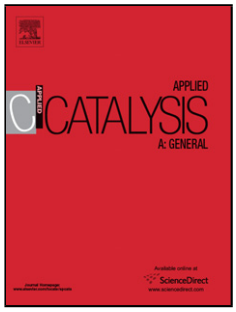

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Design, characterization and application of new ionic liquid 1-sulfopyridinium chloride as an efficient catalyst for tandem Knoevenagel–Michael reaction of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one with aldehydes

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Abstract: In this work, novel ionic liquid 1-sulfopyridinium chloride {[Pyridine–SO_3H]Cl} is synthesized, and characterized by IR, ^1H and ^{13}C NMR, UV as well as mass spectra. The ionic liquid is used as an efficient, homogeneous and reusable catalyst for the synthesis of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s by tandem Knoevenagel–Michael reaction of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one with various aromatic and hetero-aromatic aldehydes under mild reaction conditions.

Keywords: 1-Sulfopyridinium chloride {[Pyridine–SO_3H]Cl}, 3-Methyl-1-phenyl-1*H*-pyrazol-5(4H)-one, Aldehyde, 4,4′-(Arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol), Ionic liquid

1. Introduction

Pyrazolone derivatives are of importance as they have various biological activities; these compounds are essential scaffold of many commercialized drugs for brain ischemia [1], and myocardial ischemia [2]. Moreover, 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s, as an important class of pyrazolones, have been used as anti-inflammatory [3], antipyretic [4], gastric secretion stimulatory [5], antidepressant [6], antibacterial [7], and antifilarial [8] agents. These compounds have been also applied as fungicides [9], pesticides [10], insecticides [11], dyestuffs [12], and chelating as well as extracting reagents for different metal ions [12]. In spite of extensive application of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s, a few methods have been reported for their preparation. These methods include application of piperidine in ethanolic solution [13], tandem Knoevenagel-Michael reaction in benzene solution [14], application of sodium dodecyl sulfate in aqueous media [15], and electrocatalytic synthesis [16-18]. Furthermore, most of these methods are associated with limitations such as moderate yields, long reaction times, harsh reaction conditions, application of hazardous solvents and tedious workup procedures. Therefore, search for finding an efficient and capable protocol for the preparation of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s is very important.

Ionic liquids (ILs) could be considered as organocatalysts. Considering this subject, we have recently introduced a new category of ionic liquids, namely sulfonic acid

functionalized imidazolium salts (SAFIS) (in which a S-N bond has formed in the imidazole ring as five members heterocycle [19-32]), and used them as organocatalysts or organoreagents for preparation of bis(indolyl)methans [19], *N*-sulfonyl imines [20], nitro aromatic compounds [21,22], 1-amidoalkyl-2-naphthols [23], benzimidazoles [24], xanthenes [25], 1-carbamatoalkyl-2-naphthols [26], 4,4'-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5- ol)s [27], t-butyl aryl carbamates [28], 1,2,4,5-tetrasubstituted imidazoles [29], *β*-acetamido ketones [30], hexahydroquinolines [31] and trimethylsilylated hydroxyl compounds [32]. In continuation of our previous studies on the preparation and applications of acidic ILs and solid salts in organic transformations [19-31], we have prepared and characterized novel acidic ionic liquid 1-sulfopyridinium chloride {[Pyridine–SO_3H]Cl} wherein a S-N bond has formed in a six members heterocycle (Scheme S1), and utilized it as an efficient, homogeneous and reusable organocatalyst for the tandem Knoevenagel–Michael reaction of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one with aldehydes to afford 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s (Scheme 1a).

2. Experimental

2.1. Materials

All chemicals were purchased from Merck or Fluka Chemical Companies. The known products were identified by comparison of their melting points and spectral data with those reported in the literature.

2.2. Catalyst preparation (Scheme S1)

A solution of pyridine (0.395 g, 5 mmol) in CH_2Cl_2 (40 mL) was added dropwise to a stirring solution of chlorosulfonic acid (0.58 g, 5 mmol) in dry CH_2Cl_2 (40 mL) over a period of 10 min at 0 ºC. After the addition was completed, the reaction mixture was stirred for 20 min, stand for 5 min, and the CH_2Cl_2 was decanted. Afterward, the liquid residue was triturated with CH_2Cl_2 (3×10 mL), and dried under powerful vacuum at 90 °C to give [Pyridine–SO_3H]Cl as a viscous colorless oil in 95 % yield (0.929 g).

2.3. Catalyst characterization

The reaction conversions were measured by GC on a Shimadzu model GC-16A instrument using a 25m CBPI-S25 (0.32 mm ID, 0.5 μm coating) capillary column. For GC analysis, at first, the apparatus was calibrated with n-Octane as internal standard. THF was used as solvent in which the starting materials and product was dissolved in it. The conversion after doing the required program was obtained.

The ^{1}H NMR (500 or 400 MHz) and ^{13}C NMR (125 or 100 MHz) were run on a Bruker Avance DPX-250 FT-NMR spectrometer (δ in ppm).

IR spectra were run on a Shimadzu FTIR-8300 spectrophotometer.

UV-vis spectra were recorded by a Shimadzu UV-mini-1240V spectrophotometer with 1-cm quartz cells (0.5ml)

Mass spectra were obtained with a Shimadzu GC–MS-QP 1100 EX model.

Thermal gravimetry (TG) and differential thermal gravimetric (DTG) were analyzed by a Perkin Elmer (Model: Pyris 1). TG/DTG analysis (25 to 600 °C, temperature increase rate of 10 °C. min^{-1}, nitrogen atmosphere).

Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

2.4. Catalytic tests

*General procedure for the synthesis of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)s (**3a-t**) using [Pyridine–SO_3H]Cl*

A mixture of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (1.74 g, 10 mmol), aldehyde (5 mmol) and [Pyridine–SO_3H]Cl (0.0097 g, 1 mol%) in a test tube was stirred at 50 ºC. After completion of the reaction, as monitored by TLC, the reaction mixture was cooled to room temperature, extracted with warm EtOAc (20 mL) to separate the catalyst (the product is soluble in warm EtOAc; however, the catalyst is not soluble in this solvent). Then, EtOAc was evaporated and the solid residue (crude product) was triturated by a mixture of ethanol and water (9/1) to give the pure product. The recovered catalyst was washed with EtOAc (2×20 mL), dried at 90 ºC under vacuum condition, and reused for the preparation of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s according to the mentioned procedure. The catalyst was recovered and reused for five times without any significant changes in the yield and the reaction time. The pure products were identified by IR, ^{1}H and ^{13}C NMR spectra. Also mass spectrum was recorded for unknown products.

3. Results and discussion

3.1. Studies to confirm the structure of 1-sulfopyridinium chloride {[Pyridine–SO_3H]Cl}

The structure of 1-sulfopyridinium chloride was identified by IR, ^{1}H and ^{13}C NMR, UV as well as mass spectra. The spectral data include:

UV-vis (DMSO): λ_{max} 285 nm; TG/DTG analysis (25 to 600 °C): dec. point 295 °C; IR (Nujol): 750, 866, 1042, 1174, 1488, 1543, 1637, 2650-3550 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 8.11 (t, *J* = 7.45 Hz, 2H), 8.65 (t, *J* = 7.81 Hz, 1H), 8.94 (d, *J*

= 5.76 Hz, 2H), 13.67 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 127.9, 142.4, 147.1; MS: *m/z* = 196 (M^++1), 195 (M^+).

The IR spectrum of the catalyst has been displayed in Figure 1. The broad peak at 2650-3550 cm^{-1} can be related to O-H stretching of the SO_3H group. Moreover, the two peaks observed at 1042 cm^{-1} and 1174 cm^{-1} correspond to vibrational modes of N-SO_2 and O-SO_2 bonds, and confirm boding SO_3H group with the N of pyridine [22,26-29,31,32]. In other hand, the C-H stretching and bending vibrations of pyridine ring in 1-sulfopyridinium chloride appeared at 3078 and 866 cm^{-1}, respectively. The C=C and C=N vibrations assigned at 1543 and 1637 cm^{-1}, correspondingly. These mentioned peaks clearly confirmed the structure of [Pyridine–SO_3H]Cl.

Moreover, the graphical ^{1}H and ^{13}C NMR spectra of [Pyridine–SO_3H]Cl are presented in Figures S1 and S2. Here, we study ^{1}H NMR data of the catalyst. The important peak of ^{1}H NMR spectra of [Pyridine–SO_3H]Cl is related to the acidic hydrogen (SO_3H) which observed in 13.67 ppm. To confirm that this peak (13.67 ppm) is correctly related to the hydrogen of SO_3H in the compound, not hydrogen of $ClSO_3H$ (its unreacted starting material) or another possible product formed from the reaction of pyridine with $ClSO_3H$ (i.e. pyridinium chlorosulfonate), we also run the ^{1}H NMR spectra of $ClSO_3H$ and pyridinium chloride (the acidic hydrogens of pyridinium chlorosulfonate and pyridinium chloride are same) in DMSO-d_6 (the concentration of these compounds and [Pyridine–SO_3H]Cl in DMSO-d_6 for the NMR study was 0.08 $mol.L^{-1}$). In these spectra, the peaks of the acidic hydrogens of [pyridine–SO_3H]Cl, $ClSO_3H$ and pyridinium chloride were observed in 13.67, 13.45 and 11.37 ppm, respectively. The difference between the peaks of the acidic hydrogens in [pyridine–SO_3H]Cl, $ClSO_3H$ and

pyridinium chloride confirmed that the peak observed in 13.67 ppm of the ^{1}H NMR spectra of [Pyridine–SO_3H]Cl is correctly related to the SO_3H group of this compound.

UV spectra was another evidence to confirm that [Pyridine–SO_3H]Cl was really synthesized. For this purpose, UV-vis spectra of the catalyst, pyridine and pyridinium chloride were recorded. At first, some solutions of the mentioned compounds in DMSO with the same concentration were prepared. The concentration of these compounds in DMSO for UV study was 0.005 $mol.L^{-1}$. The maximum absorptions of pyridine and pyridinium chloride appeared at ca. 270 and 295 nm, correspondingly. But λ_{max} of 1-sulfopyridinium chloride {[Pyridine–SO_3H]Cl} was observed at ca. 285 nm (Figure 2). The difference between maximum absorptions of 1-sulfopyridinium chloride and other compounds (pyridine and pyridinium chloride) confirmed the preparation of the catalyst.

In another procedure, the formation of N-S bond was investigated. For this purpose, hydrogen chloride gas was transferred to a two-necks round-bottomed flask in the presence of sulfur trioxide pyridine complex as a white solid powder. HCl was reacted with this complex to give 1-sulfopyridinium chloride {[Pyridine–SO_3H]Cl} (Scheme S1). After completion of the reaction, the white solid powder was converted to a viscous colorless oil. IR, ^{1}H and ^{13}C NMR spectra of this compound showed that [Pyridine–SO_3H]Cl (produced by the another method) and this presented product was the same. The ^{1}H NMR spectra of the compound which produced by two different methods are given in Figure 3. This evidence was clearly showed that [Pyridine–SO_3H]Cl was really synthesized.

