Electrostatic Energies in the 1,4-Dichlorobenzene Polymorph Crystals: the Role of Charge Density Overlap Effects in Crystal Packing Analysis

by **Jack D. Dunitz***[a]) and **Angelo Gavezzotti***[b])

[a]) Organic Chemistry Laboratory, Swiss Federal Institute of Technology, ETH-Hönggerberg, CH-8093 Zurich
[b]) Dipartimento di Chimica Strutturale e Stereochimica Inorganica, University of Milano, I-20133 Milano

For *Dieter Seebach:*
They that go down to the sea in ships, that do business in great waters:
These see the works of the Lord, and his wonders in the deep[1]).

Electrostatic and polarization energies for the three known polymorphic crystal structures of 1,4-dichlorobenzene, as well as for one particularly stable virtual crystal structure generated by computer search, were calculated by a new accurate numerical integration method over static molecular charge densities obtained from high level *ab initio* molecular-orbital calculations. Results are compared with those from standard empirical atom-atom force fields. The new electrostatic energies, which include charge density overlap (penetration) effects, are seen to be much larger than and sometimes of opposite sign to those derived from point-charge models. None of the four polymorphs is substantially more stable than the others on electrostatic-energy grounds. Molecule-molecule electrostatic energies have been calculated for the more important molecular pairs in each of the four structures; trends are found to be very different from those indicated by point-charge energies or by total energies estimated with a parametric atom-atom force field. Conclusions based exclusively on analysis of intermolecular atom contacts and point-charge electrostatics may need to be modified in the light of the new kind of calculation.

Introduction. – Every crystal structure determined by X-ray analysis provides the answer to a question – what is the molecular structure of the compound? – and simultaneously poses a new question – why did the compound choose to crystallize in that particular crystal structure rather than in another? We can describe in precise metrical detail the intermolecular packing that is found to occur in the new crystal structure (or crystal structures, for polymorphism is turning out to be far more common than previously supposed [1]), and there is usually no shortage of ways to 'explain' the new structure in terms of local intermolecular interactions. By means of energy calculations with empirical-potential functions, we can usually confirm that the new structure corresponds to a minimum in the calculated energy hypersurface, but that is about as far as our present capabilities can go.

For a given molecule of known structure, we still have no good theory that enables us to predict its crystal structure with confidence [2]. There is no deep mystery about this. As far as we can tell, the fundamental physics of supramolecular chemistry are understood. The main problem is that, when molecules are brought into contact, the interaction energy is a complicated function of mutual orientation and distance, with the result that many different packing arrangements of a given molecule can have packing energies within a range of only a few kJ mol^{-1}. For example, for benzene, 30

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[1]) Psalm 107, 23–24.

possible crystal structures are calculated to have lattice energies within a range of 10 kJ mol^{-1} [3]. Similar considerations apply even for crystals built from large molecules where the total lattice energy may amount to several hundred kJ mol^{-1}. Hydrogen bonding is a special case, intermediate in energy between covalent and supramolecular bonding, but, even here, different H-bonding patterns with closely similar energies may be possible. Polymorphism seems to be common among all types and sizes of molecules.

Although there is no rigorous way to partition the potential energy of a crystal into component parts, all sorts of terms have come into use to describe various kinds of interaction that can be taken into account in the energy balance, at least conceptually: electrostatic interactions, donor-acceptor interactions, dipole-dipole and quadrupole-quadrupole interactions, steric repulsion, polarization energy, π-π stacking interactions, and dispersion or *Van der Waals* energy. These are used, sometimes singly and sometimes in combination, by various authors to explain *known* crystal structures in terms of simple models, but their predictive capacity is meager to say the least. At a somewhat higher level, various systems of atom-atom potentials [4] have come into use over the last half-century or so (several reviews are available, see, *e.g.*, [5]). The main assumption here is that only central forces operate between pairs of atoms in different molecules, and that the total interaction energy is the sum of the interactions between all pairs of atoms in the crystal – the additivity assumption. The individual atom-atom-interaction energies include a repulsive term with a steep rise in the energy at small interatomic distances, an attractive term designed to allow for dispersion-type interactions and, sometimes, an additional term for Coulombic interactions. With an exponential function as the repulsive term, the interaction energy between a pair of atoms can then be written as in *Eqn. 1*

$$E_{\mathrm{ij}} = A \exp(-Br_{ij}) - Cr_{ij}^{-6} + q_i q_j r_{ij}^{-1} \tag{1}$$

where A, B, C are (usually) empirical parameters, r_{ij} is the distance between atoms i and j, and q_i and q_j are the charges adopted for the Coulombic contribution. A rigorous definition of an 'atom' in this simple scheme is conspicuously missing, but by 'interatomic distances' we usually mean internuclear distances.

When devising an empirical parametric scheme, economy is a must. An extreme is *Kitaigorodski's* 'universal potential', $E(r) = 3.5\ [8600 \exp(-13r/r_o) - 0.04\ (r/r_o)^6]$, where r_o is the assumed equilibrium distance for each kind of atom pair [6]. In the UNI force field [7], which performs reasonably well in reproducing known crystal structures and predicting unknown ones, each set of parameters A, B, C is regarded as being characteristic of a given pair of elements (that is to say, no distinction is made between intermolecular $C \cdots H$ interactions in crystals of say CH_4, C_2H_4, C_2H_2, C_6H_6, *etc.*, or between intermolecular $H \cdots O$ interactions in crystals of say CH_3OCH_3, $CH_3CH{=}O$, CH_3COOH, etc.). The parameters have simply been fitted to experimental structures and sublimation enthalpies for a wide selection of organic crystals. Coulombic terms can be included in the energy calculation or not, depending on the problem. Other force fields use different parametrization methods, and others attempt to fit atom point charges (or distributed multipoles) to the electrostatic field of the molecule as obtained from a quantum-mechanical calculation, and also to estimate interatomic repulsion, polarization and dispersion terms from the calculated (or experimental) electron density in different ways. There is no general consensus on how precisely this should be done, and several schemes are currently adopted. The ultimate goal of all this is prediction and control of organic crystal structures.

