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Sample Profiles and Temperature Transients in Preparative Gas Chromatography

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Summary

This paper gives results of investigating some of the parameters involved in the operation of a preparative gas-chromatographic unit.

An elution profile for a nonabsorbed sample was noted across the column bed. Elution-rate differences indicate that the carrier gas flow rate is somewhat faster near the column wall than in the central bed. However, in at least some cases, overloading samples of absorbing solutes gave more rapid elution through the central axial portion of the column than in the near-wall portion of the column bed. Apparently, heat transfer and solute equilibrium change with concentration and temperature differences across the column bed, and both steady-state and transient temperature differences between the axis and wall have such pronounced effects that carrier gas velocity differences across the bed are of secondary importance in 1-in. I.D. columns.

Described herein is an investigation of some of the parameters affecting the maximum separable sample size and the maximum production rate of relatively nonvolatile materials in preparative gas chromatography (*14*).

Particular effort has been expended toward investigating concentration profiles along with steady- and unsteady-state temperature profiles at the inlet and outlet sections of 1-in. I.D. × 3-ft columns. The profiles were measured with pairs of thermocouples or thermistors and by sample withdrawal tubes installed at the column axis and at the column wall.

The major factors in determining separation and limiting the production rate for the various experimental operating procedures described herein are believed to be the total solute concentration

and the temperature transients as they affect the separation factor and the vapor-liquid equilibrium achieved within the 1-in. I.D. columns. Preparative scale sample injections in columns heated with Nichrome windings exhibited appreciable differences in the degree of sample resolution at the wall and central portion of the column bed; however, similar injections in oven heated columns at the best operating conditions exhibited slight sample concentration differences across the column bed. A solute concentration profile was not found for small nonoverloading samples in either Nichrome or oven heated columns, thereby giving evidence that gas velocity profile effects are small in relation to other factors affecting peak separation for the column length under investigation. Evidence that a gas velocity profile did in fact exist across the column bed was provided by a slight concentration profile noted between the wall and central bed positions of the column bed for a nonabsorbing sample.

Certain characteristics of large-scale gas-chromatography columns have been postulated (*6*) as the reason for the apparent loss of efficiency when compared to analytical scale columns. Much of the early experimental work by the investigators in this field was directed toward modifying packing procedures with the expectation that the large losses of sample resolution reported by some investigators (*3,7,10*) could be avoided. This type of experimental activity was apparently brought about by a strong conviction that the poor separations in preparative scale column were mainly due to an unfavorable carrier gas and sample velocity profile across the column bed and a relatively large rate of sample diffusion in the axial direction with only a comparatively small rate of sample diffusion in the radial direction (*10*). Velocity profiles, sample diffusion variations, and nonuniform stationary-phase loading were attributed to porosity variations across the column bed produced by an uneven distribution of the particles of column packing (*5,6,13*).

The general approach to sample scale-up in the field of preparative gas chromatography has been to determine whether the height per theoretical plate values have been preserved in the larger columns. Such measurements are normally made on nonoverloading injections. Apparently, only a limited amount of experimental work has been done in determining temperature variations and heat-transfer properties in large-diameter columns for preparative

scale sample injections and the effect that these parameters may have on the efficiency attained in those columns (*12,15*). Limited experimental work has also been done on the effects of various other operating parameters for large-scale columns (*4,9,17*).

More recently, column designs and configurations have incorporated features which are intended to correct flow and concentration profiles (*1,2,18*); however, it has not yet been made clear just how these modifications affect sample elution characteristics. A review of the experimental and commercial preparative units indicates differences of emphasis pertaining to the important scale-up parameters. Until more complete information is obtained on all the phenomena of large-scale sample elution, it is doubtful whether proper optimizing of the column and its accessories can be accomplished. It is important for scale-up purposes to know whether equilibrium factors account for the efficiency loss of a column. Or, if sample profiling is significant, the factors causing it need to be determined. Theoretical calculations for solute sample equilibrium in relation to the peak shape and separation achieved have been reported (*8,16*) which indicate that equilibrium effects can be a limiting factor in preparative gas chromatography.

In view of the state of the art of large-scale gas chromatography, it is necessary to try to determine the effects of the various parameters on sample separation. Until this information is available, successful scale-up will continue to be on an empirical rather than a theoretically predictable basis. This paper will give data on certain parameters studied using a preparative column diameter of 1 in.

EXPERIMENTAL

The equipment and column packing procedures used in this study were the same as have previously been described (*14*). Also, as described in the above reference, column heating was accomplished by one of two methods: either by external Nichrome resistance wire windings or by a constant-temperature oven.

Variations of the column and detector assembly were necessary for some experiments, as described in the following paragraphs. Ammonia-vapor-injection experiments to allow an approximation of carrier gas flow profiling were done in which the detector and exit cone were removed from the column and a piece of damp phenolphthalein saturated filter paper was placed over the exit

column end. The paper was held in place with a metal screen soldered over a 1-in. I.D. hole drilled in a thin metal plate which was securely fastened to the exit-column flange.

Thermistor studies of solute concentration profiles were carried out by placing two thermistor beads in the packing near the column exit (one in the center of the bed and one about $\frac{1}{32}$ in. from the column wall). The thermistor beads were type GC32L3 from FenWal Electronics, Inc. The beads were 0.014 in. in diameter and had a resistance at 77°F of 2200 ohms. Copper circuit leads (#30 wire) were soldered to the thermistor wire and exited from the column bed through holes drilled radially in the exit-cone Teflon gasket. The holes drilled in the gasket were only large enough to allow insertion of the #30 lead wire. The gasketing material sealed around the wires when the exit cone–column union was tightened to prevent carrier gas leakage. The thermistor beads were powered by Carle Model 100 Micro-Detector power supplies. A thermal conductivity detector was normally used in conjunction with the thermistor beads.

Axial and radial temperature profile studies were made without the detector and exit-cone assembly. Before the column was packed, two thin-walled glass tubes (2 mm I.D.) were inserted lengthwise into the column from the exit-column end to within about $\frac{1}{2}$ in. of the inlet-cone flange. One of the tubes was positioned against the column wall and the other along the central axis of the column. Tightly fitting stainless-steel coarse mesh screens ($\frac{3}{16}$-in. openings) of 1 in. O.D. were used to support the column bed and to position the tubes within the column. Three such screens were used, one of which was placed midway up the column before the column was packed. The packing process was carried out as mentioned in a previous publication (*14*). The coarse mesh screen in the midcolumn section was not an impediment during the packing operation. The remaining two screens, with a piece of glass wool between them to prevent column packing from filtering out of the column, were placed at the column exit after the packing procedure was completed. Thermocouple wire of B & S 22 gage was inserted into these tubes for steady-state measurements. Steady-state axial and radial temperature profile data were obtained by moving the thermocouples along the length of the tube. It was found in separate tests that a variation of only $\frac{1}{4}$°C occurred, because the thermocouple was within the tube rather than bare to the column packing

itself. The glass tubes used in the steady-state temperature tests were melt-sealed on the inlet-column end to prevent carrier gas channeling through the tubes. Unsteady-state radial temperature measurements during passage of a solute band were obtained with the thermocouples extending $\frac{1}{2}$ in. into the column bed from the ends of the glass tubes. Heat-transfer lag prohibited the use of thermocouples within the glass tubes in measuring unsteady-state bed temperatures. It was necessary to adjust the length of the glass tubes and to repack the column bed for each axial position investigated. A wax of high melting point was used in these experiments to seal the ends of the glass tubes protruding from the exit end of the column in order to prevent carrier gas from channeling through the tubes.

