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CHINESE CHEMICAL LETTERS

Chinese Chemical Letters 22 (2011) 147-150

www.elsevier.com/locate/cclet

Nucleophilic substitution of hydrogen in naphthalene by chloride (Cl⁻) in ionic liquids

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Abstract

Nucleophilic aromatic substitution of hydrogen in non-activated aromatic ring, a very rare phenomenon in organic chemistry, is found in ionic liquids containing Cl^- as anion under mild reaction conditions. The reaction may be carried out by the addition of the halogen-bonding adduct (Br₂Cl⁻) as nucleophile to aromatic ring carbon atom, leading to the formation of the nucleophilic substitution product.

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Keywords: Ionic liquid; Aromatic compound; Naphthalene; Nucleophilic reaction; Halogen bonding

Nucleophilic aromatic substitution of hydrogen in carbo- and heteroaromatic systems is a subject of considerable interest to chemists. The nucleophilic substitution reaction is only favored by electron withdrawing substituents on the aromatic ring in order to decrease *p*-electron density and facilitate approach of a nucleophile. The nucleophilic aromatics substitution of hydrogen in the non-activated (unsubstituted) aromatic ring is very rarely observed. Up to now, only two examples completed under the extremely overcritical conditions have been known [1,2] However, a very more surprising phenomenon was observed in our experiment, in which anionic Cl⁻ replaces hydrogen in the non-activated naphthalene in the bromination reaction of naphthalene with bromine while the ionic liquid containing Cl⁻ as anions was used as reactive medium, and the selectivity of chloronaphthalene reach up to 87% based on naphthalene. In order to explore and understand these chemical processes, the chemical behavior of bromonaphthalene was examined in detail in the ionic liquid containing Cl⁻ as anions. The result shows that no nucleophilic substitution of bromonaphthalene with Cl⁻ as prediction occurs in this system.

Negatively charged halogen atoms are capable of forming donor-acceptor bonds with halogen molecules to create the halogen-bonded prereactive complexes (halogen-bonded adducts) [3]. When Br_2 was dissolved in the ionic liquid containing Cl⁻ as anions, anion prereactive complexes [Cl-Br-Br]⁻ may be formed, and in which mid part bears some positive electric charge and each end of which is electronegative due to the induced polarization of anion Cl⁻ shown as following: {Cl^{δ}-Br^{δ +}-Br^{δ +}]. Addition of this prereactive complex as nucleophile to naphthalene ring carbon atom lead to the formation of the nucleophilic substitution products (Scheme 1).

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^{1001-8417/}\$-see front matter © 2010 Published by Elsevier B.V. on behalf of Chinese Chemical Society. doi:10.1016/j.cclet.2010.09.021



Scheme 1. Diagrammatic sketch of the reaction process of naphthalene with $R[Br_2Cl]$ (R = [BPy] (1-*n*-butylpyridinium), [Bmim] (1-*n*-butyl-3-methyl imidazolium), etc.)).

Support to the proposed reactions pathway of Scheme 1 come from the experimental results for halogenation of naphthalene at different reaction times and in different molar ratios of bromine and [BPy][Cl]. The experimental data exhibit an increase in selectivity of chloronaphthalene on going from the higher amount of the added Br_2 to the lower and suggest the occurrence of the reactive equilibrium in this ionic liquid system as follows (Eq. (1)):

$$Cl^- + Br_2 \leftrightarrow Br_2 Cl^- \tag{1}$$

In the equilibrium, the higher amount of Br_2 do not alone promote the formation of the more Br_2Cl^- , and also increase the equilibrium concentration of the electrophilic reagent Br_2 leading to the formation of bromonaphthalene and the decreasing the selectivity of chloronaphthalene at the Cl^- amount as the constant. The substitution reactions of Br_2Cl^- or Br_2 with naphthalene to give chloronaphthalene or bromonaphthalene were represented by the following equation:

$$Br_2Cl^- + naph \leftrightarrow naph - Cl + HBr + Br^-$$
⁽²⁾

$$Br_2 + naph \leftrightarrow naph - Br + HBr$$
 (3)

The reactions in Eqs. (1) and (2) possess a character of the consecutive reactions and those in Eqs. (2) and (3) display a behavior of the parallel reactions. In the course of reaction, the selectivity for the dominant nucleophilic chlorization of naphthalene in the system decreases as the reactive time increase owing to the occurrence of the electrophilic bromination and gradually approaches the value of the equilibrium state. The selectivity for 1-chloronaphthalene can reach 87% in the mixture of naphthalene (0.5 mmol), Br_2 (0.5 mmol) and [BPy][Cl] (10 mmol) at 100 °C under reflux for 10 min.

In order to deeply comprehend the nature of the interspecies interactions and further illustrate reaction procedure in this system, a series of the aromatic substituent experiments were devised. The results were shown in Tables 1 and 2. In

| Entry | Medium (10 mmol) | Con. (mol%) ^b | Sel. (mol%) ^b | | | |
|-------|--------------------------------|--------------------------|--------------------------|---------|---------------------|--|
| | | | Naph–Cl | Naph–Br | Others ^e | |
| 1 | [BPy][C1] | 65% | 81% | 19% | _ | |
| 2 | [HPy][Cl] | 65% | 78% | 22% | _ | |
| 3 | [DPy][Cl] | 66% | 76% | 24% | _ | |
| 4 | [4-MeBPy][Cl] | 54% | 66% | 34% | _ | |
| 5 | [Bmim][Cl] | 75% | 48% | 52% | _ | |
| 6 | HCl ^c | 82% | 4% | 93% | 3% | |
| 7 | $ZnCl_2^d$ | 79% | <1% | 84% | 15% | |
| 8 | FeCl ₃ ^d | 87% | <0.2% | 92% | 8% | |
| 9 | AlCl ₃ ^d | 80% | <0.2% | 90% | 10% | |

Table 1Halogenation of naphthalene in different mediaa.

