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Molecular packings and specific-bond patterns in sulfonamides

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A novel approach to the topological analysis of molecular packings and intermolecular bond patterns is described and tested on the crystal structures of 1463 sulfonamide derivates taken from the Cambridge Structural Database as well as on three newly synthesized ones. We have revealed strong correlations between local and overall topological motifs of hydrogen and halogen specific intermolecular bonds; as a rule, a particular local connection type of the molecules provides only one most preferable pattern of intermolecular bonds and *vice versa*. The molecular packings are found almost independent of existence or absence of the specific bonds and in more than 1/3 cases obey the Kitaigorodskii's model of close packing. A peculiar shape of sulfonamide molecules in some cases gives rise to a special 'butterfly' packing that is topologically less dense than the close packings. The correlations found can be used to predict main peculiarities of molecular crystals within a prospective expert system.

Introduction

Analysis of molecular packings plays an important role in understanding the structure of molecular crystals. Since the Kitaigorodskii's time it became clear that both local and overall arrangements of molecules follow some rules that were pronounced in the model of molecular close packing.[1] According to this model, each molecule in the packing of equal molecules tends to surround itself by 12 others like balls in a close packing. Other large even numbers of neighbors (10 or 14) are also possible but occur rarer. Although Kitaigorodskii analyzed very limited amount of the crystallographic data available at that time and did it by hand, his approach showed its viability and has been used until now. In 2000,[2] we have applied the concept of molecular Voronoi polyhedra to automatically study molecular packings in all organic crystal structures deposited in the Cambridge Structural Database (CSD)[3] and found that molecular coordination number 14 is more frequent than 12, while molecular centers of mass obey the Kitaigorodskii's model. At the same time, huge size of the sample (33,575 compounds) did not allow us to analyze in detail relations between topology of the molecular packings and chemical structure of the molecules.

The model of close packing assumes that intermolecular interactions are not directed and have close energy values that is characteristic for van der Walls forces. If electron exchange or ionic components are significant like in H bonds, halogen bonds, π-π interactions, or other specific bonds, one could expect a deviation from the close packing motif. On the other hand, molecular packing can influence specific intermolecular interactions since molecular crystal is a result of equilibrium between all intermolecular forces, both specific and van der Waals. From chemical point of view, the systems of such interactions can be naturally explored with the graph or network approaches, and the corresponding formalism was developed in the last decades.[4] However, to the best of our knowledge, nobody has analyzed the relations between topological properties of molecular packings and motifs of specific bonds on large samples of compounds.

Recently,[5] we proposed a universal approach to computer analysis of molecular packings and supramolecular ensembles that is based on the topological description of molecular patterns on both local and overall levels of their architecture.[2,6] This approach was shown to be perspective for creating an expert system that would allow one to predict important topological features of molecular crystals.

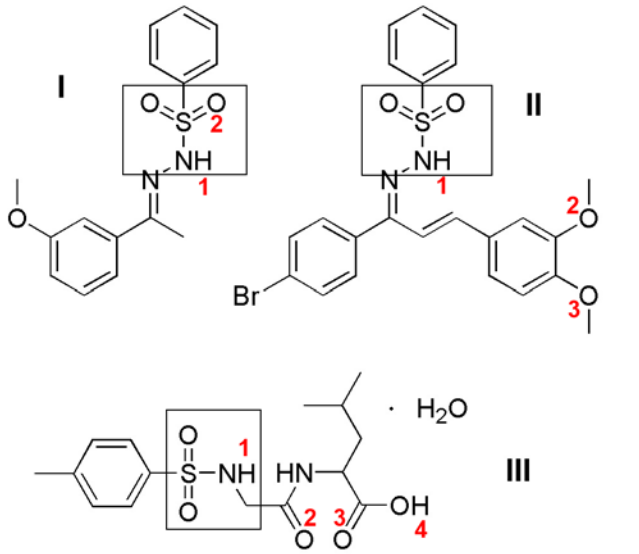
In this paper, we unite the methods of description of local and overall topological features of molecular crystals composed of sulfonamide derivates. Due to existence of electron donor atoms many sulfonamides participate in H bonding while tetrahedral geometry of the sulfur center gives rise to a complicated geometry of the whole molecule. These features can strongly influence the packing, so this kind of molecule is a good challenge for the topological methods. Our goal was to explore the relations between type of molecular packing and specific-bond patterns of the molecules. To find and check these relations we planned to study all available experimental

data on crystal structures of sulfonamides as well as to synthesize new their derivates.

Experimental

Objects

We have synthesized three new sulfonamide derivates (Scheme 1) and determined their crystal structures.



Scheme 1. Sulfonamide derivates **I-III**. Red numbers enumerate the active atoms that participate in H bonds. The sulfonamide functional groups are separated by rectangle.

Synthesis of N'-[(1E)-1-(3-methoxyphenyl)ethylidene]benzenesulfonohydrazide (I). The mixture of 3-methoxyacetophenone (5.8 mmol, 0.87g) and benzenesulfonylhydrazide (5.8 mmol, 1g) in methanol (20 mL) was refluxed for 4 hours. The progress of reaction was checked by TLC. The mixture was concentrated over rotary evaporator and left to stay in ice overnight. Precipitate obtained was filtered and washed with cold methanol. Re-crystallization in methanol gave colorless block shaped crystals. m. p. 491-493 K.

