Convenient Synthesis of Benzoate Esters Mediated by Polymer Supported Benzoyl Chloride

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ABSTRACT: Use of polymeric reagents simplifies routine acylation of alcohols because it eliminates traditional purification. We describe the use of readily available crosslinked poly(*N*-benzoyl-4-vinylpyridinium)-chloride, [P_4VP] COPh, in the solution phase synthesis of esters from alcohols or phenols in the presence of K_2CO_3 in high yields and purity. The products can be obtained by filtration and evaporation of the solvent and the polymeric reagent can be regenerated. © 2009 Wiley Periodicals, Inc. J Appl Polym Sci 115: 237–241, 2010

Key words: solid-supported reagent; esters; polymeric reagent; acylation

INTRODUCTION

Although polymeric reagents and scavengers have been used in organic synthesis for decades, development of combinatorial and parallel high throughput synthesis techniques brought this class of reagents to a wider attention. The first compound collections were based on peptides and oligonucleotides, which were stepwise, assembled on a solid-support,[1] following the concept developed by Merrifield.[2] Polymer-supported reagents especially anion exchange resins have been widely applied in organic synthesis.[3–14] These polymeric reagents are generally used in single step reactions. Their main advantage over monomeric reagents is their insolubility in the reaction medium and consequently the easier work-up by a simple filtration. The reactions can often be driven to completion by using excess of these reagents without the fear of separating the unspent reagent from the desired products. The spent polymeric reagents can usually be removed quantitatively and regenerated. In addition, anions bound to the macroporous resin have the advantage that they often react successfully in nonpolar solvents.

The ester group is an important functional group that can be synthesized in a number of different ways, such as by acylation of alcohols,[15–20] oxidation of aldehydes,[21] addition of carboxylic acids to alkenes,[22–24] reaction of carboxylic acids with diazomethane,[25,26] Bayer–Villiger oxidation of ketones,[27–29] reaction of organoboranes with α-halo esters,[30] rearrangement of α-haloketones (Favortski reaction),[31] synthesis of esters within a microreactor,[32] microwave oven synthesis of esters promoted by imidazole,[33] esterification of carboxylic acids in the presence of crosslinked polyvinyl pyridine hydrochloride as a catalyst,[34] CsF-celite as a catalyst for the synthesis of esters under microwave,[35] and especially for large scale work by reaction of carboxylate salts[36–43] or Amberlite IRA-904 supported carboxylate ion with alkyl halides or tosylates.[44] Sodium carboxylate, however, has been the reagent most widely used. Although numerous applications of solid supported reagents and scavengers are reported in literature,[3–14] only a few examples were described for ester synthesis.[14,44–53] Esterification by using, polymer-supported carboxylate,[14] or Amberlite IRA-904 supported carboxylate ion[44] with alkyl halides or tosylates, polymer-supported acids as catalyst,[45] anion exchange resin[46] polystyrylsulfonyl chloride,[47] polystyrene bound thiols,[48] basic ion exchange resin Amberlite IRA-68 as both a reagent and scavenger resin[49] resin-bound triphenylphosphine and soluble di-*t*-butylazodicarboxylate,[50] polymer-supported carbodiimide,[51] polymer-supported triazines,[52] and poly(4-vinylpyridine)[53] are instances that have been reported.

Unfortunately, each of these methods suffer from at least one of the following disadvantages: (1) yields of the reactions are low, (2) the reaction has to be carried out in the presence of phase transfer catalyst, (3) the reaction mixture has to be acidified or the reaction has to be catalyzed by a base such as pyridine, and (4) the work-up products have needed several steps, especially, in the latest method,

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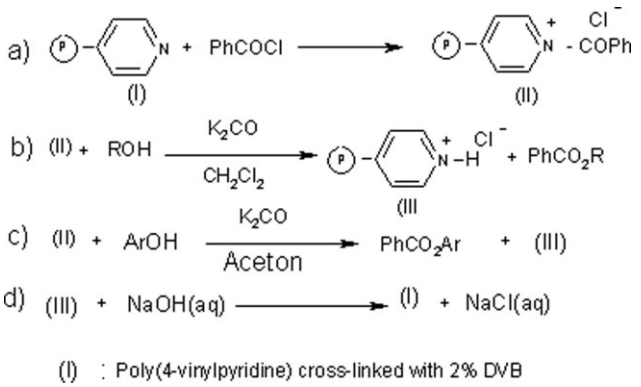


Scheme 1 Mechanism of the acyl transfer and regeneration of the polymeric reagent.

however, requires the addition of amino-functionalized silica gel to remove excess acid chloride. Polymer-supported benzoyl chloride overcomes most of the aforementioned disadvantages.

