ELECTRONIC SUPPLEMENTARY INFORMATION

Experimental details

Experiments in methanol

In order to compare the behavior of tolazamide-II crystals in tolazamide saturated solution in methanol at ambient conditions and under pressure, their recrystallization has been studied in this medium at ambient pressure. The process was carried out in drops on a hydrophobic surface and monitored using an optical microscope Nikon AZ100.

The solubility of tolazamide in methanol at ambient pressure was evaluated in the following way. First, ~15 mg of tolazamide were added to 1 ml of methanol, in order to obtain a saturated solution. After that, ~100 μL of the solution were kept in a crucible until complete evaporating of methanol. Precipitate was weighted using an Ohaus Discovery DV-214C balance. Solubility was calculated being ca. 14 mg/ml.

For an optical microsopy experiment the saturated solution of tolazamide in methanol was prepared: ~100 mg of tolazamide were added to 6 ml of methanol. Then the solution was quickly filtered and a drop was put on a glass slide with the crystal of Form II. This procedure resulted in dissolution of the crystal and subsequent solvent-assisted transformation into Form I. These phenomena were also observed at 0.1 GPa but the recrystallization was partial at this pressure that can be related to the lower solubility of tolazamide in methanol at high pressure.

Low-temperature experiments

Variable-temperature single-crystal X-ray diffraction was performed using an Oxford Diffraction Gemini R Ultra diffractometer with a kappa-geometry of the goniometer (Mo-Kα radiation, λ = 0.71073 Å, graphite monochromator, CCD detector) and an Oxford Instruments Cryojet cooling device. The temperature range was 300–100 K with a step size of 50 K (300, 250, 200, 150, 100 K on cooling and 125, 175, 225, 275 K on heating) and a cooling rate of about 150 K/h. The sample was fixed to the holder by using LV CryoOil (MiTeGen). CrysAlisPro program package[1S] was used for data collection, data reduction and unit cell refinement. The parameters related to data collection, structure solution and refinement are summarized in Tables S10 and S11.

Computational details

Periodic DFT Calculations

The choice of the dispersion correction

For more correct description of van der Waals interactions, three DFT methods with different Grimme's dispersion corrections[2S] (DFT-D2,[3S] DFT-D3[4S] and DFT-D3 with Becke-Johnson damping[5S–7S] (DFT-D3-BJ)) were tested with the PBE functional,[8S] besides the original DFT method.[9S] The choice of method was controlled *via* tag IVDW. Geometry optimization was performed for both polymorphs at two pressure points (ambient pressure and 6.1 GPa for Form I; ambient pressure and 6.8 GPa for Form II). The models for these calculations were built on the basis of the experimental single-crystal X-ray diffraction data collected at corresponding pressures. Unit cell parameters and RMSD between calculated and experimental structures (using Mercury 3.8[10S]) were used to select the most appropriate computational parameters. While it is always desired that the absolute differences between computed and experimental crystal structure parameters are minimal, this criterion is often difficult to be enforced. For the purpose of the present study, we adopted the criterion that the relative differences between volumes of polymorphs are sufficiently small, *e.g.* ($\Delta V_{I(exp-calc)} - \Delta V_{II(exp-calc)}$) and ($\Delta V_{I(exp-calc)} / V_{I(exp)} - \Delta V_{II(exp-calc)} / V_{II(exp)}$) should be minimal (Tables S12 and

S13). In this regard, the DFT-D3-BJ method[5S–7S] appeared to be reasonably accurate for tolazamide system, resulting in $\Delta V_{(exp-calc)}/V_{(exp)}$ being less than 2.3% for both polymorphs.

Since all calculations formally corresponded to T = 0 K, the calculated volumes were less than those from experiments, but within standard 3% deviation. To test the accuracy and the applicability of the calculations, additional X-Ray experiments were carried out. The two tolazamide polymorphs were cooled down to 100 K and the unit cell parameters were measured at multiple temperature points (Tables S10 and S11); no phase transitions were observed on cooling. The pressure dependencies of volumes were extrapolated to 0 K and compared with the calculated values. The difference between the computed and observed volumes was less than 1.3% for both polymorphs, thereby justifying the applied computational approach.

Enthalpies estimation

Internal energies of both polymorphs were calculated at multiple pressure points (ambient pressure, 0.7 GPa, 2.1 GPa, 4.0 GPa and 6.1 GPa for Form I; ambient pressure, 1.0 GPa, 2.5 GPa, 3.3 GPa and 6.8 GPa for Form II) starting from the experimental structure of certain polymorph at ambient pressure but letting both the atomic positions and the unit cell parameters relax during energy optimization under the corresponding pressure (ISIF=3). Investigated pressure range was extrapolated beyond experimental pressures, calculations for both forms were also performed at 8.0 GPa, 10.0 GPa, 15.0 GPa and 20.0 GPa using ambient pressure structures as starting structures with abovementioned calculation parameters.

While the first order Methfessel-Paxton method of setting partial occupancies of the wavefunctions (ISMEAR=1) was used for geometry optimizations, energies of the optimized structures were recomputed at an improved accuracy by using the tetrahedron method with Bloch correction (ISMEAR=-5). Together with this, the high plane wave cutoff (500 eV) and the dense k-point mesh (6×4×4) are consistent with the high precision setting (PREC=HIGH) recommended for variable-cell calculations.

The enthalpy was estimated as $H = U_{cryst} + PV + ZPE$, where U_{cryst} is the crystal energy calculated by the above presented periodic DFT methodology, ZPE is the zero-point energy calculated trivially from the harmonic vibrational calculation by summing up the frequencies and converting the halved sum to an energy term using the corresponding scaling factor of 1.1963×10^{-2} kJ·mol^{-1}·cm derived from fundamental expression for photon energy ($E = h \cdot \nu$). To estimate the energies of the crystal structure (U_{cryst}) at variable pressure points, overall energy of the unit cell was calculated as ($U_{cryst} = U_{inter} + U_{intra}$) without term separation. All results obtained in this work were provided and discussed only for enthalpies. Entropy was not taken into account, although the T*S term can influence on Gibbs energy. We assume the differences in the T*S terms between polymorphs to be small since the crystal symmetry does not change during phase transition II → I. This approach provides a possibility to calculate enthalpies only, saving computational time with minor inaccuracy for Gibbs energy.

When calculating enthalpies of both polymorphs, disorder observed in Form I at ambient pressure and in Form II at pressures up to 3 GPa was taken into account. Every crystal structure at every pressure with disorder was considered as a sum of two structures with a coefficient corresponding to the occupancy in the structure (*e.g.* disordered structure X with occupancies of 0.75 A and 0.25 B was calculated as H(X) = 0.75*H(A) + 0.25*H(B)). Division of disordered structure into the sum of two structures with corresponding occupancies was also used in previous work.[11S] This concept helps to calculate enthalpies of disordered structures with higher accuracy.

