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EVALUATION OF SUPERCRITICAL SULFUR HEXAFLUORIDE AS A MOBILE PHASE FOR POLAR AND NON-POLAR COMPOUNDS

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SUMMARY

The limits in the elution of non-polar and polar compounds with a supercritical sulfur hexafluoride mobile phase are determined. The compatibility of an SF_6 mobile phase with flame ionization detection during pressure programming in capillary supercritical-fluid chromatography is demonstrated. Special modifications to the split injection assembly are described. A decrease in solvent strength with increasing pressure reported in the literature was not observed. As has been indicated in the literature. SF_6 was found to exhibit low solvating power. Normal alkanes up to about $n = 30$ and polycyclic aromatic hydrocarbons of up to four rings were eluted at 100°C, but no larger compounds of either type. SF_6 has an advantage over CO_2 in that primary amines can be eluted, but it is also limited in most cases to mono-functional amines, and also to mono-functional alcohols and carboxylic acids. No adverse effects on the stationary phase or column deactivation were observed.

INTRODUCTION

Carbon dioxide is the most widely used mobile phase in supercritical-fluid chromatography (SFC). However, elution of primary aliphatic amines is not possible due to formation of insoluble salts. Ammonia has been demonstrated as a viable mobile phase[1,2] and is clearly compatible with amine compounds, but instrumental difficulties have limited its use. Research into mixed mobile phases may yield carbon dioxide-based fluids compatible with primary amines. For instance, methylamine has been used as a modifier, together with water and methanol, in carbon dioxide for the analysis of basic alkaloids[3]. It would be preferable to operate with a neat mobile phase, especially one with a low critical temperature so as to retain the possibility for analysis of thermally labile samples. Several possible mobile phases are short-chain alkanes, halocarbons, or sulfur hexafluoride. SF_6 is the only fluid among these that is compatible with flame ionization detection (FID), which provides a simple and universal detection system.

A comparison of SF_6 to other supercritical-fluid solvents[4], based on solvochromatic data, indicated that SF_6 was weakly polar yet still polarizable and not as

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strong a solvent as CO_2. Schwartz and Brownlee[5] exploited the low solvent strength of SF_6 to effect chemical class separations of hydrocarbon samples with detection via a modified FID system. N,N-Dimethylformamide was used as the injection solution solvent for a series of *n*-alkanes up to hexadecane, but it did not elute from the silica column within 20 min at 50°C and 68 bar. Hellgeth *et al.*[6] used the retention of benzene and alkyl-substituted benzene compounds in packed-column SFC to compare the solvent strength of CO_2 to SF_6. They concluded that SF_6 was a weakly solvating mobile phase and predicted that, in general, only mono-functional polar compounds could be eluted with an SF_6 mobile phase.

In this study the compatibility of an SF_6 mobile phase with FID was further evaluated under capillary column SFC conditions using pressure programming. Unusual problems encountered in split injection operation are discussed and solutions are described. The limits of SF_6 as a mobile phase for non-polar and polar aliphatic and aromatic compounds are determined, with emphasis on the possibilities for elution of amine compounds.

EXPERIMENTAL

The chromatographic system was constructed in our laboratories, and has been described in detail elsewhere[2]. It consisted of a high-pressure syringe pump (Model 8500, Varian Instruments, Walnut Creek, CA, U.S.A.), a gas chromatograph oven (Model 4100, Carlo Erba, Milan, Italy), and an electrically-acuated injection valve (Model C14W, Valco Instruments, Zug, Switzerland) mounted above the oven. The injection loop volume was 0.2 μl. Pressure was controlled from a portable computer (Model HP 75C, Hewlett-Packard, Basle, Switzerland) interfaced to the pump. The pump cylinder was equipped with a cooling jacket, through which a water–ethylene glycol solution was continuously circulated (6°C). Similar to the procedure described by Schwartz and Bronwlee[5], the FID collector assembly was protected from the corrosive action of hydrogen fluoride produced in the flame by plating a 30–50-μm layer of gold over a 0.5-μm layer of nickel (W. Fluehmann, Duebendorf, Switzerland). The effluent gases from the flame ionization detector were drawn through a vacuum scrubber (Model 412, Buchi Laboratoriums-Technik, Flawil, Switzerland) for neutralization in alkaline solution.

