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Crystal Structures from Nonempirical Force Fields

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Abstract

Until recently, structure and properties of molecular crystals could not be predicted computationally since the forces acting between the constituent molecules in crystals were not known sufficiently accurately. This situation has changed with the development of an electronic structure method called symmetry-adapted perturbation theory based on the density-functional description of monomers [SAPT(DFT)]. This method is sufficiently efficient to be applied to interactions of energetic molecules, for example to cyclotrimethylene trinitramine (RDX). Systems even larger than RDX can be treated, for example, interaction energies for the dimer of perylene, containing 64 atoms, have been computed using SAPT(DFT). The SAPT(DFT) potential developed for RDX was used in a combined molecular packing, lattice energy minimization, and molecular dynamics approach to characterize low-energy polymorphs of the RDX crystal. The lowest-energy structure corresponded to the observed crystal and the results obtained for high-density polymorphs provide new information on the polymorphism of RDX. The SAPT(DFT) method should find important applications in development of new energetic materials, including crystal design, screening molecules for co-crystallization, and identification of low-energy polymorphs.

1. Introduction

Energetic material and many other compounds of interest to national defense are crystals of organic molecules, bound by intermolecular (van der Waals) forces and dominated by the dispersion component of these forces. The knowledge of these force fields is

sufficient to predict properties of such crystals. Although intermolecular interaction energies can be computed using electronic structure methods, such methods are currently too costly to be applied to compounds of interest in the field of energetic materials. Therefore, the predictions for such systems had to be based on empirical potentials fitted to available experimental data on molecular crystals. This limits such predictions to systems used for the parametrization (in fact, also to near-experimental thermodynamic conditions). In recent years, the predictive power of theory has been examined in blind tests conducted by the Cambridge Crystallographic Data Center^[1] and found to be very low. The situation had not improved in subsequent tests, in fact, the success rate of the third test^[2] was lower than that of the previous ones. Recently, a fourth, yet unpublished test was performed, and the success rate has apparently become somewhat better.^[3,4] This is an unsatisfactory situation in view of the importance of such crystals. For example, energetic materials are crystals of large organic molecules and polymorphism of drugs is a major problem in pharmaceutical industry. This inability of theory to predict properties of molecular crystals has been considered to be one of the major issues in modern molecular science.^[5-8]

An important question for the predictions of crystal structure is how accurate the force fields should be. The failures of predictions discussed above indicate that the accuracy of the force fields used was not sufficient. Highly accurate force fields can be computed *ab initio* using wave-function (WF) based methods, but only for molecules significantly smaller than those forming molecular crystals. Density functional theory (DFT) can be applied to systems containing hundreds of atoms, but conventional DFT methods cannot describe intermolecular interactions dominated by the dispersion

component. Recently, a method has been developed which combines WF-based symmetry-adapted perturbation theory (SAPT)^[9,10] of intermolecular interactions with the Kohn-Sham DFT representation of monomers^[11–17]. This method is denoted as SAPT(DFT) or SAPT-DFT. The efficiency of the original formulations of SAPT(DFT) has been increased^[13,18–20] by applying the density-fitting method^[21]. [For the current capabilities of SAPT(DFT), and references to earlier work, see References 18 and 19.] In SAPT(DFT), the electron correlation effects inside monomers are accounted for using the DFT approach which results in a very low-cost method: SAPT(DFT) calculations take less time than supermolecular DFT calculations for interactions of monomers containing about 20 atoms. At the same time, interaction energies computed using SAPT(DFT) are as accurate as those computed using high-level WF-based methods.^[18,19,22] As an example, SAPT(DFT) has been applied to compute the complete potential surface of the water dimer^[23] and of the benzene dimer^[22], in each case giving results in excellent agreement with experimental data. These results indicate that the force fields based on SAPT(DFT) should be accurate enough to predict crystal structures. SAPT(DFT) has recently been applied to several large systems such as the pyrene dimer^[24] and the perylene dimer^[25].

