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Gel-Permeation Chromatographic Observation of Solvent–Solute Interaction of Low-Molecular-Weight Compounds

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Summary

The effect of molecular association upon gel-permeation chromatographic separations is examined. Application of a previously established GPC elution-volume/molar-volume relationship to the study of solvent/solute interactions is discussed. The use of such interactions to improve fractionating ability of GPC columns is described. Application of the GPC technique to fundamental studies of forces involved in intermolecular association is suggested.

INTRODUCTION

The application of the gel-permeation chromatographic (GPC) technique to the fractionation of small, nonpolymeric molecules has been the subject of several interesting papers (*1–5*). It has been demonstrated that both low-molecular-weight substances (*5*) and high-molecular-weight, polymeric substances (*6*) are separated on the basis of molecular volume, as opposed to either a linear dimension of a molecule (e.g., extended chain-length or an empirically arrived at effective carbon number) or molecular weight. Some data were presented for polar solutes that indicate that adsorptive forces between solute and substrate often operate to retard molecules in (or on) the gel particles. The suggestion was offered that such forces might be used to advantage to apply the GPC technique as a characterization tool in the assignment of both molecular configurations and, possibly, stereochemical conformations to substances of unknown structure.

The present paper is concerned with the observation that, under certain conditions, molecules that possess an appreciable permanent dipole emerge from a GPC column *earlier* than would be predicted on the basis of molar-volume estimates; i.e., some molecules behave as though their molar volumes are greater than one would predict on the basis of their simple molecular structures. Such observations are common and are suggestive of the existence of associative forces, possibly through solute–solute or solvent–solute interactions.

EXPERIMENTAL

Gel-permeation-chromatographic elution volumes in *o*-dichlorobenzene were determined with a Waters Model 200 gel-permeation chromatograph (manufactured by Waters Associates, Inc., Framingham, Mass.). The instrumental details have been adequately described elsewhere (7). The instrument was operated at 130°C and a flow-rate of 1 ml/min. Two-milliliter aliquots of 0.25 to 1.0% solutions were passed through four 4-ft × ⅜-in. o.d. columns in series having exclusion limits of 3×10^3, 250, 60, and 60 Å, respectively. The column substrate was a rigid, cross-linked polystyrene gel, which was prepared and characterized by Waters Associates, Inc.

Data presented for GPC fractionation in tetrahydrofuran were taken from the work reported by Hendrickson and Moore (*1*). They used four 4-ft × ⅜-in. o.d. columns in series having an exclusion limit of ~40 Å (identified as "Sx8") at 25°C and a flow-rate of 1ml/min.

Molar volumes, for the substances of interest, were estimated at 25°C and/or 130°C by a technique described earlier (*5*). A FORTRAN-language computer program, called MOLVOL, was written for the General Electric time-sharing computer which makes such calculations a simple matter. A listing of the program will be sent, together with operating instructions, upon written request.

OBSERVATIONS IN TETRAHYDROFURAN

The data for GPC fractionation of polar, low-molecular-weight substances in tetrahydrofuran are, at first glance, quite disconcerting. Whereas nonpolar hydrocarbon compounds do, indeed, elute according to their estimated molar volumes (i.e., their estimated and effective molar volumes are identical), the polar compounds elute too soon, if one compares their observed elution volumes with those elution volumes that would be predicted solely on the basis of estimated molar volumes. One would expect, if molar volumes of small polar molecules were the only consideration in determining their GPC elution volumes, that a plot of elution volume vs. log (molar volume) would result in all points lying on a single line together with the hydrocarbons. This, of course, is not what is actually observed.

The early emergence of polar substances from the GPC column, when tetrahydrofuran is used as the elution solvent, leads one to postulate at least two possible hypotheses:

1. There are certain repulsive forces operating between solute and substrate (the cross-linked polystyrene gel column packing) which prevent polar molecules from permeating the gel. If this were truly the reason for early emergence of these substances, then it would be expected to occur in most other solvents—and such is not the case!
2. The molecules are actually larger than the estimated values, either as a result of solute–solute or solvent–solute interactions resulting in weakly associated species, or, in some cases, resulting in actual reversible compound formation.