Synthesis of *N*'-[(1*E*,2*E*)-1-(4-bromophenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-ylidene] benzenesulfonohydrazide (II). The compound was prepared in two steps. Firstly 4-bromoacetophenone (5.02 mmol, 1g) and 3,4dimethoxybenzaldehyde (5.02 mmol 0.8g) was dissolved in ethanol to make a solution A. In a separate beaker sodium hydroxide (6.03 mmol, 0.24g) was dissolved 50% aqueous ethanol which will be solution B. Half of the solution A was added to B and allow it to stir for 30 mins followed by addition of another half. The mixture was stirred at room temperature for 4 hours. Precipitate obtained was filtered off and washed with cold ethanol to obtain in good yield (94%). In the second step, 3-(4-Bromo-phenyl)-1-(3,4-dimethoxy-phenyl)-propenone (1.44 mmol, 0.5g) and benzenesulfonyl hydrazide (1.44 mmol, 0.24g) were refluxed in methanol for four hours, where two drops of glacial acetic acid was used as catalyst. The solution was left as it is on bench which produces orange grains like crystals. m. p. 443-445 K.

Synthesis of 4-methyl-2-[({[(4-methylphenyl)sulfonyl]amino}acetyl)amino]pentanoic acid hydrate (III)**.** The chemicals used were purchased from international reputed suppliers and used without further purification. Glycyl L-lucine (1.44 mmol, 0.27g) was dissolved in water using 1M solution of Na_2CO_3 and the pH was adjusted 8-9. 4-Toluene sulfonyl chloride (1.31 mmol, 0.25g) was added to the above solution. Reaction progress was observed by consumption of suspended 4-Toluene sulfonyl chloride to clear solution. Then pH was adjusted to 2-3 using diluted HCl. Precipitate observed was filtered washed and recrystallized in methanol. m. p. 372-374 K**.**

X-ray data collection and structure determination. Suitable crystals of compounds **I-III** were selected and mounted, using glass fiber fixed to copper pin held on magnetic base. Agilent SuperNova (Dual source) Agilent Technologies Diffractometer, equipped with a graphite-monochromatic Cu/Mo Kα radiation was used to collect the data. The data collection was performed using CrysAlisPro software[7] at 296 K under the Cu Kα radiation. The structure solution was performed by direct methods using SHELXS–97[8] and refined by full–matrix least–squares methods on F^2 using SHELXL–97,[8] in-built with X-Seed.[9] All non–hydrogen atoms were refined anisotropically by full–matrix least squares methods.[8]

All the C-H hydrogen atoms in all three molecules were positioned geometrically and treated as riding atoms with C–H = 0.93 Å, 0.96 Å, 0.97 Å and 0.98 Å for aromatic, methyl, chiral carbon and methylene H atoms respectively. These were refined using a riding model with Uiso(H) = 1.5 Ueq(C) for methyl and Uiso(H) = 1.2 Ueq(C) for all other carbon atoms.

The N-H = 0.81(7)-0.90(6) Å, O-H = 1.10(7) - 0.88(1) Å hydrogen atom were located with difference Fourier maps and refined using riding model with Uiso (H) = 1.2 Ueq(N) and Uiso(H) = 1.5 Ueq(O). Hydrogen atoms attached to water molecule in **III** were refined using bond length and bond angle restraints with Uiso(H) = 1.5 Ueq(O).

Analysis of the Cambridge Structural Database. Using the TOPOS software we have extracted from the CSD (release 5.35, October 2013) all 1025 structures of sulfonamides that are monomolecular, *i.e.* include no other molecules except sulfonamide, and contain intermolecular H bonds. Out of them 932 structures have no other kinds of the specific intermolecular bonds under consideration, and 93 structures bear also halogen bonds. The criteria used for determination of intermolecular bonds of different types are described in the next part. In addition, we have analyzed 16 monomolecular sulfonamides containing only halogen, not hydrogen, intermolecular specific bonds. To explore the influence of intermolecular specific bonding on the type of molecular packing we have analyzed 422 monomolecular sulfonamides, in which structures the molecules are linked by van der Waals bonds only. Thus the total sample consisted of 1463 sulfonamide structures. All the structures were completely determined and contained no disordered parts of molecules.

The topological analysis of local and overall specific-bond patterns as well as molecular packings was performed with the program package TOPOS[10] following the scheme described below. The detailed information on the local and overall topologies of molecular packings and specific-bond patterns is contained in the ESI.

Method for topological analysis of molecular packings

To extract the information on general regularities from the crystallographic databases like the CSD we have to use rather simple and fast methods that allow us to process large samples of data in the same way. Quantum-mechanical approaches can analyze in detail the electron distribution and intermolecular interactions[11] but they are not suitable for bulky calculations of thousands of structures. Moreover, even quantum-mechanical methods need some simple descriptors to be comparable for different structures and usable for their classification.

