Ion Exchange Resins as a Reusable acid Catalyst for an Efficient Synthesis of Coumarins via von Pechmann reaction

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Abstract

The synthesis of coumarins via von Pechmann cyclisation reaction was carried out in the presence of catalytic amount of cation exchange resins; the reaction conditions were mild and the yields of the target products were good. The polymeric catalyst was easily recovered, purified and regenerated, ready to be used in further reactions. This protocol offers several advantages including high yield, short reaction time, easy work-up and use of relatively moderate acidic and safe catalyst. It also allows a greener process, since no waste generation and resins are reused repeatedly. Some reusable polymeric SO_3H-functionalized cation exchange resins like Amberlite IR-120, Dowex 50, X-8 100 and Tulsion T-42 have been used as catalysts. The coumarin products could simply be separated from the catalyst by filtration and the catalyst could be regenerated and reused for several times without noticeably decreasing the catalytic activity and yield.
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Keywords: *Cation exchange resin, von Pechmann, polymeric catalyst.*

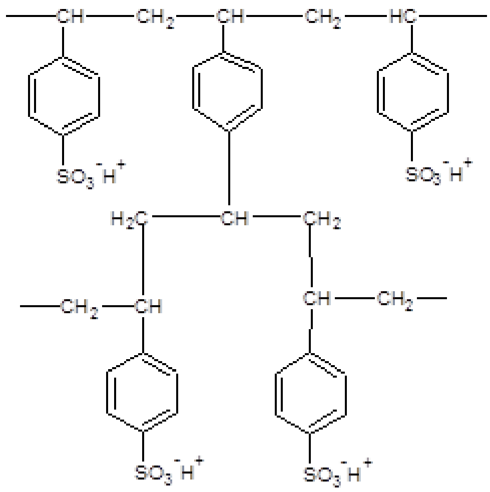
Introduction

Great progress has been made in the field of polymer chemistry over last two decades. Polymer chemistry has become famous since synthetic organic chemical reactions give a by-product which can sometimes be difficult to isolate from the desired product. On the other hand if a polymeric reagent is used in the organic synthesis, then the by-product will remain attached to the insoluble polymer and can be separated from the desired product by simple filtration. In electrophilic aromatic substitutions, non-regenerable catalysts such as metal chlorides and mineral acids are generally applied. Substitution of these by cation exchange resins result in simplified product recovery and reduction of undesirable waste stream [1-5]. We are especially interested in developing the potential use of simple, inexpensive catalysts. In recent years, organic reactions on solid phase have received considerable interest in organic synthesis because of their ease of handling, enhanced reaction rate, greater selectivity, and simple work-up. We report here the synthesis of coumarin derivatives by the Pechmann condensation using cation exchange resins.

Coumarins are an important class of compounds, and the development of new efficient synthetic strategies for the construction of coumarins is of considerable interest. Coumarin and its derivatives have attracted great interest because of their importance in the synthetic organic and medicinal chemistry. They are widely used as additives in foods, perfumes, cosmetics, pharmaceuticals [6], and in the preparation of insecticides, optical brighteners [7] and dispersed fluorescent and laser dyes [8]. Coumarins have been synthesized by several methods including Pechmann, Perkin, Knoevenagel, Reformatsky, Wittig reactions and by flash vacuum pyrolysis [9-14]. The Pechmann reaction is one of the most widely applied method for the synthesis of coumarins and its derivatives, which involves the condensation of phenols with β-ketoesters in the presence of a variety of acidic condensing agents. Several acid catalysts have been used in the conventional procedure, such as H_2SO_4 [9], $AlCl_3$ [15], P_2O_5 [16] or trifluoroacetic acid [17]. However, these catalysts have to be used in large excess, and they cannot be recovered or reused. The disposal of acidic waste leads to environmental pollution. Therefore, it is important to find the simple, recoverable and reusable catalysts for the synthesis of coumarins.

Nowadays cleaner and safer methods have been developed using microwave irradiation [18], solid acids and Lewis acids as catalysts to prompt the Pechmann condensation [19], and the search for the new readily available and green catalysts is still being actively pursued. Acidic cation exchange resins, which possess the advantageous characteristics of solid acids and mineral acids, are designed to replace traditional mineral liquid acids, such as sulfuric acid and hydrochloric acid. In fact, the use of cation exchange resins as catalysts is an area of ongoing activity. The cation exchange resins used in this work were Amberlite IR-120, Dowex 50 X-8 100 and Tulsion T-42.The main advantages of cation exchange resins are that they can be recovered, reused and they simply the purification of the final product.

