Synthesis of Nano Magnetite Fe₃O₄ Based Vanadic Acid: A Highly Efficient and Recyclable Novel Nano-catalyst for the Synthesis of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ols)

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Abstract: Nano magnetic Fe₃O₄ based vanadic acid [MNPs@VO(OH)₂] (average diameter 20–26 nm) has been synthesized by grafting VOCl₃ on the Fe₃O₄ surface nanoparticles as a retrievable supporter to produce novel heterogeneous reusable solid acid with dual ability (Bronsted and Lewis acid) followed by stirring in the air. The resultant material was characterized by scanning electron microscopy (SEM), transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD) analysis and energy-dispersive X-ray spectroscopy (EDX). Significantly, the as-prepared [MNPs@VO(OH)₂] exhibits a high catalytic activity in the synthesis of 4,4′-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ols). Additionally, the newly synthesized heterogeneous solid acid catalyst can be reused for several times without apparent loss of its catalytic activity.

Keywords: nano magnetite Fe₃O₄ based vanadic acid, 4,4′-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ols), acid catalysed reactions, heterogeneous, nanoparticles.

INTRODUCTION

NOWADAYS, the pyrazolone derivatives are an important class of heterocyclic compounds were paid much attention for their various biological activities such as antipyretic, antitumor, analgesic, antianxiety, and anti-inflammatory properties.[1] More specifically, derivatives such as 4,4′ (arylmethylene)-bis-(1*H*-pyrazol-5-ols) are applied as fungicides,[2] pesticides,[3] insecticides[4] and dyestuffs.[5]

The condensation of aldehydes with two equivalents of 3-methyl-1-phenyl-5-pyrazolone is a known used path to synthesize 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols).

Xanthan sulfuric acid,[6] phosphomolybdic acid,[7] silica sulfuric acid,[8] 3-aminopropylated silica gel,[9] sodium dodecylsulfate,[10] tetramethyl-tetra-3,4-pyridinoporphyra-zinato copper(II) methyl sulfate,[11] poly(ethyleneglycol)-bound sulfonic acid,[12] cellulose sulfuric acid,[13] lithium hydroxide monohydrate,[14] silica chloride nano particle[15] can be used as catalysts for this transformation.

However, some of these methods suffer from at least one of the following disadvantages: using the expensive catalyst at reflux condition, long reaction time, low yield, non-recovered catalyst, tedious work-up procedure and the using of large amount of catalyst. Thus, there is still a need to develop a new and convenient method for the synthesis of 4,4′-(arylmethylene)bis(1*H*-pyrazol-5-ols).

Therefore, finding an efficient and capable protocol for the preparation of 4,4′-(arylmethylene)bis(1*H*-pyrazol-5-ols) is

very important. Thus, design of novel nano magnetically separable catalytic systems have attracted attention in recent times as an interesting alternative to improve the efficient separation of heterogeneous (nano) catalysts from solutions over reaction completion by applying a simple magnet, providing improved recyclability in the designed systems.[16]

In addition, surface modification impacts the activity and selectivity of magnetite nano-catalysts.[17]

Acid catalyzed reactions have been also widely used in the modern chemical industry. It has been showed that catalytic systems that contain both Lewis and Bronsted acidity are more beneficial than Lewis or Bronsted acidic catalysts alone.[18]

Among the various transition metals as a Lewis acid, vanadium exists on the surface of the earth more plentifully and vanadium based oxidants are effectively used for various organic reactions.[19]

Vanadium and vanadium peroxides generate a number of biological and biochemical responses and have a potential as insulin-mimetic agents in the treatment of human diabetes. Moreover, vanadium is an essential prosthetic group of some haloperoxidase enzymes.[20]

Therefore, immobilization of the functionalized acid via covalent attachment to the supporting materials can combine the acid characteristics with the advantages of magnetic nanoparticles to design the acidic catalyst that facilitate catalyst recovery, recycling and reducing effluent contamination.

EXPERIMENTAL

Chemicals and Apparatus

The materials were purchased from Merck and Fluka and were used without any additional purification. All reactions were monitored by thin layer chromatography (TLC) on gel F254 plates. The synthesized catalyst was characterized by FT-IR, XRD, SEM, TEM, and elemental analysis.