We use the model of infinite periodic graph (*net*)[12] to describe the connectivity patterns between molecules and to formalize the topological features of molecular crystals. An infinite net can be transformed into a finite labeled quotient graph[13] that keeps the whole information on the structure connectivity and can be stored in an electronic database as well as processed with computer programs. To obtain the information on intermolecular interactions we use molecular Voronoi polyhedra and the Sector method.[2b] Molecular Voronoi polyhedra are composed of Voronoi polyhedra of all atoms of the molecule and their external faces correspond to intermolecular interactions (Fig. 1 left). Each atomic Voronoi polyhedron can be considered as an atomic domain in the crystal field[14] and the electron density within this domain assumed belonging to the atom. The faces of the atomic Voronoi polyhedron that separate the atom domain from the atoms of other molecules are assumed to correspond to intermolecular contacts. If the faces are direct, *i.e.* the line connecting the atoms in contact crosses the Voronoi polyhedron face, and the face is rather large (ordinarily its solid angle should exceed 1.5% of 4π steradian), the contact is considered as an interaction.

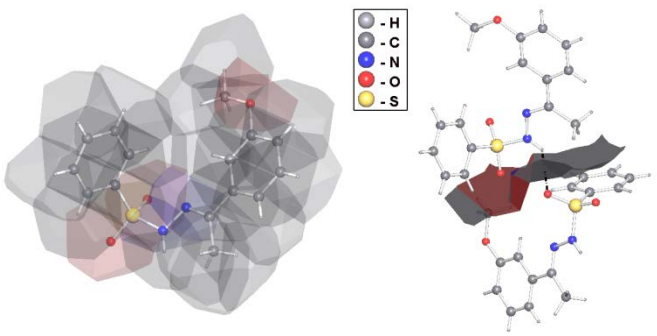


Figure 1. (Left) Molecular Voronoi polyhedron of molecule **I**; (right) two molecules **I** in the packing separated by a surface composed of the common faces of their molecular Voronoi polyhedra; the surface determines the $\Omega_{mol}(i)$ value corresponding to the intermolecular contact. H bond is shown as a dashed line.

Among intermolecular interactions we consider separately *specific* bonds that are much stronger than van der Waals interactions, namely, H bonds and halogen bonds. H bonds are identified in accordance with the geometrical criteria:[6,15] we have considered only N(O)-H…X interactions with X = N, O, F, S, or Cl and d(H…X) ≤ 2.5 Å for X = N, O, or F and 2.7 Å for X = S or Cl; d(N(O)…X) ≤ 3.5 Å for X = N, O, or F and 3.7 Å for X = S or Cl; ∠ N(O)-H…X ≥ 120°. The contact Hal…B in a fragment A-Hal…B (Hal=Cl, Br, I; A=C, N, O, F, S, Cl, Se, Br, I; B=N O F S Cl Se Br I) was referred to as a halogen bond if the solid angle for the contact Hal…B exceeded 5% of 4π steradian and ∠A-Hal…B ≥ 160°.

The local connection of the molecules is described within the scheme that we developed recently;[5b] in turn, this scheme is based on the approach proposed earlier for coordination compounds.[16] The total number of active atoms (n) of the molecule is written by letters M, B, T, K, P, G, H, O, N, D for n = 1–10; for n > 10 the record X[n] is used. The method of connecting is encoded by a superscript line of integers *mbtkpghond*… where each integer is equal to the number of molecules connected to the given one by one (m), two (b), three (t), four (k), etc. H bonds. Thus the total number of molecules connected to the given one (molecular coordination number, MCN) is equal to $m+b+t+k+p+g+h+o+n+d+\ldots$ and the total number of H bonds formed by the molecule is calculated as $m\cdot1+b\cdot2+t\cdot3+k\cdot4+p\cdot5+g\cdot6+h\cdot7+o\cdot8+n\cdot9+d\cdot10+\ldots$ The *molecular connection type symbol* (MCTS) is written as $L^{mbktpghond}$, where L is one of the letters mentioned above. In particular, in structure **III**, each sulfonamide molecule uses four active atoms to form five H bonds with two other sulfonamide molecules and three water molecules; hence, its MCTS is K^5. All three atoms of each water molecule are involved into H bonding providing a T^3 connection type (Fig. 2 top). Considering intermolecular interactions of a particular type, for example, only van der Waals interactions, only H bonds, only halogen bonds or any combination of the interactions one can get different MCTS that describe different bonding patterns.

The whole patterns are then analyzed within the concept of simplified net. The simplification procedure consists in replacing molecules by their centers of mass keeping the connectivity between the centers of mass of adjacent molecules. The resulting *underlying net* characterizes the overall topology of the molecular motif. For example, in structure **III**, the underlying net is 1-periodic (rod-like) with the 3^6(1,2) chain topology (Fig. 2 bottom; see[17] for the nomenclature of 1- and 2-periodic sphere packings). We assign the topology to one of the reference topological types by comparison of sets of topological indices that unambiguously determine the nets. The *coordination figure* of a node in the underlying net includes centers of mass of all molecules connected to the given one; this is the characteristic of the local topology of molecular packing. In Fig.2, the coordination figure of the selected molecule is the part of the underlying net that includes nodes 0-5 together with the corresponding edges.

