The Gel Permeation Chromatography of Phenolic Compounds

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Synopsis

Gel permeation chromatography, using polystyrene gel and tetrahydrofuran as solvent, has been applied to hydroxybenzophenones, esters of salicylic acid, alkylphenols, alkylated methylenediphenols, and phenol–formaldehyde condensation products. The difference between the calculated molecular volume of these phenolic compounds and that obtained by actual determination with GPC has been ascribed to tetrahydrofuran solvation of the phenolic hydroxyl group. Furthermore, it has become clear that THF solvation is affected by the steric hindrance of ortho-substituted phenol and by inactivation of the phenolic hydroxyl group resulting from internal hydrogen bonding.

INTRODUCTION

In the past few years, the application of gel permeation chromatography (GPC) to the studies on low molecular weight compounds has developed significantly.[1,2,9,17,18] However, in this field of application, problems associated with the chemical structure of the solute have come to the fore. First, molecular weight, linear dimension, molecular volume, etc.,[3-8] have been suggested as criteria for the size of a molecule; and each can give a satisfactory result under certain conditions. Second, such polar compounds as phenols, carboxylic acids, and alcohols give rise to adsorption effects[9] and solvation associated with their GPC.[10-13] Because of these effects, the apparent molecular size of the solute increases.

Among the various reports[14-18] related to GPC of phenols, Edwards et al.[16] have observed that the increase in the apparent molecular volume of the phenols resulting from solvation in THF is 55–65 cm³/mole per phenolic hydroxyl group. Hendrickson[17] has observed that the degree of solvation of phenol is 100%, while that of 2,6-di-*tert*-butyl-*p*-cresol, which is influenced by steric hindrance, is 0%.

In connection with the commercially important phenolic compounds, Coupek[19] and Howard[20] have analyzed with GPC the antioxidants found in polymers. Furthermore, Gardikes et al.,[21] Drum,[22] Quinn et al.,[23] Varishth et al.,[24] and Hagen et al.[25] have studied the application of GPC to the molecular weight distribution of phenolic resins.

The authors have realized that, in their study on the analysis by GPC of phenolic resins, phenolic antioxidants, and phenolic ultraviolet absor-

bents, it is necessary to elucidate the relationship between the structure of these compounds and solvation of THF.

In this paper, the results of observations on the various phenolic compounds made by GPC, using THF as solvent, are reported.   Relationships between the various isomers and the effluent volumes of such compounds as alkyl phenols, hydroxybenzophenones, esters of salicylic acid, and phenol–formalin condensation products, which are closely related to phenolic resins and phenolic additives, have been established, and the results obtained have been explained by the following two considerations which affect THF–phenol solvation: (a) the effect of steric hindrance of a phenolic substituted group and (b) deactivation resulting from internal hydrogen bonding in phenol.

EXPERIMENTAL

Materials

Standard materials (c.p.) used for the calibration curve were n-pentane, n-hexane, n-heptane, n-nonane, n-decane, n-undecane, n-dodecane, n-

TABLE I
Molar Volume of Aromatic Compounds

| No. | Compound | Molar volume, cc/mole | | |
		Calcd.	Found	Diff.
1	Ethylbenzene	140	100	40
2	Benzyl acetate	174	143	31
3	Benzophenone	207	143	64
4	Diphenylmethane	207	143	64
5	Bibenzyl	229	177	52
6	Benzyl ether	240	188	52
7	Phenyl benzoate	217	158	59

TABLE II
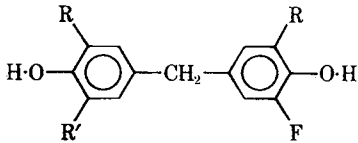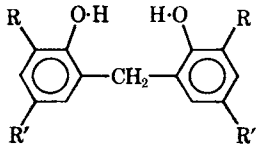#### Solvation of Tetrahydrofuran for Benzophenones, Salicylates, and Related Compounds (R_1—CO—R_2)

No.	R_1	R_2	n
1	2-Hydroxyphenyl	methyl	+0.20
2	2-Hydroxyphenyl	p-methoxyphenyl	−0.29
3	2-Hydroxyphenyl	phenoxy	+0.14
4	2-Hydroxyphenyl	p-octylphenoxy	−0.14
5	2-Hydroxy-4-octyloxyphenyl	phenyl	−0.13
6	2-Hydroxy-4-dodecyloxyphenyl	phenyl	−0.13
7	2-Hydroxyphenyl	2-hydroxyphenyl	+0.53
8	2-Hydroxyphenyl	4-hydroxyphenyl	+1.09
9	2-Hydroxy-4-methoxyphenyl	2-hydroxyphenyl	+0.16
10	4-Hydroxyphenyl	phenyl	+1.09
11	4-Hydroxyphenyl	phenoxy	+1.42
12	3-Hydroxyphenoxy	phenyl	+1.30

