

### Solubility Properties in Polymers and Biological Media. 3. Predictional Methods for Critical Temperatures, Boiling Points, and Solubility Properties ( $R_G$ Values) Based on Molecular Size, Polarizability, and Dipolarity

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**Abstract:** Critical temperatures and boiling points of 80 liquids have been correlated with parameters that describe the size, polarizability, and dipolarity of the liquids. Equations of the form  $X = X_0 + a(\text{MW})^{1/2} + b(N')^{1/2} + c\mu^2$  are given, where  $X$  is the critical temperature or boiling point, MW is the molecular weight, and  $\mu$  is the dipole moment. The  $N'$  parameter is defined by  $N' = N - N_F + 3N_{Cl} + 3N_{Br} + (3 - \mu)N_{DB} + 8$  for cycloalkanes +  $6.0(3.0 - \mu)$  for aromatics, where  $N$  is the number of atoms in the molecule and  $N_{DB}$  the number of nonaromatic carbon to carbon double bonds. The use of  $N'$  as a description of molecular polarizability is justified by linear correlation of  $(N' - N)$  with the refractive index function  $(n^2 - 1)/(2n^2 + 1)$ . For water and five alcohols, the differences between the observed critical temperatures and boiling points and values predicted by the correlation equations give estimates of the relative self-association due to hydrogen bonding in these compounds. These estimates agree well with other measures of self-association obtained from Hildebrand solubility parameters. For 28 nondipolar substances, Abraham's  $R_G$  parameter is well correlated by  $\text{MW}^{1/2}$  and  $(N')^{1/2}$ .

A good deal of attention has been devoted to methods of correlating and predicting solubilities of gaseous, liquid, and condensed phase solutes in polymers and biomedically important liquid and solid solvents.<sup>2</sup> As a prominent example, Stern, Mullhaupt, and Gareis,<sup>3</sup> approaching this problem from a polymer chemistry perspective, have demonstrated that Henry's law solubility coefficients ( $S_0$ ) of a large number of permanent gases and vapors in polyethylene correlate well with critical temperatures ( $T_c$ ) through an equation of the form of eq 1.

$$\log S_0 = A + B(T_c/T)^2 \quad (1)$$

In a recent extension of this approach into the biomedical area, Stern and Shiah<sup>4</sup> have shown that solubilities of a series of inhalation anesthetics in olive oil, human fat, silicone rubber, and natural rubber are well correlated with the solute critical temperatures and pressures according to eq 2, where  $L_0$  is the Ostwald solubility coefficient.

$$\log L_0 P_c = A + B(T_c/T) \quad (2)$$

Approaching the problem from a different direction, i.e., from a background of solution chemistry and linear solvation energy relationships, Abraham, Kamlet, Weathersby, and Taft<sup>5</sup> have recently shown that for (a) Stern and Shiah's data on the solubilities of the inhalation anesthetics in the various media and (b) solubilities of a series of inert (nondipolar)<sup>6</sup> gaseous and vapor solutes in polyethylene and hydrophilic polymers, equally good or better correlations also exist between  $L_0$  and the solute parameter,  $R_G$ , according to eq 3. The  $R_G$  parameter is a quantity determined

$$\log L_0 = a + bR_G \quad (3)$$

by Abraham<sup>7</sup> for many inert solutes (noble gases,  $\text{H}_2$ ,  $\text{CO}$ ,  $\text{N}_2$ ,  $\text{O}_2$ , alkanes, and polyalkylmetals) from best fits of their solubilities

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(2) We use the term "solvent" to refer to polymers and lipid and other biological media as well as liquid solvents.

(3) Stern, S. A.; Mullhaupt, J. T.; Gareis, P. J. *AIChE J.* 1969, 15, 64.

(4) Stern, S. A.; Shiah, S.-P. *Mol. Pharmacol.* 1981, 19, 56.

(5) Abraham, M. H.; Kamlet, M. J.; Taft, R. W.; Weathersby, P. K., submitted for publication in *J. Am. Chem. Soc.*

(6) We use the terms "inert" and "nondipolar" interchangeably to refer to solutes that do not interact with themselves or with solvents by virtue of dipole/dipole interactions.

(7) Abraham, M. H. *J. Am. Chem. Soc.* 1982, 104, 2085.

in large numbers of nondipolar and dipolar solvents to equations of the form of eq 4, where  $\Delta G_s^\circ$  is the free energy of solution and

$$\Delta G_s^\circ = -RT \ln K^H = d + lR_G \quad (4)$$

$K^H$  is the Henry's law constant. The  $R_G$  quantity in eq 4 characterizes the solute and is related to solute size, whereas  $d$  and  $l$  are characteristic properties of the solvent.

Also, as is expected of two parameters which are linear with the same solubility properties, Abraham et al.<sup>6</sup> showed a good correlation to exist between  $R_G$  of nondipolar solutes and  $T_c$ , and a better correlation between  $R_G$  and  $T_c^2$  according to eq 5. The

$$R_G = 1.542 + (6.10 \times 10^{-6})(T_c)^2 \quad (5)$$

important aspect of the complementary findings of the Stern Abraham research groups is that they demonstrate convincingly that certain relationships that had been derived for solubilities in pure liquid solvents apply equally well to solubilities in solid solvent phases (and vice versa).

The approach we describe in the present paper specifically acknowledges the hierarchical complexity that exists in solute/solvent interactions as the chemical nature of the solvent and/or solute becomes more complicated. In the order of increasing complexity, the following cases can be identified: (1) nondipolar solutes in nondipolar solvents; (2) nondipolar solutes in dipolar solvent systems; (3) dipolar non-self-associating solutes in nondipolar solvents; (4) dipolar non-self-associating solutes and solvent systems; (5) dipolar self-associating (DSA) solutes in nondipolar solvents; (6) DSA solutes in dipolar non-self-associating solvent systems; and (7) DSA solutes and solvent systems.

Now and in future papers of the present series we shall discuss the problem of describing the "Henry's law" or infinite dilution solubility coefficients for a variety of solutes in a wide variety of solvents. In many systems (types 2-7 above) substantial deviations from Henry's law (given by eq 6) can occur:<sup>8</sup>

$$p = K^H X \quad (6)$$

where  $p$  is the partial pressure of the solute above the solvent,  $K^H$  is the Henry's law constant, and  $X$  is the mole fraction of the solute

(8) Prausnitz, J. M. "Molecular Thermodynamics of Fluid Phase Equilibria"; Prentice-Hall, Inc.: Englewood Cliffs, NJ, 1969; Chapter 7.

dissolved in the solvent. Deviations from eq 6 often occur at rather low mole fraction compositions due to strong solution nonidealities in system types 2-7.<sup>8,9</sup> Fortunately, if reliable values of the infinite dilution activity coefficients,  $\gamma_1^\infty$  and  $\gamma_2^\infty$  can be estimated, either from experimental determinations or a correlation, the vapor-liquid equilibria can be predicted over the entire composition range.<sup>10</sup> Such predictions are possible even when very substantial nonidealities occur at relatively low solute concentrations. Moreover, reasonable results can often be obtained by using the infinite dilution activity coefficient for only the solute in conjunction with the Wilson equation.<sup>10</sup> If pure component vapor pressure ( $p^*$ ) data are available for the solute, the following relationship can be used to relate the values of  $K^H$ ,  $\gamma^\infty$ , and  $p^*$  for the solute:

$$K^H/p^* = \gamma^\infty \quad (7)$$

We shall also attempt to derive correlational methods for predicting  $p^*$  and  $\gamma^\infty$  in the present series of papers.

### Results and Discussion

For estimation of solubility by the methods of Stern et al.<sup>3,4</sup> or Abraham et al.<sup>5</sup> it is necessary to carry out at least one physical measurement, either of  $T_c$  or of solubility in a convenient solvent, and hence  $R_G$ . This series of papers has as its purpose to explore methods whereby  $T_c$  and  $R_G$ , and hence solubilities of nondipolar and dipolar solutes, can be estimated directly from molecular structure without recourse to any physical measurement. An example of an eventual long range application might be the prediction, prior to actual synthesis, of the relative distributions of a series of candidate pharmaceuticals between blood and lipid phases.

In the following discussion, we shall rationalize approaches for correlation of both the critical temperatures of components and the  $R_G$  values of the solutes appearing in eq 3 and 4. We shall treat the following cases of increasingly complex nature: (A) nondipolar compound, (B) dipolar non-self-associating compound, and (C) dipolar self-associating compound.

