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Sulfonated rice husk ash (RHA-SO_3H) as a highly efficient and reusable catalyst for the synthesis of some bis-heterocyclic compounds†

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Sulfonated rice husk ash (RHA-SO_3H), a newly reported solid acid catalyst, was efficiently used for the synthesis of 4,4′-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols), 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins) and bis(indolyl)methanes. The procedure gave the products in excellent yields within very short reaction times under mild and green conditions. Also this catalyst can be reused several times without appreciable loss of its catalytic activity.

Introduction

Heterocyclic compounds are widely distributed in nature and are essential to life. Pyrazoles are an important class of heterocyclic compounds that occurs widely in the pharmaceutical industry. For example, compounds containing the 2,4-dihydro-3*H*-pyrazol-3-one structural motif, including 4,4′-(arylmethylene)-bis-(1*H*-pyrazol-5-ols), have attracted interest because they exhibit a wide range of biological activities such as antimalarial,[1] antifungal,[2] anti-inflammatory,[3] antimicrobial,[4] antinociceptive,[5] analgesic,[6] fungicide,[7] and antitumor[8] activities. Additionally, they are applied as important intermediates in organic synthesis,[9] and as bis-Schiff bases.[10] 4,4′-(Arylmethylene)-bis-(1*H*-pyrazol-5-ols) were also used as pesticides,[11] antivirals[12] and ligands.[13] The main synthetic method for the preparation of this type of compounds is based on the condensation of aldehydes with 3-methyl-1-phenyl-5-pyrazolone. Therefore, a variety of catalysts and reagents have been used to facilitate this reaction.[13–20]

Coumarins are another important class of heterocycles. This importance can be attributed to their broad scope of pharmaceutical and biological activities such as anti-bacterial,[21] anti-HIV,[22] anti-Hepatitis C virus,[23] anti-tumor,[24] and anti-cancer[25] activities. Biscoumarins, the bridge substituted dimers of coumarin were also used as anti-inflammatories, antipyretics, antifungals, antiseptics,[26] anticoagulants,[27] and as urease inhibitors.[28] The preparation of 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins), a class of biscoumarins, is based on the condensation of aldehydes with 4-hydroxycoumarin. For this purpose, a variety of catalysts including piperidine,[28] I_2,[29] tetrabutylammonium bromide (TBAB),[30] sodium dodecyl sulfate (SDS),[31] $[MIM(CH_2)_4SO_3H]\,HSO_4$,[32] and $RuCl_3 \cdot nH_2O$[33] have been reported.

Indoles are also an important group of heterocyclic compounds with a broad scope of biological activities.[34] Among them, bis(indolyl)alkane derivatives have found a great deal of interest because they have many applications in pharmaceuticals. For example, they have showed antitumor,[35] antileishmanial,[36] antihyperlipidemic,[37] and anticancer[38] activities. Among various methods that have been reported for the synthesis of bis(indolyl) methanes,[39–41] the most simple and straightforward method that has been developed is based on the condensation of aldehydes with indoles. For this purpose, a variety of catalysts including I_2,[42] sulfamic acid,[43] benzyltriphenylphosphonium tribromide,[44] ceric ammonium nitrate,[45] [hmim]HSO_4 acidic ionic liquid,[46] $ZrOCl_2 \cdot 8H_2O$, camphor sulphonic acid,[47] and PEG-SO_3H[48] have been reported.

Although these procedures provide an improvement in the synthesis of the above mentioned bis-heterocyclic compounds, many of them suffer from disadvantages such as long reaction times, harsh reaction conditions, a need for excess amounts of the reagent, use of organic solvents, use of toxic reagents and non-recoverability of the catalyst. Therefore, there is still a demand for introducing simple, efficient and mild procedures with easily separable and reusable solid catalysts to overcome these problems.

