

# Supercritical and Subcritical Fluid Chromatography on a Chiral Stationary Phase for the Resolution of Phosphine Oxide Enantiomers

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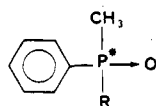
The super- and subcritical fluid chromatography separations of five enantiomeric pairs of phosphine oxides are described. The stationary phase is a classical Pirkle's phase obtained by covalent bonding of (*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine on an aminopropyl silica gel. Mobile phases are carbon dioxide, whose polarity is close to hexane, with various polar modifiers consisting of pure alcohols (MeOH, EtOH, 2-PrOH) or of alcohol-water 95:5 (v/v) mixtures. Obtained separations are very fast (less than 2 min in certain conditions) and resolution is very high ( $\approx 5$ ). The influence of temperature, the nature of the alcohol, and the addition of water to the mobile phase are examined. Better results are obtained at low temperature (subcritical conditions) and with a low polarity alcohol (2-propanol) mixed with water (95:5 v/v). Some possible explanations of these phenomena are given.

Liquid chromatography (LC) has recently received considerable attention as an analytical technique for the separation of enantiomers. The chiral stationary phase obtained by covalent bonding of (*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine on a bonded aminopropyl silica gel, first described by Pirkle et al. (1-3), allows successful enantiomeric resolution of various compounds. In most of these separations, the mobile phase is a nonpolar solvent, such as hexane, with a polar modifier, such as 2-propanol, added in small quantities, usually less than 25% by volume. A characteristic of these separations is that the analysis time may be relatively long, between 10 min and several hours (1-4).

It seemed interesting to us to use carbon dioxide whose polarity is close to that of hexane, in the super- or subcritical state, with alcohols as polar modifiers for enantiomeric separations on the Pirkle phase. The low viscosity of carbon dioxide ( $10^{-4}$  to  $10^{-5}$  Pa·s), 5-20 times lower than that of classical LC mobile phases, and, consequently, the fast diffusion of solutes (binary diffusion coefficients are about 5-20 times greater in  $\text{CO}_2$  than in LC solvents) would have as consequence a decrease in the separation time by at least a factor of 5 without any loss in efficiency (5, 6).

As an example of enantiomeric separations by super- and subcritical fluid chromatography (SFC), we chose phosphine oxides, which are chiral precursors for chiral phosphine ligands used for the synthesis of catalysts of the Wilkinson type for the homogeneous phase catalytic hydrogenation of prochiral substrates.

The chemical structure of these phosphine oxides can be represented as follows, with various substituents R.



## EXPERIMENTAL SECTION

**Apparatus.** Its design has been described elsewhere (5-7). The carbon dioxide, which is contained in a container with an eductor tube, supplies the pump of a Varian 5500 chromatograph. The cooling of the pump head is necessary to improve the pump efficiency. It is in close thermal contact with a clamp-on heat exchanger through which cold ethanol is circulated. Unfortunately, under 55 bar pressure, it is impossible to mix  $\text{CO}_2$  and liquid solvents with the proportioning valves of the Varian chromatograph, and the polar modifier was added with a Gilson pump (Model 302), which is able to pump at low flow rates (less than  $5 \mu\text{L}\cdot\text{min}^{-1}$ ). Temperature control was achieved with a constant temperature water bath (Tamson Type TX 9). A Varian UV 200 spectrophotometer was used with a special detection cell that had been modified to withstand pressures up to 350 bar. The pressure was controlled by a manually adjustable back-pressure regulator (Tescom Model 26-3220-24004).

**Reagents and Chromatographic Column.** Stainless-steel columns ( $100 \times 4.6$  mm i.d.) were packed using conventional technique with  $10 \mu\text{m}$  chiral covalently bonded silica gel (Lichrosorb  $\text{NH}_2$ , Merck). The phosphine oxides and stationary phase syntheses have been described elsewhere (1-4).

## RESULTS AND DISCUSSION

Chromatographic retention data for subcritical conditions at  $23^\circ\text{C}$  (the critical temperature of  $\text{CO}_2$  is  $31.0^\circ\text{C}$ ) compared to the liquid conditions (mixtures hexane-2-propanol) for five phosphine oxides are given in Table I.

