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Polystyrene-supported pyridinium chloroaluminate ionic liquid as a new heterogeneous Lewis acid catalyst for Knoevenagel condensation

Kaveh Parvanak Boroujeni* and Mina Jafarinasab

Department of Chemistry, Faculty of Sciences, Shahrekord University, PO Box 115, Shahrekord, Iran

Non-hygroscopic polystyrene-supported chloroaluminate ionic liquid was prepared from the reaction of Merrifield resin with pyridine followed by reaction with aluminium chloride. This Lewis acidic ionic liquid is an environmentally friendly heterogeneous catalyst for the Knoevenagel condensation of aromatic and aliphatic aldehydes with ethyl cyanoacetate. The catalyst is stable (as a bench top catalyst) and can be easily recovered and reused without appreciable change in its efficiency.

Keywords: ionic liquids, pyridinium chloroaluminate salts, polymer-supported ionic liquids, Knoevenagel condensation

One of the primary groups of ionic liquids is based on a mixture of aluminium chloride and 1,3-dialkyl-imidazolium or 1-alkyl-pyridinium chlorides.[1,2] The acidity of the resulting ionic liquid can be controlled by varying the relative amounts of $AlCl_3$ and organic chloride. Chloroaluminate melts are designated as basic when the $AlCl_3$ mole fraction is smaller than 0.5 and the melts contain the anions Cl^- and $AlCl_4^-$, a Lewis base. A neutral melt is referred to at an $AlCl_3$ mole fraction of exactly 0.5, where $AlCl_4^-$ is the only anion present. Finally, an acidic chloroaluminate melt is one in which the $AlCl_3$ mole fraction is larger than 0.5. In such acidic melts, the anions $Al_2Cl_7^-$ and $Al_3Cl_{10}^-$ exist, which act as very strong Lewis acids.[1]

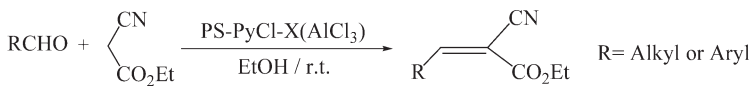
Despite having widespread application in organic synthesis either as solvents or acidic catalysts, most chloroaluminate ionic liquids suffer from one or more of the following drawbacks: laborious work-up procedures, difficulty of recovery and recycling, disposal of spent catalyst, difficult to handle, and corrosion problems. Most importantly, they are extremely hygroscopic and labile towards hydrolysis.[1] Thus, these shortcomings make them a prime target for heterogenisation. Although there are several reports on the immobilisation of ionic liquids on solid supports,[3–9] to the best of our knowledge, very few examples are known for immobilised chloroaluminate ionic liquids.[4,6]

The Knoevenagel condensation is one of the most useful and widely employed methods for carbon–carbon bond formation in organic synthesis. It is effected by treating a carbonyl compound with an active methylene compound in the presence of a catalyst. This reaction produces several important key products that include nitriles used in anionic polymerisation and the α,β-unsaturated ester intermediates employed in the synthesis of several therapeutic drugs and pharmacological products.[10,11] Several types of catalysts were introduced previously for Knoevenagel condensation such as the weak bases ammonia, primary amine and secondary amines and their salts,[12,13] $CuCl_2$,[14] $ZnCl_2$,[15] $[Ni_{0.73}Al_{0.27}(OH)_2](CO_3)_{0.135}$,[16] $LaCl_3$,[17] non-cross-linked polystyrene-supported piperazine,[18] zeolite,[19] amino group immobilised on polyacrylamide,[20] SiO_2–$HClO_4$ and SiO_2–PPA,[21] amine functionalised MCM-41,[22] ionic liquids,[23–25] silica based substituted piperidine,[26] and amino functionalised mesoporous silica.[27] However, many of the reported catalysts suffer from drawbacks such as generation of environmentally perilous waste material, tedious work-up, long reaction times, complicated operations, and the use of moisture-sensitive, expensive, hazardous, difficult to handle or unreusable catalysts. It should also be mentioned that comparing the broad application of basic catalysts, considerably less attention has been paid to the use of acid catalysts, especially heterogeneous Lewis acid catalysts, for the Knoevenagel condensation.

