This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
An ab initio quantum-mechanical theoretical framework is presented to compute thermal properties of molecular crystals. The present strategy combines dispersion-corrected density-functional-theory (DFT-D), harmonic phonon dispersion, quasi-harmonic approximation to the lattice dynamics for thermal expansion and thermodynamic functions, and quasi-static approximation for anisotropic thermo-elasticity. The proposed scheme is shown to reliably describe thermal properties of the urea molecular crystal by a thorough comparison with experimental data.

Molecular crystals have increasingly attracted great attention due to their peculiar chemical and physical properties, which make them suitable as high energy-density materials,1–3 active pharmaceutical ingredients (APIs),4–6 constituents of optoelectronic devices for their linear and non-linear optical properties,7–9 etc.

Nonetheless, from a theoretical viewpoint, they still represent a major challenge to state-of-the-art quantum-chemical methods as many kinds of chemical interactions (covalent intra-molecular, electrostatic, hydrogen-bond, long-range dispersive) need to be accurately described simultaneously. Only in recent years, different theoretical approaches have been devised in order to predict their structural and energetic properties (with the main goal of discriminating between competing polymorphs): from force-field to high-level molecular fragment-based schemes, from periodic dispersion-corrected density functional theory (DFT-D) to periodic many-body wave-function techniques.10–18 However, once a reliable and balanced description of the various chemical interactions has been achieved by means of any of the above-mentioned quantum-chemical methods, the extension of their applicability to more complex properties of technological and industrial relevance, which would greatly increase their predictiveness, such as mechanical, elastic, optical and thermodynamic responses,19–22 has to be tackled. Apart from the intrinsic high degree of complexity of the required theoretical techniques and algorithms, the main difficulty is here represented by the fact that most of those properties are largely affected by thermal effects,23–25 even at room temperature, such as zero-point energy, harmonic and anharmonic thermal nuclear motion, thermal lattice expansion, etc.

Most quantum-chemical ab initio methods describe the ground-state of a system at zero pressure and temperature. If the inclusion of pressure on computed structural and elastic properties is a relatively easy task,16,26–28 this is definitely not yet the case when temperature has to be accurately accounted for. Indeed, we are still far from having effective schemes formally developed and efficiently implemented in a solid state context, particularly so when anharmonic terms to the lattice potential have to be included into the formalism. When the harmonic approximation (HA) to the lattice potential is used, the vibrational contribution to the free energy of the crystal is assumed to be independent of volume. As a consequence, a variety of properties are wrongly described: null thermal expansion, elastic constants independent of temperature as well as the bulk modulus, equality of constant-pressure and constant-volume specific heats, infinite thermal conductivity as well as phonon lifetimes, etc.29 If the explicit calculation of anharmonic phonon-phonon interaction coefficients remains a rather computationally demanding task,30,31 with implementations often limited to a molecular, non-periodic context,32–34 a simpler, though effective, approach for correcting most of the above mentioned deficiencies of the HA is represented by the so-called quasi-harmonic approximation (QHA), which retains the same formal expression of the harmonic Helmholtz free energy $F$ and introduces an explicit dependence of phonon...
frequencies $\omega_{kp}$ on volume. Recent studies have highlighted the improved accuracy of quasi-harmonic calculations for thermal features of inorganic solids when use is made of suitable dispersion-corrected DFT methods.

In this Communication, we present a fully-integrated $ab$ initio quantum-mechanical theoretical framework for the study of thermal properties of molecular crystals, which is based on: i) use of generalized-gradient and global hybrid functionals, as a posteriori dispersion-corrected according to Grimme’s D3 proposal; ii) efficient use of both harmonic and quasi-harmonic lattice dynamical calculations for the description of phonon dispersion; iii) periodic boundary condition calculations with use of an atom-centered Gaussian-type function basis set of triple-$\xi$ quality plus polarization functions; iv) use of efficient fully-automated algorithms for the calculation of the fourth-rank elastic tensor of crystals belonging to any space group of symmetry; v) combined use of the quasi-harmonic and quasi-static approximations to include thermal effects on elastic constants; vi) full exploitation of both point-symmetry and efficient parallelization of all algorithms at all steps of the calculations.

The molecular crystal of urea, belonging to the tetragonal $P4_{2}1_{2}$ space group, is taken as a suitable test-case for a couple of reasons: i) its thermal features (anisotropic thermal lattice expansion, single-crystal elastic constants at room temperature, thermodynamic properties) have been measured in different, independent experimental studies, thus making it the optimal system for benchmarking our computational strategy; ii) a balanced description of most kinds of chemical interactions is required to properly describe it; furthermore, its peculiar molecular chain-like structure (see panel C of Figure 1) leads to a high directionality of the various interactions (from intra-chain electrostatic and hydrogen-bonds to inter-chain dispersive, etc.).

