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Chloromethylation of 2-chloroethylbenzene catalyzed by micellar catalysis

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The chloromethylation reaction of 2-chloroethylbenzene was performed successfully by micellar catalysis in the biphasic oil/water system. The effects of anionic, cationic and non-ionic surfactants on the reaction were compared. The mechanism of chloromethylation reaction and the mechanism of micellar catalysis were investigated. The results show that the micellar catalysis is an effective way to realize the chloromethylation of 2-chloroethylbenzene, and the cationic surfactant shows the most effectiveness. The longer the hydrophobic chain of the cationic surfactant is, the better the catalysis effect will be, and the addition of inorganic electrolyte into the aqueous phase can markedly promote the catalysis effect.

2-chloroethylbenzene, chloromethylation, micellar catalysis, surfactant

1 Introduction

2-Chloroethylbenzyl chloride (CEBC), especially the para-isomer, is an important organic intermediate which has widespread application in fine-chemicals, pharmaceuticals, polymers, etc.[1−5]. CEBC is traditionally prepared by chloromethylation of 2-chloroethylbenzene (CEB) in the presence of chloromethyl methyl ether and/or bis-chloromethyl ether (or reagent combinations which can result in the formation of these ethers) and stoichiometric amount of Lewis acids[6]. Selectivity and yield of the mono-chloromethyl derivatives are determined by the consecutive formation of the polychloromethylation byproducts, and the formation of diphenylmethane and diphenylethane derivatives and other byproducts, because Lewis acid is not only the catalyst of chloromethylation reaction but also the effective catalyst of Friedel-Crafts alkylation reaction[7], which are often not so high. Moreover, this method suffers from the inherent problem of using carcinogenic chloromethylethers, difficulty in post-processing and severe environmental pollution. Other methods have been tried by many domestic and international scholars in an attempt to replace the traditional one, but with no real success[8]. Micelles formed by surfactant molecules in aqueous phase, above the CMC, can allow the transfer of the lipophilic substrate into the aqueous phase by micellar solubilization, often resulting in a larger interface area between the lipophilic substrates and the hydrophilic reagents. The magnifying interface as well as electrostatic interaction and local concentrating effect[9] can often result in dramatic increase in reaction rates. In addition, micellar catalysis can effectively avoid side reactions to occur, and can enhance the selectivity of the desired compounds[10−14]. At present, micellar catalysis has been applied in various organic syntheses, such as electrophilic substitution reaction, nucleophilic substitution reaction, oxidation reaction, and hydrolysis[15−23]. In our previous paper, we once applied micellar catalysis into a single-phase system to realize the chloromethylation of 2-bromoethylbenzene successfully[24]. While investigations of single-phase systems are invaluable to understand how different factors affect these reactions, industrial production commonly employs reactant loading of 10%−50%, which is far from the maximum

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solubilization capacity of micelles[10]. Organic reactions conducted in these systems thus must work within two-phase system where a portion of reactant substrates are solubilized in the micelles and the remaining portions form emulsified droplets dispersed in the bulk aqueous phase. Under the diffusion action, the reactant substrates within the emulsified droplets can be transferred unceasingly into the micelles; at the same time, the products formed within micelles can also be transferred into the emulsified droplets continuously. Therefore, the emulsified droplets act as not only a source of reactant materials but also an acceptor of reaction products[10]. In this paper, the chloromethylation of CEB would be realized with high conversion and selectivity for mono-chloromethylation by application of micellar catalysis in biphasic oil/water system where Friedel-Crafts condensation reaction catalyzed by Lewis acid would be suppressed and the formation of byproducts such as polychloromethyl derivatives and diphenylmethane can thus be avoided. Furthermore, it is more important that the formation of carcinogenic chloromethylether and/or bis-chloromethyl ether can also be avoided because of large quantity of water in this system[25].

