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Gas chromatography of primary and secondary amines as their trifluoroacetyl derivatives

During an investigation into the volatile amines of tobacco leaf, it became necessary to devise a method for their separation and identification. However, direct gas chromatography of free amines is impaired by the tailing of peaks owing to the partial adsorption of the amines on the support material and also by the high volatility of the lower amines. To overcome this tailing effect a number of solutions have been offered including the use of an inert support such as glass beads or Teflon[1] and the deactivation of the support by treatment with sodium hydroxide[2]. Alternatively the amines may be converted to a suitable derivative such as the corresponding trifluoroacetamides. Since early work in this investigation made use of packed columns, it was decided to chromatograph the amines as their trifluoroacetyl derivatives to avoid adsorption problems. In addition, the boiling point range of the amines is decreased since conversion to the trifluoroacetamides (TFA) lowers the volatility of the lower amines and increases the volatility of the higher members. However, owing to the large number of amines encountered during the investigation it was found necessary to use capillary columns.

The separation of a number of TFA derivatives of alkylamines containing up to 22 carbon atoms on packed columns has been reported[3-5], but no comprehensive studies on capillary columns have been published.

Recent investigations into the steam volatile amines from Latakia tobacco[6] have resulted in the separation of a large number of amine TFA derivatives by capillary column GLC. The amines studied include primary aliphatic amines up to C_8, symmetrical secondary aliphatic amines up to C_5 and a number of N-methyl-alkylamines, aromatic amines and heterocyclic amines.

Experimental

The N-methyl-alkylamines were prepared in the laboratory by reacting the appropriate amine with benzaldehyde and methylating the condensation product with methyl iodide[7]. Other amines were obtained from commercial chemical suppliers.

Preparation of derivatives. The trifluoroacetamides were prepared by dissolving the amine in ether and adding trifluoroacetic anhydride in slight excess. After allowing the mixture to stand for a few minutes the solution was washed with sodium bicarbonate solution and water and then dried over magnesium sulphate. After evaporation of the ether the crude TFA derivative was either purified by vacuum sublimation in the case of solids or by distillation or preparative GLC when the derivative was a liquid.

Gas chromatography. All investigations were carried out on a Perkin-Elmer F11 gas chromatograph fitted with a flame ionisation detector. Nitrogen was used as the carrier gas. Investigations were carried out using the following stationary phases and conditions:

(a) A 50 m × 0.25 mm I.D. stainless steel capillary column coated with polyphenyl ether OS124 (PPE). Carrier gas pressure: 20 p.s.i.g. Oven temperature: programmed between 85° and 185° at 4°/min. Injection block temperature: 250°.