In continuing of our studies on the application of crosslinked poly(4-vinylpyridine) in organic synthesis,[10–14] herein, we report a novel, clean, and simple method in which alcohols or phenol react with benzoyl chloride by using excess of poly(4-vinylpyridine) crosslinked with 2% DVB and K_2CO_3 in nonaqueous solvent, such as dichloromethane for alcohols and acetone for phenols. This polymer acts as a base and acylation catalyst. To establish a simple work-up procedure, we applied an excess of polymer (5–6 equiv) to drive the esterification reaction to completion by formation of crosslinked poly(*N*-benzoyl-4-vinylpyridinium)chloride as a polymeric acylating agent and esterification step proceeds by nucleophilic displacement of alcohols or phenols in the presence of K_2CO_3 (Scheme 1).

EXPERIMENTAL

Chemicals

Chemicals were purchased from Fluka, Merck, and Aldrich chemical companies and poly(4-vinylpyridine) crosslinked with 2% DVB was purchased from Fluka. Progress of the reaction was followed by TLC using silica gel PolyGram SIL G/UV 254 plates. All products were characterized by comparison of their IR and ^{1}H-NMR spectra and physical data with those of known samples and all yields refer to the isolated pure products. FTIR and ^{1}H-NMR spectra were run on a Bruker, Equinox (model 55), and JNM-EX 90 MHz spectrophotometer, respectively.

General procedure for preparation of alkyl benzoate

To a suspension of crosslinked poly(4-vinylpyridine) (1.05 g, 5 equiv) in dry CH_2Cl_2 (10 mL), freshly distilled benzoyl chloride (281 mg, 2 mmol) was added. The mixture was stirred at room temperature or at 50°C for 30 min, 2 mmol of alcohol and 376 mg (2 mmol) of K_2CO_3 were then added and stirring continued for 1–10 h at room temperature or 0.5–8 h at 50°C. The polymer was recovered by filtration, washed twice with 5 mL of CH_2Cl_2 and regenerated by treatment successively with a solution of NaOH (10%), washing twice with distilled water and drying in a vacuum oven at 40°C, for 24 h. Evaporation of the solvent provides pure products in high isolated yields (65–97% at room temperature and 67–97% at 50°C). If further purification was needed, chromatography on silica gel [eluent: acetone/*n*-hexane (10/90)] provides highly pure products.

Preparation of *n*-propyl benzoate: A typical procedure

To a suspension of crosslinked poly(4-vinylpyridine) (1.05 g, 5 equiv) in dry CH_2Cl_2 (10 mL), freshly distilled benzoyl chloride (281 mg, 2 mmol) was added. The mixture was stirred at room temperature or at 50°C for 30 min, 212 mg (2 mmol) of *n*-propyl alcohol and 376 mg (2 mmol) of K_2CO_3 were then added and stirring continued for 5 h at room temperature or 4 h at 50°C. The polymer was recovered by filtration, washed twice with 5 mL of CH_2Cl_2 and regenerated by treatment successively with a solution of NaOH (10%), washing twice with distilled water and drying in a vacuum oven at 40°C for 24 h. Evaporation of the solvent provides pure products in high isolated yield, 288 mg (94% at room temperature or at 50°C). FTIR (neat) ν (cm^{-1}):1718, (C=O), 1602, 1585 (C=C, aromatic), 1110 and 1176, (C—O); ^{1}H-NMR (90 MHz, $CDCl_3$): δ 1.1 (3H, t, CH_3) 1.7 (2H, q, —CH_2—CH_3), 4.3 (2H, t, —CH_2—O), 7.4–8.2 (5H, aromatic).