The replacement of conventional, toxic and polluting Brönsted and Lewis acid catalysts with eco-friendly, reusable, heterogeneous catalysts is an area of current interest. In this context, there has been renewed interest in the synthesis of solid acid catalysts for organic reactions. Solid acid catalysts have many advantages compared to traditional liquid acids

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such as their efficiency, operational simplicity, easy recyclability and recoverability, non-corrosive nature and environmentally friendliness, all factors which are important in industry. Therefore, solid acid catalysts can play a significant role in the development of clean technologies.

Experimental section

Reagents and materials

Chemicals were purchased from Fluka, Merck, and Aldrich chemical companies. All yields refer to the isolated products. Products were characterized by comparison of their physical constants, and IR and NMR spectra with those of authentic samples and those reported in the literature. The purity determination of the substrate and reaction monitoring were followed by TLC on silicagel polygram SILG/UV 254 plates.

Catalyst preparation (RHA-SO_3H)

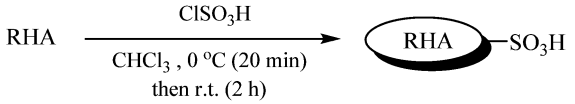
A 50 mL suction flask charged with 3.0 g of RHA and 10 mL $CHCl_3$ was equipped with a constant-pressure dropping funnel containing chlorosulfonic acid (0.7 mL) and a gas outlet tube for conducting HCl gas into water as an absorbing solution. Chlorosulfonic acid was added dropwise over a period of 20 min while the reaction mixture was stirred in an ice bath (0 °C). After addition was completed, the mixture was stirred for an additional 2 h at room temperature. Then, the mixture was filtered and the solid residue washed with methanol (20 mL) and dried at 70 °C for 1 h to afford RHA-SO_3H (3.6 g) as an earthy powder (Scheme 1).

General procedure for the synthesis of 4,4′-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) derivatives (2)

Phenylhydrazine (2 mmol) was added to a mixture of RHA-SO_3H (60 mg) and ethyl acetoacetate (2 mmol) at 80 °C, and stirred for 1 min. Then the aldehyde (1 mmol) was added and the resulting mixture was stirred for the appropriate time (Table 1). After completion of the reaction (monitored by TLC), EtOH (10 mL) was added and the catalyst was removed by filtration. Then, water was added and the precipitated product was collected by filtration in high purity.

General procedure for the synthesis of 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins) derivatives (3)

A mixture of 4-hydroxycoumarin (2 mmol), aldehyde (1 mmol), RHA-SO_3H (40 mg) and water (5 mL) in a round bottomed flask was heated at 80 °C. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was cooled to room temperature. The solid was filtered off, EtOH or CH_2Cl_2 (10 mL) was added and the catalyst was removed by filtration. The products were purified by recrystallization from aqueous ethanol.



Scheme 1 Preparation of the catalyst (RHA-SO_3H).

General procedure for the synthesis of bis(indolyl)methane derivatives (4)

A mixture of the aldehyde (1 mmol), indole (2 mmol) and RHA-SO_3H (15 mg) was heated at 80 °C under solvent-free conditions for the appropriate time. After completion of the reaction (monitored by TLC), EtOH (10 mL) was added and the catalyst was removed by filtration. Then, water was added and the precipitated product was collected by filtration in high purity.

The spectral data of the new compounds is as follows:

Compound 3m:

mp 258–260 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.50 (3H, s, CH_3), 6.08 (1H, s, CH), 7.16 (2H, d, J = 8 Hz), 7.23 (2H, d, J = 8.4 Hz), 7.39–7.45 (4H, m), 7.6 (2H, td, J_1 = 7.6 Hz, J_2 = 1.6 Hz), 8.02–8.11 (2H, m), 11.34 (1H, s, OH), 11.55 (1H, s, OH) ppm; IR (KBr, cm^{-1}): 760, 1558, 1603, 1655, 2920, 3080.