XRD patterns of all catalysts were performed on a APD 2000, Ital structure with Cu Kα radiation (k = 0.1542 nm) operating at 50 kV and 20 mA in a 2 h range of 10–70° with step size 0.01° and time step 1.0 s to assess the crystallinity of the catalyst.

The weight loss between 200 and 600 °C was determined. Semi-quantitative EDX (Röntec, Quantax/QX2) analysis was used for the characterization of element concentration and vanadium distribution within prepared catalysts. The SEM analyses were done with a TESCAN/MIRA with a maximum acceleration voltage of the primary electrons between 10 and 15 kV. Transmission electron microscope, TEM measurements were carried out on a Philips CM10 analyzer.

Typical Procedure for Synthesis of Nano Magnetic Fe₃O₄ Based Vanadic Acid

MNPs Fe₃O₄ particles (I) were prepared according to a previous report by Qu et al.[21]

MNPs Fe₃O₄ (1g) suspended in *n*-Hexane (15 ml) with sonication for 5 minutes. Then, vanadiumoxytrichloride (1 g) was dissolved in *n*-hexane (10 mL). The mixture was added drop wise to MNPs Fe₃O₄ suspension (15–20 min) and shaked for 30 minutes. The result material were separated by an external magnet, washed three times with ethanol, dried under vacuum, and shaked in the air for 48 h to promote the hydrolysis of V-Cl bonds to yield the final catalyst.

General 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 **MNPs@VO(OH)₂** (20 mg). The resulting mixture was magnetically stirred at 40 °C. The progress of the reaction was monitored by TLC. After the completion of the reaction, the catalyst was separated from the product by an external magnet and washed with ethanol (20 mL) and reused for subsequent runs. The mixture was concentrated to give the crude product. Finally, the products were purified by column chromatography on silica gel (*n*-hexane/EtOAc) or by recrystallization from ethanol.

RESULTS AND DISCUSSION

In continuation of our previously reported methodologies for designing, synthesis and applications of tasked specific heterogeneous catalysts such as silica based sulfuric,[22] phosphoric,[23] vanadic acid,[24] and magnetic nano particles[25] herein, we wish to report the synthesis and application of novel nano magnetite Fe₃O₄ based vanadic acid [MNPs@VO(OH)₂] with dual ability both as Lewis and Bronsted acid sites. The described catalyst [MNPs@VO(OH)₂] was synthesized successfully and used for the synthesis of 4,4'-(arylmethylene)bis(1*H*-pyrazol-5-ols).

Initially, Fe₃O₄ particles (I) were prepared according to a previous report. Then, nano magnetic Fe₃O₄ based
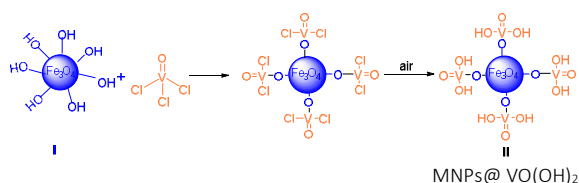
MNPs@ VO(OH)₂

Scheme 1. Synthesis of nano magnetic Fe₃O₄ based vanadic acid [MNPs@VO(OH)₂].

Figure 1. FT-IR spectra (a) Fe₃O₄ and (b) MNPs@VO(OH)₂

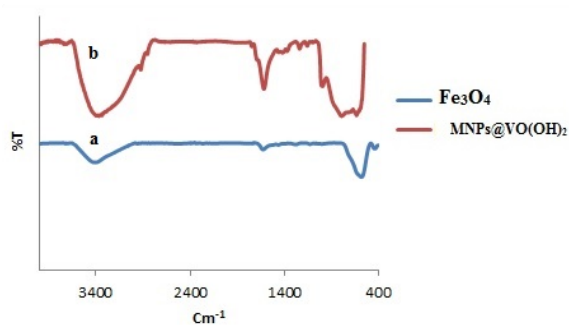**Figure 2.** The XRD of the (a) Fe₃O₄ and (b) [MNPs@VO(OH)₂].

vanadic acid [MNPs@VO(OH)₂] was synthesized by the reaction of Fe₃O₄ particles with VOCl₃ followed by stirred in the air (Scheme 1) and its structure was identified by IR, SEM, XRD and EDX.

