

Novel catalyst for environmentally friendly synthesis of acetoveratrone

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Acylated aromatic ethers are of commercial importance in fine chemicals industries, as many synthetic fragrances and pharmaceuticals contain an acyl group and these ethers are useful intermediates. Para acylated veratrole synthesized by acylation of veratrole is a useful intermediate for the production of vesnarinone, which is a cardiotoxic drug. Conventional acylation of veratrole have been carried out by using homogeneous acid catalysts such as AlCl_3 , FeCl_3 , ZnCl_2 , HF, etc. The use of these catalysts leads to many problems concerning handling, safety, corrosion and waste disposal. Thus, the search for alternatives to environmentally damaging processes has become a topic of highest priority. During the past few years, various solid acids have been tried for the acylation of veratrole. However, the conversion is still poor. Thus, there still exists scope to develop better catalysts which would catalyze the acylation of veratrole with excellent conversion and selectivity at comparatively low temperature. The present paper aims at liquid phase acylation of veratrole with acetic anhydride over silica included dodecatungstophosphoric acid (DTP) in the temperature range of 303-323 K. Effects of various parameters such as mole ratio of reactants, catalyst loading and temperature on the rates of reaction have been analyzed. The method described here is environmentally benign, and replaces the conventional and hazardous mineral acid catalyst by highly active and reusable catalyst.

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1. Introduction

The acylation of aromatic compounds is an intermediate step in the synthesis of pharmaceuticals. Para acylated veratrole synthesized by acylation of veratrole is useful intermediate for the production of vesnarinone, which is a cardiotoxic [1]. The conventional Friedel–Crafts acylation uses Lewis acid catalysts such as AlCl_3 [2], however these catalysts generate large amounts of environmentally toxic by-products; they are used in more than stoichiometric amounts, and furthermore the catalyst is non-regenerable. In this context, there is obviously a need for more environmentally friendly catalysts such as heterogeneous solid acid catalysts. During the past few years, different solid acid catalyst such as zeolites [3] metal cation exchanged clays [4], ion exchange resins [5], and supported-heteropoly acids have been used for acylation of veratrole [6]. The present work deals with acylation of veratrole by acetic anhydride using silica-included heteropoly acid as catalyst.

2 Experimental

2.1 Chemicals

Veratrole, acetic anhydride, Tetraethoxysilane (TEOS), and dodecatungstophosphoric acid (DTP) were

purchased from Merck and were used as-received.

2.2 Preparation of Silica included DTP Catalysts

The procedure described in the literature with slight modification (7) was followed for the preparation of silica-included dodeca-tungstophosphoric acid (DTP) catalyst. The silica included DTP catalyst was prepared from the hydrolysis of TEOS with aqueous solutions containing 20 % of DTP by weight. The solvent was then removed under reduced pressure in a rotary evaporator at 60 °C. The resulting solid was powdered in a mortar and dried at 120 °C for 6 h.

2.3 Catalytic studies

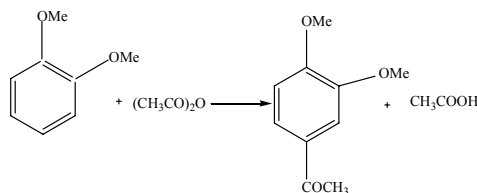
Acylation of veratrole by acetic anhydride over the different supported catalysts was carried out in a magnetically stirred glass reactor (capacity 100 cm³) fitted with a reflux condenser and a thermometer for measuring the reaction temperature. The reactor was kept in a constant temperature oil bath. The products of the acylation were analyzed by gas chromatography (GC).

In a typical experiment, the reaction mixture consisted of 80 mmol veratrole and 10 mmol mol acetic anhydride. The freshly activated catalyst (0.3 g) was added and the flask with its contents was heated at a constant temperature (30 °C) in an oil bath for 90

minutes and stirred magnetically. The progress of the reaction was monitored by withdrawing samples from the reactor and subjecting them to gas chromatographic analysis, using a 10% OV-17 column and a FID detector. The product, 3',4'-dimethoxyacetophenone was confirmed by gas chromatography–mass spectroscopy (GC-MS). The conversion is expressed as the percentage of acetic anhydride converted into the acylated product.

