

ZrCl₄ as an Efficient Catalyst for Selective Tosylation of Alcohols with *p*-Toluenesulfonic Acid¹

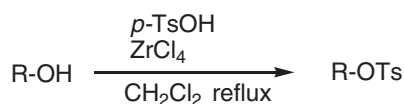
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Tosylation of alcohols has directly been carried out with *p*-toluenesulfonic acid in methylene chloride under reflux using ZrCl₄ as a catalyst. *Primary* alcohols were found to be tosylated chemoselectively over *secondary* alcohols.

Tosylation of alcohols is an important transformation in organic synthesis.² This transformation is usually achieved^{2,3} with *p*-toluenesulfonyl chloride or anhydride which is very reactive and moisture sensitive. The formation of the side products using these reagents in the presence of a base is also a problem. For direct use of *p*-toluenesulfonic acid (*p*-TsOH) as a tosylating agent, trialkyl orthoformates, alkyl ethers or esters have been employed.⁴ Recently two methods have also been developed for tosylation of alcohols with *p*-TsOH utilizing Fe³⁺-montmorillonite clay^{5a} and CoCl₂·6H₂O.^{5b} However, in the first case, the water formed in the reaction may block the acidic sites of the catalyst inhibiting the rate of the reaction while in the second case the catalyst is not suitable for tosylation of long chain alcohols which would take longer time to form the tosylates in poor yields. Herein, we wish to report a suitable method for direct tosylation of alcohols with *p*-TsOH employing ZrCl₄ as a catalyst (Scheme 1).



Scheme 1.

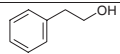
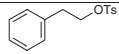
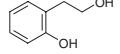
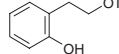
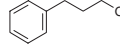
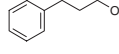
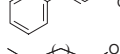
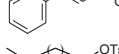
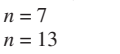
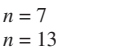
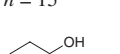
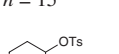
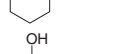
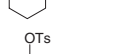

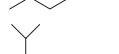
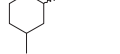
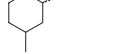
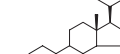
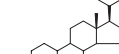
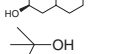
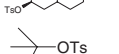
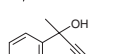
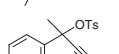
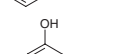
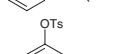
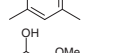
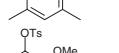
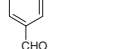
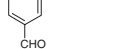
To examine the catalytic activity of different Lewis acids such as AlCl₃, SnCl₄, TiCl₄, ZrCl₄, and HfCl₄ phenyl propanol (1 equiv.) was first treated with equimolar quantity of *p*-TsOH in CH₂Cl₂ (10 mL) under reflux for 6 h in the presence of each catalyst (0.1 equiv.) separately. ZrCl₄ was found to be the most effective catalyst in term of the yield of tosylate (87%) while AlCl₃, HfCl₄, TiCl₄, and SnCl₄ formed the tosylates with the yields of 37, 28, 12, and 8%, respectively. Previously ZrCl₄ was also verified⁶ to be highly effective for direct condensation of carboxylic acids with alcohols.

The optimized condition of the present reaction was determined by tosylation of phenyl propanol (1 equiv.) with different amount of *p*-TsOH (1.0, 1.2, and 1.5 equiv.) and also using ZrCl₄ in variable quantities (0.1, 0.2, and 0.5 equiv.) Different solvents such as CH₂Cl₂, CH₃CN, and MeOH were employed and the conversion was conducted at 0 °C, room temperature and under reflux. It was observed that phenyl propanol (1 equiv.) afforded the corresponding tosylate in highest yield (94%) by heating with *p*-TsOH (1.2 equiv.) in the presence of ZrCl₄ (0.1 equiv.) in CH₂Cl₂ (10 mL) under reflux for 7 h. However, when the reaction was carried out with *p*-TsOH (1.0 equiv.) keeping all other parameters the same, the yield of the tosylate was found to be

somewhat low (86%) and the yield was not increased than 94% with *p*-TsOH in excess (1.5 equiv.) The catalyst taken in excess (0.2 and 0.5 equiv.) also retarded the yields of the tosylate (82 and 77%, respectively). The reaction conducted in CH₃CN and MeOH afforded the desired tosylate in poor yields (42 and 37%, respectively) while no product was obtained by performing the reaction at 0 °C and room temperature.

