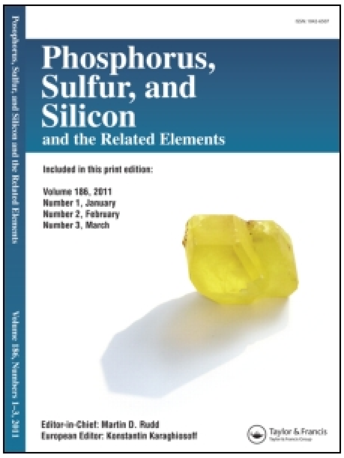

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Application of $BU_4N^+HSO_4^-$ as an Ionic Liquid and Acid Catalyst for Thioacetalization of Aldehydes and Ketones

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A variety of carbonyl containing compounds have been successfully reacted with 1,2-ethanedithiol in a thioacetylization reaction using tetrabutylammonium hydrogensulfate as a mild and efficient catalyst. Aldehydes and ketones react with good to excellent yields under mild conditions.

Keywords Acid catalyst; carbonyl compound; ionic liquid; thioacetalization

INTRODUCTION

The protection of aldehydes and ketones as thioacetal and thioketals is a widely used method, which is performed in the presence of acids, generally.[1] They are quite stable under basic or mildly acidic conditions.[2] The dithioacetals are also utilized as masked acyl anions[3] or masked methylene function groups[4] for carbon–carbon bond formation. Generally, these compounds are prepared by condensation of carbonyl compounds with thiols or dithiols employing acid catalysts including HCl,[5] PTSA,[6] $BF_3.OEt_2$,[7] $AlCl_3$,[8] $TiCl_4$,[9] $Mg(OTf)_3$,[10] $LaCl_3$,[11] $SiCl_4$,[12] WCl_6,[13] $(CH_3)_3SiCl$,[14] 5 M $LiClO_4$,[15] $SOCl_2$–SiO_2,[16] $Cu(OTf)_2$–SiO_2[17], $ZrCl_4$–SiO_2,[18] $TaCl_5$–SiO_2,[19]$CoBr_2$–SiO_2,[20] LiBr,[21a] $LiBF_4$,[22a] $InCl_3$,[23] molecular I_2,[24a] NBS,[25] and $Sc(OTf)_3$.[26]

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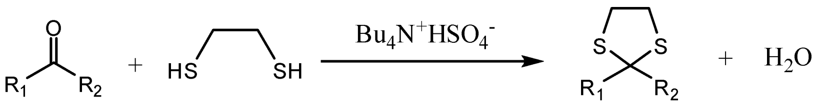
Some of these methods suffer from some drawbacks such as tedious work-up,[9,10] using relatively expensive reagents,[10–15] harsh conditions[16] or require an inert atmosphere for the reaction.[15,23–25] Therefore, an introduction of new methods and inexpensive reagents for such functional group transformations is still in demand.

Ionic liquids have attracted extensive research interest in recent years as environmentally benign solvents due to their favorable properties like non-flammability, negligible vapor pressure, reusability, and high thermal stability. They have also been referred to as *designer solvents* as their physical and chemical properties could be adjusted by a careful choice of cation and anion. Apart from this, they exhibit acidic properties. Combining these unique properties of ionic liquids they are emerging as a 'green reaction dual-purpose media' (catalyst + solvent). The use of ionic liquids as reaction medium may offer a convenient solution to both the solvent emission and catalytic recycling problem.[25–28]

RESULTS AND DISCUSSION

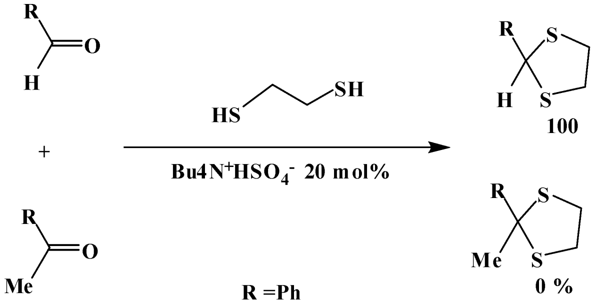
In the course of our studies on reactions under solvent-free conditions and developing new method for transformations of organic functional groups;[29–31] here, we introduce a new and environmentally benign application of $Bu_4N^+HSO_4^-$ as a mild catalyst for protection of carbonyl functional groups. This reagent is a highly chemoselective catalyst for the conversion of aldehydes in the presence of ketones to the corresponding dithioacetals under solvent-free conditions.

