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Activity and behavior of imidazolium salts as a phase transfer catalyst for a liquid–liquid phase system

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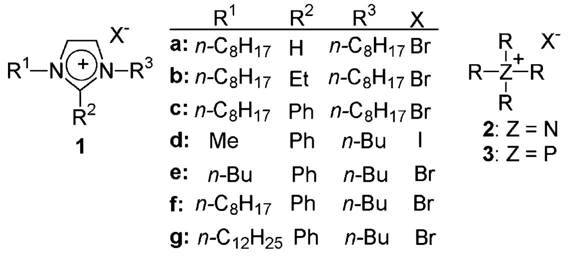
Abstract—The structure–activity relationship and behavior of *N*,*N*′-dialkylimidazolium salts as a phase transfer and/or ion-exchange catalyst in a liquid–liquid phase system were investigated for the reactions such as β-elimination reaction of alkyl halides, nucleophilic epoxidation of α,β-unsaturated carbonyl compounds, alkylation of active methylenes, and nucleophilic substitution reaction.

Imidazolium salts **1** are a well-known heterocycle but have recently been recognized as versatile molecules for use as polar organic solvents[1] (ionic liquids, when X^- is a bulky counter ion) and a precursor of stable heterocyclic carbenes[2] (when $R^2 = H$), ligating to metal atoms, and playing itself as a catalyst[3] (Fig. 1). Recently, the molecules have assumed a new aspect as a phase transfer or anion exchange catalyst. The use of imidazolium salts **1** as a phase transfer catalyst under solid–liquid biphasic conditions has been reported, which involves alkylation and Michael addition reactions of active methylene compounds and cross-aldol reaction.[4] Meanwhile, the use of **1** in organic/aqueous liquid–liquid biphasic systems has recently been reported by Lourenco and Afonso for nucleophilic alkylation and substitution reactions in CH_2Cl_2/H_2O.[5a] Kim and coworkers also reported hydrolysis of 1-chloro-2,2,2-trifluoroethane in DMF, DMSO, NMP or γ-butyrolactone/H_2O but the solvent system seems homogeneous.[5b] In these cases, only 1-*n*-butyl-3-methylimidazolium salt as an imidazolium salt was used. Compared with nitrogen and phosphorus quaternary cations **2** and **3**, the salts of which have widely been utilized as phase transfer catalysts,[6] the imidazolium cation has been reported to be more stable[6b] and is unique because its positive charge is highly delocalized to a five membered heterocyclic ring, the nature of the planar cation of which with variation of substituents might be useful for their design and functionalization as catalysts. However, the structural requirement and relationship to activity and mechanistic behavior as a catalyst have been little explored. Herein reported is the results of investigation on catalytic activity of **1** having various substituents for several reactions, which clarified the structural requirement for the use of **1** as a catalyst and gave their mechanistic aspects.



	R^1	R^2	R^3	X
a:	n-C_8H_{17}	H	n-C_8H_{17}	Br
b:	n-C_8H_{17}	Et	n-C_8H_{17}	Br
c:	n-C_8H_{17}	Ph	n-C_8H_{17}	Br
d:	Me	Ph	n-Bu	I
e:	n-Bu	Ph	n-Bu	Br
f:	n-C_8H_{17}	Ph	n-Bu	Br
g:	n-$C_{12}H_{25}$	Ph	n-Bu	Br

Figure 1. Structure of imidazolium salts **1** and quaternary salts **2** and **3**.

For the present study, imidazolium salts **1a**–**g** were prepared by the sequential alkylation of imidazole or 2-substituted imidazole, respectively, according to the conventional reaction procedure. Thus, 1-substituted or 1,2-disubstituted imidazole prepared from R^1X and imidazole or 2-substituted imidazole was alkylated with R^3X. The procedure afforded **1a**–**g** in a 83–99% yield through two steps.

