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# Ionic liquids for tetraarylporphyrin preparation

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**Abstract**—In place of widely used dichloromethane, a series of ionic liquids, ILs, was employed as a reaction medium for the one-flask preparation of tetraarylporphyrins. The porphyrin yield in the IL was comparable to that in the dichloromethane, as long as both the water content and the fluidity were conditioned to be in the optimum state. When acidic IL, [$C_4$-SAbim][$CF_3SO_3$] possessing a sulfonic acid moiety was used as the reaction medium, nothing but a black tarry by-product was obtained due to its strong acidity. However, using the acidic IL in a biphasic mode together with dichloromethane enabled porphyrins to form, even at a high reactant concentration. Furthermore, the phase-separated acidic IL was reusable for at least 10 times without any loss of catalytic activity.

## 1. Introduction

Condensation of benzaldehyde with pyrrole followed by oxidation provides tetraphenylporphyrin (TPP),[1] *N*-confused tetraphenylporphyrin (NC-TPP)[2] and black tarry by-products. By using dichloromethane as the reaction medium, Lindsey demonstrated the top yields to be ca. 50 and 39% for TPP and NC-TPP, respectively.[1] Due to the excellent yield, mild condition and convenience, the Lindsey method has since been widely applied for the syntheses of porphyrins. This method, however, entails a heavy consumption of dichloromethane and results in a waste of acid catalysts. To obtain 1.0 g NC-TPP (1.0 g TPP), for instance, as much as 5 L (2 L) dichloromethane needs to be mounted in the reaction vessel under the optimal conditions when utilising the Lindsey method,[1b] which employs methanesulfonic acid, M-SA, as the acid catalyst. We thus, feel that the need, both to reduce the use of the halogenated solvent and to heighten the reusability of the acid catalyst without any loss of the productivity in the porphyrin preparation for the green chemistry.

ILs have been widely used for various reactions[3] such as olefin oligomerisation,[4] Heck reaction,[5] hydrogenation,[6] Friedel-Crafts reaction,[7] Diels–Alder reaction,[8] and several condensation reactions.[9] However, no such application of ILs for the preparation of porphyrins has been attempted before, except for that described in our previous brief report.[10] If the green property born from IL could be applicable to the preparation of porphyrins, then it may be possible to undertake the Lindsey procedure without the need for the halogenated solvent. Our objective in this study, is to utilize ILs in the preparation of porphyrins with the aim of reducing and replacing the halogenated solvent.

In this study, we chose a series of ILs ranging from class I to class III, as shown in Chart 1, and we examined their behavior as a medium. The viscosity and water content of the ILs used are both well-known factors[11] that generally affect reactivity. Thus, these two factors in particular were carefully considered in the usage of IL as a single

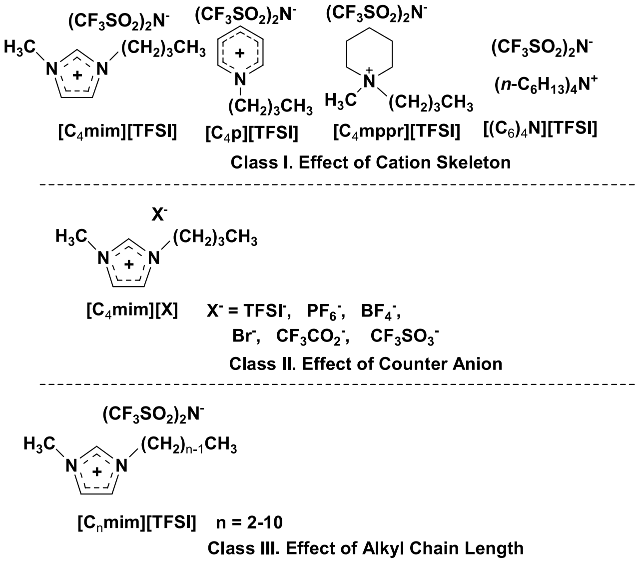

**Chart 1.**

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*Keywords*: Ionic liquid; Porphyrin; Condensation.

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homogeneous medium. As a result, the hydrophobic and moderately fluid [$C_4$mim] [TFSI] was the most appropriate medium for the porphyrin formation. However, reusing the IL as a homogeneous reaction medium was impractical due to the readily contamination of the produced by-product. In place of the homogeneous system, a biphasic mode reaction was devised for the porphyrin formation. In the case of the acidic IL, [$C_4$-SAbim][$CF_3SO_3$] in Figure 1, its usage in the biphasic mode together with dichloromethane was studied with a view to reducing the amount of halogenated solvent and reusing the acid IL.

