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Poly(4-vinylpyridine-*co*-ethylvinylbenzene) as heterogeneous reusable catalyst for the synthesis of benzoyl fumarate

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Abstract Poly(4-vinylpyridine-*co*-ethylvinylbenzene) 25 % cross-linked (with divinylbenzene) has been found to be an effective heterogeneous catalyst for the synthesis of benzoyl fumarate from aldehyde and dimethyl acetylenedicarboxy-late. Various aromatic aldehydes undergo this reaction with good yield in presence of 15 wt% of the catalyst. The catalyst was recovered and reused six times without appreciable alteration in activity. *Graphical abstract*



Keywords Benzoyl fumarate · Poly(4-vinylpyridine-*co*-ethylvinylbenzene) · Heterogeneous catalyst · DMAD · Aldehyde

Introduction

Benzoyl fumarates and their corresponding acids are known to be the vital precursors in the synthesis of many important agrochemicals, drugs as well as in

Prodeep Phukan pphukan@yahoo.com many synthetically important reactions such as Diels-Alder reaction [1-8]. While studying the photo-oxidation of furans, Scarpati and co-workers have observed the formation of benzovl fumarates [9, 10]. In the year 2003, a direct protocol for the synthesis of benzoyl fumarates was developed independently by Shi and Nair [11, 12]. Their approach involves the reaction between aldehyde and dimethyl acetylenedicarboxylate (DMAD) in presence of Lewis base such as pyridine and DMAP as catalyst. Recently, Bayat et al. observed the formation of similar structural features as byproduct during the synthesis of γ -butyrolactone [13]. There are also few reports in the literature for the synthesis of benzoyl fumarates [5, 14]. However, all these methods are based on the application of homogeneous catalysts which have the obvious problem of reusability. Application of reusable catalyst is important from the industrial as well as green chemistry point of view. We have recently reported a homogeneous reusable catalyst for the synthesis of benzoyl fumarates [15]. Subsequently, we made an improvement of the method by developing a nicotinic acid-based heterogeneous catalyst [16]. Although we are successful in synthesizing new reusable catalysts, these catalysts have to be made via multistep procedure. So, we looked for alternative commercially available catalyst to make the method more viable. Since DMAP has been proven to be the best catalyst for this particular reaction, we intended to examine the possibility of using poly(4-vinylpyridine-co-ethylvinylbenzene) 25 % cross-linked with divinylbenzene as the first case due to its commercial availability. In this paper, we describe the use of poly(4-vinylpyridine-coethylvinylbenzene) (PVPEVB) as reusable heterogeneous catalyst for the synthesis of benzoyl fumarate from aldehyde (Scheme 1).

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Scheme 1



Results and discussion

The catalyst, PVPEVB (Fig. 1) is commercially available. Initially, the reaction between 4-nitrobenzaldehyde and DMAD was taken as a model reaction to find out the optimum condition for the reaction. In a typical reaction, 5 wt% (based on the aldehyde amount) of the catalyst was added to a mixture of 4-nitrobenzaldehyde (1 mmol) and DMAD (1 mmol) in 5 cm³ DME at 0 °C under nitrogen atmosphere and the reaction was continued at room



Fig. 1 Structure of poly(4-vinylpyridine-*co*-ethylvinylbenzene), 25 % cross-linked with divinylbenzene (as per Sigma-Aldrich catalogue description)

temperature for an appropriate time. After the completion of the reaction (as indicated by TLC analysis), the catalyst was separated by filtration and washed with a small amount of DCM. The reaction mixture was concentrated and the crude material was purified by column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to get the pure product. Initial reaction in the absence of the catalyst fails to give the desired product even after 24 h of reaction (Table 1, entry 1). However, 5 wt% of catalyst and DME as solvent gives 70 % of benzoyl fumarate as product with 10 h of reaction time (Table 1, entry 2). It was observed that the reaction in other solvents such as acetonitrile and THF produced lower yield with longer reaction hours (Table 1, entries 3, 4). Only trace amount of the product formation was observed when DCM was used as solvent (Table 1, entry 5). The reaction was further investigated by increasing the catalyst amount. The reaction in presence of 15 wt% of PVPEVB produced 80 % of corresponding fumarate after 8 h of reaction (Table 1, entry 7). Further increase in catalyst loading did not improve the reaction (Table 1, entries 8, 9). Finally,

Table 1 Reaction of *p*-nitrobenzaldehyde with DMAD catalyzed by PVPEVB under different conditions

02N H +	COOMe	O COOMe	
	Solvent, 0 °C - RT	O ₂ N COOMe	

Entry	PVPEVB/wt%	Solvent	Time/h	Yield/% ^a
1	0	DME	24	0
2	5	DME	10	70
3	5	THF	14	50
4	5	CH ₃ CN	24	37
5	5	DCM	24	Trace
6	10	DME	8	74
7	15	DME	8	80
8	20	DME	8	80
9	25	DME	8	81