Gas Phase Calculations

Pair-wise interactions energy estimation

Besides the conformational landscape investigation of tolazamide molecule described in the main text, gas phase calculations were also used to estimate the relative energies of pair-wise interactions in Form I. These calculations were provided using Gaussian 09 program[12S] with M062X functional and 6-311++g(d,p) basis set. Pairs of dimer-forming molecules were extracted from crystal structures optimized at corresponding pressures (see pressures in Table S8) and treated as isolated systems. Energies of those molecular pairs were compared with energies of two individual molecules extracted from the pair one at a time. Basis set superposition error (BSSE) correction was taken into account as implemented in Gaussian 09.[12S] Results are summarized in Table S8.

Figures and Tables

Table S1. Crystal data, data collection and refinement parameters for tolazamide Form I at different pressures

For all structures: $C_{14}H_{21}N_3O_3S$, M_r = 311.40, triclinic, $P\bar{1}$, Z = 2. Experiments were carried out at 293 K with Mo-$K\alpha$ radiation using an Oxford Diffraction Gemini R Ultra X-ray diffractometer, Gaussian, Absorb-7 and Absorb-GUI.[13S] Refinement was on 191 parameters with 181 restraints for all structures. H-atom parameters were constrained.

Pressure	0.5 GPa	1.3 GPa	2.1 GPa	2.7 GPa
Crystal data				
a, b, c (Å)	6.2278 (5), 9.026 (2), 13.3215 (14)	6.0542 (6), 8.807 (3), 13.095 (2)	5.9669 (3), 8.6945 (18), 12.9785 (9)	5.9122 (3), 8.617 (4), 12.9150 (17)
α, β, γ (°)	79.608 (13), 86.913 (8), 85.990 (13)	80.05 (2), 86.260 (11), 85.728 (19)	80.432 (10), 85.884 (5), 85.774 (8)	80.610 (19), 85.576 (7), 85.688 (12)
V (Å^3)	734.09 (19)	684.8 (3)	660.93 (15)	645.9 (3)
μ (mm^{-1})	0.24	0.25	0.26	0.27
Crystal size (mm)	0.28 × 0.05 × 0.05	0.28 × 0.05 × 0.05	0.28 × 0.05 × 0.05	0.28 × 0.05 × 0.05
Data collection				
T_{min}, T_{max}	0.391, 0.481	0.391, 0.481	0.388, 0.480	0.395, 0.480
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	3799, 1000, 521	3323, 910, 469	3287, 900, 525	3208, 885, 493
R_{int}	0.132	0.147	0.133	0.138
(sin θ/λ)$_{max}$ (Å^{-1})	0.625	0.625	0.625	0.625
Refinement				
$R[F^2 > 2 \sigma(F^2)]$, $wR(F^2)$, S	0.077, 0.205, 1.03	0.075, 0.221, 1.04	0.066, 0.172, 1.03	0.073, 0.213, 1.03
No. of reflections	1000	910	900	885
Δρ$_{max}$, Δρ$_{min}$ (e Å^{-3})	0.19, -0.27	0.30, -0.21	0.21, -0.19	0.30, -0.24

Pressure	4.0 GPa	5.0 GPa	6.1 GPa
Crystal data			
a, b, c (Å)	5.8202 (3), 8.536 (5), 12.7885 (14)	5.7692 (2), 8.421 (2), 12.7212 (11)	5.7168 (4), 8.3457 (14), 12.6434 (10)
α, β, γ (°)	80.81 (2), 85.069 (6), 85.606 (14)	81.231 (12), 84.740 (5), 85.557 (9)	81.496 (1), 84.436 (7), 85.470 (11)
V (Å^3)	623.6 (4)	606.96 (16)	592.50 (12)
μ (mm^{-1})	0.28	0.28	0.29
Crystal size (mm)	$0.28 \times 0.05 \times 0.05$	$0.28 \times 0.05 \times 0.05$	$0.28 \times 0.05 \times 0.05$
Data collection			
T_{min}, T_{max}	0.391, 0.480	0.388, 0.480	0.388, 0.480
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	3065, 839, 552	3086, 834, 554	2997, 804, 558
R_{int}	0.111	0.109	0.098
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.625	0.624	0.625
Refinement			
$R[F^2 > 2 \sigma(F^2)]$, $wR(F^2)$, S	0.057, 0.136, 1.06	0.053, 0.109, 1.05	0.054, 0.126, 1.06
No. of reflections	839	834	804
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.20, -0.21	0.19, -0.20	0.20, -0.18

Computer programs: *CrysAlis PRO*,[1S] *SHELXS2014/7*,[14S] *SHELXL*,[15S] *Olex2*,[16S] *Mercury*,[10S] *PLATON*.[17S,18S]

Table S2. Crystal data, data collection and refinement parameters for tolazamide Form II at different pressures

For all structures: $C_{14}H_{21}N_3O_3S$, M_r = 311.40, triclinic, $P\overline{1}$, Z = 2. Experiments were carried out at 293 K with Mo-$K\alpha$ radiation using an Oxford Diffraction Gemini R Ultra X-ray diffractometer, Gaussian, Absorb7 and Absorb-GUI.[13S]. H-atom parameters were constrained.

Pressure	0.3 GPa	1.0 GPa	1.7 GPa	2.5 GPa
Crystal data				
a, b, c (Å)	6.3489 (4), 8.8785 (5), 13.387 (3)	6.1901 (4), 8.6946 (6), 13.321 (3)	6.0717 (3), 8.5574 (5), 13.251 (2)	5.9953 (3), 8.4598 (4), 13.189 (2)
α, β, γ (°)	81.965 (10), 85.674 (10), 84.251 (5)	81.572 (11), 86.221 (10), 83.180 (5)	81.402 (9), 86.675 (9), 82.667 (5)	81.453 (9), 86.954 (9), 82.427 (4)
V (Å^3)	742.01 (16)	703.33 (16)	674.67 (13)	655.38 (13)
μ (mm^{-1})	0.23	0.25	0.26	0.26
Crystal size (mm)	0.17 × 0.10 × 0.02	0.17 × 0.10 × 0.02	0.17 × 0.10 × 0.02	0.17 × 0.10 × 0.02
Data collection				
T_{min}, T_{max}	0.390, 0.481	0.396, 0.481	0.394, 0.481	0.391, 0.481
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	3722, 1016, 652	3542, 979, 660	3415, 939, 666	3276, 904, 643
R_{int}	0.097	0.095	0.087	0.087
(sin θ/λ)$_{max}$ (Å^{-1})	0.625	0.625	0.624	0.625
Refinement				
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.053, 0.143, 0.97	0.049, 0.135, 0.94	0.047, 0.115, 0.94	0.042, 0.114, 0.99
No. of reflections	1016	979	939	904
No. of parameters	210	210	210	210
No. of restraints	248	248	248	248
Δρ$_{max}$, Δρ$_{min}$ (e Å^{-3})	0.13, -0.19	0.14, -0.18	0.14, -0.14	0.18, -0.20

