CHROM. 13,460

GAS CHROMATOGRAPHIC ANALYSIS OF AROMATIC AMINES AS N-PERMETHYLATED DERIVATIVES

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(Received October 6th, 1980)

SUMMARY

A gas chromatographic method for the analysis of primary and secondary aromatic amines is described, based on their prior conversion into N-permethyl derivatives by treatment with formaldehyde and sodium borohydride in acidic solution. The usually difficult separation of isomers is thus easily achieved for toluidines, xylidines, anisidines and naphthylamines. Flame-ionization detector responses are enhanced and the absorption problems, which were found to be concentration dependent, are very limited.

INTRODUCTION

Primary and secondary aromatic amines are widespread industrial pollutants with toxic properties[1]. In addition, they may react with other substances in the environment, *e.g.*, nitrites, to produce other toxic products[2]. Therefore, methods to identify and determine these compounds have been developed. The present U.S. recommended analytical procedure for aromatic amines in air[3,4], which is used in most countries, employs a gas chromatograph equipped with a flame-ionization detector to determine the amines trapped from air with silica gel and dissolved in ethanol.

The method has some drawbacks: ring isomers of amines are not separated and therefore cannot be distinguished, so separate quantitative assay is impossible; it is important to remember that isomers do not usually have the same toxicity. Exposure and environmental concentration limits are set by legislation in many countries, including the U.S.A. and Italy, for *o*-toluidine and less often for *p*-toluidine. However, in general, the toxicities of isomers may differ widely in character and intensity, and may not have been well studied. Therefore, in view of the current state of legislation and possible future requirements, it is very important to have a method that is able to distinguish isomers.

Moreover, in the method currently recommended[3,4] the column with the most desirable gas chromatographic (GC) characteristics strongly binds the amines, so that amines of higher molecular weight cannot be analysed owing to the thermal stability limits of the stationary phase.

A recent paper[5] reported the simple N-permethylation of primary and secondary

aromatic amines in almost quantitative yields by treatment with formaldehyde and sodium borohydride in acidic solution.

N-Methylation of aromatic amines gives compounds with more suitable GC properties than the free amines and other derivatives[6-11] that often are less safely obtained and have to be handled with greater care, such as N-perfluoroacylamines. N-Permethylated aromatic amines can be chromatographed on a wide variety of stationary phases without serious absorption and tailing problems at relatively low temperatures. They are usually comparatively more stable than primary and secondary amines and less soluble in water, which is an advantage when an acid–base separation has to be performed.

EXPERIMENTAL

Reagents

All chemicals were commercial analytical-reagent grade materials, except for the N-permethyl derivatives of anisidines, toluidines, xylidines, mesidine and naphthylamines, which were prepared according to a described method[5]. All the compounds used for GC determinations were at least 99 % pure.

Apparatus

A variety of gas chromatographs equipped with flame-ionization detectors were used. We prepared the following columns: (A) 10 % Carbowax 20M–5 % KOH on Chromosorb W (80–100 mesh), 1 m × 2 mm I.D., stainless steel; (B)[3] Chromosorb 103 (80–100 mesh), 60 cm × 2 mm I.D., stainless steel; (C) 2.5 % SE-30 on Chromosorb G (80–100 mesh), 1 m × 2.5 mm I.D., stainless steel.

Procedures

A typical N-permethylation reaction was carried out as follows. Finely powdered sodium borohydride (3 mmol) and the aromatic amine (10^{-4} mol) were mixed in tetrahydrofuran (10 ml). The slurry obtained was slowly added to a solution of 3 M sulphuric acid (0.5 ml) and 40 % aqueous formaldehyde (0.5 ml) in tetrahydrofuran (10 ml) below 25°C with stirring. About midway through the addition, 3 M sulphuric acid (0.5 ml) was added in order to ensure a proper acidic medium until the end of the reaction. At the end of the addition, concentrated potassium hydroxide solution was then added to give a strongly basic pH. The organic phase can be analysed directly by GC. A suitable internal standard was added at the beginning when a yield evaluation was to be carried out. Peak area–weight calibrations were performed separately with the same injected amount range ($\pm15\%$) as in actual analysis. The yields given are the averages of at least three runs performed on the same amine under the same conditions.

The N-permethylation reagents were used in a larger excess than in the previously described preparative experiments[5].

RESULTS AND DISCUSSION

The proposed method starts with a pool of amine(s) concentrated by some physical and/or chemical procedure to yield a more or less diluted tetrahydrofuran
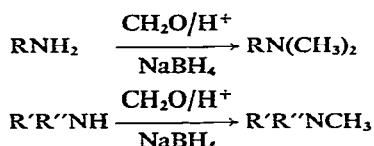
solution. The total amount of amine(s) to be derivatized may be of the order of 10^{-5} mol.

