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Poly(4-vinylpyridine)-Supported Dual Acidic Ionic Liquid: a Novel Heterogeneous Catalyst for the Synthesis of β-Acetamido Ketones

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Poly(4-vinylpyridine)-Supported Dual Acidic Ionic Liquid: a Novel Heterogeneous Catalyst for the Synthesis of β-Acetamido Ketones

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Abstract

A supported dual acidic ionic liquid catalyst was easily prepared from its starting materials and used as an environmentally friendly heterogeneous catalytic system for the synthesis of β-acetamido ketones from the four-component condensation of an aromatic aldehyde with acetophenone, acetyl chloride, and acetonitrile at room temperature. This catalyst was also applied as an efficient catalyst for the synthesis of α-aminophosphonates. The catalyst favourably combines the properties of ionic liquids and advantages of solid supports and is recoverable without loss in its catalytic activity.

Keywords poly(4-vinylpyridine)-supported ionic liquid, β-acetamido ketones; α-aminophosphonates, aldehydes, multi-component reactions

INTRODUCTION

In recent years, ionic liquids have received considerable interest as eco-friendly catalysts in green synthesis because of their unique properties.[1] One type is Brønsted acidic ionic liquids. These ionic liquids are of special important because they possess simultaneously the proton acidity and the characteristic properties of ionic liquid. Among them, SO_3H-functionalized ionic liquids with a hydrogen sulfate counteranion are of particular value as a class of dual acidic ionic liquids, because the existence of both SO_3H functional groups and hydrogen sulfate counteranions can enhance their catalytic acidities.[2–4] However, despite having the widespread application in organic synthesis, most of them suffer from one or more of the following drawbacks such as laborious work-up procedures, difficulty of recovery and recycling, disposal of spent catalyst, difficult to handle, and corrosion problems. Thus, these shortcomings make them a prime target for heterogenisation.[5–8]

β-Acetamido ketones are important synthons for a variety of biologically or pharmacologically important compounds.[9,10] These are precursors of 1,3-amino alcohols present in antibiotic nikkomycins or neopolyoxines.[11] One-pot condensation of an aldehyde with an enolisable ketone, acetyl chloride, and acetonitrile is the most convenient method for the preparation of β-acetamido ketones. Several types of catalysts were introduced previously for this purpose such as $CoCl_2$,[12] zeolite Hβ,[13] silica sulfuric acid,[14] $Sc(OTf)_3$, $Yb(OTf)_3$, and $CuCl_2$,[15] $CeCl_3.7H_2O$,[16] $ZrOCl_2.8H_2O$,[17] $FeCl_3$,[18] $La(OTf)_3$,[19] polyaniline-sulfate salt,[20] cellulose sulfuric acid,[21] and $H_5PW_{10}V_2O_{40}$.[22] Except a few, many of the above methods suffer from the drawbacks such as generation of environmentally perilous waste material, tedious work-up, high reaction temperature, long reaction times, unsatisfactory yields, complicated operations, the reaction has to be carried out under an inert atmosphere, and the use of moisture-sensitive, expensive, hazardous, difficult to handle or unreusable catalysts. In view of these, the search for finding a cost effective, mild, and simple protocol specially using green and eco-friendly catalysts for the synthesis of β-acetamido ketones is still relevant.

In a continuation of our work on the synthesis and application of poly(vinylpyridine)-supported reagents and catalysts in organic reactions,[23] herein, we now report the synthesis of poly(4-vinylpyridine-*co*-1-sulfonic acid butyl-4-vinylpyridinium)hydrogen sulfate ([P_4VPy-$BuSO_3H$]HSO_4) from the reaction of poly(4-vinylpyridine) (P_4VPy) with 1,4-butane sultone, followed by the reaction with H_2SO_4. [P_4VPy-$BuSO_3H$]HSO_4 was used as a polymer catalyst for the synthesis of β-acetamido ketones from coupling of an aromatic aldehyde with acetophenone, acetyl chloride, and acetonitrile (Scheme 1).

