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Original Resarch Article

A design for convenient and greener root towards one-pot multi-component synthesis of substituted pyrano-dichromeneo-dione and chromeno-pyrido-pyrimidinone derivatives using rice husk based heterogeneous catalyst

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ABSTRACT

In this work, a convenient and greener procedure for synthesizing substituted pyrano-dichromeno-dione and substituted chromeno-pyrido-pyrimidinone derivatives were explored using Sulphonated Rice Husk (SRH) as a novel bio-degradable, greener, heterogeneous catalyst. We designed an efficient pseudo three-component synthetic method for 7-aryl/heteroaryl substituted pyranodichromene-6, 8-dione and 7-aryl/heteroaryl substituted chromeno[4, 3-d]pyrido[1, 2-a]pyrimidinone derivatives using this greener catalyst (SRH) under reasonable reaction condition. The fundamental features of this procedure are the operational simplicity, hassle-free recovery of product, and reusability of the catalyst with excellent product yield (up to 98%). The toxic metal-free catalyst was prepared conveniently, and characterized using different spectroscopic techniques, including Fourier-transform infrared spectroscopy (FTIR), X-ray diffraction analysis (XRD), scanning electron microscopy (SEM), energy dispersive X-ray spectroscopy (EDX). Then the synthesized material was used for the greener synthetic target.

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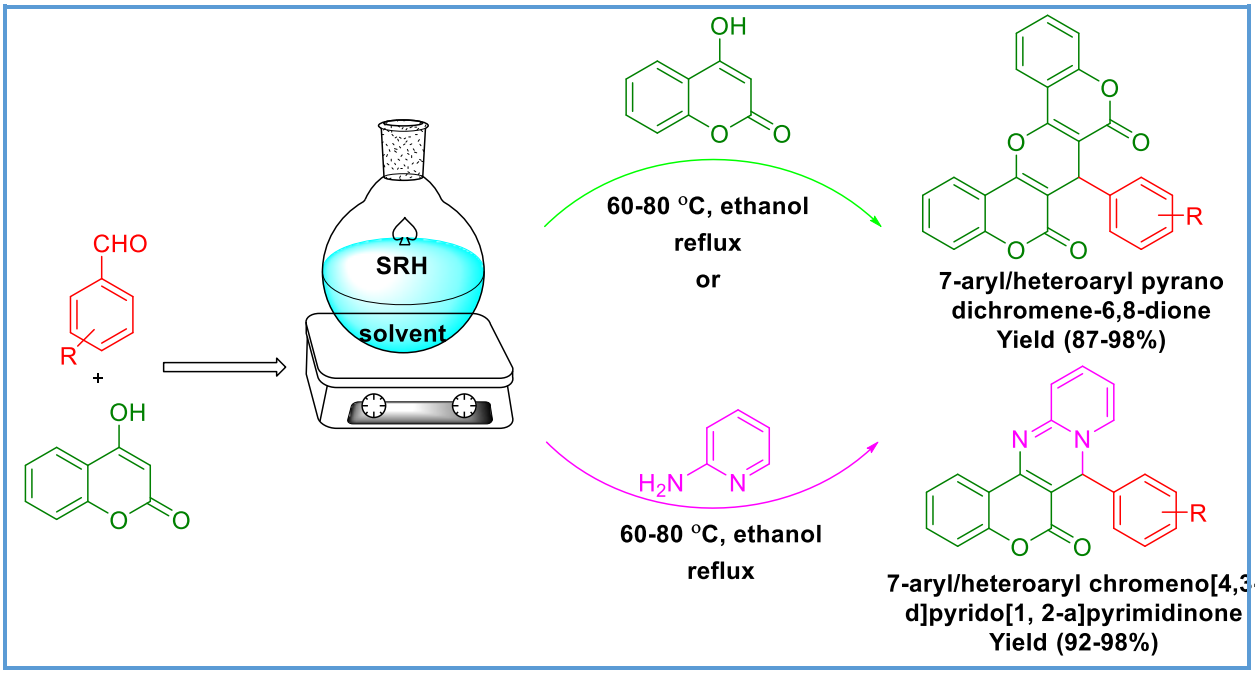
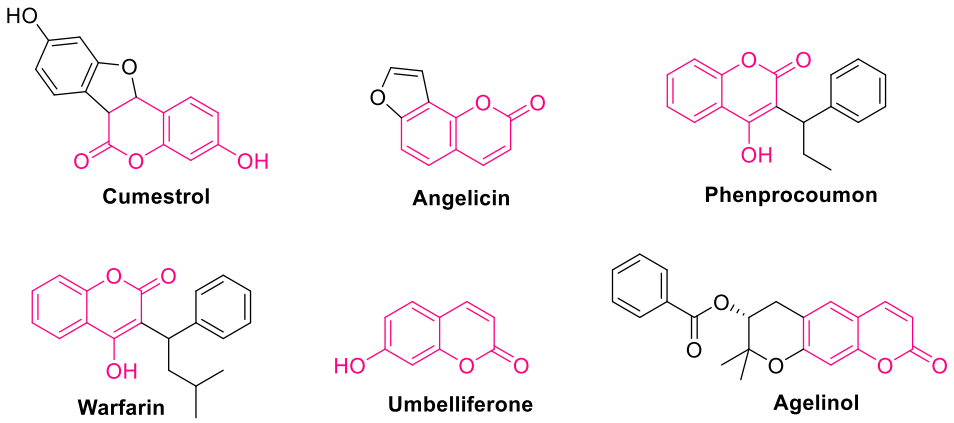
Graphical Abstract



Introduction

Coumarins are an essential class of heterocyclic compounds that contain a basic flavinoid-like skeleton. They have both natural and synthetic origins that show diverse pharmaceutical and biological activities (Scheme 1) [1]. As coumarin scaffolds are one of the essential fused ring heterocyclic bioactive compounds, researchers have made considerable effort towards the fruitful synthesis of these useful bio-active coumarine heterocycles. Coumarins can be derived from natural resources, and scaffolds can be used extensively in a laboratory to generate newer drug molecules. Their derivatives are no doubt a class of bioactive agents that show a broad range of biological activities such as anti-inflammatory [2], anticancer [3], antitubercular [4], anti-viral [5], anti-fungal [6]. Some scientific research have been made towards the synthesis of coumarin analogs to find their significant applications in medicinal chemistry. Amany coumarin derivatives have been obtained by following famous reactions procedures such as Knoevenagel, Perkin, Reformatsky, and Michael. [7] Some coumarins derivatives also showed excellent fluorescent properties, and thus a series of coumarin based molecular probes are being used to investigate drug action in cellular biological researches [8]. Among the coumarin-fused heterocycles 7-aryl substituted pyranodichromene-6, 8-dione and 7-aryl substituted chromeno[4, 3-d]pyrido[1, 2-a]pyrimidinone derivatives have attracted our keen attention for organic synthesis under green conditions. Due to having several biological and pharmaceutical activities, the chromene moiety has been generally employed in the expansion of compounds, and one-pot multicomponent reactions (MCRs) in this regard has helped us a lot because it provides convenient, energy and time-saving root over multi-step process for the synthesis of annelated coumarin derivatives. In our described project, one-pot three-component and pseudo three-component reactions have shown potential effectiveness in generating