Compound 4s:

mp 304–306 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 6.50 (1H, s, CH), 7.24 (2H, s), 7.57 (2H, d, J = 8.8 Hz), 7.68 (2H, d, J = 8.8 Hz), 8.0 (2H, dd, J_1 = 9 Hz, J_2 = 2 Hz), 8.22 (2H, d, J = 8.8 Hz), 8.40 (2H, d, J = 2.4 Hz), 11.9 (s, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 Mz): δ = 38.4, 112.6, 116.5, 117.3, 119.7, 124.3, 126.0, 128.3, 129.9, 140.1, 140.8, 146.6, 152.3; IR (KBr, cm^{-1}): 3253, 1612, 1502, 1460, 1317, 1090, 800, 733.

Compound 4t:

mp 317–319 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 3.73 (3H, s, OCH_3), 6.15 (1H, s, CH), 6.89 (2H, d, J = 8.4 Hz), 7.12 (2H, s), 7.30 (2H, d, J = 8.8 Hz), 7.55 (2H, d, J = 9.2 Hz), 7.98 (2H, dd, J_1 =

Table 1 Preparation of 4,4′-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) derivatives catalyzed by RHA-SO_3H under optimized conditions[a]

					Melting point (°C)	
Entry	Ar	Product	Time (min)	Yield (%)	Found	Reported
1	C_6H_5–	**2a**	3	91	167–169	168–170 (ref. 50)
2	2-Cl–C_6H_4–	**2b**	4	89	237–239	236–237 (ref. 14)
3	4-Cl–C_6H_4–	**2c**	3	92	206–208	207–209 (ref. 14)
4	4-Br–C_6H_4–	**2d**	3	91	212–214	215 (ref. 50)
5	4-F–C_6H_4–	**2e**	3	92	180–182	181–183 (ref. 51)
6	3-CH_3–C_6H_5–	**2f**	4	87	192–194	191–194 (ref. 50)
7	4-iso-PrC_6H_4–	**2g**	4	86	173–175	132–134 (ref. 19)
8	2-CH_3O–C_6H_5–	**2h**	6	85	212–214	210–213 (ref. 16)
9	3-CH_3O–C_6H_5–	**2i**	4	86	192–194	193–194 (ref. 50)
10	4-CH_3O–C_6H_5–	**2j**	4	91	173–175	172–174 (ref. 16)
11	2-NO_2–C_6H_4–	**2k**	5	85	220–222	221–222 (ref. 16)
12	3-NO_2–C_6H_4–	**2l**	3	90	148–150	149–150 (ref. 14)
13	4-$NO_2C_6H_4$–	**2m**	3	86	224–226	225–227 (ref. 15)
14	4-$CH_3SC_6H_5$–	**2n**	4	89	204–206	201–203 (ref. 15)
15	2-OHC_6H_4–	**2o**	4	87	228–230	227–229 (ref. 51)
16	4-OHC_6H_4–	**2p**	4	88	156–158	155–157 (ref. 15)
17	2-naphthyl–	**2q**	3	91	204–206	206–208 (ref. 18)
18	3-pyridyl–	**2r**	3	90	238–240	238–240 (ref. 18)
19	4-OHC–C_6H_4–	**2s**	8	83	208–210	209–212 (ref. 51)

[a] *Reaction conditions*: phenylhydrazine (2 mmol), ethyl acetoacetate (2 mmol) and RHA-SO_3H (60 mg) under solvent free conditions at 80 °C, and after 1 min: aldehyde (1 mmol).

9 Hz, J_2 = 2 Hz), 8.32 (2H, d, J = 2.4 Hz), 11.67 (s, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 Mz): δ = 38.1, 55.4, 112.5, 114.2, 116.7, 117.1, 121.4, 126.2, 127.8, 129.6, 136.1, 140.2, 140.6, 158.1; IR (KBr, cm^{-1}):3256, 1609, 1501, 1397, 1316, 1090, 795, 730.

