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SYNTHESIS OF 2-AMINO-4H-CHROMENE DERIVATIVES VIA THREE COMPONENT REACTION USING SODIUM BENZOATE AS A GREEN CATALYST

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ABSTRACT: To synthesize the chromene and benzochromene derivatives with the use of salt catalyst i.e sodium benzoate. This is multicomponent reaction This is carried out by using reactants benzaldehyde , malanonitrile and activated phenols like resorcinol, 1-naphthol and 2-naphthol, mixture of ethanol and water is used as a solvent. The synthesis takes place by taking care of environment and use of hazardous solvents, catalysts and chemicals is reduced.

KEYWORD: Chromene, Benzochromene, activated Phenol, Malanonitrile, Multicomponent reaction

INTRODUCTION:

In the heterocyclic compounds amino chromenes and chromenes are important as structural precursors that have gained tremendous value in organic and medicinal chemistry. Chromenes are exploited for synthesis of cosmetics, pigments [I] and potentially biodegradable agrochemicals [II]. Pharmacologically active compounds [III] are made by utilising chromene as an important precursor [III]. In the medicinal chemistry and chemical biology Chromene skeleton plays important structural part. Antimicrobial, mutagenicity, antiviral, anti-proliferative, antitumor, central nervous system activities (CNS) activities [III] are some of the important activities that are shown by Chromene skeleton. 2*H*-chromenes are utilised in synthesis of natural products. Chromene compound are used as photochromic materials. Chromenes proves to provide important biological activities such as antimicrobial [IV], antibacterial [IV], anticancer, anticoagulant, antioxidant, anti-inflammatory, anti-

tubercular, antiviral [V], anti-fungicidal, anti- anaphylactic activity [VI]. We are practicing to taking care of inexpensive and less hazardous catalysts and reagents. It is important from the industrial point of view and also should be less hazardous for environment. The increasing attention during the last decades for environmental protection has led modern academic and industrial groups to develop chemical processes with maximum yield and minimum cost whilst using nontoxic reagents, solvents and catalysts [VII]. MCRs reaction allows us to synthesize complex molecules from simple reactants and one step reaction. This is beneficial because it reduces expenses and energy and minimises the production of waste and toxic Chemicals that are hazardous for environment. It is important to carry out the synthesis of 2-amino-4*H*chromene by using energy efficient procedure. By using environment friendly catalysts and solvents and using reactants such as aldehydes, malanonitrile and activated phenols [VIII] (MCR) reaction includes two or more than two steps and isolation of intermediate do not takes place in this process, it is profitable strategy for industrial synthesis and saving time also good for environmental point of view. It helps to reduce time, energy and cost of the process [IX]. 2-amino-4*H* chromene with cyano-functionality is used as antitherapeutic effect to cure rheumatoid, psoriasis, and cancer. It also acts as pigments, laser dyes, optical brighteners, fluorescence markers, and also biodegradable agro chemicals [X]. Various methods have been performed for synthesis of chromene using catalyst such as silica nanoparticles [XI]. Because of the reasons such as to produce the desired products with the easily obtainable reactants with the help of single step without isolation of intermediate One-pot multicomponent reaction gets recognition in industrial synthesis using energy efficient way[XII] and also by taking care of principles of green chemistry. With the help of reactants such as malanonitrile, aldehyde and activated phenols or naphthol by using reflux condition and acetonitrile or DMF is used as solvent by using basic ionic liquid catalysts such as [bmim] OH amino-chromenes have been synthesized[XIII]. Various methods for preparation of heterocycles have been reported [XIV-XX]. We are trying to work on the procedure to synthesize aminochromene derivatives with the help of green solvents and green reusable salt catalyst by MCR in the organic synthesis; this gives us idea to use sodium benzoate as a green catalyst by performing condensation reaction between aldehydes, active methylene reagents and activated phenols. Sodium benzoate is the sodium salt of benzoic acid, widely used as a food preservative and a pickling agent. It appears as a white crystalline chemical compound.