The data presented in Table 1 indicate that the early emergence of polar substances is due, at least in some cases, and probably in many cases, to solvent–solute association and/or reversible compound formation. Figure 1, for example, is a plot of the data for the hydrocarbons and alcohols in Table 1. An immediate observation is the poor correlation between the estimated molar volumes and the observed elution volumes. However, if one adds to the estimated molar volumes of the alcohols the estimated molar volume of tetrahydrofuran (74.3 cm^3/g-mole) and then replots these adjusted data, the result is as shown by the X's in Fig. 1. All of the alcohols now fall on the same line as the hydrocarbons. The data for the miscellaneous compounds in Table 1 are plotted in Fig. 2. Here again, correlation is good only after the data are adjusted by adding the molar volume of tetrahydrofuran to the estimated molar volumes of the polar substances.

Three rather interesting observations may be made here:

1. Two tetrahydrofuran molar volumes (2 × 74.3) must be added to ethylene glycol. This is as one would expect, since it has two free hydroxyl groups with which to associate with solvent molecules.
2. Carbon tetrachloride falls directly in line with the hydrocarbons without any adjustment. Since this molecule is symmetrical and

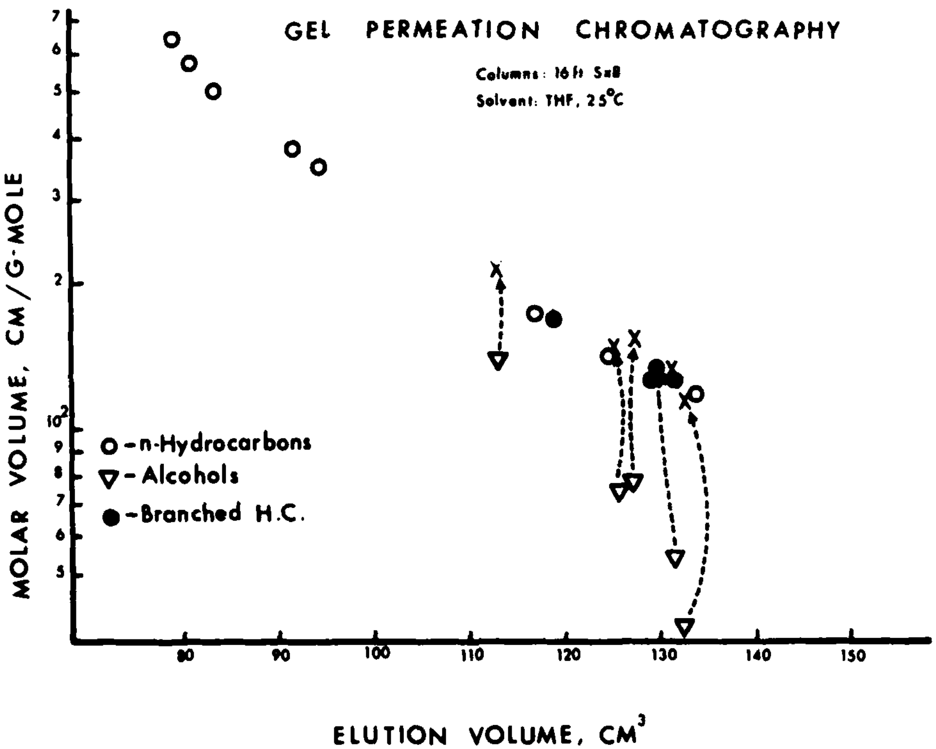

FIG. 1.

possesses no permanent dipole, it would be expected to form only comparatively weak hydrogen bonds with tetrahydrofuran.

