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Studies of Synthesis of Substituted Coumarin *via* Pechmann Condensation using Brönsted Acidic Ionic Liquid

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Abstract:

Substituted coumarins were synthesized in good yields via Pechmann condensation in Brönsted acidic ionic liquid. 3-methylimidazolinium methane sulfonate Ionic liquid was used as solvent cum catalyst in this condensation reaction.

Key Words: Brönsted acidic Ionic Liquid, Pechmann Condensation, Coumarin.

Introduction:

Coumarin itself is a natural product found in a number of plant sources, including the sweet clover and the tonka bean, although it can be synthetically produced as well. Members of this group display broad range of applications[1] as fragrances, pharmaceuticals, additives to food and cosmetics, agrochemicals, optical brightening agent, dispersed fluorescent and tunable dye lesser.[2] Biological activities like anthelmentics, hypnotic, insecticidal, and anticoagulant properties[3]. Coumarins also act as intermediates for the synthesis of fluorocoumarins. chromenes, coumarones, and 2-acylresorcinols.[4]It may be used as prodrug.

The pharmacological and biochemical properties and therapeutic applications of coumarins depend upon the pattern of substitution. Some chemicals in the coumarin family have been harnessed for their pesticides uses. Hymerocromone is a systematic insecticide that is especially effective against the Colorado beetle. Coumarin is a potent rodenticide. Coumarin is a blood thinner and used to keep blood flowing smoothly and prevent the formation of blood clots. It should not be taken while using anti-coagulants. Warfarin (Chemical in the coumarin family) is a popular anti-coagulant which can be ingested and injected depending on the need of the patient. When ingested coumarin acts as a blood thinner and it appears to be effective in treating some tumors. Coumarin is sometimes used in combination with other blood thinner for medical treatment.The carcinogenic property of coumarins have been reviewed[5,6] has their toxicity[7,8].

Besides, all these biological activities coumarins appear extensively in nature as photosensitizing agents.[9]A coumarin derivative covalently immobilized on sensing membrane as a fluorescent carrier for nitrofurazone,[10]and have been used as blue green laser dyes.[11] Coumarins, too fluoresce, notably when an electron-releasing group is present at 7-position. For example N-acetyl derivatives of 7-aminocoumarin serves as fluorescence markers for detection of proteinases.[12] Coumarin is also widely used for pumpable laser dyes or for the photographic purposes because its triplet excited-state often occurs in high yield. [16]

7-Hydroxycoumarin is used in sun screen lotion. 7-Diethylamino-4-methyl coumarin is used to sensitive a weak fluorescent second material in a mixture, designed for use as an *insitu* flaw detector in metal surfaces. Coumarins show a tendency to absorb UV light and hence they

are used as optical brightening agents.[13] in laundry and domestic detergents and as additives to fibers and paper.

Review of previous work:

Lots of methods and protocols have been developed and still developing for the synthesis of this naturally occurring widely applicable heterocycle Conmarin. Coumarin and their derivatives can be synthesized by various methods including the Perkin[14],Pechmann[15], Knoevengel[16], Reformatsky[17], Wittig[18], Michael addition of the organolithium reagent to diethylethoxymethylenemalonate,Kostanecki-Robinson Synthesis of Coumarin.

Among these Von Pechmann synthesis of coumarin involve the acid catalysed reaction between a phenol and a β-keto ester. This reaction is most widely used method for preparation of coumarins, since it proceeds from very simple starting materials and gives very good yields for various substituted coumarins. Dr.M.M.Salunkhe[19]and Bhushan Khadilkar[20] synthesised 4-substituted coumarin by using ionic liquid such as 1-butyl-3-methylimidazolium chloroaluminate and 1-butylpyridinium chloroaluminate respectively. De and Gibs reported sysnthesis of 4 – substituted coumarins via use of $BiCl_3$ catalyst. [21] Polyaniline salts are used as polymer supported acid catalyst for the preparation of substituted coumarin. Pechmann reaction using 1-butyl-3-methyl imidazolium chloride and niobium penta chloride.Pechmann Reaction in Non-Chloroaluminate trifluoromethanesulfonate imidazolium ionic liquid under Solvent-Free Conditions.[22] Synthesis of Coumarins via Pechmann Reaction in Water Catalyzed by Acyclic Acidic Ionic Liquids.[23]M. R. Didgikar *et al* reported the synthesis of coumarins Via Pechmann Condensation using silica sulfuric acid as a heterogeneous catalyst. Alum catalysed Pechmann condensation.[24] Silica gel Supported $NaHSO_4$ Catalyzed Pechmann condensation[25].LiBr-Mediated, solvent free von Pechmann reaction[26] von Pechmann reactionassisted by microwave irradiation.[27]Pechmann condensation by using zeolite,[28] clay,[29] salfonic acid[30] have also reported.