Following the approach developed in[2a] we estimate the strength of interaction between two molecules by the value of molecular

solid angle. Molecular solid angle for the interaction of a given molecule with an *i*th one is calculated with the formula:

$$\Omega_{mol}(i) = \Omega_i \Big/ \sum_i \Omega_i \times 100\%, \quad (1)$$

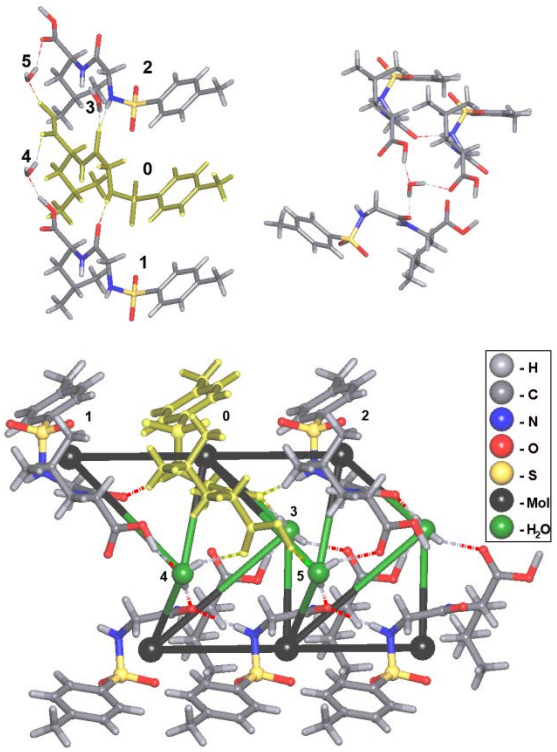


Figure 2. Structure **III**: (top left) a sulfonamide molecule 0 highlighted by yellow is connected to two other sulfonamide molecules (1, 2) and three water molecules (3-5) by four active atoms giving rise to MCTS K[5]; (top right) a water molecule is connected to three sulfonamide molecules by three active atoms giving rise to MCTS T[3]; (bottom) rod-like H-bond pattern and the corresponding fragment of the underlying net shown by black and green balls. One of the sulfonamide molecules with the center of mass No. 0 is selected in yellow; numbers 1-5 designate the centers of mass of two adjacent sulfonamide molecules (1, 2) and three water molecules (3-5). H bonds are shown by dashed lines.

where Ω_i is a sum of solid angles of the Voronoi polyhedra faces corresponding to all contacts between the two molecules; the corresponding Voronoi polyhedra faces form a surface that separates the interacting molecules (Fig. 1 right). Molecular solid angles can be applied to analyze molecular packings at different levels of interaction. If we assign weights $\Omega_{mol}(i)$ to the edges of the underlying net, different subnets can be selected that contain the edges of the weight no less than a specified value. Each subnet corresponds to a particular *representation* of the molecular packing. In this study, we draw special attention to the representations of molecular packings with MCN=12, *i.e.* corresponding to such Ω_{mol}[MCN=12] level, which is exceeded by exactly 12 $\Omega_{mol}(i)$ values for each molecule. This level is important as it is related to the model of molecular close packing,[1] according to which molecules tend to have MCN=12 in the packing.

Thus the total scheme of the topological analysis includes the following steps:
(i) Determining the infinite periodic graph that describes all intra- and intermolecular interactions; ignoring all contacts with solid angle less than 1.5%.
(ii) Searching for specific (hydrogen or halogen) bonds within the graph.
(iii) Determining molecular connection types for different kinds of molecular interactions; we have determined MCTSs for all specific contacts only, *i.e.* H bonds, halogen bonds, or the combination of both types if they coexisted in the same structure.
(iv) Building underlying nets taking into account all intermolecular contacts or specific bonds only.
(v) Generating all representations of the molecular packings that correspond to different levels of the molecular solid angle value.
We have implemented this scheme to the program package TOPOS.[10] To determine the underlying net topology we have used the TOPOS TTD Collection that currently includes almost 80,000 reference topological types.[18] We have used the conventional three-letter RCSR symbols[19] for designating topological types (for instance, face-centered cubic packing topology is referred to as **fcu**); for the topologies not included into the RCSR database the TOPOS *N*D*n* symbols[5a] were applied. In particular, the *N*D*n* symbol 12T11 designates a 12-coordinated (*N*=12) three-periodic (T) underlying net with only one non-equivalent node (there is only one number before the D symbol); the net is 11th in the list of other 12T topologies (*n*=11).

Results and Discussion

Molecular packings and H-bond patterns in compounds I-III

First we applied the algorithm of topological analysis described above to analyze structures **I-III**. Structures **I** and **II** are monomolecular, *i.e.* consist of one kind of molecule, while structure **III** contains solvate water molecules. In structures **I** and **II**, MCN=16 if one takes into account all intermolecular contacts (Table 1), while the H-bond patterns are very simple with MCTS B^2 and T^{0001} that correspond to simple chains and dimers, respectively (Fig. 3). No halogen bonds are found in structure **II** that is the only that contains halogen atoms. In structure **III** each sulfonamide molecule is connected to 14 other same molecules (Table 1) and to six water molecules, while each water molecule is surrounded by six sulfonamide molecules only; its H-bond pattern was discussed above (Fig. 2).
Analysis of molecular packings at different levels of intermolecular interactions shows that the strongest contacts in **I** and **II** provide typical patterns that we have already revealed for monomolecular benzothiazines[5a] (Table 1). For example, four contacts with $\Omega_{mol}(i)$>10% provide a diamondoid (**dia**) underlying motif in **I**, while five strongest contacts ($\Omega_{mol}(i)$>8%) in **II** lead to a **sqp** topology (Fig. 4). In **III**, water

molecules expectedly influence the packing of the sulfonamide molecules: the four strongest contacts with $\Omega_{mol}(i)$>8% give rise to a 1-periodic $3^6(1,2)$ topology[17] that rarely occurs in monomolecular packings.[5a]

