The Effective Volumes of Waters of Crystallization:

General Organic Solids

Leslie Glasser

Curtin Institute for Computation, Discipline of Chemistry

Curtin University, GPO Box U1987, Perth, WA 6845, Australia

3 Figures   ~2 400 words

Supplementary Tables S1 and S2, Figure S1

[*]Corresponding author

L. Glasser: Telephone: + 61 8 9848-3334

                    E-mail: l.glasser@curtin.edu.au

                     ORCID iD: 0000-0002-8883-0564

Abstract

Using a list of compatible hydrate/anhydrate pairs prepared by van de Streek and Motherwell, we have examined the effective volume per water of crystallization for 179 pairs of organic solids using current data from the Cambridge Crystallographic Structural Database (CSD). The effective volume is the difference per water molecule between the asymmetric-unit volumes of the hydrate and parent anhydrate, and has the mean value 24 $Å^3$. The conformational changes in the reference molecule between the hydrate and its anhydrate are shown in two Figures: one for a relatively rigid standard organic molecule and one for a more flexible linear molecule.

Using data from Nyman and Day, we have also established a generic volumetric coefficient of thermal expansion of organic solids with a value of $147 \pm 56 \times 10^{-6}$ K^{-1}.

There is a significant number of outliers to the data, negative, near zero, and large and positive. Some explanation for the existence of these outliers is attempted.

Introduction

Molecules are generally regarded as incompressible under ambient conditions; this includes the water molecule with fixed radii assigned to its constituent atoms.[1] Accordingly, we define the "effective volume" of water of crystallization as the volume difference per water of crystallization between a hydrate and its parent anhydrate, both structures corrected to room temperature.

We have recently examined effective volumes for both ionic solids[2] and non-ionic pharmaceutical systems.[3] For these systems, we observe that hydrate water effective volumes extend to a seeming upper limit of about 30 $Å^3$, which corresponds to the formula volume of liquid water under ambient conditions (but less than the 32 $Å^3$ observed for the hydrogen-bonded structure of hexagonal ice) and down towards zero as a consequence of the hydration water occupying gaps in the anhydrate, together with the anhydrate's possible structural re-arrangement. This information is of both crystal-structural and chemical/pharmaceutical value (for example, hydrates are generally less soluble than anhydrates). It also has significant thermodynamic implications since many thermodynamic properties are closely correlated with formula volumes through Volume-Based Thermodynamics (VBT).[4-5]

In the current analysis we extend this examination to waters of crystallization in non-metal-containing organic solids in general, both neutral and ionic, for simple hydrates as well as those having mixed solvates, such as ethanol/water.

Data Collection

Van de Streek and Motherwell[6] have performed a comprehensive programmatic search of the Cambridge Structural Database (CSD[7] version 5.27, November 2005) for hydrate-anhydrate pairs, ensuring that the organic moiety of the pair is stereochemically consistent while omitting metal-containing pairs because of chemical and stereochemical ambiguities which would otherwise complicate the effective volume relation. This has resulted in a list of 374 such pairs. We have manually collected from the current CSD the crystallographic data for 179 of these pairs (48%)

selected randomly, but with no chemical duplicates, at a rate of roughly three or four per alphabetically-listed group of ten. We have added a further pair for the exceptional heptahydrate of t-butanol. The data collected is the number of water molecules in the hydrate, $n(H_2O)$, the asymmetric-unit volumes of the hydrate and of the anhydrate, $V_{m,hyd}$ and $V_{m,anhyd}$, and the temperatures, T_{hyd} and T_{anhyd}, of their determination. The effective volume of the water of crystallization is calculated as the difference per water molecule between the volumes of the asymmetric-unit of hydrate and of anhydrate, with each volume corrected to the ambient temperature of 298 K using a generic volume coefficient of thermal expansion,[1] α_V, according to equation (1). (Since much of the CSD data has been reported for room temperature this correction is of limited overall significance.)

$$V_m(H_2O) = [(1+\alpha_V)(298-T_{hyd})V_{m,hyd} - (1+\alpha_V)(298-T_{anhydr})V_{m,anhyd}]/n(H_2O) \quad (1)$$

