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Catalysis

Aerosil-Supported Ionic-Liquid-Phase (ASILP) Mediated Synthesis of 2-Substituted Benzimidazole Derivatives as AChE Inhibitors

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Aerosil supported ionic liquid phase (ASILP) has been prepared by confinement of ionic liquid $[Bmim]PF_6$ on the aerosil support by adsorption interactions. This novel ASILP served as robust heterogeneous catalyst in the synthesis of biologically relevant 2-substituted benzimidazoles from *o*-phenylenediamines and aryl aldehydes in high yields under mild reaction conditions. The molecular docking studies revealed potential of 2-substituted benzimidazoles to act as acetyl cholinesterase inhibitors (AChE).

Introduction

The advent of green chemistry principles has raised a strong attention in redesigning synthetic processes so that use of hazardous substances and the generation of toxic waste can be avoided.[1] A number of strategies and scientific tools have been explored to realize sustainable chemical processes.[2] With this regard, much attention has recently been focused on the concept of supported ionic liquid phase (SILP) catalysis involving immobilization of ionic liquids (ILs) onto a surface of a porous high area support material.[3] This novel class of advanced materials constitutes one of the powerful green tools for catalyzing sustainable chemical processes. The interest in SILP catalysts stems from their interesting properties such as environmentally benign nature, high activity and selectivity, easy handling, ease of product separation and the efficient catalysts recycling. In addition, the processes applying SILP catalysts can be performed in continuous mode using fix bed reactors.[4] The concept of SILP catalysis has significantly progressed in the last few years, resulting in new applications for various organic transformations.[5] The SILP catalysts are usually prepared by depositing ILs on the surface of high area porous material either by covalent bonding or adsorption interactions.[6a,b,c] The majority of the supports used in SILP catalysis are either porous silica gels or polymer based materials.[7] In addition, carbon nanotubes,[8] active carbon cloth,[9] chitosan,[10] magnetic nanoparticles,[11] and carbon nanofibers supported on sintered metal fibers[12] have also been sporadically employed as supports. To expand the scope of SILP catalysis, it is necessary to explore new fundamental approaches to current catalytic systems. To achieve this objective, it is necessary to evaluate compatibility of new supports in the synthesis of SILP catalysts since their performance is strongly dependent upon the choice of support material. In this regard, we sought to explore the compatibility of aerosil which is commercially available, pyrogenic, amorphous silica powder with primary particles of spherical shape with average diameter of 7–40 nm with high specific surface area of 200 m^2/g. These intriguing features of aerosil spurred us to investigate its compatibility as a support in the synthesis of SILP catalysts.

Benzimidazoles are a class of pre-eminent heterocycles and the molecular scaffold of prime medicinal importance.[13] 2-Substituted benzimidazoles constitute important class of benzimidazoles that have received significant attention because of their biological activities such as antibacterial, anticancer, anti-oxidants, anti-inflammatory, anti-diabetic, antiviral, antiproliferative and antituberculosis activity.[14] Owing to their high therapeutic potential, synthesis of 2-substitiuted benzimidazoles has received increasing attention from various scientific communities. The traditional routes for synthesis of 2-substituted benzimidazoles involve the reaction between *o*-phenylenediamine and carboxylic acid or their derivatives[14] and thermal or acid promoted cyclization of *N*-(*N*-arylbenzimidoyl)-1,4-benzoquinoneimines.[15] Recently, direct condensation of *o*-phenylenediamine and aryl aldehydes is reported to be the most convenient method for the preparation of 2-substituted benzimidazoles.[16] A variety of catalyst such as TiO_2NPs,[17] UHP/12,[18] $CeCl_3$-$7H_2O$,[19] saccharose,[20] zeolite,[21] CAN /methanol,[22] solid acid Scolicite,[23] heteropoly acid,[24] imidazolium trifluoroacetate protic ionic liquid,[25] carbon disulphide,[26] CoCl2 6H2O,[27] have been reported to catalyse this

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