Friedel–Crafts alkylation reactions in pyridinium-based ionic liquids

Ying Xiao, Sanjay V. Malhotra*

Department of Chemistry and Environmental Science, New Jersey Institute of Technology, University Heights, Newark, NJ 07102, USA

Abstract

The Friedel–Crafts alkylations of benzene in pyridinium-based ionic liquids (ILs) were investigated. The effects of catalyst–IL composition, reactant composition, quantity of catalyst and reaction temperature on this reaction were studied. The reactions were found to proceed under mild conditions with conversion; a simple product isolation procedure was achieved. The ILs rendered this reaction green characteristics. The ILs could also be recycled and reused as opposed to traditional solvent–catalyst systems.
© 2004 Elsevier B.V. All rights reserved.

Keywords: Pyridinium-based ionic liquids; Alkylation; Friedel–Crafts; Iron chloride; Aluminum chloride

1. Introduction

Friedel–Crafts chemistry is of major importance both on laboratory and industrial scale. Research in this field is permanently ongoing and of high interest [1–5]. Alkylation of benzene with alkyl halides in the presence of aluminum chloride originally discovered by Charles Friedel and James M. Crafts in 1877, can be promoted by other Lewis acids, such as BF_3, $ZnCl_2$, $TiCl_4$, SbF_5, etc. The general mechanism of alkylation is shown in Scheme 1 [6].

The overall transformation of Friedel–Crafts alkylation introduces an alkyl group on an aromatic ring. Therefore, in industrial processes catalytic alkylation with alkenes is applied. However, the process has some disadvantages, such as long reaction time, formation of aluminate waste, troublesome product recovery and purification, and catalysts cannot be reused.

Recently, much attention has been focused on the use of ionic liquids as reaction media for various organic reactions, such as hydrogenation [7], oxidation [8], Diels–Alder reaction [9], Trost–Tsuji coupling [10], esterification [11], Beckman rearrangement [12], and others [13–16]. The ionic liquids are considered environmentally friendly or "green" media due to their favorable properties [17], such as chemical and thermal stability, no measurable vapor pressure, nonflammability, high ionic conductivity, also they are strongly solvating but non-coordinating. They have a profound effect on the activity and selectivity in reactions and in some cases, facilitate the isolation of products. They can be recycled and reused in most cases. All of these properties indicate that ILs may substitute volatile organic solvents.

There have been some reports on synthesis and improved reaction characteristics of the Friedel–Crafts reactions in ILs [18–22]. However, all these studies have focused only on the ILs derived from imidazole. Based on our earlier success, using pyridinium-based ionic liquids [23–25], herein, we report the application of these ionic liquids in the Friedel–Crafts alkylation.

2. Experimental

2.1. Synthesis of ionic liquids

Two ionic liquids, 1-ethyl-pyridinium trifluoroacetate ($[EtPy]^+[CF_3COO]^-$) and 1-ethyl-pyridinium tetrafluoroborate ($[EtPy]^+[BF_4]^-$), were employed in our study (Fig. 1).

* Corresponding author. Tel.: +1 973 5965583; fax: +1 973 5963586.
  E-mail address: malhotra@njit.edu (S.V. Malhotra).

(1) R—X + Lewis Acid ⇌ R⁺—X—Lewis⁻Acid

R⁺—X—Lewis⁻Acid ⇌ R⁺ + [Lewis Acid—X]⁻
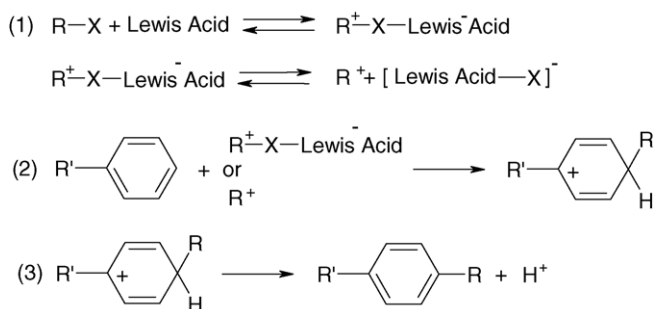
Scheme 1. General mechanism of alkylations.
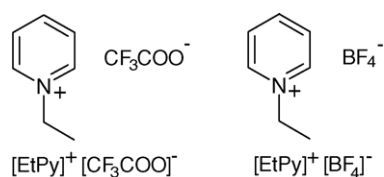

