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p-Toluenesulfonyl chloride as a new and effective catalyst for acetylation and formylation of hydroxyl compounds under mild conditions

Ardeshir Khazaei [a,*], Amin Rostami [b,*], Fatemeh Mantashlo [a]

[a] *Faculty of Chemistry, Bu-Ali Sina University, Hamedan 6517838683, Iran*
[b] *Department of Chemistry, Faculty of Science, University of Kurdistan, Sanandaj 66135, Iran*

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Abstract

The catalytic application of *p*-toluenesulfonyl chloride for efficient acetylation of various types of alcohols and phenols with acetic anhydride in solvent-free conditions is reported. Also structurally diverse alcohols were formylated using formic acid based on the use of catalytic amount of *p*-toluenesulfonyl chloride under solvent-free condition. The reactions were carried out in short reaction time and in good to excellent yields at room temperature.

Keywords: *p*-Toluenesulfonyl chloride; Hydroxyl compounds; Acetylation; Formylation

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Among the various protecting groups used for the hydroxyl function, acetyl is the most common group because of the ease of formation as well as mild conditions for deprotection [1,2]. In addition, the ester moiety is a common functional group in polymers, drugs, and biologically relevant compounds. The most commonly used reagent combination for this reaction is acid anhydride in the presence of acid or base catalysts [3–15].

Formylation is also a very important process because the formate esters serve as a useful synthetic reagent and intermediate. In addition, deformylation can be effected selectively in the presence of acetate or other ester protecting groups [1]. Furthermore if the alcoholic group is planned later in synthetic scheme, deformylation can be realized *via* direct oxidation [16]. Due to the instability of the anhydride and the acid chloride of formic acid, formylation of alcohols by formic acid and transesterification using ethyl formate are important synthetic reactions. Several catalysts, such as $Sc(OTf)_3$ [17], TMSOTf [18], PPh_3/CBr_4 [19], $In(OTf)_3$[20], $Bi(OTf)_3$ [21], $K_5CoW_{12}O_{40}\cdot 3H_2O$ [22], chloral [23], $Al(HSO_4)_3$[24], sulfuric acid ([3-(3-silicapropyl)sulfanyl]-propyl) ester [25], silphos [26], silica triflate [27] and PBBS [28] have been used for formylation of alcohols.

In continuation of our studies on catalytic application of *N*-halo compounds as organocatalyst in organic chemistry [29–31], we have found that the inexpensive and commercially available *p*-toluenesulfonyl chloride, used widely as sulfonyl transfer reagent [32], has found little application as chlorinating agent [33]. Very recently, for the first time we reported catalytic application of *p*-toluenesulfonyl chloride (*p*-TsCl) as S-halo reagent in organic transformations

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* Corresponding authors.
E-mail addresses: Khazaei_1326@hotmail.com (A. Khazaei), a_rostami372@yahoo.com (A. Rostami).

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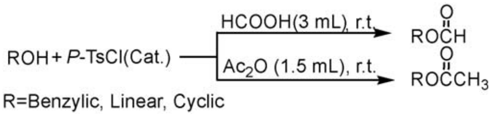
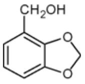
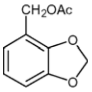
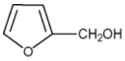
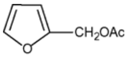
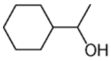
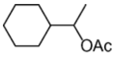
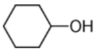
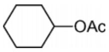
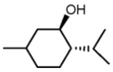
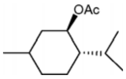
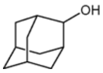
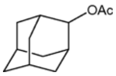
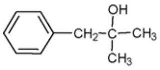
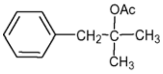
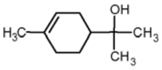
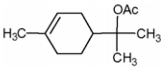
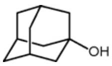
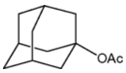


Scheme 1.

[34]. In this present research, we wish to report the catalytic application of *p*-toluenesulfonyl chloride as a source of Cl^+ for the efficient acetylation and formylation of a wide range of hydroxyl compounds under mild conditions (Scheme 1).

In order to optimize the reaction conditions, we first examined acetylation reactions of 1.0 mmol of 4-chlorobenzyl alcohol with different amounts of *p*-TsCl (0.05–0.15 mmol) and Ac_2O (1–2 mL) at room temperature under solvent-free conditions. It was observed that 0.1 mmol of *p*-TsCl in 1.5 mL of Ac_2O gave the best results and produced acetate in very short reaction time and in quantitative yields. In order to extend the scope of this acetylation reaction, the variety of hydroxyl compounds including primary, secondary, tertiary and benzylic alcohols, diols and phenols were subjected for this catalyst (Table 1). In this reaction conditions, there were no elimination products in the mixture. This

Table 1
Acetylation of alcohols or phenols (1 mmol) using Ac_2O (1.5 mL) catalyzed with *p*-TsCl (0.1 mmol) under solvent-free conditions at room temperature.

Entry	Substrate	Time (min)	Product[a]	Yield (isolated)/%
1	$4\text{-OMe–}C_6H_4CH_2OH$	9	$4\text{-OMe–}C_6H_4CH_2OAc$	87
2	$4\text{-Cl–}C_6H_4CH_2OH$	7	$4\text{-Cl–}C_6H_4CH_2OAc$	90
3	$2,4\text{-}(Cl)_2C_6H_3CH_2OH$	15	$2,4\text{-}(Cl)C_6H_3CH_2OAc$	90
4	$4\text{-F–}C_6H_4CH_2OH$	8	$4\text{-F–}C_6H_4CH_2OAc$	83
5		30		89
6		18		85
7	$PhCH_2CH_2OH$	30	$PhCH_2CH_2OAc$	85
8	$PhCH{=}CHCH_2OH$	20	$PhCH{=}CHCH_2OAc$	95
9	$CH_3(CH_2)_4CH(OH)CH_3$	25	$CH_3(CH_2)_4CH(OAc)CH_3$	93
10		43		95
11		33		96
12		83		89
13		30		86
14		180		81
15		115		75
16		25 h		87