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# Comparison of 1,1,1,2-tetrafluoroethane and carbon dioxide-based mobile phases for packed column supercritical fluid chromatography

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## Abstract

Highly polar, homogeneous mobile phases have a number of advantages over carbon dioxide-based mixed mobile phases for supercritical fluid chromatography. While these fluids have been demonstrated to have very high eluotropic strengths in capillary systems, their utility for packed columns lies in their ability to overcome the deleterious effects of residual silanol groups present on the bonded-phase surface. A particularly promising fluid, 1,1,1,2-tetrafluoroethane (HFC-134a), is characterized with respect to eluotropic strength, selectivity, efficiency and temperature effects. These results are compared to those obtained with carbon dioxide and methanol-modified carbon dioxide mobile phases on a silica column. HFC-134a displays different selectivities, efficiencies, eluotropic strength and temperature dependencies on retention than either of the two reference mobile phases. © 1997 Elsevier Science B.V.

*Keywords:* Mobile phase composition; Tetrafluoroethane; Naphthalenes

## 1. Introduction

The use of modifiers with carbon dioxide mobile phases on packed columns is nearly ubiquitous. Modifiers significantly enhance the eluotropic strength of a carbon dioxide mobile phase, thus allowing higher-molecular-mass and more polar analytes to be eluted from silica-based columns. In addition to their effect on eluotropic strength, many types of modifiers, especially alcohols, attenuate the deleterious hydrogen-bonding ability of residual silanols [1,2]. This produces more efficient, symmetrical peak profiles for polar analytes. While the preparation and use of modified-carbon dioxide

mobile phases is relatively straightforward, their use is not without problems. Addition of a modifier to a carbon dioxide mobile phase raises both the critical temperature and critical pressure of the resulting binary fluid mixture [3,4]. In addition, miscibility may become a problem under certain domains of temperature and pressure.

An alternative which has been explored for capillary supercritical fluid chromatography is the use of highly polar fluids which have reasonable critical temperatures and pressures [5–12]. Although a variety of polar fluids, such as ammonia and various chlorofluorocarbons, have been evaluated for use with capillary systems, problems with toxicity, corrosivity and environmental incompatibility have prevented these from gaining wide usage. Many fluoro-

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carbon and hydrofluorocarbon fluids have also been evaluated and have demonstrated very strong eluotropic strengths in capillary systems compared to carbon dioxide and methanol-modified carbon dioxide mobile phases [5–7].

Among the various hydrofluorocarbon fluids, 1,1,1,2-tetrafluoroethane (HFC-134a) appears to be an ideal candidate for use with both capillary and packed columns. It has a low critical pressure and a reasonable critical temperature compared to binary carbon dioxide-based mobile phases, thereby allowing for the potential of economical scalability for process separation applications. In addition, recovery of an analyte from a column effluent with a single component mobile phase is much more straightforward than from a binary mobile phase. More promising, though, is its strength as a hydrogen bond donor [7] and its high dipole moment [4]. A strong hydrogen bond-donating mobile phase may be very effective at attenuating the extraneous effects of residual silanols, while the high dipole moment should prove effective towards eluting polar compounds. HFC-134a is also comparable to pure SFC-grade carbon dioxide in both cost and UV transparency.

In this study, the effectiveness of HFC-134a as a mobile phase will be evaluated against both pure carbon dioxide and methanol-modified carbon dioxide. A bare silica column will be used in order to magnify the effects of the surface silanol interactions on analyte retention and efficiency. Probe solutes for this study will consist of a collection of well-characterized naphthalene derivatives [1,5–7] which vary by a single functional group so the effects of each type of functional group may be unambiguously determined.

## 2. Experimental

### 2.1. Chromatographic system

The chromatographic system used in this study was a Gilson SF3 system (Gilson, Middleton, WI, USA). Carbon dioxide and HFC-134a mobile phases were pumped with a Gilson model 308 pump with a thermostated head. Methanol modifier was pumped with a Gilson model 306 modifier addition pump.

