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High-Pressure Gas Chromatography and Chromatography with Supercritical Fluids. III. Fluid-Liquid Chromatography

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Summary

High-boiling substances can be separated by partition chromatography, using *n*-pentane and isopropanol under supercritical conditions as mobile carriers. At moderate temperatures (200–250°C) the volatility of heavy substances may be enhanced by a factor of as much as 10^4 by increasing the pressure from atmospheric to about 50 kg/cm^2. This enables the analysis of compounds which are too heavy for ordinary gas chromatography.

As predicted before on the basis of gas-chromatographic studies at elevated pressures, the use of supercritical mobile fluids in combination with liquid stationary phases results in an attractive separation procedure. This technique is rapid and has a high degree of flexibility. Separations according to boiling point as well as molecular type are possible.

The main features of the new chromatographic technique, for which the designation "fluid-liquid chromatography" (FLC) is proposed, are illustrated by means of several examples.

The first article of this series (*1*) described the effect of pressure on partition coefficients in gas-liquid chromatography. Using carbon dioxide as a carrier gas, we demonstrated that an increase in working pressure leads to an apparent increase of solute volatility. This phenomenon proved to be mainly caused by molecular interactions in the nonideal gas phase.

The experiments indicated that at pressures well above the critical point it might be possible to analyze compounds which are too heavy for ordinary gas chromatography. However, in our work with carbon dioxide as a carrier gas, this deduction could not be verified owing to limitations of the apparatus used.

The use of supercritical fluids as mobile carriers in chromatography seems particularly interesting as our study on the efficiency of packed columns [described in the second report of this series (2)] showed that, when properly adapted, columns operated with high-pressure gases can be nearly as efficient as normal gas-chromatographic columns. As regards separating efficiency and speed, it is anticipated that a chromatographic technique employing high-pressure gases as mobile carriers will be potentially superior to liquid chromatography.

The predictions made in the above-mentioned studies have been confirmed by the investigation covered in this article. In this work we have used mobile carriers other than carbon dioxide, which, having lower critical pressures, simplified operation under supercritical conditions.

SUPERCRITICAL MOBILE FLUIDS IN PARTITION CHROMATOGRAPHY

Whereas the use of liquids and gases as mobile carriers in partition chromatography is quite common, the behavior of supercritical fluids* under such conditions is relatively unknown. The only instance of a supercritical fluid being employed in combination with a liquid stationary phase is in a short communication by Klesper et al. (3). These authors described some experiments of an exploratory nature which, although showing that a relatively involatile substance can have a certain mobility with a supercritical carrier fluid, do not make it clear what advantage attaches to the use of such a fluid (in comparison with, e.g., liquids) that could justify the considerable experimental inconvenience inherent in their techniques. The few experiments described also fail to afford a clear insight into the effects of different operational parameters and provide little guidance as to the choice of optimum conditions.

Our efforts have therefore been primarily directed toward a better understanding of the specific features of supercritical fluids as mobile carriers in chromatography. For the sake of brevity, we shall refer to this form of chromatography as "fluid chromatography," in contrast to "gas chromatography" and "liquid chromatography." When fluid chromatography is carried out with a liquid

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* By this designation we refer to fluids at temperatures and pressures in the neighborhood of the critical point.

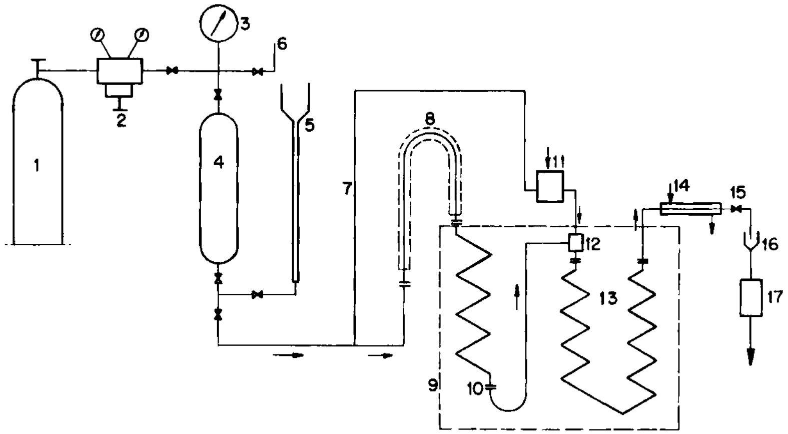

FIG. 1. Flow diagram of apparatus (the figures are explained in the text).

stationary phase (as in the present work) the technique may be called "fluid-liquid chromatography," abbreviated FLC.

EXPERIMENTAL

Systems Studied

Mobile Fluids. The following products were chosen as representatives of a nonpolar and a polar carrier fluid:

n-Pentane: $T_{crit} = 196.62°C$; $P_{crit} = 33.31$ atm; $d_{crit} = 0.238$ g/ml (*4*)

Isopropanol: $T_{crit} = 235.25°C$; $P_{crit} = 47.02$ atm; $d_{crit} = 0.2727$ g/ml (5)

The products used had a purity of about 99%.

Stationary Liquids and Solid Support. As examples of a polar and a nonpolar stationary liquid the following products were chosen:

Polyethylene glycol: PEG 6000 and PEG 1000, the number denoting the approximate mean molecular weight

Polyethylene: Alkathene, a low-density polyethylene.*

The solid support was Sil-O-Cel C 22 diatomaceous firebrick.†

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* Imperial Chemical Industries Ltd., U.K.

† Johns-Manville Corporation, U.S.A.

Apparatus and Technique

Flow Scheme of Apparatus. Figure 1 shows a flow diagram of the apparatus used in our study. Item numbers correspond to the figures in parentheses in the following description.

The reservoir for the mobile carrier is a stainless-steel cylinder (4) of 2.5-liter capacity, having a maximum working pressure of 125 atm. This reservoir is filled with the liquid mobile carrier via a glass funnel (5) with a long stem, the latter also acting as a level gauge. During the filling operation the top of the vessel is open to the atmosphere at (6).

During actual operation, the liquid in the reservoir is kept under pressure by nitrogen from cylinder (1). The nitrogen pressure is adjusted with the high-pressure reducing valve (2) and measured by means of a precision Bourdon gauge (3).

The liquid mobile carrier is heated to supercritical conditions in a preheater (8), which reduces the heat load on the thermostat. The preheater consists of an electrically heated tube (50 cm × 6 mm i.d.) filled with metal filings. The heat input is adjustable and the temperature of the tube can be measured by means of thermocouples.