The analysis time in classical LC is much larger than that in SFC. The resolution per unit of time, which allows a comparison of results obtained with both methods, is much greater in SFC than in LC for all phosphine oxides. It is interesting to note that in SFC, the addition of water to the modifier increases both selectivity and efficiency. As all the solutes examined had a similar behavior, one of them, the methyl(4-methylnaphthyl)phenylphosphine oxide, was chosen to study the influence of the different parameters (temperature, pressure, density and nature of the modifier) on selectivity, efficiency, and resolution.

The SFC enantiomeric separation of this racemate within a very short analysis time ( $<90$  s) (a) or with a high resolution ( $\approx 3.5$ ) (b) is shown in Figure 1.

**Retention and Selectivity.** As a general rule, there are two ways of influencing the retention:

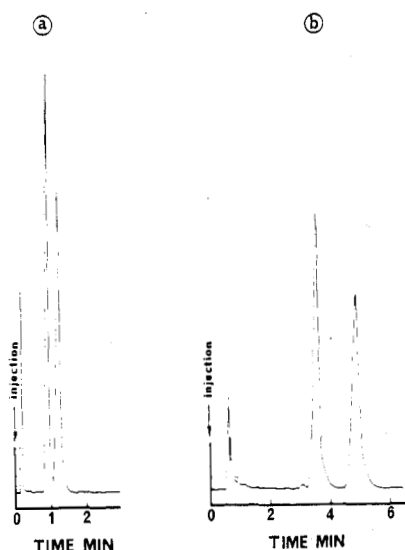
The modification of the  $\text{CO}_2$  physical state: An increase in the carbon dioxide density,  $\rho$ , results in enhanced solute solubilization and in solute retention decrease. The mobile phase density is related to pressure in a fairly predictable way.

The addition of a polar solvent (alcohol) to the carbon dioxide: Figure 2 shows, respectively, the influence of the modifier content on the solute retention and on the selectivity for three different pure alcohols and alcohol-water mixtures dissolved in carbon dioxide. The polarities of these modifiers according to Rohrschneider (8) are water (10.2) > methanol

**Table I. Structure and Retention Data for Five Racemic Phosphine Oxides Resolved on a (*R*)-*N*-(3,5-Dinitrobenzoyl)phenylglycine Stationary Phase by Supercritical Fluid Chromatography and Liquid Chromatography**

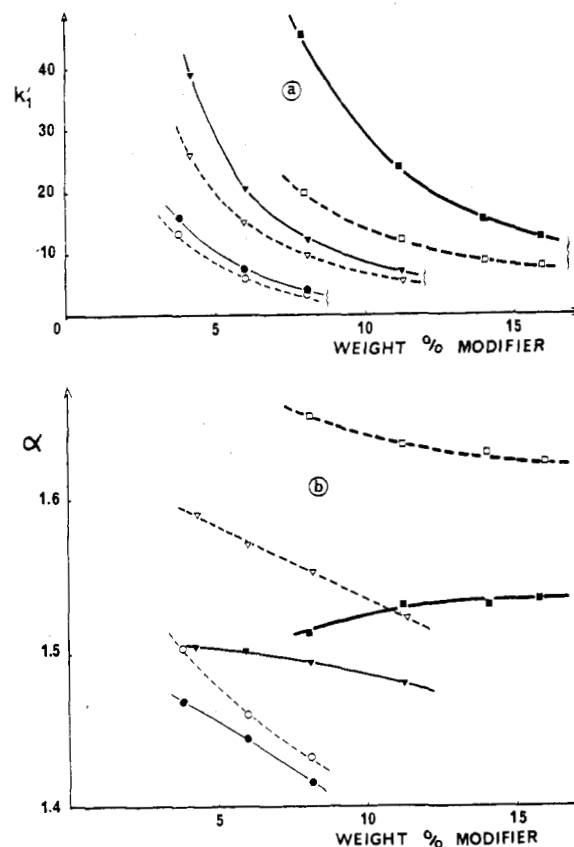
solute R	$\lambda^a$	SFC <sup>c</sup>										LC <sup>h</sup> hexane-2-propanol					
		methanol (6% w/w in CO <sub>2</sub> )					methanol-H <sub>2</sub> O (95:5 v/v) (6% w/w in CO <sub>2</sub> )										% modifier (w/w)
		$k_1'^b$	$\alpha^c$	$R_s^d$	$t^e$	$R_s/t^f$	$k_1'$	$\alpha^c$	$R_s^d$	$t^e$	$R_s/t^f$	$k_1'^b$	$\alpha^c$	$R_s^d$	$t^e$	$R_s/t^f$	
1-(4-methylnaphthyl)	280	7.54	1.43	3.48	5.89	0.59	6.04	1.45	3.69	4.86	0.76	14.0	1.49	4.0	41.2	0.097	11.7
1-(2-methoxynaphthyl)	280	8.16	1.32	2.57	5.86	0.44	6.78	1.36	2.84	5.09	0.56	6.1	1.39	3.4	16.3	0.21	22.9
9-phenanthryl	256	16.0	1.38	3.49	11.5	0.30	12.6	1.41	3.50	9.44	0.37	9.4	1.45	3.9	24.0	0.16	22.9
1-naphthyl	280	5.76	1.31	2.45	4.27	0.57	5.04	1.32	2.66	3.83	0.69	9.3	1.34	3.4	22.3	0.15	17.4
1-(2-methylnaphthyl)	256	4.3	1.16	1.32	3.05	0.43	2.38	1.16	1.38	2.69	0.51	8.9	1.19	2.0	21.9	0.095	11.7