Hofmann[1] has reported a value of the volumetric coefficient of thermal expansion of 95×10^{-6} K^{-1} for organic materials. Similarly, we have earlier[3] found a value of about 100×10^{-6} K^{-1} for paracetamol among the pharmaceutical pairs and, as noted below, now find a value of $147 \pm 56 \times 10^{-6}$ K^{-1} among general organic materials[8] (see Figures 1 and 2, and Table S1 in the Supplementary Information) with a mode value of 109×10^{-6} K^{-1}.
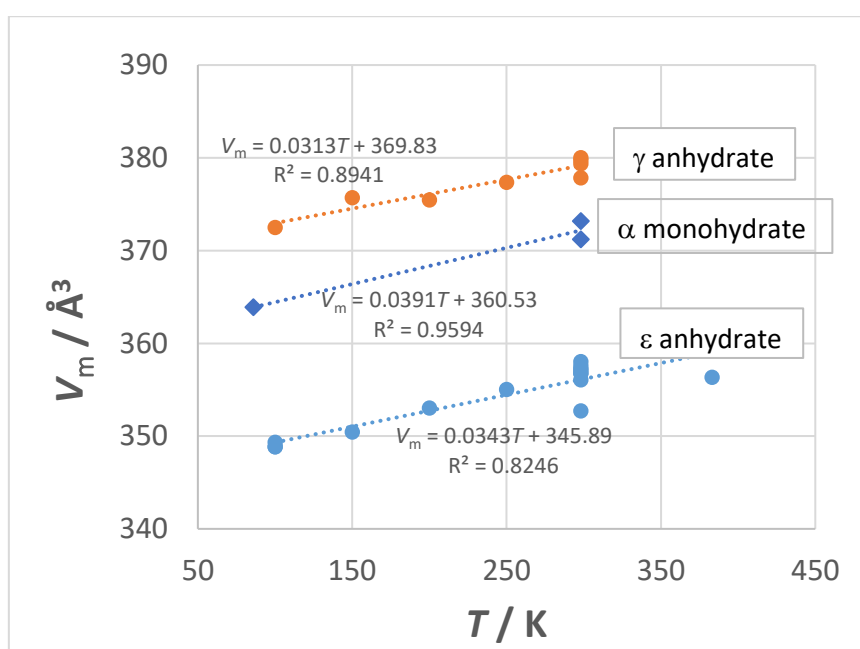
Figure 1: Asymmetric-unit volumes as a function of temperature for the hydrates (CSD refcodes PUBMII*mn*) and anhydrates (CSD refcodes PUBMUU*mn*) of hexahexanitro-azaisowurtzitane (HNIW, $C_6H_6N_{12}O_{12}$).[9] From the slopes of V_m versus T, the volumetric thermal expansion coefficients of hydrates and anhydrates $\cong 0.0355$ Å^3 K^{-1}/355 Å^3 = 100×10^{-6} K^{-1}. Only the γ anhydrate and α monohydrate are stable under ambient conditions.[10] The data for Fig. 1 are listed in Supplementary Information Table S1.

Nyman and Day have recently[8] calculated thermal data on 865 organic solids including 391 polymorphic pairs, 26 triplets and one quadruplet. Their Fig. 5(a) depicts the frequency distribution of their volumetric thermal expansion coefficient values. Using their data, we have calculated a median volumetric thermal expansion coefficient of $147 \pm 56 \times 10^{-6}$ K^{-1} which we utilise for Fig. 2, which depicts the distribution of effective volumes of water of crystallization for 163 organic hydrate/anhydrate pairs (but not including the full hexanitrohexa-azaisowurtzitane system of Fig. 1). The data for Fig. 2 may be found in our Supplementary Information as Table S2, which also includes eight negative values and eight values greater than 40Å^3 omitted from the distribution depicted in Fig. 2.
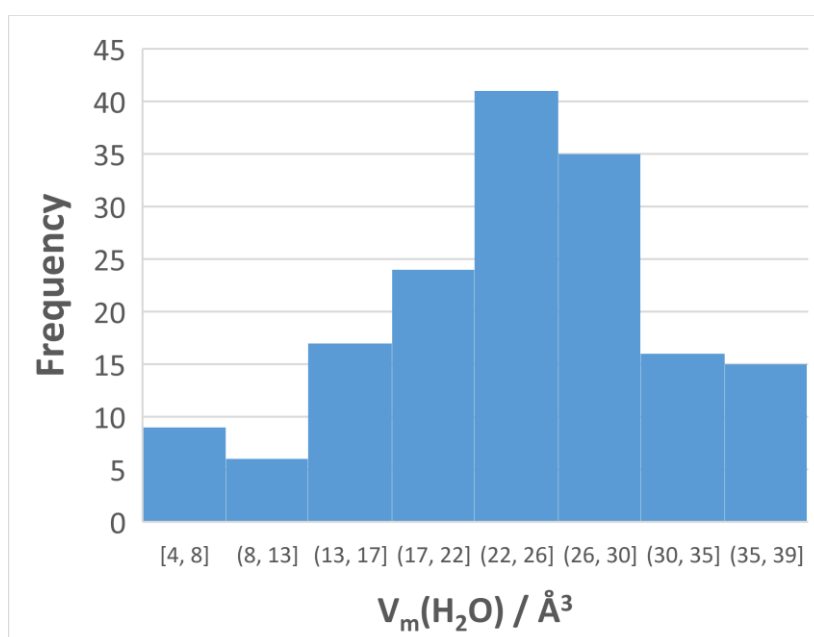
Figure 2: Distribution of effective volumes of 163 waters of crystallization for general organic solids with a generic volumetric coefficient of thermal expansion of $147 \pm 56 \times 10^{-6}$ K^{-1} to correct the experimental temperatures to 298 K according to eq (1), with a mean water effective volume of 23.8 $\pm$ 8 Å^3. Eight negative values and eight positive values larger than 40 Å^3 have been omitted from the histogram.