The mobile carrier attains the exact working temperature in a temperature-conditioning tube (10), which is an empty stainless-steel tube (4 m × 3 mm i.d.) kept in the same thermostat as the column proper. The air thermostat we used is suitable for temperatures of up to about 400°C. The temperature constancy at a level of about 200°C is better than 0.5°C, both as regards fluctuations with time and nonuniformity of temperature in the working space.

The mobile carrier enters the column (13) via a T-connection (12). Liquid samples are injected via a pneumatic injection device to be described separately. A small stream of liquid mobile carrier, withdrawn from the main liquid stream via (7), is used for flushing the sample into the column.

The effluent from the column leaves the thermostat via a capillary tube (1 m × 1 mm i.d.), the larger part of which is cooled with tap water (14). The effluent, then a liquid, leaves the cooler via a precision needle valve (15). This valve ("Speedivac" needle valve model OS 1 D*) maintains the pressure in the apparatus and serves for adjusting the flow rate to the desired value.

Nitrogen dissolved in the mobile carrier under pressure is al-

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* Edwards High Vacuum Ltd., Sussex, England.

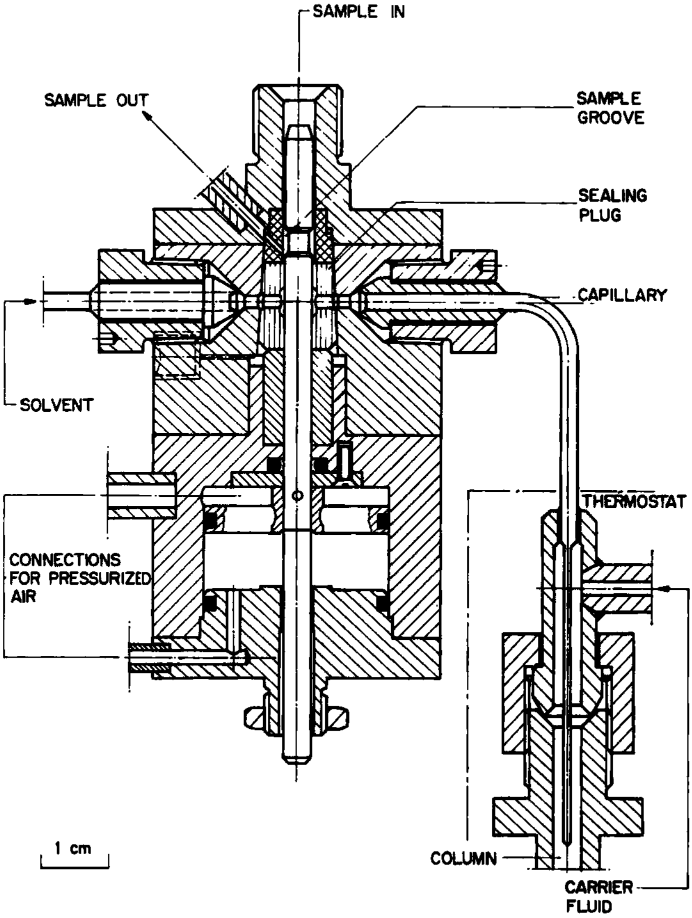

FIG. 2. Details of sample injection device.

lowed to escape from the liquid in (16); the bubble-free liquid flows via the detector (17) to waste.

Sample Injection. A pneumatic sample injector of the type used in our earlier work with carbon dioxide as a carrier (*1*) enabled operation under high pressure at room temperature or, alternatively, at reasonably high temperatures if low pressures are involved. The material of the seal (reinforced Teflon) precluded operation at elevated temperatures and high pressures simultaneously.

This difficulty has been circumvented by the arrangement shown in Figs. 1 and 2. A few drops of the sample (a dilute solution of the

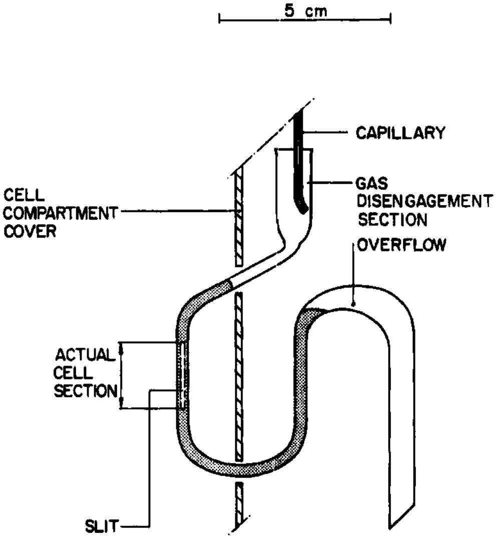

FIG. 3. Quartz UV-absorption cell.

substance to be analyzed*) are introduced into the top of the injection device shown in Fig. 2. This device is kept at room temperature. A small volume of the sample (approximately 15 μl) is transferred by a groove in the pneumatically operated stainless-steel plunger to the high-pressure part via the Teflon seal. Subsequently, a discrete amount of solvent is used for flushing this sample into the hot column via a capillary tube of about 10 cm × 0.3 mm i.d.

The volume of solvent required for a quantitative transfer is low (less than 100 μl) since the holdup of the system is also very small (about 20 μl). Column conditions are therefore hardly upset by the introduction of a relatively cold sample and solvent.

The solvent for flushing the capillary is withdrawn from the main liquid stream at the inlet side of the preheater (see Fig. 1). The small pressure drop of the latter serves as the driving force. With the setup used, it was empirically found that an injection time of about 3 sec corresponded to the right amount of solvent flowing through the injection device and capillary.

Detection. The detector was a UV absorption monitor operating

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* Usually consisting of 0.1–1 wt. % of solute in *n*-heptane or 1,2-dichloroethane. In the case of very sparingly soluble substances a saturated solution was used.

at a fixed wavelength of 2537 Å (L.K.B. "Uvicord" type 4701 A*). To prevent interference by gas bubbles, the original cell was replaced by a quartz cell which incorporated a gas separator (Fig. 3). The effective volume of this cell is of the order of 200 μl.

The 10-mV output of the electrical control unit was registered on a 2.5-mV potentiometric recorder after applying an opposing voltage of 7.5 mV. The recorder thus covered the range of 75–100% transmission.

By means of a microswitch arrangement, the exact moment of sample injection was marked on the recorder chart.

