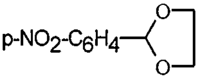
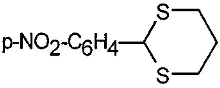
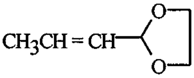
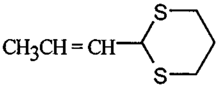
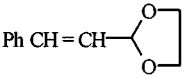
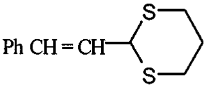
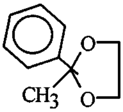
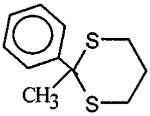
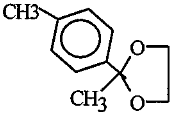
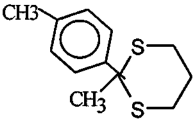
TABLE VI Transdithioacetalization of Diethyl Acetals and Ketals with Thiols, Dithiols, and 2-Mercaptoethanol Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO) in $CHCl_3$ at Room Temperature *(Continued)*

Entry	Substrate	Product	Thiol	Sub/thiol/ cat	Time (min)	Yield[a] (%)
12			$HS(CH_2)_2OH$	1/2.0/0.3	35	89
13			$PhCH_2SH$	1/3.0/0.3	45	90
14			$HS(CH_2)_3SH$	1/1.5/0.2	25	91
15			$HS(CH_2)_3SH$	1/1.5/0.2	20	91
16			CH_3CH_2SH	1/3.0/0.2	35	89
17			$HS(CH_2)_2SH$	1/2.5/0.5	100	75
18			$HS(CH_2)_3SH$	1/2.0/0.3	80	90
19			$CH_3(CH_2)_3SH$	1/3.0/0.3	85	87

[a] Isolated yield.

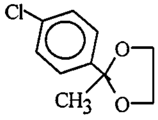
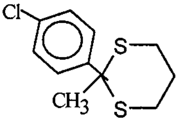
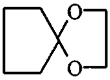
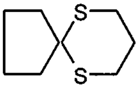
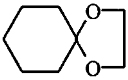
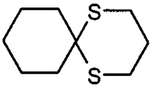
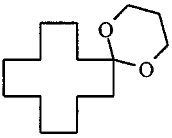
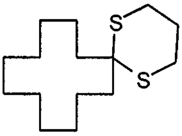
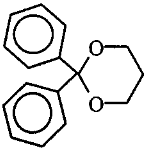
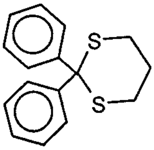
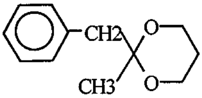
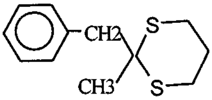
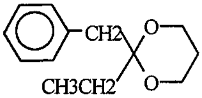
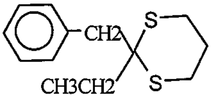
easy.[50,51] We studied the possibility of their transdithioacetalization with $HS(CH_2)_3SH$ in the presence of TABCO, NBS, and Br_2 as catalyst. The reactions were completed within short reaction times (10–25 min) and excellent yields of 1,3-dithianes (90–94%) were obtained. The

TABLE VII Transdithioacetalization of 1,3-Dioxanes and 1,3-Dioxolanes with $HS(CH_2)_3SH$ Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO) in $CHCl_3$ at Room Temperature

Entry	Substrate	Product	Sub/thiol/ cat	Time (min)	Yield[a] (%)
1			1/1.5/0.1	8	92
2			1/1.5/0.1	15	93
3			1/1.5/0.1	20	90
4			1/1.5/0.1	15	94
5			1/1.5/0.1	10	87
6			1/1.5/0.1	12	90
7			1/1.5/0.1	20	90
8			1/1.5/0.1	12	92
9			1/1.5/0.1	8	91
10			1/2.0/0.3	5	80
11			1/2.0/0.3	60	75

(Continued on next page)

TABLE VII Transdithioacetalization of 1,3-Dioxanes and 1,3-Dioxolanes with $HS(CH_2)_3SH$ Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO) in $CHCl_3$ at Room Temperature *(Continued)*