2 Experimental

2.1 Reagents and apparatus

2-Chloroethylbenzene (CEB, Jintan Chunfeng Chemical Co., Ltd.) was of chemical pure grade. Cetyltrimethylammonium bromide (CTAB, Beijing Chemical Reagent Research Institute), dodecyltrimethylammonium bromide (DTAB, Jintan Xinan Chemical Institute), sodium dodecyl sulfonates (SDS, Beijing Zhonglian Chemical reagent Plant), nonylphenol polyoxyethylene ether (NP-10, Tianjin Fuchen Chemical reagent Factory) and paraformaldehyde (Shanghai Lingfeng Chemical Reagent Co., Ltd.) were all of analytical grade. Other reagents were all commercial chemicals with analytical pure grade.

An Agilent6820 Gas Phase Chromatograph (US, Agilent Technologies) and a trace Ultra-trace DSQ GC/MS Spectrometer (US, FININIGAN) were used.

2.2 Analysis

The contents of various components in the reaction mixtures were analyzed by Agilent6820 Gas Chromatograph equipped with a DB21 capillary column (30 m ×0.25 mm×0.25 mm ID) and a hydrogen flame detector. Column temperature was set at 200℃, injection port temperature at 280℃ and detector temperature at 300℃. Inlet pressures of nitrogen gas and hydrogen gas were 65 kPa and 80 kPa respectively and the amount of test specimen was 0.1 μL.

2.3 Experimental procedure

The reaction was performed in a 1000 mL four-necked flask immersed in an oil bath kept at a given temperature and equipped with a dynamoelectric stirrer, a reflux condenser, an anhydrous HCl gas inlet and a thermometer. The reactor was charged with CEB (140.6 g, 1.0 mol) and hydrochloric acid solution (300 mL) of surfactants with the desired concentration. The mixture was stirred for 2 h in order to solubilize fully CEB in the surfactant micelle solution (the remaining portions of CEB formed emulsified droplets dispersed in the aqueous phase) and then was heated to 85℃ after the addition of paraformaldehyde (36.0 g, 1.2 mol). At the same time, anhydrous HCl gas was bubbled through the reaction mixture rapidly. After the reaction run for a period of time at constant temperature, the reaction was over. After cooling and demulsifying, the organic products were separated, neutralized with aqueous saturated sodium bicarbonate solution, washed with water until neutralization and dried over anhydrous sodium sulfate. The analyses by GC/MS were carried out subsequently to filter the resulting organic products. The conversion of CEB was calculated based on GC analysis.

In order to examine the effects of different factors such as types of surfactant, surfactant concentration, structures of surfactants and adding inorganic electrolyte on the chloromethylation of CEB, the experiments under varying conditions were carried out according to the aforementioned procedure.

3 Results and discussion

3.1 Chloromethylation of 2-chloroethylbenzene by micellar catalysis

Figure 1 shows the catalytic effects observed for the chloromethylation of CEB in the presence or absence of CTAB. As seen from Figure 1, in the absence of surfactant (CTAB), the reaction proceeded very slowly, and only 7% conversion was obtained within 8 h. Reaction performed with CTAB (its critical micelle concentration,

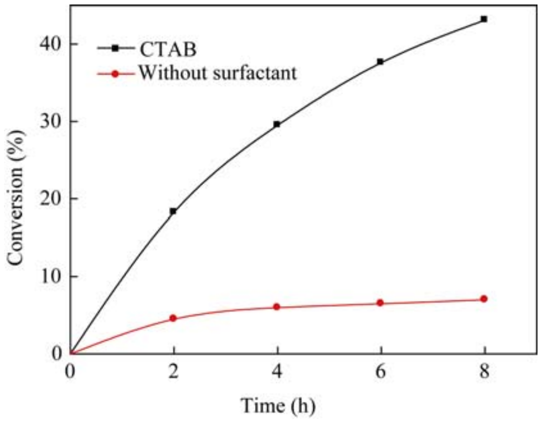


Figure 1 Relationship between conversion and reaction time in the presence and absence of CTAB. Reaction temperature: 85℃; CTAB concentration: 10 CMC.

