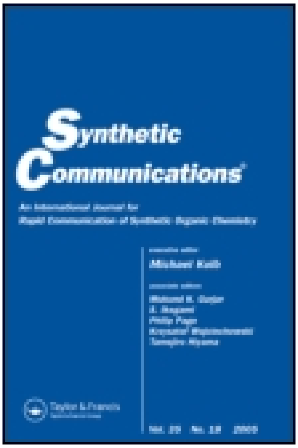

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# A Cheap, Simple, and Versatile Method for Acetylation of Alcohols and Phenols and Selective Deprotection of Aromatic Acetates Under Solvent-Free Condition

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# A Cheap, Simple, and Versatile Method for Acetylation of Alcohols and Phenols and Selective Deprotection of Aromatic Acetates Under Solvent-Free Condition

**Fatemeh Rajabi and Mohammad R. Saidi**
Department of Chemistry, Sharif University of Technology, Tehran, Iran

**Abstract:** Acyclic and cyclic acetates of various alcohols and phenols were obtained in excellent yields under mild reaction conditions in the presence of a catalytic amount of sodium hydroxide under solvent–free conditions and microwave irradiation. Selective deprotection of acetate group from the corresponding phenolic compounds was carried out in the presence of $LiClO_4.2H_2O$.

**Keywords:** Acetylation, alcohols, phenols, deprotection, solvent-free

Protection and deprotection play a significant role in organic synthesis as shown by many different methods, which have been developed for these key transformation.[1] Although few methods have been reported for the selective deprotection of aromatic acetates,[2] which are widely present in natural occurring products. Deprotection of phenolic acetate is important in multistep transformations and total synthesis.

Acetylation is one of the most common methods for the protecting of hydroxyl group, because of its facile preparation and can be easily hydrolyzed by mild basic or acidic condition.[3] Acetylation of hydroxyl groups is usually carried out with acetic anhydride or acetyl chloride under basic or acidic conditions. Many different methods for acetylation of alcohols under basic condition, such as pyridin,[4] DMAP,[5] $Bu_3P$,[6] $MgBr_2$-$R_3N$,[7]

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KF-$Al_2O_3$,[8] amino phosphanes,[9] $SiO_2$-$NaHSO_4$,[10] have been reported. A variety of acid catalysts acetylation reaction, such as $TaCl_5$,[11] TMSOTf,[12] $COCl_2$,[13] montmorillonite K-10 or KSF,[14] $Sc(OTf)_3$,[15] $Cu(OTf)_2$,[16] $In(OTf)_3$,[17] Li(OTf),[18] $La(OTf)_3$,[19] $TiCl(OTf)_3$,[20] $Sn(OTf)_3$,[21] $Sn(NTf_2)_3$,[22] $Cr(OTf)_3$,[23] $WO_3^-ZrO_2$,[24] $Bi(OTf)_3$,[25] lipase,[26] molecular sieves,[27] and $I_2$[28] were also reported in the literature.

Also pseudomonas cepacia PS lipase,[29] zeolite HSZ-360,[30] twisted amides,[31] chiral phosphines,[32] and iron complexes[33] have been used for the chemoselective acetylation. However, many of these methods have problems such as difficulty in handling the reagents, using toxic and hazardous solvents and are limited for wide applications. It was also found that the same reaction with $Ac_2O$-$Py/Al_2O_3$ was further accelerated by microwave irradiation.[34]

In the recent years, application of microwave irradiation for rapid organic synthesis as a superior, clean, and fast technique have found widespread use over the conventional heating reactions,[35,36] particularly under solvent-free conditions which are gaining more widespread uses in organic chemistry.[37–41]

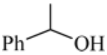
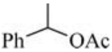
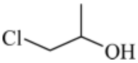
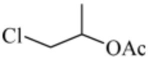
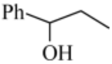
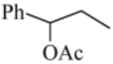
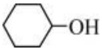
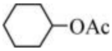
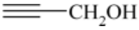
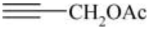
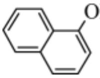
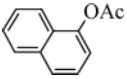
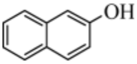
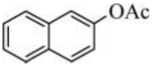
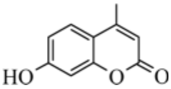
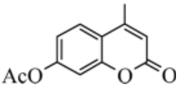
Considering the above reports and in continuation of our interests on environmentally benign solvent-free synthetic reaction and microwave-assisted organic synthesis,[42–46] herein, we describe a very simple, fast, and general protocol for the acetylation of alcohols with acetic anhydride and a catalytic amount of sodium hydroxide under microwave irradiation and solvent-free conditions.

When primary, secondary, and even tertiary alcohols were reacted with $Ac_2O$ in the presence of catalytic amounts of NaOH (ca. 0.2 equiv) under microwave irradiation and solvent-free conditions, the corresponding acetates were obtained in excellent yields. The same results were obtained when phenolic compounds were reacted with $Ac_2O$ in the presence of 0.2 equiv of NaOH, under microwave irradiation for about 1 min, (Table 1 and Scheme 1). Moreover, allylic and propargylic alcohols, diols, or triol underwent acetylation under these condition in excellent yields (Scheme 1, Table 2).

