# Zirconia Supported on Rice Husk Silica from Biowaste: A Novel, Efficient, and Recoverable Nanocatalyst for the Green Synthesis of Tetrahydro-1-benzopyrans

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Abstract—Zirconia supported silica from rice husk (an agricultural waste) has been utilized as a novel and efficient heterogeneous catalyst for the synthesis of bioactive tetrahydro-1-benzopyran derivatives via multi-component condensation of various aldehydes with dimedone and malononitrile. This protocol offers various advantages such as high yields, simple experimental work-up procedure, short reaction time, no by-products, economic availability, easy purification, and reusability of the catalyst.

**Keywords**: tetrahydro-1-benzopyrans, rice husk silica-supported zirconia, multicomponent reactions (MCR), heterogeneous reusable catalyst

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Multicomponent reactions (MCRs) have become an emerging field of research, since they facilitate multibond formation and provide new chemical scaffolds in a single step. Moreover, MCRs offer advantages in terms of operational simplicity, easy work-up and purification procedures, atom economy, energy efficiency, and environmental friendliness and have proven to be a valuable tool in organic and medicinal chemistry [1]. An example of such MCRs is the one-pot synthesis of tetrahydro-1-benzopyran derivatives that are significant heterocyclic compounds exhibiting a broad range of biological activities such as anticancer, spasmolytic, diuretic, anti-coagulant, and anti-anaphylactic activity [2]. Furthermore, they are used as cognitive enhancers and for the treatment of neurodegenerative disease, amyotrophic lateral sclerosis, AIDS associated dementia, Down's syndrome, and Parkinson's, Huntington's and Alzheimer's diseases [3]. Considering the importance of such compounds, various methods have been reported for the synthesis of tetrahydro-1-benzopyrans using different catalysts such as amino functionalized silica gel (AP-SiO<sub>2</sub>) [4], potassium phthalimide [5], PEG-1000-based dicationic ionic liquid (PEG1000-DAIL) [6], [PAPEG<sub>1000</sub>-DIL][BF<sub>4</sub>] [7], RuBr<sub>2</sub>(PPh<sub>3</sub>)<sub>4</sub> [8], sodium selenate [9], CeMg<sub>y</sub>Zr<sub>1-y</sub>O<sub>2</sub> [10], diammonium sodium hydrogen phosphate [11] and RE(PFO)<sub>3</sub> [12]. Most of the aforementioned techniques have one or more drawbacks such as high reaction temperature, prolonged reaction time, expensive catalysts, etc. Therefore an alternative, efficient, inexpensive, and green methodology for the synthesis of tetrahydro-1benzopyran derivatives is highly desirable.

In order to circumvent these obstacles, we decided to reconsider the synthetic routes using a modified silica catalyst. Silica can be obtained from rice husk (RHSi) in a very short time. Moreover, rice husk is the major waste product in the rice industry of the developing countries, which is usually discarded or burned, resulting in environmental pollution and resource wasting [13]. Therefore, it is desirable to produce value-added materials from rice husk. The catalytic activity of RHSi can be increased by the incorporation of transition metals. There have been reports on the preparation of Cu/RHSi [14], Cr/RHSi [15], Mo/RHSi [16], W/RHSi [17], Co/RHSi [18], Fe/RHSi [19], etc. These materials are good potential heterogeneous catalyst for various industrially important reactions. Despite their tremendous success, none of these catalysts was used for the synthesis of tetrahydro-1-benzopyrans. Owing to the high acidity of zirconia, we modified RHSi with zirconia to get zirconia supported rice husk silica catalyst (ZrRHSi) by precipitation method. On the other hand, the residue from the rice mill industry is used as the raw material, without any solid waste generation for the production of silica. In line with the concept of green chemistry, this method



for the preparation of ZrRHSi increases the utilization

Drawing inspiration from our experience in developing new useful methodologies for MCRs to synthesize various biologically important heterocyclic compounds [20], herein we describe the synthesis of an efficient, green, and reusable heterogeneous catalyst, namely zirconia-doped rice husk silica (ZrRHSi) and evaluate its catalytic activity towards the synthesis of tetrahydro-1-benzopyrans (Scheme 1). The proposed method offers a complementary catalytic system that allows environmentally benign synthesis of tetrahydro-1-benzopyrans. The distinguishing features of this methodology are high yield, environmentally friendly reaction process, easy workup procedure, and inexpensive catalyst. It is worth noticing that the catalyst could be regenerated and recycled without significant loss of activity for at least five cycles.

of husk as a catalyst.