Table 1. Representations of molecular packings in compounds **I-III** at different levels of van der Waals interaction. †

Structure **I**			Structure **II**			Structure **III**		
No. (*i*) of molecule	Ω_{mol} (*i*), %	Topology	No. (*i*) of molecule	Ω_{mol} (*i*), %	Topology	No. (*i*) of molecule	Ω_{mol} (*i*), %	Topology
1, 2	11.4	simple chain	1	23.8	dimer	1, 2	16.4	simple chain
3, 4	10.1	**dia**	2, 3	8.9	**hcb**	3, 4	8.4	$3^6(1,2)$
5, 6	9.3	**sxd**	4, 5	8.8	**sqp**	5, 6	6.5	4^4IIa
7, 8	6.9	**ecu**	6	6.9	**pcu**	7, 8	4.6	8L2
9, 10	4.2	**bct**	7	5.8	**kwh**	9, 10	3.2	10T15
11, 12	3.1	**fcu**	8, 9	5.2	UT	11, 12	2.3	12T11
13, 14	2.8	UT	10, 11	5.0	UT	13, 14	1.9	14T3
15, 16	2.1	UT	12	3.0	12T97			
			13, 14	1.7	UT			
			15, 16	0.6	UT			

† Only sulfonamide molecules are taken into account for **III**. UT designates unknown topology, *i.e.* not contained in the topological databases.

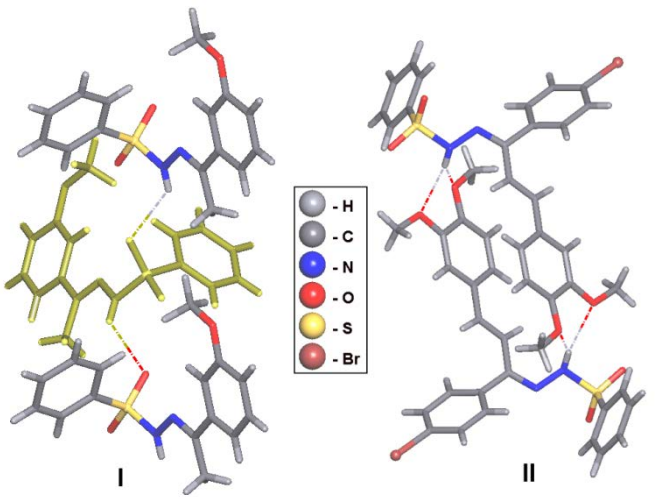


Figure 3. Connection types B^2 (left) and T^{0001} (right) of molecules **I** and **II**.

At the Ω_{mol}[MCN=12] level the representations of structures **I-III** have different topologies: **fcu**, 12T97, and 12T11, respectively. In all three cases, one can separate groups of six molecules surrounding the origin one and forming a hexagon inside the coordination figure. These groups correspond to hexagonal layers that build close packings. However, detailed analysis shows that while the 12T97 underlying net is locally close to the face-centered close packing (**fcu**), the 12T11 underlying net is essentially different. Namely, in the **fcu**-like packings there are three molecules above and below the layer, *i.e.* they are arranged in a 3+3 fashion, while in the 12T11 packing, the six molecules are combined in a 4+2 fashion (Fig. 5). Thus the 12T11 packing belongs to another ancestor packing type that will be discussed below.

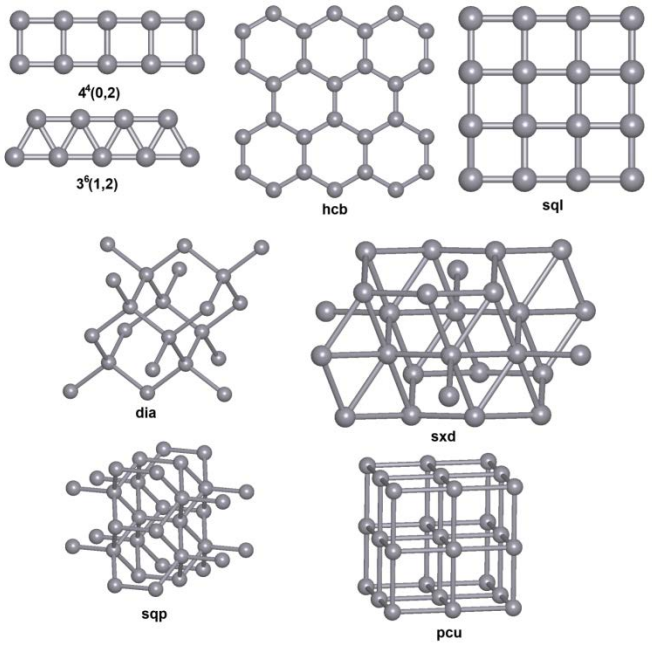


Figure 4. Important topological motifs of molecular packings and specific-bond patterns in sulfonamides.