The chromatographic column was 5 m × 100 μm I.D. deactivated fused-silica coated with a 0.5-μm film of a 100% methylpolysiloxane (SB-methyl-100, Lee Scientific, Salt Lake City, UT, U.S.A.). The column was connected to an 8 cm × 10 μm I.D. fused-silica restrictor (Infochroma, Zug, Switzerland) via a capillary column union [MVSU/005, Scientific Glass Engineering (SGE), Ringwood, Australia]; a 200-μm I.D. capillary sleeve inside the union served to eliminate dead volume and align the two capillaries. The end of the column restrictor was positioned about 2 mm below the tip of the FID jet, which was operated at 300°C. An auxiliary heating block was attached to the FID collector body and held at 250°C. This was found to eliminate spiking and noise present with either CO_2 or SF_6 mobile phases in this particular instrument (with either standard or gold-plated collectors). No differences in peak symmetry or limits to SF_6 solvating power were observed when a 50-μm I.D. frit retrictor (Lee Scientific) was tested.

Two split injection assemblies were used and are shown schematically in Fig. 1.

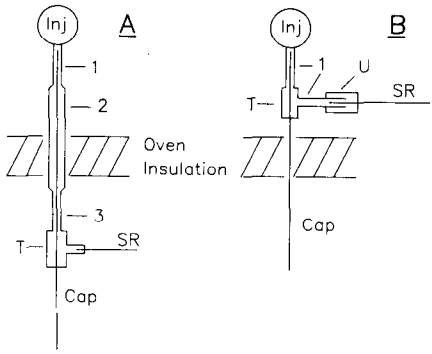

Fig. 1. Schematic diagrams of capillary SFC split injection assemblies (not to scale): (A) design used in previous experiments with 0.5-ml volume, (B) improved design used in this study with 9 μl volume. Inj = injection valve; SR = split restrictor; Cap = capillary column. U = 1/16–1/32 in. Valco reducing union. See text for description of numbered tubing sizes and T-pieces.

The first was our previous design (Fig. 1A), the second (Fig. 1B) was used to produce the chromatograms in this study. In Fig. 1A the T-piece was a 1/16 in. Swagelok union, and the stainless-steel tubing was (1) 15 mm × 0.31 mm I.D. × 1/16 in. O.D., (2) 150 mm × 2.0 mm I.D. × 1/8 in. O.D., and (3) 15 mm × 0.52 mm I.D. × 1/16 in. O.D. In Fig. 1B the T-piece was one-half of a VSU/005 union (SGE), and the tubing pieces (1) were 15 mm × 0.5 mm I.D. × 1/16 in. O.D. The splitter assembly in Fig. 1B is essentially identical to the capillary SFC splitter available from SGE with both tubing pieces reduced in length. The split restrictors were 10 μm I.D. fused-silica, 6 cm long in Fig. 1A and 10 cm long in Fig. 1B. The end of the split restrictor, in the configuration shown in Fig. 1B, was immersed in water to eliminate ice formation which causes flow irregularities.

Liquified SF_6 (SFC-grade, Scott Specialty Gases, Plumsteadville, PA, U.S.A.) was obtained in an aluminium cylinder under its own vapor pressure without an eductor tube, and was used without additional purification. A 2-μm, high flow-rate filter (SS-4FW, Nupro, Lachen, Switzerland) was installed between the cylinder and the pump.

Samples were obtained from Fluka (Buchs, Switzerland). Injection solution concentrations were about 0.5–1 mg ml^{-1} in hexane, or hexane with up to 10% dichloromethane or dichloromethane–methanol as necessary. For retention measurements, the *o*-xylene was dissolved in *n*-pentane. About 100–200 ng of each compound was injected, with some fraction of this amount entering the column. The SF_6 split ratio was 1:12 (column:split) at initial programming conditions of 100°C and 50 bar. The erroneous assumption is sometimes made in capillary SFC studies with split injection that the mobile phase split ratio is also the sample split ratio. The actual amount of sample transferred to the column in this study was not known, and would require an evaluation of the dependence of peak size on split ratio, and other factors, to make a reasonable estimate.

Data were acquired and stored via a 12-bit A/D interface (Nelson Analytical, Cupertino, CA, U.S.A.). The sampling rate was one point per second in all analyses. Chromatograms were replotted such that full-scale corresponds to the equivalent

full-scale response of a strip-chart recorder with the FID electrometer attenuation set at 2^4 (16 pA full scale deflection).

Retention parameter values of *o*-xylene were calculated using its retention time and the time of the first eluting peak of the *n*-pentane solvent (probably a smaller or branched alkane).