3. Plotted points for the "adjusted data" fall slightly above an imaginary line drawn through the hydrocarbon data. The more polar the molecule, the farther above this line is the plotted point. This phenomenon is no doubt due to moderate adsorptive forces operating between the associated solvent–solute species and the substrate.

OBSERVATIONS IN ORTHO-DICHLOROBENZENE

The data obtained with *o*-dichlorobenzene as the elution solvent further substantiate the hypothesis of solvent–solute association with GPC fractionations in tetrahydrofuran. It would be expected, a priori, if early emergence of polar substances in tetrahydrofuran is due to an increase in molar volume resulting from solvent–solute association, that moving over to a nonassociating solvent should result in all data points falling on a single line, hydrocarbons and polar compounds alike; some might fall slightly above the hydrocarbon line because of the solute–substrate adsorptive forces mentioned above, but by and large, most would fall on or near a single line.

Ortho-dichlorobenzene was selected for this critical experiment, since it would be expected to associate only weakly, if at all, with small polar molecules. Certainly any associative forces that might exist would be expected to be relatively weak in comparison to those between tetrahydrofuran (a strongly basic solvent) and other polar substances. The data obtained with *o*-dichlorobenzene are summarized in Table 2. Figure 3 is a plot of the data for hydrocarbons and alcohols. The excellent correlation of all of the data is ample support for the solvent–solute associative hypothesis discussed above. Further substantiation is shown in Fig. 4. Data are plotted for hydrocarbons

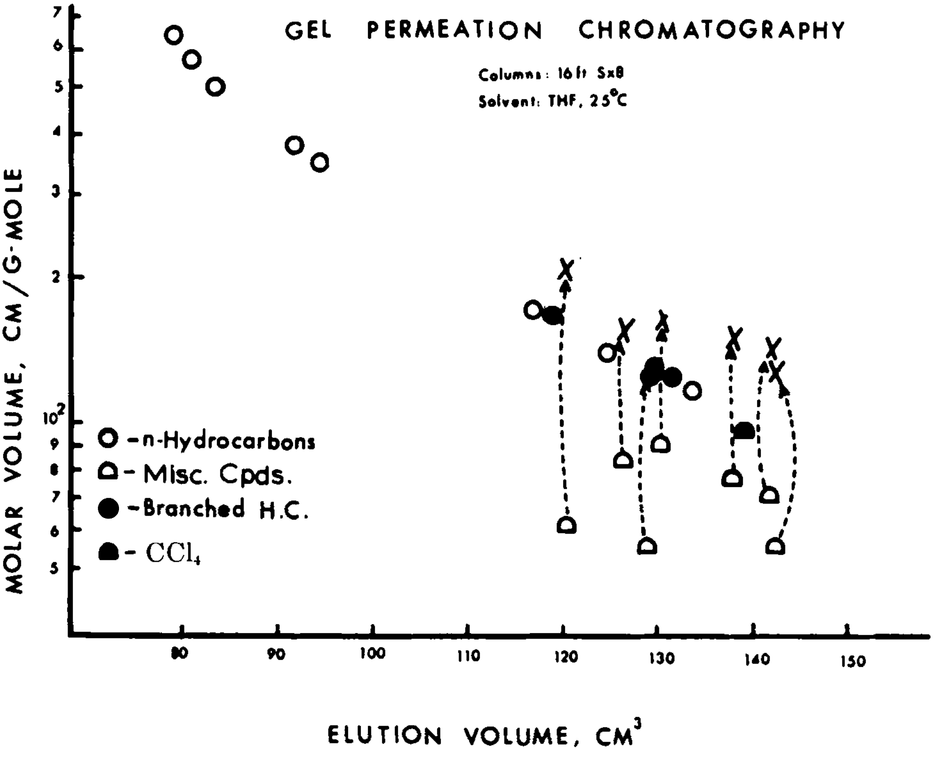

FIG. 2.