Fixed loop injections (5  $\mu$ l) were made using a Gilson model 231XL sampling injector. Detection was accomplished at 210 nm using a Gilson model 117 variable wavelength UV detector with a 7- $\mu$ l high-pressure flow cell.

### 2.2. Column

The chromatographic column used in this study was a Zorbax RX-Sil column (150 $\times$ 4.6 mm I.D.; 5  $\mu$ m particles) obtained from Mac-Mod (Chadds Ford, PA, USA).

### 2.3. Chemicals

Various 1-substituted naphthalene derivatives were obtained from Aldrich (Milwaukee, WI, USA) and were reagent grade or better. Methanol was obtained from EM Science (Gibbstown, NJ, USA). SFC-grade carbon dioxide (without helium headspace) was obtained from Scott Specialty Gases (Plumsteadville, PA, USA). HFC-134a (SUVA Grade) was obtained from DuPont (Deepwater, NJ, USA).

### 2.4. Probe samples

Solutions of the 1-substituted naphthalene derivatives were prepared in methanol to a final concentration of 50  $\mu$ g/ml.

### 2.5. Critical point determinations

Since the chromatographic system used in this study employs high-pressure mixing of carbon dioxide and methanol at 25°C, the mole fraction of the modifier was calculated for these conditions. Carbon dioxide densities were determined using NIST REF-PROP v4.0 [13]. Mixture critical points were determined using the Chueh–Prausnitz manipulation of the Redlich–Kwong equation of state [14]. Critical parameters and acentric factors for methanol were obtained from literature references [4]. Table 1 summarizes the relevant parameters for the mobile phases used in this study [13].

Table 1  
Mobile phase critical parameters

Mobile phase	$T_{bp}$ (°C)	$T_c$ (°C)	$P_c$ (bar)	Polarizability (cm <sup>3</sup> /mol)	Dipole (D)
Carbon dioxide	–56.2	30.9	73.8	14.0	1.46 <sup>a</sup>
Carbon dioxide–methanol (95:5)	n/a	49.8	101.7	n/a	n/a
HFC-134a	–26.2	101.2	40.7	13.7	2.06

<sup>a</sup> Net dipole moment for carbon dioxide is 0.00 by virtue of molecular symmetry. Effective dipole moment is 1.46 D. Mole percent of methanol in carbon dioxide at 100 bar and 25°C is 6.53 mol.% [14].

### 3. Results and discussion

#### 3.1. Stationary phase stability

One of the most important aspects regarding the use of HFC-134a with silica-based supports is the issue of system stability. Earlier citations suggest that halogenated mobile phases may degrade on silica supports [15]. To evaluate this potential problem, 1-naphthaldehyde and 1-naphthol were chromatographed on the silica support using carbon dioxide. These analytes, with their strong hydrogen bonding ability, should be sensitive probes of changes in the surface silanol chemistry. Following the injections using carbon dioxide, the mobile phase was then changed to HFC-134a and the injections repeated. The mobile phase was then switched back to carbon dioxide and the analytes reinjected. Table 2 shows that when this procedure was performed at 125°C and 200 bar, no significant change in retention was evident between the initial and final injections in pure carbon dioxide. This same experiment was performed under much more aggressive conditions (200°C and 200 bar) with no significant hysteresis. The small change in retention may be due more to differences in water content of the two mobile phases

than any surface modification [16,17]. Extended use of this system with HFC-134a at elevated temperatures and pressures showed no sign of stationary phase deterioration.

#### 3.2. Relative retention

The eluotropic strength of HFC-134a was compared to that of carbon dioxide under two sets of operating conditions. Table 3 shows that at 50°C and 200 bar, HFC-134a elutes most analytes much more readily than carbon dioxide. While most of the capacity factors obtained using HFC-134a are too low for practical separations, they illustrate the relative eluotropic strength of this mobile phase. Under these conditions, the HFC-134a mobile phase is subcritical while the carbon dioxide mobile phase is supercritical. Carbon dioxide is unable to elute highly polar derivatives such as 1-naphthylamine and 1-naphthylmethylamine, although these derivatives are readily eluted using HFC-134a. Neither of these analytes should form carbamates with carbon dioxide under these conditions due to their high  $pK_b$  values, thus negating this as a possibility for their lack of elution [18]. In general, the hydrogen bond donor/acceptor derivatives are the only derivatives which