Elution studies were done in which small sample streams were withdrawn from the wall and central bed positions at the exit end of the column. A modified exit cone and detector was used in this work. An exit cone was drilled and fitted with $\frac{3}{16}$ in. O.D. stainless-steel tubes which protruded about $\frac{1}{8}$ in. into the column bed, as shown in Fig. 1. The column packing was supported by a stain-

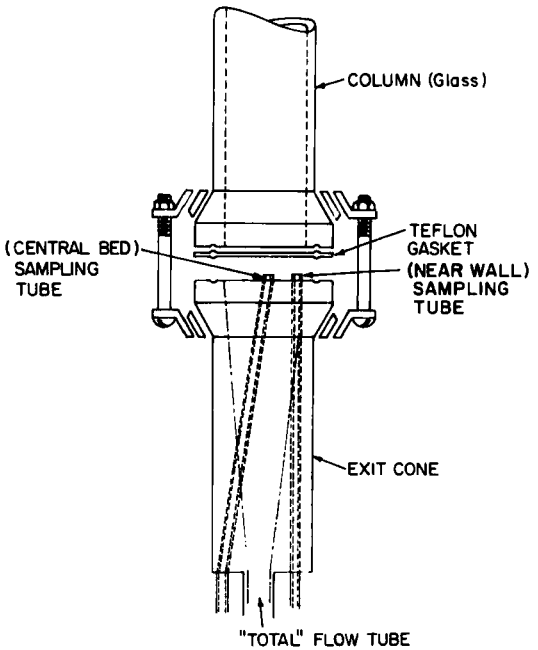

FIG. 1. Split-flow exit-cone details.

less-steel screen which was covered with a thin layer of glass wool and placed just within the mouth of the outlet cone. The eluting sample streams in the two small tubes as well as in the $\frac{3}{8}$-in. O.D. exit-cone tube all entered a special detector block in which three separate thermal-conductivity assemblies were used for independent sample analysis of the individual streams. The total flow issuing from the two small sample tubes was each about 5% of the total sample and carrier gas flow issuing from the column. The flow in the small sample tubes, as measured by a bubble meter, were found to be essentially identical; therefore, there was no need to artifically balance the flow between them. The remaining 90% of the sample and carrier gas flow will be designated as the "total" flow in the remainder of the work.

RESULTS

An earlier publication (*14*) has shown the advantage of slow sample injections and vaporization in conjunction with a hot, packed inlet cone heated about 60°C above the column operating temperature. Main emphasis in the present work was the determination of transient effects under the various operating conditions in both Nichrome and oven heated columns.

Stationary-Phase Studies on Conditioned Column Packing

The practice of operating the inlet cone at least 60°C above the operating column temperature may appear questionable because of the possibility of thermally degrading the stationary phase, particularly when the column temperature is near the maximum safe operating temperature of the column packing. Figure 2 illustrates that a loss of stationary-phase coating from the solid support occurred in the inlet section of a well-conditioned column which had been used in routine laboratory work. Coating loss is particularly noticeable in the first 10 to 12 in. of the column bed. The phase concentrations in Fig. 2 were obtained from Soxhlet extractions of various sections of packing taken from the column. As explained in succeeding sentences, it is believed that the stationary-phase weight-percentage variation shown here is principally due to a thermal degradation of the egs phase in the inlet column section rather than an elution process in which a portion of the egs phase is washed from the inlet bed by large sample injections and then deposited further down the column. An elution of the stationary-

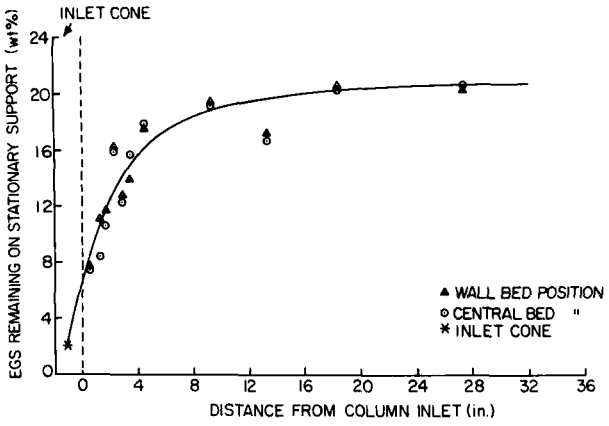

FIG. 2. Stationary-phase percentage-weight variations with distance into the column. Original column packing, 22% wt. egs.

phase elution attributed to sample overloading has been reported by Mikkelsen et al. (*11*). However, the sample volumes used by Mikkelsen et al. for injection into the columns were much larger on a cross-sectional-area basis than have been employed in this laboratory. A removal of the stationary phase due to thermal degradation rather than an elution process due to sample overloading is indicated in this work because the separations achieved were quite consistent over many repeated preparatory injections which clearly overloaded the column system. Also, inlet-cone bed samples taken from a conditioned column in which no samples were run showed essentially the same weight percentage of stationary phase remaining on the stationary support as for inlet-cone bed samples taken from a column which had been used for routine laboratory tests (shown in Fig. 2). Although stationary-phase loss is apparent in columns with a "hot," packed inlet cone, the maximum separable sample sizes and maximum production rates obtained with the modified column operation ("hot," packed inlet cone) were much higher than could be obtained with either an empty or a packed inlet cone operated at the column temperature (*14*).

Steady-State Temperature Studies

Steady-state axial temperature profiles were measured for a carefully prepared, Nichrome heated column (Fig. 3) in which Nichrome and insulating tape wrappings were spaced as evenly as

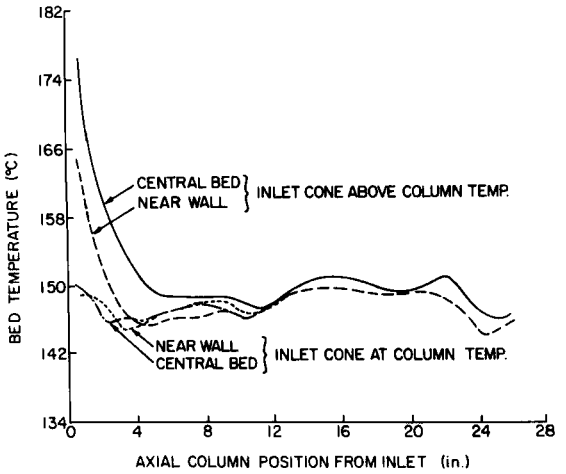

FIG. 3. Axial-bed temperature variations at steady state; 1-in. I.D. column, "evenly" Nichrome-heated.