^a Reaction conditions: naphthalene (1 mmol), Br₂ (1 mmol) and medium (10 mmol); reaction temperature 100 °C; reaction time 4 h under reflux.

^b Conversion and selectivity were determined by GC based on naphthalene.

 $^{\rm c}\,$ 1.0 g 37% HCl aqueous solution, reaction temperature: 40 $^{\circ}\text{C}.$

 d 2.0 g saturated metal chloride aqueous solution, reaction temperature: 40 °C.

^e Other product is dibromonaphthalene.

Table 2 Halogenation of different aromatics in [BPy][Cl] ionic liquid.^a

| Entry | Substrate | Con. (mol%) ^b | Sel (mol%) ^b | | | |
|-------|------------|--------------------------|-------------------------|-----|-----------------|------|
| | | | Monochloride | | Monobromide | |
| 1 | \bigcirc | 0% | CI | 0% | Br | 0% |
| 2 | | 92% | | 0% | | 100% |
| 3 | OMe | 95% | CI OMe CI | 0% | OMe Br Br | 100% |
| 4 | | 65% | CI | 81% | Br | 19% |
| 5 | | 85% | CI | 22% | Br | 78% |
| 6 | ОН | 93% | CI | 8% | OH Br | 92% |
| 7 | Br | 65% | Br | 65% | Br | 35% |
| 8 | | 69% | CI CI | 70% | Br | 30% |

^a Reaction conditions: 1 mmol substrate, 1 mmol Br₂ and 10 mmol [BPy][CI]; reaction temperature 100 °C; reaction time 4 h under reflux. ^b Conversion and selectivity were determined by GC or HPLC based on substrate.

all of the experimental results shown in Table 1, the selectivity of the chloronaphthalene in the ionic liquids are the very much higher than those in the analogous inorganic salt solutions and highest selectivity (81%) of the chloronaphthalene appears in the ionic liquid [BPy][Cl] (1-n-butylpyridinium chloride) under identical conditions. This phenomenon may be attributed to the charge-diffuse Br_2Cl^- having the much higher stability in ionic liquids than in the analogous inorganic salt solutions [4] and the ionic liquid cation exerting the hydrogen bonding donor ability on the leaving Br^- anion in the rate-determining step [5]. Of cause, the solvent dependency in nucleophilic substitution can be interpreted with reference to the nature of the charge distributions in the ground state and the activated complex in the rate-determining step [6]. It is worthy of note that the ionic liquids with different cation structures exhibit different abilities to affect the selectivity of the chloronaphthalene (Table 1, entries 1-5). This feature is in agreement with the recently reported data about nucleophilic substitution reactions in ionic liquids [5,7]. The longer or more alkyl chains on the ring of pyridine make the ionic liquid more viscous [8] and give rise to the lower selectivity of chloronaphthalene as shown in Table 1, entries 1-4. The experimental results in Table 2 clearly testify a fact that the effects inducing the increase of electron density on the aromatic ring always produce the lower selectivity of chloronaphthalene. Under the same conditions in this ionic liquid system, the selectivity of nucleophilic substitution of the aromatic hydrogen by Cl⁻ decrease on going from the feebler (Table 2, entry 7, 65%) to the stronger (Table 2, entry 6, 8%) electron releasing group located on the naphthalene ring, whenas the nucleophilic substitution reaction of aromatic hydrogen of benzene or its derivatives bearing electron releasing group with Cl^- do not occur. It further verifies that the replacement of aromatic hydrogen follows the fundamental principles of nucleophilic substitution in this ionic liquid system. Detailed reaction mechanism is in progress in our lab.

1. Experimental

[Bmim][Cl] (1-*n*-butyl-3-methylimidazolium chloride), [BPy][Cl] (1-*n*-butylpyridinium chloride), [HPy][Cl] (1-*n*-hexylpyridinium chloride), [DPy][Cl] (1-*n*-decyl-pyridinium chloride), [4-MeBPy][Cl] (4-methyl-1-*n*-butyl-pyridinium chloride) ionic liquids were synthesized according to the procedures reported previously respectively [9].

The typical reaction procedures of halogenation of aromatics are as follows: bromine (1 mmol, 0.160 g) and [BPy][Cl] (10 mmol, 1.72 g) ionic liquid were added in a 50 mL three-necked flask and stirred vigorously for 30 min at 100 °C in the N₂ atmosphere, and [BPy][Br₂Cl] was obtained. After that, naphthalene (1 mmol, 0.128 g) was added and further heated at 100 °C for 4 h under stirring. Finally, the reaction was stopped and cooled to room temperature. The products were extracted by diethyl ether (three times, 5 mL each) and quantitatively analyzed by GC using toluene as the internal standard substance. All products were determined by MS or GC–MS and FTIR.

Apparatus and instruments used for identification of the products. IR: NEXUS 670-FTIR infrared spectrometer; HPLC: Varian Pro Star 210 (Agilent XDB-C18 column); GC: Shimadzu GC-14C (Agilent DB-1 30 m, 0.25 mm); GC-MS: CP-3900GC/Saturn 2100MS system.

Acknowledgments

We thank the key project of Shanghai Science and Technology Committee (Nos. 05JC14070, 06DZ05025, 08JC1408600) for financial supports.

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