

Efficient Dichloromethylation of Some Aromatic Hydrocarbons Catalyzed by a New Ionic Liquid [C₁₂minPEG₈₀₀]Br under Homogeneous Catalysis in Aqueous Media

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A series of new imidazolium-type ionic liquids based on polyethylene glycol have been prepared. The new recyclable temperature-dependant phase-separation system comprised of [C₁₂minPEG₈₀₀]Br and methylcyclohexane was also developed and successfully applied to the dichloromethylation of some aromatic hydrocarbons to prepare dichloromethyl-substituted hydrocarbons in excellent yields. The ionic liquid could be excellently recycled without any apparent loss of catalytic activity and little loss of weight even after 8 times recycling.

Keywords: Aromatic hydrocarbons, Dichloromethylation, [C₁₂minPEG_n]Br, Temperature-dependent ionic liquid biphasic system

INTRODUCTION

Chloromethyl-substituted aromatic compounds are very important intermediates which have been widely applied in synthesis of a variety of fine or special chemicals such as pharmaceuticals, agrochemicals, dyes, flavors and fragrances, polymers, additives, *etc.* [1-3]. Procedures for chloromethylating aromatic compounds have been well documented in previous papers. The chloromethylation of aromatic hydrocarbons with hydrochloric acid and trioxane or paraformaldehyde as a formaldehyde precursor gave chloromethylated products without a catalyst, although the rate is slow and not enough for practical chemical process [4-7]. Lewis acids such as zinc chloride, stannic chloride, aluminum chloride, and boron trifluoride are well known catalysts for the reaction [8-12]. Among these acids, zinc chloride is an effective catalyst in hydrochloric acid solution [4,8,9].

However, a stoichiometric amount of catalyst to substrate is required, making the workup procedure tedious. These

catalysts, in general, suffer from the inherent problems of tedious workup procedures, corrosiveness, high susceptibility to water, difficulty of catalyst recovery, environmental hazards, waste control, *etc.* Kishida *et al.* recently reported the use of rare earth metal triflates in the chloromethylation of aromatic hydrocarbons [13-15]. However, rare earth metal triflates, particularly Sc(OTf)₃, are very expensive for the use of practical chemical processes. So, it is important to replace these catalysts with environmentally conscious catalysts that are active under mild conditions and have reasonable prices and can also be easily recovered after reactions and reused for new reactions [16].

To attain these purposes and to develop new and environment-benign procedures that address these drawbacks in the chloromethylation of aromatic hydrocarbons, we have proposed surfactant micelles, particularly CTAB, as the effective catalyst to synthesize some mono-chloromethylated hydrocarbons [17], and which have been successfully developed although we have not used them to synthesize some very useful dichloromethylated aromatic hydrocarbons such as 1,4-bis(chloromethyl)benzene [18], 4,4'-bis(chloromethyl)

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biphenyl [12,19], *etc.* [20-23].

Room temperature ionic liquids (ILs) are a special class of molten salts composed of organic cations and inorganic or organic anions. They have received considerable attention as alternatives to the traditional organic solvents. Because of their interesting physical and chemical properties, such as negligible vapor pressure, unique permittivity, high thermal stability, good solvents for both organic and inorganic substances, high electrical conductivity and wide electrochemical window, ILs have been widely used as reaction media, separation solvents, and novel electrolytes [24-29]. Up to now, examples of their applications as catalysts in the chloromethylation of aromatic hydrocarbons were seldom reported [30], and these researches are only confined to the mono-chloromethylation of certain aromatic hydrocarbons. In 2009, we developed an efficient synthetic method for 3,3',4,4'-biphenyltetracarboxylic anhydride through a key step of dichloromethylation of 4,4'-dimethylbiphenyl to synthesize 3,3'-bis(chloromethyl)-4,4'-dimethylbiphenyl catalyzed by 1-dodecyl-3-methyl-imidazolium bromide ($[C_{12}mim]Br$) in aqueous media [31]. However, the ILs are still inevitably associated with low recovery ratio, high cost, *etc.*

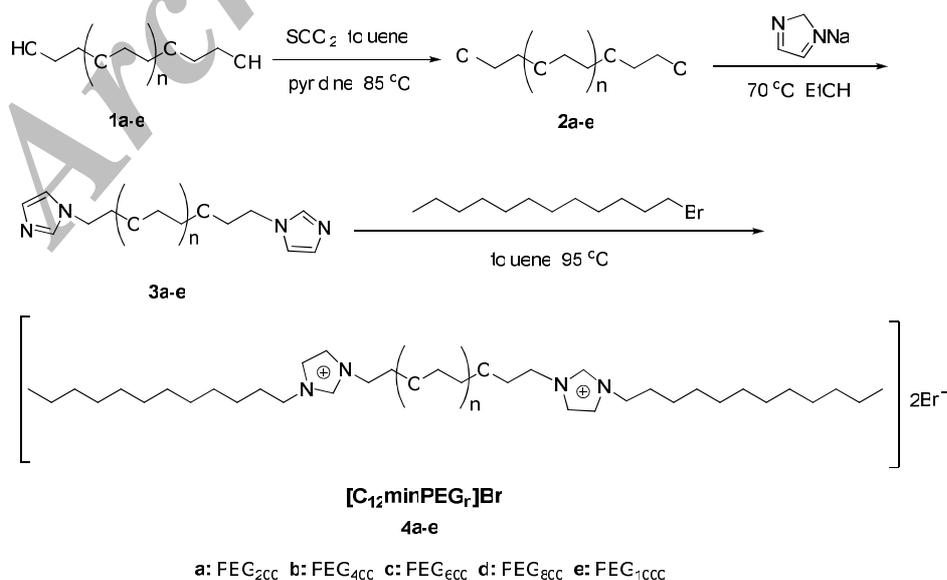
In view of both the advantages and disadvantages of homogeneous and heterogeneous catalysts, and to improve