In reactions involving mineral acids, excess of acid remaining unused has to be neutralized and involves repeated washings of the product, while resin catalyzed reactions gives yield with no production of soluble acid waste. Hence productions of environmentally harmful waste streams are minimized. A widely used cation exchange resin is that obtained by the copolymerization of styrene with a small amount of divinylbenzene followed by sulphonation. A hypothetical formulation of such a polystyrene cation exchange resin was shown in Scheme 1



Scheme 1: A hypothetical formulation of sulphonated polystyrene divinyl benzene cation exchange resin.

2. Experimental

2.1. Materials and methods

The cation exchange resins Amberlite IR-120, Dowex 50, X-8 100 and Tulsion T-42 were commercially available (Thermax Company Ltd., Pune, India). All chemicals like resorcinol, ethyl aceto acetate, n-hexane were commercially available and used without further purification. The solvents were distilled before use. The products were characterized by their physical constants (M.P.) and spectral characteristics (IR and H^1 NMR).

2.2 Activation of cation exchange resins

All resins Amberlite IR-120, Dowex 50, X-8 100 and Tulsion T-42 used in synthesis of coumarin are washed free of smaller particles by decantation. It is then allowed to soak for 10 minutes in 10% hydrochloric acid and then washed with distilled water until the washings are neutral to litmus. The resins are then dried at 50^0 for 4 hours.

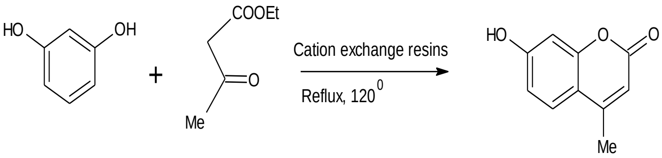
2.3. General procedure for the Pechmann condensation using cation exchange resins

Equimolar quantities of phenol (resorcinol, 10 mmol), ethyl aceto- acetate (10 mmol), 1.0 gm cation exchange resin (activated) and 10 ml solvent are heated with constant stirring in an oil bath at 120° C under reflux until all reaction ceases. The progress of the reaction was monitored by TLC. After the completion of the reaction the resin was filtered off, washed with solvent. The solvent was evaporated and reaction mixture was poured in ice-cold water when coumarin separates out as solid mass. The product was recrystalised by 40% ethanol and were analyzed by IR, ^{1}H NMR spectroscopy and physical data (M.P.) with those reported in the literature.

3. Results and discussion

Recently, considerable attention has been devoted to heterogeneous organic transformation utilizing solid acid catalysts. Among the various solid acid catalysts investigated, ion exchange resins have attracted much attention because of their suitable acidity, regeneration, reuse and simplified product recovery and reduction of undesirable waste streams. We wish to report that cation exchange resins can also affect cyclisation in the synthesis of organic compounds to give the products in yields exceeding those obtained by the common solid acid catalysts and mineral acids. Potentially the most important are sulphonic acid resins. These were shown to be as acidic as H_2SO_4 and can be used continuously at 100°C or at higher temperature for short periods. The main advantages are that they may be recovered, regenerated and reused; also they simplify the purification of products. In recent years, organic synthesis using solid acid catalysts have been of great interest in view of a flowering environmental awareness [20]. In von Pechmann reaction large quantities of concentrated sulfuric acid is used as condensing agent in the preparation of hydroxyl coumarins via condensation of phenols with β-keto esters. It has however shown by Barris-Israelstam [21] that such large amounts of acids are unnecessary since comparable yields of coumarins are obtained. The use of cation exchange resins as a condensing agent was investigated and coumarins are readily formed using such resins. The cation exchange resins used in this work are Amberlite IR-120, Dowex 50, X- 8 100 and Tulsion T-42. The resins are activated first and then used as catalyst in the condensation of phenols with β-keto esters to produce 7-hydroxy- 4- methyl coumarin. Here three steps (hydroxylation, transesterification and dehydration) are involved (Scheme 2).

The main advantage of cation exchange resins was that, they are regenerated and reused. The isolated yield was determined after each regeneration by same procedure. The catalysts can be recovered and used up repeatedly without any activity loss or product yield. The results are summarized for Amberlite IR-120 in Table 2. The isolated yield (%) of 7-hydroxy-4-methyl coumarin using n-hexane with different cation exchange resins was shown by a bar diagram (Figure 1).



