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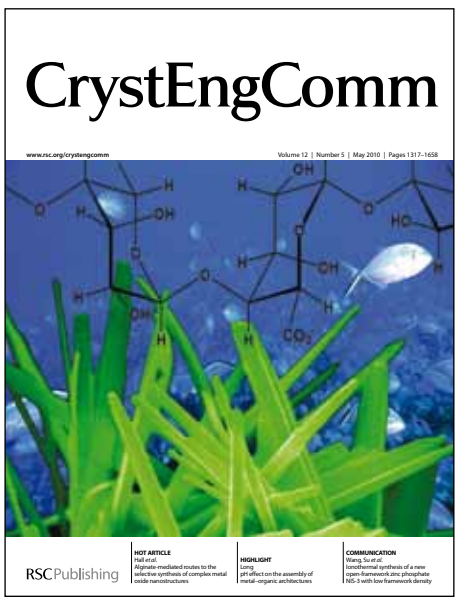

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Multilevel topological description of molecular packings in 1,2-benzothiazines

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A new method for description of molecular networks and packings is proposed and implemented into the program package TOPOS. It is shown that the method is most effective in combination with the multilevel analysis of intermolecular interactions in terms of molecular Voronoi polyhedra. The method was applied to 82 1,2-benzothiazine derivatives, 11 out of which we have synthesized for the first time. As a result, we have determined the main transformation routes of underlying nets, *i.e.* the nets of molecular centroids, at different levels of van der Waals interaction and found the most important topologies that play a key role in these routes. The method can help to create the databases of topological properties of molecular packings (the second-level databases) from the crystallographic databases (the first-level databases); this is an important step to develop predictable expert systems in materials science.

Introduction

Prediction of possible structures that can be formed from a particular set of components is one of the crucial chemical problems. At present, the structures of molecules can be reasonably predicted by quantum-mechanical methods. Moreover, chemists know many rules that govern how atoms connect to each other and in what ratio. At the same time, chemistry has already gone beyond the molecular level and deals with molecular ensembles that are usually related to the field of supramolecular chemistry. While the simulation methods have had a great progress in prediction of molecular packings that was proved by series of blind tests,[1] general supramolecular chemistry rules are not so well-determined yet. Such rules should concern the methods of connecting molecules into an ensemble like valence and hybridization rules essentially predetermine the form and topology of a molecule.

There are a lot of experimental data on supramolecular architectures stored in crystallographic databases, in particular in the Cambridge Structure Database (CSD).[2] Unfortunately, these data are not intensively used to search for general supramolecular rules because of absence of computer tools for description and rationalization of supramolecular ensembles. Moreover, crystallographic databases do not include the comprehensive information on intermolecular interactions. Thus the question is ripe how to develop tools for processing the experimental data and extracting the knowledge about preferred supramolecular motifs.

One of possible ways to cope with this problem is to use topological network approaches. Topological methods are still rather unusual in crystal chemistry; this especially concerns supramolecular and extended architectures, or in general, all chemical objects which cannot be represented as a finite set of atoms connected by valence bonds. Ordinarily, topology is discussed mainly for molecules within graph-theory approaches.[3] However, in the last 20 years the graph-theory (network) description is more and more frequently used beyond molecular objects. Patterns of intermolecular interactions, especially H bonds, were formalized in a number of nomenclatures;[4] which, however, have not been implemented into widespread software. A universal network approach to be applicable to any kind of crystal structure was launched by Wells[5] and essentially developed in the past 15 years;[6] special software (TOPOS[7] and Systre)[8] and databases (RCSR,[9] TTD and TTO)[10] were elaborated. All these approaches establish correlations between local chemical architectures (coordination figures, molecular fragments, polynuclear complex groups) and the overall structural motifs. Several reviews published in the past ten years[11] reported the most typical topological architectures of coordination networks but the occurrence of these motifs could not be predicted. Recently,[12] we have proposed an approach to creating an expert system for prediction of underlying topologies of coordination frameworks. In this paper, we will show that this approach is more universal and can be applied to other types of crystalline solids, or even to nano objects including molecular associates.

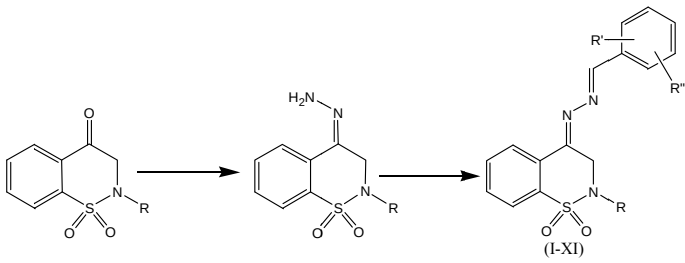
To check the approach, we have synthesized a series of molecular crystals of 1,2-benzothiazine derivatives where the molecules can form different kinds of intermolecular contacts (H bonds, halogen-halogen bonds, van der Waals interactions)

