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Supercritical Fluid (Dense Gas) Chromatography/Extraction with Linear Density Programming

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ABSTRACT

The versatility of dense gases or supercritical fluids as solvents is briefly reviewed. It is pointed out that gas density is the key parameter controlling solvent power and it is argued that density programming should replace pressure programming for chromatographic and extractive separations. Our previous theory of dense gas solubility and solubility thresholds is then used to explain why relatively high pressures are desirable for dense gas separations. The theory is also used to examine peak spacing for linear density programs to develop a special density program for uniform peak spacing.

An experimental linear density programming system utilizing CO_2 at 40°C and at pressures up to 300 atmospheres is described and factors affecting separation efficiency are evaluated. A separation of four aromatic compounds is demonstrated using programmed density extraction alone. Chromatographic columns used with polystyrene oligomers and polynuclear aromatic compounds are shown to improve the separation. The spacing of oligomers is shown to be in qualitative accord with theory. Finally, factors to be considered in optimum programming are discussed.

INTRODUCTION

Gases, when compressed, acquire some of the solvent characteristics of liquids (1). Solvent power, as measured by the Hildebrand

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solubility parameter δ, increases in rough proportion to density ρ and approaches liquid solvent power when gases are compressed to liquid densities (1-5). Consequently, the gradual compression of a suitable gas in the presence of a group of nonvolatile solutes will, by virtue of increasing solvent power, force first one of the solutes, then another, into the dense gas solution. Programmed gas compression, therefore, can be utilized for chemical separations. This was first demonstrated in this laboratory by a stepwise extraction process in which CO_2 gas, at succeeding stages of pressure, caused first the solubility of squalane at 100 atm, then dinonyl phthalate at 400 atm, and finally SE-30 at a pressure of 1200 atm (1).

Dense gases constitute versatile solvents for both extraction and chromatography. Their advantage, relative to liquids, is that they generally possess a more rapid diffusional transport and a lower viscosity (features which facilitate the chromatographic process) and their solvent power is controllable over a wide range by changes in a simple mechanical parameter, pressure. Both assets can be used to advantage in programmed compression dense gas extraction and chromatography.

Programming is most effective when a continuous increase in pressure is used such that a wide range of increasingly recalcitrant species are forced one by one into the mobile phase. This technique was first employed by Jentoft and Gouw (6,7), and later by Bartmann and Schneider (8,9) and Nieman and Rogers (10). These authors used linear pressure programs in which pressure rose in proportion to elasped time.

Our studies have shown that gas density, not pressure, is the fundamental parameter controlling solubility (1-3). The solubility parameter δ, as we have mentioned, is approximately proportional to density ρ, but it varies strongly and in a complicated manner with pressure p. The rate of change of δ with respect to p, $d\delta/dp$, is very large at low pressures and becomes very small at higher pressures. This is illustrated in Figure 1 which shows the

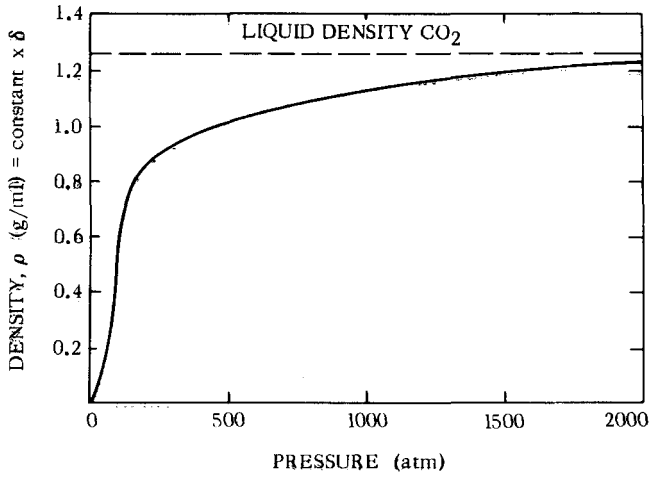

FIGURE 1. Density (and solubility parameter δ) versus pressure for carbon dioxide at 40°C.

variation of ρ (proportional to δ) with pressure for CO_2 at a temperature (40°C) only slightly higher than the critical temperature of CO_2 (31°C). It is thus expected that peak spacing and resolution over a wide density or pressure range will be less regular and less predictable with linear pressure programming than with linear density programming. This matter has been discussed by Nieman and Rogers (10). The detailed effect of linear density programs on peak spacing will be discussed in the theoretical section.

