# Acetylation of Alcohols with Acetic Anhydride Promoted by N,N,N-Trimethylanilinium Tribromide

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**Abstract**—A wide variety of alcohols were reacted with acetic anhydride at room temperature in the presence of a catalytic amount of *N*,*N*,*N*-trimethylanilinium tribromide to produce the corresponding alkyl acetates in good to excellent yields. Following this procedure, acetylation of primary, secondary, and tertiary alcohols has been performed under neutral conditions.

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Acetylation of a hydroxy group is a frequently used transformation in organic chemistry. Extensive studies have been undertaken on acetylation due to its experimental simplicity and effectiveness [1]. Esters represent an important class of intermediates which are widely used in the synthesis of fine chemicals, drugs, food preservatives, perfumes, plasticizers, and pharmaceuticals [2–6]. Many synthetic procedures for the acylation of alcohols have been emerged in the recent years, such as those utilizing acetic anhydride/1,3-dibromo-5,5-dimethylhydantoin and/or trichloroisocyanuric acid [7], acetic acid/borated zirconia [8], acetic anhydride/TaCl<sub>5</sub> [9], acetic anhydride/Bi(OTf)<sub>3</sub> [10], acetyl chloride/ZrOCl<sub>2</sub>·8H<sub>2</sub>O [11], acid chloride or acid anhydride/ZnO [12], acetic anhydride/benzyl-(triphenyl)phosphonium tribromide [13], acetic anhydride or benzoic anhydride/N,N,N',N'-tetramethylethane-1,2-diamine [14], acetyl chloride/CuO [15], acetic anhydride/LiOTf [16], acetic anhydride/Zr(OTf)<sub>3</sub> [17], etc. However, these procedures are limited by some drawbacks, in particular formation of by-products, harsh reaction conditions, low yields, toxicity of reactants, heavy metal contamination, long reaction times, etc. Therefore, introducing an efficient, general,

#### Scheme 1.

 $R = 4-i-PrC_{6}H_{4}CH_{2} (a), 4-t-BuC_{6}H_{4}CH_{2} (b), 4-BrC_{6}H_{4}CH_{2} (c),$  $2,4-Cl_{2}C_{6}H_{4}CH_{2} (d), 4-FC_{6}H_{4}CH_{2} (e), 3-FC_{6}H_{4}CH_{2} (f),$  $4-O_{2}NC_{6}H_{4}CH_{2} (g), 2-ClC_{6}H_{4}CH_{2} (h), PhCH_{2}CH_{2}OH (i),$ adamantan-2-yl (j), adamantan-1-yl (k). mild, and new procedure is called for in order to prepare alkyl acetates in the presence of an appropriate catalyst.

Taking into account the above stated, in continuation of our studies on the application of new reagents and reagent systems for transformations of organic functional group [18–25] we used N,N,N-trimethylanilinium tribromide as an efficient, green, and versatile catalyst for the acetylation of alcohols.

Initially, the reaction conditions were optimized using 2-phenylethanol (**Ii**) as model substrate. Various solvents were tested, and the results are listed in Table 1. It is seen that acetone ensured the best results in terms of reactivity, and this solvent was selected for all other acetylation reactions. We thus performed acetylation of primary, secondary, and tertiary alcohols to produce the corresponding acetates using acetic anhydride and a catalytic amount of N,N,N-trimethyl-

 
 Table 1. Acetylation of 2-phenylethanol with acetic anhydride in the presence of trimethyl(phenyl)ammonium tribromide<sup>a</sup>

Solvent	Time, h	Yield, <sup>b</sup> %
Chloroform	23	93
Acetonitrile	24	Traces
Methylene chloride	22	89
Ethyl acetate	24	No reaction
Acetone	50 min	91

<sup>a</sup> Molar ratio substrate-catalyst-acetic anhydride 1:0.1:2.5.

<sup>b</sup> Yield of the isolated compound.

Substrate	Product	Reaction time, min	Yield, <sup>b</sup> %	Substrate	Product	Reaction time, min	Yield, <sup>b</sup> %
Ia	IIa	50	95	Ig	IIg	200	94
Ib	IIb	60	98	Ih	IIh	105	98
Ic	IIc	90	94	Ii	IIi	50	91
Id	IId	170	94	Ii	IIi	24 h	No reaction
Ie	IIe	70	93	Ij	IIj	120	98
If	IIf	120	90	Ik	IIk	24 h	83°

**Table 2.** Acetylation of alcohols with acetic anhydride in the presence of trimethyl(phenyl)ammonium tribromide in acetone at room temperature<sup>a</sup>

<sup>a</sup> Molar ratio substrate-catalyst-acetic anhydride 1 : 0.1 : 2.5.

<sup>b</sup> Yield of the isolated compound.

<sup>c</sup> The product was purified by short column chromatography.

anilinium tribromide in acetone under mild conditions (Scheme 1, Table 2).

The reactions were easily carried out by mixing 1 mmol of alcohol, 0.1 mmol of N,N,N-trimethylanilinium tribromide, and 2.5 mmol of acetic anhydride in acetone, followed by stirring of the resulting mixture at room temperature for appropriate time. Finally, the reaction mixture was quenched with water, and the product was isolated by extraction with methylene chloride. No acetylation of 2-phenylethanol (**Ii**) was observed for at least 24 h in the absence of N,N,N-trimethylanilinium tribromide, whereas in the presence of the catalyst the reaction was complete in 50 min (Table 2).

In summary, we have developed an efficient, simple, and environmentally friendly procedure for the acetylation of alcohols. Mild conditions, nontoxic reactants, and easy reaction work-up are some of the notable features of this protocol.

# **EXPERIMENTAL**

The acetylated products were characterized by comparison of their spectral (IR, <sup>1</sup>H and <sup>13</sup>C NMR) and physical data with authentic samples.

Acetylation of 4-*tert*-butylbenzyl alcohol with acetic anhydride in the presence of a catalytic amount of *N*,*N*,*N*-trimethylanilinium tribromide (*typical procedure*). *N*,*N*,*N*-Trimethylanilinium tribromide, 0.038 g (0.1 mmol), was added to a solution of 0.164 g (1 mmol) of 4-*tert*-butylbenzyl alcohol and 0.255 g (2.5 mmol) of acetic anhydride in 5 ml of acetone, and the reaction mixture was stirred for 70 min at room temperature (the progress of the reaction was monitored by TLC). After reaction completion, 5 ml of water was added to the mixture under stirring, and the product was extracted with methylene chloride (5×5 ml). The extract was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> (1.5 g) and evaporated to obtain 0.202 g (98%) of 4-*tert*-buthylbenzyl acetate (**Hi**).

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