CHROMATOGRAPHIC IDENTIFICATION OF SOME INTERMEDIATES OF THE REACTION OF ANILINE WITH FORMALDEHYDE

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For the identification of the reaction products and intermediates of aniline with formaldehyde a paper chromatographic and thin-layer chromatographic method has been elaborated. The composition of the condensation products was evaluated in dependence on pH. The results confirm, in principle, the reaction scheme proposed by some authors.

The reaction of formaldehyde with aniline takes place *via* several reaction steps. The composition of the reaction mixture is dependent primarily on the pH value of the medium and on the stoichiometric excess of aniline used[1-9]. Chromatographic identification of the products and intermediary products of the reaction of aniline with formaldehyde has not been described as yet. Solvent systems currently used in chromatography of aromatic amines[10] do not afford utilisable results in the identification of the products and intermediary products of this reaction. This is due to unsharp separation and the tendency to produce elongated spots.

EXPERIMENTAL

Paper chromatography: The mobile phase is prepared by shaking 100 g of benzene with 10 g of mixture A at 20 ± 1°C. Mixture A is composed of 50 g of formamide, 50 g of dimethyl sulfoxide, and 10 g of water. The chromatographic tank is saturated with benzene vapours beforehand. Stationary phase is made by mixing 55 g of methanol and 45 g of mixture B, composed of 50 g formamide, 50 g dimethyl sulfoxide, 10 g water, and 3 g glacial acetic acid. Whatman paper No 3 is drawn through the stationare phase mixture and dried at room temperature for 30—60 min until methanol is completely evaporated. The sample is applied in the form of a 1—3% methanolic solution. After evaporation of methanol the chromatogram is developed descendently for approximately 3 h. The dried chromatogram is sprayed with the detection reagent D_1 and inspected after 1—2 h standing. After 24 hours standing the intensity of the coloration is lowered and the spot areas diminished.

Thin layer chromatography: Commercially available Silufol plates of Kavalier, Votice, were employed. The mobile phase is prepared by mixing and shaking 45 g of cyclohexane with 55 g of mixture C, at 20 ± 1°C. Mixture C is composed of 70 g dioxan, 20 g dimethylformamide, and 10 g water. The upper layer is used as the mobile phase. The sample is applied in 1—3% methanolic solution. The plates are dried after development at room temperature and sprayed with D_1, for quantitative chromatography with D_2.

Detection: Reagent D_1 is a 0·5% ethanolic solution of *p*-dimethylaminobenzaldehyde acidified with 2 ml of conc. HCl (per 100 g of solution). Reagent D_2, according to Micheel and Schweppe,

is modified by increasing the glucose content: 4 g of glucose are dissolved in a mixture of 10 ml of 85% phosphoric acid and 40 ml of water. The solution is diluted with 30 ml of ethanol and 30 ml of 1-butanol. The chromatogram is sprayed and heated at 115°C for 5—10 minutes. Quantitative evaluation is carried out with an optical densitometer ERI 65 (Zeiss, Jena), using a 560 nm filter.

RESULTS AND DISCUSSION

The reaction of aniline with formaldehyde takes place in two stages which may sometimes overlap. In the first stage formaldehyde attacks the amino group of aniline under formation of a carbinolamine. The unstable carbinolamine reacts with another aniline molecule giving rise to the first probable intermediate, N,N′-bis(phenylamino)methane. In the presence of H^+-ions an intramolecular rearrangement of the intermediate takes place gradually, first to a mixture of isomers of aminobenzylaniline, and eventually up to a mixture of isomers of bis(aminophenyl)methane.

The mechanism of this rearrangement recalls the benzidine-type rearrangements. When approximately at the boundary of both stages, the reaction mixture contains seven additional compounds as well as free aniline. However, as side-reactions also take place, as for example the formation of polymer-homologues of bis(aminophenyl)methane and the disproportionation of N,N′-bis(phenylamino)methane to aniline and the trimer of methyleneaniline, the fact must be reckoned with that the chromatographic sample may contain twelve to fifteen components.

For the separation of the sample on a single chromatogram we elaborated a system for paper chromatography, and another for thin-layer chromatography. Both systems require a thorough saturation of the chromatography chamber with the vapours of the main solvent. For paper chromatography either anhydrous formamide or dimethyl sulfoxide must be used, or their water content taken into account when weighing the mixture components. A satisfactory separation may be achieved even when the weights of water vary by ±20%, but the ensuing change of the R_F values must not be forgotten. The quality of the separation and of the R_F values is also strongly influenced by the content of acetic acid, or formic acid sometimes present in formamide. Only a formamide containing less than 0·01% of formic acid may be used. In thin-layer chromatography the moisture content in dioxan and dimethylformamide must be taken in account, and the presence of acetic and formic acids must be eliminated. In Table I R_F values of substances present in the reaction mixture at a given stage are listed. It was found that a defined relationship exists between the polymerization degree of the polymer-homologues and the R_M values (Fig. 1).

However, in thin-layer chromatography an exception was observed, when the first member of the homologous series did not fit this relationship.

The utilisability of both chromatographic methods for the identification of other aromatic amines and their derivatives has also been investigated: For single compounds the R_F values listed in Table II were found.