EXPERIMENTAL

Material and Techniques

Chemicals were either prepared in our laboratory or were purchased from Merck and Fluka. Reaction monitoring and purity determination of the products were accomplished by GLC or TLC on silica-gel polygram SILG/UV254 plates. Gas chromatography was recorded on Shimadzu GC 14-A. IR spectra were obtained by a Shimadzu model 8300 FT-IR spectrophotometer. NMR spectra were recorded on a Bruker Advance DPX-300 spectrometer. The Leco sulfur analyzer was used for the measurement of sulfur in catalyst. Melting points were determined on a Fisher-Jones melting-point apparatus and are uncorrected. Thermal gravimetric analysis (TGA) were performed by a Stanton Redcraft STA-780 with 20 °C/min heating rate in N_2. The shape and surface morphology of the samples were examined on a scanning electron microscope (SEM) (Hitachi S-3400N, Japan).

Preparation of [P_4VPy-$BuSO_3H$]HSO_4

In a round bottomed flask (50 mL) equipped with a reflux condenser, 1 g of the P_4VPy (2% DVB) was added to 1,4-butane sultone (1.5 mL) and the mixture was stirred at 100 °C for 30 h, filtered, washed with distilled water (20 mL), and dried at 80 °C overnight. Afterwards, H_2SO_4 (3 M, 5 mL) was added to the obtained resin and the mixture was stirred at room temperature for 2 h, filtered, washed with distilled water (20 mL), and dried at 80 °C overnight to give [P_4VPy-$BuSO_3H$]HSO_4.

Typical experimental procedure

To a solution of an aromatic aldehyde (1 mmol), acetophenone (1mmol), acetyl chloride (2 mmol), and acetonitrile (4 mL) was added [P_4VPy-$BuSO_3H$]HSO_4 (0.07 mmol), 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 the filtrate poured into ice-water (25 mL). The precipitated solid was filtered, washed with ice-water, and recrystallized from ethyl acetate/*n*-hexane to give the pure product.

RESULTS AND DISCUSSION

[P_4VPy-$BuSO_3H$]HSO_4 was prepared by the procedure shown in Scheme 2. At the first stage, commercially available P_4VPy (2% divinylbenzene) was reacted with 1,4-butane sultone to give the poly(4-vinylpyridine-*co*-1-sulfonate butyl-4-vinylpyridinium) ([P_4VPy-$BuSO_3$]) as a pale yellow solid. [P_4VPy-$BuSO_3$] was analyzed by elemental analysis to quantify the percentage loading of the sulfonate moiety by measuring the sulfur content, giving 0.9 mmol sulfonate moiety per gram. In a second step, the [P_4VPy-$BuSO_3$] was further treated with H_2SO_4 to form [P_4VPy-$BuSO_3H$]HSO_4 as a white cream solid. The acidic site loading in [P_4VPy-$BuSO_3H$]HSO_4 obtained by means of acid–base titration was found to be 1.7 mmol/g.[24]

For comparison, FT-IR spectra of the P_4VPy, [P_4VPy-$BuSO_3$], and [P_4VPy-$BuSO_3H$]HSO_4 were presented in Fig. 1. As can be seen in the spectrum of [P_4VPy-$BuSO_3H$]HSO_4 new peaks appeared at 1160, 1200, and 1220 cm^{-1}, which can be assigned to S=O stretching vibration.[8] Also, a new peak appeared at 1645 cm^{-1} which is ascribed to the C-N (pyridine-CH_2-) bond absorption. This observation confirms the N-alkylation of pyridine ring.

Fig. 2 shows TGA curves of P_4VPy and [P_4VPy-$BuSO_3H$]HSO_4. A weight loss was observed in each case around 100 ^oC due to the loss of moisture. In the case of [P_4VPy-$BuSO_3H$]HSO_4, the second weight loss started at about 200 ^oC is mainly assigned to the decomposition of alky-sulfonic acid groups and hydrogen sulphate counteranions. In TGA curves of P_4VPy and [P_4VPy-$BuSO_3H$]HSO_4 the last weight losses were observed at about 350 ^oC and 420 ^oC, respectively, which are attributed to the degradation of polymer backbone.

An attempt was made to investigate the morphology of [P_4VPy-$BuSO_3H$]HSO_4 catalyst using scanning electron microscopy (SEM). The SEM images of P_4VPy and [P_4VPy-$BuSO_3H$]HSO_4 are provided in Fig. 3. In the SEM photograph of [P_4VPy-$BuSO_3H$]HSO_4, it can be seen that the [P_4VPy-$BuSO_3H$]HSO_4 surface is uniform and in this catalyst the pores of P_4VPy are filled with alky-sulfonic acid groups and hydrogen sulphate counteranions.