Table 2  
Silica stationary phase stability

Mobile phase	$k'$	
	1-Naphthaldehyde	1-Naphthol
125°C/200 bar		
carbon dioxide before HFC-134a	4.68	7.18
HFC-134a	0.36	0.80
carbon dioxide after HFC-134a	4.66	7.15
200°C/200 bar		
carbon dioxide before HFC-134a	2.81	3.72
HFC-134a	0.33	0.49
carbon dioxide after HFC-134a	2.74	3.70

Table 3  
Analyte retention on silica capacity factor data

Naphthalene derivative	50°C/200 bar		200°C/100 bar		
	CO <sub>2</sub>	HFC-134a	CO <sub>2</sub>	CO <sub>2</sub> /MeOH	HFC-134a
<i>Weak hydrogen bond acceptors</i>					
H	2.26	0.04	1.19	1.06	0.25
F	2.42	0.02	1.25	1.17	0.22
Cl	2.21	0.06	2.08	1.92	0.38
Br	2.32	0.08	2.75	2.44	0.54
I	4.22	0.12	3.84	3.25	0.63
CH <sub>3</sub>	2.30	0.05	1.77	1.50	0.32
CH <sub>2</sub> CH <sub>2</sub>	4.61	0.03	2.25	1.83	0.32
C <sub>6</sub> H <sub>5</sub>	2.38	0.13	8.31	5.83	0.99
<i>Strong hydrogen bond acceptors</i>					
NO <sub>2</sub>	4.43	0.25	7.77	4.98	1.09
CH <sub>3</sub> O	2.38	0.15	3.51	2.38	0.53
CH <sub>3</sub> CH <sub>2</sub> O	2.29	0.13	3.84	2.58	0.56
(CO)H	2.31	1.15	8.16	3.54	1.36
NCS	3.28	0.19	5.82	4.63	0.74
CN	4.59	0.11	8.37	4.08	1.17
CH <sub>2</sub> CN	3.54	1.14	20.16	6.63	2.19
OCOCH <sub>3</sub>	2.05	0.08	11.11	6.15	1.34
OCOCH <sub>2</sub> CH <sub>3</sub>	1.54	0.08	12.41	6.08	1.26
OCOCH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>	1.28	0.06	14.97	6.00	1.27
<i>Hydrogen bond donor/acceptors</i>					
CH <sub>2</sub> OH	19.66	13.72	>74	4.82	3.24
CH <sub>2</sub> CH <sub>2</sub> OH	28.38	>16	>74	5.76	4.41
NH <sub>2</sub>	>30	5.07	>74	2.69	1.85
N(CH <sub>3</sub> ) <sub>2</sub>	18.00	5.65	>74	2.63	1.76
CH <sub>2</sub> NH <sub>2</sub>	>30	>16	>74	3.50	1.48
OH	5.41	3.02	>74	6.33	1.71

show any significant retention using HFC-134a under these conditions.

At 200°C and 100 bar, significant differences in eluotropic strength are still observed even though all three of the mobile phases are supercritical. Carbon dioxide is unable to elute the more polar hydrogen bond donor/acceptor derivatives ( $k' > 74$ ). Addition of 5% (v/v) methanol to the carbon dioxide mobile phase remedies this problem for the donor/acceptor analytes and has the general effect of decreasing retention for all of the other analytes as well. Most of the decrease in retention is relatively small, considering that mobile phase strength is related to the logarithm of the capacity factor [19]. The hydrogen bond donor/acceptor derivatives are the exception, showing proportionally larger decreases in retention

upon addition of methanol to the mobile phase. The amine derivatives are readily eluted, confirming their stability in carbon dioxide-based mobile phases under these conditions. As observed previously, methanol modifier acts to efficiently suppress the hydrogen bonding ability of the stationary phase [1]. An interesting observation is the reversal of elution order for the homologous naphthyl esters with the methanol-modified mobile phase compared to carbon dioxide alone.

