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ORIGINAL PAPER

1,3-Dibromo-5,5-dimethylhydantoin or *N*-bromosuccinimide as efficient reagents for chemoselective deprotection of 1,1-diacetates under solvent-free conditions

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Abstract A simple and efficient method is reported for rapid chemoselective transformation of 1,1-diacetates to the parent aldehydes using 1,3-dibromo-5,5-dimethylhydantoin or *N*-bromosuccinimide in the presence of wet SiO_2 (50%, *w*/*w*) as solid support under solvent-free conditions at room temperature. This procedure has valuable advantages, for example short reaction times, simple work-up, high yields of products, absence of solvent, and use of commercially available and non-toxic reagents.

Keywords 1,1-Diacetates · Aldehydes · Wet silica gel · 1,3-Dibromo-5,5-dimethylhydantoin · *N*-Bromosuccinimide · Solvent-free conditions

Introduction

Protection and deprotection of functional groups are important and extensively used transformations in synthetic chemistry [1, 2]. Among the different functional groups, carbonyl groups have attracted special attention in protection and deprotection reactions by virtue of their high reactivity. One useful practice for protection of carbonyl groups is 1,1-diacetylization, which has received considerable interest in recent years, because 1,1-diacetates are stable in mildly acidic and basic media and are easily prepared [3–10]. However, the search for appropriate and efficient methods for deprotection of 1,1-diacetates to the corresponding carbonyl compounds is still in high demand. In this regard, much effort has been devoted to developing numerous methodologies using various reagents such as phosphorus trichloride [11], boron triiodide–*N*,*N*-diethylaniline complex [12], mineral solid supports [13], $MoO_2(acac)_2$ [14], $FeCl_3 \cdot 6H_2O$ [15], graphite [16], $CuCl_2 \cdot 2H_2O$ [17], zirconium sulfophenyl phosphonate [18], ceric ammonium nitrate (CAN) [19], indium trichloride [20], [NO^{+}. crown. H $(NO_3)_2^{-}$] [21], Caro's acid/SiO_2 [22], $H_6P_2W_{18}O_{62} \cdot 24H_2O$ [23], $Fe_2(SO_4)_3 \cdot xH_2O$ [24], 12-molybdophoshoric acid [25], *p*-toluene sulfonic acid [26], SO_4^{2-}/SnO_2 [27], molybdenum tungsten polyoxometalates [28], $KBrO_3/MoO_3$ [29], $(NH_4)_3PW_{12}O_{40}$ [30], dodecatungstophosphoric acid ($H_3PW_{12}O_{40}$) [31], sodium hydrogen sulfate in poly(ethylene glycol) [32], indium tribromide/[bmim]PF_6 [33], indium tribromide in poly(ethylene glycol) [34], 2,6-dicarboxypyridinium chlorochromate [35], and $ZrOCl_2$ [36]. Although many of these procedures have been satisfactorily used for this propose, most suffer from one or more drawbacks, for example low yields, harsh reaction conditions, difficult work-up, and use of expensive and/or toxic reagents and solvents. In view of these limitations and also with regard to yields, reaction time, toxicity, and catalytic loading, our method is believed to be superior to those previously reported.

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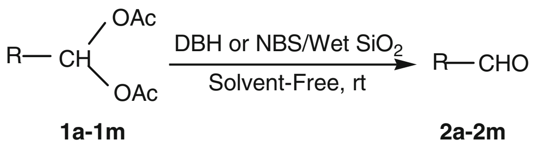
Results and discussion