Fig. 2 shows a mean value of 24 Å^3 for the effective volume of water of crystallization, which is similar to the values we have earlier reported for ionic solids and for non-ionic pharmaceutical solids (24 and 23 Å^3, respectively). The range of effective volumes is rather larger than in our earlier reports for selected molecular types, with a small number of negative values and some values even extending beyond our suggested upper limit of 40 Å^3. The effective volumes for some of these outlying data pairs are considered below.

Discussion: The Close-Packing Principle[11-13]

In the 1950's, Kitaigorodsky introduced the close-packing principle of "bumps into hollows just as a key fits into a lock"[12] for molecular solids, noting[14] that "molecules are closely packed with the minimum voids between them for the given cell". Dunitz and Gavezzotti[15] have rendered this more quantitative with their dictum "As far as the packing energy is concerned, empty space is wasted space." This may even be regarded as a modern expression of Aristotle's claim that "Nature abhors a vacuum"! It should be noted that the occupied volume tends to increase with temperature because of the anharmonicities of vibrations.

Our current analysis sets out to examine the efficiency of incorporation of the solvate water into molecular crystal structures, with the expectation that the water will require its own volume but may utilise some of the void volume of the parent crystal thus improving the packing efficiency. This efficiency may further be improved by some re-positioning and even conformational changes of the parent molecule, although the interactions with the water may, depending on circumstances, introduce some awkwardness into the packing. Examination of conformational changes in a number

of cases, using the Structure Overlay feature of the CSD Mercury program,[16] shows only minor

conformational changes of the reference molecule between the hydrate and anhydrate, as may be

seen in Fig. 3. These changes are somewhat greater in flexible linear molecules, such as amino

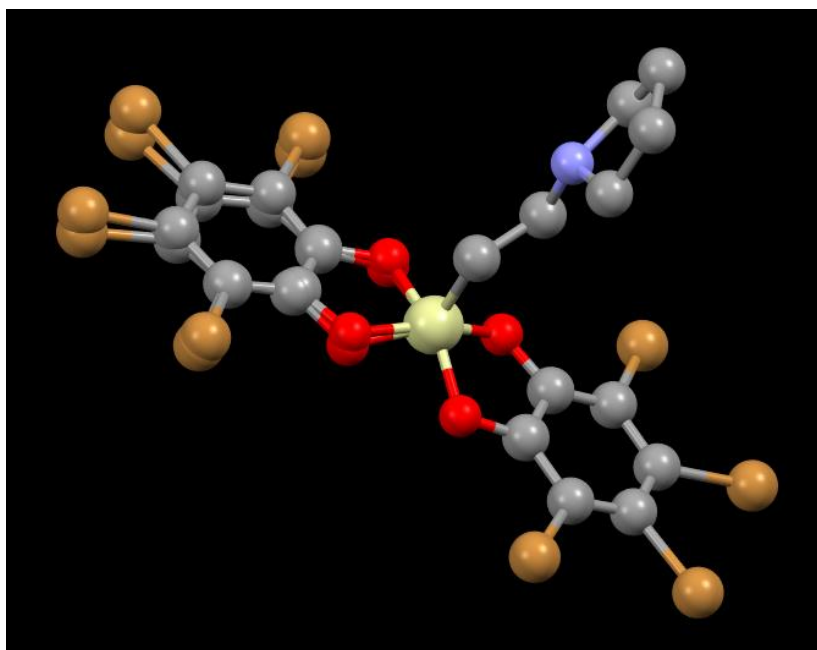acids,[2] as may be seen in Supplementary Figure S1.

Figure 3: Overlay of molecular units from the CSD files triclinic hydrate PEGVEC.cif and orthorhombic

anhydrate PEGVAY.cif illustrating the minor conformational changes between the hydrate and

anhydrate. In this view the central silicon (yellow) and nitrogen (blue) atoms have been overlaid.

This spirosilicate has the chemical formula $C_{18}H_{13}Br_8NO_4Si$ and the systematic name: bis(3,4,5,6,-

tetrabromo-1,2-benzenediolato)(2-(pyrrolidino)ethyl)silicate.[17] The Figure was prepared using the

Structure Overlay feature of the CSD Mercury program.[16]

As Fig. 2 demonstrates, the effective volume for the representative organic systems considered is

distributed around a value of 24 $Å^3$, together with some negative values and some unexpectedly

large values. We will briefly consider these wide deviations.