catalyst recovery, multiphase systems, such as phase-transfer catalysis [32,33], thermoregulated phase-transfer catalysis [34] and liquid-liquid biphasic catalysis [35], have been studied. Some novel temperature-dependent ionic liquid biphasic catalytic systems have been reported recently [36-39], and found that these temperature-dependent ionic liquids showed some advantages such as high conversions and selectivity, stability at high temperatures, easy handling and separation, excellent reusability in the reaction, *etc.*, which provide a novel route for the homogeneous catalysis and the separating and recycling of catalysts. Based on the concept of thermoregulated ionic liquid biphasic system (TRILC) and in continuation of our interest in exploring green synthetic methods using ionic liquids, we herein report a new temperature-dependent biphasic system comprised of the new recoverable ionic liquids $[C_{12}minPEG_n]Br$ (Scheme 1) and methylcyclohexane, and their applications in the synthesis of some useful dichloromethylated aromatic hydrocarbons.

EXPERIMENTAL

Reagents and Equipment

All chemicals and reagents were of analytical grade and some useful dichloromethylated aromatic hydrocarbons used as obtained. Melting points were determined on an electrothermal (Prolabo 9200) apparatus and are uncorrected.



Scheme 1. The Synthesis of $[C_{12}minPEG_n]Br$

NMR spectra were recorded on a Bruker 400-MHz spectrometer using CDCl_3 as the solvent with tetramethylsilane (TMS) as an internal standard. High performance liquid chromatography (HPLC) experiments were performed on a liquid chromatograph (Dionex Softron GmbH, America), consisting of a pump (P680) and ultraviolet-visible light detector (UVD) system (170U). The experiments were performed on Diacoverly C18 column, \varnothing 4.6 \times 150 mm. Elemental analysis were performed on a Vario EL III instrument (Elementar Analysensy Teme GmbH, Germany).

General Procedure for the Synthesis of Ionic Liquid $[\text{C}_{12}\text{minPEG}_{800}]\text{Br}$ (**4a-e**)

Step 1. A mixture of PEG_n (**1a-e**, 0.1 mol), pyridine (0.25 mol), and toluene (80 ml) was stirred in 250 ml round flask at 85 °C, then SOCl_2 (3.15 g, 0.105 mol) was added dropwise slowly, after that the mixture was stirred for 16 additional hours at 85 °C, the reaction progress was monitored by HPLC. After the reaction completed, the mixture was cooled to room temperature, then 10% HCl solution (40 ml) was added, and the organic phase was separated by decantation, the water phase (under layer) was extracted with toluene (3 \times 10 ml). The combined organic phases was washed with water (2 \times 10 ml), then dried over anhydrous Na_2SO_4 . The solvent was removed to give **2a-e**, yield 92%.

Step 2. A mixture of imidazole (0.1 mol), sodium ethoxide (0.1 mol), and ethanol (10 ml) was stirred at 70 °C for 8 h, then **2a-e** (0.05 mol) was added. After that the mixture was stirred for 20 additional hours at 70 °C, the reaction progress was monitored by HPLC. After the reaction completed, the mixture was cooled, the precipitate was filtered off, then the filtrate was extracted with a ether (3 \times 10 ml). The combined organic liquid was concentrated to give **3a-e**, yield 85%.

3a: ^1H NMR (400 MHz, CDCl_3) δ = 3.54-3.71 (m, 20H, $(\text{OCH}_2\text{CH}_2)_n$), 3.74-3.78 (m, 4H, CH_2CH_2), 4.14 (m, 4H, CH_2CH_2), 7.04-7.07 (m, 4H, $\text{CH} \times 4$), 7.57 (s, 2H, $\text{CH} \times 2$) ppm.

3b: ^1H NMR (400 MHz, CDCl_3) δ = 3.51-3.69 (m, 38H, $(\text{OCH}_2\text{CH}_2)_n$), 3.72-3.77 (m, 4H, CH_2CH_2), 4.16 (m, 4H, CH_2CH_2), 7.08-7.12 (m, 4H, $\text{CH} \times 4$), 7.79 (s, 2H, $\text{CH} \times 2$) ppm.

3c: ^1H NMR (400 MHz, CDCl_3) δ = 3.49-3.73 (m, 56H, $(\text{OCH}_2\text{CH}_2)_n$), 3.74-3.76 (m, 4H, CH_2CH_2), 4.16 (m, 4H,

CH_2CH_2), 7.14-7.17 (m, 4H, $\text{CH} \times 4$), 7.92 (s, 2H, $\text{CH} \times 2$) ppm.

3d: ^1H NMR (400 MHz, CDCl_3) δ = 3.48-3.72 (m, 74H, $(\text{OCH}_2\text{CH}_2)_n$), 3.73-3.79 (m, 4H, CH_2CH_2), 4.18 (m, 4H, CH_2CH_2), 7.16-7.21 (m, 4H, $\text{CH} \times 4$), 8.23 (s, 2H, $\text{CH} \times 2$) ppm.