but have similar shape and composition. The choice of the objects was also caused by that in recent years, there has been a rapid growth in number of literature references dealing with 1,2-benzothiazine derivatives due to their importance as analgesic and anti-inflammatory agents belonging to oxicams, a new class of non-steroidal anti-inflammatory drugs (NSAIDs).[13] These drugs are free from steroidal side-effects although they have little effect on the progression of bone and cartilage destruction.[14] Besides great therapeutic potential in asthmatic therapy,[15] these are very motivating polyfunctional heterocyclic molecules by virtue of their dynamic structural features, which include different tautomeric forms and their possible polymorphism.[16] The search for more effective anti-inflammatory agents has led medicinal chemist to explore a wide variety of chemical structures in order to inhibit cartilage destruction associated by using NSAIDs or at least reducing its severity. This led us to the synthesis of new agents using readily available starting material following facile routes to yield enough products.[17]

Experimental

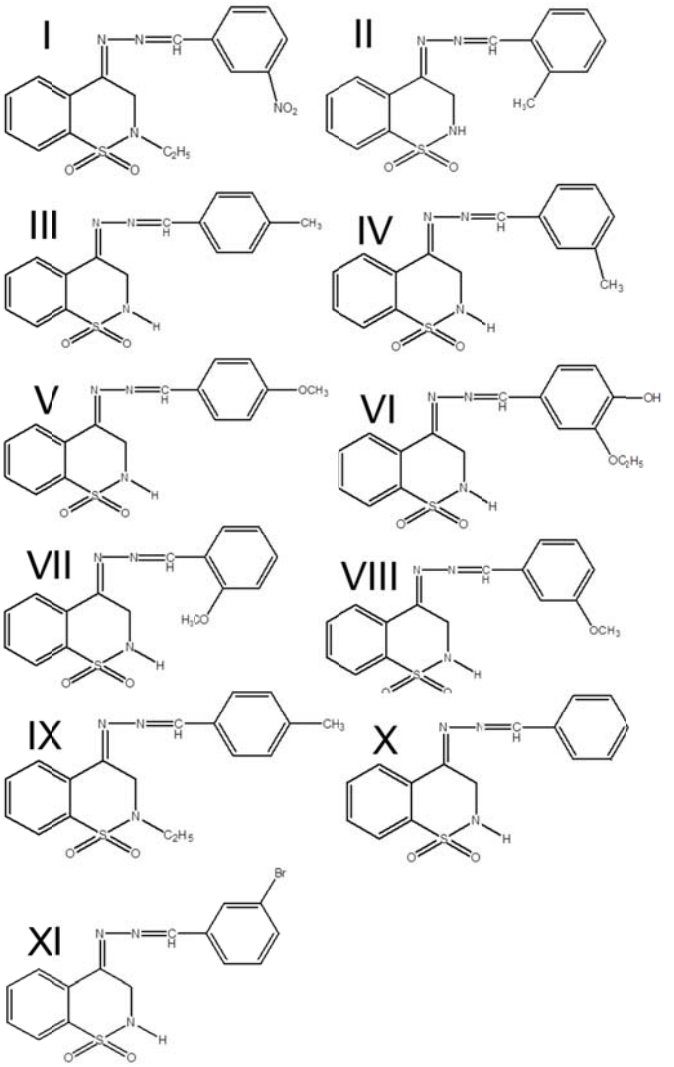
General procedures for the syntheses of 1,2-benzothiazines

According to Scheme 1 we have synthesized eleven 1,2-benzothiazine derivatives (Scheme 2). At the first stage, 1,2-benzothiazine hydrazides were obtained by the following method. The 2*H* derivative of 1,2-benzothiazine 1,1-dioxide[18] was subjected to N-ethylation[19] to get two types of the ketones as starting material. Hydrazine monohydrate (0.61 g, 12.6 mmol) was added to a solution of precursors(N-H/ethyl 2,3-dihydro-4*H*-1,2-benzothiazin-4-one 1,1-dioxide**)** (2.5 mmol) in of ethanol (20 mL) under inert atmosphere. The reaction mixture was allowed to reflux (1-2 h). After completion of the reaction it was concentrated to one third volume under reduced pressure and left overnight at room temperature. The off-white crystalline hydrazinyl derivatives thus obtained were filtered and washed with distilled water (yields: 92% & 95%, respectively).



Scheme 1. Synthesis of 1,2-benzothiazine derivatives

After this, the alcoholic solution of an appropriate aromatic aldehyde (2.36 mmol) was added to a solution of 1,2-benzothiazine hydrazides (2.36 mmol) in the same solvent under inert atmosphere. The reaction mixture was allowed to reflux for 0.5-1 h. The reaction mixture was concentrated under reduced pressure to get the di-imine products (I-XI) in significant yields.



