A Facile and Efficient One-Step Conversion of Alcohol Triphenylmethyl Ethers to the Corresponding Acetates

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Abstract: Alcohol triphenylmethyl (trityl) ethers were readily and efficiently transformed into the corresponding acetates by reaction with acetyl bromide. Triphenylmethyl ethers can also be transformed into the corresponding substituted acetates in high yields by the use of various substituted acetyl chlorides combined with sodium iodide.

Key words: one-step conversion of protecting groups, trityl ethers, acetates, acetyl bromide, sodium iodide

Alcohol triphenylmethyl (trityl) ethers are significant functional groups and protecting groups. They have been widely used for the protection of hydroxyl functions, especially in carbohydrate chemistry. While trityl ethers are generally hydrolyzed under acidic reaction conditions to afford the parent alcohols, acetates are stable under similar acidic conditions. On the other hand, several years ago, we initiated a program focused on the one-step conversion of a hydroxyl protecting group into another. As one part of this investigation, we presented that an acetyl bromide functioned as an excellent promoter in this one-step conversion of trityl ethers into the corresponding acetates. This direct conversion of THP ethers to the corresponding acetates in one pot proceeds smoothly and efficiently without a catalyst. Moreover, substituted acetates were also obtained from substituted acetyl chlorides with an equimolar amount of sodium iodide. In contrast, Bergmeier et al. have recently reported the direct conversion of trityl ethers into acetates. This reaction was performed by the treatment of trityl ethers with 2 equivalents of acetyl chloride. Longer reaction time is needed to attain higher yield of acetates. Therefore, Bergmeier's report led us to study the use of acetyl bromide in a fast direct conversion of alcohol trityl ethers to acetates.

Herein, we wish to report the protocol for the one-step conversion of trityl ethers into the corresponding acetates. This transformation allows catalyst-free acylation of trityl ethers under mild conditions, and several functional groups including benzyl ether, p-methoxybenzyl ether, p-t-butyldiphenylsilyl (TBDPS) ether, 6 the trityl ether moiety was transformed into the corresponding acetates selectively (Runs 6–9). The bis-trityl ether of an aliphatic 1,5-diol was readily converted into the corresponding bis-acetate in 93% yield using 2.5 equivalents of acetyl chloride (Run 10). Furthermore, phenolic trityl ethers were also successfully transformed into the corresponding acetates in good yields (Run 11). In this case, p-bromophenol was also obtained in 12% yield.

To study the generality of this reaction, we examined a reaction of the 1-triphenylmethoxy-3-phenylpropane with 1.2 equivalents of acetyl chloride. After the reaction mixture was stirred for 24 hours at room temperature, usual work-up afforded 3-phenylpropyl acetate in moderate yield (54%). As mentioned earlier in this text, sodium iodide accelerates the acylation of THP ethers by reaction with acetyl chloride. After evaluation of the effect of additives, it was revealed that 1.2 equivalents of sodium iodide functioned as an excellent promoter in this one-step conversion into acetate, and that the corresponding acetate was obtained in 98% yield (Table 2, Run 1). Other successful examples, of the reaction of 3-phenylpropanol trityl ether with substituted acetyl chlorides in the presence of sodium iodide are collected in Table 2. Various substituted acetates were obtained in good to excellent yields by the combination of the corresponding substitut-
Finally, we tried the direct conversion of trityl ether into the corresponding benzoate using benzoyl bromide instead of acetyl bromide. As shown in Scheme 1, the desired reaction proceeded smoothly to give benzoate in 95% isolated yield after 20 hours at room temperature. The chemistry described here is straightforward.

Scheme 1

In summary, a novel and efficient method for the direct conversion of a broad range of trityl ethers into the corresponding acetates by using only acetyl bromide was accomplished. Additionally, we found that the corresponding substituted acetates were obtained in good yields by the reaction with substituted acetyl chlorides under the influence of sodium iodide. The mild reaction conditions, wide functional group compatibility, overall efficiency, and ease of operation, render this methodology a potentially powerful addition to the list of useful direct transformations among the protecting groups of the hydroxyl function. This methodology is very significant from the viewpoint of green chemistry because it is operationally simple under very mild reaction conditions and is also atom-efficient.

Table 1  Synthesis of Various Acetates from Trityl Ethers

<table>
<thead>
<tr>
<th>Run</th>
<th>RCH$_2$COCl</th>
<th>Time (h)</th>
<th>Yield (%)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCOCl</td>
<td>6</td>
<td>98</td>
</tr>
<tr>
<td>2</td>
<td>PhCH$_2$COCl</td>
<td>10</td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td>MeOCH$_2$COCl</td>
<td>10</td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td>PhOCH$_2$COCl</td>
<td>6</td>
<td>72</td>
</tr>
<tr>
<td>5</td>
<td>(CH$_3$)$_3$CCOCl</td>
<td>10</td>
<td>82</td>
</tr>
</tbody>
</table>

$^a$ Isolated yield of purified product.

Table 2  Synthesis of Substituted Acetates from Trityl Ethers

<table>
<thead>
<tr>
<th>Run</th>
<th>RCH$_2$COCl</th>
<th>Time (h)</th>
<th>Yield (%)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCOCl</td>
<td>6</td>
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<td>10</td>
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</tr>
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</table>

$^a$ Isolated yield of purified product.

All reactions were carried out under argon atmosphere. $^1$H and $^{13}$C NMR spectra were recorded at 400 and 100 MHz on a JEOL GSX-400, respectively. The chemical shifts are reported in ppm (δ) relative to TMS in CDCl$_3$. IR spectra were recorded in cm$^{-1}$ on a JASCO FT/IR-300E. Preparative thin-layer chromatography was performed on Wakogel B-5F silica gel with Et$_2$O–hexane.

3-Phenylpropyl Acetate; Typical Procedure

AcBr (46.6 mg, 0.38 mmol) was added to 1-triphenylmethoxy-3-phenylpropane (122.5 mg, 0.32 mmol) in 1,2-dichloroethane (1.5 ml) at r.t. under an argon atm. The reaction mixture was stirred for 1 h at r.t. and quenched with phosphate buffer (pH 7). The organic materials were extracted with Et$_2$O and dried over anhyd MgSO$_4$. The solvents were evaporated and 3-phenylpropyl acetate (57.8 mg, 100%) was isolated by preparative thin-layer chromatography on silica gel (Et$_2$O–hexane, 1:3). The product gave satisfactory $^1$H NMR and IR spectra.

IR (neat): 3027, 2952, 1739, 1366, 1243, 1037, 748, 700 cm$^{-1}$.

$^1$H NMR:  δ = 1.93–2.00 (m, 2 H), 2.05 (s, 3 H), 2.69 (t, 2 H, $J$ = 7.6 Hz), 4.09 (t, 2 H, $J$ = 6.4 Hz), 7.17–7.21 (m, 3 H), 7.26–7.31 (m, 2 H).

$^{13}$C NMR:  δ = 20.95, 30.15, 32.16, 63.83, 125.98, 128.37, 128.42, 141.18, 171.16.
References


(6) TBDMS ether is prone to be converted into the acetate unlike TBDPS ether by the reaction with AcBr. See reference 3b.