RESULTS AND DISCUSSION

The compatibility of an SF_6 mobile phase with FID has been demonstrated for isobaric–isothermal conditions and where the pressure and/or the temperature were step-programmed[5]. The temperature change was from 50 to 100°C, and the pressure change was over the relatively small range of 230 to 340 bar. The packed-column flow-rates were apparently about 50–100 μl min^{-1}, and considering the injection solution concentration and peak size, then the analyses were not performed with the electrometer set at high sensitivity. We sought to determine if SF_6 was compatible under capillary column conditions, where much larger pressure changes are present and the electrometer attenuation is typically set at about 2^4 (16 pA full scale response). FID is selective for C–H bonds, but a mass-flow dependent signal could arise from the presence of hydrocarbon impurities in the SF_6 (*ca.* 5 ppm) or from ionic species formed in the flame. The fluid flow-rate through the capillary column was about 4 μl min^{-1} at initial pressure programming conditions, and was expected to have little influence on the FID signal. The resulting baselines were nearly void of any drift during large pressure changes (50 to 400 bar). This result is demonstrated in the chromatograms discussed below.

Split injection in capillary SFC has been evaluated in a number of laboratories recently with regard to reproducibility and quantitation. With SF_6 as a mobile phase, a problem was encountered that appears to be unique to such a heavy solvent molecule. Experience has shown that "humps" in chromatograms occurring after the solvent peak are usually caused by poor flow paths in the column–restrictor union, such as when the end of either capillary is broken or damaged. Similar humps were observed during initial instrument setup in this study. The humps were not reproducible in size or shape and additional noise and ghost peaks were often observed (Fig. 2). Pressure-programmed chromatograms without an injection produced no peaks, only a baseline with a very slight rise. After several complete and extremely careful assemblies of the capillary union failed to solve the problem, attention was directed to the injection system. The injector split assembly was a prototype used in early SFC experiments in our laboratory (Fig. 1A). The total volume was about 0.5 ml. With a split flow of about 40 μl min^{-1} fluid, 12 min were needed to flush the entire splitter volume. It was also noted that the density of SF_6 (*ca.* 1.6–1.7 g ml^{-1} at 50 bar) is substantially greater than the solvents being used for sample solutions: hexane, dichloromethane, and methanol. There seemed to exist the possibility that, with the large splitter volume and potential for partial miscibility, portions of the injected solvent might not be completely flushed out of the splitter and subsequently enter the column producing the humps and ghost peaks. This theory was not tested with phase equilibria studies; instead, the splitter was exchanged for one with a much smaller volume (Fig. 1B). This eliminated the humps and ghost peaks. Occasionally, some irregularities in the solvent peak shape still arise, which indicates further refinement of

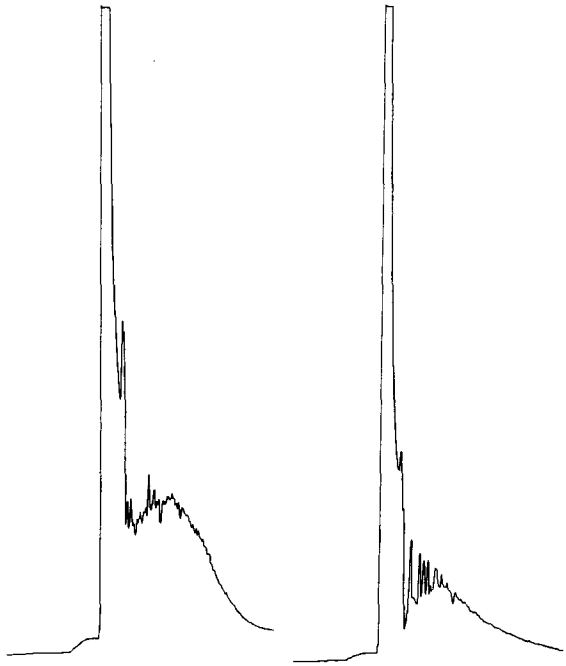

Fig. 2. Examples of unacceptable solvent peaks obtained using the split injection assembly in Fig. 1A.

the splitter assembly may be necessary. For example, most splitters are constructed of 0.5 mm I.D. tubing, which is significantly wider than the capillary SFC column used in this study (*ca.* 200 μm O.D., although wider columns are commercially available). The result is that the capillary column invariably leans against the inside wall of the splitter and is not centered in the flow path from the injection valve as would be optimal. Immiscibility of the sample solvent with the mobile phase can also cause problems. For example, when the sample solvent was about 20% or more methanol, the solvent peak was up to three times as wide as with neat hexane or dichloromethane and often interfered with detection of early eluting peaks.