We first examined the acetylation of benzyl alcohol, 1-phenyl ethanol, and 2-naphthol using $Ac_2O$ in the absence of NaOH under microwave irradiation for 5 min. In these cases low yields (*ca.* 20%) of products were obtained.

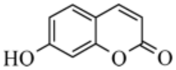
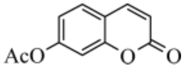
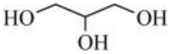
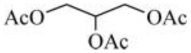
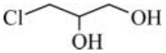
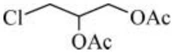
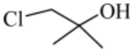
In continuation of our interest in using solid $LiClO_4$ (Azizi and Saidi,[47–49] for different organic transformations, we discovered that phenolic acetates can be easily deprotected selectively by using solid hydrated $LiClO_4$. We found out that solid hydrated $LiClO_4$ is an efficient reagent for selective deprotection of aryl acetates. Several aromatic acetates were selectively deprotected to the corresponding phenols, but aliphatic acetates were not transformed into their corresponding alcohols even after a

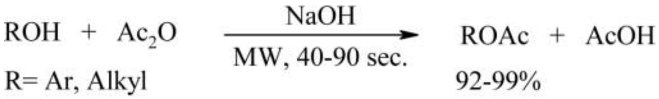
***Table 1.*** Acylating hydroxy group with $Ac_2O/NaOH$ under MW irradation

| Entry | Substrate | Product | Time (sec) | Yield (%) |
|---|---|---|---|---|
| 1 |  |  | 60 | 92 |
| 2 | $PhCH_2OH$ | $PhCH_2OAc$ | 45 | 99 |
| 3 | $Ph(CH_2)_3OH$ | $Ph(CH_2)_3OAc$ | 40 | 99 |
| 4 |  |  | 75 | 94 |
| 5 | $CH_3(CH_2)_5OH$ | $CH_3(CH_2)_5OAc$ | 70 | 99 |
| 6 | $4\text{-}MeOC_6H_5CH_2OH$ | $4\text{-}MeOC_6H_5CH_2OAc$ | 60 | 99 |
| 7 | $4\text{-}ClC_6H_5CH_2OH$ | $4\text{-}ClC_6H_5CH_2OAc$ | 70 | 97 |
| 8 | $PhCH{=}CHCH_2OH$ | $PhCH{=}CHCH_2OAc$ | 60 | 99 |
| 9 |  |  | 90 | 92 |
| 10 |  |  | 90 | 92 |
| 11 | $HOCH_2CH_2OH$ | $AcOCH_2CH_2OAc$ | 70 | 99 |
| 12 | $HO(CH_2)_3OH$ | $AcO(CH_2)_3OAc$ | 80 | 92 |
| 13 |  |  | 75 | 99 |
| 14 | $C_6H_5OH$ | $C_6H_5OAc$ | 60 | 99 |
| 15 | $4\text{-}ClC_6H_5OH$ | $4\text{-}ClC_6H_5OAc$ | 45 | 99 |
| 16 | $4\text{-}O_2NC_6H_5OH$ | $4\text{-}O_2NC_6H_5OAc$ | 45 | 99 |
| 17 | $4\text{-}BrC_6H_5OH$ | $4\text{-}BrC_6H_5OAc$ | 50 | 99 |
| 18 | $4\text{-}BrC_6H_5OH$ | $4\text{-}BrC_6H_5OAc$ | 90 | 99 |
| 19 | $4\text{-}ClC_6H_5OH$ | $4\text{-}ClC_6H_5OAc$ | 90 | 99 |
| 20 |  |  | 60 | 99 |
| 21 |  |  | 50 | 99 |
| 22 |  |  | 40 | 99 |
| 23 |  |  | 45 | 99 |

(*continued*)

***Table 1.*** Continued.

| Entry | Substrate | Product | Time (sec) | Yield (%) |
|---|---|---|---|---|
| 24 |  |  | 45 | 99 |
| 25 |  |  | 60 | 99 |
| 26 |  |  | 50 | 99 |
| 27 |  |  | 65 | 98 |



$$\underset{\text{R= Ar, Alkyl}}{\text{ROH} + \text{Ac}_2\text{O}} \xrightarrow[\text{MW, 40-90 sec.}]{\text{NaOH}} \underset{92\text{-}99\%}{\text{ROAc} + \text{AcOH}}$$

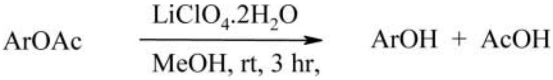
***Scheme 1.***

long reaction time. For example, when benzyl acetate is used for deacetylation in the presence of $LiClO_4 \cdot 2H_2O$, no benzyl alcohol can be obtained even after 12 h (Scheme 2, Table 2).

