

## Polymer Supported Cyanide as an Efficient Catalyst in Benzoin Condensation: An Efficient Route to $\alpha$ -Hydroxy Carbonyl Compounds

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Aromatic aldehydes are efficiently self-condensed into  $\alpha$ -hydroxy carbonyl compounds by polystyrene-supported ammonium cyanide as an excellent organocatalyst in C-C bond formation. The reaction proceeds in water under mild reaction conditions. The polymeric catalyst can be easily separated by filtration and reused several times without appreciable loss of activity.

**Key Words:** Benzoin condensation,  $\alpha$ -Hydroxy carbonyl compounds, Polymer-supported catalyst, C-C bond formation, Amberlite IRA-910CN

### Introduction

$\alpha$ -Hydroxy carbonyl group in general is important structural subunit in many biologically active compounds and is also important as precursor in stereoselective synthesis of natural products, chiral auxiliaries, and ligands.<sup>1</sup> Among the few reported synthetic strategies for introducing this moiety, the benzoin reaction remains perhaps, the most direct.<sup>2-6</sup> The benzoin condensation reaction, one of the oldest C-C bond forming reactions in organic chemistry, has been developed for self-condensation of aromatic aldehydes into  $\alpha$ -hydroxy carbonyl compounds using toxic cyanide ion in basic media.<sup>7</sup> A key intermediate in this reversible reaction is nitrile-stabilized carbanion.<sup>8</sup>

Recently, it has been shown that several nucleophilic carbenes derived from heterocyclic compounds including triazolium,<sup>2</sup> thiazolium,<sup>9</sup> thiazole, triazole, imidazole,<sup>10,11</sup> and benzimidazolium salt<sup>2</sup> are also employed as catalyst in benzoin condensation reactions. Unfortunately, these systems generally involve the use of expensive catalysts, decomposition of catalysts under the basic reaction conditions and also requirement of extended reaction times. Therefore, the development of a new and efficient protocol for this transformation under mild and more convenient conditions is still needed.

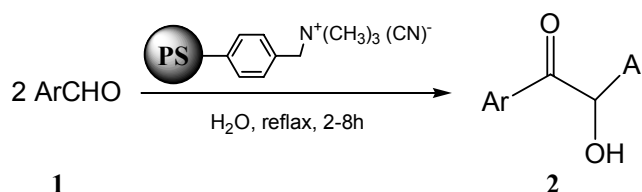
To our knowledge, there is only one report about application of polymeric catalyst in self condensation reaction of aromatic aldehydes by Castells and Dunach.<sup>12</sup> They used polymer supported  $\text{CN}^-$  as a catalyst in benzoin type condensation for just two aromatic aldehydes, benzaldehyde and furfural, in organic solvent and produced products in moderate yields and long reaction times. Also they reported furoin was obtained with the catalyst under water solvent or without solvent in low yield. In connection with the our ongoing studies on the development of a green organic synthesis using polymer-supported catalyst<sup>13</sup> and by considering the significance of all of the earlier studies in general and the development of water as an eco-friendly medium for organic reactions in particular and a valid alternative to the use of volatile and toxic organic solvents,<sup>14</sup> we decided to utilize polystyrene-supported ammo-

nium cyanide (Amberlite IRA-910CN) as an efficient functionalized polymer in benzoin condensation reaction in water. The use of water as a solvent for organic transformations offers several "green chemistry" benefits and in many reactions, significant rate enhancements are observed in water compared to organic solvents.<sup>15</sup>

### Results and Discussion

In our initial work, the benzoin condensation reaction of benzaldehyde was found to proceed efficiently in water and under reflux conditions when Amberlite IRA-910CN was employed as a polymeric catalyst. We started this study by examining the amount of polymeric catalyst in the self condensation of benzaldehyde (1 mmol). According to experiments, the best result was obtained with 0.5 g (1.5 equiv of  $\text{CN}^-$ ) polymeric catalyst and under reflux conditions. It is worthy to note that the conversion of the starting material to the product is not complete even for prolonged reaction times when the polymeric catalyst proportion is less than 0.5 g. In order to show the general applicability of the method, we extended it to a range of representative substituted benzaldehydes (Scheme 1, Table 1) under the best reaction conditions, Amberlite IRA-910CN 0.5 g (1.5 equiv of  $\text{CN}^-$ ), aldehyde (1 mmol).