3e: ^1H NMR (400 MHz, CDCl_3) δ = 3.47-3.68 (m, 92H, $(\text{OCH}_2\text{CH}_2)_n$), 3.71-3.76 (m, 4H, CH_2CH_2), 4.19 (m, 4H, CH_2CH_2), 7.24-7.32 (m, 4H, $\text{CH} \times 4$), 8.57 (s, 2H, $\text{CH} \times 2$) ppm.

Step 3. A mixture of **3a-e** (0.02 mol), 1-dodecyl bromide (0.04 mol), and toluene (10 ml) was stirred at 95 °C for 48 h, the reaction progress was monitored by HPLC, and then evaporated under reduced pressure to give the desired ionic liquid (**4a-e**) as a light brown oil, yield 87%.

4a: ^1H NMR (400 MHz, CDCl_3) δ = 0.83-0.89 (m, 6H, $\text{CH}_3 \times 2$), 1.29-1.35 (m, 18H, $\text{CH}_2 \times 9$), 1.78-1.84 (m, 4H, $\text{CH}_2 \times 2$), 3.54-3.71 (m, 20H, $(\text{OCH}_2\text{CH}_2)_n$), 3.71-3.76 (m, 4H, CH_2CH_2), 4.12-4.19 (m, 8H, $\text{CH}_2 \times 4$), 7.06-7.10 (m, 4H, $\text{CH} \times 4$), 7.61 (s, 2H, $\text{CH} \times 2$) ppm.

4b: ^1H NMR (400 MHz, CDCl_3) δ = 0.82-0.87 (m, 6H, $\text{CH}_3 \times 2$), 1.31-1.36 (m, 18H, $\text{CH}_2 \times 9$), 1.74-1.81 (m, 4H, $\text{CH}_2 \times 2$), 3.53-3.68 (m, 38H, $(\text{OCH}_2\text{CH}_2)_n$), 3.74-3.77 (m, 4H, CH_2CH_2), 4.14-4.21 (m, 8H, $\text{CH}_2 \times 4$), 7.07-7.14 (m, 4H, $\text{CH} \times 4$), 7.81 (s, 2H, $\text{CH} \times 2$) ppm.

4c: ^1H NMR (400 MHz, CDCl_3) δ = 0.81-0.88 (m, 6H, $\text{CH}_3 \times 2$), 1.30-1.35 (m, 18H, $\text{CH}_2 \times 9$), 1.72-1.79 (m, 4H, $\text{CH}_2 \times 2$), 3.52-3.76 (m, 56H, $(\text{OCH}_2\text{CH}_2)_n$), 3.76-3.79 (m, 4H, CH_2CH_2), 4.16-4.19 (m, 8H, $\text{CH}_2 \times 4$), 7.14-7.17 (m, 4H, $\text{CH} \times 4$), 7.97 (s, 2H, $\text{CH} \times 2$) ppm.

4d: ^1H NMR (400 MHz, CDCl_3) δ = 0.83-0.87 (m, 6H, $\text{CH}_3 \times 2$), 1.31-1.33 (m, 18H, $\text{CH}_2 \times 9$), 1.71-1.77 (m, 4H, $\text{CH}_2 \times 2$), 3.48-3.72 (m, 74H, $(\text{OCH}_2\text{CH}_2)_n$), 3.72-3.78 (m, 4H, CH_2CH_2), 4.15-4.17 (m, 8H, $\text{CH}_2 \times 4$), 7.16-7.21 (m, 4H, $\text{CH} \times 4$), 8.31 (s, 2H, $\text{CH} \times 2$) ppm.

4e: ^1H NMR (400 MHz, CDCl_3) δ = 0.83-0.85 (m, 6H, $\text{CH}_3 \times 2$), 1.29-1.34 (m, 18H, $\text{CH}_2 \times 9$), 1.70-1.78 (m, 4H, $\text{CH}_2 \times 2$), 3.46-3.70 (m, 92H, $(\text{OCH}_2\text{CH}_2)_n$), 3.73-3.79 (m, 4H, CH_2CH_2), 4.12-4.18 (m, 8H, $\text{CH}_2 \times 4$), 7.26-7.35 (m, 4H, $\text{CH} \times 4$), 8.62 (s, 2H, $\text{CH} \times 2$) ppm.

Typical Procedure for Dichloromethylation

The three-necked flask was loaded with aromatic

hydrocarbon (0.1 mol), paraformaldehyde (0.6 mol), conc. HCl (70 ml), [C₁₂minPEG₈₀₀]Br (0.03 mol), methylcyclohexane (70 ml). Hydrogen chloride gas was bubbled into the flask at the flow rate of 80 ml min⁻¹. The reaction mixture was stirred at an appropriate temperature for an appropriate time (Table 2). After the reaction, the reaction mixture was cooled to room temperature, the organic phase was separated by decantation, and rinsed with 5% NaHCO₃ solution (3 × 10 ml) and water (2 × 10 ml), then dried with sodium sulfate, filtered, and evaporated to dryness *in vacuo*, and the organic residue was resolved in methylene chloride and analyzed by HPLC. The crude product was recrystallized from hexane and methylene chloride and the desired product was identified by NMR and Elemental analysis or compared with authentic samples. The next run was performed under identical reaction conditions.