Preparation of phenyl benzoate: A typical procedure

To a suspension of crosslinked poly(4-vinylpyridine) (1.15 g, 6 equiv) in acetone (10 mL), freshly distilled benzoyl chloride (281 mg, 2 mmol) was added. The mixture was stirred at room temperature or at 50°C for 30 min, 212 mg (2 mmol) of phenol and 376 mg (2 mmol) of K_2CO_3 were then added and stirring continued for 1 h at room temperature or 0.5 h at 50°C. The polymeric support was recovered by filtration, washed twice with 5 mL of acetone and regenerated by treatment successively with a solution of NaOH (10%), washing twice with distilled water and drying in a vacuum oven at 40°C, for 24 h. Evaporation of the solvent provides pure products in high isolated yield, 288 mg (97% at room temperature or at 50°C). FTIR (neat) ν (cm^{-1}):1730, (C=O), 1591, 1487 (C=C,

aromatic), 1080 and 1199, (C—O); ^{1}H-NMR (90 MHz, $CDCl_3$): δ 7.0–8.2 (10H, ArH).

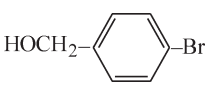
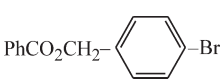
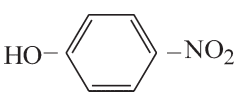
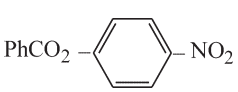
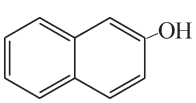
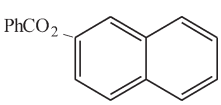
RESULTS AND DISCUSSION

Crosslinked poly(*N*-benzoyl-4-vinylpyridinium)-chloride (II) is easily prepared by using excess of poly(4-vinylpyridine) crosslinked with 2% DVB (I) and freshly distilled benzoyl chloride. This polymeric reagent used as an efficient procedure for conversion of alcohols or phenols to the corresponding alkyl or aryl benzoate under mild and heterogeneous conditions. A number of primary, secondary, and tertiary alcohols, derivatives of phenol and 2-naphthol have been selectively converted to corresponding alkyl or aryl benzoates by using (II) in the presence of K_2CO_3 in CH_2Cl_2 as solvent for alcohols and in acetone for phenols. When GLC or TLC analysis showed complete conversion of alcohols or phenols to corresponding alkyl or aryl benzoate, the mixture was filtered and washed with solvent; the solvent was evaporated to obtain the esters in good to high yields (65–97%) (Table I). The spent polymeric reagent was regenerated by stirring with a sodium hydroxide solution (10%), [Scheme 1(d)]. The reaction is believed to follow the typical transacylation pathway as shown later. The polymer acylation occurs with benzoyl chloride [Scheme 1(a)] and esterification step proceeds by nucleophilic displacement of alcohols [Scheme 1(b)] or phenols [Scheme 1(c)] in the presence of K_2CO_3.

Also the hydrochloric acid generated in the reaction was trapped by the excess of polymer, which displaces the equilibrium toward the ester formation. Among the evidence that supports this mechanism is spectroscopic observation of the acyl pyridinium ion.[15]

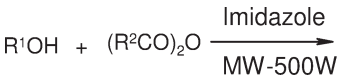
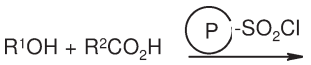
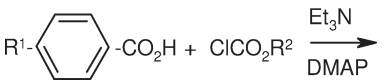
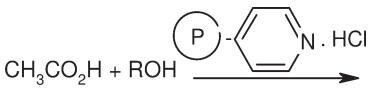
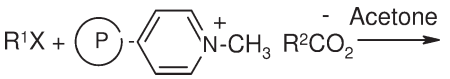
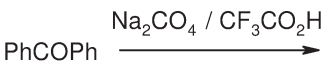
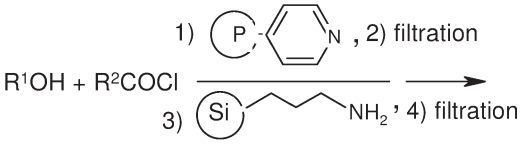
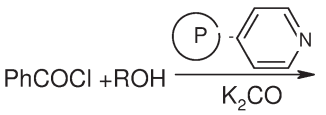
Although, CH_2Cl_2 was the most compatible solvent with the alcohols and resin, but acetone for the phenols was the most suitable solvent. We examined the scope of our procedure by reacting many available alcohols, phenols, and 2-naphthol with this benzoyl containing polymer and the results are summarized in Table I. In Table II, results of this method compared with some other reported procedures in literature.

