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Brönsted acidic ionic liquid/NH_4NO_3 as a new reagent for the deprotection of *S*,*S*-acetals under solvent-free conditions

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An efficient, mild and chemoselective method for deprotection of *S*,*S*-acetal compounds to their corresponding carbonyl compounds using 3″-methylimidazolium hydrogen sulfate/NH_4NO_3 is reported.

Keywords: Brönsted acidic ionic liquid; deprotection; *S*,*S*-acetal; 3″-methylimidazolium hydrogen sulfate; ammonium nitrate; solvent-free

1. Introduction

Ionic liquids (IL) have been frequently used as a green solvent in place of classical organic solvents in modern synthetic chemistry (*1–5*). IL are superior to conventional organic solvents due to their extremely low vapor pressure, excellent thermal stability, reusability and ability to dissolve many organic and inorganic substrates (*6*). The application of IL as solvent and catalyst has been reported for a variety of functional group transformations but their use as acid catalysts under solvent-free conditions requires more attention (*7*). IL with Brönsted acidic counter ions such as 1-hexyl-3-methylimidazolium bisulfate ([hmim][HSO_4]) (*8*), 1-butyl-3-methylimidazolium dihydrogen phosphate ([bmim][H_2PO_4]) (*8*), 1-[2-(2-hydroxy-ethoxy)ethyl]-3-methylmidazolium bisulfate ([heemim][HSO_4]) (*8*),1-butyl-3-methylimidazolium chloroaluminate ([bmim]Cl $2AlCl_3$) (*9*), and 1-butyl-3-methylimidazolium bisulfate ([bmim][HSO_4])(*10*) have been used as acid catalysts and provide a useful medium under solvent-free conditions because of their polar nature.

Protection and deprotection of reactive functional groups are essential steps in the synthesis of polyfunctional compounds. Thioacetalization is a well-known reaction that protects the carbonyl groups of aldehydes and ketones (*11*), and is frequently used as a synthetic step for the preparation of natural products (*12*). These protecting groups are useful carbonyl protecting groups due to their stability under neutral, basic and acidic conditions (*13, 14*). Therefore, the protection and deprotection of carbonyl functional groups remain crucial challenges to organic chemists.

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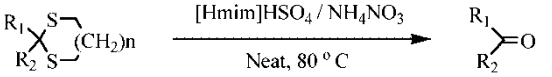
Experience shows that the critical parameters are generally the stability and cleavage of the protecting group rather than its introduction. Therefore, regeneration of the parent carbonyl group from its masked form seems to be a useful synthetic process. There are several methods for the deprotection of thioacetals (*15–22*), however, some of the systems reported suffer from drawbacks such as the presence of heavy transition metals, the use of toxic solvents, low yields, long reaction times, harsh reaction conditions and tedious work-up procedures. Thus introducing new methods, with higher efficiency, less toxicity, that are easier to handle, and which use commercially available materials are important (*20*).

During the course of our studies on the application of Brönsted acidic ionic liquid (3″-methylimidazolium hydrogen sulfate ([Hmim]HSO_4)), we have found that 3″-methylimidazolium hydrogen sulfate ([Hmim]HSO_4) has many advantages over some acidic reagents such as sulfuric acid, methanesulfonic acid, trifluoromethanesulfonic acid, and $AlCl_3$ because 3″-methylimidazolium hydrogen sulfate ([Hmim]HSO_4) is not corrosive, not destructive and it can be used as a solvent. This reagent is safe, easy to handle, environmentally benign and green. Therefore, 3″-methylimidazolium hydrogen sulfate ([Hmim]HSO_4) is an excellent candidate for acidic reagents replacement in organic reactions (*23, 24*). Herein, we wish to report the use of 3″-methylimidazolium hydrogen sulfate/NH_4NO_3 as a convenient, mild and efficient reagent for conversion of *S*,*S*-acetals to the corresponding parent carbonyl compounds (Scheme 1).



n = 0, 1
R_1 = Alkyl, Aryl, H
R_2 = Alkyl, Aryl,

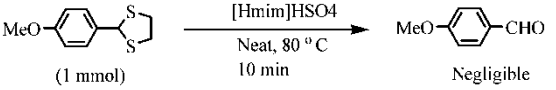
Scheme 1.

2. Results and discussion

To optimize the reaction conditions, we studied the conversion of 4-methoxyphenyl-1,3-dithiolane to 4-methoxybenzaldehyde using [Hmim]HSO_4/NH_4NO_3 in various solvents and solvent-free conditions. As shown in Table 1, in comparison to conventional methods in solvent, the yield of the reaction under solvent-free conditions is higher and the reaction time is shorter. Therefore, we employed the above conditions for the conversion of various aldehydes to the corresponding carbonyl compound under solvent-free conditions.