Because of the r^{-6} dependence of the attractive term in *Eqn. 1* and in other widely used computation schemes, intermolecular energy contributions are important only for interactions between atoms in different molecules that are in close contact, that is, between atoms on the molecular peripheries. In the calculated energy, interactions involving nonperipheral atoms at larger distances fade into insignificance. Since the peripheries of organic molecules are mostly H-atoms, this emphasis on close-contact atom pairs has led to a preoccupation in molecular recognition schemes with interactions involving these atoms, such as 'unconventional' or weak H-bonds [8]. Thus, the original H-bonding concept involving (O,N)$-$H$\cdots$(O,N) interactions has been extended to include C$-$H$\cdots$X (X = any peripheral atom) interactions. Whatever its merits for descriptive classification of crystals may be, this view is based on a serious oversimplification. The actual situation regarding intermolecular interactions may be much more complicated.

In a previous paper [9], we discussed the experimental crystal structures of the dichlorobenzenes in terms of energy calculations and qualitative geometrical arguments based largely on intermolecular contacts in the crystals. We contrasted the absence of explicit electrostatic terms in the UNI force field with their obligatory presence as an intrinsic feature of other force fields, in particular the *Williams* force field [10]. The dichlorobenzene crystal structures are characterized [11] by intermolecular Cl$\cdots$Cl distances that are markedly less than the traditional *Van der Waals* diameter of a Cl-atom (3.6 Å) and by unfavorable dispositions of C$-$Cl bond dipoles; in fact, the β-polymorph of the 1,4-isomer contains an almost linear C$-$Cl$\cdots$Cl$-$C contact with a Cl$\cdots$Cl distance as short as 3.38Å. It has been pointed out that, according to standard atom-atom potential functions, such a contact should be associated with a repulsive interaction, and that introduction of standard Coulombic charges (negative charge on Cl, positive on C) would not improve the matter. The presence of this short contact does not prevent the β-polymorph from having a packing energy quite similar to that of the other polymorphs.

The trouble with such qualitative geometric arguments is that they are based on what seems like an obvious, more-or-less standard partitioning of the structure into supposedly 'main' or 'structure-defining' interactions between certain atoms, in this case the short intermolecular Cl$\cdots$Cl contacts. But this way of looking at the structure overlooks the many-body aspect of the problem. What is important is not necessarily the interactions among individual atoms in the different molecules that attract (or, at short distances, repel) one another, however plausible that may seem, but the overall interaction between the charge densities, including their mutual polarization. This clearly calls for a different kind of computational approach: it would appear that one needs not just *a* force field, but rather *the* force field for a given molecule. Typological classification and description should give way to first principles. Recently, an accurate method for the calculation of electrostatic energies in molecular crystals has been developed [12]. Here, we apply this method to the actual and virtual crystal structures of 1,4-dichlorobenzene, consider possible applications to the refinement of existing force fields, and ask to what extent conclusions based on qualitative examination of specific atom-atom interactions are substantiated by the results of the accurate electrostatic calculations.

In passing, we once again underline the usefulness of virtual crystallography, the construction of plausible crystal structures for a given molecular structure with preconceived structural or energetic characteristics. Far from being the by-product of a frustrated crystal-structure prediction, carefully chosen virtual structures can help to illuminate the discussion of intermolecular interactions and packing effects. We include discussion of a possible orthorhombic structure, which is calculated to be particularly stable but has never been observed.

Intermolecular Interaction Energies. – The new method involves the calculation of part of the intermolecular interaction energy by direct numerical integration over electron densities [12]. It starts by a calculation of the valence-only molecular-electron density by standard quantum-mechanical programs (GAUSSIAN98 [13] was used here) at the MP2 6-31G** level. The original calculated density is expressed in terms of a large number (several millions) of charge pixels. It is then condensed by formation of super-pixels that contain the charge present in a cubic box of $n \times n \times n$ original pixels, n being called the condensation level. Charge pixels below a certain minimum charge threshold, q_{min}, usually of the order of 10^{-6} or 10^{-7} electrons, are then screened out. These measures reduce the number of pixels, N_{P}, in a molecular electron density to something of the order of 10^4. This condensed density distribution is then packed into the crystal structure, undeformed and unpolarized, just as in a rigid molecule (this is, of course, a restrictive assumption because the actual electron density of a molecule in a crystal is modified by the presence of neighbouring molecules). The electrostatic energy between any two molecules in the crystal is then obtained as a double sum of Coulombic terms over pixels, plus a pixel-nuclei and a nuclei-nuclei sum:

$$E_{\mathrm{AB}} = 1/(4\pi\varepsilon^{\circ})\ [\Sigma\Sigma\ q_i\ q_j/r_{ij} + \Sigma\Sigma\ q_i\ Z_j/r_{ij} + \Sigma\Sigma\ Z_i\ Z_j/r_{ij}] \qquad (2)$$

where q_i and Z_j are the charges on pixel i and nucleus j, respectively, r_{ij} is a pixel–pixel, pixel–nucleus or nucleus–nucleus distance in turn, and ε° is the vacuum permittivity. In addition, the electric field ε_i at any pixel within one molecule due to the electron densities of all surrounding molecules in the crystal is also evaluated, and a pixel polarizability, α_i, is defined by an empirical partitioning of atomic polarizabilities, as described in [12]. The polarization energy is then computed by the standard linear polarization formula:

$$E_{\mathrm{POL}} = 1/(4\pi\varepsilon^{\circ})\ \Sigma\Sigma\ 1/2\ \alpha_i\ \varepsilon_i^2 \qquad (3)$$

The calculated molecular electron density corresponds to that of a rigid, gas-phase molecule at 0 K and does not include dynamic polarization, that is, the deformation due to the influence of the electrostatic field of neighboring molecules. The electrostatic energy (*Eqn. 2*) is a balance between positive and negative terms. It can be either net stabilizing or destabilizing. Since the polarization energy arises from the compliance of a charge distribution to the field generated by its neighbors, its net effect is always stabilizing. Polarization is not treated explicitly in empirical schemes, being incorporated implicitly together with dispersion in the parameter C of the stabilizing term of *Eqn. 1*.