1,4-Bis(chloromethyl)benzene (5). White solid, m.p.: 98-101 °C (lit. [19] m.p.: 97-100 °C). ¹H NMR (400 MHz, CDCl₃) δ = 4.61 (s, 4H, CH₂), 7.27 (s, 4H, Ar-H) ppm. ¹³C NMR (400 MHz, CDCl₃) δ = 46.8, 128.4, 139.1 ppm. Anal. Calcd. for C₈H₈Cl₂: C, 54.86; H, 4.61; Cl, 40.52. Found: C, 54.89; H, 4.61; Cl, 40.50.

1,3-Bis(chloromethyl)-4,6-dimethylbenzene (6). White solid, m.p.: 88-90 °C (lit. [24] m.p.: 87-89 °C). ¹H NMR (400 MHz, CDCl₃) δ = 2.37 (s, 6H, CH₃), 4.69 (s, 4H, CH₂), 7.04 (s, 1H, Ar-H), 7.25 (s, 1H, Ar-H) ppm. ¹³C NMR (400 MHz, CDCl₃) δ = 17.5, 40.5, 129.2, 131.2, 134.5, 136.8 ppm. Anal. Calcd. for C₁₀H₁₂Cl₂: C, 59.09; H, 5.97; Cl, 34.94. Found: C, 59.13; H, 5.96; Cl, 34.91.

1,4-Bis(chloromethyl)-2,5-dimethylbenzene (7). White solid, m.p.: 102-104 °C. IR (KBr, cm⁻¹): 2976, 2865, 1637, 1506, 1454, 1382, 895, 806, 656. ¹H NMR (400 MHz, CDCl₃) δ = 2.34 (s, 6H, CH₃), 4.67 (s, 4H, CH₂), 7.16 (s, 2H, Ar-H) ppm. ¹³C NMR (400 MHz, CDCl₃) δ = 17.8, 40.6, 131.2, 133.7, 138.3 ppm. MS (EI, 70 eV) m/z (%): 202 (M⁺), 167, 153, 119, 105, 91, 77. Anal. Calcd. for C₁₀H₁₂Cl₂: C, 59.03; H, 5.98; Cl, 34.97. Found: C, 59.13; H, 5.96; Cl, 34.91.

1,2-Bis(chloromethyl)-4,5-dimethylbenzene (8). White solid, m.p.: 103-105 °C (lit. [22] m.p.: 102-104 °C). ¹H NMR (400 MHz, CDCl₃) δ = 2.36 (s, 6H, CH₃), 4.70 (s, 4H, CH₂), 7.14 (s, 2H, Ar-H) ppm. ¹³C NMR (400 MHz, CDCl₃) δ = 18.5, 40.7, 131.2, 134.1, 138.1 ppm. Anal. Calcd. for C₁₀H₁₂Cl₂: C, 59.07; H, 6.01; Cl, 34.92. Found: C, 59.13; H,

5.96; Cl, 34.91.

4,4'-Bis(chloromethyl)biphenyl (9). White solid, m.p.: 133-135 °C (lit. [20] m.p.: 134-136 °C). ¹H NMR (400 MHz, CDCl₃) δ = 4.63 (s, 4H, CH₂), 7.48 (m, 4H, Ar-H), 7.57 (m, 4H, Ar-H) ppm. ¹³C NMR (400 MHz, CDCl₃) δ = 46.1, 127.6, 129.4, 136.9, 140.7 ppm. Anal. Calcd. for C₁₄H₁₂Cl₂: C, 66.93; H, 4.83; Cl, 28.24. Found: C, 66.95; H, 4.82; Cl, 28.23.

6,7-Bis(chloromethyl)-1,2,3,4-tetrahydronaphthalene (10). White solid, m.p.: 110-112 °C. IR (KBr, cm⁻¹): 2946, 2832, 1643, 1510, 1447, 887, 812, 732, 667. ¹H NMR (400 MHz, CDCl₃) δ = 1.51 (s, 4H, CH₂), 2.84 (s, 4H, CH₂), 4.57 (s, 4H, CH₂), 7.16 (s, 2H, Ar-H) ppm. ¹³C NMR (400 MHz, CDCl₃) δ = 22.4, 26.1, 44.7, 127.5, 136.1, 137.3 ppm. MS (EI, 70 eV) m/z (%): 228 (M⁺), 193, 179, 145, 131, 105, 91, 77. Anal. Calcd. for C₁₂H₁₄Cl₂: C, 62.87; H, 6.17; Cl, 30.95. Found: C, 62.90; H, 6.16; Cl, 30.94.

1,4-Bis(chloromethyl)-2,5-dimethoxybenzene (11). White solid, m.p.: 125-127 °C. IR (KBr, cm⁻¹): 2981, 2859, 1635, 1504, 1462, 1386, 1157, 892, 812, 662. ¹H NMR (400 MHz, CDCl₃) δ = 3.89 (s, 6H, CH₃), 4.64 (s, 4H, CH₂), 7.21 (s, 2H, Ar-H) ppm. ¹³C NMR (400 MHz, CDCl₃) δ = 40.8, 54.7, 114.2, 126.7, 148.4 ppm. MS (EI, 70 eV) m/z (%): 234 (M⁺), 199, 185, 151, 137, 107, 77. Anal. Calcd. for C₁₀H₁₂Cl₂O₂: C, 51.04; H, 5.14; Cl, 30.17; O, 13.63. Found: C, 51.09; H, 5.14; Cl, 30.16; O, 13.61.

