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P4VP-H₂SO₄-Catalyzed Chemoselective Protection of Aldehydes to Acylal Along with Deprotection Reactions

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P4VP-H₂SO₄-CATALYZED CHEMOSELECTIVE PROTECTION OF ALDEHYDES TO ACYLAL ALONG WITH DEPROTECTION REACTIONS

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GRAPHICAL ABSTRACT

Ac₂O/ P4VP-H₂SO₄ , DCM /r.t

RCHO

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RCH(OAc)_2
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P4VP-H₂SO₄,CH₃CN

room temp. to 50° C

Abstract Poly(4-vinylpyridine)-supported sulfuric acid is an excellent reusable heterogeneous catalyst for the chemoselective synthesis of 1,1-diacetates(acylal) from aldehydes in dichloromethane at room temperature within a few minutes. The protection of salicyaldehyde generated an anhydro-dimer as single product under similar reaction conditions. The catalyst is equally applicable for the deprotection of acylal in acetonitrile. The catalyst was prepared by the wet impregnation technique.

Keywords Chemoselectivity; 1,1-diacetates; protection–deprotection; reusable catalyst; supported solid acid

INTRODUCTION

From the literature, it has been observed that the potential use of polymer-supported^[1] heterogeneous and reusable catalysts in organic transformations make reaction methods more convenient, economical, and environmentally benign. Many reactions can be carried out cleanly and rapidly in good yields. The reactions can be performed under mild conditions, and product purification is simplified because of the easy separation of insoluble solid support from the reagents and products. Poly(4-vinylpyridine) seems to be an attractive support to immobilize acidic dopants because of the basic nature of the pyridyl group. For these reasons we thought to investigate the use of poly(4-vinylpyridine)–supported sulfuric acid as reusable catalyst in protection–deprotection chemistry of carbonyl group

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RCHO $Ac_2O/P4VP-H_2SO_4$, DCM/r.t RCHO $RCH(OAc)_2$ P4VP-H_2SO₄, CH₃CN room temp. to 50⁰C

(Scheme 1) in continuation of our previous work^[2] on polymer-supported acid catalyst in organic synthesis.

The protection of carbonyl functional group as acylals is an important strategy in organic synthesis.^[3] Acylals are alternatives to acetals because of their stability in neutral as well as basic media.^[4,5] They have been applied as cross-linking reagents in cellulose and cotton^[6] industries and as stain-bleaching agents.^[7] As synthons, they have been utilized in well-known reactions of organic chemistry^[8] such as nitrile synthesis, Grignard reactions, Prins reactions, and condensation reactions such as Knoevenagel and Benzoin.

Although a large number of methods for the preparation of acylals have been reported,^[9–12] most of the existing methods suffer from many drawbacks because of one or more of the following reasons: (i) use of highly corrosive, expensive, and non recyclable Brønsted or Lewis acid catalysts, (ii) prolonged reaction times, (iii) poor yields, (iv) high temperatures, and (v) use of an excess amount of acetic anhydride. As a result, there are still real demands for the development of efficient catalytic methods for this transformation by using safe and reusable solid acid catalysts.

RESULTS AND DISCUSSION

The catalyst P4VP-H₂SO₄ was prepared by a simple wet-impregnation method^[2] and characterized with Fourier transform–infrared (FT-IR), scanning electron microscopy (SEM), thermal gravimetric analysis (TGA), and EDX studies. It is relatively nontoxic, safe to handle, and reusable after reactivation, which make the process more economical and benign. The amount of dopants present in poly(4-vinylpyridine) sulfuric acid (P4VP-H₂SO₄) was found to be 0.652 mol%. Our first approach to the protection of the carbonyl group was achieved by stirring the mixture of aldehyde (1.0 mmol), acetic anhydride (3 mmol), and P4VP-H₂SO₄ (0.0326 mol%) in organic solvent at room temperature. We observed the best results in dichloromethane out of several organic solvents such as acetonitrile, acetone, tetrahydrofuran (THF) and toluene.

To generalize the feasibility of the reaction, we examined different aldehydes (Table 1), including aromatic and aliphatic, bearing electron-withdrawing as well as electron-donating substituents, heteroatoms, and α , β -unsaturated ones. The results in Table 1 show that both aromatic and aliphatic aldehydes (entries 11 and 12) react smoothly with acetic anhydride to afford the corresponding 1,1-diacetates in good to excellent yields within less time. In the case of salicylaldehyde, we observed 85% production (Table 1, entry 8) of the anhydro dimer of o-hydroxybenzaldehyde (Scheme 2) and a minor amount of starting compound,

Scheme 1. Protection-deprotection reactions of aldehydes.

