INVESTIGATION OF THE STRUCTURE OF CHEMICAL COMPOUNDS, METHODS OF ANALYSIS, AND QUALITY CONTROL

ANALYSIS OF THE MAIN PRODUCTS OF THE NITRATION OF α-METHOXY-β-CHLOROETHYLBENZENE BY GLC

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One of the key intermediates in the industrial synthesis of chloramphenicol is p-nitro-α-methoxy-β-chloroethylbenzene (II) which is obtained by the nitration of technical α-methoxy-β-chloroethylbenzene (I) containing up to 15% α,β-dichloroethylbenzene (III) as principal contaminant. On nitrating (I) with a mixture of nitric and sulfuric acids a mixture of products was obtained containing the o-, m-, and p-isomers of (I) and (III). The composition of the reaction mass after nitration of (I) under industrial conditions was characterized only by density. A procedure for GLC analysis has been developed by us for the reliable determination of (II) in the reaction products.

According to the recommendations in [1] several sorbents were used for chromatographic separation of the nitration products. These were 10% Apiezon on Chromaton NAW-DMCS, 5% XE-60 on Chromaton, and 5 and 10% polyethyleneglycol succinate on Chromaton NAW-DMCS. Optimum separation was achieved using Chromaton NAW-DMCS (0.125-0.160 mm) with 5% polyethyleneglycolsuccinate. An analytical method with internal standard was used for the quantitative determination of the reaction mixture. o-Nitrochlorobenzene was taken for (I) and (III) and 2,4-dinitrotoluene for the remaining substances. Weight correction coefficients were determined for all compounds allowing for the percentage content of each substance in the reaction mixture. There were 13 peaks on the chromatogram, three of which were not identified. Results of statistical treatment are shown in Table 1. A chromatogram of the reaction mass obtained on nitration of technical (I) is shown in Fig. 1.

For the reliable identification and determination of the order of yield of the isomeric nitro-α-methoxy-β-chloroethylbenzenes we synthesized m- and o-nitro-α-methoxy-β-chloroethylbenzene. The remaining compounds, viz., α-methoxy-β-chloroethylbenzene [2], p-nitro-α-methoxy-β-chloroethylbenzene [2-4], α,β-dichloroethylbenzene [5], and p-nitro-α-β-dichloroethylbenzene [6] were obtained according to literature data.

The analytical method developed by us may be used in the manufacture of chloroamphenicol for determining the yield and ratios of p-, m-, and o-nitro-α-methoxy-β-chloroethylbenzenes in nitration products of technical α-methoxy-β-chloroethylbenzene.

EXPERIMENTAL

PMR spectra were recorded on a Varian XI-100 A spectrometer (USA) with tetramethylsilane as internal standard. Analyses were carried out on a LKhM-8 MD chromatograph with a thermal conductivity detector

TABLE 1. Results of Statistical Treatment of Data on Percentage Content of Nitro Isomers of α-Methoxy-β-chloroethylbenzene in Reaction Mass

Component	Content, %	Statistical characteristic							
		$\bar{x}$	S^2	S_x	$S_{\bar{x}}$	t_α	Δx_α	$x \pm \Delta x_\alpha$	$\frac{\Delta x_\alpha \cdot 100}{\bar{x}}$, %
p-Nitro-α-methoxy-β-chloroethyl benzene	66,81; 64,43; 66,03; 63,00; 65,59	65,17	2,22	1,4885	0,6657	2,776	1,848	65,17±1,848	2,84
m-Nitro-α-methoxy-β-chloroethyl benzene	21,49; 22,91; 23,65; 24,01; 24,46	23,90	0,4309	0,6564	0,2936	2,776	0,815	23,9±0,815	3,40
o-Nitro-α-methoxy-β-chloroethylbenzene	9,13; 8,37; 9,20; 9,44; 9,12	9,05	0,1616	0,402	0,1795	2,778	0,4991	9,05±0,499	5,50