In Figure 1, we report the volumetric and directional (i.e. anisotropic) thermal lattice expansion of urea, as measured experimentally (more details in the ESI) and as determined by present quasi-harmonic $ab$ initio calculations (phonons of the primitive cell evaluated at 7 distinct volumes within QHA), by minimizing $F$ with respect to the volume at each temperature. Several DFT functionals are considered: some non dispersion-corrected and a bunch of -D3 corrected ones. For the global hybrid B3LYP functional, an older dispersion-corrected version is also considered, which was specifically parametrized on molecular crystals (namely, B3LYP-D2$^*$). From $V(T)$ data reported in panel A, all non dispersion-corrected functionals are seen to poorly describe the absolute value of the equilibrium volume of the crystal, with a large overestimation by PBE, B3LYP and PBE0 and a large underestimation by LDA. On the contrary, all -D corrected functionals nicely reproduce the correct volume with deviations from each other always smaller than 1.5%. Let us stress that the sole zero-point motion effect at 0 K (seldom included, along with proper thermal effects, in most $ab$ initio studies on the relative performance of different functionals) is that of increasing the volume by about 2.6% for all -D corrected functionals. It follows that any ranking of functionals for the description of structural features of molecular crystals where zero-point and thermal effects are neglected would be rather questionable. In order to better highlight the description of thermal expansion, panel B reports the $V(T)/V(150K)$ ratio as a function of temperature. Non corrected functionals wrongly describe the thermal expansion either by largely over- or under-estimating it; all dispersion-corrected ones give a reliable description of the expansion, with a similar trend with respect to each other, PBE-D3 providing the best description at high temperatures. The anisotropy of the thermal expansion, as obtained by optimizing $a$ and $c$ as a function of the purely internal energy $E$ at different volumes, is documented in panels D and E for -D3 corrected functionals, where the $a(T)/a(150K)$ and $c(T)/c(150K)$ ratios are reported (on the same absolute scale), respectively. The thermal structural response of urea is seen to be rather anisotropic, with a much larger expansion in the $ab$ plane (inter-chain directions) than along $c$ (intra-chain direction), as expected (see also the inset of panel E where directional thermal expansion coefficients $\alpha_{\alpha}(T) = 1/x(T)\delta x(T)/\delta T$ are reported, with $x$ either $a$ or $c$). All -D3 corrected functionals nicely predict such a strong anisotropic thermal response, with an excellent description of the expansion along $a$ and just a slight underestimate of the small expansion along $c$. It should be noted that a more accurate optimization of $a$ and $c$ with respect to the free energy $F$ could be considered, which, however, would require a much larger set of calculations to be performed.
Table 1 Single-crystal independent elastic constants \( C_{\text{vu}} \) and bulk modulus \( K \) of urea (in GPa) as computed for each functional at 0 K (without zero-point effects) and at room temperature in both the isothermal (T) and adiabatic (S) conditions. Experimental adiabatic constants and bulk modulus at room temperature are also reported for comparison.

<table>
<thead>
<tr>
<th></th>
<th>( C_{11} )</th>
<th>( C_{33} )</th>
<th>( C_{44} )</th>
<th>( C_{12} )</th>
<th>( C_{13} )</th>
<th>( C_{66} )</th>
<th>( K )</th>
</tr>
</thead>
<tbody>
<tr>
<td>B3LYP-D3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 K</td>
<td>18.7</td>
<td>80.8</td>
<td>10.6</td>
<td>19.3</td>
<td>11.5</td>
<td>24.1</td>
<td>18.3</td>
</tr>
<tr>
<td>293 K (T)</td>
<td>12.3</td>
<td>70.3</td>
<td>8.9</td>
<td>13.5</td>
<td>7.9</td>
<td>17.4</td>
<td>12.5</td>
</tr>
<tr>
<td>293 K (S)</td>
<td>13.5</td>
<td>71.5</td>
<td>8.9</td>
<td>14.6</td>
<td>9.1</td>
<td>17.4</td>
<td>13.1</td>
</tr>
<tr>
<td>PBE0-D3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 K</td>
<td>16.9</td>
<td>75.3</td>
<td>10.3</td>
<td>17.1</td>
<td>10.7</td>
<td>22.1</td>
<td>16.5</td>
</tr>
<tr>
<td>293 K (T)</td>
<td>11.0</td>
<td>66.2</td>
<td>8.5</td>
<td>11.7</td>
<td>7.5</td>
<td>15.6</td>
<td>11.1</td>
</tr>
<tr>
<td>293 K (S)</td>
<td>11.9</td>
<td>67.0</td>
<td>8.5</td>
<td>12.5</td>
<td>8.4</td>
<td>15.6</td>
<td>11.7</td>
</tr>
<tr>
<td>Exp. (^{60}) 293 K (S)</td>
<td>11.7</td>
<td>54.0</td>
<td>6.2</td>
<td>10.7</td>
<td>9.2</td>
<td>10.6</td>
<td>11.1</td>
</tr>
<tr>
<td>Exp. (^{59}) 298 K (S)</td>
<td>23.5</td>
<td>51.0</td>
<td>6.2</td>
<td>-0.5</td>
<td>7.5</td>
<td>0.5</td>
<td>11.2</td>
</tr>
<tr>
<td>Exp. (^{58}) 298 K (S)</td>
<td>21.7</td>
<td>53.2</td>
<td>6.3</td>
<td>8.9</td>
<td>24.0</td>
<td>0.5</td>
<td>11.6</td>
</tr>
</tbody>
</table>