possible. Axial temperature fluctuations in the column bed in excess of 5°C were noted when the inlet cone was maintained at the column temperature. Figure 4 shows data taken on an oven heated column in which axial temperature variations along the column bed did not exceed 2°C when the inlet cone was maintained at the column temperature. Controlled column temperatures were slightly different for the two experimental runs in Fig. 4, which accounts

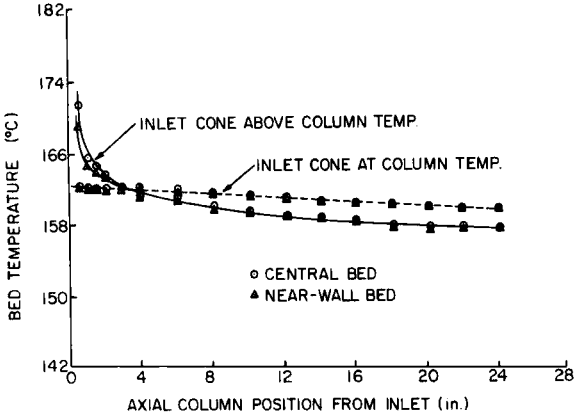

FIG. 4. Axial-bed temperature variations at steady state; 1-in. I.D. oven heated column.

for column temperatures not being the same at column bed depths sufficiently far from the inlet section as not to be affected by the inlet-cone temperature. More uniform axial temperature gradients and more uniform radial temperatures across the column bed were achieved with oven heated columns.

It is seen in Figs. 3 and 4 that the inlet-cone temperature influenced the bed temperature in both Nichrome and oven heated columns to a depth of about 10 to 12 in. A significant difference is noted in the axial temperature profiles for the center and near-wall bed positions of the inlet bed for the hot inlet-cone data in both types of columns. The fact that the central bed portion of the column could be maintained at a higher temperature than the near-wall bed suggested that this type of operation may correct the proposed solute profiling in preparative columns (*6*). The proposed solute profile is one in which the central bed portion of the solute band elutes later than the wall portion of the solute band in preparative columns, thereby forming a "bowl-shaped" concentration profile across the column bed. Maintaining the central bed at a higher temperature relative to the near-wall bed should effect a faster central bed solute elution rate, thereby tending to correct the concentration profile. However, as will be illustrated later by absorbing and nonabsorbing sample elution studies for the near-wall and central bed of 1-in. I.D. Nichrome and oven-heated columns, there was only a slight indication that solute profiling occurred across the column bed because of nonuniform gas flow. An improvement in preparative results for a hot, packed inlet cone is believed to be caused by better sample resolution as a result of an alteration of the sample band width and the axial concentration uniformity of the sample band compared to the other modes of column operation, and not by an improvement in the radial concentration profile. These predictions have resulted from experimental work, as described in the following paragraphs.

Transient Temperature Studies

Unsteady-state temperature variations have been measured in the column bed near the exit end of a Nichrome heated column during the passage of a solute band. Figure 5 is shown as an example of the concentration-temperature effects to be expected for a relatively small sample (0.1 ml methyl myristate). To give an

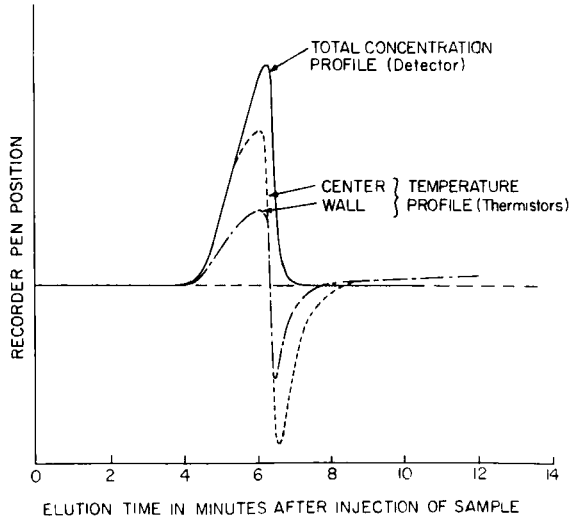

FIG. 5. Temperature variations produced in the column bed by passage of a 100-μl methyl myristate solute band at the exit-column end; 22% egs column at 155°C.

approximate idea of the temperature variations in Fig. 5, the temperature increase above the steady-state bed temperature for the central bed was about 2°C, as determined in a separate experiment. Temperature measurements on relatively small binary samples have also been made. The bed temperature was found to return to the preset column operating temperature between the peaks and

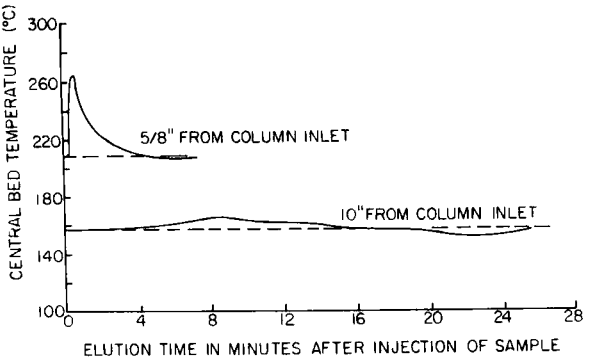

FIG. 6. Temperature variations produced in the central column bed by passage of a 5-ml methyl myristate solute band; 22% egs column at 157°C; inlet cone at 225°C.

to fluctuate during each individual peak in the same manner as shown in Fig. 5. Unsteady-state temperature measurements for large overloading samples were made with thermocouples rather than thermistor beads, because the thermistors tended to give unstable base-line response for large sample injections. The unsteady-state bed-temperature fluctuations produced by overloading samples of methyl myristate (5 ml) varied with axial position in the column, as shown for the central bed in Fig. 6. Similar results were obtained in the near-wall position with the exception that the temperature variations were not quite as pronounced as the central-bed-temperature variations. Figure 6 illustrates the large temperature variations that occurred in the column inlet in comparison to the temperature variations occurring farther down the column bed. Overheating of the inlet-bed section is to be expected, because incoming superheated vapor enters from the vaporizer and inlet cone and the high solute concentration in this portion of the column produces large exothermic heats of absorption. The cyclic temperature behavior of the unsteady-state profile for a bed position $\frac{5}{8}$ in. from the inlet flange is probably the result of a sensible heat–exothermic latent heat of absorption–endothermic latent heat of desorption process. Sensible heat effects of the incoming solute

TABLE 1

Unsteady-State Temperature Fluctuations in Inlet Column Section Produced by Passing Methyl Myristate Solute Band[a]

Sample size, ml	Bed position	Inlet-bed-temperature variations			
		Steady-state bed temp., 160°C		Steady-state bed temp., 225°C[b]	
		Heating[c]	Cooling[c]	Heating[c]	Cooling[c]
5.0	Central	36.3	7.7	64.0	4.0
5.0	Wall	13.7	4.8	62.4	6.8
3.0	Central	31.3	6.6	46.0	—
3.0	Wall	11.3	2.2	48.8	2.4
1.0	Central	20.0	4.0	22.0	—
1.0	Wall	8.0	1.3	22.2	—
0.5	Central	13.0	2.0	10.5	—
0.5	Wall	5.8	1.3	11.6	—
0.1	Central	1.3	—	1.8	—
0.1	Wall	2.4	—	1.1	—

[a] All measurements taken $\frac{5}{8}$ in. from column inlet. 20% egs, 1-in. I.D. × 3-ft-long column. Column temp., 160°C.

