Supplementary information to the article "Accuracy and reproducibility in crystal structure prediction: The curious case of ROY"

Jonas Nyman, Lian Yu and Susan Reutzel-Edens

1 Crystal energy landscape

Figure S1 shows the crystal energy landscape at the penultimate optimization stage. A subset of these structures were progressed to the final optimization with tighter convergence criteria, as shown in the article.

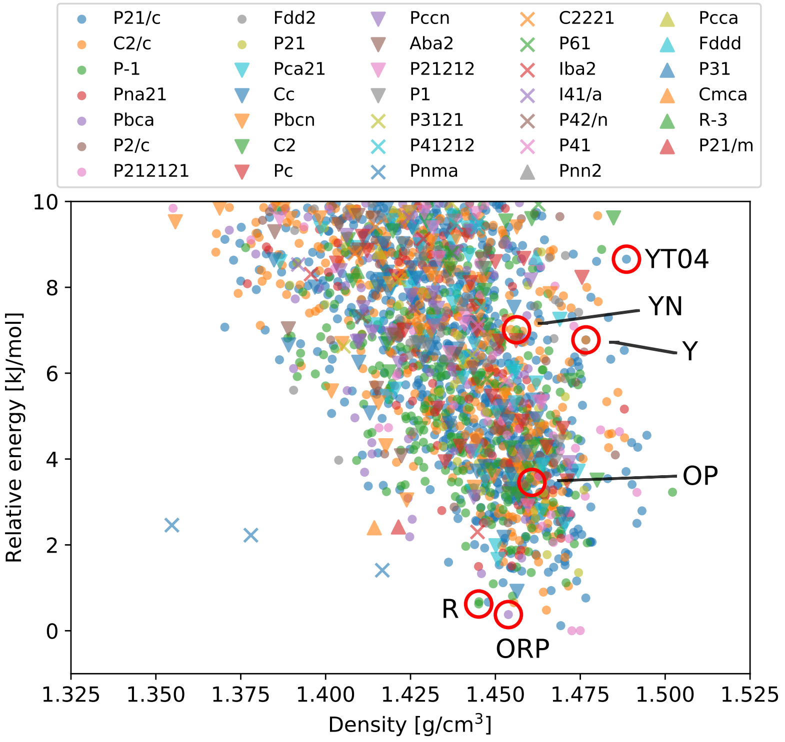


Figure S1: Crystal energy landscape with all predicted structures up to 10 kJ mol^{-1} optimized with loose convergence criteria.

2 Free energy curves

Free energy curves calculated in the harmonic approximation using crystal structures where the unit cell volumes have been optimized with PBE-D3BJ to simulate 0 K structures are shown in Figure S2.

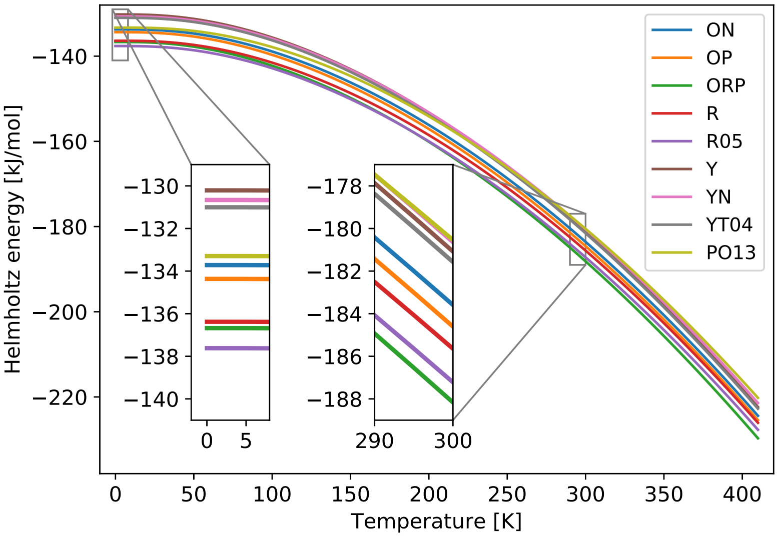


Figure S2: Harmonic approximation lattice-vibrational free energies of the ROY polymorphs, calculated relative to the gas.

Harmonic and quasi-harmonic (i.e. experimental unit cell dimensions) lattice-vibrational free energies calculated relative to Form Y are shown in figures S3 and S4.