good product yield in a hassle-free manner. It has been observed that both homogeneous and heterogeneous catalysts are capable enough to increase the productivity in MCRs. However, heterogeneous catalysts have more importance than homogeneous ones because of their easy separation and recovery from the reaction mixture. In this context, rice husk (RH) based heterogeneous support has been chosen for the synthesis of our targeted substituted pyranodichromene-6, 8-dione and chromeno[4, 3-d]pyrido[1, 2-a]pyrimidinone derivatives considering a sustainable way. Rice husk is an agricultural by-product with high silica content. The characteristics like high porosity, lightweight, and the high external surface area attracted us to use it as an excellent heterogeneous catalyst [9, 10]. There are also more reasons to select rice husk-based greener catalyst for chemical reactions due to its economic advantage, non-toxicity, high abundance, and bio-degradability. Furthermore, it is more economically cheaper than other heterogeneous materials [11]. The use of rice husk based eco-friendly catalysts and the use of safer and greener solvents are on-demand in recent years for the greener synthesis of organic compounds to achieve a sustainable goal, and so derived and modified natural substances from agricultural waste can make a significant contribution as a bio-derived catalyst in future research for the synthesis of various critical heterocyclic compounds. And following the principles of "Green Chemisty", applying the one-pot multi-component reaction technique (MCRs) along with greener catalyst (SRH), greener solvent, a versatile and powerful way has been presented in the whole work for the targeted synthesis of fused-ring coumarin derivatives. As a part of our research interest on the synthesis of substituted pyrano-dichromeneo-dione and chromeno-pyrido-pyrimidinone derivatives of biological significance, we report here the preparation of catalyst and the whole synthetic process of those above-mentioned coumarine derivatives via the simplest hassle-free route under sustainable and greener technique.



Scheme 1. Some examples of biologically active drugs containing cumarine skeleton

Experimental

Materials and methods

Crude rice-husk was collected from a nearby rice mill. The chemicals, including aldehydes, 4-hydroxycumarine, 2-aminopyride were supplied from Sigma Aldrich Chemical Co. (USA), which have been used directly without

further purification. The chemical purity of the compounds was confirmed using thin layer chromatography (TLC) on commercial aluminum baked plates of silica gel, 60 F254. NMR spectra of all the products were taken in DMSO-d_6 (TMS as an internal standard) using a Bruker 400 MHz spectrometer (operating for ^1H at 400 MHz and for ^{13}C at 100 MHz) and Bruker Advance NEO 500 MHz spectrometer (operating for ^1H at 500 MHz and for ^{13}C at 125 MHz). IR spectra of the prepared catalyst were recorded on Perkin Elmer-Spectrum RX-IFTIR spectrophotometer, Powder XRD, and SEM-EDX analysis of the prepared catalyst was carried out by Panalytical's X'pert Pro X-Ray diffractometer and JSM-IT700HR Advanced SEM Spectrometer.

General procedure for catalyst preparation

The heterogeneous catalyst (SRH) was prepared by direct sulphonation of rice husk (RH) following our previous synthetic method [12]. The rice husk (RH) was collected from a nearby rice mill and was blended finely before use. The fibrous part of the blended rice husk was first washed with dilute H_2SO_4 continuously several times, and next, the whole aggregate was thoroughly washed with water and finally by ethanol. After washing, the solvent was fully evaporated through a rotary evaporator and then thoroughly dried 5 g of chemically treated rice husk material was taken into 250 mL of a round bottom flask followed by addition of 150 mL dichloromethane (DCM). Then, 5 mL of pure Chlorosulphonic acid (98%) was added dropwise with continuous stirring until the whole suspension turned brownish and finally set to stir for 20 h on a magnetic stirrer at room temperature. After completing the reaction, the solid material was filtered off and washed with water to remove excess chlorosulphonic acid and finally acetone repeatedly to remove other organic substances till the filtrateshowed a very light brownish appearance. After leaching, the final material was dried in reduced pressure and later characterized using different spectroscopic techniques [12].

General procedure for synthesis of 7-aryl/heteroaryl-6H, 7H, 8H-pyrano[3, 2-c:5,6-c']dichromene-6, 8-dione derivatives

A mixture of 4-hydroxycumarine (2 mmol), aromatic aldehyde (1.0 mmol), and SRH (80 mg) in a 25 mL round-bottom flask was stirred at 60-80 °C for 240 min and the progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the product was extracted with ethyl acetate, and the catalyst was removed by filtration. Then ethyl acetate extract was concentrated, and the white crude product was isolated by adding petroleum ether slowly dropwise until white precipitation appeared. Then the white crude product was further purified by recrystallization in petroleum ether/ethyl acetate (v/v ratio 80/20) mixture to get the pure product. All the synthesized compounds were characterized by ^1H, and ^{13}C NMR spectroscopy and the spectral data were compared with the reported spectral data of the corresponding compound.

General procedure for synthesis of 7-aryl/heteroaryl-6a, 13a-dihydro-6H, 7H-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one derivatives

A mixture of 2-aminopyridine (1 mmol), 4-hydroxycumarine (1 mmol), aromatic aldehyde (1 mmol), and SRH (60 mg) in a 25 mL round-bottom flask was stirred at 60-80 ^oC temperature for 210 minutes. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the product was extracted with ethyl acetate, and the catalyst was separated by

simple filtration. The ethyl acetate extract were concentrated. The crude product was separated by simple precipitation with mixed solvent containing ethyl acetate and petroleum ether (1:10 v/v) slowly dropwise. Finally the obtained solid was purified by slowly washing the crude with a solvent containing ethyl acetate and petroleum ether (1:4 v/v). After isolation, all the synthesized compounds were characterized by ^{1}H and ^{13}C NMR spectroscopy, and the spectral data were compared with the reported spectral data of the corresponding compound.

Selected Spectroscopic data

7-(4-methoxyphenyl)-6H, 7H, 8H-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione (3a)

^{1}H NMR (400 MHz, DMSO): δ 3.65 (s, 3H), 6.17 (s, 1H), 6.70 (d, J = 8 Hz, 3H), 6.96 (d, J = 8 Hz, 2H), 7.18-7.24 (m, 4H), 7.45-7.49 (m, 2H), 7.78 (dd, J = 8 Hz, 2H). ^{13}C NMR (100 MHz, DMSO): δ 35.9, 55.4, 104.2, 113.6, 116.0, 120.4, 123.4, 124.6, 128.1, 131.4, 134.5, 153.0, 157.3, 165.0, 167.9.