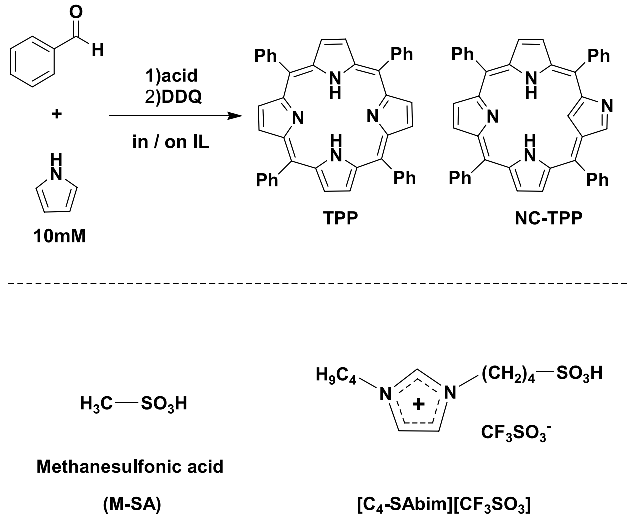


**Figure 1.** Acids and porphyrin formation.

## 2. Results and discussion

### 2.1. Classification of ILs

The IL derivatives employed in this study, can be categorized into four groups, as shown in Chart 1 and Figure 1. The relationship between the molecular structure of ILs and their role in the formation of porphyrin can be established in terms of this classification, and it is likely to be applicable to other condensation reactions.

In class I salts, five different cationic skeletons are selected in combination with the same anion, bis(trifluoromethylsulfonyl)imide $[TFSI]^-$ (Table 1). The cation structure effect on porphyrin formation will be discussed in terms of the viscosity. Class II, [$C_4$mim][X], ILs are represented by the hydrophobicity/hydrophilicity of the corresponding anions. [$C_n$mim] [TFSI]s are the class III salts in which alkyl chains of differing lengths are introduced in order to regulate both the viscosity and the hydrophobicity. Class IV imidazolium salt possesses a single sulfonic acid moiety, which acts as a catalyst, as shown in Figure 1.

**Table 1**. The class I ILs used for porphyrin preparation

| Solvent | Viscosity of IL/cP | $H_2O$ content of IL/wt% | Yield/% | |
|---|---|---|---|---|
| | | | TPP | NC-TPP |
| [$C_4$mim][TFSI] | 50.2 | 0.12 | 41 | 7 |
| [$C_4$p][TFSI] | 63.5 | 0.08 | 33 | 4.2 |
| [$C_4$mppr][TFSI] | 192 | 0.11 | 23 | 0 |
| [$(C_6)_4N$][TFSI] | 573.4 | 0.12 | 2 | 0 |
| $CH_2Cl_2$ | — | — | 8 | 38 |

[Pyrrole] = [aldehyde] = [DDQ] = 10 mM, [M-SA] = 7 mM, 22 °C, reaction time 30 min, yields were determined by HPLC analysis.

Since, porphyrin formation begins with the condensation, the ILs used were kept as dry as possible by means of a thermostatic vacuum oven, 0.08 mmHg, 60 °C, over a period of 24 h. After an IL was taken out from the drying vacuum oven, the water content was immediately measured by a Karl-Fischer moisture titrator. Although, all the ILs were dried under the same conditions, the water content varied greatly according to the salt structure, as shown in Table 2.

**Table 2**. Porphyrin preparation in class II ILs with various anions

| Solvent | Viscosity of IL/cP | $H_2O$ content of IL/wt% | Yield/% | |
|---|---|---|---|---|
| | | | TPP | NC-TPP |
| [$C_4$mim][TFSI] | 50.2 | 0.12 | 41 | 7 |
| [$C_4$mim][$PF_6$] | 289 | 0.22 | 11 | 4 |
| [$C_4$mim][$BF_4$] | 92.2 | 1.09 | 0.8 | 0.3 |
| [$C_4$mim][Br] | 1462 | 2.45 | 0.1 | 0 |
| [$C_4$mim][$CF_3CO_2$] | 71.2 | 2.1 | 0.5 | 0 |
| [$C_4$mim][$CF_3SO_3$] | 93.2 | 1.62 | 0.3 | 0.7 |

[Pyrrole] = [aldehyde] = [DDQ] = 10 mM, [M-SA] = 7 mM, 22 °C, reaction time 30 min, yields were determined by HPLC analysis.

### 2.2. Screening to cationic skeletons/class I ILs

Five cationic structures, imidazolium, pyridinium, piperidinium, and ammonium were tested to see if their solvent properties were suitable for porphyrin formation. Table 1 shows that all the ILs except for the *n*-hexylammonium bis(trifluoromethylsulfonyl)imide [$(C_6)_4N$][TFSI] can be used as the reaction medium in place of dichloromethane, except with regard to the selectivity for *N*-confusion.[12] The ammonium [$(C_6)_4N$][TFSI], however, did not work as a medium for porphyrin formation at all. While there is no appreciable difference in water content, the viscosity is reflected by the cationic skeleton structure. Since the most viscous, 573.4 cP, ammonium [$(C_6)_4N$][TFSI] and the most fluid, 50.2 cP, imidazolium [$C_4$mim][TFSI] show the worst and the best yields, respectively, viscosity can be assumed to be one of the keys to regulating porphyrin formation.

