Supporting Information:
Collective Variables for Conformational Polymorphism in Molecular Crystals

Oren Elishav,†∥ Roy Podgaetsky,†∥ Olga Meikler,‡ and Barak Hirshberg*,†¶,§

†School of Chemistry, Tel Aviv University, Tel Aviv 6997801, Israel
‡Rafael Ltd., P.O. Box 2250, Haifa 3102102, Israel
¶The Center for Computational Molecular and Materials Science, Tel Aviv University, Tel Aviv 6997801, Israel.
§The Ratner Center for Single Molecule Science, Tel Aviv University, Tel Aviv 6997801, Israel.
∥O.E. and R.P. contributed equally to this work

E-mail: hirshb@tauex.tau.ac.il

MD simulations were carried out using LAMMPS and PLUMED2. We used a time step of 1 fs, which showed energy conversion within 0.1% in an NVE simulation. In simulations of isolated molecules, the cell consisted of a single molecule of 36 atoms with the initial configuration of the CIF file after minimization (conjugate gradient). Then, we collected data on the fluctuations of the improper angles at a temperature of 50K and a pressure of 1 atm. We used a Nose’-Hoover chains thermostat and barostat with Parrinello-Rahman full-cell fluctuations.1–4 The temperature and pressure were maintained with damping parameters of 10 fs and 100 fs, respectively. Simulation of the solid consisted of four molecules (144 atoms) with the initial geometries as in the CIF file after minimization and thermalization.
of 1.1 ns. Since LAMMPS flips the simulation box, if any side length increases to 1.6 times its initial value, the cell angles can jump to complementary angles. We reversed this process when flipping occurred in all Figures for clarity. In WTMetaD simulations, upper and lower harmonic walls with a spring constant of 35 kcal mol$^{-1}$ were employed to improper angles 2, 3, and 5. The upper and lower values used are the minimum and maximum values observed from unbiased simulations of the isolated molecules.

Table S1: Lattice parameters of CL-20 polymorphs modeled with the SB-CL20-CCNN force field, at 300 K and 1 atm

| CL-20   | a(Å)  | b(Å)  | c(Å)  | α(°) | β(°)  | γ(°)  | density(g·cm$^{-3}$) |
|---------|-------|-------|-------|------|-------|-------|---------------------|
| ε       | Exp$^a$ | 8.852 | 12.556 | 13.386 | 90 | 106.82 | 90 | 2.044 |
|         | CL-20-CCNN FF | 9.023 | 12.365 | 13.86 | 88.59 | 107.26 | 90.98 | 1.971 |
| dev %   |       | 1.93 | 1.52 | 3.6 | 1.6 | 0.4 | 1.1 | 3.5 |
| β       | Exp$^a$ | 9.676 | 13.006 | 11.649 | 90 | 90 | 90 | 1.985 |
|         | CL-20-CCNN FF | 9.673 | 12.374 | 12.443 | 90.5 | 91.52 | 89.25 | 1.955 |
| dev %   |       | 0.03 | 4.9 | 6.8 | 0.55 | 1.7 | 0.8 | 1.5 |
| γ       | Exp$^a$ | 13.231 | 8.17 | 14.876 | 90 | 109.17 | 90 | 1.916 |
|         | CL-20-CCNN FF | 13.409 | 7.665 | 15.325 | 90.62 | 108.99 | 89.55 | 1.955 |
| dev %   |       | 1.34 | 6.19 | 3.02 | 0.69 | 0.16 | 0.50 | 2.0 |

$^a$ experimental values obtained from ref. 55
Figure S1: Cosines of the improper angles with an offset phase of 1.2 radians from unbiased 70 ps simulations of isolated CL-20 conformers.

Table S2: Coefficients and weights of each improper angle descriptors ($\cos(\varphi_i - 1.2)$) from MC-HLDA using all six of them.

| $\varphi_i$ | $\varphi_1$ | $\varphi_2$ | $\varphi_3$ | $\varphi_4$ | $\varphi_5$ | $\varphi_6$ |
|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| $c_i$     | -0.4712   | -0.0417   | 0.0834    | -0.8313   | -0.0899   | 0.2646    |
| $w_i(\%)$ | 22.21     | 0.17      | 0.7       | 69.11     | 0.81      | 7.0       |

Table S3: Coefficients and weights ($w_i$) for improper angle descriptors ($\cos(\varphi_i - 1.2)$) from MC-HLDA using only $\varphi_1$, $\varphi_4$ and $\varphi_6$.

| $CV_i$ | $c_1$ | $c_4$ | $c_6$ | $w_1[\%]$ | $w_4[\%]$ | $w_6[\%]$ |
|--------|-------|-------|-------|------------|------------|------------|
| $CV_1$ | -0.4342 | -0.8641 | 0.2546 | 18.8       | 74.7       | 6.5        |
| $CV_2$ | -0.822  | 0.565  | -0.074 | 67.6       | 31.9       | 0.5        |
Figure S2: Scatter plot of CL-20 polymorphs in the space of the two MC-HLDA CVs, data obtained from $\sim 70$ ps unbiased unit-cell simulations.
Figure S3: Snapshots of molecular orientation of CL-20 polymorphs during biased simulation of the solid, (a) $\epsilon$-CL-20, (b) $\gamma$-CL-20, and (c) $\beta$-CL-20.
Figure S4: (a) Average error in FES as function of block size using CV1, (b) Average error in FES as function of block size using CV2, (c) energy difference between $\epsilon$- and $\gamma$-CL-20, and (d) energy difference between $\epsilon$- and $\beta$-CL-20.