Dispersion forces are always present between molecules. They have a quantum-mechanical origin in the sense that they result from the correlated motion of the electrons in the molecules. Dispersion forces are ubiquitous in condensed phases of all chemical substances and are always attractive. An accurate calculation of such forces would be extremely complicated, but they are approximately proportional to the product of the molecular polarizabilities and inversely proportional to the sixth power of the intermolecular separation. In our electron-pixel model of intermolecular interactions, the dispersion energy can be approximated in principle, once the local polarizabilities α_i have been defined, as indicated above; however, the details of such a treatment have not yet been fully worked out. In empirical schemes, the dispersion energy is seldom evaluated separately and is usually incorporated in the second coefficient of *Eqn. 1*.

Contiguous, partly overlapping molecular-electron densities also generate exchange or *Pauli* repulsion, involving exclusion of electrons with the same spin from the same region of space. This purely quantum-mechanical effect prevents molecules from merging into each other and is at the origin of the small compressibility of condensed phases. Exchange repulsion can be taken as being proportional to overlap [14], which is also determinable in our electron-pixel scheme. As for the dispersion energy, here again the treatment is at an advanced stage of development but not yet fully worked out. We must, therefore, still resort to empirical estimates for dispersion and repulsion contributions [8], as required.

Crystal Structures of 1,4-Dichlorobenzene. – *Table 1* summarizes experimental information about the three known polymorphs of 1,4-dichlorobenzene as determined by X-ray diffraction at 100 K [11] plus the best virtual structure obtained in our previous study [9]. Since computational crystal structures are energy-optimized without regard of kinetic energies, they are formally 0 K structures. For comparison with the known structures, the virtual crystal structure (in space group *Pbca*) was expanded to obtain estimated unit-cell parameters at 100 K and at room temperature. This was done by assuming a 2% cell volume increase for each 100 K, as judged from

Table 1. *1,4-Dichlorobenzene Polymorphs: Structural Data, Short Atom-Atom Contacts and Lattice Energies Computed by* Williams (*W*) *or UNI Force Field Potentials*

Phase	Space group, temperature	Z	V_{cell}/ Å^3	Cl···Cl/Å	Cl···H/Å	$-E(W)$/ kJ mol^{-1}	$-E$(UNI)	$-E$qq[a])/kJ mol^{-1}	
								ESP	MUL
α	$P2_1/a$, 100 K	2	306.8	3.73	2.89, 3.01, 3.02	64.7	65.5	4.8	0.9
β	$P\bar{1}$, 100 K	1	153.5	3.39	2.97, 3.00, 3.03	63.7	65.7	4.0	0.2
β	$P\bar{1}$, r.t.	1	159.4	3.42	2.99, 3.03	–	63.8	–	–
γ	$P2_1/c$, 100 K	2	305.4	3.80, 3.82	2.89, 3.10	60.9	66.4	5.7	7.9
Virtual	*Pbca*, 0 K	4	579.6	3.62	2.91	63.4	68.3	3.5	6.1
	Pbca, 100 K	4	593.6	–	–	64.0	71.0	3.5	–
	Pbca, 298 K	4	615.1	–	–	64.0	71.4	3.5	–

[a]) Coulombic point charge energies by ESP or *Mulliken* charges (see text).

measurements of the β-phase [15] and in line with statistics on the expansion coefficients of organic compounds [16]. Lattice energies computed with the *Williams* force field and the UNI force field are around 60 to 65 kJ mol^{-1} for all four polymorphs but give different energy ordering. For comparison, the experimental heat of sublimation of 1,4-dichlorobenzene (unknown polymorph) is 64.9 kJ mol^{-1} [17]. As shown experimentally, the γ-phase is the most stable one at low temperature, but this is not reflected by either of the computational schemes.

Table 1 also includes the electrostatic energy calculated for each structure with estimated point charges on the atomic nuclei (corresponding to the third term in *Eqn. 1*) for both *Mulliken* and ESP charges. The former are derived from *Mulliken* population analysis [18] and the latter by optimal fitting of atomic charges to reproduce the calculated electric field of the molecule as closely as possible. The charges themselves are quite different (ESP in parentheses): Cl, $+0.004$ (-0.097), C(Cl), -0.130 (-0.001), C(H), -0.093 (-0.070), H, $+0.156$ ($+0.119$), and, correspondingly, so are the calculated electrostatic energies. Both kinds of atomic charge are in common use but they have no real theoretical basis, since the charge of an atom in a molecule can neither be measured nor defined in a unique manner. In any case, *Table 1* shows that, for these crystal structures, the electrostatic energy given by both kinds of atom point charges is less than 10% of the lattice energy calculated with the respective force fields of the exp-6 type (the first two terms in *Eqn. 1*).

In calculations based on *Eqn. 1*, each term corresponds only in a very rough manner to what it is supposed to represent. The electrostatic energy (as given by the third term) comes out merely as a small correction factor. In our more rigorous calculation, the electrostatic energy is many times more stabilizing than that obtained by localized atomic point charges. However, since total lattice energies calculated by *Eqn. 1* compare favorably with sublimation energies, the only possible conclusion is that the electrostatic energy is already implicitly included, although in an indirect and somewhat cryptic manner, in the balance of the first two terms of *Eqn. 1*.

Electrostatic and Polarization Energies. – Results of calculations made with the new electrostatic-energy program at the MP2 6-31G** level are shown in *Table 2*. The molecules have slightly different dimensions in the four polymorphs, but the maximum difference in molecular electronic energy between them is only *ca.* 1 kJ mol^{-1}. The untreated charge densities consisted of $99 \times 107 \times 169$ points, for a step of 0.088 Å. Differences between the two levels of condensation are small, but they are large enough to reverse the energy ordering between α- and β-phases, for example. The electrostatic energies in *Table 2* are seen to be many times larger than those estimated by the point-charge models and to be slightly less than half of the lattice energies as given by the empirical force fields (*Table 1*).