### 2.3. Screening of counter anions/class II ILs

The counter anion on the 1-butyl-3-methylimidazolium, $C_4$mim, divides the class II salts into water-soluble and water phase-separable groups. When the former, [$C_4$mim] [$BF_4$], [$C_4$mim][Br], [$C_4$mim][$CF_3CO_2$], and [$C_4$mim] [$CF_3SO_3$], were used as the solvent, porphyrins were obtained at less than 1% in total yield. On the other hand, the latter, [$C_4$mim][TFSI] and [$C_4$mim][$PF_6$], produced porphyrins at 49 and 15% in total yield, respectively. The gap in the yield between [$C_4$mim][TFSI] and [$C_4$mim][$PF_6$] would seem to originate from their difference in viscosity. The amount of water remaining in the former ILs is five to

20 times more than that in the latter ILs. Water content of more than 1 wt% in the water-soluble IL would perturb the condensation between pyrrole and benzaldehyde, resulting in a poor porphyrin yield.

### 2.4. Intended addition of water

To exemplify that the contained water disturbs the condensation reaction, a certain amount of water was intentionally added to the [$C_4$mim][TFSI]. Five [$C_4$mim][TFSI]s possessing a different water content were prepared for porphyrin formation. Figure 2 shows the relation between porphyrin yield and water content, in addition to the change in viscosity. When the water content in [$C_4$mim][TFSI] was increased, the yields of both TPP and NC-TPP deteriorated in accordance with decreasing viscosity, from 50 cP down to 33 cP. It is obvious that porphyrins are noticeably less obtainable if the amount of water which remains exceeds 1.0 wt%. In general, increasing fluidity of a viscous medium results in facilitating a reaction. Nevertheless, Figure 2 demonstrates the opposite result as to the relation between yield and viscosity. The effect of the disadvantage due to the remaining water outways the benefit stemming from the fluidity increase, as long as the water content ranges below 50 cP.

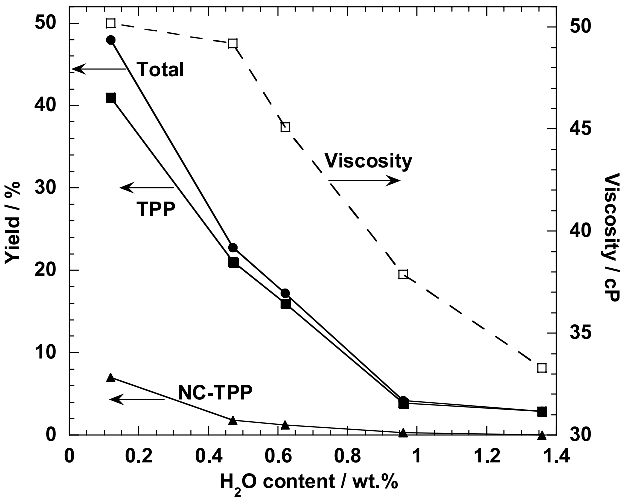


**Figure 2.** Porphyrin preparation in [$C_4$mim][TFSI] with various amounts of water content.

### 2.5. Alkyl chain length effect in class III, $C_n$mims

In the case, where the viscosity is below 50 cP, as shown in Figure 2, how much water exists is much more important than how low the viscosity is. To examine the influence of a viscosity of more than 50 cP on the yield of porphyrins, a set of [$C_n$mim][TFSI]s, $n=2, 3, 4, 5, 6, 7, 8, 9$, and 10, was used for the condensation reaction.

Figure 3 compares the viscosity with the contained water in terms of the alkyl chain length, and shows the relation between porphyrin yield and these two features. It can be confirmed[13] that the viscosity varies with the alkyl chain length, that is, as the alkyl chain becomes longer, the salt becomes more viscous and more hydrophobic. The viscosity for [$C_{10}$mim][TFSI] and for [$C_2$mim][TFSI] is more than double and nearly half of that for [$C_4$mim][TFSI], respectively. In contrast, the amount of water, which remains shows the opposite tendency with regard to alkyl chain length. As long as the water, which remains in the ILs with a longer alkyl than butyl chain length (from [$C_5$-mim][TFSI] to [$C_{10}$mim][TFSI]) is less than one-sixth that in the [$C_4$mim][TFSI], then the [$C_2$mim][TFSI] and [$C_3$-mim][TFSI] contain more water than the [$C_4$mim][TFSI] does. In particular, the amount of water remaining in the [$C_2$mim][TFSI] is four times that in the [$C_4$mim][TFSI].

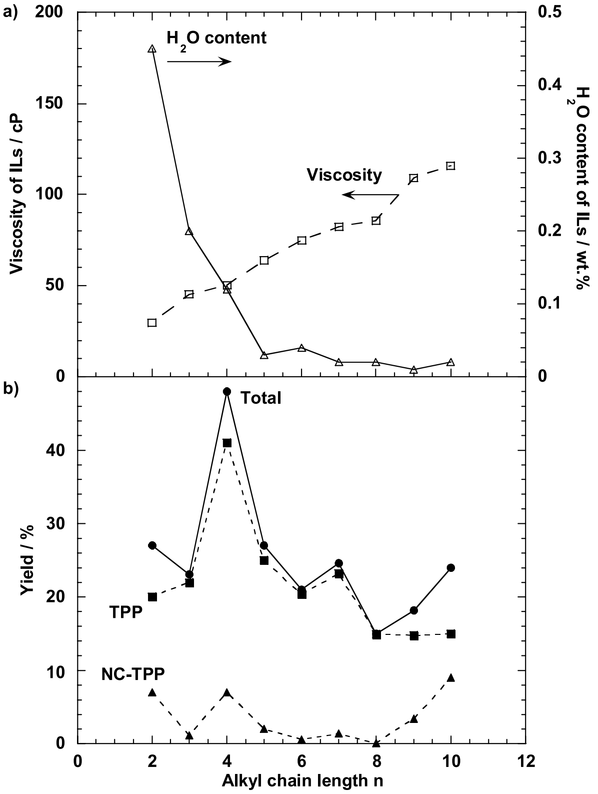


**Figure 3.** The relationship between alkyl chain length $n$ ($n=2$–10) of [$C_n$mim][TFSI] and porphyrin yield, viscosity, and water content; (a) viscosity and water content of the class III ILs, (b) porphyrin productivity in the class III ILs.