7-phenyl-6H, 7H, 8H-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione (3b)

^{1}H NMR (400 MHz, DMSO): δ 6.24 (s, 1H), 7.02-7.08 (m, 3H), 7.11-7.15 (m, 2H), 7.22-7.29 (m, 4H), 7.45-7.50 (m, 2H), 7.77 (q, 2H). ^{13}C NMR (100 MHz, DMSO): δ 36.6, 103.9, 116.0, 120.5, 123.4, 124.6, 125.3, 127.2, 128.2, 131.4, 142.9, 153.0, 165.1, 168.2.

7-(2-chlorophenyl)-6H, 7H, 8H-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione (3c)

^{1}H NMR (400 MHz, DMSO): δ 6.12 (s, 1H), 7.08-7.18 (m, 3H), 7.21 (d, J = 8 Hz, 4H), 7.37 (d, J = 4 Hz, 1H), 7.44-7.77 (m, 2H), 7.78 (d, J = 8 Hz, 2H). ^{13}C NMR (100 MHz, DMSO): δ 36.6, 103.3, 115.9, 120.4, 123.4, 124.5, 126.5, 127.5, 129.8, 130.9, 131.3, 133.2, 140.9, 152.9, 164.4, 168.2.

7-(2-bromophenyl)-6H, 7H, 8H-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione (3d)

^{1}H NMR (400 MHz, DMSO): δ 5.99 (s, 1H), 7.02 (t, 1H), 7.17-7.22 (m, 5H), 7.38 (dd, J=8 Hz, 2H), 7.46 (t, 2H), 7.77 (d, J = 8 Hz, 2H). ^{13}C NMR (100 MHz, DMSO): δ 38.8, 103.4, 116.0, 120.4, 123.4, 124.5, 127.0, 127.8, 131.1, 131.3, 133.3, 152.9, 164.3, 168.1.

7-(4-hydroxyphenyl)-6H, 7H, 8H-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione (3e)

^{1}H NMR (400 MHz, DMSO): δ 6.12 (s, 1H), 6.52 (d, 2H), 6.84 (d, 2H), 7.17-7.22 (m, 4H), 7.44-7.48 (m, 2H), 7.77 (dd, J = 8 Hz, 2H), 8.90 (s, 1H). ^{13}C NMR (100 MHz, DMSO): δ 35.8, 104.3, 115.0, 115.9, 120.5, 123.3, 124.6, 128.0, 131.3, 132.8, 153.0, 155.1, 165.1, 168.1.

7-(4-fluorophenyl)-6H, 7H, 8H-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione (3f)

^{1}H NMR (400 MHz, DMSO): δ 6.21 (s, 1 H), 7.02-7.08 (m, 3 H), 7.11-7.15 (m, 2 H),7.22-7.29 (m,4 H), 7.45-7.50 (m, 2H), 7.77 (q, 2H). ^{13}C NMR (100 MHz, DMSO): δ 36.6, 103.9, 116.0, 120.5, 123.4, 124.6, 125.3, 127.2, 128.2, 131.4, 142.9, 153.0, 165.1, 168.2.

7-(2-methylphenyl)-6H, 7H, 8H-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione (3g)

^{1}H NMR (400 MHz, DMSO): δ 1.96 (s, 3H), 6.09 (s, 1H), 6.97 (s, 3H), 7.22-7.27 (m, 5H), 7.47 (s, 2H), 7.80 (d, J = 5.6 Hz, 2H). ^{13}C NMR (100 MHz, DMSO): δ 21.6, 36.5, 105.2, 116.1, 120.0, 123.6, 124.6, 126.3,127.7, 128.3, 131.6, 137.0, 142.1, 152.9, 165.2, 168.9.

7-phenyl-6H, 7H-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one (4a)

^{1}H NMR (500 MHz, DMSO): δ 6.31 (s, 1H), 6.81-6.83 (m, 1H), 6.94-7.08 (m, 1H), 7.12-7.15 (m, 1H), 7.17-7.27 (m, 4H), 7.48-7.52 (m, 2H), 7.83-7.92 (m, 4H). ^{13}C NMR (125 MHz, DMSO): δ 36.0, 103.3, 112.0, 113.0, 115.3, 119.8, 122.7, 124.0, 124.7, 126.5, 127.6, 130.8, 136.5, 142.2, 143.5, 152.4, 154.1, 164.6, 167.7.

7-(4-methoxyphenyl)-6H, 7H-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one (4b)

^{1}H NMR (500 MHz, DMSO): δ 3.68 (s, 3H), 6.21 (s, 1H), 6.74 (d, 2H), 6.99 (d, J = 8 Hz, 2H), 7.20-7.26 (m, 3H), 7.48-7.51 (m, 2H), 7.80 (d, J = 1.5 Hz, 1H), 7.82 (d, J = 1.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO): δ 35.2, 54.7, 103.5, 111.7, 113.0, 114.4, 115.3, 119.8, 122.7, 123.9, 127.4, 130.7, 131.6, 134.0, 139.4, 141.8, 152.3, 155.5, 156.6, 164.4, 167.5.

7-(2-chlorophenyl)-6H, 7H-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one (4c)

^{1}H NMR (500 MHz, DMSO): δ 6.10 (s, 1H), 6.82 (m, 1H), 6.96 (d, J = 10 Hz, 1H) 7.11-7.25 (m, 5H), 7.42 (dd, J = 5 Hz, 1H), 7.47-7.50 (m, 2H), 7.81-7.92 (m, 3H). ^{13}C NMR (125 MHz, DMSO): δ 36.0, 102.6, 112.0, 113.1, 115.3, 119.8, 122.8, 123.9, 125.8, 126.9, 129.2, 130.2, 130.7, 132.6, 136.2, 140.2, 143.7, 152.3, 153.9, 163.8, 167.6.

7-(4-bromophenyl)-6H, 7H-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one (4d)

^{1}H NMR (500 MHz, DMSO): δ 6.24 (s, 1H), 6.80-6.83 (m, 1H), 6.94 (d, J = 10 Hz, 1H), 7.05-7.07 (m, 1H), 7.21-7.27 (m, 3H), 7.33-7.36 (m, 1H), 7.49-7.52 (m, 1H), 7.81-7.92 (m, 4H). ^{13}C NMR (500 MHz, DMSO): δ 35.7, 102.9, 111.9, 112.9, 115.3, 117.7, 119.7, 122.8, 124.0, 128.9, 130.4, 130.9, 136.7, 141.8, 143.5, 152.4, 154.1, 164.3, 167.6.

7-(4-fluorophenyl)-6H, 7H-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one (4e)

^{1}H NMR (500 MHz, DMSO): δ 6.27 (s, 1H), 6.79-82 (m, 1H), 6.92 (d, J = 9 Hz, 1H), 6.93-7.0 (m, 2H), 7.11-7.14 (m, 1H), 7.21-7.27 (m, 3H), 7.49-7.52 (m, 1H), 7.82-7.92 (m, 3H). ^{13}C NMR (125 MHz, DMSO): δ 35.5, 103.3, 111.9, 112.7, 114.0, 114.2, 115.3, 119.8, 122.8, 124.0, 128.2, 128.2, 130.8, 137.0, 138.1, 138.1, 143.2, 152.4, 154.3, 159.1, 161.0, 164.4, 167.7.