In a crystal, the electron density of one molecule overlaps a little with those of the neighboring ones. On the one hand, overlap means electron-electron repulsion, but, on the other hand, the peripheral fringes of the electron density of one molecule come into closer contact with the nuclei of neighboring molecules. Before exchange repulsion and nucleus-nucleus electrostatic repulsion come drastically into play, there is a borderline region where net repulsion or attraction depends on a very subtle balance. This energy contribution due to overlap is present in our calculation but is missing in localized,

Table 2. *Coulombic and Polarization Energies of 1,4-Dichlorobenzene Polymorphs by the Electron-Pixel Integration Method*

	Number of e-pixels a)		Number of molecules b)	$-E$(coul) /kJ mol^{-1}		$-E$(pol) /kJ mol^{-1}	
	$n=4$	$n=5$		$n=4$	$n=5$	$n=4$	$n=5$
α	12009	6531	213	25.8	24.5	6.6	6.5
β	11995	6524	223	23.5	24.9	6.7	6.6
γ	12018	6542	221	26.3	26.0	7.0	7.0
Pbca, 0 K	12015	6519	225	29.2	33.6	10.6	10.3
Pbca, 100 K	12015	6519	225	25.6	–	8.4	–
Pbca, r.t.	12015	6519	205	21.6	–	6.1	–

a) All e-pixels with charge less than 10^{-7} electrons are screened out. b) All molecules with distance between centers of mass < 20 Å are included.

point-charge schemes. The difference between the rigorous electrostatic energy and the electrostatic energy obtained by a contracted computational scheme, such as a point-charge approximation or a distributed multipole scheme, is known as the penetration energy. [19] It has been shown [12] that the present method of calculating electrostatic energies qualifies as rigorous in this respect.

As mentioned, the virtual *Pbca* structure was expanded to obtain estimated unit-cell parameters at 100 K and at room temperature. This expansion produces an increase in all interatomic intermolecular distances in the crystal, and the calculated electrostatic and polarization energies are extremely sensitive to this. Thus, the relatively small changes in cell dimensions on passing from 0 to 300 K lead to a 40% decrease in both types of energy contribution, underlining the critical importance of closest possible packing for maximizing the lattice energy in crystals. As we have remarked elsewhere: as far as the packing energy is concerned, empty space is wasted space [20].

Polarization energies also are significantly different among the four structures, but their trend is the same as the trend in electrostatic energies, in partial justification of the neglect of the former in all empirical force fields. The polarization energies amount to *ca.* 10% of the lattice energies, and the sum of electrostatic and polarization energies is thus considerably less than the sublimation enthalpy for all four structures. This is not too surprising as the two quantities are not comparable, because of our temporary neglect of other contributions (exchange and dispersion energies). As discussed in [12], for some crystal structures the sum of electrostatic and polarization energies is larger than the sublimation enthalpy, for some it is smaller. However, as compensation for these deficiencies in the present calculations, the electrostatic energies in *Table 2* are not subject to arbitrary assumptions about atomic charges and are in that sense rigorous.

The *Pbca* structure was calculated to have the best packing energy according to the empirical chargeless UNI force field, and it also has the best electrostatic and polarization energies according to the new calculations. Thus, the failure of the chargeless UNI force field to predict the observed structures as the most stable ones is not due to its lack of explicit electrostatic terms. Yet, this apparently very favorable *Pbca* structure has never been observed. The reasons for this are open to discussion, one possibility being the unfavorable nucleation or growth rate of the corresponding crystal embryos in solution or in the melt.

Molecular-Packing Analysis. – For a detailed examination of the molecular packing, the lattice electrostatic energy has been partitioned over each pair of neighbour molecules in the various polymorphs (*Tables 3–6*). Each pair is characterized by a center of mass distance (d), a symmetry operator (S screw, T translation), and a molecule-molecule total energy as calculated by the UNI force field, as well as the electrostatic energy. This kind of partitioning is possible for the electrostatic energy, which is additive over molecules, but it is meaningless for the polarization energy because the polarizing electric field at any point in one molecule results from the contributions of all surrounding molecules.

Table 3. *1,4-Dichlorobenzene, α-Structure: Molecule–Molecule Distances and Energies between Close Neighbors*

Pair label	Symmetry operation[a]	d/Å	$E(4)$[b]/kJ mol^{-1}	$E(5)$[c]/kJ mol^{-1}	$E(\mathrm{UNI})$[d]/kJ mol^{-1}
A	T (0,0, ± 1)	3.92	− 4.8	− 2.8	− 23.4
B	T (0, ± 1,0)	5.74	− 5.6	− 5.2	− 12.4
C	T (0,1,1; 0, − 1, − 1)	6.95	− 4.7	− 5.2	− 6.3
D	S (1/2,1/2,0; − 1/2,1/2,0); (− 1/2, − 1/2,0; 1/2, − 1/2,0)	7.87	− 2.1, − 2.3	− 2.3, − 2.4	− 4.5
E	S (1/2,1/2,1; − 1/2,1/2, − 1); (− 1/2, − 1/2, − 1; 1/2, − 1/2,1)	7.49	− 2.6, − 2.9	− 2.7, − 3.0	− 4.0
F	T (0,1, − 1; 0, − 1,1)	6.95	+ 0.1	+ 0.2	− 1.8

[a] For each pair, the symmetry operation is either translation (T) or screw axis (S). [b] Electrostatic energy, condensation level 4. [c] Electrostatic energy, condensation level 5. [d] Energy by the UNI empirical force field.

Table 4. *1,4-Dichlorobenzene, β-Structure: Molecule–Molecule Distances and Energies between Close Neighbors.* See footnotes to *Table 3*.

