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New and efficient technique for the synthesis of ε -caprolactone using KHSO₅ as an oxidising agent in the presence of a phase transfer catalyst

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1. Introduction

The Baeyer–Villiger (BV) reaction is one of the most important transformations in organic chemistry [1,2]. Nearly a century ago, just one year after potassium peroxomonosulphate (KHSO₅) was first described, the BV oxidation was reported by Baeyer and Villiger [3]. Although KHSO₅ has since been replaced by organic peracids, hydrogen peroxide and alkyl hydroperoxides [4,5], the use of KHSO₅ in the BV reaction has recently increased. KHSO₅ is a versatile oxidising agent and is commercially available as the stable triple salt (2KHSO₅·KHSO₄·K₂SO₄, e.g., oxone[®]), which is easy to handle, non-toxic and relatively inexpensive. As a result, the triple salt has been studied as a routine reagent for epoxidation reactions, the oxidation of aldehydes to carboxylic acids and other oxidation processes for the synthesis of fine chemicals [6,7].

Oxone[®] has also been used as an oxidising agent in the BV oxidation. However, to use oxone[®], an aqueous reaction medium must be employed, which can cause the products of the reaction to hydrolyse. Alternatively, anhydrous potassium peroxomonosulphate on silica can also be used (SiO₂·KHSO₅) [8,9]. Moreover, in the synthesis of lactones, selected ionic liquids have been used as solvents for KHSO₅ [10].

In the present study, BV oxidation was achieved with $KHSO_5$ in the presence of a phase transfer catalyst (PTC). Until now, only one report on the use of PTC for the oxidation of ketones to lactones

ABSTRACT

A new method for the synthesis of ε -caprolactone based on the Baeyer–Villiger oxidation of cyclohexanone was developed. In the proposed reaction, potassium peroxomonosulphate was used as an oxidising agent under phase transfer catalysis conditions. The effects of the reaction parameters, including the type of phase transfer catalyst, the concentration of the oxidising agent, the type of organic solvent and temperature, were investigated. When dichloromethane was used as an organic solvent and an adequate amount of water was added to the reaction mixture, the highest yield and selectivity for ε -caprolactone were achieved at 40 °C.

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has been presented. However, in the aforementioned study, borax and H_2O_2 was used as the oxidising agent [11]. Borax forms peroxy species with H_2O_2 , which can be transferred into the organic phase. Herein, we present the synthesis of ε -caprolactone from cyclohexanone using potassium peroxomonosulphate as an oxidising agent.

2. Experimental

2.1. Materials

All the phase transfer catalysts used in the present study were commercially available materials. Tetrabutylammonium bromide (TBAB) and tetrabutylphosphonium bromide hydrosulphate (TBPB) were obtained from Fluka Chemie AG. Benzyltributylammonium chloride (BTBAC) and tributylmethylammonium chloride (TBMAC) were purchased from Merck. 18-Crown-6, dibenzo-18-crown-6 and dicyclohexano-18-crown-6 were obtained from Fluka. 2KHSO₅·KHSO₄·K₂SO₄, n-decane and cyclohexanone (99% pure) were purchased from Acros Organics.

2.2. Experimental procedure

2.2.1. Analysis

¹H NMR and ¹³C NMR spectra were recorded at 300 MHz and 75 MHz in CDCl₃, respectively (Varian Unity Inova plus, TMS as the internal standard). GC analysis was performed on a PerkinElmer chromatography equipped with a PerkinElmer Elite-624 column (30 m, 0.53 mm ID, 3 μ m df), and decane was used as an internal standard.

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2.2.2. Kinetics measurments

Cyclohexanone (10.2 mmol), decane (an internal standard, 0.5 g), 2KHSO₅·KHSO₄·K₂SO₄ (10.2 mmol), H₂O (10 cm³) and an organic solvent (30 cm³) were introduced into a three-neck round bottom flask (150 cm³) equipped with a mechanical stirrer and a condenser. The vessel was placed in a temperature-controlled oil bath with an accuracy of ± 1 °C, and a phase transfer catalyst (1.02 mmol) was added to the flask. The reaction was stirred at 40°C for 6h and was monitored by GC. Samples were taken from organic layer after 15, 30, 60, 90, 150, 240, 360 min and analyzed by GC. When the reaction was complete, phases were separated. When hexane or toluene was used as the organic solvent, dichloromethane (25 cm³) was added to the post-reaction mixture to dissolve the product. The organic layer was washed with water (10 cm^3) and 5% aqueous NaOH $(3 \times 10 \text{ cm}^3)$ to remove all residual peroxy compounds and phase transfer catalyst. Next, the crude mixture was washed with water $(2 \times 10 \text{ cm}^3)$, dried over anhydrous MgSO₄ and the solvent was evaporated under vacuum. The crude, concentrated mixture was analysed by NMR.

