

Gas chromatography of N-chloroethyl and N,N-bis-(chloroethyl) carbamates

The N-chloroethyl urethanes represent an interesting class of compounds in their intimate structural relationship to nitrogen mustard derivatives. Such compounds have been assayed colorimetrically via γ -(4-nitrobenzyl)-pyridine (NBP)¹⁻⁷. This reagent has also been employed in the study of comparative chemical and biological activities of such alkylating agents⁸. The colored product formed by the NBP-alkylating agent couple has been described by BARDOS and his coworkers⁸. Alkylating agents have alternately been studied by a cytotoxic metabolic inhibition test^{9,10} and by fluorimetry¹¹. The analysis of β -chloroethyl carbamate included in a group of simple carbamates, and a diverse selection of N-substituted urethanes as analyzed by gas chromatographic means has been reported earlier^{12,13}.

The object of this note is to report the gas chromatographic elution pattern of the N-chloroethyl urethanes on several chromatographic liquid phases.

Experimental

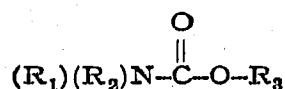
The N-chloroethyl carbamate standards employed in this study were obtained from BASF, Ludwigshafen, Germany. Gas chromatographic analysis was carried out on (1) 15 % Versilube F-50 copper and (2) 10 % SE-30 stainless steel columns housed in an F&M model 1502 dual column oven containing a hot-wire detector and operated from an F&M model 500 gas chromatograph; on a (3) 4 % QF-1 glass column in an F&M model 1609 flame ionization gas chromatograph; and on a (4) 5 % Dow-11 glass column in an Aerograph model 600-B containing an electron capture detector. Specific analytical operating conditions are given in the footnotes to Table I.

Results and discussion

The results of chromatographic analysis of the chloroethyl carbamates on the various liquid partitioning phases are given in Table I. The relative elution behavior followed a similar pattern on all of the columns employed with no reversals being noted. The best resolution appeared to be obtained on Dow-11. The effective number of plates for the elution of N,N-bis-(2-chloroethyl) ethyl carbamate, however, indicated Versilube F-50 (66 plates/ft.) was slightly more efficient than Dow-11 (60 plates/ft.). The greatest number of total effective plates was obtained on the QF-1 column (300 plates), while the lowest efficiency was observed on SE-30 (22 plates/ft.). As would be expected, the order of elution on such relatively non-polar phases was found to be a function of molecular weight. It should be mentioned that several peaks were obtained on the electron capture detector for all of the carbamates analyzed. The elution results reported by electron capture refer to the principal component detected on the recorder chart. Gas chromatographic analysis on a selective phase (Carbowax 20 M) was also attempted initially. The alkyl carbamates eluted successfully, but the aryl derivatives, and the 2,4,6-trichlorophenyl carbamate derivative in particular, were extremely retained on this substrate. Even on a non-selective phase such as QF-1, elution of the samples required a column operating temperature in the vicinity of 200°.

This study of the chromatographic behavior of chloroethyl carbamates is being extended to other classes of chlorinated carbamates.

TABLE I
GAS CHROMATOGRAPHY OF CHLOROETHYL CARBAMATES



R_1	R_2	R_3	Relative retention ^a			
			Dow-11 ^b	QF-1 ^c	Versilube F-50 ^d	SE-30 ^e
Methyl	2-chloroethyl	methyl	0.020	0.036	0.031	0.036
Methyl	2-chloroethyl	ethyl	0.028	0.045	0.038	0.043
2-Chloroethyl	2-chloroethyl	ethyl	0.12	0.12	0.10	0.12
2-Chloroethyl	2-chloroethyl	<i>p</i> -tolyl	1.0	1.0	1.0	1.0
2-Chloroethyl	2-chloroethyl	<i>p</i> -chlorophenyl	1.5	1.3	1.4	1.2
2-Chloroethyl	2-chloroethyl	2,4,6-trichlorophenyl	3.1	1.9	2.6	2.3

^a Relative to N,N-bis-(2-chloroethyl) *p*-tolyl carbamate as 1.0. Retention of this derivative was 5.6 min on QF-1, 5.9 min on SE-30, 6.3 min on Dow-11, and 23.3 min on Versilube F-50.

^b 5% w/w on 60-80 mesh Chromosorb W, 3 ft. by 0.125 in. O. D. glass column. Operating conditions: column 150°; injection port 70 V; detector 150°; output sensitivity 1 ×; input impedance 10⁷; detector titanium tritide 250 mc; nitrogen carrier 35 ml/min.

^c 4% w/w on 80-100 mesh Chromosorb W (HMDS pretreated), 6 ft. by 0.25 in. glass column. Operating conditions: column 198°; injection port 70 V; detector 210°; range 1000; flame ionization detector; hydrogen 74 ml/min; air 400 ml/min; nitrogen carrier 60 ml/min.

^d 15% w/w on 60-80 mesh Chromosorb W (HMDS pretreated), 4 ft. by 0.125 in. copper column. Operating conditions: column 195°; injection port 235°; detector 250°; filament current 150 mA; hot-wire detector; helium carrier 26 ml/min.

^e 10% w/w on 60-80 mesh Chromosorb W, 8 ft. by 0.125 in. stainless steel column. Operating conditions: column 195°; injection port 235°; detector 250°; filament current 150 mA; hot-wire detector; helium carrier 33 ml/min.

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