On the Additivity of Molar Attraction Constants

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Abstract—A statistically significant test of the additivity of molar attraction constants on an increment or functional group basis indicates that there may be some limitations regarding its validity. An approximate additivity, however, may be operational and have some practical value.

Keyphrases ☐ Molar attraction constants—additivity ☐ Additivity, incremental—molar attraction constants

The molar attraction constant (F), a physical constant associated with the solubility parameter (δ) concept is thought to be an additive quantity (1) such that it can be calculated as a sum of empirically determined constants or increments for the individual functional groups comprising a given chemical structure. The relationship between δ and F can be expressed as

$$\delta = (E/V)^{1/2} = (EV)^{1/2}/V = F/V = \Sigma F_i/V \qquad \text{(Eq. 1)}$$

where E is the cohesive energy, V the molar volume, F the molar attraction constant for an entire molecule, and F_i the value for each functional group comprising the molecule. Classically, these F_i values have been of practical importance in that they provide a simple means for calculating solubility parameters (2) and more recently they have been used to correlate biological activity with chemical structure (3). A table of F_i values for some functional organic groups has been compiled (1).

Although F can be shown to be additive on a molar basis (3), its additivity on an incremental basis has not been validated. The objective then is to test this additivity in a statistically unobjectionable way. This is necessary because often the apparent additivity of a physical constant is misleading in that incremental contributions to such a constant are masked by a second additive quantity. Such a second quantity if exactly additive may camouflage less noticeable inaccuracies in the parent quantity. In particular, Exner (4–7) has shown that in the case of molar quantities such as molar volume, parachor, and molar refractivity, smaller changes of the measured values are over-shadowed by the influence of the molecular weight (M) and that M itself being strictly additive can cause an approximate additivity of the whole expression. He has suggested that the influence of such interfering quantities can be eliminated simply in a homologous series of the type $X(CH_2)_nH$ according to the following:

$$F = F_c + xF_h \qquad \text{(Eq. 2)}$$

$$\phi = \phi_c + x\phi_h \qquad \text{(Eq. 3)}$$

where F is the parent quantity, ϕ the interfering additive quantity, x the number of homologous units, and where the subscripts c and h refer to the increments for the constant and homologous part of the molecule, respectively.

Solving Eq. 3 for x, substituting into Eq. 2, and rearranging gives

$$F/\phi = F_h/\phi_h + (\phi_h F_c - \phi_c F_h)/\phi_h[1/\phi] \qquad \text{(Eq. 4)}$$

In the case of molar attraction constants one needs to test the additivity of F without the influence of V or M as suggested by Eq. 1. This requires plots of F/V *versus* $1/V$ and F/M *versus* $1/M$ as suggested by Eq. 4. Such plots for different series of the type $X(CH_2)_nH$ should give several straight lines having a common point of intersection (F_h/ϕ_h) on the y-axis if the quantity F is exactly additive.

RESULTS AND DISCUSSION

Linear correlations between F/V and $1/V$ and between F/M and $1/M$ have been made using values of F calculated from experimental values of $\delta(F = \delta V)$. The experimental values of δ were taken from *References* 2 and 8, while values for V were calculated using densities (ρ) reported in *Reference* 9 ($V = M/\rho$). The resultant parameters pertinent to the correlations are tabulated in Tables I and II where r is the correlation coefficient and n is the number of members of a series used in the correlation. As seen in Tables I and II, the intercepts in both types of plots are quite widespread which indicates some inaccuracies in the additivity of F and suggests that F is at best only approximately additive. Using a value of 16.58 for the molar volume of a methylene group (5) gives a range of 127 to 177 for F (F_{CH_2} = intercept $\times$ V_{CH_2}) when analyzed from F/V *versus* $1/V$ plots. Similarly, using a molecular weight of 14 for a methylene group gives a range of 95 to 126 for F (F_{CH_2} = intercept $\times$ M_{CH_2}) when analyzed from F/M *versus* $1/M$ plots. These ranges are large, do not agree well, and are probably outside the variability attributable to experimental errors in δ and V.

From the slopes (Eq. 4) one is able to calculate the respective F_c values or the contribution to F made by the constant part of the chemical structure (ester, alcohol, *etc.*). F_c values so calculated, however, also contain the contribution made by one hydrogen if the functional group is terminal (*e.g.*, alcohols) or two hydrogens if the functional group is central (*e.g.*, ketones). Consequently, to obtain the F_i value for the descriptive functional group in each series, the proper correction has to be made. Such corrected group constants are also given in Tables I and II and correspond to the respective functional group given in parentheses. The corresponding values reported by Small (1) are also included for comparison. In general, the group constants calculated by Eq. 4 are in poor agreement with the previously reported values. These differences may in part be due to the fact that only aliphatic straight-chain series have been used in the analysis whereas Small's values were determined for the general case. The inaccuracies or poor additivity