As a first approximation, one may characterize the intermolecular potential function,  $\Phi(r)$ , for the above classes of compounds using the Stockmayer expression,<sup>11</sup> which reduces to the form of the simpler Lennard-Jones expression for nondipolar compounds (type A above) since the dipole moment,  $\mu$ , of the component is in this case zero. The Stockmayer expression is given by eq 8,

$$\Psi(r) = 4\epsilon_0[(\sigma/r)^{12} - (\sigma/r)^6 - (\mu^2/r^3)g(\theta)] \quad (8)$$

where  $\epsilon_0$ ,  $\sigma$ , and  $\mu$  are the potential well depth, collision diameter, and dipole moment of the molecule, and the exponent function  $g(\theta)$  is a complex function of the angle separating the neighboring molecules.

For non-hydrogen-bonding compounds we have<sup>11</sup>

$$\sigma = 0.785V_c^{1/3} \quad (9a)$$

$$\epsilon_0 = 0.897T_c k \quad (9b)$$

where  $k$  is Boltzmann's constant,  $T_c$  is the compound's critical temperature, and  $V_c$  is the critical volume in cm<sup>3</sup>/mol. For hydrogen-bonding materials we have<sup>11</sup>

$$\sigma = 36.9V_c^{1/3}Z_c^{2.75} \quad (10a)$$

$$\epsilon_0 = 0.00331(T_c/Z_c^4) \quad (10b)$$

where  $Z_c = P_c V_c / RT_c$  and  $P_c$  is the critical pressure of the compound expressed in atmospheres.

On the basis of the above molecular-scale considerations, some important conclusions can be suggested. If one considers compounds in class A, the dipolar term may be neglected, and one needs to consider only the factors that affect  $V_c$  and  $T_c$  of the

Table I. Data Used in Correlations for Nondipolar Compounds

no.	compound	MW <sup>1/2</sup>	N <sup>1/2</sup>	T <sub>c</sub> , K	BP, K	R <sub>G</sub>	calcd, eq 24
1.	He	2.00	1.00	5.1	0.9	1.32	1.29
2.	H <sub>2</sub>	1.41	1.41	33.2	14.0	1.54	1.38
3.	Ne	4.49	1.00	44.3	24.4	1.39	1.49
4.	Ar	6.31	1.00	151.1	87.5	1.75	1.64
5.	Kr	9.15	1.00	209.3	116.5	1.95	1.87
6.	Xe	11.46	1.00	289.7	161.2	2.19	2.06
7.	Rn	14.90	1.00	377.2	211.3	2.39	2.34
8.	N <sub>2</sub>	5.29	1.41	126.0	77.3	1.64	1.69
9.	O <sub>2</sub>	5.66	1.41	154.3	90.1	1.74	1.73
10.	CO	5.29	1.41	134	81.6	1.71	1.70
11.	CH <sub>4</sub>	4.00	2.24	191.9	111.7	1.90	1.88
12.	C <sub>2</sub> H <sub>6</sub>	5.48	2.83	305.2	185	2.26	2.21
13.	C <sub>3</sub> H <sub>8</sub>	6.63	3.32	369.8	231	2.47	2.47
14.	n-C <sub>4</sub> H <sub>10</sub>	7.62	3.74	425	272.6	2.70	2.70
15.	n-C <sub>5</sub> H <sub>12</sub>	8.49	4.12	469.6	309.2	2.89	2.90
16.	n-C <sub>6</sub> H <sub>14</sub>	9.27	4.47	507.2	342.0	3.11	3.09
17.	n-C <sub>7</sub> H <sub>16</sub>	10.00	4.80	540	371.5	3.32	3.26
18.	n-C <sub>8</sub> H <sub>18</sub>	10.68	5.10	569	398.6	3.52	3.42
19.	c-C <sub>3</sub> H <sub>6</sub>	6.48	4.12	397.8	240.1		
20.	c-C <sub>5</sub> H <sub>10</sub>	8.37	4.80	511.8	322.3	3.02	3.13
21.	c-C <sub>6</sub> H <sub>12</sub>	9.17	5.10	553.4	353.8	3.24	3.30
22.	(CH <sub>3</sub> ) <sub>4</sub> C	8.49	4.12	456.9	282.6	2.73	2.90
23.	(C <sub>2</sub> H <sub>5</sub> ) <sub>4</sub> C	11.31	5.39	590	419.3	3.68	3.58
24.	i-C <sub>4</sub> H <sub>10</sub>	7.62	3.74	408.1	270	2.61	2.70
25.	C <sub>6</sub> H <sub>6</sub>	8.83	5.48	562.5	353.1		
26.	1,4-C <sub>6</sub> H <sub>4</sub> (CH <sub>3</sub> ) <sub>2</sub>	10.34	6.00	617	410		
27.	1,3,5-C <sub>6</sub> H <sub>3</sub> (CH <sub>3</sub> ) <sub>3</sub>	10.95	6.25	653	437.8		
28.	CF <sub>4</sub>	9.38	1.00	225.2	145.3	1.70	1.89
29.	C <sub>2</sub> F <sub>6</sub>	11.75	1.41	292.8	194.1		
30.	SF <sub>6</sub>	12.08	1.00	318.6	209.1	1.98	2.11
31.	(CH <sub>3</sub> ) <sub>3</sub> Sn	13.36	4.12			3.14	3.30
32.	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> Sn	15.31	5.39			4.02	3.90
33.	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> Pb	17.98	5.39			4.17	4.12

compound to adequately characterize its properties. The primary factors controlling  $V_c$  of a material are its molecular weight (MW) and the number of atoms in the molecule ( $N$ ). Also, correlation is strong between  $T_c$  of a compound and  $V_c$  and molecular polarizability (which, at a given MW, also depends on  $N$ ) for compounds in class A, so one can again reasonably expect that  $N$  and MW will be the most important variables for consideration in critical temperature correlations of nondipolar compounds. The exact functional dependency of a given property on MW and  $N$  cannot, of course, be generally predicted a priori. We have therefore approached the problem in an empirical fashion.

**Correlations of  $T_c$  for Nondipolar Compounds.** The data used in the correlations<sup>12</sup> are assembled in Table I and include results for the noble gases, some aliphatic and aromatic hydrocarbons, the inert<sup>6</sup> inorganic gases, H<sub>2</sub>, CO, N<sub>2</sub>, and O<sub>2</sub>, some tetraalkyltin and lead compounds with hydrocarbon-like properties, and some fluorinated gases. All the compounds in Table I have zero dipole moments.

Our various attempts to relate critical temperatures to functions of MW and  $N$  led to the following findings: (a) In all cases, correlations with MW<sup>1/2</sup> and N<sup>1/2</sup> led to better statistical goodness of fit than corresponding correlations with MW and  $N$ , MW<sup>1/2</sup> and  $N$ , or MW and N<sup>1/2</sup>. (b) The correlations for compounds 1-18 and 22-24 of Table I (i.e., excluding the cycloalkanes, the aromatics, and the fluorinated compounds) led to eq 11 as the multiple linear regression equation, with  $r$  (the correlation

$$T_c \text{ (in K)} = -114.7 + 27.1(\text{MW})^{1/2} + 82.1(N)^{1/2} \quad (11)$$

coefficient) = 0.993 and sd (the root mean square deviation) = 21.4 K. (c)  $T_c$  values calculated for the cycloalkanes and the aromatic hydrocarbons through eq 11 were much lower than observed, undoubtedly because of the enhanced polarizability characteristics of the latter type of compounds, which are evidenced by the following  $n^2_D$  values: *n*-hexane, 1.375; cyclohexane,

(9) Prausnitz, J. M.; Anderson, T. F.; Grens, E. A.; Eckert, C. A.; Hsieh, R.; O'Connell, J. P. "Computer Calculations for Multicomponent Vapor-Liquid and Liquid-Liquid Equilibria"; Prentice-Hall, Inc.: Englewood Cliffs, NJ, 1980; Chapter 4.

(10) Reid, R. C.; Prausnitz, J. M.; Sherwood, T. K. "The Properties of Gases and Liquids", 3rd ed.; McGraw-Hill: New York, 1977; Chapter 8.

(11) Reid, R. C.; Sherwood, T. K. "The Properties of Gases and Liquids", 2nd ed.; McGraw-Hill: New York, 1966; Chapter 3.

(12) Critical temperatures and dipole moments were from: "CRC Handbook of Chemistry and Physics", 60th ed.; Weast, R. C., Ed.; CRC Press: Boca Raton, FL, 1979.