The experimental determination of thermo-elastic parameters of molecular crystals is rather problematic due to general difficulties in growing crystals of adequate size, performing measurements on very soft samples, and dealing with low-symmetry space groups (i.e. high number of independent elastic constants \( C_{\text{vu}} \) to be determined). From a theoretical point of view, temperature-dependent elastic constants could be obtained as second free energy density derivatives with respect to the strain: \( C_{\text{vu}}^F(T) = 1/V(T) \partial^2 F/\partial e_v \partial e_u \), which, however, would require the costly calculation of phonons at several strained lattice configurations. \(^{65}\) A simpler way to obtain those thermo-elastic quantities is represented by the quasi-static approximation (QSA), \(^{49,50}\) which, taking advantage of the \( V(T) \) relation obtained through the QHA, consists in evaluating static internal-energy specific heat can indeed be obtained by summing on top of the harmonic thermodynamic quantities such as the isothermal bulk modulus. Such thermodynamic properties of molecular crystals requires the accurate lattice-dynamical evaluation of phonon dispersion (i.e. of out-of-plane intermolecular vibrations). From computed phonon frequencies, harmonic thermodynamic quantities such as the constant-volume specific heat \( C_V \) and entropy \( S \) can be derived through the vibration partition function within standard statistical mechanics. Experimentally measured specific heats (via calorimetric techniques) refer to the constant-pressure \( C_P \) case, which might significantly differ from the \( C_V \) one when lattice expansion is large, as in the case of molecular crystals. The QHA offers a way to evaluate such quantity, again enabling a direct comparison with experimental data. The constant-pressure specific heat can indeed be obtained by summing on top of the harmonic constant-volume one the term: \( C_P(T) - C_V(T) = \alpha_v \partial^2 \ln(T) V(T) / \partial T^2 \), where \( \alpha_v \) is the volumetric thermal expansion coefficient and \( k^T \) the isothermal bulk modulus. Such thermodynamic properties of urea are reported in Figure 2 as a function of temperature, as obtained at the PBE-D3 level of theory (thermodynamic proper-

\[ C^S_{\text{vu}}(T) = C^F_{\text{vu}}(T) + \frac{TV(T)\alpha_v(T)\lambda_v(T)}{C_v(T)} \quad (1) \]

\[ C_P(T) - C_V(T) = \alpha_v(T)k^T(T)V(T)/T^2 \quad (2) \]
ties have been shown to be very insensitive to different choices of DFT functionals. A direct space, frozen-phonon, approach is here adopted, which consists in computing phonon frequencies on super-cells of the primitive lattice: a $3 \times 3 \times 3$ super-cell is used (i.e. containing 432 atoms), which corresponds to a sampling of phonon dispersion over 27 $k$-points within the first Brillouin zone in reciprocal space. In the right panel, the computed entropy is compared with the experimentally measured one by Anderson et al. The dashed line corresponds to a $\Gamma$-only calculation of vibration frequencies (i.e. to entirely neglecting the effect of phonon dispersion), while the continuous line to a converged description of phonon dispersion, which confirms the crucial role of collective intermolecular vibrations in predicting reliable thermodynamic properties of molecular crystals. The same consideration also applies to the specific heat case (left panel). Here, we shall note that the correction given in Eq. (2) is essential in order to recover the correct behavior (i.e. slope) of the specific heat at high temperatures when comparing with the experiment (see difference between thin, $C_V$, and thick, $C_P$, continuous lines).

To summarize, we have presented a multifaceted ab initio theoretical framework for the evaluation of a variety of thermal properties (structural, elastic, thermodynamic) of molecular crystals, which has been implemented into a development version of the CRYSTAL14 program by some of the present authors. The anisotropic thermal expansion, adiabatic single-crystal elastic constants and thermodynamic properties of urea have been shown to be reliably described within the proposed approach. Zero-point and thermal effects (often neglected in quantum-mechanical studies) are documented to be crucial for the accurate prediction of these properties and for a rigorous assessment of the relative performance of different theoretical methods.

Prof. Piero Ugliengo is gratefully acknowledged for having stimulated this work as well as Prof. Roberto Orlando for his fundamental contribution in the implementation of the -D3 correction.

References