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One-pot three-component synthesis of 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-*1H*-pyrazol-5-ols) using silica vanadic acid as heterogeneous and recyclable catalyst with dual ability

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Abstract

Silica vanadic acid (oxo-vanadium has been supported on silica) with Lewis and Bronsted acid site is introduced as an efficient, reusable, and heterogeneous catalyst for tandem Knoevenagel–Michael reaction of two equivalents of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one with various aromatic aldehydes for the synthesis of 4,4′-(arylmethylene)bis(1*H*-pyrazol-5-ol)s at room temperature. The present methodology offers several advantages over existing methodologies, such as excellent yields, short reaction time, simple procedure, easy work-up, mild reaction conditions, and synthesis of wide range of products. This procedure gave the products in excellent yields within very short reaction times over other vanadium(V) compounds. Also this catalyst can be reused six times without appreciable loss of its catalytic activity.

Keywords: Silica vanadic acid (SVA), Dual ability, Multi-component reactions, Bis(pyrazolyl)methanes, Heterogeneous catalysis.

1. Introduction

Acid catalyzed reactions have been widely used in the modern chemical industry. As a kind of environmentally friendly catalyst, Bronsted and Lewis acidic catalyst have attracted much attention from researchers due to the combination of the advantages of Bronsted and Lewis acid [1].

Development of heterogeneous catalysts for fine chemicals synthesis has become a major area of research. One of the major drawbacks of the homogeneous catalysts is the difficulty in separating the relatively expensive catalysts from the reaction mixture at the end of the process. Therefore the use of reagents and catalysts on supporters has received significant attention.

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Nowadays, the pyrazolone derivatives were paid much attention for their various biological activities such as antitumor, antianxiety, antipyretic, analgesic, and anti-inflammatory properties [2].

More specifically, derivatives such as 4,4′-(arylmethylene)-bis-(1*H*-pyrazol-5-ols) are applied as fungicides [3], pesticides[4], Insecticides[5] and dyestuffs [6–7]. The condensation of aldehydes with two equivalents of 3-methyl-1-phenyl-5-pyrazolone is a known used route for synthesizing 4,4′-(arylmethylene)bis(1H-pyrazol-5-ol)s. Xanthan sulfuric acid [8], phosphomolybdic acid [9], silica sulfuric acid [10], 3-aminopropylated silica gel [11] , sodium dodecylsulfate [12], tetramethyl-tetra-3,4-pyridinoporphyrazinato copper(II) methyl sulfate [13], poly(ethyleneglycol)-bound sulfonic acid [14], cellulose sulfuric acid [15], lithium hydroxide monohydrate [16], 1,3,5-tris(hydrogensulfato) benzene [17], sulfuric acid([3-(3-silicapropyl)sulfanyl]propyl)ester [18], 2-hydroxy ethyl-ammonium acetate [19], N-(3-silicapropyl)-N-methyl imidazolium hydrogen sulfate [20], benzyltriethylam-monium chloride [21], ceric ammonium nitrate [22], silica-bonded S-sulfonic acid [2] and 1,3-disulfonic acid imidazolium tetrachloroaluminate [23], can be used as catalysts for this transformation.

All of these methods while offering some advantages also suffer from different drawbacks such as the use of organic solvents or expensive catalysts, longer reaction times, high temperature, low yields, tedious work-up procedure and the use of large amount of catalyst. So there is still a need to develop a new and convenient method for the synthesis of 4,4′-(arylmethylene)bis(1H-pyrazol-5-ol)s.

2. Experimental procedure

2.1. Typical Procedure for synthesis of bis(pyrazolyl)methanes

To a solution of an aldehyde (1 mmol), 3-methyl-l-phenyl-5-pyrazolone (2 mmol), and 4-5 drop ethanol was added SVA (10 mg) and the resulting mixture was magnetically stirred at room temperature. The progress of the reaction was monitored by TLC. After the completion of the reaction, the catalyst was filtered off and washed with ethanol (20 mL), and the filtrate was concentrated on a rotary evaporator under reduced pressure to give the crude product. Whenever required, the products were purified by column chromatography on silica gel (*n*-hexane/EtOAc) or by recrystallization from ethanol.

3. Results and discussion

In continuation of our previously reported studies to synthesis of new silica supported catalysts for organic transformations [24], we propose a simple strategy to create Bronsted acid site on V=O supported silica. Silica vanadic acid (SVA) was synthesized by the grafting of vanadiumoxy trichloride onto silica gel, followed by stirring in the air for 72 hours to promote the intermediate species (II) [25-27] which is a much stronger oxidant than H_2O_2. Therefore, our goal in undertaking this line of investigation was twofold: (i) synthesis of heterogeneous catalyst with Lewis and Bronsted site. (ii) It act as an oxidation agents with V=O band.