As shown in Figure 3b, all the ILs used, except for [$C_4$mim][TFSI], provided TPP in yields of 20±5%. Only the [$C_4$mim][TFSI] produced twice as much TPP as the other ILs with an alkyl chain length shorter or longer than the butyl chain length. Increasing the alkyl chain length makes an IL, which is viscous enough to limit diffusion of the substrates in return for reducing the amount of remaining water, due to increased hydrophobicity. When the viscosity ranges beyond 50 cP, the former as to the diffusing factor governs the porphyrin formation. On the other hand, in the case of [$C_2$mim][TFSI] and [$C_3$-mim][TFSI], the large amount of remaining water is the leading reason for an impaired reaction. This is why butyl [$C_4$mim][TFSI] shows the maximum TPP productivity against the alkyl chain length. In other words, the butyl chain is an optimal point of length in the trade-off relation between the remaining water and the viscosity.[14]

## 2.6. [$C_4$-SAbim][$CF_3SO_3$] and M-SA

Davis et al. reported[15] [$C_4$-SAbim][$CF_3SO_3$] catalyzed esterification,[15] and Friedel-Crafts alkylation.[16] Since, the acid moiety in [$C_4$-SAbim][$CF_3SO_3$] also seems to catalyze porphyrin formation, the acidic IL was compared with the typical acid catalyst, M-SA. Entries 2–5 in Table 3 summarize the results. The acidity of neat [$C_4$-SAbim][$CF_3SO_3$] is too strong to form the aromatic rings, as shown in entry 2. Hence, the acidic IL is diluted with the widely used [$C_4$mim][TFSI] and tested as entry 3. Since, the acid concentration generally affects porphyrin formation, as shown in entries 4 and 5, the concentration of [$C_4$-SAbim][$CF_3SO_3$] in [$C_4$mim][TFSI] was set to be the same as that of 7 mM M-SA. Entry 3 shows that the [$C_4$mim][TFSI] solution of [$C_4$-SAbim][$CF_3SO_3$] produced TPP and NC-TPP in yields of 46 and 5%, respectively, without the addition of any acid catalyst. The total yield, 51% in entry 3, is larger than that of the M-SA catalyzed reaction, 44% in entry 5. This fact indicates that similar to M-SA, the diluted [$C_4$-SAbim][$CF_3SO_3$] with [$C_4$mim][TFSI] acts as an effective catalyst to form a porphyrin ring, apart from the selectivity for TPP and NC-TPP.[12]

It is true that the hydrophobic and moderately fluid [$C_4$mim][TFSI] containing [$C_4$-SAbim][$CF_3SO_3$] allows us to conduct the porphyrin synthesis without using the halogenated solvent in excellent yield, as well as the hydrophobic IL possessing M-SA as shown in Table 2. However, both of the two acidic systems utilizing the [$C_4$mim][TFSI] have a serious problem when using them as a homogeneous reaction medium. It is the contamination stemmed from the tarry by-products with which the formation of the porphyrin ring is impaired as described below. To avoid the fatal defect, we have devised the following biphasic mode reaction.

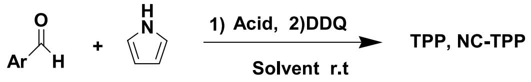
## 2.7. Biphasic reaction of acidic IL and dichloromethane

As confirmed above, well-devised ILs are employable as the reaction medium for porphyrin formation in place of the widely used halogenated solvent. However, the ILs used are unlikely to be reused for the reaction due to the difficulty in removing the dissolved black tarry by-products from the ILs. Unlike the porphyrins, the tar, which emerged from the oxidation step could not be taken away from the non-volatile IL by extraction with a halogenated solvent. Thus, the difficulties entailed in reusing of the costly ILs become a serious problem for green synthesis. To avoid the inherent demerit arising from the tar contamination without losing any productivity with regard to porphyrins, we devised a biphasic reaction arising from the interface between dichloromethane and the acidic IL.

Prior to monitoring the reaction, we confirmed the miscibility between dichloromethane and [$C_4$mim][TFSI] containing the acid catalyst, M-SA or [$C_4$-SAbim][$CF_3SO_3$]. Mixing [$C_4$mim][TFSI] with dichloromethane, at broad volume ratio ranging from 1/20 to 20/1, shows a single phase, not the phase-separated situation regardless of the added acid. Furthermore, the tested imidazolium ILs shown in Table 2 all are well miscible with dichloromethane regardless of the counter anion. As opposed to these homogeneous situations, undiluted [$C_4$-SAbim][$CF_3SO_3$] itself is fortunately immiscible with dichloromethane as shown in Figure 4, thereby enabling us to perform a biphasic mode reaction. The phase-separated situation not only permits us to readily recycle the ILs, it might also suppress the dissolution of the [$C_4$-SAbim][$CF_3SO_3$] into dichloromethane. The superior immiscibility of the acidic IL would originate from the hydrophilic, that is, oleophobic sulfonic acid moiety.