<sup>a</sup>Detection wavelength (nm). <sup>b</sup>Capacity factor of the first eluted enantiomer. <sup>c</sup>Selectivity between the enantiomers. <sup>d</sup>Resolution. <sup>e</sup>Analysis time (min) [retention time of the last eluted solute]. <sup>f</sup>Resolution per unit of time (min<sup>-1</sup>). <sup>g</sup>SFC: Flow rate for CO<sub>2</sub>, 3.5 mL·min<sup>-1</sup>; modifier, 0.25 mL·min<sup>-1</sup>; column, 10 × 0.46 cm i.d.; subcritical conditions, 20 °C, 260 bar, CO<sub>2</sub> density 0.97 g·cm<sup>-3</sup>. <sup>h</sup>LC: Mobile phase, hexane-2-propanol; flow rate, 2 mL·min<sup>-1</sup>; column, 25 × 0.46 cm i.d.; temperature, 40 °C.



**Figure 1.** Chiral separation of methyl-1-(4-methylnaphthyl)phenylphosphine oxide on Pirkle's phase with (a) a high speed or with (b) a high resolution: column, 100 × 4.6 mm i.d.; detection, UV at 280 nm; stationary phase, 10  $\mu$ m aminopropyl Lichrosorb NH<sub>2</sub> silica bonded with (*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine. (a) Mobile phase: CO<sub>2</sub>-methanol-H<sub>2</sub>O (91.8-7.6-0.51) (w/w). Flow rates: CO<sub>2</sub>, 10 mL·min<sup>-1</sup>; methanol-H<sub>2</sub>O (95:5) v/v, 1.0 mL·min<sup>-1</sup>. Inlet pressure, 275 bar; outlet pressure, 230 bar; temperature, 20 °C. (b) Mobile phase: CO<sub>2</sub>-methanol-H<sub>2</sub>O (94-5.63-0.37) (w/w). Flow rates: CO<sub>2</sub>, 3.5 mL·min<sup>-1</sup>; methanol-H<sub>2</sub>O (95:5) v/v, 0.25 mL·min<sup>-1</sup>. Inlet pressure, 270 bar; outlet pressure, 255 bar; temperature, 23 °C.

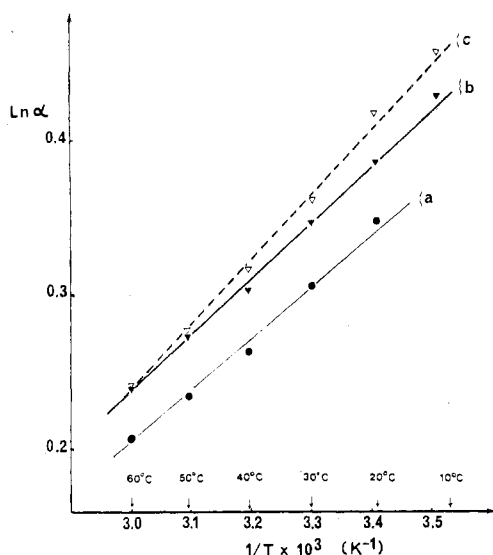
(5.1) > ethanol (4.3) > 2-propanol (3.9). The modifier molecule competes with the solute on the specific sites of the stationary phase. Therefore, the higher the modifier concentration, the lower the retention. In addition, the less polar the alcohol, the greater the capacity factors and the selectivities. These results are in good agreement with those published by Horvath (9) for classical liquid chromatography. A small addition of water (5% in the modifier, that is, from 0.2% to 0.5% in the mobile phase) greatly decreases the solute retention (Figure 2a). As in adsorption chromatography, this effect is much more significant when the modifier is less polar (that is, when the modifier polarity is greatly lower than that of water (10)). Addition of water increases the selectivity (Figure 2b). We think that water adsorption on the residual silanol groups decreases their adsorption energy (11) and results in an enhanced chiral recognition of the stationary phase due to a minimization of the nonspecific polar adsorption. Figure 3 shows the variation of log  $\alpha$  vs. the temperature reciprocal ( $K^{-1}$ ). At a given temperature, the selectivity values remain constant (within 1%) when the carbon dioxide pressure varies