We have prepared Brönsted acidic type ionic liquid by using easy convenient method from cheap and easily available starting materials and using this new ionic liquid,two derivatives of coumarin were synthesised.

Materials and Methods:

All reagents used were chemically pure or analytical reagent grade. Purity of organic compounds was checked by TLC. IR spectra of samples were measured in KBr pellets on Perkin Elmer 257-FTIR ^{1}HNMR recorded on 300MHz Bruker NMR Instrument.

General Procedure of Synthesis of Ionic Liquid:

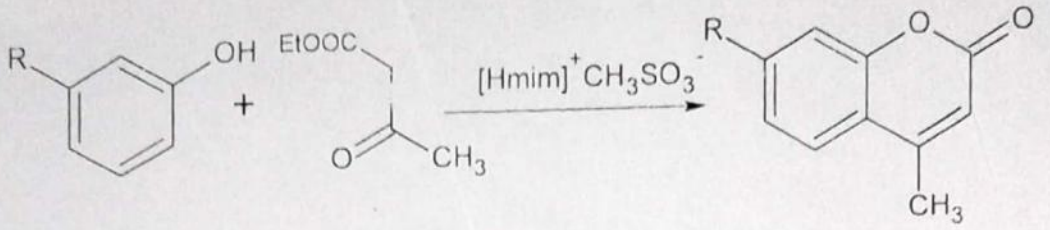
0.01 mol 1-Methylimidazole was placed in a round bottom flask and cooled to 0^0 C. 0.01 mol methane sulfonic acid was added slowly with stirring. The mixture was stirred for 5 minute at room temperature to get 3-methylimidazolinium methane sulfonate.

General Procedure of Synthesis of Substituted Coumarin via Pechmann Condensation using IL $[Hmim]^+ CH_3SO_3^-$:

From a) Resorcinol b) 3 – Amino Phenol

27

The mixture of a)110mgm resorcinol (1mmol) b) 109 mgm 3-amino phenol (1mmol) mgm. ethylacetoacetate (1mmol) and ionic liquid $[Hmim]^+CH_3SO_3^-$ was heated at 75°c for min. testing with the help of TLC confirmed the completion of reaction. Then reaction mixture was cooled to room temperature and poured into 10 gm. crushed ice. The crystalline product was collected by filtration under suction, and washed with cold H_2O.Purified the product by recrystallization from appropriate solvents.



Phenol Ethylacetoacetate Coumarin Derivatives

R = a) OH b) CH_3

Result & Discussion:

Sr. No.	Starting material	Temperature	Time	Yield	Melting Point
a	Resorcinol + Ethyl acetoacetate	75°c	30 min.	95%	185°c
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The Derivatives of Coumarine are all well known. The Physical Properties like colour physical constant and spectral data of ours prepared compounds are found good agreement with previously reported data.

Conclusion:

We have presented an efficient and very simple an alternative method for preparation of coumarin derivatives via Pechmann condensation using Brönsted Acidic Ionic Liquid. Short reaction time with higher yields and easy work up of the reactions are the advantages of this methodology.

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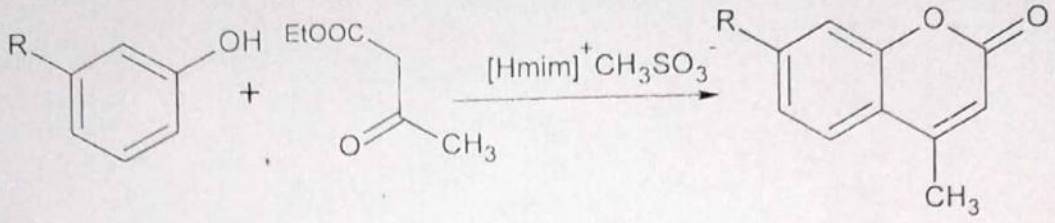

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