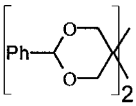
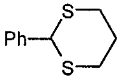
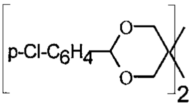
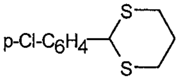
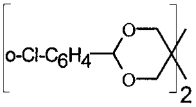
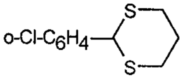
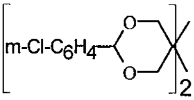
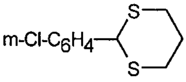
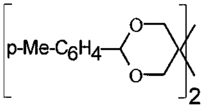
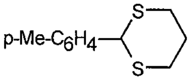
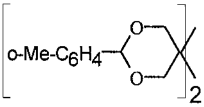
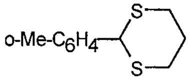
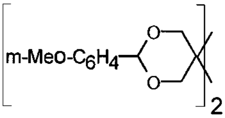
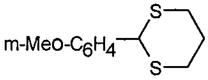
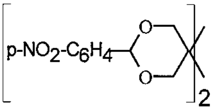
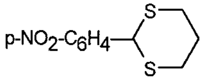
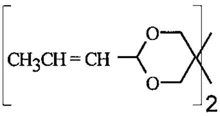
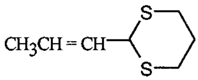
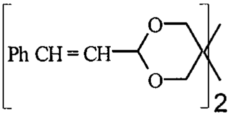
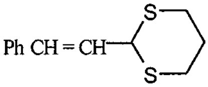
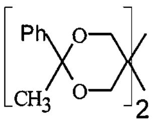
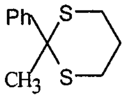
Entry	Substrate	Product	Sub/thiol/ cat	Time (min)	Yield[a] (%)
12			1/2.0/0.3	60	84
13			1/1.5/0.2	25	89
14			1/1.5/0.2	15	90
15			1/1.5/0.2	30	89
16			1/2.0/0.4	120	82
17			1/2.0/0.3	50	87
18			1/2.0/0.3	65	89

[a] Isolated yield.

results obtained using NBS as representative catalyst are shown in the Table VIII.

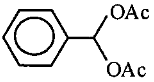
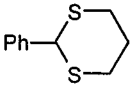
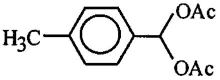
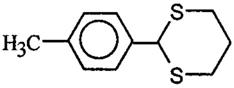
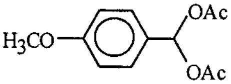
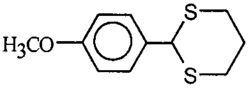
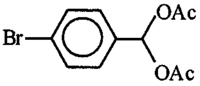
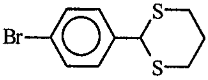
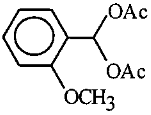
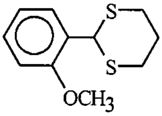
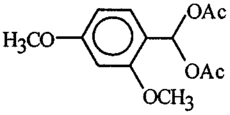
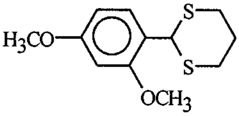
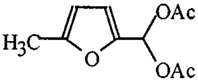
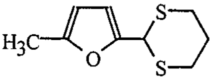
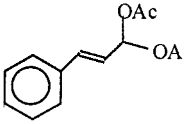
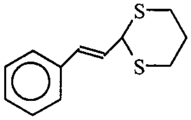
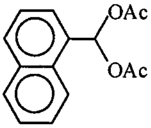
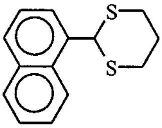
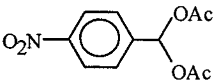
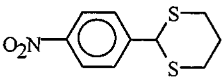
By use of these catalysts, acylals (geminal diacetates), [Scheme, X = $(OAc)_2$, R′ = H], as stable derivatives of aldehydes were also converted to their corresponding 1,3-dithianes with $HS(CH_2)_3SH$ in high yields and short reaction times (5–18 min). The results obtained in the presence of NBS as catalyst are shown in the Table IX.