Pressure	3.3 GPa	4.0 GPa	4.7 GPa	5.5 GPa
Crystal data				
a, b, c (Å)	5.9272 (3), 8.3697 (4), 13.124 (2)	5.8787 (3), 8.2985 (4), 13.070 (2)	5.8398 (3), 8.2425 (4), 13.031 (3)	5.7996 (3), 8.1816 (4), 12.978 (3)
α, β, γ (°)	81.580 (8), 87.185 (8), 82.254 (4)	81.714 (8), 87.395 (8), 82.183 (4)	81.891 (8), 87.556 (8), 82.156 (4)	82.064 (9), 87.702 (9), 82.134 (4)
V (Å^3)	637.89 (12)	624.86 (12)	614.97 (13)	604.02 (13)
m (mm^{-1})	0.27	0.28	0.28	0.29
Crystal size (mm)	$0.17 \times 0.10 \times 0.02$	$0.17 \times 0.10 \times 0.02$	$0.17 \times 0.10 \times 0.02$	$0.17 \times 0.10 \times 0.02$
Data collection				
T_{min}, T_{max}	0.399, 0.481	0.392, 0.481	0.392, 0.481	0.391, 0.481
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	3135, 869, 642	3135, 866, 647	3104, 856, 641	3047, 841, 629
R_{int}	0.085	0.082	0.083	0.085
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.625	0.625	0.625	0.625
Refinement				
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.042, 0.078, 1.11	0.044, 0.101, 1.10	0.043, 0.108, 1.07	0.041, 0.097, 1.04
No. of reflections	869	866	856	841
No. of parameters	191	191	191	191
No. of restraints	184	184	184	184
$\Delta\rho_{max}, \Delta\rho_{min}$ (e Å^{-3})	0.14, -0.16	0.17, -0.16	0.17, -0.18	0.15, -0.17

Pressure	6.1 GPa	6.8 GPa
Crystal data		
a, b, c (Å)	5.7694 (3), 8.1369 (4), 12.941 (3)	5.7365 (3), 8.0902 (4), 12.894 (2)
α, β, γ (°)	82.207 (9), 87.842 (9), 82.147 (4)	82.422 (8), 88.028 (8), 82.178 (4)
V (Å^3)	596.16 (12)	587.59 (11)
m (mm^{-1})	0.29	0.29
Crystal size (mm)	$0.17 \times 0.10 \times 0.02$	$0.17 \times 0.10 \times 0.02$
Data collection		
T_{min}, T_{max}	0.391, 0.481	0.390, 0.481
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	3006, 824, 629	2957, 809, 599
R_{int}	0.079	0.084
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.625	0.625
Refinement		
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.044, 0.103, 1.06	0.050, 0.119, 1.10
No. of reflections	824	809
No. of parameters	191	86
No. of restraints	184	0
$\Delta\rho_{max}, \Delta\rho_{min}$ (e Å^{-3})	0.19, -0.17	0.21, -0.26

Computer programs: *CrysAlis PRO*,[1S] *SHELXS2014/7*,[14S] *SHELXL*,[15S] *Olex2*,[16S] *Mercury*,[10S] *PLATON*.[17S,18S]

Table S3. Parameters of the third-order Tait equations of state for tolazamide Forms I and II

Form	I		II	
Fitted data	*experimental*	*calculated*	*experimental*	*calculated*
Temperature (K)	293	0	293	0
V_0 (Å^3)	774.6(6)	732.0(8)	784.2(2)	730.3(10)
a	9.6	8.4	11.1	6.4
b (GPa^{-1})	1.5	0.9	1.7	0.7
c	0.010	0.014	0.009	0.020
K_0 (GPa)	6.4(3)	10.7(2)	5.8(2)	11.9(5)
K_0'	9.0(3)	7.5(1)	9.2(2)	6.9(1)

Table S4. The volumes differences between tolazamide polymorphs at different pressure points based on the calculated data and the data from Tait equations of state describing experimental and calculated data*

Pressure, GPa	$\Delta V = V_{II} - V_{I}$, Å^3, based on:		
	calculated data	Tait equations of state describing calculated data	Tait equations of state describing experimental data
8.0	4.56	4.84	3.11
10.0	4.24	4.49	2.80
15.0	3.84	3.46	1.82
20.0	2.24	2.22	0.74

*provided these forms still exist at these pressures in reality

Table S5. The differences between the enthalpies of tolazamide polymorphs and their constituents (internal energies, zero-point energies (ZPE) and the PV terms) at different pressure points*

Pressure, GPa	$\Delta H = H_{II} - H_I$, kJ/mol	$\Delta U = U_{II} - U_I$, kJ/mol	$\Delta ZPE = ZPE_I - ZPE_{II}$, kJ/mol	$\Delta(PV) = P(V_{II} - V_I)$, kJ/mol
ambient	6.1	9.6	-3.5	0.0
8.0	69.7	49.4	-1.7	21.9
10.0	74.4	52.1	-3.3	25.6
15.0	89.3	56.6	-2.0	34.7
20.0	96.8	71.6	-1.8	27.0

*provided these forms still exist at these pressures in reality

Table S6. Angles between the principal axes of the strain ellipsoid and unit cell directions for tolazamide forms I and II (pressure increase from ambient pressure point to 6.1 GPa for Form I and from ambient pressure point to 6.8 GPa for Form II). Results are obtained using WinStrain program[19S] at infinitesimal lagrangian approximation

Form	Axis	Angle with unit cell direction (°)		
		a	*b*	*c*
I	1	138.4(0.3)	63.6(0.4)	61.0(0.1)
	2	125.1(0.4)	148.9(0.3)	103.1(0.3)
	3	70.7(0.2)	105.1(0.2)	32.4(0.1)
II	1	39.8(0.1)	122.8(0.1)	80.3(0.1)
	2	125.6(0.1)	146.9(0.1)	110.1(0.1)
	3	74.5(0.1)	86.2(0.1)	157.5(0.1)

Table S7. Hydrogen bonds distances *vs* pressure for two polymorphs of tolazamide and distances between the benzene rings (calculated as distances between two centroids) for Form I, using Mercury program[10S]

Tolazamide I				Tolazamide II				
Pressure (GPa)	N2-H2···O3 (-x,1-y,1-z)		Distance between benzene rings (Å)	Pressure (GPa)	N1-H1···O1 (-x+1, -y+2, -z+1)		N2-H2···O3 (-x, -y+1, -z+1)	
	$D···A$ (Å)	3σ (Å)			$D···A$ (Å)	3σ (Å)	$D···A$ (Å)	3σ (Å)
0.5	2.85	0.06	3.992	0.3	3.047	0.024	3.01	0.018
1.3	2.82	0.09	3.863	1.0	2.95	0.021	2.961	0.015
2.1	2.85	0.06	3.793	1.7	2.906	0.021	2.907	0.015
2.7	2.85	0.06	3.773	2.5	2.863	0.021	2.868	0.015
4.0	2.831	0.054	3.717	3.3	2.846	0.018	2.821	0.012
5.0	2.773	0.054	3.675	4.0	2.815	0.021	2.792	0.015
6.1	2.746	0.054	3.646	4.7	2.803	0.021	2.783	0.015
				5.5	2.777	0.021	2.738	0.015
				6.1	2.788	0.021	2.751	0.015
				6.8	2.762	0.024	2.714	0.015

Table S8. Stabilization energy of pair-wise interactions and distances between the benzene rings (calculated as distances between two centroids, using Mercury program[10S]) in the calculated tolazamide Form I structures at different pressures.

