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Low-Waste Process for Preparing Ketopantolactone, with Electrochemical Recovery of Bromine

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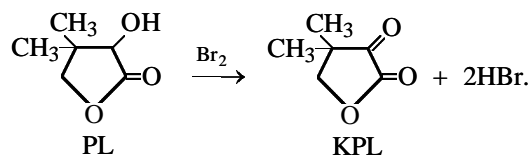
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Abstract—The process parameters of dehydrogenation of pantolactone with bromine in chloroform and the possibility of bromine recycling by electrolysis of hydrogen bromide formed in the synthesis of ketopantolactone were studied.

Ketopantolactone (KPL) shows promise for pharmaceutical industry. The known methods for its preparation are based on oxidative dehydrogenation of pantolactone (PL).

There are published data on oxidation of PL with oxygen in the presence of a catalyst [1, 2], as well as with calcium hypochlorite [3–5], potassium bromate [6, 7], bromine [8–10], and organic peroxides [11]. These data show that PL is catalytically oxidized at 180–300°C and elevated pressure, which requires complex equipment; the target product undergoes partial tarring. With chlorine or calcium hypochlorite, abundant nonutilizable wastewater is formed. The reaction with bromine as dehydrogenating agent proceeds by the scheme:



This scheme suggests formation of an equivalent amount of hydrogen bromide, which is suitable for high-yield recovery of recyclable bromine. This option was recognized as the most promising and was technologically developed.

In [10], dehydrogenation of PL with bromine in refluxing carbon tetrachloride was recommended; the reaction is complete within 5–8 h. In [9], this period was reduced to 1 h by adding a minor amount of water to the reaction mixture.

Presently, carbon tetrachloride is considered unsuitable as solvent for environmental reasons and its production is to be closed [12]. Therefore, we re-

placed carbon tetrachloride with chloroform in our experiments. Next, the possibility of recovery of bromine from an aqueous solution of hydrogen bromide formed in the synthesis was analyzed.

The initial experiments on dehydrogenation of PL in chloroform failed. The reaction was incomplete even after refluxing the PL solution in chloroform with bromine for 14 h, probably because of the lower boiling point of CHCl_3 , compared to CCl_4 . The situation was substantially improved by introducing minor amounts of water to the reaction mixture: When 10 ml of water was added to 60 ml of chloroform, the reaction was complete after heating for 3.5 h. However, further increase in the content of water decreased the weight of the target product. For example, upon adding 60 ml of water, the yield of KPL after refluxing for 5 h was only 48%, and at water content below 10% the reaction was decelerated and HBr evaporated.

An important role is also played by the PL concentration in chloroform. Table 1 shows that, at the PL : chloroform ratio of 1 : 7.5, the KPL yield remains fairly high, but falls dramatically with the amount of chloroform decreasing further; the reaction does not go to completion despite longer heating time. Thus, we developed a procedure for preparing KPL in 92–95% yield.

All the above-described experiments were performed in a 150-ml reactor charged with 4 g of PL. To test the suitability of the process for large-scale application, we carried out an experiment in a 2-l reactor charged with 100 g of PL, 900 ml of chloroform, 160 ml of water, and 137 g of bromine. The very first run showed that, on passing to a larger reactor,

Table 1. Influence of the PL concentration in chloroform on the yield of KPL (4 g of PL, 5.27 g of Br₂)

CHCl ₃ , ml	Water, g	PL : CHCl ₃ ratio	Yield of KPL, %
40	1.0	1 : 10	82.8*
30	5.5	1 : 7.5	91.8
20	5.0	1 : 5.0	80.0
10	2.5	1 : 2.5	30.0**

* 7-h refluxing. ** The reaction was incomplete in 8 h.

Table 2. Influence of the electrolysis mode on the degree of bromine recovery (anolyte volume 500 ml)

HBr charge, g	I, A	Q, A h	Br ₂ obtained	
			g	%
196	10	58	112	64
217	10 → 5	78	197	87
213	10 → 5	71	176	86
213	10 → 5 → 2	72	194	91

the reaction is significantly decelerated: Upon refluxing of the mixture for 3 h 50 min, only 47% of the charged PL reacted. Upon further refluxing for 3 h 30 min, PL was 75% converted. Our attempt to accelerate the reaction by illuminating the reaction mixture with a 300-W incandescent lamp was successful: Upon 45-min illumination, PL fully entered into the reaction, and the yield of isolated KPL was 85%.