To evaluate the efficiency of this system, we examined the reaction of 4-methoxyphenyl-1,3-dithiolane with [Hmim]HSO_4 without using NH_4NO_3 (Scheme 2). We found that NH_4NO_3 is necessary for this conversion.

As shown in Table 2, by using this method different kinds of *S*,*S*-acetals including aromatic dithioacetal containing electron-withdrawing and electron-donating substituents, α,β-unsaturated dithioacetal and aliphatic dithioacetal were treated with [Hmim]HSO_4/NH_4NO_3 under solvent-free conditions at 80 °C. The corresponding carbonyl compounds were obtained in good to high



(1 mmol) Negligible

Scheme 2.

Table 1. Dethioacetalization of 4-methoxyphenyl-1,3-dithiolane in the presence of $[Hmim]HSO_4/NH_4NO_3$.

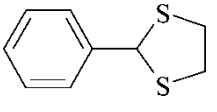
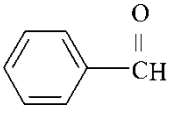
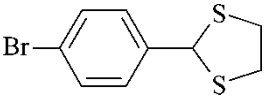
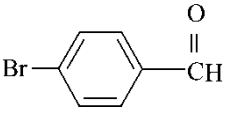
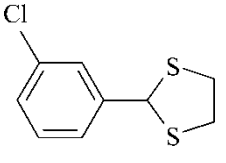
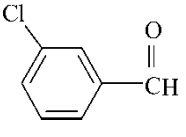
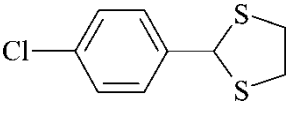
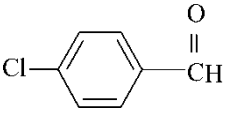
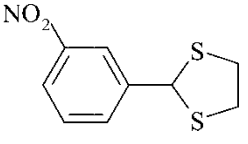
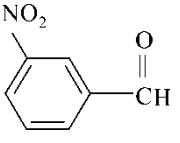
Entry	Solvent[a]	Yield (%)[b]	Time (min)
1	Dichloromethane	0	40
2	Acetonitrile	Trace	40
3	Ethylacetate	10	40
4	1,2-Dichloroethane	40	40
5	Cyclohexane	0	40
6	Solvent-free[c]	92	10

Notes: [a]The reaction was carried out in 5 ml of solvents at reflux conditions.
[b]The yields refer to isolated pure products.
[c]The reaction was carried out with 3 mmol of $[Hmim]HSO_4$ at 80 °C.

yields. The products were obtained by simple extraction with ethylacetate. By using this method we did not observe any by-products such as over oxidation to carboxylic acid (Table 2, entries 1–16) or nitration of aromatic rings. The possible mechanism for this reaction is outlined in Scheme 3.

In conclusion, we have developed a simple, mild, inexpensive, environmentally safe method for deprotection of *S*,*S*-acetals. High yields and short reaction times are noteworthy features of the reported method.

Table 2. Deprotection of various *S*,*S*-acetals in the presence of $[Hmim]HSO_4/NH_4NO_3$ under solvent-free conditions at 80 °C.[a,b]

Entry	Substrate	Product	Time (min)	Yield (%)
1			10	80
2			15	87
3			15	85
4			15	90
5			20	90

(*Continued*)

Table 2. Continued.

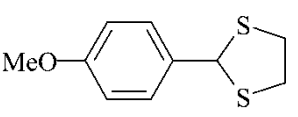
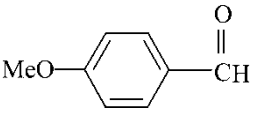
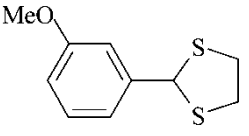
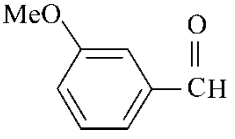
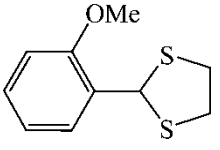
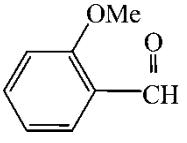
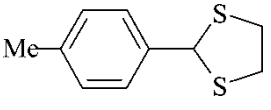
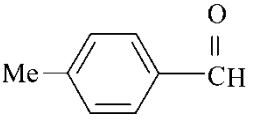
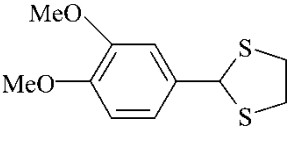
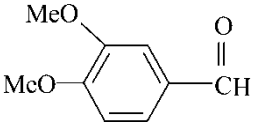
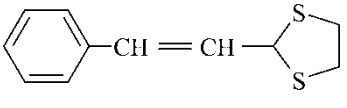
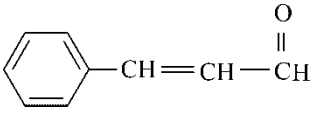
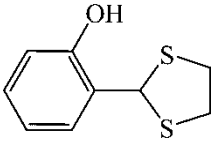
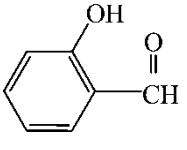
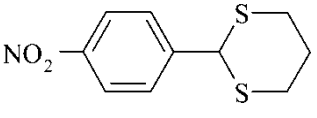
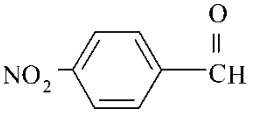
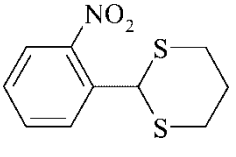
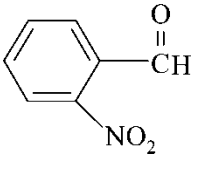
Entry	Substrate	Product	Time (min)	Yield (%)
6			10	92
7			12	88
8			12	90
9			20	88
10			15	90
11			12	90
12			35	80
13			15	91
14			20	90

