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Note

A paper chromatographic method for the separation and determination of the condensation products of aromatic amines with formaldehyde in acidic medium

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In order to elucidate the mechanism of the technically important reaction of aromatic amines with formaldehyde, a kinetic investigation of the initial steps of this reaction was carried out. For the analysis of aqueous acidic reaction mixtures, paper chromatography was preferred to thin-layer chromatography because of the ease of extraction of the coloured spots for spectrophotometric determination. The solvent systems described in the literature¹⁻⁶ for the chromatographic separation of aromatic amines were unsuitable for the separation of the acidic reaction mixtures because of inadequate separations and elongation of the spots produced. We report here a paper chromatographic method for separating and determining the reactants and products in the reaction of aniline and substituted anilines with formaldehyde in acidic medium.

EXPERIMENTAL

Materials

Aniline, *m*-toluidine, *o*-toluidine, *N*-methylaniline, *N*-ethylaniline, *N,N*-dimethylaniline and *N,N*-diethylaniline were reagent-grade materials (BDH, Poole, Great Britain), twice distilled before use.

N-(*n*-Propyl)aniline (b.p. 220–222°) and *N*-(*n*-butyl)aniline (b.p. 235–238°) were prepared by standard methods⁷.

4,4'-Diaminodiphenylmethane (diamino-DPM) (m.p. 92°) was isolated from an aniline-formaldehyde reaction mixture according to the method described by Scanlan⁸.

2,4'-Diamino-DPM (m.p. 88°) was prepared by the catalytic reduction of 2,4'-dinitro-DPM (m.p. 118°) with hydrogen at 50 p.s.i. in the presence of Raney nickel⁹.

2,2'-Diamino-DPM (m.p. 158°) was prepared by the reduction of 2,2'-dinitro-DPM (m.p. 205°) with hydrogen at 50 p.s.i. in the presence of Raney nickel^{10,11}.

4,4'-Diamino-3,3'-dimethyl-DPM (m.p. 158°), 4,4'-diamino-2,2'-dimethyl-DPM (m.p. 123°), *N,N'*-dimethyldiamino-DPM (b.p. 212–215° at 6 mm), *N,N'*-diethyldiamino-DPM (b.p. 235–236° at 6 mm), *N,N'*-dipropyldiamino-DPM (b.p. 216–220° at 6 mm) and *N,N'*-dibutyldiamino-DPM (b.p. 250–256° at 6 mm) were prepared by the method described by Wagner¹².

p,p'-Tetramethyldiamino-DPM (m.p. 89°) was prepared by a standard method¹³.

p,p'-Tetraethyldiamino-DPM (b.p. 236° at 6 mm) was isolated from a reaction mixture of two equivalents of diethylaniline, one equivalent of formaldehyde and one equivalent of hydrochloric acid. The reaction mixture was steam distilled in order to separate the unreacted amine and the required product was recovered from the residue and purified by distillation under reduced pressure.

The solvents used were analytical-grade materials (BDH).

Chromatographic techniques

Solutions of the compounds in dilute hydrochloric acid (1–10 μ l of 0.02 *M* amine or 0.01 *M* diamino-DPM) were spotted individually and as mixtures of the corresponding mono- and dinuclear amines on Whatman No. 1 filter-paper and developed by the ascending technique in a chromatographic chamber containing the solvent (see below) for about 10–12 h, during which time the solvent rose a distance of about 30 cm. The paper was then taken out, dried at room temperature for 45 min and worked up using one of the three procedures outlined below.

Procedure A. In the case of the primary amines, the paper was first sprayed with nitrous acid prepared by mixing ice-cold solutions of 2 ml of 2 *N* hydrochloric acid and 1 ml of 2.5% sodium nitrite and diluting to 10 ml with water. It was then sprayed with a solution of β -naphthol (0.1 g) in 10 ml of 1 *N* sodium hydroxide solution. The red spots were cut out while moist and extracted with 5 ml of a 0.2 *N* solution of sodium hydroxide in 50% aqueous ethanol.

Procedure B. Secondary amines were made visible by spraying with a 0.8% ethanolic solution of 2,6-dichloroquinone chlorimide (5 ml) mixed with 15 ml of 40% sodium acetate solution. The bluish green spots were extracted with 5 ml of ethanol.