When these derivatives are chromatographed using HFC-134a at 200°C and 100 bar, retention of all the various probe analytes decreases significantly compared to either carbon dioxide or methanol-modified carbon dioxide. As observed at 50°C, the strong hydrogen bond acceptor derivatives show relatively

long retention times compared to the other derivatives. All of the hydrogen bond donor/acceptor derivatives are readily eluted. Interestingly, the selectivity for the naphthyl esters is different from either

of the two other mobile phases. Fig. 1 compares the elution profiles for 1-phenylnaphthalene using HFC-134a and methanol-modified carbon dioxide. Not only does HFC-134a produce efficient peak profiles,

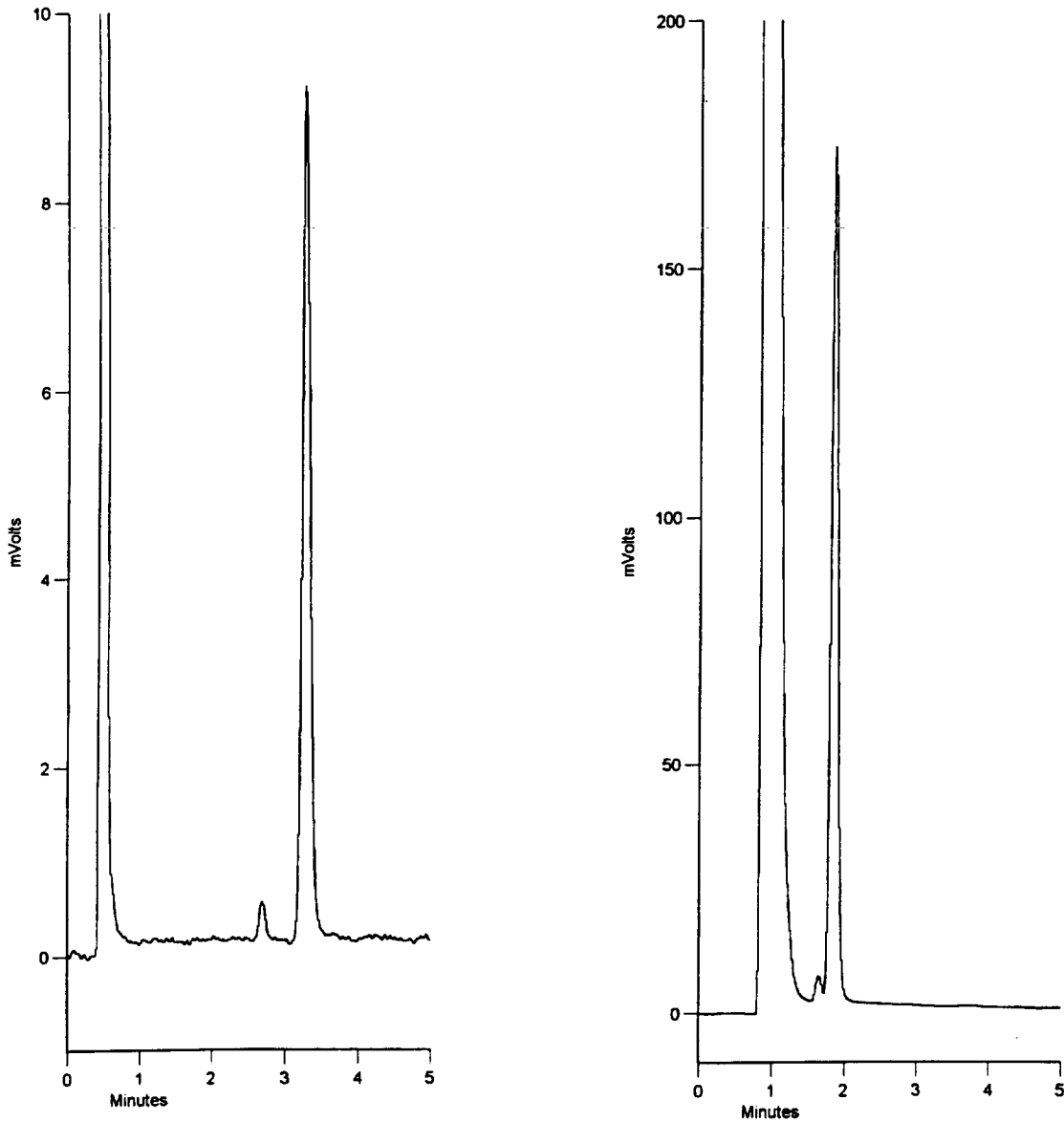


Fig. 1. Chromatograms of 1-phenylnaphthalene eluted with: (a, left) carbon dioxide–methanol (95:5, v/v), and (b, right) HFC-134a; at 100 bar/200°C. Injection volumes, solute concentrations and detector settings were identical for these two separations. Detection wavelength was 210 nm.

but the improvement in signal-to-noise is approximately 20-fold over the methanol-modified mobile phase.

### 3.3. Selectivity

The differences in mobile phase selectivities warrant further analysis. An attempt was made to characterize the relative selectivities using linear solvation energy relationship (LSER; solvatochromic) techniques [1,7,20]. This type of analysis was unsuccessful due to the significant contribution from adsorptive interactions to the overall retention process. Current LSER analysis techniques do not work well when the retentive process deviates significantly from a partition-type mechanism.