At 95°C, the retention time of *o*-xylene increased over the pressure range 250–310 bar in a phenyl packed-column SFC system[6]. This increase was suggested to show a concurrent decrease in solvent strength, resulting from decreased mass transfer rates of the solute from the stationary to the mobile phase. The decreased mass transfer rates were attributed to slower solute diffusivity in the mobile phase, which is a result of increased density and viscosity. The pressure–density isotherm of SF_6 at 95°C is shown in Fig. 3.

If the solvent strength decreases under these conditions, then a decrease in retention should also be present in capillary SFC. The retention parameters of *o*-xylene at 95°C over the pressure range 50–350 bar (Table I and Fig. 4) obtained in our capillary SFC system show continuously increasing solvent strength. All retention parameters decrease, and the mobile phase linear velocity increases. The relatively constant capacity factor (k') values at 200–350 bar probably reflect the fact that

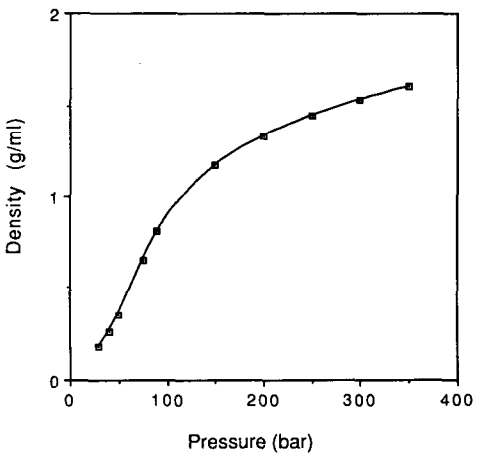

Fig. 3. Pressure–density isotherm of SF_6 at 95°C, calculated from the Peng–Robinson equation of state[7]. Solid line added for clarity.

o-xylene still has a slight affinity for the stationary phase, even though the peak elutes during the last part of the solvent peak at 200 bar and is only a barely detectable shoulder at 350 bar. At such low retention as $k' = 0.08$, the surface of the stationary phase is in contact with a mixture of solvent and mobile phase, disregarding possible swelling and uptake of solvent or mobile phase. Thus, the solute retention is not solely affected by the mobile and stationary phases. Even so, the adjusted retention time (t'_R) values in Table I show continuously decreasing retention, indicative of increasing solvent strength. Since retention time only indicates the position of a peak in a chromatogram, the effect observed by Hellgeth *et al.*[6] was not indicative of a decrease in solvent strength. The effect could have been a consequence of decreased flow-rates (not specified in ref. 6) arising from the increased viscosity and density, or of a lack of thermal equilibrium as has been reported with a carbon dioxide mobile phase[8].

TABLE I

RETENTION PARAMETERS OF *o*-XYLENE IN CAPILLARY SFC AT 95°C

Parameters are: retention time of unretained solute (t_0), *o*-xylene retention time (t_R), adjusted retention time ($t'_R = t_R - t_0$), capacity factor ($k' = t'_R/t_0$), and mobile phase linear velocity (u).

Pressure (bar)	t_0 *(min)*	t_R *(min)*	t'_R *(min)*	k'	u *(cm s^{-1})*
50	11.77	18.77	7.00	0.59	0.71
75	11.00	13.19	2.19	0.20	0.76
90	10.23	11.64	1.41	0.14	0.81
150	6.82	7.44	0.62	0.091	1.22
200	5.31	5.75	0.44	0.083	1.57
250	4.41	4.77	0.36	0.082	1.89
300	3.81	4.13	0.32	0.084	2.19
350	3.40	3.68	0.28	0.082	2.45

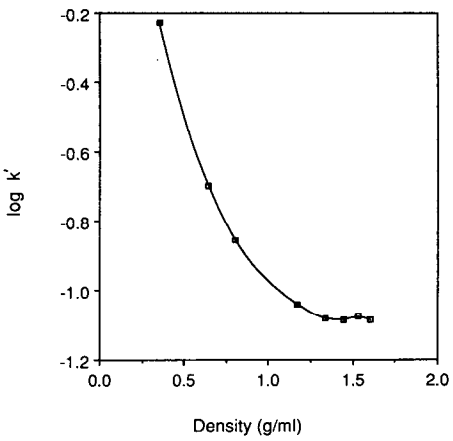

Fig. 4. Retention of *o*-xylene *vs.* SF_6 density at 95°C, densities calculated as in Fig. 3.

