Gas-Liquid Chromatography and Structure-Retention Time Relationship of Anhalonium Alkaloids and Related Bases

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Gas-liquid chromatographic separation of 18 anhalonium alkaloids and related bases has been studied employing 1 per cent methylsiloxane polymer (containing about 5 per cent phenyl substitution) as the liquid phase. The GLC behavior of these closely related compounds suggested a structure-retention time relationship. In general, *N*-monomethylation of primary and secondary amines, *O*-methylation, or *C*-monomethylation of the bases studied was found to decrease the retention time, while introduction of hydroxyl, methoxyl, or methylenedioxy group, or an unsaturation, produced an increase in retentivity. These changes in retention time may be attributed to the changes in polarity of amino and/or phenolic hydroxyl groups brought about by substitution in or adjacent to these groups.

THE PRACTICAL utility of gas-liquid chromatography in the field of natural products is well established (1). In alkaloid work this technique is now commonly employed for the purpose of identification of bases in crude fractions, and in their separation and estimation (2, 3). In the last few years, several significant gas chromatographic studies on biological amines have been reported (4, 5). The gas chromatography of amines, alkaloids, and amino acids has been recently reviewed by Fales and Pisano (5).

During our studies (6) on the alkaloids of *Anhalonium lewinii* three groups of closely related bases, β-phenylethylamines, tetrahydroisoquinolines, and dihydroisoquinolines, became available. The main difference among these compounds is found in variations in or near the polar amino and/or phenolic hydroxyl groups (7). Fales and Pisano have suggested that in polar compounds such as these, contribution to the over-all interaction from various functional groups on the molecules will be related to the polarity and configuration of the groups, and chances for separation will be most favorable when a polar column is used for their chromatography.

This paper presents the results of gas chromatographic study on anhalonium alkaloids and related bases wherein polar methylsiloxane containing ∽5% phenyl substitution was employed as the liquid phase.

EXPERIMENTAL

Apparatus.—A Chromalab gas chromatograph equipped with hydrogen flame detector was used.

Column.—The column was made[1] of glass tube, 12 ft. in length and having an inner diameter of 4 mm. The liquid phase in the column was 1% methylsiloxane containing ∽5% phenyl substitution [2] and the solid support was Gas-Chrom P, 100 to 140 mesh. The column temperature was maintained at 180°, and argon at 20 p.s.i. was employed as the carrier gas. Other pertinent column conditions have been recorded in Table I.

TABLE I.—CONDITIONS FOR GAS-LIQUID CHROMATOGRAPHY OF ANHALONIUM ALKALOIDS AND RELATED BASES

Col. packing	1% methylsiloxane containing ∽5% phenyl substitution on Gas-Chrom P, 100 to 140 mesh
Col. temp.	180°C.
Cell temp.	240°C.
Flash heater temp.	210°C.
Carrier gas	Argon at 20 p.s.i.
Hydrogen flow rate	32 ml./min.
Current sensitivity	3×10^{-8} amp.

Method.—Samples of 1-μl. quantities of 1% solution of the bases in ethanol were injected into the flash heater zone. When the acid salts of alkaloids were chromatographed, samples were prepared in 1% ethanolic solution of diethylamine. A Hamilton microsyringe was used for sample injection.

RESULTS AND CONCLUSIONS

Table II summarizes the gas chromatography of anhalonium alkaloids and related bases. Results indicate that under the conditions employed and using methylsiloxane containing ∽5% phenyl substitution as the liquid phase in the column separation of these closely related compounds could be achieved. The following conclusions could be arrived at regarding the relationship of their structure and retention time.

1. *N*-Monomethylation of primary and secondary amines, *O*-methylation, or *C*-monomethylation of the bases studied resulted in a decrease in retention time. Although there was an increase in molecular weight corresponding to a methylene group, the observed decrease[3] in retention time of the phenol ether and the alkylated amine could be rationalized as due to the corresponding decrease in polarity of the derivatives as compared to their parent compounds. The decrease in retention of *C*-methyl derivative, as compared to its lower homolog, may be hypothesized as due to an interference of methyl group in permitting the molecule to be adsorbed on

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[1] For the preparation of column, see *Reference 5*.

[2] A gift to the Laboratory of Metabolism, National Heart Institute, U. S. Public Health Service, Bethesda, Md., from Dr. Arthur Martellock, General Electric Silicone Products Division, Waterford, N. Y.

[3] While this manuscript was in preparation, Ikekawa *et al.* (9) have reported similar observations during the gas chromatography of morphinan derivatives.

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