The catalytic activity of [P_4VPy-BuSO_3H]HSO_4 was studied in the synthesis of β-acetamido ketones by the condensation of aldehydes with acetophenone, acetyl chloride, and acetonitrile at room temperature (Table 1). The optimum molar ratio of [P_4VPy-BuSO_3H]HSO_4: aldehyde: acetyl chloride was found to be 0.07:1:2. Various types of substituted benzaldehydes were smoothly converted into the corresponding β-acetamido ketones (entries 1-8). Salicylaldehyde afforded the corresponding product without any acetylation of hydroxyl group (entry 9). Aliphatic aldehydes did not yield the desired product (entry 10). The reaction of benzaldehyde with acetophenone and acetonitrile in the absence of acetyl chloride failed to produce the corresponding product. This observation indicated that the presence of acetyl chloride is necessary in this reaction. Also, the reaction of benzaldehyde with acetophenone, acetyl chloride, and benzonitrile (instead of acetonitrile) led to the formation of the corresponding β-benzamido ketone in 88% yield after 1 h. This demonstrates that in this reaction, nitrile acts as a nucleophile according to the mechanism proposed in Scheme 3. We believe that [P_4VPy-BuSO_3H]HSO_4 activates the aldehyde group for nucleophilic attack as well as facilitating enolization of acetophenone.

Recently, we used polystyrene-supported Al(OTf)$_3$ as a polymer catalyst for the synthesis of α-aminophosphonates by the condensation of amines and aldehydes with diethyl phosphite.[25] Along this line, in this study, we observed that [P_4VPy-BuSO_3H]HSO_4 is also an effective catalyst for the synthesis of α-aminophosphonates (Scheme 4).

[P_4VPy-BuSO_3H]HSO_4 recovered after a reaction can be washed with water and used again at least five times without appreciable change in its efficiency (Scheme 5).

A comparison of the present procedure, using $[P_4VPy\text{-}BuSO_3H]HSO_4$, with selected previously known protocols is collected in Table 2. As it is seen in addition to having the general advantages attributed to the solid supported catalysts, $[P_4VPy\text{-}BuSO_3H]HSO_4$ has a good efficiency compared to other recently reported catalysts

CONCLUSION

In conclusion, we have synthesized $[P_4VPy\text{-}BuSO_3H]HSO_4$ as a polymer-supported dual acidic ionic liquid. $[P_4VPy\text{-}BuSO_3H]HSO_4$ can act as an efficient catalyst for the synthesis of β-acetamido ketones and α-aminophosphonates. The significant advantages of this methodology are high yields, short reaction times, simple work-up procedure, and easy preparation and handling of the catalyst. In addition, the use of this catalyst has resulted in a reduction in the unwanted and hazardous waste that is produced during conventional homogeneous processes. Finally, this solid catalyst can be recovered unchanged and used again.

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24. 1 gr of dry [P_4VPy-BuSO_3H]HSO_4 was added to 10 mL aqueous solution of NaCl (2 M) and the resulting mixture was stirred for 24 h and then titrated potentiometrically with aqueous solution of NaOH (0.01 mol/Lit) as titrant and phenolphthalein as an indicator.

