Synthesis and Characterization of Functionalized Amino Coumarins in Ionic liquid

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ABSTRACT

Reductive amination of carbonyl compounds was carried out by using aliphatic quarternary ammonium based ionic liquids. 2, 3-dihydroxy-N, N, N-tributylpropanaminum chloride (DTPTf) ionic liquid was synthesized, characterized and used for reductive amination of carbonyl compounds in the presence of sodium borohydride. These preliminary results are encouraging and advocate dual role of ionic liquid as a medium and reducing agent for proficient conversion of aldehydes to amines, however, reductive amination reaction needs to be established for other substituents.

Keywords: reductive amination, Ionic liquid, thiazolyl Coumarin.

1. INTRODUCTION

Coumarin, 2H-1-benzopyran-2-one is a natural product found in the plant kingdom\(^1\)-\(^3\). The Coumarin ring system has an easier acceptability in the biological system compared to its isomeric chromones and flavones\(^4\). Coumarin derivatives with substituents like hydroxy, acetyl, amino have proved to be potential chelating agents. Some of the Coumarin derivatives exhibit distinct physiological, photodynamic and bacteriostatic activity\(^5\). Quercioli reported that these compounds are having sedative, vasodilating, tuberculostatic, antibacterial and antifungal properties\(^6\). The authors present interest concerns with the synthesis of amino coumarins in task specific ionic liquids by reductive amination of carbonyl compounds to avoid the use of hazardous solvents. Coumarins are considered as building blocks for the construction of pharmaceuticals\(^7,8\) and agrochemicals. Reductive amination of carbonyl compounds\(^9\) is one of the convenient methods to synthesize biologically active amines. To achieve the minimum use of the hazardous reagents and improved selectivity of reductive amination reaction, there has been emphasis on green chemistry. Room temperature ionic liquids are identified as green solvents for organic synthesis\(^10,11\). Keeping in view of the
environmental pollution ecofriendly solvent is used to carry out the reaction. The task specific ionic liquid used in the present work has already reported by the author which is a significant one pot three component reaction.

2. EXPERIMENTAL SECTION

2.1. General Reaction

Chemicals and solvents used in the experiment were commercially available. Homogeneity/purity of all the products were assayed by thin-layer chromatography (TLC) on OH
OH
N N+
OH
OH
X +
X- 120
6h

Scheme 1 Synthesis of 2,3-dihydroxy-N,N,N-tributylpropanaminium halide ionic liquid X=Cl

Ar + Ar NH2 IL IL

Scheme 2 General reaction for asymmetric reductive amination

Alumina-coated plates (Merck). Product samples in methanol (MeOH) were loaded on TLC plates and developed in CHCl3: MeOH (9.5:0.5, v/v). When slight impurities were detected by iodine vapor/UV light visualization, compounds were further purified by chromatography on silica gel columns (100 - 200 mesh size, CDH). Purity of the compounds was finally re-checked by TLC. In the present study 2, 3-dihydroxy-N, N, N-Tributylpropanaminium Chloride ionic liquid was prepared by the reported procedure and by using the IL as a reaction medium synthesis of some functionalized amines carried by reductive amination procedure.

2.2. Reductive Amination of 3-(2- Amino-4-Thiazolyl) Coumarin and Pyridine-2-carboxaldehyde

A solution of 2.44g (0.01mol) 3-(2- Amino-4-Thiazolyl) Coumarin and pyridine-2-carboxaldehyde 1.07g (0.01mol) are mixed in 0.25 g (0.0008 mol) ionic liquid 1 at room temperature for 30 minutes followed by the addition of NaBH4. At the end of the reaction,
diethyl ether was added. The organic layer was separated, washed with water, dried (Na$_2$SO$_4$), and filtered. The filtrate was evaporated to afford the N-[(2-pyridyl) methyl] - 3-(2- Amino-4-Thiazolyl) Coumarin. m.p 198°C Crystallization from ethanol afforded 86% product. [analytical calc.found (%): C, 64.56; H, 3.30; N, 12.49; C$_{18}$H$_{12}$N$_3$O$_2$S requires (%): C, 64.85; H, 3.33; N, 12.61.

2.3. Synthesis of N-[(2-thienyl) methyl]-3-(2- Amino-4-Thiazolyl) Coumarin

3-(2-amino-4-thiazolyl) Coumarin (2.44g 0.01mol) and thiophene-2-carboxaldehyde (1.12g 0.01mol) are mixed in 0.25 g (0.0008 mol) of ionic liquid at room temperature for 90 minutes at 70°C followed by the addition of NaBH$_4$. After completion of the reaction, the reaction mixture was extracted with ethyl acetate. The extract was dried over anhydrous Na$_2$SO$_4$ and evaporated to afford the product 85.6%. m.p 198°C [analytical calc.found (%): C, 60.12; H, 2.85; N, 8.19; C$_{17}$H$_{11}$N$_2$O$_2$S requires (%): C, 64.85; H, 3.33; N, 12.61.

3. RESULTS AND DISCUSSION

Two novel aminocoumarins have been synthesized by reductive amination process using ecofriendly liquid solvent medium and characterized. The synthesized novel substituted amino coumarins are stable at room temperature and are non-hygroscopic in nature. They are insoluble in water; sparingly soluble in methanol and fairly soluble in dimethylformamide. These amines display a strong absorption band around 1720cm$^{-1}$ suggesting υ(CO) of lactone in N-[(2-pyridyl) methyl]-3-(2- Amino-4-Thiazolyl) Coumarin and at 1724 cm$^{-1}$ for N-[(2-thienyl) methyl]-3-(2- Amino-4-Thiazolyl) Coumarin. A small intensity band appears at 1590 cm$^{-1}$ indicating due to CH-NH. A small intensity band at 1420 cm$^{-1}$ is due to υ(CN) of pyridine and at 779 cm$^{-1}$ is due to υ(CS) of N-[(2-thienyl) methyl]-3-(2- Amino-4-Thiazolyl) Coumarin.

CONCLUSION

In conclusion, we have synthesized novel functionalized amino coumarins by asymmetric reductive amination by using cleaner technology under neutral conditions. The outcome of this research is motivating, yet more research on synthesized IL required to be applied for various reductive amination reactions. The biological activity of amino coumarins has to be pursued yet.

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