7-(4-hydroxy-3-methoxyphenyl)-6H, 7H-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one (4f)

^{1}H NMR (500 MHz, DMSO): δ 3.54 (s, 3H), 6.19 (s, 1H), 6.52-6.54 (m, 1H), 6.58 (d, 1H), 6.82 (s, 1H), 6.94 (d, J = 10 Hz, 1H), 7.21-7.25 (m, 3H), 7.47-7.51 (m, 1H), 7.82-7.87 (m, 3H), 8.53 (broad s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 35.5, 55.5, 103.7, 111.6, 112.0, 112.9, 114.8, 115.3, 119.2, 119.9, 122.7, 124.0, 130.7, 133.0, 136.6, 143.5, 144.0, 146.8, 152.3, 154.1, 164.5, 167.6.

Results and Discussion

The prepared catalyst was characterized by FTIR spectroscopy first, and the comparison with FTIR spectrum of rice husk indicated the transformation of rice husk into sulphonated rice husk (SRH) (Figure 1). The new broadband at 3420 cm^{-1} and the band at 1100 cm^{-1} denote the incorporation of –SO_3H groups into rice husk after sulphonation. The band with a peak 1100 cm^{-1} represents the symmetric and asymmetric stretching of S=O bonds of –SO_3H groups, and the broadened band at 3420 cm^{-1} represents the -OH groups vibration after the incorporation of –SO_3H groups [13]. Scanning electron microscopy (SEM) analysis and powder X-ray diffraction (p-XRD) have also made a clear path for confirming the prepared catalyst from the rice husk. The powder XRD

analysis shows characteristic peaks at 2θ=20.83º, which is a broad peak indicating some carbon composed aromatic sheets oriented randomly (Figure 1) [14].

The rough surfaces in SEM images of SRH were considered to be result from sulphonation of rice husk material (Figure 2). This is an indication of a good change in surface morphology after sulphonation. The Comparison of EDX images of SRH and RH also reflecting visible change in the elemental composition and considerable changes in atomic weight percentage of certain elements such as C, Si, O, and S was noticed from the EDX data analysis of RH and SRH (Figure 2). For further support, EDX data are included in supporting information.

The above promising data analysis and literature survey has given us a good confirmation that the heterogeneous catalyst (SRH) has been formed without any doubt and not demand any further quantitative analytical support and is now finally ready for suitable organic reactions to be used up as heterogeneous catalyst under greener reaction condition.

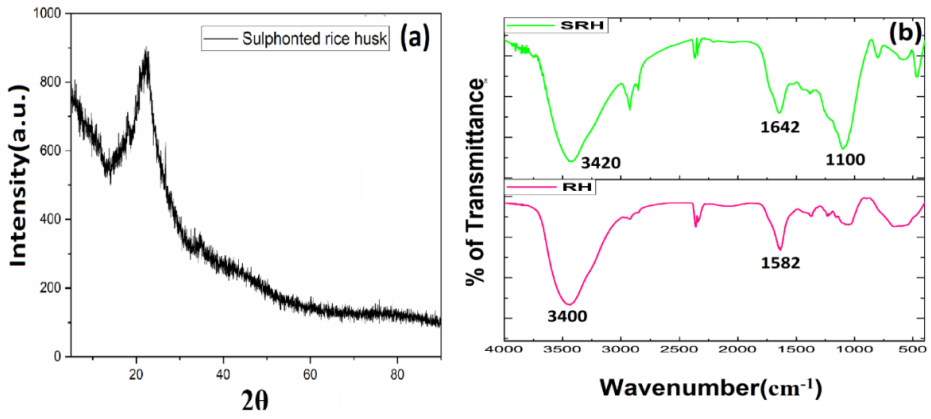


Figure 1. a) Powder XRD image of SRH, and b) FTIR images of RH & SRH

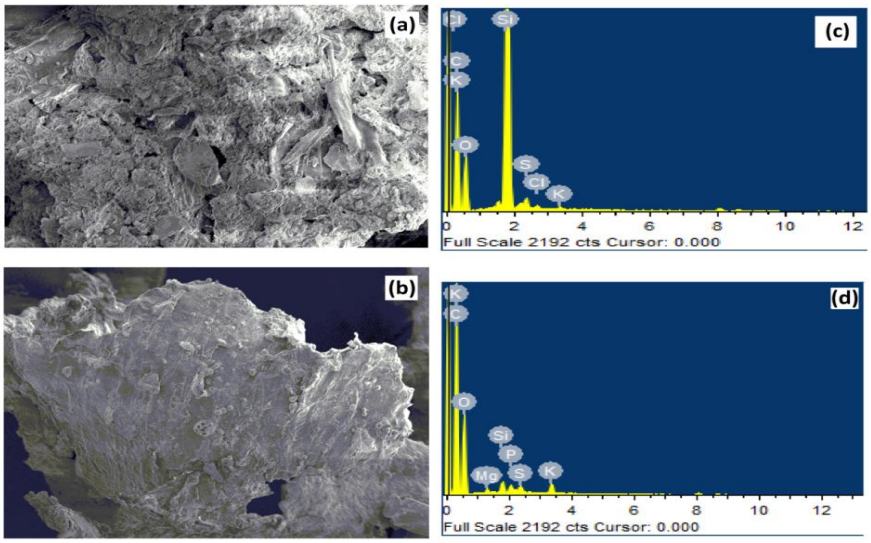
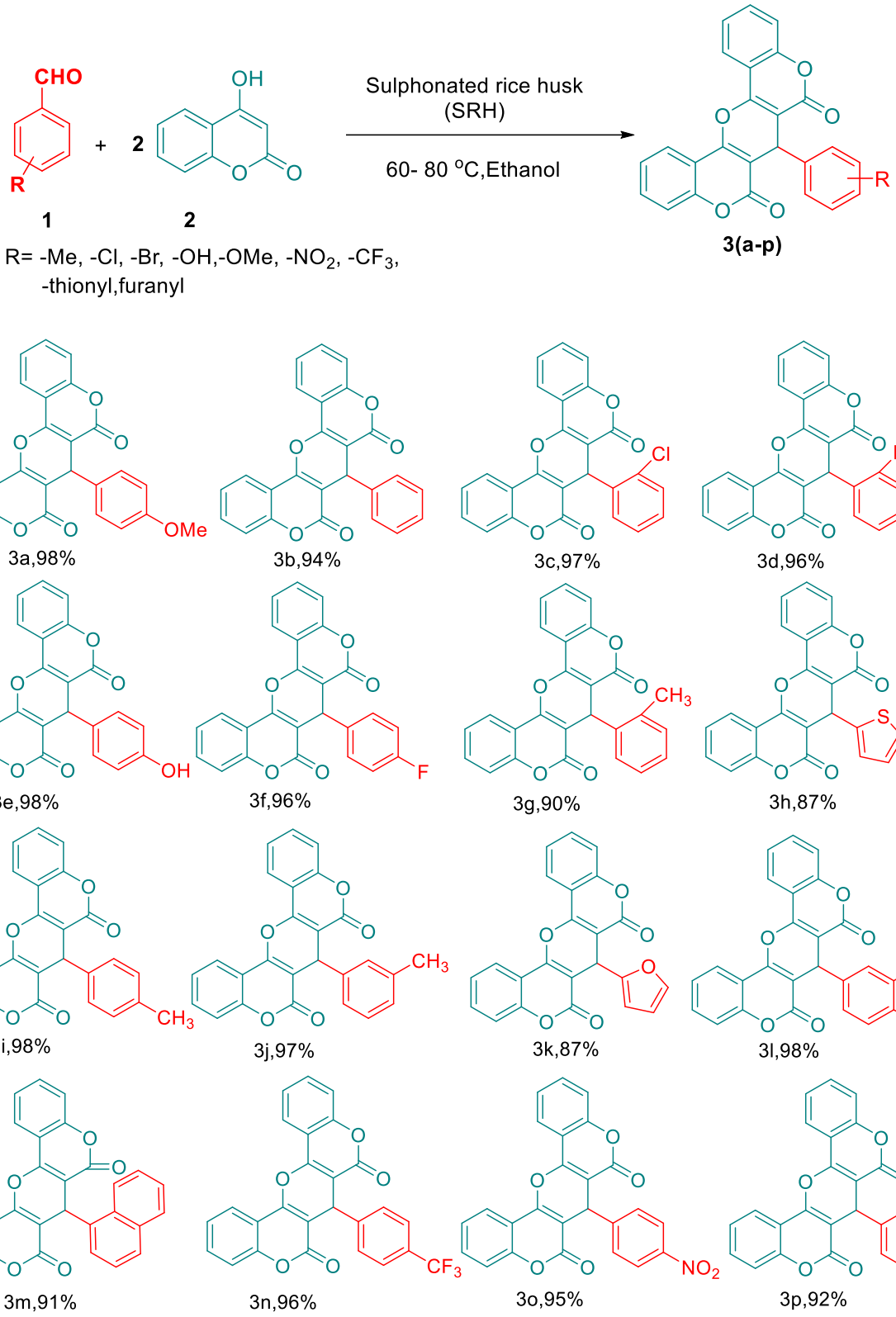