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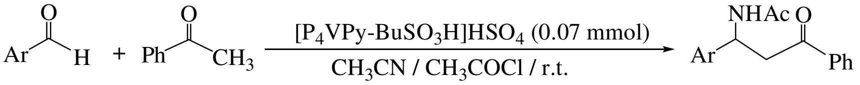
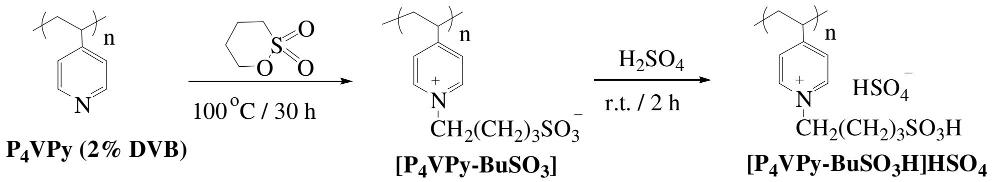
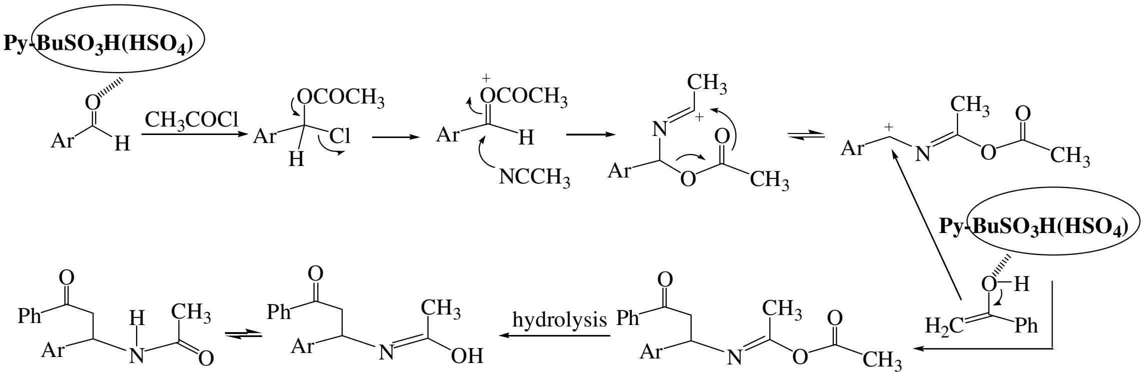


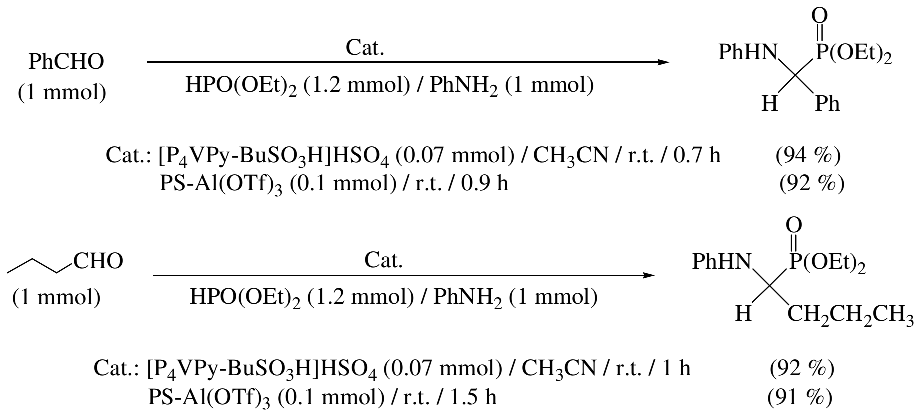
SCH. 1.



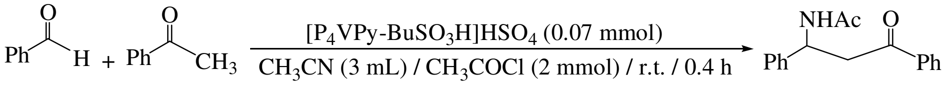
SCH. 2.



SCH. 3.



SCH. 4.



Run No.	1	2	3	4	5
Isolated yield (%)	94	94	93	90	90

SCH. 5.