Scheme 2. Molecules of 1,2-benzothiazines synthesized in this study.

X-ray data collection and structure determination

Suitable crystals of compounds were chosen for single crystal diffraction studies and mounted on Agilent SuperNova (Dual source) Agilent Technologies Diffractometer, equipped with a graphite-monochromatic Cu Kα radiation. The data was collected using CrysAlisPro software[20] at 296 K. The structures solution were performed by direct methods using SHELXS–97[21] and refined by full–matrix least–squares methods on F2 using SHELXL–97,[21] in-built with X-Seed.[22] All non–hydrogen atoms were refined anisotropically by full–matrix least squares methods.[21] All the C-H hydrogen atoms were positioned geometrically and treated as riding atoms with C–H distances of 0.93 Å for aromatic, 0.96 Å for methyl and 0.98 Å for methylene H atoms. These were refined using a riding model with $U_{iso}(H) = 1.5\ U_{eq}(C)$ for methyl and $U_{iso}(H) = 1.2\ U_{eq}(C)$ for all other carbon atoms. The N-H hydrogen atoms were

located with difference Fourier maps and refined using riding models.

Analysis of the Cambridge Structural Database

To make a comprehensive overview of molecular crystals containing 1,2-benzothiazine derivatives we have screened the CSD (release 5.34, October 2012) and found 71 monomolecular structures (see the ESI), *i.e.* consisting of only one kind of 1,2-benzothiazine molecule, although, they could contain several symmetry non-equivalent molecules of the same kind. We did not consider the structures where benzothiazine molecules cocrystallize with other molecules.

Voronoi approach to description of intermolecular interactions

To determine intermolecular interactions from the crystallographic data we have used the method of molecular Voronoi polyhedra.[23] An intermolecular contact considered if Voronoi polyhedra of the corresponding atoms had a common face. The strength of the bonding was estimated by the value of the solid angle (Ω) of the face expressed in percentage of the total solid angle of 4π steradian. This criterion was shown to be more universal than other geometrical criteria of bond strength, including bond valences, and especially useful to study non-valence interactions (see the review[24] and references therein). The contacts with Ω≤1.5% were ignored as they correspond to a typical experimental error of the Ω values. To distinguish H bonds and specific bonds with participation of halogen atoms we have applied additional geometrical criteria.[25] Namely, the contact H…B in a fragment A-H…B (A, B=N, O) was considered as an H bond if all the following criteria were hold: d(H…B) ≤ 2.5 Å; d(A…B) ≤ 3.5 Å; ∠A-H…B ≥ 120°. The contact Hal…B in a fragment A-Hal…Hal (Hal=Cl, Br, I; A=C, N, O, F, S, Cl, Se, Br, I) was referred to as a specific bond if ∠A-Hal…Hal ≥ 160°. Below we apply the term "van der Waals interactions" to all intermolecular interactions that are not H bonds or specific bonds according to the criteria mentioned above, but obey the Ω≤1.5% criterion.

Graph-theory approach to description of intermolecular interactions

In the graph-theory approach, an extended atomic structure is described as an infinite graph (network), whose vertices and edges correspond to atoms and interatomic bonds, respectively. This representation keeps only the information about structure connectivity, and ignores geometrical properties like interatomic distances, bond angles, etc. As a result, rather far relations can be found between the extended architectures that differ by chemical composition and geometrical form. If a chemical compound contains complex groups like molecules, clusters, synthons, polynuclear complex groups, etc. , these groups are squeezed to their centers of gravity to give a so-called *underlying net*, *i.e.* the net that shows the method of connecting the complex groups (structural units). The set of structures that have the same underlying net topology irrespective of the internal structure of the complex groups are considered belonging to the same *isoreticular series*. The reference topologies of underlying nets are gathered in the RCSR database[9] and TOPOS TTD collection;[10] these sources are used to classify chemical structures into isoreticular series. Several nomenclatures designate the reference topologies; here we use two of them: the three-letter RCSR symbols[9] and TOPOS *N*D*k*-*n* symbols.[11c] *N*D*k*-*n* symbol is used in two forms: for periodic nets the short form *N*D*n* is applied, where *N* is a sequence of degrees (coordination numbers) of all independent nodes of the underlying net; D is one of the letters C, L, or T designating the dimensionality of the net (C – chain, L – layer, T – three-periodic framework); *n* enumerates non-isomorphic nets with a given N*D* sequence. For finite (molecular) graphs the symbol *N*M*k*-*n* is applied, where *k* is the number of nodes (atoms) in the graph.

An important question, why some isoreticular series are very long while others contain the only representative, leads us to search for possible causes that invoke a particular underlying net topology. One of the obvious causes is the local topology that describes the method of connecting every structural unit with surrounding structural units;, the primitive element of the local topology in an underlying net is *coordination figure*. Thus the relation "coordination figure - underlying net" is an important point in prediction of extended architectures.