[b] Inlet-bed section maintained 65°C above column temperature by Nichrome windings.

[c] Heating and cooling above or below stationary-state bed temperature at that bed position (°C).

vapor are comparable to latent heat effects of the solute absorption-desorption process. The bed-temperature variations occurring at sufficient distances that the sensible effects of the incoming sample vapor are negligible are predominantly the latent heat of absorption and desorption effects, as illustrated by the profile obtained 10 in. from the inlet flange.

The inlet-bed section was further studied because of the high solute concentration and large temperature effects inherent in that portion of the column. Table 1 is a summary of the temperature

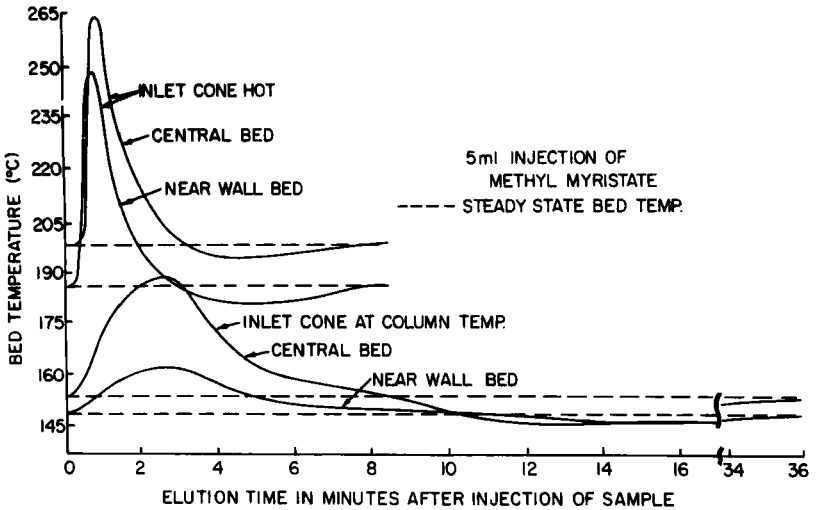

FIG. 7. Comparison of unsteady-state temperature in inlet-column section produced by passing solute band. Temperature probes $\frac{1}{8}$ in. from column inlet; 20% egs column at 150°C.

maxima and minima observed for various sample sizes of methyl myristate with the inlet-cone temperature either maintained at or above the column temperature. Temperature variations of less than 0.5°C are not recorded in this table. Figure 7 is an example of the data shown in Table 1. It is seen that the temperature variations were significantly greater for an inlet cone heated above the column temperature than when the inlet cone was maintained at the column temperature. Also, the temperature variation was of much shorter duration and the central and near-wall bed-temperature fluctuations were much more similar to each other when the inlet

cone was maintained above the column temperature than when the inlet cone was maintained at the column temperature.

In the unsteady-state temperature measurements, sample elution from the section of packing in question is not expected to be complete, at least until after the minimum temperature of the temperature fluctuation has been recorded (see Fig. 5). An estimated concentration profile for the methyl myristate injection into a column with the inlet cone maintained at the column temperature as shown in Fig. 7 would be a very broad peak of relatively low concentration. This indicates that appreciable band spreading may be occurring, which would be injurious to efficient sample separation. In comparison, the heated-inlet-cone data in Fig. 7 indicates that a band of relatively high initial concentration has passed rapidly through the inlet section of the column.

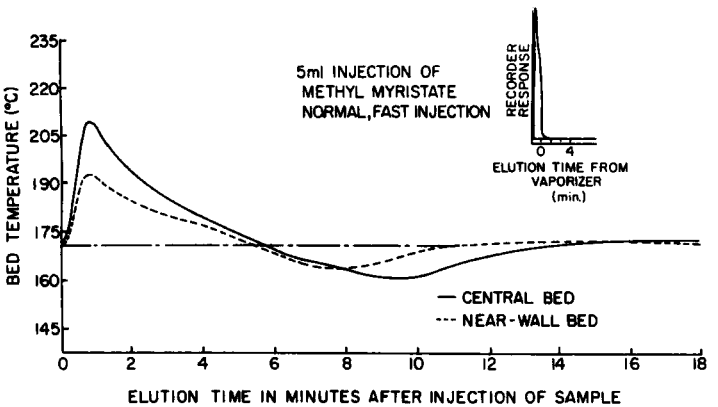

FIG. 8. Unsteady-state temperature in inlet-column section produced by passing solute band in oven heated column; temperature probes $\frac{3}{8}$ in. from column inlet; 20% egs column at 160°C; inlet cone at 220°C.

Methyl myristate samples (5 ml) were also injected into oven-heated columns. Figure 8 illustrates unsteady-state temperature variations noted for a rapid sample injection into a column having a heated inlet cone. The eluent from the vaporizer was also recorded and is included in Fig. 8. The vaporization profile indicates that the sample was rapidly vaporized. The unsteady-state temperature profile obtained for this sample indicates that the band passing through the column had a high initial concentration and was of relatively short duration. Injections of methyl myristate, having a com-

parable vaporization profile as shown in Fig. 8, were than made into the column when the inlet cone was maintained at the column temperature. The temperature variations recorded, as in the Nichrome heated column, were of reduced magnitude but of greatly extended length when compared to the heated-inlet-cone data. The temperature variations produced in the oven heated column by passing solute bands were not as large as noted in the Nichrome heated columns under comparable operating conditions. Heat-transfer characteristics for the oven column and connecting cone were much better than for the corresponding Nichrome heated columns, thereby probably accounting for lower temperatures of the carrier gas and sample vapor entering into the column and also for reduced temperature fluctuations of the column-bed variations brought about by sample absorption and desorption.

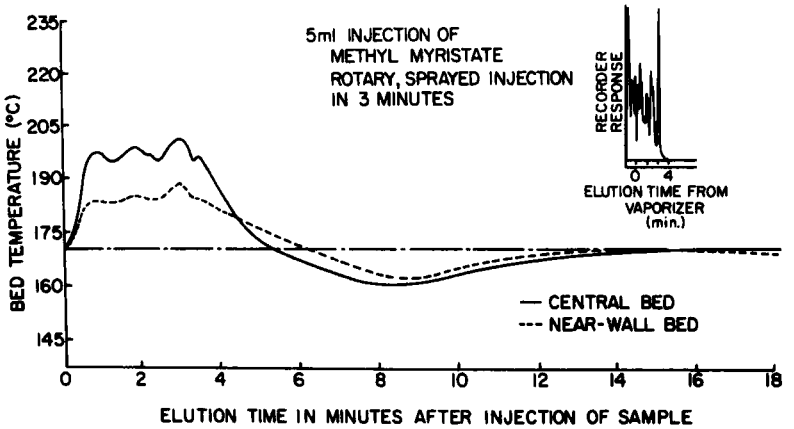

FIG. 9. Unsteady-state temperature in inlet-column section produced by passing solute band in oven heated column; temperature probes $\frac{1}{8}$ in. from column inlet: 20% egs column at 160°C; inlet cone at 220°C.

