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SELECTIVE PREPARATION OF KEY INTERMEDIATES FOR THE SYNTHESIS OF GEMINI SURFACTANTS BY PHASE-TRANSFER CATALYSIS

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Abstract

A comparison of liquid-liquid and solid-liquid PTC for the selective synthesis of diglycidyl ether from protected pentaerythritol and epichlorohydrin is presented. Solid-liquid PTC was found to be more useful than liquid-liquid PTC because the use of water or other solvents can be avoided and higher yields and selectivity are achieved. It was proved that etherification takes place in the solid phase-organic phase system even in the absence of the phase-transfer catalyst. However, the use of tetrabutylammonium bisulfate as catalyst is essential due to its crucial effect on the enhancement of the rate of etherification and on the improvement of the selectivity to diglycidyl ether, which is higher than 98%.

Keywords: Diglycidyl ether, epichlorohydrin, protected pentaerythritol, selective etherification, phase-transfer catalysis, gemini surfactants

INTRODUCTION

In the last decade, the development of new surfactants having at least two hydrophobic chains and two ionic or polar groups became the subject of intense investigation due to their unique properties. Geminis, the common name for this type of surfactants, can be orders of magnitude more surface-active than comparable conventional surfactants, and their aggregation behavior and micelle shape are drastically different from those of single-chain surfactants [1]. Widespread applications as industrial or household and personal care products have already been found [2]. The selective synthesis of intermediates to avoid mixtures of products is a key factor in the synthetic route to geminis.

Polyglycidyl ethers are useful intermediates for building up the complex structures of geminis [3]. Recently, we reported the use of pentaerythritol diglycidyl ethers as key intermediates for the synthesis of new anionic geminis [4]. These versatile ethers have been synthesized selectively from protected pentaerythritol and epichlorohydrin in the presence of potassium hydroxide in dimethyl sulfoxide (DMSO). Even though this method is useful in laboratory synthesis, it is inconvenient in large-scale preparation because of the expensive make-up and recovery of DMSO. Therefore, to avoid the use of aprotic polar solvents is especially attractive for production purposes.

Since phase-transfer catalysis (PTC) was reported as a convenient method for etherification in two-phase systems [5], long-chain alkyl glyceryl ethers [6], glycol diglycidyl ethers [7], and *N*-acyldiethanolamine diglycidyl ethers [8] have been synthesized under PTC conditions. In previous works, most experiments were conducted in the presence of 48-95% aqueous NaOH solutions, while only a few were carried out directly with NaOH pellets. Recently, solid-liquid PTC has been reported as an advantageous procedure for the synthesis of some monoalkylglycidyl ethers because it improves yields and avoids the use of aqueous NaOH solution [9].

In the present study, an attempt has been made to improve the selectivity of the phase-transfer catalyzed reaction for the preparation of diglycidyl ether from protected pentaerythritol and epichlorohydrin (Scheme 1). Yields and selectivity for liquid-liquid and solid-liquid reaction systems are compared, and some key factors in achievement of the highest selectivity for diglycidyl ether formation (as required for the synthesis of geminis) are discussed.
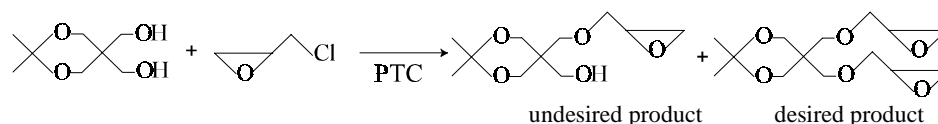
Scheme 1

EXPERIMENTAL

Tetrabutylammonium bisulfate (99%) (TBAB), epichlorohydrin (99%) and sodium hydroxide (97%, 20-40 mesh beads) were purchased from Aldrich Chemical Co. All these chemicals were used without further purification. Protected pentaerythritol (1,5-dioxaspiro[5,5]undecano-3,3-dimethanol) was synthesized and purified as previously reported [10].

Reaction experiments were carried out in a 100-mL three-neck conic-bottomed flask fitted with an efficient mechanical stirrer (100-1000 rpm). The reaction flask was placed in a thermostated water bath and the temperature of the reaction mixture was kept within ± 0.2°C. The stirring rate was controlled so that the organic phase in the mixture was finely dispersed.

