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Review Article

The Nature of Stacking Interactions between Organic Molecules Elucidated by Analysis of Crystal Structures

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Many planar organic molecules are stacked in infinite columns in the crystalline state. Observations of this in the early years of X-ray crystallography and subsequent discussions about the importance of stacking interactions are reviewed. A survey is made of discussions of the nature of stacking interactions, with special attention paid to the role of charge-transfer interactions in binary molecular complexes. Modern theories and models for intermolecular interactions and quantum-mechanical calculations based on these models are described. As the experimental data for stacking interactions in the gas phase are limited, it is argued that use should be made of the large amount of crystallographic data in order to test the validity of the models.

A survey is made of structural features which may be used for analyzing stacking interactions from crystal structures, such as molecular overlap, electron densities, changes in molecular structure, interplanar distance and interatomic distances in the stack. Special attention is paid to the use of molecular-packing analysis based on atom-to-atom potentials and a comparison between experimental structures and minimum-energy structures calculated by this method. It seems difficult to explain all differences according to the present models for intermolecular interactions.

With the establishment of X-ray crystallography in the first decades of this century a direct determination of bond distances and angles in molecules was possible for the first time. The importance of this has to some extent overshadowed the importance of another kind of information gained from the crystal structures; how the molecules are packed together in the crystal lattice. This information has been essential for the understanding of intermolecular forces. Although the existence of hydrogen bonds had been suggested before, X-ray investigations gave the first clear picture of such bonds, even before a direct localization of hydrogen atom positions by this method was possible.

A striking feature concerning the packing of organic molecules in crystals which was discovered in the early years of X-ray crystallography is that many planar or nearly planar molecules form infinite stacks with approximately parallel molecular planes separated by interplanar distances of approximately 3.3–3.6 Å. The structure determinations of Robertson *et al.* showed this to be the usual packing for polyaromatic hydrocarbons such as pyrene[1] and coronene.[2] In his classical work on phthalocyanines Robertson also found that this class of molecule forms stacks.[3,4]

For molecules with smaller ring systems the packing turned out to be more variable, although many examples of stack formation were observed for such molecules. Lonsdale found in 1929 that hexamethylbenzene molecules pack in this way in the crystal lattice.[5]

Binary complex between aromatic or unsaturated organic molecules of the kind known today as charge-transfer complexes or electron-donor–acceptor complexes were first discovered in 1858.[6] The first crystal structure of such a complex, between *p*-iodoaniline and 1,3,5-trinitrobenzene, was published in 1943.[7] Since then a large number of crystal structures of similar complexes have been reported.[8,9] In the majority of them the partner molecules are stacked alternately in infinite columns, but several complexes are also known where each of the partner molecules forms segregated stacks. Some of the complexes are of great technical interest as they show considerable electrical conductivity. Some molecules able to form such complexes may also form salts which show superconductivity at low temperatures.[10] In such salts these molecules, which are in ionic state, form stacks.

Considerable interest in the biological importance of stacking interactions grew up, especially after 1960. In

1938 Astbury and Bell concluded from X-ray fibre diagrams of sodium thymonucleate that these indicate a spacing of 3.3–3.4 Å between 'flat or flattish nucleotides standing out perpendicularly to the long axis of the molecule.'[11] In the more detailed double-helix structure of DNA, suggested and later confirmed,[12,13] the bases are situated over each other corresponding to the way free molecules are situated in stacks. It is known from the results of X-ray investigations that free nucleic acid bases form such stacks in the crystalline state,[14] and from NMR investigations even in the liquid state.[15]

The fact that many polyaromatic hydrocarbons are highly carcinogenic, and the observation that many planar molecules are able to intercalate between the bases in DNA, causing disturbances in the double helix replication, has led to theories about a possible role of stacking interactions in the development of certain forms of cancer.[16,17]

Other kinds of biological processes in which the role of stacking interactions has been discussed are those involving flavins and flavin derivatives.[18–20] Most flavin derivatives have been shown to form stacks in the crystalline state, and the stacking interaction has been suggested to be of importance for the activity of flavin coenzymes in redox reactions in living organisms.

Early discussions about the nature of stacking interactions

The main points in the theory of the kind of attractive force between molecules which is usually classified as the van der Waals force were developed around 1930, mainly by London *et al.*[21,22] According to this theory these forces consist of dispersion forces, or London forces, dipole–dipole forces, or electrostatic forces, and induced dipole forces, or polarization forces. The repulsive forces which act at small distances were described in 1927 by Heitler and London.[23]

These theories explain well why the packing of organic molecules in crystals usually seems to follow approximately the principle of closest packing. For many planar molecules the observed formation of stacks conforms well with this principle. For binary complexes of stacked, planar organic molecules it has seemed necessary to assume additional forces in order to explain the complex formation. The observation that most of these compounds are coloured and show absorption bands in their UV or visible spectra also indicate that these complex formations are of a special kind. Pfeiffer[24] suggested in 1927 that the bonding in the complexes occurs through the saturation of 'residual valences' in the component molecules. Briegleb and Schachowskoy[25] suggested in 1932 that the formation of complexes between aromatic nitro compounds and aromatic hydrocarbons is due to induced dipole forces caused by the polar nitro groups.

The first theory for such complexes which was generally accepted was formulated around 1950 by Mulliken.[26] According to his theory, the ground-state wavefunction for the complex has the form of eqn. (1),

$$\psi = a\psi_0(\mathrm{D,A}) + b\psi_1(\mathrm{D^+ - A^-}) \qquad (1)$$

where $\psi(\mathrm{D,A})$ is the properly antisymmetrized no-bond wavefunction, and $\psi(\mathrm{D^+ - A^-})$ represents transfer of an electron from the donor, D, to the acceptor, A. In most complexes $a \gg b$. There is also an excited state given by eqn. (2),

$$\psi^* = a^*\psi_1(\mathrm{D^+ - A^-}) - b^*\psi_0(\mathrm{D,A}) \qquad (2)$$

where $a^* \approx a$ and $b^* \approx b$.

In accordance with this description the complexes have been called charge-transfer complexes. The binary complexes of stacked, planar organic molecules are only one of several classes of charge-transfer complexes.

Mulliken's theory successfully explained many spectroscopic results, and the attractive forces accompanying the charge-transfer process were for many years believed to be the dominant part of the intermolecular forces in these complexes. It has also been suggested that charge-transfer interactions in some cases are an important part of the stacking interactions in crystals with only one kind of molecule (self-complexes), such as in naphthoquinones.[27]

When Mulliken introduced his theory he predicted that the knowledge of charge-transfer interactions would open new ways for understanding intermolecular interactions in biological systems.[26] This view obtained considerable support from many others, among them Szent-Gyørgyi,[18] who formulated a theory concerning cancer in which charge-transfer interactions play an important part.[28] Many research projects based on this theory have been carried out. The discussions mentioned earlier concerning the biological significance of stacking interactions have to some extent been discussions about the biological significance of charge-transfer interactions.

About 20–25 years ago scepticism concerning the importance of charge-transfer interactions for the ground-state stabilization of complexes began to be widespread. This scepticism was based on many kinds of experimental results.

As a consequence of his theory Mulliken suggested that the mutual arrangement of molecules held together by charge-transfer forces should obey the 'overlap and orientation principle': The overlap between the highest filled molecular orbital of the donor and the lowest unfilled one of the acceptor should be a maximum.[29] Based on this principle he predicted structures for various kinds of charge-transfer complexes. Many of these predictions turned out to be wrong. Most clearly this was demonstrated for complexes between lone-pair donors and halogen acceptors.[30] For complexes with alternately stacked planar molecules, the picture is not so clear and will be discussed later.