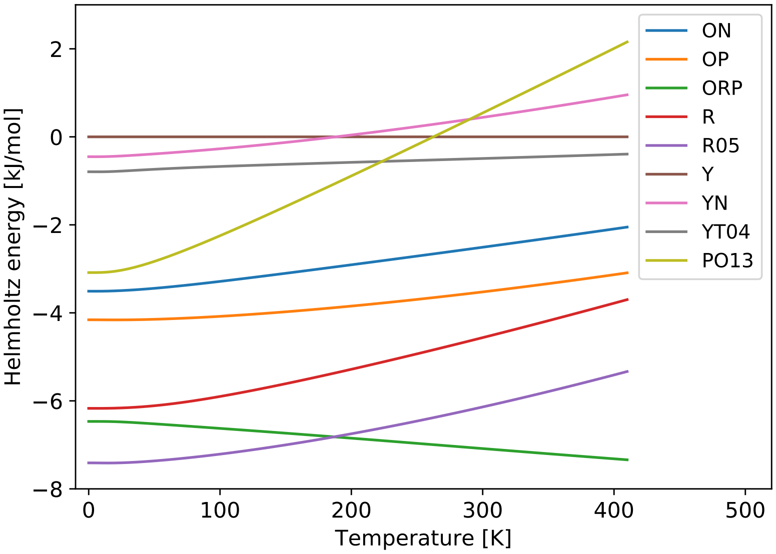


Figure S3: Harmonic approximation lattice-vibrational free energies of the ROY polymorphs, calculated relative to Form Y.

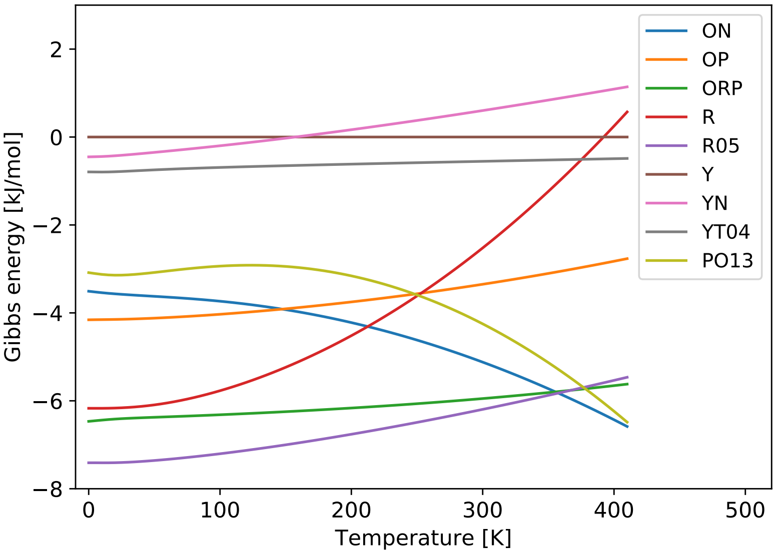
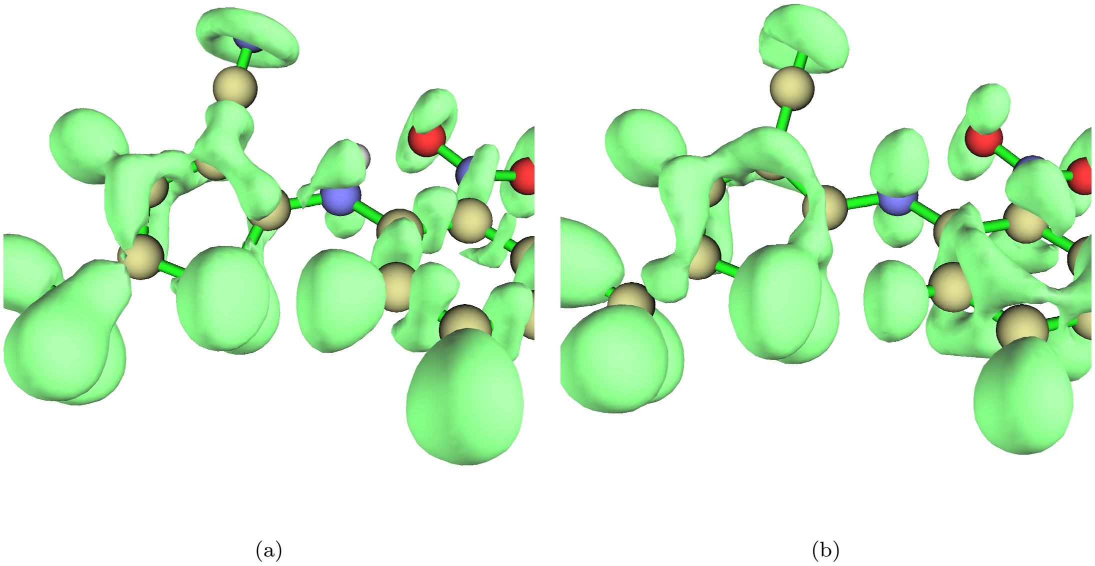


