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HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY OF COMPOUNDS OBTAINED DURING THE PRODUCTION OF N-NITROSODIPHENYLAMINE

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SUMMARY

The conditions for the high-performance liquid chromatographic separation of a mixture of compounds obtained during the production of N-nitrosodiphenylamine were established. Silica gel with 20-μm spherical particles was used as the stationary phase and *n*-pentane–methanol as the mobile phase. Elution data for diphenylamine, N-nitrosodiphenylamine, 4-nitrodiphenylamine, 4-nitrosodiphenylamine, aniline, carbazole and toluene were measured using *n*-pentane containing 2, 4 and 6% (w/w) of methanol. The eluate was monitored by means of a UV detector at 254 nm. A procedure for the determination of a low content (0.1–2%, w/w) of diphenylamine in N-nitrosodiphenylamine is described.

INTRODUCTION

N-nitrosodiphenylamine (N-NODFA) is an important diphenylamine (DFA) derivative with many uses, *e.g.*, as a stabilizer for certain types of explosives, as a polymerization catalyst and as a nitrosation agent in organic synthesis. N-NODFA is also an important intermediate in the production of rubber industry chemicals. It has not been found to be toxic[1], but it is suspected of being carcinogenic as are other nitrosamines[2].

In view of the above, the development of a suitable method for the determination of N-NODFA is desirable. Determinations of N-NODFA (and other nitroso compounds) using titration with chromium(II) chloride[3] and reduction with tin(II) chloride[4] with subsequent bromination have been described. There is also a semi-quantitative determination of N-NODFA by means of a "spot test"[5,6]. A photometric determination[7] is based on the formation of a coloured palladium–N-NODFA complex. Further, both N-NODFA and DFA can be determined by spectrophotometric methods[8], especially in the UV region[9], and by polarography[10,11]. However,

most spectral measurements, in both the UV[12,13] and IR[14–17] regions, were concerned with structural studies of N-NODFA and similar compounds[18–21].

Thin-layer chromatography (TLC) permits the simultaneous determination of DFA, N-NODFA and their derivatives, as well as of products of their decomposition[22–25].

High-performance liquid chromatography (HPLC) is a very useful method for the analysis of these compounds, which are characterized by a low thermal stability. The main advantages are the rapidity of the analysis and the possibility of determining also impurities present in low concentrations. The determination is not affected by the presence of other compounds of the same type, in contrast to chemical and photometric methods.

N-NODFA is obtained by a nitrosation of DFA following the scheme

$$C_6H_5 \cdot NH \cdot C_6H_5 + NaNO_2 + H_2SO_4 \rightarrow C_6H_5 \cdot N(NO) \cdot C_6H_5$$

DFA N-NODFA

The reaction is carried out in toluene. The aim of this work was to develop a method for the determination of small amounts of DFA in the presence of N-NODFA. In addition to these two compounds, it is necessary to separate chromatographically aniline and carbazole originating in technical diphenylamine, and 4-NODFA and 4-NO_2DFA as nitrosation by-products.

EXPERIMENTAL

Apparatus

A Varian 8500 liquid chromatograph (Varian, Palo Alto, Calif., U.S.A.) with a syringe pump was used. Sample injection was performed by the stop-flow technique, with a 5- or 10-μl syringe (Micromesure AG Hamilton, Bonaduz, Switzerland) directly into the column, using a septumless injection device. A fixed-wavelength (254 nm) UV detector (Varian) was employed and the chromatograph was operated at ambient temperature. Chromatograms were recorded on a Varian A25 dual-pen strip-chart recorder.

Columns

(1) A stainless-steel column (50 cm × 2 mm I.D.) manufactured in the Laboratory of Synthetic Fuels was packed by the tap–fill method with 20-μm spherical particles of Pragosil 20 silica gel. This material was manufactured in collaboration between the Nuclear Research Institute, Řež, and the Prague Institute of Chemical Technology.

(2) A stainless-steel column (25 cm × 2 mm I.D.) MicroPak SI 10 (Varian) was also used.

Materials

N-NODFA, DFA, 4-NODFA, 4-NO_2DFA and 4-toluidine were obtained from the Department of Organic Technology, Institute of Chemical Technology, Prague. Aniline and carbazole were obtained from commercial sources.

Mobile phase

n-Pentane (VEB Jenapharm-Laboratorchemie, Apolda, G.D.R.) and methanol (Lachema, Brno, Czechoslovakia) were dried over Nalsit A 4 activated molecular sieve, distilled in glass using a calcium chloride closure to prevent access of moisture and stored over activated molecular sieves.

