

Polymer-Supported Carboxylate as a New Polymeric Reagent for Synthesis of Alkyl Esters

Mohammad Ali Karimi Zarchi,* BiBi Fatemeh Mirjalili, and Nahid Ebrahimi

Department of Chemistry, College of Science, Yazd University, Yazd, Iran. *E-mail: makarimi@yazduni.ac.ir

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Polymer supported reagents especially anion exchange resins have been widely applied in organic synthesis.¹⁻⁸ 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 workup 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 non-polar solvents.

The ester group is an important functional group that can be synthesized in a number of different ways such as acylation of alcohols,⁹ oxidation of aldehydes,¹⁰ addition of carboxylic acids to alkenes,¹¹ reaction of carboxylic acids with diazomethane,¹² Bayer-Villiger oxidation of ketones,¹³ reaction of organoboranes with α -halo esters,¹⁴ rearrangement of α -haloketones (Favorskii reaction)¹⁵ and especially for large scale operation by reaction of carboxylate salts¹⁶ or Amberlite IRA-904 supported carboxylate ion¹⁷ with alkyl halides or tosylates. Sodium carboxylate, however, has been the reagent most widely used. Unfortunately, each of these methods suffer from at least one of the following disadvantages: (1) the 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) tedious work-up procedure.

Polymer-supported carboxylate ion overcomes most of the above mentioned disadvantages. In this study we wish to report an important, efficient, and easy method for preparation of alkyl acetate or alkyl formate esters from crosslinked poly(4-vinylpyridinium) acetate (I) or crosslinked poly(4-vinylpyridinium) formate (II) with alkyl halides (Scheme 1).

While there are numerous applications of solid-supported reagents and scavengers only a few examples for the formation of esters were described. Solid-supported acids were used as catalysts in the esterification of carboxylic acids with alcohols.¹⁸ Carboxylates, generated with solid-supported organic bases, were alkylated with alkyl halides.¹⁷

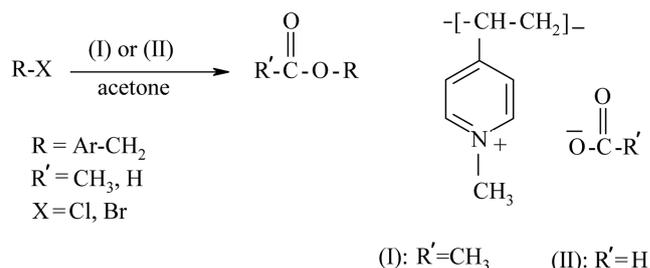
Solid-supported organic bases were also used as scavenger

resins in the esterification of benzyl alcohol with benzyl chlorides, giving clean benzyl esters in high yields.¹⁹ A modification of the Mitsunobu reaction with resin-bound triphenylphosphine and soluble di-*t*-butylazodicarboxylate was described, that allowed for the isolation of pure products without chromatography.²⁰ A very recent report described the alkylation of carboxylic acids with carbenium ions, generated from polymer-supported triazines, for the ester formation.²¹

We report here a convenient and general procedure for the synthesis of esters from alkyl halides and polymer-supported carboxylate ion that readily prepared from employing the commercially available poly(4-vinylpyridine) (2% cross-linked with DVB) resin as the solid-supported condensation reagent. Crosslinked poly(*N*-methyl-4-vinylpyridinium) acetate (I) and crosslinked poly(*N*-methyl-4-vinylpyridinium) formate (II) were prepared by an exchange reaction between crosslinked poly(*N*-methyl-4-vinylpyridinium) iodide with a slight excess of sodium acetate or sodium formate solution in water. Using these heterogeneous reagents converted benzyl halides to benzyl acetate or benzyl formate esters in acetone under reflux condition.

The advantages of this method are: 1) the reaction can be performed in non-aqueous medium; 2) an excess of the reagent can be used; 3) the product can be obtained by simple filtration and evaporation of the solvent; and 4) the polymeric reagent is easily regenerable with a sodium acetate or sodium formate solution.

Crosslinked polymers (I) and (II) can be easily prepared and used as mild and efficient polymeric reagents for conversion of benzyl halides to the corresponding benzyl acetate and benzyl formates. It was proved that acetone is the best solvent for these reactions. In these conversions, the best molar ratio of reagent/substrate proved was 1.5, but



Scheme 1

Table 1. Conversion of benzyl halides to their corresponding benzyl acetate or benzyl formates with polymer (I) or polymer (II) in acetone under reflux condition

Entry	Substrate	Product	Molar ratio Substrate : Reagent	Polymeric reagent	Time (h)	Isolated Yield (%)
1	4-Bromo-benzyl bromide		1 : 1.5	(I)	6	80
			1 : 1.5	(II)	6	85
2	Benzyl bromide		1 : 1.5	(I)	8	80
			1 : 1.5	(II)	6	85
3	3-Chloro-benzyl bromide		1 : 1.5	(I)	6	80
			1 : 1.5	(II)	6	80
4	2-Bromo-propio-phenone		1 : 1.5	(I)	6	90
			1 : 1.5	(II)	6	95
5	1-(Chloromethyl) naphthalene		1 : 1.5	(I)	6	85
			1 : 1.5	(II)	6	90
6	Benzyl chloride		1 : 1.5	(I)	6	80
			1 : 1.5	(II)	6	80
7	4-Me-benzyl bromide		1 : 2	(I)	6	70
			1 : 1.5	(II)	8	80
8	4-Nitro-benzyl bromide		1 : 1.5	(I)	8	90
			1 : 1.5	(II)	6	95
9	Bromodiphenyl methane		1 : 2	(I)	10	80
10	2-Bromobenzyl bromide		1 : 2	(I)	8	70

for secondary benzyl halides, 2-substituted benzyl halides and benzyl halides with electron donor group on their rings, was 2. The capacities of these polymers were determined by potentiometric titration of filtrates with a 0.1 N solution of silver nitrate. The capacity of polymer (I) was 0.86 mmol/g of the polymer, and the capacity of polymer (II) was 0.91 mmol/g of the polymer. As expected, capacity of polymer (II) is greater than polymer (I), because acetate ion is more steric than the formate ion and hence the polymer (II) reacts faster than polymer (I) with benzyl halides (Table 1).