Other reasons for the scepticism were the results of thermodynamic measurements. For complexes between

tetracyanoethylene and methylated benzenes or polyaromatic hydrocarbons the measured enthalpies of formation showed no clear relationship either with the ionization potentials of the hydrocarbons or with the frequencies of the charge-transfer bands in the spectra of the complexes.[31] A similar lack of relationship was demonstrated for complexes of iodine.[32]

The assumption that an important contribution of charge-transfer forces is necessary for the formation of binary complexes was contradicted by the discovery of crystalline complexes with alternately stacked molecules of tetramethyluric acid[33–35] or polyfluorinated hydrocarbons[36,37] with various aromatic donors. In these complexes no charge-transfer bands were observed in their spectra, and, in addition, the low electron affinities of these molecules make the existence of important charge-transfer interactions seem highly questionable.

Much of the scepticism concerning the importance of charge-transfer interactions was summarized in a review article by Hanna and Lippert.[32] Some of their arguments were criticized, especially by Mulliken and Person.[38] One result of these discussions is that the term 'electron-donor–acceptor complex' is now often preferred to 'charge-transfer complex'.

Theoretical studies of intermolecular interactions

Theoretical studies of intermolecular interactions which may be compared with experimental results are hampered by two major problems:

(1) The majority of precise experimental data for intermolecular interactions are from the crystalline state. In this state a large number of molecules are involved in the interactions. Because of limitations in computer capacity, lattice-energy calculations are possible only when very simple analytical expressions are used for the energy. Atom-to-atom potentials and the more sophisticated potentials derived by Claverie *et al.*[39,40] are examples of such expressions, and calculations of this kind will be discussed later.

(2) The majority of organic molecules, including those involved in stacking interactions, are of such a size that *ab initio* quantum-mechanical calculations are difficult, even if they are limited to a single pair of molecules. Semiempirical methods have usually been preferred for these molecules. Castella *et al.*[41] have used such methods to calculate the potential-energy surface for a series of complexes between large aromatic hydrocarbons and benzene derivatives. By a combination of *ab initio* and semiempirical methods for the benzene–tetracyanoethylene complex Emery *et al.*[42] have calculated line shapes of the charge-transfer bands which agree well with the experimental ones and a geometry for the complex which agrees reasonably well with crystal structures of related complexes.

Ab initio calculations with acceptable approximations are possible only for isolated pairs of very small molecules. However, such calculations may give a qualitative description and a set of concepts which may also be useful for a discussion of interactions between larger molecules, and thus of the nature of stacking interactions.

Cioslowski *et al.*[43] have used *ab initio* methods to calculate electron densities between the partner molecules of the benzene–tetracyanoethylene complex, which conform well with a definition of weak bonds suggested by Bader *et al.*[44]

Morokuma and Kitaura[45] have used a variation approach to *ab initio* studies of intermolecular interactions. Based on the calculations, they tried to separate contributions from electrostatic, polarization, exchange, dispersion and charge-transfer interactions. The sum of these contributions was, however, different from the calculated total energy, and an additional 'mixing' term had to be added to account for this difference. The method was used to calculate the various contributions in some complexes with coordinative bonds, some hydrogen-bonded systems, and charge-transfer complexes between some simple donors and halogen acceptors. The calculated equilibrium distances between the partner molecules in the charge-transfer complexes were, however, considerably larger than those observed in, or estimated from, crystal structures of the same or similar complexes.

Nagata and Aida[46] have performed *ab initio* studies of the pairing and the stacking interactions in nucleic acid bases in nucleic acids, and used the partition scheme of Morokuma and Kitaura for analysis of the stacking interactions. They found that the stacking interaction between the bases is a principal factor in determining the conformation of nucleic acids. The dispersion energy was found to contribute most to the stacking interaction, while the contribution of charge-transfer energy for all pairs of overlapping bases is close to 50% of that of the dispersion energy.

The partition scheme used by Mulliken and Kitaura corresponds closely to a traditional description of intermolecular interactions. A somewhat different scheme has been developed by Røeggen.[47] Røeggen used an extended geminal model for his *ab initio* calculations. In the derivation of his formulae a partition scheme appears in which the total energy is the sum of distortion energies for the partner molecules, and the Coulombic energy, the exchange energy and the correlation energy for the interaction between the distorted molecules. In a modified partition scheme the Coulombic energy is further divided into the electrostatic energy, which corresponds to the interaction between undistorted molecules, and the induction energy, which corresponds to the additional interaction due to the distortion of the molecules.

Based on this method, calculations have been performed for charge-transfer complexes between ammonia and halogen acceptors,[48] and between water and halogen acceptors.[49] The equilibrium distance for the H_3N–Cl_2 complex is much shorter than that found by Morokuma and Kitaura, but the distance in both this complex and the H_2O–Cl_2 complex is still ca. 0.2 Å longer than that

estimated from, or observed in, crystal structures of similar complexes. In all these complexes the distortion is mainly an approach of lone-pair electrons of N or O into a 'vacant' space in the vicinity of a halogen nucleus, an effect which is closely related to charge transfer.

Røeggen's partition scheme illustrates how the interaction between electron donor and acceptor molecules may be described without use of the charge-transfer concept. The term will, however, still be used in the discussions of the nature of stacking interactions in this article.

In some articles the discrepancies between calculated equilibrium distances and distances found in crystals are explained as results of the crystal forces in the crystalline state.[50] The results of gas-phase studies of intermolecular interactions are thus important, both for a direct comparison with results of calculations on isolated systems, and for an evaluation of the effect of the crystal forces by comparison with crystal structures.

Studies of intermolecular interactions in the gas phase and in solution

Valuable information about the nature of stacking interactions between molecules in the gas phase may be obtained from jet-beam studies. Castella *et al.*[51] have used such methods to study the stacking interactions in a series of anthracene and perylene complexes with benzene derivatives in a supersonic expansion. The fluorescence spectra and the results of fluorescence decay time measurements were discussed on the basis of the computed potential-energy surfaces.[41] The interplanar distance in the perylene–aniline complex in the ground electronic state was roughly estimated as 3.0–3.6 Å. No accurate experimental determination of interplanar distances between stacked molecules in the gas phase have been reported.

Various methods have been used to determine the interatomic distances and potentials in the gas phase for small molecules, such as molecular beam spectroscopy, measurement of elastic differential cross-section in molecular beam scattering, measurement of the second virial coefficient and analysis of transport data.[52–54] These methods are, however, not applicable to larger molecules.

Only a very limited number of direct structure determinations of molecular complexes in the gas phase have been performed. The hydrogen-bond distances found by electron diffraction in the dimeric forms of formic acid[55] and acetic acid[56] are ca. 0.1 Å longer than those found in the crystal structures of these compounds.[57,58] In the microwave structure of the complex between trimethylamine and trifluoroiodomethane the N---I distance and the overall geometry of the complex are very close to those observed for similar complexes in the crystalline state.[59] These results indicate that, when gas-phase results are not available, crystallographic results may be a reasonable guideline for the estimation of geometries of complexes in the gas phase.