Pair label	Symmetry operation	d/Å	$E(4)$/kJ mol^{-1}	$E(5)$/kJ mol^{-1}	$E(\mathrm{UNI})$/kJ mol^{-1}	E_{qq}[a]
A	T (0,0, ± 1)	3.88	− 4.3	− 5.3	− 23.9	+ 2.0
B	T (0, ± 1,0)	5.87	− 4.6	− 4.1	− 11.8	− 2.2
C	T (1,0,1; − 1,0, − 1)	6.83	− 5.6	− 6.0	− 7.1	− 2.2
D	T (± 1,0,0)	7.30	− 4.0	− 5.0	− 6.7	− 1.9
E	T (0,1,1; 0, − 1, − 1)	6.98	− 5.1	− 4.2	− 6.5	− 1.9
F	T (1,1,1; − 1, − 1, − 1)	8.75	+ 0.8	+ 0.8	0	+ 0.7
G	T (− 1,1,0; 1, − 1,0)	9.56	− 1.0	− 1.4	− 1.2	+ 1.0

[a] Electrostatic energy calculated by point-charge methods.

Tables 3–6 list the molecule-molecule energies $E(4)$ and $E(5)$ calculated for different condensation levels. They are seen to vary by 1–2 kJ mol^{-1}. This is disturbing for the discussion of fine detail of crystal packing but it is almost unavoidable. Net electrostatic energies are tiny differences between two large numbers; on the one hand, the sum of the nuclei-nuclei and electron-electron repulsion energies, of the order of 500,000 kJ mol^{-1}, and the overall electron-nuclei attraction energy, which is of the same order of magnitude. The resulting net energies may differ slightly depending on several factors, including condensation level, screen-out threshold, symmetrization of the

Table 5. *1,4-Dichlorobenzene, γ-Structure: Molecule–Molecule Distances and Energies between Close Neighbors.* See footnotes to *Table 3.*

Pair label	Symmetry operation	d/Å	$E(4)$/kJ mol^{-1}	$E(5)$/kJ mol^{-1}	E(UNI)/kJ mol^{-1}
A	S (0,1/2,1/2; 0, – 1/2,1/2); (0, – 1/2, – 1/2; 0,1/2, – 1/2)	4.87	– 4.7, – 5.1	– 5.0, – 5.6	– 15.9
B	T (0,± 1,0)	6.02	– 6.4	– 6.9	– 10.5
C	T (1,0,1; – 1,0, – 1)	7.17	– 6.3	– 4.5	– 5.6
D	S (1,1/2,1/2; 1, – 1/2,1/2); (– 1, – 1/2, – 1/2; – 1,1/2, – 1/2)	7.63	– 2.1, – 2.3	– 2.2, – 2.3	– 2.1
E	T (0,0,± 1)	7.41	+ 0.1	+ 0.1	– 1.1
F	T (1, – 1,1; – 1,1, – 1)	9.37	– 0.4	– 0.4	– 2.3
G	T (1,1,1; – 1, – 1, – 1)	9.37	+ 0.5	+ 0.5	0

Table 6. *1,4-Dichlorobenzene,* Pbca *Virtual Structure: Molecule–Molecule Distances and Energies between Close Neighbors.* See footnotes to *Table 3.*

Label	Symmetry operation	d/Å	$E(4)$/kJ mol^{-1}	E(UNI)/kJ mol^{-1}
A	S along b	5.55	– 6.5	– 12.7
B	S along a	5.94	– 7.7	– 8.7
C	S along c	6.46	– 1.6	– 8.0
D	T (0,± 1,0)	6.99	+ 2.8	– 3.6
E	T (0,0,± 1)	8.63	+ 0.3	– 1.3

electron-density distribution, and merely that the 'atoms' in our model are not spherical but agglomerates of cubes. (This factor alone causes the electrostatic energy of an Ar crystal to deviate from zero by 1–2 kJ mol^{-1} even at the best condensation level.) However, the differences between calculations at different condensation levels must cancel themselves out to some extent, because they are about the same for total electrostatic energies as for individual molecular pair energies. There are also small differences (up to 0.4 kJ mol^{-1}) between electrostatic energies of pairs related by symmetry-equivalent screw axes. These can probably be attributed to lack of precise rotational invariance of the electron-density distribution.

The electrostatic energies of all molecule-molecule pairs for distances up to 20 Å are shown graphically in *Fig. 1* for the α-structure, and quite similar results are obtained for the others. For all four crystal structures, the pair-pair energies converge to zero for distances greater than about 10 Å. Furthermore, the four structures have quite similar molecule-molecule energy distributions (see also *Tables 3–6*), showing that, as far as electrostatic energy is concerned, there are no major differences in the coordination patterns. Not more than four or five molecular pairs make significant contributions to the electrostatic energy; they are the closest pairs and also those that give the highest UNI energy contributions. However, some of the electrostatic pair energies are calculated to be slightly destabilizing ($E_{el} > 0$), whereas none are destabilizing according to UNI potentials, which include dispersion, polarization, and electrostatic energies in an unspecified mixture.

Coming to packing details, we note first that, for the α- and β-structures, the three closest neighbor pairs A, B, C, all involving translationally related molecules, are practically the same (*Tables 3* and *4*). The A interaction involves molecular stacking

