

# An efficient and selective tosylation of alcohols with *p*-toluenesulfonic acid<sup>☆</sup>

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**Abstract**—Silica chloride has been found to be an efficient catalyst for facile tosylation of alcohols directly with *p*-toluenesulfonic acid in methylene chloride under reflux. The process is associated with selective tosylation of *secondary* alcohols over *primary* alcohols.

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Tosylation of alcohols is widely used in organic synthesis.<sup>1</sup> Tosylation is generally carried out<sup>2</sup> with *p*-toluenesulfonic acid in methylene chloride under reflux. However, these tosylating agents are very reactive and moisture sensitive. *p*-Toluenesulfonic acid (*p*-TsOH) has also been used<sup>3</sup> as a tosylating agent but in this case expensive reagents such as trialkyl orthoformates, alkyl ethers or esters are also used. Recently, the synthesis of sulfonates has been carried out with organic base adducts of arylsulfonyls such as 1-phenylsulfonylbenzotriazole and 1-(benzenesulfonyl)- and 1-(*p*-toluenesulfonyl)-3-methylimidazolium triflates but an appreciable amount of side products were formed.<sup>4</sup> Two other methods using Fe<sup>3+</sup>-montmorillonite clay<sup>5a</sup> and CoCl<sub>2</sub>·6H<sub>2</sub>O<sup>5b</sup> have been used for direct tosylation with *p*-TsOH. However, in the first case *primary* and *secondary* alcohols behaved very similarly (e.g., MeOH and cyclohexanol both took 3 h to generate the corresponding tosylates in yields of 82% and 86%, respectively) while in the second method, tosylation of long-chain alcohols required longer times to give the products but in poor yields (e.g., 1-decanol gave the corresponding tosylate in 26% yield after 10 h). Thus there are a limited number of suitable direct tosylation methods for alcohols with *p*-TsOH and there is still a need to develop efficient protocols for this purpose.

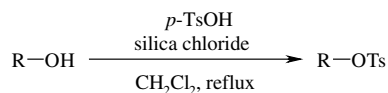
In continuation of our work<sup>6</sup> on the development of novel synthetic methodologies, we recently observed that silica chloride is an efficient heterogeneous catalyst for tosylation of alcohols with *p*-TsOH (Scheme 1).

Several alcohols were treated with *p*-TsOH in the presence of silica chloride in CH<sub>2</sub>Cl<sub>2</sub> under reflux to give the tosylation products (Table 1). *Primary* and *secondary* alcohols (except long-chain alcohols) afforded the products in very high yields. However, with long-chain alcohols the yields were only moderate (51–63%). *Secondary* alcohols required less time than *primary* alcohols. Thus a *secondary* alcohol can be tosylated chemoselectively in the presence of *primary* alcohols. As an example, when a mixture of 1-octadecanol and cyclohexanol were refluxed with *p*-TsOH in CH<sub>2</sub>Cl<sub>2</sub> in the presence of silica chloride the two compounds were converted into the corresponding tosylates in yields of 7% and 95%, respectively (Scheme 2). The selective tosylation was also observed by reacting a compound containing both *primary* and *secondary* hydroxyl groups with *p*-TsOH in the presence of silica chloride (Scheme 3). The yield of the mono-tosylate derived from the *secondary* alcohol moiety was 86% while that of di-tosylated product was only 8%. Cholesterol (entry k), even though a more complex *secondary* alcohol, produced the tosylated product efficiently and in good yield (84%).

**Keywords:** Alcohols; *p*-TsOH; Tosylation; Silica chloride; Selectivity.

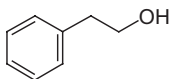
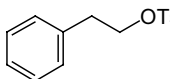
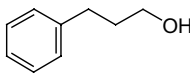
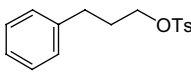
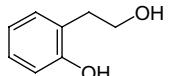
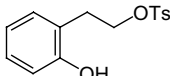
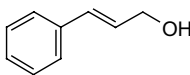
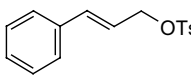
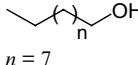
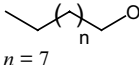
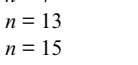
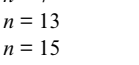
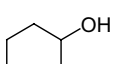
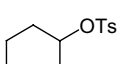
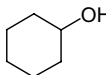
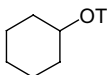


