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Polymeric sulfonate of piperazine as an inexpensive and recyclable catalyst for Knoevenagel condensation

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Polymeric sulfonate of piperazine (Amberlite® 200 H/piperazine) has been found to be an inexpensive and reusable catalyst for Knoevenagel reaction between aldehydes and activated methylene compounds. The preparation and rejuvenation of the presented polymer-supported catalyst is very simple from the standpoint of experimental operation. The reusability of this catalyst has also been studied.

Keywords: Polymer-supported catalyst, polymeric sulfonate, piperazine, Knoevenagel reaction

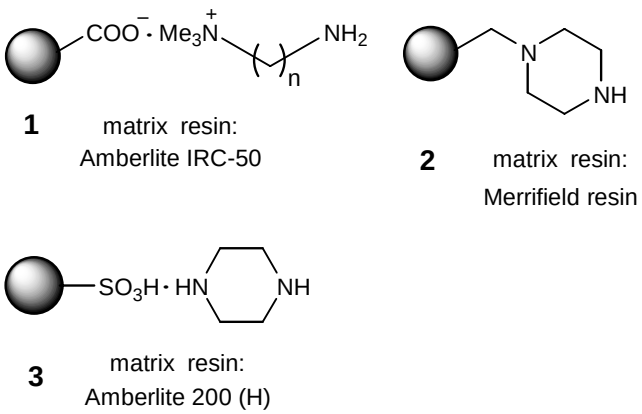
IPC: **Int.Cl.[7] C 07 D**

Knoevenagel condensation is a base catalyzed, convenient method to convert carbonyl groups into alkenes under mild conditions. The usual Knoevenagel catalysts are ammonia and ammonium salts, primary and secondary amines and their salts[1].

In recent years, there has been a tremendous upsurge of interest in various chemical transformations mediated by polymer-supported catalysts and a large number of chemical reactions were found to be facilitated by this type of catalysts, and associated literature is extensive[2]. As an important class of heterogeneous catalysts, immobilized molecular catalysts can combine the advantages of heterogeneous and homogeneous catalysts[3]. One of the advantages of insoluble polymeric catalysts is their easy recovery from the reaction system which prevents the release of toxic chemicals into the environment. Hence, their greater use may be beneficial from the environmental point of view. Although many catalysts are described in the organic chemists' reports, there are still formidable challenges in the design of new immobilized molecular catalysts. In the search for efficient heterogeneous Knoevenagel catalysts, up to now, efforts were largely focused on the basic anion-exchange resins[4], natural and synthetic inorganic solid bases[5], and organically modified inorganic solids[6]. However, the number of papers dealing with the use of polymer-supported amines in Knoevenagel condensation is extremely scarce.

Saito and co-workers have reported a synergic acid-base catalyst containing aminoalkyl groups bound to a carboxylic acid-type cation exchange resin (Amberlite® IRC-50) through ion pairs with the intramolecular ω-trimethylammonium groups (**Scheme I**, resin 1)[7]. It has been proved earlier that piperidine is a highly active catalyst for Knoevenagel condensation[1]. More recently, Simpson's group described the resin-bound piperazine, prepared *via* the reaction between Merrifield's resin and piperazine, as a piperidine equivalent (**Scheme I**, resin 2)[8].

Herein is reported a facile and efficient preparation and use of a polymer-supported catalyst (**Scheme I**,



Scheme I

resin 3) for Knoevenagel reaction (**Scheme I**). The catalyst was easily rejuvenated by washing with organic solvents (*e.g.* ethanol), and could be reused several times with little loss of catalytic activity.

Amberlite® 200 in H^+ form, an easily available (staple product manufactured by Rohm & Haas Co.) macroporous cation exchange resin containing sulfonic acid groups, was chosen as a solid support in the present experiments. As immobilized catalytic species, piperazine is a more common and cheaper reagent than the previously reported ω-trimethylamnio ethylamine[7]. Compared with the piperazine covalently bonded to Merrifield's resin described in the literature[8], a noteworthy feature of our catalyst is its simplicity in preparation. Amberlite® 200 (H) resin was treated with piperazine in deionized water at rt for 0.5 hr. Subsequent filtration, washing, and drying of the polymer gave the catalyst as gray beads, characterized by FT-IR spectroscopic data as illustrated in **Figure 1**.