A qualitative comparison of mobile phase selectivities may be made by comparing the capacity factors obtained using HFC-134a versus those obtained using the carbon dioxide-based mobile phases. Fig. 2 shows the correlation obtained at 50°C and 200 bar for HFC-134a and carbon dioxide. For this comparison, hydrogen bond donor/acceptor derivatives were not included. The difference in functional group selectivity between these two systems is substantial. Weak hydrogen bond-accepting derivatives (halogen, alkyl and aryl derivatives) show proportionally lower retention using HFC-134a than hydrogen bond acceptor derivatives. Among the

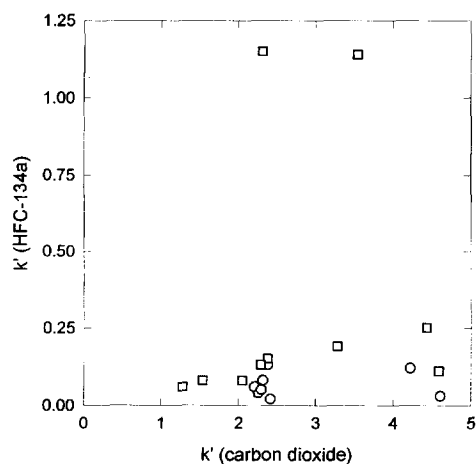


Fig. 2. Selectivity comparison between HFC-134a and carbon dioxide for: (○) weak hydrogen bond acceptors; and (□) strong hydrogen bond acceptor derivatives on silica at 50°C and 200 bar.

strong hydrogen bond-accepting derivatives, a large difference in functional group selectivity is evident, as indicated by the relatively long retention times for 1-naphthaldehyde and 1-naphthylacetonitrile. It is uncertain how many of these differences in selectivity are due to the fact that under these conditions, HFC-134a is subcritical while carbon dioxide is supercritical.

In Fig. 3, the relative selectivities are compared under conditions where both HFC-134a and carbon dioxide are supercritical. Again, hydrogen bond donor/acceptor derivatives were not included. Under these conditions, fewer differences in functional group selectivity are evident. Strong hydrogen bond acceptor derivatives show slightly more selectivity differences than other derivatives, but much less selectivity than observed at 50°C. In Fig. 4, HFC-134a is compared to methanol-modified carbon dioxide under the same temperature and pressure conditions. Hydrogen bond donor/acceptor derivatives are included in this plot since both mobile phases elute all of these derivatives. It is clear that there is a significant difference in functional group selectivity between these mobile phases with only the weak hydrogen bond-accepting derivatives showing any sort of retention correlation between the two mobile phases.