Table II. Data Used in the Correlations for Dipolar Compounds<sup>a</sup>

no.	compound	MW <sup>1/2</sup>	N' <sup>1/2</sup>	μ <sup>2</sup>	(T <sub>c</sub> ) <sub>obsd</sub>	(T <sub>c</sub> ) <sub>calcd</sub> <sup>eq 8</sup>	(ΔΔT <sub>c</sub> ) <sub>D</sub>	(BP) <sub>obsd</sub>	(BP) <sub>calcd</sub> <sup>eq 14</sup>	(ΔΔBP) <sub>D</sub>
1.	Et <sub>3</sub> N	10.15	4.69	0.44	533.2	534.1	-1.1	362.6	350.6	12.0
2.	EtOEt	8.60	3.87	1.32	466.5	430.4	36.1	307.7	279.4	28.3
3.	EtOAc	9.38	3.74	3.17	523.3	440.9	82.3	350.3	285.9	64.4
4.	acetone	7.62	3.16	8.29	508.7	347.8	160.9	329.6	322.6	107.0
5.	2-butanone	8.49	3.61	7.29	535.6	406.8	128.7	352.7	263.0	89.7
6.	CH <sub>3</sub> NO <sub>2</sub>	7.81	2.64	11.97	587.8	296.6	291.2	373.9	186.4	192.8
7.	CH <sub>3</sub> CN	6.40	2.45	15.36	547.8	258.8	289.0	355	161.6	193.4
8.	CHF <sub>3</sub>	8.37	1.41	2.72	299	229	70	190.9	138.3	52.5
9.	CH <sub>3</sub> F	5.83	2.00	3.42	317.7	207.8	109.9	194.7	126.5	68.1
10.	CHCl <sub>3</sub>	10.93	3.74	1.02	536	482.4	53.6	334.8	313.2	21.6
11.	CH <sub>2</sub> Cl <sub>2</sub>	9.22	3.46	2.96	510	414.5	95.5	313.0	267.5	45.5
12.	CH <sub>3</sub> Cl	7.10	2.83	3.42	416.9	307.7	109.2	248.9	195.1	53.8
13.	CH <sub>3</sub> CH=O	6.63	2.65	7.24	460.8	280.8	180.0	293.9	176.8	117.1
14.	C <sub>6</sub> H <sub>5</sub> Cl	10.60	4.78	2.86	632.3	556.1	76.2	405.1	365.3	39.8
15.	C <sub>6</sub> H <sub>5</sub> F	9.80	4.40	2.96	560.1	501.9	58.2	358.1	330.1	28.1
16.	C <sub>6</sub> H <sub>5</sub> CN	10.15	2.46	17.47	699.1	360.1	339.0	465	228.2	236.8
17.	C <sub>6</sub> (CH <sub>3</sub> ) <sub>6</sub>	12.73	6.93	0.00	767.1	783.7	-16.6	538	522.5	15.5
18.	C <sub>6</sub> H <sub>5</sub> OCH <sub>3</sub>	10.39	5.08	1.82	641.6	574.2	67.4	428.6	378.3	50.3

<sup>a</sup> Temperatures in K.

1.426; benzene, 1.502. (d) The T<sub>c</sub> values calculated through eq 11 for SF<sub>6</sub>, CF<sub>4</sub>, and C<sub>2</sub>F<sub>6</sub> were higher than observed, again most probably because of differing polarizability characteristics, the polarizabilities of perfluoro compounds being considerably less than those of corresponding hydrogen compounds; compare n<sup>20</sup><sub>D</sub> of 1.271 for perfluoro-*n*-octane with 1.397 for *n*-octane. (e) Critical temperatures of CCl<sub>4</sub>, CBr<sub>4</sub>, and CFCl<sub>2</sub>CFCl<sub>2</sub> (not included in Table I) were higher than called for by eq 11, as were those for CH<sub>2</sub>=CH<sub>2</sub> and CH<sub>2</sub>=CHCH<sub>3</sub>, again most probably because of polarizability effects. (f) To account for these different polarizability characteristics, a parameter, N', was defined as follows:

$$N' = N - N_F + 3N_{Cl} + 3N_{Br} + 3N_{DB} + 8 \text{ for cycloalkanes} + 18 \text{ for nondipolar aromatics} \quad (12)$$

where N<sub>F</sub>, N<sub>Cl</sub>, N<sub>Br</sub>, and N<sub>DB</sub> are the numbers of fluorine, chlorine, bromine, and nonaromatic double bonds in the molecule, respectively. (g) The multiple-parameter least-squares correlation of T<sub>c</sub> with MW<sup>1/2</sup> and N'<sup>1/2</sup> for compounds 1–30 of Table I led to eq 13. It is seen that including the compounds with the

$$T_c \text{ (in K)} = -107 + 26.8(MW)^{1/2} + 79.3(N')^{1/2} \quad (13)$$

$$r = 0.994, \text{ sd} = 21.1 \text{ K}$$

different polarizability characteristics causes only nominal differences in the intercepts and coefficients of MW<sup>1/2</sup> and (N')<sup>1/2</sup> between eq 11 and 13, and the correlation coefficients and standard deviations (near 21 K over a temperature range from 5 to 653 K) are also similar. On this basis, it was considered unnecessary to "fine tune" the definition of N' of nondipolar solutes beyond the precision shown in eq 12.

#### Correlations of T<sub>c</sub> for Dipolar Non-Self-Associating Compounds.

Equation 13 applies only to nondipolar and very weakly dipolar species and breaks down seriously for closely related but more strongly dipolar compounds that, because of dipole/dipole interactions which stabilize the liquid phase, have higher critical temperatures than are called for by eq 13. To quantify these dipolar effects, we have defined by eq 14 a quantity, (ΔΔT<sub>c</sub>)<sub>D</sub>,

$$(\Delta\Delta T_c)_D = (T_c)_{\text{obsd}} - (T_c)_{\text{calcd}}^{\text{eq13}} \quad (14)$$

the increment in critical temperature due to dipole/dipole interactions. Values of (T<sub>c</sub>)<sub>obsd</sub>, (T<sub>c</sub>)<sub>calcd</sub> and (ΔΔT<sub>c</sub>)<sub>D</sub> are assembled in Table II, together with gas phase electric dipole moments and values of MW<sup>1/2</sup> and (N')<sup>1/2</sup> for 18 compounds of varying dipolarity which are not self-associated by hydrogen bonding.

If one now reconsiders eq 8 and 9 for the dipolar molecules, the principal new physical parameter to be taken into account is the dipole moment, μ. The function g(θ), which accounts for the angle between the dipoles of interacting molecules is complex, and its contribution may be neglected for the purposes of the present discussion.

Our attempts at correlations of T<sub>c</sub> with functions of μ led to the following conclusions: (a) correlations of (ΔΔT<sub>c</sub>)<sub>D</sub> with μ<sup>2</sup> showed better statistical goodness of fit than corresponding correlations with μ, as might be expected, since the dipolar effect involves interactions between the dipoles of at least two molecules. (b) The correlation for the aliphatic compounds of Table II (i.e., compounds 1–13) led to regression eq 15. (c) The weakly dipolar

$$(\Delta\Delta T_c)_D = 23.6 + 18.9\mu^2 \text{ K} \quad (15)$$

$$r = 0.964, \text{ sd} = 22.7 \text{ K}$$

aromatic compounds fit eq 13–15 reasonably well, but the observed T<sub>c</sub> values of the aromatic compounds with the larger dipole moments, fluoro- and chlorobenzene and benzonitrile, are significantly lower than called for by eq 13–15 and the definition of N' in eq 12.

[The latter results were not surprising to us in the light of an observation by Taft, Abboud, and Kamlet<sup>13</sup> that, although polarizabilities of aromatic solvents tend to increase slightly with increasing dipolarity (e.g., compare the n<sup>20</sup><sub>D</sub> values of benzene, 1.501; benzonitrile, 1.529; nitrobenzene, 1.566), polarizability contributions to solvent effects of aromatics decrease with increasing solvent dipolarity. The rationale for such an effect will be described in detail in a future paper. For present purposes it suffices to say that a dipolar molecule like nitrobenzene, adjacent to another dipolar molecule, is configured so that its most dipolar moiety (the nitro group) is oriented toward the dipole of the neighboring molecule, and the less dipolar, more polarizable moiety (the ring) is away from that dipole. As a consequence, the average distance, r, between the dipole of one molecule and the polarizable center of the other will be greater for nitrobenzene than for a nondipolar molecule like toluene, which is oriented to minimize r and maximize the dielectric stabilization of the system by London forces. Since the dispersion effect is usually considered to vary with a higher power of r, typically r<sup>3</sup>, the polarizability contribution to solvent effects (or to effects on T<sub>c</sub> and BP of liquids) will be significantly smaller for nitrobenzene than for toluene, even though the f(n<sup>2</sup>) term is larger for the former compound than for the latter.]

