SYNLETT Spotlight 322

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Ytterbium Trifluoromethansulfonate

Compiled by Tran Anh Tuan

Tran Anh Tuan was born in Quangninh, Vietnam, in 1982 and began studying chemistry at the National University of Hanoi, Vietnam, in 2000. After receiving the post master degree at the University of Paris-Sud XI, France, in 2005, he joined the group of Prof. David Bonnaffé and is currently undertaking a Ph.D. project financed by the French ministry of education and research. His research, under the supervision of Dr. Christine Le Narvor, is focused on the synthesis and functionalization of glycosaminoglycan fragments.

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Introduction

Ytterbium trifluoromethansulfonate [$Yb(OTf)_3$] has been widely used in organic syntheses in the last few years.[1] $Yb(OTf)_3$ is a strong Lewis acid[2] due to the hard character of Yb^{3+} ion and the presence of electron-deficient triflate in its coordination sphere. In contrast to traditional Lewis acids, such as $AlCl_3$, BF_3, $TiCl_4$, and $SnCl_4$, which are often used in stoichiometric amounts, only catalytic amounts of $Yb(OTf)_3$ are necessary. Moreover it can be easily recovered and reused without loss of activity. Interestingly, $Yb(OTf)_3$ remains catalytically active in the presence of many Lewis bases containing nitrogen, oxygen, phosphorus or sulfur atoms. The resulting water-compatibility of $Yb(OTf)_3$[3] is one of its well-known advantages, with respect to traditional Lewis acids that are very sensitive and easily decomposed or deactivated in the presence of small amounts of water. The most interesting point from a synthetic point of view is that $Yb(OTf)_3$-catalyzed reactions are clean, while $Yb(OTf)_3$ is regarded as environmentally friendly catalyst. Ytterbium triflate is prepared by heating ytterbium(III) oxide or chloride in an aqueous trifluoromethansulfonic acid solution (Scheme 1).[4,5]

$$Yb_2O_3 + 6\ TfOH \longrightarrow 2\ Yb(OTf)_3 + 3\ H_2O$$

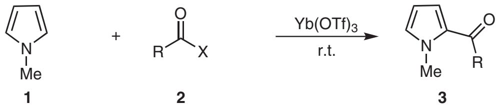
$$YbCl_3 + 3\ TfOH \longrightarrow Yb(OTf)_3 + 3\ HCl$$

Scheme 1

This reagent has been used in numerous organic transformations,[1] e.g. in aldol reactions,[6] Kharasch-type additions,[7] glycosylations,[8] Friedel–Crafts acylations,[9] dealkoxyacetylations,[10] syntheses of β-enaminones,[11] etc. This article describes some major applications in organic synthesis in the recent years.

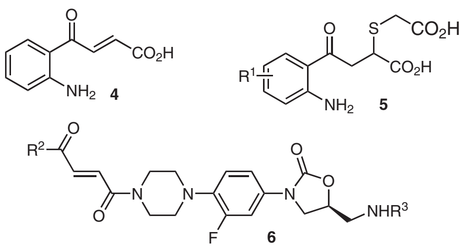
Abstracts

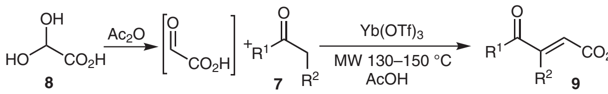
(A) *Friedel–Crafts Acylation:*
The acylation of 1-methylpyrrole has been reported recently.[12] The reaction is carried out in [bpy][BF_4] with a catalytic amount of $Yb(OTf)_3$ (10 mol%) at room temperature. Good yields were obtained (80–93%), but the reaction fails without catalyst. Moreover, the catalyst can be recycled three times without loss of activity.