TABLE III

Solvation of Tetrahydrofuran for Phenols

|	Substituent at[a]				Elution volume, cc	Molar volume, cc/mole		
No.	o-	o'-	m-	p-		Calcd.	Found	n
1	—	—	—	OH	159	120	275	2.10
2	—	—	—	NO$_2$	162	134	220	1.32
3	—	—	—	Cl	163	129	205	1.20
4	—	—	—	—	164	108	183	1.20
5	—	—	—	B	159	197	265	1.11
6	—	—	—	M	164	130	188	1.00
7	—	—	—	BZ	196	219	255	0.74
8	—	—	B	—	160	197	255	1.00
9	—	—	M	—	164	130	188	1.00
10	—	OH	—	—	161	120	235	1.65
11	—	Cl	—	—	163	129	195	1.09
12	—	M	—	—	164	130	183	0.94
13	—	B	M	—	159	219	265	0.86
14	—	M	—	M	163	152	196	0.84
15	—	B	—	—	161	197	237	0.80
16	—	B	—	B	157	286	320	0.73
17	—	NO$_2$	—	—	170	134	120	0.18
18	Cl	Cl	—	—	165	150	176	0.64
19	M	B	—	—	160	219	245	0.64
20	M	M	—	—	165	152	177	0.63
21	M	M	—	M	164	175	190	0.51
22	M	B	—	B	157	308	320	0.48
23	B	B	—	—	159	286	263	0.08
24	B	B	—	M	158	308	285	0.08
25	B	B	—	B	156	374	345	0.00
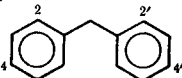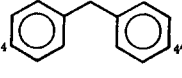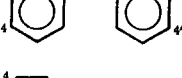
[a] M = methyl, B = tert-butyl, BZ = benzyl.

TABLE IV

Solvation of Tetrahydrofuran for Alkylated Methylenediphenols

Structure	R	R'	n
	H	H	2.32
	tert-butyl	methyl	1.27
	tert-butyl	tert-butyl	0.04
	H	H	1.44
	tert-butyl	methyl	0.46
	tert-butyl	ethyl	0.42
	tert-butyl	tert-butyl	0.54

eicosane, n-octacosane, n-hexatriacontane, methyl caproate, ethyl caproate, dimethyl adipate, ethyl heptylate, methyl nonoate, ethyl caprylate, dimethyl sebacate, methyl laurate, ethyl laurate, methyl palmitate, ethyl palmitate, dibutyl sebacate, methyl stearate, ethyl oleate, ethyl stearate, and butyl stearate. Polypropylene oxide samples with known molecular weights (790,1220,2020, and 3900) were supplied by Waters Associates.

TABLE V
Solvation of Tetrahydrofuran for Phenol–Formaldehyde
Condensation Products

No.	Structure	Hydroxyls at	Elution volume, cc	n_0	n
1		2,2'	157.5	1	1.44
2		2,4'	155.5	2	1.98
3		4,4'	154.5	2	2.32
4		2,2',2''	153.5	1	1.66
5		4,2',4''	150.0	3	3.32
6		4,2',2''	152.5	2	2.22
7		2,6',4''	151.5	3	2.60
8		2,6',2''	153.0	2	2.14
9		4,6',4''	150.5	3	3.04
10		4,6',2''	151.5	2	2.60

Aromatic model compounds (Table I), benzophenones and related compounds (Table II), and phenols (Table III) were all c.p. grade and were used as purchased. Alkylated bisphenols[26] (Table IV) and the phenol-formaldehyde condensates[27] (Table V) were prepared according to the methods in the literature. Tetrahydrofuran was distilled once before use.

Gel Permeation Chromatography

A Water Model 200 GPC was used under the following operating conditions: solvent, tetrahydrofuran; temperature, 50°C; flow rate, 1 ml/min; sensitivity, 1×; injection time, 120 sec; concentration, 0.1%; columns, a series of four columns ($^3/_8$ in. × 4 ft) packed with polystyrene gel of nominal pore sizes 10^5, 10^4, 10^3, and 10^2 Å, respectively, supplied by Waters Associates.

RESULTS AND DISCUSSION

The calculated molar volume (cc/mole) for each compounds was obtained by summing up the atomic volumes and the structural correction factors given in the table of Le Bas.[28] The calibration curve (Fig. 1) was

drawn by plotting the elution volume versus the calculated molar volume
for the standard materials and polypropylene oxide. Using the calibration
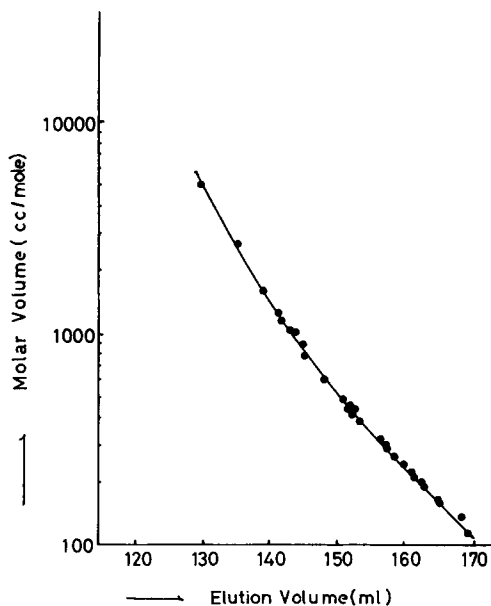curve, the apparent or observed molar volumes of other compounds were

Fig. 1. Calibration curve obtained with linear hydrocarbons, esters, and polypropylene
oxides.

given as the molar volumes corresponding to their observed elution volumes.