As illustrated in a previous publication (*14*), a slow sample injection sprayed onto the wall of an empty vaporizer cavity gave improved column performance in terms of maximum separable sample size and maximum production rate. Figure 9 shows the vaporization profile and inlet-bed unsteady-state temperature measurements for a slow methyl myristate (5 ml) injection. In comparison to Fig. 8, the temperature variation in Fig. 9 indicates that a solute band of rather uniform axial concentration, having essentially the same over-all elution time, passed through the inlet sec-

tion of the column. High initial solute concentration, as in the case of rapid sample injection, was not indicated for the slow injections. The temperature variations recorded indicate that appreciable band spreading did not occur for slow sample injections.

Slow rates of sample injection into a column with a heated inlet cone apparently have the advantage of producing solute bands of more uniform axial concentration than samples injected in a rapid manner into the same system. A more uniform axial concentration in the solute band should have the effect of minimizing overloading effects at any point during passage of the band and, as a consequence, the separation factor should be maintained at a higher value throughout the column length, thereby resulting in better sample resolution. Extremely wide solute bands have resulted from sample injections made into columns having the inlet cone maintained at the column temperature. Such excessive band spreading is not desirable in preparative columns because it will result in reduced sample production rates.

Concentration Profile Studies

A series of experiments with a modified detector system which simultaneously recorded central and near-wall bed concentrations along with the concentration of the "total" elution flow were made to determine solute concentration profiles. Figures 10 and 11 show 100- and 200-μl injections (C_{14}/C_{16} methyl ester mixture), respectively, made into a Nichrome heated egs column for which the

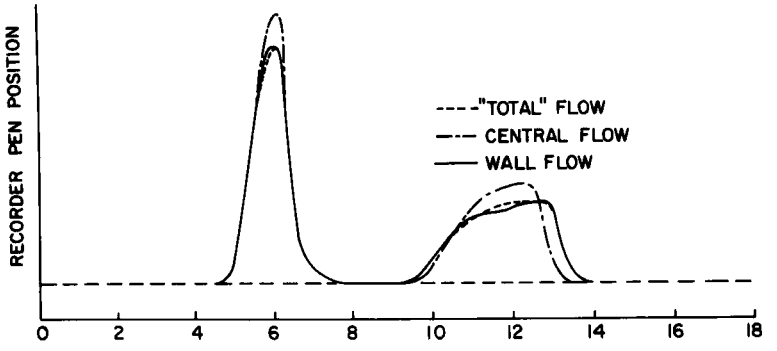

FIG. 10. Column exit concentration profiles, 22% egs column at 162°C, empty, 100λ C_{14}/C_{16} injection.

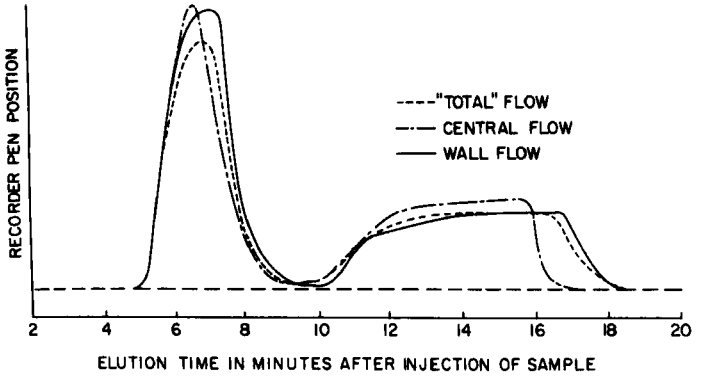

FIG. 11. Column exit concentration profiles, 22% egs column at 162°C; inlet cone 162°C, empty; 200λ C_{14}/C_{16} injection.

inlet cone was empty of column packing and run at the column temperature. Injections of 100, 300, and 500 μl were also made into the same column, in which the inlet cone was packed and maintained about 60°C above the column temperature as shown in Figs. 12, 13, and 14, respectively. All sample injections were made in a rapid manner. First of all, a lack of solute profiling was shown in each case as the first peak of the binary sample began to elute. Only slight concentration profiles appeared at the end of the second peak for both 100-μl injections mentioned above. Significant concentra-

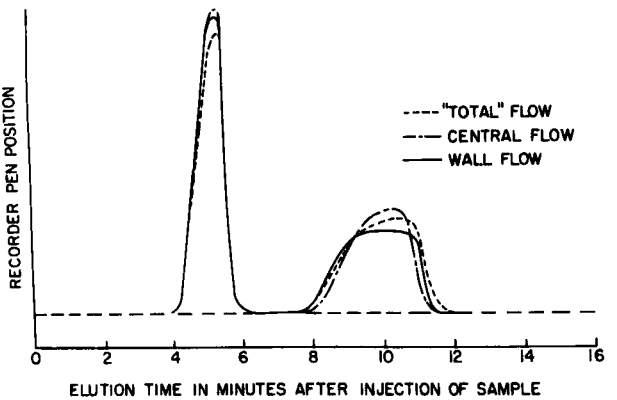

FIG. 12. Column exit concentration profiles, 22% egs column at 164°C; inlet cone 230°C, packed; 100λ C_{14}/C_{16} injection.

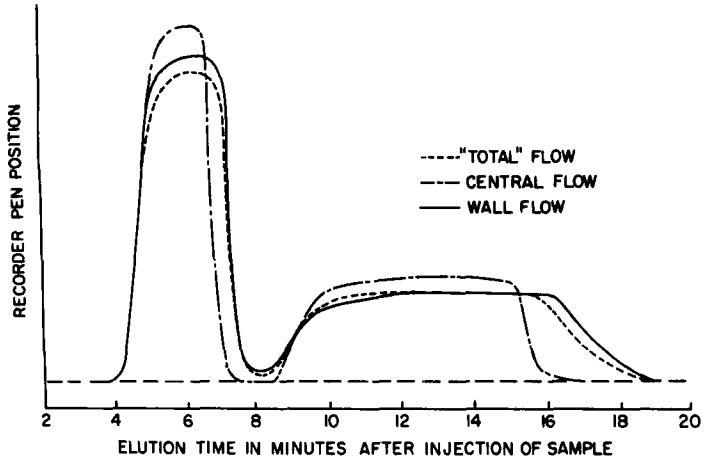

FIG. 13. Column exit concentration profiles, 22% egs column at 164°C; inlet cone 230°C, packed; 300λ C_{14}/C_{16} injection.

tion profiling existed for all other samples at the end of the first peaks and the beginning and end of the second peaks, as shown in Figs. 11, 13, and 14. Figures 13 and 14 show that a better sample resolution occurred in the central bed than in the near-wall position when the inlet cone was maintained above the column temperature. Band spreading in both the central and near-wall bed positions appeared to limit the maximum separable sample size when the inlet cone was maintained at the column temperature.