In continuation of our research on the development of synthetic methodologies using solid acid catalysts, we now wish to introduce polystyrene-supported pyridinium chloroaluminate ionic liquid (PS-PyCl-X$AlCl_3$) as an effective heterogeneous catalyst for the Knoevenagel condensation of aldehydes with ethyl cyanoacetate (Scheme 1).

Poly[styrene-*co*-(1-((4-vinylphenyl)methyl)pyridinium) chloroaluminate] (PS-PyCl-X$AlCl_3$) was prepared by the procedure shown in Scheme 2. In the first stage, commercially available Merrifield resin (2% divinylbenzene, 2.1 mmol Cl per gram) was reacted with pyridine to give the poly[styrene-*co*-(1-((4-vinylphenyl)methyl)pyridinium) chloride] (PS-PyCl). The PS-PyCl was analysed by elemental analysis to quantify the percentage loading of the pyridinium moiety by measuring the nitrogen content, giving 1.89 mmol Py per gram. The PS-PyCl was further treated with excess amounts of $AlCl_3$ in refluxing toluene to form PS-PyCl-X$AlCl_3$. The resulting pale brown solid was reasonably stable to air and moisture and could be kept as a bench top catalyst for more than 1 year without appreciable change in its efficiency. We believe that the hydrophobic nature of polystyrene protects the water-sensitive Lewis acid from hydrolysis by atmospheric moisture until it is suspended in an appropriate solvent where it can be used in a chemical reaction. The atomic absorption technique gave 3.3 mmol Al per gram of PS-PyCl-X$AlCl_3$. Considering the aluminium and pyridine contents of PS-PyCl-X$AlCl_3$, it is clear that the $AlCl_3$ mole fraction ($AlCl_3$/$AlCl_3$+Py) in this catalyst is larger than 0.5 and thus we can imagine that it is the Lewis acid $Al_2Cl_7^-$ (as the predominant aluminium species) that plays an important role in the catalytic activity in PS-PyCl-X$AlCl_3$.[1,4]

For comparison, the FT-IR spectra of the Merrifield resin, PS-PyCl, and PS-PyCl-X$AlCl_3$ are presented in Figure 1. The IR spectra of PS-PyCl showed absorption peaks due to the pyridine ring at 3020, 2900, 1640, 1500, 1475, 775 cm^{-1}.[28] As can be seen in the spectrum of PS-PyCl-X$AlCl_3$, when $AlCl_3$ was complexed with PS-PyCl new peaks appeared at 575, 500, 430, 385 cm^{-1}, which can be assigned to Al-Cl stretching modes of the $Al_2Cl_7^-$ anion.[29]



Scheme 1

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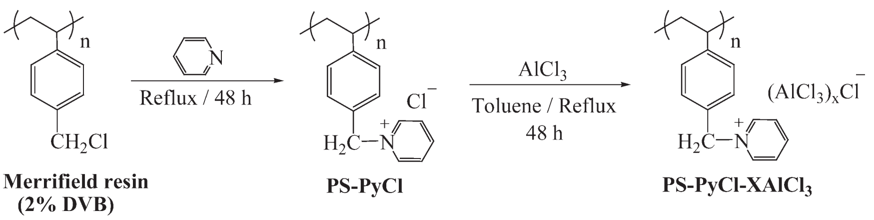
* Correspondent. E-mail: parvanak-ka@sci.sku.ac.ir