In the same study[6], at 224 bar, the retention time of *o*-xylene decreased over the temperature range of 50 to 75°C. This effect was also used to support the theory of decreased solvent strength of SF_6, although the effect of increased solute volatility was also noted to be a factor. Under these same conditions, the retention parameters of *o*-xylene in CSFC (Table II and Fig. 5) indicate that the solute volatility over-compensates for the decrease in density occurring as the temperature increases at constant pressure (Fig. 6).

A mixture of normal aliphatic hydrocarbons was chromatographed (Fig. 7). The alkanes up to $n = 30$–32 were eluted, but the longer alkanes of $n = 36$ and 40 did not elute. This limit in chain length is considerably lower than that found with a CO_2 mobile phase. It is possible that alkanes longer than $n = 30$–32 might elute under different conditions, at a higher temperature for example.

A mixture of four polycyclic aromatic hydrocarbons (PAHs) was injected and pressure programmed at 10 bar min^{-1} from 50 to 400 bar at 100°C. Naphthalene (128 g mol^{-1}), phenanthrene (178 g mol^{-1}), and chrysene (228 g mol^{-1}) eluted, although the chrysene peak was small and broad. Coronene (300 g mol^{-1}) did not elute under these conditions. The limit in molecular weight for PAHs is then about 250 g mol^{-1},

TABLE II

RETENTION PARAMETERS OF *o*-XYLENE IN CAPILLARY SFC AT 224 BAR

Temperature (°C)	t_0 (min)	t_R (min)	t'_R (min)	k'	u (cm s^{-1})
50	5.60	6.31	0.71	0.127	1.49
60	5.48	6.05	0.58	0.105	1.52
70	5.29	5.81	0.52	0.098	1.58
80	5.11	5.58	0.47	0.092	1.63
95[a]	4.86	5.26	0.40	0.082	1.72

[a] Values interpolated from data in Table I.

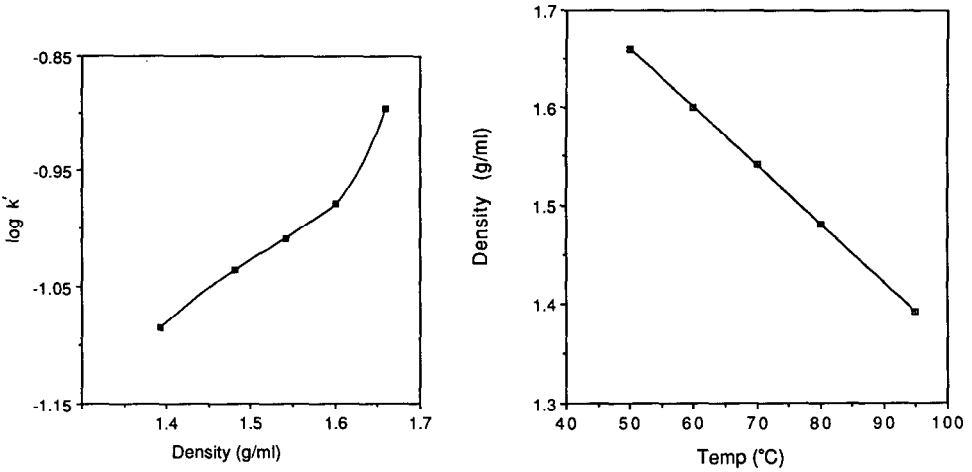

Fig. 5. Retention of *o*-xylene *vs.* SF_6 density at 224 bar, densities calculated as in Fig. 3.

Fig. 6. Temperature–density isobar of SF_6 at 224 bar, calculated as in Fig. 3.

corresponding to compounds such as perylene or benzo[*a*]pyrene. 1,2,4-Trichlorobenzene (TCB) was added to this sample solution (hexane and dichloromethane) to dissolve the coronene. TCB eluted between naphthalene and phenanthrene. The limitations in the elution of aliphatic and aromatic hydrocarbons with an SF_6 mobile