2. RDX CRYSTAL

In order to test the capabilities of SAPT(DFT), we have decided to investigate a crystal built of cyclotrimethylene trinitramine (RDX) monomers under essentially the same conditions as in the blind tests, i.e., without any use of experimental information about the crystal except for the monomer's geometry within the crystal taken from measurements of Reference 26. The *ab initio*-optimized monomer geometry is very close to the geometry observed in crystals^[27], so that the use of the former geometry would give essentially identical results. One should point out, however, that there exists a monomer structure with energy very close to that of the global minimum geometry.^[27] This structure could not be excluded a priori to be the one appearing in the crystal and in a completely first-principles approach one should develop an RDX dimer potential also for this monomer's structure.

A simplified version of the SAPT(DFT) RDX dimer potential of Reference 28 has been used to generate a large number of RDX crystal polymorphs using the molecular packing and lattice minimization methods available in the MOLPAK/WMIN computer code packages.^[29] The development of a simplified version was necessary since WMIN codes cannot use the original form of the potential.^[28] The simplified version was

obtained by refitting the atom-atom potentials u_{ab} with the standard Buckingham-type formula:

$$a_{ab}e^{-\beta_{ab}r_{ab}} + \frac{q_a q_b}{r_{ab}} - \frac{C_6^{ab}}{r_{ab}^6}, \quad (1)$$

where r_{ab} is the atom-atom distance and q_a , q_b are the atomic charges of Reference 28. The sites were located at the atomic positions of the monomers. The parameters C_6^{ab} were fitted to the long-range only SAPT(DFT) interaction energies using combining rules: $C_6^{ab} = \sqrt{C_6^{aa}C_6^{bb}}$... The parameters α_{ab} and β_{ab} were fitted to the complete set of SAPT(DFT) interaction energies using the numerical procedure described in Reference 28. The simplification of the potential had only a small impact on crystal predictions. We can judge this based on the results of isothermal-isostress (N_sT) molecular dynamics (MD) simulations (see below) which could be performed with both potentials: the cell vectors of the time-averaged geometry differed by 0.2–0.7% in the two cases.

The molecular packing part of the MOLPAK/WMIN codes sampled 51 most common space-symmetry groups to produce 50,653 candidate structures for each group. For the 500 most dense structures, the lattice parameters and monomer orientational parameters were optimized (within restrictions of a given space group) using WMIN. From these 500 polymorphic structures, the 13 lowest-energy structures have been selected for the N_sT MD simulations at ambient conditions. The N_sT MD simulations were performed using the original SAPT(DFT) RDX dimer potential.^[28] No symmetry constraints were used in this step. Note that this potential has already been used in Reference 28 in N_sT MD simulations for the crystal of RDX, but only for the experimentally observed polymorph, i.e., no crystal structure predictions were attempted. After the equilibration phase, the simulations were used to generate time-averaged information about the RDX crystal structure. This was accomplished by averaging the molecular parameters for each of the symmetry-equivalent molecules in all unit cells within the simulation supercell. For comparison, similar calculations were performed with the empirical RDX dimer potential of Sorescu, Rice, and Thompson (SRT)^[30] (fitted on the properties of the RDX crystal) and the 11 lowest-lying configurations were selected for the molecular dynamics simulations.

In Figure 1, a plot of lattice potential energies and densities of the resulting crystal structures is presented. Our lowest energy structure is essentially identical to the experimental structure. It is separated from other structures by a fairly substantial gap, so that our prediction is unambiguous. The agreement achieved by

our first-principle approach is even better than that achieved by the empirical SRT potential despite the fact that the experimental information we compare to was used in fitting of this potential. Although the SRT potential does predict the correct lowest-energy structure, its predictions for other polymorphs are very different from the SAPT(DFT) predictions: the pattern of points in Figure 1 is quite different in the two cases and the distributions of points cannot be made to overlap by translations. Since SAPT(DFT) description of any low-energy polymorph should be equally accurate as the description of the lowest-energy polymorph, we conclude that the empirical potentials are not well suited to investigate polymorphism of crystals. The main reason is that the empirical potentials may describe well only the regions of the configuration space which are probed by the lowest energy crystal for which experimental information is available. As shown in Reference 28, this is the case for the RDX dimer: the SRT and SAPT(DFT) potentials are very close to each other for the crystal closest neighbor dimer configuration, but not for other configurations corresponding to various local minima. Since the latter configurations dominate the interactions in some polymorphs, the SRT potential cannot describe these polymorphs well.

