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Analysis of supramolecular architectures: beyond molecular packing diagrams

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Current trends in crystal engineering are critically discussed based on experimental charge density analysis for quantifying various interatomic interactions, from weak van der Waals to coordinate bonds, as applied to the design of crystalline materials.

Since the pioneering works of Kitaigorodskii,[1] the molecular structural chemistry has developed some ideas on how to interpret and thus to predict a crystal packing pattern. The studies of Schmidt have shown that one can successfully use crystal packing peculiarities to control photochemical reactions in a solid state.[2] The latter works are generally considered the ‘starting point’ of a new branch of structural chemistry – crystal engineering. According to the most rigorous definition by Desiraju, the crystal engineering is ‘the understanding of intermolecular interactions in the context of crystal packing and in the utilization of such understanding in the design of new solids with desired physical and chemical properties’.[3] Thus, the success of crystal engineering is directly related to our knowledge of various intermolecular interactions, their nature, energy, mutual influence, *etc*.

Despite some progress in this branch of physical chemistry and emerging of special journals (Crystal Growth and Design, Crystal Engineering Communications), the prediction of crystal structures and the control over molecular self-assembly in solids is not so encouraging as it should be for the successful ‘crystal synthesis’. As it was ironically noted in a review,[4] the greatest achievement in crystal engineering of these 40 years can be formulated as ‘viewing crystal structures as networks’, and the exponential growth of the works in this field is not due to the real understanding of molecular self-assembly upon the crystal formation but mostly a result of the technical progress – the appearance of excellent program suits (such as Platon[5] and Mercury[6]) that facilitate the crystal packing analysis and, in particular, its graphical representation. As a consequence, each crystallographer and/or synthetic chemist can just in seconds fetch out numerous intermolecular contacts and see wonderful 1D, 2D or 3D periodic arrangements of molecules; this makes them feel involved in the self-assembly in crystals and adds one more work on ‘crystal pseudoengineering’.

Among various concepts that have been successfully used in the crystal engineering is the concept of supramolecular synthon proposed by Desiraju.[7] The significance of this idea can be illustrated in part by the fact that up to date one of the first works introducing it was cited more than 2300 times, according to the Web of Knowledge. Among various supramolecular synthons, the most handy are those in which functional groups are assembled by hydrogen bonds, while in the case of all other specific interactions the behavior of a system upon crystal formation is very hard to control and thus to predict, as one may expect. Furthermore, even after the successful supramolecular synthesis of a particular 1D or 2D associate, the final crystal structure can be too far from the expected one. As the non-limiting examples, we can suggest the supramolecular control of spontaneous resolution.[8] The idea that the choice of specific functional groups able to trigger the formation of some definite homochiral supramolecular aggregate (such as helix, for instance) does make it possible to obtain a homochiral self-assembled structure, but unfortunately the whole crystal crystallizes in a racemic space group since the above assemblies are interlinked by weak C–H···O and H···H interactions and the like, which cannot be predicted or controlled to the same extent as the strong H-bonds are.[9] Note that, if the crystal design is tailored to a certain practical task, the requirements on the space group of crystalline materials (such as chiral or polar) become the real necessity. The examples are materials for non-linear optics and terahertz technologies.[10]

As a consequence, if a synthetic crystallographer needs to obtain a specific crystal packing for the whole crystal and does not deal with metal-organic frameworks, to make this ‘synthesis’ successful is the same as to take the jack pot in Las Vegas. Of course, there are some extremely good classes of compounds for crystal design, *i.e.*, rigid molecules with several functional groups capable of participating in a small number of highly predictive supramolecular synthones,[8(*c*)] but the whole situation for the 3D control of organic crystals with various functional groups (and thus competitive interactions and cooperative effects)

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or with a big portion of aliphatic groups (and thus a significant portion of weak van der Waals interactions) is still a serious problem, and any receipt to accomplish this is like a receipt of Smoke Bellew to win in roulette in the well-known Jack London's story.[11]