Further experiments showed that, under intensive illumination, the reaction was complete within 15–20 min, but the yield of KPL decreased to 70–79%. Thus, illumination intensifies not only oxidative dehydrogenation but also side reactions, which have, most probably, the radical nature. By varying the power of the light source and the distance separating it from the reactor, we empirically chose the conditions at which the reaction was complete within 2 h and the yield of KPL based on the reacted PL was within 82–85%.

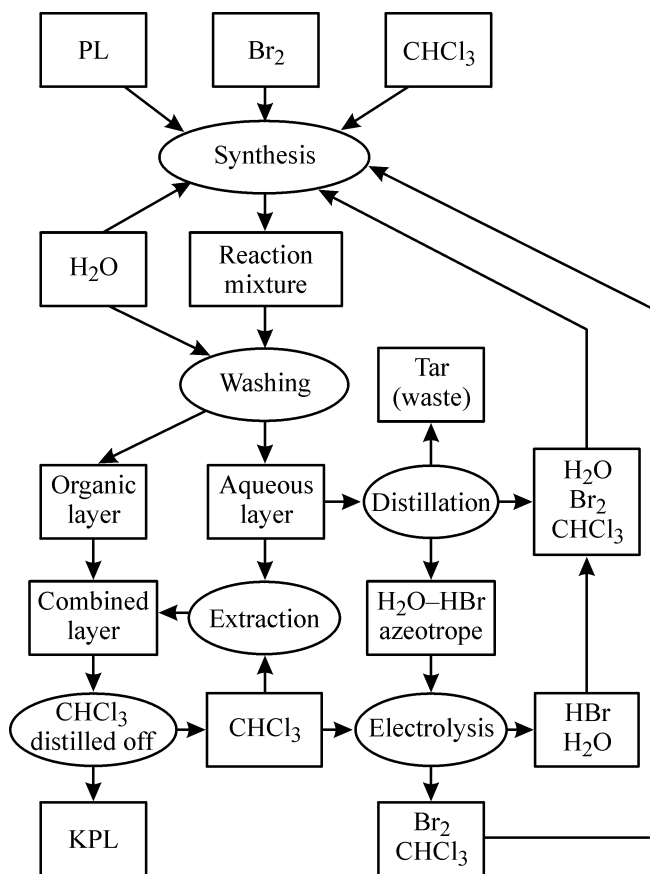
To free the HBr solution from organic impurities, the aqueous layer was distilled on a film evaporator. First, water containing unchanged bromine and chloroform dissolved in the aqueous layer was distilled off at 100–102°C. Then the vapor temperature increased, and the HBr–H₂O azeotrope containing 48% hydrogen bromide was distilled off at 123–124°C. The bottoms contained ca. 8 g of a thick tar composed, most probably, of the products of side reactions accompanying the dehydrogenation of PL. The distilled-off aqueous phase, containing bromine and chloroform, was re-

cycled, and the HBr–H₂O azeotrope was subjected to electrolysis for recovery of bromine.

Bromine was recovered in the cathode chamber of a filter-press electrolyzer under permanent extraction of the evolving bromine with chloroform. Electrolysis was performed in the batch mode, the current lowered stepwise. The initial current density was 0.25 A cm⁻²; after 50% of the calculated amount of electricity *Q* was passed, it was decreased to 0.10 A cm⁻², and the remaining 15% of the electricity was applied at a current density of 0.05 A cm⁻². In this mode, it is possible to recover over 90% of the bromine present in solution in the form of bromide ions. The effect of a stepwise decrease in the current density is clearly illustrated by Table 2. It is reasonable to utilize the depleted anolyte containing 3–5% HBr instead of water in further KPL synthesis.

In the experiments utilizing the generated bromine-containing solutions, the yield of KPL was 83 and 88%. A control run with pure reactants under the identical conditions gave an 85% yield.

The general flowsheet of the suggested process is shown below.



Flowsheet of the KPL synthesis involving bromine recovery.

EXPERIMENTAL

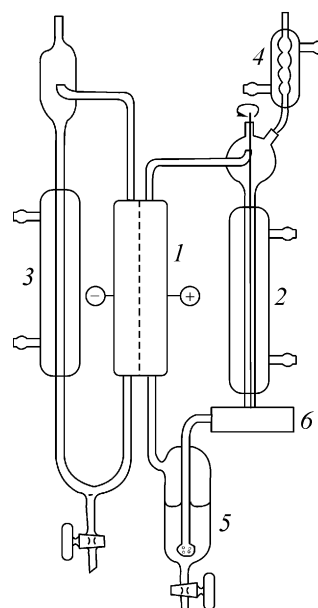
In this study, we used *DL*-pantolactone (mp 74–77°C). The other reactants (bromine and chloroform) were of chemically pure grade.