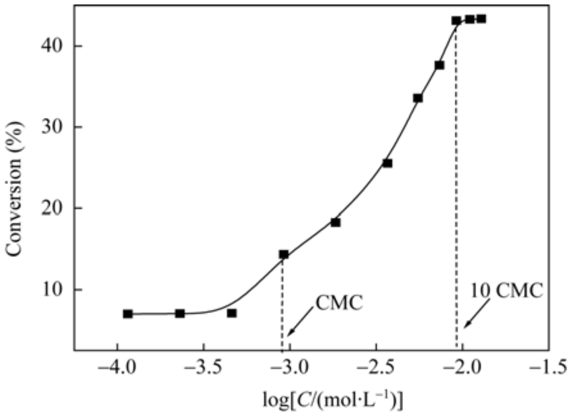


Figure 2 Relationship between conversion and concentration of CTAB. Reaction time: 8 h; reaction temperature: 85℃.

CMC, is 9.20×10^{-4} mol·L^{-1}[26]) at a concentration of 9.20×10^{-3} mol·L^{-1} (10 CMC) proceeded very rapidly and the CEB conversion reached 43% at the same interval, which demonstrated the high efficiency of micellar catalysis, as expected. When no surfactant (CTAB) was used, under the stirring conditions, the reaction system was a suspension with two phases and the interface area between oil phase and aqueous phase was very small, so the reaction rate of chloromethylation occurred at the interface is quite low. However, when CTAB was used, there were numerous micelles in the reaction system and CEB was solubilized in these micelles, resulting in a larger oil-water interfacial area and a higher reaction rate compared to the system without CTAB. Because the used amount of CEB in our research system was very high, except one portion was solubilized in the micelles, the other portions formed O/W emulsion. Under the diffusion action, the reactant materials (CEB) within the emulsified droplets could be transferred unceasingly into the micelles; simultaneously, the chloromethylated products formed within micelles could also be transferred into the emulsified droplets continuously. Therefore, the emulsified droplets acted as a continuous source of reactant materials and a sink into which the resulting products (CEBC) entered, so that the chloromethylation reaction of CEB could keep going. This process was probably analogous to the emulsion polymerization one[9,10].

The influence of CTAB concentration on the conversion of CEB at the same temperature (85℃) and reaction time (8 h) is shown in Figure 2. When CTAB concentration was very small (below CMC), conversion of CEB was quite low, and did not change with CTAB concentration nearly. However, when CTAB concentration reached to CMC, the conversion of CEB increased sharply, and increased continuously with an increase in CTAB concentration. The facts fully reveal the efficiency of micellar catalysis once more. When the concentration of CTAB was smaller than CMC, CTAB was dissolved by the molecular state in the water phase, and the micellar concentration together with the resulting CEB solubilizing capacity seemed too low to induce a significant micellar catalysis process. Once the concentration of CTAB reached CMC, micelles were formed, CEB was solubilized in the micelles, the interface area of oil phase/water phase was magnified suddenly, the rate of the chloromethylation reaction occurring at the interface was accelerated abruptly, so the conversion of CEB appears a break point at CMC. Hereafter, the number of micelles increased with the increasing CTAB concentration, and the solubilization capacity of CEB thus increased continuously, so the rate of the reaction speeds up and the conversion is enhanced. And it can be found that under the present experimental conditions the optimum CTAB concentration is 10 CMC, namely, 9.20×10^{-3} mol·L^{-1}.

3.2 Mechanism and effects of surfactant type on chloromethylation

In order to explore the reaction mechanism of chloromethylation, three types of cation (CTAB), anionic (SDS) and nonionic (NP-10) surfactants were used to catalyze the chloromethylation of CEB in micelle solutions.