Reactions were followed by withdrawing samples of the reaction mixture (0.25 mL) during the course of the reaction, and continued until the increase in yield was negligible. The crude of reaction was filtered and washed with dichloromethane (2 × 25 mL) and diethyl ether (4 × 25 mL). The combined organic extracts were analyzed by GLC analysis using a Shimadzu GC-17AATF chromatograph equipped with a methyl silicone capillary column (30 m × 0.32 mm, 0.25 µm film thickness) and flame ionization detector.

Liquid-liquid PTC

A mixture of 1,5-dioxaspiro[5.5]undecane-3,3-dimethanol (843.5 mg, 3.90 mmol), 50 % aqueous sodium hydroxide (35.6 mL, 890.0 mmol) and epichlorohydrin (3.0 mL, 39.0 mmol) was heated to the desired temperature (30 or 40°C) under vigorous stirring (700 rpm). The phase-transfer catalyst, TBAB (132.4 mg, 0.39 mmol, 10 mol %), was added all at once, and the temperature of the reaction mixture was kept constant until the reaction was completed. The reaction was stopped when the yield of diglycidyl ether (monitored by GC) did not increase any more with increasing reaction time. Yields and selectivity were calculated based on the amounts of products estimated by GC. Results are summarized in Table 1.

Solid-liquid PTC

A mixture of 1,5-dioxaspiro[5.5]undecane-3,3-dimethanol (843.5 mg, 3.90 mmol), sodium hydroxide pellets (0.936 g, 23.4 mmol), water (0.1 mg, 1 wt.%) and TBAB (132.4 mg, 0.39 mmol, 10 mole %) was heated to the desired temperature (30 or 40°C) under vigorous stirring (700 rpm). Epichlorohydrin (3.0 mL, 39.0 mmol) was added all at once, and the temperature of the reaction mixture was kept until the reaction was completed. The progress of all reaction products was followed as described above for the aqueous phase-organic phase reaction system. Values of yields and selectivity are summarized in Table 2.

RESULTS AND DISCUSSION

The low solubility of the protected pentaerythritol in water proved to be a limiting factor in determining the diol/NaOH ratio to be used in the aqueous phase-organic phase reaction system. Only a large excess of 50 % aqueous NaOH solution over alcohol ensures a fast and complete dissolution of the diol with an efficient alkoxide anions formation. For this reason, diol/NaOH equivalent ratios as large as 100-fold had to be used at 30°C. The amount of TBAB was increased gradually from 2 to 30 mole % for optimization purposes. The phase-transfer catalyzed reaction did not take place using 2 mole % TBAB (Table 1, run 1). However, when 10 mole % TBAB was used, the yield of diglycidyl ether reached 41 % in about 120 min (Table 1, run 2). The rate of reaction increased significantly with increasing the amount of TBAB from 20 to 30 mole %, but the maximum yields of diglycidyl ether only increased from 47 to 51 % (Table 1, runs 3 and 4). Indeed, these yields could be achieved in 90 min using 20 mole % TBAB or in less than 40 min with 30 mole % TBAB. Despite the fact that the yield only rose to about 50%, the selectivity was nearly 100 %.

The large excess of the aqueous NaOH solution seems to be responsible for these results. When the Na$^+$/TBA$^+$ ratio is very large, the conversion of the alkoxide anions from the sodium to ammonium form is difficult. Therefore, the phase-transfer process is inefficient and a significant amount of catalyst is needed to enhance the rate of etherification, as observed. A significant amount of alkoxide anions remains in the aqueous phase without being extracted by the TBA$^+$ catalyst; consequently, ethers are obtained in low yields. The lack of monoglycidyl ether formation, as desired, can be explained by the large OH$^-$/alkoxide anions ratio, and it will be discussed once some additional experimental evidence be presented.

Attempts to improve the yield of diglycidyl ether were made by decreasing the NaOH equivalents to the minimum amount below which the diol is insoluble. An ultrasonic bath was used to attend to the dissolution process. The lowest admissible diol/NaOH ratio was 1/45 equivalent, which is still a very large excess. Then, the diol/epichlorohydrin ratio was gradually increased from 10 to 30, using an amount of catalyst in the range of 3-10 mole % TBAB. In a final choice, a diol/epichlorohydrin/NaOH ratio of 1/20/45 was used for 4 mole % TBAB. The overall yield of glycidyl ethers was 95%, but the selectivity was 55.8 % (Table 1, run 5). This significant increase of the yield was achieved with an undesirable loss of the selectivity. To explain this behavior we give the following explanation.

