Effect of internal rotation on surface and volume of molecules with 1,3-dioxa moiety

T. BLEHA

Polymer Institute, Centre for Chemical Research,
Slovak Academy of Sciences, CS-842 36 Bratislava

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The van der Waals surface envelope was calculated for molecules with O—X—O segment (where X is a tetrahedral centre) as a function of the torsional angles of X—O bonds. Merely small differences were found between the surface and the volume of energetically stable conformers. The conformational variation of the surface was not substantially affected by an inclusion of lone electron pairs in the calculation. The implications of torsional variation of molecular surface on the microthermodynamical surface and on the Gibbs energy of solvation in Sinanoglu's solvophobic theory have been discussed. The limitations have been pointed out for the use of molecular surface as the sole criterion of the extent of solute solvation.

Рассчитаны поверхности ван-дер-ваальсовых оболочек для молекул с фрагментом O—X—O (где X — тетраэдрический центр), как функция торсионных углов связей X—O. Обнаружены лишь небольшие различия в поверхностях и объемах энергетически стабильных конформеров. На конформационную зависимость поверхности не оказывает существенного влияния включение в расчет неподеленных электронных пар. Обсуждается эффект торсионной зависимости молекулярной поверхности на микротермодинамическую поверхность и гиббсову энергию сольватации в сольвофобной теории Синаноглу. Отмечены ограничения применимости молекулярной поверхности как единственного критерия степени сольватации растворенного вещества.

A great deal of the physicochemical properties of substances can be correlated with the molecular size, *i.e.* with the molecular volume or the molecular surface. The determination of the size of individual molecules continues to be a problem; the quantities extracted from the experimental measurements in the gaseous and liquid phases are used most frequently. The typical examples are van der Waals atom radii r_W, the analogous volumes of atoms (or atomic groups) or the effective molecular cross sections σ derived from various experimental methods.

The correlation of the molecular size with the macroscopic properties is less straightforward for molecules in which an internal rotation is possible. Recent experimental and theoretical studies [1—5] indicate the nonidentical value of volume and surface for various rotational isomers. Besides, since the solvation energy of solute molecules strongly depends on their size, the difference in surface or volume can bring about the shift of the conformational equilibrium in solution in comparison with the gaseous state even for the nonpolar molecules [5, 6].

A reliable estimation of the changes in van der Waals molecular surface ($\mathbf{S}_W$) or volume (V_W) can be found from the model computations in which a molecule is approximated by a geometrical body formed by the mutually interlocking spheres corresponding to atoms (or to atomic groups) with the radius r_W. By the variation of torsional angles in molecule the conformational dependence of $\mathbf{S}_W$ can be calculated. This paper reports the results of calculation of the van der Waals surface envelope for molecules with the two oxygen lone electron pairs at a tetrahedral centre. This class of molecules is an object of our interest for some time even [7—9] due to their special stereochemical behaviour — the preference of synclinal position to antiperiplanar one — which is termed as the anomeric or *gauche* effect.

Methods and parameters

Conformational changes of the van der Waals surface have been investigated for three molecules of the general formula CH_3—O—X—O—CH_3 where X is CH_2, PO_2^-, and $Si(CH_3)_2$, *i.e.* dimethoxymethane (DMM), dimethylphosphate anion (DPM^-), and dimethoxydimethylsilane (DDMS), respectively. Torsional angles φ_1 and φ_2 correspond to the rotation around X—O bonds with the values of 180° in antiperiplanar (*ap*) conformation and of ±60° in synclinal (*sc*) conformations. Apart from the internal rotation the completely rigid molecular geometry was assumed with parameters from Ref. [7] (Table 1, geometry *B*) for DMM and from Ref. [9] for DMP^-. In DDMS the bond lengths 0.1425 nm, 0.1632 nm, and 0.1842 nm were assigned for C—O, O—Si, and Si—C bonds, respectively, with the tetrahedral bond angles except the C—O—Si angle which was put 123.6°; all that based on the data for the structurally similar molecule [10].

Using the standard Hermann's program (QCPE No. 235) [11] the molecular surface has been determined. The surface is computed by numerical integration and in addition to the input geometry data the program requires the choice of van der Waals radii of atoms and atomic groups. We assumed r_W/nm: 0.12, 0.17, 0.15, 0.19, 0.18 and 0.21 for H, C, O, Si, and P atoms and CH_3 group, respectively. The methyl groups on the central silicon atom have been regarded as quasiatoms with the latter value of r_W. The torsional angle was changed by 10° increment. The complete conformational hypersurface $\mathbf{S}_W(\varphi_1, \varphi_2)$ has been constructed for DMM only. In the remaining cases the sections of latter hypersurface corresponding to $\varphi_2 = 180°$ have been computed, which was sufficient for comparison of the molecular surface of *ap* and *sc* conformations. The theoretical and experimental studies on the volume changes at internal rotation [1—5] concentrated so far just on this *sc—ap* difference.