TABLE VIII Transdithioacetalization of Cyclic Diacetals with $HS(CH_2)_3SH$ Catalyzed by N-Bromosuccinimide (NBS) in $CHCl_3$ at Room Temperature

Entry	Substrate	Product	Sub/thiol/ cat	Time (min)	Yield[a] (%)
1			1/2.5/0.15	10	90
2			1/2.5/0.2	20	90
3			1/2.5/0.2	25	91
4			1/2.5/0.2	18	92
5			1/2.5/0.1	10	94
6			1/2.5/0.1	15	91
7			1/2.5/0.1	12	92
8			1/2.5/0.2	25	90
9			1/2.5/0.2	10	94
10			1/2.5/0.1	15	90
11			1/3.0/0.2	25	90

[a] Isolated yield.

TABLE IX Transdithioacetalization of Acytals with $HS(CH_2)_3SH$ Catalyzed by N-Bromosuccinimide (NBS) in $CHCl_3$ at Room Temperature

Entry	Substrate	Product	Sub/thiol/ cat	Time (min)	Yield[a] (%)
1			1/1.5/0.1	5	94
2			1/1.5/0.1	10	95
3			1/1.5/0.1	10	93
4			1/1.5/0.1	15	93
5			1/1.5/0.1	12	90
6			1/1.5/0.1	10	90
7			1/1.5/0.1	12	93
8			1/1.5/0.1	10	90
9			1/1.5/0.1	18	91
10			1/1.5/0.1	15	90

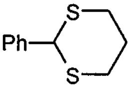
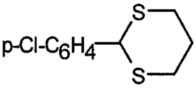
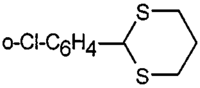
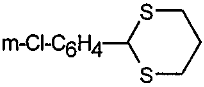
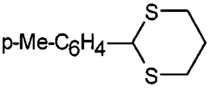
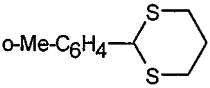
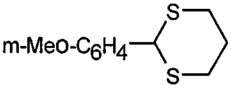
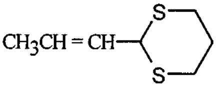
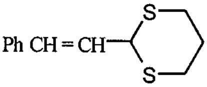
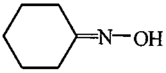
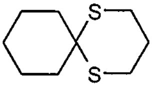
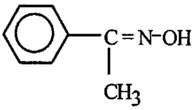
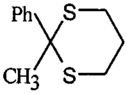
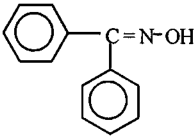
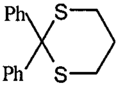
[a] Isolated yield.

Aldehydes and ketones are generally purified and characterized via their corresponding crystalline oximes or hydrazones that may be employed for further synthetic manipulation. Therefore, in-situ preparation of dithioacetals from oximes and hydrazones is a useful synthetic transformation. In the process of in-situ conversion of benzaldehyde oxime to its 1,3-dithiane with $HS(CH_2)_3SH$ and TABCO, NBS and Br_2 as catalysts (0.2 molar equivalent), it was observed that these catalysts are not efficient for this transformation at room temperature. For example, in the case of Br_2 which is more efficient than the other two catalysts, benzaldehyde oxime was converted to 2-phenyl-1,3-dithiane only in 55% yield after 48 h at room temperature. We therefore performed the transdithioacetalization of oximes under reflux condition in the presence of Br_2 as catalyst. Both aldoximes and ketoximes reacted under reflux condition with 1,3-propanedithiol and furnished their corresponding 1,3-dithianes (Table X). In comparison with kaolinitic clay, which was not able, to convert acetophenone oxime to its dithioacetals in refluxing CCl_4 (0% yield is reported)[41] with this method, the reaction produces 2-methyl-2-phenyl-1,3-dithiane in 70% yield.