**Figure 2.** Influence of the modifier concentration on the retention of the first eluted enantiomer of the methyl-1-(4-methylnaphthyl)phenylphosphine oxide (a) and on the selectivity (b) at a temperature of 20 °C: pressure, 260 bar; column and stationary phase as in Figure 1; flow rate of CO<sub>2</sub>, 3.5 mL·min<sup>-1</sup>; detection, UV at 280 nm; modifier (●) methanol, (○) methanol-H<sub>2</sub>O (95:5) (v/v), (▼) ethanol, (▽) ethanol-H<sub>2</sub>O (95:5) (v/v), (■) 2-propanol, (□) 2-propanol-H<sub>2</sub>O (95:5) (v/v).

between 60 and 270 bar. Since the pressure and density are linked at a given temperature, the influence of the CO<sub>2</sub> density  $\rho$  on the selectivity is small compared to that of temperature and of the nature of the modifier. As is illustrated in Figure 3, these two last parameters can induce great variations of selectivity: from a thermodynamic point of view, the lower the temperature, the higher the selectivity. The linear dependence of log  $\alpha$  on the reciprocal of the temperature can be expressed as

$$\ln \alpha = \ln \frac{K_2}{K_1} = -\frac{\Delta(\Delta G^\circ_i)}{RT} \quad (1)$$



**Figure 3.** Effect of the temperature on the selectivity between the enantiomers of the methyl-1-(4-methylnaphthyl)phenylphosphine oxide for various modifiers: mobile phase (a) CO<sub>2</sub>-methanol (91.8-8.2) (w/w), (b) CO<sub>2</sub>-ethanol (91.9-8.1) (w/w); (c) CO<sub>2</sub>-ethanol-H<sub>2</sub>O (91.8-7.68-0.51) (w/w); flow rates (a) CO<sub>2</sub>, 3.5 mL·min<sup>-1</sup>; methanol, 0.35 mL·min<sup>-1</sup>; (b) CO<sub>2</sub>, 3.5 mL·min<sup>-1</sup>; ethanol, 0.35 mL·min<sup>-1</sup>; (c) CO<sub>2</sub>, 3.5 mL·min<sup>-1</sup>; ethanol-H<sub>2</sub>O (95:5) v/v, 0.35 mL·min<sup>-1</sup>. Each selectivity point is a mean of the selectivities at various pressures (60-270 bar).

where  $K_i$  is the distribution coefficient of the solute  $i$  between the two phases and  $\Delta G^\circ_i$  is the net free energy of distribution of the enantiomers between the two phases. Introducing  $\Delta G^\circ_i = \Delta H^\circ_i - T\Delta S^\circ_i$ , we can write

$$\ln \alpha = \frac{\Delta(\Delta S^\circ_i)}{R} - \frac{\Delta(\Delta H^\circ_i)}{RT} \quad (2)$$