[EtPy]⁺ [CF₃COO]⁻   [EtPy]⁺ [BF₄]⁻

Fig. 1. Pyridinium-based ionic liquids.

These ILs were prepared following the literature method [26,27].

A general synthetic procedure could be described as follows: trifluoroacetic acid or tetrafluoroboric acid (0.2 mol) were slowly added to a stirred slurry of silver(I) oxide (0.1 mol) and distilled water (50 ml). To avoid photodegradation of silver(I) oxide, the reaction mixture was fully covered with aluminum foil. The reaction mixture was stirred continuously until the reaction was complete, which was indicated by the formation of a solution. A solution of *N*-ethyl-pyridinium bromide (0.2 mol) was added to the reaction mixture. As reaction took place and ILs formed, a yellow precipitate of silver(I) bromide started to be observed. The mixture was stirred at room temperature for a certain time until no more precipitate formed. The precipitate of silver(I) bromide was filtered off, and then the solvent was removed by rotary evaporation under vacuum at about 65 °C. The resulting ionic liquids were put in an oven overnight at 65 °C to remove the moisture.

2.2. Alkylation of benzene

The utility of ionic liquids [EtPy]⁺[CF₃COO]⁻ and [EtPy]⁺[BF₄]⁻ was investigated in alkylation of benzene (**1**) with 1-bromopropane (**2**), 1-chlorobutane (**3**) and benzyl chloride (**4**) (Scheme 2). The ILs were applied as such and with aluminum or iron chloride added.

In a typical reaction [28], the specified amount of catalyst (anhydrous FeCl₃ or AlCl₃) was added to pyridinium-based ionic liquid, and the mixture continuously stirred at 45 °C until the catalyst completely dissolved. Benzene (**1**) and alkyl halides (**2**, **3**, **4**) were directly added to the catalyst–IL solution. Two phases, i.e. ionic liquid and organic were formed and the mixture was stirred (250 rpm) at the desired reaction temperature for 4 h. The molar ratio of benzene:alkyl halide:ionic liquid was maintained at 2:1:1. At the end of the reaction, the organic layer could be easily decanted from the catalyst–IL system, and any organic residues were removed by extraction with diethylether.

2.3. Analytical method

The reaction samples and products were analyzed using a Varian CP-3800 Gas Chromatograph equipped with SPB^TM-5 column, 30 m × 0.25 mm × 0.25 μm.

3. Results and discussion

3.1. Alkylation of benzene with 1-bromopropane

As shown in Scheme 2 Eq. (1), both *iso*-product (**5**) and *n*-product (**6**) were obtained in the alkylation of benzene and 1-bromopropane. Since the reaction proceeds via formation of a carbocation intermediate, this may undergo a hydride shift to form a more stable cation. In reactions with 1-bromopropane, the primary propyl cation undergoes a hydride shift to form the more stable isopropyl cation. Therefore, major product in each case is isopropylbenzene. Table 1 shows the results of reaction of benzene with 1-bromopropane in different catalyst–IL system at room temperature and at 50 °C.
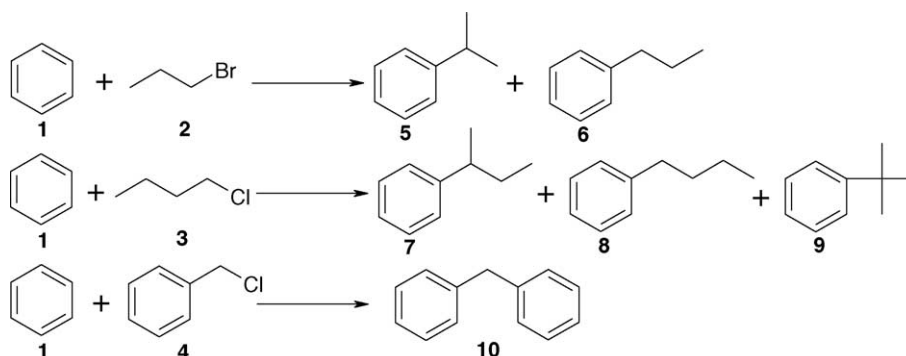
Scheme 2. Friedel–Crafts alkylation reactions with benzene.

