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STUDY OF THE MODES OF CONVERSION OF p-NITRO-α-METHOXYSTYRENE INTO p-NITRO-α-BROMOACETOPHENONE

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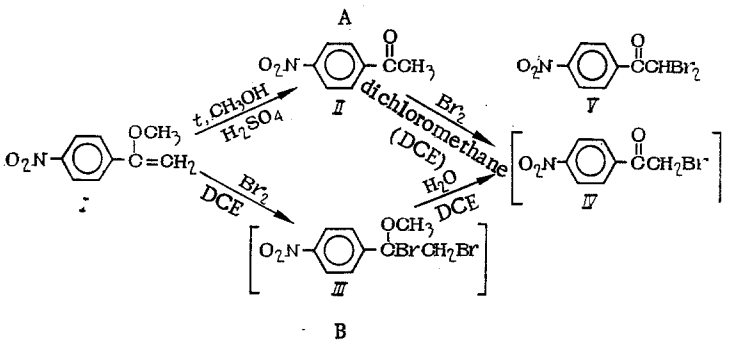
UDC 615.332 (Laevomycetinum).012.1.002.62

During the production of laevomycetin and syntomycetin, p-nitro-α-bromoacetophenone (IV) is prepared from p-nitro-α-methoxystyrene (I) by two methods.



According to method A, (I) is hydrolyzed in aqueous methanol in the presence of catalytic amounts of sulfic acid while the reaction mixture is boiled [1]. The solution of p-nitroacetophenone (II) purified by charcoal is cooled to 18-20°, and (II), which separates out, is filtered, dried, and used in dry dichloroethane for the preparation of (IV).

According to method B, (I) is brominated in dry dichloroethane [1, 2], and 1-(p-bromophenyl)-1-methoxy-1,2-dibromoethane (III) thus formed is hydrolyzed to (IV). Then the solution is dried by azeotropic distillation of water with dichloroethane, and used for the preparation of the urotropin complex.

A gas–liquid chromatographic (GLC) analysis of the solution of the bromoketone (IV) obtained by the above methods showed that in both cases the yield and the quality of the required product are practically the same. The product obtained after bromination contains not only the required compound (IV) but also up to 5-7% of p-nitro-α,α-dibromoacetophenone (V) and its equivalent amount of ketone (II). The formation of (V) can be explained by acid-catalyzed bromination of (IV) (method A) and the disproportionating action of hydrogen bromide (methods A and B).

If the above methods for the preparation of (IV) are compared, it is seen that method A is more labor and raw-material consuming, requires a more complex apparatus, and has a more prolonged production cycle. Therefore, in the present work, we studied the process of preparation of (IV) by method A, without isolation of ketone (II), and we also considered the problem of the possible preparation of the required bromoketone from compound (III) by its thermal dissociation.

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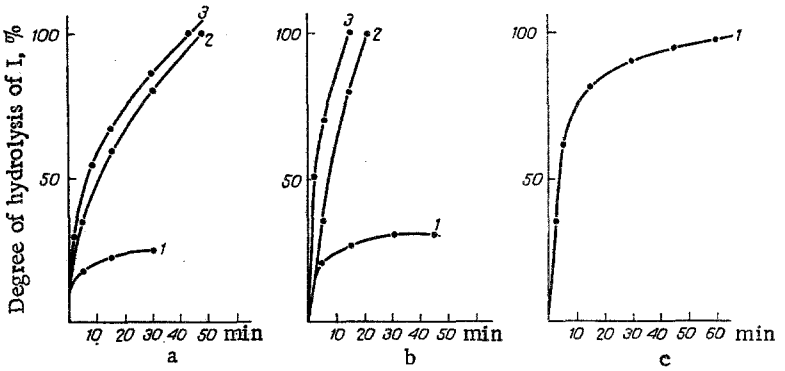

Fig. 1. Dynamics of the hydrolysis of p-nitro-α-methoxystyrene in dichloroethane as a function of temperature at different concentrations of hydrogen bromide in the aqueous phase. Ratio between the aqueous and organic phases 1:1 by volume, rate of stirring 80-100 rpm. Temperature: a) 10°; b) 30°; c) 83°. Concentration of hydrogen bromide in water: 1) 1; 2) 10; 3) 20%.