Preparation of Columns. The Sil-O-Cel C 22 firebrick was coated with polyethylene in the following way:

One part (by weight) of polyethylene was dissolved in about 4 parts of decalin by heating to boiling. This was done under an atmosphere of nitrogen in a rotating evaporator. The required amount of Sil-O-Cel was added and the mixture was heated under nitrogen at 160–180°C for some time (with the evaporator rotating) to allow the solution to be absorbed in the pores. The solvent was then distilled off slowly in a stream of nitrogen, while the mixture was being rotated. After cooling, the packing was sieved through a 40-mesh sieve to remove some clotted particles. The maximum loading obtainable in a single operation is about 10 wt. %. With higher loadings the solution is either too viscous or not all the solution is absorbed by the pores, resulting in the formation of a caked mass.

The coating of the firebrick support with polyethylene glycol was carried out in a similar way, using methanol as a solvent. However, owing to the better solubility of the polyglycols and the lower viscosity of the solution, the coating procedure was less critical and larger amounts of a stationary phase could be loaded onto the support.

The columns used in the present work were filled and coiled by the procedures usually followed in GLC.

Determination of Partition Coefficients. As the amounts of stationary liquid in the columns were only approximately known—some bleeding occurred during startup and when operating under severe conditions—we measured k' values (capacity ratios) rather than true partition coefficients (k). These quantities are related by the equation:

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* L.K.B. Produkter A.B., Stockholm, Sweden.

$$k' = k \frac{V_L}{V_G}$$

where V_G and V_L are the volumes of the mobile phase and the stationary phase in the column.

k' is found experimentally by measuring the elution time of a solute (t_R) and the holdup time of a nonpartitioning substance (t_G) at a constant flow rate, with the aid of the equation:

$$t_R = (1 + k')t_G$$

At the conditions adopted, the net retention of benzene is sufficiently small to permit the use of this substance for determining t_G without serious error.

In most of the experiments the average velocity of the carrier fluid in the column amounted to a few centimeters per second. The pressure drop across the column was, as a rule, below 2 kg/cm^2. Pressures reported are pressures at the column inlet.

RESULTS AND DISCUSSION

Stability of Columns

Apart from some bleeding occurring with newly prepared columns (presumably caused by the stripping-off of contaminants and degradation products of a lower molecular weight, already present in the stationary liquid or formed during the coating procedure), the columns proved to be reasonably stable at pressures below 50 kg/cm^2. Under the conditions adopted in most of the experiments, PEG 6000 and Alkathene columns did service in a large number of analyses. Some columns were used for months.

The bleeding rate increases very rapidly with increasing pressure and becomes quite appreciable with *n*-pentane at pressures above 50 kg/cm^2. We have, therefore, refrained from carrying out systematic experiments with the present systems at pressures exceeding 50 kg/cm^2.

Effect of Operational Parameters on Speed of Elution and Separation Pattern

Effect of Pressure. As a typical example of the dependence of partition coefficients on pressure, Fig. 4 shows some results of mea-

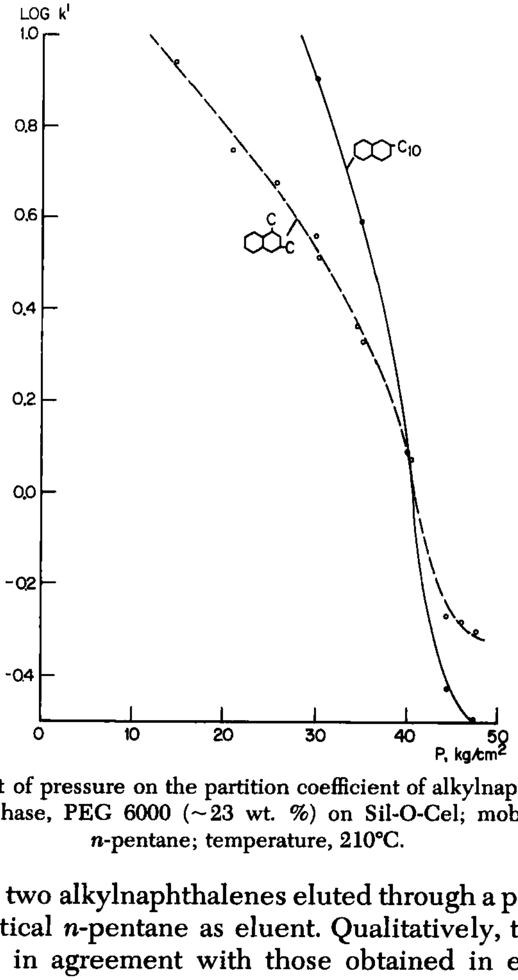

FIG. 4. Effect of pressure on the partition coefficient of alkylnaphthalenes. Stationary phase, PEG 6000 (~23 wt. %) on Sil-O-Cel; mobile phase, *n*-pentane; temperature, 210°C.

surements on two alkylnaphthalenes eluted through a polar column with supercritical *n*-pentane as eluent. Qualitatively, the shape of the curves is in agreement with those obtained in earlier work with CO_2 (*1*).

Figure 4 not only illustrates the great influence of pressure on the partition coefficient (hence, on the speed of elution), but also serves to demonstrate the possibility of changing the elution pattern by applying different pressures. At lower pressures, 1,3-dimethylnaphthalene (bp 263°C) elutes before 2-*n*-decylnaphthalene (bp 387°C). As in normal GLC, the elution proceeds in the order of increasing boiling points. The polar stationary phase may be expected to have some specific affinity for dimethylnaphthalene, in

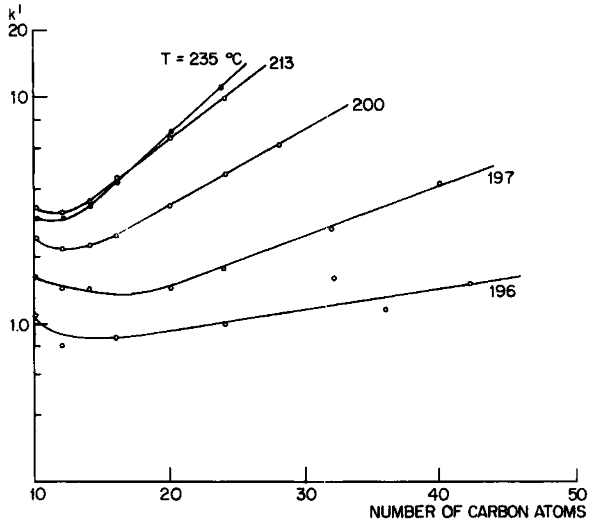

FIG. 5. Partition coefficients of di-*n*-alkyl phthalates as a function of carbon atom number at various temperatures. Stationary phase, PEG 6000 (~23 wt. %) on Sil-O-Cel; mobile phase, *n*-pentane; pressure, 35 kg/cm^2.

contrast with the more paraffinic decylnaphthalene, but obviously this effect is completely overshadowed by the large difference in boiling points. In other words, at low pressures light/heavy selectivity dominates over type selectivity.