Results and discussion

Figs. 1—3 show the variation of molecular surface as a function of the torsional angle φ_1 when $\varphi_2 = 180°$, that means, when the second half of the molecule is in an extended conformation. In comparison of calculated quantities the emphasis is laid

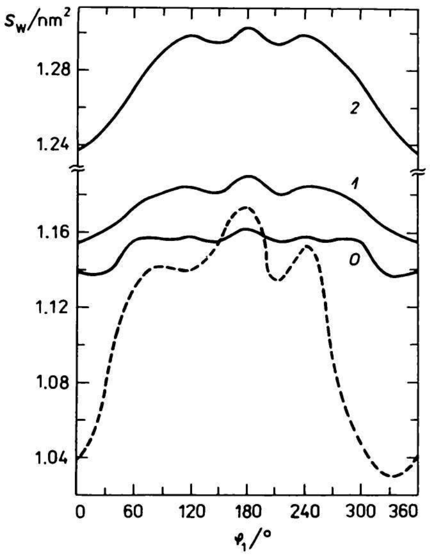

Fig. 1. Variation of molecular surface S_W in DMM with torsional angle φ_1 when $\varphi_2 = 180°$ (full lines) and $\varphi_2 = -60°$ (dashed line). Calculation without lone pairs (0), with lone pairs at $d = 0.05$ nm (*1*) and at $d = 0.1$ nm (*2*).

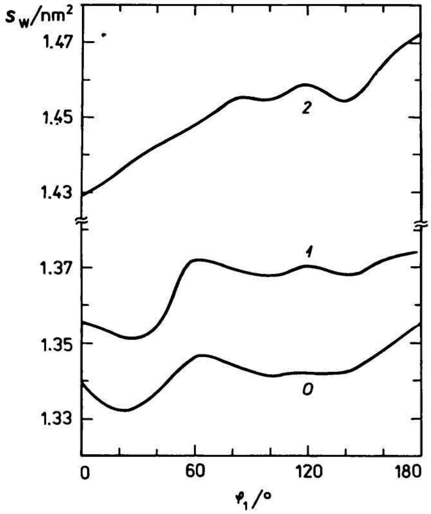

Fig. 2. Variation of molecular surface S_W in DMP$^-$ with torsional angle φ_1 when $\varphi_2 = 180°$. Specification of curves as in Fig. 1.

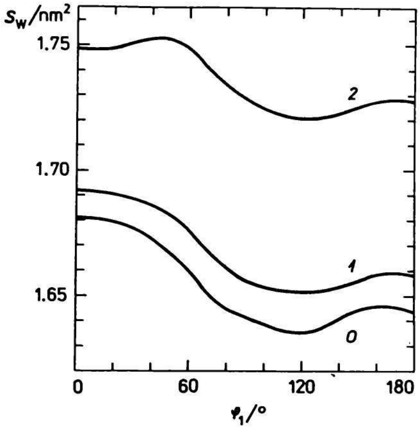

Fig. 3. Variation of molecular surface S_W in DDMS with torsional angle φ_1 when $\varphi_2 = 180°$. Specification of curves as in Fig. 1.

on the relative changes of S_W with the rotation; the absolute values of surface being of the less importance. From the general correlation $S \sim V^{2/3}$ it is assumed that also the relative surface changes at the internal rotation are proportional to the relative volume changes. As is seen in Figs. 1 and 2 a minimum of molecular surface is located in the vicinity of synperiplanar (*sp*) conformation with $\varphi_1 = 0°$ as could be expected due to the maximum overlap of groups in this position. On the contrary, in DDMS the presence of bulky methyl groups on central silicon results in a decrease of overlap in position with $\varphi_1 = 0°$ as compared with *ap* position or, in other words, in an increase of molecular surface. The torsional changes of surface as demonstrated by curves in Figs. 1—3 are rather inconspicuous and lie within the three per cent range. The differences in surface of the stable rotational isomers, for example between *ap* and *sc* conformation, are even smaller. In these molecules *sc* conformation is usually more stable and is shifted close to *sp* position with minimum of φ_1 about 30° or 40° [7—9]. Our preliminary CNDO/2 and PCILO quantum chemical calculations indicate that in DDMS the energetically stable isomer is located even at $\varphi_1 = 0°$. The variation of surface with internal rotation would be probably further diminished by presuming the relaxed geometry of molecules instead of the rigid one. One can expect that such changes of internal geometry occur especially in the regions of the large repulsion (as is *sp* position of DMM) and they would diminish the steric overlap of groups and enlarge the molecular surface.

