Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

SUPPORTING MATERIALS

Correlations between secondary structure- and protein-protein interface-mimicry: The Interface Mimicry Hypothesis

Jaru Taechalertpaisarn,[a] Rui-Liang Lyu,[a] Maritess Arancillo,[a] Chen-Ming Lin,[a] Lisa M. Perez,[b] Thomas R. Ioerger,[c] and Kevin Burgess[a]*

[a]Department of Chemistry and [b]Laboratory For Molecular Simulation, Texas A & M University, Box 30012, College Station, TX 77842-3012, USA. [c]Department of Computer Science, Texas A & M University, College Station, TX 77843-3112.

E-mail: burgess@tamu.edu

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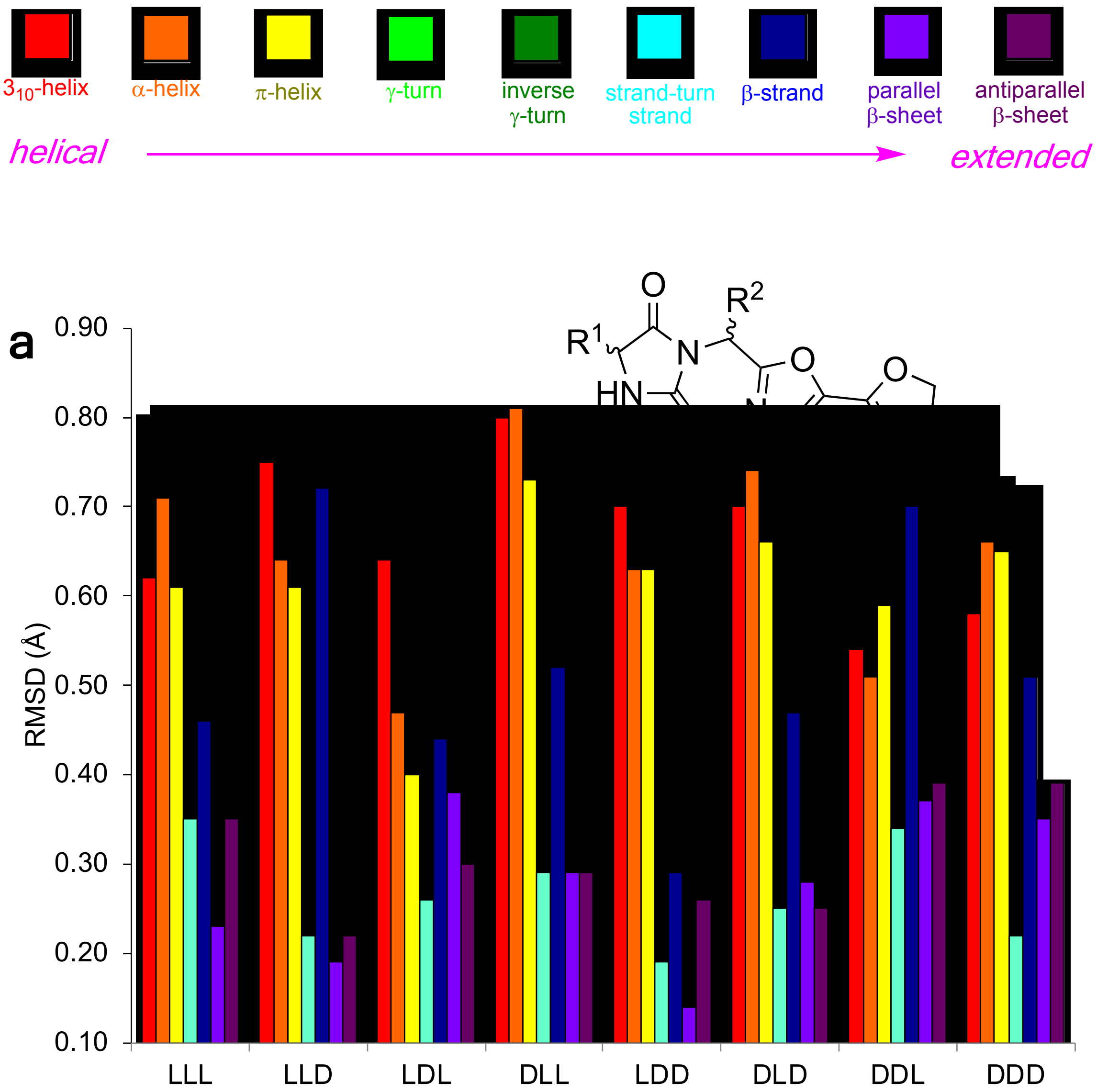
A. EKO Procedures