| Entry | Substrate | Product | Time | Yield ^a (%) | Mp Reported (°C) | Mp Found (°C) |
|-------|---|--|--------|---------------------------|--------------------------------|---------------------|
| 1 | онс | CH(OAc)2 | 15 min | 100 | 44–46 ^[5] | 46 |
| 2 | | O ₂ N-CH(OAc) ₂ | 10 min | 100 | 125 ^[9b] | 125 |
| 3 | СНО | CH(OAc) ₂ | 5 min | 100 | 85.5– 86.5 ^[15a] | 86 |
| 4 | О2N СНО | O ₂ N CH(OAc) ₂ | 5 min | 100 | 64–66 ^[5] | 65 |
| 5 | онс-Сі | CI-CH(OAc) ₂ | 5 min | 100 | 79–80 ^[15a] | 80 |
| 6 | ОНСОМе | MeO-CH(OAc) ₂ | 20 min | 50 | 64–65 ^[15a] | 65 |
| 7 | ОНС | Me-CH(OAc) ₂ | 30 min | 80 | 68–70 ^[5] | 70 |
| 8 | ОН | | 5 min | 85 | 130 ^[13b] | 128 |
| 9 | онс-Он | MeOCO-CH(OAc) ₂ | 19 h | 50 | 57 ^[16] | 57 |
| 10 | онс———————————————————————————————————— | MeOCO CH(OAc) ₂ | 25 min | 100^{b} | 57 | 57 |
| 11 | СНО | CH(OAc) ₂ | 30 min | 100 | Oil ^[15b] | Oil |
| 12 | СНО | CH(OAc) ₂ | 5 min | 10 | Oil ^[15a] | Oil |
| 13 | СНО | CH(OAc) ₂ | 24 h | 10 | 84–87 ^[5] | 86 |

Table 1. P4VP-H₂SO₄-catalyzed acylal formation of different aldehydes with acetic anhydride

(Continued)

| Entry | Substrate | Product | Time | Yield ^a (%) | Mp Reported (°C) | Mp Found (°C) |
|-------|-----------|----------------------|--------|---------------------------|------------------------|---------------------|
| 14 | СНО | _ | 5 min | Polymer | _ | _ |
| 15 | | _ | 12 h | NR | _ | _ |
| 16 | o | _ | 12 h | NR | _ | _ |
| 17 | ≻o | _ | 12 h | NR | _ | _ |
| 18 | | _ | 12 h | NR | _ | _ |
| 19 | CHO | CH(OAc) ₂ | 2 h | 60 | 110 ^[17] | 110 |
| 20 | СНО | CH(OAc) ₂ | 30 min | 80 ^c | 110 | 110 |

Table 1. Continued

⁴All products were characterized by ¹H NMR, ¹³C NMR, FT-IR, and TLC comparison with authentic samples prepared by reported methods.

^bThe reaction was carried out using a 1: 6 ratio of substrate and acetic anhydride.

^cThe reaction was carried out using a 1:4 ratio of substrate and acetic anhydride.

whereas the sulfuric acid-catalyzed method^[13] provides only 65% of the dimer. Definitely, the advantages of our experimental conditions are the reusability of the catalyst, safe handling and easy separation of products.

After completion of the reactions, the catalyst was recovered by filtration and reused four times with minimal difference in yield (98-100%) in each cycle within 5 min through the reaction of m-nitro-benzaldehyde and acetic anhydride in dichloromethane. The FT-IR spectra of the used catalyst also showed similar absorption patterns with original IR spectra of P4VP-H₂SO₄ acid (Fig. 1).



Scheme 2. Synthesis of anhydrodimer of salicyaldehyde.

The keto group of acetophenone and other aliphatic ketones such as cyclohexanone, acetone and butanone remained unreactive under the experimental condition (Table 1, entries 15–18) within 12 h, which showed the chemoselective nature of P4VP-H₂SO₄ catalyst for the protection of aldehyde to acylal group. The reaction of cinnamaldehyde (Table 1, entry 13) formed only 10% acylal product during 24 h. Furaldehyde, under the described (Table 1, entry 14) experimental conditions, formed an unidentified polymer. The reaction of 1-naphthaldehyde showed 60% conversion (Table 1, entry 17) with 1:3 molar ratios of aldehyde and acetic anhydride in 2 h. The increasing amount of acetic anhydride completed the reaction (Table 1, entry 18) within 30 min.

The catalyst was again investigated for the deprotection of acylals to aldehydes. Table 2 shows the results of the deprotection of acylals to the corresponding aldehydes using catalytic amounts of P4VP-H₂SO₄ in acetonitrile at different temperatures. It was observed that at room temperature the reaction takes more time (Table 2, entries 1, 4, 5, 8, and 9) to complete the conversion.



Figure 1. FT-IR spectrum of P4VP (A), P4VP-H₂SO₄ (B), and reused P4VP-H₂SO₄ (C).