TABLE 1

GPC Data in Tetrahydrofuran[a]

Compound	Elution volume, cm^3	Molar volume,[b] cm^3/g-mole	Adjusted molar volume,[c] cm^3/g-mole
A. Aliphatic hydrocarbons:			
n-Pentane	133.8	117	—
n-Heptane	124.6	141	—
n-Nonane	117.0	174	—
n-Octadecane	94.5	350	—
n-Eicosane	91.8	382	—
n-Octacosane	83.2	503	—
n-Dotriacontane	80.8	573	—
n-Hexatriacontane	79.1	642	—
2-Methylpentene-1	131.4	125	—
4-Methylpentene-1	129.0	125	—
3-Methylpentane	129.5	133	—
2,2,4-Trimethylpentane	119.0	169	—
B. Alcohols:			
Methanol	132.5	39	114
Ethanol	131.4	57	131
n-Propanol	127.3	77	152
iso-Propanol	125.8	74	148
n-Heptanol	113.1	139	213
C. Miscellaneous compounds:			
Ethylene glycol	120.3	62	136 210[d]
Aniline	126.6	84	159
Acetic acid	129.0	56	130
Chloroform	130.5	91	165
Ethyl formate	138.0	78	152
Acetone	142.0	71	145
Acetonitrile	142.5	55	130
Carbon tetrachloride	139.0	96	—

[a] Data taken from Ref. (*1*).

[b] Estimated by the method of Lydersen discussed in Ref. (*5*), at 25°C, rounded to the nearest cm^3/g-mole.

[c] Estimated molar volume + 74.3 (estimated molar volume for THF), rounded to nearest cm^3/g-mole.

[d] Estimated molar volume + 2(74.3), rounded to nearest cm^3/g-mole.

and a series of other compounds possessing permanent dipoles of varying magnitudes. Here, again, all data points fall on or near a single line, with minor retardation of some molecules due, presumably, to solute–substrate adsorptive phenomena.

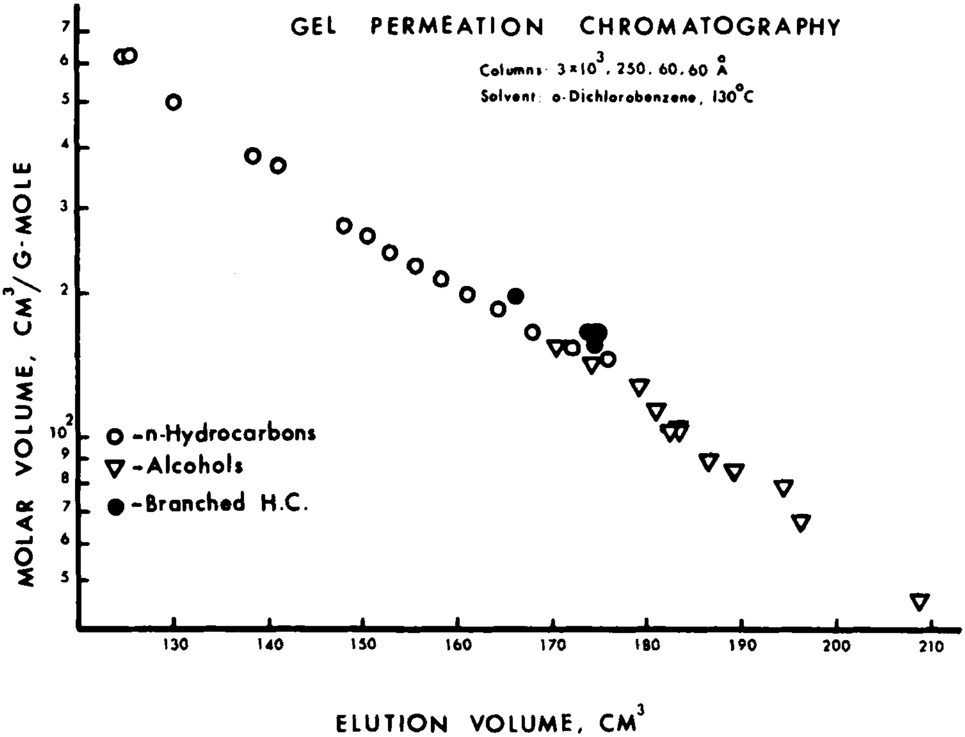

FIG. 3.

