Acta Crystallographica Section D
Biological Crystallography
ISSN 0907-4449

Alternative models for two crystal structures of *Candida albicans* 3,4-dihydroxy-2-butanone 4-phosphate synthase

Isolde Le Trong and Ronald E. Stenkamp*

Departments of Biological Structure and Biochemistry, Biomolecular Structure Center, University of Washington, Seattle, WA 98195, USA

Correspondence e-mail: stenkamp@u.washington.edu

Received 26 October 2007
Accepted 5 November 2007

PDB References: 3,4-dihydroxy-2-butanone 4-phosphate synthase, native, 2ris, r2rissf; D-ribulose 5-phosphate complex, 2riu, r2riusf.

Reinterpretation of the space-group symmetry is reported for two crystal structures of *Candida albicans* 3,4-dihydroxy-2-butanone 4-phosphate synthase (PDB codes 1tks and 1tku). The two structures reported in space group *P*1 with a dimer in the asymmetric unit can be described as *C*-centered monoclinic structures with one subunit in the asymmetric unit.

Two crystal structures of 3,4-dihydroxy-2-butanone 4-phosphate synthase (DHBPS) from *Candida albicans* have been deposited in the Protein Data Bank (Echt *et al.*, 2004). PDB entry 1tks contains a model for the unliganded enzyme, while PDB entry 1tku is a D-ribulose 5-phosphate (Ru5P) complex of the protein. The structures are isomorphous (see Table 1) and were solved in space group *P*1 with two identical polypeptide chains in the asymmetric unit. The authors reported the presence of a noncrystallographic twofold rotation axis that relates the two chains in what is believed to be the physiologically important dimer.

We re-examined these structures after surveying *WHAT_CHECK* results (Hooft *et al.*, 1996) for PDB entries with more than one molecule in the asymmetric unit. The small r.m.s. deviations from an average structure for the two molecules in the asymmetric unit attracted our attention, as did the nearly 90° γ angles for the two triclinic unit cells.

Visual inspection shows that the dyad relating the two subunits is collinear with the *b* axis of the triclinic unit cell and applies to the entire crystal. Thus, the crystal structures possess monoclinic symmetry. This is also seen in the deposited diffraction data.

An alternate description of the crystal structures is possible in space group *C*2 with a single subunit in the asymmetric unit. The transformation used to convert the reflection indices to the monoclinic cell was $h_{\rm monoclinic} = -k_{\rm triclinic} + 2l_{\rm triclinic}$, $k_{\rm monoclinic} = -k_{\rm triclinic}$, $l_{\rm monoclinic} = h_{\rm triclinic}$. Averaging of the replicate measurements related by the 2/*m* monoclinic symmetry resulted in $R_{\rm merge}$ values of 0.034 and 0.024 for the diffraction data for PDB entries 1tks and 1tku, respectively. The number of unique reflections was reduced from 43 263 to 24 177 for the free enzyme and from 39 344 to 20 361 for the Ru5P complex. The triclinic data sets were reported as being 84.4% and 77.3% complete (Echt *et al.*, 2004). (We have been unable to confirm the 77.3% value owing to an inconsistency between the reported number of reflections and the resolution limits for the Ru5P complex.) The reindexed monoclinic sets were 91.9% and 93.0% complete for the enzyme and Ru5P complex, respectively. Table 1 contains a comparison of the triclinic and monoclinic unit-cell parameters.

An initial model was oriented and positioned in the monoclinic cell with *MOLREP* (Collaborative Computational Project, Number 4, 1994) using the *A* chain of 1tks as the probe. Water molecules from 1tks were added to the model if they were within 4 Å of atoms in the *A* chain, if they had a matching water molecule bound to the *B* chain and if they were located in a peak higher than 1σ in a difference electron-density map calculated for the *MOLREP* solution. A refined model for the free enzyme served as the initial model for the Ru5P complex. Superposition of the *A* chain of 1tku, along with its waters

Table 1
Unit-cell parameters for the PDB entries for 3,4-dihydroxy-2-butanone 4-phosphate synthase.

Molecular form	Native enzyme		Ru5P complex	
PDB code	1tks	2ris	1tku	2riu
Space group	*P*1	*C*2	*P*1	*C*2
a (Å)	40.4	109.5	40.2	109.6
b (Å)	48.1	48.1	47.9	47.9
c (Å)	59.8	40.4	59.8	40.2
α (°)	66.2	90.0	66.4	90.0
β (°)	72.0	70.2	72.3	70.6
γ (°)	89.9	90.0	89.9	90.0
No. of molecules per ASU	2	1	2	1
Reference	Echt *et al.* (2004)	This work	Echt *et al.* (2004)	This work

Table 2
Comparison of refinement statistics for the triclinic and monoclinic models.