Clearly, to predict and to obtain a particular crystal structure, one needs to have a correct method to perform the retrospective analysis of a crystal packing, *i.e.*, to find not only strong but also moderate and, that is the most important, weak intermolecular interactions. It is also helpful to estimate the input of the above interactions into the crystal formation. Unfortunately, in most cases, scientists still use only geometrical criteria, such as van der Waals radii (VDWRs).[12] This approach has clear drawbacks: (i) any set of VDWRs is just some arbitrary values with no physical meaning; (ii) almost all VDWRs are isotropic, which is not true for most atoms; (iii) VDWRs should be used with great caution for the search of weak interactions; (iv) VDWRs can hardly be used for a comparison of various types of interactions. Sure enough, there are different approaches that can, to some extent, overcome the problems described for VDWRs, such as Hirshfeld surfaces,[13] PIXEL integration method,[14] Voronoi–Dirichlet polyhedral,[15] just to name a few, but in these cases there are no clear definition of a bonding interaction and/or they cannot be used for the direct estimation of an interaction energy.

The important alternative to the purely geometric approach is the R. F. W. Bader's 'Atoms in molecules' theory (QTAIM).[16] As the QTAIM approach requires only the electron density distribution function $\rho(r)$ for topological analysis, it can be applied to both experimental X-ray diffraction data and quantum chemical investigations.[17] This theory of atoms in molecules has provided us with a definition of an atom as a region in a real space bounded by a zero-flux surface, for which all the properties computable for a molecule and defined locally can be calculated.[16] Among these properties are electron populations (and thus atomic charges), electron energy, various electric moments, *etc*.[16,18] Note that in the case of energy densities – potential [$v(r)$], kinetic [$g(r)$] and electron energy [$h_e(r)$] densities – the corresponding values can be obtained from the experimental data only through a some sort of approximation since for their direct estimation one needs a wave function, which cannot be reconstructed with a sufficient accuracy from high-resolution X-ray data. To estimate the energy density, it was proposed[19] to use the Kirzhnits approximation[20] for the kinetic energy density function $g(r)$. Accordingly, the $g(r)$ function is described as $(3/10)(3\pi^2)^{2/3}[\rho(r)]^{5/3} + (1/72)|\nabla\rho(r)|^2/\rho(r) + (1/6)\nabla^2\rho(r)$, in conjunction with the local virial theorem $[2g(r) + v(r) = (1/4)\nabla^2\rho(r)]$ leading to the expression for $v(r)$ and allowing one to estimate the electron energy density $h_e(r)$.[16] Note that this approximation for $g(r)$ not only gives an opportunity to define correctly the type of an interatomic interaction[†] but makes it possible to obtain the electron localization function (ELF)[21] and the localized-orbital locator[22] directly from experimental X-ray diffraction data.

Within the QTAIM theory, any bonding interaction is manifested in $\rho(r)$ as a (3, –1) critical point [bond critical point (BCP)] and a gradient path (the so-called bond path) linking two interacting atoms. The values of $\rho(r)$, $-\nabla^2\rho(r)$, $h_e(r)$ and other properties at this BCP produce information on the nature of the test interaction.[16,18,†] Among the clear benefits of this criteria for a chemical bond is its unique dichotomic nature. In contrast to any localization procedure and a consequent analysis of orbital occupancies or values of some diagonal elements in corresponding matrixes, such a definition does not contain the words 'more' or 'not less than' some arbitrary value. As a consequence, it can be equally used for classical chemical bonds (*e.g.*, C–C) and weak interactions such as H···H. In most cases, the molecular graph obtained according to QTAIM and one formally proposed basing on a 'chemical intuition' or the textbooks coincide.

At the same time, there are some examples when the 'chemical intuition' and the qualitative chemical concepts give opposite results; these are extensively discussed in the literature and are the main critics of QTAIM. Surprisingly, in some works one can find mutually annihilating claims to QTAIM definition of a chemical bond: (group A) any shortened contact (even forced in nature) corresponds to an attractive interaction, such as intramolecular H···H interactions in biphenyl,[23] a He···C in inclusion complex of helium in adamantane;[24] or (group B) 'unambiguous' (according to the general chemical concepts) bonds, such as metal–metal in the clusters of 3*d* metals and metal···C in various π-complexes,[26] do not correspond to the bonding interaction within the QTAIM theory. As a rule, these two groups of works ignore the 'results' of their opponents. Any counterarguments that can be easily found in the literature – the absence of BCP for shortened C···C transannular interactions in [2.2]paracyclophane (for group A)[27] and the presence of BCP for Pd···Pd intramolecular contacts in carboxylate complexes with four bridging ligands (for group B)[28] – are not taken into consideration. The general problem of this critics is the fact that there is no other clear definition of a chemical bond that can be used to give an unambiguous answer to the above questions whether or not these bonds exist. Thus, the careful analysis of the above works and others devoted to the correctness of QTAIM definition of chemical bonding in a particular system is mainly based on the 'poorly parameterized chemical intuition'.