1,2-Bis(chloromethyl)-4,5-dimethoxybenzene (12). White solid, m.p.: 118-121 °C. IR (KBr, cm⁻¹): 2978, 2864, 1638, 1510, 1459, 1385, 1162, 894, 808, 665. ¹H NMR (400 MHz, CDCl₃) δ = 3.90 (s, 6H, CH₃), 4.65 (s, 4H, CH₂), 7.18 (s, 2H, Ar-H) ppm. ¹³C NMR (400 MHz, CDCl₃) δ = 40.7, 54.8, 114.3, 126.8, 148.4 ppm. MS (EI, 70 eV) m/z (%): 234 (M⁺), 199, 185, 151, 137, 107, 77. Anal. Calcd. for C₁₀H₁₂Cl₂O₂: C, 51.03; H, 5.16; Cl, 30.18; O, 13.61. Found: C, 51.09; H, 5.14; Cl, 30.16; O, 13.61.

1,3-Bis(chloromethyl)-4,6-dimethoxybenzene (13). White solid, m.p.: 112-114 °C. IR (KBr, cm⁻¹): 2986, 2857, 1642, 1506, 1467, 1384, 1155, 887, 814, 668. ¹H NMR (400 MHz, CDCl₃) δ = 3.92 (s, 6H, CH₃), 4.68 (s, 4H, CH₂), 7.10 (s, 1H, Ar-H), 7.29 (s, 1H, Ar-H) ppm. ¹³C NMR (400 MHz, CDCl₃) δ = 40.6, 54.6, 97.3, 114.8, 133.2, 154.7 ppm. MS (EI, 70 eV) m/z (%): 234 (M⁺), 199, 185, 151, 137, 107, 77. Anal. Calcd. for C₁₀H₁₂Cl₂O₂: C, 51.05; H, 5.15; Cl, 30.19; O, 13.61. Found: C, 51.09; H, 5.14; Cl, 30.16; O, 13.61.

RESULTS AND DISCUSSION

The initial study was carried out using biphenyl as the substrate to optimize the reaction conditions, the dichloromethylation of biphenyl was carried out in oil-water biphasic system in the presence and absence of $[C_{12}\text{minPEG}_{800}]\text{Br}$ at first. As shown in Fig. 1, in the absence of $[C_{12}\text{minPEG}_{800}]\text{Br}$, the chloromethylation reaction proceeded very slowly, the yield was less than 12% after 24 h, and the selectivity was only 67%. The results mean that hydrochloric acid does not work as an effective catalyst for the chloromethylation. Reaction performed with $[C_{12}\text{minPEG}_{800}]\text{Br}$ at a catalytic amount of 0.3 equiv was proceeded very rapidly and the yield reached 90% in a shorter time (10 h), the selectivity was increased to 98%. However, the selectivity and the yield were not enhanced significantly with further increase in the reaction time.

Figure 2 shows the influences of the amount of $[C_{12}\text{minPEG}_{800}]\text{Br}$ on the dichloromethylation. The yield and the selectivity increased with the amount of $[C_{12}\text{minPEG}_{800}]\text{Br}$ and reached maximum at 0.3 equiv. of the promoter was used. By further addition of $[C_{12}\text{minPEG}_{800}]\text{Br}$, the yield and selectivity were not changed significantly. The subsequent experiments on optimum conditions revealed that 10 h and 0.3 equiv of the promoter were necessary to complete the reaction. Besides $[C_{12}\text{minPEG}_{800}]\text{Br}$, four other types of ionic liquids, $[C_{12}\text{minPEG}_{200}]\text{Br}$, $[C_{12}\text{minPEG}_{400}]\text{Br}$, $[C_{12}\text{minPEG}_{600}]\text{Br}$ and $[C_{12}\text{minPEG}_{1000}]\text{Br}$ were tested as catalysts in the reaction (Table 1, entries 2-5); it was observed that $[C_{12}\text{minPEG}_{800}]\text{Br}$ and $[C_{12}\text{minPEG}_{1000}]\text{Br}$ resulted in the best performance, providing 98% and 97% high yields, respectively. Considering all the factors comprehensively, $[C_{12}\text{minPEG}_{800}]\text{Br}$ was selected as the best catalyst precursor. The different catalytic abilities of ILs may be attributed to their different abilities of forming homogeneous catalysis mediums with methylcyclohexane. Under the same conditions, the IL that forms homogeneous catalysis medium in combination with methylcyclohexane, will lead to a larger increase in the effective reactant concentration, which increases the encounter probability between biphenyl and reactive species. Thus, faster reaction rate and higher yield of the reaction is obtained.