In this paper we have utilized CO_2 gas at pressures up to 330 atmospheres for the linear density programming. While this maximum is considerably below the 2000 atm we have used in nonprogrammed work, it is considerably above the critical pressure of CO_2 (75.3 atm). Our work suggests that a range of pressures and densities at least this high is necessary for the versatile handling of strongly interacting solutes of an intermediate molecular weight (200-1000) and for polymers of high molecular weight. While a cursory inspection of Figure 1 shows that about half of the liquid density is achieved at 100 atm, we note that innumerable species require den-

sities very close to liquid densities to become soluble in the dense gas. Such densities require pressures much higher than 100 atm, as Figure 1 clearly illustrates. The theoretical basis of the need for such high densities will be presented in the theory section.

All of the results reported here were obtained with CO_2 at 40°C. The 40°C temperature corresponds to a reduced temperature T_r (temperature/critical temperature) of 1.03. The value $T_r = 1.03$ is, in our experience, a useful compromise. Lower values lead to large and sometimes erratic changes with minor temperature fluctuations and higher values require higher pressures to reach the desired gas densities.

Carbon dioxide was chosen because it has a convenient critical temperature (31°C), a high liquid density solubility parameter of $\delta_{liq} = 11.0$, no UV absorption, and a wealth of data applying to it from our previous studies.

THEORY

Our previous studies have shown that the solubilities in dense gases of solutes of intermediate and high molecular weight increase abruptly with increasing pressure and density. Consequently, there is a rather distinct level of compression at which the solubility first becomes observable. This level is designated by the threshold pressure p^* or the threshold density ρ^*. More fundamentally, there is a unique threshold level δ^* of the solubility parameter δ for each solute, and p^* and ρ^* simply represent the compression levels necessary to reach δ^*.

Giddings, Myers, and King have derived an equation for δ^*/δ_o, the threshold solubility parameter relative to the solute solubility parameter (2). The proportionality between solubility parameter and density makes it possible to equate the ratio δ^*/δ_o to $\rho^*/\rho_{\delta o}$, the threshold density relative to the density of the gas at the point where its solubility parameter equals that of the solute.

With this substitution and other minor changes, their Equation 7 becomes

$$\frac{\rho^*}{\rho_{\delta o}} = 1 - \left[\left(\frac{RT\ \rho_o}{M^*\ \delta_o^2}\right) \ln\ K^*\right]^{\frac{1}{2}} \tag{1}$$

where R is the gas constant, T the absolute temperature, M* the threshold molecular weight of solute (that molecular weight barely soluble at a detectable level at density ρ^*), ρ_o the solute density and K* the threshold value of the distribution coefficient between phases. In the cited paper the value $K^* \sim 8 \times 10^6$ was suggested on the basis of experimental evidence. We round off ln (K*) to 16. Inserted in the equation, this value yields

$$\frac{\rho^*}{\rho_{\delta_o}} = 1 - \frac{4}{\delta_o}\left(\frac{RT\ \rho_o}{M^*}\right)^{\frac{1}{2}} \tag{2}$$

Solving for M*, we obtain

$$M^* = \frac{16RT\rho_o}{\delta_o^2} \frac{\rho_{\delta o}^2}{(\rho_{\delta o} - \rho^*)^2} \tag{3}$$

Equation 3 approximates the upper molecular weight value that can be detected at density ρ^*. The equation shows that M* falls off very rapidly as density ρ^* drops below ρ_{δ_o}. Thus a doubling of $(\rho_{\delta o} - \rho^*)$ from 0.1 to 0.2 g/mL, which represents a change in ρ^* of only 0.1 g/mL, cuts the workable molecular weight range M* by a factor of 4. If ρ_o and thus $\rho_{\delta o}$ are fairly high, corresponding to moderately polar or otherwise strongly interacting solutes, very high pressures may be needed to reach the ρ^* corresponding to the molecular weight range desired.