Recently, 1,3-dibromo-5,5-dimethylhydantoin (DBH) and *N*-bromosuccinimide (NBS) have gained much attention as oxidation and bromination agents in organic reactions [37–39]. These compounds are relatively non-toxic, commercially available, inexpensive, and stable to air and moisture. In this work we examined the catalytic ability of DBH and NBS in the solvent-free deprotection of 1,1-diacetates to the corresponding aldehydes using wet SiO_2 as a solid support. To achieve this, 1,1-diacetates **1a–1m** were reacted with DBH or NBS in different molar ratios with or without use of wet SiO_2 to yield the corresponding aldehydes **2a–2m** (Scheme 1). According to the experimental data reported in Tables 1 and 2, the best results were obtained when the reactions were carried out using wet SiO_2. It is found that both aromatic and aliphatic 1,1-diacetates were efficiently converted to their parent aldehydes with DBH and NBS, respectively, in 72–96% and 68–94% yields (Tables 1, 2) under mild reaction conditions. It is important to note that no conversion of the 1,1-diacetates to aldehydes was observed when the reactions were carried out in the absence of either of these reagents.

Synthetically, chemoselectivity in chemistry is regarded as one of the most important aspects of organic reactions. In this regard, the selectivity of this method was investigated by conducting a competitive reaction on a 1:1 mixture of 1,1-diacetates derived from benzaldehyde and acetophenone (Scheme 2). As the ^{1}H NMR spectral analysis indicated, only the benzaldehyde diacetate was chemoselectively converted to benzaldehyde whereas the acetophenone diacetate remained intact under the same reaction condition. As a result, this procedure can be regarded as potentially useful for chemoselective deprotection of aldehyde diacetates in the presence of ketone diacetates.

Although the mechanism of this reaction is not yet fully understood, one possibility is suggested in Scheme 3. It is based on:

1. reduction of reaction rates when dry SiO_2 is used; and
2. the similar reactivities of aromatic and aliphatic aldehyde diacetates in these reactions.



Scheme 1

Table 1 Conversion of 1,1-diacetates **1a–1m** to aldehydes **2a–2m** catalyzed by wet SiO_2-supported DBH

Entry	R	Aldehyde	Catalyst[a]	Time (min)	Yield (%)[b,c]
1	C_6H_5	**2a**	2.5	3	84
2	2-ClC_6H_4	**2b**	3	5	90
3	4-ClC_6H_4	**2c**	2.5	4	96
4	2-$CH_3C_6H_4$	**2d**	2.5	4	84
5	4-$CH_3C_6H_4$	**2e**	2.5	5	72
6	2-HOC_6H_4	**2f**	2.5	5	90
7	4-CNC_6H_4	**2g**	3	4	74
8	2-$NO_2C_6H_4$	**2h**	3.25	4	80
9	3-CH_3O-2-$NO_2C_6H_4$	**2i**	3	4	84
10	$C_6H_5CH{=}CH$	**2j**	2	2	75
11	CH_3CH_2	**2k**	2.25	3	84
12	$CH_3(CH_2)_2$	**2l**	2.25	4	90
13	$(CH_3)_2CH$	**2m**	2.25	4	86

[a] Amount of catalyst used for 1 mmol of substrate

[b] Products were characterized by physical and spectral (^{1}H, ^{13}C NMR, and IR) analysis and the results were compared with data reported in the literature

[c] Isolated yields

Table 2 Conversion of 1,1-diacetates **1a–1m** to aldehydes **2a–2m** catalyzed by wet SiO_2-supported NBS

Entry	R	Aldehyde	Catalyst[a]	Time (min)	Yield (%)[b,c]
1	C_6H_5	**2a**	3	4	92
2	2-ClC_6H_4	**2b**	3.5	5	90
3	4-ClC_6H_4	**2c**	3.5	6	90
4	2-$CH_3C_6H_4$	**2d**	4	6	80
5	4-$CH_3C_6H_4$	**2e**	4	6	70
6	2-HOC_6H_4	**2f**	2.5	5	81
7	4-CNC_6H_4	**2g**	3.25	5	68
8	2-$NO_2C_6H_4$	**2h**	4	4	79
9	3-CH_3O-2-$NO_2C_6H_4$	**2i**	4	4	87
10	$C_6H_5CH{=}CH$	**2j**	3	3	80
11	CH_3CH_2	**2k**	2.25	3	87
12	$CH_3(CH_2)_2$	**2l**	2.5	4	94
13	$(CH_3)_2CH$	**2m**	3.5	6	80