R = Me, CH_2Me, $(CH_2)_2Me$, C_6H_5, Bn, CH_2Cl
X = Cl, OAc

(B) *Crotonation:*
3-Acylacrylic acids possess a high potential in the synthesis of biologically or pharmaceutically active compounds, such as **4**,[13] **5**,[14] and **6**.[15] Recently, Gorobets and co-workers described a new facile protocol for the synthesis of aromatic and heteroaromatic 3-acylacrylic acids **9** in good yields (54–78%).[16] Aromatic ketones **7**, glyoxylic acid monohydrate **8**, and $Yb(OTf)_3$ (2.5 mol%) are reacted under microwave irradiation.





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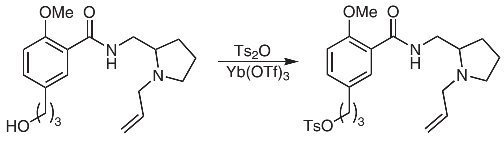
(C) *Tosylation:*
Most tosylations use triethylamine or pyridine as a base in the reaction of appropriate alcohols with the tosylating agents.[17] In 2004, Schirrmacher and Comagic[18] reported the low-yielding tosylation of **10** using TsCl and pyridine. Gratifyingly, when $Yb(OTf)_3$ is used,[18] the tosylation with Ts_2O proceeded in excellent yield (85%). These conditions were also applied for several primary and secondary alcohols and provided the tosylates in good yields (75–89%).



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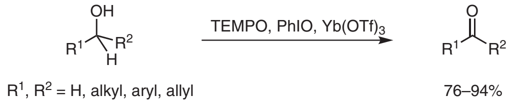
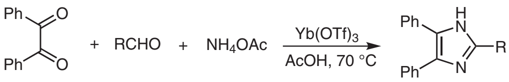
(D) *TEMPO-Mediated Oxidation:*
Vatèle described a new method for the oxidation of alcohols with iodosylbenzene relying on the utilization of the TEMPO/PhIO system as oxidizing source.[19] However, when 4-phenyl-butan-1-ol was treated with PhIO and TEMPO, only 5% of 4-phenyl-butan-1-al was obtained. In the presence of $Yb(OTf)_3$ (2 mol%), the expected aldehyde was obtained in good yield (83%). The triflate can also catalyze the oxidation of several primary or secondary alcohols into the corresponding aldehydes or ketones in good to excellent yields (76–94%).



(E) *One-Pot Multicomponent Synthesis of Substituted Imidazoles:*
$Yb(OTf)_3$ has been used for the synthesis of substituted imidazoles through three-component condensation of benzil **12**, aldehydes and ammonium acetate.[20] It was found that conventional Lewis acids, such as $AlCl_3$ and $FeCl_3$, gave low yields (45–60%) despite using 20 mol%. In contrast, the expected imidazole was obtained in excellent yield (95%) using only 5 mol% of $Yb(OTf)_3$. Moreover, the catalyst can be recovered from water by simple extraction and reused giving good yields. This procedure can also be utilized in condensations with different aromatic aldehydes in good yields (73–97%).



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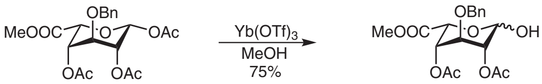
(F) *Selective Anomeric Deacetylation:*
Selective anomeric deacetylation is a key step in the oligosaccharide synthesis. $Yb(OTf)_3$ can promote the selective anomeric deacetylation of compound **14** (an important synthon involved in the synthesis of heparin sulphate fragments).[21,22] The reaction is carried out using catalytic amounts of $Yb(OTf)_3$ (5 mol%) and gave compound **15** in good yield (75%). However, $Nd(OTf)_3$ proved to be a superior catalyst. This protocol also gave good yields (61–85%) when applied to other sugar peracetates, such as α- or β-D-glucopyranose or β-D-xylopyranose peracetates. One of the most striking features is that Yb^{3+} and Nd^{3+} catalyzed the transesterification of the anomeric acetate without catalyzing the methyl glycoside formation.



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