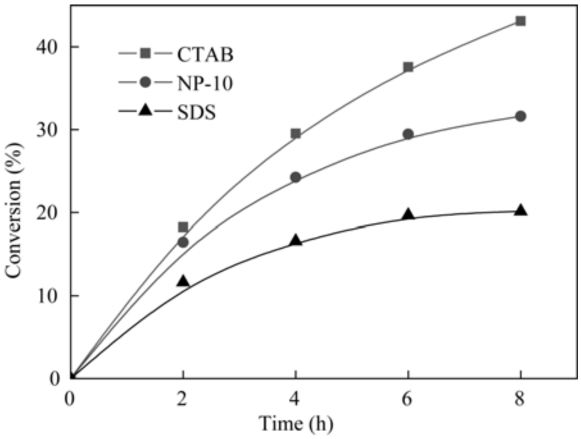


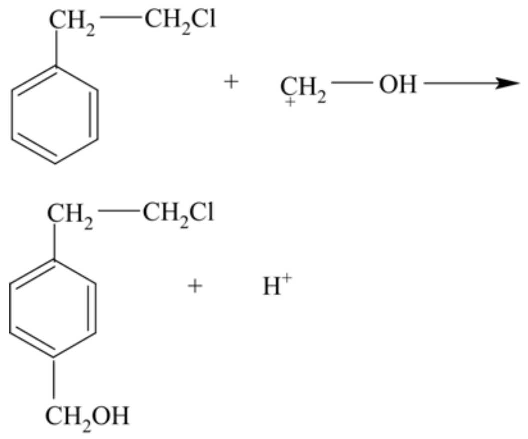
Figure 3 Relationship between conversion and reaction time for three types of surfactants. Concentration of the surfactant: 10 CMC; reaction temperature: 85℃.

Figure 3 shows the conversion varied with the change of the reaction time at the same temperature (85℃) and with a concentration condition of 10 CMC.

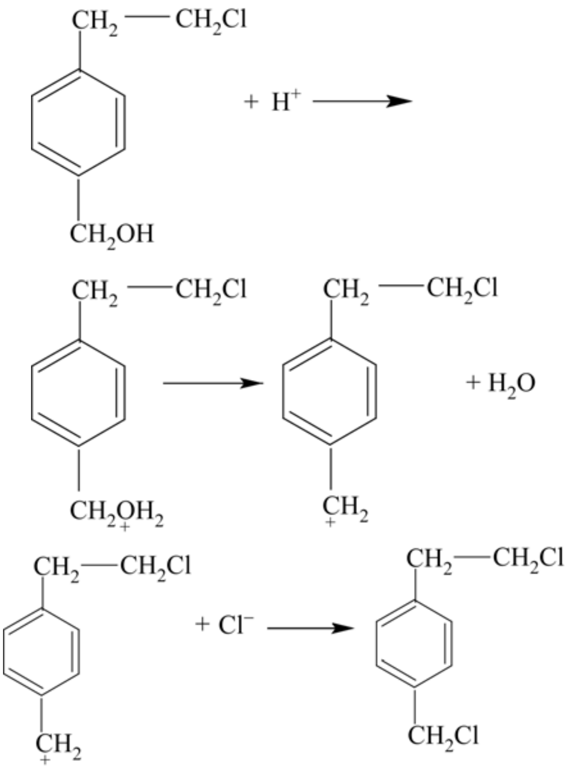
As seen from Figure 3, the catalytic ability of these surfactants was evidently different and decreased in the order CTAB>NP-10>SDS. The difference was probably caused by two reasons: (1) the mechanism of chloromethylation and (2) the different micellization behavior (critical micelle concentration CMC and micellar aggregation number N_{agg} and so on). The reaction mechanism of chloromethylation for CEB consists of electrophilic substitution reaction and nucleophilic substitution reaction, which can be expressed as follows:

Electrophilic substitution reaction:

$$CH_2{=}O + H^+ \longrightarrow \underset{+}{C}H_2{-}OH \qquad (1)$$


(2)

Nucleophilic substitution reaction:


(3)

(4)

Scheme 1 Mechanism of chloromethylation reaction of CEB.

