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Sodium Hydrogen Sulfate in Poly(ethylene glycol). An Efficient Recyclable System for the Deprotection of 1,1-Diacetates

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Summary. Poly(ethylene glycol) was used as the solvent for selective deprotection of 1,1-diacetates (acylals) with easy recyclability of solvent and sodium hydrogen sulfate catalyst. This method is high yielding, fast, clean, safe, and therefore very suitable for practical organic synthesis.

Keywords. Sodium hydrogen sulfate; Poly(ethylene glycol); Deprotection; 1,1-Diacetates; Aldehydes.

Introduction

The selective protection or deprotection of a functional group is one of the important and widely carried out transformations in multistep synthesis of complex organic molecules [1]. In recent years, 1,1-diacetates have been introduced as suitable protection groups for aldehydes [2] owing to their stability in neutral and basic medium and ease of preparation [3]. In addition, they can be converted into other useful functional groups by reaction with appropriate nucleophiles [4] and used as carbonyl surrogates for asymmetric synthesis [5]. The synthesis of aldehyde enantiomers by lipase-catalysed resolution of the corresponding acylals has been reported [6]. However, the final stages of chemical manipulation require their cleavage so as to regenerate the parent aldehydes. Therefore, considerable interest has been focused on mild and selective methods. Consequently, reagents have been developed for this transformation, which include hydrochloric acid [7], sulfuric acid [8], montmorillonite clays [9], expansive graphite [10], zeolite [11], the boron triiodide-*N,N*-diethylaniline complex [12], ceric ammonium nitrate coated on silica gel [13], neutral alumina under irradiation [14], $CeCl_3 \cdot 7H_2O/NaI$ [15], CBr_4 [16], $NO^+ \cdot crown \cdot H(NO_3)_2^-$ [17], $AlCl_3$ [18], zirconium(IV) chloride [3f], $BiCl_3$ [19a], 2,6-dicarboxypyridinium chlorochromate [19b], layered

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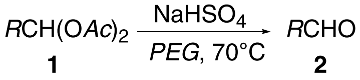

$$\underset{\mathbf{1}}{RCH(OAc)_2} \xrightarrow[PEG,\ 70^\circ C]{NaHSO_4} \underset{\mathbf{2}}{RCHO}$$

Scheme 1

zirconium sulfophenyl phosphonate [20], $Sc(OTf)_3$ [21], base-catalysed cleavage by sodium hydroxide or aqueous potassium carbonate [22], and potassium phenoxides [23]. Recently, β-cyclodextrin in aqueous medium has also been reported for this conversion [24]. However, most of these methods are associated with drawbacks including the use of harmful organic solvents and non-available, costly reagents, harsh reaction conditions, low yields, and difficulties to separate and recover the catalyst. Therefore, the development of an efficient and versatile catalytic system for the deprotection of 1,1-diacetates is highly interesting.

In recent years, liquid polymers or low melting polymers have emerged as alternative green reaction media with unique properties such as thermal stability, commercial availability, nonvolatility, immiscibility with a number of organic solvents, and recyclability. Poly(ethylene glycol)s are preferred over other polymers because they are inexpensive, nonhalogenated, easily degradable, and of low toxicity [25]. Many organic reactions have been carried out using *PEGs* as solvent or co-solvent, such as the *Heck* reaction [26], asymmetric dihydroxylation [27], *Suzuki* cross-coupling [28], oxydehydrogenation of alcohols and cyclic dienes, oxidation of sulfides, the *Wacker* reaction [29], and partial reduction of alkynes [30]. The use of *PEG* as a recyclable solvent system for the metal mediated radical polymerisation of methyl methacrylate and styrene has also been reported [31]. In view of the emerging importance of *PEG* as novel reaction media, we wish to report a mild and highly efficient method for the selective deprotection of 1,1-diacetates using sodium hydrogen sulfate as catalyst in *PEG* (MW 2000) (Scheme 1).