To accommodate a similar trend in effects of polarizability on critical temperatures of dipolar aromatics and dipolar olefins and to fit the results for compounds 14–17 of Table II (and some of the compounds of Table IV) to eq 15, we have modified the definition of N' as follows:

$$N' = N - N_F + 3N_{Cl} + 3N_{Br} + (3.0 - \mu)N_{DB} + 8 \text{ for cycloalkanes} + 6.0(3.0 - \mu) \text{ for aromatics} \quad (16)$$

Accordingly, N' remains N + 18 for aromatics and N + 3N<sub>DB</sub> for olefins with zero dipole moments. With dipolar aromatics and olefins, however, polarizability contributions to N' decrease with increasing μ and turn negative at μ > 3.0 D.

Table III. Data Used in the Correlations for Self-Associating Compounds<sup>a</sup>

no.	compound	MW <sup>1/2</sup>	N' <sup>1/2</sup>	μ <sup>2</sup>	(T <sub>c</sub> ) <sub>obsd</sub>	(T <sub>c</sub> ) <sub>calcd</sub> <sup>eq 13</sup>	(ΔΔT <sub>c</sub> ) <sub>SA</sub>	(BP) <sub>obsd</sub>	(BP) <sub>calcd</sub> <sup>eq 16</sup>	(ΔΔBP) <sub>SA</sub>
1.	H <sub>2</sub> O	4.24	1.73	3.42	647.3	218.8	428.5	373.1	131.7	241.4
2.	MeOH	5.66	2.45	2.89	513.1	302.6	210.4	337.8	190.0	147.7
3.	EtOH	6.78	3.00	2.86	516.1	375.2	140.9	351.6	240.3	111.3
4.	<i>n</i> -PrOH	7.75	3.46	2.82	536.7	436.4	100.2	370	282.7	87.2
5.	<i>i</i> -PrOH	7.75	3.46	2.76	508.1	435.3	72.8	355.6	281.9	73.6
6.	<i>n</i> -BuOH	8.60	3.87	2.76	562.9	490.2	72.7	390	320.9	70.0

<sup>a</sup> Temperatures in K.

[The terms for the aromatics and olefins in eq 16 are similar in concept to the "reducing functions of *n*" proposed by Taft et al. to rationalize polarizability contributions to solvent effects,<sup>13,14</sup> except that other "reducing polarizability functions", when applied to solvent effects, have gone to zero for aromatics with dipole moments near 4.2D rather than turning negative as in eq 16. It is not completely clear (however, see below) why a negative polarizability contribution should lead to optimal correlations of critical temperatures for the more dipolar aromatic compounds.]

Continuing seriatim with our findings for the dipolar compounds: (d) With *N'* now defined by eq 16, the correlation for the 18 aliphatic and aromatic compounds of Table II is given by eq 17. That the standard deviation for eq 17 is only 1 K higher

$$(\Delta\Delta T_c)_D = 19.3 + 19.0\mu^2 \text{ K} \quad (17)$$

$$r = 0.967, \text{ sd} = 22.0 \text{ K}$$

than for antecedent eq 13, despite the increased complexity of the molecular interactions, serves to support our assumption that the dipolar effect varies with the square of the dipole moment. That the intercept in eq 17 is smaller than the standard deviation suggests that the relationship does, indeed, involve a direct proportionality. (e) To combine all the effects into a single equation, we next carried out a multiple parameter least squares correlation of *T<sub>c</sub>* for the 48 compounds of Tables I and II with MW<sup>1/2</sup>, (*N*)<sup>1/2</sup>, and μ<sup>2</sup> as the independent variables. The result is given by eq 18. A plot of calculated vs. observed *T<sub>c</sub>* values is shown in Figure

$$T_c \text{ (in K)} = -99.9 + 26.6(\text{MW})^{1/2} + 78.9(\text{N})^{1/2} + 20.3\mu^2 \quad (18)$$

$$r = 0.993, \text{ sd} = 22.1 \text{ K}$$

1. It is seen that the coefficients of μ<sup>2</sup> are similar in eq 17 and 18 and that the coefficients of MW<sup>1/2</sup> and (*N*)<sup>1/2</sup> and the intercepts are similar in eq 13 and 18, despite the fact that the 18 *T<sub>c</sub>* values in Table II did not contribute to the determination of the latter terms in eq 13. This lends confidence that the effects of the properties which control critical temperatures of nondipolar and dipolar non-self-associating compounds are being dealt with in a satisfactory manner in eq 18.

**Correlations of Boiling Points.** Following the same sequence of steps as with the critical temperatures, we have correlated the boiling points, BP, of the same 48 compounds with MW<sup>1/2</sup>, (*N*)<sup>1/2</sup>, and μ<sup>2</sup>. The correlations are given by eq 19 for the 30 non-dipolar

$$\text{BP (in K)} = -87.5 + 17.6(\text{MW})^{1/2} + 55.7(\text{N})^{1/2} \quad (19)$$

$$r = 0.994, \text{ sd} = 13.1 \text{ K}$$

$$(\Delta\Delta\text{BP})_D = 11.9 + 12.82\mu^2 \text{ K} \quad (20)$$

$$r = 0.982, \text{ sd} = 12.3 \text{ K}$$

$$\text{BP (in K)} = -86.6 + 17.7(\text{MW})^{1/2} + 56.1(\text{N})^{1/2} + 13.5\mu^2 \quad (21)$$

$$r = 0.994, \text{ sd} = 13.4 \text{ K}$$

(13) Taft, R. W.; Abboud, J.-L. M.; Kamlet, M. J. *J. Am. Chem. Soc.* **1981**, *103*, 1080.

(14) A representative "reducing function of *n*" is given by *P* (polarizability effect) = [f(*n*) - 0.19](1 - 0.23μ), where f(*n*) = (n<sup>2</sup> - 1)/(2n<sup>2</sup> + 1). The (1 - 0.23μ) term in this equation is near unity for nondipolar aromatic solvents like benzene and approaches zero for the more dipolar aromatics like nitrobenzene and benzonitrile. The [f(*n*) - 0.19] term is near zero for the less polarizable aliphatic solvents and larger for the more polarizable aromatics.

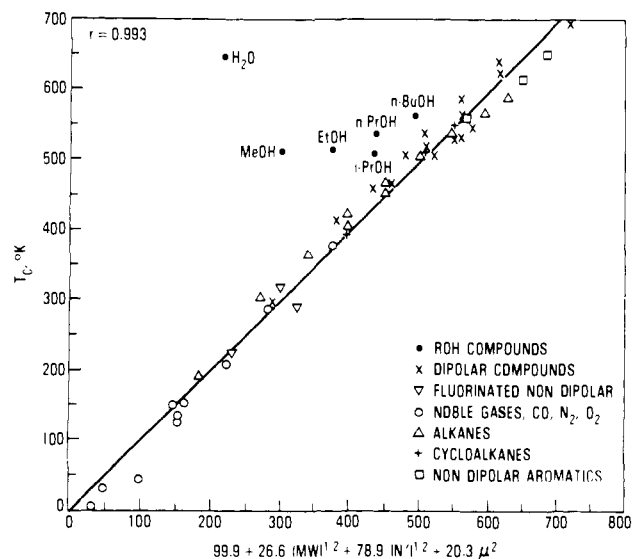


Figure 1. Observed critical temperatures plotted against values calculated through eq 18.

compounds of Table I, eq 20 for the 18 dipolar compounds of Table II, and eq 21 for all 48 compounds. It is seen that, although the correlation coefficients are similar, the standard deviations for eq 19–21 are about 2/3 as large as those for the corresponding *T<sub>c</sub>* correlations. Also, the ratios of the coefficients of MW<sup>1/2</sup>, (*N*)<sup>1/2</sup>, and μ<sup>2</sup> are 1.00/2.97/0.76 in eq 18 and 1.00/3.16/0.76 in eq 21. These similar ratios suggest that the molecular size, polarizability, and dipolarity have similar relative influences on critical temperatures and boiling points. Further, the coefficients of the independent variables in eq 21 and 18 are in the ratios of 0.665 for MW<sup>1/2</sup>, 0.711 for (*N*)<sup>1/2</sup>, and 0.658 for μ<sup>2</sup>, which is in accord with Guldberg's original observation that the ratio of the normal boiling point to the critical temperature is relatively constant for many organic and inorganic materials and approximately equal to 2/3.<sup>15</sup>

The correlations leading to eq 13–18 and 19–21 were restricted to compounds for which critical temperatures, normal boiling points, and gas-phase electric dipole moments were reported in the same data source.<sup>12</sup> We have carried out further tests of eq 18–21 on an additional series of compounds for which boiling points, but not critical temperatures, were listed in that same handbook. These are discussed in detail below, together with a comparison with other calculational methods.

