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Process Optimization of Biphenile Chloromethylation

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Abstract Optimization of the biphenile chloromethylation process with paraphormaldegide has been done in the presence of $ZnCl_2$ with HCl gas by the Box–Wilson method of mathematical planning of experiment. The 4,4'–(dichloromethyl)–biphenile yield dependence on the biphenile - paraphormaldegide ratio, temperature and reaction duration has been studied. A mathematical model of the process has been developed and optimal conditions for the biphenile chloromethylation procedure has been determined.

1. Introduction

The well known chlorometilation reaction is of great importance, since chlorine derivatives of aromatic compounds are intermediate products of synthesis of medicines, as well as chemicals protecting plants, dyes and others [1]. There is no any publication concerning procedure for producing 4,4'-(dichloromethyl)-biphenile. For this reason the biphenile chloromethylation reaction has been studied.

A 4,4'-(dichloromethyl)-biphenile is an intermediate component used in production of various classes of compounds which are in wide use in human life. Particularly, they are used in production of optical bleaches [2, 3] consumption of which in the world reaches to about 60-80 thousand tons per year [4]. It is also used in production of cleaning powder [5], thermoresistant and chemically resistant polymers [6]. Therefore, optimization and development of technological process to synthesize a 4,4'-(dichloromethyl)-biphenile is of practical interest.

In the papers [7] and [8] there were described procedures for production of 4,4'-(dichloromethyl)-biphenile in the presence of zinc chloride adding HCl gas in the reaction mixture (63% yield) and with aqueous HCl solution in the trichloroacetic acid (80% yield and 90% purity).

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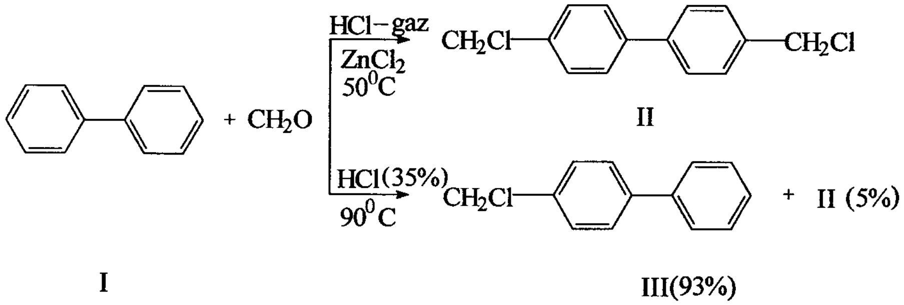

Our experiments on biphenile chloromethylation (I) with heating in concentrated HCl [9] have shown that monocloromethylphenile (III) was produced with 90% yield. Add of HCl gas in the reaction mixture and in the presence of zinc chloride, the yield of the 4,4'-(dichlormethyl)-biphenile (II) was 90% with 95% purity. Therefore, to develop a technological scheme to produce a 4,4'-(dichloromethyl)-biphenile it was necessary to make optimization of the process.

2. Results and discussion

To optimize a synthesis of a 4,4'-(dichloromethyl)-biphenile we used the Box-Wilson method of mathematical modeling of experiments [10]. There were performed preliminary monofactor experiments to study a dependence of the 4,4'-(dichloromethyl)-biphenile yield on temperature, reaction duration and amount of waterless zinc chloride. A biphenile chloromethylation reaction has been performed at the constant molal ratio of the biphenile-paraphormaldegide-$ZnCl_2$ which was 1.5:3.3:1, and different temperatures - 40, 45, 50, 55, 60, 65, 70 o C duration of the reaction was 9 hours (Fig.1).

At the temperature of 40 and 45℃ the reaction was not completed fully, and residual monochloromethylbifenile up to 6% presented in the reaction chemical mixture. At the temperature of 50℃, the reaction completed fully with a maximum yield of 90.3% and purity of 95%. Further temperature increasing resulted in decreasing the 4,4'-(dichloromethyl)-biphenile yield due to formation of by-products up to 15%. In this connection we have selected

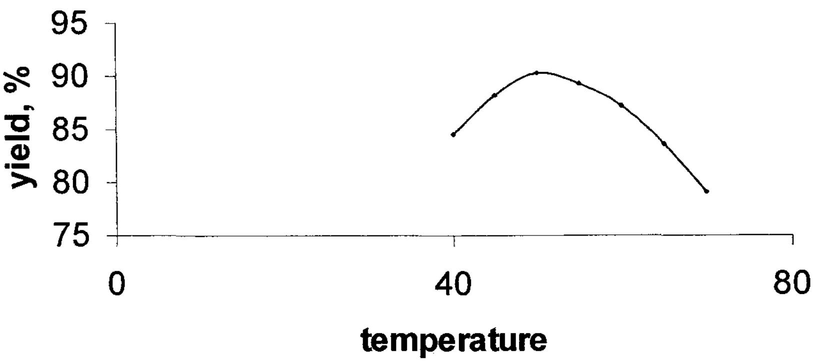

Fig. 1. Dependence of 4,4'-(dichloromethyl)-biphenile on the reaction temperature