Results and discussion

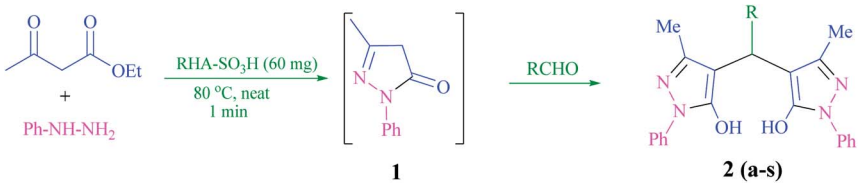
Very recently, we have reported the preparation and characterization of sulfonated rice husk ash (RHA-SO_3H) as a new solid acid catalyst and its applicability in the chemoselective preparation and deprotection of 1,1-diacetates.[49]

On the basis of the information obtained from the studies on RHA-SO_3H, we anticipated that this reagent could be used as an efficient solid acid catalyst for the promotion of the reactions which need the use of an acidic catalyst to speed them up. Therefore, we were interested in investigating the applicability of this reagent in the promotion of the synthesis of 4,4′-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols), 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins) and bis(indolyl)methanes.

At first, we focused our attention on studying the synthesis of 4,4′-(aryl methylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols). For optimization of the reaction conditions, the reaction between phenylhydrazine, ethyl acetoacetate and 4-chlorobenzaldehyde to form the corresponding product was selected as a model reaction and the various conditions including the amount of catalyst, solvent and temperature were examined. Finally, the optimal reaction conditions for this reaction were determined as shown in Scheme 2. Any further increase in the amount of catalyst or temperature did not improve the reaction time or yield.

After optimization of the reaction conditions and in order to establish the effectiveness and the acceptability of the method, we explored the protocol with a variety of simple, readily available substrates under the optimal conditions. The results were presented in Table 1. It was observed that under similar conditions, a wide range of aromatic aldehydes containing electron-withdrawing as well as electron-donating groups, such as Cl, Br, F, CH_3, OCH_3, NO_2, iso-Pr, SCH_3 and OH in the ortho, meta, and para positions of the benzene ring, easily converted to the corresponding 4,4′-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) in short reaction times with good to excellent isolated yields (Table 1, entries 1–16). As can be seen, the effect of the nature of the substituents on the aromatic ring did not show very obvious effects in terms of yields and times under the selected reaction conditions, while the steric effects showed a very small influence on the reaction times (Table 1, entries 2, 8 and 11). Furthermore, 2-naphthaldehyde, a polycyclic aromatic aldehyde, also provided the desired product in very good yields (Table 1, entry 17). Pyridine-3-carbaldehyde, a heterocyclic aldehyde, was also used as a substrate under these conditions and the desired product was successfully obtained with high yield (Table 1, entry 18). This method was also found to be useful for the usage of dialdehydes. In this reaction, 4 equivalents of 3-methyl-1-phenyl-5-pyrazolone successfully condensed with 1 equivalent of terephthaldialdehyde, and di-4,4′-(phenylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) was obtained with high yield in a short time which shows the practical synthetic efficiency of this reaction (Table 1, entry 19).

After the successful application of RHA-SO_3H as a solid acid catalyst in the synthesis of 4,4′-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols), we decided to use it in the condensation



Scheme 2 One-pot synthesis of 4,4′-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols).