The X-ray diffractogram of ZrRHSi is depicted in Fig. 1. The observed PXRD pattern is in well agreement with the standard JCPDS data. The broad peak at  $2\theta \approx 22.3^{\circ}$  indicates an amorphous form of silica. The absence of any more characteristic peaks confirms a strong interaction of zirconia with silica. No peaks corresponding to zirconium or other impurities were observed as the amount of zirconia was only 10 wt %. This also indicates that Zr<sup>4+</sup> ions were just well dispersed in the silica matrix. A similar observation was reported for the tin-doped rice husk silica [21].

Next, the SEM study was performed to examine the morphology of the synthesized ZrRHSi catalyst. From Fig. 2 it is clear that incorporation of zirconia did not change the porous surface of silica and that zirconia was uniformly dispersed on the silica surface. To evaluate the composition of the catalyst, ZrRHSi was subjected to EDX studies. The atom percentages observed for O, Si, and Zr were 37.5, 48.3, and 14.2, respectively. The thermal stability of ZrRHSi was examined by TG-DTA analysis. The initial weight loss at 25–120°C was assigned to the removal of surface adsorbed hydration water. The catalyst is stable till 800°C. There was no loss of physisorbed or chemisorbed  $ZrO_2$  from the silica surface, which is in accordance with the earlier report [22].

After successful characterization, we have found that ZrRHSi can be used as an efficient catalyst for the



Fig. 1. X-Ray powder diffraction pattern of ZrRHSi.



Fig. 2. SEM image of ZrRHSi.

Entry no.	ZrRHSi, g	Time, <sup>a</sup> min	Yield, <sup>b</sup> %
1	0	120	30
2	0.02	30	40
3	0.04	30	55
4	0.06	30	60
5	0.08	30	75
6	0.10	30	90
7	0.12	30	90
8	0.14	30	90

Table 1. Optimization of the amount of ZrRHSi

<sup>a</sup> Reaction conditions: dimedone (2 mmol), aldehyde (1 mmol), malononitrile (1 mmol), ethanol (15 mL), temperature 80°C. <sup>b</sup> Isolated yield.

cyclocondensation reactions. The optimal conditions were found by varying different reaction parameters. The reaction between an aryl aldehyde, dimedone, and malononitrile was carried out in the presence of 0.02 g of ZrRHSi. When water was used as solvent at 26°C for 10 h, no product formation was observed. The reaction mixture charred under microwave irradiation, and only 40% of the product was formed on ultrasonication. Surprisingly, the desired product was obtained in a good yield within 30 min on heating under

solvent-free conditions in an oil bath. In all these cases, the Knoevenagel condensation product was formed.

We also evaluated different solvents for this condensation and found that ethanol gives excellent yields. In the next stage, different amounts of ZrRHSi were used for the cyclocondensation of 4-methoxybenzaldehyde, malononitrile, and dimedone. The maximum yield (90%) was observed with 10 mol % of the catalyst (Table 1, entry no. 6). An increase in the amount of ZrRHSi did not improve the yield (Table 1, entry

**Table 2.** Synthesis of tetrahydro-1-benzopyrans using ZrRHSi as catalyst

Entry no.	R	Product <sup>a</sup>	Time, min	Yield, <sup>b</sup> %	mp, °C	
					found	reported
1	Н	4a	60	94	231–233	230–232 [23]
2	4-NO <sub>2</sub>	4b	90	93	178-179	177–178 [24]
3	3-NO <sub>2</sub>	4c	120	90	213-214	210–212 [23]
4	4-Br	4d	110	92	201-203	201–203 [12]
5	4-OMe	4e	120	89	193–194	190–192 [25]
6	4-OH	4f	130	90	208-209	205–207 [26]
7	2,4-Cl <sub>2</sub>	4g	140	88	250-251	249–250 [11]
8	4-Me	4h	130	93	217-218	216–218 [5]
9	4-CN	4i	140	90	228-229	227–230 [11]
10	3,5-Br <sub>2</sub>	4j	130	92	217-218	_
11	4-C1	4k	140	95	213-214	210–213 [27]
12	4-NMe <sub>2</sub>	41	150	94	224–225	223–225 [26]
13	Naphthalen-2-yl	4m	170	85	253-255	253–255 [25]
14	4-MeOC(O)	4n	150	95	258-259	257–259 [25]
15	2-ОН	40	150	87	214–215	_

