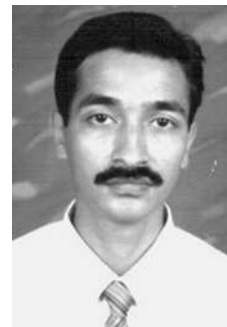


SYNLETT Spotlight 62

Tris(trifluoromethanesulfonato)indium

Compiled by Ashim Jyoti Thakur



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

Ashim Jyoti Thakur was born in Diphu, a small hilly town in Assam, India in 1974. He received a BSc (Chemistry) degree in 1995 and MSc (Chemistry) degree in 1997 from Gauhati University, Guwahati, India and was awarded a PhD(2002) from Dibrugarh University, Dibrugarh, India working in the Medicinal Chemistry Division of Regional Research Laboratory (CSIR), Jorhat 785 006, India under the guidance of Dr. J. S. Sandhu, FNA. During doctoral tenure he worked on synthetically modified pyrimidine moiety and development of synthetic methods. Currently he is a Senior Research Fellow (CSIR) in the same institution working in the same area under the supervision of Dr. Dipak Prajapati, Sc. E-II. His research interests include asymmetric synthesis of bio-potent molecules and green chemistry.

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Introduction

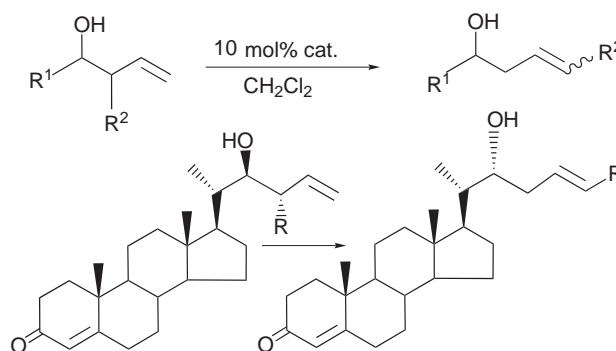
Tris(trifluoromethanesulfonato)indium or indium(III) triflate $[\text{In}(\text{OTf})_3]$ constitute one of the most important catalyst among the lanthanide triflates and indium based reagents. In recent years, indium(III) triflate has received increasing attention both as a reagent and catalyst for organic reactions.¹ It is a mild, selective, and water tolerant Lewis acid in several C–C and C-heteroatom bond forming reactions. In contrast to classical Lewis acids, which often are required in stoichiometric quantities, $\text{In}(\text{OTf})_3$ readily promotes a range of reactions in catalytic quantities soluble both in organic solvents and aqueous media. In some cases the presence of water even improves their activity. Moreover, the solubility of this reagent in water means that they can be readily recov-

ered unchanged from the aqueous phase of reaction mixtures on work up and subsequently reused, a very crucial point as far as green chemistry is concerned, for which it is gaining popularity and momentum in current research. This catalyst finds application in thioacetalization and transthoacetalization of carbonyl compounds,¹² acylation of alcohols and amines,¹³ tetrahydropyranlation and depyranlation of alcohols,¹⁴ regioselective ring opening of activated aziridines with arenes.¹⁵

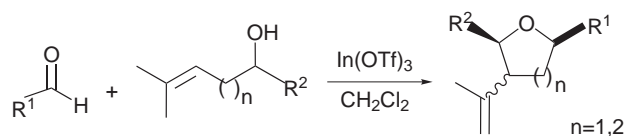
Preparation: $\text{In}(\text{OTf})_3$ is prepared from the corresponding oxide (In_2O_3) and triflic acid (TfOH) in water.² The water formed in the reaction is evaporated under reduced pressure after filtering the unreacted oxide. The resulting white powder is dried in vacuo.

Abstracts

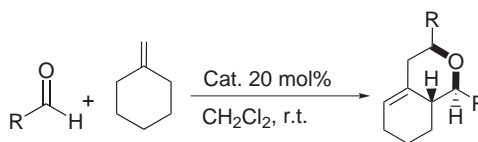
(A) Loh et al.³ have reported the $\text{In}(\text{OTf})_3$ catalyzed conversion of branched homoallylic alcohols to the thermodynamically preferred linear regioisomers followed by its utilization for the construction of steroidal side chains with anti-Cram stereoselectivity.