Equation 2 can also be used to investigate the spacing between peaks (as in a homologous series) as density increases in a linear fashion with time. Thus, we obtain from Equation 2 the following derivative

$$\frac{d\rho^*}{dM^*} = \frac{2\ \rho_{\delta_o}(RT\rho_o)^{1/2}}{\delta_o\ M^{*3/2}} \tag{4}$$

which shows that the increment in density (and time) between successive peaks with a fixed increment in molecular weight gradually decreases as $1/M^{*3/2}$. This result is in accord with expectations since the density or time increment must become zero as ρ^* approaches ρ_{δ_o}, the density at which, theoretically, solutes of infinite molecular weight become soluble.

While peak spacing with linear density programs are not expected to be uniform, it will be more regular than with linear pressure programs where peak spacing depends on T_r through a complicated equation-of-state effect. However, we note that in the concave down portion of Figure 1 the decreasing density increments per unit time in a linear pressure program partially compensate for the decreasing peak spacing expected in a linear density program. Thus, the linear pressure program may not be as bad as expected based on the highly variable slope of Figure 1. However, theoretical analysis of the problem is complicated by the necessity of using a realistic equation of state and will not be attempted here.

We should point out that if we want to achieve uniform peak spacing we must have

$$\frac{dM^*}{dt} = \frac{dM^*}{d\rho^*} = \frac{d\rho^*}{dt} = \text{constant} \tag{5}$$

which will serve to specify the necessary $d\rho^*/dt$ values and, by integration, the kind of density program $\rho^*(t)$ necessary for uniform peak spacing. If we use Equation 4 to obtain $dM^*/d\rho^*$ (substituting for M^* given by Equation 3 in Equation 4), we find the necessary program to be of the form

$$\rho^* = \rho_{\delta_o} - 1\Bigg/\left[\frac{(dM^*/dt)\delta_o^{\,2}t}{16\ RT\ \rho_o\rho_{\delta_o}^{\,2}} + c\right]^{1/2} \tag{6}$$

where c is a constant of integration. If we wish to start the program such that $\rho^* = 0$ at time $t = 0$, c becomes $1/\rho_{\delta o}^2$.

The above theoretical conclusions rest on the validity of Equation 1, admittedly an approximation. Reasonable agreement between Equation 1 and experimental threshold data has been demonstrated (2). In the light of more recent and still unpublished results from our laboratory, however, it is clear that the equation is valid only for liquids or for solids with a melting point not substantially higher than the operating temperature. To reach this condition for high melting point solids, increased experimental temperatures and carrier gases with correspondingly large critical temperatures should be chosen. Failure to do this leads to a considerably depressed--often unobservable--solubility.

EXPERIMENTAL

Apparatus

A diagram of the linear density programming apparatus is shown in Figure 2. The pressure source consisted of an Aminco #46-14021 (Silver Springs, Md.) air operated 2-stage 2000 atm gas compressor and a 1 liter pressure reaction vessel (Aminco #46-16875) used as a ballast tank. The pressure of the source was controlled by a solid state relay circuit coupled to an Aminco #14164 3000 atm pressure gauge. System plumbing included 0.101 cm and 0.05 cm I.D. and 0.317 cm O.D. 316 stainless steel tubing connected by type HF2 fittings and valves from High Pressure Equipment Co. (Erie, Pennsylvania). The compressor, ballast tank, and connecting tubing were shielded by a 0.635 cm thick steel plate box heated to 40 ± 1^0C. Gas held at 420 atm in the ballast tank was fed to a Consolidated Controls (Bethel, Conn.) Series #1B high pressure regulator. Linear gas density programming was accomplished by driving the pressure regulator with an electronically controlled variable speed motor (G.K. Heller, Floral Park, N.Y., T2-100). The rotation rate was regulated