The calculated surface S_W depends obviously on the radii r_w and on the rather arbitrary selection of their values. However, a simulation of atoms by spheres even in the case of atoms with the lone electron pairs as oxygens is the more questionable approximation in this approach. In literature the discussion continues on the real size of electron lone pairs and on the most suitable way of their simulation. The quantum chemical calculations and the deformational maps from the X-ray diffraction experiment unequivocally confirm the unsymmetrical character of the electron density distribution in heteroatoms (of oxygen type) bonded in molecule. In semiempirical calculations of potential energy of molecules the effect of lone pairs is most frequently accounted for by the inclusion of the additional centres of electron density "quasiatoms" located in accord with the expected hybridization on heteroatom [12—14]. In the calculation of surface S_W we have used an analogous procedure. The radius $r_W = 0.12$ nm was assigned [12] to each of lone pairs on oxygen atoms and they were located in the direction of sp^3 hybridization. Their distance from the centre of oxygen atom represents a parameter of calculation d for which two values 0.05 nm and 0.1 nm were taken. The plots of surface S_W calculated with the four additional lone pairs are also shown in Figs. 1—3. It can be seen that the inclusion of lone pairs evidently increases the molecular surface but does not qualitatively change the character of the conformational dependence of S_W.

The complete map of van der Waals surface has been constructed for DMM with the lone pairs assumed at $d = 0.05$ nm. The map $S_W(\varphi_1, \varphi_2)$ is of a very simple form with the only distinctive minimum in *sp*,*sp* conformation ($S_W = 0.966$ nm^2) and with one maximum in *ap*,*ap* conformation ($S_W = 1.187$ nm^2). In the map the drop of molecular surface is confined to the area formed by the rotation of φ_1 and φ_2 about ±60° from *sp*,*sp* position; the rest of the map being rather flat. The difference between maximum and minimum of surface on the map is about 20 %. The section of the map for $\varphi_2 = 60°$ (Fig. 1) provides the idea about the form of the map and contains also the stable conformers *sc*,-*sc* with surface 1.135 nm^2 and -*sc*,-*sc* with surface 1.048 nm^2. Evidently, the value of S_W at $\varphi_1 = 180°$ for this section is identical to S_W at $\varphi_1 = 60°$ and the section $\varphi_2 = 180°$.

There exist attempts to utilize van der Waals surface or volume of molecule in the prediction of stable conformations of molecules [15]. Comparison of the map $S_W(\varphi_1, \varphi_2)$ or its sections in Fig. 1 with the analogous map of potential energy for DMM [7] documents the limitations of such approach. The most stable conformation of DMM is not *ap*,*ap* as it would follow from Fig. 1 (with the maximum surface or minimum of steric overlap) but, *sc*,-*sc* conformation. Electrostatic (dipole-dipole) and electronic (delocalization) effects which are responsible for the shift of conformational equilibrium in DMM into *sc*,-*sc* position (anomeric effect [7—9]) are not taken into account in the prediction of stable conformations based on S_W or V_W.

From comparison of values in Figs. 1—3 with the data for n-hexane and higher alkanes [5, 6] it seems that in molecules with 1,3-dioxa group the torsional changes of surface are smaller than in n-alkanes and can be of the opposite sign. For example, the interconversion of central C—C bond to *sc* conformation in all--*ap*-hexane brings about a 3.5 % decrease of molecular surface. An analogous *sc*—*ap* difference in DDMS for $d = 0.05$ nm is positive and only 1.2 % (or 2 % for the *sp*—*ap* difference).

Besides the correlation of molecular surface and volume with the macroscopical properties of substances the molecular surface is frequently used also as a measure of solute—solvent interaction [16] and in expressing the "accessible" surface of molecule needed not only for solvation [17] but also as a criterion of probability of the bimolecular reaction with other reagent [18]. Van der Waals geometrical envelope S_W plays a central role mainly in Sinanoglu's solvophobic theory [16] of solvation where it assists in determining the "microthermodynamical" surface of molecule in solution.