After the addition of a suitable inert internal standard to the mixture to be analysed, the solution is mixed with sodium borohydride and carefully poured into a solution of acidic formaldehyde in the cold. The reaction takes just the time required for the addition of the reagents. After addition of a solution of potassium hydroxide, the organic phase is ready for GC analysis.

The amines which were derivatized and the yields of the reactions are given in Table I.

TABLE I

ABSOLUTE GC YIELDS OF N-PERMETHYLATED AROMATIC AMINES

$$RNH_2 \xrightarrow[\text{NaBH}_4]{\text{CH}_2\text{O/H}^+} RN(CH_3)_2$$

$$R'R''NH \xrightarrow[\text{NaBH}_4]{\text{CH}_2\text{O/H}^+} R'R''NCH_3$$

The reported yields are the averages of at least three identical experiments carried out on a 10^{-4} molar scale. A weighed amount of an appropriate inert internal standard was added to the amine to be methylated. Internal standard to N-permethylated amine peak-area ratios were determined on the intact reaction mixtures after addition of concentrated potassium hydroxide.

Amine	Yield of N-permethylated amine (%)	Amine	Yield of N-permethylated amine (%)
Aniline	98	Mesidine (2,4,6-trimethylaniline)	96
o-Toluidine	99	o-Anisidine	92
m-Toluidine	98	m-Anisidine	100
p-Toluidine	98	p-Anisidine	99
2,3-Xylidine	100	Diphenylamine	100
2,4-Xylidine	99	α-Naphthylamine	94
2,5-Xylidine	96	β-Naphthylamine	96
2,6-Xylidine	99		
3,4-Xylidine	100		
3,5-Xylidine	97		

The effect of N-permethylation on the GC separation of isomers was dramatic. Under the usual conditions of GC analysis[3,4], the separation of isomers fails: toluidines gave a perfectly symmetrical peak, but a single peak for a mixture of all three isomers; the peak shape adversely affected any quantitative evaluation of the poorly separated isomers of anisidines and xylidines.

Figs. 1, 2 and 3 show the GC profiles for the N-permethyl derivatives of toluidines, anisidines and xylidines, respectively. Although the peak shape was optimal before and after N-permethylation, the separation of isomers was greatly improved, only 2,4- and 2,5-permethylxylidine emerging in a single peak. The environmentally perhaps more dangerous o-toluidine was eluted at less than half the retention time of the other two isomers.
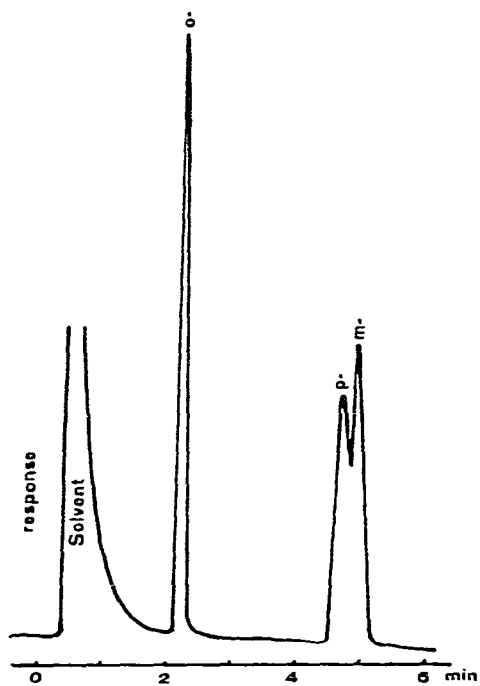
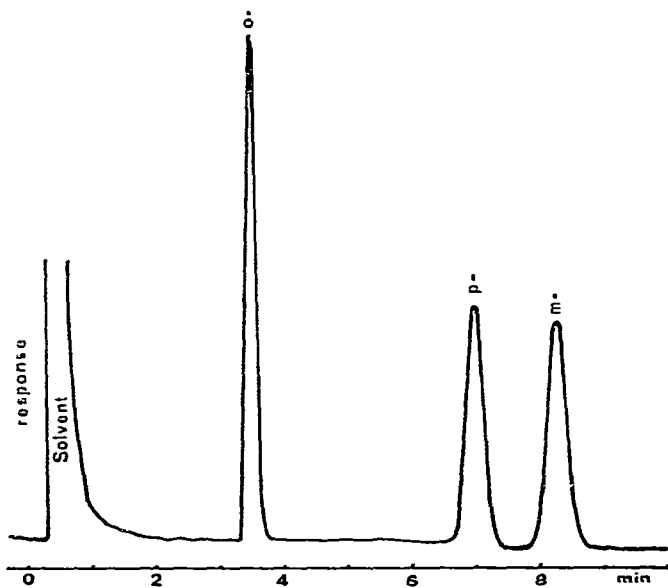Fig. 1. GC profiles of N-permethylated toluidines on column A at 180°C.