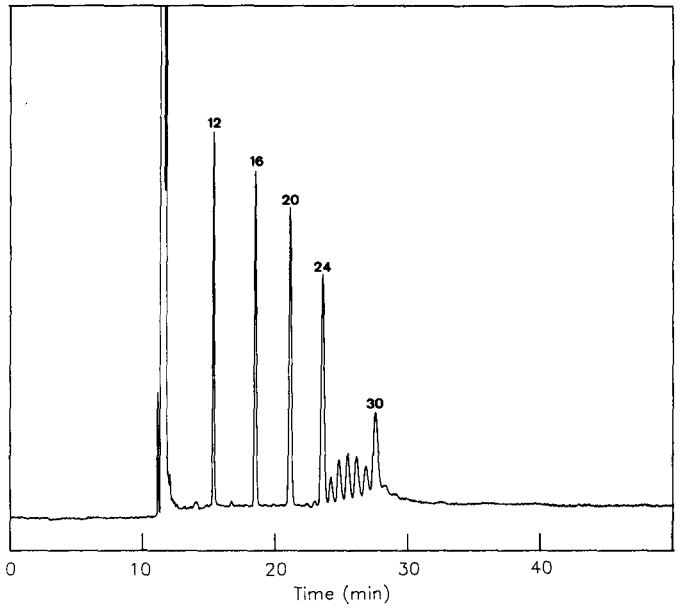

Fig. 7. Capillary SFC chromatogram of a mixture of *n*-alkanes, peak numbers represent alkyl chain length. Conditions: 100°C, pressure programmed at 10 bar min^{-1} from 50 to 400 bar after 10 min inital-pressure hold time, column described in text.

phase imply that application to hydrocarbons group analysis[5] is likewise limited to samples of fairly low molecular weight.

Very little data exist to evaluate the solvating power of SF_6 towards polar compounds. Several polar compounds were injected to assess the limits of SF_6 solvating power for polar compounds. Mono-, di-, and, in some cases, poly-substituted compounds were used. The major functional groups included were hydroxyl, carboxylic acid, and amine, and a few compounds were of mixed functionality. Most of these test compounds can be easily eluted by gas chromatography, and they are used in this study as simple probes for the determination of the properties of an SF_6 mobile phase in capillary SFC.

Considering that benzoic acid[9] is soluble in SF_6, it was expected that aliphatic alcohols (Fig. 8) and a carboxylic acid would elute (Fig. 9). The carboxylic acid peak shows overloading typical on a methylpolysiloxane stationary phase. No information was available as to the solubility of amines in SF_6. Two aliphatic amines were eluted with virtually no peak tailing (Fig. 10). This is the first report of the elution of primary aliphatic amines by SFC with FID. Short-term retention time reproducibility of these amines was excellent, about 0.03% relative standard deviation. Another primary amine which also contains a tertiary amine function (Fig. 11) eluted close to the solvent peak. N-Methylethanolamine eluted even earlier at 12 min under the same programming conditions, also with symmetric peak shape. The aromatic diamine compound *m*-diaminobenzene eluted with symmetric peak shape, but the necessity of adding a signficant amount of methanol to effect dissolution in the injection solution resulted in poor solvent peak shape. In this case the FID signal did not completely return to baseline (*ca.* 10% offset) until 3 min after the end of the solvent peak and at

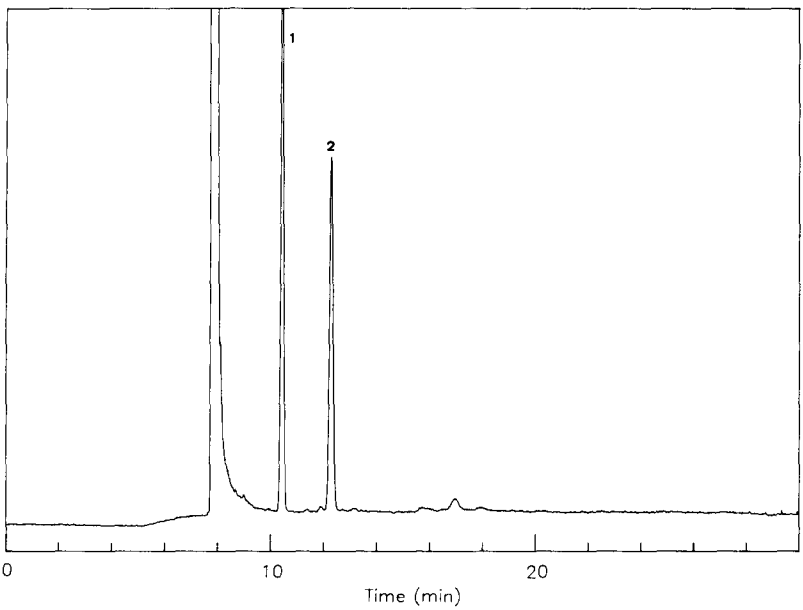

Fig. 8. Capillary SFC chromatogram of (1) 1-decanol and (2) 1-tetradecanol. Conditions: 100°C, pressure programmed from 50 to 300 bar at 20 bar min^{-1} after 5 min at initial pressure.