Initially, we tried the protection of aldehydes **1** to the corresponding dithioacetals **2** by 1,2-ethanedithiol in the presence of catalytic amounts of $Bu_4N^+HSO_4^-$ at room temperature under solvent-free conditions. This reaction gave dithioacetal derivatives in 73–91% yield after 20–85 min. The reaction was tried using a wide variety of aldehydes and ketones containing electron-withdrawing and electron-donating substituents (Scheme 1, Table I). The reaction proceeds efficiently for carbonyl compounds at ambient temperature under mild conditions.

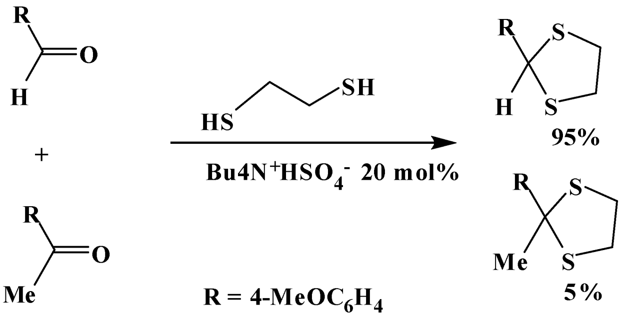


R_1=phenyl, R_2= H, CH_3

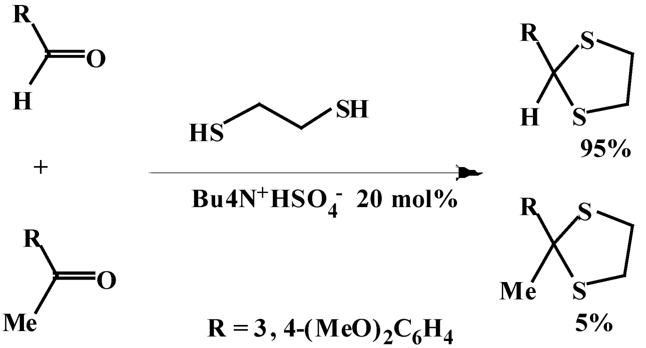
SCHEME 1



Eq. 1



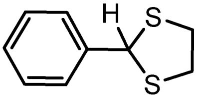
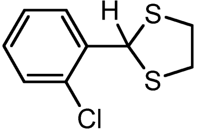
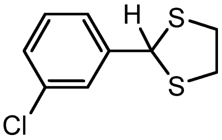
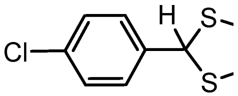
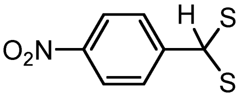
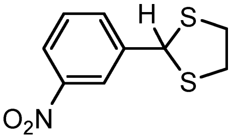
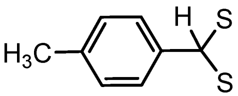
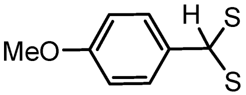
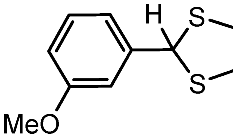
Eq. 2