Moreover, it is well-known that sulfur trioxide pyridine complex [$C_5H_5N^{+}SO_3^{-}$] has produced by the dropwise addition of chlorosulfonic acid (1 equiv.) to pyridine (2

equiv.) dissolved in dichloroethane at low temperature (Scheme S2) [33-35]. In these conditions, in each time, there were excess amount of pyridine besides $ClSO_3H$ in the reaction mixture; thus, 1 equiv. of pyridine (as a nucleophile) attacks to the sulfur of $ClSO_3H$ to give [Pyridine–SO_3H]Cl, and another 1 equiv. of pyridine acted as a base and abstracts the acidic hydrogen of [Pyridine–SO_3H]Cl to afford $[C_5H_5N]^+SO_3^-$ and $[C_5H_5NH]Cl$. In the synthesis of [Pyridine–SO_3H]Cl, we added 1 equiv. of pyridine dropwise to 1 equiv. of chlorosulfonic acid at low temperature. In these conditions, in each time, there were excess amount of $ClSO_3H$ besides pyridine in the reaction mixture; thus, when pyridine reacted with $ClSO_3H$, and [Pyridine–SO_3H]Cl formed, there is no base in the reaction media to abstract the acidic hydrogen of the compound to afford $[C_5H_5N]^+SO_3^-$ and $[C_5H_5NH]Cl$. Also, according to the literature [33,35], in the reaction of pyridine with chlorosulfonic acid at low temperature, the reaction route was the nucleophilic substitution (substitution of Cl of $ClSO_3H$ by the nitrogen of pyridine), not the acid–base reaction (abstraction of the hydrogen of $ClSO_3H$ by pyridine to give $[C_5H_5N–H][ClSO_3]$).

The amount of acid sites in [Pyridine-SO_3H]Cl was determined by titration of aqueous solution of [Pyridine-SO_3H]Cl (0.1 M) with NaOH (0.1 M). It was found that three mole of NaOH reacts with one mole of [Pyridine-SO_3H]Cl. It means that the catalyst was hydrolyzed to pyridinium chloride and sulfuric acid (Scheme S3). This result indicates that the catalyst has one acidic-SO_3H group (Scheme S3).

In another study, thermal gravimetric (TG) and derivative thermal gravimetric (DTG) analysis of 1-sulfopyridinium chloride was investigated at range of 25 to 600 °C, with a temperature increase rate of 10 °C.min^{-1} in a nitrogen atmosphere. The

corresponding diagrams are shown in Figure 4. In TG pattern, we observed multi-stage decomposition pattern in [Pyridine–SO_3H]Cl. Some weight losses were observed about 18%, 40% and 14% which can be related to loss of HCl, SO_3 and CH_2=CH_2, respectively. Therefore, 1-sulfopyridinium chloride could be applied as catalysts below 200 °C, and decomposed after 200 ºC.

3.2. The synthesis of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)s ***3a-t*** *using [Pyridine-SO_3H]Cl*

After full characterization of [Pyridine-SO_3H]Cl, we examined its catalytic activity for the preparation of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s. For this purpose, as a model reaction, the condensation of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (**1**) (2 mmol) with 4-nitrobenzaldehyde (1 mmol), was examined in the presence of different quantities of the 1-sulfopyridinium chloride, at range of 25-70 °C under solvent-free conditions (Scheme 1a). The results are summarized in Table 1. Interestingly, 1 mol% of [Pyridine–SO_3H]Cl was sufficient to afford the product in excellent yields and in very short reaction times at 50 °C (Table 1, entry 3). No improvement in the reaction results was observed by increasing the amount of the catalysts and the temperature. The solvent-free condensation was also tested at 50 °C without catalyst in which the reaction was not progressed even after long reaction time (2 h).

The results of catalytic tests in the solvent-free reaction of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (**1**) with 4-nitrobenzaldehyde over [Pyridine-SO_3H]Cl at 50 °C (variation of conversion or yield with time), are shown in Fig. 5. It was found that after 8 min of the reaction, conversion of (**1**) was 96%.

To compare the efficiency of solution conditions versus the solvent-free conditions, a mixture of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (**1**) (2 mmol) and 4-nitrobenzaldehyde (1 mmol) in the presence of [Pyridine–SO_3H]Cl was heated in an oil-bath (50 °C) in various solvents for 90 min. Low yields of the product was obtained, even after elongated reaction times (Table 2). In the solvent-free conditions, the starting materials (3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one and 4-nitrobenzaldehyde) and the catalyst formed a homogeneous system in the reaction media. This homogeneous system was changed to a bi-phase system when the reaction was examined solvents including $CHCl_3$, EtOAc, EtOH, CH_3CN and CH_2Cl_2; because the starting materials were soluble in the mentioned solvents, but the ionic liquid was insoluble. Therefore, the catalytic activity of [Pyridine–SO_3H]Cl decreased in these solvents. In the case of H_2O solvent, [Pyridine-SO_3H]Cl was soluble in water, but the starting materials were insoluble; moreover, the catalyst hydrolyzed in the aqueous media. Therefore, the yield also decreased when H_2O was applied as solvent. Therefore, the solvent-free reaction was more efficient.

After optimization of the reaction conditions, the condensation of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one with various aryl and hetero-aryl aldehydes was examined in the presence of 1 mol% [Pyridine–SO_3H]Cl at 50 °C in the absence of solvent, in order to assess the scope and the generality of the catalyst. The results are displayed in Table 3. As it is shown in Table 3, arylaldehydes possessing electron-releasing substituents, electron-withdrawing substituents and halogens on their aromatic rings were utilized successfully in the reaction, and gave the desired products in high yields and in very short reaction times. The catalyst was also efficient when hetero-arylaldehydes were applied in

the reaction (Table 3, entries **3i**, **3j** and **3k**). Interestingly, the condensation of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2 eq.) with terephthaldehyde (1 eq.) in the presence of [Pyridine–SO_3H]Cl (2 mol%) at 50 °C under solvent-free conditions, afforded di-4,4'-(arylmethylene)-bis(3-methyl-1-phenylpyrazol-5-ol) **5** in 78 % yield within 15 min (Scheme 1b). Thus, the catalyst was general and highly efficient.

3.3. Comparison of the efficiency of [Pyridine–SO_3H]Cl with the recently reported catalysts for the synthesis of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)s

To compare the efficiency of our catalyst with the reported catalysts for the synthesis of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s, we have tabulated the results of these catalysts to perform the condensation of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one with 4-nitrobenzaldehyde, in Table 4. As Table 4 indicates, [Pyridine–SO_3H]Cl has remarkably improved the synthesis of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s in different terms {reaction time, yield and turn-over frequency (TOF)}. The TOF values were calculated by the equation TOF = Yield (%)/[Time (min)×Catalyst amount (mol%)]. The reaction times were shorter, and the yields and TOFs were higher when our catalysts were utilized.