2.2.3. Synthesis of ε -caprolactone

Cyclohexanone (0.102 mol), 2KHSO₅·KHSO₄·K₂SO₄ (0.102 mol), $H_2O(100 \text{ cm}^3)$ and $CH_2Cl_2(300 \text{ cm}^3)$ were introduced into a threeneck round bottom flask (750 cm³) equipped with a mechanical stirrer and a condenser. The vessel was placed in a temperaturecontrolled oil bath with an accuracy of ± 1 °C, and TBAB as a phase transfer catalyst (10.2 mmol) was added to the flask. The reaction was stirred at 40 °C for 6 h. When the reaction was complete, phases were separated. The organic layer was washed with water (50 cm^3) and 5% agueous NaOH $(3 \times 50 \text{ cm}^3)$ to remove all residual peroxy compounds and TBAB. Next, the crude mixture was washed with water $(2 \times 50 \text{ cm}^3)$, dried over anhydrous MgSO₄ and concentrated. The crude product was chromatographed with hexane/ethyl acetate (v/v 3/1) as the eluent. The solvent was evaporated under vacuum and ε -caprolactone was obtained with 77%. ¹H-NMR (300 MHz, CDCl₃, TMS): δ = 4.23 (m, 2H); 2.63 (m, 2H); 1.77 (m, 6H); 13 C NMR (CDCl₃): δ = 175.55; 68.53; 33.75; 28.57; 28.07; 22.23; b.p. 235 °C.

3. Results and discussion

The oxidation of the cyclohexanone to ε -caprolactone was selected as a model reaction. The synthesis of ε -caprolactone is of great importance in the chemical industry. Currently, ε -caprolactone is prepared through the oxidation of cyclohexanone using O₂/acetaldehyde (BASF) or peroxyacetic acid (Perstorp).

Potassium peroxomonosulphate, the active compound in the triple salt (2KHSO₅·KHSO₄·K₂SO₄), was selected as an alternative oxidising agent to organic peroxyacids for the Baeyer-Villiger reaction. However, because potassium peroxomonosulphate is only soluble in water, it was essential to find a solvent system to carry out to the synthesis of ε -caprolactone.

In our preliminary studies (Table 1), it was found out that the oxidation process in a two-phase system consisting of organic phase (cyclohexanone dissolved in dichloromethane) and inorganic solid phase (2KHSO₅·KHSO₄·K₂SO₄) conducted at 40 °C did not proceed. ε -Caprolactone was not detected, and the conversion of cyclohexanone was not observed. Although high conversions were obtained after water was added to the reaction mixture, the synthesis of ε -caprolactone was not achieved. Rather, the product of lactone hydrolysis, 6-hydroxyhexanoic acid, was detected in the crude mixture. Thus, the results suggested that the BV lactone product was sensitive to hydrolysis.

Phase transfer catalysis is a powerful method that allows reactions to be conducted in a two phase system (liquid–liquid or liquid–solid). The role of the PT catalyst is to facilitate the transfer

Table 1

The effect of the addition of water (10 cm³) and phase transfer catalyst (TBAB, 1.02 mmol) on the oxidation of cyclohexanone. Reaction conditions: cyclohexanone, 1.0 g, 10.2 mmol; 2KHSO₅·KHSO₄·K₂SO₄, 6.3 g, 10.2 mmol; dichloromethane, 30 cm³; decane, 0.5 g, 3.5 mmol; temperature, 40 °C; 800 rpm.



of the reactant from one phase to another. This technique allows for acceleration of the reaction rate and easy separation of reaction mixtures. With phase transfer catalysis, good selectivity for hydrolytically unstable reagents can be obtained despite the presence of water in the reaction medium [12,13].

In the present study, TBAB, the most common PT catalyst, was added to the studied reaction systems, which consisted of an organic phase and inorganic phase (a solid triple salt or a triple salt and water). As a result, only in the system with water high yields of ε -caprolactone were obtained, and by-products were not detected (Table 1). Thus, to achieve BV oxidation with KHSO₅, water and a phase transfer catalyst are necessary.