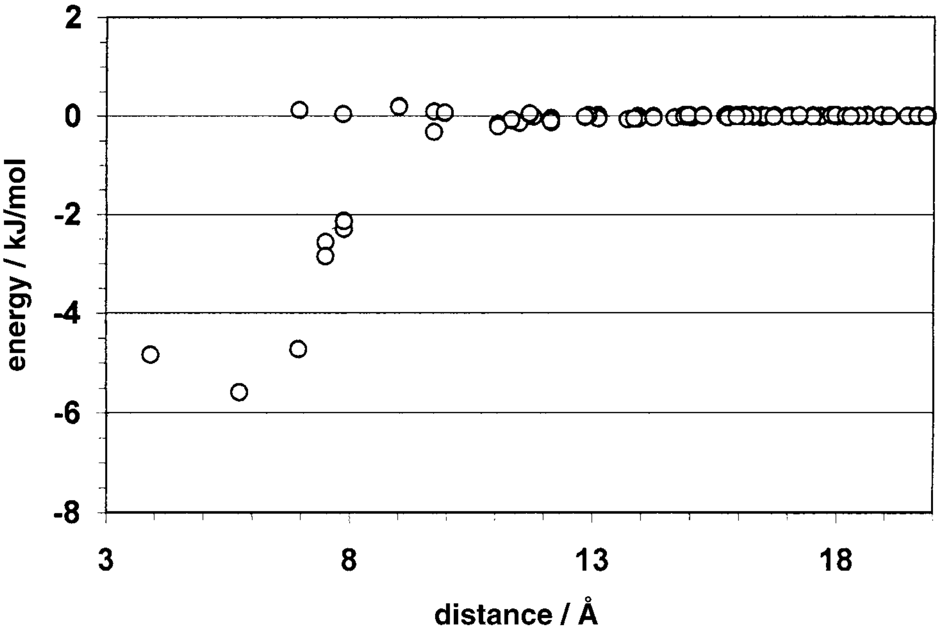

Fig. 1. *1,4-Dichlorobenzene, α-structure: dependence of the electrostatic molecule-molecule energy on distance between molecular centers of mass.* The trend is the same in all polymorphs and independent of computational details.

along the short crystal axis (3.92 Å in α, 3.88 Å in β), as illustrated in *Fig. 2*. As the electrostatic energy for this pair is only -3 to -5 kJ mol^{-1}, compared with the corresponding UNI energy of *ca.* -24 kJ mol^{-1}, we can assume that the major part of the interaction energy comes here from the dispersion term; interestingly, the point-charge electrostatic energy for this pair is destabilizing. The B interaction involves a slipped stack along a 5.7–5.8 Å translation (*Fig. 3*) and again the electrostatic energy is less than half the UNI energy for both α- and β-structures. This same motif appears in the B pair of the γ-structure. Finally, the C interaction involves displacement by 6.8–6.9 Å almost in the plane of the benzene ring (*Fig. 4*). Although the molecule-molecule distance in the C pair is greater than in the A and B pairs, its electrostatic energy is the lowest and in this case quite comparable with the corresponding UNI energy. As seen in *Fig. 4*, the C arrangement is characterized by quite short intermolecular H···Cl contacts (2.970 Å).

The remarkably short C–Cl···Cl–C contact distance of 3.38 Å in the β-structure occurs in the translation related G pair (*Table 4* and *Fig. 5*). This is the prototype of the nearly linear type-I contact of *Desiraju* and *Parthasarathy* [21], which is frequently observed in Cl-containing organic compounds. In spite of the short Cl··· Cl distance and the unfavorable disposition of bond dipoles, the electrostatic-energy contribution for this molecular pair is *ca.* -1 kJ mol^{-1} and, hence, slightly stabilizing. A similar result is obtained for the UNI energy. Although the juxtaposition of negative charges on the Cl-atoms is energetically unfavorable as far as localized point charges are concerned,

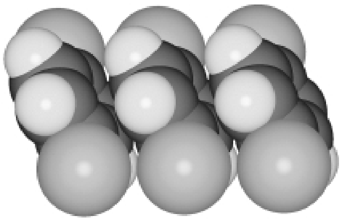

Fig. 2. *The A-motif* (see *Tables 3* and *4*) *in the α- and β-structures.* The Cl ··· Cl distance is 3.92 Å.

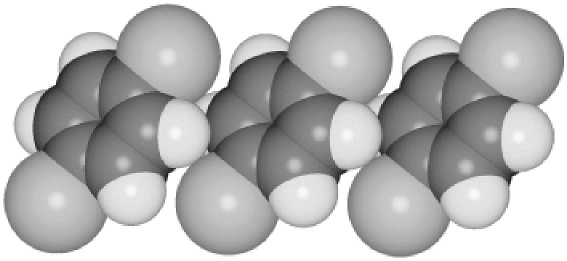

Fig. 3. *The B-motif* (see *Tables 3* and *4*) *in the α- and β-structures*

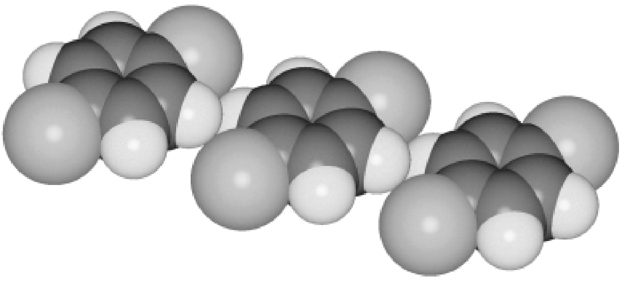

Fig. 4. *The C-motif* (see *Tables 3* and *4*) *in the α- and β-structures.* The shortest Cl ··· H distances are *ca.* 2.97 Å.

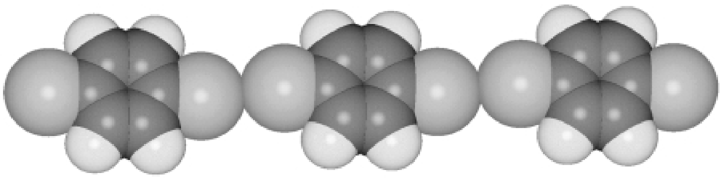

Fig. 5. *The controversial G-motif in the β-structure with head-on C–Cl groups.* The Cl ··· Cl distance is 3.39 Å.

penetration effects may be assumed to stabilize the system. In any case, the linear type-I interaction evidently plays only a very minor role as far as its contribution to the lattice energy is concerned. We note that the F pair in the γ-structure corresponds to a similar type-I contact with a longer Cl ··· Cl distance of 3.82 Å, and is likewise insignificant as

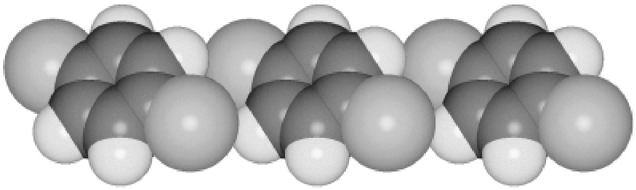

Fig. 6. *Another kind of translational pattern found in the β-* (D- and E-motifs) *and γ-* (C-motif) *structures.* Note the short Cl ··· H distances (*ca.* 3.03 Å).

far as its electrostatic energy is concerned. Other nearest-neighbor pairs involving translation are the D and E pairs of the β-structure, and the C pair of the γ-structure (*Fig. 6*). These seem to be stabilized by confrontation of positively charged H-zones and negatively charged Cl-zones, with Cl ··· H contact distances of *ca.* 3 Å.

