This article was downloaded by:
On: *25 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK

Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

Some Aspects of Pressure-Induced Equilibrium Shifts in Chromatography

J. Calvin Giddings[a]
[a] Department of Chemistry, University of Utah, Salt Lake City, Utah

To cite this Article Giddings, J. Calvin(1966) 'Some Aspects of Pressure-Induced Equilibrium Shifts in Chromatography', Separation Science and Technology, 1: 1, 73 — 80
To link to this Article: DOI: 10.1080/01496396608049435
URL: http://dx.doi.org/10.1080/01496396608049435

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

SEPARATION SCIENCE, 1(1), 73–80 (1966)

Some Aspects of Pressure-Induced Equilibrium Shifts in Chromatography

J. CALVIN GIDDINGS
DEPARTMENT OF CHEMISTRY, UNIVERSITY OF UTAH, SALT LAKE CITY, UTAH

Downloaded At: 14:52 25 January 2011

Summary

The possible advantages of pressure-induced equilibrium shifts in chromatography are explored. First, the subject of pressure-induced increases in migration rates is discussed, particularly in the light of solubility relationships already established in the high-pressure literature. Second, the more subtle equilibrium shifts leading to an enhancement of selectivity are studied. The practical implication of these equilibrium shifts are emphasized.

The prospects of very high inlet pressures (say 10^2 to 10^4 atm) in chromatography are promising in two complementary ways. First, the ultimate column efficiency (number of theoretical plates) and speed of analysis are proportional to the pressure drop available for pushing fluid through columns (*1*,*2*). This subject has already been explored at some length theoretically (*1–4*); a beginning has barely been made toward experimental verification and exploitation (5).

Second, pressure variations almost universally shift equilibrium constants in one way or another. Since chromatographic migration rates depend upon the equilibrium distribution of solutes between phases, it is worth making a broad inquiry into the benefits that might accrue through such controlled equilibrium shifts. This is the object of the present note. To start with, the potential of pressure-induced migration in chromatography will be discussed.

Downloaded At: 14:52 25 January 2011

PRESSURE-INDUCED MIGRATION

Quite often separation is unattainable because substances do not migrate at a measurable velocity. To remedy this, a very large shift in equilibrium is needed. Such large changes are most readily obtained with gases; this leads us quite directly (but not exclusively) to the technique of gas chromatography.

It is generally recognized that gas chromatography is unexcelled in resolution and separation speed. However gas chromatography is applicable only to the separation of fairly volatile compounds. This excludes a great number of important chemical species, among them being many kinds of macromolecules, inorganic compounds, highly polar species, and ions. This restriction is particularly unfortunate from the standpoint of biochemical separations (*6*).

Recently this author pointed out (*7*) that at pressures of the order of 1000 atm, gas chromatography would converge with classical liquid chromatography. "At such [gas] densities intermolecular forces become very large, and are undoubtedly capable of extracting big molecules from the stationary phase." In this way "nonvolatile" components become volatile, thus removing the most serious limitation (volatility) to present gas-chromatographic practice. Klesper and co-workers have indeed observed an enhancement in the migration of porphyrins at pressures to 140 atm (*8*). Below we elaborate to some extent on the chromatographic potential of that broad and essentially unexplored continuum between dilute gases and bulk liquids.

Quite fortunately, some guidelines for pressure-induced migration can be inferred from the literature of high-pressure chemistry (*9*). Thus ionic (and presumably polar) substances dissolve in high-pressure polar gases and nonionic substances in nonpolar gases. The application of such ordinary solubility rules would undoubtedly make it possible to induce migration in a selective fashion and to control the loss (bleeding) of stationary phase or adsorbent.