To assess the generality of this catalyst, a variety of aldehydes were converted to the corresponding olefinic products in excellent yields using activated methylene compounds such as malononitrile and ethyl cyanoacetate (**Scheme II**, **Table I**). The work-up of these reactions is quite simple: only a filtration to remove the catalyst followed by evaporation of the solvent is required. Moreover, the catalyst was easily rejuvenated by washing with small amounts of organic solvents (*e.g.* ethanol), and could be reused several times with little loss of activity.

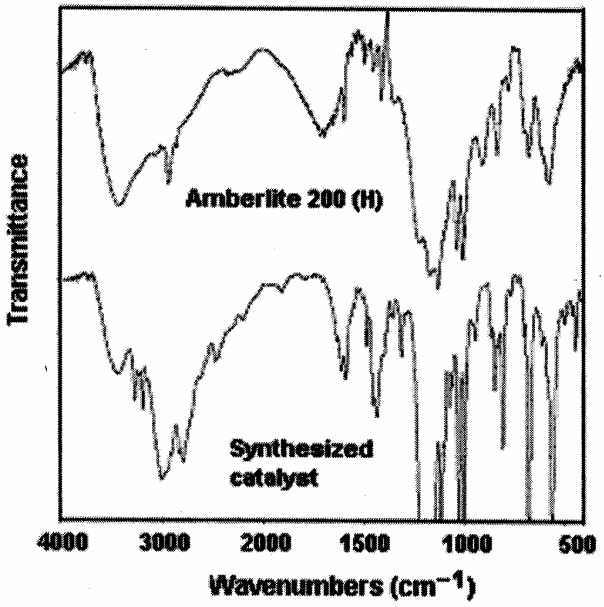


Figure 1 — FT-IR spectra of starting resin and polymeric sulfonate of piperazine

Other experiments were conducted to study the reuse of polymeric piperazine monosulfonate in the subsequent reactions. The catalyst was recovered simply by filtration and washing with ethanol, and the catalytic activity of the recovered catalyst was compared with that of fresh catalyst by using the reaction of benzaldehyde with malononitrile catalyzed by as-synthesized catalyst as a model reaction. The results obtained are gathered in **Table II**. The yields remain around 80% clearly illustrating the reusability of the catalyst. This reaction was repeated four times by recycling the same batch of catalyst. The catalyst was washed with ethanol before every run. It is noted that even higher yields were obtained in the third run than in the first run. It should be noted, however, this catalyst must be kept away from strong bases or acids (both inorganic and organic) to avoid the run off of supported piperazine.

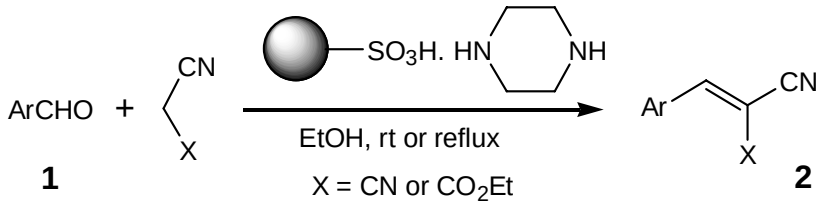
For catalysts covalently bonded on gel polystyrene resin, the catalytic activity is dependent on the choice of solvents to a large extent, as the swelling condition affects the mass transfer in gel networks by which substrates access active sites. Merrifield's resin is poorly swelled in polar solvent such as ethanol. In contrast, the use of macroporous resin ensures that the mass transfer in the large apertures of resin occurs much faster than in the relatively dense gel structure of Merrifield's resin, so the reaction is faster and requires no previous swelling before use due to the rigid structure. Furthermore, the use of macroporous resin facilitates the washing and regeneration process because the impurities in the macroscopic void are much easier to remove than those in gel networks, avoiding the troublesome steps of regeneration work-up.

In conclusion, the presented catalyst has clear advantages including high activity, easily available starting materials, simple preparation and regeneration, and environmental friendliness.

Experimental Section

Melting points were recorded on WRS-1 capillary apparatus and are uncorrected. IR spectra were obtained on a Nicolet Nexus 470 infrared spectrometer in KBr discs and ^{1}H NMR spectra were recorded on a Bruker AC 200 spectrometer with TMS as internal standard. Reagents and solvents were purchased and used without further purification.

