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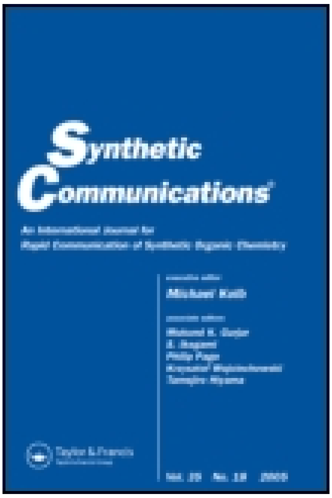

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Synthesis, Characterization, and Catalytic Behavior of Methoxy- and Dimethoxy-substituted Pyridinium-Type Ionic Liquids

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SYNTHESIS, CHARACTERIZATION, AND CATALYTIC BEHAVIOR OF METHOXY- AND DIMETHOXY-SUBSTITUTED PYRIDINIUM-TYPE IONIC LIQUIDS

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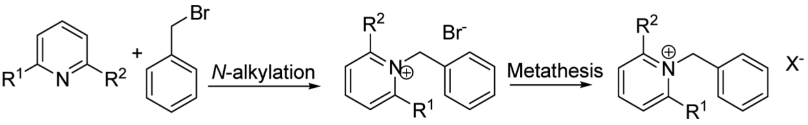
GRAPHICAL ABSTRACT



Abstract *Synthesis of methoxy-substituted pyridinium-type ionic liquids from a nontoxic and easy method is described. Catalytic behaviors of synthesized ionic liquids were investigated with various concentrations for the Mannich reaction. We have observed that methoxy- and dimethoxy-substituted pyridinium bromides showed better catalytic behavior than other ionic liquids.*

Keywords Catalysis; dimethoxy; Mannich reaction; methoxy; pyridinium

INTRODUCTION

Ionic liquids play crucial roles in synthetic organic chemistry, catalytic reactions, electrochemistry, and engineering.[1–5] Ionic liquids act as immobilization media and ionic transition-metal catalysts, which are retained during separation.[6–11] Major disadvantages of the catalysts are insufficient stability, reusability, and deactivation of single-phase catalyst. Carbon–carbon coupling bond formations from Suzuki coupling reaction between some nitrile-functionalized pyridinium ionic liquids showed good catalytic activity.[12–16] Depending on the counterions, the behavior of the catalyst varies.[17] Zhao et al. reported the Mitsunobu reaction in the presence of pyridinium as well as imidazolium salts as nucleophilic reagents.[18] Ni et al. reported that chiral pyridinium ionic liquids are highly efficient catalysts for Michael addition reaction with considerable yield.[19] Some of the pyridinium salts act as effective coupling reagents for the synthesis of carboxycylic ester.[20] Microwave-assisted esterification reaction between the α-amino acid and substituted alcohol in the presence of pyridinium-type ionic liquids showed better catalytic

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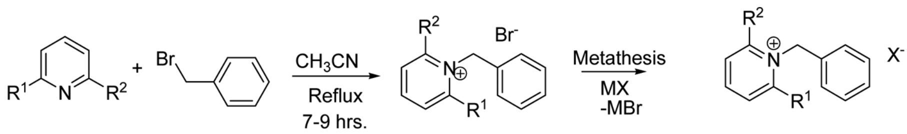
behaviors.[21] Pyridinium-based ionic liquids showed good catalytic activity in the Marita–Baylis–Hillman reaction as well as reduction reaction.[22] We report herein the synthesis of mono- and dimethoxy-substituted pyridinium with different counteranions and examin the catalytic activity of our synthesized ionic liquids in the Mannich reaction.

RESULTS AND DISCUSSION

1-Methoxy/1,6-dimethoxy pyridine (1.0 equiv.) is treated with benzyl bromide (1.05 equiv.) in the presence of a minimum amount of dry acetonitrile under refluxing conditions for about 7–9 h, followed by evaporation to give pyridinium salts of compounds **1** and **2** from 90 to 96% of yield. Followed by anion exchange reaction (metathesis) with various inorganic salts in the presence of a minimum amount of water (environmentally friendly solvent) at room temperature with stirring for about 1 h gives the anion exchanged product. Completion of the metathesis reaction is confirmed with aqueous solution of $AgNO_3$. We have to separate the ionic liquids from metallic bromide, which is not easy because the usual solvent extraction is not feasible due to the water-soluble nature of both metallic bromide and ionic liquids, so we have to apply a special technique for isolation (Soxhlet extraction) in the presence of dry tetrahydrofuran (THF) for 1 h under reflux to give metallic bromide-free ionic liquids with good yield. The synthesized compounds are confirmed by both spectral and analytical data.