3.4. Recovering and reusing the catalyst

In another study, recyclability of the catalyst was examined upon the condensation of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one with 4-nitrobenzaldehyde. After completion the reaction, the reaction mixture was extracted by the warm EtOAc and separated from the catalyst. The recycled catalyst was triturated with CH_2Cl_2, and

used for another reaction. We observed that the catalytic activity of the catalyst was restored within the limits of the experimental errors for five successive runs (Table 5). [Pyridine–SO_3H]Cl was also characterized by TG, UV, ^{1}H NMR and IR spectra after its application in the reaction. These spectra were same as those of the fresh catalyst (Figure 6).

3.5. Effect of impurity of water on the catalytic activity of 1-sulfopyridinium chloride

The ionic liquid is sensitive to moisture and water. To study effect of impurity of water on the catalyst activity, the condensation of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (1.74 g, 10 mmol), aldehyde (5 mmol) using [Pyridine–SO_3H]Cl (0.0097g, 1 mol%) was examined in the presence of different amounts of H_2O at 50 ºC (Table 6). As Table 5 indicates, 12 mmol of H_2O did not affect significantly on the catalytic activity of [Pyridine–SO_3H]Cl; however, more increasing the amount of H_2O decreased their activity. This can be attributed to hydrolysis of the catalyst to pyridinium chloride and H_2SO_4 in the peresence of very excess amount of water. In the synthesis of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s, water produces as a side product (Scheme 6); due to this point, after any cycle of recovery and before reusing the catalyst, it was heated at 90 ºC under vacuum to dry and remove the produced water during the reaction.

4. Conclusions

In summary, we have reported the synthesis of 4,4'-(arylmethylene)-bis(3-methyl-1-phenylpyrazol-5-ols) using 1-sulfopyridinium chloride [Pyridine–SO_3H]Cl as a new, homogeneous and reusable catalyst in a green recyclable media. The promising points for

the presented methodology are efficiency, generality, high yield, relatively short reaction time, low cost, cleaner reaction profile, ease of product isolation, simplicity, and finally compliance with the green chemistry protocols.

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Figure captions

Figure 1. IR spectrum of 1-sulfopyridinium chloride {[Pyridine–SO_3H]Cl} in comparison with pyridine.

Figure 2. UV spectra of pyridine, pyridinium chloride and [Pyridine–SO_3H]Cl} at room temprature in DMSO (the concentration of these compounds in DMSO was 0.005 $mol.L^{-1}$).

Figure 3. ^1H NMR spectra of the compound which produced by two different methods. (the concentration of [Pyridine–SO_3H]Cl in DMSO-d_6 as solvent for the NMR study was 0.08 $mol.L^{-1}$).

Figure 4. Thermal gravimetric (TG) and derivative thermal gravimetric (DTG) analysis of 1-sulfopyridinium chloride at range of 25 to 600 °C, with a temperature increase rate of 10 °C.

Figure 5. Variation of the reaction conversion and yield with time on the solvent-free condensation of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2 mmol) with 4-nitrobenzaldehyde (1 mmol) in the presence of [Pyridine–SO3H]Cl (1 mol%) at 50 °C.

Figure 6. The characterization of reused catalysts after five runs using TG (a), UV-vis (b) 1HNMR (c) and IR (d) spectra.

Table 1. Effect of different amounts of catalysts and temperature on the synthesis of 4,4´-(arylmethylene)-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)s.[a]

Catalysts	Mol% of Catalyst[a]	Temp. (°C)	Time (min)	Yield[b]/Conv.[c] (%)
[Pyridine–SO_3H]Cl	0.5	50	8	71/74
[Pyridine–SO_3H]Cl	1	50	8	94/96
[Pyridine–SO_3H]Cl	3	50	8	94/96
[Pyridine–SO_3H]Cl	1	25	15	trace
[Pyridine–SO_3H]Cl	1	70	8	94/96
-	-[d]	50	3 h	28/33

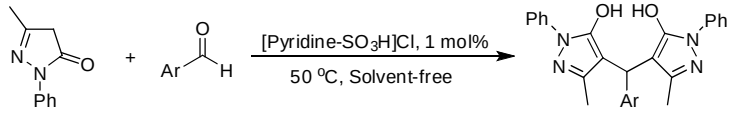
[a]The reactions were carried out by the condensation of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2 mmol) with 4-nitrobenzaldehyde (1 mmol) in the absence of solvent. [b]Isolated yield. [c]Conversion. [d]The reaction was carried out in the absence of solvent and catalyst.

Table 2. Effect of various solvents on the synthesis of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)s.[a]

Entry	Solvent	Temp. (°C)	Time (min)	Yield[b]/Conv.[c] (%)
1	$CHCl_3$	50	30	40/44
2	EtOAc	50	30	33/37
3	EtOH	50	30	29/32
4	H_2O	50	30	10/14
5	CH_3CN	50	30	25/28
6[d]	CH_2Cl_2	Reflux	30	50/54

[a]The reaction was carried out by the reaction of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2 mmol) with 4-nitrobenzaldehyde (1 mmol) in the presence of [Pyridine–SO_3H]Cl (1 mol%). [b]Isolated yield. [c]Conversion. [d]The reaction was carried out under reflux condition.

