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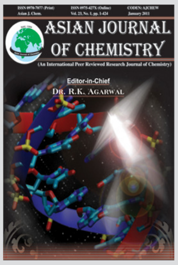

NOTE

An Eco-friendly and Mild Process for Deacetylation Reactions in Water

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A convenient methodology has been developed for the removal of a variety O-acetyl group in water. The reaction is promoted by sodium bicarbonate at room temperature. This method offers an efficient green alternative to the existing protocols since the reaction is preceded in water which is a cheap, non-toxic and non-volatile solvent.

Key Words: Deacetylation, Water, Solvent, Sodium bicarbonate.

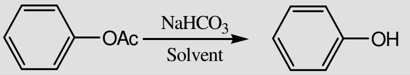
Solvent usage is often an integral part of synthetic processes, whether it is in academic or industrial sector[1]. The choice of specific solvent for a desired synthetic process can have profound economical and environmental implications. Wide array of research endeavors have focused to find out "green" reaction media, but water can undoubtedly be considered the safest solvent available[2]. Therefore synthetic organic reactions in aqueous media at ambient temperature have able to attract great interest. Among the various organic transformations commonly encountered in contemporary organic synthesis, the choice of the protection and deprotection strategy is of high importance in multifunctional molecules including the total synthesis of natural products[3]. A large variety of protective groups have been developed along with numerous methods for their removal. The acyl group is very useful for protection of hydroxyl group and it has been employed widely in the synthesis of natural products and in carbohydrate chemistry as it is easy to introduce and several methods exist to cleave it[4]. Various reagents such as HCl[5], $NaBH_4$[6], Sm/I_2[7], $TsOH/SiO_2$[8], Zn/MeOH[9], lanthanide triflates[10], $BF_3{\cdot}OEt_2$[11], $I_2/MeOH$[12], $HClO_4$-SiO_2[13], mesoporous supported Co(II)[14], tin-based alkoxide anion[15], has been commonly used for deprotection of acetyl group. Although these methods have certain applicabilities, most have associated drawbacks such as operational complexity, harsh reaction conditions, use of costly, difficult to obtain and environmentally unacceptable reagents and low yields. Therefore, development of simple and environmentally friendly method for deacetylation of alcohols utilizing inexpensive and readily available reagent at room temperature is still desirable. In our previous attempt we were able to cleave steroidal, alicyclic and aromatic acetates to respective alcohols in aqueous medium under the influence of *Pseudomonas fluorescens*[16].

All ^1H NMR spectra were recorded at 300 MHz using $CDCl_3$ as solvent and TMS as the internal reference. IR spectra were scanned either as a liquid flim on a KBr.

General procedure for the deacetylation reaction: A round bottomed flask was charged with acetate (1 mmol) and $NaHCO_3$ (6 mmol) and the mixture was stirred in water (8 mL) at room temperature for required time. After completion, the reaction mixture was diluted with water (20 mL) and extracted with ether (20 mL × 3). Combined extract was washed with brine (20 mL × 3) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the products were confirmed by comparing the ^1H NMR and IR spectral data with authentic samples.

The present work investigates whether sodium bicarbonate, a mild reagent[17], could remove acetyl group to furnish free alcohols under mild conditions. To test this rotation, a series of reactions were carried out using phenyl acetate as a substrate under different conditions. The results were summarized in Table-1. It has been seen from Table-1 that, in presence of sodium bicarbonate (9 mmol), deacetylation proceeded to afford phenol with quantitative yield (Table-1, entry 1). Use of methanol as solvent, in present reaction conditions also gave the desired product in excellent yields (Table-1, entry 2). But significant variations in yields were observed in chloroform and only 35 % yield of deacetylated product were obtained (Table-1, entry 3) use of mix solvent (water/methanol, 1:1) leads to excellent product yields (Table-1, entry 4). This method works well with 6 mmol of $NaHCO_3$ in water (Table-1, entry 5 *versus* 6). Several examples illustrating this mild procedure

TABLE-1
DEACETYLATION OF PHENYL ACETATE UNDER DIFFERENT CONDITIONS*



Entry	Solvent	$NaHCO_3$ (mmol)	Time (h)	Yield (%)**
1	Water	9	5	98
2	Methanol	9	5	98
3	Chloroform	9	5	35
4	Methanol/water (1:1)	9	5	99
5	Water	6	6	97
6	Water	3	10	65

*Phenyl acetate (1 mmol) and 8 mL solvent was used. **Isolated yields.

for deacetylation of alcohols are presented in (Table-2). The general efficiency of this reaction is evident from the variety of acetates including aromatic (Table-2, entries 1-8) alicyclic (Table-2, entry 9-11), secondary (Table-2, entry 12) and benzylic (Table-2, entry 13), were deacetylated in excellent yields and functional groups such as chloro, bromo, nitro and methoxy were not affected during the reaction. The aromatic acetate bearing an electron withdrawing group at the *p*-position (Table-2, entries 3, 4, 6 and 7) proceeded with a faster reaction rate than non-aromatic analogues (Table-2, entries 9-12).

TABLE-2
DEACETYLATION OF ACETATES WITH $NaHCO_3$*

$$R{-}O{-}COMe \xrightarrow[\text{Water, rt}]{NaHCO_3} R{-}O{-}H$$

Yield up to 98%

Entry	R	Product	Time (h)	Yield (%)
1	Phenyl	Phenol	5	98
2	*p*-Methylphenyl	*p*-Methylphenol	6	90
3	*p*-Chlorophenyl	*p*-Chlorophenol	4	97
4	*p*-Nitrophenyl	*p*-Nitrophenol	3	98
5	*p*-Methoxyphenyl	*p*-Methoxyphenol	7	88
6	*p*-Acetophenyl	*p*-Acetophenol	4	85
7	*p*-Bromophenyl	*p*-Bromophenol	4	95
8	2-Napthyl	2-Naphthol	9	85
9	Cyclohexyl	Cyclohexanol	7	80
10	Cyclopentyl	Cyclopentanol	8	70
11	Cycloheptyl	Cycloheptanol	7	76
12	1-Phenylethanyl	1-Phenylethanol	8	85
13	Benzyl	Benzyl alcohol	8	80

*All the products were characterized by ^1H NMR and IR spectra.

In conclusion, a mild, efficient and facile process is developed for the deprotection of various O-acetates in water under the influence of $NaHCO_3$. The reaction is proceed under mild conditions and resulted high yields of the parent hydroxyl compounds. Further work on acetate cleavage using chiral organic base is in progress.

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