In order to confirm the modification of the magnetite surface, the FT-IR spectrum of the prepared materials were obtained and have been shown in Figure 1.

Figure 1. shows the FT-IR spectra of the MNPs (a) and MNPs@VO(OH)₂ (b). The Fe−O stretching vibration near 592 cm⁻¹ and the O-H stretching vibration at 3429 cm⁻¹ were observed for the Fe₃O₄ (Figure 1a). The introduction of VO(OH)₂ to the surface of MNPs is confirmed by the bands at 786.7 and 1007 cm⁻¹ assigned to the V−O and V=O respectively, and the bands at 3384 assigned to the O−H stretching vibration.

XRD patterns of (a) Fe₃O₄ and (b) [MNPs@VO(OH)₂] are shown in Figure 2. As shown in Figure 2a, weak diffraction peaks with 2θ at 30°, 35.4°, 43°, 53.4, 57.4°, and 62.4° which are attributed to the (2 2 0), (3 1 1), (4 0 0), (4 2 2), (5 1 1) and (4 4 0) phases of Fe₃O₄, respectively.

In Figure 2b, we can observe that the XRD pattern of the [MNPs@VO(OH)₂] is similar to the pattern of Fe₃O₄ nanoparticles because the structure of [MNPs@VO(OH)₂]
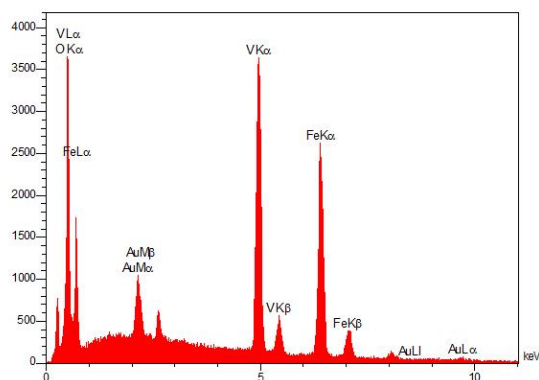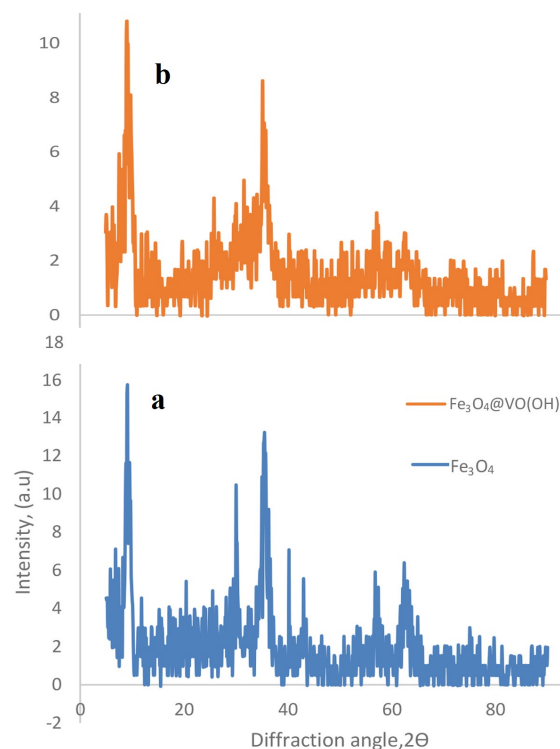
can be remained after the surface modification with VO(OH)₂ and new peaks attributable to these groups could not be detected in the XRD. However, the crystallinity of the samples clearly decreases after the coating process and the catalyst was going to amorphous structure. These results provide further evidence that functionalization on the nano magnetite take place.[26]

The EDX elemental analysis is shown in Figure 3. From the spectrum, it can be seen that iron, oxygen and vanadium elements present in the [MNPs@VO(OH)₂] samples which is in good agreement with the proposed catalyst structure (Figure 3).