Here, we will not discuss the results obtained by the authors who tried to analyze the physical meaning of BCP from the first principles and its significance for theoretical chemistry (see, *e.g.*, ref. 29); but accepting it for a fact, we will show what the QTAIM analysis can give to a crystallographer (or any other researcher) for the qualitative and, more importantly, quantitative analysis of supramolecular organization in a crystal. Jumping ahead, we would also like to mention that the excellent agreement between the QTAIM estimates and the quantum chemical calculations and/or thermochemical data can serve as an independent proof of the correctness and significance of inter- and intramolecular interactions fetched out by means of the topological analysis of $\rho(r)$.

For a long time, most of the works involving the QTAIM analysis were mainly devoted to the analysis of the presence of inter- and intramolecular interactions and to the elucidation of their nature.[17,30] Their results are still of great importance for theoretical chemistry; for instance, the QTAIM approach was successfully used to investigate the chemical bonding pattern in atranes and various hypercoordinated silicon compounds,[30(e),31] phosphine oxides,[32] metal carbonyl complexes and various π-complexes,[30(c),33] to analyze the delocalization of charge in carboranes,[34] the nature of stereoelectronic effects,[35] *etc*.

Although such works have shed light on some aspects of chemical bonding and reactivity and thus helped to resolve many problems of theoretical chemistry, in particular, related to organo-

[†] According to the AIM theory, interatomic interactions fall into 'shared' and 'closed-shell' types (R. F. W. Bader and H. Essen, *J. Chem. Phys.*, 1984, **80**, 1943). Shared interactions are characterized by negative $\nabla^2\rho(r)$ values and high $\rho(r)$ values in BCP, while for closed-shell interactions (ionic bonds, some van der Waals complexes, *etc.*), the value of $\nabla^2\rho(r)$ is positive and that of $\rho(r)$ is small. However, a positive $\nabla^2\rho(r)$ value is not a unique criterion for a closed-shell interaction. The necessary condition for this type of interaction to occur is a positive value of the energy density, which is related to $\nabla^2\rho(r)$ by the equation: $h_e(r) = v(r) + g(r) = g(r) - (1/4)\nabla^2\rho(r)$. The value of $h_e(r)$ may still be negative if the absolute value of the potential energy density (*a priori* negative) exceeds the kinetic one. Therefore, the bonds that are characterized by a positive value of $\nabla^2\rho(r)$ and a negative value of $h_e(r)$ are referred to as an intermediate type of interatomic interactions.

element and organometallic compounds, in supramolecular chemistry their contribution in understanding the molecular self-assembly to a crystal is not so straightforward. While the set of intermolecular interactions obtained through the topological analysis of $\rho(r)$ is much more theoretically justified than those based solely on the geometrical criteria, such set by itself can hardly be used to quantify the energetic aspect of aggregation. Furthermore, topological parameters in BCP, in particular $\rho(r)$ values, cannot be directly applied to various types of interactions, for its absolute value depends not only on the interatomic distance but also on the nature of interacting atoms and their surrounding. Thus, any correlation relating the strength of a particular intermolecular interaction with a value of $\rho(r)$ in its BCP, such as of a X–H···O hydrogen bond, cannot be equally used for Cl···Cl interactions and even for X–H···S ones.

Note that the energy of the atoms contains information on all the interactions that exist in a particular crystal; thus, it cannot be used to elucidate the role of a particular interaction in the supramolecular organization. Although the atomic energies clearly give a lot of highly relevant information,[18] they are difficult to use for the analysis of intermolecular interactions. Furthermore, the integral values of the energy for atoms and/or functional groups must be compared with reference values (ideally, those in an isolated molecule) and/or those for formally equivalent fragments having different surroundings in a crystal. As a consequence, this approach is more successful for the analysis of stereoelectronic interactions[35] rather than supramolecular organization.