Procedure C. For tertiary amines, the spray reagent was prepared by mixing ice-cold solutions of 0.5% *p*-nitraniline in 2 *N* hydrochloric acid (5 ml) and 1 ml of a 2.5% solution of sodium nitrite. Urea (4 g) was added in order to remove the excess of nitrous acid and the solution was buffered with 15 ml of 40% sodium acetate solution. The brown spots, when extracted with 5 ml of 0.2 *N* hydrochloric acid in 80% aqueous ethanol, yielded bright red solutions.

Quantitative evaluations were made from the Beer's law plots of the absorbance of the coloured extracts measured with a Beckman DU2 spectrophotometer at their respective λ_{\max} values (Table I). The mean error in the determinations was 3%.

RESULTS AND DISCUSSION

In contrast to the phenol-formaldehyde reaction, the products of the condensation of aromatic amines with formaldehyde are complex and pH dependent because the amino group can also take part in the reaction. In neutral and slightly acidic media, primary amines react almost instantaneously to give the cyclic trimer of the Schiff's base, *viz.* anhydroamineformaldehyde, *e.g.* (C₆H₅NCH₂)₃ (ref. 14). Secondary amines, under the same conditions, react very fast to yield anhydroaminobenzyl alcohol-type compounds (–NRC₆H₃–CH₂–)_{*n*} (refs. 15 and 16). *p*-Toluidine reacts in a different manner to yield the so-called Tröger's base¹⁷.

However, the reactions of aniline, *o*- and *m*-toluidines and *N*-alkyl and *N,N*-

TABLE I

R_F VALUES OF THE COMPOUNDS EXAMINED AND THE λ_{max} VALUES OF THEIR COLOURED EXTRACTS

No.*	Compound	R_F	λ_{max} .
1	Aniline	0.51	443
2	2,2'-Diamino-DPM	0.40	440
3	2,4'-Diamino-DPM	0.26	440
4	4,4'-Diamino-DPM	0.20	440
5	<i>o</i> -Toluidine	0.59	445
6	3,3'-Dimethyl-4,4'-diamino-DPM	0.42	443
7	<i>m</i> -Toluidine	0.58	445
8	2,2'-Dimethyl-4,4'-diamino-DPM	0.38	442
9	<i>p</i> -Toluidine	0.60	443
10	N-Methylaniline	0.54	653
11	N,N'-Dimethyldiamino-DPM	0.29	650
12**	N-Ethylaniline	0.62	653
13**	N,N'-Diethyldiamino-DPM	0.50	653
14**	N-(<i>n</i> -Propyl)aniline	0.69	655
15**	N,N'-Di-(<i>n</i> -propyl)diamino-DPM	0.58	650
16**	N-(<i>n</i> -Butyl)aniline	0.75	653
17**	N,N'-Di-(<i>n</i> -butyl)diamino-DPM	0.63	653
18	N,N-Dimethylaniline	0.50	500
19	N,N'-Tetramethyldiamino-DPM	0.23	500
20**	N,N-Diethylaniline	0.66	510
21**	N,N'-Tetraethyldiamino-DPM	0.53	510

* 1-9 developed using Procedure A; 10-17 developed using Procedure B; 18-21 developed using Procedure C.

** Using paper sprayed with 5 *N* HCl.

dialkylamines with formaldehyde at high acid concentrations proceed at a moderate rate to yield the corresponding diamino-DPMs when the amine:formaldehyde ratio is two or more. In order to separate and determine the products and reactants in this case, we found the solvent system methanol-benzene-amyl alcohol-8 *N* hydrochloric acid (10:20:60:12) to be very suitable.

Whereas primary amines and their diamino-DPMs could be separated satisfactorily using 4 *N* hydrochloric acid, a higher acid concentration (8 *N*) was necessary in order to avoid tailing and to provide good separations in the case of secondary and tertiary amines. The tailing which arises in the case of less basic amines, *viz.*, N-ethylaniline, N-propylaniline, N-butylianiline, N,N-diethylaniline and their diamino-DPM derivatives on account of the change in pH during development can be obviated by using paper sprayed with 5 *N* hydrochloric acid and dried prior to development.

Increasing the amyl alcohol concentration or benzene content makes the mobile phase less polar and results in lower R_F values and better separations. However, when deciding the optimum amyl alcohol concentration, the increase in development time as the amyl alcohol content increases must also be taken into account.

The suggested solvent system affords a method of separation of the amines from their diamino-DPMs and yields well defined circular spots suitable for quantitative spectrophotometric determination.

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