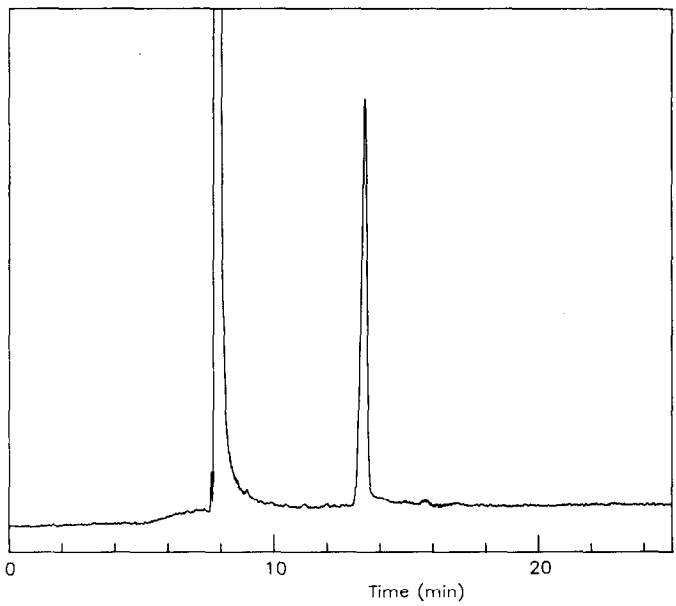

Fig. 9. Capillary SFC chromatogram of tetradecanoic acid. Conditions: same as in Fig. 8.

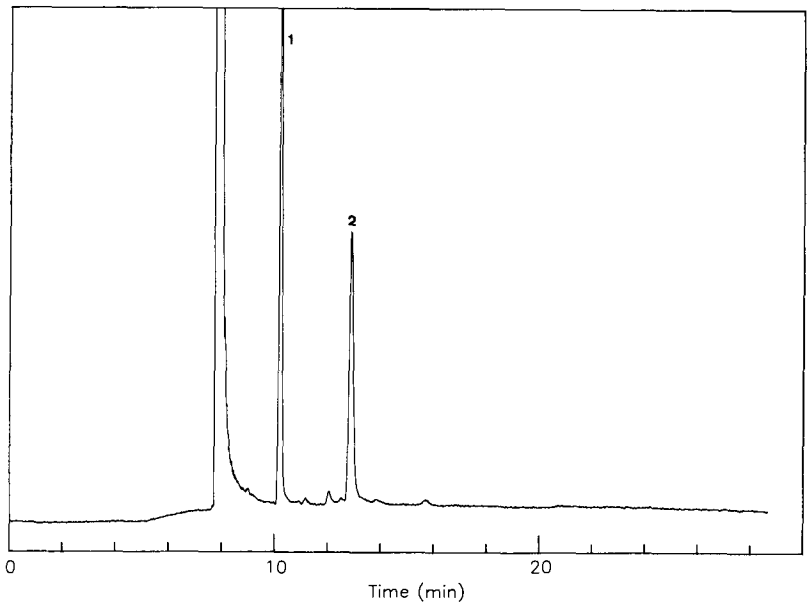

Fig. 10. Capillary SFC chromatogram of (1) 1-aminodecane and (2) 1-aminohexadecane. Conditions: same as in Fig. 8.