The situation is different, however, at high pressures. As we had found in our earlier work (*1*) the light/heavy selectivity diminishes at higher pressures, increasing the possibility that type selectivity may dominate. Figure 4 shows that such is the case at pressures exceeding 40 kg/cm^2, the more paraffinic decylnaphthalene eluting before dimethylnaphthalene. In this region of fluid chromatography the elution proceeds in the order which can be expected for LLC with a polar stationary phase.

Effect of Temperature. Some results of measurements on the homologous series of di-*n*-alkyl phthalates are shown in Fig. 5. In our earlier work (*1*) we observed that in homologous series the logarithm of the partition coefficient may be expected to be a linear function of the carbon number. In the present case, this linear relationship holds fairly well for the higher members (from di-*n*-butyl phthalate on).

It is seen that at a constant pressure somewhat above the critical point, a decrease in temperature (in the region slightly above the critical point) effects a considerable lowering of the partition coefficients. This can be interpreted as an increase of volatility. In this region of fluid chromatography the effect of temperature is, therefore, opposite to that in normal GLC.

The effect of temperature is particularly great in the neighborhood of the critical point; from the curves for 200, 197, and 196°C in Fig. 5, it can be seen that a difference of a few degrees centigrade may well change the partition coefficient by a factor of 2 or even more.

In Fig. 5 the curves for 235 and 213°C cross. This phenomenon can be better understood from Fig. 6, where log k' has been plotted against the temperature. It is seen that the curve of diethyl phthalate passes through a maximum. At temperatures below this maximum the temperature derivative of k' is positive. With increasing temperatures the solute molecules are less inclined to remain in the

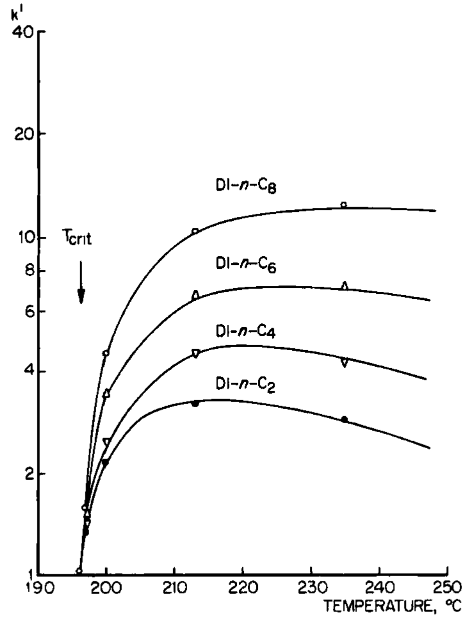

FIG. 6. Effect of temperature on the partition coefficients of some di-*n*-alkyl phthalates. Conditions: see Fig. 5.

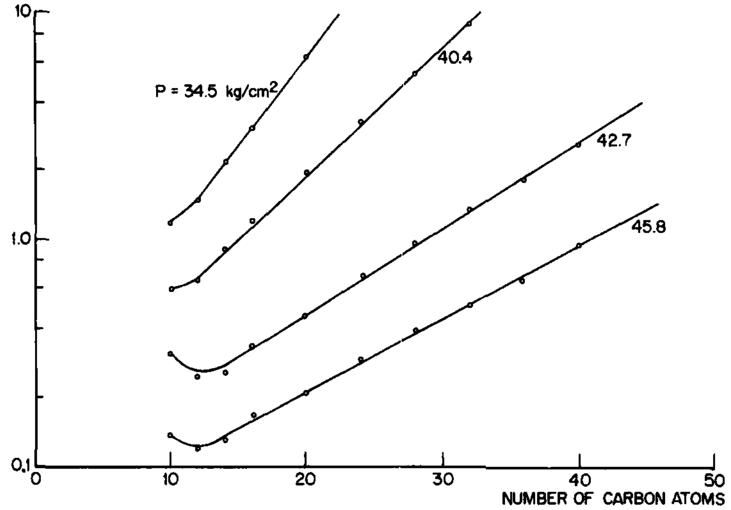

FIG. 7. Partition coefficients of di-*n*-alkyl phthalates on a nonpolar column with a nonpolar mobile phase. Stationary phase, Alkathene (~ 10 wt. %) on Sil-O-Cel; mobile phase, *n*-pentane; temperature, 213°C.

fluid phase as molecular interactions here decrease due to a lower fluid density.

At temperatures above the maximum, the role of molecular interactions in the gas phase is less important and an increase in temperature lowers *k'* by increasing the solute volatility as in normal GLC. The temperature derivative of *k'* is determined by a heat of transition (vaporization), which is positive in the temperature above the maximum.

With larger solute molecules, molecular interactions in the fluid phase are stronger. The temperature at which a transition from a positive to a negative slope occurs may shift to higher values. As can be seen from Fig. 6, the maximum in the curve of dioctyl phthalate evidently lies above 235°C. In the temperature range of 213 to 235°C the temperature derivative of *k'* is positive for this solute, whereas it is negative for diethyl phthalate. The lines corresponding to operating temperatures of 213 and 235°C in Fig. 5 must, therefore, cross somewhere between these two members of the dialkyl phthalate series.

Effect of the Nature of Mobile and Stationary Phases. Figures 7, 8, and 9 show the results of *k'* measurements for the homologous series of di-*n*-alkyl phthalates with different combinations of polar and nonpolar mobile and stationary phases.

Neglecting the first members of the series and considering the straight parts of the curves only, we may infer that the light/heavy selectivity (as follows from the slopes) is generally highest in Fig. 9 and lowest in Fig. 8. Figure 7 (completely nonpolar system) depicts an intermediate situation.

This is more clearly illustrated in Fig. 10, where curves for different phase systems are compared with the equality of k' for di-*n*-hexyl phthalate (the lowest member in the straight parts considered) as a criterion for comparison. Taking the completely nonpolar system as a reference, it is evident that the slope is lower with a polar stationary phase. In the latter case, higher members of the phthalate series possessing long paraffinic chains are less well retained than they would be if they had the same "polar character" as the lower members.