Table 1
The Friedel–Crafts alkylation of benzene (**1**) with 1-bromopropane (**2**)[a]

Entry	Catalyst–solvent	Conversion (%) room temperature (50 °C)	Selectivity to major product (%)
1	$[EtPy]^+[BF_4]^-$	17 (43)	65 (72)
2	$[EtPy]^+[CF_3COO]^-$	29 (51)	71 (76)
3	$AlCl_3–[EtPy]^+[BF_4]^-$	60 (81)	75 (84)
4	$AlCl_3–[EtPy]^+[CF_3COO]^-$	72 (91)	78 (93)
5	$FeCl_3–[EtPy]^+[BF_4]^-$	56 (80)	74 (81)
6	$FeCl_3–[EtPy]^+[CF_3COO]^-$	71 (90)	77 (89)

[a] Molar ratio of benzene:1-bromopropane:catalyst:IL = 2:1:2:1.

As data shows, the yields of Friedel–Crafts alkylation are dependent on the catalyst–solvent composition. It is note worthy that the reaction does occur in ionic liquids even in the absence of a catalyst (entries 1 and 2), which would make this system truly green. However, the low conversions suggested the need of a catalyst for the reaction. A comparison of the results of ILs containing aluminum chloride, considered environmentally hazardous, with iron chloride based system shows the same catalytic activity. This indicated that the $FeCl_3$–IL system can efficiently replace $AlCl_3$–IL in the Friedel–Crafts alkylations. Also, a comparative study of two different temperatures (room temperature and 50 °C) showed that higher product conversion and selectivity are obtained at higher temperature. This could be because increased temperature provides thermodynamically stable 2° cation *iso*-product compared to 1° cation *n*-product. However, further increasing the temperature to 75 °C resulted in decreased yield and selectivity of the desired product, while unidentified byproducts formed. In all case, we note, the results with $[EtPy]^+[CF_3COO]^-$ are better than those with $[EtPy]^+[BF_4]^-$ though they have the same cation, which indicates the anions of ILs are critical for the reactions.

$FeCl_3$–$[EtPy]^+[CF_3COO]^-$ gave the best performance in the Friedel–Crafts alkylations and also it is much more friendly to the environment compared with aluminum chloride.

In order to investigate the catalytic activity of $FeCl_3$–IL system, reactions with various amounts of $FeCl_3$ were studied with different IL compositions in the Friedel–Crafts reactions of benzene and bromopropane at room temperature for 4 h. We kept the molar ratio of benzene:bromopropane:ionic liquid of 2:1:1 constant and changed the quantity of $FeCl_3$. The $FeCl_3$–IL systems were studied separately in two different ILs. The results are summarized in Fig. 2.

Fig. 2 shows that better results are obtained with increased amount of $FeCl_3$. However, when the quantity of $FeCl_3$ is more than two equivalent of ionic liquid, the catalytic activity did not change any more. Similar descriptions have also been reported by others [20,21]. Therefore, reactions of benzene with other alkyl halides were studied with 2 equiv. $FeCl_3$.