The influences of the amount of paraformaldehyde on the dichloromethylation are shown in Fig. 3. No reaction occurred

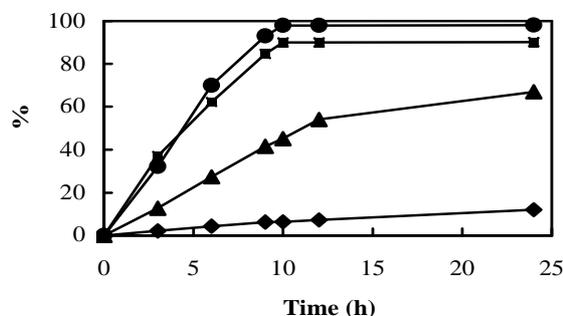


Fig. 1. Influences of the presence and absence of $[C_{12}\text{minPEG}_{800}]\text{Br}$ on the yield and selectivity dichloromethylation: yield (no IL, ◆), yield (with IL, ■), selectivity (no IL, ▲), selectivity (with IL, ●). Reaction conditions: BP (0.1 mol), paraformaldehyde (0.6 mol), $[C_{12}\text{minPEG}_{800}]\text{Br}$ (0.03 mol), conc. HCl (70 ml), methylcyclohexane (70 ml), anhydrous hydrogen chloride gas (80 ml min^{-1}), 70 °C:

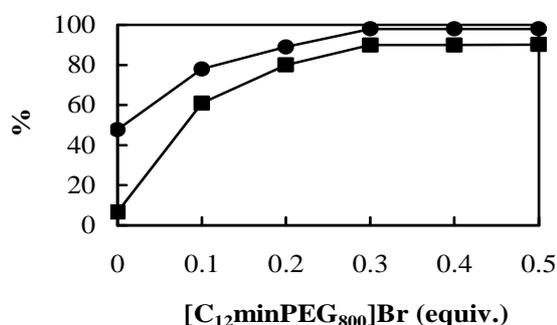


Fig. 2. Influences of amount of $[C_{12}\text{minPEG}_{800}]\text{Br}$ on the yield (■) and selectivity (●) of dichloromethylation. Reaction conditions: BP (0.1 mol), paraformaldehyde (0.6 mol), conc. HCl (70 ml), methylcyclohexane (70 ml), anhydrous hydrogen chloride gas (80 m min^{-1}), 70 °C, 10 h.

in the absence of paraformaldehyde, and an increase in the amount of paraformaldehyde enhanced the reaction yield and selectivity until a $(\text{CH}_2\text{O})_n/\text{BP}$ ratio of 6 is reached. However, further addition of formaldehyde resulted in the decrease of

Table 1. Synthesis of 4,4'-Bis(chloromethyl)biphenyl with [C₁₂minPEG_n]Br/methylcyclohexane^a

Entry	Ionic liquid	Time (h)	Yield (%) ^b	Selectivity (%) ^c
1	[C ₁₂ minPEG ₈₀₀]Br	10	90	98
2	[C ₁₂ minPEG ₂₀₀]Br	14	72	88
3	[C ₁₂ minPEG ₄₀₀]Br	12	79	91
4	[C ₁₂ minPEG ₆₀₀]Br	10	84	95
5	[C ₁₂ minPEG ₁₀₀₀]Br	10	91	97

^aReaction conditions: BP (0.1 mol), paraformaldehyde (0.6 mol), [C₁₂minPEG_n]Br (0.03 mol), conc. HCl (70 ml), methylcyclohexane (70 ml), anhydrous hydrogen chloride gas (80 ml min⁻¹), 70 °C. ^bIsolated yield. ^cIsolated selectivity.

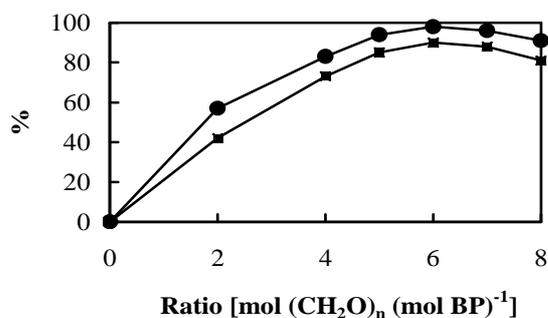


Fig. 3. Influences of amount of paraformaldehyde on the yield (■) and selectivity (●) of dichloromethylation. Reaction conditions: BP (0.1 mol), [C₁₂minPEG₈₀₀]Br (0.03 mol), conc. HCl (70 ml), methylcyclohexane (70 ml), anhydrous hydrogen chloride gas (80 ml min⁻¹), 70 °C, 10 h.

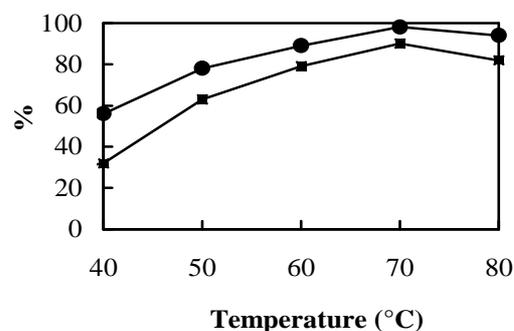


Fig. 4. Influences of temperature on the selectivity (●) and yield (■) of dichloromethylation. Reaction conditions: BP (0.1 mol), paraformaldehyde (0.6 mol), conc. HCl (70 ml), methylcyclohexane (70 ml), [C₁₂minPEG₈₀₀]Br (0.03 mol), anhydrous hydrogen chloride gas (80 ml min⁻¹), 10 h.

the yield. This is due to the formation of poly(chloromethyl)biphenyls, as observed in the LC chromatogram, although we did not identify their structures. Figure 4 shows the influences of reaction temperature on the dichloromethylation. The catalytic activities increased with increasing reaction temperature. Maximum yield and selectivity was reached at 70 °C; however, the yield and the selectivity decreased with further increase in temperature.