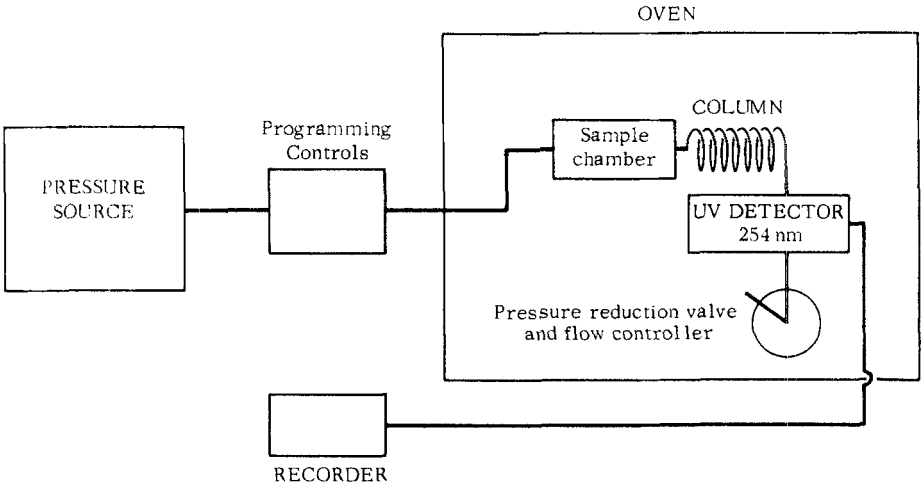

FIGURE 2. Schematic diagram of the linear density programming dense gas chromatograph.

by a cam cut to give the necessary pressure change to yield a linear increase in density. (A detailed description of this device is given in Reference 12). The outlet flow from this regulator was filtered through a meter-long charcoal column before entering the chromatograph oven. A Heise (Newtown, Conn.) CM-3012 pressure gauge was used to monitor pressure.

The oven was a 30 cm square galvanized steel box insulated with 2.54 cm of fiber glass. Temperature was maintained to 40 $\pm$ 0.5°C. Dense gas was fed to the sample cell, then through the chromatographic column to the detector, and finally reduced to atmospheric pressure by a pressure reduction valve. The sample was deposited from solution onto glass wool inside a 1.58 mm O.D., 1.01 mm I.D. tube which was inserted into a high pressure tee fitting placed in the system such that dense gas could be forced through the tube and subsequently led to the column (12).

The high pressure UV detector system is described elsewhere (12). Gas from the detector cell was reduced to atmospheric pres-

sure by a pressure reduction valve (12). The outlet flow was controlled by an electronic thermistor feedback circuit controlling the pressure reduction valve. Output of the detector was recorded on a Varian (Palo Alto, Calif.) G-200 strip chart recorder.

Materials

The gas used in this study was U.S. Welding C.P. grade carbon dioxide. Column packing materials were GC-Durapak (Carbowax 400 bonded to Porasil C, 37-75 micron, Waters Associates, Milford, MA) and Chromasorbs P and W (both from Johns-Manville, Denver, Co). All columns were constructed using 0.635 cm O.D. and 0.203 cm I.D. 316 stainless steel tubing packed by standard dry column techniques. Benzene, chloroform, toluene, pentadecylphenol, eicosanoic acid, naphthalene, 1,3,5-triphenylbenzene, anthracene, 9,10-diphenylanthracene, 2,3-benzanthracene, hexaphenylbenzene and pentacene were obtained from Aldrich Chemical Company (Milwaukee, Wisconsin). The 600, 900, and 2100 molecular weight polystyrenes were obtained from Pressure Chemical Company (Pittsburgh, Pennsylvania); phenanthrene was obtained from Matheson, Coleman and Bell (Norwood, Ohio); diethylstilbestrol dipalmitate was obtained from Alfred Bader Chemical Company (Milwaukee, Wisconsin); phenylstearate was obtained from Eastman Organic Chemicals (Rochester, New York); and Antioxidant #330 was obtained from Ethyl Corporation (Orangeburg, South Carolina).

Procedure

The sample material was dissolved in toluene or benzene to a concentration of 20 mg/mL. Approximately 40 to 50 µL of the solution was placed on the substrate in the sample tube and the tube inserted into the chromatographic system. The system was pressurized to 272 atm and the flow rate at the pressure reduction valve was set at 60 mL/min.

