



Review

Synthetic applications of *p*-toluenesulfonyl chloride: A recent update

Thangaraj Devadoss

Department of Pharmaceutical Chemistry, Shri Vile Parle Kelavani Mandal's Institute of Pharmacy, Behind Gurudwara, Mumbai Agra National Highway, Dhule, Maharashtra 424001, India

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ABSTRACT

The *p*-toluenesulfonyl chloride is one of the most common reagents for converting the poor leaving group (OH) into a good leaving group (OTs). Activating the hydroxyl group enables the chemists to prepare a wide range of functional groups from the hydroxyl compound. Besides, it acts as a protecting agent, chlorinating agent, dehydrating agent, arylating agent, and catalyst. This review describes the recent synthetic applications of *p*-toluenesulfonyl chloride and discusses the mechanism of reactions wherever applicable.

1. Introduction

The reagent *p*-toluenesulfonyl chloride is a derivative of *p*-toluenesulfonic acid. Alternatively, it is called *p*-tosyl chloride and abbreviated as *p*-TsCl or TsCl [1]. The chemical properties of *p*-TsCl are almost parallel with an acid halide [2]. Fig. 1 represents the chemical structure of *p*-toluenesulfonyl chloride.

In organic chemistry, *p*-toluenesulfonyl chloride is a well-known reagent for transforming the poor leaving group into a good leaving group, particularly for the OH group [3]. This transformation facilitates the organic chemists to synthesize alkyl halide, epoxide, oxetane, and aziridine from alcohol, vicinal diol, 1,3-diol, and *N*-aryl- β -amino alcohol, respectively [4–7]. The chemical structure of the *p*-toluenesulfonyl chloride permits the organic chemists to introduce the tosyl group to primary alcohol over secondary alcohol. Besides, it allows regioselective mono and ditosylation of hydroxyl groups in carbohydrates [8].

The well-established tosylation procedure of alcohols required one equivalent of alcohol, one and a half equivalent of tosyl chloride, and two equivalents of pyridine in chloroform (Scheme 1) [9].

Selecting the appropriate base enables chemists to selectively introduce the tosyl group to the amino group over the hydroxyl group and vice versa (Scheme 2). The strong base favors the *O*-tosylation, while the weak base directs the tosylation toward the amino group [10].

In 2001, Bouzide *et al.* successfully sulfonylated a variety of primary and secondary alcohols under neutral conditions, silver oxide, and potassium iodide [11]. This neutral condition is favorable for the substrate bearing the base or acid-sensitive functional groups.

Many researchers explored the dehydrating nature of *p*-TsCl, dehydration of urea derivatives, primary amides, and formamides afforded carbodiimides, nitriles, and isocyanides, respectively [12–14]. Further, it acts as a carboxyl group activator for simple carboxylic acids, amino acids, and protected amino acids. This activation process allows the chemists to prepare functional groups like esters, amides, thioesters, amides, and ketones from carboxylic acids [15–18].

The *p*-TsCl not only converts the poor leaving group into a good leaving group but also serves as a source of a chlorine atom, aryl group, and arylsulfonyl group and serves as a catalyst in many reactions [4, 19–22].

The objective of the current review is to discuss the synthetic applications of *p*-TsCl from the year 2000 to till date.

2. Synthetic applications of *p*-toluenesulfonyl chloride

The synthetic utilities of *p*-toluenesulfonyl chloride are discussed elaborately in the following subheadings.

2.1. Tosylating agent

2.1.1. Tosylation of alcohols

Tosylation is one of the strategies to activate the hydroxyl groups. As discussed in the introduction, most commonly, tosylation is performed in the presence of a base, (Schemes 1, 2).

In 2000, Martinelli and their team members introduced the tosyl group selectively to one of the hydroxyl groups in diols with the help of dibutyltin oxide [23]. In the cyclic diols (cyclopentane-1,2-diol and

E-mail address: tdevadoss@gmail.com.

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