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Note

Formation of amine-N-trifluoroacetyl derivatives from the amine hydrochloride salts

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Analysis of aqueous extracts of the Murchison meteorite for low-molecular-weight organic compounds revealed the presence of aliphatic amines¹. However, it became desirable to separate the amines from the other organic compounds in the meteorite extract and analyze them separately in order to obtain mass spectrometric (MS) confirmation. Initially the amines were partially separated from other volatile compounds by acidifying the sample with hydrochloric acid, carefully evaporating the water to remove interfering volatile compounds, and then adding base to regenerate the free amines. However, the free amines are difficult to separate as the free bases in aqueous solution and especially difficult to analyze by gas chromatography (GC) and by combined GC-MS. Therefore a suitable derivative was sought which did not require extraction of the amines into an organic solvent (because of low efficiency, potential loss through volatilization, and non-selectivity for amines) and which could be formed directly in aqueous solution or from the amine hydrochloride salts.

The benzene-soluble dinitrophenyl derivatives of amines can be formed by reacting aqueous solutions of the amines with sodium dinitrophenyl sulfonate². This reagent reacts satisfactorily with primary amines, but slowly and incompletely with secondary amines. These derivatives did not separate completely and required high temperatures to elute them from GC columns containing methyl and phenyl silicone stationary phases. In addition, the mass spectra of many of the various isomers are not easily distinguishable from each other³. On the other hand, the N-trifluoroacetyl derivatives of aliphatic amines are easily separated by GC⁴⁻⁶, and their mass spectra have been characterized⁷. The N-trifluoroacetyl (N-TFA) derivatives were formed by the addition of trifluoroacetic anhydride (TFA)₂O, to a solution of the free amines in an organic solvent. This note describes a procedure for the direct trifluoroacetylation of the C₁-C₆ aliphatic amine hydrochloride salts, thus obviating the regeneration of the very volatile free amines for derivatization purposes.

EXPERIMENTAL

All of the C₁-C₄ as well as some of the C₅ and *n*-C₆ aliphatic amines were used in this study. A sample of each amine listed in Table I containing 1 mg/ml of the free

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TABLE I

RETENTION ORDER AND RETENTION TIMES OF THE AMINE N-TFA DERIVATIVES ON A CAPILLARY AND PACKED COLUMN CONTAINING FFAP LIQUID PHASE

Amine	N-TFA retention time (min)	
	Capillary column	Packed column
Dimethyl	13.4	—
Diethyl	15.3	4.9
<i>tert.</i> -Butyl	16.1	6.8
<i>tert.</i> -Amyl	19.6	8.6
Isopropyl	22.1	9.6
N-Methyl- <i>n</i> -butyl	22.9	12.4
<i>sec.</i> -Butyl	25.2	13.6
Ethyl	28.8	15.6
Isobutyl	30.4	17.3
<i>n</i> -Propyl	31.4	18.5
Methyl	31.7	18.6
<i>n</i> -Butyl	36.4	21.1
Isoamyl	38.9	22.6
<i>n</i> -Amyl	41.7	23.7
<i>n</i> -Hexyl	47.2	26.4
Ammonia	50.9	28.8

amine in water, was acidified to about pH 1 with hydrochloric acid. An aqueous solution containing all of the amines studied was treated similarly. The water was removed with rotary evaporation at 40°. The sample of the amine hydrochloride mixture left a viscous yellow liquid which was rendered more crystalline with the addition and evaporation of 10 ml diethyl ether (three times). Approximately 2 mg of the amine hydrochloride mixture were added to a PTFE-lined screw cap vial followed by 2 ml of (TFA)₂O (in the hood). The vial was tightly capped and placed in a boiling water bath for 5 min. During this heating period the solution bubbled slightly as the amine hydrochlorides slowly dissolved to form the N-TFA derivatives. The method described is similar to that used by Cruickshank and Sheehan⁸ to form N-TFA amino acid methyl esters from the amino acid methyl ester hydrochlorides. Following reaction each vial was cooled and 3 ml of dichloromethane were added. The excess (TFA)₂O, trifluoroacetic acid, hydrochloric acid, and dichloromethane were removed at 0° with rotary evaporation leaving clear or slightly yellowish liquids with a characteristic sweet odor for each sample. A few milliliters of dichloromethane were added and the solution was dried by submerging the vial for several seconds in a liquid nitrogen bath to freeze out the water or by adding a few milligrams of anhydrous sodium sulfate (previously washed and heated to 550°). The samples of individual amine N-TFA derivatives and the mixture were analyzed in a Perkin-Elmer 3920 gas chromatograph by injecting each sample onto a 46 m × 0.05 cm I.D. stainless-steel capillary column dynamically coated with FFAP (Carbowax 20M terminated with 2-nitroterephthalic acid) and on a 180 × 0.32 cm O.D. stainless-steel column packed with 10% FFAP on 80–100 mesh Chromosorb W. The capillary column was held at 80° for 8 min and then temperature programmed at 2°/min to a final temperature of 150° with a helium flow-rate of 3 ml/min. The packed column was held at 50° for 2 min and then temperature programmed to 200° at 5°/min with a flow-rate

of 30 ml/min. The elution order and retention times of the amines on the two columns are compared in Table I.

The elution order is very dependent on the degree of branching with the most highly branched compounds eluting first and the derivative of ammonia eluting last of the compounds studied. The analysis time was only about one half as long on the packed column, but the derivatives of dimethyl- and diethylamine were not resolved from the solvent and the derivatives of *n*-propylamine and methylamine were not resolved from each other. However, the faster elution time and higher maximum operating temperatures with a packed column would allow separation of higher molecular weight homologs.

It is believed that the method described here for the formation of amine TFA derivatives from the hydrochloride salts will be of great utility in analyzing dilute aqueous solutions of amines because the aqueous amine solution can be evaporated to dryness following formation of the hydrochloride salts, thus allowing concentration of the amines to a very small final volume while evaporating potentially interfering low-molecular-weight compounds which may otherwise be derivatized with (TFA)₂O and interfere with the analysis. In addition, the derivatives are easily synthesized, easily separated by GC, and positively identifiable from their mass spectra.

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