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Deprotection of Thioacetals Using $K_2S_2O_8$/[*bmim*]Br as a Mild and Efficient Reagent under Solvent-Free Conditions

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Summary. A straightforward and effective procedure for the deprotection of thioacetals to the corresponding carbonyl compounds using potassium persulfate and the ionic liquid [*bmim*]Br under solvent-free conditions is reported. A variety of aliphatic and aromatic 1,3-dithiolanes or 1,3-dithanes was deprotected to the corresponding carbonyl derivatives by this procedure.

Keywords. Ionic liquid; 1,3-Ditholane; 1,3-Dithiane; Solvent-free; Deprotection.

Introduction

The protection of carbonyl groups is essential in multistep syntheses until the electrophilic nature of the C=O group is to be exploited. Among carbonyl protecting groups, dithioacetals constitute an important class of compounds as acyl anion equivalents [1] or masked methylene functions in carbon–carbon bond forming reactions. These substrates are versatile [2] due to their straightforward preparation and also to their stability under basic or mildly acidic conditions [3]. The final step in the multistep synthesis involves the deprotection of the thioacetal to the original carbonyl group. Dethioacetalization of thioacetals under mild reaction conditions into the corresponding carbonyl compound is an important transformation, but is not a straightforward process. Many procedures are available in literature for this purpose [4], however, it is not always an easy process. Therefore, various hydrolytic [5] or oxidative deprotection methods [6] have been reported.

Recently, the use of $KMnO_4$, $BaMnO_4$, and MnO_2 in aprotic solvents for the selective deprotection of thioacetals has been reported [7]. However, some of the mentioned methods suffer from drawbacks like high temperatures or long reaction times, and often involve using toxic metal ions and solvents, which are detrimental to the environment. Therefore, there is still a need for an efficient, less expensive, and safer method for the deprotection of thioacetals. The toxic and volatile nature of many organic solvents, particularly chlorinated hydrocarbons that are widely used as solvents in organic synthesis, has introduced a serious threat to the environment. Therefore design of solvent-free reactions [8] and use of alternative green solvents like water [9], supercritical fluids [10], and ionic liquids [11] have received intensive attention in recent years. Although ionic liquids have been successfully employed as solvents with catalytic activities for a variety of important reactions [11], their use as catalyst under solvent-free conditions has not been explored to any great extent [12]. The high cost of most of the conventional ionic liquids prompted us to initiate an investigation to explore the use of a catalytic amount of less expensive and readily available ionic liquids for the dethioacetalization to carbonyl compounds.

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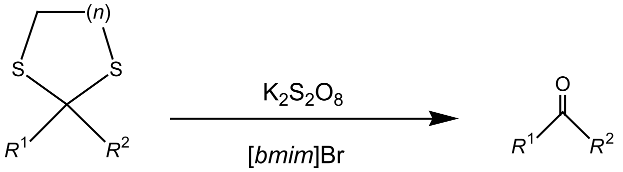
Results and Discussion

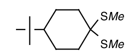
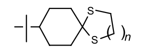
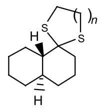
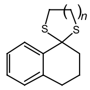
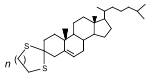
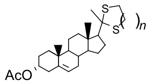


(R^1 = H, Alkyl, R^2 = Aryl), n = 1 or 2

Scheme 1

In continuation of our ongoing program to develop environmentally benign methods under solvent-free conditions [13–15], we wish to report an efficient method for the deprotection of thioacetals to their corresponding carbonyl compounds. The process readily proceeds under solvent-free conditions using potassium persulfate ($K_2S_2O_8$) in the presence of 1-butyl-3-methylimidazolium bromide [*bmim*]Br as an ionic liquid (Scheme 1). Potassium persulfate is a mild and inexpensive oxidizing agent, which can not be easily used in a common organic solvent. However, using this reagent in the presence of a catalytic amount (10 mol%) of [*bmim*]Br as an ionic liquid without using any organic solvent and under almost

Table 1. Deprotection of various dithioacetals in the presence of $K_2S_2O_8$/[*bmim*]Br under solvent-free conditions at 70–80°C[a, b]