Figure S4: Quasi-harmonic approximation lattice-vibrational free energies of the ROY polymorphs, calculated relative to Form Y.

3 Electron localization functions

The electron localization function (ELFπ) and the localized-orbit locator function (LOLπ) were calculated on 6-311G(d,p) wavefunctions of a single ROY molecule calculated with PBE, B3LYP, B2PLYP and MP2 (dispersion correction has no effect on the wavefunction). Only electrons in π-type orbitals were included.

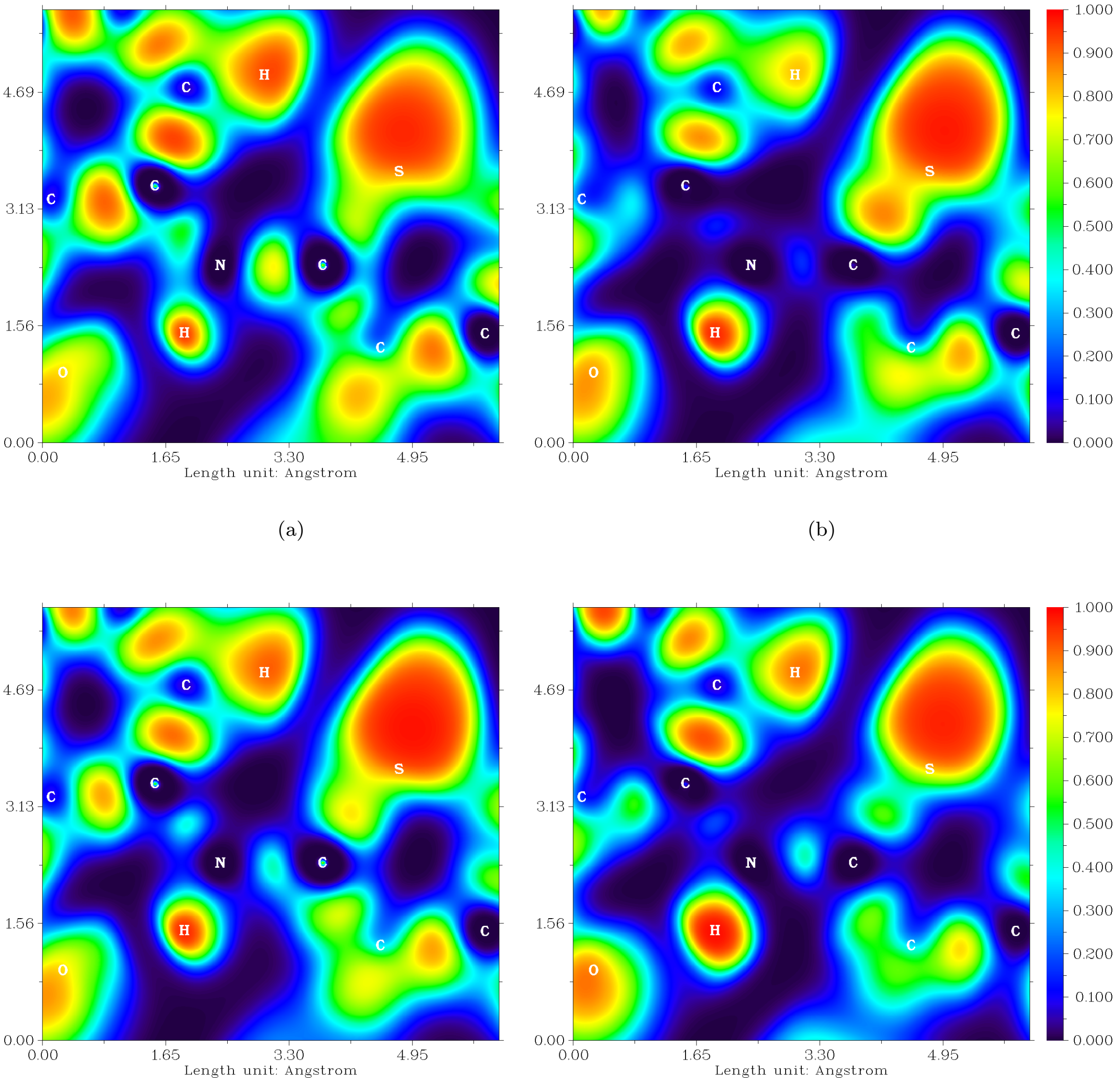
The ELFπ functions of the PBE and B2PLYP wavefunctions were plotted as density iso-surfaces over the whole ROY molecule, see Figures S5(a) and (b).