Given all the above problems, the correlation by Espinosa *et al.* (CEML),[36] which was proposed for weak hydrogen bonds and interconnected the energy of an interaction (E_{int}) with the potential energy density $v(r)$ in its BCP, was a long-awaiting remedy for many tasks and problems of crystal engineering. This astonishingly simple correlation states that the value of E_{int} is equal to one half of the potential energy density in the corresponding BCP. Although this correlation did not receive the theoretical justification up to date (as it is rather common for functions that are based on the electron density and its derivatives), it was shown to perform very well for a wide range of interactions (see below).

First, we have tested it for $Cr(C_6H_6)_2$[37] and [2.2]paracyclophane;[38] their crystals are formed by the weakest interactions C–H···H–C and C–H···C, *i.e.*, the interactions for which the interatomic distance (2.30–2.70 and 2.80–3.06 Å for H···H and H···C) exceeds the sum of the corresponding VDWRs and which in most structural works are considered normal van der Waals contacts (Figure 1). Within the charge density analysis in these crystals, we have not only obtained all the basic information, such as the deformation electron density (DED), $\nabla^2\rho(r)$ and ELF maps, the occupancy of 3*d*-orbitals for the chromium atom, the topological parameters in BCPs of intramolecular bonds and atomic charges, but we have also fetched out all the bonding interactions and estimated their energy (E_{int} values of 0.5–0.8 kcal mol^{-1}). It was reasonable to propose that the total value for all the above intermolecular contacts would give the lattice energy (E_{lat}), which in turn is related to the enthalpy of sublimation The perfect agreement between our estimates of E_{lat} {17 and 22 kcal mol^{-1} in $Cr(C_6H_6)_2$ and [2.2]paracyclophane} and the available thermochemical data – the sublimation enthalpy (18.7±1.5 and 23.0±1 kcal mol^{-1}) – was a rather unexpected success. Of course, the same E_{lat} values can be obtained in a simpler way by means of the atom–atom potential method, but our approach gives not only a theoretically justified set of intermolecular interactions but also a great deal of additional information. Furthermore, the obtained data on the character and the strength of intermolecular interactions were used to evaluate the barrier to rotation of benzene rings and to twist motion of ethylene bridges in the crystals of $Cr(C_6H_6)_2$ and [2.2]paracyclophane, respectively. Similar results were obtained for aryl-substituted icosahedron carboranes,[34(*b*),(*c*)] in which, in addition to the above C–H···H–C interactions, the main contribution to E_{lat} is from the C–H···H–B interactions, *i.e.*, the prototypes of the so-called dihydrogen bond[39] formed by hydrogen atoms with opposite charges.

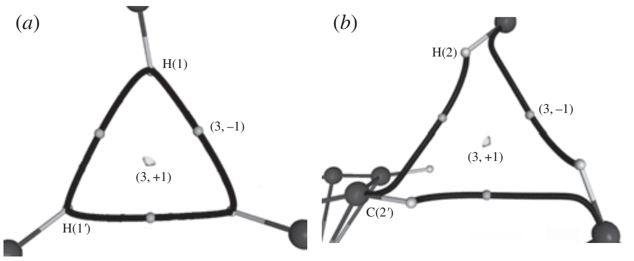

Figure 1 Bond paths for (*a*) H···H and (*b*) H···C intermolecular interactions in the crystal of $Cr(C_6H_6)_2$. Reprinted with permission from K.A. Lyssenko *et al. J. Phys. Chem. A*, 2006, **110**, 6545. © 2006, American Chemical Society.

The above approach was also shown to be valid for the evaluation of much stronger interactions, as, for example, N–H···O hydrogen bonds (4.0–10.9 kcal mol^{-1}) in the α-polymorphic form of glycine, for which we have also obtained a really good agreement between the E_{lat} (31.2 kcal mol^{-1}) and the sublimation enthalpy (32.5 kcal mol^{-1}). Note that, in this crystal, the contribution of N–H···O bonds to E_{lat} is ~79%, while the rest is from weak C–H···O and C···C interactions.[40]