For many phenolic compounds, the apparent molar volumes thus ob-
tained are larger than their calculated molar volumes obtained by using
the table of atomic volumes. These increments are attributed to tetra-
hydrofuran solvating them.

In addition, as shown in Table I, an additional correction of 30 cc/mole
was found to be necessary for each benzene ring in benzene derivatives.

Consequently, the average number n of solvating tetraphydrofuran
molecule is given as follows:

$$n = \frac{\text{apparent molar volume} - \text{calculated molar volume} + 30 \times B}{88.3}$$

where B = number of benzene rings in the solute molecule and 88.3 =
calculated molar volume of tetrahydrofuran (cc/mole).

As given in Table II, 2-hydroxyacetophenone, 2-hydroxybenzophenones,
and 2-hydroxybenzoates are not solvated (compounds 1–6, n = −0.29 to
0.20) despite their hydroxyl groups. This is explained by assuming the

intramolecular hydrogen bond between the hydroxyl and the carbonyl groups as follows:
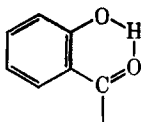
For 2,2'-dihydroxybenzophenones, the solvation is still considerably hindered (compounds 7 and 9, n = 0.16 and 0.50), but the 2,4'-isomer is solvated (compound 8, n = 1.09) similarly to the 4- or 3-hydroxy compounds (compounds 10, 11, and 13, n = 1.09 to 1.42).

Table III gives the solvation of substituted phenols in which the intramolecular hydrogen bond is also suggested for nitrophenol (compound 17, n = 0.18), whereas the para isomer shows unhindered solvation (compound 2, n = 1.32). The solvation for catechol (compound 10, n = 1.65) is less than that for hydroquinone (compound 1, n = 2.10), probably due to steric hindrance.

Table III also shows the steric hindrance of alkyl groups toward solvation; solvation does not occur for 2,6-di-*tert*-butyl-substituted phenols (compounds 23–25, n = 0.00–0.08), whereas it develops as the alkyl groups becomes less bulky or as they are more separated from the hydroxyl group.

For para-substituted phenols, the solvation is in the order of the substituent; nitro, chloro, hydrogen, *tert*-butyl, methyl, benzyl, suggesting the effect of the acidity of the phenols. The chlorine atom shows steric hindrance equal to that of the methyl group (compounds 11 versus 12, 18 versus 20).

Table IV shows similar steric hindrance of ortho-alkyl groups for methylenediphenols; but by comparing 4,4'-methylenediphenols with 2,2'-isomers, it is shown that the hydroxybenzyl group in the ortho position hinders the solvation less than the ortho-*tert*-butyl group. It was observed for 2,2'-methylenediphenols that the bulky substituents in the 5- or 5'-positions (para to hydroxyl) also hinder the solvation.

Table V shows the numbers, both observed (n) and the calculated (n_0), of tetrahydrofuran solvated to phenol–formaldehyde condensates. The latter (n_0) was obtained by assuming that all of the pairs of hydroxyl groups in 2,2'-positions form hydrogen bonds, which was described by Szymanski et al.[29]:

compound, n_0 = 2
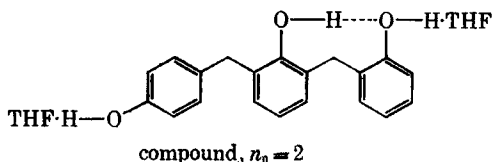
The results given in Table V support the presence of such hydrogen bonds. The results also agree with those reported by J. Kumanotani et al.[30] for

the NMR spectrum of novolak resins dissolved in pyridine where the ring current effect of the solvating pyridine was diminished by the presence of the "high ortho" structure of the novolak. It is thus considered very advantageous to apply both NMR spectrum and gel permeation chromatography for the characterization of novolak resin. These are being investigated in our laboratory.

SUMMARY

Solvation of the phenol–THF system has been elucidated by the comparison made between the calculated molecular volume and the actual volume of phenols determined by gel permeation chromatography using tetrahydrofuran as solvent.

1. THF will not exhibit solvation with a phenol in which its hydroxyl group is involved in the formation of an internal hydrogen bond, for example, with phenols that possess an ortho-carbonyl group, o,o'-dihydroxydiphenyl methane, etc.

2. Bulky ortho-substituted groups will impede solvation of THF, especially 2,6-di-*tert*-butylphenols will not form solvation at all.

3. Acidity of phenols will promote solvation.

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