We report that synthesis of oxirane from the Mannich reaction is accelerated by our synthesized ionic liquids (Scheme 1). The reaction of aniline (1.0 equiv.), phenol (1.0 equiv.), and formaldehyde (2.0 equiv.) under room temperature with stirring is considered as a model reaction to study the catalytic activity of ionic liquids with different concentrations. In the same reaction, there is no positive response in the absence of catalyst even in the thermal conditions; therefore our ionic liquid plays a crucial role to promote the Mannich reaction.

The procedure is optimized using different concentrations of ionic liquids. From this, we observed that the yield of oxirane formation is maximum at 1.60×10^{-5} mmol of ionic liquid concentration with less reaction time compared to 7.21×10^{-6} mmol and 1.07×10^{-5} mmol concentration of ionic liquid in which the yield and reaction time are not appreciable. From that result, the concentration of catalysts plays an important role to increase the yield and reduce reaction time. We concluded that the optimum concentration of ionic liquids plays a major role to increase the percentage of yield and reduce the reaction period.



1-2

3-8

1 = R^1 = OMe; R^2 = H,

2 = R_1 = OMe; R_2 = OMe,

3 = R^1 = OMe; R^2 = H;X = BF_4,

4 = R^1 = OMe; R^2 = OMe; X= BF_4,

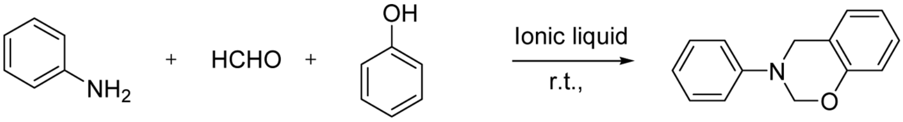
5 = R^1 = OMe; R^2 = H; X = PF_6,

6= R_1 = OMe; R^2 = OMe; X= PF_6,

7= R^1 = OMe; R^2 = H; X = CF_3SO_3,

8= R^1 = OMe; R^2 = OMe; X = CF_3SO_3

Scheme 1. Synthesis of ionic liquids.



Scheme 2. Catalytic activity of ionic liquid with different concentrations.

Table 1. 7.21×10^{-6} mmol concentration

	IL with Br^-		IL with BF_4^-		IL with PF_6^-		IL with $CF_3SO_3^-$	
Reaction	MP	DMP	MP	DMP	MP	DMP	MP	DMP
Time (h)	1.45	2	1.45	2	2	2.15	2	2.05
Yield (%)	72	69	68	66	65	62	60	58

Table 2. 1.07×10^{-5} mmol concentration

	IL with Br^-		IL with BF_4^-		IL with PF_6^-		IL with $CF_3SO_3^-$	
Reaction	MP	DMP	MP	DMP	MP	DMP	MP	DMP
Time (min)	30	38	30	42	30	35	30	36
Yield (%)	88	84	80	77	74	70	69	66

Table 3. 1.60×10^{-5} mmol concentration

	IL with Br^-		IL with BF_4^-		IL with PF_6^-		IL with $CF_3SO_3^-$	
Reaction	MP	DMP	MP	DMP	MP	DMP	MP	DMP
Time (min)	15	20	15	22	15	25	15	22
Yield (%)	92	92	98	92	98	96	96	92

Notes. MP, methoxypyridinium; DMP, dimethoxypyridinium.

CONCLUSION

We prepared the methoxy/dimethoxy pyridinium-type ionic liquids using a nontoxic and easy method. We have investigated the homogeneous catalytic activity of synthesized ionic liquids **1–8**. We found that the oxirane formation is appreciable only in the presence of a catalyst. We observed that monomethoxy-substituted pyridinium ionic liquid shows better catalytic activity than dimethoxy-substituted pyridinium compounds. The monomethoxy pyridinium ionic liquids show the catalytic activity in the following order: $Br^- > PF_6^- > BF_4^- > CF_3SO_3^-$. Our synthesized pyridinium-type ionic liquids acted as potential catalyst even at low concentrations.

EXPERIMENTAL

General Procedure for Synthesis of Mono- and Dimethoxy Pyridinium Bromides 1 and 2

1-Methoxy/1,6-dimethoxy pyridine (9.163×10^{-3} mmol) treated with benzyl bromide (1.8784×10^{-2} mmol) in the presence of 30 mL dry CH_3CN under refluxing condition between 7 and 9 h followed by evaporation gave *N*-alkylated products **1** and **2**.

Ionic liquid 1. Yield: 96%; liquid; MS: 280; ^1H NMR (D_2O) δ: 4.50 (s, 2H), 5.06 (s, 3H), 7.09–7.51 (m, 9H); ^{13}C NMR (D_2O) δ: 52.2, 56.2, 115.4, 121.5, 125.8, 128.7, 129.1, 134.5, 143.8, 148.3, 157.8. Anal. calculated for $C_{13}H_{14}BrNO$: C, 55.73; H, 5.04; N, 5.00. Found: C, 54.04; H, 4.94; N, 4.88.