In comparison with the reaction of oximes, TABCO, NBS, and Br_2 were found to have similar efficiency for transdithioacetalization of hydrazones, imines and enamines. We studied transdithioacetalization of imines and enamines with $HS(CH_2)_3SH$ in the presence of Br_2 as a representative catalyst. Conversion of these compounds to their corresponding 1,3-dithiane was occurred at room temperature with excellent yields (Table XI, entries 1–7). We also extended our studies for transdithioacetalization of phenylhydrazones of both aldehydes and ketones with Br_2 as catalyst in the presence of $HS(CH_2)_3SH$. The reactions were occurred at room temperature and produced the corresponding 1,3-dithianes in high yields (Table XI, entries 8, 9).

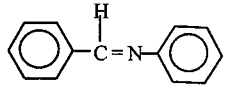
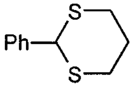
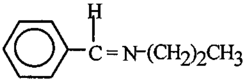
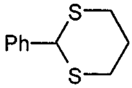
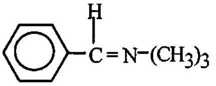
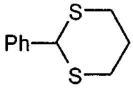
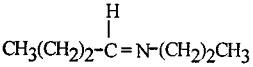
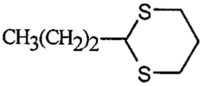
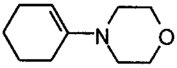
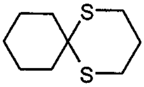
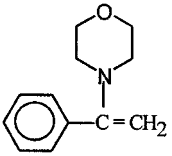
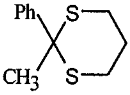
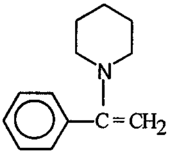
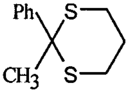
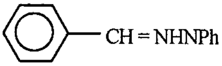
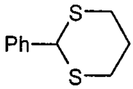
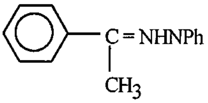
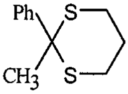
In order to study the chemoselectivity of these catalysts, different binary mixtures were selected and their competitive reactions with $HS(CH_2)_3SH$ were studied. Very high chemoselectivity behavior of TABCO, NBS, and Br_2 for transdithioacetalization reactions has been noticed. By this method, benzaldehyde diacetate was exclusively converted to its 1,3-dithiane in the presence of acetophenone (Table XII, entry 1). 4-methyl acetophenone diethyl acetal was quantitatively converted to its 1,3-dithiane in the presence of 4-methyl acetophenone (Table XII, entry 2). Excellent chemoselectivity in the transdithioacetalization of binary mixtures such as benzaldehyde diethyl acetal and benzaldehyde diacetate (Table XII, entry 3), 4-chlorobenzaldeyde diethyl acetal and 4-chlorobenzaldehyde diacetate (Table XII, entry 4), 2-methyl-2-(4-chlorophenyl)-1,3-dioxolane and 4-chlorobenzaldehyde

TABLE X Transdithioacetalization of Oximes with $HS(CH_2)_3SH$ Catalyzed by Bromine (Br_2) in $CHCl_3$ Under Reflux Conditions

Entry	Substrate	Product	Sub/thiol/cat	Time (min)	Yield[a] (%)
1	Ph-CH=N-OH		1/5.0/0.8	10	90
2	$\text{p-Cl-C}_6\text{H}_4\text{-CH=N-OH}$		1/5.0/0.8	11.5	89
3	$\text{o-Cl-C}_6\text{H}_4\text{-CH=N-OH}$		1/5.0/0.8	12	87
4	$\text{m-Cl-C}_6\text{H}_4\text{-CH=N-OH}$		1/5.0/0.8	11	89
5	$\text{p-Me-C}_6\text{H}_4\text{-CH=N-OH}$		1/5.0/0.8	9	92
6	$\text{o-Me-C}_6\text{H}_4\text{-CH=N-OH}$		1/5.0/0.8	10	90
7	$\text{m-MeO-C}_6\text{H}_4\text{-CH=N-OH}$		1/5.0/0.8	8	91
8	$\text{CH}_3\text{CH=CH-CH=N-OH}$		1/5.0/0.8	75	85
9	Ph CH=CH-CH=N-OH		1/5.0/0.8	10	89
10			1/5.0/0.8	15	85
11			1/7.0/1.0	24	70
12			1/10.0/2.0	48	50

[a] Isolated yield.