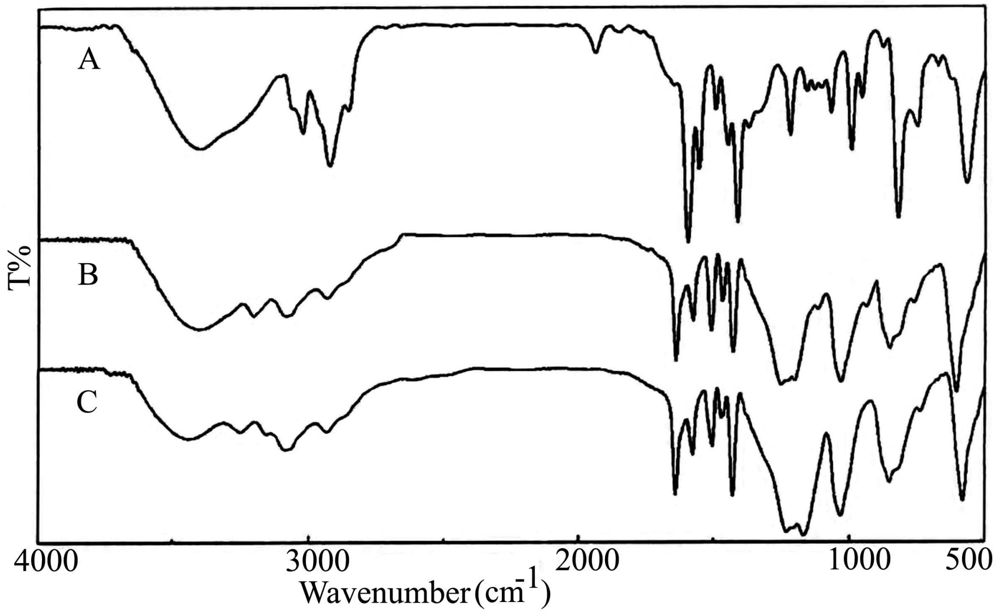


FIG. 1. FT-IR spectra of P_4VPy (A), [P_4VPy-$BuSO_3$] (B), and [P_4VPy-$BuSO_3H$]HSO_4 (C).

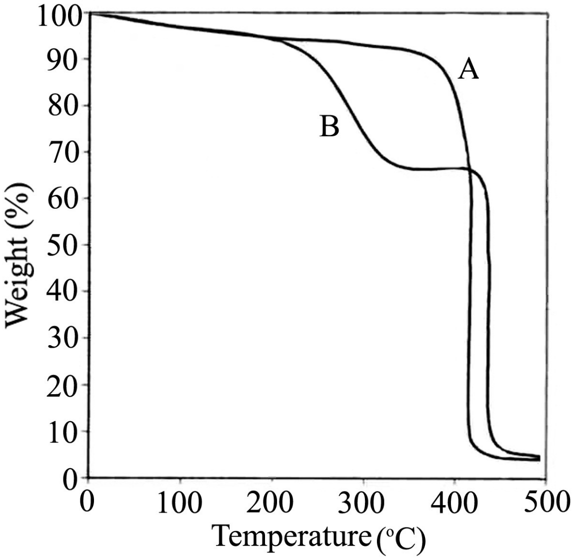
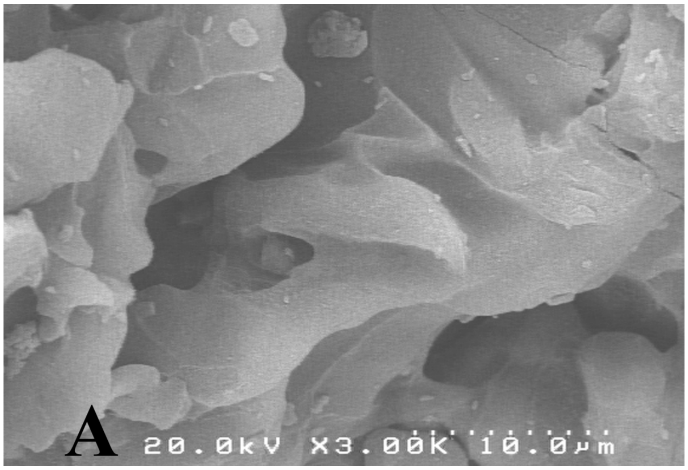