First, we investigated the nucleophilic epoxidation of α,β-unsaturated ketone **4** to **5** in the presence of a

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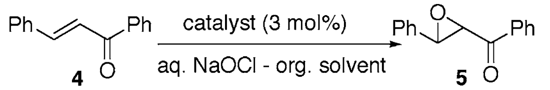
catalytic amount (3 mol %) of imidazolium salts **1** in the two-phase system of aqueous NaOCl solution and an organic solvent, and evaluated the efficiency of various **1** having different substituents. The results are summarized in Table 1, in which the relative efficiency value was calculated based on the yields of **5** observed after an appropriate reaction time. In the actual experiments, the reactions were highly dependent on the stirring efficiency. Therefore, to avoid errors arising from stirring efficiency, the reactions were performed using the same type and size of vessels and magnetic stirring bars with the same stirring rate and the reaction with **1c** was always carried out as the standard when the reactions with other catalysts were performed. Values for efficiency shown in Table 1 were calculated as a ratio of yield of **5** with each catalyst toward that with **1c** in toluene under the same reaction conditions. As can be seen from Table 1, imidazolium salts, except for 2-unsubstituted **1a**, exhibited catalytic activity for the transformation. The systematic structure–activity relationship was observed among compounds **1d–g** which have a phenyl group at the 2-position of imidazolium ring and N-substituents with different chain length at the 1- and 3-positions: Increase of the total carbon number of chains at the 1- and 3-positions increased catalytic activity, presumably due to enhanced solubility of (imidazolium)$^{+-}$X and/or (imidazolium)$^{+-}$OCl in the organic solvent utilized. Actually, **1d** which is nearly insoluble in toluene could not catalyze the reaction in a toluene–water system. As illustrated in Figure 2, **1** may act as an ion-exchanging agent in the reaction media, that is, an (imidazolium)$^{+-}$OCl generated catalytically from (imidazolium)$^{+-}$X might be an active species.

To clarify the reason why 2-unsubstituted imidazolium salt **1a** could not catalyze the reaction of **4** to **5**, **1a** was treated with aqueous NaOCl/CH_2Cl_2 and it was found that under oxidative conditions **1a** was decomposed to give the corresponding urea derivative and unknown compounds (Eq. 1).[7]

Table 1. Relative efficiency of catalysts for the nucleophilic epoxidation of **4** to **5** with aqueous NaOCl



Catalyst	Total C-number[a]	Relative efficiency[b]	
		Toluene	CH_2Cl_2
No	—	No reaction	No reaction
TBAB	—	0.56	0.93
1a	16	0	0
1b	16	0.98	0.83
1c	16	1.00 (Standard)[c]	0.93
1d	5	0	0.86
1e	8	0.77	0.96
1f	12	0.96	0.91
1g	16	1.12	1.07

[a] Total carbon-number of the substituents at the 1- and 3-positions of the imidazolium ring.

[b] The value is shown as the ratio of yield of **5** with each catalyst toward that with **1c** in toluene under the same reaction conditions.

[c] Compound **5** was obtained in 92% isolated yield by the reaction with 3 mol % of **1c** for 24 h at room temperature.

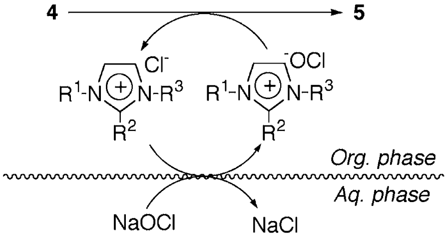
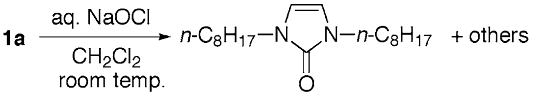


Figure 2. Possible mechanism of epoxidation of **4** to **5**.

 (1)

Since an imidazolium salt **1c** solved in toluene and acted as an ion-exchange catalyst for the reaction of Table 1, a **1c**/toluene/H_2O system was utilized to nucleophilic substitution reaction (Eq. 2). As expected, the conversion of alkyl bromide to the iodide proceeded in the presence of an imidazolium salt **1c**, and **1c** was a better catalyst than TBAB (n-Bu_4NBr) under the given conditions.

$$n\text{-}C_{12}H_{25}\text{-Br} \xrightarrow[\text{3M KI aq.- toluene, 40 °C, 20 h}]{\text{catalyst (3 mol \%)}} n\text{-}C_{12}H_{25}\text{-I} \quad \begin{array}{r}\text{no cat.: 0\%}\\ \text{TBAB: 7\%}\\ \textbf{1c}\text{: 68\%}\end{array} \qquad (2)$$