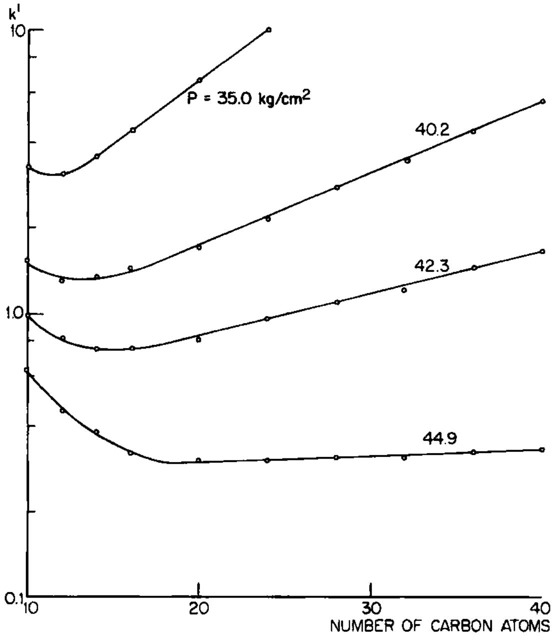

FIG. 8. Partition coefficients of di-*n*-alkyl phthalates on a polar column with a nonpolar mobile phase. Stationary phase, PEG 6000 (~23 wt. %) on Sil-O-Cel; mobile phase, *n*-pentane; temperature, 213°C.

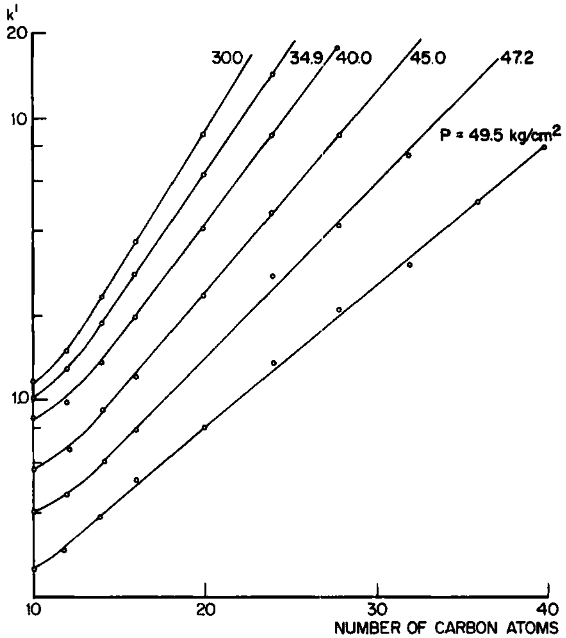

FIG. 9. Partition coefficients of di-*n*-alkyl phthalates on a nonpolar column with a polar mobile phase. Stationary phase, Alkathene (~10 wt. %) on Sil-O-Cel; mobile phase, isopropanol; temperature, 245°C.

With the polar mobile fluid the situation is reversed, the higher members here being less readily eluted than the lower ones.

Figure 10 demonstrates that a proper choice of the phases can ensure that either a light/heavy selectivity or a type selectivity dominates. With the light/heavy selectivity low, as in the PEG 6000/*n*-pentane system, conditions become favorable for separation according to type in wide-boiling mixtures. With volatility and polar effects reinforcing each other, as in the Alkathene/isopropanol system, we may compensate for the fact that FLC generally has a lower light/heavy selectivity than GLC.

As an illustration of a light/heavy separation with the Alkathene/isopropanol system, Fig. 11 shows the separation of phthalates according to molecular size.

Figures 12(A) and (B) demonstrate the type selectivity of the PEG 6000/*n*-pentane system. Figure 12(A) represents the separation of dimyricyl phthalate from diphenyl phthalate. It is noteworthy that the more highly paraffinic ester is eluted well before the more highly aromatic ester, notwithstanding the difference of 48 carbon atoms. Figure 12(B) shows the separation of phthalates of approximately the same molecular weight but differing in the nature of the alcohol groups.

Applicability of FLC to Substances of Low Volatility

Besides demonstrating the type of selectivity attainable, Fig. 12(A) also serves to illustrate the possibilities of FLC for heavy substances. Dimyricyl phthalate ($C_{68}H_{126}O_4$, MW 1006, a substance obviously too heavy for normal GLC) is eluted within a few minutes from a column of 2 m length.

It is of interest to compare FLC with GLC as regards the applicability to heavy substances. Such a comparison may well be made on the basis of polynuclear hydrocarbons as solutes. These com-

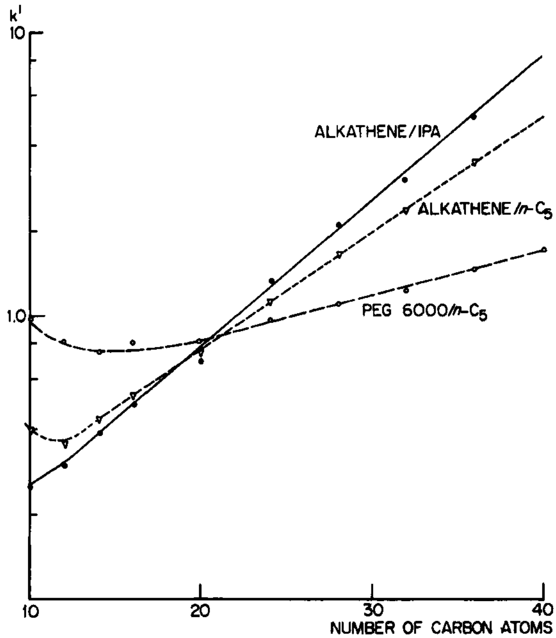

FIG. 10. Effect of phase system on the partition coefficients of di-*n*-alkyl phthalates. Mobile fluids: *n*-pentane, $T = 213°C$, $P = 42$ kg/cm^2; isopropanol, $T = 245°C$, $P = 49.5$ kg/cm^2. Stationary phases: Alkathene (~10 wt. %) and PEG 6000 (~23 wt. %) on Sil-O-Cel.