(a) (b)

Figure S5: ELFπ iso-density (at 0.7) for the (a) PBE and (b) B2PLYP wavefunctions. In the left (PBE) figure, note spurious charge transfer to the C-N bond in the amino moiety and from the phenyl ring to the nitro-group nitrogen.

The ELFπ-function and LOLπ functions were also plotted in the plane intersecting the amino-moiety, see Figures S6 and S7. Since π-bonds extend above and below the atomic plane, the LOLπ-function was also calculated on a parallel plane 0.63 Å above the atomic plane, see Fig S8.



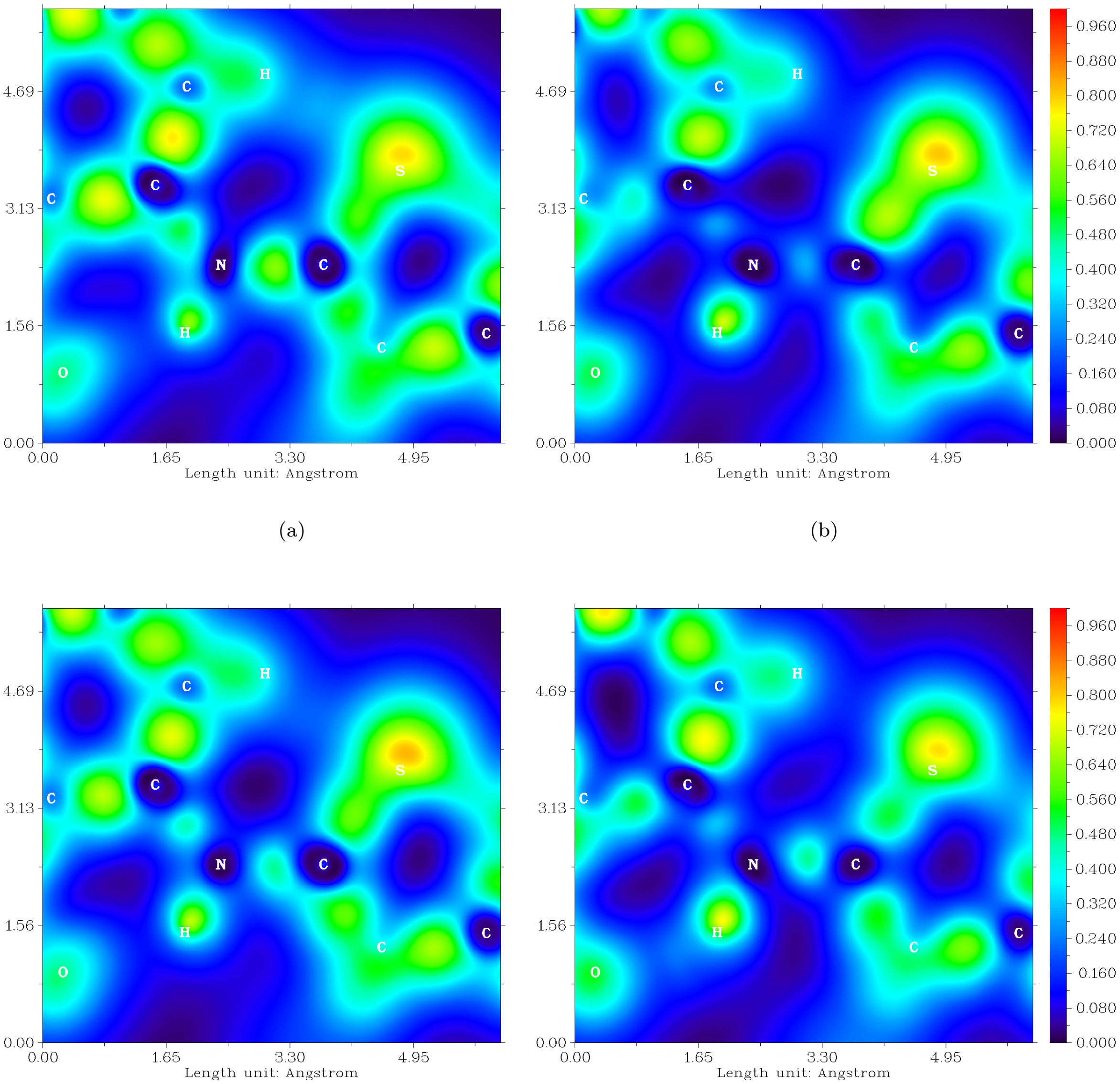
(a)