Figure 2. a) SEM image of SRH, b) SEM image of RH, c) EDX image of SRH, and d) EDX image of RH

The generality of the reaction was observed with a variety of aromatic and heterocyclic aldehydes with electron-donating and electron-withdrawing substituent at *ortho*, *meta,* and *para* position (Scheme 2). The targeted compounds (**3a-3o**) are successively synthesized using sulfonated rice husk (SRH) as an efficient catalyst under greener reaction conditions and within a short reaction time. Initially, the reaction was carried out by taking anisaldehyde (1 mmol), 4-hydroxycumarine (2 mmol) at a time in a 25 mL round bottom flask, and in the presence of a catalyst the expected product was obtained with an excellent yield. Satisfactory yield was obtained in 90 mg of SRH catalyst in ethanol solvent at 80 ^{0}C temperature (Table 1, entry 2). However, in the absence of a catalyst the formation of the desired product was not obtained (Table 1, entry 11, 12). With decreasing the amount of catalyst, the yield of the product decreased slightly along with reaction temperature and time of the reaction. The optimized condition was determined by taking anisaldehyde (1 mmol) and 4-hydroxycoumarine(2 mmol) in a 25 mL round bottom flask fitted with a condenser. It was observed that at 70 ^{o}C with minimum 70 mg of catalyst SRH in ethanol, giving best result with yield up to 96% (Table 1, entry 6). From this optimization table (Table 1), it is clear that SRH catalyst is suitable for one-pot synthesis of 7-aryl/heteroaryl-6*H*, 7*H*, 8*H*-pyrano[3, 2-c:5,6-c']dichromene-6, 8-dione with excellent yield in a short reaction time.

The amount of the catalyst and time of the reaction was further rechecked to report the accurate, optimized condition of the reaction. Taking this as a model reaction (Scheme 2), a few experiments were carried out to compare the catalyst efficiency of (SRH) with other conventional homogeneous acid and base catalysts as well as metal catalysts also (Table 2 entry 1-10). It was observed that the results of most of the acid catalysts, as well as base catalysts in ethanol, showed good activity at 70 °C (Table 2, entry 1, 3, 5, 7, 8) and the comparison of results to that of the performance of SRH revealed a satisfactory result over other homogeneous catalysts concerning reaction time and yield of the product (Table 2, entry 10). The progress of the reaction was monitored by thin layer chromatography (TLC), and the pure product was obtained by recrystallization in petroleum ether/ethyl acetate (v/v ratio 80/20) mixture. Role of methanol (Table 1, entry 7, 12) and water (Table 1, entry 13, 14, 15, 16) have also been observed, and it was observed that the product yield in methanol is relatively unaltered to that of ethanol. In distilled water, the reaction did not happen due to damage of the catalyst in the water medium. Observation with the addition of water into ethanol solvent revealed that the role of water is unfriendly until the ratio of ethanol/water exceeds 3:1 (v/v) (Table 1, entry 15) with a decreased amount of yield. The catalyst can sustain its activity in alcohol/water mixed solvent with a minimum quantity of water with a satisfactory product yield. For the greener aspect of reaction, methanol is advised to be avoided for its toxicity and adversity in the reaction medium. From the optimized reaction condition, it is clear that SRH catalyst is undoubtedly suitable for synthesizing 7-aryl/heteroaryl-6*H*, 7*H*, 8*H*-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione with excellent yield in a short reaction time. The effectiveness of SRH over other acid catalysts was established as it requires a short reaction time and is easily separable from the reaction mixture (Table 2, entry 10).



