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Note

Gas chromatography of aromatic acids after pyrolysis of their trimethylphenylammonium salts

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A number of problems occur in the gas chromatography (GC) of aromatic acids due to their considerable polarity, *viz.*, tailing of peaks, long elution times and poor reproducibility. Therefore methods of converting the acids into volatile esters have been applied using various esterification reagents such as diazomethane, anhydrous methanol-hydrogen chloride, methanol-boron trifluoride, potassium ethylsulphate^{1-8,13}, etc. Methyl esters of acids were obtained by Prelog and Picentanida⁹ by means of thermal decomposition of the tetramethylammonium salts of the acids. Trimethylamine is formed as a by-product of the decomposition. This method was applied by Fuson *et al.*¹⁰ to the methylation of some sterically hindered acids and the yields of the methyl esters obtained were in the range 60-90% at pyrolysis temperatures of 200-250°. A 0.2 M methanolic solution of trimethylanilinium hydroxide is an efficient methylation reagent available from Pierce (Rockford, Ill., U.S.A.) under the trade name Methelute. This reagent is also recommended for the evaluation of a number of pharmaceuticals.

Robb and Westbrook¹¹ found that the yields of esters were dependent both on the overall concentration of tetramethylammonium salt (minimum 20 µg/µl) and on the pyrolysis temperature (minimum 300°) when pyrolyzing tetramethylammonium salts of aliphatic mono- and dicarboxylic acids directly inside the vaporizers of commercial GC units. These workers also reported higher conversions of aromatic acids and of hydroxy- and dicarboxylic acids, except for oxalic, malonic, citric and malic acids which are decomposed to lower-molecular-weight products at 365°.

We have used trimethylphenylammonium hydroxide in studies of the methylation of a series of aromatic acids and have shown that this reagent gives volatile methyl esters at pyrolysis temperatures above 250°.

EXPERIMENTAL

Gas chromatography

A Fractovap Model C, Series 200, Type P-AID/f temperature-programmed gas chromatograph (Carlo Erba, Milan, Italy) was equipped with a flame ionization detector (FID) and following columns:

(1) stainless steel (2.3 m × 2 mm I.D.) packed with 15% Carbowax 20M on silanized Celite C22 (60-80 mesh);

(2) glass (2.5 m \times 2 mm I.D.) packed with 3% OV-17 on Chromaton N-AW-DMCS (0.16–0.20 mm) (Lachema, Brno, Czechoslovakia).

Temperatures: vaporizer and FID, 320°; column, 150 or 180°. Carrier gas (nitrogen) flow-rate, 20 ml/min. The sample (1 μ l) was injected using a Hamilton 10- μ l microsyringe.

Gas chromatography–mass spectrometry (GC–MS)

The products of pyrolysis were identified using a GC–MS system consisting of a JGC-20 KFP gas chromatograph connected via a double-jet molecular separator to a JMS 01-SG2 double-focusing electron-impact ionization mass spectrometer (JEOL, Tokyo, Japan). A similar OV-17 column to that described above was used with a length of 2 m and a helium flow-rate set to give an ion source pressure of 3.5×10^{-6} – 3.6×10^{-6} Torr (467–480 μ Pa) at GC inlet pressures of 1.2 kg/cm² (117.7 kPa) or 1.3 kg/cm² (127.5 kPa) and column temperatures of 130 or 150°, respectively. The sample (1 μ l) was injected using a 10- μ l MS 10 Terumo microsyringe and the temperature of vaporizer and molecular separator was 300°. Mass spectra at a resolution of $R_{10\%} = 1000$ were obtained under the following conditions: temperature of ionization chamber, 305°; energy of ionizing electrons, 75 eV; ionizing current (trap current), 200 μ A; accelerating voltage, 10 kV; scanning rate, 20–300 a.m.u. in 5 sec.

Procedure

A 0.2 M solution of trimethylphenylammonium hydroxide in methanol was prepared from the corresponding iodide according to Cundiff and Markunas¹². 2-Methylnaphthalene was employed as internal standard to quantitate the yield of the methylation reaction studied. *Ca.* 15 mg of the aromatic acid were weighed into a micro test-tube, 0.5 ml of a methanolic solution of the internal standard were added (*ca.* 40 mg/ml) followed by one drop of methanolic phenolphthalein solution and 1 ml of 0.2 M trimethylphenylammonium hydroxide. The micro test-tube was then sealed by a serum cap and after thorough mixing a 1- μ l aliquot of the resulting solution was injected into the chromatograph.