Dichloromethane (10 mL) was placed on the [$C_4$-SAbim][$CF_3SO_3$] (3 mL) in a test tube, having formed the interface ($\phi$ 1.6 mm, 200 $mm^2$) had been formed at 22 °C. This biphasic solution was allowed to stand for 10 min. Adding neat pyrrole (14.5 mM) and benzaldehyde (14.5 mM) onto the upper solution immediately resulted in the appearance of color in the dichloromethane phase. The color stemming from the precursors of the porphyrins (porphyrinogen) heightened over time, as shown in Figure 4. Unlike the dichloromethane solution, the IL phase was not colored at all during the reaction period. After 20 min, the dark brown dichloromethane solution was separated from the IL phase and then oxidized by the addition of powdered DDQ

**Table 3**. Porphyrin preparation utilizing [$C_4$-SAbim][$CF_3SO_3$][a] at a low reactant concentration



| Entry | Acid/$mm^2$ or mM | Solvent | [Reactant]/mM | Time[b]/min | Yield/% | |
|---|---|---|---|---|---|---|
| | | | | | TPP | NC-TPP |
| 1[a] | Interface 200 $mm^2$ at [$C_4$-SAbim][$CF_3SO_3$]/$CH_2Cl_2$ | $CH_2Cl_2$ | 14.5 | 20 | 43 | 10 |
| 2[c] | [$C_4$-SAbim][$CF_3SO_3$] neat | [$C_4$-SAbim][$CF_3SO_3$][d] | 10 | 5 | 0 | 0 |
| 3[c] | [$C_4$-SAbim][$CF_3SO_3$] 7 | [$C_4$mim][TFSI] | 10 | 30 | 46 | 5 |
| 4[e] | M-SA 0.32 | $CH_2Cl_2$ | 10 | 480 | 43 | 10 |
| 5[e] | M-SA 7 | $CH_2Cl_2$ | 10 | 30 | 5 | 39 |

Reaction condition; 22 °C, [aldehyde] = [pyrrole], [oxidant] = [reactant].

[a] This work; yields were determined after recrystallization.

[b] Condensation time.

[c] This work; yields were determined by HPLC analysis.

[d] The viscosity is 3185 cP and the water content is 1.85 wt%.

[e] Lindsey Method; data from Ref. 1, yields were determined by HPLC analysis without recrystallization.

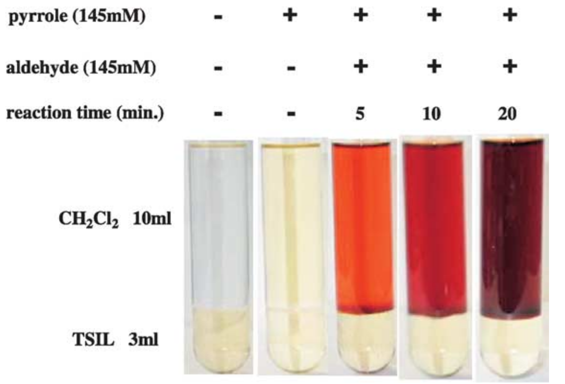


**Figure 4.** Photograph showing colour change due to condensation reaction at the interface between $CH_2Cl_2$ and acidic IL. Room temperature +/−: denotes the presence/absence, respectively.

(342 mg, 14.5 mM) at 22 °C. Triethylamine (100 μL) was added to the black solution which formed, in order to quench the dissolved acid. Subsequent treatments for the isolation of porphyrins were conducted according to the literature.[1] Recrystallized TPP and NC-TPP were obtained at yields of 43 and 10%, respectively (Table 3, entry 1). Table 3 compares the present biphasic reaction with the Lindsey method[1] using M-SA in dichloromethane. It is obvious that the biphasic procedure is broadly comparable in yield to the single homogeneous reaction (entries 1, 4, and 5), regardless of the selectivity[12] for the ordinal and *N*-confused porphyrins.

To minimize the amount of dichloromethane solvent, we examined the formation of porphyrins at a 10-fold higher reactant concentration, 145 mM, on the interface (Table 4, entry 1). The isolated yield of TPP at 145 mM on the acidic IL interface was as little as 16% less than that at 14.5 mM (Table 3, entry 1), but two to eleven times more than that at 100 mM of the homogeneous condensation employing M-SA. This fact means that, in spite of some loss in efficiency, the interfacial reaction using $[C_4\text{-SAbim}][CF_3SO_3]$ is suitable for the case of a high reactant concentration, when compared to the homogeneous reaction. Separating the acid catalysis from the reaction medium is beneficial for increasing the production of porphyrins, particularly at a high concentration. This knowledge leads to a reduction in the amount of halogenated solvent, which needs to be used.

