SHORT COMMUNICATION

Selective Nitration of Phenol to *ortho*-Nitrophenol using Dilute Nitric Acid by Microemulsion of Cetytrimethylammonium Bromide (CTAB) in Isooctane

Gen-sheng Yang[†], Jie-hua Shi and Jinghua Li

College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310032, P.R. China

Abstract—The paper reports near-selective nitration of phenol to *ortho*-nitrophenol using CTAB microemulsion solution in the presence of dilute nitric acid. The difference betweem the selective nitration of different kinds of surfactants such as AOT (anionic surfactant) and CTAB (cationic surfactant) has been investigated. All these experimental results indicate that microemulsions can be selective to give the *ortho*-phenol.

Key words: CTAB, Microemulsion, Selective Nitration, Phenol, *o*-Nitrophenol, *p*-Nitrophenol

INTRODUCTION

Microemulsions are a transparent or translucent pseudo-homogeneous mixture of oil (which may be an organic solution of a water-insoluble compound), water (which may contain mineral acid or a salt), and surfactants or a mixture of surfactant and cosurfactant (alcohol), with high thermodynamical stability [Lindman and Danielson, 1981; Langevin, 1986; Holmberg, 1994]. Since Hoar and Schulman first described these systems in 1943, microemulsions have been of great interest in pharmaceutical and cosmetic applications because of their transparent appearance, long stability, and ease of preparation and high solubility of drug [Choi et al., 1999]. They have also been proposed as good solvents for nonpolar organic molecules as well as inorganic salts, and thus appear to be excellent media for facilitating reactions between different species. The pseudo-ternary phase diagram of such systems can be divided into various regions, among which the *type I* and the *type II* regions are of general importance. The *type I* region consists of an oil-in-water type of microemulsion in equilibrium with an excess oil phase, whereas the *type II* region consists of a water-in-oil type of microemulsion in equilibrium with an excess aqueous phase. During the last two decades, a concert effort has been made to understand the structure, dynamics and interactions of microemulsions, mainly because of some of their applications. The microemulsion droplet can be considered as a microreactor where chemical reactions can occur within the small domain provided by the droplet. In addition, microemulsions have recently been used to effect separation and purification. Despite the number of studies highlighting the beneficial effects of microemulsions in enhancing the reaction rates, relatively few studies deal with the related issue of selectivity of desired components, except Chhatre et al. [1993].

The nitration of phenol is normally carried out by initial sulfonation of the compound by sulfuric acid, followed by nitration with nitric acid [Schofield, 1980]. Many scientists have explored phenol and its derivatives for selective nitration. However, no notable region selectivity is observed in the nitration except by Chhatre et al.

[1993]. Chhatre et al. have reported near selectivity of phenol to *ortho*-nitrophenol using a microemulsion solution of sodium salt of dioctyl sulfosuccinate (AOT) in the presence of dilute nitric acid. Their study indicated that microemulsions, besides enhancing the reaction rates, could also be selective to give the desired product.

In the present paper, we investigated the pseudo-ternary phase diagrams of systems containing water, oil (isooctane), Cetytrimethylammonium bromide (CTAB) and co-surfactant of a short chain alcohol butanol and described the results of the experimental investigation of selective nitration of phenol to *ortho*-nitrophenol using microemulsion solution of cetytrimethylammonium bromide (CTAB) in isooctane. The difference between the selective nitration of different kinds of surfactants such as AOT (anionic surfactant) and CTAB (cationic surfactant) is presented alongside the experimental results.