Substrate	R^1	R^2	n	Time/min	Yield/%[c]	Mp/°C or Bp/°C/torr (Ref. [13])
2a	4-*Me*OC$_6$H$_4$	H	2	10	80	141–143/50 (141–143/50)
2b	3,4-(*Me*O)$_2$C$_6$H$_3$	H	2	10	80	81–83 (82)
2c	4-O$_2$NC$_6$H$_4$	H	1	15	78	104–106 (104–106)
2d	C$_6$H$_5$	CH$_3$	2	10	90	200–2002/760 (200–2002/760)
2e	C$_6$H$_5$	C$_6$H$_5$	2	10	87	46–48 (47–49)
2f	CH$_3$(CH$_2$)$_9$CH$_2$	H	2	22	84	239–240/760 (240/760)
2g		–	–	25	90	170–172/760 (169–171/760)
3a	C$_6$H$_5$	*Me*	1	10	81	201–202/760 (200–202/760)
3b	4-BrC$_6$H$_4$	*Me*	1	10	86	49–52 (49–52)
3c	2-O$_2$NC$_6$H$_4$	H	2	10	88	43–45 (42–43)
3d	3-O$_2$NC$_6$H$_4$	H	2	25	90	54–56 (55–58)
3e	4-O$_2$NC$_6$H$_4$	H	2	20	83	81–83 (82)
3f		–	1	20	80	170–172/760 (169–171/760)
3g		–	2	20	85	
3h		–	1	25	80	57–59 (57–59)
3i			2	25	76	57–59 (57–59)
3j	4-ClC$_6$H$_4$	H	2	10	78	45–48 (45–47)
3k	4-ClC$_6$H$_4$	*Me*	2	12	75	231–232/760 (232/760)
3l	4-Br-C$_6$H$_4$	CH$_2$Br	2	15	85	107–110 (108–110)
3m		–	1	12	90	127/13 (127/13)
3n		–	2	15	78	127/13 (127/13)
3o	*Ph*	H	2	10	80	176–1178760 (176–1178760)
3p	2-*Me*OC$_6$H$_4$	H	2	15	87	37–39 (37–39)
3q	*Me*O$_2$CCH$_2$CH$_2$	*Me*	1	20	88	192–193/760 (193–195/760)
3r	*Me*O$_2$CCH$_2$CH$_2$	*Me*	2	25	85	192–193/760 (193–195/760)
3s		–	1	25	75	79–81 (79–82)
3t		–	2	25	81	79–81 (79–82)
3u		–	1	32	78	148–150 (148–150)
3v		–	2	25	84	148–150 (148–150)

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[a] The yields refer to the isolated products after purification. [b] All products were characterized by physical data and their IR, TLC, GC, NMR spectra, and Mp or Bp

neutral conditions at 70–80°C in reaction times of 10–25 min provided products in high yields (75–90%).

To optimize the reaction conditions and evaluate the synergy between $K_2S_2O_8$, ionic liquid, and solvent-free conditions several experiments were done. When we treated 1 mmol of 4-methoxyphenylthiolane with 1 mmol $K_2S_2O_8$ in the absence of the ionic liquid in refluxing acetonitrile the yield of 4-methoxybenzaldehyde after 1 h refluxing was 45%. Reaction of 4-methoxyphenylthiolane with 1 mmol of $K_2S_2O_8$ in the presence of a catalytic amount (10 mmol%) of [*bmim*]Br in refluxing acetonitrile resulted in 4-methoxybenzaldehyde and 4-methoxybenzoic acid after 1 h in 35 and 15%. We also reacted 1 mmol of 4-methoxyphenylthiolane with 1 mmol of $K_2S_2O_8$ in the absence of ionic liquid under solvent-free conditions grinding the latter reaction mixture in a mortar for 30 s and keeping it at 70–80°C for 1 h. The yield of the conversion to the corresponding benzaldehyde was 40%. Only in the case of grinding a mixture of $K_2S_2O_8$ in the presence of a catalytic amount (10 mmol%) of [*bmim*]Br at 65–70°C the deprotection of thioacetal to the corresponding carbonyl compounds in low reaction time was high.

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

Experimental

Typical Procedure for Dethioacetalization of p-Chlorophenyl-1,3-dithiolane Using $K_2S_2O_8$/[bmim]Br

A mixture of 0.21 g *p*-chlorophenyl-1,3-dithiolane (1 mmol), 0.27 $K_2S_2O_8$ (1 mmol), and 0.03 g [*bmim*]Br (10 mol%) was ground for 1 min in a mortar with a pestle and kept at 65–70°C for the time specified in Table 1. The progress of the reaction was followed by TLC/GC. After the reaction was completed (Table 1), filtration through a sintered glass funnel followed by transfer into a separatory funnel and washing with $NaHCO_3$ (5%) drying (Na_2SO_4), and removing the solvent under reduced pressure. The residue was purified through a short column of silica gel (cyclohexane/*EtOAc*, 3/1) to obtain 0.11 g (78%) pure *p*-chlorobenzaldehyde.

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