Scheme 1 shows a plausible mechanism for the chloromethylation of CEB. Firstly, depolymerization of paraformaldehyde under the acidic condition yields formaldehyde which reacts with proton to yield hydroxymethyl cation and the electrophilic substitution reaction occurs by subsequent attack of the hydroxymethyl cation on benzene ring of CEB to give 2-chloroethylbenzyl alcohol; then 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.

In the chloromethylation reaction process, it is probable that the nucleophilic substitution reaction of anion Cl^- attacking the benzyl carbonium ion is the most important step or rate-controlling step. Obviously, when CTAB was used as catalyst, the cationic head groups charged with a part of positive charge was advantageous to the nucleophilic substitution reaction of anion Cl^-; however, when SDS was used, the anionic head groups charged with negative charge strongly repelled the anions Cl^- and played an inhibition role in the nucleophilic substitution reaction. Therefore, the catalytic action of CTAB is stronger than that of SDS. For NP-10, because there was neither promoter action nor inhibition action on the nucleophilic substitution reaction, its catalytic action came between them.

3.3 Effect of structure of cationic surfactants on micellar catalysis

In order to examine the effect of the structure of cationic surfactant on the micellar catalysis, two kinds of cationic surfactants, CTAB and DTAB, were used, and the experimental results are shown in Figure 4.

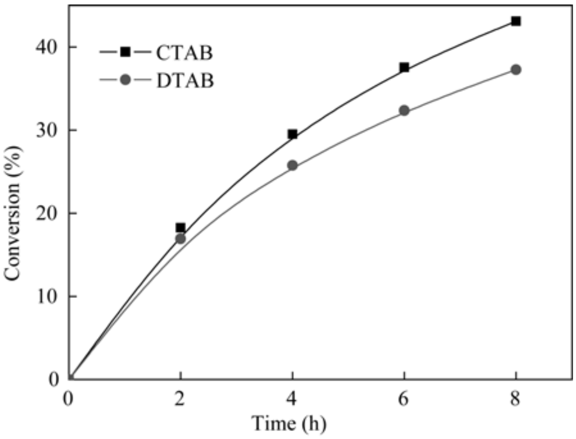


Figure 4 Effect of surfactant structure on micellar catalysis. Reaction temperature: 85℃; concentration of the surfactant: 10 CMC.

As shown in Figure 4, the conversion of CEB catalyzed by CTAB is higher than that catalyzed by DTAB under the same reaction conditions, which indicated that the catalytic action of CTAB was stronger than that of DTAB. The primary reason causing the difference should be ascribed to their different molecular structures. CTAB and DTAB belong to identical series of cationic surfactants, and the longer the hydrophobic carbon chain, the lower the CMC and the greater the aggregate number (N_{agg}). So CTAB has a lower CMC (9.2×10^{-4} mol·L^{-1}) and a greater N_{agg} (61) than DTAB (CMC: 1.5×10^{-2} mol·L^{-1} and N_{agg}: 50[26]). Thereby, at the same concentration, there was more CEB solubilized in CTAB micelles which resulted in a higher rate of chloromethylation reaction and a greater conversion of CEB in a given reaction time.

3.4 Effect of adding inorganic electrolyte on micellar catalysis

The addition of inorganic electrolyte (NaCl) can significantly influence micellization behavior of surfactants, and also influence the micellar catalysis effect. Figure 5 shows that the conversion of CEB varied with the change of NaCl concentration in different micellar catalysis systems.

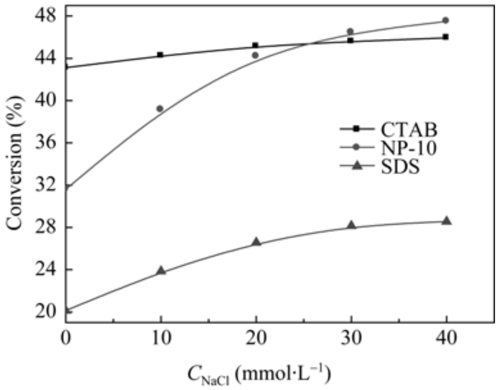


Figure 5 Effect of adding inorganic electrolyte on micellar catalysis. Reaction temperature: 85℃; reaction time: 8 h; concentrations of the surfactants: 10 CMC.

