

Direct Oxidation of Aldehydes to Methyl Esters with Urea Hydrogen Peroxide and *p*-Toluenesulfonyl Chloride



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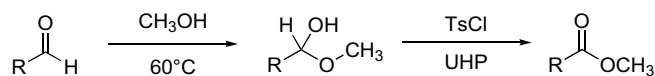
Abstract: Combination of urea hydrogen peroxide and *p*-toluenesulfonyl chloride in methanol was proved to be facile and highly efficient for the oxidative methyl esterification of various aldehydes to the corresponding carboxylic methyl esters.

Keywords: Aldehydes, esters, oxidation, peroxides, *p*-toluenesulfonyl chloride, organic chemistry.

1. INTRODUCTION

Carboxylic acid ester is a very important functionality in organic chemistry and can be found in the sub-structure of many natural products, pharmaceuticals, advanced materials, and fine chemicals [1]. Traditionally, carboxylic acid esters have been prepared by the nucleophilic substitution reaction of carboxylic acids or their derivatives with alcohols in the presence of the various acidic or basic promoters [2]. In recent years, direct oxidative esterification of aldehydes has gained considerable attention [3]. This protocol usually involved the formation of hemiacetal intermediates by the reactions of aldehydes with alcohols and subsequent oxidation in the presence of various oxidants such as iodine [4], *N*-iodosuccinimide [5], pyridinium hydrobromide perbromide [6], manganese dioxide [7], siloxanes-palladium [8], and peroxovanadium [9]. However, these methods are generally associated with certain drawbacks such as harsh reaction conditions, low yields, long reaction times, and limited range of applicable aldehydes. In the last decade, much interest has aroused on the direct esterification of aldehydes using aqueous hydrogen peroxide as a main oxidant in combination with a variety of transition-metal complexes such as V₂O₅ [10], methyltrioxorhenium [11], titanosilicate [12], iron-copper oxide [13] and iron perchlorate [14]. Recently, methyl esterification of aromatic aldehydes with hydrogen peroxide in combination with metallic Lewis acids such as calcium chloride [15], magnesium chloride [15] and zinc bromide [16] has also been reported. However, only a few methods which involved hemiacetal intermediates have been known for the direct esterification of aldehydes under metal-free reaction conditions. For example, the use of highly

concentrated 50% aqueous H₂O₂ solution [17] or reagent combination of iodine-iodobenzene diacetate was reported earlier [18]. However, these methods also suffered from disadvantage like harsh reaction conditions low yield and limited range of aldehydes. Therefore, the development of efficient oxidative system for the conversion of aldehydes to methyl esters under safe and environmentally friendly metal-free conditions would be highly appealing. Urea hydrogen peroxide (UHP) has received great attention as a safe dry alternative to aqueous hydrogen peroxide [19]. UHP proved to be a valuable oxidant in various important organic reactions due to its high thermal stability, ease of handling, and environmentally benign properties. In the course of our ongoing interest in the development of sustainable and practical oxidation methodologies, we have found that combination of UHP and *p*-toluenesulfonyl chloride (TsCl) in methanol represents an excellent oxidative system for the conversion of aldehydes to the corresponding methyl esters. In consideration of environmentally friendly reactions, this protocol is attractive, because both UHP and TsCl are inexpensive and avoid the use of the toxic transition-metal complexes. Initially, we used benzaldehyde as a model substrate and tested for the direct oxidative esterification of aldehydes to methyl esters.



Scheme (1). Conversion of aldehydes to methyl esters.

2. RESULTS AND DISCUSSION

Treatment of benzaldehyde with UHP (5.0 equiv.) and TsCl (1.0 equiv.) in 3 mL of methanol for 6 h at 60°C pro-

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vided methyl benzoate in 93% yield. When the reaction was performed using aqueous 35% H₂O₂ instead of UHP, the methyl benzoate was obtained in significantly lower yield of 75%. In the absence of TsCl, the reaction failed to give the desired methyl benzoate. It is thought the actual oxidant should be *p*-toluenesulfonyl peroxyacid formed *in situ* by the reaction of UHP and TsCl. Until now, only limited examples of oxidative reactions utilizing sulfonic peroxyacid were known. For example, polymer supported sulfonic peroxyacid formed *in situ* by the reaction of sulfonic acid moiety on the polymer surface with hydrogen peroxide were applied for the dihydroxylation of olefins [20] or the oxidation of aldehydes to carboxylic acids [21]. In addition, resin supported sulfonic peroxyacid formed *in situ* by the reaction of perfluorinated resin with hydrogen peroxide was utilized in direct esterification of aldehyde to esters in the presence of magnesium sulfate for the narrow range of aldehyde substrates [22]. To

the best of our knowledge, there is no precedent for the utilization of organic sulfonic peroxyacid for the effective oxidative esterification of aldehyde. We initially examined the effect of the variation of alcohols on the present protocol. As shown in Table 1, various alcohols such as ethanol, *n*-propanol, isopropanol, and *t*-butanol gave the desired products in the range of modest to good yields whereas phenol gave unreacted benzaldehyde. Methanol gave the highest yield among all the tested alcohols.