**Critical Temperatures and Boiling Points of Self-Associating (Hydrogen-Bonded) Liquids.** In addition to the molecular size, polarizability, and dipole/dipole effects quantified by eq 18 and 21, self-association (via hydrogen bonding)<sup>16</sup> stabilizes the liquid relative to the vapor state. This effect serves to further increase the normal boiling points and critical temperatures of amphiprotic R-OH compounds, which can act simultaneously as hydrogen bond donors (acids) and acceptors (bases). Accordingly, in an extension of our previous reasoning, we have defined by eq 22a and 22b two quantities, (ΔΔT<sub>c</sub>)<sub>SA</sub> and (ΔΔBP)<sub>SA</sub>, the increments

(15) Guldberg, C. M. *Z. Phys. Chem.* **1980**, *5*, 374.

(16) Although dipole/dipole effects lead to a sort of self-association, we use here the term self-association to refer to hydrogen bonding by amphiprotic compounds acting simultaneously as donors (acids) and acceptors (bases).

$$(\Delta\Delta T_c)_{SA} = (T_c)_{obsd} - (T_c)_{calcd}^{eq18} \quad (22a)$$

$$(\Delta\Delta BP)_{SA} = (BP)_{obsd} - (BP)_{calcd}^{eq21} \quad (22b)$$

in critical temperatures and boiling points due to self-association by hydrogen bonding.

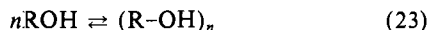
Values of  $(\Delta\Delta T_c)_{SA}$  and  $(\Delta\Delta BP)_{SA}$  for water and some alcohols are assembled in Table III together with the data used in the calculations. Also, the results for the R-OH compounds are included in the plot of  $(T_c)_{obsd}$  vs.  $(T_c)_{calcd}^{eq18}$  in Figure 1. The  $(\Delta\Delta T_c)_{SA}$  terms correspond to the vertical displacements of the R-OH data points from the regression line.

It is seen in the table and the figure that, as might be expected, the increments in  $T_c$  and BP increase with decreasing steric effects of R in R-OH, the increments being relatively similar for 1-butanol and 2-propanol, increasing slightly on going to 1-propanol, somewhat more so on going to ethanol and methanol, and sharply on going to water. Indeed, for water, the self-association contributions to  $T_c$  and BP outweigh the contributions of molecular size, polarizability, and dipolarity combined. [The 131.7 K boiling point in Table III for hypothetical non-self-associated water compares with a value of 161 K estimated by Taft and Sisler<sup>17</sup> by extrapolation of a linear relationship of normal boiling points of the group 6 hydrides (H<sub>2</sub>Te, H<sub>2</sub>Se, H<sub>2</sub>S) with period numbers].

Also of interest are the ratios of the self-association contributions to  $T_c$  and BP for the various R-OH compounds. These are listed, as follows, together with corresponding critical pressure values.

	$(\Delta\Delta T_c)_{SA} / (\Delta\Delta BP)_{SA}$	$P_c$ , atm
H <sub>2</sub> O	1.775	218.3
MeOH	1.424	78.5
EtOH	1.265	63
<i>n</i> -PrOH	1.115	51
<i>i</i> -PrOH	0.989	47
<i>n</i> -BuOH	1.038	43.6

The ratios, which are also seen to increase with decreasing size of R in R-OH, are rationalized as follows. The extent of stabilization of the liquid phase relative to the vapor phase by hydrogen bonding depends on the equilibrium constant for the reaction given by eq 23, the  $\Delta\Delta$  term being larger the higher the



equilibrium constant. This reaction is exothermic from left to right, so that the higher temperatures at the critical points tend to shift the equilibria in the direction of dissociation. However, since  $(R-OH)_n$  occupies less volume than  $nR-OH$ , the higher pressures at the critical points tend to shift the equilibria in the direction of association. The opposing trends just about offset one another for *n*-butanol and 2-propanol, but the higher critical pressures dominate increasingly on going to 1-propanol, ethanol, methanol, and water. Indeed, there is a fair correlation between the  $(\Delta\Delta T_c)_{SA} / (\Delta\Delta BP)_{SA}$  ratios and the logarithms of the critical pressures, the linear regression equation being given by eq 24. The

$$(\Delta\Delta T_c)_{SA} / (\Delta\Delta BP)_{SA} = -0.673 + 1.10 \log P_c \text{ (in atm)} \quad (24)$$

$$n = 6, r = 0.974$$

dependence of  $T_c$  on  $P_c$  suggested by eq 24 is consistent with our earlier analysis of effects contributing to critical temperatures (eq 8-10).<sup>18</sup>

**Comparisons with Other Measures of Self-Association.** We were also interested in examining how the  $(\Delta\Delta T_c)_{SA}$  and  $(\Delta\Delta BP)_{SA}$  values for the R-OH compounds compared with other properties that depend on the extent of self-association, but we found such information to be quite sparse in the literature. The most comprehensive and informative study is by Abboud and co-workers,<sup>19</sup>

who have reported the following dimerization constants,  $K_d$ , in cyclohexane solvent: *t*-BuOH, 22; *i*-PrOH, 39; *n*-PrOH, 47; EtOH, 48; MeOH, 56. They also concluded that tetramerization ( $K_{dd}$ , for dimerization of dimers) is over an order of magnitude more important than dimerization. For the couple MeOH/*t*-BuOH, they found  $(K_d)_{MeOH} / (K_d)_{t-BuOH}$  in CCl<sub>4</sub> = 1.83 and  $(K_{dd})_{MeOH} / (K_{dd})_{t-BuOH}$  = 3.49. These results are qualitatively and quantitatively consistent with our findings.

Abboud and co-workers<sup>19</sup> also observed that their association constants appeared to depend primarily on the steric influence of R, and hence were nicely correlated with Taft's steric parameter,  $E_s$ .<sup>20</sup> Accordingly, we have also carried out correlations of the  $\Delta\Delta$  terms with the  $E_s$  values of R in R-OH, and we have found the correlation coefficients and the standard deviations to be 0.989 and 18.6 K for the linear regression of  $(\Delta\Delta T_c)_{SA}$  with  $E_s$  and 0.981 and 11.6 K for the regression equation with  $(\Delta\Delta BP)_{SA}$ . [However, the  $E_s$  values for the R groups considered here are also approximately linear with the corresponding substituent polarizability measures,  $\sigma_\alpha$  (values of which will be published shortly), with a correlation coefficient of 0.975. Hence, the relative self-association terms for the R-OH compounds may be governed by steric or electronic effects, or, more probably, by a combination of both.]

Another measure of the extent of self-association is the self-association contribution to the Hildebrand solubility parameter,  $\delta_{SA}$ , defined as follows:

$$\delta_{SA} = \delta_H - \delta_C \quad (25)$$

where  $\delta_H$  is the Hildebrand solubility parameter, as determined from the molal heat of vaporization,<sup>21</sup> and  $\delta_C$  is the corresponding solubility parameter, as determined for R-OH solvents from correlations of the solubilities of nondipolar solutes.<sup>22,23</sup> We have recently reported the following  $\delta_{SA}$  values:<sup>24</sup> H<sub>2</sub>O, 5.3; MeOH, 3.2; EtOH, 2.1; *n*-PrOH, 1.7; *i*-PrOH, 1.5; *n*-BuOH, 1.6. Correlations of the  $\Delta\Delta$  terms with  $\delta_{SA}$  are given by eq 26 and 27.

$$(\Delta\Delta T_c)_{SA} = -68.5 + 93.9\delta_{SA} \text{ K} \quad (26)$$

$$r = 0.998, \text{ sd} = 6.3 \text{ K}$$

$$(\Delta\Delta BP)_{SA} = 7.8 + 44.7\delta_{SA} \text{ K} \quad (27)$$

$$r = 0.995, \text{ sd} = 6.1 \text{ K}$$

It is particularly important that the intercept in eq 27 is smaller than the standard deviation of antecedent eq 21, as this suggests that the relationship involves a direct proportionality as would be required if  $\delta_{SA}$  and  $(\Delta\Delta BP)_{SA}$  were both proportional to self-association energies. The nonproportionality in eq 26 may be because the  $T_c$  values are at different critical pressures. These excellent correlations between the completely independently derived measures of self-association lend confidence that our extractions of the self-association terms from the complex mixtures of effects influencing the critical temperatures and boiling points are approximately correct.