In addition, the catalytic system could be typically recovered and reused for subsequent reactions with no appreciable decrease in yields and reaction rates (Fig. 5). The recycling process performed as follows. The upper layer of

methylcyclohexane (organic layer), containing product, was removed by decantation and the lower layer of catalytic system (aqueous layer) was concentrated to remove generated water through water knockout drum. Fresh substrates and methylcyclohexane were then recharged to the [C₁₂minPEG₈₀₀]Br catalytic system, and the mixture was heated to react once again. Only 4.0% loss of weight was observed after 8 times recycling.

With these results in hand, the catalytic system was then applied to some other aromatic hydrocarbons as summarized in Table 2. It is seen that aromatic hydrocarbons such as xylene, dimethoxybenzene and 1,2,3,4-tetrahydronaphthalene

Efficient Dichloromethylation of Some Aromatic Hydrocarbons

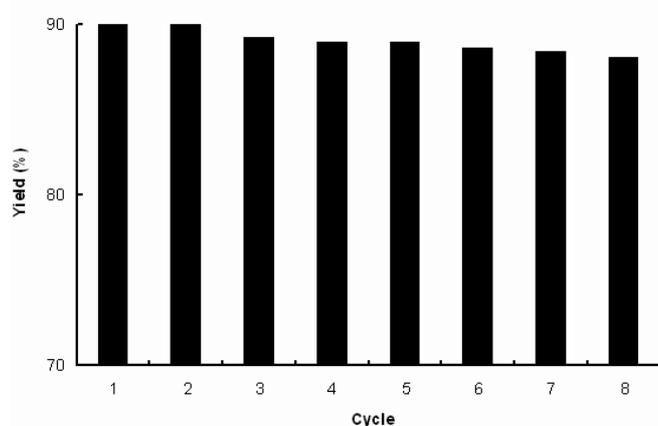


Fig. 5. Repeating reactions using recovered $[C_{12}minPEG_{800}]Br$. Reaction conditions: BP (0.1 mol), paraformaldehyde (0.6 mol), methylcyclohexane (70 ml), recovered catalytic system ($[C_{12}minPEG_{800}]Br/conc. HCl$), anhydrous hydrogen chloride gas ($80 ml min^{-1}$), $70 ^\circ C$, 10 h.

have been successfully resulted in the formation of corresponding dichloromethyl-substituted products in good to high yields (Table 2, entries 2-4, 6 and 7-9), although the yields of **8**, **10** and **12** were a little lower, in contrast to other products **6**, **7**, **9**, **11** and **13**, and their selectivities were only 90%, 92% and 89%, respectively. While in the case of benzene, as a less active substrate for the dichloromethylation, much lower selectivity and yield were obtained even under more drastic reaction conditions (Table 2, entry 1).

The excellent catalytic abilities of $[C_{12}minPEG_{800}]Br$ /methylcyclohexane suggest the dichloromethylation among aromatic hydrocarbons, hydrochloric acid, formaldehyde, methylcyclohexane and $[C_{12}minPEG_{800}]Br$ has a particular mechanism.

A review of the literatures [40-42] shows that the chloromethylation by treatment with formaldehyde and HCl, $^+CH_2OH$ and chloromethyl cation ($^+CH_2Cl$) are the species frequently suggested. It is highly impossible that the $^+CH_2Cl$ exists in any chloromethylation systems, particularly in aqueous solutions under mild conditions. The dichloromethylation belongs to the further reaction on the basis of the mono-chloromethylation. This has been well confirmed by the experiment of benzene (Table 2, entry 1),

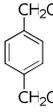
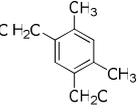
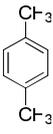
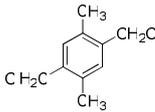
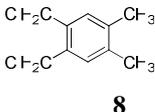
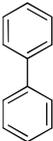
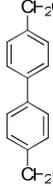
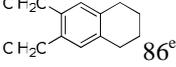
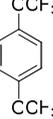
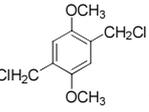
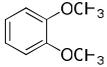
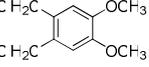
which resulted in 27% yield of the mono-chloromethylated product benzyl chloride. Based on the experimental results obtained and literature reports, a possible mechanism for the dichloromethylation of aromatic hydrocarbons is shown in Scheme 2.

Before the chloromethylation, there exists an obvious oil-water biphasic system, and the lower layer (water phase) consists of $[C_{12}minPEG_{800}]Br$, hydrochloric acid and formaldehyde, and the upper layer (oil phase) consists of methylcyclohexane and aromatic hydrocarbons (substrates). During the process of chloromethylation, the oil-water biphasic system disappears and a homogeneous reaction medium is formed. It is considered that the activation of formaldehyde is a first step for the enhancement of the chloromethylation. Firstly, depolymerization of paraformaldehyde by acid catalysis of hydrochloric acid yields formaldehyde which reacts with proton (H^+) to yield hydroxymethyl cation ($^+CH_2OH$). Then, an electrophilic substitution reaction occurs by subsequent attack of the $^+CH_2OH$ on benzene ring of aromatic hydrocarbons to give aromatic carbinol. The resulting alcohol under the action of acid gives a benzyl carbonium ion and water very rapidly. Finally, the benzyl carbonium ion reacts with anions Cl^- to yield the desired products. After the completion of the reaction, a complete phase-separation is occurred again after being cooled to room temperature; the upper layer of methylcyclohexane, containing product was removed by decantation. Then the lower layer containing $[C_{12}minPEG_{800}]Br$ and hydrochloric acid, was concentrated to remove water produced in the reaction through water knockout drum, for the recycling. The thermoregulated biphasic behavior of $[C_{12}minPEG_{800}]Br$ (*i.e.*, mono-phase at high temperature and bi-phase at room temperature) plays a very important role in the chloromethylation process; in fact, it will results in local concentration of the reacting species and, consequently, in a large increase in the effective reactant concentration and excellent catalytic effects.