Other, completely different motifs appear in the monoclinic structures, along screw axes or glide planes (*Fig. 7*). To this category belong the D and E pairs of the α-structure, as well as the D-motif in the γ-structure. Of the same type, but more closely packed, is the A-motif in the γ-structure (*Fig. 8*). These motifs seem to gain stabilization from diffuse interactions that are not easily sorted out, but including juxtaposition of positively charged H-zones and negatively charged Cl-zones. The Cl ··· H distances here are in a quite normal range.

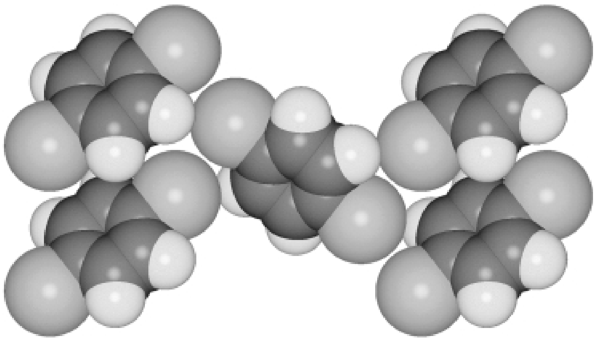

Fig. 7. *A typical, loose herring-bone pattern in the monoclinic α-* (D- and E-motifs) *and γ-* (D-motif) *structures*

Finally, *Fig. 9* shows a prototypical electrostatically destabilizing arrangement, appearing in the F pair of the β-structure and the G pair in the γ-structure. Although the H ··· H distances of 4.6 Å are longer than normal contact distances and would hardly have been considered worth discussing in traditional packing analyses, the electrostatic interaction between positively charged H-zones is significantly different from zero. Here, penetration effects are insignificant because the H-atom electron cloud is very contracted. Both these examples of electrostatically destabilized pairs involve parallel molecules with H ··· H confrontation, and so does the D pair in the virtual *Pbca* structure (*Fig. 10*). This is the most extreme in this respect with an electrostatic energy of $+2.8$ kJ mol^{-1}, although the corresponding UNI energy is stabilizing (-3.6 J mol^{-1}). Such electrostatically destabilized pairs are rather common in organic crystal structures [12].

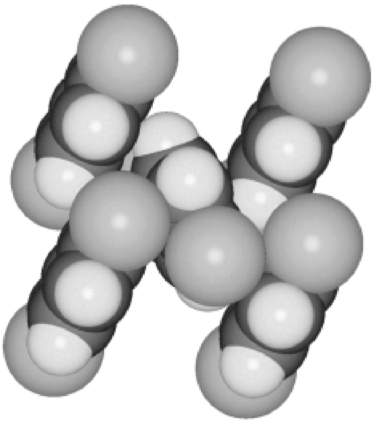

Fig. 8. *A more closely packed herring-bone pattern in the* γ-*structure* (A-motif)

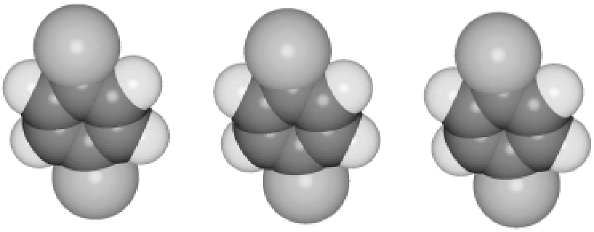

Fig. 9. *An electrostatically destabilizing pattern found in the* β *structure* (F-motif) *with shortest H ··· H distance of 4.62 Å*

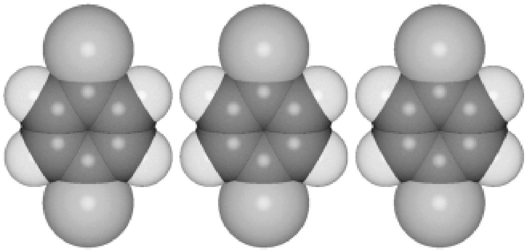

Fig. 10. *An electrostatically destabilizing pattern found in the virtual* Pbca *structure with shortest H ··· H distance of 2.72 Å and Cl ··· Cl distance 6.99 Å*

It would appear from the above analysis that, in the three observed crystal structures of 1,4-dichlorobenzene and in the best virtual structure obtained by force-field calculation, electrostatic stabilization can arise from a variety of molecule-molecule interactions, involving mainly C ··· H or Cl ··· H intermolecular contacts. Stacking seems to be slightly more efficient in this respect than herring-bone patterns. In particular, the $P\bar{1}$ space group of the β-structure requires all molecules to be parallel, so that herringbone patterns are impossible; the structure nevertheless gets along very well with sheared parallel planes.