## 2.8. Need of interface

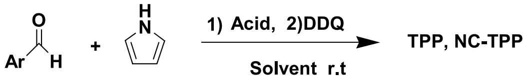
Increasing the concentration of the M-SA and/or the reactants generally results in a low yield of porphyrins due to oligomer formation,[1a] as shown in Table 4. When dichloromethane solution, which was saturated or partially dissolved with $[C_4\text{-SAbim}][CF_3SO_3]$ (Table 4, entries 7 and 8) was applied as a homogeneous single phase, low yields, 7–11% TPP and 2–4% NC-TPP, were observed similar to the dichloromethane solution of M-SA (Table 4, entries 9 and 10). These facts indicate that the presence of the acidic IL phase through the interface helps facilitate the condensation in the dichloromethane phase, even at a high reactant concentration.

## 2.9. Reusing acidic IL at a high reactant concentration

In addition to the above benefit, another advantage, which results form devising the separated phase of the $[C_4\text{-SAbim}][CF_3SO_3]$ is its reusability. Table 5 shows the relation between the repeated use of $[C_4\text{-SAbim}][CF_3SO_3]$ and the preparation of TPP, NC-TPP, tetra-*p*-tolylporphyrin (TTP), and *N*-confused tetra-*p*-tolylporphyrin (NC-TTP). To reduce the amount of dichloromethane as much as possible, the reactant concentration was set to be 145 mM, which was more than 10 times that which had been explored for the optimum concentration in the Lindsey method.[1] After the condensation, the upper dichloromethane phase was removed from the acidic IL phase. Fresh dichloromethane solution of the reactants was added to the remaining $[C_4\text{-SAbim}][CF_3SO_3]$, being as a single phase in the test tube, in order to start the biphasic reaction again. On the other hand, powdered DDQ was added to the removed dichloromethane solution and the porphyrins, which formed were isolated. The area of the interface was ca. 200 mm$^2$. This procedure was repeated 10 times at 22 °C, without supplying any acid catalysts.

In addition, the manner in which vigorous shaking of the phase-separated system affects the reaction was estimated

**Table 4**. $[C_4\text{-SAbim}][CF_3SO_3]/CH_2Cl_2$ biphasic system for porphyrin formation at a high reactant concentration



| Entry | Acid/mm$^2$ or mM | Solvent | [Reactant]/mM | Time[a]/min | Yield/% | |
|---|---|---|---|---|---|---|
| | | | | | TPP | NC-TPP |
| 6[b] | Interface 200 mm$^2$ at $[C_4\text{-SAbim}][CF_3SO_3]/CH_2Cl_2$ | $CH_2Cl_2$ | 145 | 10 | 27 | 4.2 |
| 7[c] | $[C_4\text{-SAbim}][CF_3SO_3]$ | $CH_2Cl_2$ | 145 | 10 | 7 | 2 |
| 8[d] | $[C_4\text{-SAbim}][CF_3SO_3]$ | $CH_2Cl_2$ | 145 | 10 | 11 | 4 |
| 9[e] | M-SA 50 | $CH_2Cl_2$ | 100 | 8 | 12 | 12 |
| 10 | M-SA 100 | $CH_2Cl_2$ | 100 | 10 | 2.4 | 6.8 |

Reaction condition; 22 °C, [aldehde] = [pyrrole], [oxidant] = [reactant].

[a] Condensation time.

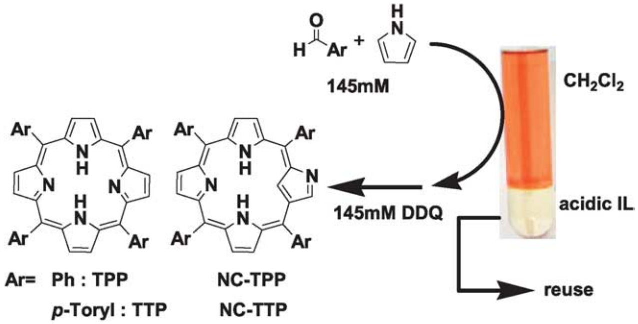
[b] This work; yields were determined after recrystallization.

[c] $CH_2C1_2$ was placed on the $[C_4\text{-SAbim}][CF_3SO_3]$ phase for 10 min without shaking. Yields were determined by HPLC analysis.

[d] $CH_2C1_2$ was pre-equilibrated with the $[C_4\text{-SAbim}][CF_3SO_3]$ by shaking for 5 min with a vortex mixer. Yields were determined by HPLC analysis.

[e] Lindsey Method; data from Ref. 1, Yields were determined by HPLC analysis.

**Table 5**. Reuse of [$C_4$-SAbim][$CF_3SO_3$] at high reactant concentrations



| Cycle | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| | Without shaking | | | | With shaking | Without shaking | | | | |
| TPP (%) | 27 | 24 | 24 | 26 | 1.4 | 16 | 7 | 16 | 15 | 16 |
| NC-TPP (%) | 4 | 4 | 4 | 4 | 4.7 | 2 | 2 | 7 | 3 | 3 |
| | | | | | Without shaking | | | | | |
| TTP (%) | 30 | 31 | 30 | 28 | 27 | 28 | 28 | 29 | 28 | 31 |
| NC-TTP (%) | 6 | 4 | 4 | 6 | 7.1 | 6 | 6 | 7 | 6 | 5 |

[Pyrrole] = [aldehyde] = [DDQ] = 145 mM, 22 °C, reaction time 10 min, isolated yields were determined after recrystallization.

for the repeated porphyrin preparations. Among the repeated cycles for TPP/NC-TPP formation, only the fifth cycle involved vigorous shaking of the biphasic system, whereas the other cycles, the first to the fourth and the sixth to the tenth, were kept as a silent interface without shaking during the reaction period. For the TTP/NC-TTP reaction, on the other hand, no shaking treatment was applied at all.