**Correlations of Abraham's  $R_G$  Parameter.** We have also correlated Abraham's  $R_G$  values of nondipolar solutes<sup>7</sup> with  $MW^{1/2}$  and  $(N')^{1/2}$  (which means, in effect, that these parameters also correlate solubilities of Abraham's 28 nondipolar solutes in large numbers of nondipolar and dipolar non-self-associating and

(20)  $E_s$  values used in the correlation: H, +1.24; CH<sub>3</sub>, 0.00; C<sub>2</sub>H<sub>5</sub>, -0.07; *n*-C<sub>3</sub>H<sub>7</sub>, -0.36; *n*-C<sub>4</sub>H<sub>9</sub>, -0.39; *i*-C<sub>3</sub>H<sub>7</sub>, -0.47 [Taft, R. W. in "Steric Effects in Organic Chemistry"; Newman, M. S., Ed.; Wiley: New York, 1956; Chapter 13].

(21) Hildebrand, J. H.; Scott, R. L. "The Solubility of Nonelectrolytes", 3rd ed.; Dover Publications: New York, 1964. Hildebrand, J. H.; Scott, R. L. "Regular Solutions"; Prentice-Hall: Englewood Cliffs, NJ, 1962.

(22) We have shown earlier<sup>23</sup> that free energies of solution of nondipolar solutes in dipolar and nondipolar solvents are well correlated by equations of the form  $\Delta G_s = (\Delta G_s)_0 + h\delta$ , where  $\delta$  is the Hildebrand solubility parameter. The  $\delta_C$  values were obtained from the best fits to the above equations of solubilities of multiple inert solutes in R-OH solvents.

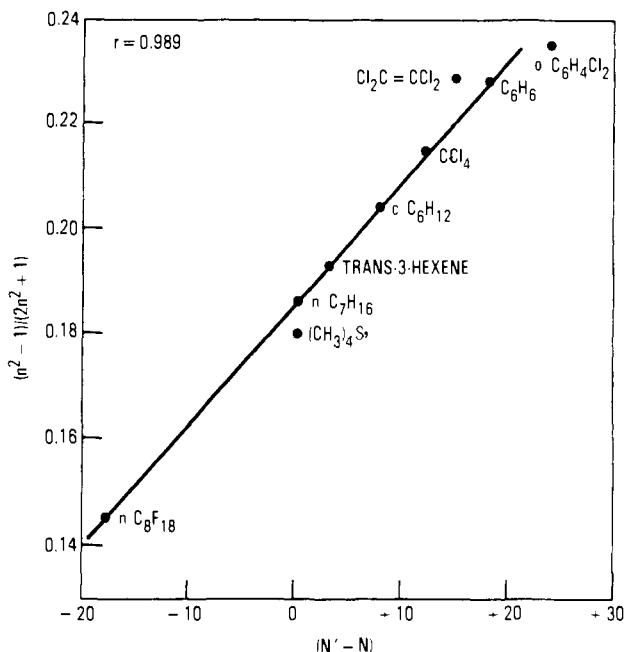
(23) Kamlet, M. J.; Carr, P. W.; Taft, R. W.; Abraham, M. H. *J. Am. Chem. Soc.* **1981**, *103*, 6062.

(24) Kamlet, M. J.; Doherty, R. M.; Taft, R. W.; Abraham, M. H. *J. Am. Chem. Soc.* **1983**, *105*, 6741.

(17) Taft, R. W.; Sisler, H. H. *J. Chem. Educ.* **1947**, *24*, 1945.

(18) Because of the differing ratios of the self-association terms, the usual generalizations regarding  $T_c$ /BP relationships break down for water and the alcohols.

(19) Frange, B.; Abboud, J.-L. M.; Benamou, C.; Bellon, L. *J. Org. Chem.* **1982**, *47*, 4553.



**Figure 2.** Polarizability function  $(n^2 - 1)/(2n^2 + 1)$  plotted against  $(N' - N)$ .

self-associating solvents). The multiple linear regression is given by eq 28. Observed and calculated results are assembled in Table

$$R_G = 0.766 + 0.0815(MW)^{1/2} + 0.349(N')^{1/2} \quad (28)$$

$$n = 28, r = 0.993, sd = 0.095$$

I, where it is seen that, unlike the BP correlation, where calculated results for the  $R_4Sn$  and  $R_4Pb$  compounds were on the high side (see below), the calculated  $R_G$  values for these compounds bracket the experimental results.

Since MW strongly influences solute size and weakly influences polarizability (as evidenced from the following  $n_D^{20}$  values: *n*-hexane, 1.375; *n*-heptane, 1.387; *n*-octane, 1.397) whereas  $N'$  varies weakly with size and strongly with polarizability (see below) we can ascertain from the ratios of the coefficients of  $MW^{1/2}$  and  $(N')^{1/2}$  whether  $T_c$ , BP, and  $R_G$  are influenced equally by molecular size and polarizability and, if not, which property has the greater influence on which parameter. The ratios of the coefficients are 1/2.97 for  $T_c$ , 1/3.16 for BP, and 1/4.28 for  $R_G$ , which suggests that critical temperatures and boiling points are relatively more influenced by molecular size, while  $R_G$  (and hence solubilities of nondipolar solutes) are more influenced by solute polarizability. The differing ratios may explain why experimental  $R_G$  values show better linearity with  $T_c^2$  ( $r = 0.992$ ) than with  $T_c$  ( $r = 0.972$ ).<sup>5</sup> The lesser relative dependence on solute MW may also explain why the tetraalkyltin and -lead compounds fit the  $R_G$  correlation better than the BP correlation (see below).

Equation 28 can be used to predict additional  $R_G$  values of nondipolar and dipolar solutes. It should be understood, however, that an experimental  $R_G$  value of a nondipolar solute, typically obtained by averaging individual estimates from solubilities in a number of solvents and eq 4, is more reliable than and preferable to a calculated value from eq 28. The experimental average deviations are usually considerably smaller than the standard deviation of eq 28.

For dipolar solutes, however, solute dipole/solvent dipole (or induced dipole) effects also influence free energies of solution, so that "experimental"  $R_G$  values of any such solutes are more difficult to determine, and, at the present writing, the  $R_G$  parameter for such solutes necessarily remains a calculated value from eq 28, which is considered to measure contributions of molecular size and polarizability to solubility properties. In future papers of this series, we shall show that solubilities of dipolar solutes in nondipolar and dipolar solvents are well correlated through equations which involve multiple dependences on

$(R_G)_{\text{calcd}}$  eq 28, a solute dipolarity parameter (either  $\mu$  or  $\pi^*$ ) and, if necessary, a solute hydrogen bond acidity and/or basicity parameter ( $\alpha$  and/or  $\beta$ ).<sup>25</sup>

**Correlation of  $N'$  with a More Fundamental Parameter.** Equations 18 and 21 measure molecular size, polarizability, and dipolarity contributions to  $T_c$  and BP. While there is no question that molecular size is related to MW and molecular dipolarity to  $\mu$ , the relationship between molecular polarizability and  $N'$  is less obvious. Also, we do not now know of any obvious reason why the relationships should be with the square roots of MW and  $N'$ .

As to the significance of  $N'$ , however, we can now show that, although arrived at by Edisonian fitting of the data, it does turn out to have a meaningful and satisfying relationship to a more fundamental parameter. Listed below are  $(N' - N)$  values for nine compounds of different polarizability classes and with zero dipole moments, together with the refractive index function  $(n^2 - 1)/(2n^2 + 1)$ , a frequently used measure of molecular polarizability.