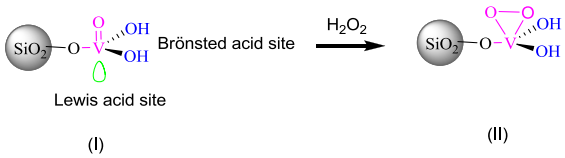
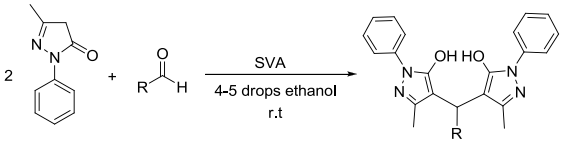


Figure 1. Silica Vanadic Acid (SVA) (I) in situ converted to peroxovanadium species (II) in the presence of H_2O_2 (II)

Herein, we prepared SVA according to our previously reported procedure [28-30] and wished to used it as a heterogeneous and recyclable catalyst with dual ability in the synthesis of 4,4’-alkylmethylene-bis(3-methyl-5-pyrazolones)(Scheme 1)



1 2 3

R: Aryl,, Hetero aryl

Scheme 1. Tandem Knoevenagel–Michael reaction of 1-phenyl-3-methyl-5-pyrazolone with aldehydes catalyzed by SVA.

For optimizing the reaction conditions, the reaction of 3-methyl-1-phenyl-5-pyrazolone **1** (2 mmol) with

benzaldehyde (1 mmol), in the presence of different amount of catalyst and temperatures was investigated under solvent-free conditions. The best result was obtained with 0.01 g of SVA at room temperature. The reaction was completed within 30 min and the expected product (Entry 6, table 1) was obtained in 95% yield. This reaction was also examined in the absence of catalyst under solvent free conditions in which the reaction did not noticeable progress even after 2 hours (Entry 8, table 1).

Table 1. Optimization of the catalyst amount and temperature on the reaction of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one with benzaldehyde.

Entry	Amount of catalyst (g)	Temperature (°C)	Time (min)	Yield[a] (%)
1	0.05	60	20	90
2	0.03	40	20	93
3	0.01	40	20	90
4	0.005	40	20	50
5	0.03	RT	30	96
6	0.01	RT	30	95
7	0.005	RT	40	35
8	-	RT	120	14

Reaction conditions: benzaldehydes (1 mmol), 3-methyl-l-phenyl-5-pyrazolone (2 mmol), catalyst, 4-5 drop ethanol at different temperature.
[a] Isolated yield

In order to understand the preferred catalyst to other vanadium(V) compounds, 3-methyl-1-phenyl-5-pyrazolone **1** was treated with ammonium vanadate and vanadium pentoxide under optimum reaction conditions instead of SVA as a catalyst (Table 2). We found that this modified silica gel improved reaction process toward increasing the reaction yield and decreasing the reaction time.

Table 2. Catalytic activity of different vanadium(V) oxide (8% mol) on the reaction of methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one with benzaldehyde at room temperature

Entry	catalyst	Time (min)	Yield (%)
1	SVA	30	95
2	Ammonium vanadate	120	58
3	V_2O_5	120	45

After optimization of the reaction conditions, to explore the efficiency and the scope of the presented protocol, 3-methyl-1-phenyl-5-pyrazolone was treated with structurally diverse aromatic aldehydes under the optimized reaction conditions in the presence of SVA as catalyst. The corresponding results are depicted in table 3.

As table 3 indicates, all aldehydes (including benzaldehyde and arylaldehydes bearing halogens, electron-withdrawing or electron releasing substituents) were successfully reacted with 3-methyl-1-phenyl-5-pyrazolone to give the corresponding 4,4'-(arylmethylene)-bis(3-methyl-1-phenylpyrazol-5-ol) derivatives in good to excellent.

Table 3. The preparation of Synthesis of bis(pyrazolyl)methanes 3a–n using SVA as catalyst at room temperature.

Reaction conditions: Aldehydes (1 mmol), 3-methyl-l-phenyl-5-pyrazolone (2 mmol), SVA (10 mg), 4-5 drop ethanol at 40 °C.
[a] Isolated yields.

Entry	R	Product	Time (min)	Yield[a] (%)	M.p. °C (lit.)[Ref]
1	C_6H_5	3a	30	95	168–170 (171–172)[12]
2	2-Cl-C_6H_4	3b	65	80	235–236 (236–237)[12]
3	3-Cl-C_6H_4	3c	30	90	150–152 (153–154)[12]
4	4-Cl-C_6H_4	3d	30	87	213–215 (207–209)[12]
5	2-NO_2-C_6H_4	3f	80	75	221–223 (224–225)[12]
6	4- NO_2-C_6H_4	3g	55	90	229–231 (230–232)[12]
7	2-Br-C_6H_4	3h	70	85	249-251 (248-250)[31]
8	2-Me-C_6H_4	3i	30	86	201–203 (203–204)[12]
9	4-Me-C_6H_4	3j	30	90	201–203 (203–204)[12]
10	2-OMe-C_6H_4	3k	75	72	210-212 (210−213)[17]
11	4- OMe-C_6H_4	3l	65	73	175-177 (155−157)[17]
12	2-Naphthyl	3m	30	85	205–207 (206−208)[12]
13	2-Furyl	3n	30	89	190–193 (189–191)[12]

The reusability of the catalysts is one of the most important benefits and makes it useful for commercial applications. Thus the recovery and reusability of SVA were investigated. For this purpose, condensation of 3-methyl-1-phenyl-5-pyrazolone with benzaldehydes was studied. The reaction mixture was extracted by ethanol and separated from the catalyst. Recovered SVA was washed with ethanol and has been also use at least 6 times without any noticeable loss of catalytic activity.