TABLE I

RELATIVE RETENTION TIMES OF TRIFLUOROACETYL DERIVATIVES OF AMINES

No.	*TFA derivative*	*PPE*	*Apiezon L.*	*SE-30*	*DEGS*
1	Ethylamine	0.12	0.05	0.08	0.05
2	*n*-Propylamine	0.20	0.13	0.14	0.73
3	Isopropylamine	0.09	0.05	0.07	0.32
4	*n*-Butylamine	0.40	0.26	0.28	0.96
5	Isobutylamine	0.24	0.18	0.20	0.77
6	*sec.*-Butylamine	0.19	0.14	0.17	0.61
7	*tert.*-Butylamine	0.06	0.05	0.09	0.23
8	*n*-Amylamine	0.66	0.46	0.48	1.19
9	Isoamylamine	0.55	0.38	0.32	1.07
10	*n*-Hexylamine	0.94	0.72	0.73	1.39
11	*n*-Heptylamine	1.22	1.00	1.00	1.68
12	*n*-Octylamine	1.52	1.28	1.39	1.86
13	Allylamine	0.20	0.10	0.12	—
14	Dimethylamine	0.09	0.05	0.07	0.12
15	Diethylamine	0.19	0.18	0.20	0.27
16	Diisopropylamine	0.27	0.33	0.35	—
17	Di-*n*-propylamine	0.48	0.52	0.53	0.50
18	Diisobutylamine	0.66	0.75	0.76	—
19	Di-*n*-butylamine	1.00	1.00	1.00	1.00
20	Di-*sec.*-butylamine	0.69	0.81	—	0.70
21	Diisoamylamine	1.22	1.28	1.29	—
22	Di-*n*-amylamine	1.37	1.39	1.50	—
23	N-Methyl-ethylamine	0.13	0.13	0.12	0.20
24	N-Methyl-isopropylamine	0.19	0.18	0.20	0.19
25	N-Methyl-*n*-propylamine	0.24	0.22	0.23	—
26	N-Methyl-isobutylamine	0.31	0.32	0.32	0.35
27	N-Methyl-*n*-butylamine	0.43	0.41	0.41	0.46
28	N-Methyl-isoamylamine	0.55	0.53	0.54	0.60
29	N-Methyl-*n*-amylamine	0.71	0.65	0.64	—
30	Diallylamine	0.40	0.68	0.39	—
31	Aniline	1.34	0.94	0.85	2.08
32	*o*-Toluidine	1.44	1.09	1.00	1.90
33	*m*-Toluidine	1.60	1.21	1.13	—
34	*p*-Toluidine	1.64	1.24	1.17	—
35	2,3-Dimethylaniline	1.87	1.47	1.35	2.30
36	2,4-Dimethylaniline	1.77	1.39	0.88	—
37	2,5-Dimethylaniline	1.68	1.34	1.24	2.17
38	2,6-Dimethylaniline	1.74	1.34	0.97	2.27
39	3,4-Dimethylaniline	2.02	1.58	1.47	2.45
40	*o*-Ethylaniline	1.57	1.24	1.17	2.02
41	*p*-Ethylaniline	1.89	1.49	1.50	—
42	Pyrrole	0.31	0.52	0.53	—
43	Pyrroline	0.66	0.43	0.39	0.79
44	Pyrrolidine	0.80	0.52	0.48	0.80
45	Piperidine	0.80	0.65	0.58	0.76
46	(±)-1-Phenethylamine	1.60	1.15	1.13	2.18
47	2-Phenethylamine	1.93	1.39	1.35	2.39
48	1,2,5,6-Tetrahydropyridine	0.81	0.63	—	0.89

(b) A 50 m × 0.25 mm I.D. stainless steel capillary column coated with Apiezon L. Carrier gas pressure: 20 p.s.i.g. Oven temperature: programmed between 95° and 195° at 4°/min. Injection block temperature: 250°.

(c) A 30 m × 0.25 mm I.D. stainless steel capillary column coated with silicone rubber SE-30. Carrier gas pressure: 20 p.s.i.g. Oven temperature: programmed between 90° and 180° at 4°/min. Injection block temperature: 250°.

(d) A 15 m × 0.5 mm I.D. stainless steel support-coated column containing

diethylene glycol succinate. Carrier gas pressure: 10 p.s.i.g. Oven temperature: programmed between 50° and 180° at 3°/min. Injection block temperature: 230°.

Results and discussion

The relative retention times of all the compounds analysed on four stationary phases are shown in Table I. The internal standard used throughout was di-*n*-butylamine and all retention values were measured from the solvent peak.

It is impossible to resolve the mixture of 48 compounds on any one of the stationary phases, but identifications may be made by careful choice of columns. It is noteworthy that the derivatives of isopropylamine and dimethylamine are inseparable on the three non-polar columns, whereas the DEGS column distinguishes them easily. A similar effect is observed for N-methyl-isopropylamine and diethylamine.

If the relative retention times of the aliphatic derivatives obtained on the SE-30 and DEGS columns are plotted against each other, primary and secondary amines lie on two separate curves and this property may be used to distinguish an unknown amine.

The aromatic amines are generally well separated, but occasionally they possess the same retention time as higher members in the aliphatic series. The only aromatic amines which cannot easily be separated are *m*-toluidine and (±)-1-phenethylamine, but their retention times on Apiezon L are sufficiently different for them to be adequately distinguished.

The heterocyclic amines were all separated with the exception of pyrrole and pyrrolidine, which give coincident retention values on Apiezon L. Pyrrole is unique in that the derivative may produce two peaks when chromatographed, owing to trifluoroacetylation taking place either on the N-atom in the usual way to form N-trifluoroacetyl-pyrrole or on the C-2 atom giving 2-trifluoroacetylpyrrole. The formation of both compounds is, however, dependent upon the conditions employed, but since 2-trifluoroacetylpyrrole is preferentially formed, it may be the only one to appear when chromatographed; for this reason this peak has been used to identify pyrrole during the present investigation. In order to identify the two peaks, a sample of pure 2-trifluoroacetylpyrrole was prepared by reacting pyrrole with trifluoroacetic anhydride in dry benzene at 0° and purifying the product by vacuum sublimation, m.p. 46–47° (ref. 8).

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