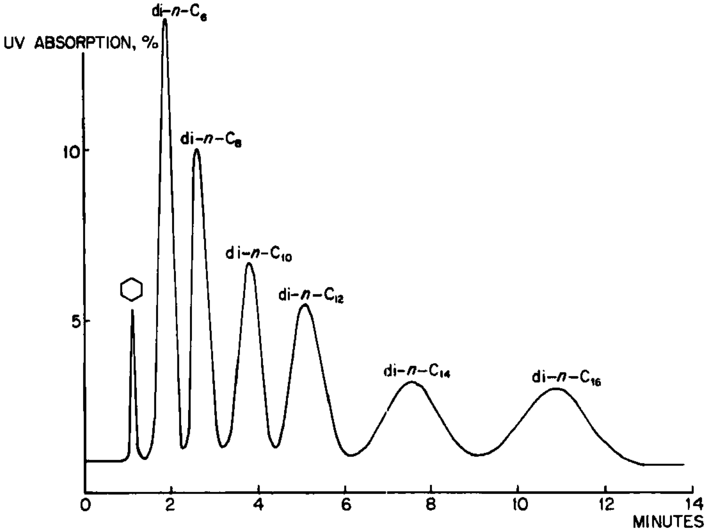

FIG. 11. Separation of phthalates according to molecular weight. Column, 2 m × 6 mm i.d. with Alkathene (~10 wt. %) on Sil-O-Cel (50/70 mesh); mobile phase, isopropanol; temperature, 245°C; pressure, 49.5 kg/cm^2.

pounds have been the subject of many GLC studies [e.g., (*6–13*)], being particularly well suited to high-temperature GLC because of their exceptionally high thermal stability.

In Fig. 13 FLC is compared with GLC at the same temperature and with high-temperature GLC. All curves pertain to nonpolar stationary liquids at the same loading (about 5 wt. % on firebrick support).

A comparison of the lower FLC curve with the upper curve (GLC at the same temperature*) affords some idea of the "gain in volatility" obtained by using a supercritical fluid instead of a low-pressure gas. The increase in volatility amounts to nearly 10^3 for substances boiling at about 450°C. Extrapolating the upper curve, we can predict with some assurance that the increase in volatility for a substance boiling at 600°C should be of the order of 10^4.

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* The data used for constructing this curve were not based on direct measurements, but calculated from results obtained by Abraham and Mark (*11*) on lightly loaded (2 wt. %) Celite columns. We assumed that the packing density of Sil-O-Cel C 22 firebrick is twice that of Celite and that the net retention is proportional to the percentage of liquid on support.

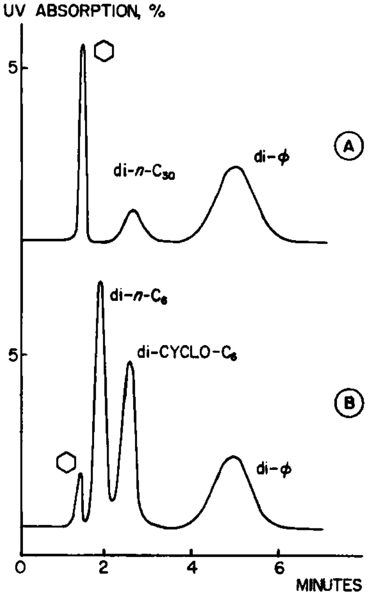

FIG. 12. Separation of phthalates according to type. Column, 2 m × 6 mm i.d. with PEG 6000 (~23 wt. %) on Sil-O-Cel (120/140 mesh); mobile phase, *n*-pentane; temperature, 213°C; pressure, 44.9 kg/cm^2.

The middle curve represents typical high-temperature GLC conditions. If we take a k' value of the order of 10^2 as a practical upper limit for an analytical separation,* we may deduce that high-temperature GLC has its limit at a solute boiling point of about 600°C, at least for substances of high thermal stability. By using higher operating temperatures (if permitted by the stability of the solute) and somewhat lower liquid loadings, it may be possible to shift the boiling point barrier by, for instance, 100°C, but there the possibilities may well be exhausted.

The situation is definitely more favorable with FLC, since an extrapolation of the lower curve of Fig. 13 suggests that this technique should still be applicable to substances with boiling points between 900 and 1000°C (with the same criterion as before). The operating conditions corresponding to the lower curve are far from extreme and are still well away from operational limits.

* This means that for a column of a few meters length operated with carrier gas velocities of a few centimeters per second, the analysis time will be of the order of 1 hr.

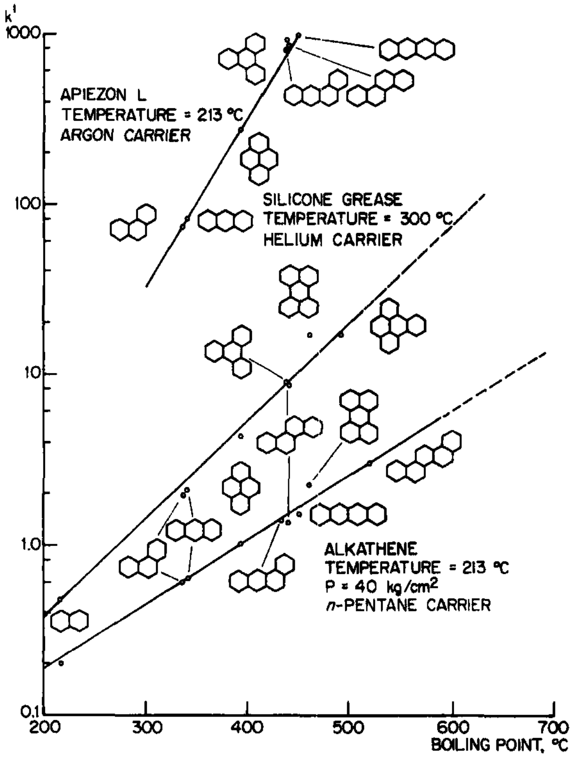

FIG. 13. Comparison of FLC (lower curve) with GLC at the same temperature (upper curve) and high-temperature GLC (middle curve). Liquid loadings of columns: approximately 5 wt. %.