This approach allows one not only to accurately reproduce the energy of a crystal lattice but also to compare the energy of polymorphic forms.[41] It was demonstrated with two polymorphs of paracetamol as an example. The latter are known to violate the so-called density rule stating that the 'rational' (dense) crystal packing should correspond to a more stable polymorphic form. The charge density analysis of these two modifications, **I** (monoclinic) and **II** (orthorhombic) with the former being the most stable but having a smaller density than that of phase **II**, has revealed that the H-bond energy calculated according to CEML in **I** (10.8 and 6.0 kcal mol^{-1} for the O–H···O and N–H···O bonds, respectively) is higher than that in **II** (9.2 and 4.6 kcal mol^{-1}, respectively) by 3 kcal mol^{-1}. This, apparently, leads to a greater stability of polymorph **I**. The experimental values of ΔH_{sub} for the two modifications also indicate that **I** is more stable; however, they differ by only 2 kJ mol^{-1}. As a result, one can assume that other interactions, *i.e.* those of the C–H···O, C–H···π, H···H, and π···π types, compensate for the discrepancy between the thermochemical data and the CELM energies of the H-bonds. Indeed, the inverse relation between the energies of these interactions is observed in the two polymorphs: the 'weak' interactions are stronger in phase **II**, and the H-bonded layers in it are packed more densely [d_{calc} is 1.338(1) and 1.383(1) g cm^{-3} in **I** and **II**]. Thus, such interactions, although they are usually neglected, can be rather competitive with strong H-bonds. This has a clear impact on the properties of a crystalline material, the density of the polymorphs in this case.

The total interaction energy for polymorphs **I** (23.6 kcal mol^{-1}) and **II** (21.3 kcal mol^{-1}) of paracetamol reproduced the trend for their relative stability, although the corresponding difference was larger than that found in a thermochemical investigation.[42] As a result, the approach based on the comparison of the total interaction energies obtained from X-ray diffraction data can be used to determine the stability of polymorphic modifications. It is valid even in the case of the 'isoenergetic' phases (such as in paracetamol), when the energy difference is within the experimental error in the thermochemical measurements.

The estimated E_{int} values for H-bonds and other strong interactions (*e.g.*, I···O and I···I) can also be compared with quantum chemical data. Indeed, such estimations on different levels of theory have shown that E_{int} values well coincide with those typically obtained as the difference of the corresponding values for aggregates and isolated species.[43] The good agreement was also found between the E_{int} values and those derived from the spectroscopic parameters, such as X–H frequency downshift and according to Iogansen's equation.[44] Note that CEML correlation is the best choice for charged systems,[40(*a*)] for which the energy difference-based approach indicates the destabilizing character of the interionic binding. In this case, the CEML not only provides the interaction strength with the sufficient accuracy but also does not fail to predict the attractive nature of H-bonds between likely charged ions, which are considered truly stabilizing by a majority of chemists. This benefit of CEML allowed performing the systematic investigations of anion···anion (such as Cl^-···Cl^-, NO_3^-···NO_3^-) interactions in various organic and inorganic compounds, which revealed that these types of interactions play a significant role in supramolecular organization in many crystals and make significant contribution to their lattice energy.[45]

In particular, the similarity between anion···anion (AA) and cation···cation (CC) interactions and classical cation···anion (CA) bonds was demonstrated within the charge density analysis in the crystals of glycinium trifluoroacetate, glycinium naphthalene-1,5-disulfonate monohydrate and glycine α-polymorph.[40] In the first two structures, a great number of bonding CC and AA interactions, mainly the contacts C–H···O, were found in addition to the CA bonds. Based on their CEML energies, it was shown that the strength of the interactions C–H···O did not depend on their type. Although this conclusion is intuitive, any quantum chemical calculation of a CC pair formed by such a contact C–H···O will show that it does not lead to any gain in energy. The presence of numerous H···O interactions with different nature of the fragments involved also allowed testing whether their length (d) correlated with the attributed energy (E_{int}) (Figure 2).[40]

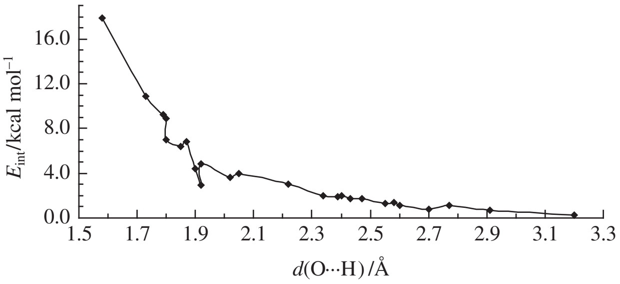

Figure 2 Dependence of the interaction energy on the interatomic distance O···H for hydrogen bonds and the interactions C–H···O in the crystals of glycinium trifluoroacetate, glycinium naphthalene-1,5-disulfonate monohydrate and α-polymorph of glycine. The figures from ref. 40.