Reaction conditions: 4-nitrobenzaldehyde (1 mmol), DMAD (1 mmol), 5 cm³ solvent, 0 °C to rt

^a Isolated yield

Table 2 Synthesis of benzoyl fumarates using PVPEVB catalyst



Entry	Ar	Yield/% ^a
1	$C_{6}H_{5}$ (1a)	60
2	$4-BrC_{6}H_{4}$ (1b)	79
3	$4-ClC_{6}H_{4}$ (1c)	74
4	$4-FC_{6}H_{4}$ (1d)	70
5	$4-NO_2C_6H_4$ (1e)	80
6	$4-MeOC_{6}H_{4}$ (1f)	68
7	$4-MeC_{6}H_{4}$ (1g)	53
8	$C_{10}H_7$ (1h)	61
9	3-BrC ₆ H ₄ (1i)	68
10	$3-ClC_{6}H_{4}$ (1j)	70

Reaction conditions: aldehyde (1 mmol), DMAD (1 mmol), PVPEVB (15 wt%), 5 cm3 DME, 0 °C to rt, 8 h

^a Isolated yield

15 wt% of catalyst (based on the aldehyde amount), 1 mmol of aldehyde, 1 mmol of DMAD in DME and 8 h of reaction time was found to be the optimum condition for the reaction. After optimization the protocol has been extended to a variety of aldehydes and the results are presented in Table 2.

The efficiency of this method is evident from the high yield of benzoyl fumarates formed from various substituted benzaldehydes. It was observed that the presence of electron withdrawing group enhances the yield of the reaction (Table 2, entries 2–6). On the other hand, electron donating group results in the lower product yield (Table 2, entry 7). It was further observed that para-substituted aldehyde shows better results compared to the corresponding meta-substituted aldehyde (Table 2, entries 3, 4, 8, 9). This reaction was found to be less effective for aliphatic aldehyde.

Reusability of the catalyst was tested with 4-nitrobenzaldehyde. After the completion of the reaction, the solvent was removed and 5 cm³ DCM was added to the crude reaction mixture. The reaction mixture was passed through a filter paper to remove the insoluble polymeric catalyst. The residue in the filter paper was washed with DCM, dried under vacuum, and kept in a desiccator for 24 h before reuse. Initially, after the first use, the recovery percentage of the catalyst was found to be 98 % in comparison to the first use of the catalyst. The recovered catalyst was reused. We have reused the catalyst six times without appreciable loss in activity. The slight decrease in yield in the subsequent step can be attributed to the small

Table 3 Reusability of the catalyst

Entry	Catalyst reused	Catalyst recovered/% ^a	Yield/% ^b
1	1st	98	80
2	2nd	97	79
3	3rd	95	79
4	4th	92	78
5	5th	91	77
6	6th	89	76

Reaction conditions: 4-nitrobenzaldehyde (1 mmol), DMAD (1 mmol), 5 cm^3 DME, 0 °C to rt, 8 h

^a With respect to first use

^b Isolated yield

decrease in the catalyst recovery. After the sixth run, the yield was found to be 76 with 89 % of catalyst recovery (Table 3, entry 6).

The mechanism of this reaction has already been proposed by Shi et al. [11]. In this case, the pyridine moiety attached to the polymer takes part in the mechanism. Thus, the pyridine subunit of the polymeric catalyst produces a zwitterionic intermediate by interacting with DMAD, which subsequently reacts with aldehyde followed by intermolecular proton transfer. Expulsion of the catalyst at the final stage results in the formation of the product.

In conclusion, we have developed an efficient heterogeneous and reusable catalytic protocol for the synthesis of benzoyl fumarate from aldehyde and DMAD in presence of a catalytic amount of poly(4-vinylpyridine-*co*-ethylvinylbenzene). Use of a commercially available catalyst makes this methodology convenient for direct applications. The method is suitable for various aromatic aldehydes to obtain the product in high yield. Moreover, the catalyst can be reused six times without appreciable loss in activity.

Experimental

The catalyst poly(4-vinylpyridine-*co*-ethylvinylbenzene) 25 % cross-linked (with divinylbenzene) was purchased from Sigma-Aldrich Corporation.

Typical experimental procedure for polymer catalyzed synthesis of benzoyl fumarate

A solution of 0.142 g DMAD (1 mmol) and 0.045 g 4-nitrobenzaldehyde (1 mmol) in 5 cm³ anhydrous DME was cooled to 0 °C under nitrogen atmosphere. PVPEVB (15 wt%) was then added and the reaction was stirred at room temperature for 8 h. After the completion of the reaction, the reaction mixture was filtered and the residue was washed with DCM. The combined filtrate was concentrated and purified by column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to get the pure product **1e** with 80 % yield.

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