TABLE XI Transdithioacetalization of Imines, Enamines, and Phenylhydrazones with $HS(CH_2)_3SH$ Catalyzed by Bromine (Br_2) in $CHCl_3$ at Room Temperature

Entry	Substrate	Product	Sub/thiol/ cat	Time (h)	Yield[a] (%)
1			1/1.5/0.1	8	93
2			1/1.5/0.1	5	95
3			1/1.5/0.1	5	95
4	 $CH_3(CH_2)_2-\overset{H}{C}=N-(CH_2)_2CH_3$		1/1.5/0.1	15	91
5			1/1.5/0.1	12	92
6			1/1.5/0.1	10	90
7			1/1.5/0.1	8	90
8			1/1.5/0.1	12	93
9			1/1.5/0.1	10	90

[a] Isolated yield.

TABLE XII Selective Dithioacetalization of Carbonyl Compounds with $HS(CH_2)_3SH$ Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO, Method A), N-Bromosuccinimide(NBS, Method B) and Bromine (Br_2, Method C) in $CHCl_3$ at Room Temperature

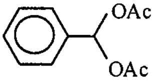
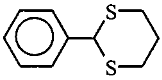
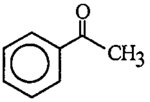
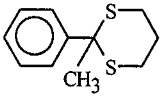
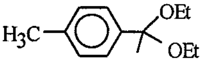
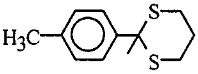
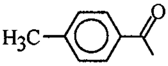
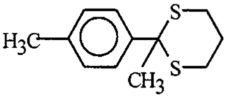
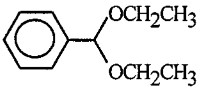
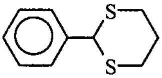
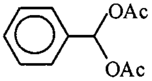
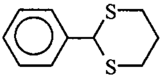
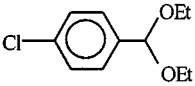
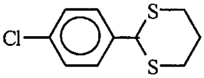
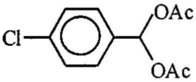
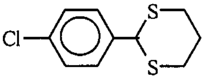
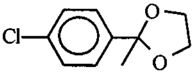
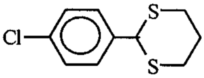
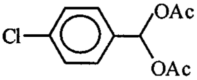
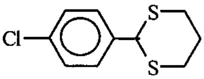
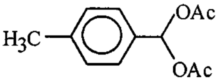
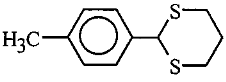
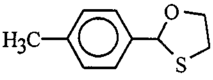
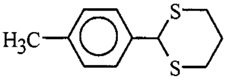
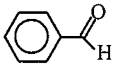
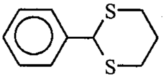
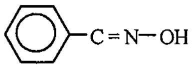
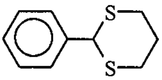
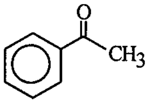
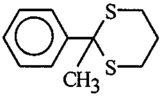
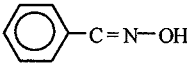
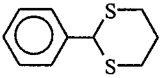
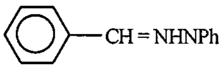
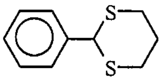
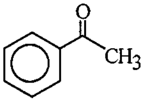
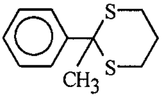
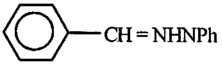
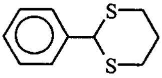
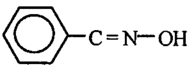
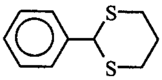
Entry	Substrate 1 Substrate 2	Product 1 Product 2	Sub 1/sub 2/thiol/ cat, method	Time (min), [h]	Yield[a] (%)
1			1/1/1.5/0.2, A	(5)	100
					0
2			1/1/1.5/0.1, B	(12)	100
					0
3			1/1/1.5/0.2, C	(5)	100
					0
4			1/1/1.5/0.2, A	(7)	100
					0
5			1/1/1.5/0.2, A	(5)	100
					0
6			1/1/1.5/0.2, A	(5)	100
					0

