

Short communication

Ferric perchlorate: A novel and highly efficient catalyst for direct acetylation of THP ethers with acetic acid

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Abstract

A mild and efficient method for direct acetylation of THP ethers into corresponding acetates with acetic acid, catalyzed by ferric perchlorate is described.

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1. Introduction

During the multistep synthesis of natural products, the efficiency of the synthetic protocol employed often depends largely on protection and the deprotection of the functional groups involved. To this end, protecting groups have been playing a crucial role during the synthesis of complex natural products. Therefore, protection and deprotection of alcohols play an essential role in synthetic strategy [1]. Amongst various reagents used for protection of alcohols, 3,4-dihydro-2-pyran is employed for the protection of hydroxy group owing to the outstanding stability of tetrahydropyranyl ethers under a variety of conditions in various organic syntheses including peptide, nucleotide and carbohydrate chemistry [2]. On the other hand, acetylation of alcohols in an important and routinely utilized transformation in organic synthesis [3]. The most commonly used reagent combination for this reaction uses acetic anhydride in the presence of acid or base catalysts [4].

Although there are several method for deprotection of THP ethers [5–8] and conversion of alcohols into acetates, methods for direct conversion of THP ethers to acetate are limited and even those suffer from serious drawbacks. The method available for the direct conversion of THP ethers to the corresponding

acetates include $\text{FeCl}_3/\text{Ac}_2\text{O}$, AcOH/AcCl , $\text{Ti}/\text{Ac}_2\text{O}$, bismuth salts, $\text{Cu}(\text{OTf})_2/\text{Ac}_2\text{O}$ and ZrCl_4 [9–14].

We have recently reported ferric perchlorate as Lewis acid catalyst in protection and deprotection of THP ethers [15]. Due to importance of protection–deprotection protocol and advantages of one-pot reaction and our continuous interest in catalytic reactions [16], in this paper, we wish to describe that ferric perchlorate in catalytic amount can convert THP ethers directly to the corresponding acetates in high yields in a one-pot reaction in the presence of acetic acid.

2. Experimental

All products were known and their physical and spectroscopic data were compared with those of authentic samples. The purity of compounds was determined by GC analysis. Yields refer to GC analysis.

Acetylation of tetrahydropyranyl benzyl ether: typical procedure. To a stirred mixture of tetrahydropyranyl benzyl ether (5 mmol, 0.92 g) and acetic acid (2.5 ml), $\text{Fe}(\text{ClO}_4)_3$ (0.05 mmol, 0.025 g) was added and stirring continued at ambient temperature, for 10 min. The progress of reaction was monitored by TLC (eluent: petroleum ether:ethyl acetate, 4:1). Upon completion of reaction a solution of 10% sodium bicarbonate (15 ml) was added, and extracted with CH_2Cl_2 (2×15 ml), the organic phase dried with anhydrous calcium chloride

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Table 1
Catalytic direct acetylation of THP ethers using $\text{Fe}(\text{ClO}_4)_3$ in acetic acid

Entry	Substrate	Product	Time (min)	Yield (%) ^a
1			10	96
2			60	83
3			60	86
4			30	87
5			45	91
6			60	85
7			60	92

^a Yields refer to GC analysis.

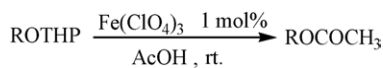
and the solvent evaporated to dryness to give the products (Table 1).

3. Results and discussion

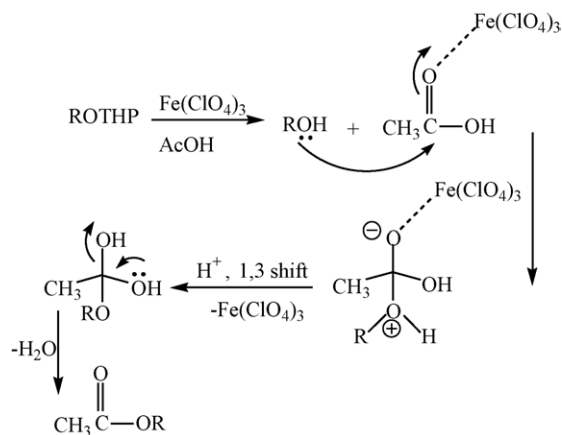
In view of emerging importance of direct deprotection and protection in multistep synthesis and our general interest in protection and deprotection protocols [17–21] we expedited direct deprotection of THP ethers to their corresponding acetates using inexpensive and available ferric perchlorate. Although there are limited method for direct conversion of THP ethers to acetates most of them have utilized relatively expensive and sometimes unavailable acetic anhydride (not easy to purchase for being reagent of conversion of morphine to heroin) and corrosive acetyl chloride. In addition use of acetic anhydride as an acetylating agent is inherently wasteful since half of the every acid anhydride molecule is lost as carboxylic acid and the use of HOAc (as solvent) with lanthanide triflate [22] whilst efficient, is expensive.

In this paper, we wish to describe a new method for direct deprotection and acetylation of THP ethers using acetic acid in the presence of catalytic amount of $\text{Fe}(\text{ClO}_4)_3$. Various THP ethers were converted to their acetates in a one-pot reaction (Scheme 1).

Primary and secondary THP ethers, both allylic and propargylic underwent deprotection and acetylation without any trace of by product. The reaction was performed by stirring a mixture of THP ethers (5 mmol) and $\text{Fe}(\text{ClO}_4)_3$ (0.05 mmol) in acetic acid (2–5 ml) at ambient temperature for the selected time to afford the corresponding acetate in good to high yields (85–96%). Our results are summarized in Table 1.



Scheme 1.



Scheme 2.

The plausible role of $\text{Fe}(\text{ClO}_4)_3$ for this direct acetylation of THP ether may be the regeneration of alcohols from THP ethers without over-oxidation of them to carbonyl compounds or over oxidation to carboxylic acids. Although Fe(III) reagents are known to be strong oxidant [23], Fe(III) of ferric perchlorate in this reaction behaves as a powerful and highly selective Lewis acid. The oxidation potential of ferric perchlorate in methanol is only 0.70 eV [24]. After regeneration of alcohol, $\text{Fe}(\text{ClO}_4)_3$ may activate the acyl moiety by coordination, starting the acetylation process with permanent regeneration of $\text{Fe}(\text{ClO}_4)_3$ which is concomitant for catalytic nature of this compound in this reaction, followed by lose of water (Scheme 2).

4. Conclusion

We have clearly demonstrated that THP ethers can directly and selectively deprotected and acetylated in the presence of catalytic amount of ferric perchlorate with inexpensive and available acetic acid. Ferric perchlorate is a hygroscopic compound, which is readily prepared by the reaction of ferric hydroxide

and can be stored for a long time in desiccators, it is not toxic, expensive and explosive even when heated in solution.

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