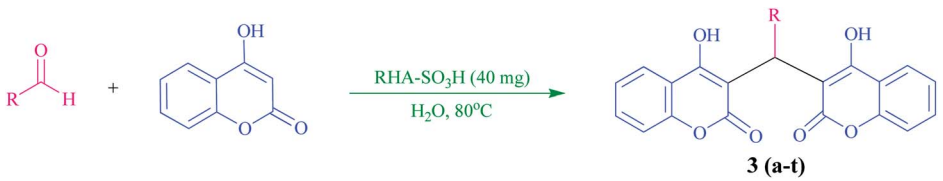
of 4-hydroxycoumarin with aldehydes leading to biscoumarins. For this purpose and to obtain the optimum reaction conditions, the reaction between 4-nitrobenzaldehyde and coumarin to its corresponding biscoumarin was studied as a model reaction in different conditions. In order to chose the reaction media, different solvents such as dichloromethane, diethyl ether, ethanol and water as well as solvent free conditions were used, and the best results were obtained in water. Finally, we found that the best result was obtained using 1 mmol aldehyde, 2 mmol 4-hydroxycoumarin and 40 mg RHA-SO_3H as the catalyst in 5 mL H_2O 80 °C, as shown in Scheme 3.

Subsequently, to reveal the generality of this method, the condensation was carried out with a variety of substrates using RHA-SO_3H under the optimal conditions. For this purpose, a broad range of aromatic, aliphatic and heterocyclic aldehydes were reacted with 4-hydroxycoumarin and the corresponding 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins) were obtained in high yields and short reaction times, as shown in Table 2. Various aromatic aldehydes containing electron-withdrawing or electron-donating groups (Cl, Br, CH_3, OCH_3, NO_2, $N(CH_3)_2$, SCH_3 and OH) and also α,β-unsaturated aldehydes (cinnamaldehyde and 2-nitrocinnamaldehyde) were efficiently condensed with 4-hydroxycoumarin in very good yields and times (Table 2, entries 1–16). Furthermore, using this method, heterocyclic aldehydes (indole-3-carbaldehyde, pyridine-3-carbaldehyde and pyridine-4-carbaldehyde), and 3-phenylpropionaldehyde as an aliphatic aldehyde were converted to the corresponding products in good to high yields (Table 2, entries 17–20).

In the next step, RHA-SO_3H solid acid catalyst was used in the condensation of indoles with aldehydes leading to bis(indolyl)methanes. For this purpose and to obtain the optimum reaction conditions, the reaction between 4-nitrobenzaldehyde and indole was studied as a model reaction in different conditions and the best result obtained using 1 mmol aldehyde, 2 mmol indole and 15 mg RHA-SO_3H at 80 °C under solvent free conditions (Scheme 4).

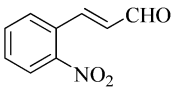
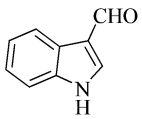
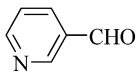
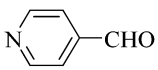
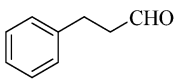
After optimization of the reaction conditions, a broad range of aromatic and heterocyclic aldehydes were reacted with different indole derivatives (indole, 2-methyl indole and 5-nitro indole) and the corresponding bis(indolyl)methanes were obtained in high yields and short reaction times, as shown in Table 3. Various aromatic aldehydes containing electron-withdrawing or electron-donating groups (Cl, Br, NO_2, OCH_3 and OH), α,β-unsaturated aldehyde (cinnamaldehyde) and polycyclic aromatic aldehyde (2-naphthaldehyde) were efficiently condensed with indole in very good yields and times (Table 3, entries 1–12). This method was also found to be useful for the usage of dialdehyde. In this reaction, 4 equivalents of indole successfully condensed with 1 equivalent of terephthaldialdehyde and di-bis(indolyl)methanes were obtained with good yield which shows the practical synthetic efficiency of this reaction (Table 3, entry 13). 2-Methyl indole and 5-nitro indole were also successfully used in the synthesis of bis(indolyl) methanes under the selected conditions (Table 3, entries 14–20). It should be noted that indoles with electron-donating substituents (CH_3) were converted to the desired products in shorter times than indoles with electron-withdrawing substituents (NO_2). Furthermore, under this catalytic system, the application of ketones such as acetophenone was not successful and no product was obtained which indicates the chemoselectivity of the protocol and that aldehydes are more reactive than ketones due to higher electrophilicity of aldehydes in comparison with ketones.