Outlook. – In contrast to force-field calculations based on *Eqn. 1*, the electrostatic energy calculated with *Eqn. 2* is parameter-free and exact (apart from rounding-off errors arising from condensation level, imperfect symmetrization, *etc*). The polarization energy calculated with *Eqn. 3* does depend on an empirical partitioning of atomic polarizabilities, as described earlier, but it is not adjustable in the sense that force-field parameters are. Thus, as far as our new calculations go, the results are more rigorous than those derived from parametric schemes. However, unlike the latter, they cannot be compared quantitatively with experimental lattice energies because the missing parts – exchange repulsion and dispersion energies – are of magnitude comparable to the electrostatic and polarization energies that are included. The value of our results is not that they yield approximate lattice energies but rather that they shed new light on crystal-packing factors and sometimes run counter to widespread interpretations of the structural evidence based on parametric models. Even if, as foreseen, the pixel-pixel approach will be adapted to the full calculation of intermolecular energies, the question will arise as to whether it will be applicable to crystal-structure prediction for large molecules or to the prediction of protein folding. This may not be possible with present computational power, but we are encouraged to believe that it will be before very long.

One rather clear result in *Tables 1* and *2* is that electrostatic energies derived from atomic point charges (*Mulliken* or ESP) are much smaller than the actual electrostatic energies. There are also differences in sign and, hence, in the chemical meaning of the message conveyed by the calculation. The comparison of UNI energies with electrostatic energies (*Tables 3–6*) suggests that, to make up for this deficiency, UNI energies contain a considerable electrostatic component, with the implication that large dispersion energies tend to go together with large electrostatic energies. Similar considerations apply to other parametric schemes. They yield good lattice energies but give a false impression of the importance of the underlying energy terms.

The introduction of penetration energy may change the current view of electrostatically attractive or repulsive intermolecular atom contacts in crystals. Compared with point-charge models, even those adapted to reproduce the electrostatic field of the molecules, penetration effects produce a substantial increase in intermolecular electrostatic energies. In some cases, this completely alters the chemical interpretation. Although the numerical results change a little with condensation level, these calculations clearly show that in this head-on approach the electrostatic energy of the dimer is not monotonic destabilizing, as is the point-charge energy, but stays essentially close to zero until the sharp onset of repulsion at a Cl $\cdots$ Cl distance just below 3.4 Å. A very similar conclusion was reached in a careful quantum-chemical study [22] of chloromethane dimers, using *ab initio* intermolecular perturbation theory (IMPT). As a check, these calculations for chloromethane dimers have been repeated with our scheme, and the same results were obtained for electrostatic energies within a few kJ mol^{-1}. Similarly, the total electrostatic energy of the hexachlorobenzene crystal is calculated to be stabilizing but it is destabilizing according to a point-charge energy calculation [12]. Thus, interpretations of the Cl $\cdots$ Cl interactions in crystal structures based on simple localized charge distributions are unreliable and should be regarded with reserve²). Indeed, the extent to which Cl ··· Cl interactions play a significant role in steering the molecular arrangement within a crystal depends not directly on electrostatic factors but rather on dispersion. On the other hand, confrontation of H-atoms in the mutual approach of molecules is always electrostatically repulsive according to the rigorous calculations, a result that will come as no surprise. Penetration plays a lesser role here because the H-atom charge is so small and contracted.

One question in packing analysis that may be of concern in the light of our results is, to what extent do r^{-1} interactions between molecular charge distributions translate into interactions between individual atoms? Ever since *Kitaigorodski*'s pioneering work on crystal packing [6] and with the development of atom-atom potential schemes, attention has been focussed almost exclusively on the role of interactions between atoms in different molecules that are 'in contact'. By this is generally meant that the separation between the atoms concerned is less than R^{eq}, the distance where the atom-atom potential curve has zero slope, where attractive and repulsive forces exactly balance. These zero-slope distances vary somewhat among atom-atom potentials preferred by different authors, but not by much. According to this picture, the dominating features of a molecular crystal structure involve the points where molecules come into contact with one another, and much of the literature on the interpretation of observed crystal structures has been concerned with the identification of recurring patterns and the assessment of the relative importance of various localized structure-directing interactions. The analysis of close intermolecular contacts is especially appealing in terms of atom-atom pair potentials and has indeed been of great help in estimating values of the adjustable parameters of such force fields to reproduce observed contact distances.

However, it is obvious that the only atoms that can come into contact with those of neighboring molecules in molecular organic crystals are those on the molecular peripheries (mostly limited to univalent H, F, Cl, *etc.*, but also divalent O and trivalent N). To balance the net intermolecular attraction, the forces between pairs of atoms in intermolecular contact must be repulsive (although they may correspond to negative potential energy, *i.e.*, be stabilizing). In empirical force fields of the type described by *Eqn. 1*, the role of contact atom pairs in stabilizing the crystal structure is greatly overemphasized because of the r^{-6} dependence of the attraction-energy term. The distances between other noncontact pairs are large enough that their contributions in an r^{-6} dependence scheme become negligible. On the other hand, the new electrostatic-energy calculation with its r^{-1} dependence shows that stabilizing interactions between electrons in one molecule and atomic nuclei in the other are important at much longer distances. Thus, the contact atom pairs that occur in molecular crystals should not necessarily be considered as the prime promoters of the intermolecular

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²) As an extreme example, consider a vastly oversimplified electrostatic interpretation involving the dipole moment of chlorobenzene, 1.69 D. The C−Cl bond distance is *ca.* 1.72 Å, so, if the charge separation is assumed to be localized in this bond, equal and opposite charges of 1 q (q = electronic charge) are associated with each atom. For such charges, the electrostatic energy for the head-on C−Cl ··· Cl−C approach of two such molecules at a Cl ··· Cl distance of 3.38 Å would amount to *ca.* 400 kJ mol⁻¹, compared with the correct result of approximately zero. Even if the 'length' of the dipole is taken as the length of the molecule (*ca.* 5.2 Å), the approach energy would still amount to an impossible value.

attraction but rather as a result of longer-range effects. This change in outlook, if confirmed by further analyses, suggests that we may need to revise some of the conclusions derived from too-exclusive attention to close intermolecular contacts in crystals – and other supramolecular assemblies as well. While concepts such as surface complementarity will doubtless retain their validity in the broad context of molecular recognition, they may have to be modified to take into consideration electrostatic forces extending past the surface atoms into the interior of the interacting molecules.

The molecular pictures in this paper were drawn with the program SCHAKAL [23].

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