Table 4. Reusability of SVA as a catalyst for the preparation of bis(pyrazolyl)methane 3a

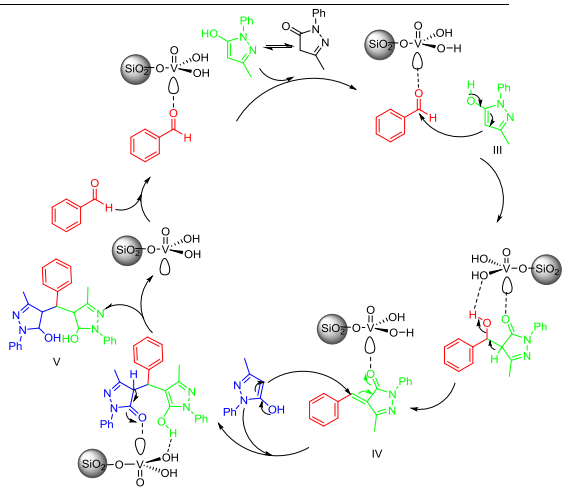
Entry	Cycle	Time (min)	Yields (%)
1	1st run	30	95
2	2st run	30	94
3	3st run	30	95
4	4st run	30	93
5	5st run	30	90
6	6st run	40	82

The major advantages of the present protocol over existing methods can be seen by comparing our results with the most popular recently reported procedures, as shown in Table 5. The reaction of benzaldehyde with 3-methyl-5-pyrazolones for the preparation 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) (entry 1, Table 4) was chosen as a model reaction and the comparison is in terms of reaction time, reaction conditions and percentage yields. Shorter reaction time and milder reaction condition was obtained using SVA instead of Bronsted acid catalyst. So, it can be suggested that V=O centers would be the active sites of the SVA, which participate in the activation of aldehyde functional group. SVA not only functioned as a Lewis acid but also as a Bronsted acid in the reaction mechanism. Therefore when this catalyst (entry 1, Table 5) compared with Bronsted acid catalyst (entries 2-9, Table 5) lower reaction temperature and time with higher yield obtained by SVA. The catalysis results showed that the cooperation of Lewis and Bronsted acid sites in the catalytic procedure can increase the catalytic efficiency of SVA.

Table 5. Comparison of the efficiencies of a number of different reported catalysts with SVA in the condensation of benzaldehyde with 2 equivalents of 3-methyl-l-phenyl-5-pyrazolone.

Entry	Catalyst	Solvent/Temperature .(°C)	Time (min)	Yield (%)	Ref
1	SVA	Solvent free/r.t	30	95	This work
2	Sodium dodecyl sulfate	H_2O/Reflux	60	86.8	[32]
3	Silica-bonded S-sulfonic acid	EtOH/Reflux	120	80	[2]
4	Silica sulfuric acid	EtOH-H_2O/70	60	93	[33]
5	Silica-bonded ionic Liuid[spipim]HSO_4	EtOH/Reflux	120	89	[20]
6	Silica-bonded N-propylpiperazinesulfamic acid	Solvent free	45	93	[34]
7	1,3-disulfonic acid imidazolium tetra chloroaluminate {[Dsim]$AlCl_4$}	Solvent free	60	86	[24]
8	[P_4VPyBuSO_3H]HSO_4	EtOH/Reflux	42	95	[35]
9	SASPSPE	EtOH/Reflux	180	90	[18]

We believe that the silica vanadic acid activates the aldehyde group for nucleophilic attack by 3-methyl-1-phenyl-*1H*-pyrazol-5-ol (III) to form (IV) which undergoes Michael addition with second molecule of 3-methyl-1-phenyl-1*H*-pyrazol-5-ol to form the product (V) [36-37].



Scheme 2. Plausible mechanism for the formation of bis(pyrazolyl)methanes 3a.

4. Conclusion

In conclusion, the present method is an operationally simple, clean and highly efficient procedure for the synthesis of of bis(pyrazolyl)methane derivatives using a catalytic amount of SVA. In addition low cost, easy availability, recyclable, moderate Lewis and Bronsted acidity and heterogeneous catalyst, excellent yields of products, short reaction time, simple experimental and usage of room temperature makes this method practical for the synthesis of 4,4′-(arylmethylene)bis(3-methyl-1-phenyl-pyrazol-5-ols).

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