Recently,[12] we have proposed an approach that uses correlations between chemical composition, local and overall topology of coordination compounds to develop an expert system for prediction of periodic motifs in coordination polymers. Below we extend this approach to supramolecular architectures and molecular crystals.

To describe the topology of supramolecular complexes we use the concept of molecular connection type that is formalized with *molecular connection type symbol* (MCTS). MCTS generalizes the symbol of ligand coordination type[26] that we used recently[12] to specify the method of connection of ligands with metal atoms in coordination polymers. Like the ligand symbol, MCTS has the general view $L^{mbtkpghond\ldots}$, where *L* is a capital letter that designates the number of atoms (*n*) in the molecule that participate in the intermolecular contacts under consideration. This letter is M, B, T, K, P, G, H, O, N, D for *n*=1-10 or X[*n*] for *n*>10. The line of integers *mbtkpghond*… contains the numbers of other molecules, to which a given molecule is connected by one (*m*), two (*b*), three (*t*), etc. intermolecular contacts; the terminal zero numbers are not shown in the line. MCTS essentially predetermines coordination figure of the molecule; the sum *m*+*b*+*t*+*k*+*p*+*g*+*h*+*o*+*n*+*d*+… is equal to molecular coordination number, *i.e.* the number of molecules connected to the given one. Let us first consider some simple examples.

In compound **III**, each molecule forms two H bonds N-H…N with participation of one N and one H atom (Fig. 1a), so *L*=B (two atoms participate in the intermolecular contacts under consideration), and each of the two bonds connects the molecule with a different molecule, so *m*=2 (two molecules are connected to the given one by one bond each) and all other numbers *btkpghond*… are equal to zero. Hence MCTS looks

like B^2 and designates a bridge type of the molecule coordination.

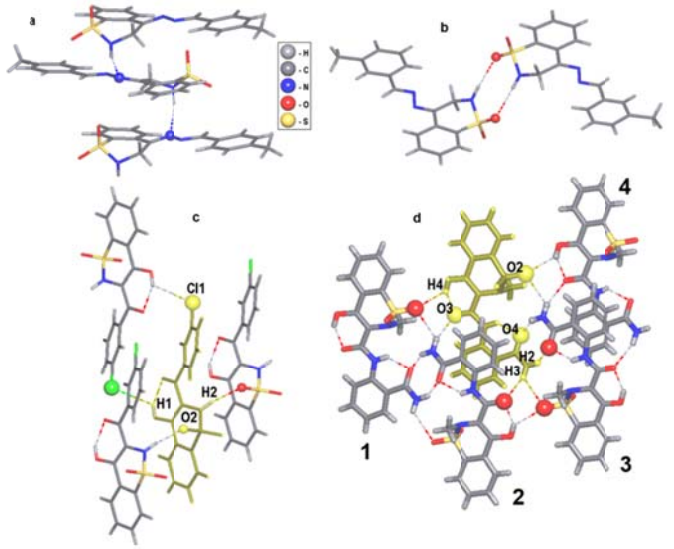


Figure 1. Coordination types of H-bonded molecules in (a) compound **III** (B^2); (b) compound **IV** (B^{01}); (c) (3-chlorophenyl)(4-hydroxy-1,1-dioxido-2H-1,2-benzothiazin-3-yl)methanone (KUTNIX) (K^{21}); (d) N-(2-carbamoylphenyl)-4-hydroxy-2-methyl-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide (BUFJES) (G^{2101}). In all cases, the atoms participating in intermolecular bonds are shown as balls. For KUTNIX and BUFJES, the molecules, for which MCTS is determined, are highlighted in yellow.

The molecules in compound **IV** also form two H bonds each but both bonds connect the same molecule (Fig. 1b). This means that m=0 (there are no molecules connected the given one by one H bond), while b=1 (one molecule is connected by two H bonds); MCTS = B^{01}.

H bonded molecules in other compounds obtained in this work have one of these two MCTS, which are most typical for 1,2-benzothiazines. However, the complete list of 1,2-benzothiazines taken from the CSD contains few examples of other coordination types. In particular, (3-chlorophenyl)(4-hydroxy-1,1-dioxido-2H-1,2-benzothiazin-3-yl)methanone (KUTNIX)[27§] is coordinated with the K^{21} type: each molecule is connected to three other molecules (m+b=2+1=3); two of them are connected with one H bond each, while the third one is connected with two H bonds (Fig. 1c). The most complex coordination type occurs for N-(2-carbamoylphenyl)-4-hydroxy-2-methyl-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide (BUFJES).[28] In this molecule, there are six atoms participating in intermolecular H bonds (there are intramolecular H bonds as well but they are not included into MCTS), hence L=G (Fig. 1d). With atoms H4 and O2 the molecule is connected to two other molecules (1 and 4); m=2. Atoms H3 and O3 participate in two H bonds with molecule 2, *i.e.* b=1. At last, molecule 3 is connected by four H bonds with participation of H2, H3, O2, and O4 atoms that gives rise to k=1. As a result, MCTS is G^{2101} and molecular coordination number is 2+1+0+1=4.