In the course of various high-pressure experiments a measurable gas-phase solubility has been noted for such unlikely materials as minerals, electrolytes, and polymers (*9,10*). Thus we have every reason to believe that the range of gas chromatography could be extended to many "nonvolatile" inorganics, ions, macromole-

Downloaded At: 14:52 25 January 2011

cules, and related chemical systems. (The separation of some gases into two phases at high pressure even makes the development of a gas-gas partition system conceivable for these separations.) Although in extreme cases the technique might be closer, physically, to liquid than to gas chromatography, it should be possible to retain many of the advantages of gas systems, including some of the versatility in detection equipment.

From the above it is clear that even at ordinary temperatures, with a proper choice of gas and stationary phases, one should be able to induce the migration of increasingly large and complex molecules as the pressure is raised (in some cases it may, of course, be desirable to combine high temperature with high pressure). It is important to know what limits, if any, exist on the complexity of species thus affected. In theory there is essentially no limit. For instance, one should be able to induce the migration of most extremely large, polar molecules (e.g., the transfer RNA's, M.W. ~23,000) that are soluble in some solvent (and possibly some that are not). The reason is that even above the critical point adequate compression can produce any desired density. A great variety of gases—polar, nonpolar, unsaturated etc.—exist with critical points sufficiently low that the gas phase can be used at reasonably low temperatures. The diversity of gas types is illustrated by the following examples: NH_3 ($T_c = 132°C$), C_2H_2 (36°), A (−122°), CO_2 (31°), COS (105°), Cl_2 (144°), C_2N_2 (128°), C_2H_6 (32°), C_2H_4 (8°), He (−268°), HCl (51°), HBr (90°), CH_3F (45°), N_2 (−147°), N_2O (36°), PH_3 (51°), C_3H_8 (96°), SiF_4 (−2°), and, somewhat higher, H_2O (374°). It is clear that one could go a long way toward finding a gas (or gas mixture) with properties suitable for a given problem. Advantage might also be found in using these substances somewhat below the critical temperature, where fairly high densities can be obtained at moderate temperatures and pressures.

A significant advantage to pressure-induced migration would likely be the profound effect of pressure changes and the ease of controlling pressure. At present if one needs to promote migration or selectivity in any form of chromatography, the chemical system or the temperature must be changed. The latter is often confined to a narrow range and, in addition, changes giving an enhanced migration almost invariably reduce selectivity, and vice versa (*1*). Pressure, of the high magnitude proposed here, provides a simple control for the degree of interaction of solute with the parent phases. Changes would have a large effect on both migration and selectivity (see below). One can envision a heterogeneous mixture from which successive jumps in pressure cause the migration of increasingly complex molecules. An enormous molecular weight range could perhaps be covered in this fashion. This approach, in some ways analogous to programmed-temperature gas chromatography, would have the advantage that high pressure, unlike high temperature, is not inherently a source of molecular decomposition. (The technique is perhaps more similar to gradient elution liquid chromatography, except that no chemical change is involved.)

From the above, the advantages of high-pressure gas chromatography would appear to be multiple in number and straightforward in application. Some problems should be pointed out. Beyond the difficulties of operating high-pressure flow systems, one could not often use a conventional detector system operating at atmospheric pressure, because the species which had been induced to migrate would cease moving as it reached low-pressure regions. To maintain the induced migration, the outlet of the column would need to be held at an elevated pressure. In this way, unfortunately, one loses much of the pressure drop which is so advantageous to column efficiency and speed. Nonetheless, pressure drops of a hundred atmospheres (which exceeds anything now used) could no doubt be maintained except for the very high molecular weight species, which would be so sensitive to slight changes in pressure. Possibly one could superimpose a temperature gradient on the pressure gradient in the latter case to maintain the delicate equilibrium.

Downloaded At: 14:52 25 January 2011

Although the enhancement of migration through pressure increases most obviously applies to gas chromatography, the effect would not be entirely absent in liquid chromatography. This is indicated by observed changes in ionization, solubility, and other equilibrium constants with pressure (9). These shifts, smaller in magnitude, fall within the context of the discussion below.