Next, we studied the behavior of imidazolium salts as catalysts under the basic conditions required for basic β-elimination reaction of alkyl halide to alkene (Eq. 3) and nucleophilic alkylation of the compounds having a acidic proton (Eq. 4). The β-elimination reaction of alkyl halide was performed as follows: A mixture of aqueous 50% NaOH (1 mL), toluene (1 mL), and $PhCH_2CH_2Br$ (1.5 mmol) was stirred at room temperature (22–24 °C) in the absence or presence of imidazolium salt **1** or TBAB (5 mol %). It was found that imidazolium salts **1a** and **1c** could effectively catalyze the reaction as well as TBAB. It was noted that 2-unsubstituted imidazolium **1a** as well as substituted **1c** could equally exhibit catalytic activity, while **1a** could not catalyze nucleophilic epoxidation of **4** to **5** and decomposed under the oxidative conditions. The time course of the reactions with **1c** and TBAB was traced by GC analyses and is shown in Figure 3. A control experiment without catalyst did not afford the product styrene at all. Time versus log(1 − x) plots (x = conversion, $0 \leqslant x \leqslant 1$) for both reactions catalyzed by **1c** and TBAB fit well to simple lines when the conversion was less than 80% (<~10 h), where the reaction could be considered as an expected pseudo-first order under the conditions in the presence of large excess of a base and a relatively small amount of catalyst to the substrate halide. The results indicate that catalyst **1c** was stable and did not

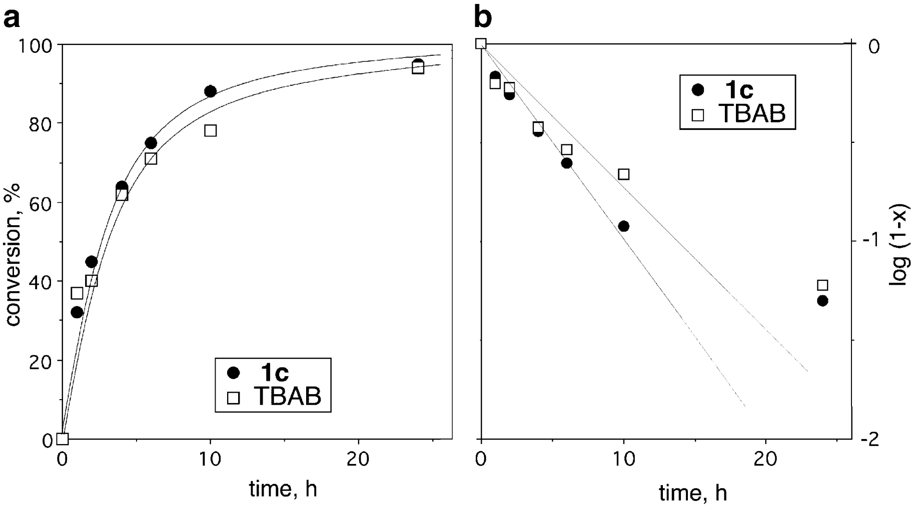


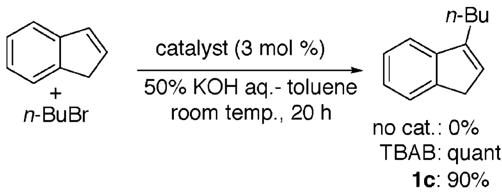
Figure 3. Reaction time course (a) and time versus log(1 − x) plots (b) of elimination reaction of $PhCH_2CH_2Br$ in aqueous NaOH–toluene. (x = conversion ($0 \leqslant x \leqslant 1$)).

change the structure of its cation counterpart during the reaction.

$$PhCH_2CH_2Br \xrightarrow[\text{50\% NaOH aq.-toluene, room temperature}]{\text{catalyst (3 mol \%)}} PhCH{=}CH_2 \ \text{quant. (48 h)} \qquad (3)$$

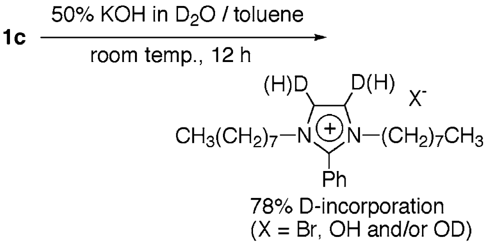
catalyst: **1a**, **1c** or n-Bu_4NBr

Deprotonation and alkylation reaction of the compounds having an acidic proton illustrated in Eq. 4 was investigated. Thus, **1c** as well as TBAB were effective for the alkylation of indene in an aqueous KOH–toluene system to give selectively mono-alkylated compound in a good yield (Eq. 4).[8]