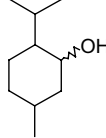
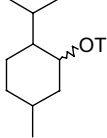
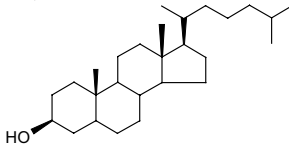
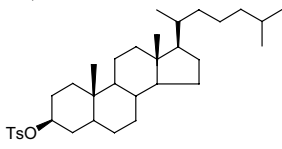


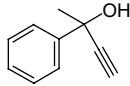
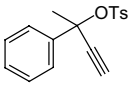


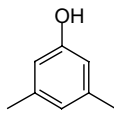
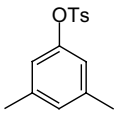
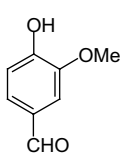
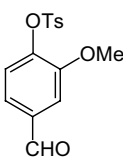
<sup>☆</sup> Part 48 in the series, 'Studies on novel synthetic methodologies'.

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Scheme 1.

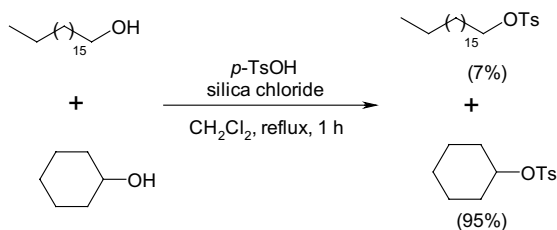
**Table 1.** Tosylation of alcohols using silica chloride<sup>a</sup>

Entry	Substrate	Product	Time (h)	Isolated yield (%)
a			2.0	86
b			1.5	91
c			2.0	89
d			2.5	80
e			3.0	63
f			4.0	54
g			4.5	51
h			1.0	95
i			2.5	87
j			2.0	94
k			1.5	84
l			10	0
m			10	0
n			10	0
o			10	0
p			10	0

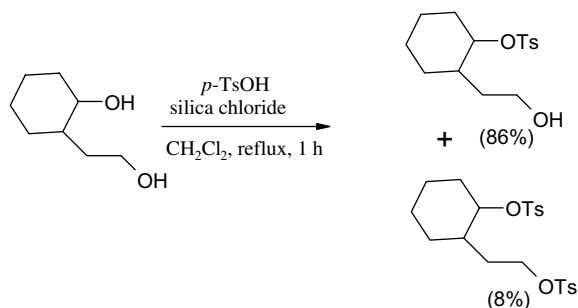
<sup>a</sup>The structures of the products were established from their spectral (<sup>1</sup>H NMR and MS) data.

Phenols and *tertiary* alcohols did not undergo tosylation under the present experimental conditions even after 10h.

The catalyst, silica chloride can easily be prepared<sup>7</sup> from the readily available materials, silica gel and thionyl chloride. It does not dissolve and so can easily be re-



Scheme 2.



Scheme 3.

moved from the reaction mixture. The only by-product of the reaction is water and thus there is no problem relating to removal of side products and the experimental procedure itself is very simple.<sup>8</sup> The structures of the products were established from their spectral (<sup>1</sup>H NMR and MS) data.

In conclusion, we have developed a convenient, facile and selective method for direct tosylation of alcohols with  $p$ -TsOH using silica chloride as a heterogeneous catalyst.  $p$ -TsOH is a cheaper tosylating agent than  $p$ -TsCl or  $p$ -Ts<sub>2</sub>O. The present method is more environmentally benign over the generally practiced tosylation with  $p$ -TsCl/pyridine, which produces large amounts of salt effluents. We feel our protocol is an attractive alternative to the existing procedures for tosylation of alcohols.

## Acknowledgement

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- General procedure for tosylation*: The alcohol (1 mmol) and  $p$ -TsOH (1.2 mmol) were dissolved in  $\text{CH}_2\text{Cl}_2$  (10 mL). Silica chloride (100 mg) was added and the mixture was heated under reflux. The reaction was monitored by TLC. After completion, the reaction mixture was filtered and the concentrated filtrate was subjected to column chromatography over silica gel using EtOAc–hexane (1:4) as eluent to obtain analytically pure tosylate.