Following the above reaction condition different alcohols were now heated under reflux with *p*-TsOH in CH₂Cl₂ in the presence of ZrCl₄ to form the tosylates (Table 1). *Primary* alcohols afforded the products in very high yields. Even long-chain

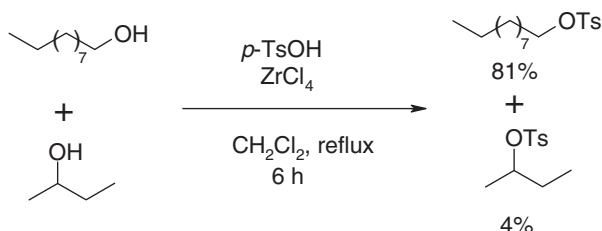
Table 1. Tosylation of alcohols using ZrCl₄^{a,b}

Entry	Substrate	Product	Time /h	Isolated Yield / %
a			6	95%
b			6.5	92
c			7	94
d			6.5	90
e			7	85
f			10	82
g			10	79
h			10	54
i			12	58
j			12.5	55
k			10	51
l			14	0
m			14	0
n			14	0
o			14	0

^aThe structure of the products were established from spectral (¹H NMR and MS) data.

^bThe starting material was the remainder in the case of a secondary alcohol and it could be recovered.

alcohols were also converted smoothly to the tosylation products. However, *secondary* alcohols took longer times to produce the tosylates in moderate yields. Thus the present catalyst catalyzes chemoselectively the tosylation of *primary* alcohols over *secondary* alcohols. To verify this, a mixture of 1-decanol and 2-butanol was treated with *p*-TsOH in the presence of $ZrCl_4$ in CH_2Cl_2 under reflux for 6 h (Scheme 2). The two compounds were converted into the corresponding tosylates in yields of 81 and 4%, respectively.



Scheme 2.

The present method was found to be unsuitable for tosylation of *tertiary* alcohols and phenols. In the first case steric factor of the intermediates may be the possible reason of not forming the tosylates while in the second case $ZrCl_4$ creates weak polarization of the $O=S<$ bond of *p*-TsOH and a phenol having poor nucleophilicity is incapable to attack the sulphur atom.

The catalyst, $ZrCl_4$ is easily available and less costly. It is now commercially utilized for its efficient catalytic activity as well as mildness. The experimental procedure for tosylation is simple⁷ and there is no problem for removal of side products. The structures of the tosylates were settled from their spectral (¹H NMR and MS) data.

In conclusion, we have demonstrated that $ZrCl_4$ is an efficient catalyst for direct tosylation of alcohols with *p*-TsOH and it catalyzes selectively the tosylation of *primary* alcohols over *secondary* alcohols. The method is economic as *p*-TsOH

is cheaper than *p*-TsCl and *p*-Ts₂O, and it is also more simple and eco-friendly than the methods using the latter two reagents as there is no problem here related to side products. The present procedure is thus expected to find useful applications for direct tosylation of alcohols.

The authors thanks CSIR, New Delhi for financial assistance.

References and Notes

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- General procedure for tosylation : To a solution of an alcohol (1 mmol) and *p*-TsOH (1.2 mmol) in CH_2Cl_2 (10 mL) $ZrCl_4$ (0.1equiv., 25 mg) was added. The mixture was heated under reflux and the reaction was monitored by TLC. After completion, the mixture was filtered and the filtrate was concentrated. The residue was subjected to column chromatography over silica gel using EtOAc-hexane (1:4) as eluent to produce pure tosylate.