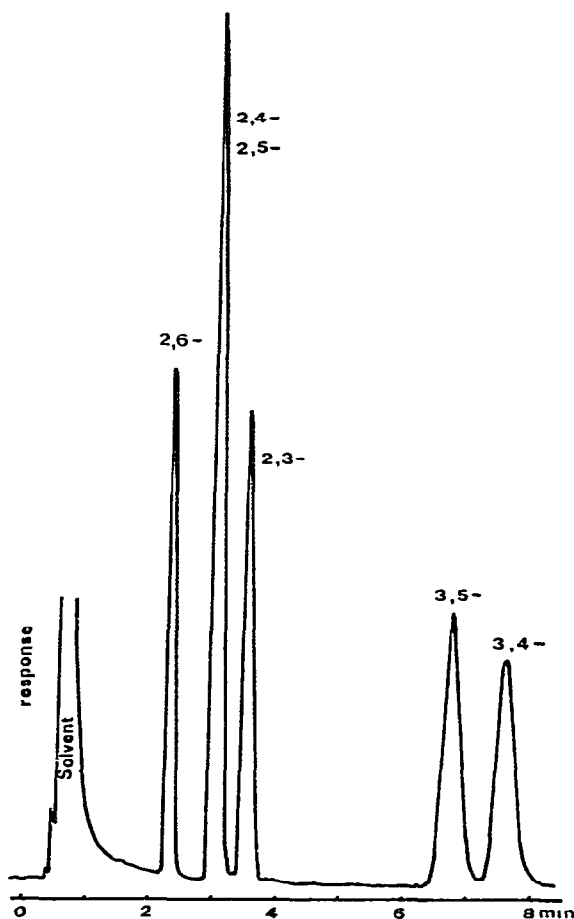Fig. 2. GC profiles of N-permethylated anisidines on column A at 200°C.

Fig. 3. GC profiles of N-permethylated xylidines on column A at 200°C.

The stationary phase recommended for the analysis of primary aromatic amines[3,4] (column B) completely held up the important α- and β-naphthylamines, whereas column C did not separate them adequately (Fig. 4a). A good separation, however, could be readily obtained on the same column after N-perfluoropropionylation[12]; a partial separation has been reported on a different silicone stationary phase[13], but tailing and, perhaps, absorption were extensive. We previously used GC with nematic stationary phases to obtain a complete separation of the two isomers[14], but no concentration, absorption or background (bleeding) study was carried out; also, these stationary phases can be used only in the nematic temperature range, which limits the flexibility of the method. Complete separation was achieved with N-permethyl derivatives (Fig. 4b).

Another advantage of N-permethylation resides in a much reduced absorption by the stationary phase and its solid support. That this was the case was strongly suggested by the shape of the peaks (no tailing), but we carried out a quantitative determination for aniline to evaluate this effect. According to expectation[15], the
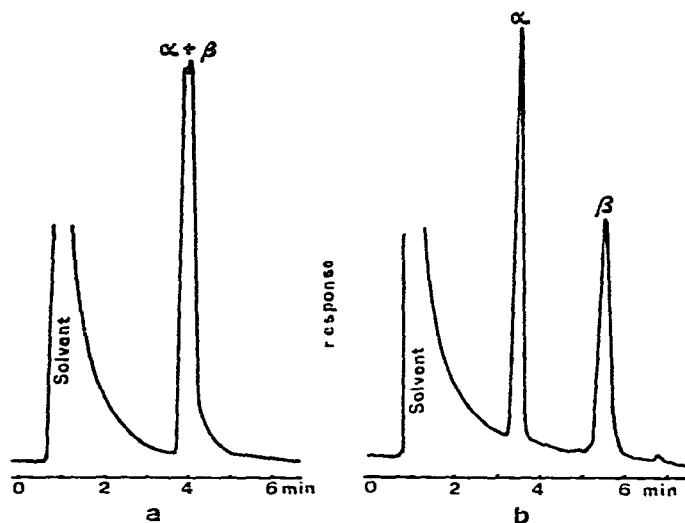
Fig. 4. GC profiles of (a) unmethylated naphthylamines and (b) N-permethylated naphthylamines on column C at 200°C.

RMR[16] for N,N-dimethylaniline was higher than that for aniline. When the amount of the two anilines and a hydrocarbon standard injected was decreased 100-fold, from 1 μmol to 10 nmol, the RMR difference for the two compounds widened considerably, indicating increasing absorption. Actually, N,N-dimethylaniline also showed a decrease in RMR, but to a much lesser extent. This result, incidentally, indicates a potential pitfall in the quantitative analysis of these compounds (Table II).

TABLE II

·EFFECT OF SAMPLE SIZE ON THE RMR OF ANILINE AND N,N-DIMETHYL-ANILINE

GC profiles were obtained upon elution from column A (see Experimental) at 100°C and 130°C for N,N-dimethylaniline and aniline, respectively.

Amine	Sample size (nmol)	$RMR_{n\text{-}heptane}$
Aniline	600	580
	6	384
N,N-Dimethylaniline	600	778
	6	640

ACKNOWLEDGEMENTS

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