Molecular form	Native enzyme		Ru5P complex	
PDB code	1tks	2ris	1tku	2riu
Space group	*P*1	*C*2	*P*1	*C*2
Resolution	20–1.6	20–1.6	20–1.66	20–1.7
R factor (overall)	0.192	0.204	0.184	0.185
$R_{\rm free}$	0.219	0.229	0.218	0.215
No. of unique reflections	43264	24177	39461	20361
No. of protein atoms	3034	1527	3034	1522
No. of water molecules	676	137	672	158
No. of ligand atoms	—	—	28	14
Average *B* values (Å^2)				
Protein	12.9	11.3	12.1	13.1
Solvent	28.3	16.8	28.0	20.6
Ligand	—	—	27.8	27.5
R.m.s. deviations				
Bond lengths (Å)	0.005	0.008	0.005	0.007
Bond angles (°)	1.19	1.10	1.27	1.13
Ramachandran quality, residues in				
Most favored regions (%)	88.9	90.5	89.9	91.0
Additional allowed regions (%)	11.1	8.9	10.1	8.4
Generously allowed regions (%)	0	0.6	0	0.6
Reference	Echt *et al.* (2004)	This work	Echt *et al.* (2004)	This work

and ligand, permitted transfer of the ligand model to the monoclinic structure.

The structural models were refined using *REFMAC*5 (Murshudov *et al.*, 1997) from the *CCP*4 suite (Collaborative Computational Project, Number 4, 1994). $R_{\rm free}$ (Brünger, 1993) was calculated using 5% of the reflections. $\sigma_{\rm A}$-weighted $|F_{\rm o}| - |F_{\rm c}|$ and $2|F_{\rm o}| - |F_{\rm c}|$ electron-density maps (Read, 1986) were examined with *XtalView* (McRee, 1999) for manual adjustments of the models. The final *R* (and $R_{\rm free}$) values for the two structures were 0.205 (0.229) and 0.186 (0.215). Additional details concerning the refinement are included in Table 2. *PROCHECK* (Laskowski *et al.*, 1993) was used to monitor and validate the final models. Coordinates and structure factors for these reinterpretations of the two structures have been deposited in the PDB and assigned identification codes 2ris and 2riu. The net effect of this change of space-group assignment on the molecular structure is very small. The enzyme and ligand models for the monoclinic structures are very similar to the triclinic structures. R.m.s. differences among the structures are provided in Table 3. The protein and ligand molecules are all as similar as the two copies in the original triclinic models.

The major differences between the monoclinic and triclinic structures concern the numbers of water molecules included in the structural models. The triclinic structures contained 676 and 672 water molecules for the enzyme and its D-ribulose-5-phosphate complex, respectively. These numbers are reduced to 130 and 151, respectively, for the monoclinic models. The large reduction beyond the factor of two expected for the smaller asymmetric units probably comes from a reduction in the number of water molecules fitted to noise peaks in the electron-density maps.

Table 3
R.m.s. distances between superposed protein models (Å).

R.m.s. distances were calculated for superposed models using *XtalView* (McRee, 1999). Residues 5–70 and 90–200 contributed to the values. The gap between residues 70 and 90 omitted about ten residues from the model and covered a segment of polypeptide not seen in the electron-density maps. The values in each entry in the table are (from top to bottom) r.m.s. distance for the C^{α} atoms, for main-chain atoms (N, C^{α}, C, O) and for all atoms.

	2ris	1tks chain *A*	1tks chain *B*	2riu	1tku chain *A*	1tku chain *B*
2ris	—	0.069 0.072 0.180	0.073 0.075 0.540	0.098 0.099 0.236	0.100 0.104 0.224	0.103 0.107 0.560
1tks chain *A*		—	0.072 0.072 0.571	0.120 0.122 0.293	0.103 0.105 0.221	0.111 0.112 0.595
1tks chain *B*			—	0.116 0.118 0.540	0.101 0.102 0.586	0.099 0.101 0.191
2riu				—	0.057 0.060 0.276	0.059 0.062 0.534
1tku chain *A*					—	0.040 0.040 0.573
1tku chain *B*						—

The similarity of the two molecules in the triclinic asymmetric units was noted in the original structure report (Echt *et al.*, 2004), although the r.m.s. deviations reported there differ from those in Table 3. Differences in the particular residues contributing to the r.m.s. values probably account for this. No description of the different packing environments for the two molecules in the triclinic asymmetric unit was provided in the original structure report. In the monoclinic structure interpretations, the two subunits in the dimers are in equivalent positions and identical in the symmetric homodimers.

This work was supported by the Royalty Research Fund of the University of Washington. We thank Ethan Merritt for helpful discussions.

References

Brünger, A. T. (1993). *Acta Cryst.* D**49**, 24–36.
Collaborative Computational Project, Number 4 (1994). *Acta Cryst.* D**50**, 760–763.
Echt, S., Bauer, S., Steinbacher, S., Huber, R., Bacher, A. & Fischer, M. (2004). *J. Mol. Biol.* **341**, 1085–1096.
Hooft, R. W. W., Vriend, G., Sander, C. & Abola, E. E. (1996). *Nature (London)*, **381**, 272.
Laskowski, R. A., MacArthur, M. W., Moss, D. S. & Thornton, J. M. (1993). *J. Appl. Cryst.* **26**, 283–291.
McRee, D. E. (1999). *J. Struct. Biol.* **125**, 156–165.
Murshudov, G. N., Vagin, A. A. & Dodson, E. J. (1997). *Acta Cryst.* D**53**, 240–255.
Read, R. J. (1986). *Acta Cryst.* A**42**, 140–149.