Scheme 2: The Pechmann condensation between resorcinol and ethyl acetoacetate catalyzed by different cation exchange resins.

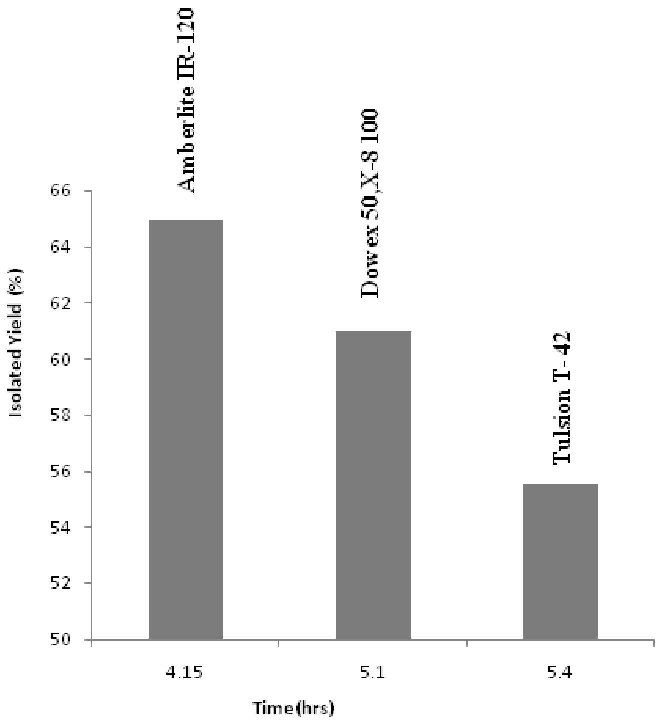


Figure 1: Bar diagram showing isolated yield (%) of 7-hydroxy-4-methyl coumarin with different cation exchange resins using n-hexane at 120°C.

3.1. Effect of cation exchange resin and solvent

The effect of cation exchange resin on the rate of the reaction and percentage yield was investigated by using three types of resins, Amberlite IR-120, Dowex 50, X- 8 100 and Tulsion T-42. It was found that Amberlite IR-120 was more successful. The observation of Table 1 reveals that the time required for the condensation of resorcinol with ethyl aceto acetate in presence of Amberlite IR-120 is less than other resins. Thus, the rate of the reaction was increased substantially and the yield too, being improved to some extent. Amberlite IR-120 is a "Gel'' type cation exchange resin of the Styrene DVB (divinyl benzene) type. It should have effective pore size and volume. Its structure should permit adequate diffusion of reagents into the relative sites, a phenomenon which depends upon the extent of swelling or solvation. To investigate the effect of solvent, we have carried out the reaction in presence and absence of the solvent. A non-polar compound, n-hexane was used as solvent. The rate of reaction and yield too was increased to some extent when the reaction was carried out in presence of solvent.

4. Conclusions

In conclusion, we have demonstrated a method using some commercially available cation exchange resins, Amberlite IR-120, Dowex 50, X-8 100 and Tulsion T-42 as a reusable acid catalyst for an efficient synthesis of 7-hydroxy-4-methyl coumarin by the condensation of resorcinol with ethyl aceto acetate. The simple workup procedure, mild reaction condition and reusable eco-friendly catalyst are the advantages of the present protocol. We feel that, the process will be practically useful for acid catalyzed cyclisation reactions.

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Table 1: Synthesis of 7-hydroxy-4-methyl coumarin at 120°C in presence of n-hexane using different cation exchange resins.

Sr. No.	Starting materials	Cation exchange resin	Reaction time (hrs.)	Isolated yield (%)	Physical constant (M.P. in °C)
1.	Resorcinol + Ethyl aceto acetate	Amberlite IR-120	4.15	64.95	180 / 179 [R]
2.	Resorcinol Ethyl aceto acetate	Dowex 50, X- 8 100.	5.10	60.98	179 / 179 [R]
3.	Resorcinol Ethyl aceto acetate	Tulsion T- 42	5.40	50.56	180 / 179 [R]

Table 2: Isolated yield (%) of 7-hydroxy-4-methyl coumarin with Amberlite IR-120 after regeneration.

Cation exchange resin	Initial yield (%)	Yield after regeneration (%)			
		1st	2nd	3rd	4th
Amberlite IR-120	64.95	64.94	64.95	64.95	64.90