Speed and Efficiency of Separations

Our previous work (2) on the separating efficiency of packed GLC columns operated at high pressures showed that in such columns the plate height is mainly determined by the slowness of mass transfer by diffusion in the gas-filled pores of the packing (apart from the contribution by packing irregularity, which can—at least theoretically—be made sufficiently small by a suitable packing technique or by the use of narrow columns). This intragranular mass-transfer resistance can be diminished by reducing the particle size. Fortunately, there is little objection to the use of fine packings in FLC, since high-pressure gases and supercritical

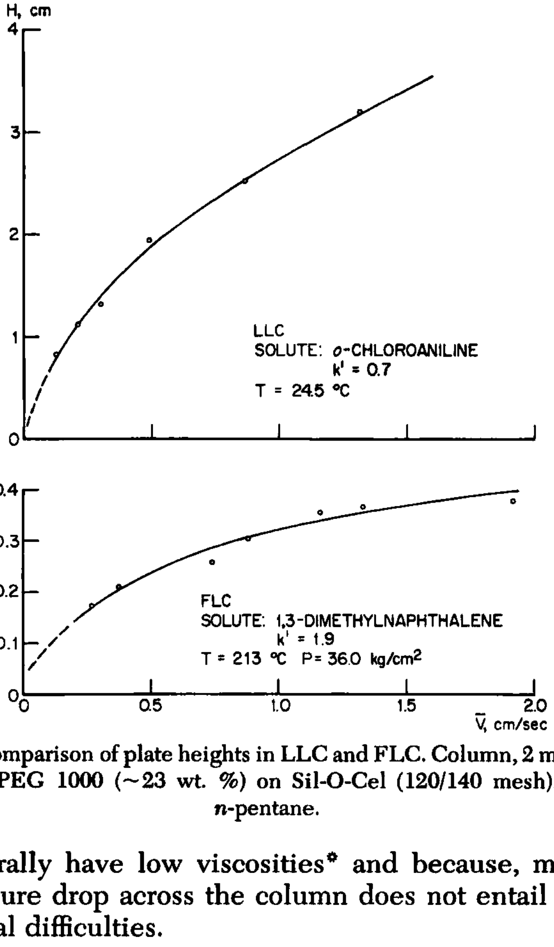

FIG. 14. Comparison of plate heights in LLC and FLC. Column, 2 m × 6 mm i.d. with PEG 1000 (~23 wt. %) on Sil-O-Cel (120/140 mesh); eluent, *n*-pentane.

fluids generally have low viscosities* and because, moreover, a larger pressure drop across the column does not entail additional experimental difficulties.

In this respect the situation is definitely more favorable in FLC than in LLC. Diffusivities are generally considerably lower in liquids than in supercritical fluids, while viscosities are higher.* If efficiency and speed of GLC separations were to be attained in LLC, the particle size must be so small that excessively large pressure drops would develop across columns other than extremely

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* The viscosity of supercritical *n*-pentane at 210°C and 35 kg/cm^2 is 0.0221 cP (*14*). Most liquids employed as eluents in liquid chromatography have viscosities of 0.5–2 cP.

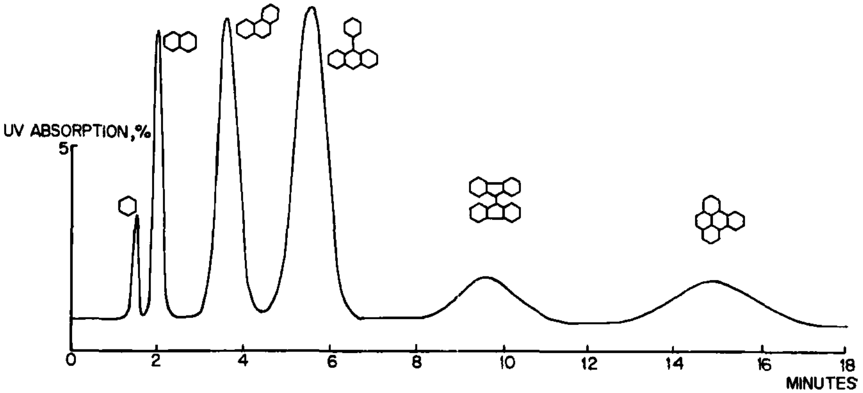

FIG. 15. Separation of some aromatic hydrocarbons. Pressure, 42 kg/cm^2; *other conditions as given in Fig. 12.*

short ones at the high eluent rates. Actually, LLC columns rarely exceed 1 m in length, while mobile phase velocities are as a rule about two orders of magnitude lower than in GLC.

The superiority of FLC over LLC is demonstrated by the experiments shown in Fig. 14, where one and the same column is operated under LLC and FLC conditions. Plate heights of a few milli-

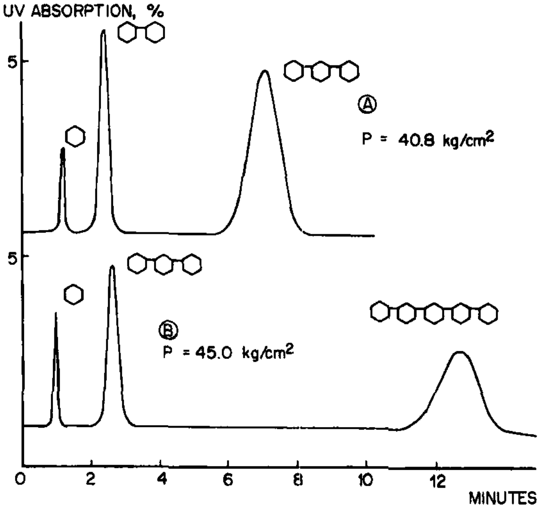

FIG. 16. Separation of polyphenyls. Conditions except pressure as given in Fig. 12.

meters are obtained[*] at mobile phase velocities of 1–2 cm/sec in FLC.

With liquid pentane as a mobile carrier, such velocities lead to excessive plate heights (upper curve in Fig. 14; note the difference in ordinate scales). In LLC operation, plate heights comparable to the ones in FLC are obtained only at velocities below 0.1 cm/sec.

With supercritical pentane as a mobile carrier, the pressure drop across the column considered is about 0.5 kg/cm^2 at a velocity of 1.5 cm/sec. With liquid pentane at a comparable velocity, the pressure drop is about 5 kg/cm^2.

Miscellaneous Examples of Separations by Means of FLC

Separations of Aromatic Hydrocarbons. Figure 15 is a chromatogram obtained from a synthetic mixture of unsubstituted aromatic hydrocarbons with boiling points of up to about 500°C. The diminished light/heavy selectivity (as compared with GLC) is evident from the fact that a boiling range of about 400°C can be covered in one run at constant operating conditions.

Figures 16(A) and (B) show the separation of bi-, *m*-tri-, and *m*-quinquephenyl. It can be observed that with supercritical pentane at 213°C and 45 kg/cm^2, the last compound (bp 576°C) can be eluted within a short time. It is of interest to compare this result with those of previously conducted GLC experiments at unusually high temperatures.

Smith and Gudzinowicz (*15*) succeeded in eluting *m*-quinquephenyl in a programmed-temperature operation in which the temperature was increased up to 370°C. They used a silicone gum rubber column.