(b)

(c)

(d)

Figure S6: ELFπ in the plane of the amino group, calculated on (a) PBE, (b) B2PLYP, (c) B3LYP and (d) MP2 wavefunctions. Note excessive π-density between atoms in the amino-moiety in the left figures.



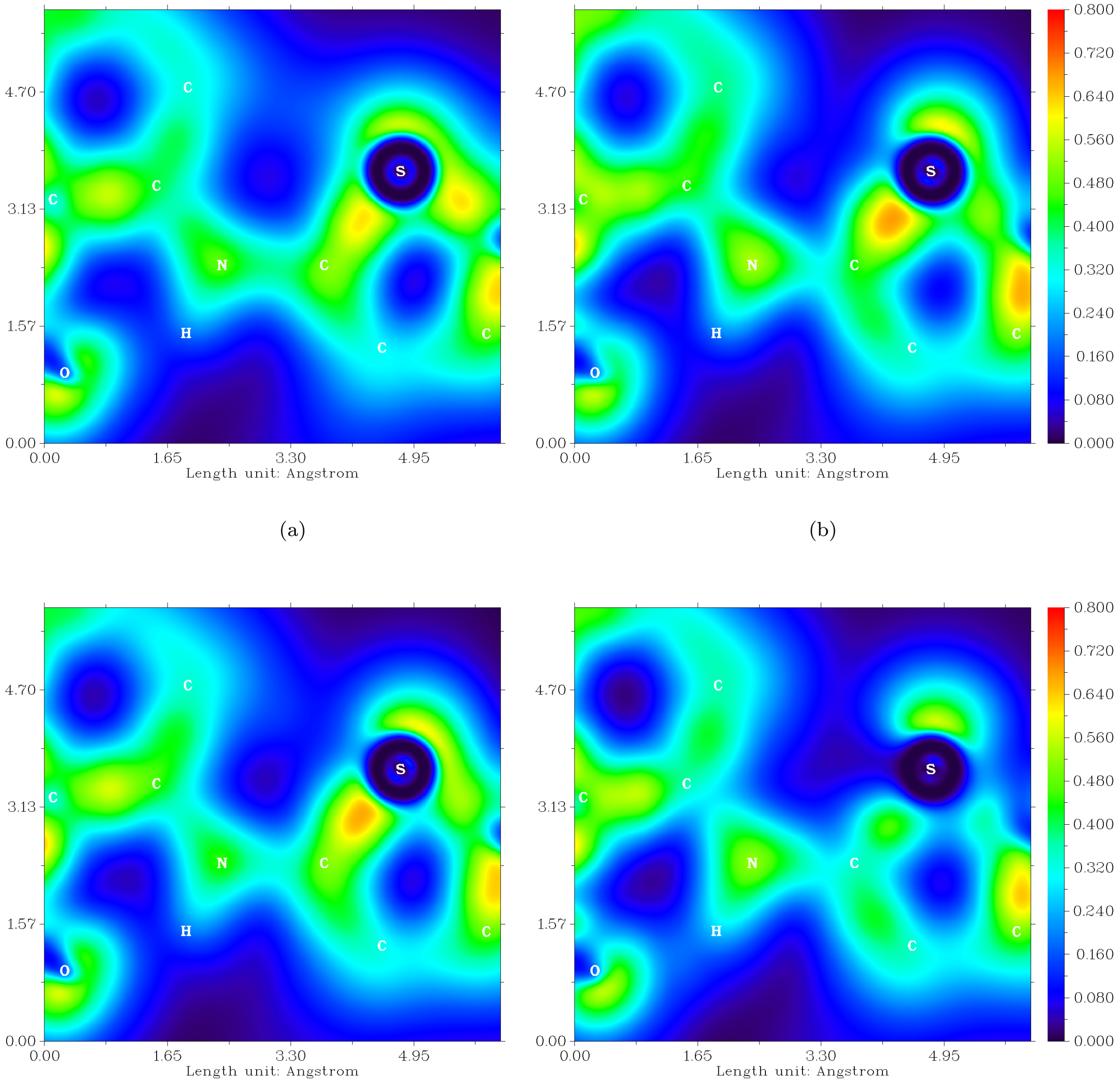
(a)