Furthermore, CEML can be used to evaluate the cooperative effects of H-bonding. As it was shown for piperidine-2-carboxylic acid tetrahydrate, the strength of H-bonds formed between water molecules[46] steadily increases (from 5.5 to 7.2 kcal mol^{-1}) upon the increase in the size of the H-bonded ring (from 4 to 6) (Figure 3). The presence of a positively charged amino acid moiety in this crystal made it possible to estimate the role of a solute in the aggregation of water molecules, in particular, the charges and dipole moments of water molecules.

The role of H-bonds and water molecules in charge transfer processes is of great importance for the design of electrochemical devices. The extensive investigations of various structures contains onium ions (H_3O^+, $H_5O_2^+$, $H_7O_3^+$, *etc.*) and sulfo acid moieties[47] have shown a nearly linear correlation between the total energy of the cation–anion H-bonds and a value of the charge transfer in a crystal. As a consequence, in some of these salts, the positive charge of the onium ion becomes as small as +0.2e; the latter promotes the formation of a new type of interactions (H_3O-lp)$^+$···π-system (Figure 4).[47(*c*)] Note that the charges of water molecules in the above hydrates were close to zero, thus indicating that water molecules mainly act as channels for charge transfer from cations to anions.

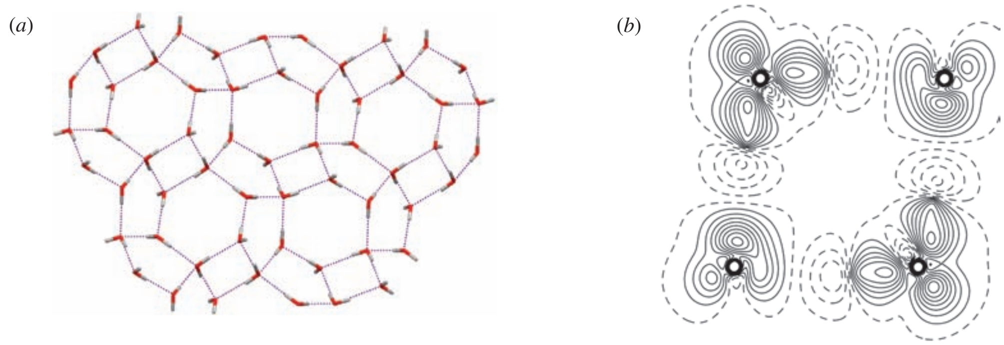

Figure 3 (*a*) Fragment of an H-bonded water layer in the crystal of piperidine-2-carboxylic acid tetrahydrate and (*b*) a deformation electron density map in the area of a four-membered ring. The figures from ref. 46. © 2006, Wiley Periodicals, Inc. Reproduced with permission.

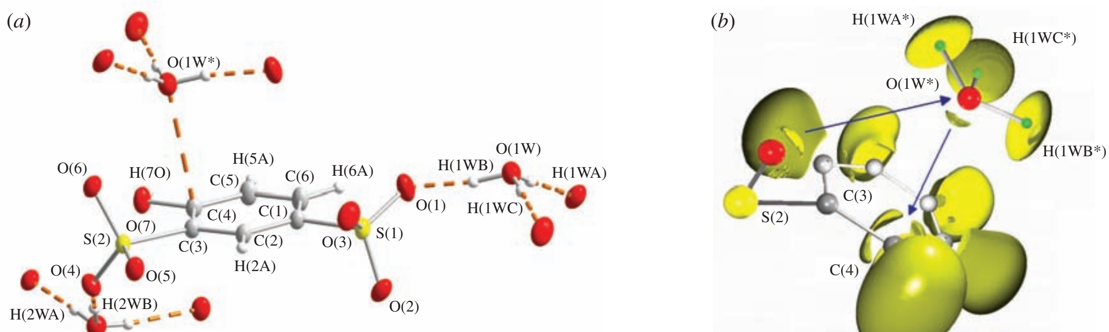

Figure 4 (*a*) General view of bis(oxonium) 4-hydroxy-1,3-benzenedisulfonate and (*b*) the experimental ELF 3D-distribution in the area of the oxonium–π interaction. The figures from ref. 47(*c*). © 2011, Wiley Periodicals, Inc. Reproduced with permission.