TABLE XII Selective Dithioacetalization of Carbonyl Compounds with $HS(CH_2)_3SH$ Catalyzed by 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO, Method A), N-Bromosuccinimide(NBS, Method B) and Bromine (Br_2, Method C) in $CHCl_3$ at Room Temperature *(Continued)*

Entry	Substrate 1 Substrate 2	Product 1 Product 2	Sub 1/sub 2/thiol/ cat, method	Time (min), [h]	Yield[a] (%)
7			1/1/1.5/0.2, C	(5)	100
					0
8			1/1/3.0/0.4, C	[3]	90
					10
9			1/1/3.0/0.4, C	[3]	85
					15
10			1/1/3.0/0.4, C	[3]	75
					25

[a] Yields based on NMR and GC (n-heptane was used as internal standard).

diacetate (Table XII, entry 5), and 4-methylbenzaldehyde diacetate and its 1,3-oxathiolane (Table XII, entry 6) was observed. We also observed excellent chemoselectivity for dithioacetalization of aldehydes and ketones in the presence of oximes and hydrazones. Benzaldehyde was exclusively converted to 2-phenyl-1,3-dithiane with 1,3-propanedithiol in the presence of benzaldoxime (Table XII, entry 7). Acetophenone was transformed to 2-methyl-2-phenyl-1,3-dithiane in the presence of benzaldoxime with the ratio of 90/10 after 3h (Table XII, entry 8). Benzaldehyde phenylthydrazone was converted to its 2-phenyl-1,3-dithiane in the presence of acetophenone with the ratio of 85:15 (Table XII, entry 9).

Benzaldehyde phenylhydrazone was also reacted in the presence of benzaldoxime with the ratio of 75:25 after 3 h (Table XII, entry 10). As it was observed in the competitive transdithioacetalization reactions, oximes are less reactive than their carbonyl compounds or hydrazones derivatives.

The mechanism of the reaction is not very clear to us. In our studies for acetalization of carbonyl compounds, we observed that NBS, TABCO, and Br_2 could act as efficient catalysts. Since in these reactions no HBr is produced, it could be concluded that the catalytic activity of these compounds could well be attributed to the presence of electrophilic bromine in the reaction. Similarly in the case of dithioacetalization and transdithioacetalization reactions, these compounds can act as source of electrophilic halogen, however, the catalytic action of anhydrous HBr produced through coupling of some thiol to disulfide cannot be ruled out.

CONCLUSION

In conclusion, the presented catalysts are efficient, mild, readily available, and cheap for the protection of carbonyl compounds as their cyclic S,S-acetal and ketals, acyclic S,S-acetals and ketals and 1,3-oxathiolanes in high yields. The use of NBS and TABCO is advantageous over molecular bromine due to ease of handling and safety aspects. Transdithioacetalization of a wide range of compounds such as acetals, ketals, diacetals, acylals, imines, enamines, and hydrazones can also be performed with these catalysts at room temperature. In addition, the excellent chemoselectivity observed for dithioacetalization of carbonyl compounds and transdithioacetalization of different functionalities makes this method a useful contribution in organic synthesis.

EXPERIMENTAL

General

All yields refer to isolated products unless otherwise stated. The products were identified by comparison of their physical and spectral data (IR and NMR) with those obtained for known samples. The purity of the products was determined with TLC on silica-gel polygram SIL G/UV 254 plates or GC analysis. IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. The NMR spectra were recorded on a Bruker Avance DPX instrument (250 MHz).