3.2. Alkylation of benzene with 1-chlorobutane

Results of alkylation of benzene with 1-chlorobutane in different catalyst–IL system are shown in Table 2.

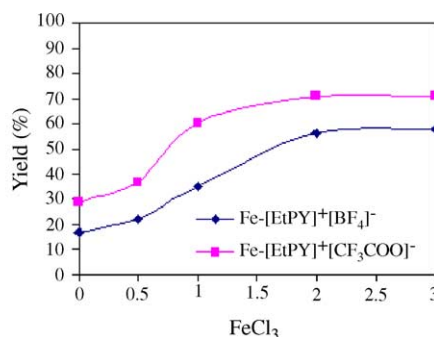| Benzene:1-Bromo-propane:IL:FeCl₃ (molar ratio)	$[EtPy]^+[BF_4]^-$	$[EtPy]^+[CF_3COO]^-$
	Conv. (%)	
2:1:1:0	17	29
2:1:1:0.5	22	37
2:1:1:1	35	60
2:1:1:2	56	71
2:1:1:3	58	71

Fig. 2. The alkylation of benzene and 1-bromopropane with different content of $FeCl_3$.

Table 2
The Friedel–Crafts alkylation of benzene (**1**) with 1-chlorobutane (**3**)

Entry	Catalyst–solvent	Conversion (%) room temperature (50 °C)	Selectivity to major product (%)
1	$[EtPy]^+[BF_4]^-$	21 (45)	66 (75)
2	$[EtPy]^+[CF_3COO]^-$	34 (55)	76 (80)
3	$AlCl_3–[EtPy]^+[BF_4]^-$	68 (87)	76 (88)
4	$AlCl_3–[EtPy]^+[CF_3COO]^-$	77 (96)	81 (93)
5	$FeCl_3–[EtPy]^+[BF_4]^-$	67 (88)	74 (87)
6	$FeCl_3–[EtPy]^+[CF_3COO]^-$	77 (94)	83 (94)

Table 3
The Friedel–Crafts alkylation of benzene (**1**) with benzyl chloride (**4**)

Entry	Catalyst–solvent	Conversion (%) room temperature (50 °C)
1	$[EtPy]^+[BF_4]^-$	<1 (6)
2	$[EtPy]^+[CF_3COO]^-$	<1 (12)
3	$AlCl_3–[EtPy]^+[BF_4]^-$	21 (47)
4	$AlCl_3–[EtPy]^+[CF_3COO]^-$	35 (59)
5	$FeCl_3–[EtPy]^+[BF_4]^-$	20 (44)
6	$FeCl_3–[EtPy]^+[CF_3COO]^-$	33 (56)

As in Scheme 2 Eq. (2) shows that 'sec-' (**7**), 'n-' (**8**) and 'tert-' (**9**) products were obtained in this alkylation. We would expect *tert*-butylbenzene, thermodynamically most stable of the three, to be the major product. However, interestingly *sec*-butylbenzene is the major product.

As Table 2 shows, slightly better conversions and product selectivity are obtained compared to data in Table 1. This could be because the electronegativity of Cl^- is stronger than that of Br^-, which could enhance the electrophilicity of the intermediate carbocation and promote the reactions. Comparable results are obtained in $AlCl_3$–IL and $FeCl_3$–IL systems. In the reactions with 1-chlorobutane, higher conversions are seen at 50 °C. Also, $[EtPy]^+[CF_3COO]^-$ turns out to be a better medium than $[EtPy]^+[BF_4]^-$, which also indicate the anions of ILs are important for the reactions. One interesting thing, we note, is that when we raise the temperature, the selectivity to *sec*-butylbenzene also increases, which seems to be in contrast with the general mechanism of the reactions. So far, we do not know the reasons, and further investigation is underway.