Note that H-bonds, especially with high energy (greater than 20–30 kcal mol^{-1}), do not correspond to the closed-shell interactions, for which CEML was proposed, but are of an intermediate type.[†,43(c),(d)] As a result, it was proposed that CEML is also valid for other intermediate interactions, such as almost all the coordinate bonds. We have tested this correlation for Gd–OH_2, Gd–N(phenanthroline), Gd–Cl,[48] and Au–P[49] bonds. In all cases, a quite good agreement between the CEML estimates and the *ab intio* data has been observed. In particular, the E_{int} value for Au–P bond was 57.9 kcal mol^{-1}, while the dissociation energies of MeAu–PPh_3 and AuCl–PH_3 complexes were 58.9 and 53.2 kcal mol^{-1}, respectively, according to LCGTO-LDF and MP2 calculations.[49] Note that, as in the case of $Cr(C_6H_6)_2$ (see above), the X-ray diffraction investigation allows one not only to analyze the peculiarities of Au–P bonding (Figure 5) but also to evaluate charge transfer between the AuCl and PPh_3 species. In addition, we were able to study the crystal packing of this compound in the quantitative level, in particular, to estimate the energy (0.7–0.8 kcal mol^{-1}) of weak Au···H (2.96–3.3 Å) interactions.

The use of CEML for the analysis of coordinate bonds, such as M–X (M = Si, Ge, Sn, Hg and Rh; X = H, F, O, N, C, Cl and H), based on both the X-ray diffraction data and DFT studies clearly demonstrated its validity for the interactions with energies up to 100 kcal mol^{-1}.[50]

Therefore, we can conclude that, starting from closed-shell H···H interactions (E_{int} = 0.2–0.5 kcal mol^{-1}) to H-bonds and coordinate bonds belonging to the intermediate type with E_{int} up to ~100 kcal mol^{-1}, one can use the CEML for at least semiquantitative estimation of the interaction energy.

Although C–H···H–C interactions and most of the so-called weak H-bonds (X–H···π, C–H···O, *etc*.) are clearly weaker than the corresponding coordinate bonds, they may govern not only the formation of a supramolecular organization but also the stabilization of complexes. Thus, it was shown that previously unknown trimeric homochiral cyclo-$(PdLCl)_3$ (L is *ortho*-palladated chiral *N*-isopropylbenzylamine) was stabilized by the C–H···H–C and N–H···π interactions with the energies of 1.0–1.2 and 1.1–1.6 kcal mol^{-1}, respectively (Figure 6).[51] A detailed analysis of intramolecular interactions in its dimer and trimer revealed that the latter structure can gain as much as ~7 kcal mol^{-1} due to their existence. Although these interactions could be somewhat weakened in solution, even a half of this value would be enough to stabilize this trimer in solution, at least at low temperatures, as it was proved by VT-NMR studies indicating that the molar ratio between the dimers and trimers was 2.1 : 1.0 (at 233 K).

Weak H-bonds and similar interactions may also play a significant role in the charge redistribution between molecules, as in the crystals with several independent species in a unit cell. Their investigations made it possible, for the first time, to analyze the pseudosymmetry phenomena on the quantitative level and to demonstrate how small variations in the energy of intermolecular interactions would be able to cause a pronounced redistribution of charges in a crystal.[52]

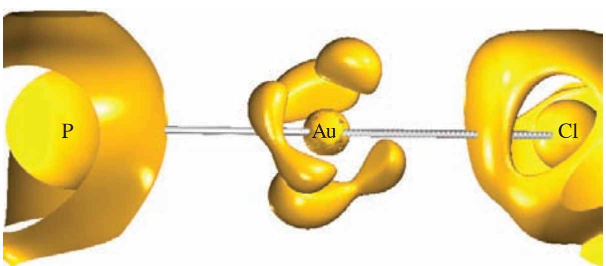

Figure 5 3D map of ELF in the area of Au, P and Cl atoms. Reprinted with permission from A. O. Borissova *et al*., *J. Phys. Chem. A*, 2008, **112**, 11519. © 2008, American Chemical Society.