Charge-transfer complexes in solution have been studied extensively, mainly by spectroscopic methods.[60] Most of the results concern the transition from the ground state to the excited state, but give little information about the ground-state structure. Analysis of Raman spectra have been used to estimate the interplanar distance between the partner molecules in the complex between hexamethylbenzene and tetracyanoethylene in dichloromethane solution.[61] The estimated distance in the ground state, 3.28 Å, is very close to that found in the crystalline state, 3.28 Å at 113 K[62] and 3.35 Å at room temperature.[63]

Experimental data from the gas phase useful for analysis of stacking interactions are thus very limited. Even data from solution concerning the ground state are limited. It is thus important to find methods to analyze such interactions from the large amount of data from the crystalline phase.

Molecular-packing analysis based on atom-to-atom potentials

In the atom-to-atom potential method a simple analytical expression for the interatomic potential for each pair of non-bonding atoms is used to calculate the packing energy of a crystal lattice with a large number of molecules. The popularity of the method is very much a result of a book by Kitaigorodsky.[64] The method has been reviewed by Kitaigorodsky,[65] Mason,[66] Mirsky[67] and more recently by Pertsin and Kitaigorodsky.[68]

In the majority of calculations based on this method one of the following two analytical expressions is used for the potential: the Lennard-Jones potential, eqn. (3), or the Buckingham potential, eqn. (4).

$$E = \Sigma\Sigma - A_{jk} r_{jk}^{-6} + B_{jk} r_{jk}^{-12} + q_i q_j r_{jk}^{-1} \quad (3)$$

$$E = \Sigma\Sigma - A_{jk} r_{jk}^{-6} + B_{jk} \exp(-C_{jk} r_{jk}) + q_i q_j r_{jk}^{-1} \quad (4)$$

All interatomic distances r_{jk} in the crystal up to a certain limit may be included in the sums. A typical value for this limit is 10 Å, where at least the first two terms become negligible. The first term in the two expressions is the attractive dispersion term, which may be derived from London's theory.[22] The second term is the repulsive exchange term, and was introduced for the first expression by Lennard-Jones[69] and for the second expression by Buckingham.[70] It now seems to be generally accepted that the latter expression is slightly more correct and is most frequently used.[66]

The third term in the expressions, the Coulombic term, was at first considered unimportant by Kitaigorodsky.[65] It has been shown, however, that although the term is relatively small for the interaction between neutral molecules, it may be important when the method is used to predict crystal structures, as in the case of benzene.[71]

Usually net atomic charges, q, are placed at the nuclear positions. However, the calculation of such charges raises

many problems.[67] Williams and Houpt[72] have recommended a potential-derived charge model in which those charges are used which reproduce the surrounding electric potential as well as possible. They showed, however, that better results may be obtained when charges are also located on the extensions of and on the centers of covalent bonds. Stone and Price[73] have discussed the weaknesses of using isotropic charge distributions. A different method for calculating the electrostatic interactions has been introduced by Hirschfeld,[74] where the molecular charge density is decomposed into atomic fragments, and each fragment is represented by its net charge, and dipole and quadropole moments localized at the atomic nucleus.

The atom-to-atom potential method may be used not only to calculate the lattice energy in a crystal with an experimentally determined structure, but also to find the structure which gives the lowest calculated energy, the minimum energy structure, by moving and rotating the molecules in the cell and varying the cell constants. The mathematical procedures for this have been described by Williams.[75]

The atom-to-atom potential method has been used for a large variety of purposes. For an unknown structure with known space group and cell parameters the minimum energy structure may be calculated and used as a starting point for the least-squares refinement in an X-ray structure determination.[76] Gavezotti[77] has used the method together with the Cambridge Structural Database[78] for a systematic analysis of the packing and for describing the potential surface of fused-ring aromatic hydrocarbons. Williams and Xiao[79] have used the method to analyze the molecular packing in dimers of benzene, naphthalene and anthracene at different intermolecular distances and orientations.

The compounds chosen for the atom-to-atom potential calculations mentioned above are those where only classical van der Waals interactions are expected to be present, and the calculations are based on the assumption that the analytical potential expression describes such interactions approximately correctly. When hydrogen bonds are present different expressions may be used for the hydrogen-bond energies.[68,80,81] When other kinds of interactions are expected to be present the calculated minimum-energy structures may be compared with the experimental structures and the differences analyzed in order to elucidate additional interactions. This kind of analysis will be discussed later.

By calculating the minimum-energy structure of an isolated complex and comparing this with the minimum-energy structure in the crystal an estimation may be made of the influence of crystal forces on intermolecular distances. For the complex between *N*,*N*-dimethylaniline and hexafluorobenzene, where the minimum-energy crystal structure is very close to the experimental crystal structure,[82] the interplanar distance in the minimum-energy structure is only 0.001 Å longer in the isolated complex than in the crystal.[83]

The analytical potential expression for the intermolecular interactions may be combined with expressions for intramolecular interactions. Busing[84] has prepared a computer program in which intramolecular bond energies are also included. Allinger *et al.*[85,86] have used expressions for intermolecular potentials in addition to various intramolecular potentials in molecular mechanics programs for crystals.

The atom-to-atom potential expressions described above have some obvious shortcomings. The partitioning of the energy in the three separate terms is in itself questionable. The problems of calculating the electrostatic energy has been mentioned already. In addition, some effects are neglected. Caillet and Claverie[87] have derived a potential expression where non-additive effects such as polarization and multipole interactions are also included. Calculations based on this expression have been performed for several compounds, among them nitrobenzene, where the molecules form stacks in the crystalline state. The polarization energy calculated for this compound is ca. 3% of the total interaction energy.

Analysis of stacking interactions based on crystal structures

Molecular overlap. It might be expected that the way in which adjacent molecules in the stack overlap highly depends on the nature of the stacking interactions. For molecular complexes Herbstein[8] has introduced the term 'overlap diagram', which is the projection onto the average plane of two (or three, if necessary) successive molecules in the stack. The term may also be used for the overlap in crystals with only molecules of the same kind.

Kitaigorodsky[65] has pointed out that the overlap diagram for unsubstituted fused aromatic hydrocarbons shown in Fig. 1a, where all C atoms take up the same positions with respect to their nearest neighbours, should give the densest packing and thus be expected to be preferred. This is approximately the overlap observed for pyrene[1] and coronene.[2] For graphite, however, a completely different overlap diagram, shown in Fig. 1b, is observed.[88]

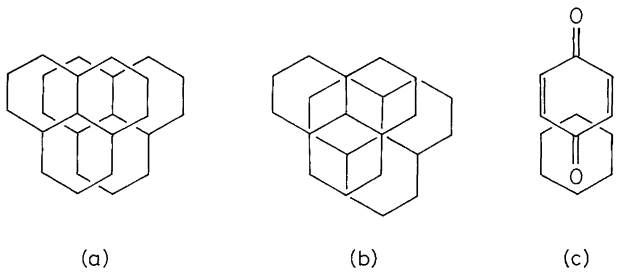


Fig. 1. Overlap diagram for the densest packing of aromatic rings (a),[65] for graphite (b)[88] and for many molecular complexes containing *p*-benzoquinone (c).[95]

Bugg[89] has pointed out that for purine derivatives the polar regions of one molecule usually overlap the polarizable ring system of the adjacent molecule, which indicate that polarization forces are important in such compounds. However, a large variety of overlap diagrams have been observed for such molecules, even in different crystal modifications of the same compound.[90]

For molecular complexes the influence of charge-transfer interactions should be easily recognized from the overlap diagrams if the overlap and orientation principle holds for such interactions. There seem to be different opinions on this point. Goldberg[91] has performed calculations on several complexes of 7,7,8,8-tetracyanoquinodimethane (TCNQ) based on the iterative extended Hückel method and found that the overlap observed in the crystal structures of these compounds agrees well with the overlap and orientation principle. Later, Shaanan and Shmueli[92] published a number of structures of such complexes and explained the observed overlap diagrams relatively well from this principle, with the addition of some electrostatic effects. For other classes of complexes, however, the overlap diagrams differ clearly from those predicted from the overlap and orientation principle. This does not necessarily mean that charge-transfer interactions are unimportant in these complexes.