In order to show the merit of the selected procedures, Table 4 compares our results obtained from the synthesis of 4,4′-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols), 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins) and bis(indolyl)methanes in the presence of RHA-SO_3H with the same results reported in the literature. This method avoids disadvantages of the other procedures such as long reaction times, toxic reagents, high temperature, organic solvents, excess reagents and low yield. It is also important to note that the reported procedures for the synthesis of 4,4′-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s are based on the condensation of aldehydes with



Scheme 3 Synthesis of 3,3′-(arylmethylene)-bis-(4-hydroxycoumarin) derivatives in the presence of RHA-SO_3H.

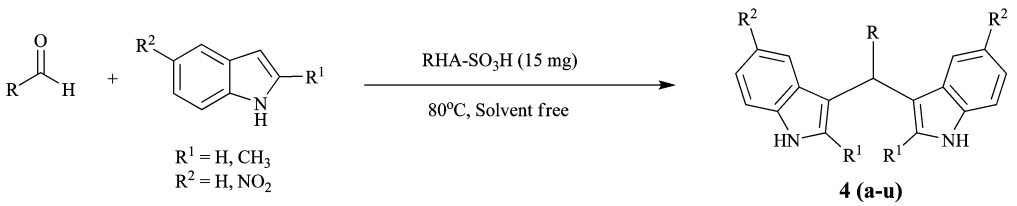
Table 2 Preparation of 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins) derivatives catalyzed by RHA-SO_3H[a]

Entry	Aldehyde	Product	Time (min)	Yield (%)	Melting point (°C) Found	Reported
1	C_6H_5–	**3a**	15	90	232–234	230–232 (ref. 31)
2	2-Cl–C_6H_4–	**3b**	45	89	205–207	201–203 (ref. 32)
3	3-Cl–C_6H_4–	**3c**	25	91	230–232	228–230 (ref. 31)
4	4-Cl–C_6H_4–	**3d**	25	93	257–259	257–258 (ref. 29)
5	4-Br–C_6H_4–	**3e**	20	90	269–271	268–270 (ref. 29)
6	2-NO_2–C_6H_4–	**3f**	35	92	211–212	200–202 (ref. 32)
7	3-NO_2–C_6H_4–	**3g**	15	94	236–238	234–236 (ref. 31)
8	4-NO_2–C_6H_4–	**3h**	10	95	233–235	232–234 (ref. 32)
9	2-CH_3–C_6H_4–	**3i**	60	88	218–220	218–220 (ref. 31)
10	3-CH_3O–C_6H_4–	**3j**	15	94	256–258	238 (ref. 28)
11	4-CH_3O–C_6H_4–	**3k**	15	92	249–251	249–250 (ref. 32)
12	4-$(CH_3)_2N$–C_6H_4–	**3l**	25	94	221–223	222–224 (ref. 31)
13	4-CH_3S–C_6H_4–	**3m**	20	93	258–260	—
14	2-OHC_6H_4–	**3n**	50	89	250–252	254–256 (ref. 32)
15	C_6H_5–CH=CH–	**3o**	20	92	192–194	196 (ref. 28)
16		**3p**	60	90	190–192	190–192 (ref. 33)
17		**3q**	45	87	241–243	240–244 (ref. 29)
18		**3r**	40	88	271–273	274–276 (ref. 52)
19		**3s**	20	93	269–271	261–263 (ref. 52)
20		**3t**	70	90	197–199	190 (ref. 28)

[a] *Reaction conditions*: 4-hydroxycoumarin (2 mmol), aldehyde (1 mmol), RHA-SO_3H (40 mg) and water (5 mL) at 80 °C.