From the first cycle through the tenth final cycle, no shaking TTP/NC-TTP preparations, the yields for isolated TTP and NC-TTP ranged from 27 to 31% and from 3.9 to 6.4%, respectively. Despite having used high reactant concentrations, constant yields appeared for all the cycles. On the other hand, the influence of shaking on the isolated yields was studied for the TPP/NC-TPP preparations. Prior to the vigorous shaking, yields of ca. 25 and 4.2% for TPP and NC-TPP, respectively, had been maintained from the first to the fourth cycle, similar to the case of the TTP/NC-TTP preparations. Vigorous shaking of the fifth cycle immediately brought a brown color into the acidic IL phase and dramatically reduced the TPP yield down to 1.4%. Although, the silent interface without shaking was set again for the subsequent condensations from the sixth to the final cycle, the isolated yields of TPP could not reach the values noted prior to the shaking. It was impossible to remove the color from the contaminated, non-volatile IL even by extraction with a halogenated solvent, into which the by-products could readily be dissolved. This fact means that once the acidic IL phase is contaminated with the by-products, the productivity for porphyrins never recovers to the original level.

Based on these results, it can be said that the continually recycled usage of acidic [$C_4$-SAbim][$CF_3SO_3$] does not affect the porphyrin yield at all, as long as the contamination arising from the by-products is not transported through the interface by shaking. It is useful to note again that the dichloromethane phase can produce more porphyrins just by being placed on the silent acidic IL, than by being shaken vigorously with the IL.

## 3. Conclusion

These results demonstrate that the formation of tetraarylporphyrin derivatives in IL is an observable phenomenon. The water content and the viscosity of the used salt affect the reactivity in IL. In the case of the widely used $C_n$min ILs, in particular, the trade-off relation between water content and fluidity is relevant to the porphyrin yield. Balancing the two factors as equal priorities is crucial for porphyrin preparation.

Using the acidic IL, [$C_4$-SAbim][$CF_3SO_3$] as a reaction medium is unfavourable for porphyrin formation due to its strong acidity and high viscosity of as much as 3185 cP, in addition to the remaining water, which can comprise as much as 1.85 wt%. Despite these demerits, utilizing acidic IL as a biphasic mode with dichloromethane represents superiority both with regard to the reusability of the IL phase and porphyrin productivity in a high reactant concentration. The presence of the interface may act to stop the supply of more acid than is necessary. Further, investigation into the spatial distribution of the TILS around the interface is currently under way in our laboratory.

## 4. Experimental

### 4.1. Materials

Pyrrole (TCI, 99%), benzaldehyde (Wako, 98%), *p*-tolualdehyde (Wako, 95+%) and DDQ (TCI, 97%), $CH_2Cl_2$ (Kishida, 98%) were used as received. All other reagents were of a reagent grade and were used as received from Aldrich without further purification. Column chromatography was conducted using Aluminium oxide 90 Active basic (MERCK) and silica gel BW-300SP (FUJI SILYSIA).

### 4.2. Synthesis of used ILs

[$C_4$-SAbim][$CF_3SO_3$], 3-butyl-1-(butyl-4-sulfonyl) imidazolium trifluoromethyl-sulfonate was synthesized according to the published procedures[15] and the other ILs ranging from [$C_4$mim][TFSI] to [$C_{10}$mim][TFSI] were synthesized according to the published general procedures.[11] These ILs included [$C_4$mim][TFSI], [$C_4$p][TFSI], [$C_4$mppr]-[TFSI], [$n$-$(C_6H_{13})_4$][TFSI], [$C_4$mim][$PF_6$], [$C_4$mim][$BF_4$], [$C_4$mim][Br], [$C_4$mim][$CF_3CO_2$], [$C_4$mim][$CF_3SO_3$], [$C_2$-mim][TFSI], [$C_3$mim][TFSI], [$C_5$mim][TFSI], [$C_6$mim]-[TFSI], [$C_7$mim][TFSI], [$C_8$mim][TFSI], [$C_9$mim][TFSI], and [$C_{10}$mim][TFSI]. All the prepared ILs were dried in a vacuum oven (0.08 mmHg, 60 °C, EYELA, VOS-301SD) for at least 24 h and such condition was maintained until the subsequent experiment.

### 4.3. Determination of water content and viscosity

The water content was determined by Karl-Fischer titration using a Karl-Fischer moisture titrator MKC-510N (KEM) at room temperature. The viscosity was measured with a DV-II+Pro Programmable Cone/Plate (CPE-51) Viscometer (BROOKFIELD) at 22 °C via an external temperature controller. Each sample comprised 0.5 mL and measurements were conducted in triplicate. For the experiments of Figures 2 and 3, in particular, after determining the values, the measured samples were immediately mounted into a vessel for porphyrin preparation.