FIG. 2. TGA curves of P_4VPy (A) and [P_4VPy-$BuSO_3H$]HSO_4 (B).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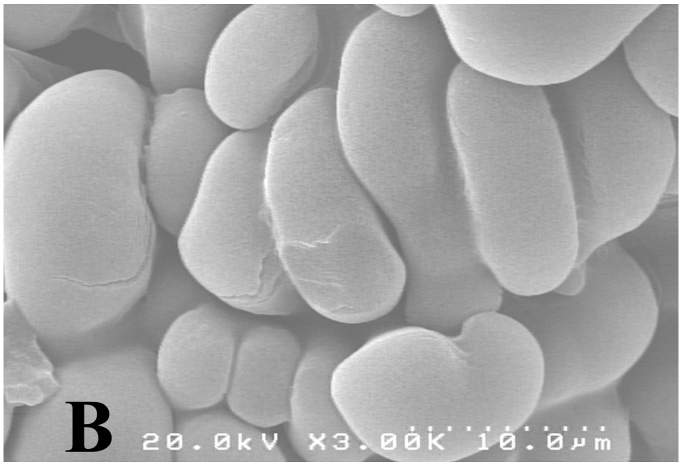
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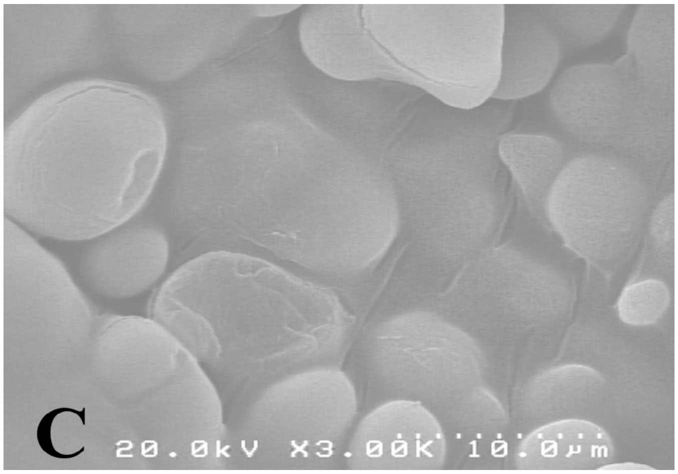
C
20.0kV X3.00K 10.0μm

FIG. 3. SEM photographs of P_4VPy (A), [P_4VPy-$BuSO_3H$]HSO_4 (B) and [P_4VPy-$BuSO_3H$]HSO_4 after five uses (C).

TABLE 1

Synthesis of β-acetamido ketones using [P_4VPy-$BuSO_3H$]HSO_4.

Entry	Ar	Time (h)	Yield (%)[a]	Mp (°C) (Lit. (Ref.))
1	Ph	0.4	94	104-106 (103-105)[9]
2	4-$CH_3C_6H_4$	0.5	94	111-113 (112)[17]
3	4-$CH_3OC_6H_4$	0.5	92	111-113 (110-112)[17]
4	4-ClC_6H_4	0.4	94	148-150 (144-146)[22]
5	4-BrC_6H_4	0.4	92	149-151 (148-150)[18]
6	3-BrC_6H_4	0.4	93	105-106 (101-103)[22]
7	4-$NO_2C_6H_4$	0.3	92	155-157 (154)[17]
8	2-$NO_2C_6H_4$	0.4	90	194-196 (191-192)[17]
9	2-HOC_6H_4	0.5	90	131-133 (129-131)[22]
10	CH_3CH_2CHO	1	–	–

[a]Isolated yields. All products are known compounds and were identified by comparison of their physical and spectral data with those of the authentic samples.

TABLE 2

Comparison of the catalytic activity of [P_4VPy-$BuSO_3H$]HSO_4 against other reported catalysts for the coupling of benzaldehyde with acetophenone, acetyl chloride, and acetonitrile.

Entry	Catalyst	Temp. (°C)	Time (h)	Yield (%)
1	$CoCl_2$[a]	80	1	64[12]
2	Zeolite Hβ[a]	28	8.5	87[13]
3	Silica sulfuric acid	80	1	91[14]
4	$Sc(OTf)_3$	r.t.	30	82[15]
5	$CeCl_3.7H_2O$	r.t.	7	96[16]
6	$ZrOCl_2.8H_2O$	r.t.	5	90[17]
7	$FeCl_3$	r.t.	8	88[18]
8	$La(OTf)_3$[b]	85	4	87[19]
9	Polyaniline-sulfate salt	80	1	90[20]
10	Cellulose sulfuric acid[c]	80	1	97[21]
11	$H_5PW_{10}V_2O_{40}$	80	0.7	80[22]
12	$[P_4VPy\text{-}BuSO_3H]HSO_4$	r.t.	0.4	94

[a] With 4-chlorobenzaldehyde instead of benzaldehyde.

[b] With 4-fluorobenzaldehyde instead of benzaldehyde.

[c] With dimedone instead of benzaldehyde.