TABLE I

R_F Values of Compounds Present in the Product of the Reaction of Aniline with Formaldehyde Polymer-homologues are characterized by the general formula ($n = 1$—3).

$$H_2N-\text{⬡}-CH_2-\left[\text{⬡}-CH_2\right]-\text{⬡}-NH_2$$
$$\underset{NH_2}{|}\Big]_n$$
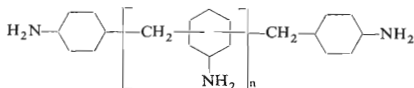
Compound	Paper	Thin layer
4,4'-Bis(aminophenyl)methane	0·21	0·20
4,2'-Bis(aminophenyl)methane	0·39	0·35
2,2'-Bis(aminophenyl)methane	0·57	0·79
Trimer of methyleneaniline	0·96	1·0
N,N'-Bis(phenylamino)methane	0·58	0·68
4-Aminobenzylaniline	0·61	0·45
2-Aminobenzylaniline	0·86	0·73
Monomer-homologue ($n = 1$)	0·14	0·15
Dimer-homologue ($n = 2$)	0·10	0·05
Trimer-homologue ($n = 3$)	0·06	0·02

FIG. 1

Relationship Between the R_M Values and the Polycondensation Degree of Polymer-Homologues (n)

1 Paper chromatography, 2 thin-layer chromatography.
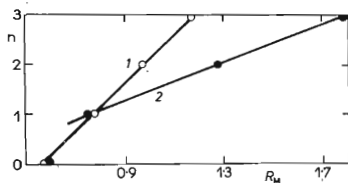
Quantitative evaluation was made use of in the condensation of aniline with formaldehyde at various pH values. The reaction was carried out at 25°C, using three moles of aniline to which one mol of 37% formaldehyde was added dropwise, regularly, over 2 h. The reaction was considered complete when the content of the unreacted formaldehyde in the mixture dropped below 0·1%. The mean error of quantitative chromatography is 4%. In principle, the results confirm the existing views on the course of the reaction of aniline with formaldehyde, as well as on the effect of pH on the composition of the reaction mixture. If the reaction takes place at a relatively high pH value the main product (95%) is N,N'-bis(phenylamino)methane accompanied by 5%

Substance	Paper	Thin layer
Benzidine	0·10	0·13
Diphenyline	0·29	0·32
o-Benzidine	0·71	0·75
o-Aminodiphenylamine	0·86	0·90
p-Aminodiphenylamine	0·42	0·44
Aniline	0·51	0·63
1-Naphthylamine	0·56	0·63
2-Naphthylamine	0·55	0·58
Diphenylamine	0·88	0·92
o-Phenylenediamine	0·12	0·34
m-Phenylenediamine	0·05	0·21
p-Phenylenediamine	0·02	0·07
o-Nitroaniline	0·53	0·62
m-Nitroaniline	0·38	0·51
p-Nitroaniline	0·15	0·28
o-Aminophenol	0·10	0·32
m-Aminophenol	0·04	0·19
p-Aminophenol	0·02	0·04
o-Chloroaniline	0·00	0·91
m-Chloroaniline	—	0·45
p-Chloroaniline	—	0·30
o-Toluidine	—	0·82
m-Toluidine	—	0·41
p-Toluidine	—	0·13
p-Dimethylaminophenylamine	0·20	0·25
4,4′-Bis(aminophenyl) sulfone	0·02	0·06
4,2′-Bis(aminophenyl) sulfone	0·15	0·18
4,4′-Bis(amino-3-dimethylphenyl)methane	0·54	0·62

of trimeric methylaniline. A reaction carried out at pH 7·0—7·5 affords in addition to N,N′-bis(phenylamino)methane (65%) also 4-(22%) and 2-(13%) aminobenzylaniline. At pH 5·0—5·5 the content of N,N′-bis(phenylamino)methane is already distinctly lower (18%), but the content of 4-aminobenzylaniline (48%) increases and the content of 2-aminobenzylaniline decreases (8%). The presence of 4,4′- (18%), 4,2′- (4%) and 2,2′- (1%) bis(aminophenyl)methane in the reaction mixture indicates that the rearrangement to the second degree is beginning to take place. At pH 1·0 to 1·5 N,N′-bis(phenylamino)methane could be no longer found in the reaction mixture

and the content of 4- (29%) and 2- (2%) aminobenzylaniline indicates that the rearrangement to the second degree is accelerated. This is also shown by the increase of the content of 4,4'-bis(aminophenyl)methane (45%), while the decrease of the content of 4,2'- (2%) and the disappearance of 2,2'-bis(aminophenyl)methane indicates that the increase in H^+ content leads to the suppression of the formation of isomers. In addition to the mentioned substances the reaction mixture also contains polymerhomologues (21%). It may be stated with a certain reserve that the first detectable reaction intermediate in the reaction of aniline with formaldehyde is undoubtedly N,N'-bis(phenylamino)methane. If H^+-ions are present in the reaction mixture a substantial rearrangement to the first degree can be observed (aminobenzylanilines are the product) and with increasing H^+-ion concentration the rearrangement to the second degree begins to appear (the content of the product of the terminated reaction increases). Hence, it may be supposed as very probable that the rearrangement of N,N'-bis(phenylamino)methane is indeed affected primarily by the acidity of the reaction medium and that it takes place even at room temperature.

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Translated by Ž. Procházka.