### 4.4. Intended addition of water to [$C_4$mim][TFSI]

Shaking the phase-separable [$C_4$mim][TFSI] (2 mL) with distilled water (2 mL) by a vortex mixer for 5 min followed by separation with centrifuging (3,000 ppm, 10 min) produced water-saturated [$C_4$mim][TFSI]. By mixing the water-saturated [$C_4$mim][TFSI] ($H_2O$ 1.36 wt%) with the freshly vacuumed-dried [$C_4$mim][TFSI] ($H_2O$ 0.12 wt%), three [$C_4$mim][TFSI]s containing water to the amount of 0.47, 0.62, 0.96 wt% were prepared.

### 4.5. HPLC analysis of porphyrins

Prior to performing HPLC analysis, the crude reaction mixture containing black tarry by-products was first pre-treated through column chromatography applying basic alumina with chloroform eluent. Then HPLC analysis was performed using a JASCO PU-2089 with a quaternary pump, a thermostatic column compartment to be set at 30 °C, and a diode array UV–vis detector. A silica gel analytical column was selected (nakalai tesque, COSMOSIL, 4.6 mm by 250 mm) with the gradient solvent between hexane and acetone ranging from 95–50/5–50 vol%, respectively. The gradient ratio for the mixing was conditioned to be as follows: 0 min, 5% acetone/95% hexane, 0–30 min, linear increase to 50% acetone/50% hexane. TPP and NC-TPP were eluted at 7 min and 13 min, respectively. The Soret band absorption wavelengths, 417 and 438 nm, were set as the detective monitor for TPP and NC-TPP, respectively.

### 4.6. Protocol for porphyrin preparation using ILs

In the present porphyrin syntheses, the Lindsey method was applied both for the single homogeneous mode and for the biphasic mode, due to its wide generality and excellent productivity. The reaction temperature, concentrations, and time period are the same as the best conditions for NC-TPP in dichloromethane. The procedure outline is as follows: standing dichloromethane or IL solution of benzaldehyde (10 mM) and pyrrole (10 mM) in the presence of M-SA (7 mM) at 22 °C for 30 min followed by the addition of powdered DDQ (10 mM) provides TPP, NC-TPP, and black tarry by-products. The remaining acid was quenched by the addition of 6 M equiv of triethylamine (TEA) to the used acid. The target porphyrins were isolated by the same procedure as described in the literature.

**4.6.1. A single homogeneous solution mode.** For Tables 1 and 2, Figures 2 and 3. Into 1 mL IL solution of 10 mM benzaldehyde and 10 mM pyrrole at 22 °C, M-SA was added to be 7 mM. After standing at the temperature for 30 min, neat DDQ (10 mM) was added followed by the addition of 6 M equiv of TEA to the acid.

For entries 7 and 8 in Table 4. At first, dichloromethane pre-equilibrated with [$C_4$-SAbim][$CF_3SO_3$] was prepared in two ways. In the case of entry 8, 10 mL dichloromethane were vigorously shaken with 3 mL [$C_4$-SAbim][$CF_3SO_3$] for 5 min in a vortex mixer. The mixture was centrifuged (3,000 rpm) for 10 min to separate clearly the two phases. On the other hand, for entry 7, 10 mL dichloromethane were placed on the silent surface of 3 mL [$C_4$-SAbim][$CF_3SO_3$] without shaking and this was left to standing for 10 min. Into each 1 mL of dichloromethane solution, pyrrole and benzaldehyde were added to be each 145 mM, and this was left to stand for 10 min without the addition of any acid at 22 °C. Into the reaction mixture, DDQ was added to be 145 mM, and then the remaining acid was quenched by the addition of 6 M equiv of TEA to the acid.

**4.6.2. Biphasic ($CH_2Cl_2$/[$C_4$-SAbim][$CF_3SO_3$]) mode.** Placing 10 mL dichloromethane on the silent surface of 3 mL [$C_4$-SAbim][$CF_3SO_3$] in a test tube forms the interface of ca. 200 $mm^2$. The interface was left to stand for 10 min at 22 °C. Into the upper dichloromethane phase, pyrrole and the corresponding aldehyde were added to be each 145 mM. Although, the dichloromethane phase was immediately coloured, the [$C_4$-SAbim][$CF_3SO_3$] phase was not coloured at all. The condensation reaction in the upper dichloromethane phase was quenched within 10 min. The dichloromethane phase was taken out from the [$C_4$-SAbim][$CF_3SO_3$] phase and the oxidation with DDQ was conducted in the separated dichloromethane solution in order to prevent contamination of the acidic IL phase. The separated dichloromethane phase was oxidized by the addition of DDQ (14.5 or 145 mM). The crude reaction mixture containing black tarry by-products was pre-treated with column chromatography on basic alumina with $CH_2Cl_2$ eluent followed by a second column chromatography on silica gel with MeOH/$CH_2Cl_2$ eluent. The first red fraction and the second brown fraction were collected as TPP and NC-TPP, respectively. Recrystallization with $CH_2Cl_2$/hexane produced TPP and NC-TPP, each as shiny violet crystal.

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