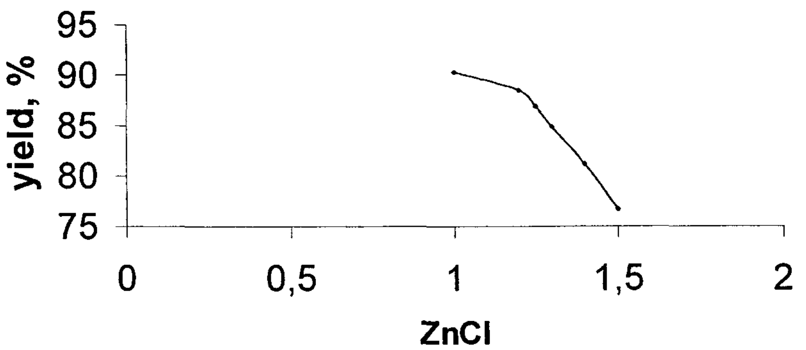

Fig.2. Dependence of 4,4'-(dichloromethyl)-biphenile on the amount of $ZnCl_2$

optimum temperature of 50℃ and studied yield of dichloromethyl derivative at different amounts of zinc chloride. Duration of the reaction was 9 hours. The results of the experiments have been shown in Fig.2.

From the Fig.2 it can be seen that increasing amount of waterless zinc chloride results in decreasing the reaction product yield. The experiments have also shown that when the portion of $ZnCl_2$ was less than 50% of the initial amount the reaction failed.

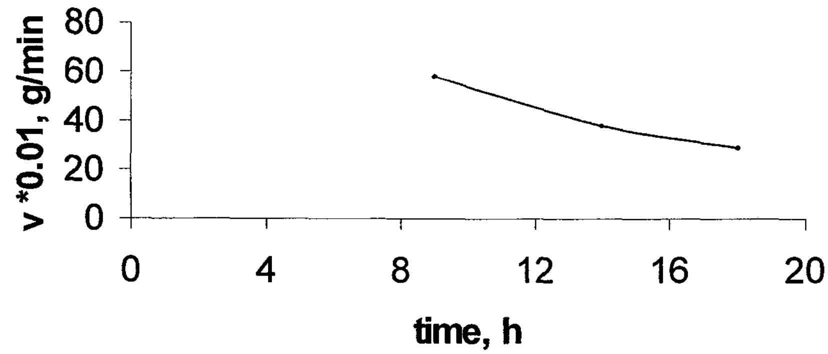

Fig.3. Dependence of the mean rate of HCl entering on the reaction duration

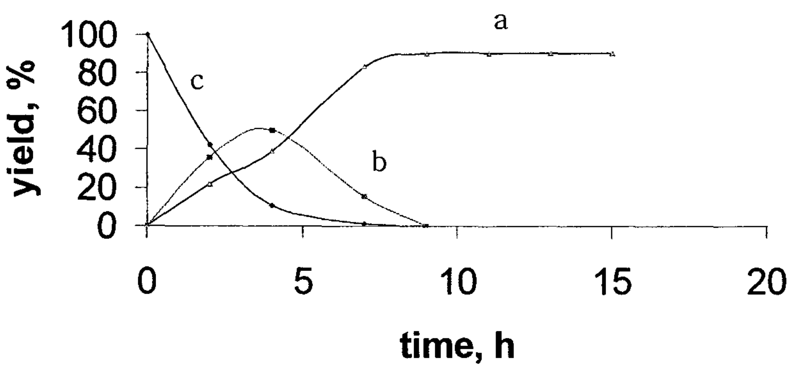

Fig.4. Dependence of 4,4'-(dichloromethyl)-biphenile on the reaction process duration

The next set of experiments was aimed at the study of duration of the reaction process on the 4,4'-(dichloromethyl)-biphenile yield. Duration of the biphenile chloromethylation reaction depends on the amount of HCl-gas coming in during reaction process. In this connection we have determined the mean rates of HCl-gas entering at different reaction duration, namely, 9, 14 and 18 hours. The results are shown in Fig. 3.

It was revealed that increase of mean rate of HCl coming in the reaction mixture leads to decreasing duration of the reaction process. Dependence of the biphenile chloromethylation reaction product yield on

Table 1. Parameters and variation ranges

Parameters	Variation levels -1	0	+1	Variation ranges
x1	50	60	70	10
x2	9	13.5	18	4.5
x3	1	1.25	1.5	0.25

the 1.5:3.3:1 molal ratio of the biphenile-paraphormaldegide-$ZnCl_2$ at the 50℃ is shown in Fig. 4 (a). There also are shown changes of 4-chloromethylbiphenile (b) and biphenile (c).