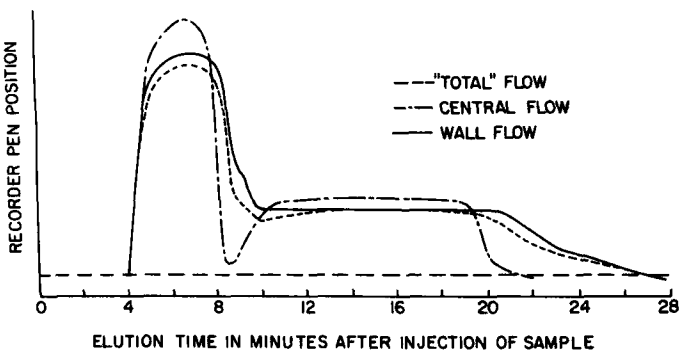

FIG. 14. Column exit concentration profiles, 22% egs column at 164°C; inlet cone 230°C, packed; 500λ C_{14}/C_{16} injection.

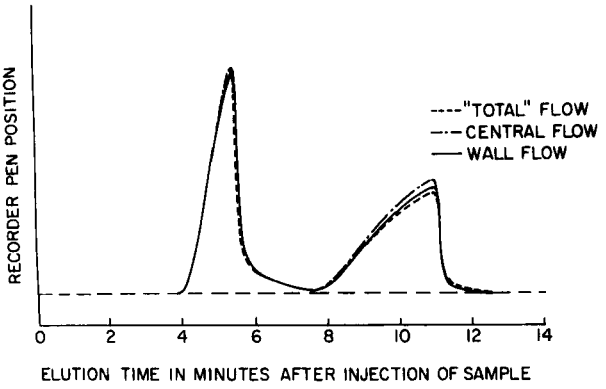

FIG. 15. Column exit concentration profiles, 20% egs oven column at 160°C; inlet cone 160°C, empty; 200λ C_{14}/C_{16} injection.

Elution profiles have also been investigated for oven-heated columns. The maximum separable sample size (Fig. 15) appeared to be limited by band spreading for an egs oven column in which the inlet cone was unpacked and operated at the column temperature. Figure 16 illustrates the maximum separable sample size, injected in a rotary sprayed manner, in the egs oven column with a packed inlet cone operated 60°C above the column temperature in which essentially no solute profiling or resolution differences occurred across the column bed.

Figures 17 through 22 illustrate the results of exit concentration

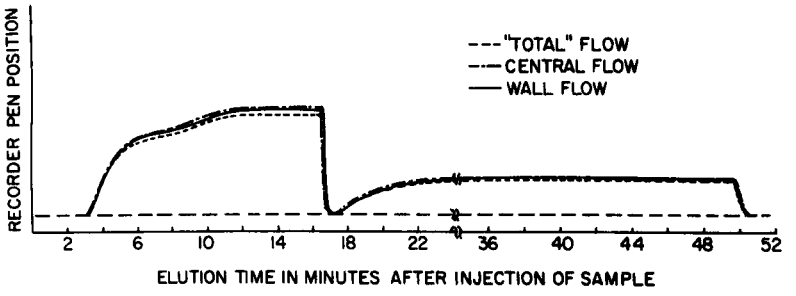

FIG. 16. Column exit concentration profiles, 20% egs oven column at 160°C; inlet cone 220°C, packed; 4000λ C_{14}/C_{16} injection; slow, rotary injection in 55 sec.

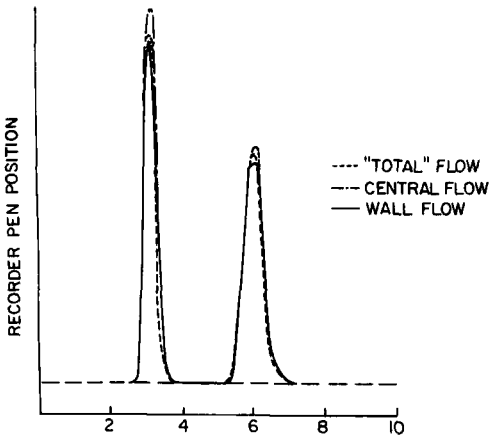

FIG. 17. Column exit concentration profiles 17% SE30 oven column at 215°C; inlet cone 215°C, empty; 50λ C_{14}/C_{16} injection.

profile studies done in SE30 oven columns. Figures 17 and 18 illustrate that when the inlet cone was unpacked and operated at the column temperature, there was very little difference noted in the wall and central bed solute concentration for small sample sizes and that the maximum separable sample size appeared to be

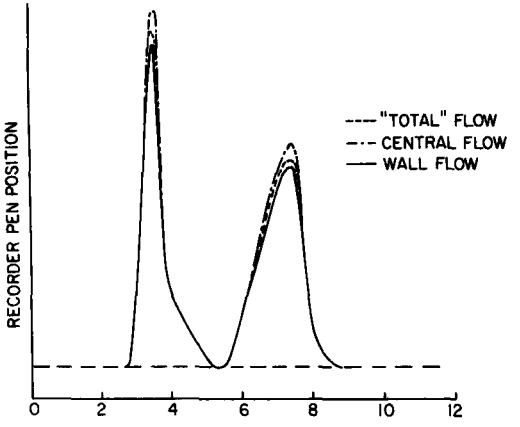

FIG. 18. Column exit concentration profiles 17% SE30 oven column at 215°C; inlet cone 215°C, empty; 500λ C_{14}/C_{16} injection.

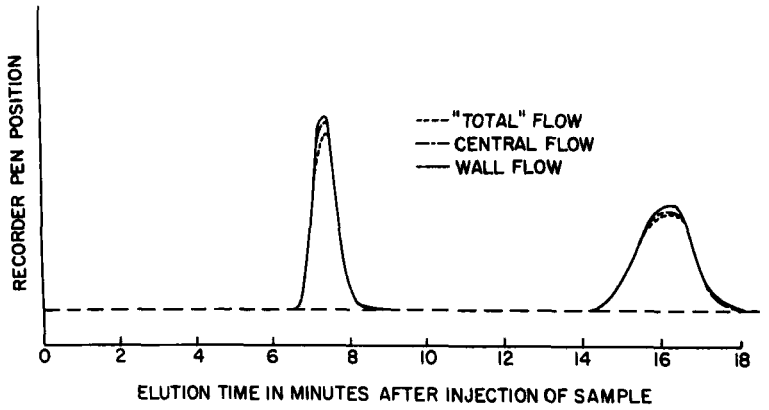

FIG. 19. Column exit concentration profiles 17% SE30 oven column at 190°C; inlet cone 270°C, packed; 50λ C_{14}/C_{16} injection.