Correction factors were determined by the same procedure, the acid being replaced by a corresponding methyl ester and the methylation reagent by the same volume of anhydrous methanol.

RESULTS AND DISCUSSION

Of the two stationary phases examined, the OV-17 phase is more suitable and permits a good separation of methyl esters from the solvent as well as from N,N-dimethylaniline arising from the pyrolysis. The peaks are narrower, even at lower column operating temperatures, and their elution times are substantially shorter than with the Carbowax 20M column. Only the methyl benzoate peak is overlapped by N,N-dimethylaniline, which therefore excludes the analysis of benzoic acid.

In a series of substituted benzoic acids, the isomeric methylbenzoic acids exhibited almost identical correction factors, the mean value of which could be used for the calculations. A similar relation can be assumed to exist for isomers of acids having other substituents. With the exception of aminobenzoic acids which produced

TABLE I
YIELDS OF METHYL ESTERS FROM VARIOUS AROMATIC ACIDS

Acid	Yield (%)
<i>o</i> -Methylbenzoic	95
<i>m</i> -Methylbenzoic	85
<i>p</i> -Methylbenzoic	90
<i>p</i> -Chlorobenzoic	103
<i>m</i> -Chlorobenzoic	88
<i>m</i> -Nitrobenzoic	100
<i>p</i> -Nitrobenzoic	94

no peaks of methyl esters under the given reaction conditions, the benzoic acids having chloro, iodo, nitro, 2,4-dichloro and 4-chloro-3-nitro substituents were methylated successfully.

The ester yields are listed in Table I and were at least 85%. Products of thermal decomposition of the trimethylphenylammonium salts were identified by comparing their elution times with those of standard compounds (if available) and/or by measuring the mass spectra of the effluents from the chromatographic column. In addition to *N,N*-dimethylaniline and the methyl esters of the acids listed in Table I, the methyl esters of *o*-chloro-, *o*- and *m*-iodo-, 2,4-dichloro-, 4-chloro-3-nitro-, *o*-, *m*- and *p*-hydroxy- and *o*-, *m*- and *p*-methoxy-benzoic acids were identified by GC-MS. The mass spectra of the methylation products of isomeric hydroxybenzoic acids have confirmed the fact that the esterification of a carboxyl group takes place at the same time as the partial methylation of a hydroxyl group. Thus, in addition to the peak of a hydroxybenzoic acid methyl ester, a peak of a methoxybenzoic acid methyl ester also occurs on the chromatogram. The ratio of the methoxy- to the hydroxybenzoic acid methyl ester (the former deluting before the latter) was found to be 2:1 by comparing the peak areas for the *meta* and *para* isomers. The esters of the *ortho* isomers are eluted in the reverse order with the methoxy-to-hydroxy peak-area ratio being 1:6. The occurrence of an intense violet colour of phenolphthalein in all of the experiments is evidence of the presence of an excess of trimethylphenylammonium hydroxide.

The dependence of the ester yield for *p*-chlorobenzoic acid on vaporizer temperature is in a good agreement with the conclusions of Robb and Westbrook¹¹ who investigated the similar relation for benzoic acid in other types of gas chromatograph. However, a differential thermal analysis experiment showed that the pyrolysis of the isolated trimethylphenylammonium salt of benzoic acid can be completed quantitatively even at 250°.

The results obtained indicate that the described procedure may be applicable to routine qualitative GC analyses of aromatic carboxylic acids. In individual series of isomers, the *ortho* isomer can be easily distinguished from the *meta* and *para* isomers whose separation from each other, however, is generally poor on the OV-17 column and requires another type of stationary phase. A quantitative application is possible after a determination of the conversion factors for a larger series of mixtures of acids. Common types of gas chromatographs can be used without any modification for analyses by the described procedure, and the reagents required are readily available. Because of its simplicity and rapidity, the method fulfils the requirements of modern analysis.

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