To solve the first problem, we studied the dynamics of hydrolysis of (I) in dichloroethane in the presence of hydrobromic, hydrochloric and sulfuric acids. The rate of stirring and the ratio between the phases were kept constant, and the concentration of the acid in the aqueous phase and the reaction temperature were varied. The experimental data obtained with hydrobromic acid as the aqueous phase are shown in Fig. 1. Similar results were also obtained with sulfuric and hydrochloric acids of corresponding concentrations. The composition of the reaction mixture during hydrolysis was determined by GLC. From the results it follows that the rate of hydrolysis of (I), other conditions being equal (temperature, rate of stirring, ratio between the phases), depends appreciably on the concentration of hydrobromic acid used. Figure 1 shows that when 1% hydrobromic acid is used, the rate of hydrolysis of (I) is suitable for industrial purposes at the boiling point of the reaction mixture only. With 10-20% acid it is possible to hydrolyze (I) at fairly high rate at low temperatures (see Fig. 1a, b). We attempted to reduce the volume of the apparatus at the plant, and further studied the possibility of decreasing the amount of the hydrobromic acid employed. It was found that with 30% hydrobromic acid, it is possible to quantitatively hydrolyze (I) in dichloroethane after 1 h at 18-20°. Hydrobromic acid is taken in such an amount that 3-3.5 equivalents of water could be introduced per 1 equivalent of (I). The dichloroethane layer was washed from methanol and hydrogen bromide, and the solution of ketone (II) was azeotropically dried. The latter was brominated under conventional conditions [1]. According to the GLC data and the melting point, the product obtained did not differ from that obtained from (I) by the existing technology.

It was interesting to study also the possibility of converting compound (III) into the bromoketone (IV), omitting the stage of hydrolysis of (III), and hence bringing the reaction products into a contact with hydrogen bromide. In analogy to the reaction with α,β-dihaloethyl alkyl ethers [4], compound (III) should split off methyl bromide on heating, and become converted into (IV). Methyl bromide can thus be used as such [5], or be converted into bromine by the method of catalytic oxidation of alkyl halides described in literature [6].

The thermolysis of a 15% solution of (III) in dichloroethane was studied in the temperature range of 40-83° (boiling the reaction mixture). We assumed that the reaction proceeds according to mechanism E1, and determined the main kinetic parameters (the rate constant of the reaction at 60° was $4.8 \cdot 10^{-3}$ min^{-1}, the activation energy of thermolysis, 16 kcal/mole). It was found that the complete dissociation of (III) is achieved after 9 h of boiling the reaction mixture. However, analysis of the reaction solution after the thermolysis showed that in this case also a product is formed, which contains 5-8% of an admixture of (V) and its equivalent amount of ketone (II). The appearance of (V) during the thermolysis of (III) can be explained if it is assumed that compound (III) can brominate p-nitro-α-bromoacetophenone.

We have showed already the possibility of brominating with compound (III) in the case of acetophenone (VI). When a solution of (III) in dichloroethane is mixed with an equivalent amount of acetophenone and held for 3 h at 18-20°, about 60% of (VI) was converted into α-bromoacetophenone (VII). When the temperature was increased to 60°, α,α-dibromoacetophenone (VIII) appeared in appreciable amounts together with α-bromoacetophenone. In these processes, methyl bromide and p-nitroacetophenone were also formed. We did not study the mechanism of the side process of bromination of (IV) by compound (III), since this was beyond the scope of the present research.

Thus, during the preparation of bromoketone (IV) by method A, it is possible to exclude the isolation of (II) by carrying out the hydrolysis of (I) in dichloroethane in the presence of an aqueous solution of a mineral acid. Hydrogen bromide obtained as a byproduct in the bromination of ketone (II) can be used as the acid catalyst. By introducing into the industrial production the above method of hydrolysis of (I) in a heterogeneous medium, it is possible to appreciably decrease the labor-consuming character of the process, to omit the use of the toxic methyl alcohol, and also to shorten the production cycle during the production of bromoketone (IV) by scheme A. Moreover, it was shown that compound (III) can be converted into bromoketone (IV) by heating the dry solution of(III) in dichloroethane.

EXPERIMENTAL METHOD

The study was carried out on a gas chromatograph "Tsvet-4" with a flame-ionization detector. Conditions of analysis: a 300 × 0.3 cm column of stainless steel with 10% polymethylsiloxane OV-101 on Gas-Chrom Q (60-80 mesh). Temperature of vaporizer 280°, and of column 210°. Gas carrier — helium, consumption 40 ml/min. Ratio between consumption of helium, hydrogen and air was 1:1:7.5. Size of the sample was 1 microliter, unit scale $200 \cdot 10^{-8}$. The impurities were identified by adding pure substances — indicators. A quantitative analysis was carried out by the method of internal normalization of peak areas using calibration coefficients (without taking the solvent into account). An analysis of the reaction mixture during a study of the brominating action of compound (III) on acetophenone was carried out under similar conditions. The values of the calibration coefficients were 1 for (II) and (VI), 1.63 for (VII), 3.94 for (IV), 1.91 for (VIII), 5.8 for (V), and 1.22 for (I). The relative error of the determination did not exceed ±1%.