3.3. Alkylation of benzene with benzyl chloride

Table 3 shows the results of alkylation of benzene with benzyl chloride at different temperatures, catalyst and solvent conditions. In this reaction, the product conversion decreased significantly compared to previous cases.

The catalyst–IL still shows better results than the pure IL. Also, in all cases, the results with $[EtPy]^+[CF_3COO]^-$ are better than those with $[EtPy]^+[BF_4]^-$. Both $FeCl_3$–IL and $AlCl_3$–IL systems show comparable efficiency.

3.4. Recycle and reuse of FeCl₃–IL

We investigated the reusability and efficiency of ionic liquid with or without catalysts. The recycling process involved washing the used ionic liquids with diethyl ether. Any organic residue left in the ionic liquid layer could be separated by the ether wash. The IL layer was then separated and dried under reduced pressure at 65 °C. Successive runs were performed with the recovered ionic liquid $[EtPy]^+[BF_4]^-$ or $[EtPy]^+[CF_3COO]^-$ for the alkylation between benzene and 1-chlorobutane (Scheme 2, Eq. (2)) at 50 °C for 4 h.

As results in Table 4 shows, both ionic liquids could be recovered quantitatively and almost without loss of activity and selectivity. This is evident from the fact that the conversion of the Friedel–Crafts alkylations is not affected even after the third run with the recovered ionic liquid. However, yields of the ionic liquid recovery from the used catalyst–IL system were relatively low.

As can be seen in Table 5, although the $FeCl_3$–IL system can be recovered efficiently, the conversion dropped dramatically. After third trial, yields of the alkylation product

Table 4
Recycling of ionic liquids in the alkylation of benzene and 1-chlorobutane

Recycling #	$[EtPy]^+[BF_4]^-$		$[EtPy]^+[CF_3COO]^-$	
	Recovered[a] (wt.%)	Converted[b] (%)	Recovered[a] (wt.%)	Converted[b] (%)
0	–	45 (75)	–	55 (80)
1	94	43 (73)	93	53 (75)
2	92	44 (74)	92	51 (78)
3	93	41 (72)	93	50 (76)

[a] Isolated yield
[b] Values in parenthesis indicate selectivity to major product.

Table 5
Recycling of Fecl₃–IL in the alkylation of benzene and 1-chlorobutane

Recycling #	$FeCl_3–[EtPy]^+[BF_4]^-$		$FeCl_3–[EtPy]^+[CF_3COO]^-$	
	Recovered[a] (wt.%)	Conversion[b] (%)	Recovered[a] (wt.%)	Conversion[b] (%)
0	–	88 (87)	–	94 (94)
1	88	75 (84)	90	82 (92)
2	85	67 (83)	86	76 (90)
3	89	65 (81)	87	75 (91)

[a] Isolated yield.
[b] Values in parenthesis indicate selectivity to major product.

dropped compared with the fresh catalyst–IL system. On the other hand, product selectivity remained nearly unaffected.

4. Conclusion

The pyridinium-based ILs are suitable media for Friedel–Crafts alkylation of benzene. The reactions proceed at a better rate at relatively lower temperature, yielding high product conversion. The $[EtPy]^+[CF_3COO]^-$–$FeCl_3$ was found to be the best solvent–catalyst system which can efficiently substitute the aluminum catalysis system. Applications of the pyridinium-based ILs as solvents for number of other reactions are under investigation in our laboratory.