Baxter and Keen (*16*) analyzed *m*-quinquephenyl in a time comparable to ours in an isothermal run at 445°C. Operation at this extremely high temperature was possible only by employing a specially prepared polyphenyl tar as stationary phase.

Figure 17 demonstrates how, under conditions of pronounced type selectivity, a separation of hydrocarbons according to aro-

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[*] It is probable that better results can be achieved with FLC, because these plate heights include appreciable contributions from the detection system and unevenness of flow in the packing. The column was filled and coiled in the way which is usual in GLC. Nevertheless, our present results adequately demonstrate the difference between FLC and LLC.

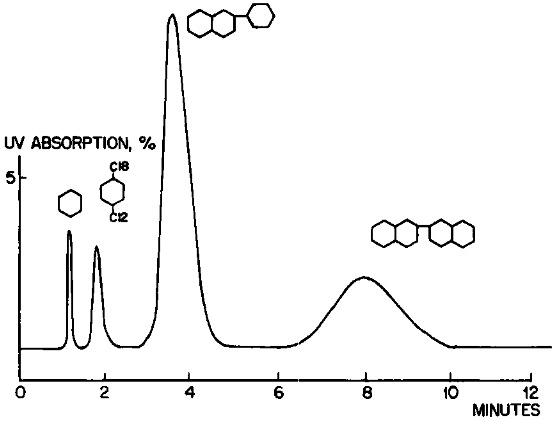

FIG. 17. Separation of some hydrocarbons according to ring number. Pressure, 41.9 kg/cm^2; other conditions as given in Fig. 12.

matic ring number may be obtained. 1-Dodecyl-4-octadecylbenzene ($C_{36}H_{66}$, estimated boiling point about 500°C) is eluted well before 2-phenylnaphthalene ($C_{16}H_{12}$, bp 345°C), notwithstanding the differences in boiling points and the number of carbon atoms.

Figure 18 shows the ready separation of two isomeric hydrocarbons, viz., 1,1′-binaphthyl (bp > 360°C) from 2,2′-binaphthyl (bp 452°C).

Separation of Heavy Oxygenated Compounds. Heavy products of nearly equal molecular weight and structure, but differing in functional groups, may be separated by FLC. This is demonstrated in

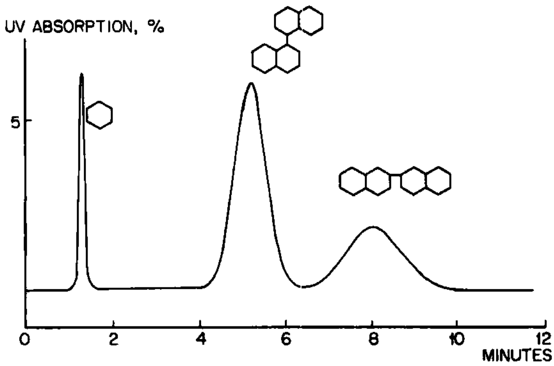

FIG. 18. Separation of isomeric binaphthyls. Pressure, 41.9 kg/cm^2; other conditions as given in Fig. 12.

Figs. 19(A) and (B), showing the separation of an alcohol from a ketone and an ether from a ketone, respectively.

CONCLUSIONS

The main points emerging from our study may be summarized as follows.

Applicability of FLC to Heavy Substances

FLC can be applied to substances of such low volatility that they lie beyond the limits of normal GLC. As compared with GLC at the same temperature, the "gain in volatility" may be as high as 10^4.

Flexibility of FLC

FLC is a very versatile chromatographic technique because the elution speed and the separation pattern are variable within wide limits to suit a particular separation. By proper choice of parameters, it may be ensured that either a class separation or a separation ac-

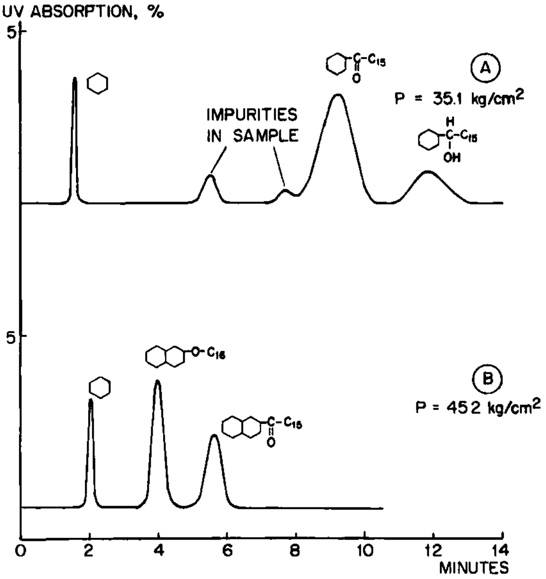

FIG. 19. Separation of oxygenated compounds of near-equal molecular weight. Conditions except pressure as given in Fig. 12.

cording to boiling point dominates. In this respect, FLC may be regarded as a cross between GLC and LLC, combining features of both.

It owes this flexibility to the great effects of pressure and temperature, as well as the freedom of choosing the desired phase combination. Stationary and mobile phases of the same polarity may be combined, provided that the former has a sufficiently high molecular weight. This is a definite advantage over LLC, where the requirement of immiscibility means that in general only liquids of a widely different polarity can be combined.

Since temperatures in FLC are not necessarily very high, a large number of high-molecular-weight products of various polarities may be regarded as eligible for the role of immobile phase. In this respect the situation is definitely more favorable here than in high-temperature GLC, where the stringent demands on thermal stability limit the choice to only a few stationary phases, all being relatively nonpolar.

Speed and Efficiency of FLC Separations

While probably not quite so fast and efficient as in normal GLC, the separations by FLC are at any rate much faster and more efficient than in LLC. This conclusion is not only supported by the results of plate-height measurements, but also by the chromatograms shown. In nearly all these examples, the separation was achieved within 15 min.

Operational Aspects

With the setup as described in the present study, an analysis by means of FLC is almost as easy as analysis by GLC. Very little manipulation is required. Possibilities of automation, a feature of GLC, should also be present in FLC.

As the speed of elution depends very much upon both temperature and pressure, it may be advantageous in many instances to use a programming technique. The profits to be gained from such an operation should be comparable to the advantages of programmed-temperature GLC over isothermal GLC.

Our work has been confined to aromatic substances in view of the UV-absorption detector employed. It will be clear that a more universal type of detector is required for a general application of FLC. Ideally, such a detector should possess a high sensitivity and low internal volume, and preferably be based on detection in the fluid phase.

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