An interesting phenomenon was observed when toluene and hexane were used as the solvent. As shown in Fig. 1, the type of organic solvent had a significant effect on the oxidation of cyclohexanone. For instance, when hexane was used as the organic solvent, 100% conversion of cyclohexanone was obtained within 30 min. ε -Caprolactone is not soluble in hexane and is only partially soluble in toluene; thus, the reaction rate may have increased due to the formation of a separate layer based on the insoluble product. Unfortunately, in the aforementioned layer, the desired product was exposed to the effects of water, and ε -caprolactone was hydrolysed, and in hexane only 6-hydroxyhexanoic acid was



Fig. 1. Variation of the conversion of cyclohexanone with the time on stream during the reaction of cyclohexanone with $2\text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$ in the presence of different solvents (30 cm^3): (\blacklozenge) hexane; (\blacksquare) toluene; (\blacktriangle) dichloromethane. Reaction conditions: cyclohexanone, 1.0 g, 10.2 mmol; $2\text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$, 6.3 g, 10.2 mmol; TBAB, 1.02 mmol; H_2O , 10 cm³; decane, 0.5 g, 3.5 mmol; temperature, $40 \circ \text{C}$; 800 rpm. Y – yield of ε -caprolactone after 6 h.



Fig. 2. Variation of the conversion of cyclohexanone with the time on stream during the reaction of cyclohexanone with 2KHSO₅·KHSO₄·K₂SO₄ in the presence of different phase-transfer catalysts (1.02 mmol): (\blacklozenge) BTBAC; (\blacksquare) TBMAC; (\bigstar) TBAB; (\bigcirc) TBPB. Reaction conditions: cyclohexanone, 1.0 g, 10.2 mmol; 2KHSO₅·KHSO₄·K₂SO₄, 6.3 g, 10.2 mmol; H₂O, 10 cm³; decane, 0.5 g, 3.5 mmol; dichloromethane, 30 cm³; temperature, 40 °C; 800 rpm. Y – yield of ε -caprolactone after 6 h.

obtained. Although hydrolysis product was also observed in the presence of toluene, the partitioning phenomenon was less significant. For instance, after 150 min, 48% ε -caprolactone was obtained, and the conversion of cyclohexanone was 93%. Alternatively, in dichloromethane, the lactone was completely protected from hydrolysis.

Variations in the catalytic activity of selected catalysts over time were compared under otherwise identical conditions. Several quaternary ammonium salts were evaluated, including TBAB, BTBAC, TBMAC, TBPB (Fig. 2), 18-crown-6, dicyclohexano-18-crown-6 and dibenzo-18-crown-6 (Fig. 3). As shown in the figures, all of the catalysts were highly active in the BV oxidation of cyclohexanone. Nevertheless, the highest initial reaction rate was observed in the presence of BTBAC and dibenzo-18-crown-6.

The standard amount of water used in the experiments $(10.2 \text{ mmol of a triple salt}, 10.2 \text{ mmol of cyclohexanone in } 30 \text{ cm}^3 \text{ of dichloromethane})$ was 10 cm^3 . To evaluate the effects of the water concentration, the model reaction was performed with 1, 2, 3, 4, 5



Fig. 3. Variation of the conversion of cyclohexanone with the time on stream during the reaction of cyclohexanone with $2\text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$ in the presence of different phase-transfer catalysts (1.02 mmol): () dibenzo-18-crown-6; () divergence of a stream of the stream o



Fig. 4. Variation of the conversion of cyclohexanone with the time on stream during the reaction of cyclohexanone with $2\text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$ in the presence of different amounts of water: (\diamondsuit) 20 cm^3 ; (\square) 10 cm^3 ; (\bigstar) 5 cm^3 , (\bigcirc) 4 cm^3 ; (\bigcirc) 3 cm^3 ; (\square) 2 cm^3 ; (\square) 20 cm^3 ; (\square) 10 cm^3 ; (\bigstar) 5 cm^3 , (\bigcirc) 4 cm^3 ; (\bigcirc) 3 cm^3 ; (\square) 2 cm^3 ; (\square) 10 cm^3 ; (\square) 20 cm^3 ; $20 \text{$

and 20 cm³ of water. It was found that in the presence of PT catalyst the reaction rate and yield of lactone increase with the rise of amount of water in the reaction system. As shown in Fig. 4, the highest initial rate was observed with 20 cm³ of water, but traces of hydroxy acid (<1%) were observed as a by-product. However, the highest yield of ε -caprolactone was obtained with 10 cm³ of water, and no by-products were observed. As shown in Fig. 5, the reaction rate for the oxidation of cyclohexanone was slower at room temperature than at 40 °C.