CONSEQUENCES OF SOLVENT–SOLUTE ASSOCIATION

The observation that solvent–solute interactions can play an important role in the gel-permeation-chromatographic behavior of polar molecules leads one to postulate some possible new applications of the GPC technique. The fact that the *effective* molecular volume of a substance is changed by association with the solvent can be made use of in optimizing GPC separations of polar from nonpolar and polar from other polar substances. Apparently the associative forces observed here are strong enough to hold solvent and solute molecules together tightly enough to survive repeated passage into and out of the cross-linked gel network in the GPC column.

A mixture of two substances having identical molecular volumes would not normally be separable by GPC. However, if only one of the species were polar, then GPC fractionation of such a mixture might be feasible if a great enough increase in the molecular volume of the polar

TABLE 2

GPC Data in *o*-Dichlorobenzene[a]

Compound	Elution volume, cm^3	Molar volume,[b] cm^3/g-mole
A. Aliphatic hydrocarbons:		
n-Pentane	176.0	148
n-Hexane	172.2	152
n-Heptane	168.0	167
n-Octane	164.4	183
n-Nonane	161.2	199
n-Decane	158.4	215
n-Undecane	155.7	226
n-Dodecane	153.1	243
n-Tridecane	150.7	262
n-Tetradecane	148.2	276
n-Octadecane	141.3	357
n-Eicosane	138.3	389
n-Octacosane	130.0	505
n-Pentatriacontane	125.4	626
n-Hexatriacontane	124.5	624
2,2,4-Trimethylpentane	166.4	198
3-Methylpentane	173.5	161
2-Methylpentene-1	174.5	158
4-Methylpentene-1	174.1	164
B. Alcohols:		
Methanol	208.8	46
Ethanol	196.4	67
n-Propanol	189.7	85
iso-Propanol	186.8	90
n-Butanol	183.6	104
iso-Butanol	184.4	105
sec-Butanol	182.5	105
tert-Butanol	181.2	113
Allyl alcohol	194.4	79
n-Pentanol	179.3	123
n-Hexanol	174.6	142
n-Heptanol	170.6	156
C. Carboxylic acids:		
Acetic	202.3	62
Propionic	191.6	80
n-Butyric	186.9	98
n-Valeric	180.7	116
n-Hexanoic	176.6	133
n-Heptanoic	172.0	151
n-Octanoic	169.0	169

TABLE 2 (*Continued*)

Compound	Elution volume, cm^3	Molar volume,[b] cm^3/g-mole
D. Aromatics:		
Benzene	186.3	105
Toluene	180.0	123
Ethylbenzene	175.5	142
o-Xylene	175.4	131
m-Xylene	174.6	134
p-Xylene	174.6	135
Chlorobenzene	182.2	116
Iodobenzene	181.3	124
E. Miscellaneous compounds:		
Cyclohexane	181.1	124
Bromocyclohexane	176.6	145
Cyclohexanol	181.3	124
Acetonitrile	195.0	64

[a] Data obtained with four columns in series having exclusion limits of 3×10^3, 250, 60, and 60 Å, respectively, at 130°C and 1 ml/min flow rate.

[b] Estimated by the method of Lydersen discussed in Ref. (*5*), at 130°C rounded to nearest cm^3/g-mole.

species resulted from association with the solvent. This approach might even be extended to mixtures of polymeric substances having polar groups either pendant along the chain or present as end-groups.