When the injection system had come to equilibrium ~15 min after pressurization, the linear density program was started. The pres-

sure was allowed to increase from 27.2 to approximately 300 atm in such a way that the density rose at a rate of 0.005 or 0.01 g/mL-min, from 0.047 g/mL to 0.9 g/mL.

RESULTS AND DISCUSSION

In a linear density programmed chromatograph two mechanisms of separation are present: a continuous "solvent extraction" in the sample cell and differential retention in the chromatographic column. In order to maximize efficiency, the rate of density change must be optimized with respect to the extraction process in the injection cell, flow rate, and column length. If the density is increased too rapidly, the process will not take proper advantage of density programming as components will be extracted and migrated too close together. Similarly, if column length is too great or flow too slow, differential migration between components will be diminished by late elution and pressures exceeding optimum levels.

Once the threshold density of a component is reached, it is advantageous if that component is extracted quickly and completely so that it can be totally removed from subsequent components. To that end, glass wool, Chromosorb P, and Chromosorb W were tested to determine which material was most suitable for use as a solid support on which to deposit the sample solutions. Each of these materials was placed in the sample cell, variable quantities of an anthracene-chloroform solution placed on them, and the cell inserted into the system. The sample was run without a chromatographic column to determine the effectiveness of extraction. A heavy loading produced a broad peak highly skewed toward the front edge with an abrupt tail. Optimum loading was 50 μL or less of the sample solution which presumably formed a thin coating leading to rapid extraction. This study also showed that glass wool and Chromosorb W allowed higher levels of sample loading than Chromosorb P before excess skewing occurred. Glass wool was finally chosen for use because it was easily handled in the sample cell.

The thickness of the deposited sample is, of course, especially critical when considering solute mixtures instead of single components. When the threshold density is reached for a component, that compound will begin to dissolve leaving insoluble components behind in the surface layer of the deposit. The soluble molecules in the inner layers must diffuse out, a slow process which can broaden the zone. As an extreme case of this, we found that a mixture of hexaphenylbenzene (an insoluble component) and anthracene in toluene failed to yield any observable peak even though anthracene is very soluble in carbon dioxide. The absence of a peak persisted with repeated injections regardless of gas density or sample concentration. In other cases where two soluble species are present which dissolve at different densities, the two may elute together if the coating is too thick. In all cases the sample loading should be minimal to reduce zone broadening and component overlap.

The threshold pressure and density of a number of components were determined by running the individual compounds listed in Table 1 without a chromatographic column. The threshold density was calculated from the point on the chromatogram where the component was first detected.

Several mixtures of the compounds shown in Table 1 were run to determine the minimal density difference necessary for separation without a column. Two programmed density rates were tested; the pertinent data are listed in Table 2. Comparison of results for the two program rates indicates that the slower rate yields slightly better resolution than the faster rate. Specifically, to obtain unit resolution by extraction alone, a threshold density difference $\Delta\rho^*$ of 0.15 g/mL is needed at a program rate of 0.01 g/mL-min while a 0.01 g/mL difference is required for the 0.005 g/mL-min program. Figure 3 illustrates the $\Delta\rho^*$ requirement by showing the separation of four components each having a $\Delta\rho^*$ of at least 0.1 g/mL with respect to its neighbors. We emphasize that this separation is obtained by extraction alone, without the benefit of a chromatographic column. It is very likely that further studies of injection cell

TABLE 1

Threshold Densities and Pressures for Various Compounds in CO_2 at 40°C

Compound	Molecular Weight	Threshold Density g/cc	Threshold Pressure atm
Benzene	78	0	0
Phenyl Stearate	360	0.015	7
Pentadecylphenol	304	0.035	17
Eicosanoic Acid	312	0.084	41
Naphthalene	128	0.100	46
Phenanthrene	178	0.120	49
1,3,5-Triphenylbenzene	306	0.175	64
Anthracene	178	0.251	76
Antioxidant #330	774	0.300	81
9,10-Diphenylanthracene	330	0.310	82
2,3 -Benzanthracene	228	0.495	89
Pentacene	278	0.900	270
Polystyrene 600	600	0.236	73
Polystyrene 900	900	0.350	83
Polystyrene 2100	2100	0.640	100
Diethylstilbestrol Dipalmitate	774	0.290	80

