

TiCl₃(OTf)/[bmim]Cl Assisted One-Pot Multicomponent Reaction for The Synthesis of Spiro-Thiazolidinone Derivatives

Siddheshwar D. Jadhav¹, Sandip V. Mahamuni², Umesh S. Shelake³, Dattatray B. Yedage^{1*}

¹Department of Chemistry, Willingdon College, Sangli, Maharashtra, India¹

²Department of Chemistry, Sadguru Gadge Maharaj College, Karad, Satara, Maharashtra, India²

³Department of Chemistry, Rajarshi Chhatrapati Shahu College, Kolhapur, Maharashtra, India³

^{*}dbyedagedb@gmail.com

Abstract: Multicomponent reactions (MCRs) are efficient strategies for the development of biologically active heterocyclic compounds; however, the development of economical and ecofriendly catalytic systems remains a challenge. This study aims to explore an efficient catalytic system TiCl₃(OTf)/[bmim]Cl for the synthesis of spirothiazolidinones under mild reaction conditions. This protocol offers a sustainable and efficient way for the development of bioactive heterocycles, highlighting the potential use of ionic liquid- TiCl₃(OTf) catalytic systems.

Keywords: Ionic liquid, TiCl₃(OTf)/[bmim]Cl, multicomponent reaction (MCR), spirothiazolidin-4-ones

1. INTRODUCTION

Multistep reactions always produce waste and require additional isolation procedures that often include traditionally used volatile organic compounds as well as hazardous and costly solvents after each step. Multicomponent reactions (MCRs) are very powerful synthetic strategies in chemistry where three or more reactants react in a single step to form a desired product. MCRs are having high atom economy, cost effective, can be carried out at mild reaction conditions and useful in rapid generation of structurally diverse biologically active molecules. [1]

In 2008, TiCl₃OTf-ionic liquid as an catalyst for the synthesis of thioamides was reported by J. Noei, and A.R. Khosropour.[2] Recently, Habib Firouzabadi and co-workers reported the use of TiCl₃(OTf) solid trichloro titanium(IV) trifluoromethanesulfonate catalyzed acylation of -OH and -SH under neat conditions.[3] Benzoylation and transesterification of alcohols, phenols and thiols was also reported at higher temperature under solvent-free conditions. In 2015, Asadollah Farhadi and coworkers employed TiCl₃(OTf) solid catalyst with ionic liquid in MCR to synthesize 3,4-dihydropyrimidin-2(1H)-ones/ thiones.[4]

Spiro compounds have been categorized with notable biological activities, such as antimycobacterial, anti-inflammatory, antiviral, and antitumor activities.[5-7] Heterocyclic moieties that contain a thiazolidin-4-one ring are also accompanying with pharmacological effects, such as antioxidant,[8] antitubercular,[9] anti-inflammatory,[10] antibacterial,[9] antifungal,[11] cytotoxic,[11] anticancer,[10] antiproliferative,[12] antihyperglycemic and antidyslipidemic agents.[13] Over the last three decades, many synthetic methodologies have been developed for the synthesis of spirothiazolidin-4-ones and 4-thiazolidinones using wide range of catalytic systems. Some methods use 1-butyl-3-methylimidazolium and 1-methylimidazolium with inorganic anions like PF₆, BF₄, and PTSA,[14] sulfonated mesoporous silica,[15] urea-choline chloride as a deep eutectic solvent with carbon-SO₃H as a solid acid catalyst,[16] and CuSO₄.5H₂O (10 mol%) with PEG-400,[17] DCC,[18] HBTU,[19] deep eutectic solvent,[20] MCM-41-supported