In the theory of the solvent effect on conformational equilibrium the Gibbs energy difference of two conformers is given as a sum of the isolated molecule change and the solvation term

$$\Delta G = \Delta G_{\mathrm{isol}} + \Delta G_{\mathrm{solv}} = \Delta E_{\mathrm{isol}} + P\Delta V_{\mathrm{isol}} - T\Delta S_{\mathrm{isol}} + \Delta G_{\mathrm{elst}} + \Delta G_{\mathrm{disp}} + \Delta G_{\mathrm{cav}} \qquad (1)$$

On the right-hand side of the last equation there are the differences of static potential energy, entropy, and volume of two conformers of isolated molecule and the solvation term expressed as a sum of changes in the electrostatic and dispersion Gibbs energy of solvent—solute interactions and the Gibbs energy difference of cavity formation in solvent.

Sinanoglu showed [16] that all the last three terms on the right-hand side of eqn (*1*) depend on molecular surface or volume. This connection is especially evident in the cavity term ΔG_{cav} which is determined as a product $k_{\mathrm{g}}S_{\mathrm{W}}\gamma$, where γ is the macroscopic surface tension and k_{g} is a function which converts the molecular surface to the microthermodynamical surface. In the case of dramatic torsional changes of surface it may happen that ΔG_{cav} term would be the dominant term in eqn (*1*) and it would determine the stable conformation in solution. Results in Figs. 1—3 show that this situation is quite improbable in molecules with 1,3-dioxa group on tetrahedral centre since the calculated differences of surface between stable conformers are very small. In this way the present calculations support the assumption from the analysis of solvent effect on conformation of DMM [8] and DMP^- [19] about exaggerated and unreliable values of ΔS_{W} when calculated with an approximation of molecule as a parallelepiped [20] and when the false values of ΔS_{W} negatively influence also the ΔG_{cav} and ΔG_{disp} terms. In both molecules the ΔG_{elst} term exhibits the most important influence on their conformation in solution. Coincidentally, it seems that similarly as the electrostatic forces are dominant in the intramolecular preference of *sc* position in DMM (anomeric effect) [8, 14] the electrostatic stabilization of conformers by solvent is the most important factor also in the interaction of DMM with solvent.

The torsional dependence of surface of DMP^- shown in Fig. 2 is directly connected with the calculations of accessible surface in nucleic acids [17, 18] where the macromolecular chain and bulky substituents (bases) partially restrict solvent or reactant accessibility to the phosphate groups. The accessible surface is calculated by moving the solvent (reactant) molecule along van der Waals geometrical envelope and it is possible to separate the contribution of individual atoms or groups to the total surface. As an oversimplification it is assumed [17] that those conformations which have the maximum accessible surface will be the most solvated and stabilized ones. Calculations of solvation energy of DMP^- show [19], however, that for the section $\varphi_2 = 180°$ the dominant electrostatic term in eqn (*1*) prefers *sp* position with maximum dipole moment to *ap* position which possesses maximum surface according to Fig. 2. Generally, maximum surface guarantees for the maximum Gibbs energy of solvation in certain special cases only according to the solvophobic-solvophilic classification of interaction [16].

Differences of van der Waals surface in Figs. 1—3 can be simply recalculated on the corresponding changes of conformational volume ΔV_{W}. This conversion results in $-3.55\ \mathrm{cm^3\ ml^{-1}}$ for *sc*—*ap* difference in V_{W} of n-hexane [5]. Recent measurement of Raman spectra of n-heptane at higher pressure led to — 1.8 $cm^3 mol^{-1}$ for overall volume changes ΔV between *sc* and *ap* conformations [2, 3]. Accordingly, a simplified recalculation of surface on volume change seems to result in a partial overestimation of ΔV_W. We should mention in addition that a different procedure for calculation of volume V_W [21], also based on the calculation of overlapping spheres, resulted in only minimal differences between van der Waals volume of *sc* and *ap* conformers of hexane [22].*

By differentiation of eqn (*1*) according to pressure an expression for the isothermal volume changes ΔV of two conformers in solution is obtained. Conformational volume ΔV is determined by a sum of the inherent changes of isolated molecule ΔV_{isol} and volume changes due to the interaction with solvent ΔV_{solv}. The first term can be approximately replaced by change of van der Waals volume ΔV_W for the two most stable conformers in solution which in general may be different from those in vapour phase. The term ΔV_{solv} can be further decomposed to three contributions, similarly as in eqn (*1*). Hence, the torsional dependences shown in Figs. 1—3 reflect the volume difference of conformers in vapour phase only. The picture can substantially change in solution due to the contribution of ΔV_{solv} and the latter term can even determine the sign and size of the overall volume changes ΔV That is documented by recent treatment of the volume changes between *sc* and *ap* conformations of 1,2-dichloroethane and 1,2-dibromoethane [3] where it was shown that both inherent van der Waals overlap of halogens and solvation volume estimated on the basis of ΔG_{elst} only contribute equivalently to the experimental values of ΔV (from — 1.8 to — 4.5 $cm^3 mol^{-1}$).