<sup>a</sup> Compounds **4b**–**4d**, **4f**–**4i**, **4k**, **4l**, and **4n** were reported previously and were identified by comparison of their physical properties with those described in the respective literature. Compounds **4a**, **4e**, **4j**, **4m**, and **4o** were characterized by <sup>1</sup>H and <sup>13</sup>C NMR spectra.



nos. 7, 8). The effect of temperature was also investigated. As expected, the yield increased from 28 to 90% as the temperature was changed from 25 to 80°C.

Encouraged by these results, we subsequently employed a variety of aromatic aldehydes to explore the generality of the proposed procedure to synthesize numerous tetrahydro-1-benzopyrans. Aromatic aldehydes including those with electron-donating and electron-withdrawing substituents provided the desired product in high to excellent yields as shown in Table 2. After scrutinizing the result (Table 2), it became clear that variation in the yield was very small with aldehydes containing both electron-withdrawing (Table 2, entry nos. 2-4, 7, 9-11) and electron-donating substituents (Table 2, entry nos. 5, 6, 8, 12). From the viewpoint of green chemistry, recoverability and reusability of catalysts are highly crucial. The ZrRHSi catalyst along with the solid product was separated from the reaction mixture and washed with ethyl acetate to get solid ZrRHSi which was then dried at 110°C for 2 h and reused for the model reaction. The results (Fig. 3), demonstrated that there was almost no appreciable change in the activity of ZrRHSi which can be used successively for at least four runs.

A possible mechanism is shown in Scheme 2. The reaction involves activation of the aldehyde by ZrRHSi, followed by attack of dicyanomethanide to form Knoevenagel adduct **A**, which further reacts with the enol form of dimedone to give intermediate **B**. The



**Fig. 3.** Reusability of ZrRHSi; reaction conditions: dimedone (2 mmol), benzaldehyde (1 mmol), malononitrile (1 mmol), ethanol (15 mL), temperature 80°C, ZrRHSi (0.1 g).

latter undergoes cyclization to tetrahydro-1-benzopyran. This successfully confirms the key role of ZrRHSi in the synthesis of various tetrahydro-1benzopyrans.

In summary, a reliable and practical method has been developed for the synthesis of tetrahydro-1benzopyran derivatives. Environmentally benign nature of ZrRHSi, economic aspects, reusability, and multicomponent reaction conditions are the other remarkable advantages of the proposed methodology. We feel that this economically viable methodology will prove to be a greener and good alternative to the existing methods for the synthesis of tetrahydro-1-benzopyrans.

## EXPERIMENTAL

All chemicals and solvents used were commercial products and were used without further purification. The crystal structure of the catalyst was characterized by X-ray powder diffraction using a PANalytical Xpert Pro X-ray diffractometer (Cu  $K_{\alpha}$  radiation,  $\lambda 0.154$  nm; scanning rate 2 deg/min). Scanning electron micrograph was obtained from Quanta ESCM, FEI instrument with EDAX. Thermal analysis of the catalyst was performed in a DSC-TG Analyzer Standard instrument (SDT Q600, V20.9, Build 20) at a heating rate of 10 deg/min in a nitrogen atmosphere. Thin layer chromatography (silica gel F<sub>254</sub> plates) was used to monitor the reaction progress; TLC plates were visualized under a UV lamp. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker AMX instrument (400 MHz for <sup>1</sup>H and 100 MHz for <sup>13</sup>C) using DMSO- $d_6$  as solvent and tetramethylsilane as reference.

**Zirconia supported on rice husk silica (ZrRHSi).** The raw material, rice husk, was collected from a local rice mill (Bangalore, India). The husk was mixed with concentrated aqueous HCl, and the mixture was refluxed for 3 h. The treated husk was washed with water, dried at 110°C for 12 h, and burned at 600°C in a muffle furnace for 6 h to get amorphous white silica. Colloidal silica was mixed with a required amount of a zirconyl nitrate solution, and aqueous ammonia (1:1) was added dropwise to this mixture until precipitation was complete. The precipitate was washed, dried, and calcined at 500°C for 5 h.