The GPC technique might be applicable to the fundamental study of forces resulting from various types of molecular interactions:

(a) dipole–dipole;
(b) dipole–induced dipole;
(c) ion-pair formation;
(d) complex formation.

The application of the principles discussed above not only would be useful in merely observing the formation of such associated species, but could be applied to the examination of the strengths of the bonds thus formed and the equilibria involved by studying the effects of varying such parameters as temperature and concentration.

A new tool is now offered to the physical chemist for studying solvation and intermolecular association, not by observing a "shadow" produced by the associated species (as with spectral methods, for example) but by direct application of a "yardstick" held in one hand

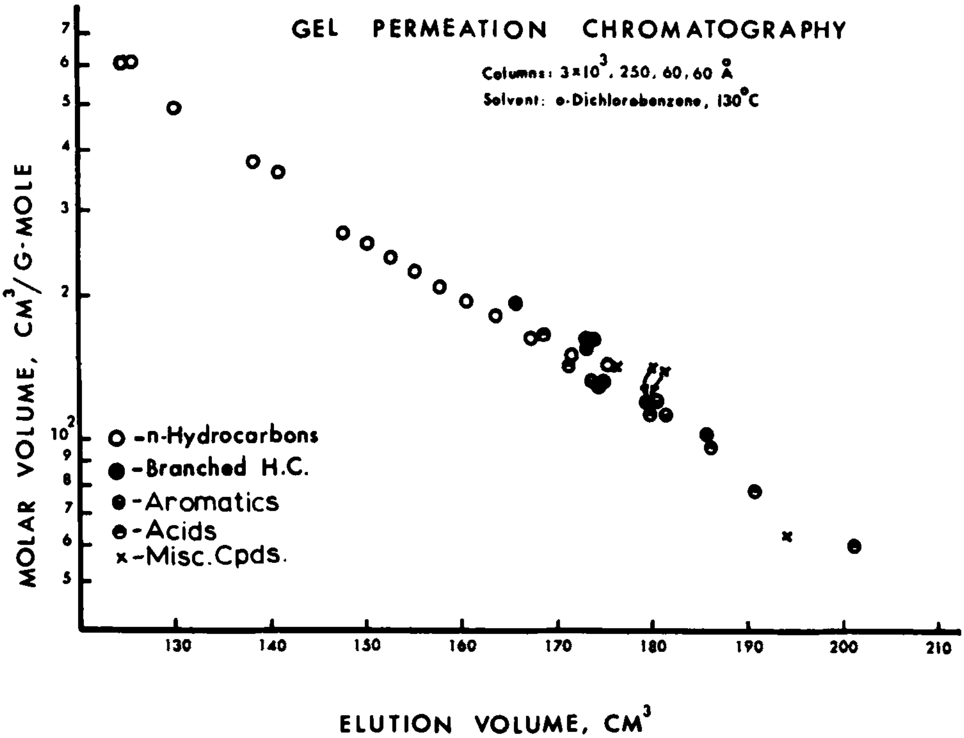

FIG. 4.

(the calibrated GPC column) to the actual associated species held in the other hand.

REFERENCES

1. J. G. Hendrickson and J. C. Moore, *J. Polymer Sci.*, **A4**, 167 (1966).
2. W. B. Smith and A. Kollmansberger, *J. Phys. Chem.*, **69**, 4157 (1965).
3. J. G. Hendrickson, *Anal. Chem.*, **40**, 49 (1968).
4. G. D. Edwards and Q. Y. Ng, *Polymer Preprints*, Division of Polymer Chemistry, American Chemical Society Meeting, Chicago, Sept., 1967, p. 1326.
5. J. Cazes and D. R. Gaskill, *Separ. Sci.*, **2**, 421 (1967).
6. Z. Grubisic, P. Rempp, and H. Benoit, *Polymer Letters*, **5**, 753 (1967).
7. J. Cazes, *J. Chem. Educ*, **43**, A567, A625 (1966).

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