EXPERIMENTAL:

All the melting points were determined in open capillaries in a paraffin bath and are uncorrected. The progress of the reactions was monitored by TLC.

General Procedure for synthesis of 2-amino-4-aryl-7-hydroxy 4*H*-chromene-3 Carbonitrile 1a

Method A

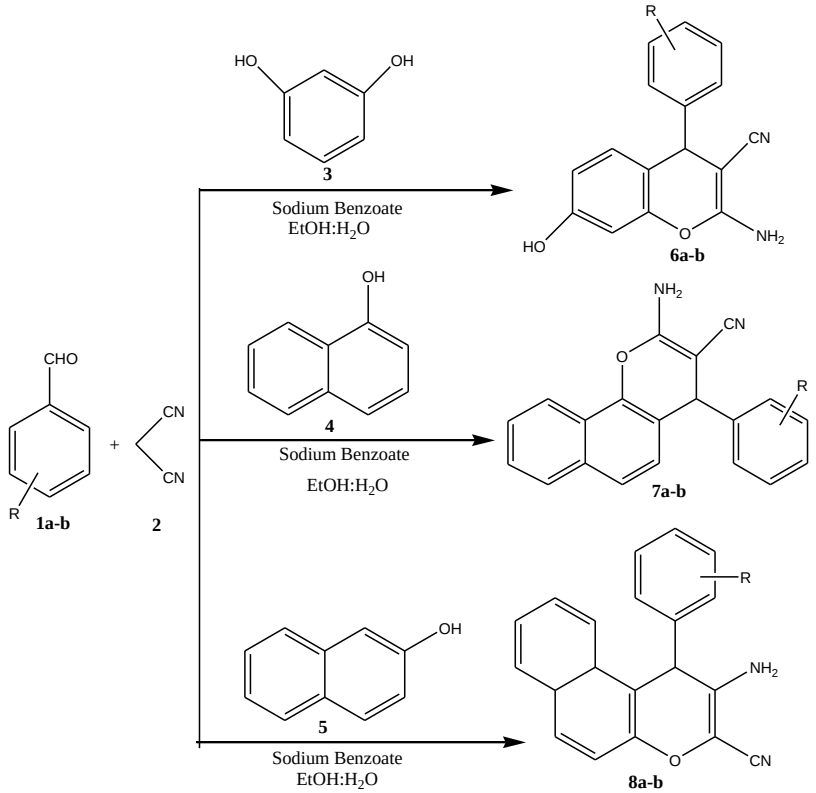
A mixture of appropriate benzaldehyde (1mole), malanonitrile (1mole), resorcinol (1mole) and sodium benzoate as a catalyst is added (1mole) to this mixture (1:1) ratio of ethanol and water is added as a solvent. The reaction mixture is stirred for 150 minutes. The progress of reaction is monitored by TLC. When the product obtained it is extracted with ethyl acetate, then 4 ml water is added remove the water layer. Catalyst is removed with aqueous layer as catalyst is soluble in water. the organic layer is dried by adding sodium sulphate. the dried material is then recrystallized with ethanol. Pale yellow crystals are obtained. (MP:-209-215 ^{o}C)

Method B

A mixture of appropriate benzaldehyde (1mole), malanonitrile (1mole), resorcinol (1mole) and sodium benzoate as a catalyst is added (1mole) to this mixture (1:1) ratio of ethanol and

water is added as a solvent. The reaction mixture is stirred for 150 minutes. The progress of reaction is monitored by TLC. The precipitate obtained is filtered and washed with water. Catalyst is removed with water. Dry and crude product is recrystallized with ethanol. Pale yellow crystals are obtained. (M.P-208-218 ^{o}C)

RESULT AND DISCUSSION: We have performed the synthesis of 2-amino-4*H*-derivative by three component efficient reaction between aromatic aldehydes, malanonitrile and resorcinol, α-naphthol and β-naphthol by using ethanol and water as a solvent by using sodium benzoate as an efficient catalyst at room temperature. The method gives efficient and improved pathway for the synthesis of chromenes in terms of short reaction time and reusable and green catalyst. The catalyst is soluble in water and easy to recover or remove and reaction proceeds in short period of time.