It can be seen from this figure that HCl gas coming in the reaction mixture longer than 9 hours does not increase the 4,4'-(dichloromethyl)-biphenile yield. A similar relation was observed at the mean HCl-gas rates during 14 and18 hours reaction process, respectively.

main parameters having effect on the biphenile chloromethylation process can be considered x1 = temperature of the reaction (oC), x2 = duration of the reaction process and x3 = the waterless zinc chloride portion relative to its initial amount.

For optimization of the process a full factor experiment 23 with expanded planning matrix was used. Results of the experiments carried out are presented in Table 2.

Table 2. Planning matrix and the results of the experiments

No	x0	x1	x2	x3	x1x2	x1x3	x2x3	x1x2x3	y1	y2	y	S2	y	(y-y)2
1	+	−	−	−	+	+	+	−	90.1	90.5	90.3	0.08	88.68	2.62
2	+	+	−	−	−	−	+	+	79.0	79.2	79.1	0.02	79.28	0.03
3	+	−	+	−	−	+	−	+	66.9	68.5	67.7	1.28	69.30	2.56
4	+	+	+	−	+	−	−	−	61.2	59.0	60.1	2.42	59.90	0.04
5	+	−	−	+	+	−	−	+	77.2	76.2	76.7	2.25	77.14	0.19
6	+	+	−	+	−	+	−	−	68.9	73.5	71.2	10.5	72.18	0.96
7	+	−	+	+	−	−	+	−	61.1	55.3	58.2	8.41	57.76	0.96
8	+	+	+	+	+	+	+	+	55.0	52.6	53.8	2.88	52.80	1.00

On the base of these experiments, the

Results of statistical analysis (G0.95 (1.8)

$$y = 69.63-3.59x1-9.69x2-4.66x3+0.58x12+1.11x13+0.71x23-0.31x123 \quad (1)$$

$$y = 69.63-3.59x1-9.69x2-4.66x3+1.11x13 \quad (2)$$

b_1	x_1= 3.59 10 = 35.9	b_1	x_1/ 20 = 1.795 2°C
b_2	x_2= 9.69 4 = 38.76	b_2	x_2 / 20 = 1.938 2 h
b_3	x_3= 4.66 0.25 = 1.165	b_3	x_3/ 20 = 0.058 0.006%

= 0.6798, Gexp = 0.3789; S2rep = 3.49; S2adq = 5.07; t0.05 (8) = 2.31; F0.95 (5.8) = 3.7; F_{exp} = 1.45) have shown that the model is adequate since $F_{exp} < F_{tab}$. From the results given in Table 2 the following regression function have been derived:

After estimation of significance of the equation (1) coefficients by Student criteria the following mathematical model of the process has been received:

This equation was used for the program of sharp rising on the surface of response function in order to determine optimum conditions for the maximum 4,4'-(dichloromethyl)-biphenile yield. The variables in these experiments were temperature, reaction duration and amount of waterless zinc chloride. Intervals (or steps) of the variables were taken bjxj / 20:

Table 3. Results of the sharp rise experiments

N	x1	x2	x3	y1	y2	y
9	60	13.5	1.25	86.8	89.4	88.1
10	58	11.5	1.19	88.6	89.8	89.2
11	56	9.5	1.13	90.1	89.9	90.0
12	54	7.5	1.07	87.6	89.4	88.5

The results of the sharp rise experiments are given in the Table 3.

It can be seen from the table that the best result has been received in the experiment No1. Parameter variation in the sharp rise experiments did not improve the reaction yield. This can be explained by the fact that increasing the reaction duration leads to increasing mean HCl -gas rate coming in the reaction chemical mixture; a high HCl-gas rate leads to getting away the solvent, that leads to decreasing a solubility of the reagents at the initial stage of the reaction, and, therefore, leads to lowering the 4,4'-(dichloromethyl)-biphenile yield. On the other hand, increase of waterless zinc chloride leads to increasing intermediate layer that lessens the reaction product yield.

3. Conclusions

The carried out experiments and use of the Box - Wilson mathematical model made it possible to make optimization of the biphenile chloromethylation process and determine optimal conditions for this process. Optimal values of the main parameters responsible for the maximum 4,4'-(dichloromethyl)-biphenile yield have been determined to be:

- molal ratio of the biphenile-paraphormaldegide-$ZnCl_2$ 1.5:3.3:1;
- temperature 50℃;
- duration of the reaction process 9 hours.

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