PRESSURE-INDUCED SELECTIVITY

The inducement of migration, to be significant, would usually require a large shift in equilibrium. The above-mentioned changes in selectivity (reflected by the difference, ΔK, in distribution constants between designated species) would require a *differential*

Downloaded At: 14:52 25 January 2011

shift in equilibrium, but only of a small magnitude. Thus if two chromatographic zones migrated at identical rates ($\Delta K = 0$), making separation impossible under normal conditions, a differential shift yielding the value ΔK would lead to nearly complete separation in a column with N plates, where *(1)*

$$N = 16/[(\Delta K/K)\ (1 - R)]^2 \tag{1}$$

in which K is the mean distribution coefficient for the two close-lying solutes and R, also a mean value, is the ratio of zone velocity to the flow velocity of the mobile phase. If a differential shift of 5% is induced ($\Delta K/K = 0.05$), a column of about 10,000 plates would make the separation possible for most solutes ($R \sim 0.2$). Only 2500 plates would be needed for a 10% differential shift. It should be possible to achieve or exceed these plate numbers in high-pressure columns.

The appropriate question, then, is whether differential shifts of 5 or 10% can be induced by pressure. The magnitude of differential equilibrium shifts at high pressure among similar solutes in two-phase systems has not been studied, to this author's knowledge. [A low-pressure shift, using gases, has been discussed by Desty et al. *(11)*.] We shall discuss what is involved and make some estimates of what is needed to achieve these shifts.

At low pressures, equilibrium states are determined primarily by the degree of interaction between molecules. With increasing pressure a new factor grows in importance: molecular volume and the ability of molecules to crowd together efficiently to reduce this volume. These forces often act in opposition; the open structure of ice *I*, optimal at low pressures, cannot exist at high pressures. Thus the appearance of the volume factor should lead to equilibrium shifts, both total and differential, the magnitude depending on how well solute and solvent interlock and on changes in the solvent structure in both mobile and stationary phases.

Consider two solutes, A and B, having distribution coefficients K_A and K_B for the transfer from mobile to stationary liquid phases. The shift in each K with pressure is given by *(12)*

$$\mathscr{R}T(\partial \ln K/\partial p)_T = -\delta \bar{V}^\circ \tag{2}$$

where $\delta \bar{V}^\circ$ is the standard-state partial molar volume change for the transfer of solute between phases. The differential shift is accounted for by subtracting one such equation from another, giving

$$\mathcal{R}T(\partial/\partial p)[\ln(K_B/K_A)] = -\Delta(\delta\bar{V}^\circ) \tag{3}$$

where $\Delta(\delta\bar{V}^\circ)$ is the difference in $\delta\bar{V}^\circ$ between the two solutes. If for convenience we assume K_B and K_A identical at low pressures, the effect of increasing pressure is reflected in $\Delta K = K_B - K_A$. Upon replacing K_B by $K_A + \Delta K$ in the above equation, and restricting its application to relatively small values of $\Delta K/K$, we find that

$$\mathcal{R}T(\partial/\partial p)(\Delta K/K) = -\Delta(\delta\bar{V}^\circ) \tag{4}$$

At moderate compressions, for which partial molar volumes are not much affected, this integrates to the simple form

$$\Delta K/K = -p\,\Delta(\delta\bar{V}^\circ)/\mathcal{R}T \tag{5}$$

Equation (5) shows that at $T = 300°\text{K}$, an absolute $\Delta K/K$ value of 0.1 (the "10%" shift mentioned above) can be achieved when the product, $p\,\Delta(\delta\bar{V}^\circ)$, equals about 2500 atm cm^3/mole. Thus if the volume increment term is 1 cm^3/mole, 2500 atm would bring about separation; if it is 5 cm^3/mole, 500 atm would suffice.

The magnitude of $\Delta(\delta\bar{V}^\circ)$ is rather hard to estimate in general. That volume changes are caused by a variation in chemical state are well known. Chemical reactions, which represent severe chemical changes, often involve volume increases or decreases of up to 30 cm^3/mole. Isomerization commonly involves 0 to 5 cm^3/mole.