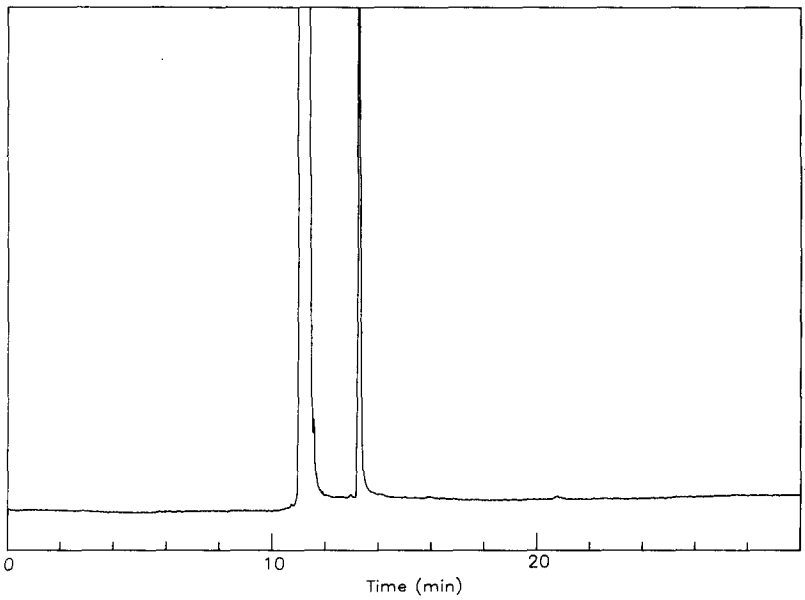

Fig. 11. Capillary SFC chromatogram of 3-diethylamino-1-propylamine. Conditions: same as in Fig. 8, except for 10 min inital-pressure hold time.

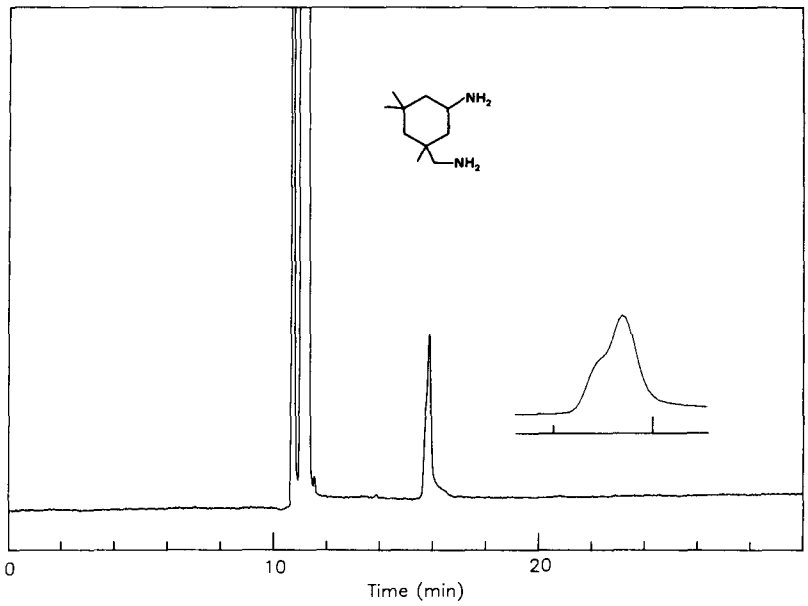

Fig. 12. Capillary SFC chromatogram of isophoron diamine, inset is expanded view. Conditions: same as in Fig. 11.

that point there was a rapid drop in the signal to baseline. This could indicate, together with the injection phenomenon noted above, that there is only limited miscibility of methanol in SF_6. This would hinder the use of methanol as a modifier in SF_6, although other alcohols may be more miscible. Isophoron diamine, an aliphatic diamine, eluted with slight peak tailing (Fig. 12). It was also barely separated into the *cis* and *trans* isomers as shown by the expanded area in Fig. 12. N-Methylethylenediamine apparently eluted but this could not be confirmed due to proximity to the solvent peak. Several other compounds were also eluted with excellent peak shape but are not shown here: anthraquinone, dioctylamine, and several trialkyl amines.

The following polar compounds, injected and pressure programmed at 10 bar min^{-1} from 50 to 400 bar at 100°C, were not eluted by SF_6 capillary SFC: 1,10-decanediol, 1,6-diaminohexane, 1,12-diaminododecane, diethylenetriamine, 4,4′-diaminodiphenylmethane, caffeine, and *p*-aminobenzoic acid. Since *m*-diaminobenzene eluted, it was surprising that 4,4′-diaminodiphenylmethane did not elute. It was assumed that since decanediol did not elute that a similar dicarboxylic acid also would not elute. The prediction by Hellgeth *et al.*[6] that SF_6 would be limited to only mono-functional polar compounds appears to be generally valid.

The column surface deactivation is critical to elution of polar compounds. Initially, an older column was used during the instrument setup. Injection of the aliphatic alcohols produced peaks wih some tailing, while no peaks were seen for injection of the aliphatic amines or acid. The column was replaced by one which was highly deactivated and the results described in this study were obtained. After three weeks of continuous use, the column was tested by gas chromatography for activity and was found to produce almost no tailing for diols or aliphatic amines, similar to the peak shapes initially reported by Woolley *et al.*[10]. SF_6 does not degrade this stationary phase or adversely affect column activity. It is probable that other common stationary phases are also resistant but should be tested.

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