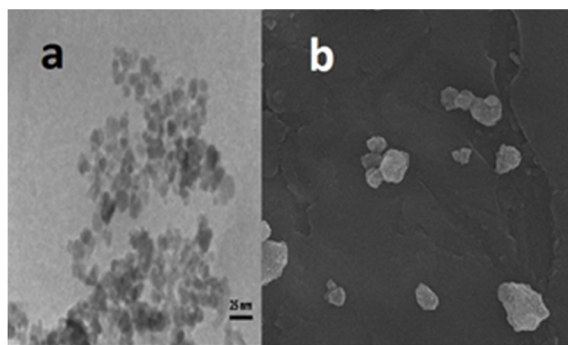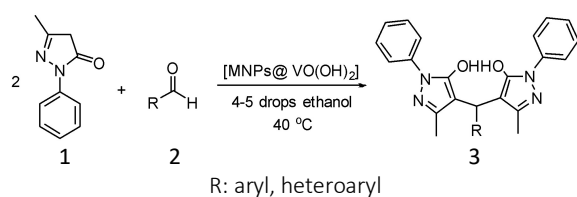TEM and SEM images of the synthesized catalyst

Figure 3. EDX analysis for [MNPs@VO(OH)₂].

Figure 4. The TEM (a) and SEM (b) of the [MNPs@VO(OH)₂].

Scheme 2. Tandem Knoevenagel–Michael reaction of 1-phenyl-3-methyl-5-pyrazolone with aldehydes catalyzed by [MNPs@VO(OH)₂].

were recorded and showed in Figure 4. The average diameter of the catalyst is around 25 nm with an approximate spherical shape.

The activity of the catalyst was subsequently investigated upon characterization in the synthesis of bis(pyrazolyl)methanes (Scheme 2).

To optimize the reaction conditions, the solvent-free condensation of 3-methyl-1-phenyl-5-pyrazolone (1) (2 mmol) with benzaldehyde (1 mmol), as model reaction using different amounts of catalyst at range of 25–60°C was examined (Table 1). The best results were obtained using 0.02 g of [MNPs@ VO(OH)₂] at 40°C. 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 [MNPs@VO(OH)₂] as catalyst. The corresponding results are depicted in Table 2.

The results reported in Table 2 showed that a variety

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	Catalyst / g	Temperature/ °C	Time/ min	Yield[a] (%)
1	0.04	60	10	92
2	0.04	40	10	93
3	0.02	40	10	90
5	0.01	40	10	75
6	0.005	40	20	46
3	0.04	25	30	78
5	0.01	25	30	75
6	0.005	25	30	35

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

of aromatic aldehydes with electron releasing groups (methoxy, methyl), electron withdrawing substituents (nitro), in the ortho, meta and para positions of the benzene ring, polycyclic aromatic (naphthyl) and heterocyclic aldehyde (furyl, pyridyl) reacted efficiently with two equivalents of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one to afford the product 3a–p in a short experimental time (5–45 min) with high yields (72–96 %).

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 [MNPs@VO(OH)₂] were investigated. For this purpose, condensation of 3-methyl-1-phenyl-5-pyrazolone with

Table 2. The preparation of bis(pyrazolyl)methanes 3a–p using [MNPs@VO(OH)₂] as catalyst at 40 °C

Entry	R	product	Time (min)	Yield[a] (%)	M.p. °C (lit.)[Ref]
1	C₆H₅	3a	10	90	168–170 (171–172)[27]
2	4- NO₂C₆H₄	3b	5	95	229–231(230–232)[27]
3	3- NO₂C₆H₄	3c	5	96	145–147 (149–150)[27]
4	2-NO₂C₆H₄	3d	10	94	221–223 (224–225)[27]
5	4-FC₆H₄	3e	5	87	181-183 (182–184)[28]
6	4-ClC₆H₄	3f	10	85	213–215 (207–209)[27]
7	3-ClC₆H₄	3g	10	89	150–152 (153–154)[27]
8	2-ClC₆H₄	3h	10	92	235–236 (236–237)[27]
9	3-BrC₆H₄	3i	15	84	173–175 (172–175)[29]
10	4-MeC₆H₄	3j	15	87	201–203 (203–204)[27]
11	2-MeC₆H₄	3k	15	79	201–203 (203–204)[27]
12	2-MeOC₆H₄	3l	30	72	210-212 (210–213)[28]
13	4-MeOC₆H₄	3m	45	74	175-177 (155–157)[28]
14	2-Naphthyl	3n	10	91	205–207 (206–208)[27]
15	2-Furyl	3o	10	83	190–193 (189–191)[27]
16	2-Pyridyl	3p	10	79	228–231 (230–232)[27]