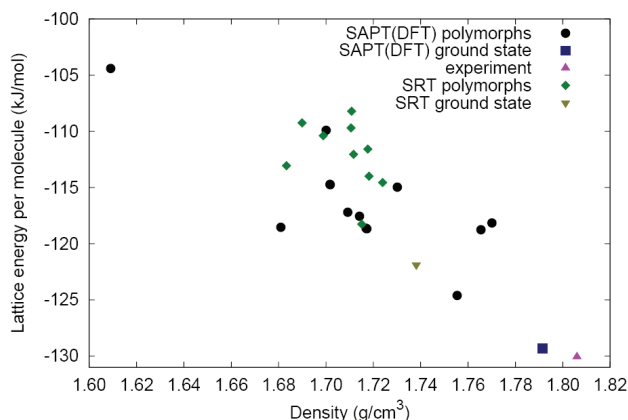


Figure 1. Correlation between the density and lattice energy per molecule for the 13 polymorphic structures of the RDX crystal from MD simulations using the SAPT(DFT) potential and comparison to simulations using the empirical SRT potential of Reference 30. The point corresponding to the observed crystal is denoted by a red up-triangle.

The excellent agreement of SAPT(DFT) predictions for the RDX crystal with experiment indicates that this method can be reliably used for other molecular crystals. Such predictions can be done entirely from first principles so that the method can be used even for compounds for which no experimental data are available and methods based on empirical force fields cannot be used. Therefore, this method should find applications in crystal design, in particular in development of novel energetic

materials and (opto)electronic devices, screening molecules for co-crystallization, and identification of low-energy polymorphs of pharmaceutical compounds.

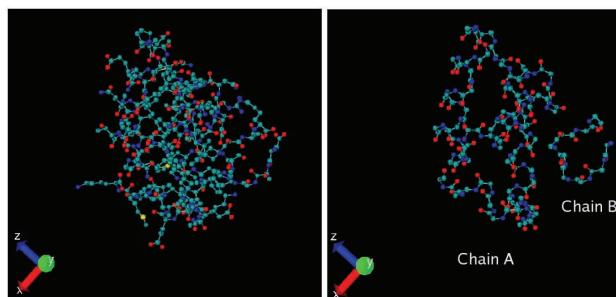


Figure 2. Dimer of TAP UBA (chain A) and nucleoporin peptide (chain B)

3. Linearly-Scaling SAPT(DFT)

Whereas many of the applications mentioned above can be pursued with the current version of the SAPT(DFT) codes, the present scaling of SAPT(DFT), as the fifth power of system size, will not allow applications to dimers containing much more than about 50 atoms. However, for large systems the scaling can be reduced to linear if calculations are properly localized to only some fragments of such systems. A general strategy for a linear SAPT(DFT) approach was outlined in Reference 31. This paper also presented applications of this approach to the electrostatic component of interaction energies for cases with a localized intermolecular contact region. Recently, the method has been extended to dimers with extended contact areas such as two parallel polymers or two parallel planar molecules. The new algorithm groups atoms of the monomers into domains and calculates interdomain contributions either with the electron density overlap effects or from simple asymptotic formulas. This approach should enable us to calculate electrostatic interactions of monomers containing several hundred atoms. Using this algorithm, we have reproduced the exact electrostatic interaction energies of dimers containing two long parallel alkane chains, e.g., $C_{36}H_{74}$ - $C_{36}H_{74}$, to within about one percent. The approximate method was then applied to systems for which exact calculations are not possible. One example of such application, currently under development, is shown in Figure 2. No hydrogens are displayed in either panel. The left panel shows all heavy atoms, whereas, the right panel only the atoms of the backbone. The dimer shown in Figure 2 is a biomolecule with known crystallographic structure.^[32] It is a complex between the transporter associated with antigen processing (TAP), also known as nuclear export factor (NFX1), ubiquitin-associated (UBA) monomer (chain A) and F_xFG nucleoporin peptide (chain B), where F stands of

phenylalanine and FG for phenylalanine-glycine peptides. These biomolecules are important in the field of nuclear transport.^[32,33]

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