Scheme 2. Synthesis of 7-aryl/heteroaryl-6*H*, 7*H*, 8*H*-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione derivatives [a]

Table 1. Optimisation table for the synthesis of **3a** under variable reaction conditions

Entry	Catalyst (mg)	Solvent	Temperature (°C)	Time (min)	Yield (%)[a]
1	90	Ethanol	90	310	98
2	90	Ethanol	80	280	98
3	85	Ethanol	80	260	98
4	85	Ethanol	80	240	96
5	80	Ethanol	70	220	96
6	70	Ethanol	70	190	96
7	70	Methanol	70	190	96
8	65	Ethanol	60	190	94
9	60	Ethanol	60	180	94
10	60	Ethanol	60	160	92
11	None	Ethanol	70	190	-
12	None	Methanol	70	190	-
13	70	H_2O	70	190	-
14	70	Ethanol/H_2O(6:1)	70	190	84
15.	70	Ethanol/H_2O(3:1)	70	190	78
16.	70	Ethanol/H_2O(1:1)	70	190	54

[a] Isolated yield

Table 2. Comparison of catalyst efficiency for the synthesis of **3a**

Entry	Catalyst	Solvent	Temperature (°C)	Time (min)	Yield (%)[a]
1	PTSA (60 mg)	Ethanol	70	190	83
2	PEG-200 (3 mL)	-	70	240	70
3	H_2SO_4 (3 mL)	-	70	220	80
4	Glycerol (5 mL)	-	70	220	72
5	AcOH (0.1 mL)	Ethanol	70	190	74
6	Fe_3O_4 (60 mg)	Ethanol	70	190	81
7	K_2CO_3 (60 mg)	Ethanol	70	190	70
8	Et_3N (2 mL)	-	70	190	95
9	$FeCl_3$ (60 mg)	Ethanol	70	180	78
10	SRH (70 mg)	Ethanol	70	190	96

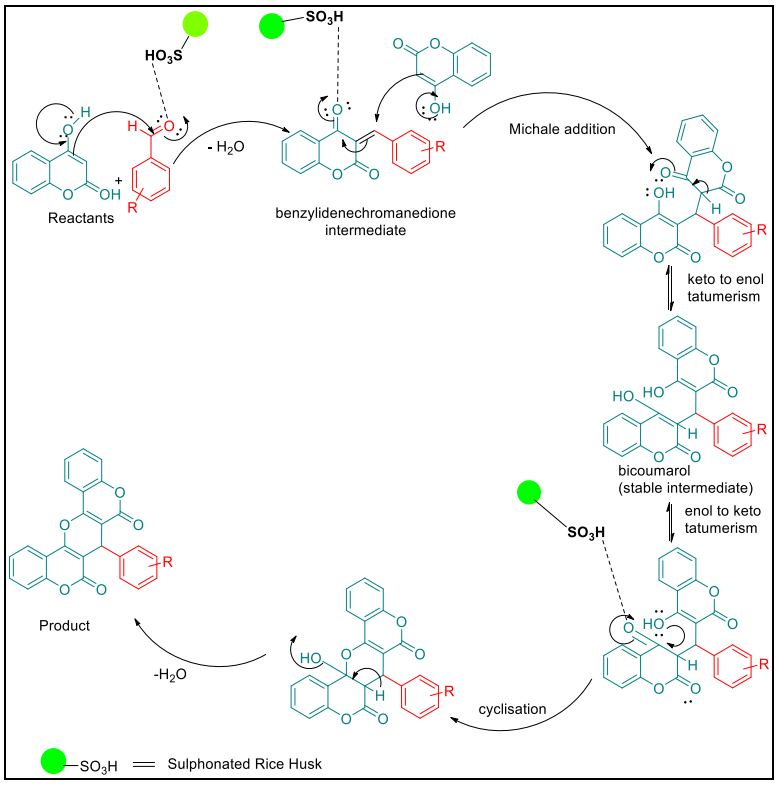
[a]Isolated yield

Mechanism

A plausible mechanism (Scheme 3) for the synthesis of 7-aryl/heteroaryl-6*H*, 7*H*, 8*H*-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione derivatives is established by considering the porosity, active rough surface and the acidic behavior of the surface of the catalyst. At the very first step of the reaction, as usual, protonation occurs at aldehyde oxygen of aromatic aldehyde, and then a condensation reaction starts with 1 mol 4-hydroxycoumarine giving a aryledine-chromanedione intermediate, and after that fast Michael addition reaction occurs between another remaining 1 mol of 4-hydroxycoumarine and aryledine-chromanedione intermediate to give bis-coumarol as another intermediate [15]. Finally, an intramolecular cyclization followed with the expulsion of 1 mol of water results in the formation of the desired product 7-aryl/heteroaryl-6*H*, 7*H*, 8*H*-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione.

Initially, the reaction was carried out with anisaldehyde (1 mmol), 4-hydroxycumarine (1 mmol), 2-aminopyridine (1 mmol) in a 25 mL

round bottom flask. Excellent yield was observed for various aldehydes in the presence of 80 mg of SRH catalyst in ethanol solvent at 70 ^{o}C temperature with a reaction time of 190 min. From the optimization table (Table 3) it is clear that with decrease in the amount of catalyst, the yield of the product decreases slightly, and in the absence of catalyst yield of the product was diminished (Table 3, entry 10, 11). The performance of the reaction is almost similar in methanol (Table 3, entry 5 and 12). However, for the greener aspect, ethanol is a safer solvent than methanol to achieve the maximum yield. The role of water in ethanol and methanol was also observed in this case, and the results reflected short of lower yield than that of pure ethanol and methanol. It may be due to the reduced efficacy of the catalyst in the presence of water. From the optimized condition, it is clear that the SRH catalyst is suitable for converting 7-aryl/heteroaryl-6a, 13a-dihydro-6*H*, 7*H*-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one derivatives with excellent yield in a short reaction time. It was observed that at 60 °C using minimum amount of catalyst SRH (60 mg) in ethanol gave the best result (Table 3, entry 7). The progress of the reaction was monitored by thin layer chromatography (TLC). Finally, the off white solid crude product was isolated from concentrated ethylacetate extract of the reaction mixture by adding mixed solvent containing ethyl acetate and petroleum ether (1:10 v/v) slowly dropwise. Finally the obtained solid was purified by slowly washing the crude with a solvent containing ethyl acetate and petroleum ether (1:4 v/v). The generality of the reaction was observed with a variety of aromatic and heterocyclic aldehydes with electron-donating and electron-withdrawing substituents at *ortho*, *meta,* and *para* position also under optimized reaction condition and the targeted compounds (**4a-4j**) are successively synthesized using SRH as efficient catalyst under green reaction condition (Scheme 4).

