Communications to the Editor

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NOVEL SUBSTITUENT ENTROPY CONSTANT $\sigma_{s°}$ REPRESENTS THE MOLECULAR CONNECTIVITY χ AND IT RELATED INDICES

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The novel substituent entropy constant $\sigma_{s°}$ represents the molecular connectivity χ, one of the QSAR descriptors developed by molecular topology. It is closely correlated with chromatographic retention data, such as retention time Rt or RT, and with retention index R.I. and specific retention volume Vg. Also, water solubility, boiling point and partition coefficient are represented by $\sigma_{s°}$.

KEYWORDS—— substituent entropy constant $\sigma_{s°}$; molecular connectivity; branching index; chromatographic retention data; boiling point; water solubility; partition coefficient; chromatographic polar effect constant σ_c^*

In the previous reports,[1)] the validity of the substituent entropy constant $\sigma_{s°}$ has been extended in the field of the QSAR, together with the substituent enthalpy constant σ_i and σ_π.[2)] Furthermore, a cluster analysis of the current QSAR descriptors revealed that this constant is appropriate as an independent descriptor representing the contribution from the entropy term.

Kier et al.[3)] proposed, as an effective QSAR descriptor, the molecular connectivity χ, developed from the branching index of hydrocarbons presented by Randić.[4)] This descriptor, which originated from the molecular topology, is closely related to a number of physical constants, such as chromatographic retention time Rt or RT,[5)] retentin index R.I.,[6)] specific retention volume Vg,[6)] water solubility S,[7)] boiling point Tb,[7)] partition coefficient log P[8)] and chromatographic polar effect constant σ_c^*.[9)]

This communication deals with the correlation of the substituent entropy constant $\sigma_{s°}$ with χ and R.I. as QSAR descriptors, with chromatographic retention data, and with the other physical constants cited above.

In the first step, the branching index of C_3——C_8 hydrocarbons and molecular connectivity index χ can be correlated with S°_{298} instead of $\sigma_{s°}$, because the two descriptors above are originally "non-energetic".

The results are as follows:

Branching Index B.I.[4)]

$$B.I. = 0.053(\pm 0.002)\ S^\circ_{298} - 1.995$$

$$n = 39,\ r = 0.994,\ F = 3131^{**},\ SE = 0.01$$

Connectivity Index χ[3]

$\chi = 0.051(\pm 0.003)\ S^{\circ}_{298} - 1.823$

$n = 77,\ r = 0.972,\ F = 1287^{**},\ SE = 0.04$

Retention Time Rt[5a] of Alkanes

$\log Rt = 7.86(\pm 0.41)\ \sigma_{s^\circ} - 0.48$

$n = 18,\ r = 0.995,\ F = 1630.7^{**},\ SE = 0.01$

Retention Time RT[5b] of Alkanes and Alkenes

$\log RT = 7.53(\pm 0.64)\ \sigma_{s^\circ} - 0.27$

$n = 35,\ r = 0.972,\ F = 574.4^{**},\ SE = 0.02$

Retention Index R.I.[6]

Aliphatic series and stationary phase = Apiezone-L

$\log R.I. = 1.44(\pm 0.23)\ \sigma_{s^\circ} + 0.26(\pm 0.22)\ |\sigma_i| + 2.33$

$n = 26,\ r = 0.945,\ F = 95.3^{**}.\ SE = 0.04$

Aromatic series and statinary phase = SE-30

$\log R.I. = 2.29(\pm 0.49)(\sigma_{s^\circ})^2 + 1.26(\pm 0.97)\ |\sigma_i| - 0.73(\pm 0.73)\ |\sigma_\pi| + 3.06$

$n = 9,\ r = 0.994,\ F = 133.8^{**},\ SE = 0.004$

Specific Retention Volume Vg[6]

$\log Vg = 8.76(\pm 0.49)\ (\sigma_{s^\circ})^2 + 0.07$

$n = 19,\ r = 0.994,\ F = 1443.3^{**},\ SE = 0.01$

Boiling Point Tb[7] of Aliphatic Alcohols

$Tb = 471.76(\pm 35.74)\ \sigma_{s^\circ} - 28.80$

$n = 52,\ r = 0.996,\ F = 704.7^{**},\ SE = 1.28$

Water Solubility S[7] of Aliphatic Alcohols and Alkanes

$\ln S = -45.55(\pm 2.07)\ \sigma_{s^\circ} + 34.85(\pm 1.89)\ |\sigma_i| - 2.98$

$n = 27,\ r = 0.995,\ F = 1107.8^{**},\ SE = 0.09$

Partition Coefficient log P[8] in H_2O/n-Octanol

$\log P = 13.07(\pm 1.67)\ \sigma_{s^\circ} - 11.12(\pm 3.12)\ |\sigma_i| - 1.24$

$n = 42,\ r = 0.943,\ F = 155.8^{**},\ SE = 0.07$

Monosubstituted benzenes with electron donating substituents

$\log P = 10.48(\pm 1.42)\ \sigma_{s^\circ} - 4.15(\pm 0.47)\ |\sigma_\pi| + 0.46$

$n = 8,\ r = 0.998,\ F = 549.5^{**},\ SE = 0.03$

Chromatographic Polar Effect Constant σ_c^*[9] of Aliphatic Hydrocarbons

$\sigma_c^* = 0.78(\pm 0.50)(\sigma_{s^\circ})^2 - 0.83(\pm 0.29)\ \sigma_{s^\circ} - 15.00(\pm 1.03)\ |\sigma_i| + 0.53$

$n = 38,\ r = 0.986,\ F = 394.9^{**},\ SE = 0.002$

These results suggest that the novel substituent entropy constant σ_{s° represents the topological index, chromatographic retention data, and some characteristics of the solvents.

EXPERIMENTAL

1. Regression Analysis

The regression analyses were carried out using the program NEC TSS LIBRARY TSS/LIB-6 and our own programs coded in BASIC language. The values of SE are obtained from the equation $SE = [\ Sse/(n-k)(n-k-1)]^{1/2}$, where n = number of observations, k = number of independent variables and Sse = sum of squares of residuals.

2. Calculation

All numerical treatments were carried out with an NEAC S-900 computer at the

Computation Center, Osaka University, with a personal computer NEC PC-8001.

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