

Recyclable Polymeric π -Acid Catalyst Effective on Mannich-Type Reaction in Water

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Polymer-supported dicyanoketene acetal (poly-DCKA-1), synthesized by copolymerization of a DCKA bearing a 4-vinylbenzyl group with ethyleneglycol dimethacrylate, was found to be an excellent recyclable catalyst for the three-component Mannich-type reaction of aldehydes, aromatic amines, and TMS enolate of ethyl isobutyrate in water as the sole solvent.

Key words polymer; π -acid catalyst; aqueous media; Mannich-type reaction; recycle

Organic reactions in water have recently been recognized as useful tool for the synthesis of compounds because water is a cheap, safe, and benign solvent to the environment.^{1–4)} Development of insoluble reagents with high efficiency in synthetic reactions^{5–9)} has recently attracted much attention for their convenience of manipulation and recycling from the viewpoint of green chemistry.^{10,11)} In this context, polymeric modification of reagents, especially of reaction promoters and catalysts effective in organic reactions in water, is a promising methodology.^{12–16)} In our study on the development of dicyanoketene acetals (DCKAs) as novel π -acid catalysts,^{17–21)} we have reported that a certain polymer-supported DCKA (poly-DCKA-1), prepared by copolymerization of a DCKA carrying a styrene functionality with ethyleneglycol dimethacrylate (EGDMA), effectively catalyzes the reactions of acetals, monothioacetalization,^{22,23)} cyana-tion,^{23,24)} and Mukaiyama aldol reaction with silicone nucleophiles,^{23,24)} and Mannich-type reaction of imines with silicone enolates in acetonitrile.²⁵⁾ The polymer was found also to catalyze hydrolysis of acetals and silyl ethers in an aqueous system.^{26,27)}

Two-component Mannich-type reaction of aldimines with silyl enolates and three-component reactions using aldehydes, amines, and silyl enolates are useful tools for synthesis of β -aminocarbonyl compounds.²⁸⁾ Many Lewis acidic,^{29–34)} Brønsted acidic,^{35–38)} combined Lewis–Brønsted acidic,³⁹⁾ and Lewis basic catalysts^{40,41)} working on the reactions effi-

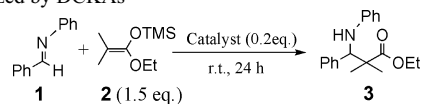
ciently in water have emerged recently. In our project on the creation of new polymer-modified DCKA catalysts working in water, we have investigated the catalytic activities of poly-DCKA-1 and a new solid catalyst (poly-DCKA-2) of the ether type, which were developed from DCKA-3 with a primary hydroxyl group that appears versatile for functionalization, in Mannich-type reactions. We now report on poly-DCKA-1 as a highly efficient and recyclable catalyst promoting aqueous Mannich-type reactions of various imines including unstable imines prepared *in situ* from aromatic and aliphatic aldehydes.

First, the new DCKAs (DCKA-1 and DCKA-2) were prepared as monomeric standard DCKAs (Chart 1). DCKA-1 was obtained from tetracyanoethylene (TCNE) and 2-benzyl-1,3-propanediol according to the general procedure⁴²⁾; DCKA-2 by benzylation of DCKA-3, which was prepared from TCNE and 2-hydroxy-2-methyl-1,3-propanediol; and DCKA-4 by alkylation of DCKA-3 with 4-vinylbenzylchloride, respectively.⁴³⁾ A polymer-supported DCKA (poly-DCKA-2) was prepared by copolymerization of DCKA-4 with EGDMA in the presence of AIBN as a radical initiator in refluxing toluene.⁴⁴⁾

The catalytic activities of poly-DCKA-1 and the new DCKAs (DCKA-1, DCKA-2, and poly-DCKA-2) synthesized were investigated in the two-component Mannich-type reaction using benzylidene aniline (**1**) and TMS-enolate (**2**), prepared from ethyl isobutyrate, in water and acetonitrile (CH_3CN) as a solvent at room temperature. A mixture of imine (**1**) (1.0 eq), TMS-enolate (**2**) (1.5 eq), and a catalyst (0.2 eq) in a solvent was stirred for 24 h. Results including the data of dicyanoketene ethyleneacetal (DCKEA) as a standard catalyst are summarized in Table 1. Poly-DCKA-1 showed high activity, providing a β -aminoester (**3**) not only in CH_3CN (85% yield), but also in water (84% yield), although the simple DCKA-1 gave **3** in poor to moderate yields. However, while appreciable catalytic activity was observed for DCKA-2, poly-DCKA-2 was almost completely inactive in water.

Three-component Mannich-type reaction of benzaldehyde, aniline, and **2** was carried out for assay of catalytic activity of the DCKAs. The results are summarized in Table 2,⁴⁵⁾ which

Table 1. Mannich-Type Reaction of Benzylidene Aniline with a Silyl Enol Ether Catalyzed by DCKAs



Entry	Catalyst	Solvent	Yield (%)
1	None	Water	14
2	DCKEA	Water	35
3	DCKEA	CH_3CN	28
4	DCKA-1	Water	64
5	DCKA-1	CH_3CN	34
6	DCKA-2	Water	45
7	DCKA-2	CH_3CN	5
8	Poly-DCKA-1	Water	84
9	Poly-DCKA-1	CH_3CN	85
10	Poly-DCKA-2	Water	7
11	Poly-DCKA-2	CH_3CN	30