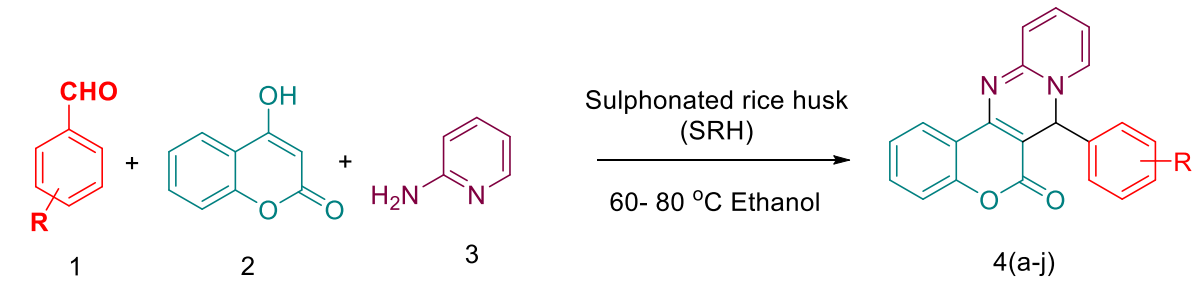


Scheme 3. The plausible mechanism for the synthesis of 7-aryl/heteroaryl-6*H*,7*H*,8*H*-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione

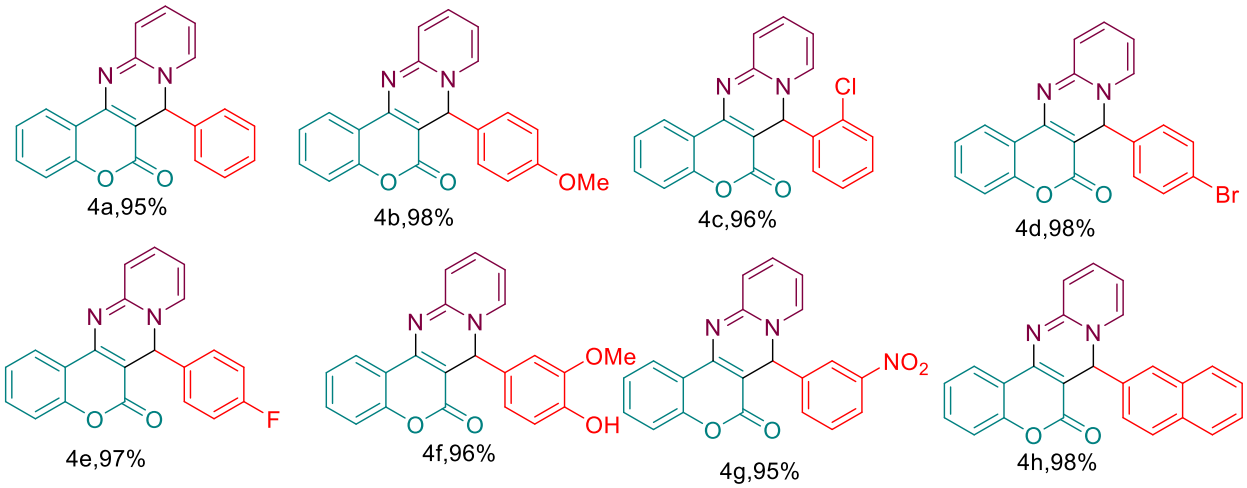
Table 3. Optimisation table for the synthesis of **4b** under variable reaction conditions

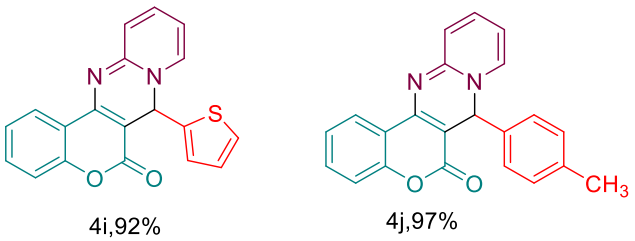
Entry	Catalyst (mg)	Solvent	Temperature (°C)	Time (min)	Yield (%)[a]
1	100	Ethanol	90	320	98
2	90	Ethanol	90	280	98
3	80	Ethanol	80	260	98
4	80	Ethanol	70	230	96
5	70	Ethanol	70	210	96
6	60	Ethanol	70	180	96
7	60	Ethanol	60	180	94
8	60	Ethanol	60	160	92
9	50	Ethanol	50	160	80
10	None	Ethanol	70	215	53
11	None	Methanol	70	220	53
12	70	Methanol	70	190	96
13	80	H_2O	70	190	-
14	80	Ethanol/H_2O(6:1)	70	220	92
15	80	Ethanol/H_2O(3:1)	70	250	82
16	80	Ethanol/H_2O(1:1)	70	300	72

[a]Isolated yield

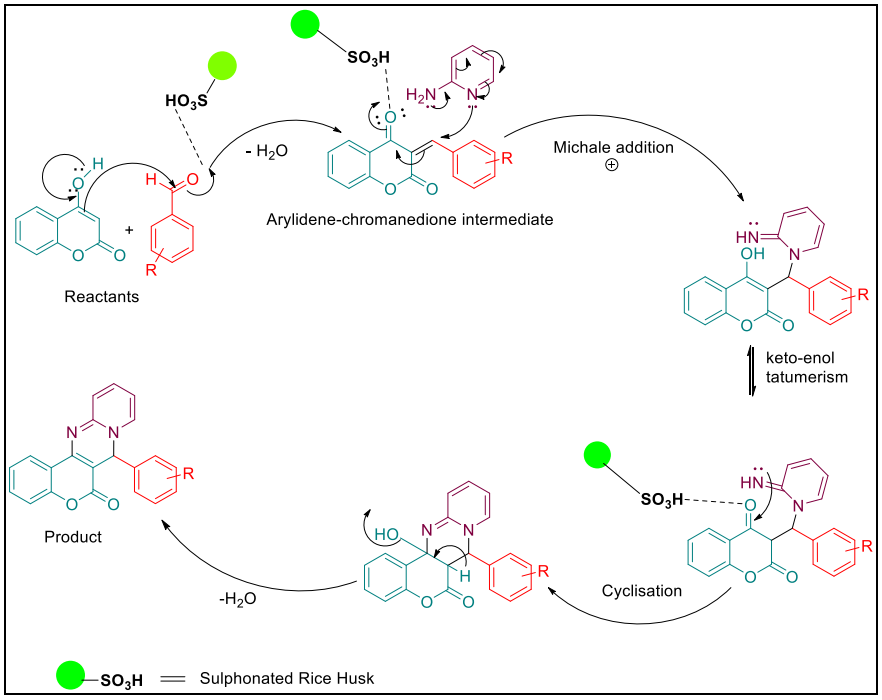


R= -Me, Et, -Cl, -Br, -F,-OH, -OMe, -NO_2,thionyl





Scheme 4. Synthesis of 7-aryl/heteroaryl-6a, 13a-dihydro-6*H*, 7*H*-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one derivatives using sulphonated rice husk[a]



Scheme 5. The plausible mechanism for the synthesis 7-aryl/heteroaryl-6a, 13a-dihydro-6*H*, 7*H*-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one derivatives

Mechanism

A plausible mechanism of synthesis (Scheme 5) of 7-aryl/heteroaryl-6a, 13a-dihydro-6*H*, 7*H*-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one derivatives are established by considering the acidic behavior of the catalyst. Initially a fast protonation at aldehyde oxygen followed by condensation reaction with 1 mol of 4-hydroxycoumarine to give a aryledine-chromanedione intermediate and then Michael addition reaction occurs between 2-aminopyridine and aryledine-chromanedione followed by intramolecular cyclization along with fast condensation results in the formation of desired 7-aryl/heteroaryl-6a, 13a-dihydro-6*H*, 7*H*-chromeno[4, 3-d]pyrido[1, 2a]pyrimidin-6-one derivatives [15].