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Table 2. Continued.

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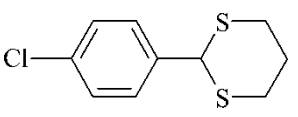
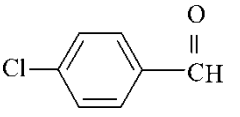
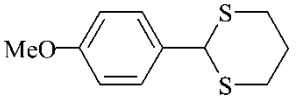
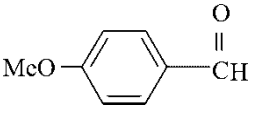
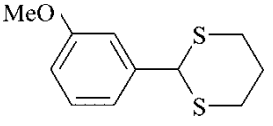
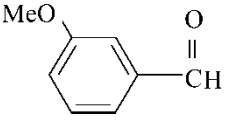
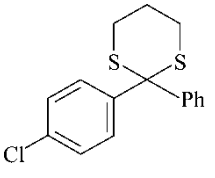
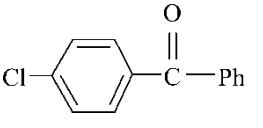
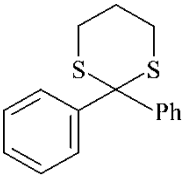
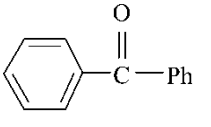
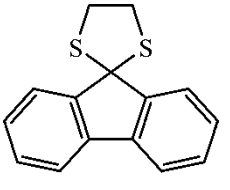
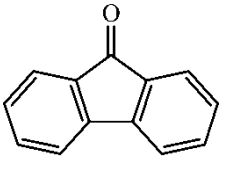
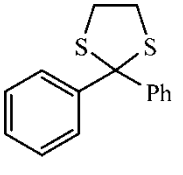
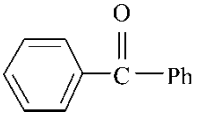
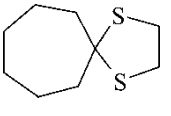
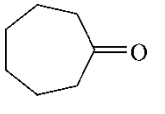
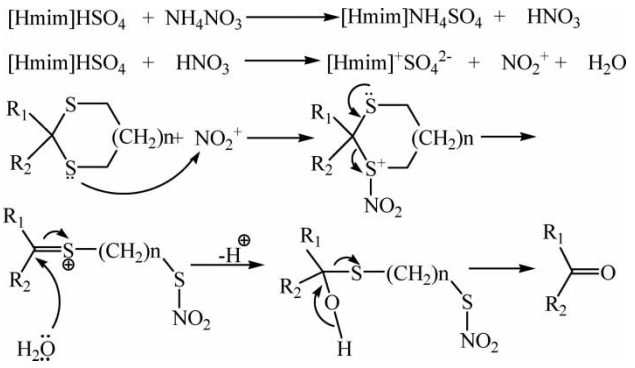
15			15	88
16			15	85
17			15	82
18			80	88
19			80	90
20			80	88
21			80	89
22			140	70

Notes: [a]The yields refer to the isolated products after purification.
[b]All of the products were characterized by physical data and their spectra (IR, ^{1}HNMR, TLC and GC).



Scheme 3.

3. Experimental procedure

3.1. *General*

Products were characterized by comparison of authentic samples (IR, ^{1}HNMR spectrum, melting point, mixed melting point and co-TLC analysis) with those obtained by literature methods (*20*) or alternative methods of synthesis. All melting points (mps) were taken on a Gallenkamp melting apparatus and are uncorrected. ^{1}HNMR spectra were recorded on a Varian 250 NMR spectrometer operating at 250 MHz. The spectra were measured in CCl_4 and $CDCl_3$ relative to TMS (0.00 ppm). GC analysis was run with a Shimadzu GC-14A. IR spectra were recorded on a Shimadzu 435 IR spectrophotometer. Spectra of solids were performed using KBr pellets. [Hmim]HSO_4 was prepared according to a previously reported method (*22*).