For benzene derivatives the overlap and orientation principle predict a direct superposition of the molecules.[60] Such an overlap is observed only for a few complexes. A large variety of overlap diagrams for complexes of such molecules have been observed with a certain predominance of diagrams corresponding approximately to the overlap of two single rings in Fig. 1a.[8,9] This may be interpreted as a result of the influence of dispersion forces. However, Mayoh and Prout,[93] using PPP π-electron theory for their calculations, obtained results which disagree with the orientation and overlap principle and indicate that this overlap also gives the maximum contribution of charge-transfer forces. According to the calculations the charge-transfer forces are not very sensitive to variations in the relative orientation of the overlapping molecules, neither for this class of complex nor for most other classes. This result agrees well with the frequent occurrence of orientational disorder in such complexes. The calculations indicate that the lowest charge-transfer state contributes to only a small part of the charge-transfer energy.

For complexes which serve as models for possible biologically important interactions the degree of overlap is also often regarded as an indication of charge-transfer interactions. Such interactions have thus been assumed for a series of complexes between protonated or methylated guanine bases and tryptophanes, where there is a considerable overlap between the indole ring and the guanine base.[94]

In some complexes the overlap diagrams indicate that other kinds of interactions have a dominating effect. Prout and Wallwork[95] have pointed out that in many complexes containing *p*-benzoquinone or its derivatives the C = O bond is localized above the ring centres and nearly parallel to C–C bonds of the adjacent ring, as shown in Fig. 1c, and interpreted this as being due to the effect of polarization forces.

In general, it is difficult to draw conclusions concerning the influence of charge-transfer interactions in the complexes from overlap diagrams alone, as these do not seem to form any coherent pattern. One obvious reason for this is the disturbing effect of steric factors caused by the shapes of the partner molecules, especially by bulky substituents. More reliable conclusions from overlap diagrams can probably be drawn when such diagrams are compared for compounds having relatively equal shapes. Another possibility is to compare the observed overlap diagrams with the minimum-energy overlap diagrams calculated by the atom-to-atom potential method. Examples of this well be discussed later.

Electron densities. Krebs Larsen *et al.*[96] have determined the crystal structure of the complex between perdeuteropyrene and tetracyanoethylene at liquid nitrogen temperatures. By integration of the charge density over the volume of the tetracyanoethylene molecule, they found a very small transfer of charge from tetracyanoethylene to perdeuteropyrene, i.e. in the opposite direction to that expected. They concluded, however, that this effect is probably not significantly different from zero, and that a possible transfer in the expected direction must be less than 0.15 *e*. This result has been an additional argument for the sceptics concerning the significance of the charge-transfer effect in the ground state of this kind of complex. The result also shows that changes in electron density resulting from stacking interactions are difficult to observe with X-ray crystallographic methods at the present stage.

Changes in molecular structures as a result of stacking interactions. Krebs Larsen *et al.* also tried to find an effect of complexation on bond lengths in the perdeuteropyrene–tetracyanoethylene complex by comparison with those found in the structures of the partner molecules. They concluded that this effect in perdeuteropyrene is at most a few thousandths of an ångstrom. The effect may possibly be somewhat larger in tetracyanoethylene, but as the molecule has an orientational disorder in this complex, it is difficult to draw safe conclusions even about this.

This example illustrates well how difficult an analysis of stacking interactions from changes in molecular structure may be. In most cases the effects are too small to be detected, at least in room-temperature structures. Very often the molecules in this kind of complex have orientational disorder, which makes an accurate determination of bond distances and angles difficult. If the disorder disappears at low temperature, the transformation into the low-temperature modification is often accompanied by formation of twinned crystals. In some cases, however, when the stacking interactions are very strong, or one of

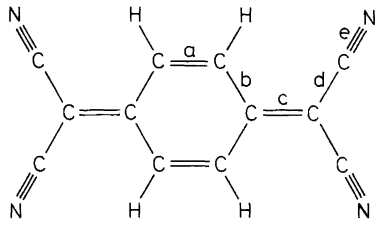


Fig. 2. Bonds in 7,7,8,8-tetracyanoquinodimethane which depend on the transfer of charge in molecular complexes. After Ref. 97.

the partner molecules is relatively flexible, significant effects of complex formation on molecular structures may be observed.

TCNQ is an acceptor which forms strong charge-transfer complexes, some of them with an ionic ground state. Flandrois and Chasseau[97] have compared bond distances in this molecule for a large series of complexes. They showed that there is a prolongation of the distances *a*, *c* and *e* (Fig. 2) and a shortening of *b* and *d* as a result of the transfer of charge. The change in *b*–*c* and *c*–*d* may amount to several hundredths of an ångstrom. By assuming a linear relationship between these changes and the degree of charge-transfer and using an estimate made by other methods of the transfer in one of the complexes, they were able to estimate the transfer in the ground state for the whole series of complexes, ranging from 0 to 1.0 *e*. The authors also reported similar changes in bond lengths in *N*-methylphenazine on complexing with TCNQ.

Krygowski *et al.*[98] have calculated the energy needed to bring the observed geometries for *N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine (TMPDA) and TCNQ in a series of salts and complexes into their Kekulé structures, 'the HOSE values', and found a correlation between this energy and the charges of the molecules or ions. They suggest this as a method to estimate the degree of charge transfer in complexes.

Herbstein *et al.*[99] have found that in the crystal structure of the 1:2 complex between 9,10-dihydroanthracene and 1,3,5-trinitrobenzene the 9,10-dihydroantracene molecule has a planar or nearly planar shape. In the structure of the pure compound they found that the molecule has a folded shape with a dihedral angle between the benzene rings of 144.7°. The authors also argued that the phenothiazine molecule seems to be more planar in its complex with 1,3,5-trinitrobenzene[100] than in the pure compound.[101]

Some examples will be shown later of the effect of complexation on the tetrahedral character of the amino group in aromatic amines.

Interplanar distance between adjacent molecules in the stack. The interplanar distance in the stack is very often used as an indication of the strength of the stacking interaction. A quite common view is that a distance below 3.40 Å, which is regarded as the van der Waals distance between aromatic rings, indicates some interactions in addition to the van der Waals interaction. That this is an oversimplification is apparent from the fact that the interplanar distance also varies strongly for pure aromatic hydrocarbons, and decreases as the size of the ring system increases. In pyrene it is 3.53 Å,[1] in coronene 3.40 Å[2] and in graphite 3.35 Å.[88]

For charge-transfer complexes the use of the interplanar distance as a measure of the strength is especially common. There is no doubt that the short distances observed in may complexes of TCNQ are results of strong interactions. In the 1:1 complex between TMPDA and TCNQ, which shows considerable electrical conductivity, the interplanar distance is 3.27 Å.[102] Spectroscopic data indicate that this complex has an ionic ground state.[8] The amino group is planar, unlike that found in pure TMPDA,[103] and other structural features indicate that this molecule has a cationic character in the complex. An analysis of the TCNQ structure based on the method of Flandrois and Chasseau[97] indicates a transfer of 0.5 *e* between the partners. Also in some other TCNQ complexes showing electrical conductivity distances well below 3.4 Å have been observed.[104]

Complexes between TCNQ and tetrathiofulvalene derivatives are also well known organic conductors. In some of these the molecules are stacked alternately with interplanar distances of more than 3.5 Å,[105,106] probably due to the size of the sulfur atoms. In other complexes in this series segregated stacks for each of the components are observed. The interplanar distance in the TCNQ stacks in these complexes are close to 3.2 Å.[107]

In a large number of compounds $(TCNQ)_2^-$ units are formed.[8,9] These units form stacks, possibly charge-transfer complexes between anions and neutral molecules. The interplanar distances range from 3.24 to 3.36 Å.