Obviously, the conversion of CEB increased slowly with increase in NaCl concentration. When NaCl was added into the CTAB system, the electrostatic repellent action of the cationic head groups was partly counterbalanced by anion Cl$^-$, which promoted accumulation of CTAB molecule resulting in the decrease in its CMC and increase in aggregating number and micelle size. These results would be advantageous to allowing the total amount of CEB solubilization in CTAB micelle solution to increase, which thus promoted the micellar catalysis action and enhanced the conversion of CEB. The effect of NaCl was most pronounced for SDS, one reason was the decrease in CMC of SDS and the increase in CEB solubilization in the micellar solution; another was that the electrostatic repellent action of the anionic head groups was also partly counterbalanced by cation Na$^+$, reducing the inhibiting effect of anionic head groups of SDS on the nucleophilic substitution reaction of anion Cl$^-$, and resulting in speeding up of chloromethylation reaction of CEB. When NaCl was added into the NP-10 system, the cation Na$^+$ would be combined on the surface of NP-10 micelles, so that NP-10 micelle surface was charged positively which would attract anion Cl$^-$ strongly and thus would accelerate distinctly the nucleophilic substitution reaction; higher solubilization ability of NP-10 micelles containing NaCl was another factor resulting in higher reaction rate of CEB chloromethylation, even higher than that in CTAB system.

In addition, for the ionic surfactants, adding the inorganic electrolyte NaCl into the micelle solution would reduce the intramolecular electrical repulsion and cause compact arrangement of surfactant molecules in the palisade layer, which reduced the possible solubilization position of CEB, and thus reduced the solubilization capacity of CEB in the micelle solution and the concentration of CEB in the micelle surface, leading to a retarding effect. Therefore, as seen from Figure 5, the conversion rates of CEB tended to become slow when the concentration of NaCl was high.

3.5 Selectivity

It is well known that micellar catalysis can be used to improve the selectivity for target compounds. Tables 1 and 2 show the experimental results. When no surfactant micelles were used, the selectivity was very low, however, the selectivity was very high in the micellar catalysis systems. The addition of inorganic electrolyte NaCl could further improve the selectivity.

Table 1 Selectivity in mono-chloromethylation of 2-chloroethylbenzene in the presence of surfactants[a)]

Surfactant	2 h	8 h
CTAB	88.7	83.5
NP-10	87.4	78.6
SDS	84.9	73.8
No surfactant	75.3	61.9

a) Reaction temperature: 85℃; reaction time: 8 h; concentrations of the surfactant: 10-fold CMC.

Table 2 Selectivity in mono-chloromethylation of 2-chloroethylbenzene in the presence of surfactants and NaCl[a)]

Surfactant	NaCl (mmol·L^{-1})	2 h	8 h
CTAB	10.0	92.8	89.6
	30.	93.9	91.2
NP-10	10.0	94.2	91.8
	30.0	96.3	94.7
SDS	10.0	90.5	86.2
	30.0	91.5	86.5

a) Reaction temperature: 82℃; reaction time: 8 h; concentration of surfactants: 10-fold CMC.

4 Conclusions

In this research, micellar-catalyzed chloromethylation reaction of CEB in an oil-water biphasic system was carried out successfully for preparation of 2-chloroethylbenzyl chloride. When no surfactants were used, the interface area between oil phase and water phase was very small, so the rate of chloromethylation reaction occurring at the oil-water interface was quite low; however, when surfactant micelles were formed, CEB was solubilized into numerous micelles, the interface area of oil phase/water phase was magnified suddenly and the rate of chloromethylation reaction was accelerated abruptly. Cationic surfactants are more suitable for the chloromethylation reaction of CEB. Furthermore, the structure of cationic surfactant and the addition of inorganic electrolyte can influence the micellization behavior of surfactant, and the micellar catalysis effect as well. The selectivity for mono-chloromethylation was remarkably improved in the micellar solutions.

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