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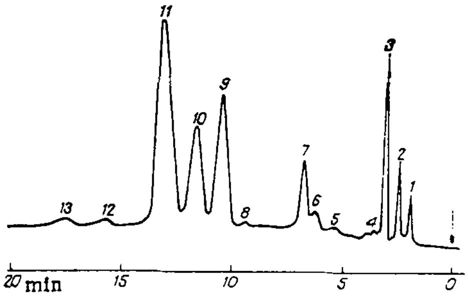

Fig. 1. Chromatogram of reaction mixture. 1) α-Methoxy-β-chloroethylbenzene; 2) α,β-chlorobenzene; 3) o-nitrochlorobenzene; 4) first unknown contaminant; 5) second unknown contaminant; 6) third unknown contaminant; 7) o-nitro-α-methoxy-β-chloroethylbenzene; 8) supposedly o-nitro-α,β-dichloroethylbenzene; 9) 2,4-dinitrotoluene; 10) m-nitro-α-methoxy-β-chloroethylbenzene; 11) p-nitro-α-methoxy-β-chloroethylbenzene; 12) supposedly m-nitro-α,β-dichloroethylbenzene; 13) p-nitro-α,β-dichloroethylbenzene.

with a metal column of length 3 m and internal diameter 0.3 cm under the following conditions. Evaporator temperature was 275°C, detector temperature 240°C, column temperature (programmed 140-200°C at 12°C/min), min), carrier gas consumption 40 ml/min), carrier gas consumption 40 ml/min, detector current 100 mA.

m-Nitro-α-methoxy-β-chloroethylbenzene. Chlorine (6 g; 0.16 mole) was passed at 20°C through a solution of m-nitrostyrene (12 g; 0.08 mole) in methanol (75 ml) and the mixture was then stirred at this temperature for 3 h. The methanol was evaporated, chloroform (50 ml) and water (30 ml) were added to the residue, the organic layer was separated, washed with water (30 ml), and dried over sodium sulfate. The solvent was evaporated and the residue was recrystallized from methanol. m-Nitro-α-methoxy-β-chloroethylbenzene (11.3g; 0.05 mole) was obtained in 62.5% yield of mp 52-55°C. Found, %: C 50.10; H 4.68; N 6.50. $C_9H_{10}NO_3Cl$. Calculated, %: C 50.12; H 4.68; N 6.50. PMR spectrum (deuterochloroform), δ ppm: 3.34 singlet (OCH_3), 4.45 triplet (CH), 3.38-3.8 multiplet (CH_2Cl), 8.13 doublet 2-CH), 8.09 multiplet (4-CH), 7.4-7.7 multiplet (5,6-CH).

o-Nitro-α-methoxy-β-chloroethylbenzene. α-Methoxy-β-chloroethylbenzene (17.06g; 0.1 mole) was added slowly to a mixture (39 g) containing nitric acid (10g; 0.16 mole), sulfuric acid (23g; 0.24 mole), and water (6 g) cooled to 10°C. The mixture was stirred for 2 h at this temperature poured into ice-water (100ml). The solid was filtered off and washed on the filter with cold methanol (30 ml). p-Nitro-α-methoxy-β-chloroethylbenzene (7.55g; 0.035 mole) of mp 58-59.0°C was obtained. The filtrate was extracted with dichloroethane (3 × 30 ml). The organic layer was washed with water (2 × 20 ml) and the dichloroethane evaporated. The residue (13.5g) was distilled in a vacuum of 4 mm Hg. Three fractions were obtained of bp 83-136, 136, 136, and 136.5-150°C. o-Nitro-α-methoxy-β-chloroethylbenzene (1.8g; 0.005 mole) was obtained by crystallization from ethanol of the fraction with bp 136°C and had mp 72-75.5°C. Found, %: C 50.20; H 4.50; N 6.50. $C_9H_{10}NO_3Cl$. Calculated, %: C 50.12; H 4.68; N 6.50. PMR spectrum (deuterochloroform), δ ppm: 3.32 singlet (OCH_3), 4.97 quadruplet (CH), 3.6-4.0 multiplet (CH_2Cl), 8.0 quadruplet (3-CH), 7.4-7.85 multiplet (4,5,6-CH).

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