Our interest is to synthesize the substituted chromenes and benzochromenes by using sodium benzoate as a green catalyst and green solvents like ethanol and water. When the solvent is not used reaction takes more time to proceed by using energy efficient procedure. We started the synthesis by allowing reaction of a mixture of aromatic aldehydes, malanonitrile and resorcinol in equimolar amount (mole ratio 1:1:1) by using stirring condition at room temperature containing catalytic amount of sodium benzoate and the solvents used in this reaction is the mixture of ethanol and water in the ratio (1:1) to give 2-amino-4aryl-7 hydroxy-4*H* Chromene-3-carbonitriles.2-naphthol give the above one-pot three-component reactions for extended periods. When solvent is not used in above reaction takes more time to proceed even if we provide the temperature and gives minimum yield when, a mixture of ethanol and water was used as a solvent in the previous reactions, the three phenols gave the desired products in good yields at room temperature. Some of the products were sticky solids but after recrystallization it appeared as crystals. We can remove or recover catalyst by filtration/washing process with water or extraction process because catalyst we have used is soluble in water. All known compounds were identical in all physical and spectroscopic

aspects with the others which are the structures of the isolated products were confirmed on the basis of their elemental analysis and spectral data.

The structure of the isolated product 6**a** was confirmed on the basis of LCMS data shows that a sharp broad peak is obtained. at the retention time 1.54. at this retention time mass obtained is 265.14 (m+2). and the reported mass of the product is 264. Furthermore in the ^{1}H NMR the presence of aromatic protons shows value in between 7.2-7.4 ppm protons adjacent to the OH group shows value 6.8 ppm and 6.9 ppm. The presence of NH_2 group is confirmed with value 4.8 ppm, OH proton give signal at 9.7ppm. Aromatic protons adjacent to the OH group shows value 6.8ppm and 6.5ppm. Aromatic protons that are adjacent to the CN group show the value 6.4ppm due to de-shielding effect.

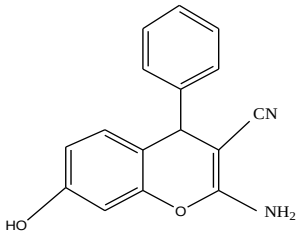
Table No 1- Synthesis of substituted 2 amino chromenes by using sodium benzoate

Sr. no	R	Substrate	Products	time(minutes)	M.P[3] (^{o} C)	Yield (%)[a]
1	H	Resorcinol	6a	150	220-222	90
2	H	1-naphthol	7a	150	208-210	82
3	H	2-naphthol	8a	180	278-280	80
4	4-Cl	Resorcinol	6b	150	164-169	92
5	4-Cl	1-naphthol	7b	180	232-234	85
6	4-Cl	2-naphthol	8b	180	188-191	82

[a]Isolated Yields.

SPECTRAL ANALYSIS:

All known compounds were identical in all physical and spectroscopic properties with the structure of isolated product on the basis of their elemental analysis and spectral data.



2-amino-4phenyl-4H-benzo(h)chromene-3-carbonitrile

^{1}H NMR (DMSO-d6, 400 MHz ppm): 4.6 (s, 2H, NH_2), 6.4 (s, 1H, H-Ar), 6.5 (d, 1H, H-Ar), 6.8 (d, 1H, H-OH), 6.9 (d, 2H, H-Ar), 7.2 (t,3H, Ar-H),7.3(dd, 2H, Ar-H), 9.7 (s, 1H, O-H)
LCMS: m/z 265.14(m+2)

CONCLUSION:

We have found a new way of synthesizing amino chromenes of expected biological and chemical characteristics using energy efficient, green, and environment friendly procedure by using salt catalyst i.e. sodium benzoate, as an green, reusable and efficient catalyst for this reaction by taking care of 12 principles of green chemistry.

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