Effecient and Mild Ytterbium (III)-catalyzed Tosylation of Alkohols

S. Comagic, R. Schirrmacher

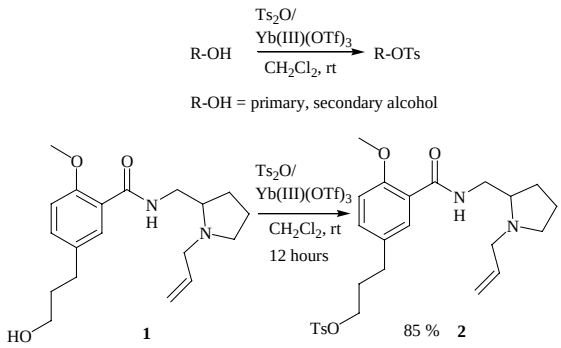
Institute for Nuclear Chemistry, Fritz-Srassmann-Weg 2, University of Mainz, 55128 Mainz, Germany

The development of mild and efficient methods for the tosylation of alcohols is constantly receiving attention due to the fact that tosylates (Ts = para-toluenesulfonyl) are among the most common leaving groups in organic synthesis. Most methods use triethylamine or pyridine as a base in the reaction of appropriate alcohols with tosylating agents. Special problems arise when TsCl/pyridine is used which is present in excess (10 equiv.) and can facilitate side reactions in more complex compounds.

In search for milder conditions for tosylation reactions, the catalytic effect of ytterbium (III) trifluoro-methanesulfonate ($Yb(III)(OTf)_3$) as a catalyst for the tosylation of a variety of primary and secondary alcohols with Ts_2O was investigated. This water-tolerant re-usable Lewis acid catalyst has been applied in a wide variety of reactions. The synthetic use of lanthanide (III)-catalyst for a ring opening in the aminolysis of epoxides and oxetanes has been reported. These applications led us to use the oxophilicity of Yb(III) to polarize and weaken the oxygen-sulfur bond making nucleophilic attacks of alcohols easier.

To prove the general feasibility of this catalysis, primary as well as sterically more challenging secondary alcohols were reacted at room temperature with Ts_2O in the presence of a catalytic amount of $Yb(III)(OTf)_3$. In nearly every case, the corresponding tosylates were obtained in an average yield of 80% after work-up. The reaction time varied between 10 min and several hours.

Typical scheme for tosylation:



e.g.: tosylation of a D2-like receptor ligand

Tosylation of alcohols: Typical procedure

To a solution of Ts_2O (1.2 eqiv.) in CH_2Cl_2 (2 mL), $Yb(III)(OTf)_3$ (10 mg, 16 µmol) was added and the suspension was stirred for 10 min until most of the solid was dissolved. The alcohol was added in pure form to the solution under continuous stirring. After the reaction was complete (TLC monitored: with n-hexane/ ethylacetate), the mixture was poured into a saturated $NaHCO_3$ solution, extracted with CH_2Cl_2 (3 x 20 mL) and the organic phase was dried over Na_2SO_4. The solvent was evaporated and purification was achieved with short column chromatography on silicagel with ethylacetate/ n-hexane.

[1] Fieser, M., Reagents for Organic Synthesis; Vol. 1; Wiley: New York, 1967, 1179
[2] Kobayashi, S., Synlett 1994, 689
[3] Chini, M.; Crotti, P.; Favero, L.; Maccia, F.; Pineschi, M., Tetrahedron Lett. 1994, 35, 433
[4] Comagic, S., Schirrmacher, R., Synthesis 2004, accepted for publication