Table I—Test of Additivity: F/M *versus* $1/M$

Series	Intercept	Slope	r	n	Group Constant Eq. 4	Group Constant *Ref.* 1
Alkanes (H)	9.81	114	0.992	7	67	80–100
Alcohols (OH)	10.69	245	0.993	7	370	—
Nitriles (CN)	10.26	205	0.986	5	415	410
Ketones (CO)	7.69	288	0.980	9	384	275
Esters (COO)	8.39	153	0.911	12	404	310
Acids (COOH)	11.27	45	0.617	3	496	—
Chlorides (Cl)	8.41	99	0.951	3	339	270
Iodides (I)	8.44	−561	0.998	4	453	425
Sulfones (OSO)	9.18	231	0.987	3	702	—

Table II—Test of Additivity: *F/V versus 1/V*

Series	Intercept	Slope	*r*	*n*	Group Constant Eq. 4	Group Constant *Ref.* 1
Alkanes (H)	8.73	−194	0.997	7	33	80–100
Alcohols (OH)	8.95	218	0.998	7	452	—
Nitriles (CN)	8.60	167	0.965	5	457	410
Ketones (CO)	6.68	236	0.985	9	437	275
Esters (COO)	7.04	201	0.936	12	482	310
Acids (COOH)	9.12	201	0.978	3	452	—
Chlorides (Cl)	6.99	149	0.949	3	381	270
Iodides (I)	6.76	215	0.999	4	501	425
Sulfones (OSO)	7.61	527	0.999	3	—	—

of F does not appear to be related to a variability in F_c values since the described plots give excellent linear correlations with constant slopes. An attempt has been made to account for the variability in F_i values by considering the variation in chain length in a homologous series (10). The observed variations and inconsistencies, however, are most probably due to the poorly additive nature of F.

Deviations from strict additivity do not necessarily discredit the practical use of F. One must decide what sort of inaccuracies can be tolerated for an intended purpose. The calculation of F from group constants which are only approximately additive may be valuable on an operational basis. For example, in diols such as ethylene glycol, diethylene glycol, and propylene glycol, calculated values for a single OH group are 273, 273, and 278, respectively, while in hetero-functional analogs such as carbitol, the values for an OH group cluster around 325. Such dependencies on compound type place even further limitations on the additivity of F. Nonetheless, there is a practical usefulness for an apparent additivity of F on a constitutive basis when used within the limits of recognized restrictions.

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Preparation of Some Substituted Imidazolidine-2,4-diones

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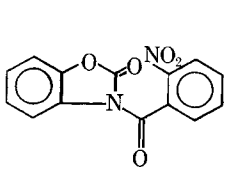
Abstract □ Heating 2-benzoxazolinone or 5-chloro-2-benzoxazolinone with aminoacid esters resulted in the formation of 3-(2-hydroxyphenyl) imidazolidine-2,4-dione derivatives. Results of preliminary pharmacological tests are reported.

Keyphrases □ Imidazolidine-2,4-diones—synthesis □ Pharmacological screening—imidazolidine-2,4-diones □ IR spectrophotometry—structure □ NMR spectroscopy—structure

Heating of 2-benzoxazolinone with aniline (1) and hydrazine hydrate (2) was observed to yield a substituted urea and a semicarbazide derivative, respectively. A similar rearrangement was noted (3) when the hydrogenation of 3-(2-nitrobenzoyl)-2-benzoxazolinone (I) resulted in the formation of 1-hydroxy-3-(2-hydroxyphenyl) quinazoline-2,4-dione (II). More recently, 3-(2-hydroxyphenyl) - 5 - (4 - hydroxybenzyl)imidazolidine - 2,4-dione (III) was produced when 2-benzoxazolinone was heated with ethyl tyrosinate (4). The latter observation prompted a study to determine whether the initial reaction in the rearrangement was an acylation at Position 3 of the benzoxazolinone ring or an attack of the carbonyl group by the amino moiety of the aminoacid ester.



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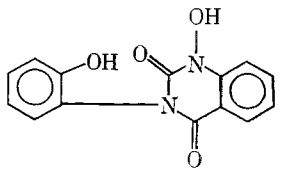
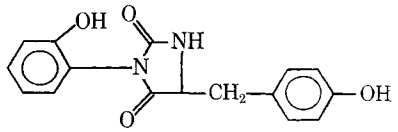


II



III

The acylation of 2-benzoxazolinone (IV*a*) or the potassium salt of IV*a* with ethyl benzoate or ethyl butyrate at different temperatures failed to occur. On the other hand, refluxing IV*a* with benzylamine, pyrrolidine, and 4-pipecoline in each case provided a urea derivative (VII) which was readily detected by the appearance of a 1650–1630 cm.$^{-1}$ carbonyl band in the IR spectrum. These observations, together with the fact that ureas containing an appropriate carbethoxy group spontaneously form cyclic derivatives (5, 6), indicate that the