Scheme 2

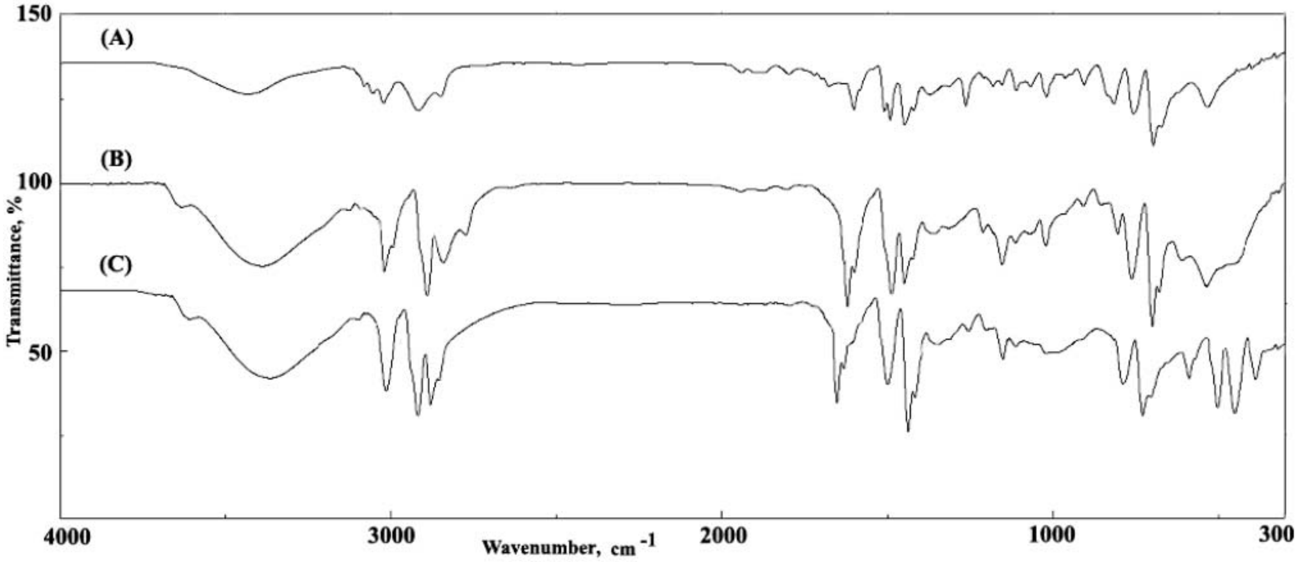
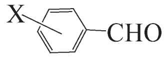


Fig. 1 FT-IR spectra of (A) Merrifield resin, (B) PS-PyCl, and (C) PS-PyCl-XAlCl$_3$.

In order to explore the catalytic activity of PS-PyCl-XAlCl$_3$, we studied the Knoevenagel reaction of aromatic and aliphatic aldehydes with ethyl cyanoacetate (Table 1). The best results in terms of yield as well as reaction time were obtained at room temperature in ethanol which proved to be the solvent of choice among other organic solvents. The optimum molar ratio of PS-PyCl-XAlCl$_3$ to aldehyde was found to be 0.1:1. Variously substituted aromatic aldehydes, with electron donating or electron withdrawing groups, cleanly and rapidly reacted with ethyl cyanoacetate to give the corresponding Knoevenagel products (entry 1a–h). Aliphatic aldehydes needed slightly more time to produce the corresponding products in good yields (entries 2–4). Also, 2-pyridyl aldehyde and 2-furaldehyde gave the desired products (entries 5 and 6). The reaction failed to proceed with ketones due to hindered and non favourable electronic structure (entry 7).