Diethyl ether was dried over sodium, distilled and stored over molecular sieves. 2-Propanol (Lachema) of analytical-reagent grade was used without further treatment.

Qualitative analysis

Three test mixtures were prepared, as follows. (i) For observing the resolution (R_s) of the chromatographic peaks of DFA and N-NODFA, a solution of both standards in methanol was prepared with ratios resulting in approximately equal responses on the UV detector set at 254 nm. (ii) The second test mixture was used for estimating the feasibility of quantitative monitoring of both components, the ratio of their concentrations being 1:100. (iii) The third test mixture contained, in addition to N-NODFA and DFA, the following components: toluene (nitrosation medium), aniline and carbazole (impurities in DFA), and 4-NODFA and 4-NO_2DFA (nitrosation by-products).

Three mobile phases were tried: (A) *n*-pentane–2-propanol (99:1, w/w); (B) *n*-pentane–diethyl ether (50:50, w/w); (C) *n*-pentane–methanol. The proportion of methanol in system C was varied from 2 to 6% (w/w) at flow-rates from 10 to 120 ml/h, while evaluating (a) the possibility of separating all seven compounds, *i.e.*, toluene, N-NODFA, DFA, aniline, carbazole, 4-NO_2DFA and 4-NODFA, and (b) the possibility of separating N-NODFA and DFA with a resolution (R_s) sufficiently large for the quantitative determination of low contents (0.1–2%) of DFA in N-NODFA to be feasible.

Retention data were measured for the *n*-pentane–methanol system at methanol concentrations of 2, 4 and 6% (w/w) and with a flow-rate of 40 ml/h.

Quantitative analysis

Quantitative analyses were performed on a 50-cm stainless-steel column packed with Pragosil 20. *n*-Pentane containing 2% (w/w) of methanol was used as the mobile phase at a flow-rate of 20 ml/h. An external standard method was used and calibration graphs were constructed for N-NODFA and DFA. The contents of both components were determined from a single chromatogram obtained on a dual-pen strip-chart recorder. The input terminals of both channels were connected with each other and with the detector output. The voltages chosen for recording the N-NODFA and DFA peaks was 10 and 1 mV, respectively, at a UV detector sensitivity set at 0.08 absorbance unit full scale.

RESULTS AND DISCUSSION

A satisfactory separation of the compounds studied was not achieved with the eluents *n*-pentane–diethyl ether and *n*-pentane–2-propanol. On the other hand, the system *n*-pentane–methanol was found to give good separations of N-NODFA, DFA and the other compounds.

All of the compounds were separated on the column packed with Pragosil 20, the peaks being symmetrical. When the MicroPak SI 10 column was used, strong adsorption of aniline on the column occurred, making the detection of low contents of this compound impossible. There was also considerable tailing of all of the other compounds studied. Further work was therefore performed with the column packed with Pragosil 20. Fig. 1 shows a chromatogram of a test mixture on the MicroPak SI 10 column. All subsequent chromatograms were obtained on the Pragosil 20 column.

Table I gives the retention data measured at methanol concentrations of 2, 4 and 6% (w/w) and a flow-rate of 40 ml/h.

When using the mobile phase containing 2% (w/w) of methanol, the compounds are eluted in the following sequence: toluene, N-NODFA, DFA, aniline,

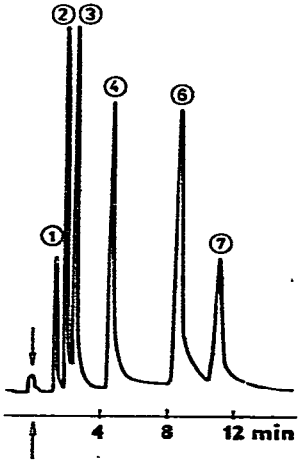

Fig. 1. Separation of a test mixture on MicroPak SI 10 column (25 cm × 2 mm I.D.). Mobile phase *n*-pentane–methanol (96:4, w/w); flow-rate, 30 ml/h; pressure, 3 MPa. Peaks: 1 = toluene; 2 = N-NODFA; 3 = DFA; 4 = carbazole; 6 = 4-NO_2DFA; 7 = 4-NODFA.

TABLE I

RETENTION VALUES

k' = capacity factor, calculated from the equation $k' = (t_R - t_0)/t_0$, where t_R (sec) is the sample retention time and t_0 (sec) is the hold-up time.