CONCLUSIONS

A series of new imidazolium-type ionic liquids based on polyethylene glycol (PEG) have been prepared. It was found that the $[C_{12}minPEG_{800}]Br$ /methylcyclohexane system results

Table 2. Synthesis of Some Dichloromethyl-Substituted Aromatic Hydrocarbons with [C₁₂minPEG₈₀₀]Br /Methylcyclohexane^a

Entry	Substrate	Temperature (°C)	Time (h)	Selectivity (%) ^b	Products and yields (%) ^c
1		80	14	72	 70 ^d 5
2		60	8	100	 93 6
3		60	8	100	 94 ^e 7
4		60	8	90	 84 8
5		70	10	98	 90 9
6		60	8	92	 86 ^e 10
7		60	8	100	 96 ^e 11
8		60	8	89	 83 ^e 12

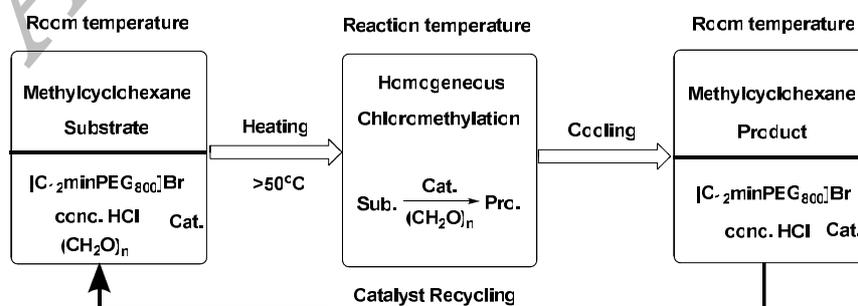
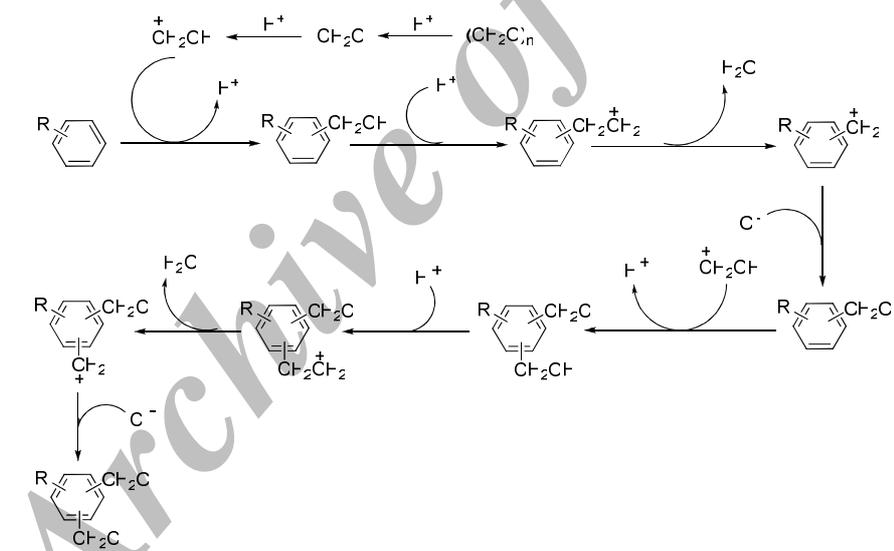
Efficient Dichloromethylation of Some Aromatic Hydrocarbons

Table 2. Continued

9		60	8	100		95 ^e
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13

^aReaction conditions: aromatic hydrocarbon (0.1 mol), paraformaldehyde (0.6 mol), [C₁₂minPEG₈₀₀]Br (0.03 mol), conc. HCl (70 ml), methylcyclohexane (70 ml), anhydrous hydrogen chloride gas (80 ml min⁻¹). ^bIsolated selectivity. ^cIsolated yield. ^d27% Yield of the mono-chloromethylated product benzyl chloride was obtained. ^eNew compounds.



Scheme 2. Possible mechanism for dichloromethylation of aromatic hydrocarbons

in an excellent temperature-dependent phase behavior for the dichloromethylation of some aromatic hydrocarbons, which is capable of converting aromatic hydrocarbons into the corresponding dichloromethyl-substituted products in good to excellent isolated yield under homogeneous catalysis in aqueous media. [C₁₂minPEG₈₀₀]Br could be efficiently recovered by simple decantation after reaction without any apparent loss of catalytic activity and little loss of weight even after 8 times recycling. Mild reaction conditions, ease of workup, high yields, stability, easy isolation of the compounds, good thermoregulated biphasic behavior of the IL, and excellent recycle-ability of the catalyst are all the attractive features of this methodology. Further aspects of the catalysis of the proposed system and its application to other organic synthesis are under investigation.

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