Eq. 3

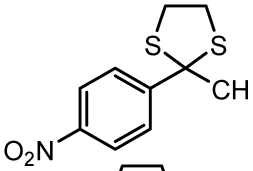
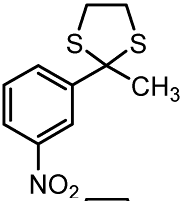
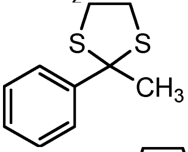
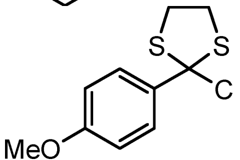
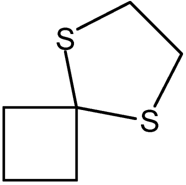
Moreover, this procedure is highly chemoselective, providing the selective protection of an aldehyde in the presence of a ketone. Treatment of an equimolar mixture of benzaldehyde and acetophenone in the presence of 1,2-ethanedithiol and catalytic amount of $Bu_4N^+HSO_4^-$ (20 mol%) under solvent-free conditions produced only 1,2-dithiolane derivative of benzaldehyde while the acetophenone is completely recovered, this competitive reaction illustrating the chemoselectivity of the present method (Equation (1)). The other competition reactions are shown in Equations (1–3).

TABLE I Thioacetalization of Aldehydes and Ketones with 1,2-Ethanditithiol Catalyzed by Tetrabutylammonium Hydrogen Sulfate as an Ionic Liquid

Entry	Substrate	Product	Time (min)	Yield (%)
1	C_6H_5CHO		27	83
2	2-ClC_6H_5CHO		33	79
3	3-ClC_6H_5CHO		30	88
4	4-ClC_6H_5CHO		26	90
5	4-$O_2NC_6H_5CHO$		20	91
6	3-$O_2NC_6H_5CHO$		24	89
7	4-$H_3CC_6H_5CHO$		29	82
8	4-$MeOC_6H_5CHO$		38	78
9	3-$MeOC_6H_5CHO$		35	81

(Continued on next page)

TABLE I Thioacetalization of Aldehydes and Ketones with 1,2-Ethandithiol Catalyzed by Tetrabutylammonium Hydrogen Sulfate as an Ionic Liquid *(Continued)*

Entry	Substrate	Product	Time (min)	Yield (%)
10	4-$O_2NC_6H_5COCH_3$		53	84
11	3-$O_2NC_6H_5COCH_3$		51	82
12	$C_6H_5COCH_3$		65	76
13	4-$MeOC_6H_5COCH_3$		85	73
14	Cyclobutanone		60	76

[a]Yields refer to pure isolated products and were characterized by comparison of their physical and spectral data (IR, ^{1}HNMR, m.p., or b.p.) with authentic samples.[31] [b]Reactions were carried out in room temperature for aldehydes and at reflux conditions for ketones.

In summary, we have reported the synthesis of thioacetals and thioketals using a mild reagent ($Bu_4N^+HSO_4^-$). The reaction of aldehydes and ketones having withdrawing groups on their aryl ring to the corresponding thioacetals and thioketals resulted in corresponding products in less time and with higher yields.

EXPERIMENTAL

General

All yields refer to isolated products after purification. All of the products were characterized by comparison of their spectral (IR, ^{1}H NMR, TLC, and GC) and physical data (melting or boiling points) with those of authentic samples.[31] All ^{1}H NMR spectra were recorded at 300 MHz in $CDCl_3$ relative to TMS as an internal standard. All ^{13}C NMR spectra were recorded at 75 MHz in $CDCl_3$ relative to TMS as an internal standard. All of the reactions were carried out in a mortar in a hood with strong ventilation.

Typical Procedure

A solution of benzaldehyde (5 mmol, 0.53 g), 1,2-ethanditiol (7 mmol, 0.65 g), and $Bu_4N^+HSO_4^-$ (1 mmol, 0.33 g) in 10 ml dichloromethane was stirred for 27 min in room temperature, and the reaction was monitored by TLC. After compilation of the reaction, the solvent was evaporated via rotary evaporator then 10 ml diethyl ether was added to the remaining mixture and the solution was washed with NaOH solution 10% to remove the excess thiol. This solution was dried on magnesium sulfate and purified via column chromatography.

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