In addition to those observed in TCNQ complexes, short interplanar distances indicating strong stacking interactions are found in some fluoranil complexes[108–110] and in the complex between TMPDA and chloranil.[111] In the latter complex, which has been shown by spectroscopic methods to be ionic in the ground state,[8] the TMPDA molecule is planar and the interplanar distance is 3.28 Å.

In spite of these examples it is difficult to find a clear correlation between interplanar distance and strength of the stacking interactions when all kinds of charge-transfer complexes are considered. In their review article Prout and Kamenar state: 'Perhaps the most interesting feature – is the complete lack of any systematic relationship associated with mean interplanar spacing'.[9] One obvious reason for this is the effect of steric repulsion due to bulky substituents, which may be more important than differences in strength of the charge-transfer interaction. The large distance of 3.55 Å found in the hexamethylbenzene–TCNQ complex may be explained as an effect of such repulsion,[112] although it is hard to understand why it is 0.20 Å shorter in the hexamethylbenzene–fluoranil complex at room temperature.[110] A factor which may be responsible for a part of this difference, and which com-

plicates such comparisons of interplanar distances, is that the charge-transfer interaction in some cases may lead to a molecular overlap with large steric hindrance and thus increase the interplanar distance.

Distances between atoms in adjacent molecules in the stack. In some complexes intermolecular distances between specific atoms in the stack indicate a strong interaction. In the complex between *N,N*-dimethylaniline and fluoranil[113] (Fig. 3) the distance between the N atoms of the amino group and the C atom of the carbonyl group is 3.03 Å. From this result, the finding that the amino group has a more tetrahedral character than in the hexafluorobenzene complex with the same amine, and the interplanar distance, which is much shorter on the lone-pair side of the N atom than on the other side (Fig. 3), it was concluded that in this complex there is a strong charge-transfer interaction where the lone pair is strongly involved. The short N---C = O distance may, however, also be seen in relation to the short O---C = O distances found in many crystal structures.[114] These have been considered to be results of the strong dipole nature of the carbonyl group.

Ohashi[115] has observed short distances, 3.173 and 3.293 Å, between N atoms of amino groups and ring C atoms attached to cyano groups in the complex between *N,N*-dimethylamino-*p*-phenylenediamine and 1,2,4,5-tetracyanobenzene, and discussed these in relation to the corresponding short distances in the complexes of 1,2,4,5-tetracyanobenzene with TMPDA and with diamino-*p*-phenylenediamine, 3.152 and 3.164 Å, respectively.[116,117] He concluded that these distances indicate charge-transfer interactions in which the N atoms are involved. He also compared the tetrahedral character of the amino groups, the out of plane positions of the amine N atoms, the C(ring)–N(amine) bond distance, and the quiniod character of the 1,2,4,5-tetracyanobenzene molecules in the area where the amino groups overlap, and found that the variations in these structural parameters are as expected if the strength of the interaction increases with the electron-donating power of the amine.

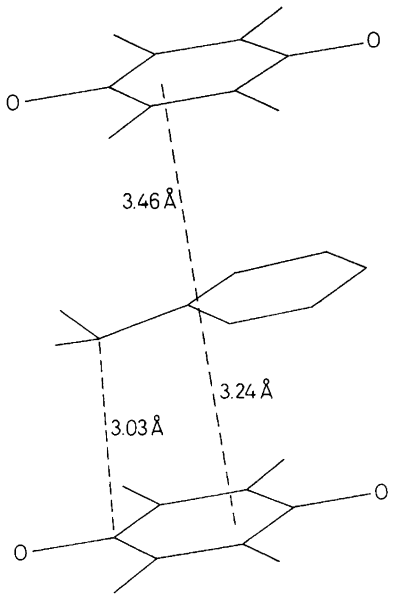


Fig. 3. Crystal structure of the complex between *N,N*-dimethylaniline and fluoranil. After Ref. 113.

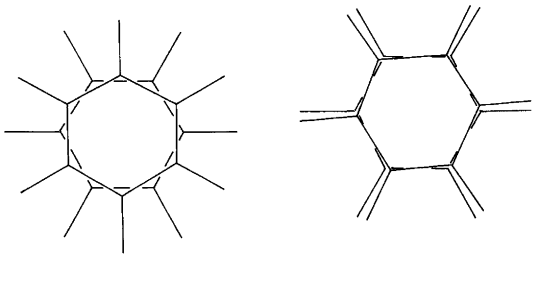
An observation of an intermolecular distance shorter than the van der Waals distance does not necessarily mean that there are interactions in addition to normal van der Waals interactions. Atoms belonging to bulky groups, e.g. methyl groups, may well be forced within the van der Waals distance from atoms in neighbouring molecules in order to reduce distances between other atoms forced apart by these bulky groups. In general, discussions of intermolecular distances are often based on the simple assumption that the atoms consist of hard spheres into which neighbouring atoms are unable to penetrate unless forces stronger than van der Waals forces are present. Such an interpretation of the van der Waals distance was never intended by those who introduced the concept. Pauling described the van der Waals distance as the distance 'at which the attractive forces are balanced by the characteristic repulsion force between atoms'.[118] All atoms in the crystal contribute to the attractive forces, not only the nearest neighbours, and a precise definition of the van der Waals distance thus requires a specification of these forces. Using Buckingham potentials Williams and Houpt[72] have found that distances where the calculated repulsive force between neighbouring atoms is 10^{-10} N correspond well with the sums of Pauling's van der Waals radii. The non-spherical shape of many atoms, which has been demonstrated by Nyburg and Faerman,[119] is another factor which makes it unrealistic to base an analysis of intermolecular interactions on a simple use of van der Waals radii.

Differences between experimental structure and minimum-energy structure calculated by the atom-to-atom potential method. The potentials used in the atom-to-atom potential method give a much more realistic picture of the intermolecular forces than those based on the assumption of hard spheres. It is therefore more reasonable to discuss differences between experimental structures and minimum-energy structures calculated by this method than to discuss intermolecular distances differing from the van der Waals distance. If the atom-to-atom potentials are assumed to describe the ordinary van der Waals interactions approximately correctly, differences between experimental structures and minimum-energy structures must be due to other kinds of interaction. The large number of examples reported where these differences are very small[120] may justify such an assumption. For aromatic molecules it is, however, often found that the rings are overlapping directly in the minimum-energy structure, whereas they are somewhat displaced in the overlap diagram for the experimental structure. Hunter and Sanders[121] have shown that when charges of the π-electrons are placed above and below the ring plane, a much better agreement is obtained.