Table S4: Lattice parameters of the CL-20 defect forms

| Form     | $a$ [Å] | $b$ [Å] | $c$ [Å] | $a$ [$^\circ$] | $b$ [$^\circ$] | $c$ [$^\circ$] |
|----------|---------|---------|---------|----------------|----------------|----------------|
| II, IV   | 8.909   | 12.230  | 13.438  | 80.421         | 117.323        | 94.53          |
| III      | 7.997   | 14.304  | 16.034  | 120.444        | 111.43         | 86.764         |
| $\gamma_{defect}$ | 10.234  | 13.084  | 11.356  | 88             | 98             | 89             |
Figure S5: FES of independent simulations with different seeds. Each seed was randomly chosen. The simulations were run for $150 - 500$ ns.
Figure S6: Preliminary supercell 2x2x2 WT-MetaD simulations: (a) CV obtained as an average over the corresponding values of all molecules in the supercell, as in the main text, and (b) cell parameters of the supercell using the average CV. Transitions from epsilon to a defect, gamma, and then beta phases are observed. (c) CV based on a switching function counting the number of epsilon molecules in the supercell, and (d) cell parameters of the supercell using the switching function CV. A transition from the epsilon to the gamma phase is observed.

Table S5: Lattice parameters and densities of CL-20 polymorphs from DFT calculations

| Polymorphs   | a[Å]   | b[Å]   | c[Å]   | α[°]  | β[°]  | γ[°]  | ρ[gr cm⁻³] |
|--------------|--------|--------|--------|-------|-------|-------|------------|
| β_{experiment} | 9.676  | 13.006 | 11.649 | 90    | 90    | 90    | 1.985      |
| β_{DFT}      | 9.515  | 13.063 | 11.419 | 90    | 90    | 90    | 2.048      |
| β_{error} [%] | 1.66   | 0.44   | 1.97   | 0     | 0     | 0     | 3.2        |
| γ_{experiment} | 13.231 | 8.170  | 14.876 | 90    | 109.15| 90    | 1.916      |
| γ_{DFT}      | 13.085 | 8.170  | 14.675 | 90    | 109.012| 90    | 1.96       |
| γ_{error} [%] | 1.1    | 0      | 1.35   | 0     | 0.13  | 0     | 2.3        |
| ϵ_{experiment} | 8.852  | 12.556 | 13.386 | 90    | 106.82| 90    | 2.044      |
| ϵ_{DFT}      | 8.805  | 12.474 | 13.259 | 90    | 106.34| 90    | 2.08       |
| ϵ_{error} [%] | 0.53   | 0.65   | 0.95   | 0     | 0.45  | 0     | 1.8        |
We applied DFT to investigate the stability of all observed intermediate and defect forms. The γ-form with slightly different lattice parameters observed in our MetaD simulations did not converge during cell relaxation. Thus, it is possible this form is an artifact of the applied force field.

Table S6: Lattice parameters and densities of the stable CL-20 intermediate form (I) from DFT calculations

| Form      | a [Å]  | b [Å]  | c [Å]  | a [°]  | b [°]  | c [°]  | ρ [gr cm⁻³] |
|-----------|--------|--------|--------|--------|--------|--------|-------------|
| I_MD−initial | 9.128  | 12.186 | 14.578 | 80.421 | 117.323 | 94.53  | 2.015       |
| I_DFT     | 8.851  | 12.378 | 14.269 | 81.336 | 114.818 | 94.323 | 2.0728      |
| I_error [%]| 3.04   | 1.57   | 2.12   | 1.14   | 2.14   | 0.22   | 2.83        |

References

(S1) Shinoda, W.; Shiga, M.; Mikami, M. Rapid Estimation of Elastic Constants by Molecular Dynamics Simulation under Constant Stress. *Physical Review B* 2004, 69, 134103.

(S2) Tuckerman, M. E.; Alejandre, J.; López-Rendón, R.; Jochim, A. L.; Martyna, G. J. A Liouville-operator Derived Measure-preserving Integrator for Molecular Dynamics Simulations in the Isothermal–isobaric Ensemble. *Journal of Physics A: Mathematical and General* 2006, 39, 5629.

(S3) Parrinello, M.; Rahman, A. Polymorphic Transitions in Single Crystals: A New Molecular Dynamics Method. *Journal of Applied Physics* 1998, 52, 7182.

(S4) Martyna, G. J.; Tobias, D. J.; Klein, M. L. Constant Pressure Molecular Dynamics Algorithms. *The Journal of Chemical Physics* 1998, 101, 4177.

(S5) Nielsen, A. T.; Chafin, A. P.; Christian, S. L.; Moore, D. W.; Nadler, M. P.; Nissan, R. A.; Vanderah, D. J.; Gilardi, R. D.; George, C. F.; Flippen-Anderson, J. L. Synthesis of Polyazapolycyclic Caged Polynitramines. *Tetrahedron* 1998, 54, 11793–11812.