MATERIALS

Phenol crystals (AR grade) were obtained from Shanghai Chemistry Reagent Company (China) and were purified by recrystallization. Benzene (AR grade) procured from Hangzhou Chemistry Reagent Company (China) was purified by distillation and used as a solvent for phenol. Cetytrimethylammonium bromide (AR grade), CTAB, was obtained from Shanghai Chemistry Reagent Import and Export Company (China) and was used as a surfactant and was purified by recrystallization twice by using ethanol and ether. AR grade sodium salt of dioctyl sulfosuccinate, AOT, was purchased from Sigma and used as a surfactant without further purification. Nitric acid, which was also obtained from Hangzhou Chemistry Reagent Company, was used in a diluted form. Isooctane (AR grade) was purchased from Shanghai Chemical Reagent Company (China). AR grade *n*-butanol was purchased from Hangzhou Reagent Company and used as co-surfactant without further purification. The twice-distilled water was obtained from our laboratory.

In this work, the chromatographic experiments were performed on 1102 gas chromatography equipped with FID (Shanghai Analytical Instrument Plant, China) and CDMC-1EX chromatographic data processor (Shanghai Institute of Calculate Technology, China).

EXPERIMENTAL

[†]To whom correspondence should be addressed.
E-mail: gensheng@mail.hz.zj.cn

1. Construction of Pseudo-Ternary Phase Diagrams

Phase diagrams were constructed by using a traditional titration method. The samples were prepared at twenty points of different compositions. Appropriate amounts of CTAB, isooctane and cosurfactant, butanol were weighed into glass vials and the samples were stirred until a clear solution was obtained. The mixing ratio of CTAB to cosurfactant butanol was 1 : 3 (mol ratio). The sealed glass vials were placed in an incubator at 30 °C. Titrated with water drop by drop, the mixing solution was vigorously shaken with the mixer. After this procedure, samples were kept in the incubator at 30 °C for a few days. After equilibrium was reached, the mixtures were both checked visually for clarity. The transition between the clear isotropic solution and two-phase region was determined by visual observation of the samples.

The pseudo-ternary phase diagrams were represented as a ternary diagram, which contained three components of water, oil (isooctane), and surfactant/co-surfactant. The boundary of the phase diagram was drawn within a tiny error.

2. Selective Nitration

In all the experimental runs 100 ml of the aqueous phase was reacted with 25 ml of organic phase. A stirred cell reactor was maintained at 30 °C by thermostatic bath. Its temperature was maintained with an accuracy of ±2 °C. The reactor was provided with a two-blade stirrer. The stirrer was positioned in such a way that half of the width of its blade was in the phenol-benzene mixture and the other half was in the microemulsion. The interface was stirred with extreme care to avoid splashing, and the stirring rate was maintained at 50 rpm and with an accuracy ±2 rpm.

There are three sets in the experiments. In the first set (runs 1-9), three different microemulsions of *type I* (oil-inwater type) were prepared and used for conducting the reactions. The oil-inwater type microemulsion solutions were prepared according to Pseudo-Ternary Phase Diagrams as described above, and the only difference was the substitution of nitric acid for water. The solution thus prepared was then equilibrated with an excess of pure benzene. The excess of benzene was then used to prepare the phenol-benzene mixtures of varying concentrations. In the second set (runs 10-18), the nitric acid with concentrations similar to those in Set 1 was used to contact with phenol-benzene mixtures of varying concentrations. The twice distilled water was substituted for microemulsion. This was done in order to compare the results with those obtained in runs 1-9. In the third set of experiments, AOT, surfactant, was substituted for CTAB. Some experiments were done in the similitude of runs 1-18. This was done in order to compare the results with those obtained in Set 1. The microemulsion and the mixture were then contacted in the stirred cell reactor described above.

After 5 minutes of each reaction, the mixture was demulsified with diethyl ether, its reaction product was extracted, and it was analyzed immediately on the gas chromatograph for its composition.