Since the tetrabutylammonium hydroxide is soluble in the organic phase, the formation of ion pairs between OH$^-$ and TBA$^+$ may be important in determining

the selectivity because the monoglycidyl ether can undergo etherification to diglycidyl ether in their presence. For large OH⁻/alkoxide anions ratios, the tetrabutylammonium hydroxide formation is expected to a great extent; the result is a facile conversion of the monoglycidyl ether to diglycidyl ether yielding, in consequence, to high selectivity. But, if the presence of tetrabutyl-ammonium hydroxide in the organic phase decreases, as expected for lower ratios, the etherification of the monoglycidyl ether in the organic phase is more difficult and, then, the process is less selective.

Table 1

Etherification of 1,5-dioxaspiro[5.5]undecane-3,3-dimethanol with epichlorohydrin using TBAB as phase-transfer catalyst in liquid-liquid reaction systems

Run	TBAB (mole %)	Diol/Epichlor./NaOH wt.% NaOH	Time (h)	Yield of ethers (%)		Selectivity (%)
				Monoglycidyl	Diglycidyl	
1	2	1 / 10 / 228 50% NaOH	2	0	0	0
2	10	1 / 10 / 228 50% NaOH	2	0	41	> 99
3	20	1 / 10 / 228 50% NaOH	2	0	47	> 99
4	30	1 / 10 / 228 50% NaOH	2	0	51	> 99
5	4	1 / 20 / 45 50% NaOH	5	42	53	55.8

Yields and selectivity values reached after the reaction was completed at 30°C

Consequently, large excesses of aqueous NaOH solution should be avoided to achieve good yields, while they are needed to obtain a high selectivity. These opposing effects prompted us to carry out the etherification in solid-liquid reaction system avoiding the use of aqueous NaOH solution.

The epichlorohydrin and the products themselves were used as solvent to carry out the reaction without other solvents. The solid-phase consisted of diol and NaOH pellets, containing 1 wt.% of water. The amount of TBAB was increased gradually from 0 to 10 mole %. A diol/epichlorohydrin/NaOH ratio of 1/10/6 equivalents was adopted. Table 2 summarizes the yields and selectivity after the etherification was completed at 40°C. It was found that etherification takes place even in the absence of the phase-transfer catalyst; the overall yield of ethers was 89 % and the selectivity was 53.9 % (Table 2, run

6). The partial lipophilic character of the diol and the strong desiccant effect of the NaOH pellets seem to have great importance on this result. Since the diol is rather soluble in epichlorohydrin, it is present in the organic phase (epichlorohydrin). Then, the etherification can readily occur in the presence of a desiccant source, as NaOH pellets, in the organic phase.

Table 2

Etherification of 1,5-dioxaspiro[5.5]undecane-3,3-dimethanol with epichlorohydrin using TBAB as phase-transfer catalyst in solid-liquid reaction systems

Run	TBAB (mole %)	Diol/Epichlor./NaOH wt.% NaOH	Time (h)	Yield of ethers (%)		Selectivity (%)
				Monoglycidyl	Diglycidyl	
6	0	1 / 10 / 6 99 % NaOH	5	41	48	53.9
7	10	1 / 10 / 6 99% NaOH	1.5	< 1	92	98.9
8	4	1 / 10 / 6 99% NaOH	3	< 1	85	98.8

Yields and selectivity values reached after the reaction was completed at $40^{\circ}C$

However, the use of TBAB is essential due to its crucial effect on the improvement of the rate of etherification and the selectivity. When a 10 mole % TBAB was used, the diglycidyl ether was obtained in good yield (92 %) and excellent selectivity (98.9 %) after 1.5 h (Table 2, run 7). The reaction time increased with decreasing amount of TBAB, but yields and selectivity were not significantly modified, as expected. These results indicate that TBAB is again a key factor to enhance the phase-transfer rate through the formation of ion pairs between alkoxide anions and TBA^+ and to improve the selectivity as discussed before.

It can be concluded that the PTC carried out in solid phase-organic phase proved to be the most efficient two-phase system for the preparation of the diglycidyl ether. This method is highly selective and avoids the expensive use of aprotic polar solvents or large excesses of aqueous NaOH solutions. These advantages determine the usefulness of this method for the large-scale preparation of this type of key intermediates for the synthesis of gemini surfactants.

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