3-methyl-1-phenyl-5-pyrazolone, while our method is based on the one-pot condensation of phenylhydrazine, ethyl acetoacetate and aldehydes. On the basis of the obtained results we believe that the reaction proceeds *via* the *in situ* generation of 3-methyl-1-phenyl-5-pyrazolone (**1**) which in reaction with aldehydes produces the desired products. This comparison also clarifies an important point about the catalyst. As it can be seen, rice husk and rice husk ash are also able to catalyze this type of reaction, but in much longer reaction times than RHA-SO_3H. These results give clear evidence for the truth that the presence of SO_3H groups in the catalyst is necessary to obtain the best performance.

The reusability of the catalyst was also checked in three types of the above mentioned reactions. For this purpose, the model reactions were studied again under the optimized reaction conditions. Upon completion, the catalyst was removed by filtration, washed with dichloromethane, dried and reused for the same reaction. This process was carried out over three runs in each series of the reactions. The obtained results showed that the reactions led to the desired products without significant



Scheme 4 Synthesis of bis(indolyl)methane derivatives in the presence of RHA-SO_3H.

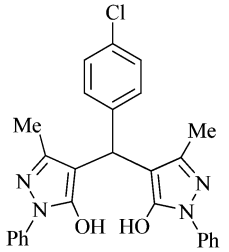
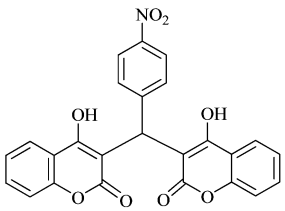
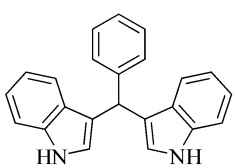
Table 3 Preparation of bis(indolyl)methane derivatives catalyzed by RHA-SO_3H[a]

Entry	Ar	R^1	R^2	Product	Time (min)	Yield (%)	Melting point (°C) Found	Reported
1	C_6H_5–	H	H	**4a**	8	91	128–130	126–127 (ref. 42)
2	2-Cl–C_6H_4–	H	H	**4b**	18	88	94–95	75–76 (ref. 53)
3	4-Cl–C_6H_4–	H	H	**4c**	6	91	86–88	78–88 (ref. 47)
4	4-Br–C_6H_4–	H	H	**4d**	8	90	110–112	112–113 (ref. 29)
5	2-NO_2–C_6H_4–	H	H	**4e**	8	89	138–140	139–141 (ref. 43)
6	3-NO_2–C_6H_4–	H	H	**4f**	4	93	220–222	219–221 (ref. 53)
7	4-NO_2–C_6H_4–	H	H	**4g**	3	94	237–239	222–224 (ref. 53)
8	3-CH_3O–C_6H_4–	H	H	**4h**	13	91	163–165	165 (ref. 55)
9	4-CH_3O–C_6H_4–	H	H	**4i**	22	92	186–188	186–188 (ref. 48)
10	4-OHC_6H_4–	H	H	**4j**	60	88	122–124	124–125 (ref. 54)
11	C_6H_5–CH=CH–	H	H	**4k**	8	90	100–102	100–101 (ref. 33)
12	2-Naphthyl–	H	H	**4l**	20	90	200–202	201–203 (ref. 53)
13[b]	–C_6H_4–	H	H	**4m**	25	86	193–195	194 (ref. 56)
14	C_6H_5–	CH_3	H	**4n**	2	91	257–259	250–253 (ref. 47)
15	4-Cl–C_6H_4–	CH_3	H	**4o**	2	92	249–251	247–248 (ref. 53)
16	4-CH_3O–C_6H_4–	CH_3	H	**4p**	4	93	213–215	102–103 (ref. 48)
17	4-NO_2–C_6H_4–	CH_3	H	**4q**	2	95	240–242	241–243 (ref. 47)
18	3-Indolyl–	CH_3	H	**4r**	12	87	271–273	270–272 (ref. 57)
19[b]	4-NO_2–C_6H_4–	H	NO_2	**4s**	60	94	304–306	—
20[b]	4-CH_3O–C_6H_4–	H	NO_2	**4t**	60	93	317–319	—
21	Acetophenone	H	H	**4u**	120	0	—	—