TABLE 2

Programmed Flow Rates used for Mixtures Separated by Extraction

Rate of Density Gain	Outlet Flow Rate (1 atm)	$\Delta\rho^*$ of Solutes for Unit Resolution
0.01 g/mL-min	69 cc/min	0.15 g/mL
0.005 g/mL-min	36 cc/min	0.10 g/mL

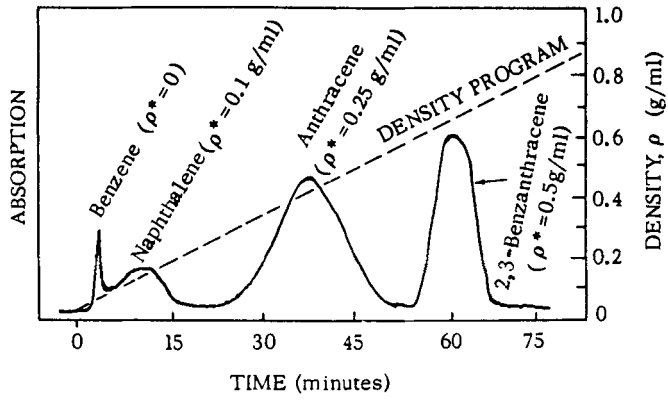

FIGURE 3. Separation of aromatic compounds by continuous extraction using linear density programming at a rate of 0.01 g/mL-min.

design and sample deposition would lead to reduced $\Delta\rho^*$ values and increased programming rates such that very rapid separations would result perhaps bettering chromatography in speed for simple separations involving intermediate or high molecular weight components.

Extraction studies were also done with several polystyrene polymers whose threshold density values are listed in Table 1. When the 600 and 900 nominal molecular weight polymers were mixed together, a broad peak similar to that for 600 molecular weight polystyrene alone was obtained. When 600 and 2100 molecular weight polystyrenes were mixed, one broad peak resulted with no apparent separation. Since these polymers contain the same oligomers but in differing concentration ratios, no overall separation of the samples was expected. Furthermore, the threshold densities of the oligomers are too similar to be differentiated by density programming alone. For oligomer resolution, a chromatographic column is required.

In the next phase of the study Carbowax 400/Porasil C was used in two columns 20 cm and 100 cm long. The outlet flow rates, chosen as those leading to satisfactory resolution with the 600 molecular weight polystyrene, were 34 mL/min for the 20 cm column and 69 mL/

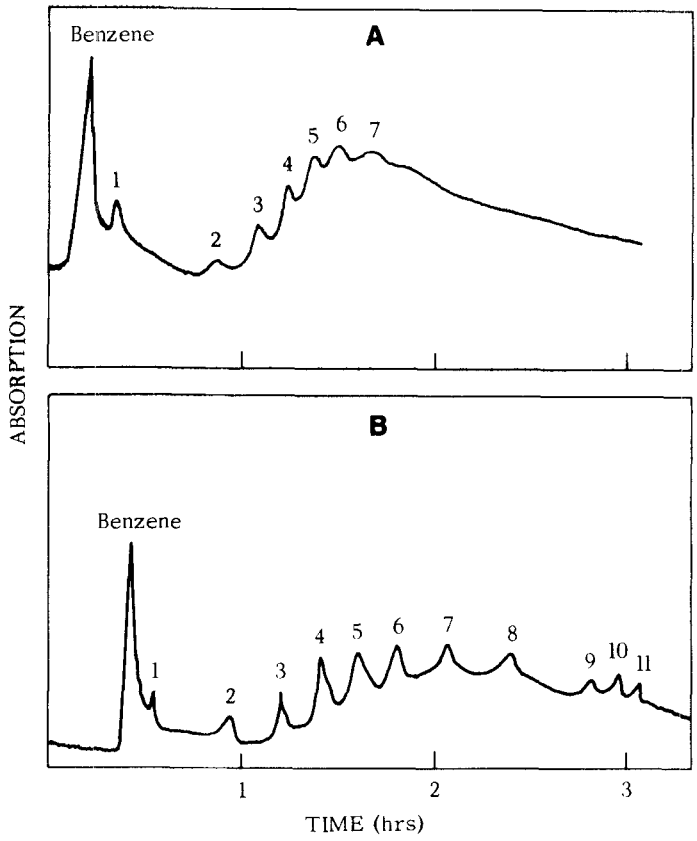

FIGURE 4. Separation of 600 MW polystyrene oligomers with linear density programming using Carbowax 400 columns 20 cm long (A) and 100 cm long (B).