MCTS allow one to recognize different kinds of connection of the same molecule or to find different molecules with the same connection type. If there are molecules with different connection types like in cocrystals, in crystals containing solvate molecules, or in monomolecular packings with several different molecules MCTS are united into *molecular crystal formula* according to the stoichiometric ratio. Thus in our sample there are only two examples with two symmetry non-equivalent H-bonded molecules of the same composition and structure. In the packing of N-(2-chlorophenyl)-4-hydroxy-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide (HUDLUO),[29] molecules i and ii have MCTS $\mathbf{T}^{21}$ and B^2, respectively, thanks to intermolecular H bonds i-1 (H1 and O4 atoms), i-2 (O4 atom), i-ii (H3-O8 atoms), and ii-3 (H5 atom) (Fig. 2). The ratio of molecules i and ii is 1:1, hence molecular crystal formula looks like B^2T^{21}. In compound **X**, both molecules have the same coordination type (B^2) so molecular crystal formula has the same view (B^2).

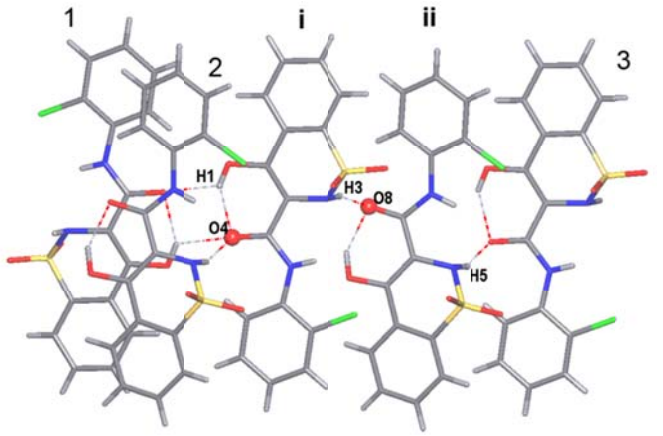


Figure 2. Coordination types of H-bonded molecules in N-(2-chlorophenyl)-4-hydroxy-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide (HUDLUO).

The correlations between coordination figure and overall topology have been intensively discussed for coordination polymers,[11b,c] but not for molecular crystals. Moreover, MCTS contains more detailed information on the local topological properties of molecular packings and can be easily stored in the crystallographic databases to be used for an automated analysis of molecular crystals. To illustrate this point, we have implemented the MCTS concept into the TOPOS program package and applied it for the study of the 1,2-benzothiazine derivatives.

Multilevel description of intermolecular contacts

One of important problems of the topological analysis of molecular crystals concerns different strengths of intermolecular interactions. Taking into account weaker or stronger van der Waals interactions, specific (e.g. halogen-halogen) or H bonds, one can obtain different underlying nets for the same molecular crystal. It is meaningless to say that one or another underlying net is "better" than others – each net describes the topology of the crystal at some level of interactions. This approach allows us to find relations between different structures. In this study, we use molecular solid

angles[23a] to estimate intermolecular interactions. Molecular solid angle (Ω_{mol}) is determined as a normalized sum of solid angles (Ω_i) of Voronoi polyhedra faces corresponding to all intermolecular contacts; it characterizes the total common surface of interacting molecules. We applied the TOPOS procedure of generation representations[30] to the set of Ω_{mol} and obtained a number of underlying nets for each molecular packing. Thus in compound **IX** there can be chosen seven levels of intermolecular interactions according to Ω_{mol} values for van der Waals contacts (Table 1). We skip the contacts 13-16 with Ω_{mol}<1% and unite the weakest contacts 9-12 to the same group. Note that the Ω_{mol} values do not strictly correlate with the distances between molecular centroids since the form of the benzothiazine derivatives is essentially anisotropic.

Table 1. Different levels of van der Waals interactions in compound **IX**. The distances are computed between centroids of the origin molecule and a given molecule

No. of molecule	Distance, Å	Ω_{mol}, %	Topology
1	5.480	17.6	1M2-1 (dimer)
2	4.920	16.5	2C1 (chain)
3	6.632	13.5	**hcb** (layer)
4	7.058	8.0	**sql** (layer)
5, 6	8.350	6.1	**hxl** (layer)
7, 8	12.891	5.8	**hex** (framework)
9, 10	14.589	4.4	
11, 12	15.589	4.2	**fcu** (framework)
13, 14 (skipped)	8.461	0.9	
15, 16 (skipped)	14.701	0.7	