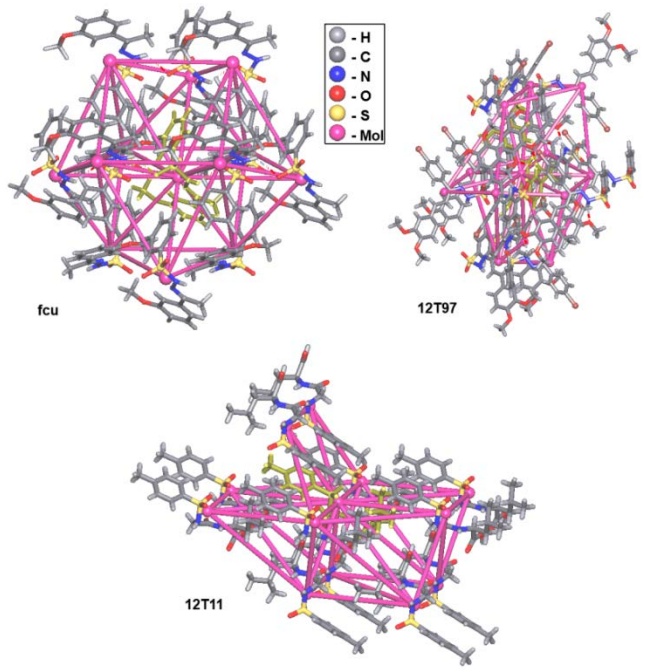


Figure 5. Molecular packings in structures **I** (top left), **II** (top right) and **III** (bottom). The central hexagons of the coordination figures correspond to close-packed hexagonal layers of molecules. The origin molecules are selected in yellow.

Specific-bond patterns in sulfonamides

H-bond patterns. Analysis of H-bond patterns in the 932 sulfonamides containing only hydrogen bonds shows that there occur totally 44 different connection types, among which the most preferable are B^{01} and B^{2}. Other rather frequent connection types (K^{4}, K^{21} and K^{02}) include four active atoms. In most cases, the sulfonamide groups participate in H bonding in accordance with Scheme 1 providing two active atoms; additional active atoms are located in other functional groups of the molecules. The correlation between MCTS and overall topology of the H-bond pattern is rather strong: there are a few possible underlying topologies for each connection type (Table 2). Compounds **I-III** have typical local and overall motifs of H-bond patterns, which are collected in Table 2.

Table 2. Most abundant connection types and the corresponding H-bonded motifs in sulfonamides

MCTS	Occurrence, %	Underlying net	Correlation MCTS-underlying net, %
B^{01}	33.9	dimer	100
B^{2}	30.7	simple chain	100
K^{4}	7.8	**sql** layer	76.0
		3^{6}(1,2) chain	14.7
		dia framework	5.3
		others (2)	4.0
K^{21}	6.3	**hcb** layer	59.6
		4^{4}(0,2) ladder	40.4
K^{02}	4.6	simple chain	100

Totally, the H-bond patterns belong to 41 kinds of underlying nets; the most abundant are dimer and simple chain patterns that correspond to B^{01} and B^{2} connection types. Other important pattern topologies are 2-periodic square lattice (**sql**), honeycomb net (**hcb**) as well as 1-periodic 4^{4}(0,2) and 3^{6}(1,2). The list of existing connection types is also essentially limited for each underlying topology (Table 3). For each H-bond pattern there is one prevailing MCTS of a high correlation level (>74%).

Halogen-bond patterns. Since the sulfonamide group itself cannot provide halogen bonding, such kind of specific bond can exist in the structures under consideration only thanks to halogen-substituted radicals. The number of sulfonamides, in which there are no H bonds while halogen specific bonds exist, is not so large to analyze the correlations between local and overall topologies of the structural motifs; however the general tendencies are similar to those in H-bond patterns. Out of the 16 sulfonamides, in 12 (75.0%) the halogen-bond motif is simple chain (MCTS = B^{2}); in two structures – dimers (MCTS = M^{1}) and in two structures[20] a 2-periodic **sql** pattern occurs. In both two **sql** motifs, a K^{4} connection type is realized that is the most frequent also in the **sql** H-bond patterns (Table 3).

Mixed specific-bond patterns. Our analysis of the structures where hydrogen and halogen bonds coexist reveals that the distributions of local and overall topologies of their patterns taken *separately* are similar to those considered above (see the ESI). This means that different types of specific bonds do not significantly influence each other in sulfonamides. The integral patterns that include both types of intermolecular bonding are hence 'sums' of the one-kind-bond patterns. Indeed, combinations of the most typical motifs of hydrogen and halogen bonds, namely dimers, simple chains and **sql** net, produce the most frequent integral patterns, namely simple chain, **hcb** and **sql** layers, 4^{4}(0,2) ladder and **pcu** (primitive cubic) framework according to the schemes shown in Fig. 6.