Table 3. The preparation of 4,4'-(arylmethylene)-bis(3-methyl-1-phenylpyrazol-5-ol)s using 1-sulfopyridinium chloride {[Pyridine–SO_3H]Cl} as catalyst at 50 °C.[a]



1 2 3a-t

Entry	Ar	Time (min)	Yield[b]/Conv.[c] (%)	mp. °C (lit.)
3a	C_6H_5	11	89/92	168-170 (171-172)[15]
3b	4-ClC_6H_4	8	94/97	213-215 (207-209)[15]
3c	3-ClC_6H_4	8	92/96	150-152 (153-154)[15]
3d	2-ClC_6H_4	8	91/95	235-236 (236-237)[15]
3e	4-$EtOC_6H_4$	10	87/91	184-186(186-188)[18]
3f	4-$NO_2C_6H_4$	8	94/96	229-231(230-232)[15]
3g	3-$NO_2C_6H_4$	9	96/98	145-147 (149-150)[15]
3h	2-$NO_2C_6H_4$	9	93/96	221-223 (224-225)[15]
3i	2-Thienyl	16	80/85	189-190 (190-192)[18]
3j	2-Furyl	10	71/76	190-193 (189-191)[18]
3k	2-Pyridyl	10	77/81	228-231 (230-232)[18]
3l	3-BrC_6H_4	8	93/96	173-175 (172-175)[18]
3m	4-MeC_6H_4	10	90/93	201-203 (203-204)[15]
3n	4-FC_6H_4	8	88/91	143-150
3o	2-BrC_6H_4	8	92/95	248-250
3p	4-Cl-3- $NO_2C_6H_4$	9	96/98	232-238
3q	2,5-di$MeOC_6H_4$	10	84/86	133-141
3r	4-BrC_6H_4	8	90/93	203-209
3s	4-CNC_6H_4	8	93/96	214-219
3t	2-Naphtyl	11	90/92	203-207

[a]The amounts of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one, aldehyde and [Pyridine–SO_3H]Cl in all reactions were 10, 5 and 0.05 mmol, respectively, and the reactions were carried out at 50 ºC under solvent-free condition. [b]Isolated yield. [c]Conversion.

Table 4. Comparison of the results on the synthesis of 4,4'-((4-nitrophenyl)methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) catalyzed by our new catalysts with those obtained by the recently reported catalysts.[a]

Reaction Condition	Catalyst loading	Time (min)	Yield[b] (%)	TOF[c] (min^{-1})	Ref.
[Pyridine–SO_3H]Cl, solvent-free, 50 ºC	1 mol%	8	94	11.7500	-[c]
Silica-bonded S-sulfonic acid (SBSSA), EtOH, reflux condition	18 mol%	40	90	0.1250	36
[Dsim]$AlCl_4$, solvent-free, 90 ºC	1 mol%	40	91	2.2750	27
PEG-400, 110 ºC	282 mol%	60	94	0.0055	18
3-Aminopropylated silica gel, CH_3CN, r.t.	30 mol%	10	98	0.3266	37
Poly(ethylene glycol)-bound sulfonic acid (PEG-SO_3H), water, reflux condition	1.5 mol%	15	93	4.1333	17
p-Toluenesulfonic acid, solvent-free, 50 ºC	1 mol%	25	20	0.8000	-[d]
$ClSO_3H$, solvent-free, 50 ºC	1 mol%	17	93	5.4705	-[d]

[a]The reactions were carried out by the condensation of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one with 4-nitrobenzaldehyde. [b]Isolated yield. [c]Turn-over frequency. [d]Our work.

Table 5

Recycling experiments for 1-sulfopyridinium chloride.[a]

Entry	Cycle	Time (min)	Yield[b] (%)
1	1st run	8	94
2	2st run	8	92
3	3st run	9	91
4	4st run	10	89
5	5st run	11	88

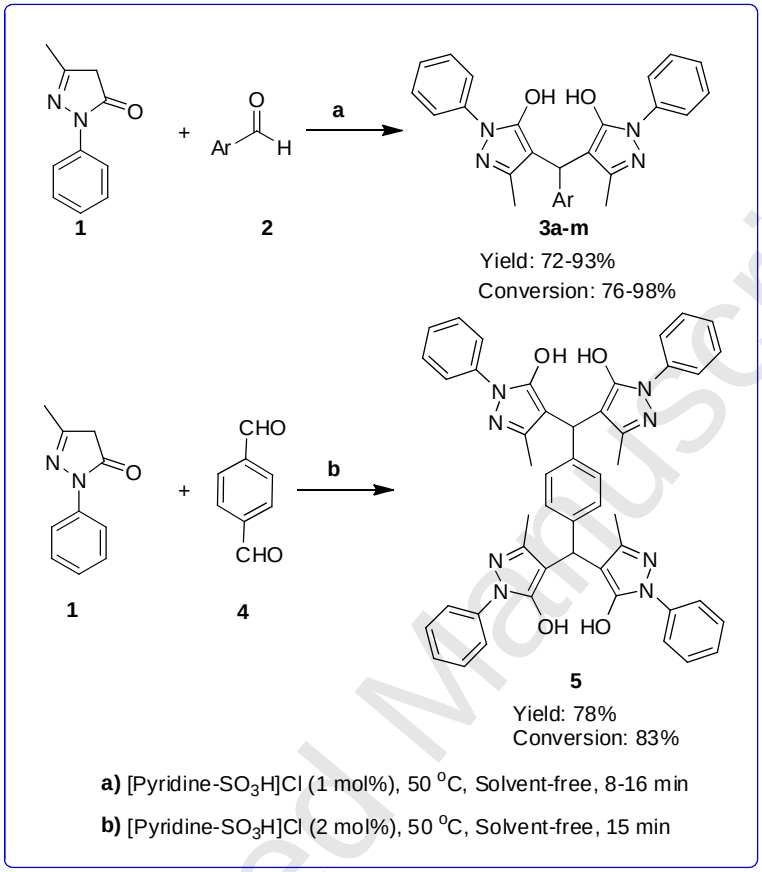
[a]The reaction of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (2 mmol) with 4-nitrobenzaldehyde (1 mmol) in the presence of reused [Pyridine–SO_3H]Cl (1 mol%) under solvent-free conditions at 50 ºC. [b]Isolated yield.