To optimise the reaction conditions, the oxidation of cyclohexanone was performed at a ketone: triple salt molar ratio of 1:0.5 and 1:1.5 (which is equivalent to 1:1 and 1:3 ketone: KHSO₅, respectively) (Fig. 6). The results indicated that the rate of the reaction increased with an increase in the KHSO₅ concentration because the extraction of lipophilic pairs ($Q^+HSO_5^-$) into the organic phase was more efficient. However, to minimise the overall cost of the process, the reaction was conducted at a 1:1 ketone: triple salt ratio.



Fig. 5. Variation of the conversion of cyclohexanone with the time on stream during the reaction of cyclohexanone with 2KHSO₅·KHSO₄·K₂SO₄ at different temperatures: (\blacklozenge) 40 °C; (\blacksquare) room temperature. Reaction conditions: cyclohexanone, 1.0 g, 10.2 mmol; 2KHSO₅·KHSO₄·K₂SO₄, 6.3 g, 10.2 mmol; TBAB, 1.02 mmol; H₂O, 10 cm³; decane, 0.5 g, 3.5 mmol; dichloromethane, 30 cm³; 300 rpm. Y – yield of ε -caprolactone after 6 h.



Scheme 1. BV reaction in two-phase system under PTC conditions.



Fig. 6. Variation of the conversion of cyclohexanone with the time on stream during the reaction of cyclohexanone with 2KHSO₅·KHSO₄·K₂SO₄ at different molar ratios cyclohexanone:KHSO₅: (\blacklozenge) 1:3; (\blacksquare)1:2; (\blacktriangle)1:1. Reaction conditions: cyclohexanone, 1.0 g, 10.2 mmol; TBAB, 1.02 mmol; H₂O, 10 cm³; decane, 0.5 g, 3.5 mmol; dichloromethane, 30 cm³; temperature, 40 °C; 800 rpm. *Y* – yield of ε -caprolactone after 6 h.

To summarize, the experimental results demonstrate that the oxidation reaction of cyclohexanone by oxone conducted in a two-phase liquid–liquid system consisting of organic phase (cyclohexanone dissolved in dichloromethane) and inorganic phase (2KHSO₅·KHSO₄·K₂SO₄ dissolved in water) is very rapid both in the presence and absence of a phase transfer catalyst. Moreover, the oxidation reaction without PTC is even faster than in the presence of the PTC. However, in the reaction conducted without catalyst the only product is 6-hydroxyhexanoic acid in 100% selectivity, whereas the addition of PTC leads exclusively to ε -caprolactone being produced (selectivity of lactone was 100%).

We postulate different mechanisms for these two cases:

1. When the oxidation is conducted without the PT catalyst, we assume that the reaction takes place only at the boundary between organic and aqueous phases. Oxone does not dissolve in the organic phase and that is why KHSO₅ cannot enter the organic phase. Evidence for that comes from the experiment in which a two-phase system consisting of a water solution of oxone and dichloromethane was stirred for 6 h at room temperature. After that the phases were separated and the organic phase was concentrated and then analysed by the iodometric determi-

nation of peroxy compounds. We have not found any traces of $\rm HSO_5^-$ in the organic phase.

2. In the case of the reaction carried out in the presence of PT catalyst, HSO₅⁻ can enter the organic phase in the form of lipophilic pairs Q⁺HSO₅⁻ which are continuously extracted from the inorganic phase into the organic phase, where the BV reaction occurs (Scheme 1). The extraction of Q⁺HSO₅⁻ was confirmed by iodometric titration. The concentration of HSO₅⁻ in organic phase was around 8%.

4. Conclusions

In conclusion, an efficient method for the synthesis of ε caprolactone using a commercially available, safe, stable and inexpensive oxidising agent (KHSO₄) was developed. The use of phase transfer catalysts enabled the transfer of reactive species from the inorganic phase to the organic phase and protected the lactone from hydrolysis. Compared to the use of peroxyacids or hydrogen peroxide as the oxidant, the proposed method is relatively inexpensive, the reagents are readily available, ε caprolactone is obtained in high yield, the product was easily isolated, the reaction time was relatively short, and mild reaction conditions were employed. Thus, the proposed process is suitable for the industrial scale synthesis of ε -caprolactone.

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