Since one frequently wishes to separate isomers, it is worth looking at isomerizations more closely. It is helpful to note that $\Delta(\delta\bar{V}^\circ) = \delta(\Delta\bar{V}^\circ)$, where, it will be recalled, δ represents a change in phase and Δ a change from compound A to compound B (thus $\Delta\bar{V}^\circ$ is the volume change due to isomerization). One experimental result that is indicative of the quantities involved is the keto-enol tautomerism of aceto-acetic ester (*9,12*). The sign of $\Delta\bar{V}^\circ$ changes from positive to negative in going from polar to nonpolar solvents. Water, compared to many solvents, gives $\delta(\Delta\bar{V}^\circ) \sim 7$ cm^3/mole, a value adequate for very significant differential shifts.

Although the foregoing is based on the concept of nearly constant partial molar volumes and a relatively fixed liquid structure, moderate pressure changes often induce structural variations which should have a significant effect. High pressures generally

Downloaded At: 14:52 25 January 2011

lead to a more ordered liquid structure, tending either to liquid crystals or, if too severe, solids (*9*). This ordering would no doubt lead to useful differential changes; liquid crystals have already been shown to possess excellent selectivity based on molecular shape (*13,14*). Coupled with this, the promotion of ionization, hydrogen bonding, and other changes by pressure would undoubtedly have a significant influence on various chromatographic separation processes at high pressures.

Needless to say, many separation processes besides chromatography depend upon a differential equilibrium between phases. Although high pressures would be very difficult to obtain in the larger of these systems, the same rules would apply quite generally. For instance, Goranson has suggested that differential changes in freezing temperatures be used in fractional crystallization (*15*). The possibility that pressure-induced equilibrium (and transport) shifts might be used in a broad class of separation processes needs to be explored more systematically.

Downloaded At: 14:52 25 January 2011

Acknowledgment

This investigation was supported by Public Health Service Research Grant GM 10851-09 from the National Institutes of Health.

REFERENCES

1. J. C. Giddings (ed.), *Dynamics of Chromatography* (Vol. 1 of Chromatographic Science), Part 1, Dekker, New York, 1965.

2. J. H. Knox, *J. Chem. Soc.*, **1961**, 433.

3. J. C. Giddings, *Anal. Chem.* **36**, 1890 (1964).

4. J. C. Giddings, *Anal. Chem.*, **37**, 60 (1965).

5. M. N. Myers and J. C. Giddings, *Anal. Chem.*, in press.

6. C. J. O. R. Morris and P. Morris, *Separation Methods in Biochemistry*, Wiley (Interscience), New York, 1964.

7. J. C. Giddings, A critical evaluation of the theory of gas chromatography, *5th Intern. Symp. Gas Chromatography*, Brighton, England, Sept. 1964, to be published.

8. E. Klesper, A. H. Corwin, and D. A. Turner, *J. Org. Chem.*, **27**, 700 (1962).

9. S. D. Hamann, *Physico-Chemical Effects of Pressure*, Butterworth, London, 1957.

10. P. Ehrlich and E. B. Graham, *J. Polymer Sci.*, **45**, 246 (1960).

11. D. H. Desty, A. Goldup, G. R. Luckhurst, and W. T. Swanton, in *Gas Chromatography 1962*, (M. van Swaay, ed.), Butterworth, London, 1962, p. 67.

12. S. D. Hamann, in *High Pressure Physics and Chemistry* (R. S. Bradley, ed.), Vol. 1, Academic Press, New York, 1963, Chap. 7, p. ii.

13. H. Kelker, *Z. Anal. Chem.* **198,** 254 (1963).

14. M. J. S. Dewar and J. P. Schroeder, *J. Am. Chem. Soc.*, **86,** 5235 (1964).

15. R. W. Goranson, *Sci. Monthly,* **51,** 524 (1940).

Received by editor November 20, 1965
Submitted for publication December 30, 1965

Downloaded At: 14:52 25 January 2011