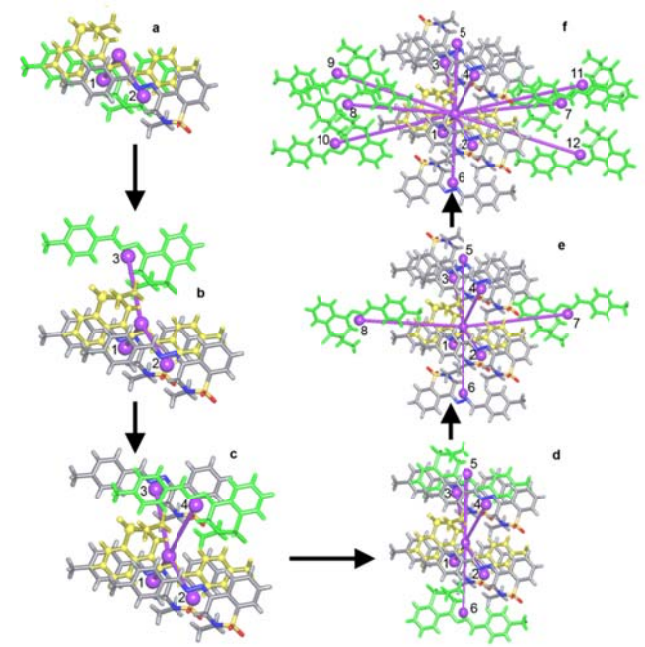


Figure 3. Transformation route for the underlying topologies in the crystal structure of compound **IX**: (a) 2C1 chain; (b) **hcb** layer; (c) **sql** layer; (d) **hxl** layer; (e) **hex** framework; (f) **fcu** framework. The numbering of molecular centroids (violet balls) in coordination figures corresponds to Table 1. The origin molecule is in yellow; the molecules connected at different levels of interaction are in green.

Table 1 and Fig. 3 show the way of assembling molecules into a 3D packing: the strongest contacts to molecules 1 and 2 lead to dimer and chain ensembles, the third contact to molecule 3 gives rise to a honeycomb (**hcb**) layer. As will be shown below, almost all compounds under consideration follow this topological scheme. Next steps are also quite typical: the layered structure is kept after molecules 4-6 are involved in the interaction; a square lattice (**sql**) and a hexagonal close-packed layer (**hxl**) are formed. Weaker contacts (7-12) yield a 3D framework with a primitive hexagonal packing (**hex**) and finally with face-centered cubic close packing topology (**fcu**). Note that the coordination figures of the nodes in the underlying nets are geometrically similar to those for the idealized nets that are collected in the ESI.

Results and Discussion

Analysis of intermolecular contacts shows that compounds **III**, **IV**, **V**, **VI**, **X**, **XI** contain hydrogen bonds while in other structures the molecules are linked only by van der Waals interactions. No specific halogen-halogen bonding was found in the single halogen-containing compound **XI**. Structure **X** contains two symmetry non-equivalent sorts of molecules with similar coordination by H bonds but different patterns of van der Waals contacts (Table 2). So we have studied all the structures at two levels, considering all types of intermolecular contacts or taking into account only H bonds.

Analysis of H bonds is the most typical for crystallochemical description of molecular crystals. At this level, MCTS has the simplest view because of relatively small number of such intermolecular bonds. In our case, compounds **IV**, **VI** have MCTS B^{01} while compounds **III**, **V**, **X**, **XI** have MCTS B^2 that characterizes two possible H bond patterns: consisting of dimers or chains, respectively. Emphasize that while B^{01} type of coordination predetermines dimers, B^2 can lead to finite ring associates, nonetheless such topologies do not occur in the benzothiazine packings.

Table 2. Transformation routes for the underlying net topologies of compounds **I**-**XI** at different levels of van der Waals interaction

Compound	Transformation route†
I	2C1 → **hcb** → **hxl** → **tcg-x**
II	2C1 → **hcb** → **sql** → **bcu-x**
III	2C1 → **dia** → **pcu** → **tcg-x**
IV	1M2-1 → SP1 → **sql** → **bnn** → **sxd** → **ecu** → UT
V	2C1 → **sql** → **bnn** → **cco** → **hcp**
VI	2C1 → **hcb** → **dia** → UT
VII	2C1 → **sql** → **sxd** → **ecu** → UT
VIII	2C1 → **hcb** → **sql** → UT
IX	2C1 → **hcb** → **sql** → **hxl** → **hex** → **fcu**
X	2C1 → **hcb** → UT 1M2-**1** → 2C1 → **sql** → UT
XI	2C1 → **sql** → **sxd** → **bct** → **bcu-x**

† UT – underlying net with unknown topology, *i.e.* the topology that is not described in RCSR or the TOPOS TTD collection.

Van der Waals bonding is more diverse both in the number of interactions between 1,2-benzothiazine molecules and in the

bond strength. It is the case to apply the multilevel analysis. Such analysis shows that the number of possible topologies of molecular packings at various levels of bonding is essentially limited (Table 2, Fig. 4; the pictures of all the nets are given in the ESI).