Into a 2-l flask equipped with a reflux condenser and a stirrer, 100 g of PL, 960 ml of chloroform (870 ml of recycled and 90 ml of fresh), 150 ml of water (or depleted anolyte), and 137 g of bromine were introduced. The reaction mixture was illuminated with a 300-W incandescent lamp and refluxed for 2 h. The reaction was regarded as complete when no traces of PL were revealed by gas chromatography. The reaction mixture was transferred into a separatory funnel; for better separation of the aqueous layer, 40 ml of water was added. The separated organic layer was washed with 40 ml of water. This water was combined with the separated aqueous layer, which was a concentrated solution of hydrogen bromide. The resulting aqueous layer was treated with chloroform (2 × 30 ml). The extract was combined with the organic layer, and chloroform was distilled off. The hot bottoms were transferred into a beaker for crystallization. After 1 h, the crystalline KPL precipitate had a constant weight of 83.7 g, mp 64–66°C. The waste was ca. 350 ml of an aqueous hydrogen bromide solution containing 127 g of HBr and 11.7 g of bromine.

Distillation of the aqueous layer on the film evaporator yielded 84 ml of a fraction containing water, bromine, and chloroform, 255 ml of the HBr–H₂O azeotrope, and 8 g of the bottoms containing the reaction by-products.

The HBr–H₂O azeotrope mixture was electrolyzed in a filter-press electrolyzer with the anode and cathode spaces separated by a NAFFION-403 membrane. A stainless-steel plate served as cathode, and DEZ-3 graphite used in chlorine production, as anode. Prior to being used, graphite was impregnated with a paraffin–polyethylene melt. The electrodes and the membrane were separated by 4 mm. The catholyte circulation was effected by a gas lift system, and anolyte circulation, by a rotary pump. The solution leaving the anolyte entered a backup reservoir where it passed through a chloroform layer. The bromide formed on the anode was dissolved in a chloroform layer. When the required concentration was reached, the solution of bromine in chloroform was fed to synthesis of KPL. The figure presents the general view of the setup for bromine recovery.

The anode chamber of the electrolyzer was charged with 500 ml of a 33.4% solution of HBr containing



Schematic of the setup for electrochemical recovery of bromine: (1) electrolyzer, (2) anode circuit cooler, (3) cooler at the cathode off-gas line, (4) reflux condenser, (5) backup reservoir, and (6) rotary pump.

213.4 g of the bromide ion. As anolyte was used 150 ml of a HBr solution of the same concentration. Chloroform (80 ml) was poured into the backup reservoir. Electrolysis was performed in three steps at current densities of 0.25, 0.10, and 0.05 A cm⁻², respectively. The anolyte temperature during electrolysis was kept within 12–15°C. After each step, the solution of bromine in chloroform was discharged from the backup reservoir, and a fresh portion of chloroform (88 ml) was added. A total of 188.4 g of bromine dissolved in 240 ml of chloroform was obtained in our experiment. Waste anolyte consisted of 490 ml of the aqueous solution of HBr containing 24.7 g of HBr. Bromine was recovered to 88%. The waste anolyte

Table 3. Major parameters of a typical run*

Step no.	<i>I</i> , A	<i>I/S</i> , A cm ⁻²	<i>τ</i> , h	<i>V</i> , V	<i>Q</i> , A h	Br ₂ obtained, g	CE, %
1	10	0.25	3.6	7.5	36.0	100.3	93.3
2	5	0.124	4.4	5.0	22.0	55.4	84.4
3	2	0.05	6.8	3.2	13.6	32.6	80.5
Total						188.4	88.0

* *S* is the electrode surface area; *V*, voltage; and CE, current efficiency.

was used in the synthesis instead of water. The electrolysis mode and bromine yields in each step are presented in Table 3.

CONCLUSIONS

(1) Pantolactone can be dehydrogenated with bromine in chloroform.

(2) At the pantolactone : chloroform : water ratio of 1 : 7.5 : (0.85–0.90) in the reaction mixture, keto-pantolactone can be prepared in 82–85% yield. The process can be accelerated 3–4-fold by illuminating the reaction mixture.

(3) A method for electrochemical recovery of bromine and its recycling was developed. Three percent of bromine is lost in the developed scheme.

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