[a] *Reaction conditions*: aldehyde (1 mmol), indole (2 mmol), RHA-SO_3H (15 mg) at 80 °C under solvent free conditions. [b] 30 mg catalyst was used.

changes in terms of yield and reaction time which clearly demonstrates practical recyclability of RHA-SO_3H. Further pH analysis of the recovered catalyst showed a loading of 2.28 mmol H^+ g^{-1}. This result suggests that the catalytic nature of RHA-SO_3H remains unchanged after each run and leaching of the acid species did not occur during the course of the reaction.

Table 4 Comparison of the results obtained from the synthesis of 4,4′-(4-chlorophenylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ol), 3,3′-(4-nitrophenylmethylene)-bis-(4-hydroxycoumarins) and 3,3′-(phenylmethylene)-bis-(1*H*-indole) in the presence of RHA-SO_3H with those obtained using other catalysts

Product	Catalyst (loading)	Reaction conditions	Time (min)	Yield (%)
	SDS (5 mol%)	Reflux/H_2O	1 h	91.5 (ref. 14)
	Silica-bonded S-sulfonic acid (100 mg)	Reflux/EtOH	50	90 (ref. 15)
	$[HMIM]HSO_4$ (10 mol%)	EtOH,))), r.t.	45	90 (ref. 16)
	PEG-SO_3H (1.5 mol%)	Reflux/H_2O	30	94 (ref. 17)
	Silica sulfuric acid (80 mg)	70 °C/EtOH–H_2O	70	90 (ref. 18)
	SASPSPE (100 mg)	Reflux/EtOH	2.2 h	85 (ref. 19)
	$[Sipmim]HSO_4$ (150 mg)	Reflux/EtOH	1 h	90 (ref. 20)
	Rice husk (60 mg)	Reflux/EtOH	3 h	80 (This work)
	Rice husk ash (60 mg)	Reflux/EtOH	1.5 h	85 (This work)
	RHA-SO_3H (60 mg)	80 °C/solvent free	3	92 (This work)
	Piperidine (a few drop)	r.t./EtOH	4 h	96 (ref. 28)
	I_2 (10 mol%)	100 °C/H_2O	28	95 (ref. 29)
	TBAB (10 mol%)	100 °C/H_2O	25	91 (ref. 30)
	SDS (20 mol%)	60 °C/H_2O	3 h	98 (ref. 31)
	RHA-SO_3H (40 mg)	80 °C/H_2O	10	95 (This work)
	Sulfamic acid (10 mol%)	r.t./solvent free	30	92 (ref. 43)
	$(PhCH_2PPh_3)^+Br_3^-/SiO_2$ (10 mol%)	90 °C/solvent free	16	80 (ref. 44)
	$[hmim]HSO_4$ (1 mol%)	r.t./EtOH	1 h	97 (ref. 46)
	$ZrOCl_2 \cdot 8H_2O$ (5 mol%)	r.t./H_2O–EtOH	3 h	93 (ref. 47)
	$FeCl_3$–RiH (150 mg)	80 °C/EtOH	15	92 (ref. 53)
	RHA-SO_3H (15 mg)	80 °C/solvent free	8	91 (This work)

Conclusions

In conclusion, we have used RHA-SO_3H as a highly powerful solid acid catalyst for the simple and efficient synthesis of 4,4′-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols), 3,3′-(arylmethylene)-bis-(4-hydroxycoumarins) and bis(indolyl) methanes. The procedure has several advantages such as high reaction rates, ease of preparation and handling of the catalyst, simple and green experimental procedure and use of an inexpensive and reusable catalyst. Furthermore, this process avoids problems associated with organic solvent and liquid acid use, which makes it a useful and attractive strategy in view of the economic and environmental advantages. Further work to explore this catalyst in other organic transformations is in progress.

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