General Procedure for Dithioacetalization of Carbonyl Compounds with TABCO, NBS, or Br_2 as Catalyst in $CHCl_3$ at Room Temperature

To a solution of carbonyl compound (1 mmol) and the appropriate catalysts (Tables I–III) in $CHCl_3$ (5 mL), thiol or dithiol (Tables I–III) was added at room temperature. The reaction mixture was stirred for the appropriate time. The progress of the reaction was monitored by TLC or GC. After completion of the reaction, an aqueous solution of NaOH (5%, 25 mL) was added and the mixture was extracted with $CHCl_3$ (3 × 25 mL). The organic layer was then separated and washed with saturated solution of NaCl (20 mL) followed by H_2O (20 mL). The organic layer was separated and dried over anhydrous Na_2SO_4. Removal of the solvent gave almost pure cyclic and acyclic S,S-acetals and ketals in excellent yields (Tables I–III). Further purification, if necessary, was performed by column chromatography on a short column of silica gel using petroleum ether (40–60°C)/ethyl acetate (9:1) as eluent. Products were characterized by spectroscopic (^{1}H NMR, ^{13}C NMR, IR, MS) analysis and also by comparison with the known samples prepared according to the literature.[3–36]

General Procedure for Oxathioacetalization of Carbonyl Compounds with TABCO as Catalyst in $CHCl_3$

To a solution of carbonyl compound (1 mmol) and TABCO as catalyst (Table V) in $CHCl_3$ (5 mL), 2-mercaptoethanol was added at room temperature. The reaction mixture was stirred for the appropriate time. The progress of the reaction was monitored by TLC or GC. After completion of the reaction, an aqueous solution of NaOH (5%, 25 mL) was added and the mixture was extracted with $CHCl_3$ (3 × 25 mL). The organic layer was then separated and washed with saturated solution of NaCl (20 mL) followed by H_2O (20 ml). The organic layer was separated and dried over anhydrous Na_2SO_4. Purification was performed by vacuum distillation to afford desired product in good yield (Table V). Products were characterized by spectroscopic (^{1}H NMR, ^{13}C NMR, IR, MS) analysis and also by comparison with the known samples prepared according to the literature.[48,49]

General Procedure for Transdithioacetalization of Acetals, Diacetals, Ketals, Acylals, Enamines, Imines, Hydrazones and Oximes Catalyzed by TABCO, NBS, or Br_2

To a solution of acetal, ketal, acylal, enamine, imine, phenylhydrazone, or oximes (1 mmol) and thiol or dithiol (Tables VI–XI) in $CHCl_3$ (5 mL), the appropriate catalyst (TABCO, NBS, or Br_2) was added and the mixture was stirred at room temperature for the appropriate time

(Tables VI–IX, XI). The reaction of oximes was carried out under reflux condition (Table X). TLC or GC monitored the progress of the reaction. After completion of the reaction, aqueous solution of NaOH (5%, 25 mL) was added and the mixture was extracted with $CHCl_3$ (3 × 25 mL). The organic layer was then separated and washed with saturated solution of NaCl (20 mL) followed by H_2O (20 mL). The organic phase was dried over anhydrous Na_2SO_4. Purification was performed by column chromatography on silica gel and petroleum ether (40–60°C)/ethyl acetate (9:1) was used as eluent. Products were characterized by comparison of their spectral data with samples prepared according to the literature.[3–36]

General Procedure for Transoxathioacetalization of Acetals and Ketals with TABCO as Catalyst in Chloroform

To a solution of acetals and ketals (1 mmol) and TABCO (0.1–0.3 mmol) in $CHCl_3$ (5 mL), 2-mercaptoethanol was added at room temperature (Table VI, entries 8–10, 12). The reaction mixture was stirred for the appropriate time. The progress of the reaction was monitored by TLC or GC. After completion of the reaction, aqueous solution of NaOH (5%, 25 mL) was added and the mixture was extracted with $CHCl_3$ (3 × 25 mL). The organic layer was then separated and washed with saturated solution of NaCl (20 mL) followed by H_2O (20 mL). The organic phase was dried over anhydrous Na_2SO_4. Purification was performed by vacuum distillation to afford the desired products in high yield. Products were characterized by comparison of their spectral data with those of samples prepared according to the literature.[48,49]

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