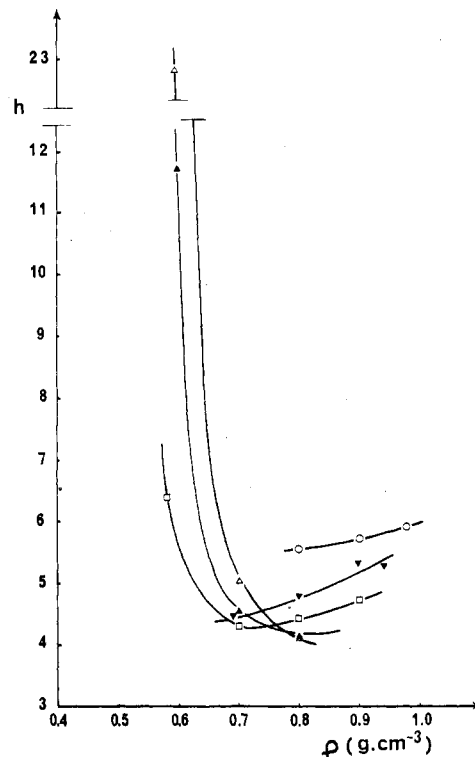
where  $\Delta H^\circ_i$  and  $\Delta S^\circ_i$  are, respectively, the enthalpy and entropy variations associated with the retention process of solute  $i$ .

The slope of the curve varies if water is present in the modifier. As the slope is related to the enthalpic term, the addition of water probably entails a modification in the retention mechanism.

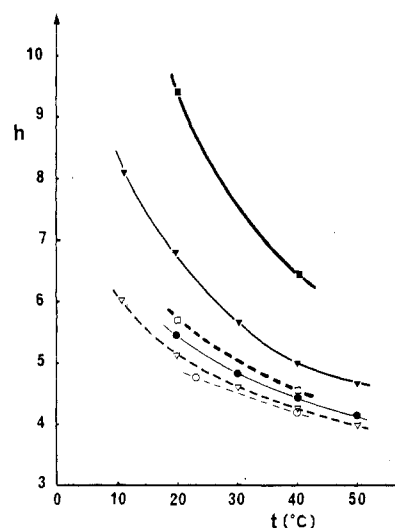
**Kinetics.** Supercritical and subcritical fluids in chromatography show faster kinetics than liquid phases. The fast solute diffusion in the carbon dioxide allows the use of high flow rates without any loss in efficiency. Even under subcritical conditions, the solute diffusion coefficients  $D_m$  are still higher than those found in liquids (for naphthalene at 20 °C,  $D_m = 9.3 \times 10^{-9} \text{ m}^2\cdot\text{s}^{-1}$  in subcritical CO<sub>2</sub> at a density of 0.9 g·cm<sup>-3</sup> (12, 13) and  $D_m = 3 \times 10^{-9} \text{ m}^2\cdot\text{s}^{-1}$  in hexane).

In a supercritical fluid, the compressibility is a crucial factor, and therefore the efficiency per unit of time can vary greatly with the CO<sub>2</sub> physical state. Therefore, it is necessary to quantify the influence of different parameters, such as temperature, density, and the nature of the modifier on the efficiency.

**Influence of the CO<sub>2</sub> Physical State.** Figure 4 shows plots of the reduced plate height  $h$  vs. the CO<sub>2</sub> density at various temperatures ( $h = H/d_p$  where  $H$  is the height equivalent to a theoretical plate and  $d_p$  is the particle diameter). At high density ( $\rho \geq 0.8 \text{ g}\cdot\text{cm}^{-3}$ ), where the CO<sub>2</sub> compressibility  $K_T$  is low ( $K_T = (1/\rho)(\partial P/\partial \rho)_T < 2 \times 10^{-3} \text{ bar}^{-1}$ ), efficiency increases with temperature and slightly decreases with the density  $\rho$ . These two tendencies can be explained by the variations of the solute diffusion in the mobile phase. It is well-known that, in SFC,  $D_m$  is a decreasing function of the density and an increasing function of the temperature at constant density (5, 12).