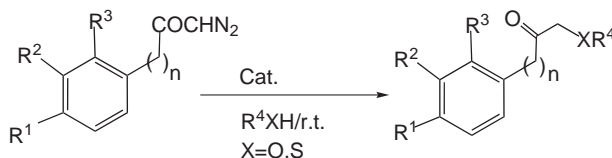
(B) Intramolecular 3,5-oxonium-ene cyclization reaction catalyzed by $\text{In}(\text{OTf})_3$ in dichloromethane afford both tetrahydropyran and tetrahydrofuran rings.⁴ A tandem 2-oxonia[3,3]-sigmatropic rearrangement/cyclization reaction of homoallylic alcohols with the corresponding aldehydes catalyzed by $\text{In}(\text{OTf})_3$ selectively afford dimethyltetrahydrofurans and methylenedimethyltetrahydro furans.⁵



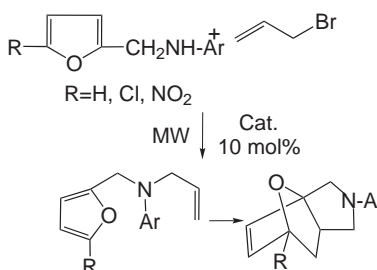
(C) An atom economic and efficient synthetic construction of tetrahydropyran rings using $\text{In}(\text{OTf})_3$ – catalyzed self-tandem carbonyl-ene, intramolecular (2,5)-oxonium-ene cyclization between aldehydes and methylene cyclohexane is reported. This method provides a facile assembly of tetrahydropyran units for the synthesis of natural products containing tetrahydropyran groups.⁶



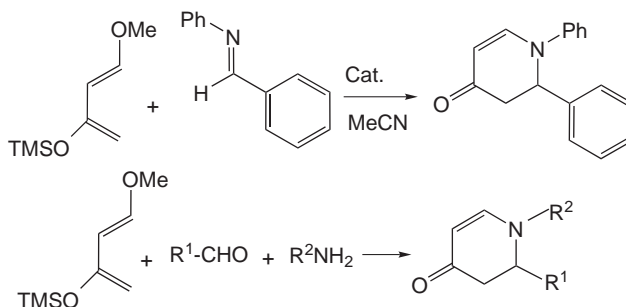
(D) Facile O–H insertion reactions of α -diazoketones with aliphatic/aromatic alcohols or benzenethiol have been developed in the presence of $\text{In}(\text{OTf})_3$ as a catalyst. These reactions provide good yields of α -alkoxy ketones. A comparative study with other Lewis acids establishes the reactivity of indium triflate in O–H insertion reactions of α -diazoketones with no Wolf rearrangement product.⁷



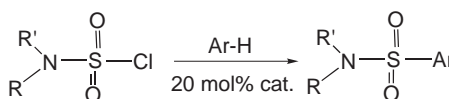
(E) $\text{In}(\text{OTf})_3$ is found to be an effective (reusable) catalyst for one step intramolecular Diels–Alder reaction of furans⁸ in the solid state under Microwave irradiation (8–10 mins, 80–90% yields). The reaction is less effective under thermal conditions (20–30 mins, 40–45% yields) and takes several days at room temperature, and undergo retro Diels–Alder reaction when purified by distillation. It should be noted that the yield of second (83%) and even third (80%) runs are comparable to that of first run (85%).



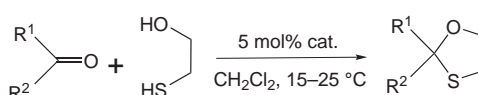
(F) At a loading as low as 0.5 mol% it can catalyse the hetero Diels–Alder reaction of Danishefsky's diene and imines. A three component coupling reaction between aldehydes, amines, and Danishefsky's diene to afford tetrahydropyridine derivatives proceeds similarly in high yields.⁹



(G) A practical synthesis of sulfonamides¹⁰ is achieved through this indium catalyst by the sulfamylation of aromatics. The reaction gives consistently good results with activated aromatics across a range of sulfamoyl chlorides but isolated yields are low with deactivated substrates such as chlorobenzenes. An intramolecular sulfamylation is also possible.



(H) This catalyst finds important applications in protection-deprotection chemistry also. In the presence of 5 mol% of this catalyst both activated and deactivated aromatic aldehydes including a sterically hindered one such as mesitaldehyde, aliphatic aldehydes and cinnamaldehyde react rapidly with 2-mercaptoethanol (1.5 equiv) in dichloromethane as the solvent at 15 °C to afford the corresponding 1,3-oxathiolanes in good to excellent yields.¹¹



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