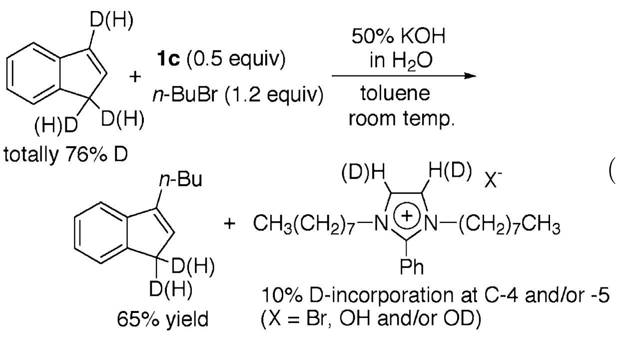


(4)

To clarify an active species as a base and the structural stability of **1** under the basic conditions, we carried out the following experiments: The ^{1}H NMR spectra of the residue obtained by the reaction of **1c** with an excess amount of KOH in toluene/H_2O and the following concentration of the organic phase indicated an imidazolium ring structure similar to **1c**, peaks of which had somewhat different chemical shifts from those of **1c**. As revealed from Eq. 5, protons at the 4- and 5-positions could be exchanged with the protons of solvent(s) by a deprotonation/protonation pathway under the basic conditions.[9] Meanwhile, as shown in Eq. 6, it was found that the reaction of deuterated indene (totally 76%D at 1- and 3-positions)[10] and n-BuBr in toluene–50% KOH in H_2O with 50 mol % of **1c**, which gave the corresponding alkylated indene in good yield and recovered **1c** with 10% of deuterium incorporation at the C4 (or C5) position. The deuterium incorporation thus observed was apparently larger than the total D/H ratio included in the mixture of the substrates, reagents (**1c** and KOH), and solvent (H_2O). It is pointed out that the reaction under basic conditions at least involves the C4- (or C5-) anion of **1c**, which can act as a base for deprotonation of indene.



(5)



(6)

Based on these results, a possible mechanism for the elimination reaction of alkyl halides and alkylation of indene is illustrated in Figure 4. The imidazolium bromide **1** can react with MOH (M = K or Na) on the surface between the organic and aqueous phases to give imidazol-4-ylidene **A**, which may deprotonate an acidic proton of the substrate to occur the elimination or alkylation reaction and generate (imidazolium)$^{+-}$X again. In addition, a catalytic cycle involving an

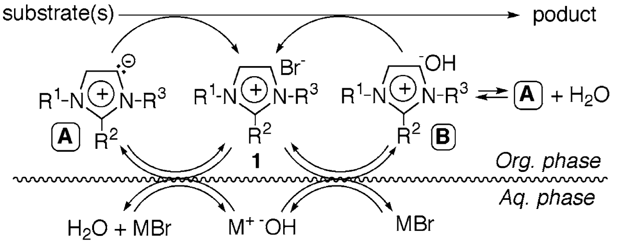
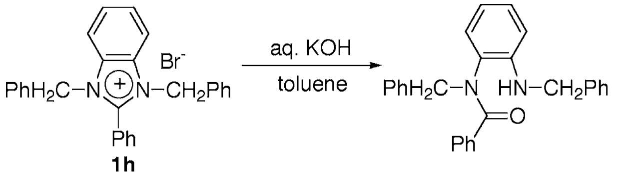


Figure 4. Possible mechanism of elimination reaction and proton-exchange reaction of the imidazolium.

(imidazolium)$^{+-}$OH (**B**), derived from **1** by an ion-exchange reaction, as an active base cannot be ruled out. An anion **A** may also be generated through the formation of **B**.

In contrast to imidazolium **1a**–**g**, the benzo derivative of imidazolium salt **1h**[11] could not catalyze the β-elimination reaction shown in Eq. 2. It was found that the reaction of **1h** with KOH gave the corresponding ring-opening product (Eq. 7).



(7)

In summary, we have reported the structural requirement and structure–activity relationship of 1,3-disubstituted and 1,2,3-trisubstituted imidazolium as a phase transfer catalyst in a liquid–liquid phase system under various reaction conditions. In addition to a similar ion-exchanging mechanism to that for usual phase transfer catalysts such as quaternary ammonium salts, it was suggested that the reaction under the basic conditions may involve an imidazol-4-ylidene compound as an active species. These results might be useful for further application and design of imidazolium salts as a phase transfer catalyst.

Acknowledgment

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