Pressure (GPa)	Distance between stacked benzene rings (Å)	Stabilization energy of pair-wise interactions (kJ/mol)
0.0001	3.984	-42.9
0.7	3.909	-45.8
2.1	3.757	-48.9
4.0	3.691	-46.7
6.1	3.621	-42.0
8.0*	3.564	-36.6
10.0*	3.529	-30.0
15.0*	3.436	-9.3
20.0*	3.358	14.1

*provided Form I still exists at these pressures in reality

Table S9. Root-mean-square deviations (RMSD) of atomic positions between the molecules in structures of Form I/II at ambient pressure and other pressure points (as implemented in Mercury 3.8)[10S]

Form I		Form II	
Pressure, GPa	RMSD, Å	Pressure, GPa	RMSD, Å
0.5	0.051	0.3	0.035
1.3	0.070	1.0	0.073
2.1	0.091	1.7	0.103
2.7	0.092	2.5	0.138
4.0	0.112	3.3	0.256
5.0	0.118	4.0	0.255
6.1	0.133	4.7	0.253
		5.5	0.256
		6.1	0.257
		6.8	0.258

Table S10. Experimental unit cell parameters of tolazamide Form I at different temperatures

	Temperature (K)	*a*, *b*, *c* (Å)	α, β, γ (°)	*V* (Å³)
cooling	293	6.3558 (3), 9.2184 (5), 13.5140 (7)	78.983 (5), 87.259 (4), 85.808 (5)	774.66 (7)
	250	6.3346 (3), 9.1641 (5), 13.4642 (7)	79.222 (4), 87.305 (4), 85.936 (4)	755.95 (7)
	200	6.3064 (5), 9.1298 (7), 13.3984 (11)	79.397 (7), 87.344 (7), 85.986 (7),	745.14 (11)
	150	6.2738 (2), 9.0824 (4), 13.3414 (5)	79.449 (4), 87.415 (3), 86.013 (4)	738.80 (5)
	100	6.2433 (2), 9.0724 (4), 13.3119 (5)	79.359 (4), 87.461 (3), 85.933 (3)	760.32 (5)
heating	125	6.2586 (2), 9.0748 (4), 13.3249 (5)	79.432 (3), 87.442 (3), 85.970 (3)	765.43 (5)
	175	6.2891 (3), 9.0960 (4), 13.3659 (5)	79.436 (4), 87.381 (3), 86.026 (4)	741.73 (6)
	225	6.3186 (5), 9.1502 (8), 13.4244 (11)	79.314 (7), 87.303 (7), 85.948 (7)	749.41 (11)
	275	6.3453 (3), 9.1929 (3), 13.4917 (7)	79.103 (5), 87.266 (4), 85.857 (4)	760.32 (7)
	293	6.3506 (6), 9.2241 (9), 13.4984 (13)	79.091 (8), 87.215 (8), 85.815 (8)	765.43 (13)

Table S11. Experimental unit cell parameters of tolazamide Form II at different temperatures

|	Temperature (K)	a, b, c (Å)	α, β, γ (°)	V (Å^3)
cooling	293	6.4954 (3), 9.0530 (4), 13.4630 (6)	82.471 (3), 85.251 (4), 85.839 (4)	780.61 (6)
	250	6.4476 (3), 9.0146 (5), 13.4866 (7)	82.361 (4), 85.369 (4), 85.554 (4)	772.61 (7)
	200	6.3938 (3), 8.9799 (4), 13.5211 (7)	82.132 (4), 85.599 (4), 85.342 (4)	764.78 (6)
	150	6.3349 (8), 8.9444 (11), 13.5491 (15)	81.970 (10), 85.922 (10), 85.275 (10)	756.22 (15)
	100	6.3093 (11), 8.9247 (15), 13.578 (3)	81.865 (16), 86.143 (16), 85.170 (16)	753.0 (2)
heating	125	6.3217 (8), 8.9383 (12) 13.5516 (16)	81.886 (10), 85.956 (10), 85.210 (11)	754.09 (17)
	175	6.3687 (5), 8.9670 (6) 13.5480 (9)	82.031 (6), 85.711 (6), 85.265 (6)	762.04 (9)
	225	6.4252 (16) 9.004 (2) 13.532 (4)	82.36 (2), 85.43 (2), 85.47 (2)	771.6 (3)
	275	6.4865 (18) 9.042 (2) 13.468 (4)	82.42 (2), 85.53 (2), 85.74 (2)	779.0 (4)
	295	6.5009 (15) 9.062 (2) 13.471 (3)	82.514 (19), 85.284 (19), 85.885 (18)	782.7 (3)

Table S12. Unit cell parameters and volumes for Form I at ambient pressure and 6.1 GPa: comparison of experimental (T=298K) values with those calculated with different dispersion corrections

Pressure	Method	Value	a, Å	b, Å	c, Å	α, °	β, °	γ, °	V, Å³
ambient pressure	DFT-D2	Parameter	6.1922	8.8124	14.1210	77.183	80.707	79.440	732.735
		Δ	0.1648	0.4062	0.6064	1.814	6.495	6.371	42.128
		δ	2.592	4.406	4.487	2.296	7.448	7.424	5.4368
	DFT-D3 (zero damping)	Parameter	6.2685	8.9530	14.2464	76.939	81.505	80.021	762.143
		Δ	0.0885	0.2656	0.7318	2.058	5.697	5.790	12.720
		δ	1.39	2.881	5.415	2.605	6.533	6.747	1.6415
	DFT-D3 (Becke-Johnson damping)	Parameter	6.2580	8.9486	14.2026	76.862	81.342	79.924	757.479
		Δ	0.0990	0.2700	0.6880	2.135	5.860	5.887	17.384
		δ	1.56	2.929	5.091	2.703	6.720	6.860	2.2435
	DFT without dispersion corrections	Parameter	6.4567	9.3467	14.4757	75.539	83.753	81.710	834.655
		Δ	0.0997	0.1281	0.9611	3.458	3.449	4.101	59.792
		δ	1.57	1.390	7.112	4.377	3.955	4.779	7.7716
	Experiment	Parameter	6.3570	9.2186	13.5146	78.997	87.202	85.811	774.863
6.1 GPa	DFT-D2	Parameter	5.8539	7.9443	13.1613	81.866	74.877	79.169	577.575
		Δ	0.1371	0.4014	0.5179	0.370	9.559	6.301	14.925
		δ	2.398	4.810	4.096	0.454	11.32	7.372	2.5190
	DFT-D3 (zero damping)	Parameter	5.8416	8.0975	13.3159	80.743	76.772	78.885	597.156
		Δ	0.1248	0.2482	0.6725	0.753	7.664	6.585	4.656
		δ	2.183	2.974	5.319	0.924	9.077	7.704	0.7858
	DFT-D3 (Becke-Johnson damping)	Parameter	5.8276	8.0457	13.3100	81.079	76.524	78.770	591.324
		Δ	0.1108	0.3000	0.6666	0.417	7.912	6.700	1.176
		δ	1.938	3.595	5.272	0.512	9.370	7.984	0.1985
	DFT without dispersion corrections	Parameter	5.9043	8.2367	13.4558	80.037	77.609	79.231	621.827
		Δ	0.1875	0.1090	0.8124	1.459	6.827	6.239	29.327
		δ	3.280	1.306	6.425	1.790	8.085	7.300	4.9497
	Experiment	Parameter	5.7168	8.3457	12.6434	81.496	84.436	85.470	592.500