Catalyst recyclability experiment

To check the recyclability of the catalyst, a model reaction was performed between anisaldehyde (1.8 mmol), 4-hydroxycoumarine

(1.8 mmol), 2-aminopyridine (1.8 mmol) in the presence of 110 mg of sulfonated rice husk following the optimized reaction condition (Scheme 4, **4b**). After successfully completing each reaction steps, the reaction mixture was extracted with ethyl acetate until the catalyst was thoroughly washed off. The catalyst was further washed with ethanol at the end finally then it was finally dried under vaccum vacuum vacuum, and the recovered catalyst weight was measured (Figure 3).

After every recovery step of the catalyst, the following reaction was repeated following optimized reaction condition with a required proportion of the reactants to that of the weight of the recovered catalyst (Table 4). Amount of catalyst, aldehyde, reaction time, temperature, and yield percentage of the product has been shown in the Table 4. The catalyst was readily recovered from the reaction mixture with minimum loss by centrifugation.

Also, it was found to retain its acidic property, even after the 5th run for this particular model reaction. This was further supported by FTIR spectra of the recovered SRH catalysts after successive reactions (Figure 4).

Figure 3. Recyclability experiment

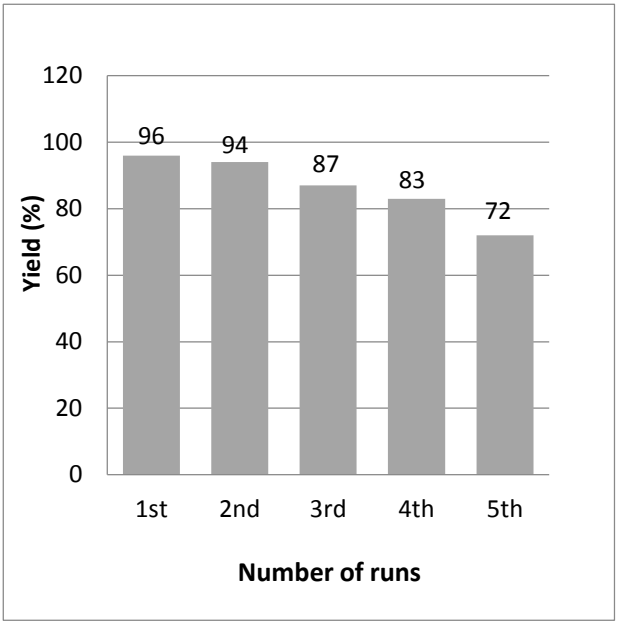


Table 4. Table for the amount of recovered catatyst with isolated product yield

Entry	Catalyst (mg)	Aldehyde (x mmol)	Temperature (°C)	Time (min)	Yield (%)[a]
1	110	1.80 mmol	70	180	96
2	80	1.30 mmol	70	180	94
3	60	0.90 mmol	70	180	87
4	50	0.75 mmol	70	180	83
5	40	0.60 mmol	70	180	72

[a]Isolated yield after reaction of anisaldehyde (x mmol), 4-hydroxycoumarine (x mmol), 2-aminopyridine (x mmol)

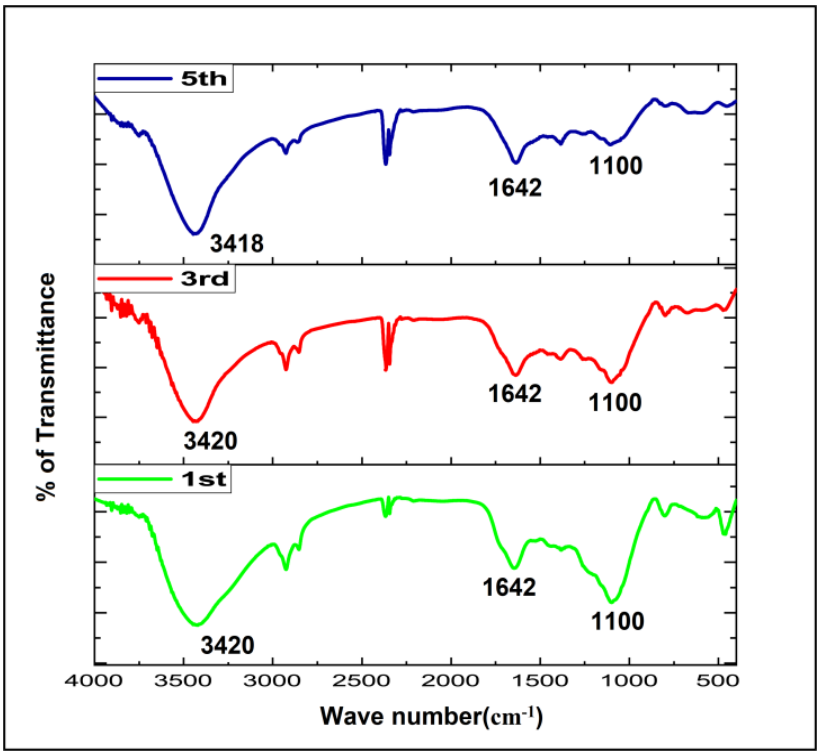


Figure 4. FTIR spectra of reused catalysts after 1st , 3rd, and 5th and run

Conclusions

In this research study, a simple and greener methodology for the synthesis of several 7-aryl/heteroaryl-6*H*, 7*H*, 8*H*-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione and 7-aryl/heteroaryl-6a, 13a-dihydro-6*H*, 7*H*-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one derivatives from commercially available aldehydes has been established. We have introduced a new greener method using newly developed cheaper heterogeneous catalyst Sulphonated rice husk (SRH) for the synthesis of 7-aryl/heteroaryl-6*H*, 7*H*, 8*H*-pyrano[3, 2-c:5, 6-c']dichromene-6, 8-dione and 7-aryl/heteroaryl-6a, 13a-dihydro-6*H*,7*H*-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one derivatives with excellent yield. This heterogeneous catalyst is found to be highly efficient for the synthesis 7-aryl/heteroaryl-6*H*, 7*H*, 8*H*-pyrano[3, 2-c:5, 6-c']dichromene-6,8-dione and 7-aryl/heteroaryl-6a, 13a-dihydro-6*H*, 7*H*-chromeno[4, 3-d]pyrido[1, 2-a]pyrimidin-6-one derivatives in short reaction time. The catalyst is recyclable up to 5th run for above mentioned model reaction and has broad aspect to catalyze a wide range of multi-component reactions bearing condensation and cyclisation steps.

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Disclosure Statement

No potential conflict of interest was reported by the authors.

Supporting Information

Additional supporting information related to this article can be found, in the online version, at DOI: 10.22034/ajgc.xxxx.
Supplementary data include experimental details, ^{1}H NMR, ^{13}C NMR spectra of all the synthesized compounds (**3a-3p**), (**4a-4j**) and EDX data of the prepared catalyst (PDF).

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