BULLETIN

OF THE

KOREAN CHEMICAL SOCIETY

ISSN 0253-2964 BKCSDE 25(9)
Volume 25, Number 9 September 20, 2004

Communications

Facile and Efficient Method for the Acetylation of Alcohols under Microwave Irradiation

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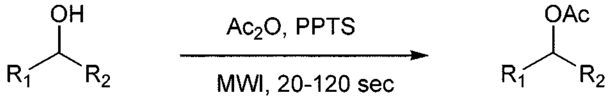
Received April 29, 2004

Key Words : Acylation, Alcohols, PPTS, Microwave, Solvent-free

Acylation reactions continue to be one of the most employed reactions for the protection of alcohols. In particular, protection of alcohols into the corresponding acetate esters has attracted much attention due to the ease of preparation and high stability of acetate esters.[1-2] Acetylation of alcohols are commonly carried out by the reaction of alcohols with acetic anhydride or acid chloride in the presence of bases such as pyridine,[3] 4-(dimethylamino)-pyridine,[4] and KF-Al_2O_3.[5] It also have been reported that a number of acids such as *p*-toluenesulfonic acid[6] and montmorillonite clays[7] could facilitate the alcohol acetylations. Much of the recent endeavors have been concentrated on the system using metal triflates such as TMSOTf,[8] $Sc(OTf)_3$,[9] $Bi(OTf)_3$,[10] $Cu(OTf)_2$,[11] and LiOTf[12] for the efficient acetylation reaction of alcohols. Although, all of the above mentioned methods has some degree of generality, most of them have one or more practical drawbacks that associated with hazardous reagents, long reaction times, toxic organic solvents, rigorous reaction conditions, and tedious experimental procedures. Furthermore, some of the metal triflates are not commercially available and their preparation and handling required stringent conditions. Therefore, development a facile and environment friendly method for the acetylation of alcohols utilizing inexpensive and readily available reagent is still quite be desirable. Pyridinium *p*-toluenesulfonate (PPTS) has often been employed in the protection of alcohols as tetrahydropyran ethers[13] and trimethylsilyl ethers.[14] However, to the best of our knowledge, the PPTS promoted acetylation reaction of alcohols has been unprecedented.



Scheme 1

Microwave irradiation technique has rapidly gained in popularity as it dramatically accelerates a variety of organic transformations.[15] Especially, microwave-promoted reactions in conjunction with environmentally benign solvent-free conditions has attracted fast growing interest as time and energy saving protocol throughout the organic synthesis.[16] Very recently, an example of microwave-promoted acetylation of aromatic alcohols has been reported by the reaction of alcohols with acetic anhydride in the presence of stoichiometric amount of imidazole for 3 min.[17]

As a continuation of our investigations on organic reactions performed under solvent-free microwave irradiation conditions, we now wish to report our results on rapid and facile preparation of acetate esters by the reaction of a variety of alcohols with acetic anhydride utilizing PPTS as a reaction promoter. Treatment of alcohols with acetic anhydride (1.5 equiv.) in the presence of PPTS (1.0 equiv.) under microwave irradiation in domestic microwave oven for 20-120 sec provided the corresponding acetate esters in very high yields. At the present reaction conditions, the use of PPTS is found to be crucial for the success of the reactions. For example, when a mixture of 1-octanol and acetic anhydride without PPTS was heated under microwave

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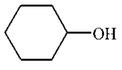
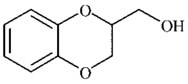
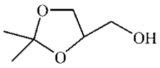
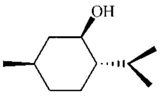
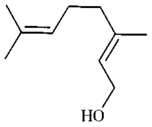
Table 1. Acetylation of alcohols under microwave irradiation

Entry	R_1	R_2	Yield (%)[a]
1	Ph	H	94
2	4-(Me)C_6H_4	H	92
3	4-(Cl)C_6H_4	H	95
4	2-(NO_2)C_6H_4	H	95
5	4-(NO_2)C_6H_4	H	92
6	Ph	CH_3	87
7	$PhCH_2$	H	94
8	$PhCH_2(CH_2)_3CH_2$	H	95
9	$PhCH_2OCH_2$	H	94
10	PhCH=CH	H	95
11	Ph	Ph	90
12	PhCO	Ph	87
13	n-C_7H_{15}	H	92
14	n-C_6H_{13}	CH_3	93
15	$HOCH_2CH_2OCH_2$	H	90
16			92
17			98
18			97
19			97
20			92

[a]Isolated yields.

irradiation for prolonged reaction time (3 min), no detectable formation of acetylated product was observed as judged by TLC analysis. To test the scope of this protocol, a variety of alcohols with different structural features were examined. As can be seen in the Table 1, all of the reactions studied for the aromatic and aliphatic alcohols were successfully afforded the acetylated products in excellent yields. Primary and secondary alcohols are acetylated equally well at the present conditions. By contrast, when the present method was subjected to a tertiary alcohol, triphenylmethanol, no reaction was observed and the starting alcohol remained unaffected. Acetylation of a dihydroxy compound, di(ethylene glycol), under present conditions using twice amounts of Ac_2O and PPTS smoothly gave diacetylated product (entry **15**). Allylic alcohols could also be acetylated cleanly in highly satisfactory manner (entries **10** and **20**). Moreover, the acetylation of alcohols containing acid-labile functionalities successfully gave the corresponding acetate esters in very high yields (entries **17** and **18**), which reflect very low acidity of the present reaction conditions. These results coupled with fast reactions clearly demonstrate the practical advantages of the present new protocol over existing alternative methods. General experimental procedure is as follows: An alcohol (1.0 mmol), acetic anhydride (0.153 g, 1.5 mmol), and pyridinium *p*-toluenesulfonate (0.251 g, 1.0 mmol) were mixed and placed in a 50 mL of glass tube. The reaction mixture was inserted in an alumina bath inside household microwave oven and irradiated (700 W) 1-6 times for a period of 20 sec with 10 sec intervals. The reaction mixture was extracted with dichloromethane (2 × 25 mL) and washed with saturated aqueous sodium bicarnonate solution (2 × 25 mL) and water (40 mL). The dichloromethane layer was separated and dried over $MgSO_4$. The solvent was evaporated *in vacuo* to give almost pure product. Further purification by flash column chromatography (SiO_2, ethyl acetate : hexane = 1 : 3) provided desired acetate ester.

In summary, we have newly found that PPTS can efficiently mediated the acetylation of various alcohols with acetic anhydride under microwave heating in solvent-free conditions.

Acknowledgment. We thank the KOSEF (R-01-1999-000-00036-0) for financial support of this work.

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