	$(N' - N)$	$(n^2 - 1)/(2n^2 + 1)$
$CCl_4$	12	0.215
<i>n</i> - $C_6H_{14}$	0	0.186
<i>c</i> - $C_6H_{12}$	8	0.204
$C_6H_6$	18	0.228
$Cl_2C=CCl_2$	15	0.229
<i>n</i> - $C_8F_{18}$	-18	0.145
<i>trans</i> -3-hexene	3	0.193
1,4- $C_6H_4Cl_2$	24	0.235
$(CH_3)_4Si$	0	0.180

The two sets of properties are nicely linear with one another, the regression being given by eq 29. A plot of the correlation by eq 29 is shown in Figure 2.

$$(n^2 - 1)/(2n^2 + 1) = 0.1857 + 0.00231(N' - N) \quad (29)$$

$$r = 0.989, sd = 0.0041$$

**Further Tests of the Correlations.** As has been mentioned earlier, all the data in Tables I and II are from the same handbook,<sup>12</sup> and the correlations leading to eq 18 and 21 were restricted to compounds for which critical temperatures, normal boiling points, and gas phase dipole moments were available from that source. As further tests of the above correlations, we have compared normal boiling points calculated through eq 21 with experimental values from that same source for some additional compounds. It was assumed that, because of the parallelisms between eq 18 and 21, conclusions regarding BP will also apply to  $T_c$ . The results are assembled in Table IV.

It is seen that agreement between calculated and observed values is satisfactory for the first 25 compounds of Table IV (the average error of 11.2 K compares with a 13.4 K standard deviation of eq 21) but that eq 21 overcalculates the normal boiling points of crotonaldehyde, dimethylformamide, dimethylacetamide, and the tetraalkyltin and -lead compounds. The differences for the tetraalkylmetals cause us no concern. Correlation equations 18 and 21 are intended for use in *interpolative* situations, and the calculations for these compounds involve significant molecular weight *extrapolations* (it is seen that among these four compounds the errors increase with increasing MW). The dependences on the square roots of MW and  $N'$  were chosen for simplicity in calculation, and it may well be that a lower exponent of MW would bring the tetraalkylmetal results into line without significantly affecting the fits for the other compounds. [It was mentioned earlier (and is shown in Table I) that the tetraalkylmetal results did fit the  $R_G$  correlation (eq 28) reasonably well, possibly because of the lesser relative dependence of  $R_G$  on MW.]

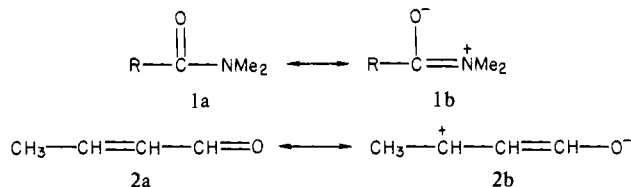
Of greater interest to us are the results for dimethylformamide, dimethylacetamide, and crotonaldehyde. Despite the fact that these involve interpolative values of MW,  $N'$ , and  $\mu$ , the calculated boiling points for these compounds are on the high side by more

(25) Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.*, in press.

Table IV. Comparison between Observed and Predicted Normal Boiling Temperatures Using the Present Method (eq 21) and the Literature Method (eq 30)

compound	BP obsd	calcd eq 21	K diff	% diff	calcd eq 30	K diff	% diff
C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	483.9	495.0	+11.9	+3	314	-170	-35
C <sub>6</sub> H <sub>5</sub> Br	429	441.7	+12.7	+3	492	+63	+15
C <sub>6</sub> H <sub>5</sub> COOEt	486	475.9	-10.1	-2	369	-110	-23
(CH <sub>3</sub> ) <sub>2</sub> SO	462	458.6	-3.4	-1	220	-239	-52
CH <sub>3</sub> Br	287.7	276.7	-11.0	-4	246	-31	-11
(CH <sub>3</sub> ) <sub>3</sub> As	325.0	319.2	-5.8				
(CH <sub>3</sub> ) <sub>4</sub> Si	299.6	310.7	+11.1				
CH <sub>2</sub> =CH <sub>2</sub>	169.4	175.5	+6.1	+4	164	-5	-3
CH <sub>2</sub> =CHCH=CH <sub>2</sub>	268	267	-1.0	0	249	-28	-10
CCl <sub>2</sub> =CCl <sub>2</sub>	394	398.1	+4.1	+1	437	+43	+11
CH <sub>3</sub> CH=CH <sub>2</sub>	225.7	216.2	-9.5	-4	220	-6	-3
cis-CH <sub>3</sub> CH=CHCl	305.9	312.2	+6.3				
trans-CH <sub>3</sub> CH=CHCl	310.5	323.1	+12.6				
ClCH <sub>2</sub> CH=CH <sub>2</sub>	318	321.8	+3.8				
CH <sub>2</sub> =CHBr	288.9	305.9	+17.0	+6	358	+71	+24
CH <sub>2</sub> =CCl <sub>2</sub>	310	319.3	+9.3	+3	196	-114	-37
CH <sub>2</sub> =CHCH=O	326.1	329.0	+2.9				
CH <sub>2</sub> =CHCN	351	379.7	+28.7				
cis-ClCH=CHCl	333.4	339.5	+6.1				
CH <sub>2</sub> =C(CH <sub>3</sub> )CH=O	341.5	347.3	+5.8				
HCOOEt	327.6	302.3	-25.3	-8	216	-112	-34
C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	475.1	454.9	-20.1	-4	355	-120	-25
<i>o</i> -C <sub>6</sub> H <sub>4</sub> Cl <sub>2</sub>	453.6	469.2	+15.6	+3	408	-46	-10
(CH <sub>3</sub> ) <sub>3</sub> P	310.9	288.9	-22.0				
PCl <sub>3</sub>	348.6	331.0	-17.6				
Differences Greater than 30 K between Eq 21 and Observed Values							
trans-CH <sub>3</sub> CH=CHCH=O	377	423.7	+46.7				
HCON(CH <sub>3</sub> ) <sub>2</sub>	425	474.7	+49.9	+12	264	-161	-38
HCON(CH <sub>3</sub> ) <sub>2</sub>	438	491.5	+53.5	+12	299	-139	-32
(CH <sub>3</sub> ) <sub>4</sub> Sn	351	381	+30				
(C <sub>2</sub> H <sub>5</sub> ) <sub>4</sub> Sn	454	486	+32				
(CH <sub>3</sub> ) <sub>4</sub> Pb	383	434	+51				
(C <sub>2</sub> H <sub>5</sub> ) <sub>4</sub> Pb	473	534	+61				
Average relative error				4.4%	22.3%		

than three standard deviations of eq 21. It may not be coincidental that for these three compounds there is significant resonance enhancement of the dipole moment (via canonical structures 1b and 2b). The reported dipole moments of DMF and DMA are



near 3.8 D,<sup>12</sup> whereas best fits to eq 21 would require dipole moments near 3.5 D.<sup>26,27</sup> Also, eq 17, 18, 20, and 21 carry with them the implicit assumption that dipole moments do not differ significantly between the vapor and liquid phases and that they are not very sensitive to temperature. It may be that this assumption is less valid for the resonance enhanced dipoles than for the other dipoles.

[This effect may also explain why a negative polarizability contribution of the ring in eq 16 leads to best fits to  $T_c$  and BP of the dipolar aromatics. To some extent these also involve resonance enhanced dipoles. Thus, if we had used a zero contribution of the ring, as we do in solvent effect correlations, the calculated  $T_c$  and BP values for these compounds would have been higher than observed. By including the negative polarizability contribution, we may introduce an offsetting error to compensate for the resonance enhanced dipole effect.]

(26) Abboud and co-workers<sup>27</sup> have reported that for "select solvents" (aliphatic non-self-associating solvents with a single dominant dipole),  $\pi^*$  values are very nearly proportional to molecular dipole moments. Taken with  $\pi^* = 1.00$  and  $\mu = 3.95$  for Me<sub>2</sub>SO, the  $\pi^*$  of 0.88 for both DMF and DMA would be consistent with a dipole moment near 3.5D.

(27) Abboud, J.-L. M.; Kamlet, M. J.; Taft, R. W. *J. Am. Chem. Soc.* **1977**, *99*, 8327.