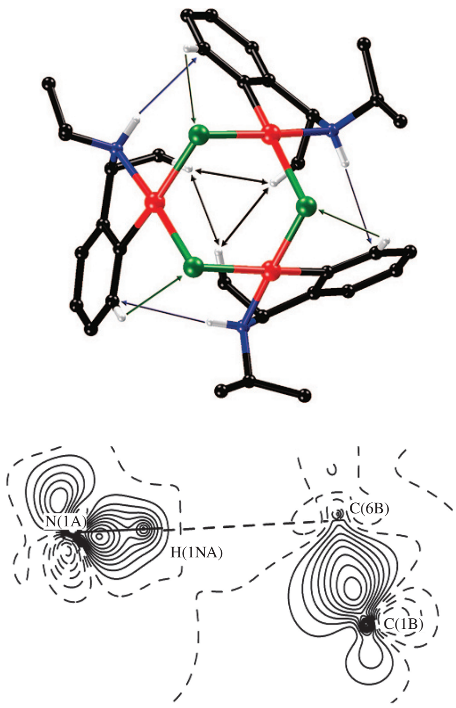

Figure 6 Schematic representation of secondary interactions in cyclo-$(PdLCl)_3$ trimers and a deformation electron density map in the area of intramolecular N–H···π bonds. Reprinted with permission from S. Z. Vatsadze *et al*., *Organometallics*, 2009, **28**, 1027. © 2009, American Chemical Society.

Moreover, the detailed analysis of electron density may be a rather convenient tool for the design of functional materials, although for the investigations of this type a combined approach, *i.e.*, the use of different physicochemical methods, is clearly required.

As the examples of such investigations, we can mention the analysis of sunflower, octathio[8]circulene $C_{16}S_8$.[53] The combination of Raman, IR, UV-vis, X-ray diffraction powder and high-resolution single crystal investigations demonstrated that S···S interactions were the reason for the red color of one of its forms; it was also shown that much less ordered white form of sulflower had much weaker intermolecular interactions. These results gave an idea that its white form could be soluble, while the red one is not. Indeed, the former form appeared soluble in common solvents, which opened the way for the studies of its chemical and electro-optical properties.

A similar combined investigation of lanthanide adducts with different amounts of 1,10-phenanthroline, chloride ions and water molecules in the inner and outer coordination spheres $[LnCl_1Phen_2(H_2O)_3]Cl_2(H_2O)$ (Ln = Eu, Gd and Tb), $[EuCl_2Phen_2(H_2O)_2]Cl_1(H_2O)$ and $[EuCl_2Phen_1(H_2O)_4]Cl_1(H_2O)$ allowed analyzing the influence of inner- *vs.* outer-sphere ligands on the Ln–X bond lengths in terms of net atomic charges, bond energies, and electron transfer from the ligands to the metal ion. It was found that the energy of extended non-covalent interactions occurring in the second coordination sphere (H-bonding and π-stacking) was comparable to that of Ln–ligand bonds.[48] The luminescence properties of the three Eu adducts were interpreted within the results of the topological analysis of electron density distribution function therein. An intraligand charge transfer state was identified, and its contribution to the ligand-to-europium energy transfer process was analyzed. The outcome of this study was that specific interionic interactions, which are usually not considered in theoretical calculations or in the interpretation of the luminescence properties of rare earth complexes, played an important role in the sensitization of Eu luminescence.[48]

Clearly, the topological analysis of an electron density function in a crystal, in particular, in conjunction with CEML, can be used to resolve many problems in structural and theoretical chemistry. Thus, if a researcher has (i) a well-formed crystal (ii) with the ordered crystal structure and (iii) the strong reflection power and also (iv) sufficient time and patience not to publish ORTEP pictures only, then using the topological analysis of electron density within QTAIM supplemented by E_{int} values from CEML, he/she can 'in one pot' obtain an accurate molecular geometry, a standard crystal packing diagram, atomic displacement parameters; fetch out all the bonding interactions, analyze their nature, estimate atomic charges and energies, E_{lat} values and finally, in the ideal case, interconnect such a great amount of information with the physicochemical properties of a bulk material.

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