RESULTS AND DISCUSSION

1. Determination of the Ternary Microemulsions of CTAB/n-Butanol/Isooctane/Water System

The phase behavior of microemulsion of cetytrimethylammonium bromide (CTAB) in isooctane was investigated. Then we repeated the process by using dilute nitric acid that was substituted
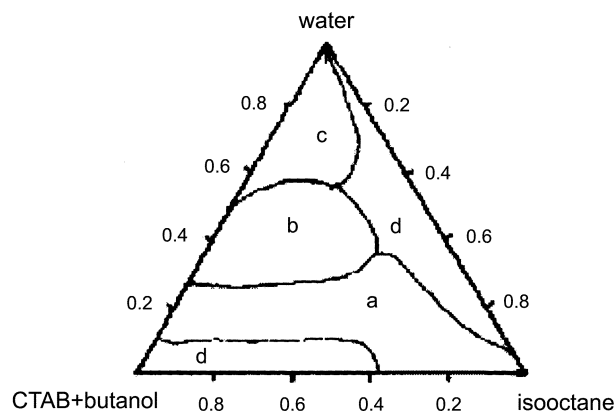

Fig. 1. Pseudo ternary phase diagram.
a : w/o microemulsion   c : o/w microemulsion
b : liquid crystal   d : two phase

for water. The phase diagram of this system is presented in Fig. 1.
2. Selective Nitration

The composition of 100 ml solution of the aqueous phase used in each set is as shown in Table 1. The results of reactions carried out under microemulsion conditions are shown in Table 2 and Table 3, respectively, using nitric acid (no surfactant). Tables 2 and 3 show the product ratio of selectivity between *o*-nitrophenol and *p*-nitrophenol. It is obvious that the selectivity of formation of *o*-nitrophenol was higher than that of *p*-nitrophenol. The two-phase nitration of phenol carried out by Thompson and Zeegers [1989] yielded 55.1% *o*-nitropenol and 41% *p*-nitropenol (the ratio of *o*-nitropenol to

Table 1. Composition of 100 ml aqueous phase solution used in this work

Run no.	Concentration of HNO$_3$ (mol/liter)	CTAB added (g)	n-Butanol (ml)	Isooctane (ml)
1-3	2.03	5.00	3.90	17.40
4-6	3.06	7.46	5.60	11.60
7-9	4.01	10.00	8.00	6.00
10-12	2.03	0.00	0.00	0.00
13-15	3.06	0.00	0.00	0.00
16-18	4.01	0.00	0.00	0.00

Table 2. Nitration reactions of phenol under microemulsion medium

Run no.	HNO$_3$ mol/*l*	Phenol (g)	Ratio of *o*-nitrophenol to *p*-nitrophenol
1	2.03	3.4	1.3
2	2.03	1.8	1.2
3	2.03	0.8	1.1
4	3.06	3.4	2.0
5	3.03	1.8	2.0
6	3.06	0.8	3.5
7	4.01	3.4	1.7
8	4.01	1.8	2.8
9	4.01	0.8	3.6

Table 3. Nitration reactions of phenol with dilute nitric acid (no surfactant)

Run no.	HNO$_3$ mol/l	Phenol (g)	Ratio of o-nitrophenol to p-nitrophenol
10	2.03	3.4	1.2
11	2.03	1.8	1.3
12	2.03	0.8	1.4
13	3.06	3.4	1.0
14	3.06	1.8	1.4
15	3.06	0.8	1.8
16	4.01	3.4	0.3
17	4.01	1.8	0.6
18	4.01	0.8	1.1

Table 4. Nitration reactions of phenol under different microemulsion at constant concentration medium of phenol

Run no.	HNO$_3$ mol/l	Average of ratio of o-nitrophenol to p-nitrophenol in CTAB solution	Average of ratio of o-nitrophenol to p-nitrophenol in AOT solution
1-3	2.03	1.2	3.4
4-6	3.06	2.5	2.1
7-9	4.01	2.7	1.6