Table 1 Knoevenagel condensation of aldehydes with ethyl cyanoacetate in the presences of PS-PyCl-XAlCl$_3$[a]

Entry	Aldehyde	Time /h	Yield /%[b]	M.p./°C or B.p./°C /mmHg	
				Found	Reported[Ref.]
1					
	a. X= H	0.7	94	51	49–50[30]
	b. X= 4-CH$_3$	1	93	93	91.5–92.5[30]
	c. X= 4-OCH$_3$	1.1	92	79	79[32]
	d. X= 4-Cl	0.6	93	91	90[32]
	e. X= 2-Cl	0.6	94	50	49–50[30]
	f. X= 2-NO$_2$	0.5	96	97	90–100[30]
	g. X= 4-NO$_2$	0.5	97	171	171–172[30]
	h. X= 4-OH	1	93	174	172–173[30]
2	Ph-CH=CHCHO	1.3	90	115	116[32]
3	PhCH$_2$CHO	1.3	90	92	87–90[31]
4	*n*-PrCHO	1.4	90	71–73/3	70–71/3[31]
5	2-pyridyl aldehyde	1	94	97	95–96[33]
6	2-furaldehyde	0.9	93	91	93[32]
7	PhCOCH$_3$	2	5	–	–

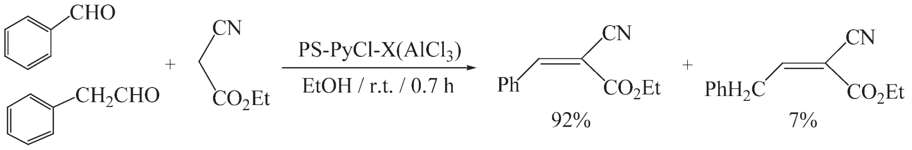
[a] Ratio of aldehyde:ethyl cyanoacetate is 1:1. All reactions were carried out in EtOH at room temperature in the presence of 0.1 mmol of PS-PyCl-XAlCl$_3$.

[b] Isolated yields. All products are known compounds and were identified by comparison of their physical and spectral data with those of the authentic samples.

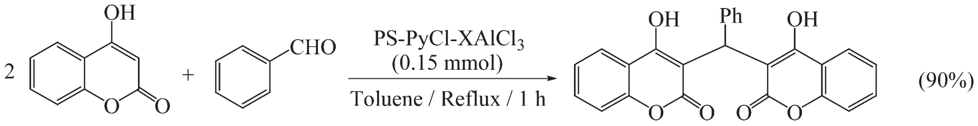
To find out whether the reaction takes place in the solid matrix of PS-PyCl-XAlCl$_3$ or whether AlCl$_3$ simply released in ethanol is responsible for the Knoevenagel reaction, PS-PyCl-XAlCl$_3$ was added to ethanol and the mixture was stirred at room temperature for 2 h. When, the catalyst was filtered off and the filtrate was analysed for its aluminium content, it showed negligible release of AlCl$_3$. Moreover, the filtrate was found to be inactive for the Knoevenagel reaction of aldehydes with ethyl cyanoacetate. These observations indicate that PS-PyCl-XAlCl$_3$ is stable under the reaction conditions, and there is no leaching of acid moieties during the reactions.

To explore the selectivity of the present method, equimolar mixtures of aromatic and aliphatic aldehydes were allowed to react with ethyl cyanoacetate in the presence of PS-PyCl-XAlCl$_3$. As shown in Scheme 3, the catalyst was able to discriminate between aromatic and aliphatic aldehydes.

It is noteworthy that Salunkhe and co-workers used 1-butylpyridinium chloroaluminate ionic liquid as a catalyst for Knoevenagel condensation, which was moisture sensitive and readily hydrolysed.[23] They found that two reactions, Knoevenagel and Michael, competing to give different ratios of two products, which led to undesirable by-products. It was pleasing to observe that, we did not observe any side reactions such as Michael addition or hydrolysis of the ester moiety, due to the mild catalytic activity of PS-PyCl-XAlCl$_3$ and the mild reaction conditions.



Scheme 3



Scheme 4

One notable achievement of PS-PyCl-XAlCl$_3$ is a one-pot synthesis of biscoumarinyl methane derivatives by a two-component one-pot domino Knoevenagel-type condensation/ Michael reaction between 4-hydroxycoumarin and aromatic aldehydes. For example, 4-hydroxycoumarin and benzaldehyde were reacted in refluxing toluene in the presence of PS-PyCl-XAlCl$_3$ to give the desired 3,3′-phenylmethylenebis-(4-hydroxycoumarin) in 90% yield (Scheme 4).