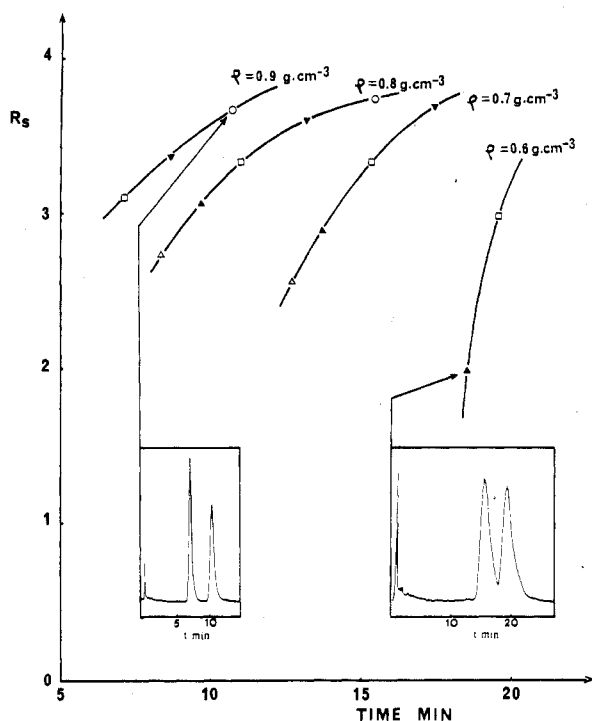


**Figure 4.** Variation of the reduced plate height  $h$  with the CO<sub>2</sub> density  $\rho$  for various temperatures: column and stationary phase as in Figure 1; mobile phase, CO<sub>2</sub>-methanol (95.2-4.8) (w/w); flow rate, CO<sub>2</sub> 3.5 mL·min<sup>-1</sup>, methanol 0.2 mL·min<sup>-1</sup>; detection, UV at 280 nm; temperature, (○) 20 °C, (▼) 30 °C, (□) 40 °C, (▲) 50 °C, (△) 60 °C.



**Figure 5.** Variation of the reduced plate height with the temperature for various modifiers added to carbon dioxide: column and stationary phase as in Figure 1; carbon dioxide density, 0.85-0.9 g·cm<sup>-3</sup>; flow rate, CO<sub>2</sub> 3.5 mL·min<sup>-1</sup>; modifier 0.35 mL·min<sup>-1</sup>; modifier, (■) 2-propanol, (□) 2-propanol-H<sub>2</sub>O (95:5) (v/v); (▼) ethanol, (▽) ethanol-H<sub>2</sub>O (95:5) (v/v), (●) methanol, (○) methanol-H<sub>2</sub>O (95:5) (v/v).

At low density ( $\rho < 0.7 \text{ g}\cdot\text{cm}^{-3}$ ), the compressibility of the CO<sub>2</sub> cannot be neglected any more (for  $0.6 < \rho < 0.7 \text{ g}\cdot\text{cm}^{-3}$  and  $T > 30 \text{ °C}$ ;  $10^{-2} < K_T < 10^{-1} \text{ bar}^{-1}$ ). Under these conditions there appears a density gradient in the chromatographic column due to the pressure drop. The first consequence is an apparent efficiency decrease, but the limiting factor is not kinetics but thermodynamics: the capacity factor spreads out. This phenomenon increases in importance with the solute retention (in the present case at  $\rho = 0.6 \text{ g}\cdot\text{cm}^{-3}$  and for capacity factor values between 40 and 50, that is, for residence times of 20 min). At these densities, plates theory



**Figure 6.** Variation of the resolution  $R_s$  between the enantiomers of the methyl-1-(4-methylnaphthyl)phenylphosphine oxide vs. the separation time at constant density: column and stationary phase as in Figure 2; mobile phase, CO<sub>2</sub> 3.5 mL·min<sup>-1</sup>, methanol 0.2 mL·min<sup>-1</sup> (along the different curves, the temperature varies and the pressure is chosen so that to keep constant the carbon dioxide density); detection, UV at 280 nm; temperature, (O) 20 °C, (▼) 30 °C, (□) 40 °C, (▲) 50 °C, (Δ) 60 °C.

is no longer valid and the measured efficiency values have lost all physical significance. In conclusion, to obtain a classical efficiency, we must operate at densities greater than 0.7 g·cm<sup>-3</sup>.

**Influence of the Nature of the Modifier.** Figure 5 shows the influence of various modifiers at the same content in carbon dioxide on the efficiency as a function of the temperature. As has been noticed above, efficiency is increasing with temperature because of the high density (0.9 g·cm<sup>-3</sup>). The column efficiency is greater when the polarity of the modifier is high ( $N_{\text{methanol}} > N_{\text{ethanol}} > N_{\text{2-propanol}}$ ). Furthermore, small quantities of water in the modifier (5% v/v) can drastically increase the chromatographic column efficiency. The im-