(b)

(c)

(d)

Figure S7: LOLπ in the plane of the amino group, calculated on (a) PBE, (b) B2PLYP, (c) B3LYP and (d) MP2 wavefunctions.



(a) (b) (c) (d)

Figure S8: LOLπ 0.63 Å above the plane of the amino group, calculated on (a) PBE, (b) B2PLYP, (c) B3LYP and (d) MP2 wavefunctions.

4 Single crystal X-ray diffraction of ON

A large needle was picked from a primordial sample of Form ON, isolated at Eli-Lilly in 1994. This sample, stored at room temperature for 23 years, shows no signs of degradation or phase transition, and Form ON thus appear to be indefinitely metastable at ambient conditions. The needle was cut into a single crystal, approximately $0.2 \times 0.1 \times 0.05$ mm in size, and mounted on a Bruker SMART APEX2 diffractometer equipped with an Incoatec I X-ray tube. Diffraction was performed with monochromated Cu K_α radiation ($\lambda = 1.54178$ Å), beam diameter 0.5 mm. The crystal was cooled to 100 K with a stream of cryogenic nitrogen gas. Bragg reflections were recorded with a Bruker APEX II Quazar CCD detector. Indexing and unit cell determination was performed with the OLEX 2 program. The data was corrected for absorption by SADABS.[1] The crystal structure was solved by direct methods using SHELXS and refined to $R = 3\%$ against F^2 by full-matrix least-squares using SHELXL.[2, 3] Non-hydrogen atoms were refined anisotropically. In addition, the thermal expansion was studied by determining the unit cell dimensions of the same crystal at 150 K, 200 K, 250 K and at room temperature. A CIF file 'ROY_ON_100K.cif' is included, which contains atomic coordinates, thermal displacement parameters, refinement details and the raw hkl reflection data.

Table S1: Results of single crystal X-ray diffraction of Form ON at 100 K.

Space group	$P2_1/c$
a	3.8517(2) Å
b	18.458(2) Å
c	16.3545(12) Å
β	92.481(3)°
Volume	1161.61(17) Å^3
Mol. weight	259.28 g/mol
Z	4
Z'	1
Density	1.483 g/cm^3
R	0.0308
wR	0.0765

Table S2: Form ON thermal expansion.

Temp. [K]	a [Å]	b [Å]	c [Å]	β [°]	Vol. [Å^3]
100	3.852	18.458	16.354	92.481	1161.6
150	3.871	18.481	16.360	92.872	1168.9
200	3.894	18.543	16.371	93.233	1180.1
250	3.921	18.595	16.381	93.574	1192.0
RT	3.946	18.638	16.390	93.881	1202.8

This structure has also been deposited as CCDC Accession Code 1877411. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

5 Supplementary crystal structure data

The entire set of predicted crystal structures are provided as two CIF files.
The first file 'ROY_final_predicted.cif' contains the 1077 lowest-energy structures that were optimized with tighter convergence criteria. A larger set of 2765 structures optimized at the same level of theory, but with looser convergence criteria is also included in the CIF file 'ROY_loose_convergence_predicted.cif'.

We also include the experimental polymorphs optimized with PBE-NP in the CIF files 'ROY_experimental_PBE-NP_optimized.cif' and 'ROY_experimental_TMFF_optimized.cif'.

The proposed structure for polymorph RPL, #22 is included in the CIF file 'Structure_#22.cif'.

References

[1] Lennard Krause, Regine Herbst-Irmer, George M Sheldrick, and Dietmar Stalke. Comparison of silver and molybdenum microfocus x-ray sources for single-crystal structure determination. *J. Appl. Cryst.*, 48(1):3–10, 2015.

[2] George M Sheldrick. Shelxt–integrated space-group and crystal-structure determination. *Acta Cryst. A*, 71(1):3–8, 2015.

[3] George M Sheldrick. Crystal structure refinement with shelxl. *Acta Cryst. C*, 71(1):3–8, 2015.