Results and Discussion

As shown in Table 1, treatment of phenylmethanediol diacetate (**1c**) in *PEG* in the presence of $NaHSO_4$ at 70°C afforded benzaldehyde in 95% yield. In a similar reaction, various 1,1-diacetates **1** underwent deprotection smoothly to give the corresponding aldehydes **2** in excellent yield. The reactions are mild and no side products or decomposition are observed. In the absence of catalyst, the reaction did not yield any product even after a long reaction time. Lower catalyst loading can be used with only a marginal drop in reaction rate. In these cases, lower temperature can also be applied but results in a longer reaction time. It should be mentioned that the cleavage of (*m*-nitrophenyl)methanediol diacetate (**1o**) and (*p*-nitrophenyl)methanediol diacetate (**1p**) require a little longer reaction time, possibly due to the strongly electron-withdrawing nitro substituent, which is in agreement with the reaction in an organic solvent.

The tolerance of various functional groups under the reaction conditions is noteworthy. Thus acid sensitive or oxidizable groups, such as methoxy, benzyloxy, methylenedioxy, nitro, chloro, and double bonds survive. The phenolic acetate functions (**1m** and **1n**) remain also unaffected under these reaction conditions.

Table 1. Selective cleavage of 1,1-diacetates using $NaHSO_4$ in *PEG* at 70°C

	Substrate	Time/min	Yield/%[a]
1a	$CH_3(CH_2)_4$-CH(O*Ac*)$_2$	30	85
1b	$CH_3(CH_2)_8$-CH(O*Ac*)$_2$	35	88
1c	*Ph*-CH(O*Ac*)$_2$	20	95
1d	4-*MePh*-CH(O*Ac*)$_2$	18	94
1e	2-*Me*O*Ph*-CH(O*Ac*)$_2$	17	93
1f	4-*Bn*O*Ph*-CH(O*Ac*)$_2$	15	92
1g	2-Cl*Ph*-CH(O*Ac*)$_2$	30	96
1h	4-Cl*Ph*-CH(O*Ac*)$_2$	40	97
1i	3,4-(OCH_2O)*Ph*-CH(O*Ac*)$_2$	16	96
1j	4-F*Ph*-CH(O*Ac*)$_2$	25	95
1k	2-Furyl-CH(O*Ac*)$_2$	25	90
1l	*Ph*CH=CHCH(O*Ac*)$_2$	30	93
1m	4-*Ac*O*Ph*-CH(O*Ac*)$_2$	18	92
1n	3-*Me*O-4-*Ac*O*Ph*-CH(O*Ac*)$_2$	20	93
1o	2-NO_2*Ph*-CH(O*Ac*)$_2$	120	95
1p	4-NO_2*Ph*-CH(O*Ac*)$_2$	150	93

[a] Yields refer to isolated products

Therefore the present procedure is a selective deprotection of aryl aldehyde diacetates to aryl aldehydes in the presence of the phenol acetates.

To check the reusability of solvent as well as the catalyst, the reaction mixture was extracted with diethyl ether, and *PEG* and sodium hydrogen sulfate were solidified and used in a further cleavage of **1** by charging with same substrate. The product obtained was of the same purity and yield as in the first run. *E.g.*, the treatment of **1c** in *PEG* in the presence of $NaHSO_4$ at 70°C afforded benzaldehyde in 95%, 94%, 92%, 93%, and 91% yields over five cycles.

In conclusion, we have developed an alternative cleavage procedure for 1,1-diacetates using *PEG* as the solvent. The simple procedure combined with ease of recovery and reuse of this novel catalytic system is expected to contribute to the development of a green strategy for the deprotection of 1,1-diacetates in protective group chemistry.

Experimental

All products were characterized by comparison of their spectral and physical data with those of authentic samples. Boiling points and melting points are uncorrected. ^1H NMR spectra were recorded on a BRUKER AC-P-200 spectrometer, using $CDCl_3$ as solvent and *TMS* as internal standard. IR spectra were obtained on a FTS-135 spectrometer. 1,1-diacetates **1** were prepared according to the procedure reported in Ref. [32].

General Procedure for the Deprotection of 1,1-Diacetates **1**

A mixture of 1 mmol **1**, 0.12 g $NaHSO_4$ (1 mmol), and 2 g *PEG*-2000 was placed in a 25-cm^3 round-bottomed flask and was stirred and heated at 70°C. After completion of the reaction (monitored by TLC), the reaction mixture was cooled, and extracted with $3 \times 10\,cm^3$ of diethyl ether. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel to afford pure **2**. The remaining *PEG* and $NaHSO_4$ were further washed with ether and would be recycled for subsequent reactions.

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