References

[1] M. Bandini, A. Melloni, A. Umani-Ronchi, Angew. Chem. Int. ed. 43 (2004) 550.
[2] G.R. Meima, G.S. Lee, J.M. Garces (Eds.), Fine Chemicals through Heterogeneous Catalysis, Wiley–VCH Verlag GmbH, Weinheim, Germany, 2001, p. 151.
[3] H. Yao, C.A. Wilkie, ACS Symp. Ser. (Fire Polym.) 797 (2001) 125.
[4] I.N. Jung, B.R. Yoo, Adv. Organometall. Chem. 46 (2000) 145.
[5] J.S. Wilkes, NATO ASI Ser. C: Math. Phys. Sci. (Molten Salt Chem.) 202 (1987) 405.
[6] F.A. Carey, R.J. Sundberg, Advanced Organic Chemistry: Reactions and Synthesis, Part B, 4th ed., Plenum Press, New York, 2002 (Chapter 6).
[7] M. Berthod, J.M. Joerger, G. Mignani, M. Vaultier, M. Lemaire, Tetrahedron: Asymm. 15 (2004) 2219.
[8] H. Xie, S. Zhang, H. Duan, Tetrahedron Lett. 45 (2004) 2013.
[9] I. Meracz, T. Oh, Tetrahedron Lett. 44 (2003) 6465.
[10] C. De Bellefon, E. Pollet, P. Grenouillet, J. Mol. Catal. A: Chem. 145 (1999) 121.
[11] Y. Gu, F. Shi, Y. Deng, J. Mol. Catal. A: Chem. 212 (2004) 71.
[12] J. Peng, Y. Deng, Tetrahedron Lett. 42 (2001) 403.
[13] D. Zhao, M. Wu, Y. Kou, E. Min, Catal. Today 74 (2002) 157.
[14] H. Zhao, S.V. Malhotra, Aldrichim. Acta 35 (2002) 75.
[15] H. Olivier-Bourbigou, L. Magna, J. Mol. Catal. A: Chem. 182/183 (2002) 419.
[16] C.M. Gordon, Appl. Catal. A: Gen. 222 (2001) 101.
[17] S.V. Malhotra, H. Zhao, Phys. Chem. Liq. 42 (2004) 215.
[18] Z. Zhao, Z. Li, G. Wang, W. Qiao, L. Cheng, Appl. Catal. A: Gen. 262 (2004) 69.
[19] P. Formentin, H. Garcia, Catal. Lett. 78 (2002) 115.
[20] K. Qiao, Y. Deng, J. Mol. Catal. A: Chem. 171 (2001) 81.
[21] J.A. Boon, J.A. Levisky, J.L. Pflug, J.S. Wilkes, J. Org. Chem. 51 (1986) 480.
[22] C. Decastro, E. Sauvage, M.H. Valkenberg, W.F. Holderich, J. Catal. 196 (2000) 86.
[23] Y. Xiao, S.V. Malhotra, Tetrahedron Lett. 45 (2004) 8339.
[24] H. Zhao, R. Luo, S.V. Malhotra, Biotechnol. Prog. 19 (2003) 1016.
[25] H. Zhao, S.V. Malhotra, Biotechnol. Lett. 24 (2002) 1257.
[26] J.D. Holbrey, K.R. Seddon, J. Chem. Soc., Dalton Trans. (1999) 2133.
[27] H. Zhao, S.V. Malhotra, R. Luo, Phys. Chem. Liq. 41 (2003) 487.
[28] General experimental procedure: the catalyst, anhydrous $AlCl_3$ or $FeCl_3$ (16 mmol), was slowly added to pyridinium-based ionic liquid (8 mmol), the mixture was stirred at 45 °C until the catalyst completely dissolved. Benzene (16 mmol) and alkyl halides (**2**) or (**3**) or (**4**) (8 mmol) were directly added to the catalyst–IL solution. Two phases were formed and the reaction mixture was stirred (250 rpm) at the desired reaction temperature for 4 h. After reaction was over, the mixture was diluted with 3 mL water and 3 mL petroleum ether and shaken vigorously. The organic layer was separated from ionic liquid. Any leftover organic material was extracted with diethyl ether and the ionic liquid was dried at 65 °C under vacuum to remove moisture and then reused. The combined organic extracts were washed with water (3 mL) followed by brine (3 mL). Evaporation of solvent under reduced pressure gave the product which was dried over Na_2SO_4.