Analysis of experimental crystal structures by comparison with minimum-energy structures may also reduce the significance of points which seem striking from a more simple analysis. In the complex between *N,N*-dimethylaniline and hexafluorobenzene, the overlap diagram is approximately the same on both sides of the amine in spite of the different steric conditions caused by the partly tetrahedral character of the amino group.[122] From this observation it has been argued that there must be a specific interaction between the π-orbitals in this complex.[37] By atom-to-atom potential calculations, however, approximately the same overlap diagrams were also found in the minimum-energy structure.[82] This shows that the different steric conditions on the different sides of the amine are of minor importance. In the complexes between hexafluorobenzene and methylated benzenes the benzene rings of adjacent molecules in the stack are twisted 30° relative to each other in complexes with two and three methyl groups, whereas they become more parallel as the number of methyl groups increases.[37] It has been suggested that this may be due to an influence of charge-transfer forces in the latter complexes.[123] The same trend is also observed, however, for the minimum-energy structures, and can thus be explained as a result of ordinary van der Waals interactions.[82]

Fig. 4 shows the overlap diagram for the experimental structure and for the minimum-energy structure of the complex between hexamethylbenzene and fluoranil.[82] In this case the difference is relatively large and may be interpreted as a result of a strong charge-transfer interaction in the complex.

When the molecular overlap in the experimental structure is different from that in the minimum-energy structure, it may be difficult to compare the interplanar distances. To avoid this problem one may minimize the energy by starting with the experimental structure and varying only the crystallographic axes, thus keeping the overlap unchanged. The term optimum density structure has been used for the minimum-energy structure obtained in this way.[82] The results of such density optimizations may also give information about the strength of the interactions between neighbouring stacks. For room temperature structures with large thermal vibrations all the axes will normally decrease in such an optimization.



(a) (b)

Fig. 4. Overlap diagram for the experimental structure (major orientation) (a) and for the minimum energy structure (b) of the complex between hexamethylbenzene and fluoranil. After Ref. 82.

Table 1 shows the relative shifts of the axes in density optimizations for some hexafluorobenzene and fluoranil complexes.[82] For some of the hexafluorobenzene complexes the decrease is largest for the stack axis, which indicates that the stacking interaction is weak for these complexes. Other results of the analysis indicate that weak C–H---F interactions between different stacks are important in these complexes. For other hexafluorobenzene complexes the relative decrease is of the same magnitude for all axes, whereas for the hexamethylbenzene-hexafluorobenzene complex and for the fluoranil complexes the stack axis decreases much less than the other axes, or even increases, indicating stacking interactions stronger than ordinary van der Waals interactions. A surprising result from this analysis is that there seem to be more additional stacking interactions in the hexafluorobenzene complex with hexamethylbenzene than in those with aromatic amines, which are regarded as stronger electron donors.

Calculations similar to those described have also been made for some methylated adeninium compounds. In these compounds there are hydrogen bonds, and the parameters in the analytical potentials for hydrogen-bonding H atoms were modified in such a way that the hydrogen bond distances in the minimum-energy structures were approximately as in the experimental structures. In *N,N*-dimethyladeninium picrate stacks of alternating ions with an interplanar distance of 3.34 Å has been observed.[124] This has been interpreted as an indication of charge-transfer interactions between these ions. However, an analysis based on atom-to-atom potential calculations indicates that this distance is as expected when only van der Waals interactions are present.[125] For some other compounds with stacks containing only *N,N*-dimethyladeninium ions, an increase by more than 0.05 Å has been found in the stack axis in the optimum density structure relative to that in the experimental structure, which indicates additional stacking interactions.[126,127]

Table 1. Shifts in crystallographic axes (%) in the packing-density optimization for some complexes containing hexafluorobenzene (HFB) or fluoranil. For each compound the stack axis is marked with an asterisk. From Ref. 82.

Compound	Δ*a*	Δ*b*	Δ*c*
p-Xylene – HFB	−2.3	−2.9	−3.7*
Mesitylene – HFB	−2.4	−0.8	−4.2*
Durene – HFB	−3.4	−0.5	−2.4*
Hexamethylbenzene – HFB	−2.0	−2.3	−0.3*
N,N-Dimethylaniline – HFB[a]	0.5*	−0.3	0.1
N,N,3,5-Tetramethylaniline – HFB	−2.3*	−3.3	−2.6
TMPDA – HFB[b]	2.4	−2.5*	−2.4
Durene – fluoranil	1.8*	−4.0	−0.9
Hexamethylbenzene – fluoranil[c]	−1.5	−0.5	3.4*

[a]Experimental structure at 120 K. [b]Major orientation of TMPDA. [c]Experimental structure at 223 K. Major orientation of fluoranil.

In the crystal structure of 8-azaguanine stacks have been observed with a remarkably short interplanar distance of 3.25 Å.[128] A possible contribution of charge-transfer interactions and a possible relationship between this and the anticarcinogenic effect of this compound was discussed. This structure has later been redetermined and a disordered pattern of hydrogen bonds has been found.[129] The authors suggested that this disorder may be the main reason for the biological effect. Because of the large number of N atoms in this ring system it is difficult to estimate from the van der Waals radii the expected interplanar distance if only van der Waals interactions were present. By the atom-to-atom potential method, however, an interplanar distance of 3.39 Å has been calculated for the optimum density structure.[130] The experimental distance is thus remarkably short, and indicates some kind of additional stacking interaction.

Atom-to-atom potential calculations are thus well suited to reveal unusual interactions which may be present, but normally it is not possible to conclude anything about the nature of these unusual interactions from such calculations. In order to obtain this, additional terms may be added to the potential expression. Basilevsky *et al.*[131] have added a term for the quantum-chemical interactions between π-electrons, using the PPP method for the calculation of this term. A good agreement between calculated and experimental structure has been obtained by this method for a series of molecular complexes containing tetracyanoethylene, and it was concluded that in these complexes there are significant charge-transfer interactions in addition to the van der Waals interactions.

Finally, it must be emphasized that differences between experimental structures and calculated minimum-energy structures may well be results of the shortcomings of the atom-to-atom potentials used to describe the van der Waals interactions. Some care must therefore be shown when conclusions are drawn from this kind of analysis.

Concluding remarks

In the preceeding sections only a small part of the large amount of information concerning stacking interactions in crystal structures has been reviewed. Some of the examples show that the nature of such interactions may be more complicated than those described as classical van der Waals interactions or charge-transfer interactions. The problem is how to make use of all this information in order to obtain a better understanding of the nature of the interactions.

Analysis based on effects of stacking interactions on molecular structures and on electron densities in the crystals may be more fruitful when the accuracy in the determination of atomic positions and electron densities has been improved.

Analysis based on differences between experimental structures and minimum-energy structures calculated by the atom-to-atom potential method seems to represent an improvement relative to those based on some of the criteria used earlier. This kind of analysis in combination with use of the Cambridge Structural Database[78] may turn out to be fruitful. Further improvement may be obtained when some of the problems of the atom-to-atom potential method have been overcome. In order to elucidate the reasons for the observed differences, terms for calculated additional interactions may be added to the ordinary potential expression. However, it seems at present unreasonable to believe that all observed differences can be classified according to known concepts.

An improved understanding of the nature of stacking interactions therefore depends not only on the methods used for analyzing the crystal structures, but also on the models and concepts provided by theoreticians for this kind of interaction.