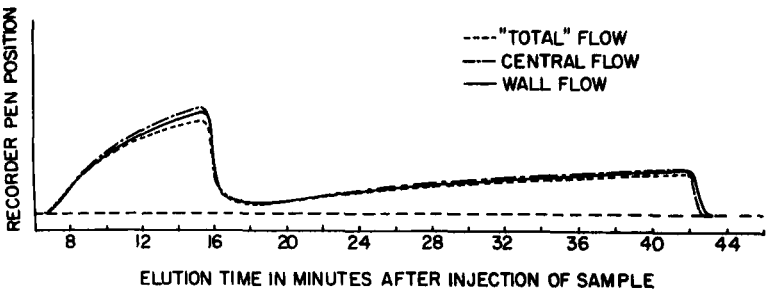

FIG. 20. Column exit concentration profiles 17% SE30 oven column at 190°C; inlet cone 285°C; 5000λ C_{14}/C_{16} injection; normal, fast injection.

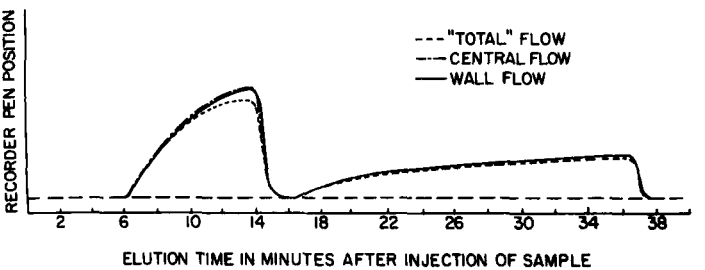

FIG. 21. Column exit concentration profiles 17% SE30 oven column at 190°C; inlet cone 285°C, packed; 5000λ C_{14}/C_{16} injection; slow, rotary injection in 45 sec.

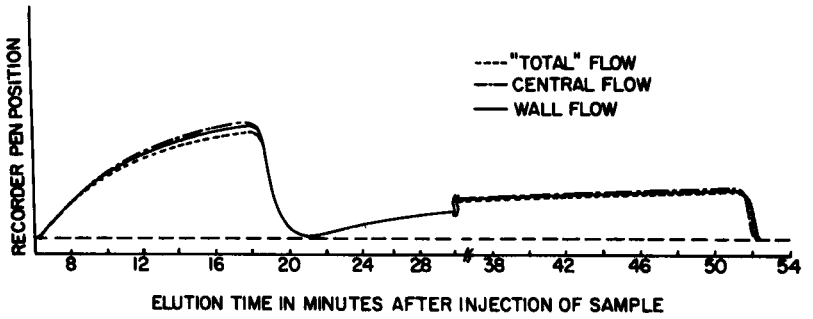

FIG. 22. Column exit concentration profiles 17% SE30 oven column at 190°C; inlet cone 270°C, packed; 7000λ C_{14}/C_{16} injection.

limited by solute-band spreading. Next, a series of injections were made in which the inlet cone was filled with column packing and heated above the column temperature. Essentially no solute-concentration-profile differences could be detected at the wall and central bed positions, as shown in Fig. 19. Figures 20 and 21 illustrate that a better sample resolution resulted when the sample (5.0 ml) was injected in a slow rotary manner (Fig. 21) rather than in a rapid manner (Fig. 20). In comparison to the sample in Fig. 20, which did not show complete separation, the sample in Fig. 21 was completely resolved and had a faster elution rate. Only a slight solute concentration profile existed at end of the second peak for the sample in Fig. 20. The sample injected in a slow, rotary manner in Fig. 21 exhibited even less solute profiling. The maximum separable sample size for the SE30 column at these operating conditions is illustrated in Fig. 22. Again, only a negligible amount of solute profiling occurred under these conditions.

Several observations can be made from the solute-concentration-profile measurements. First, the noted lack of concentration profiling evident in the initial elution of the first component of all binary samples and the lack of profiling for the entire first and second peaks for nonoverloading samples indicates that carrier gas velocity differences across the column bed and unequal stationary-phase distribution effects may not be significant factors in determining concentration profiling or extreme losses of sample resolution for the 1-in. I.D. × 3-ft-long columns used here. The results were the same for a column having either a packed or unpacked inlet cone operated either at or above the column temperature. Samples as low

as 16 μl of the C-14/C-16 methyl ester mixture also indicated that sample profiling was insignificant and that HETP values were essentially identical in the central and near-wall bed positions. In addition, thermistor beads have been used at the inlet of the sample tubes of the sample profile detector in the central and near-wall bed positions to accurately signal the arrival of nonoverloading and overloading solute bands at the individual bed positions. This was done to verify that the relative elution times of the several elution streams in the thermal conductivity detector were correct. For the small samples, the central bed sample arrival time was about ½ sec later than in the near-wall bed position. Compared to the normal sample elution times utilized in gas chromatography ranging upward from several minutes, a difference in sample elution time across the column bed of up to several seconds is insignificant. The noted lack of sample profiling for relatively slowly eluting samples in these 1-in. I.D. columns may be due to sufficient radial diffusion, which would tend to produce uniform sample bands across the column bed.

Nonabsorbing Sample Concentration Studies

The elution of a nonabsorbing sample injection of nitrogen into a helium carrier gas stream was indicated by thermistors at the exit of a column. The samples of nitrogen were injected as rapidly as possible directly into the vaporizer block in a manner analogous to absorbing sample injections. The sample concentration profiles which were observed did not appear to vary significantly with the various operating conditions (e.g., when the column was run with

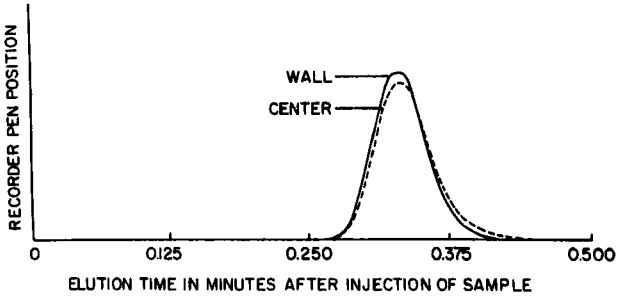

FIG. 23. Velocity profile measurements for the wall and column axis; 5 ml N_2 injection into He carrier gas; egs column at 156°C, inlet cone 224°C, packed.

an empty versus a packed inlet cone). An example of the concentration profiles obtained in the central and near-wall bed positions is shown in Fig. 23. For the 3-ft column in question, the nitrogen began to elute in the central and near-wall beds in essentially the same time. The first nitrogen molecules eluting from the column bed had an apparent average velocity within the column system of about 10.9 ft/min. The maximum nitrogen concentration in the central and near-wall bed positions occurred at essentially the same time. The apparent average velocity of the nitrogen molecules eluting at the peak maxima was 9.12 ft/min. A difference in the apparent average nitrogen molecule velocity at the two bed positions occurred at the end of the nitrogen band, with the near-wall nitrogen molecules having an apparent average velocity of 7.16 ft/min compared to a 6.62 ft/min average velocity for the central bed molecules. The near-wall nitrogen molecules therefore eluted on the average about 8% faster than the central bed molecules for the latter portion of the peak. In extreme cases, other nitrogen-injection-data runs have shown up to a 4% faster near-wall nitrogen elution for the initial portion of the band and up to a 13% faster near-wall nitrogen elution in the latter portion of the band compared with the central bed nitrogen-elution rate. Nitrogen peak maxima for both bed positions were found to occur simultaneously.