Table S13. Unit cell parameters and volumes for Form II at ambient pressure and 6.8 GPa: comparison of experimental (T=298 K) values with those calculated with different dispersion corrections

Pressure	Method	Value	a, Å	b, Å	c, Å	α, °	β, °	γ, °	V, Å³
ambient pressure	DFT-D2	Parameter	6.4937	8.9344	13.5647	82.706	85.370	87.258	777.504
		Δ	0.0104	0.1335	0.0806	0.196	0.110	1.419	6.748
		δ	0.160	1.472	0.598	0.230	0.129	1.653	0.8604
	DFT-D3 (zero damping)	Parameter	6.5196	8.9668	13.6038	82.673	85.308	87.157	785.526
		Δ	0.0155	0.1011	0.1197	0.163	0.048	1.331	1.274
		δ	0.238	1.115	0.8877	0.198	0.056	1.551	0.1624
	DFT-D3 (Becke-Johnson damping)	Parameter	6.5141	8.9592	13.5835	82.683	85.314	87.152	783.048
		Δ	0.0100	0.1087	0.0994	0.173	0.054	1.313	1.204
		δ	0.154	1.199	0.737	0.210	0.063	1.530	0.1535
	DFT without dispersion corrections	Parameter	6.5950	9.1103	13.7044	82.685	85.232	87.027	813.158
		Δ	0.0909	0.0424	0.2203	0.175	0.028	1.188	28.906
		δ	1.40	0.468	1.634	0.212	0.033	1.384	3.6858
	Experiment	Parameter	6.5041	9.0679	13.4841	82.510	85.260	85.839	784.252
6.8 GPa	DFT-D2	Parameter	5.9831	7.8552	12.7630	84.593	86.176	82.460	591.116
		Δ	0.2466	0.2350	0.1310	2.171	1.852	0.282	3.541
		δ	4.299	2.905	1.016	2.634	2.104	0.343	0.6026
	DFT-D3 (zero damping)	Parameter	6.0044	7.9256	12.7879	84.361	86.015	82.679	599.675
		Δ	0.2679	0.1646	0.1061	1.939	2.013	0.501	12.100
		δ	4.670	2.035	0.8229	2.353	2.287	0.610	2.0593
	DFT-D3 (Becke-Johnson damping)	Parameter	6.0061	7.9290	12.7929	84.234	85.999	82.868	600.439
		Δ	0.2696	0.1612	0.1011	1.812	2.029	0.690	12.864
		δ	4.700	1.993	0.7841	2.198	2.305	0.840	2.1893
	DFT without dispersion corrections	Parameter	6.0821	8.1203	12.8885	83.775	85.781	83.691	627.742
		Δ	0.3456	0.0301	0.0055	1.353	2.247	1.513	40.167
		δ	6.025	0.372	0.043	1.642	2.553	1.841	6.8361
	Experiment	Parameter	5.7365	8.0902	12.8940	82.422	88.028	82.178	587.575

Figure S1. Calculated enthalpy difference (a), internal energy difference (b) and PV difference (c) of Form II and Form I versus pressure. Calculation of enthalpies, internal energies and PV term in experimental range was provided at corresponding experimental pressures for Form I and II, which were different due to the limitations of experimental techniques. All phases are assumed to be preserved also above 7 GPa
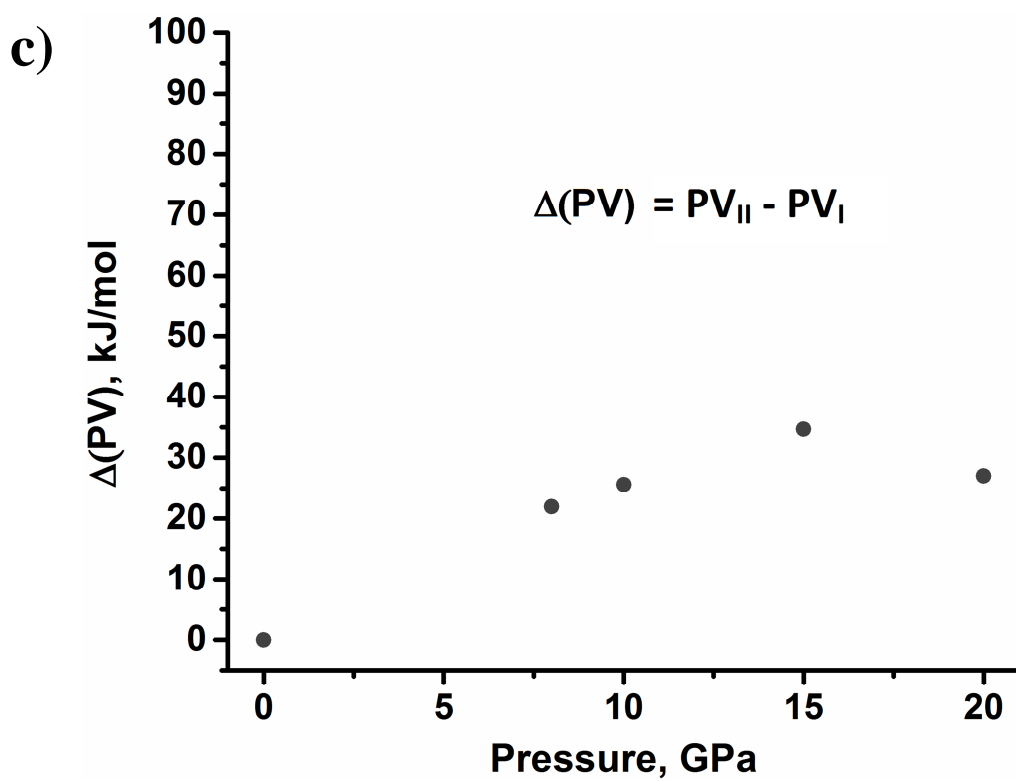
c)