TABLE I
Preparation of Esters[a] from Alcohols or Phenols by Using Crosslinked Poly(*N*-benzoyl-4-vinylpyridinium)chloride, at Room Temperature or at 50°C

Entry	Substrate	Product[b]	Reaction time (h)	Yield[c] (%)
1	CH_3OH	$PhCO_2CH_3$	4 (3)[d]	97 (97)[d]
2	C_2H_5OH	$PhCO_2C_2H_5$	5 (4)	95 (96)
3	*n*-C_3H_7OH	$PhCO_2C_3H_7$	5 (4)	94 (94)
4	*n*-C_4H_9OH	$PhCO_2C_4H_9$	7 (5)	91 (93)
5	*n*-$C_5H_{11}OH$	$PhCO_2C_5H_{11}$	7 (5)	91 (92)
6	*n*-$C_7H_{15}OH$	$PhCO_2C_7H_{15}$	10 (8)	85 (87)
7	*n*-$C_{10}H_{21}OH$	$PhCO_2C_{10}H_{21}$	10 (8)	83 (84)
8	$(CH_3)_2CHOH$	$PhCO_2CH\ (CH_3)_2$	10 (8)	65 (67)
9	$(CH_3)_3COH$	$PhCO_2C\ (CH_3)_3$	24 (24)	0 (0)
10	PhOH	$PhCO_2Ph$	1 (0.5)	97 (97)
11	$Ph(CH_2)_2OH$	$PhCO_2(CH_2)_2Ph$	10 (8)	84 (85)
12	$Ph(CH_2)_3OH$	$PhCO_2(CH_2)_3Ph$	10 (8)	86 (85)
13			10 (8)	81 (83)
14			2 (1)	93 (94)
15			2 (1)	96 (96)

[a] The reactions were performed in CH_2Cl_2 with alcohols and 5 equiv of crosslinked poly(4-vinylpyridine), but in acetone with phenols and 6 equiv of crosslinked poly(4-vinylpyridine).
[b] The structures were confirmed by comparison of the boiling point, IR, and ^{1}H-NMR spectra with those of authentic specimen.
[c] Isolated yields.
[d] Values in the parentheses corresponded to the reactions that take place at 50°C.

TABLE II
The Comparison of the Reaction Conditions of Different Methods of Ester Synthesis

Entry	Reaction conditions	Temp. (°C)/time	Yield (%)	Ref.
1		MW-500 W/3 min	63–90[a]	33
2		r.t /0.25–22 h	87–100[b]	47
3		0.0/24 h	68–97[a]	32
4		80/1 h	3–100[a]	34
5		56/6–10 h	70–95[a]	14
6		MW-900 W/5–8 min	82–90[a]	35
7		r.t/14 h	76	29
8		r.t /1–10 h	27–96[a]	53
9		r.t /1–10 h	65–97[a]	This work

[a] Isolated yield.
[b] Purity product.

In summary, we demonstrated the use of crosslinked poly(*N*-benzoyl-4-vinylpyridinium)chloride as an efficient polymeric reagent for the suspended solution phase synthesis of esters from alcohols or phenols. In this method, commercially available crosslinked poly(4-vinylpyridine) was used as a base, scavenger, and catalyst. Esters were obtained in good yields and high purity by simple filtration. Exploitation of this reagent to improve the performance of other nucleophilic displacement is under investigation.

The esterification reactions were performed under mild and completely heterogeneous conditions at room temperature or at 50°C (with increase in temperature, the reaction time decreases). The products can be obtained simply by filtration and evaporation of the solvent. The results and reaction conditions are given in Table I. Because acidity of phenols is greater than alcohols, in the presence of a base such as K_2CO_3, phenols react faster than alcohols (entries 10, 14, and 15 in Table I). The relative reactivity of alcohols toward esterification was observed the following order, $CH_3OH > 1^\circ > 2^\circ > 3^\circ$, which is in accord with a nucleophilic substitution process (Table I).

CONCLUSION

We believed this procedure using crosslinked poly(4-vinylpyridine) presents a useful and convenient alternative to the existing method for synthesis of alkyl or aryl esters from alcohols or phenols. Further application of this system in organic synthesis is currently under investigation.

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