These selectivity plots suggest that, under super-

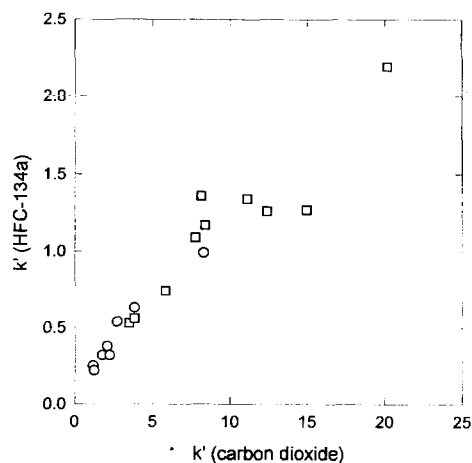


Fig. 3. Selectivity comparison between HFC-134a and carbon dioxide for: (○) weak hydrogen bond acceptors; and (□) strong hydrogen bond acceptor derivatives on silica at 200°C and 100 bar.

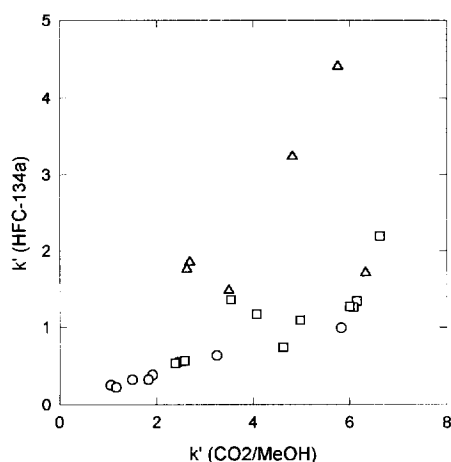


Fig. 4. Selectivity comparison between HFC-134a and methanol-modified carbon dioxide for: (○) weak hydrogen bond acceptors; (□) strong hydrogen bond acceptor; and (△) amine and hydroxyl derivatives on silica at 200°C and 100 bar.

critical conditions, HFC-134a behaves in a manner similar to carbon dioxide with respect to weak hydrogen bond accepting and some of the strong hydrogen bond-accepting derivatives. That is, HFC-134a, with its strong hydrogen bond donor ability, does not preferentially elute hydrogen bond acceptor derivatives. While formation of a strong hydrogen-bonding interaction is expected to occur in the mobile phase, this effect may be offset by some mechanism which results in increased retentivity. This may occur by virtue of a layer of adsorbed HFC-134a at the chromatographic surface under supercritical conditions which enhances retention of hydrogen bond acceptor derivatives by making the Gibbs layer substantially stronger in hydrogen bond-donating ability [21,22]. This surface layer may be relatively impervious to hydrogen bond donor derivatives and prevent excessive retention (Table 3).

Similar conclusions may be drawn when compar-

ing HFC-134a versus methanol-modified mobile phases. Here, the main difference is that hydrogen bond donor/acceptor derivatives are proportionally more retained in HFC-134a. A methanol layer at the chromatographic surface may be more stable than a layer of HFC-134a due to its ability to self-associate via intermolecular hydrogen-bonding interactions. This stabilized layer may be more effective at blocking the surface silanol functional groups than the HFC-134a layer, which does not have the ability to self-associate. These observations are consistent with earlier observations with modified carbon dioxide mobile phases wherein self-associating modifiers were more effective at blocking the extraneous effects of residual silanols than modifiers which are not capable of self-association [1].

### 3.4. Efficiency

A comparison of the relative efficiencies for HFC-134a versus carbon dioxide-based mobile phases is given in Table 4. Three derivatives were chosen to represent the three major types of derivatives: weak hydrogen bond acceptor, strong hydrogen bond acceptor and hydrogen bond acceptor/donor functional groups. At 50°C and 200 bar, HFC-134a showed inferior reduced plate height values for the phenyl and isothiocyanate derivatives compared to carbon dioxide. 1-Naphthol showed a significant improvement in efficiency compared to carbon dioxide, although neither mobile phase produces desirable reduced plate heights.