POLY(4-VINYLPYRIDINE)-SUPPORTED SULFURIC ACID

| Entry | Substrate | Temp (°C) | Time | Product | Yield (%) ^a |
|-------|---------------------------------------|-----------|--------|------------------------|------------------------|
| 1 | CI-CH(OAc) ₂ | rt | 12 h | 4-Chlorobenzaldehyde | 80 |
| 2 | CI-CH(OAc) ₂ | 50 | 45 min | 4-Chlorobenzaldehyde | 100 |
| 3 | О2N СНО | 50 | 1 h | m-Nitrobenzaldehyde | 100 |
| 4 | CH(OAc) ₂ | rt | 12 h | Benzaldehyde | 85 |
| 5 | CH(OAc) ₂ | rt | 2 h | Butanal | 80 |
| 6 | O ₂ N-CH(OAc) ₂ | 50 | 1 h | p- Nitrobenzaldehyde | 100 |
| 7 | | 50 | 1 h | o- Nitrobenzaldehyde | 100 |
| 8 | MeO-CH(OAc) ₂ | rt | 2.5 h | p- Anisaldehyde | 80 |
| 9 | Me CH(OAc) ₂ | rt | 4 h | p-Tolualdehyde | 85 |
| 10 | MeOCO-CH(OAc) ₂ | 50 | 45 min | p- Hydroxybenzaldehyde | 96 |
| 11 | CH(OAc) ₂ | rt | 1.5 h | Pentanal | 100 |
| 12 | CH(OAc) ₂ | 50 | 1 h | 1-Naphthaldehyde | 95 |

Table 2. Deprotection of 1,1-diacetates to aldehydes in acetonitrile

^aIsolated yield.

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EXPERIMENTAL

All chemicals are commercially available and were used without further purification. The products were identified by comparison of their FT-IR and ¹H NMR spectroscopic data with those of authentic compounds (prepared by known method) and literature reported data.^[5,13–17]

General Procedure for the Synthesis of 1,1-Diacetate from Aldehydes

The polymer-supported catalyst (0.0326 mol%) was added to a stirred solution of aldehyde (1 mmol), acetic anhydride (3 mmol), and dichloromethane (2 ml) in a 50-ml round-bottom flask at room temperature. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion, the mixture was diluted with dichloromethane and filtered to recover the catalyst. The organic solution was washed with NaHCO₃ solution and dried over anhydrous sodium sulfate. The dichloromethane solution was evaporated under reduced pressure, and the crude product was found to be almost pure product. All the compounds were characterized by taking ¹H NMR, ¹³C NMR, and IR.

General Procedure for the Deprotection of 1,1-Diacetate to Aldehydes

The polymer-supported catalyst (0.0326 mol%) was added to a stirred solution of 1,1-diacetate (1 mmol) in acetonitrile (4 ml) (at room temperature or 50 °C) in a 50-ml round-bottom flask with a reflux condenser. The progress of the reaction was monitored by TLC. After completion, the catalyst was recovered by filtration, and the filtrate was extracted with dichloromethane and dried over anhydrous sodium sulfate. The dichloromethane solution was evaporated under reduced pressure to give the corresponding aldehydes in pure form.

Spectral Data of Selected Compounds

1,1-Diacetate-1-(3-nitrophenyl)methane (Table 1, Entry 4). Mp 65 °C; ¹H NMR (CDCl₃, 400 MHz): $\delta = 8.39$ (s, 1H), 8.28–8.24 (dd, J = 8.2, 1.2 Hz, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.72 (s, 1H), 7.61–7.57 (t, J = 8 Hz, 1H), 2.14 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.7$, 148.4, 137.6, 133.0, 129.8, 124.7, 122.0, 88.4, 20.9. FT-IR (KBr): 2963, 1760, 1533, 1358, 1255, 1203, 1091, 1016, 809, 685 cm⁻¹. CHN analysis, C₁₁H₁₁O₆N, calculated (%) C, 52.17; N, 5.53; H, 4.34. Found: C, 52.19; N, 5.57; H, 4.35.

1,1-Diacetoxy pentane (Table 1, Entry 11). Oil; ¹H NMR (CDCl₃, 400 MHz): $\delta = 6.78$ (t, J = 5.5 Hz, 1H), 2.08 (s, 6H), 1.75–1.78 (m, 2H), 1.35–1.37 (m, 4H), 0.91 (t, J = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 169$, 90.6, 32.9, 25.8, 22.3, 20.8, 13.9; FT-IR (KBr): 2953, 2870, 2381, 1759, 1441, 1371, 1247, 1208, 1114, 1004 cm⁻¹. CHN analysis: C₉ H₁₆O₄, calculated (%) C, 57.44; H, 8.50. Found: C, 57.47; H, 8.52.

CONCLUSION

In this report, we have successfully demonstrated the catalytic activity of $P4VP-H_2SO_4$ and its use as a simple, ecofriendly, reusable, and efficient heterogeneous acid catalyst for the chemoselective synthesis of 1,1-diacetates from aldehydes in dichloromethane at room temperature along with deprotection reaction in acetonitrile.

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