#### Comparison with a Group Contribution Literature Approach.

To evaluate the results in Table IV in the context of "current state of the art" literature methods, the values of BP calculated from eq 21 are compared in Table IV with a number of values obtained by using a calculational procedure involving additivity of group contributions. Specifically, the Lyderson approach<sup>10,28</sup> was used for the prediction of  $V_c$ ,  $P_c$ , and the reduced boiling point,  $\theta = \text{BP}/T_c$ , according to eq 30a-c. An expression suggested by Reid,

$$P_c = \text{MW}/(\sum \Delta_p + 0.34)^2 \text{ atm} \quad (30a)$$

$$V_c = 40 + \sum \Delta_v, \text{ cm}^3/\text{mol} \quad (30b)$$

$$\theta = 0.567 + \sum \Delta_T - (\sum \Delta_T)^2 \quad (30c)$$

$$V_b = V_c(0.422 \log P_c + 1.981) \text{ cm}^3/\text{mol} \quad (30d)$$

$$\text{BP} = (\theta/V_b^{0.18}) \exp[(2.77V_b^{0.18}/\theta) - 2.94] \text{ K} \quad (30e)$$

eq 30d,<sup>10</sup> was then used to estimate  $V_b$ , the molar volume at the boiling point, from  $V_c$  and  $P_c$ . Finally, another expression suggested by Reid,<sup>10</sup> eq 30e, was employed for the final prediction of BP from  $\theta$  and  $V_b$ .

The  $\Delta_p$ ,  $\Delta_v$ , and  $\Delta_T$  terms in eq 30a-c refer to the individual group contributions tabulated by Lyderson<sup>28</sup> for the various functional groups, such as CH<sub>3</sub>, -CH<sub>2</sub>-, >CH-, >C=, -C≡, F, Cl, Br, -O-, -O- in ring, OH in alcohol, OH in phenol, >C=O, >C=O in ring, -NH<sub>2</sub>, -NH-, >N-, -C≡N, NO<sub>2</sub>, etc. It is evident from the above that, for any but the simplest compounds, estimation of BP by the Lyderson-Reid method involves a cumbersome calculation.

Reid points out in the later edition of his book<sup>29</sup> that predictive methods for BP are often rather poor, and our calculations using eq 30 substantiate this observation for many of the compounds.

(28) Lyderson, A. L. *Rep. Univ. Wis. Eng. Exp. St.* **1955**, *3*.

(29) See ref 11.



Moreover, as is the case with many group contribution methods, all the group  $\Delta$  values were not available for compounds in Table IV having other than the usual functionality. The approximate methods embodied in eq 18, and 21 avoid this problem but have the disadvantage that a knowledge of the dipole moment is required. Fortunately, the "current state of the art" in prediction of dipole moments from chemical structures is relatively quite advanced.<sup>30</sup>

A rather unexpected conclusion is reached on consideration of the absolute and the percentage differences between the observed values of BP in Table IV and the values predicted by the two calculational methods. For this limited data set, the simpler calculational method produces a clearly significantly superior estimate of BP. Clearly, a much wider range of compounds would be required for study before such a surprising conclusion could be fully validated, but the fact that the compounds in Table IV were randomly selected for consideration serves as strong presumptive evidence for the superiority of eq 21.

**Additional Methods for Prediction of  $T_c$  and BP.** There have been a large number of attempts to predict values of  $T_c$ , due at least in part to the importance of  $T_c$  in chemical engineering.<sup>31,32</sup> Relationships have been suggested between  $T_c$  and a variety of physical and molecule properties, the most successful being based on the connection between  $T_c$  and BP. Gambill<sup>32</sup> has advocated either Lydersen's equation, eq 30c, or Eduljee's equation, eq 31,

$$BP/T_c = \sum \Delta_T/100 \quad (31)$$

and lists  $\Delta_T$  values for both equations. The average error in  $BP/T_c$  is about 1% in either equation. However, the prediction of  $T_c$  via eq 30c or 31 necessitates the measurement of a physical property, BP, whereas the aim of the present program is to take advantage of the advanced "state of the art" in dipole moment predictability to predict  $T_c$  without recourse to any physical experiment.

There have been a number of equations put forward relating  $T_c$  to molecular structure, but the only relationship that has proven to be in any way successful is that between  $T_c$  and the parachor,  $P$ , defined by Sugden as  $P = (MW)\gamma^{1/4}/\rho$ . In this equation,  $\gamma$  is the surface tension and  $\rho$  the liquid density. It might be thought that the use of the parachor also requires measurements of physical properties  $\gamma$  and  $\rho$ , but since the parachor is to some extent additive, it is possible to obtain a set of atomic and structural constants that can be used to predict  $P$ , and thence  $T_c$ . Thus Herzog<sup>33</sup> lists a rather complete set of such constants derived from Mumford and Phillips,<sup>34</sup> and Meissner and Redding<sup>31</sup> give constants derived from Sugden's original work.

We have used these constants to calculate parachors for compounds 11–31 of Table I and have correlated the calculated parachors with  $T_c$  and with  $T_c^2$ . It became evident that, just as for the correlations via eq 11, predicted values of  $T_c$  for cycloalkanes and aromatic hydrocarbons were lower than observed and predicted values for the fluorinated compounds were higher than observed. For the remaining open-chain aliphatic hydrocarbons and the hydrocarbon-like  $Me_4Sn$ , we found the correlations were quite successful using the Mumford–Phillips  $P$  values (eq 32) or

$$(T_c)^2 = -16\,239 + 988 \log P \quad (32)$$

$$r = 0.996, \text{ sd} = 14.4 \text{ K}$$

$$(T_c)^2 = -19\,758 + 1009 \log P \quad (33)$$

$$r = 0.996, \text{ sd} = 14.6 \text{ K}$$

the Sugden  $P$  values (eq 33). We considered that there was little to be gained by carrying this line of investigation further, as it was clearly evident that additional terms would need to be added to eq 32 and 33 for compounds with differing dipolarity and polarizability characteristics and we saw no advantage to offset the increased complexity of still another group additivity method over eq 18.

It is of interest, however, that if we define another quantity,  $(\Delta\Delta T_c)_{SA^*}$ , as the difference between observed  $T_c$  values and values calculated through eq 32 and 33, we obtain the following results:

	Mumford–Phillips	Sugden
H <sub>2</sub> O	411.2 K	460.4 K
MeOH	195.4	240.5
EtOH	141.7	178.9
<i>n</i> -PrOH	113.8	146.5
<i>i</i> -PrOH	87.7	124.3
<i>n</i> -BuOH	94.7	124.3

The correlation coefficients of the linear regression equations of  $(\Delta\Delta T_c)_{SA^*}$  vs.  $(\Delta\Delta T_c)_{SA}$  are (Mumford–Phillips) 0.9976 and (Sugden) 0.9989. That the correlations are so good despite the fact that dipolarity and polarizability effects are not taken into account in the calculation of  $(\Delta\Delta T_c)_{SA^*}$  we attribute to the fact that the latter properties are either quite similar for the alcohols and water or vary linearly with the  $\Delta\Delta$  terms. We consider these correlations to be a further independent substantiation of our estimates of the relative self-association energies.

Two additional boiling point correlations deserve comment. We have mentioned that Taft and Sisler<sup>17</sup> observed a linear relationship of boiling points of non-hydrogen-bonding group 6 hydrides with period number. They also observed similar relationships for the H, CH<sub>3</sub>, and C<sub>2</sub>H<sub>5</sub> derivatives of the group 4, 5, 6, and 7 elements that allowed estimates of boiling points to within several degrees. Hine and Ehrenson,<sup>35</sup> using a group additivity approach involving separate contributions by F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>, and CH, have estimated boiling points of 44 halo- and polyhalomethanes, with an average error of 2.4 K.

In conclusion, we wish to point out that in this series of papers we will attempt to develop predictational methods for properties that have until now been best estimated in the chemical engineering community by the so-called UNIFAC method.<sup>36</sup> The latter approach has yielded an accurate and fundamentally satisfying means of accounting for the solution behavior of the seven solute/solvent systems listed earlier, but it is rather complex to apply and is sometimes hampered by the lack of data for specific group contributions of interest. The primary advantage of the present methods, which are based on solute size, polarizability, dipolarity, and hydrogen bonding effects, is in their greater simplicity. Whether this greater simplicity can be achieved without excessive sacrifice in precision relative to UNIFAC remains to be determined.

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(33) Herzog, R. *Ind. Eng. Chem.* **1944**, *36*, 997. See also Pilcher and Ward (Pilcher, R. W.; Ward, J. M. *J. Chem. Eng. Data* **1958**, *3*, 193) for additional correlations.

(34) Mumford, S. A.; Phillips, J. W. C. *J. Chem. Soc.* **1929**, 2112.

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