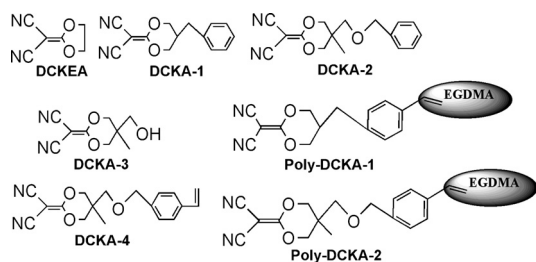


Chart 1. Monomeric and Polymer-Supported DCKAs

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Table 2. Three-Component Mannich-Type Reaction Catalyzed by DCKAs

$$\text{PhCHO} + \text{PhNH}_2 \xrightarrow[\text{(1.0 eq.)}]{\text{(1.0 eq.)}} \xrightarrow[\text{r.t., 30 min.}]{\text{Solvent}} \xrightarrow[\text{r.t., 24 h.}]{\text{Catalyst (0.2 eq.) } \text{2 (1.5 eq.)}} \text{3}$$

Entry	Catalyst	Solvent	Yield (%)
1	DCKA-1	Water	51
2	DCKA-1	CH ₃ CN	29
3	DCKA-2	Water	73
4	DCKA-2	CH ₃ CN	Trace
5	Poly-DCKA-1	Water	91
6	Poly-DCKA-1	CH ₃ CN	51
7	Poly-DCKA-2	Water	12
8	Poly-DCKA-2	CH ₃ CN	35

Table 3. Three-Component Mannich-Type Reaction Using Various Aldehydes Catalyzed by Poly-DCKA-1 in Water

$$\text{RCHO} + \text{R}'\text{NH}_2 \xrightarrow[\text{r.t., 30 min.}]{\text{Water}} \xrightarrow[\text{r.t., 24 h.}]{\text{Poly-DCKA-1 (0.2 eq.) } \text{2 (1.5 eq.)}} \text{R}'\text{NH}-\text{C}(\text{R})=\text{O}$$

Entry	RCHO	R'NH ₂	Yield (%)
1	<i>p</i> -MeO-C ₆ H ₄ -CHO	PhNH ₂	70
2	<i>p</i> -NO ₂ -C ₆ H ₄ -CHO	PhNH ₂	41
3	<i>p</i> -Cl-C ₆ H ₄ -CHO	PhNH ₂	70
4	2-Furyl-CHO	PhNH ₂	64
5	PhCH ₂ CHO	PhNH ₂	35
6	PhCH ₂ CH ₂ CHO	PhNH ₂	52
7	(<i>E</i>)-PhCH=CHCHO	PhNH ₂	64
8	PhCHO	<i>p</i> -MeO-C ₆ H ₄ -NH ₂	84
9	PhCHO	<i>o</i> -MeO-C ₆ H ₄ -NH ₂	75

Table 4. Recycling Experiment of Mannich-Type Reaction Using Poly-DCKA-1 as a Catalyst in Water

$$\text{PhCHO} + \text{PhNH}_2 \xrightarrow[\text{2 (1.5 eq.)}]{\text{H}_2\text{O, r.t., 24 h.}} \text{3}$$

Cycle	Two-component system			Three-component system		
	1st	2nd	3rd	1st	2nd	3rd
Yield (%)	84	85	80	91	90	88

shows the remarkable efficiency of poly-DCKA-1 in water among the DCKAs examined.

Table 3 demonstrates the generality of the catalytic function of poly-DCKA-1 in the aqueous three-component Mannich-type reaction of **2**, aniline, and anisidines, and various aldehydes including aliphatic ones, which produce unstable imines.⁴⁵⁾

Poly-DCKA-1 could be used repeatedly without appreciable loss of catalytic activity in the three-component Mannich-type reaction as well as the two-component reaction after a simple operation to recover the catalyst⁴⁶⁾ (Table 4).

In conclusion, the novel recyclable solid catalyst poly-DCKA-1, which contains neither proton nor metal, was found highly effective in the Mannich-type reaction in water.

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- 43) DCKA-**1** was obtained in 79% yield from TCNE and 2-benzylpropane-1,3-diol, which was synthesized from diethyl malonate by benzylation followed by reduction with LiAlH_4 . DCKA-**2** and DCKA-**4** were synthesized in 68% and 81% yield, respectively, by benzylation and *p*-vinylbenzylation of DCKA-**3** bearing a primary hydroxyl group which was prepared from TCNE and 2-methyl-2-hydroxymethylpropane-1,3-diol.
- 44) A new polymer-supported DCKA (poly-DCKA-**2**) was synthesized as a colorless powder by refluxing mono-DCKA-**3** with an equivalent molar amount of EGDMA in toluene for 2 h in the presence of AIBN (0.05 eq). Poly-DCKA-**2** thus obtained was found to contain 2.06 mmol/g of the DCKA unit by elemental analysis.
- 45) An appreciable decrease in the yield of the desired **3** was observed when a mixture of all the reagents including the catalyst (DCKA-**1**) and water was stirred at once, although the reason for the phenomenon was not obvious. Thus reaction conditions so that an aldehyde and an amine were treated in water for 30 min at room temperature to make the corresponding imine before addition of the catalyst and **2** were adopted in the three-component Mannich-type reaction.
- 46) The catalyst was recovered by filtration, followed by washing successively with water and ethyl acetate and drying *in vacuo* at room temperature for 4 h, and then reused.