p-Nitro-α-bromacetophenone (IV) according to Method A (without isolation of ketone (II)). Compound (I) (35.8 g, 0.2 mole) is dissolved in 250 ml of dichloroethane, 15.4 g of a 30% hydrobromic acid is added, and the mixture is stirred (80-120 rpm) for 1 h at room temperature. The mixture is then left for 10 min to settle, and the lower hydrobromic acid layer is separated. The dichloroethane solution of (II) is washed with water from hydrogen bromide to neutral reaction of the washings, and then dried by azeotropic distillation of water with dichloroethane. A solution is obtained which contains, according to the GLC data, 32.4 g of (II) (98%), mp 81-83°. The dried solution of (II) is heated to 30°, and 31.4 g of bromine is added dropwise. When the reaction mixture is completely decolorized, hydrogen bromide is removed by passing a current of nitrogen. The product obtained contains, according to the GLC data (without taking the solvent into account), 92.5% of (IV), 1.5% of (II) and 6% of (V). Yield of (IV) 93%, calculated on (II).

p-Nitro-α-bromoacetophenone (thermolysis of (III)). Compound (I) (35.8 g, 0.2 mole) is dissolved in 250 ml of dichloroethane, 31.4 g of bromine is added, and the mixture is heated to boiling for 9 h. The end of thermolysis of (III) is determined by the absence of acid after treating the sample with water, while the composition of the product is determined by the GLC method. The yield and the composition of the product are practically the same as those obtained from (I) without the isolation of ketone (II), or in accordance with the present technology by methods A or B.

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BIOCHEMICAL PURIFICATION OF WASTEWATERS FROM THE PRODUCTION OF SYNTHETIC VITAMINS A, B_1, B_2 AND C

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The wastewaters from the production of synthetic vitamins contain various organic and inorganic compounds [1, 2]. Many of these compounds undergo biochemical destruction with difficulty, or inhibit the oxidation of other compounds. We have already determined [3] the conditions of biochemical decontamination of industrial wastewaters from the production of vitamins A, B_1 and C, the wastes of which were taken in the ratio of 1:74:5, respectively. Because of the increase in the production output of vitamins and changes in the technology of their preparation, in the present work we studied possible biochemical purification of the total waste of the Belgorod vitamin combinate, containing mainly the wastes from the production of vitamins A, B_1, B_2, and C.

To find the optimum conditions for biochemical purification of the total waste, we used a two-stage laboratory model of an aeration tank mixer. The choice of this system was based on the high effectiveness of the purification and the stability of operation of the equipment used for the purification when the content of organic contaminations in the total waste is increased. The advantages of the two-stage system are that each stage forms a biocenosis of the active sludge, maximally adapted to the conditions of treatment of the contaminations, and that the oxygen from the air fed in is effectively utilized. The model was prepared from plexiglass. The aeration tank had a capacity of 5 liters, the regenerator of 1.5 liters, the sedimentation tank, 0.65 liters. The capacity of the aeration tank and the regenerator of stage (II) were the same as those used at stage (I).

The unpurified wastewaters are characterized by different reaction of the medium (pH 5.0-11.0) and a high concentration of organic contaminations, of up to 2150 mg O_2/liter according to chemical oxygen demand (COD, dichromate oxidation) and up to 1570 mg/liter according to the total biochemical oxygen demand (BOD_{total}). Other indices of the unpurified wastewater delivered to the aeration tank after the neutralization and settling are given in Table 1.

Since in the wastewater which we studied, the nitrogen and phosphorus present were insufficient for carrying out an effective biochemical purification, they were added in the form of ammonium nitrate and potassium monophosphate, in amounts calculated so that the ratio BOD_5:N:P = 100:5:1 [4].

The model of the aeration tank mixer worked for 24 h per day at room temperature.

The control of the operation of the aeration tank mixer was carried out according to the basic sanitary-chemical and microscopic factors, determined daily. Every 10 days we carried out a complete complex of hydrochemical investigations. The consumption of air was determined in relation to the concentration of the dissolved oxygen, which was maintained within 1.5-2 mg/liter in the aeration tanks of stages (I) and (II). The aeration period was 24 h. The growth and the adaptation of the spontaneous microflora of the active sludge was continued for 120 days. The initial COD value of the waste passed to the aeration tank was 100 mg O_2/liter. When stable indices of the purified liquid were obtained, the concen-

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