Compound	*Proportion of methanol in mobile phase*					
	2%		*4%*		*6%*	
	k'	t_R	k'	t_R	k'	t_R
Toluene	0.21	97	0.19	96	0.18	95
N-NODFA	1.8	222	1.7	215	1.6	208
DFA	2.5	280	2.3	264	2.1	248
Aniline	6.8	624	6.0	566	5.2	500
Carbazole	8.6	769	6.0	566	4.7	457
4-NO_2DFA	22.3	1873	13.0	1129	9.3	824
4-NODFA	26.8	2238	15.0	1288	10.5	925

carbazole, 4-NO_2DFA and 4-NODFA .The mobile phase containing 4% (w/w) of methanol does not separate aniline and carbazole, and with 6% (w/w) of methanol carbazole is eluted before aniline, the sequence of the other compounds remaining unchanged. Fig. 2 shows the behaviour of the retention times when the concentration of methanol in the mobile phase is changed, measured at two different flow-rates. Fig. 3 illustrates the separation of a test mixture at flow-rates of 20 and 120 ml/h.

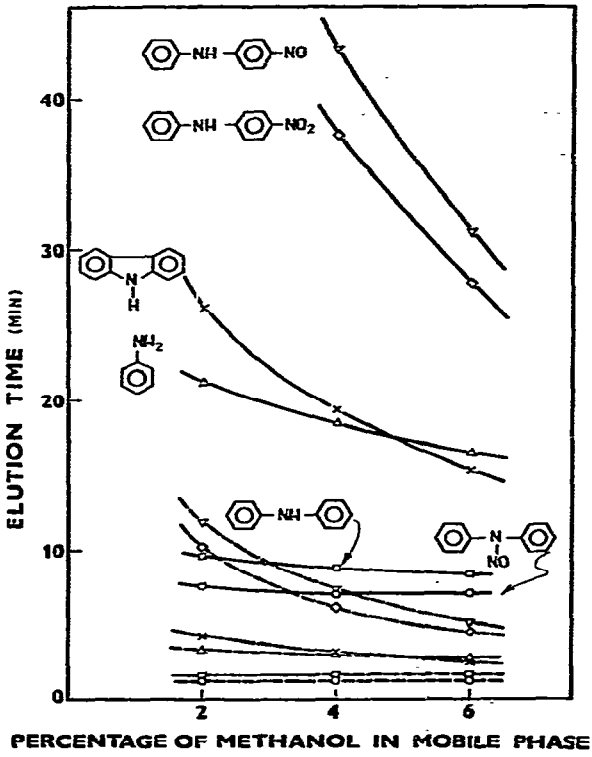

Fig. 2. Dependence of the elution time on the composition of the mobile phase, using a column (50 cm × 2 mm I.D.) packed with Pragosil (20 μm). Solid line, flow-rate 20 ml/h, pressure 1.5 MPa; broken line, flow-rate 120 ml/h, pressure 8 MPa.

The resolution (R_s) for N-NODFA and DFA is given in Table II for various concentrations of methanol in the mobile phase and for various flow-rates of the mobile phase. The R_s values presented are the averages of three measurements.

As the minor component (DFA) is eluted on the descending slope of the major component (N-NODFA), from the point of view of quantitative monitoring of DFA the resolution must be greater the smaller is the amount of this minor component that has to be determined. For concentrations of DFA in N-NODFA in the range of 0.1–2% the value of R_s should be about 3, which can be achieved by using a flow-rate of 10–20 ml/h and *n*-pentane containing 2% (w/w) of methanol as the mobile phase.

If some compounds with longer elution times are present (*e.g.*, 4-NO_2DFA or

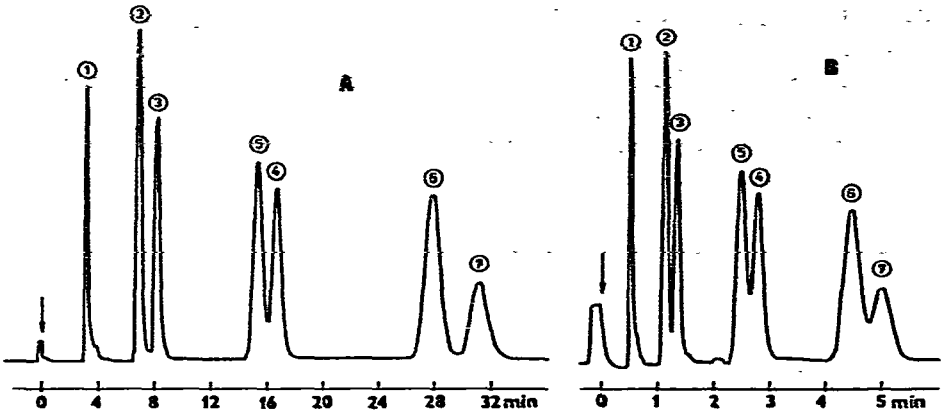

Fig. 3. Influence of flow-rate on separation, using a column (50 cm × 2 mm I.D.) packed with Pragosil (20 μm). Mobile phase, *n*-pentane–methanol (94:6, w/w). A, Flow-rate 20 ml/h, pressure 1.5 MPa; B, flow-rate 120 ml/h, pressure 8 MPa. Peaks: 1 = toluene; 2 = N-NODFA; 3 = DFA; 4 = carbazole; 5 = aniline; 6 = 4-NO_2DFA; 7 = 4-NODFA.