References

1. Robertson, J. M. and White, J. G. *J. Chem. Soc.* (1947) 358.
2. Robertson, J. M. and White, J. G. *J. Chem. Soc.* (1945) 607.
3. Robertson, J. M. *J. Chem. Soc.* (1935) 615.
4. Robertson, J. M. *J. Chem. Soc.* (1936) 1195.
5. Lonsdale, K. *Proc. R. Soc. London, Ser. A123* (1929) 494.
6. Fritzsche, J. *J. Prakt. Chem. 73* (1858) 282.
7. Powell, H. M., Huse, G. and Cooke, P. W. *J. Chem. Soc.* (1943) 153.
8. Herbstein, F. H. In: Dunitz, J. O. and Ibers, J. A., Eds., *Perspectives in Structural Chemistry*, Wiley, New York 1971, Vol. 4, Chap. 3.
9. Prout, C. K. and Kamenar, B. In: Foster, R., Ed., *Molecular Complexes*, Elek, London 1973, Vol. 1, Chap. 4.
10. Bechgaard, K. In: Pierrot, M., Ed., *Structure and Properties of Molecular Crystals*, Elsevier, Amsterdam 1990, Chap. 5.
11. Astbury, W. T. and Bell, F. O. *Nature (London) 141* (1938) 747.
12. Watson, J. D. and Crick, F. H. C. *Nature (London) 171* (1953) 737.
13. Arnott, S., Dover, S. D. and Wonacott, A. J. *Acta Crystallogr., Sect. B25* (1969) 2192.
14. Bugg, C. E., Thomas, J. M., Sunderalingam, M. and Rao, S. T. *Biopolymers 10* (1971) 175.
15. Ts'o, P. O. P. In: Fasman, G. and Timisheff, Eds., *Fine Structure of Proteins and Nucleic Acids*, Dekker, New York 1970.
16. Bergman, E. D. In: Pullman, B., Ed., *Molecular Associations in Biology*, Academic Press, New York 1968, and references therein.
17. Hopfinger, A. J. *Intermolecular Interactions and Biomolecular Organization*, Wiley, New York 1977, Chap. 8, and references therein.
18. Szent-Gyørgyi, A. *Introduction to Submolecular Biology*, Academic Press, New York 1960.
19. von Glehn, M., Kierkegaard, P., Norrestam, R., Rønnquist, O. and Werner, P.-E. *Acta Crystallogr. 24* (1970) 3701.
20. Fritchie, C. F. Jr. and Johnston, R. M. *Acta Crystallogr., Sect. B31* (1975) 454.
21. Eisenschitz, R. and London, F. *Z. Phys. 60* (1930) 491.
22. London, F. *Trans. Faraday Soc. 33* (1937) 8.
23. Heitler, W. and London, F. *Z. Phys. 44* (1927) 455.

24. Pfeiffer, P. *Organische Molekülverbindungen*, 2nd. edn., F. Enke, Stuttgart 1927.
25. Briegleb, G. and Schachowskoy, T. *Z. Phys. Chem., Teil B19* (1932) 255.
26. Mulliken, R. S. *J. Am. Chem. Soc. 74* (1952) 811.
27. Gaultier, J., Hauw, C. and Breton-Lacombe, M. *Acta Crystallogr., Sect. B25* (1969) 231.
28. Szent-Gyørgyi, A. *Proc. Natl. Acad. Sci. USA 74* (1977) 2844.
29. Mulliken, R. S. *Recl. Trav. Chim. 75* (1956) 845.
30. Hassel, O. and Rømming, C. *Quart. Rev. (London) 16* (1962) 1.
31. Dewar, M. J. S. and Thomson, C. C. *Tetrahedron Suppl. 7* (1966) 97.
32. Hannah, M. W. and Lippert, J. L. In: Foster, R. Ed., *Molecular Complexes*, Elek, London 1973, Vol. 1, Chap. 1.
33. Damiani, A., de Santis, P., Giglio, E., Liquori, A. M., Puliti, R. and Ripamonti, A. *Acta Crystallogr. 19* (1965) 340.
34. Damiani, A., Giglio, E., Liquori, A. M., Puliti, R. and Ripamonti, A. *J. Mol. Biol. 23* (1965) 113.
35. Damiani, A., Giglio, E., Liquori, A. M. and Ripamonti, A. *Acta Crystallogr. 23* (1967) 675.
36. Swinton, F. L. In: Foster, R. Ed., *Molecular Complexes*, Elek, London 1974, Vol. 2, Chap. 2.
37. Dahl, T. *Acta Chem. Scand., Ser. A42* (1988) 1.
38. Mulliken, R. S. and Person, W. B. *J. Am. Chem. Soc. 91* (1969) 3409.
39. Caillet, J. and Claverie, P. *Acta Crystallogr., Sect. A31* (1975) 448.
40. Claverie, P. In: Pullman, B., Ed., *Intermolecular Interactions. From Diatomics to Biopolymers*, Wiley, New York 1978, Chap. 2.
41. Castella, M., Millie, P., Piuzzi, F., Caillet, J., Langlet, J., Claverie, P. and Tramer, A. *J. Phys. Chem. 93* (1989) 3941.
42. Emery, L. C., Sheldon, J. M., Edwards, W. D. and McHale, J. L. *Spectrochim. Acta, Part A48* (1992) 715.
43. Cioslowski, J., Mixon, S. T. and Edwards, W. D. *J. Am. Chem. Soc. 113* (1991) 1083.
44. Bader, R. F. W., Slee, T. S., Kremer, D. and Kraka, E. *J. Am. Chem. Soc. 105* (1983) 5061.
45. Morokuma, K. and Kitaura, K. In: Ratajczak, H. and Orville-Thomas, W. J., Eds., *Molecular Interactions*, Wiley, New York 1980, Vol. 1.
46. Nagata, C. and Aida, M. *J. Mol. Struct. (Theochem) 179* (1988) 451.
47. Røeggen, I. *J. Chem. Phys. 79* (1983) 5520.
48. Røeggen, I. and Dahl, T. *J. Am. Chem. Soc. 114* (1992) 511.
49. Røeggen, I. and Dahl, T. *To be published.*
50. Kollman, P., Dearing, A. and Kochanski, E. *J. Phys. Chem. 86* (1982) 1607.
51. Castella, M., Millie, P., Piuzzi, F., Caillet, J., Langlet, J., Claverie, P. and Tramer, A. *J. Phys. Chem. 93* (1989) 3949.
52. Novick, S. E., Davies, P., Harris, S. J. and Klemperer, W. *J. Chem. Phys. 59* (1973) 2273.
53. Burgmans, A. L. J., Farrar, J. M. and Lee, Y. T. *J. Chem. Phys. 64* (1976) 1347.
54. Aziz, R. A. and Slaman, M. *J. Mol. Phys. 58* (1986) 679.
55. Almenningen, A., Bastiansen, O., Motzfeldt, T. *Acta Chem. Scand. 23* (1969) 2848.
56. Derissen, J. *J. Mol. Struct. 7* (1971) 67.
57. Holtzberg, F., Post, B. and Fankuchen, I. *Acta Crystallogr. 6* (1953) 127.
58. Nahringbauer, I. *Acta Chem. Scand. 24* (1970) 453.
59. Legon, A. C., Millen, D. J. and Rogers, S. C. *J. Chem. Soc., Chem. Commun.* (1975) 580.
60. Foster, R. *Organic Charge-Transfer Complexes*, Academic Press, London 1969.
61. Britt, B. M., Lueck, H. B. and McHale, J. L. *Chem. Phys. Lett. 190* (1992) 528.
62. Maverick, E., Trueblood, K. N. and Bekoe, D. A. *Acta Crystallogr., Sect. B34* (1978) 2777.
63. Saheki, M., Yamada, H., Yosioka, H. and Nakatsu, K. *Acta Crystallogr., Sect. B32* (1976) 662.
64. Kitaigorodsky, A. I. *Organic Chemical Crystallography*, Consulants Bureau, New York 1955.
65. Kitaigorodsky, A. I. *Molecular Crystals and Molecules*, Academic Press, New York 1973.
66. Mason, R. In: Dunitz, J. D. and Ibers, J. A. *Perspectives in Structural Chemistry*, Wiley, New York 1970, Vol. 3.
67. Mirsky, K. In: Schenk, H., Olthof-Hazekamp, R. and van Koningsveld, H., Eds., *Computing in Crystallography. Proceedings of International Summer School 1978*, Delft Univ. Press, Delft 1978.
68. Pertsin, A. J. and Kitaigorodsky, A. I. *The Atom-to-Atom Potential Method*, Springer, Berlin 1987.
69. Lennard-Jones, J. E. *Proc. R. Soc. London 43* (1931) 461.
70. Buckingham, R. A. *Proc. R. Soc. London, Ser. A168* (1938) 264.
71. Williams, D. E. *Acta Crystallogr., Sect. A30* (1974) 71.
72. Williams, D. E. and Houpt, D. J. *Acta Crystallogr., Sect. B42* (1986) 286.
73. Stone, A. J. and Price, S. L. *J. Phys. Chem. 92* (1988) 3325.
74. Hirshfeld, F. L. *Theor. Chim. Acta 44* (1977) 129.
75. Williams, D. E. *Acta Crystallogr., Sect. A28* (1972) 629.
76. Cradwick, P. D., Hall, D. and Wood, M. K. *Acta Crystallogr., Sect. B33* (1977) 2380.
77. Gavezotti, A. *J. Am. Chem. Soc. 113* (1991) 4622 and references therein.
78. Allen, F. H., Kennard, O. and Taylor, R. *Acc. Chem. Res. 16* (1983) 146.
79. Williams, D. E. and Xiao, Y. *Acta Crystallogr., Sect. A49* (1993) 1.
80. Lippincott, E. R. and Schroeder, R. *J. Chem. Phys. 23* (1955) 1099.
81. Hagler, A. T., Huler, E. and Lifson, S. *J. Am. Chem. Soc. 96* (1974) 5319.
82. Dahl, T. *Acta Crystallogr., Sect. B46* (1990) 283.
83. Dahl, T. *Unpublished work.*
84. Busing, W. R. *Acta Crystallogr., Sect. A28* (1972) S252.
85. Allinger, N. L. and Lii, J.-H. *J. Comput. Chem. 8* (1987) 1146.
86. Allinger, N. L. and Young, H. Y. *J. Am. Chem. Soc. 111* (1989) 8551.
87. Caillet, J. and Claverie, P. *Acta Crystallogr., Sect. A31* (1975) 448.
88. Nelson, J. B. and Riley, D. P. *Proc. Phys. Soc. 57* (1945) 477.
89. Bugg, C. In: Bergman, E. D. and Pullman, B., Eds., *The Purines – Theory and Experiment*, Israel Academy of Sciences and Humanities, Jerusalem 1972.
90. Takenaka, A., Shibata, M. and Sasada, Y. *Acta Crystallogr., Sect. C42* (1986) 1336.
91. Goldberg, I. *Theor. Chim. Acta 40* (1975) 271.
92. Shaanan, B. and Shmueli, U. *Acta Crystallogr., Sect. B36* (1980) 2076 and references therein.
93. Mayoh, B. and Prout, C. K. *J. Chem. Soc., Faraday Trans. 2, 68* (1972) 1072.
94. Ishida, T., Doi, M., Ueda, H., Inoue, M. and Scheldrick, G. M. *J. Am. Chem. Soc. 110* (1988) 2286.
95. Prout, C. K. and Wallwork, S. C. *Acta Crystallogr. 21* (1966) 449.
96. Krebs Larsen, F., Little, R. G. and Coppens, F. *Acta Crystallogr., Sect. B31* (1975) 430.
97. Flandrois, S. and Chasseau, D. *Acta Crystallogr., Sect. B33* (1977) 2744.
98. Krygowski, T. M., Anulewics, R. and Kruszewski, J. *Acta Crystallogr., Sect. B39* (1983) 732.
99. Herbstein, F. H., Kapon, M. and Reisner, G. M. *Acta Crystallogr., Sect. B42* (1986) 181.