min for the 100 cm column. Figures 4A and 4B show the separation of 600 molecular weight polystyrene oligomers on the two columns using a programmed density rate of 0.01 g/mL-min. Clearly the chromatographic columns lead to the resolution of oligomers whereas extraction alone is unable to provide separation. We note that a more complete resolution of oligomers has been obtained using supercritical n-pentane at high temperatures with pressure programming (12).

Figures 4A and 4B confirm the prediction made in the theory section that peak spacing will decrease with elapsed time when using linear density programming. Unfortunately, a quantitative test of the theory is not possible because of the unknown delay (retention) time added to each oligomer's threshold extraction time by the column. Ideally, the theory should be tested in a pure extraction experiment but, as we have noted, oligomer resolution was not possible in our system without a column.

Finally, Figure 5 (compared to Figure 3) shows that the resolution of polynuclear aromatics can be enhanced by using a chromato-

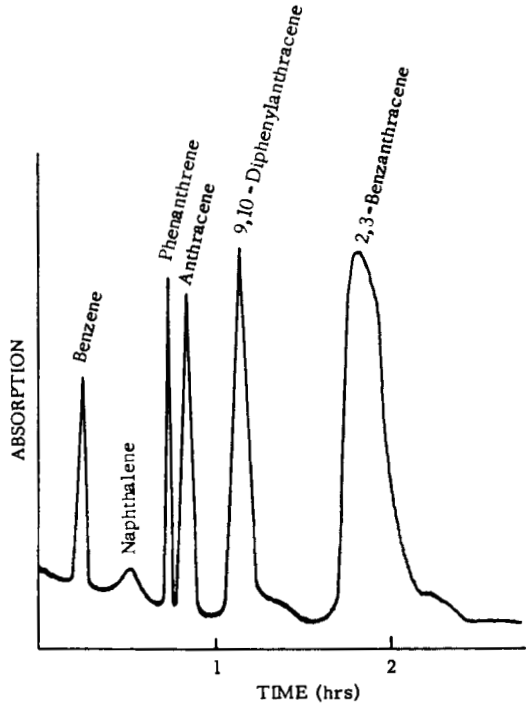

FIGURE 5. Separation of polynuclear aromatics on the 100 cm Carbowax 400 column using a density program rate of 0.01 g/mL-min.

graphic column in conjunction with the differential extraction process.

CONCLUSIONS

This study shows that the search for optimal programming is a rather complicated matter in programmed compression dense gas chromatography. The programming of compression is unlike the programming of temperature in programmed temperature chromatography where the simplest program (linear) leads to rather even peak spacing within a homologous series. In the programmed compression case the most common approach--linear pressure programming--fails even to deal with the principal parameter (density) governing peak migration. Linear density programming, as employed here, deals directly with the principal parameter of migration, but whether it does so optimally is open to question. We have shown both experimentally and theoretically that peak spacing is not uniform with linear density programs but probably can be made to approach uniformity by the special density program of Equation 6. However, uniform spacing may not always be optimal: it may be worthwhile in some cases to submerge detail for higher molecular weight components in order to speed the separation toward completion.

Clearly, optimum programming depends upon the needs and objectives of experimental work. We have provided here a theoretical approach for converting those needs into the appropriate density based program. Furthermore, we have demonstrated the experimental feasibility of one such density program (linear) and have shown experimentally how density based programming can be approached. With the present growth of interest in dense gases for various extractive and chromatographic separations, density based programming should assume prominence as the best means to exploit the variable solvent power of these versatile solvents.

CREDIT

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