Table 3. Most abundant H-bonded motifs and the corresponding connection types in sulfonamides

Underlying net	Occurrence, %	MCTS	Correlation underlying net-MCTS, %
simple chain	39.6	B^{2}	78.7
		K^{02}	12.1
		K^{002}	5.8
		T^{02}	2.6
		others (3)	0.9
dimer	35.9	B^{01}	97.1
		others (4)	2.9
sql layer	7.9	K^{4}	74.7
		G^{22}	18.7
		$\mathbf{P^{22}}$	4.0
		others (2)	2.6
hcb layer	4.3	K^{21}	87.2
		G^{03}	7.7
		T^{21}	5.1
4^{4}(0,2) ladder	2.8	K^{21}	85.2
		P^{03}	7.4
		T^{21}	3.7
		T^{3}	3.7
3^{6}(1,2) ladder	1.3	K^{4}	84.6
		T^{4}	15.4

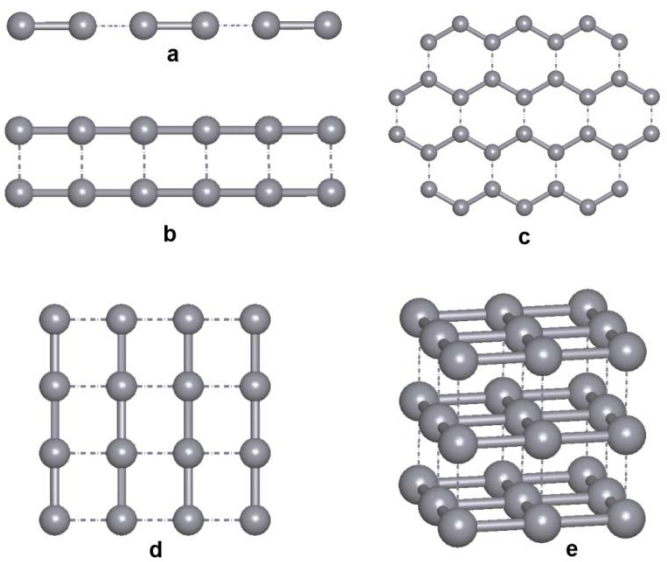


Figure 6. Methods of assembling mixed specific-bond patterns: (a) dimer + dimer + … = simple chain (b) ; two simple chains + dimers = 4^{4}(0,2) ladder; (c) simple chain + dimer + … = **hcb** layer; (d) simple chain + simple chain + … = **sql** layer; (e) **sql** layer + simple chain = **pcu** framework. Hydrogen and halogen bonds are shown by different types of edges (solid and dashed lines); the balls correspond to molecular centers of mass.

Molecular packings in sulfonamides

Comparison of overall topologies of molecular packings in the 1025 + 16 = 1041 sulfonamides containing specific bonds and 422 sulfonamides where the framework is supported only by van der Waals interactions shows that the general features of their distributions are similar. At the Ω_{mol}[MCN=12] level the most frequent are the close packing motifs **fcu** and **hcp** (hexagonal close packing) (Table 4).

Table 4. Most abundant motifs of molecular packings in sulfonamides

1041 structures with specific bonds		422 structures without specific bonds	
Underlying net	Occurrence, %	Underlying net	Occurrence, %
fcu	23.8	**fcu**	25.8
hcp	12.5	**hcp**	11.4
bcu-x-12-*Cmcm*	3.1	**bcu-x**-12-*Cmcm*	3.1
12T11	2.1	12T11	1.7
12T5	1.8	12T5	1.4

Thus the specific bonds do not significantly influence the molecular packings that in more than 1/3 cases obey the Kitaigorodskii's model. It is notable that the close packings are realized in spite of a peculiar 'butterfly' shape of sulfonamide molecules (Fig. 7). This shape, however, in some cases, gives rise to a special packing **bcu-x**-12-*Cmcm*[21] that is topologically less dense than the close packings; it has only 33 molecule-molecule contacts within the coordination figure compared to 36 contacts in close packings. This arrangement can also be called 'butterfly' packing due to peculiar form of the coordination figure (Fig. 7). From geometrical point of view the difference between close and 'butterfly' packings can be conceived as a different arrangement of molecules with respect to the close packed hexagonal layer as was discussed above (Fig. 5). A detailed analysis shows that other packing topologies can be obtained from one of the close packings or the 'butterfly' packing by adding, removing or reorganizing some molecule-molecule contacts. For example, the 12T5 and 12T11 packing types (Table 4; *cf.* Fig. 5) are similar to the 'butterfly' packing, but have the same number (36) of the molecule-molecule contacts in the coordination figure as close packings.

Conclusions

Analysis of molecular packings and various motifs of linked molecules is an important part in understanding the structure and properties of molecular crystals as well as of supramolecular ensembles. The tools described and tested in this paper can help the chemist to formalize and facilitate such analysis. As a result, large samples of crystallographic data can be processed to find new structural correlations. Thus we showed that local and overall topologies of specific-bond motifs in sulfonamides are strongly interrelated, while hydrogen and halogen bonds weakly influence the molecular packings. We revealed that albeit the sulfonamide molecules form a close packing in many cases, one more 'butterfly' packing type is typical for them. Such kinds of correlations can be used to predict main peculiarities of molecular crystals within a prospective expert system.[5]