It must be noted here that one should be cautious of crediting the apparent average velocity differences at the wall and central bed positions as arising entirely within the column bed and thereby referring to these apparent velocity profiles as carrier gas velocity profiles. True carrier gas velocity profiles arising because of imperfections in the column bed should produce results in which the wall and central bed peaks are essentially identical in shape and in which the central bed peak should be displaced everywhere equidistant from the peak eluting at the column wall. However, radial sample diffusion across the column bed is expected to occur and correct, to some degree, the concentration profiles produced by the carrier gas velocity profile. The data discussed above illustrate that the latter portion of the peak exhibits tailing tendencies which are probably not produced within the column bed but which may be the result of inefficient sample injection and/or sample tailing produced upon elution from the vaporizer cavity and passage through the inlet cone. The elution profiles have been found to be generally quite similar, except for peak tailing.

Samples of ammonia vapor injected into the vaporizer block and detected by a piece of moist phenolphthalein-activated filter paper covering the exit end of the column bed also indicated that carrier gas flow is more rapid at the column wall. The ammonia vapor was detected first at the column wall as a pink annular ring. This annular ring then spread inward to the center of the column bed within about 2 to 3 sec.

Although the experimental work described above does not measure velocity profiles directly, the methods do have the advantage of being simple to conduct. Also, in a practical sense, the results which include superimposed carrier gas velocity profile and radial sample diffusion effects do permit some tentative conclusions as follows.

It should be noted at this point that if one were to estimate the shape of absorbing sample bands at the two bed positions studied on the basis of nonabsorbing sample concentration profiles, the conclusion would be that absorbing solute bands should elute more rapidly in the near-wall position for both the initial and final sections of the peak. This type of peak behavior has not been observed with nonoverloading, absorbing samples, as noted previously in the 3-ft columns studied. Peak elution characteristics for the nonoverloading absorbing samples were found to be nearly identical in the two bed positions. In some cases, for example, see Figs. 14 and 20, overloading, absorbing samples have shown exactly the opposite effect, in that the sample elution in the central bed is more rapid than in the near-wall bed positions at the end of the sample peaks. Apparently heat-transfer characteristics and solute equilibrium have pronounced effects on the eluting solute bands and differences in the solute elution rate brought about by carrier-gas-velocity variations across the 1-in. I.D. bed are of secondary importance for the system studied.

DISCUSSION

The experimental results for 1-in. I.D. × 3-ft preparative columns presented in this work may be summarized briefly as follows:

1. An uneven elution rate of a nonabsorbed sample has been noted across the column bed. Although radial sample diffusion tends to reduce the concentration profiling of such samples, elution-rate differences indicate that the carrier gas flow is somewhat faster near the column wall than in the central bed.

2. Radial and axial temperature gradients were noted in Nichrome and oven heated columns.

3. Both axial and radial temperature gradients were noticeably less in oven heated columns than for Nichrome heated columns.

4. A variation in the percentage by weight of solvent phase remaining on the solid support was found to exist in the axial direction in the inlet end of the columns that had been used in regular laboratory experiments.

5. Negligible radial solute concentration gradients were found at the end of the 3-ft columns for small sample injections in which peak distortion did not occur, in both Nichrome and oven heated columns for various operating conditions.

6. Significant solute concentration gradients and sample resolution differences across the column bed were found for overloading samples in Nichrome heated columns; however, small and essentially negligible radial solute concentration gradients and resolution differences across the column bed were found for overloading samples in oven heated columns at the best operating conditions.

7. The slow-sample-injection technique described herein appeared to produce solute bands of relatively uniform concentration over their axial length and to limit temperature fluctuations within the column, which resulted in better sample resolution.

It is not possible at this time to describe in detail the exact way that various factors such as axial and radial temperature gradients, axial stationary-phase concentration gradients, and varying concentration levels within the solute band may affect the elution process within the column. It has been found, however, that the manner of column heating and sample injection have a pronounced effect on the results obtained in these columns. The achievement of high sample production rates has been dependent on choosing proper operating conditions so that the full potential of the system is realized. It has been found that the sample elution characteristics of preparative scale samples under certain operating conditions show essentially no concentration profiling and that the sample resolution may be limited by the separational power of the column.

The present paper demonstrates that radial velocity profiles in carrier gas flow are among the less serious limitations in preparative scale work with 1-in. I.D. × 3-ft columns, so that other factors must be found to explain the limitations. The single underlying factor that appears to affect the preparative results shown here is not

sample profiling because of physical defects in the column bed, but sample resolution, which is a direct result of the separation factor and phase equilibrium attained for a given sample injection.

The good results of analytical scale gas chromatography are probably in large measure due to very large separational factors that exist at very low solute separations. The increase in solute concentration required for successful preparative gas chromatography is normally accompanied by a decrease in solute separation factors. The solute concentration must not be increased beyond the point where the resulting decrease in the separation factor prevents clean separation. Slow introduction and vaporization of the sample was beneficial probably because it permitted the introduction of large samples of solute without creating excessive solute concentrations within a narrow sample band. The large samples entered into the column as relatively long zones of low, but relatively uniform, axial concentration. Rapid injection and rapid vaporization gave poorer preparative results because the samples entered as relatively short zones having a high initial concentration. The absence of a bad effect on separation when a large sample is introduced as a relatively long slug is not too surprising in the light of the computations of Sumantri (*16*). Although his work dealt with only one component, and with a limited range of sample sizes and adsorption isotherms, the computations did indicate that the eluting sample bandwidth would be widened only slightly (6%) by a tenfold increase in sample introduction time.

The magnitude and character of the transient temperature changes found to exist in preparative gas chromatography were more pronounced than anticipated. These very sizeable transient temperature phenomena that occur as a solute band passes down a preparative column accentuate and complicate the changes in separation factors and phase equilibrium constants. Thus a better production rate is associated with the lesser temperature transient that occurs with slow sample introduction. Many similar correlations can be noted, but there are also various unexpected results.

The temperature and concentration effects just noted differentiate preparative scale from analytical scale chromatography. It is not unreasonable to think that even the same separational process (chromatography) operating at the opposite extremes of sample loading should exhibit some diffferences in design and operating requirements. A satisfactory understanding of all the complex

interrelations that determine the results of preparative gas chromatography will require experimental study of other major variables, including especially representative data on the variation of separation factors with solute concentration and with temperature. When this is available, empirical and subjective designs and procedures will give way to a realistic model, and computations will lead to the desired objective understanding of optimum designs and procedures.

Acknowledgment

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