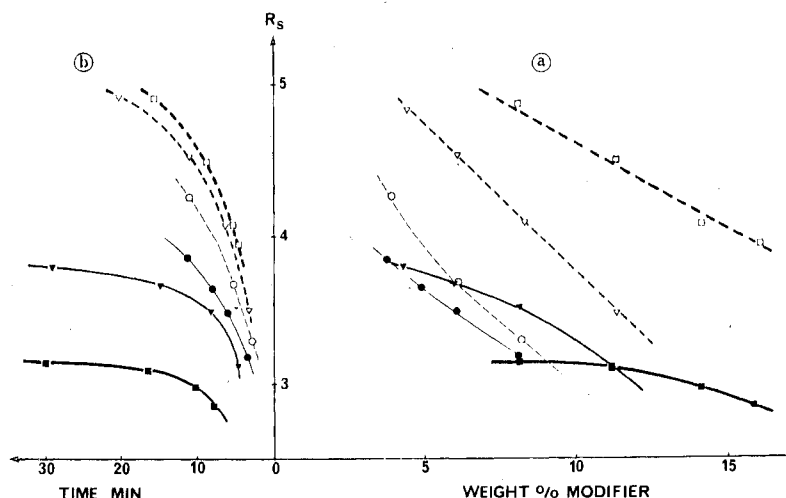
provement observed with additional water is much more important with 2-propanol than with methanol, that is, when alcohol polarity is low. An explanation may be suggested: The decrease in the solute diffusion coefficient produced by the modifier depends on its viscosity ( $\eta_{\text{methanol}}^{25^\circ\text{C}} = 0.53 \times 10^{-3} \text{ Pa}\cdot\text{s}$ ;  $\eta_{\text{ethanol}}^{25^\circ\text{C}} = 1.08 \times 10^{-3} \text{ Pa}\cdot\text{s}$ ;  $\eta_{\text{2-propanol}}^{25^\circ\text{C}} = 1.9 \times 10^{-3} \text{ Pa}\cdot\text{s}$ ). The diffusion of solutes is faster in a CO<sub>2</sub>-methanol mixture than in a CO<sub>2</sub>-2-propanol mixture, and, accordingly, the efficiency with CO<sub>2</sub>-methanol is greater than with CO<sub>2</sub>-2-propanol. This explanation, however, cannot apply to the influence of water. The small quantity of water (here, 0.5 % v/v in the mobile phase) cannot increase the molecular solute diffusion to an extent corresponding to the large efficiency variations observed, particularly, for 2-propanol-water mixtures.

In that case, a complementary interpretation may be proposed: As described in the retention section, the addition of water induces a cancellation of the adsorption phenomenon. The kinetics of adsorption may be slower than that of the interaction between racemate and chiral moieties resulting in a faster overall rate of the chromatographic process.

**Resolution.** Resolution,  $R_s$ , is the most important factor in chromatography. It takes into account kinetics and thermodynamics. At high density, efficiency increases with temperature. But, it has been shown that the lower the temperature, the higher the selectivity. A compromise is necessary and the optimum chromatographic conditions are found in the subcritical range.

**Influence of the CO<sub>2</sub> Physical State.** On Figure 6, plots of the analysis time vs. resolution for various densities,  $\rho$  are represented. On each isodensity curve, pressure and temperature are chosen such as to keep  $\rho$  constant. It is obvious that high resolution is obtained for densities greater than 0.7 g·cm<sup>-3</sup>, that is, where efficiency reaches optimal values. When the CO<sub>2</sub> density increases, the resolution for a given separation time increases. Two cases must be considered according to the density value.

(a) Density lower than 0.7 g·cm<sup>-3</sup>: In this area, the apparent efficiency is decreasing with density (capacity factor in the chromatographic column spreads out). Consequently, the resolution decreases according to the square root of this efficiency. (b) Density greater than 0.7 g·cm<sup>-3</sup>: In this density range, we have demonstrated that, at a given temperature, selectivity and efficiency are, at first approximation, constant. On the other hand, analysis time decreases with the carbon dioxide density. Thus, the highest resolution per unit of time is obtained at high density ( $\rho \approx 0.97 \text{ g}\cdot\text{cm}^{-3}$ ), under elevated



**Figure 7.** Variation of the resolution  $R_s$  between the enantiomers of methyl-1-(4-methylnaphthyl)phenylphosphine oxide with (a) the concentration of modifier and with (b) the separation time at a temperature of 20 °C: column and stationary phase as in Figure 1; pressure, 260 bar; flow rate of CO<sub>2</sub>, 3.5 mL·min<sup>-1</sup>; detection, UV at 280 nm; modifier (■) 2-propanol, (□) 2-propanol-H<sub>2</sub>O (95:5) (v/v), (▼) ethanol, (▽) ethanol-H<sub>2</sub>O (95:5) (v/v), (●) methanol, (○) methanol-H<sub>2</sub>O (95:5) (v/v).

pressure (250 bar) and at subcritical temperature (20 °C).