Table 6

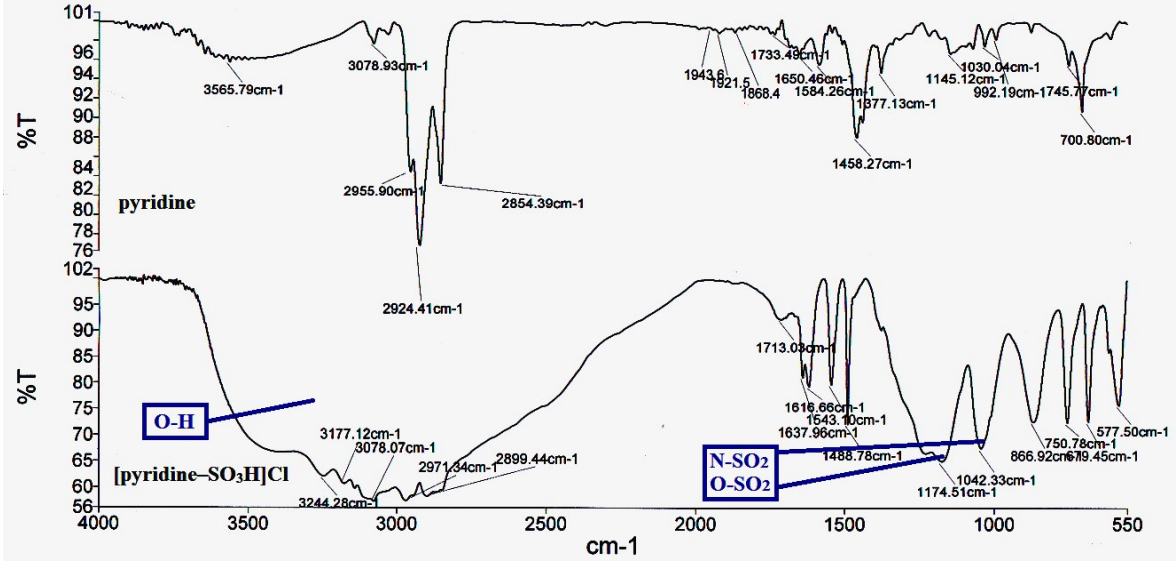
Effect of impurities of water on the condensation of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one and 4-nitrobenzaldehyde.[a]

Entry	Water Amount (mmol)	Time (min)	Yield[b]/Conv.[c] (%)
1	1	8	94/96
2	2	12	94/96
3	4	19	93/95
4	6	22	91/94
5	8	26	90/92
6	10	30	89/91
7	12	41	88/90
8	14	60	78/81

[a]The amounts of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one, aldehyde and [Pyridine–SO_3H]Cl in all reactions were 10, 5 and 0.05 mmol, respectively, and the reactions were carried out at 50 ºC under solvent-free condition. [b]Isolated yield. [c]Conversion.



Scheme 1. a) The preparation of 4,4′-(arylmethylene)-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol)s by the condensation of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one with arylaldehyde using [Pyridine–SO_3H]Cl (1 mol%) as catalyst at 50 ºC under solvent-free conditions. **b**) The preparation of di-4,4'-(arylmethylene)-bis(3-methyl-1-phenylpyrazol-5-ol) by the condensation of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one with terephthaldehyde using [Pyridine–SO_3H]Cl (2 mol%) at 50 ºC under solvent-free conditions.



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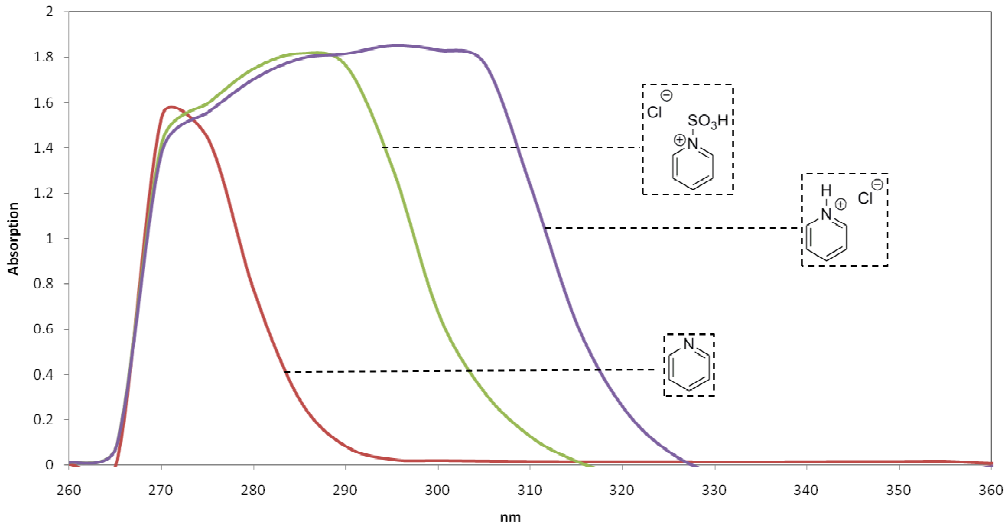