The following correlations can be revealed from the multilevel analysis:

(i) In most cases, the strongest contacts give dimers (1M2-1) or simple chain (2C1) as was found for H bonds. No ring structures are found.

(ii) The whole packing motif, when all contacts are taken into account, corresponds to 12-coordinated face-centered cubic (**fcu**), hexagonal close packing (**hcp**) or 14-coordinated body-centered cubic (**bcu-x**) or **tcg-x** nets. However, the topology of the whole packing is not as characteristic as for the strongest contacts: in many cases, the overall topology is not contained in the electronic databases like RCSR or TOPOS TTD collection (Table 2). This is due to strong difference between stronger and weaker van der Waals contacts in the packing of 1,2-benzothiazines: the weaker are the contacts the less characteristic is the corresponding topology (*cf.* Tables 1 and 3).

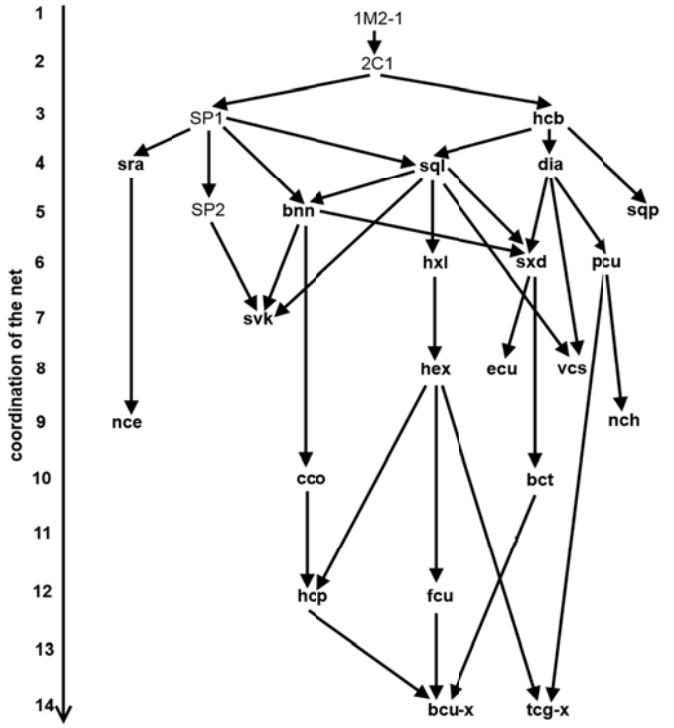


Figure 4. The scheme of transformations of the underlying net topologies of 1,2-benzothiazines at different levels of chemical interaction. Increase of the net connectivity from top to bottom corresponds to decrease of the strength of van der Waals interaction between molecules.

(iii) There are two main methods of assembling dimers or chains into a 3D packing. The most typical one follows the plane motif up to 4-coordinated square plane net (**sql**) or 6-coordinated hexagonal close packed net (**hxl**). The second route passes through 4-coordinated diamondoid (**dia**) and 6-coordinated primitive cubic (**pcu**) nets; here 3D motif appears immediately. The intermediate net in both routes is honeycomb (**hcb**); it is the most common for the 3-coordinated motifs. One of the ways (1M2-1 → 2C1 → **hcb** → **sql** → **hxl** → **hex** → **fcu**) was considered above in Table 1 and Fig. 3. The second (rarer) route can be seen in compound **III** (Table 3, Fig. 5). Simple chains 2C1, where the molecules are connected both by strongest van der Waals interactions (1, 2) and by H bonds, are organized into a **dia** 3D framework by van der Waals interactions of the second level (3, 4). Two additional molecules (5, 6) involved into the interactions of the third level transform the diamondoid framework into a primitive cubic lattice (**pcu**). Further addition of eight rather weak contacts results in the **tcg-x** framework. There is one more rare route passing through 3-coordinated 1D sphere packing (SP1; $4^4(0,2)$ according to the nomenclature of Koch and Fischer).[31] However this route not always leads to new topologies like 2D sphere packing (SP2; 4^4Ib);[32] it can also follow a typical way through the **sql** net as occurs in compound **IV** (Table 2).