$\Delta(PV) = PV_{II} - PV_{I}$
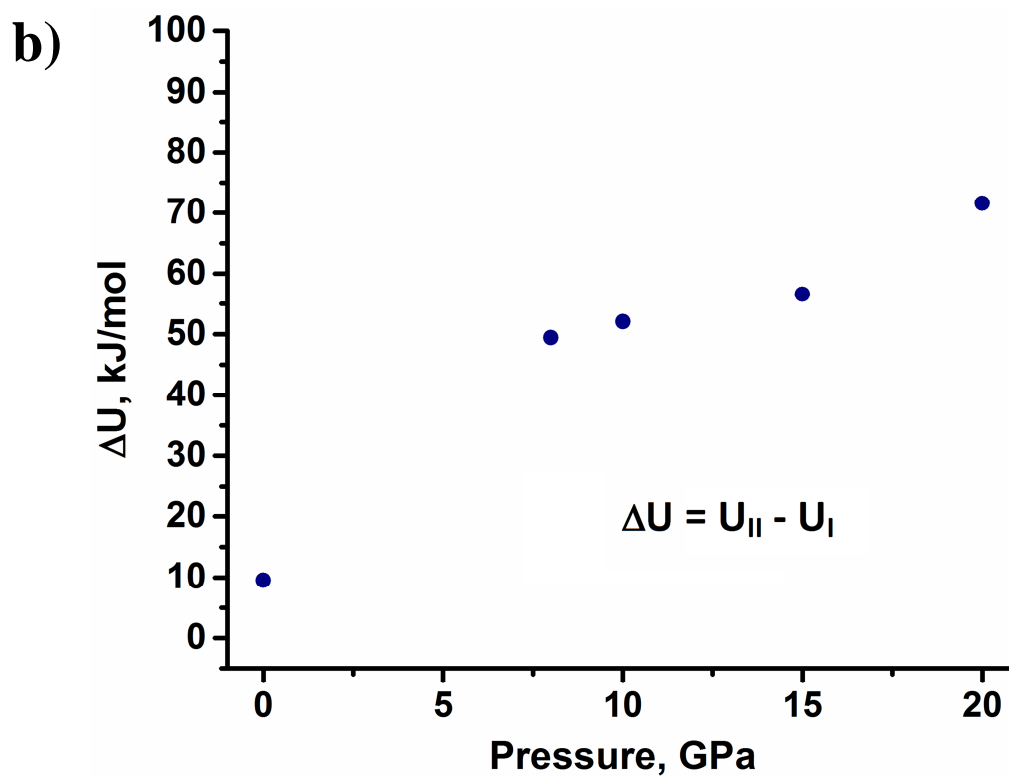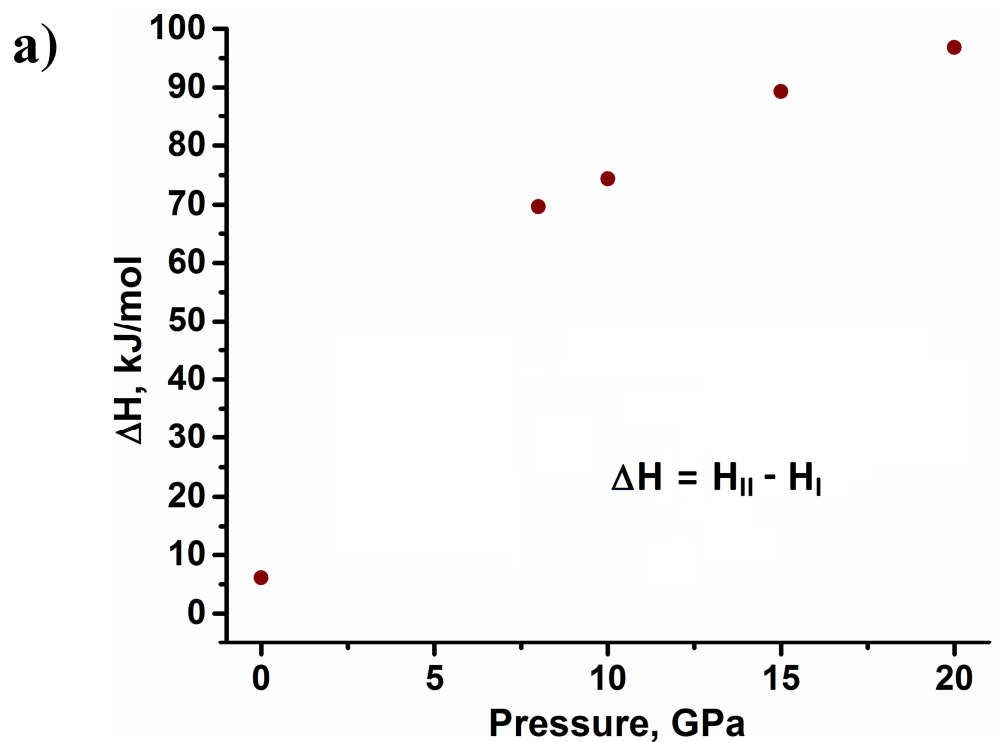
Figure S2. Site occupancy factors for two possible conformations of azepane ring
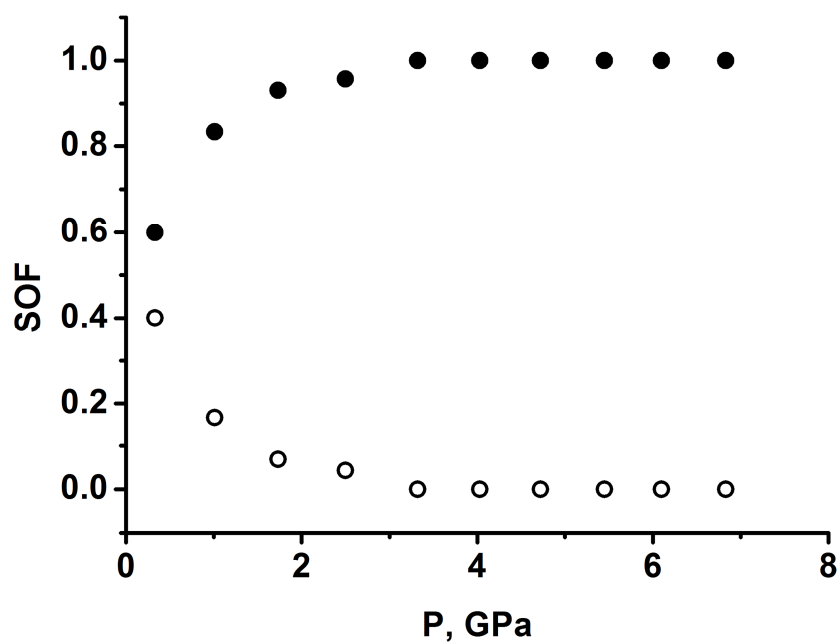
Figure S3. Conformational landscape of tolazamide C5-C4-S1-N1 dihedral angle. From this and the next (Fig. S4–S7) figures one can see that tolazamide polymorphs I and II are conformational polymorphs, whereas II and III – not.