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NUMERICAL INTEGRATION OF THE VAN DER WAALS ENVELOPE OF THE SUBSTITUENTS

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Summary. The numerical integration of the van der Waals envelope of the substituent is performed by means of Monte Carlo method. The resulted van der Waals volumes of 29 substituents show a good correlation with molar refractivity.

1. Introduction

This paper presents a Monte Carlo method to compute the van der Waals volume (WV, $\mathring{A}^3$) of substituents, molecules, ions or radicals. The method is useful in QSAR (QSAR is the abbreviation for Quantitative Structure-Activity Relationships) because WV is a bulk steric parameter with clear physical meaning.

The WV values for 29 substituents are reported, and a correlation between molar refractivity and WV is computed.

2. Numerical integration of the van der Waals envelope

In order to integrate the van der Waals envelope, the chemical species are described by the cartesian coordinates and van der Waals radii of their atoms.

For the calculations of coordinates the standard values of bond lengths and bond angles can be used, and van der

Waals radii listed in ref. 1 or 2.

The van der Waals volume (WV, $\mathring{A}^3$) is given by the equation :

$$WV = a \text{ Card } N_I / \text{Card } N_T \qquad (1)$$

where a stands for the volume of the parallelipiped which circumscribes the considered van der Waals envelope, and Card denotes the cardinal.

N_T is the set of uniform random points generated within the parallelipiped of volume a and N_I is the subset of N_T whose points fall within the considered van der Waals envelope.

We note that the precision of WV values strongly depends on the values of a and N_T. Because the value of a is imposed by the considered van der Waals envelope, we may choose the value of Card N_T. In general, Card $N_T \geqslant 300000$ assures a precision of 99,5% for the computed WV's. WV's may be computed, according to the relation (1), by means[3] of our program NOVA.

3. Applications

Using the NOVA program, we computed WV values for the substituents listed in Table 2. WV^a and WV^b values were computed by means of the van der Waals radii from refs. 1 and 2 :

Table 1. Van der Waals radii, r_W [$\mathring{A}$] .

Atom	H	C	N	O	F	Cl	Br	I
r_W, ref.1	1.20	1.57	1.50	1.40	1.35	1.80	1.95	2.15
r_W, ref.2	1.24	1.54	1.37	1.27	1.18	1.63	1.79	2.02

Table 2. MR and WV values

No.	Substituent	MR	WV[a]	WV[b]
1.	CH_3	5.7	23.08	24.86
2.	CH_2Cl	10.5	41.71	38.16
3.	CH_2Br	13.4	46.40	41.08
4.	CH_2I	18.6	57.12	51.14
5.	CHF_2	5.2	31.41	26.76
6.	CF_3	5.0	34.55	27.33
7.	$CHCl_2$	15.3	55.97	46.19
8.	F	0.8	10.29	6.85
9.	Cl	5.8	24.44	18.29
10.	Br	8.7	31.01	24.03
11.	H	1.0	7.22	7.91
12.	I	14.0	41.52	34.39
13.	NO_2	6.7	26.69	20.84
14.	$C(O)CH_3$	11.2	37.87	36.15
15.	NH_2	4.4	19.40	18.29
16.	CN	5.5	23.38	20.43
17.	CH_2OH	7.2	31.12	30.71
18.	COOH	6.9	31.38	28.17
19.	OH	2.6	14.78	13.04
20.	CO_2	6.1	28.42	24.13
21.	$n\text{-}C_4H_9$	19.6	68.05	70.01
22.	$CH_2C(O)CH_3$	15.1	56.33	56.00
23.	CH_2OCH_3	12.1	48.09	48.32
24.	$CHBrCH_3$	18.0	61.92	57.34
25.	SCH_3	13.5	23.92	24.75
26.	CBr_3	28.6	89.04	72.83
27.	CCl_3	20.1	70.53	56.07
28.	$C(OH)(CH_3)_2$	16.4	57.98	58.27
29.	$n\text{-}C_3H_7$	15.0	53.85	53.51

The obtained WV^b are generally smaller than WV^a because of the smaller van der Waals radii given by Boyd (excepting the value for hydrogen).

Our WV's may be used to compute the proportion of the steric (i.e., van der Waals volume) vs electronic component within the molar refractivity (MR). There resulted the following MR vs WV equations :

$$MR = -1.966 + 0.323\ WV^a \qquad (2)$$

($r = 0.95$, $s = 2.01$, $F = 128.53$, $EV = 0.91$)

$$MR = -1.455 + 0.343\ WV^b \qquad (3)$$

($r = 0.93$, $s = 2.38$, $F = 87.84$, $EV = 0.87$)

Further details concerning MR may be found in ref. 4.

Equations (2) and (3) show approximately the same variation of MR with WV.

The explained variance (EV) computed for the equation (2) or (3), namely about 0.9, indicates that the relative proportion of the steric vs. the electronic component within MR is about 9:1.

4. Conclusions

1. We developed an easy to use Monte Carlo method to compute van der Waals volume of any chemical specie. The computed values of the van der Waals volume of 29 substituents are reported.
2. Using the Monte Carlo computed van der Waals volumes, we proved that the relative proportion of the steric vs. electronic component within MR is about 9:1.

References

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