[a] Amount of catalyst used for 1 mmol of substrate

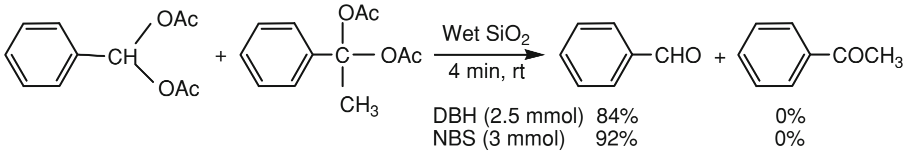
[b] Products were characterized by physical and spectral (^{1}H, ^{13}C NMR, and IR) analysis and the results were compared with data reported in the literature

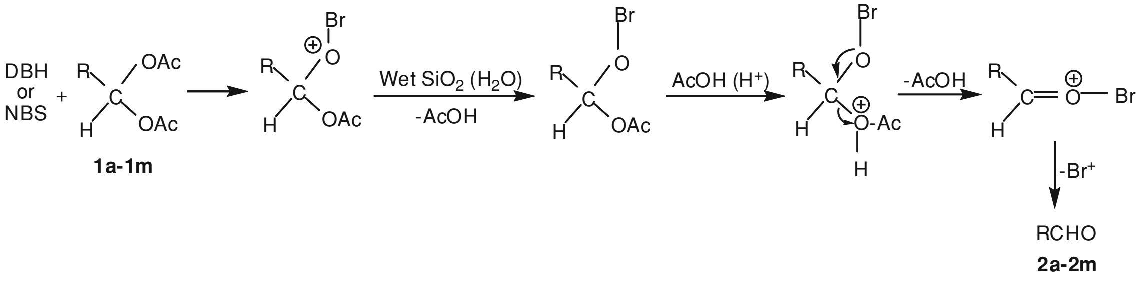
[c] Isolated yields

As shown in this mechanism, possible in-situ release of bromide ion by DBH and NBS occurs [40, 41], and this ion subsequently attacks one of the oxygen atoms in the acetate to promote the hydrolysis step.

In conclusion, we have developed a rapid, selective, simple, and efficient procedure for deprotection of

Scheme 2





Scheme 3

1,1-diacetates derived from aldehydes. This reaction proceeds rapidly at room temperature to afford the product in excellent yield with no side product formation. Short reaction times, high yields, mild conditions, easy workup, absence of the solvent in the reaction, and the use of non-toxic, commercially available, and inexpensive reagents are the main advantages of this method that make it environmentally friendly and industrially applicable.

Experimental

IR spectra were recorded on a Shimadzu 435-U-04 spectrophotometer (KBr). ^{1}H and ^{13}C NMR spectra were obtained by use of a Jeol FT NMR 90-MHz spectrometer; compounds were dissolved in $CDCl_3$ and TMS was used as internal reference. Melting points were determined on a stuart SMP3 apparatus. 1,1-Diacetates were prepared according to the literature [5, 6].

General procedure for deprotection of 1,1-diacetates

A mixture of 1,1-diacetates **1a–1m** (1 mmol) and DBH (2.25–3.25 mmol) or NBS (2.25–4 mmol) and 0.1 g wet SiO_2 (50% *w*/*w*) was placed in a mortar and pulverized at room temperature for an appropriate time (Tables 1, 2). After complete conversion of the substrate, as indicated by TLC, 10 cm^3 Et_2O was added and the mixture was then directly absorbed on silica gel. Purification was accomplished by simple column chromatography using ethyl acetate and *n*-hexane as eluents. The pure products were obtained in good to excellent yields (Tables 1, 2).

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