As shown in Table 1, in the presence of polymeric catalyst, the self condensation of aromatic aldehydes possessing chloride or a strong electron-accepting group such as CN and  $\text{NO}_2$  proceeded to give the corresponding benzoin in good yields (entries 2-7) and in all cases a very clean reaction was



Scheme 1

**Table 1.** Benzoin condensation reactions of various aromatic aldehydes catalyzed by Amberlite IR-910CN

Entry	Aldehyde	Product	IR Spectra (OH, CO) (cm <sup>-1</sup> )	Time (h)	Yield <sup>a</sup> (%)
1			3414, 1680	2.5	80
2			3459, 1665	2.0	85
3			3465, 1682	2.5	80 <sup>b</sup>
4			3383, 1702	2.5	70
5			3407, 1704	2.0	80
6			3424, 1690	2.15	80
7			3419, 1692	2.15	75
8			-	3.5	15 <sup>b</sup>

<sup>a</sup>Crude yields. <sup>b</sup>Determined by GC analysis.

observed. As expected, benzoin condensation reaction of aromatic aldehydes possessing a strong electron-donating group such as OH proceeded with difficulty and produced product in low yield. The structure of all the products were settled from their analytical and spectral (IR, <sup>1</sup>H NMR) data and by direct comparison with authentic samples.

The most ideal synthetic methodology could be defined as a system wherein 100% atom economy is preserved, the solvent is recycled to the fullest extent and the catalyst or excess of reagent remains throughout in the solvent medium and without losing activity for several runs. Thus, the noteworthy advantage of this polymeric catalyst lies in its reusability. Table 2 demonstrates the usability of the catalyst after 3 replicate self condensation of *p*-chlorobenzaldehyde to cor-

**Table 2.** Reusability of the catalyst<sup>\*</sup>

Experiment	No. of cycles	Time(h)	Yield (%)
1	1	2.5	80
2	2	2.5	77
3	3	2.5	75

<sup>\*</sup>All reactions were carried out under similar condition.

responding benzoin. It is noticeable to mention that no toxic cyanide ions were detected in aqueous reaction media (Ag-NO<sub>3</sub> test).

In conclusion, polystyrene-supported ammonium cyanide (Amberlite IRA-910CN) has been proved to be an effective

and stable polymeric catalyst in benzoin condensation reaction. Application of this heterogeneous polymeric catalyst in C-C bond formation reaction eliminates the use of the organic reaction medium, avoids the use of toxic materials, and allows the recovery and re-use of the catalyst due to the heterogeneous nature of reaction. Thus, we believe the present methodology opens an environmentally benign access route to different types of  $\alpha$ -hydroxy ketones.

### Experimental Section

Chemicals were purchased from Fluka, Merck and Aldrich Chemical Companies. Aldehydes were distilled before use. Yields refer to isolated crude products. The purity determination of the products and reaction monitoring were accomplished by TLC on silica gel polygram SILG/UV 254 plates. IR spectra were recorded on a BOMEM MB-Series 1998 FT-IR spectrometer.

**Preparation of polymer supported cyanide catalyst.** Amberlite IRA-910CN, which is not commercially available, was easily prepared from the corresponding chloride form via exchange of the anion by using a 10% aqueous NaCN solution. Amberlite IRA-910 Cl<sup>-</sup> form; 16-50 mesh (10 g), was stirred for 6 h in the cyanide solution (100 mL). It was then, filtered off and washed several times with water before drying under vacuum at 50 °C. The activity of polymer supported cyanide anion was found to be in the range 3.0-3.2 mmol/g of dry resin.

**Preparation of  $\alpha$ -hydroxy ketones using polystyrene-supported ammonium cyanide as catalyst.** To a suspension of pure aromatic aldehyde (1.0 mmol) and water (5 mL), Amberlite IRA-910CN (0.5 g) was added, and the resulting mixture was magnetically stirred under reflux conditions. Progress of the reaction was monitored by TLC, using carbon tetrachloride-ethylacetate (5:1) as eluent. After completion of

the reaction, the polymeric catalyst was filtered off and washed with ethyl acetate. The filtrate was extracted with ethyl acetate and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent in vacuo gave the desired product. Further purification was achieved by crystallization in ethanol.

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