PS-PyCl-XAlCl$_3$ recovered after a reaction can be washed with ethanol and used again at least five times without any noticeable loss of catalytic activity (Table 2).

In conclusion, we have synthesised a polymer-supported pyridinium chloroaluminate ionic liquid as a new heterogeneous Lewis acid catalyst that favorably combines the properties of an ionic liquid and the advantages of a solid support. This polymer catalyst has an activity in Knoevenagel reactions comparable to that of 1-butylpyridinium chloroaluminate ionic liquid as far as we tested but offers its own advantages originating from being supported on a polymeric matrix, enhanced stability (as a bench top catalyst), reusability, high chemoselectivity, easier handling, and the simplification of product work-up, separation, and isolation.

Experimental

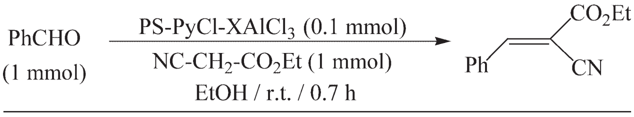
Chemicals were either prepared in our laboratory or were purchased from Merck and Fluka. Capacity of the catalyst was determined by atomic absorption technique using a Philips atomic absorption instrument. Reaction monitoring and purity determination of the products were accomplished by TLC on silica-gel polygram SILG/UV$_{254}$ plates. IR spectra were obtained by a Shimadzu model 8300 FT-IR spectrophotometer. NMR spectra were recorded on a Bruker Advance DPX-300 spectrometer.

Synthesis of PS-PyCl-XAlCl$_3$: In a round bottomed flask (100 mL) equipped with a reflux condenser, a solution of Merrifield resin (1 g, 2% DVB) in pyridine (10 mL) was refluxed for 48 h. Afterwards, the mixture was filtered, washed with distilled water (20 mL) and dried at 80 °C overnight (Yield: 89.4%). Then, 1 g of the obtained resin was added to a solution of AlCl$_3$ (0.5 g) in toluene (10 mL) and stirred under reflux for 24 h under N$_2$ atmosphere. Afterward, AlCl$_3$ (0.4 g) was added again and the mixture was stirred for 24 h and filtered and then the excess of AlCl$_3$ was removed by extraction with ethanol in an Soxhlet apparatus (Yield: 85.7%).

Knoevenagel reaction; typical procedure

To a solution of aldehyde (1 mmol) and ethyl cyanoacetate (1 mmol) in ethanol (5 mL) was added PS-PyCl-XAlCl$_3$ (0.1 mmol), and the resulting mixture was magnetically stirred at room temperature. The progress of the reaction was monitored by TLC. After the completion of the reaction, the catalyst was filtered off and washed with EtOH (2×5 mL) and the filtrate was concentrated on a rotary evaporator under reduced pressure to afford the crude product. Whenever required, the products were purified by column chromatography on silica gel (*n*-hexane/EtOAc). The spent catalyst from different experiments was washed with EtOH and used again without further drying.