The products were identified by their FT-IR and $^1\text{H-NMR}$ spectral data and by comparison of their TLC with those of authentic samples. As expected, benzyl bromides were reacted as alkylating agents better than benzyl chlorides. It was found that an electron acceptor group on the ring of benzyl halides increased the positive charge on the bonded carbon to the leaving group and the yield of the reaction increased (Table 1).

Experimental Section

General. Chemicals were purchased from Fluka, Merck and Aldrich chemical companies. Yields refer to isolated products. Crosslinked poly(4-vinyl pyridinium) carboxylate ion was synthesized according to our procedure. The carboxylic ester products were characterized by comparison of their FT-IR and $^1\text{H-NMR}$ spectral data and by comparison of their TLC chromatogram with those of authentic samples. The FT-IR and $^1\text{H-NMR}$ spectra were recorded on a Magna-FT-IR, T. M, Nicollet (model 550) and Perkin-Elmer Hitachi (60 MHz) spectrophotometer respectively.

Preparation of quaternized crosslinked poly(4-vinylpyridinium) iodide. Crosslinked poly(4-vinylpyridine) (1.0 g) was added to an excess methyl iodide in a round-bottomed flask (50 mL) and stirred for 24 hrs at room temperature. The mixture was filtered and washed with acetone. It was then dried under vacuum at 40 °C. The weight of the dried poly(4-vinylpyridinium) iodide was 2.3 g.

Preparation of quaternized crosslinked poly(4-vinylpyridinium) acetate (I). Crosslinked poly(4-vinylpyridinium) iodide (2.3 g) was added to an excess aqueous acetate solution in a round-bottomed flask (100 mL) and stirred for 24 h at room temperature. The mixture was filtered and washed with distilled water (5×10 mL). It was then dried under vacuum at 40 °C. The weight of the dried poly(4-vinylpyridinium) acetate was 1.67 g. The capacity of the polymer was determined by potentiometric titration of filtrates with 0.1 N solution of silver nitrate and it was equal to 0.86 mmol of acetate ion per gram of polymer.

Preparation of quaternized crosslinked poly(4-vinylpyridinium) formate (II). Crosslinked poly(4-vinylpyridinium) iodide (2.3 g) was added to an excess aqueous solution of sodium formate in a round-bottomed flask (100 mL) and stirred for 24 h at room temperature. The mixture was filtered and washed with distilled water (5×10 mL). It was then dried under vacuum at 40 °C. The weight of the dried poly(4-vinylpyridinium) formate was 1.54 g. The

capacity of the polymer was determined by potentiometric titration of filtrates with a 0.1 N solution of silver nitrate and it was equal to 0.91 mmol of acetate ion per gram of polymer.

General procedure for reaction of benzyl halides with crosslinked poly(4-vinylpyridinium) acetate (I) or formate (II). To a mixture of benzyl halide (1 mmol) and acetone (10 mL) in a round-bottomed flask (100 mL), 1.5-2.0 mmol of polymer (I) or polymer (II) was added, and the mixture was stirred at reflux for 6-10 h. Reaction monitoring was accomplished by TLC with chloroform/*n*-hexane (70 to 30) as eluent. The products were obtained in 30-95% yields. The spent polymeric reagent was regenerated by treatment with sodium acetate or sodium formate solution.

Preparation of 4-bromobenzyl acetate with polymer (I), a typical procedure. To a suspension of crosslinked poly(4-vinylpyridinium) acetate (I) (1.72 mmol, 2.0 g) in acetone (10 mL) was added 4-bromobenzyl bromide (1.15 mmol, 0.29 g). The mixture was stirred for 6 h at reflux condition. Reaction monitoring was accomplished by TLC with chloroform/*n*-hexane (70 to 30) as eluent. The product was obtained in 80% yield (0.21 g) by preparative TLC., FT-IR: ν_{max} (neat) 1736 (C=O, ester), 1490 (C=C), 1012, 1226 (C-O), 1377 (CH₂ and CH₃) 800 (p-subst) cm⁻¹. $^1\text{H NMR}$ (60 MHz, CDCl₃): δ 2.0 (3H, s, CH₃) 5.0 (2H, s, CH₂) 7.0-7.4 (4H, arom)

Preparation of 4-bromobenzyl formate with polymer (II), a typical procedure. To a suspension of crosslinked poly(4-vinylpyridinium) formate (II) (1.81 mmol, 2.0 g) in acetone (10 mL) was added 4-bromobenzyl bromide (1.2 mmol, 0.3 g). The mixture was stirred for 6 h at reflux condition. Reaction monitoring was accomplished by TLC with chloroform/*n*-hexane (70 to 30) as eluent. The product was obtained in 85% yield (0.20 g) by preparative TLC., FT-IR: ν_{max} (neat) 1724 (C=O, ester), 1489, 1595 (C=C), 1011, 1155 (C-O), 1430 (CH₂) 808 (p-subst) cm⁻¹. $^1\text{H NMR}$ (60 MHz, CDCl₃): δ 5.0 (2H, s, CH₂) 7.0-7.4 (4H, arom), 8.2 (1H, s).

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