100. Fritchie, C. J. Jr. *J. Chem. Soc. A* (1969) 1328.
101. Bell, J. D., Blount, J. F., Briscoe, O. V. and Freeman, H. C. *J. Chem. Soc., Chem. Commun.* (1968) 1656.
102. Hanson, A. W. *Acta Crystallogr. 19* (1965) 610.
103. Ikemoto, I., Katagiri, G., Nishimura, S., Yakushi, K. and Kuroda, H. *Acta Crystallogr., Sect. B35* (1979) 2264.
104. Zobel, D. and Ruban, G. *Acta Crystallogr., Sect. B39* (1983) 638 and references therein.
105. Chasseau, D. and Leroy, F. *Acta Crystallogr., Sect. B37* (1981) 454.
106. Chasseau, D., Gaultier, J., Fabre, J. M. and Giral, L. *Acta Crystallogr., Sect. B38* (1982) 1632.
107. Kistenmacher, T. J., Phillips, T. E. and Cowan, D. O. *Acta Crystallogr., Sect. B30* (1974) 763 and references therein.
108. Hanson, A. W. *Acta Crystallogr. 16* (1963) 1147.
109. Bernstein, J. and Regev, H. *Cryst. Struct. Commun.* (1980) 581.
110. Dahl, T. *Acta Chem. Scand 44* (1990) 56.
111. de Boer, J. D. and Vos, A. *Acta Crystallogr., Sect. B24* (1968) 720.
112. Colton, R. H. and Henn, D. E. *J. Chem. Soc. B* (1970) 1532.
113. Dahl, T. *Acta Chem. Scand., Ser. A35* (1981) 701.
114. Bolton, W. *Acta Crystallogr. 17* (1964) 147.
115. Ohashi, Y. *Acta Crystallogr., Sect. B29* (1973) 2863.
116. Ohashi, Y., Iwasaki, H. and Saito, Y. *Bull. Chem. Soc. Jpn. 40* (1967) 1789.
117. Tsuchiya, H., Marumo, F. and Saito, Y. *Acta Crystallogr., Sect. B29* (1973) 659.
118. Pauling, L. *The Nature of the Chemical Bond*, 3rd edn., Cornell Univ. Press, New York 1960, p. 258.
119. Nyburg, S. C. and Faerman, C. H. *Acta Crystallogr., Sect. B41* (1985) 274.
120. Williams, D. E. and Cox, S. R. *Acta Crystallogr., Sect. B40* (1984) 404.
121. Hunter, C. H. and Sanders, J. K. M. *J. Am. Chem. Soc. 112* (1990) 5525.
122. Dahl, T. *Acta Crystallogr., Sect. C41* (1985) 931.
123. Dahl, T. *Acta Chem. Scand., Ser. A29* (1975) 699.
124. Dahl, T. *Acta Chem. Scand., Ser. B40* (1986) 226.
125. Dahl, T. *Unpublished work.*
126. Dahl, T. *Acta Chem. Scand. 47* (1993) 38.
127. Dahl, T. and Fossli, D. *Acta Chem. Scand. To be published.*
128. Mackintyre, W. M., Sing, P. and Werkema, M. S. *Biophys. J. 5* (1965) 697.
129. Sletten, J., Sletten, E. and Jensen, L. H. *Acta Crystallogr., Sect. B24* (1968) 1692.
130. Dahl, T. *Unpublished work.*
131. Basilevsky, M. V., Weinberg, N. N. and Zhulin, V. M. *Theor. Chim. Acta 59* (1981) 373.

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