Ionic liquid 2. Yield: 90%; liquid; MS: 310; ^1H NMR (D_2O) δ: 4.56 (s, 2H), 5.06 (s, 6H), 7.22–7.48 (m, 8H); ^{13}C NMR (D_2O) δ: 52.2, 56.2, 115.4, 121.5, 125.8, 128.7, 129.1, 148.3, 157.8. Anal. calculated for $C_{14}H_{16}BrNO_2$: C, 54.21; H, 5.20; N, 4.52. Found: C, 54.08; H, 4.94; N, 4.38.

General Procedure for Metathesis Reaction: Preparation of Ionic Liquids 3–8

1-Methoxy/1,6-dimethoxy pyridinium bromide (1.0 equiv./1.784×10^{-3} mmol) and 1.03 equiv. inorganic salt ($NaBF_4$, K_4PF_6, and $LiCF_3SO_3$) are mixed with 10 mL of deionized water at room temperature with stirring for about 1 h to give anion-exchanged products **3–8**.

Ionic liquid 3. Yield: 80%; mp 160 °C; MS: 287; ^1H NMR (D_2O) δ: 4.52 (s, 2H), 5.05 (s, 3H), 7.11–7.66 (m, 9H); ^{13}C NMR (D_2O) δ: 52.4, 56.1, 115.0, 121.4, 125.4, 128.2, 128.9, 134.1, 143.6, 148.1, 157.3. Anal. calculated for $C_{13}H_{14}BF_4NO$: C, 54.39; H, 4.92; N, 4.88. Found: C, 54.24; H, 4.84; N, 4.74.

Ionic liquid 4. Yield: 87%; mp 240 °C; MS: 317; ^1H NMR (D_2O) δ: 2.63 (s, 2H), 3.75 (s, 6H), 7.05–7.14 (m, 8H); ^{13}C NMR (D_2O) δ: 52.4, 56.1, 115.0, 121.4, 125.4, 128.2, 128.9, 134.1, 143.6, 148.1, 157.3. Anal. calculated for $C_{14}H_{16}BF_4NO_2$: C, 53.03; H, 5.09; N, 4.42. Found: C, 52.96; H, 4.84; N, 4.34.

Ionic liquid 5. Yield: 83%; mp 130 °C; MS: 345; ^1H NMR (D_2O) δ: 4.49 (s, 2H), 5.02 (s, 3H), 7.16–7.69 (m, 9H); ^{13}C NMR (D_2O) δ: 52.3, 56.3, 115.1, 121.1, 125.4, 128.2, 128.9, 134.1, 143.5, 148.1, 157.1. Anal. calculated for $C_{13}H_{14}F_6NOP$: C, 45.23; H, 4.09; N, 4.06. Found: C, 45.18; H, 4.00; N, 3.94.

Ionic liquid 6. Yield: 85%, mp 220 °C; MS: 375; ^1H NMR(D_2O) δ: 2.60 (s, 2H), 3.73 (s,6H), 4.52 (s, 2H), 5.05 (s, 6H), 7.18–7.76 (m, 8H); ^{13}C NMR (D_2O) δ: 52.2, 56.2, 115.4, 121.5, 125.8, 128.7, 129.1, 134.5, 143.8, 148.3, 157.8. Anal. calculated for $C_{14}H_{16}F_6NO_2P$: C, 44.81; H, 4.30; N, 3.73.

Ionic liquid 7. Yield: 85%; liquid; MS: 349; ^1H NMR (D_2O) δ: 4.54 (s, 2H), 5.10 (s, 3H), 7.13–7.70 (m, 9H); ^{13}C NMR (D_2O) δ: 52.2, 56.3, 115.1, 121.4, 125.4, 128.4, 128.9, 134.4, 143.5, 148.4, 157.1. Anal. calculated for $C_{14}H_{14}F_3NO_4$: C, 48.14; H, 4.04; N, 4.01. Found: C, 48.12; H, 4.00; N, 3.94.

Ionic liquid 8. Yield: 87%; mp 170 °C, MS: 378; ^{1}H NMR (D_2O) δ: 4.50 (s, 2H), 5.09 (s, 6H), 7.07–7.69 (m, 8H); ^{13}C NMR (D_2O) δ: 52.2, 56.2, 115.4, 121.5, 125.8, 128.7, 129.1, 134.5, 143.8, 148.3, 157.8. Anal. calculated for $C_{15}H_{16}F_3NO_5S$: C, 47.49; H, 4.25; N, 3.60. Found: C, 47.36; H, 4.16; N, 3.58.

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