[11S, 20S] Form III (CCDC No. 1025481) has been included into the conformational landscape analysis for the sake of completeness. However, Form III is less important for this particular study.
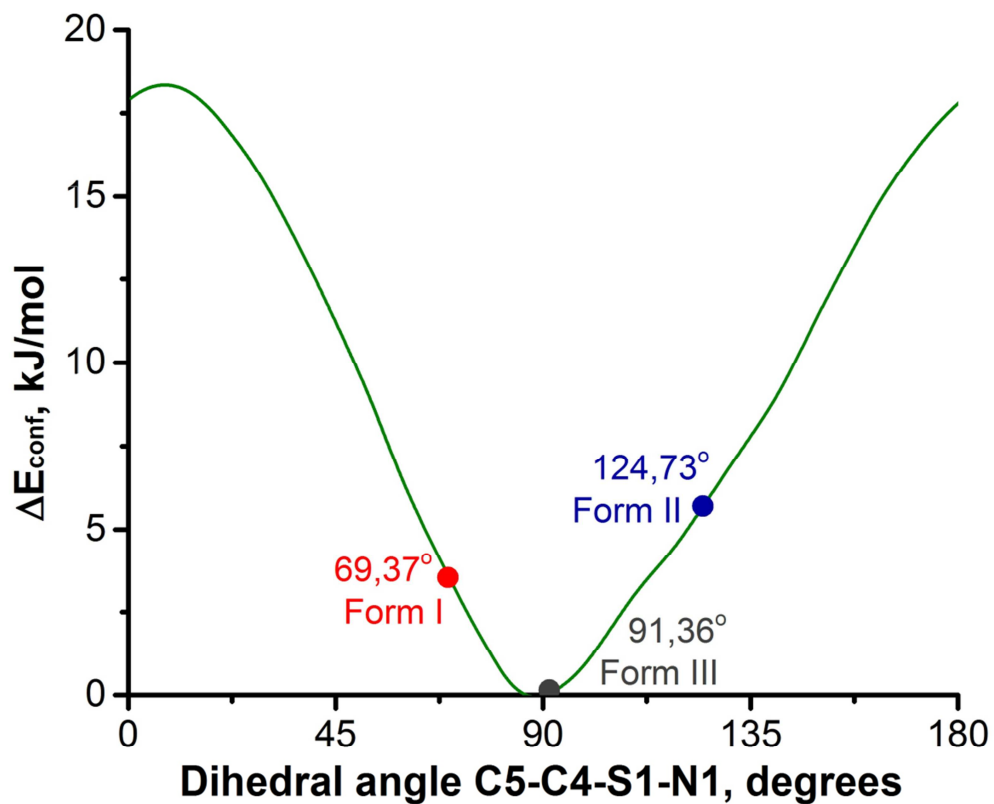
Figure S4. Conformational landscape of tolazamide C4-S1-N1-C8 dihedral angle*. Form III (CCDC No. 1025481) has been included into the conformational landscape analysis for the sake of completeness. However, Form III is less important for this particular study.
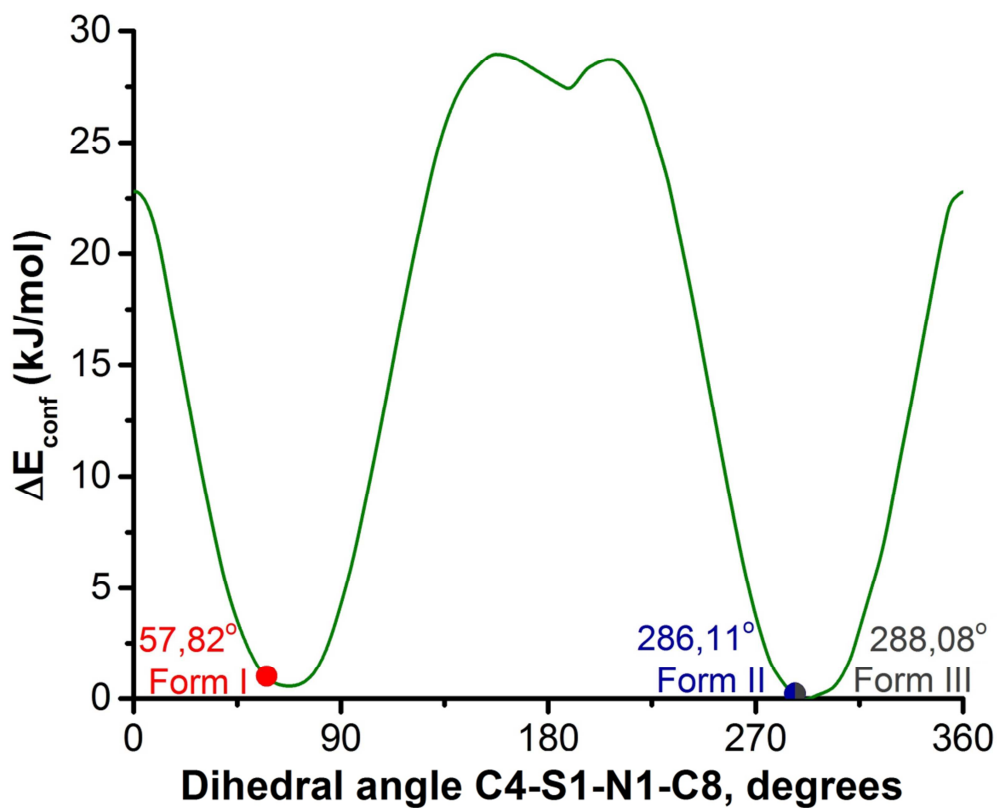