At 200°C and 100 bar, the reduced plate heights for the phenyl and isothiocyanate derivatives were larger using HFC-134a than those obtained with carbon dioxide or methanol-modified carbon dioxide. 1-Naphthol showed better efficiencies with HFC-134a than with either of the other mobile phases.

Table 4  
Analyte efficiency on silica reduced plate height data

Derivative	50°C/200 bar		200°C/100 bar		
	CO <sub>2</sub>	HFC-134a	CO <sub>2</sub>	CO <sub>2</sub> /MeOH	HFC-134a
C <sub>6</sub> H <sub>5</sub>	7.1	11.0	21.9	12.1	26.4
NCS	6.0	12.9	18.8	17.8	26.9
OH	134.2	63.6	eno	70.0	27.9

eno, elution not observed.

These observations support the earlier speculation that HFC-134a is effective at blocking the hydrogen bond-accepting ability of the silica surface. The uniformity of reduced plate heights, especially at supercritical conditions using HFC-134a, suggests that the relatively high reduced plate heights may result from linear velocity effects [23]. Under these conditions, HFC-134a has a viscosity of 380 microPoise (at a density of 0.3892 g/ml) while carbon dioxide has a viscosity of 277 microPoise (at a density of 0.1224 g/ml) [13]. In general, higher viscosity mobile phases show better efficiencies at lower linear velocities, although it is uncertain where the optimum linear velocity for HFC-134a lies with respect to the operating conditions employed in these studies.

### 3.5. Temperature effects

The effect temperature has on retention was investigated for two derivatives at 100 bar. Fig. 5 shows that, over the temperature range of 100–200°C, retention decreases as temperature increases using pure carbon dioxide for both derivatives. This behavior is typical for these types of systems and represents the domain where the analyte heat of adsorption on the stationary phase is higher than the analyte's ideal heat of solution [24–26]. Addition of methanol to the mobile phase results in similar behavior, but with lower capacity factors. The slopes are slightly different due to differences in heats of adsorption and solution [26].

The data obtained using HFC-134a is quite different than that of the other mobile phases. Both analytes show increasing retention as a function of temperature. It appears that these temperatures are in the range where the analyte heat of adsorption is smaller than the ideal heat of solution. Again, this observation is consistent with the formation of an adsorbed layer of HFC-134a at the silica surface. Within this temperature range, there is no apparent point where the energies balance and retention begins to decrease as the balance shifts towards exothermic adsorption. Whether this indicates that the analyte heat of adsorption using HFC-134a is smaller than that for carbon dioxide-based mobile phases for a given set of conditions or whether the

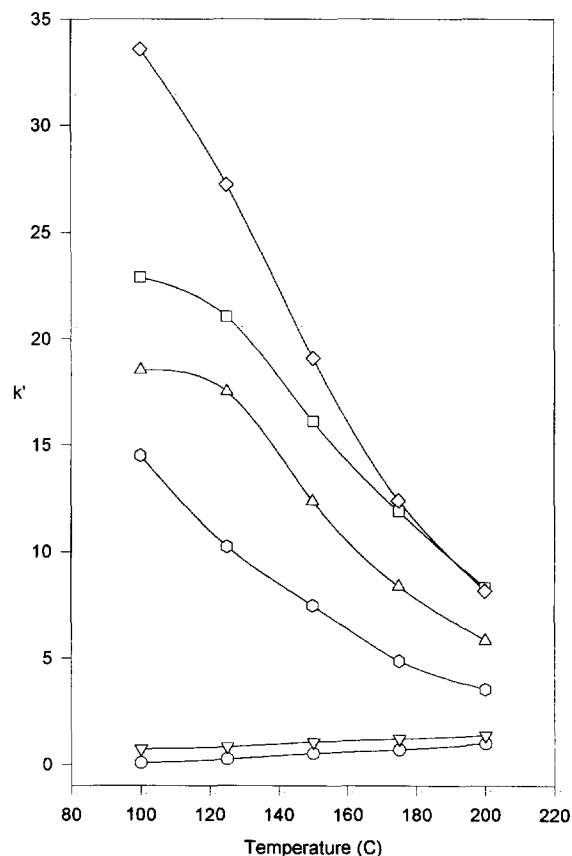


Fig. 5. Effect of temperature on retention on silica at 100 bar for: (□) 1-phenylnaphthalene in carbon dioxide; (△) 1-phenylnaphthalene in methanol-modified carbon dioxide; (○) 1-phenylnaphthalene in HFC-134a; (◇) 1-naphthaldehyde in carbon dioxide; (◊) 1-naphthaldehyde in methanol-modified carbon dioxide; and (▽) 1-naphthaldehyde in HFC-134a.