General procedure for the synthesis of tetrahydro-1-benzopyrans. A mixture of aromatic aldehyde (1 mmol), dimedone (2 mmol), malononitrile (1 mmol), ZrRHSi (0.1 g), and ethanol (15 mL) was stirred at 80°C for 2 h. The progress of the reaction was monitored by TLC using ethyl acetate–hexane (3:7) as eluent. The mixture was diluted with 10 mL of water, and the solid precipitate was filtered off. The catalyst was recovered by washing the solid residue with ethyl acetate. The crude product obtained from the ethyl acetate layer was subjected to silica gel column chromatography (ethyl acetate-petroleum ether, 3:7). The recovered solid catalyst was kept aside for reuse.

**2-Amino-4-(4-methoxyphenyl)-7,7-dimethyl-5oxo-5,6,7,8-tetrahydro-4H-1-benzopyran-3-carbonitrile (4e).** Yield 89%, white solid, mp 193°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.03 s (3H), 1.11 s (3H), 2.21 d (2H, J = 4 Hz), 2.44 s (2H), 3.76 s (3H), 4.36 s (2H), 6.81 d (2H, H<sub>arom</sub>, J = 4 Hz), 7.15 d (2H, H<sub>arom</sub>, J = 8 Hz), 7.26 s (2H). <sup>13</sup>C NMR spectrum,  $\delta_{\rm C}$ , ppm: 27.66, 32.16, 34.74, 40.67, 50.69, 55.19, 63.88, 76.68, 113.97, 118.67, 128.6, 135.45, 157.33, 158.61, 161.19, 195.89.

**2-Amino-4-(3,5-dibromophenyl)-7,7-dimethyl-5oxo-5,6,7,8-tetrahydro-4H-1-benzopyran-3-carbonitrile (4j).** Yield 92%, white solid, mp 217°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 0.99–1.22 m (6H), 2.39 s (2H), 2,59–2.71 m (2H), 4.07 d (1H, J = 4 Hz), 5.83 s (1H, NH<sub>2</sub>), 6.23 s (1H, H<sub>arom</sub>), 7.42 s (1H, H<sub>arom</sub>), 7.69 s (1H, H<sub>arom</sub>). <sup>13</sup>C NMR spectrum,  $\delta_{\rm C}$ , ppm: 26.93, 27.35, 32.14, 41.23, 44.69, 50.52, 76.68, 108.53, 112.23, 116.13, 121.98, 129.90, 135.52, 146.9, 164.53, 167.31, 197.01.

**2-Amino-7,7-dimethyl-4-(naphthalen-1-yl)-5oxo-5,6,7,8-tetrahydro-4H-1-benzopyran-3-carbonitrile (4m).** Yield 85%, white solid, mp 253°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.07 s (3H), 1.13 s (3H), 2.16–2.27 m (2H), 2.51–2.53 m (2H), 4.48 s (2H), 5.27 s (1H), 7.23–7.81 m (7H). <sup>13</sup>C NMR spectrum,  $\delta_{\rm C}$ , ppm: 27.83, 28.85, 30.66, 32.19, 40.73, 50.57, 64.20, 76.68, 114.64, 118.54, 122.28, 123.26, 129.41, 134.89, 157.39, 161.73, 195.76.

**2-Amino-4-(2-hydroxyphenyl)-7,7-dimethyl-5oxo-5,6,7,8-tetrahydro-4***H***-1-benzopyran-3-carbo-<b>nitrile (40).** Yield 87%, white solid, mp 214°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.03 s (3H), 1.11 s (3H), 2.21 d (2H, *J* = 4 Hz), 2.44 s (2H), 4.35 s (2H), 4.85 s (1H), 6.73 d (2H, H<sub>arom</sub>, *J* = 8 Hz), 7.10 d (2H, H<sub>arom</sub>, *J* = 8 Hz), 7.26 s (2H). <sup>13</sup>C NMR spectrum,  $\delta_{\rm C}$ , ppm: 27.67, 28.84, 30.9, 34.74, 40.69, 50.7, 76.68, 114.64, 118.54, 122.28, 123.26, 129.41, 134.89, 157.39, 161.73, 195.76.

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### CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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