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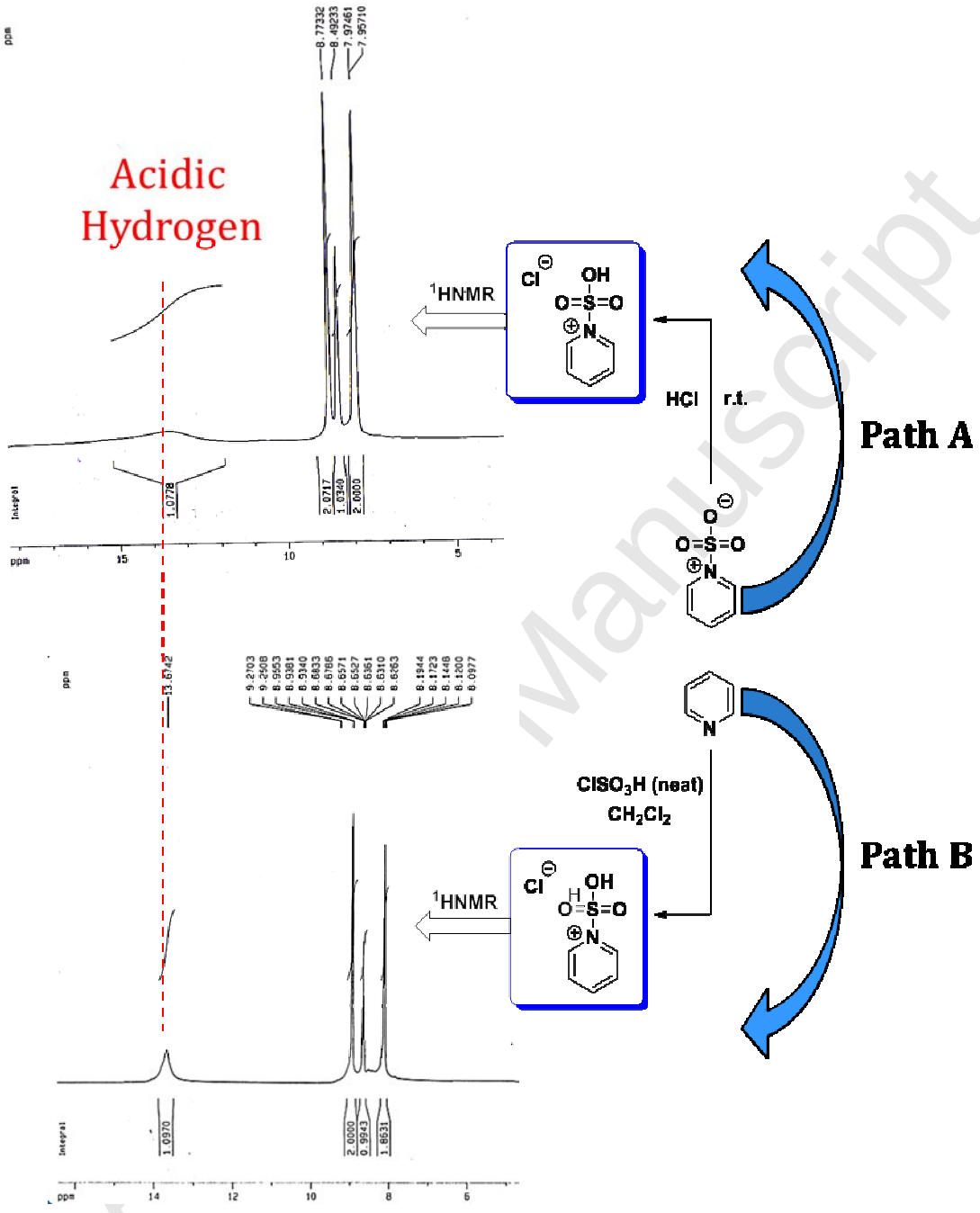

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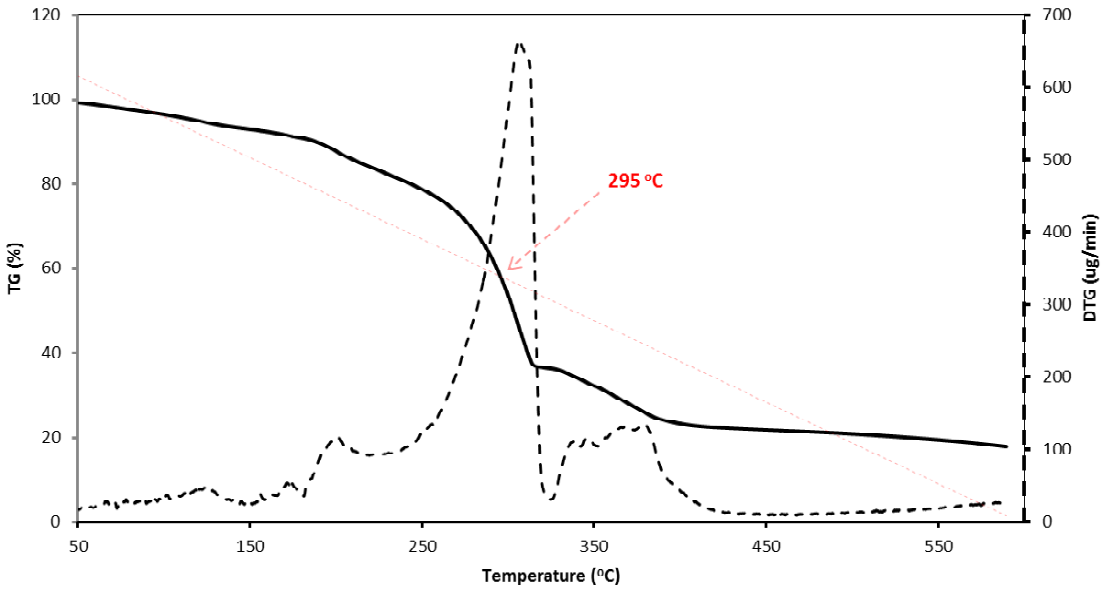

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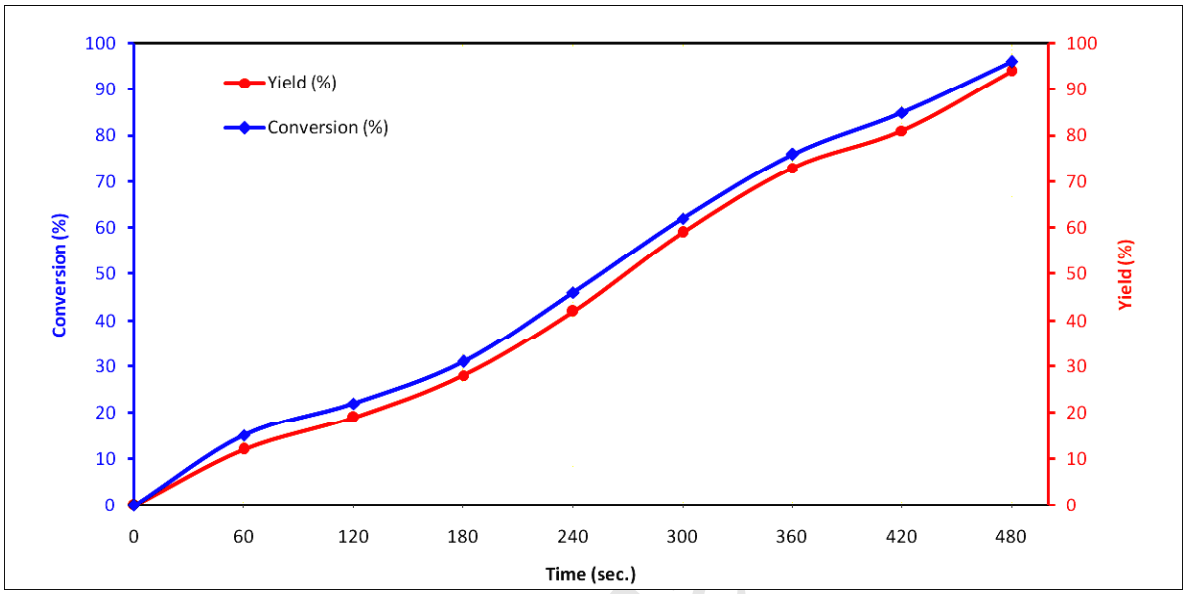