Table 3. Different levels of van der Waals interactions in compound **III**. The distances are computed between centroids of the origin molecule and a given molecule

No. of molecule	Distance, Å	Ω_{mol}, %	Topology
1, 2	5.580	16.7	2C1 (chain)
3, 4	7.669	10.3	**dia** (framework)
5, 6	12.514	6.6	**pcu** (framework)
7, 8	13.970	4.6	
9, 10	10.675	4.4	
11, 12	16.181	4.3	
13, 14	10.666	2.7	**tcg-x** (framework)
15, 16 (skipped)	11.466	0.3	

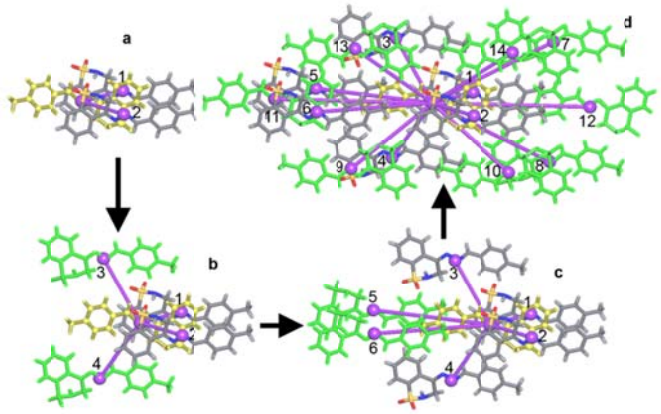


Figure 5. Transformation route for the underlying topologies in the crystal structure of compound **III**: (a) chains 2C1; (b) **dia** framework; (c) **pcu** framework; (d) **tcg-x** framework. The numbering of molecular centroids (violet balls) in coordination figures corresponds to Table 3. The origin molecule is in yellow; the molecules connected at different levels of interaction are in green.

(iv) There are important topologies that can produce many high-coordinated underlying nets after forming additional van der Waals contacts and/or are the result of transformation of many low-coordinated underlying nets. Such important topologies are junction points in Fig. 4; taking into account the

importance of the corresponding routes (see the previous item (iii)) the following nets should be mentioned: 3-coordinated **hcb**; 4-coordinated **sql** and **dia**; 5-coordinated **bnn**; 6-coordinated **sxd**; 7-coordinated **svk**; 8-coordinated **hex**; 14-coordinated **bcu-x**. Most of them were noticed as important for other classes of chemical compounds.[11,25a]

(v) Molecular connection types are not as characteristic for van der Waals bonding as for H bonded patterns; more characteristic is coordination figure or molecular coordination number. For example at rather high level of strength of van der Waals contacts that corresponds to Ω_i>10%, molecules in compounds **I**, **III**, **VIII**, **IX**, and **X** have molecular coordination number 12, but their MCTSs are different: X[16]^{2631}, X[12]^{66}, X[16]^{470001}, X[17]$^{0(11)01}$, and X[14]^{4503}, respectively.

The results obtained show that molecules of a particular kind prefer to be organized in particular topological packing motifs. For example, the honeycomb motif is well known in crystal chemistry and the most abundant in 2-periodic 3-coordinated underlying nets,[12] but there are also frequent 3-periodic motifs **srs** and **ths**.[11] Why do these motifs not occur in 1,2-benzothiazines? Apparently, one of the reasons is that the 1,2-benzothiazine molecules are planar and can form the largest number of intermolecular contacts being in a coplanar orientation that promote a 2-periodic motif. This feature also provides some other motifs based on close-packed layers, like **hxl**, **hex**, **fcu**, or **hcp**.

Conclusions

The method of multilevel topological description of molecular packings proposed in this paper can be applied to molecules of any chemical composition and nature, organic, metal-organic or inorganic, connected by intermolecular interactions of any kind. Importantly, this approach can essentially facilitate formalization of the motifs of interconnecting molecules and storing this information in an electronic form. This information can then be used to find relations between the organization of a molecular packing and supramolecular ensembles at different levels of chemical interaction as well as between different molecular packings or ensembles. Among the theoretical methods of materials science, such approach could complement the quantitative methods of mathematical modeling, like quantum-mechanical methods, since it allows one to solve a number of tasks that require analysis of large samples of data, namely:

- to find typical coordination types of a molecule in packings;
- to analyze the relations between the local coordination of a molecule and the packing motif as a whole;
- to understand what peculiarities of the molecular composition and structure influence the local and overall topological motifs of the packings.

In general, the method proposed will help to create the databases of topological properties of molecular packings (the second-level databases) from the crystallographic databases (the first-level databases); this is an important step to develop predictable expert systems in materials science.[12]

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Notes and references

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† Electronic Supplementary Information (ESI) available: crystallographic data on compounds **I-XI** (CCDC reference numbers 968345-968355); list of Reference Codes of 71 crystal structures taken from the CSD; pictures of all underlying nets mentioned in the text. See DOI: 10.1039/b000000x/

§ Hereafter the CSD Reference Codes are given in parentheses.

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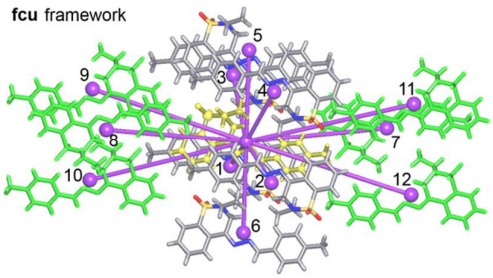

A new method for description of molecular networks and packings is proposed and implemented into the program package TOPOS.