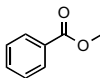

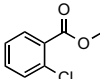
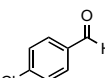
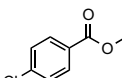
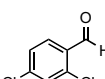
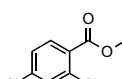
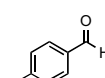
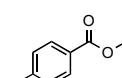
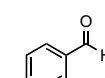
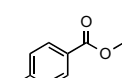
Encouraged by the excellent methyl benzoate formation, this protocol was explored for the oxidative methyl esterification of a variety of aldehydes. It was noted that the present reaction conditions exhibit excellent reactivity with various aromatic, aliphatic and heterocyclic aldehydes as shown in Table 2. In most cases, the oxidation of aldehydes exclusively afforded the corresponding methyl ester in high yield.

Table 1. Influence of different alcohols for the conversion of benzaldehyde to esters using UHP/TsCl^a.

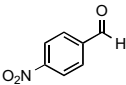
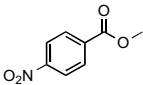
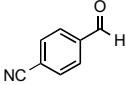
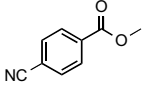

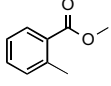
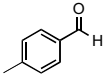
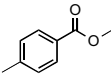

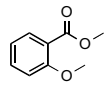
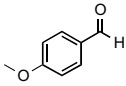
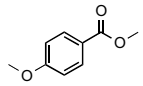

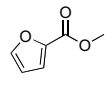

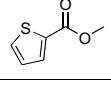
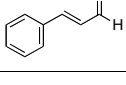
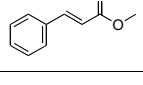
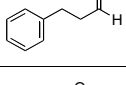
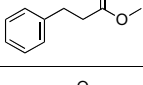

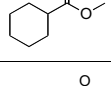
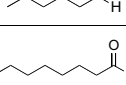
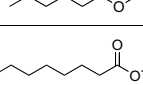
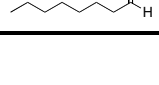
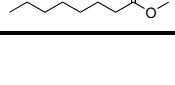
Entry	Solvent	Time (h)	Yield (%) ^b
1	MeOH	6	93
2	Ethanol	10	78
3	<i>n</i> -propanol	15	56
4	2-Propanol	20	50
5	<i>t</i> -Butanol	20	15
6	Phenol	24	N.R. ^c

^aReaction conditions: benzaldehyde (1.0 mmol), UHP (4.0 mmol), TsCl (1.0 mmol), alcohol (3 mL), 60°C. ^bIsolated yield. ^cNo reaction.

Table 2. Oxidative esterification of aldehydes to methyl esters using UHP/TsCl.

Entry	Substrate	Product	Time (h)	Yield (%) ^a
1			6	93
2			8	84
3			8	93
4			8	80
5			8	95
6			8	88

(Table 2) Contd....

Entry	Substrate	Product	Time (h)	Yield (%) ^a
7			8	98
8			8	98
9			8	88
10			8	96
11			8	84
12			8	80
13			7	82
14			4	86
15			7	83
16			8	98
17			7	76
18			8	70
19			8	75

^aIsolated yield.

Aromatic aldehydes with electron-donating or electron-withdrawing groups also provided the corresponding methyl esters in high yields. Aromatic aldehydes with ortho-substituents also provided the desired methyl carboxylates in high yields (entries **2**, **4**, **9** and **11**). In addition, the reaction worked well for 3-phenyl propanal (entry **16**). Moreover, an enal as *trans*-cinnamaldehyde was successfully converted to the methyl *trans*-cinnamate under the present reaction conditions in high yield (entry **15**).

We also attempted direct esterification of cyclic and acyclic aliphatic aldehydes to give high yields of corresponding methyl esters (entries **17**, **18** and **19**). In all of the examined cases, the carboxylic acid by-product had not been detected. In most of the hydrogen peroxide mediated methyl

esterification protocols reported earlier, electron rich aromatic aldehydes and heterocyclic aldehydes provided lower yields [16], hence this method can be served as a viable alternative method.

It is thought that the reaction presumably proceeds through oxidation of hemiacetal intermediate with *p*-toluenesulfonyl peroxyacid similar to that of the peroxide mediated conversion of alcohol to ester reported previously [23].

3. EXPERIMENTAL

A general experimental procedure for the esterification of aldehydes is as follows: An aldehyde (1 mmol) was reacted

with urea hydrogen peroxide (5 mmol) and *p*-toluenesulfonyl chloride (1 mmol) in 3 mL of methanol at 60°C for 6-8 h. After completion of the reaction, the solvent was removed *in vacuo* and the residue was dissolved in ethyl acetate (20 ml), washed with saturated sodium bicarbonate solution (20 ml) and dried over anhydrous sodium sulfate. After removal of solvent, the crude product was purified by column chromatography (230-400 mesh silica gel, *n*-hexane/ethyl acetate = 1/4). Purification of the product with silica gel flash column chromatography with ethyl acetate: hexane (1:4) eluent yielded the pure methyl carboxylic ester.

CONCLUSION

In conclusion, we have developed a novel and effective method for the oxidative methyl esterification of a variety of aldehydes by use of the reagent combination of UHP and TsCl. This method employs readily available and inexpensive reagents in metal-free reaction conditions which makes it an economical, safer and greener alternative to existing methods.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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