TABLE II

RESOLUTION (R_s) FOR N-NODFA AND DFA

R_s calculated from the relationship

$$R_s = \frac{2(t_D - t_N)}{W_N + W_D}$$

where t_N = elution time for N-NODFA; t_D = elution time for DFA; W_N = peak width of N-NODFA, measured at the base; W_D = peak width of DFA, measured at the base.

Proportion of methanol in mobile phase (%)	*Flow-rate of mobile phase (ml/h)*				
	10	*20*	*40*	*80*	*120*
2	3.3	2.7	2.6	1.9	1.6
4	2.4	2.4	2.2	1.7	1.4
6	2.3	1.7	1.7	1.3	1.1

4-NODFA), the time of analysis is longer under these conditions. If the determination of all compounds by a single analysis is required, isocratic conditions and a programmed flow-rate can be used. Fig. 4 shows a chromatogram obtained by using a programmed flow-rate. The slope of the programmed flow-rate was recorded simultaneously together with the chromatogram on dual-pen strip-chart recorder.

Fig. 5 illustrates the analysis of a sample containing a small amount of DFA in addition to N-NODFA. A dual-pen strip-chart recorder with different sensitivities in the two channels was used in this instance.

The determination of DFA in addition to N-NODFA using *p*-toluidine as an internal standard was unsuccessful. Some samples prepared from technical N-NODFA changed their composition very rapidly after addition of *p*-toluidine, as a result of a reaction between N-NODFA and *p*-toluidine.

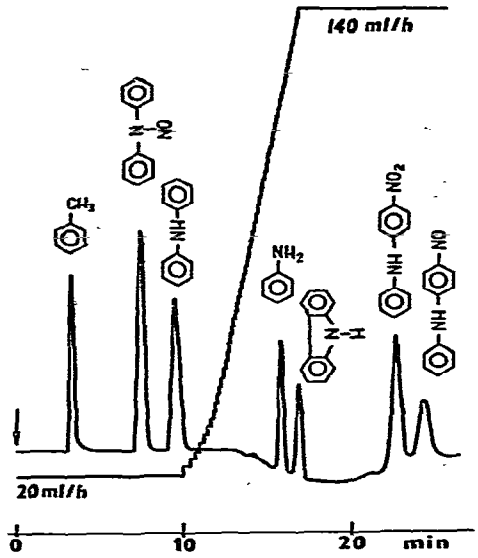

Fig. 4. Chromatogram of test mixture illustrating the use of flow-rate programming. Mobile phase, *n*-pentane–methanol (98:2, w/w). Flow-rate: from 20 to 140 ml/h. The column (50 cm × 2 mm I.D.) was packed with Pragosil (20 μm).

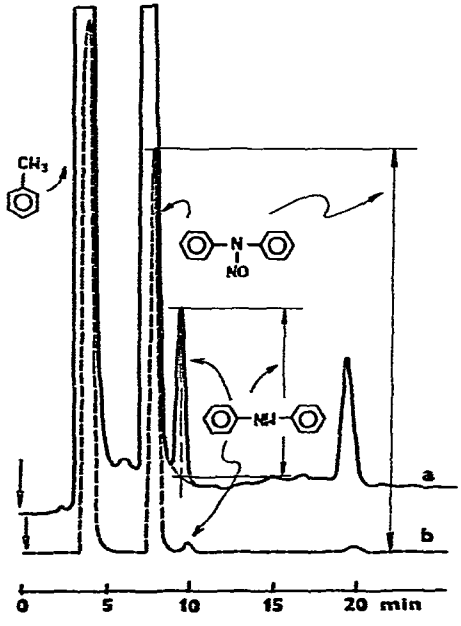

Fig. 5. Analysis of a sample containing a small amount of DFA in addition to N-NODFA. A dual-pen strip-chart recorder with different sensitivities (1 and 10 mV) on the two channels was used. The column (50 cm × 2 mm I.D.) was packed with Pragosil (20 μm).

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