**Influence of the Nature of the Modifier.** The variation of the resolution with the nature of the mobile phase is shown in Figure 7a. We must emphasize that the addition of water to the modifier increases resolution while reducing the separation time. The lower the modifier polarity, the greater is this effect. Thus, with 2-propanol, the addition of water leads to an increase of about 50% in resolution, while the separation time, as clearly illustrated in Figure 7b, is about 2 times lower.

### CONCLUSION

Carbon dioxide super- and subcritical fluid chromatography, in conjunction with polar modifiers, permits the improvement of both column performance and resolution in the separation of enantiomers on chiral stationary phases. By choice of proper conditions and suitable modifiers, higher resolutions per unit of time than in classical liquid chromatography are obtained.

Selectivity mainly depends on the nature of the polar modifier and on temperature, as in liquid chromatography, whereas the mobile phase density has no influence. Moreover, the retention mechanism of phosphine oxides seems to be similar in SFC and in LC. As a consequence, super- and subcritical fluid chromatography on a Pirkle phase can probably resolve all the racemics already separated in liquid chromatography in a shorter separation time.

### ACKNOWLEDGMENT

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**Registry No.** CO<sub>2</sub>, 124-38-9; MeOH, 67-56-1; EtOH, 64-17-5; 2-PrOH, 67-63-0; H<sub>2</sub>O, 7732-18-5; methyl(4-methylnaphthyl)phenylphosphine oxide, 98687-96-8; methyl(2-methoxynaphthyl)phenylphosphine oxide, 98687-97-9; methyl(1-phenanthryl)phenylphosphine oxide, 98687-98-0; methyl(1-naphthyl)phenylphosphine oxide, 37775-99-8; methyl(2-methylnaphthyl)phenylphosphine oxide, 98687-99-1.

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## Investigation of Retention and Selectivity Effects Using Various Mobile Phases in Capillary Supercritical Fluid Chromatography

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**The influence of various mobile phases on the retention and selectivity of a polarity-test mixture in capillary supercritical fluid chromatography (SFC) was investigated. Capacity ratios and selectivities were obtained under equivalent chromatographic operating conditions using supercritical carbon dioxide, nitrous oxide, and ethane mobile phases and a relatively nonspecific 5% phenyl poly(methylphenylsiloxane) stationary phase. A 2.5% (w/w) mixture of methanol in carbon dioxide was also evaluated. In addition, chromatographic efficiency was compared at similar  $k'$  for each fluid. Carbon dioxide and nitrous oxide exhibited similar solvating power with only slight differences in selectivity. Ethane, being less polar, displayed the poorest solvating power for the polar solutes and offered greater differences in selectivity. The greatest differences in selectivity were observed at lower temperatures and higher densities. The carbon dioxide-methanol fluid mixture displayed different selectivity than pure carbon dioxide, but not to the same extent as reported for packed column SFC.**

Interest in supercritical fluid chromatography (SFC) is expanding. Supercritical fluids possess favorable properties

which render them attractive as mobile phases for chromatography. The density of a supercritical fluid approaches that of a liquid (and thus has similar solvating characteristics), but solute diffusivity remains higher and viscosity is lower (1), which allows higher chromatographic efficiencies per unit time to be achieved relative to liquid mobile phases (2). Consequently, the potential advantages of both liquid and gas chromatography are combined. Furthermore, the solvating power of a supercritical fluid mobile phase is continuously variable and controllable as a function of pressure (or density). This property allows pressure-programming techniques to be used in SFC in an analogous fashion to temperature programming in gas chromatography or gradient elution in liquid chromatography if the pressure drop across the chromatographic column is minimal (3). Thus, pressure programming ranges in SFC are less restrictive for capillary column operation. In addition, several fluids have low critical temperatures that provide favorable conditions for the analysis of thermally labile compounds.

As in liquid chromatography, there are a number of fluids available in SFC for mobile phases that offer a range of polarity and selectivity. However, current SFC practice and technology have been limited to relatively few fluids. Undoubtedly, the most popular fluid is carbon dioxide, which has been used extensively in both packed column (4-7) and