*irregular curve near maximum is the result of interpolation, but obviously does not affect important data

Figure S5. Conformational landscape of tolazamide S1-N1-C8-N2 dihedral angle. Form III (CCDC No. 1025481) has been included into the conformational landscape analysis for the sake of completeness. However, Form III is less important for this particular study.
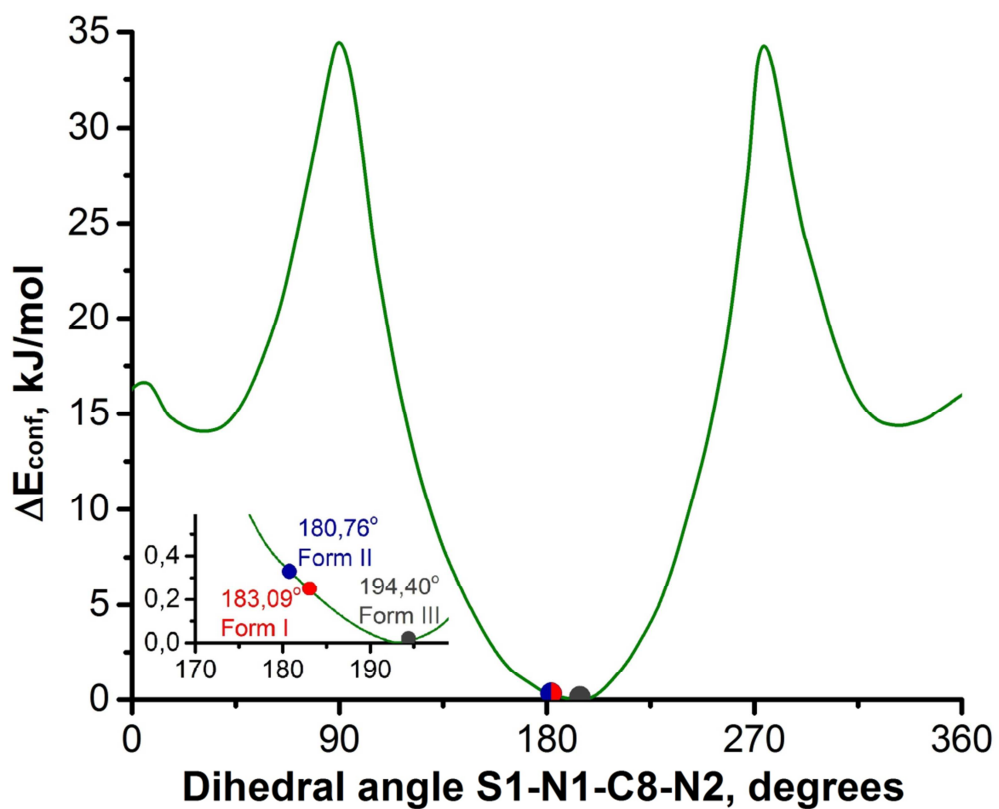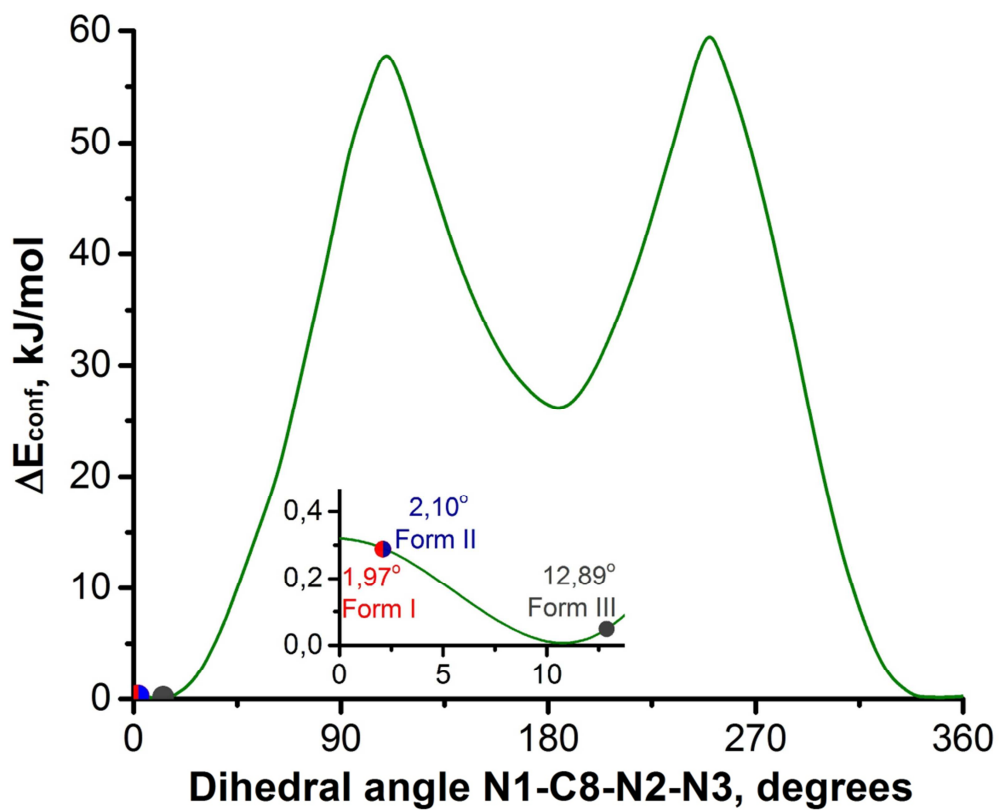
Figure S6. Conformational landscape of tolazamide N1-C8-N2-N3 dihedral angle. Form III (CCDC No. 1025481) has been included into the conformational landscape analysis for the sake of completeness. However, Form III is less important for this particular study.
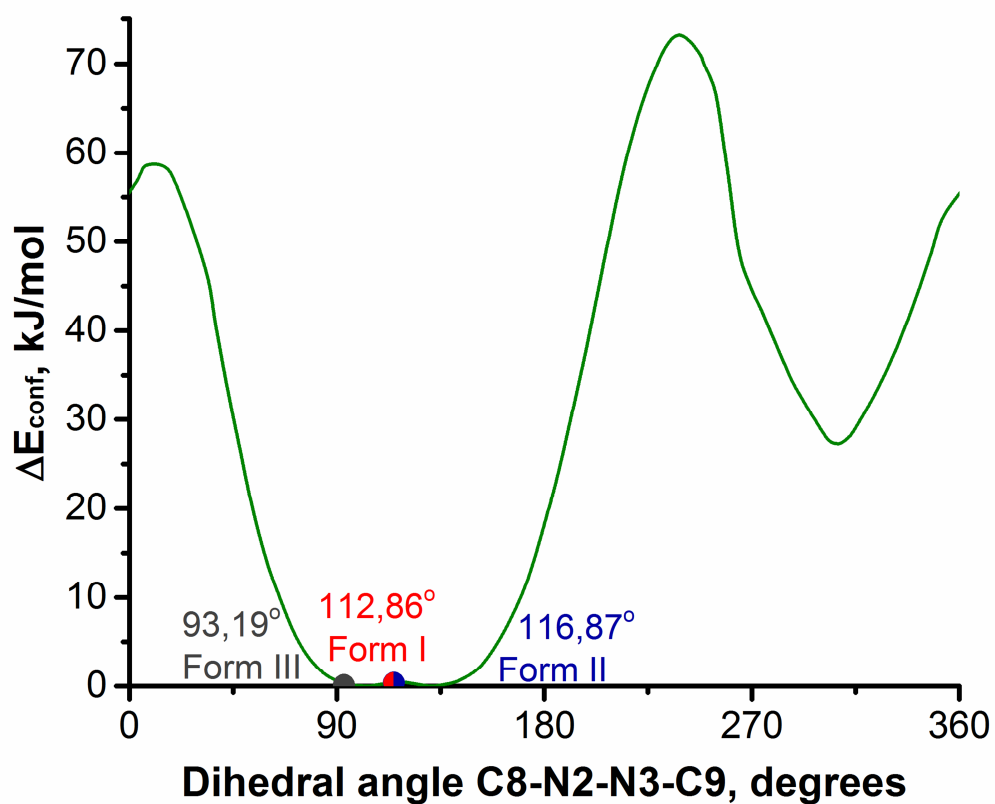
Figure S7. Conformational landscape of tolazamide C8-N2-N3-C9 dihedral angle. Form III (CCDC No. 1025481) has been included into the conformational landscape analysis for the sake of completeness. However, Form III is less important for this particular study.

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