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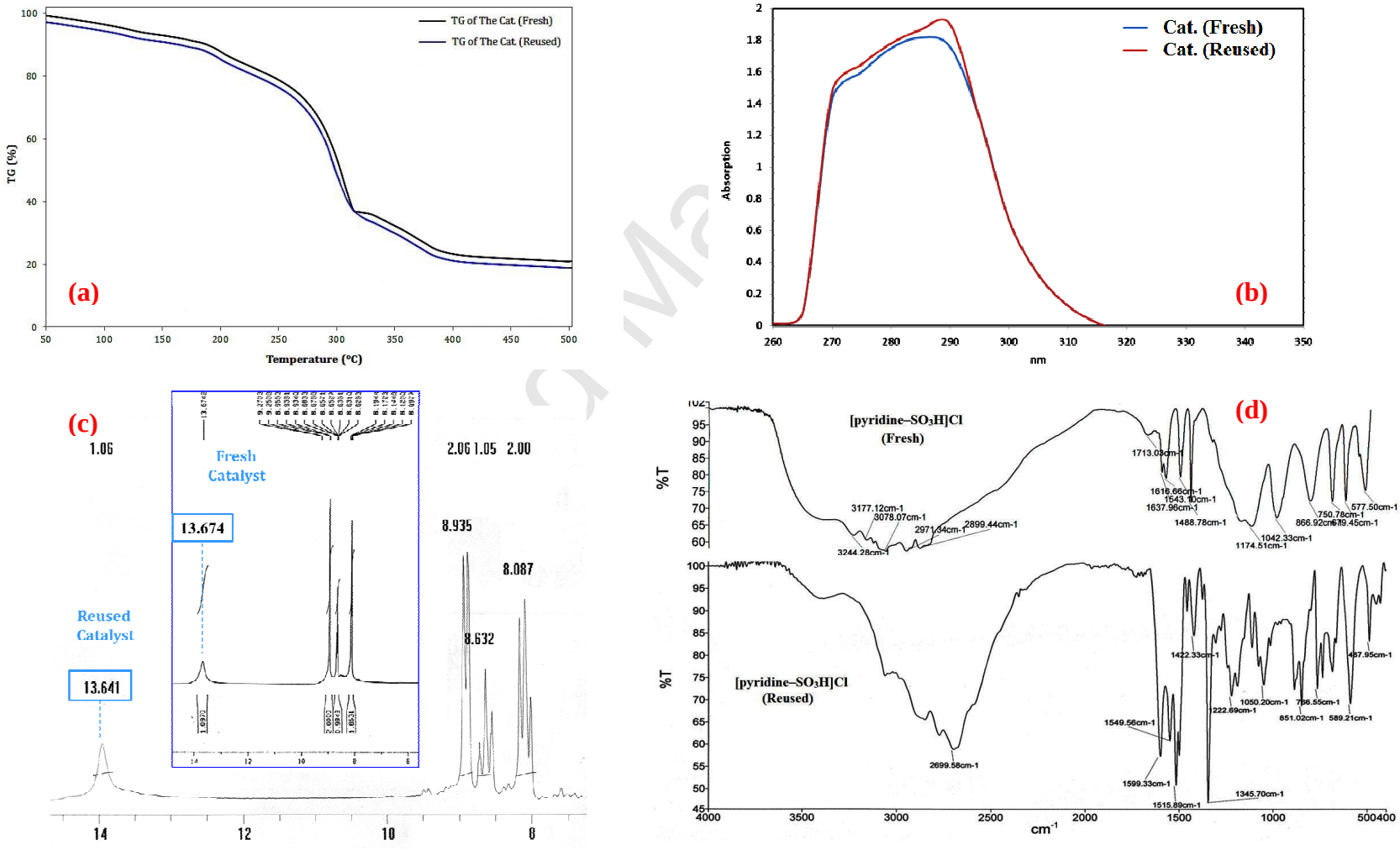

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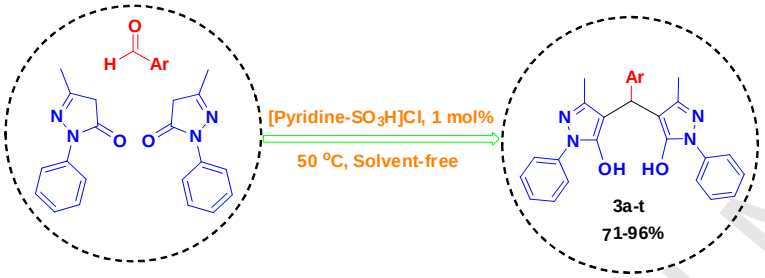
Graphical Abstract



Tandem knoevenagel-michael reaction

Highlights

Catalytic system based on 1-sulfopyridinium chloride was synthesized.
This catalyst was characterized by IR, ^{1}H as well as ^{13}C NMR, UV and mass spectra.
This catalytic system was successfully tested in Knoevenagel–Michael reaction.
The yield of products was obtained 72-93% for 8-16 min under mild conditions.