Reaction conditions: Aldehydes (1 mmol), 3-methyl-1-phenyl-5-pyrazolone (2 mmol), MNPs@VO(OH)₂ (20 mg), 4–5 drop ethanol at 40 °C.
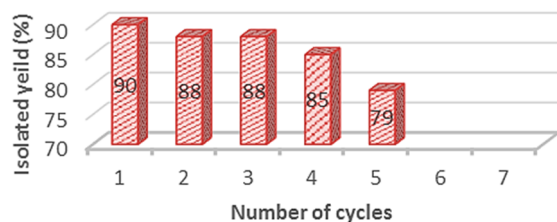[a] Isolated yield.

Figure 5. The reaction of 3-methyl-1-phenyl-5-pyrazolone with benzaldehydes in the presence of recycled [MNPs@VO(OH)₂] within 10 min.

benzaldehyde was studied. It catalysts were easily collected by means of a magnet, washed with ethanol and dried to be reused in subsequent reactions. Recovered [MNPs@VO(OH)₂] was washed with ethanol and has been also use at least 5 times without any noticeable loss of catalytic activity (Figure 5).

We believe that the [MNPs@VO(OH)₂] activates the aldehyde group for nucleophilic attack by 3-methyl-1-phenyl-1*H*-pyrazol-5-ol (IV) 2 to form (V) which undergoes Michael addition with second molecule of 3-methyl-1-phenyl-1*H*-pyrazol-5-ol to form the product (VI) (Scheme 3). [30]

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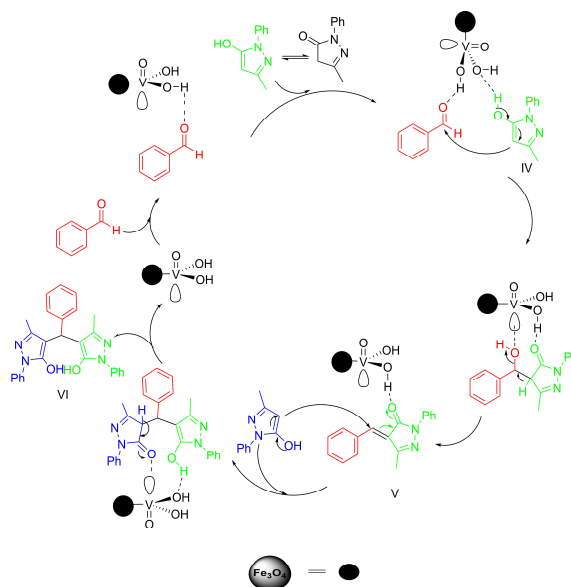
Scheme 3. Plausible mechanism for the formation of bis(pyrazolyl)methanes.

CONCLUSION

In conclusion, we have described the development of a mild efficient and simple method for the one-pot three-component condensation reaction of aromatic aldehydes with 1-phenyl-3-methylpyrazol-5-one in ethanol for the synthesis of 4,4'-(arylmethylene)bis(1*H*-pyrazol-5-ol) derivatives, catalyzed by [MNPs@VO(OH)₂] as a new and heterogeneous organic catalyst at 40°C. The catalyst is characterized by FT-IR, XRD, TEM, SEM and EDX. The procedure has several advantages such as high reaction rates, ease of preparation and handling of the catalyst, simple experimental procedure and use of a reusable catalyst.

Table 3. 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	Our catalyst	EtOH/40	10	90	This work
2	Sodium dodecyl sulfate	H₂O/Reflux	60	86.8	[10]
3	Silica-bonded S-sulfonic acid	EtOH/Reflux	120	80	[1]
4	Silica sulfuric acid	EtOH-H₂O/70	60	93	[31]
5	Silica-bonded ionic Liuid[spipim]HSO₄	EtOH/Reflux	120	89	[32]
6	{[Dsim]AlCl4}	Solvent free /50	60	86	[33]
7	[P₄VPyBuSO₃H]HSO₄	EtOH/Reflux	42	95	[34]
8	SASPSPE	EtOH/Reflux	180	90	[35]
9	SBPPSA	Solvent free /80	45	93	[36]

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