Preparation of polymer supported catalyst. Amberlite® 200 resin (5.00 g) was stirred with a solution of piperazine (1.50 g) in deionized water (10



1 **2**

SchemeII

Table I—Knoevenagel reaction catalyzed by polymeric sulfonate of piperazine

Compd [b]	R	X	Time (min)	Yield (%) [a]
2a	C_6H_5-	CN	60 (rt)	83
2b	C_6H_5-	COOEt	40 (reflux)	86
2c	4-Cl-C_6H_4-	CN	35 (rt)	89
2d	4-Cl-C_6H_4-	COOEt	40 (reflux)	94
2e	4-OH-C_6H_4-	CN	30 (rt)	90
2f	4-OH-C_6H_4-	COOEt	25 (reflux)	96
2g	3-MeO-4-OH C_6H_3-	CN	90 (rt)	72
2h	3-MeO-4-OH C_6H_3-	COOEt	50 (reflux)	79
2i	3-O_2N-C_6H_4-	CN	30 (rt)	88
2j	3-O_2N-C_6H_4-	COOEt	30 (reflux)	91
2k	Furyl	CN	45 (rt)	76
2l	Furyl	COOEt	150 (rt)	80

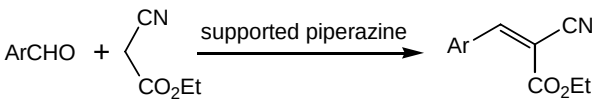
[a]Isolated yields

[b]All products were known compounds and characterized by m.p., IR and ^{1}H NMR spectra

mL) for 0.5 hr at rt. The catalyst thus obtained was separated by filtration and thoroughly washed with deionized water (10 mL×2) and absolute ethanol (10 mL×2) and dried under vacuum at rt to constant weight. A loading of 2.75mmole of piperazine per gram of as-synthesized dry catalyst was determined by elemental analysis.

General procedure. To a stirred suspension of polymeric catalyst (1.00 g) and aromatic aldehyde (10 mmole) in absolute ethanol (10 mL) was added activated methylene compounds (11 mmole). The reaction mixture was stirred under ambient or refluxing conditions (until the aldehyde disappeared, as indicated by TLC). On completion of the reaction, the mixture was filtered and the catalyst was washed with hot ethanol (5 mL×4), and the filtrate and washings were combined. The solvent was removed under reduced pressure and the resulting crude product was purified by recrystallization from aqueous ethanol (90%) to give pure olefinic products.

Table II — The reuse of reported catalyst



Run	Time (min)	Yield (%) [a]
1	40	86
2	40	81
3	40	82
4	40	78

[a] Isolated yields

Selected ^{1}H NMR data

2b: ^{1}H NMR ($CDCl_3$): δ_H 1.42 (t, *J*=7.2 Hz, 3H, CH_3), 4.40 (q, *J*=7.2 Hz, 2H, CH_2), 7.49-7.58 (m, 3H, ArH), 7.99 (d, *J*=7.6 Hz, 2H, ArH), 8.28 (s, 1H, CH=). **2c**: ^{1}H NMR ($CDCl_3$): δ_H 7.72 (d, *J*=8.8 Hz, 2H, ArH), 7.74 (s, 1H, CH=), 7.79 (d, *J*=8.8 Hz, 2H, ArH). **2f**: ^{1}H NMR ($CDCl_3$): δ_H 1.40 (t, *J*=7.3Hz, 3H, CH_3), 4.39 (q, *J*=7.1Hz, 2H, CH_2), 6.44 (s, 1H, OH), 6.96 (d, *J*=8.3 Hz, 2H, ArH), 7.98 (d, *J*=8.3 Hz, 2H, ArH), 8.21 (s, 1H, CH=). **2g**: ^{1}H NMR ($CDCl_3$): δ_H 3.98 (s, 3H, CH_3O), 6.44 (s, 1H, OH), 7.02 (d, *J*=8.3 Hz, 1H, ArH), 7.43 (d, *J*=8.3 Hz, 1H, ArH), 7.66 (s, 1H, ArH), 7.79 (s, 1H, CH=). **2j**: ^{1}H NMR ($CDCl_3$): δ_H 1.39 (t, *J*=7.2 Hz, 3H, CH_3), 4.39 (q, *J*=7.2 Hz, 2H, CH_2), 7.69(m, 1H, ArH), 8.28 (s, 1H, CH=), 8.36 (m, 1H, ArH), 8.69 (1H, t, *J*=1.9 Hz, ArH). **2k**: ^{1}H NMR ($CDCl_3$): δ_H 6.72 (q, *J*=1.6 Hz, 1H), 7.36 (d, *J*=3.6 Hz, 1H), 7.52 (s, 1H), 7.81 (d, *J*=1.2 Hz, 1H).

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