Although in molecules with 1,3-dioxa group the changes of S_W and V_W look as unimportant ones, an opposite situation may sometimes arise when these changes are large and their reliable prediction is necessary in order to correlate macroscopical properties or to calculate this solvent effect. The method used in this paper represents a very appropriate alternative for this purpose. More crude approximations of molecule, *e.g.* by parallelepiped [20] are not sensitive enough and the use of molar volume or other macroscopic property is unable to provide the conformational dependence of molecular size. Other indirect methods can lead to the controversial results as recently in Ref. [23] where the larger inherent volume was assigned to the coiled conformation of alkane chain than to the extended one in apparent contradiction with experimental and theoretical findings for conformational volume of short alkanes [5, 6], which obviously should affect the computed solvation energy. Calculation of inherent volume or surface of solute molecule

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* Molar volume of 1,1,2-trichloroethane is by mistake quoted in Ref. [5] as 192.1 $cm^3 mol^{-1}$ instead of the correct value 92.7 $cm^3 mol^{-1}$. The author is grateful to Dr. Terryn for bringing this error to his attention.

must be an indispensable part of every more rigorous attempt to determine the effect of solvent on conformational equilibrium of flexible molecules.

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References

1. Christian, S. D., Grundes, J., and Klaboe, P., *J. Chem. Phys. 65,* 496 (1976).
2. Schoen, P. E., Priest, R. G., Sheriden, J. P., and Schnur, J. M., *J. Chem. Phys. 71,* 317 (1979).
3. Taniguchi, Y., Takaya, H., Wong, P. T. T., and Whalley, E., *J. Chem. Phys. 75,* 4815 (1981).
4. Pratt, L. R., Hsu, C. S., and Chandler, D., *J. Chem. Phys. 68,* 4202 (1978).
5. Bleha, T., Gajdoš, J., and Tvaroška, I., *J. Mol. Struct. 68,* 189 (1980).
6. Bleha, T., *Makromol. Chem., Rapid Commun. 2,* 35 (1981).
7. Tvaroška, I. and Bleha, T., *J. Mol. Struct. 24,* 249 (1975).
8. Tvaroška, I. and Bleha, T., *Collect. Czech. Chem. Commun. 45,* 1883 (1980).
9. Mlýnek, J., Bleha, T., and Tvaroška, I., *Chem. Zvesti 34,* 3 (1980).
10. Carleer, R., van der Enden, L., Geise, H. J., and Mijlhoff, F. C., *J. Mol. Struct. 50,* 345 (1978).
11. Hermann, R. B., *J. Phys. Chem. 76,* 2754 (1972).
12. Allinger, N. L. and Chung, D. Y., *J. Amer. Chem. Soc. 98,* 6798 (1976).
13. Plyamovatyi, A. Kh., Dashevskii, V. G., and Kabachnik, M. Yu., *Dokl. Akad. Nauk SSR 234,* 1100 (1977).
14. Tvaroška, I. and Bleha, T., *Biopolymers 18,* 2537 (1979).
15. Zanotti, G., Spadon, P., and Del Pra, P., *J. Polym. Sci., Polym. Chem. Ed. 17,* 2283 (1979).
16. Sinanoglu, O., *Int. J. Quantum Chem. 18,* 381 (1980).
17. Ponnuswamy, P. K. and Thiyagarajan, P., *Biopolymers 17,* 2503 (1978).
18. Lavery, R., Pullman, A., and Pullman, B., *Theor. Chim. Acta 57,* 233 (1980).
19. Bleha, T., Mlýnek, J., and Tvaroška, I., *Collect. Czech. Chem. Commun. 46,* 1722 (1981).
20. Beveridge, D. L., Kelly, M. M., and Randa, J. J., *J. Amer. Chem. Soc. 96,* 3769 (1974).
21. Terryn, B. and Barriol, J., *J. Chim. Phys. 78,* 207 (1981).
22. Terryn, B., private communication.
23. Raudino, A., Zuccarello, F., and Buemi, G., *J. Chem. Soc., Faraday Trans. 2 77,* 1331 (1981).

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