heat of solution is larger with HFC-134a, or both, remains to be determined.

What may be determined is that the shift to a higher critical temperature for HFC-134a has little to do with this observed behavior. Fig. 6 shows the same data plotted against reduced temperature ( $T/T_R$ ). While the data do not all completely overlap, it is readily apparent that the behavior differs irrespective of reduced temperature. Retention is clearly increasing in the reduced-temperature domain where retention in methanol-modified carbon dioxide is decreasing.



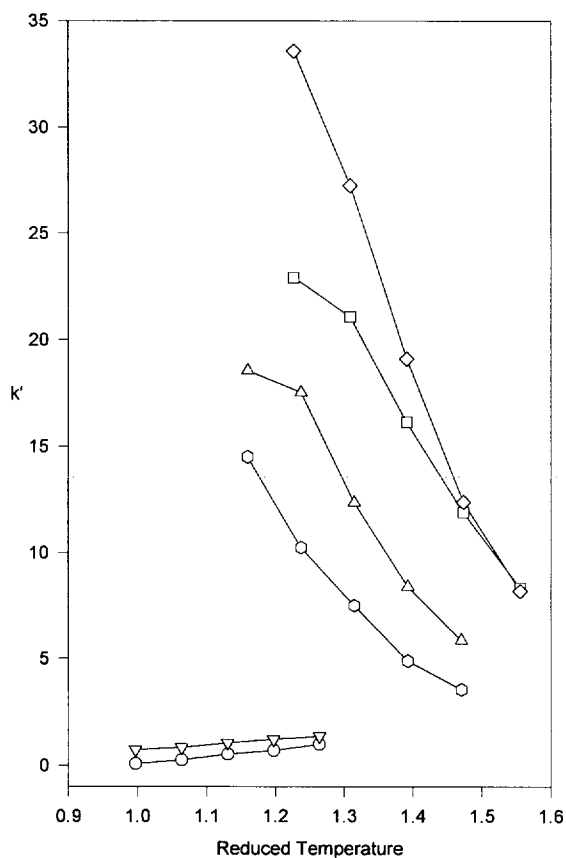


Fig. 6. Effect of reduced temperature on retention on silica at 100 bar for: (□) 1-phenyl naphthalene in carbon dioxide; (△) 1-phenyl naphthalene in methanol-modified carbon dioxide; (○) 1-phenyl naphthalene in HFC-134a; (◇) 1-naphthaldehyde in carbon dioxide; (○) 1-naphthaldehyde in methanol-modified carbon dioxide; and (▽) 1-naphthaldehyde in HFC-134a.

#### 4. Conclusions

HFC-134a was demonstrated to be a useful alternative to carbon dioxide-based mobile phases for packed-column chromatography on silica supports. The elutropic strength of HFC-134a was shown to be much higher than carbon dioxide-based mobile phases for all types of analytes. Hydrogen bond-accepting derivatives showed higher relative retention times than other derivatives, regardless of temperature. The selectivity obtained using HFC-134a differed significantly from either carbon dioxide or methanol-modified carbon dioxide, suggesting

its utility as an alternative mobile phase for method optimization. Peak reduced plate heights obtained using HFC-134a were superior for hydrogen bond donor/acceptor derivatives, but inferior to carbon dioxide-based mobile phases for other types of derivatives. Further investigation will determine the source of the higher reduced plates for these compounds. HFC-134a also displayed rather unique temperature dependencies on retention compared to carbon dioxide-based mobile phases.

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