p-nitrophenol was about 1.34). The current industrial method [Booth, 1987] employs nitration of chlorobenzene using mixed acid (30% HNO$_3$, 56% H$_2$SO$_4$, 14% H$_2$O), followed by hydrolysis NaOH at 130 °C. The method produces 34-36% of o-nitrophenol, 63-65% of p-nitrophenol and about 1% of m-nitrochlorobenzene. And the selectivity ratio of o-nitrophenol to p-nitrophenol was 0.55. Chhatre et al. [1993] reported that the selectivity of formation of o-nitrophenol was considerably improved (to more than 65%, and to even more than 88% in some cases) through carrying out the reactions in the microemulsion condition (the surfactant is AOT). In the present report we found that the ratio of selectivity of formation of o-nitrophenol and p-nitrophenol was improved in microemulsion of CTAB in isooctane (the highest ratio of o-nitrophenol to p-nitrophenol was 3.63). The mechanism for achieving such an improvement can be explained as below. Phenol has a hydroxyl group which is more hydrophilic than its phenyl group. As a result, when phenol is in the state of interfacial conditions, it orients in such a case that the phenyl group remains extended toward the organic phase, whereas the hydroxyl group protrudes into the aqueous phase. This makes the attack of the nitroniumm ion more likely toward the ortho-carbon atom of phenol, rather than the para-carbon atom that is relatively far from the interface. Nevertheless, we do get an amount of para- and other nitrophenols that include di- and trinitrophenols.

Table 3 shows that the ratio of o-nitrophenol to p-nitrophenol increased inversely when the initial amount of phenol decreased. It may be that phenol solubility in the organic phase isooctane of the microemulsion system was limited, so excess of phenol was dissolved in aqueous phase of the microemulsion system in which the content was nitric acid. Evidently, the product of o-nitrophenol was less and the ratio of o-nitrophenol to p-nitrophenol decreased.

Table 2 shows that the ratio of o-nitrophenol to p-nitrophenol increased relatively when the concentration of HNO$_3$ increased at constant concentration of phenol. Table 4 also shows that the tendency of the average ratio increased as the nitric acid concentration increased in the microemulsion of CTAB; the tendency is inverse in the microemulsion of AOT from Table 4. The phenomenon may be that AOT and CTAB are different types of surfactants. CTAB is a cationic surfactant and AOT is an anionic surfactant. Due to the influence of electric charge state, the cation head of CTAB can be attracted by nitrate ion, so the attack opportunity at ortho-C of phenol may increase when the concentration of nitric acid increases.

CONCLUSION

On the basis of the results reported in this paper, near-selective nitration of phenol o-position can be carried out under microemulsion of CTAB system by using dilute nitric acid. Also, the process of nitration as a whole becomes safer and more economical. Due to the influence of electric charge state of different types of surfactants, the nitration condition and tendency are not same.

REFERENCES

Booth, G., "Ullmann's Encyclopedia of Industrial Chemistry," B. Elvers, S. Hawkins and G. Schulz Eds., Vol. A17, VCH Publishers, FRG (1987).

Chhatre, A. S., Joshi, R. A. and Kulkarni, B. D., "Microemulsions as Media for Organic Synthesis: Selective Nitration of Phenol to ortho-Nitrophenol Using Dilute Nitric Acid," *J. Colloid Interface Sci.*, **158**, 183 (1993)

Choi, S.-Y., Oh, S.-G., Bae, S.-Y. and Moon, S.-K., "Effect of Short-Chain Alcohols as Co-surfactants on Pseudo-ternary Phase Diagrams Containing Lecithin," *Korean J. Chem. Eng.*, **16**(3), 377 (1999).

Holmberg, K., "Organic and Bioorganic Reactions in Microemulsions," *Adv. Colloid and Interface Sci.*, **51**, 137 (1994).

Langevin, D., "Microemulsion and Liquid-crystals," *Mol. Cryst. Liq. Cryst.*, **138**, 259 (1986).

Lindman, B. and Danielson, I., "The Definition of Microemulsion," *Colloids and Surfaces*, **3**, 391 (1981).

Schofield, K., "Aromatic Nitration," Cambridge Uni. Press, London/New York (1980).

Thompson, M. J. and Zeegers, P. J., "A Theoretical Study on the Two-phase Nitration of Phenols," *Tetrahedron*, **45**(1), 191 (1989).