3.2. *Dethioacetalization of p-chlorophenyl-1,3-dithiolane using [Hmim]HSO_4/NH_4NO_3: typical procedure*

In a round bottom flask, a mixture of *p*-chlorophenyl-1,3-dithiolane (0.216 g, 1 mmol), [Hmim]HSO_4 (0.54 g, 3 mmol), NH_4NO_3 (0.10 g, 1.2 mmol) was stirred for 15 min at 80 °C. The progress of the reaction was followed by TLC/GC. After the reaction was completed, ethylacetate (2 × 10 ml) was added to the reaction mixture and after vigorous stirring was extracted and then washed with $NaHCO_3$ (5%). The organic layer was dried over anhydrous Na_2SO_4 and the solvent removed under reduced pressure. The residue was purified through a short column of silica gel (cyclohexane/EtOAc, 3:1) to obtain a pure product of *p*-chlorobenzaldehyde (0.126 g, 90%, mp: 45–47 °C).

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References

(1) Welton, T. *Chem. Rev.* **1999,** *99,* 2071–2084.
(2) Sheldon, R. *Chem. Commun*. **2001,** 2399–2407.
(3) Holbrey, J.D.; Seddon, K.R. *Clean Prod. Process.* **1999,** *1,* 223–226.

(4) Cole, A.C.; Jensen, J.L.; Ntai, I.; Tran, K.L.T.; Weaver, K.J.; Forbes, D.C.; Davis, J.H., Jr. *J. Am. Chem. Soc.* **2002,** *124,* 5962–5963.
(5) Morrison, D.W.; Forbes, D.C.; Davis, J.H., Jr. *Tetrahedron Lett.* **2001,** *42,* 6053–6055.
(6) Kwan, J.; Kim, M.-J. *J. Org. Chem.* **2002,** *67,* 6845–6847.
(7) Li, T.-S.; Zhang, Z.-H.; Yang, F.; Fu, C.-G. *J. Chem. Res.* **1998,** *1,* 38–39.
(8) Fraga-Dubreuil, J.; Bourahla, K.; Rahmouni, M.; Bazureau, J.P.; Hamelin, J. *Catal. Commun.* **2002,** *3,* 185–190.
(9) Potdar, M.K.; Mohile, S.S.; Salunkhe, M.M. *Tetrahedron Lett.* **2001,** *42,* 9285–9287.
(10) Singh, V.; Kaur, S.; Sapehiyia, V.; Singh, J.; Kad, G.L. *Catal. Commun.* **2005,** *6,* 57–60.
(11) Greene, T.W. *Protective Groups in Organic Synthesis*; Wiley: New York, 1981.
(12) Kunz, H.; Waldmann, H. *Comprehensive Organic Synthesis*; Trost, B.M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 6.
(13) Corey, E.J.; Seebach, D. *J. Org. Chem*. **1966,** *31,* 4097–4099.
(14) Mori, Y.; Kohchi, Y.; Suzuki, M. *J. Org. Chem*. **1991,** *56,* 631–637.
(15) Iranpoor, N.; Firouzabadi, H.; Shaterian, H.Z. *Tetrahedron Lett.* **2003,** *44,* 4769–4773.
(16) Hajipour, A.R.; Zarei, A.; Khazdooz, L.; Ruoho, A.E. *Synthesis* **2006,** 1480–1484.
(17) Corey, E.J.; Erickson, B.W. *J. Org. Chem*. **1971,** *36,* 3553–3560.
(18) Hajipour, A.R.; Ruoho, A.E. *Sulfur Lett.* **2002,** *25,* 151–154.
(19) Olah, G.; Vankar, D.; Arvanaghi, M.; Prekash, G. *Synthesis* **1979,** 720.
(20) Hajipour, A.R.; Khoee, S.; Ruoho, A.E. *Org. Prep. Proced. Int.* **2003,** *35,* 527–581.
(21) Kamal, A.; Reddy, P.S.M.M.; Reddy, R. *Tetrahedron Lett*. **2003,** *44,* 2857–2860.
(22) Gupta, N.; Sonu; Kad, G.L.; Singh, J. *Catal. Commun.* **2007,** *8,* 1323–1328.
(23) Hajipour, A.R.; Rafiee, F.; Ruoho, A.E. *Synlett* **2007,** 1118–1120.
(24) Hajipour, A.R.; Khazdooz, L.; Ruoho, A.E. *Catal. Commun.* **2008,** *9,* 89–96.