Fig.1 provides a clear example of the problematic issues. The asymmetric-unit volumes of the ε

anhydrate of hexahexanitro-azaisowurtzitane are smaller than those of hydrate, leading to a range

of positive values for the ambient effective volume of about 27, 31 and even 69 $Å^3$ for the water of crystallization depending upon the particular combination of CSD Refcode crystals chosen. By contrast, the γ anhydrate yields an effective volume of -26 $Å^3$. A value in the usual range is observed if the unstable β parent phase is selected as the anhydrous reference (see Table 2, PUBMUU03). What seems to be the issue here is that the structures of the hydrate and of the parent anhydrate may be wildly incommensurate so that hydration is of an essentially different structure to that of the anhydrate with which it is being compared, in addition to possible errors in the crystal structures such as missing hydrations and/or solvation by other solvates when crystallized from mixed solvents.

We have examined a few of the most egregious outliers in order to identify what might be the relevant issues. In general we note that one of the crystalline space groups may have very low symmetry such as triclinic, with the implication that packing and stacking may be difficult with a complex-shaped molecule - but we do not have an explanation for all the outliers. (i) Examining examples of negative effective water volumes: for LEZKAC/FIQFER, the hydrate water has been distributed over four sites; for RAVBUL/NAFMEM, the anhydrate is triclinic and there is a mixed solvate: water plus dichloromethane; for PEGVEC/PEGVAY, the hydrate is triclinic while the material is an organic silicate (see Fig. 3). (ii) Correspondingly, examining examples with excessively positive effective hydrate volumes: for YAKWAJ/BISMEV04 the anhydrate structure was determined at the high pressure of 0.4 GPa; for both NIMSIM/NINSEI and DOFTAT/DOFSUM the hydrate is described as a clathrate; for EDUHIU/EDUGOZ and NABWET/NABWAP both hydrates are triclinic.

(iii) Some hydrate/anhydrate pairs (such as GAFVOY/VUXBAR and JEDTOB/TPEPHO07) have very similar asymmetric-unit volumes leading to near-zero values for the effective volume of the water of crystallization. It is perhaps possible that both of each pair are hydrates but that water has been missed from the structure of the supposed anhydrate.

Conclusions

The effective volumes per water molecule of waters of crystallization are distributed around 24 $Å^3$, so that this value may be used with some confidence in the prediction of the crystal structures and volume-related thermodynamic properties of hydrated organic materials. However, there are some large negative and positive values as well as some near-zero values, which require special explanation in order to justify, as noted above. It seems necessary to regard such values as special-case outliers requiring deeper analysis.

A generic value of $147 \pm 56 \times 10^{-6}$ K^{-1} has been established for the volumetric coefficient of thermal expansion of organic solids. It seems most appropriate to compare hydrate/anhydrate pairs whose structures have been determined at ambient temperature or, at least, at similar temperatures.

Supplementary Information

Table S1: data for Fig.1; Table S2: data for Fig. 2; Figure S1: Structure Overlay for arginine dihydrate and arginine.

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Title: The Effective Volumes of Waters of Crystallization: General Organic Solids

Author: Leslie Glasser
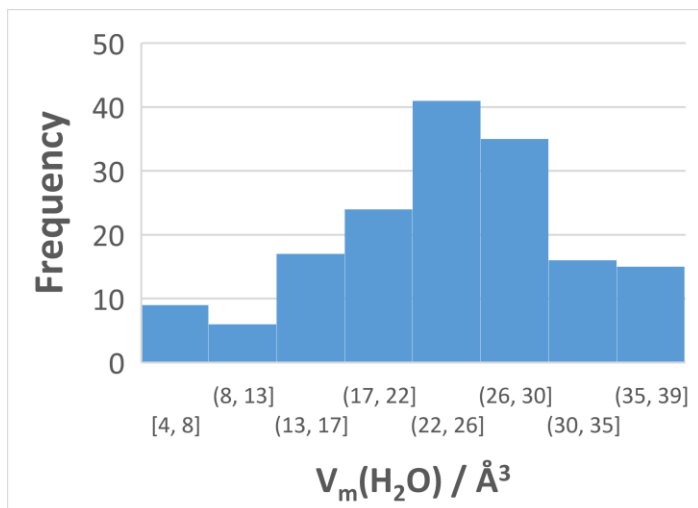
Synopsis: The effective volumes of waters of crystallization have been determined for 163 hydrate/parent systems, yielding a mean value of 24 $Å^3$. A generic value of $147 \pm 56 \times 10^{-6}$ K^{-1} has been established for the volumetric coefficient of thermal expansion of organic solids.

These results may be helpful in assessing and predicting hydrate crystal structures and volume-related thermodynamic properties.