In conclusion, the results obtained in this study reveal that a clean, fast, simple, efficient, environmentally benign and solvent-free acetylation of hydoxyl groups can be carried out with $Ac_2O$ and small amount of sodium hydroxide which is a very cheap and common reagent (although, a solvent was used in the workup step). This method also is very useful for acetylation of hydroxyl compounds that have an acid-sensitive group such as OMe and for diols and triol. Also we have found that solid hydrated lithium perchlorate, which is used as a cheap and recyclable reagent in comparism with many other Lewis acid, is a simple and efficient reagent for selective deprotection of aryl acetates.

## EXPERIMENTAL

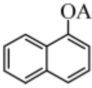
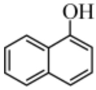
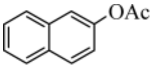
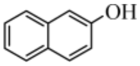
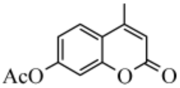
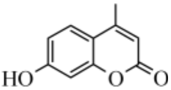
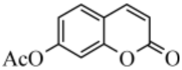
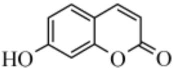
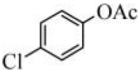
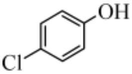
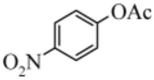
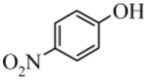
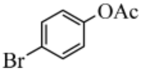
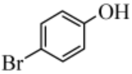
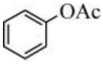
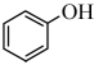
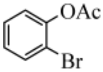
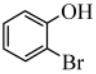
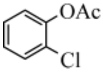
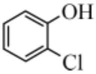
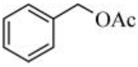
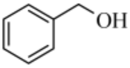
NMR spectra were recorded on a Bruker ACF 500 using chloroform-d as solvent. Infrared spectra (IR) were measured on a Perkin-Elmer 1600 FT-IR spectrometer. Column chromatography was performed on silica gel, Merck grade 60. $CH_2Cl_2$ or ether was distilled before use. Lithium perchlorare was purchased from Across. Other chemicals were purchased from Fluka and Merck.



$$\text{ArOAc} \xrightarrow[\text{MeOH, rt, 3 hr,}]{\text{LiClO}_4\text{.2H}_2\text{O}} \text{ArOH} + \text{AcOH}$$

***Scheme 2.***

*Table 2.* Deprotection of acetyl group from aromatic acetate by solid $LiClO_4$

| Entry | Substructure | Product | Time (hr) | Yield (%)[a] |
|---|---|---|---|---|
| 1 |  |  | 2.5 | 68 |
| 2 |  |  | 2.5 | 71 |
| 3 |  |  | 3.0 | 57 |
| 4 |  |  | 3.0 | 65 |
| 5 |  |  | 3.0 | 60 |
| 6 |  |  | 3.0 | 52 |
| 7 |  |  | 3.5 | 55 |
| 8 |  |  | 3.0 | 61 |
| 9 |  |  | 3.5 | 62 |
| 10 |  |  | 3.5 | 60 |
| 11 |  |  | 12 | 0.0[b] |

[a] Isolated yields.

[b] The same results were obtained for the other aliphatic acetates.

## General Procedure for Acetylation of Hydroxyl Groups with NaOH Under Solvent-free Condition

A mixture of alcohols, diols, or phenols (5 mmol), acetic anhydride (10–30 mmol, depending on the alcohol)[1], and NaOH (1–3 mmol, depending on the alcohol)[1] were placed in a sealed teflon container (screw cap type, 50 ml) and subjected to microwave irradiation in a conventional

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[1] For alcohols 10 mmol of acetic anhydride and 10 mmol of NaOH was used; for diol 20 mmol of acetic anhydride and 20 mmol of NaOH was used; for triol 30 mmol of acetic anhydride and 30 mmol of NaOH was used.

microwave oven with 30–40% of high power for 1 to 2 min (Table 1). After cooling, the mixture was diluted with $CH_2Cl_2$ (20 mL) and washed with water (2 × 20 mL), dried over $MgSO_4$, and evaporated to give the crude products. Further purification was carried out by column chromatography on basic alumina eluting with ethyl acetate/hexane, if needed. All compounds were characterized on the basis of spectroscopic data (IR, NMR, MS) and by comparison with those reported in the literature.

### General Procedure for Deprotection of Aromatic Acetates Using $LiClO_4 \cdot 2H_2O$ Under Solvent-free Condition

Aromatic acetate (2 mmol), $LiClO_4 \cdot 2H_2O$ (2 mmol), and MeOH (2 mmol) were placed in a 5 mL flask and stirred at room temperature for the time shown in Table 2. After the reaction was complete, dichloromethane (10 mL) was added and the precipitated $LiClO_4$ was recovered by filtration. The filtrate was extracted with 5% sodium hydroxyl (2 × 20 mL). After neutralizing with 5% HCl, the product was extracted with dichloromethane (2 × 10 mL), dried with $MgSO_4$. The solvent removed by using a rotary evaporator. Further purification was carried out by column chromatography on basic alumina eluting with ethyl acetate/hexane, if needed. All compounds were characterized on the basis of spectroscopic data (IR, NMR, MS) and by comparison with those reported in the literature.

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