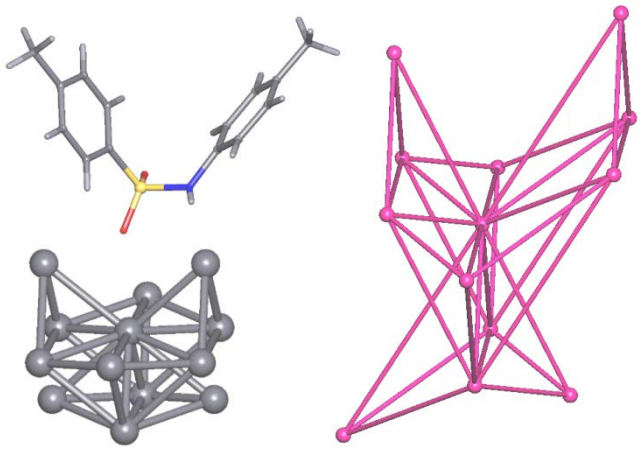


Figure 7. (Top left) 4-Methyl-*N*-(4-methylphenyl)benzenesulfonamide molecule[22] and (right) coordination figure in the underlying net of the corresponding **bcu-x**-12-*Cmcm* molecular packing; (bottom left) coordination figure in the idealized **bcu-x**-12-*Cmcm* net.

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† Electronic Supplementary Information (ESI) available: crystallographic data on compounds **I-III** (CCDC reference numbers 989765-989767); Tables S1-S10 with distributions of connection types and overall topological motifs in molecular packings and specific-bond patterns in the 1463 sulfonamide derivates. See DOI: 10.1039/b000000x/.

1 A. I. Kitaigorodskii, *Molecular Crystals and Molecules*, Academic Press, New York, 1973.
2 (a) E. V. Peresypkina and V. A. Blatov, *Acta Cryst.*, 2000, **B56**, 501; (b) E. V. Peresypkina and V. A. Blatov, *Acta Cryst.*, 2000, **B56**, 1035.
3 F. H. Allen, *Acta Cryst.*, 2002, **B58**, 380.

4 (a) J. Grell, J. Bernstein and G. Tinhofer, *Cryst. Rev*. 2002, **8**, 1; (b) (a) L. Öhrström and K. Larsson, *Molecule-Based Materials: The Structural Network Approach*, Elsevier, Amsterdam, 2005; (c) V. A. Blatov, D. M. Proserpio, Ch. 1 in *Modern Methods of Crystal Structure Prediction*, ed. A. R. Oganov, Wiley-VCH, Weinheim, 2011.
5 (a) F. Aman, A. M. Asiri, W. A. Siddiqui, M. N. Arshad, A. Ashraf, N. S. Zakharov, and V. A. Blatov, *CrystEngComm*, 2014, **16**, 1963; (b) P. N. Zolotarev, M. N. Arshad, A. M. Asiri, Z. M. Al-amshany and V. A. Blatov, *Cryst. Growth Des*., 2014, **14**, 1938.
6 I. A. Baburin and V. A. Blatov, *Acta Cryst*., 2007, **B63**, 791.
7 *CrysAlis PRO*. Agilent Technologies, Yarnton, England, 2012.
8 G. M. Sheldrick, *Acta Cryst*., 2008, **A64**, 112.
9 L.J. Barbour, *J. Supramol. Chem*., 2001, **1**, 189.
10 V. A. Blatov, *Struct. Chem*., 2012, **23**, 955; http://www.topos.samsu.ru.
11 (a) G. Gilli and P. Gilli, *The Nature of the Hydrogen Bond: Outline of a Comprehensive Hydrogen Bond Theory*, Oxford University Press, New York, 2009; (b) A. Gavezzotti, *Top Curr. Chem*. **2012**, *315*, 1.
12 O. Delgado-Friedrichs, M. D. Foster, M. O'Keeffe, D. M. Proserpio, M. M. J. Treacy and O. M. Yaghi, *J. Solid State Chem.*, 2005, **178**, 2533.
13 S. J. Chung, T. Hahn, W. E. Klee, *Acta Cryst*., 1984, **A40**, 42.
14 V. A. Blatov, *Cryst. Rev*., 2004, **10**, 249.
15 (a) T. Steiner, *Angew. Chem. Int. Ed. Engl*. 2002, **41**, 48; (b) P. Metrangolo, H. Neukirch, T. Pilati and G. Resnati, *Acc. Chem. Res*. 2005, **38**, 386.
16 V. N. Serezhkin, A. V. Vologzhanina, L. B. Serezhkina, E. S. Smirnova, E. V. Grachova, P. V. Ostrova and M. Yu. Antipin, *Acta Cryst*., 2009, **B65**, 45.
17 E. Koch and W. Fischer, *Z. Kristallogr*. 1978, **148**, 107.
18 V. A. Blatov, D. M. Proserpio, *Acta Cryst*. 2009, **A65**, 202.
19 M. O'Keeffe, M. A. Peskov, S. J. Ramsden and O. M. Yaghi, *Acc. Chem. Res*., 2008, **41**, 1782; http://rcsr.anu.edu.au/.
20 (a) R. Minkwitz,P. Garzarek, F. Neikes, A. Kornath and H. Preut, *Z. Anorg. Allg. Chem*., 1997, **623**, 333; (b) S. Mukherjee, R. Sivappa, M. Yousufuddin, C. J. Lovely, *Synlett*, 2010, 817.
21 V. A. Blatov, *Acta Cryst*., 2007, **A63**, 329.
22 I. U. Khan, S. Sharif, M. Akkurt, A. Sajjad and J. Ahmad, *Acta Cryst*., 2010, **E66**, o786.