3. Results and discussion

Acylation of veratrole with acetic anhydride was carried out over the silica-included DTP catalysts at 60 °C for 90 minutes. The molar ratio of veratrole to acetic anhydride (8:1) were used for all the catalytic runs. The product, 3',4'-dimethoxyacetophenone was confirmed by gas chromatography–mass spectroscopy. The reaction scheme is represented as follows.



3.1 Effect of catalyst quantity

The effect of catalyst loading was studied over a range of 0.1–0.4 (Fig. 1). The conversion of acetic anhydride was found to increase with increase in catalyst amount, which is due to the proportional increase in the number of active sites and the additional active sites do not increase the adsorption of reactants at a given concentration and so the conversion of acetic anhydride does not increase much. Hence all further experiments were carried out using 0.3 g catalysts.

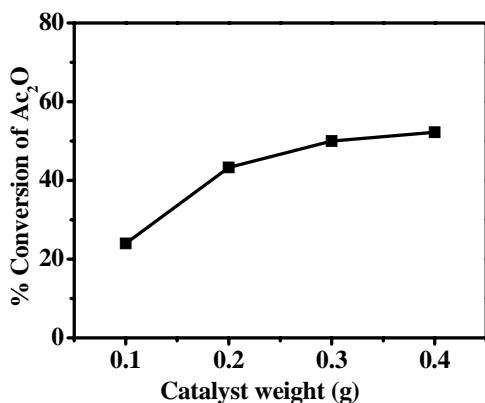


Fig. 1. Effect of catalyst quantity.

3.2 Effect of temperature

The effect of temperature on conversion was studied under otherwise similar conditions at 30, 40 and 50 °C, respectively (Fig. 2). The conversion was found to increase significantly on increasing the temperature.

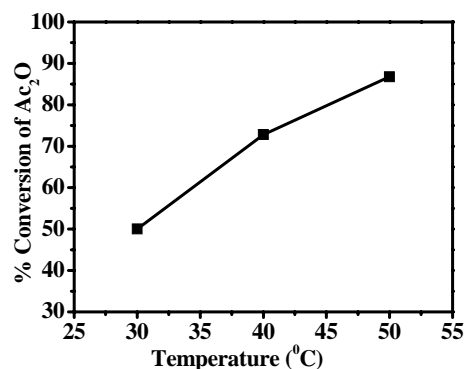


Fig. 2. Effect of temperature.

4. Conclusion

The liquid-phase acylation of veratrole with acetic anhydride was studied using silica-included heteropolycyclic acid. High conversion in the acylation of veratrole with acetic anhydride was achieved under mild conditions. The catalysts can be recovered and reused, with the avoidance of toxic waste generated by conventional Lewis acid catalysts.

Acknowledgments

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References

- [1] R. V. Jasra, Y. Badheka, S. Muthusamy, US Patent application 10/341606, 2003.
- [2] G. A. Olah, Interscience Monographs on Organic Chemistry: Friedel–Crafts Chemistry, p. 973.
- [3] C. Guinard, V. Pedron, F. Richard, R. Jacquot, M. Spagnol, J. M. Coustard, G. Perot, Appl. Catal. A **234**, 79 (2002).
- [4] B. M. Choudary, M. Sateesh, M. L. Kantam, K. V. R. Prasad, Appl. Catal. **171**, 55 (1998).
- [5] B. M. Choudary, M. L. Kantam, M. Sateesh, K. K. Rao, P. L. Santhi, Appl. Catal. A **149**, 257 (1997).
- [6] G. D. Yadav, H. G. Manyer, Microp. Mesop. Mater. **63**, 85 (2003).
- [7] Yusuke Izumi, Katsunori Hisano, Tomoko Hida, Appl. Catal. **181**, 277 (1999).

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