Table 2 Recovery of PS-PyCl-XAlCl$_3$



Use	1	2	3	4	5
Yield/%	94	92	91	90	90

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References

1 P. Wasserscheid and W. Keim, *Angew. Chem. Int. Ed.*, 2000, **39**, 3772.
2 J.P. Hallett and T. Welton, *Chem. Rev.*, 2011, **111**, 3508.
3 C. DeCastro, E. Sauvage, M.H. Valkenberg and W.F. Hölderich, *J. Catal.*, 2000, **196**, 86.
4 M.H. Valkenberg, C. DeCastro and W.F. Hölderich, *Top. Catal.*, 2001, **14**, 139.
5 D.W. Kim and D.Y. Chi, *Angew. Chem. Int. Ed.*, 2004, **43**, 483.
6 H.W. Bae, J.S. Han, S. Jung and M. Cheong, *Appl. Catal. A: Gen.*, 2007, **331**, 34.
7 D.W. Kim, H.J. Jeong, S.T. Lim, M.H. Sohn and D.Y. Chi, *Tetrahedron*, 2008, **64**, 4209.
8 Q. Bao, K. Qiao, D. Tomida and C. Yokoyama, *Catal. Commun.*, 2009, **10**, 1625.
9 N. Fontanals, S. Ronka, F. Borrull, A.W.Trochimczulk and R.M. Marce, *Talanta*, 2009, **80**, 250.
10 G. Marciniak, A. Delgado, G. Leclerc, J. Velly, N. Decker and S. Schwarts, *J. Med. Chem.* 1989, **32**, 1402.
11 J. March, *Advanced organic chemistry*, 4th edn, John Wiley, Chichester, 1992.
12 L.F. Tietze and U. Beifuss, *Comprehensive organic synthesis*, ed. B.M. Trost, Pergamon, Oxford, 1991.
13 G. Cardillo, S. Fabbroni, L. Gentilucci, M. Gianotti and A. Tolomelli, *Synth. Commun.*, 2003, **33**, 1587.
14 O. Attanasi, P. Fillippone and A. Mei, *Synth. Commun.*, 1983, **13**, 1203.
15 P.S. Rao and R.V. Venkatratnam, *Tetrahedron Lett.*, 1991, **32**, 5821.
16 U. Costantino, M. Curini, F. Montanari, M. Nocchetti and O. Rosati, *J. Mol. Catal. A: Chem.*, 2003, **195**, 245.
17 A.V. Narsaiah and K. Nagaiah, *Synth. Commun.*, 2003, **33**, 3825.
18 G. Yang, Z. Chen, G. Xu and X. Nie, *Catal. Commun.*, 2004, **5**, 75.
19 X. Zhang, E.S.M. Lai, R. Martin-Aranda and K.L. Yeung, *Appl. Catal. A: Gen.*, 2004, **261**, 109.
20 B. Tamami and A. Fadavi, *Catal. Commun.*, 2005, **6**, 747.
21 S. Kantevari, R. Bantu and L. Nagarapu, *J. Mol. Catal. A: Chem.*, 2007, **269**, 53.
22 K.M. Parida and D. Rath, *J. Mole. Catal. A: Chem.*, 2009, **310**, 93.
23 J.R. Harjani, S.J. Nara and M.M. Salunkhe, *Tetrahedron Lett.*, 2002, **43**, 1127.
24 N. Jiang, H. Jin, Y.H. Mo, E.A. Prasetyanto and S.E. Park, *Microporous Mesoporous Mater.*, 2011, **141**, 16.
25 H.R. Shaterian, M. Arman and F. Rigi, *J. Mol. Liq.*, 2001, **158**, 145.
26 C. Mukhopadhyay and V. Ray, *Catal. Commun.*, 2011, **12**, 1496.
27 J. Mondal, A. Modak and A. Bhaumik, *J. Mol. Catal. A: Chem.*, 2011, **335**, 236.
28 R.J. Gale and R.A. Osteryoung, *Inorg. Chem.*, 1980, **19**, 2240.
29 M.E. Peach, V.L. Tracy and T.C. Waddington, *J. Chem. Soc. (A)*, 1969, 366.
30 S. Wang, Z. Ren, W. Cao and W. Tong, *Synth. Commun.*, 2001, **31**, 673.
31 C. Su, Z.C. Chen and Q.G. Zheng, *Synthesis*, 2003, 555.
32 J.A. Cabello, J.M. Campel, A. Garcia, D. Luna and J.M. Marinas, *J. Org. Chem.*, 1984, **49**, 5195.
33 W. Flitsch and S. Kahner-Grone, *Chem. Ber.*, 1982, **115**, 871.