The QMD was performed according to the procedure described before.[1, 2] After energy minimization in the QMD process, all conformers within 3.0 kcal/mol of the lowest energy conformer were clustered into families with similar RMSDs (< 0.5 Å) based on Cα – Cβ coordinates. The conformer having lowest energy in each family was selected as a representative. These representatives were systematically aligned on the Cα – Cβ coordinates of interface residues on > 240,000 protein-protein complexes recorded in the PDB, and the results were sorted based on RMSDs of Cα – Cβ coordinates.[1]

B. EKOS, EKO, and DSSP/STRIDE data for chemotype 2



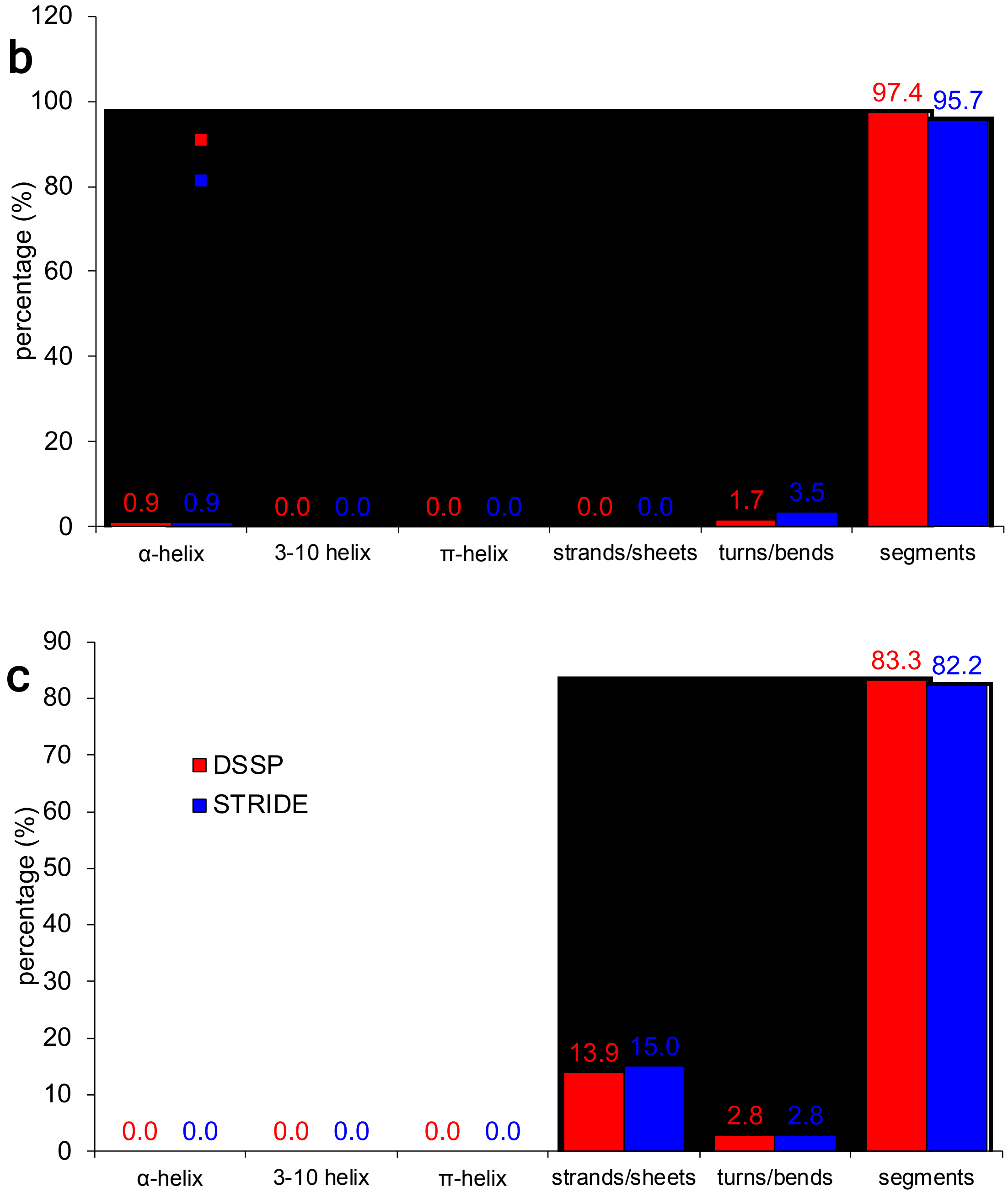
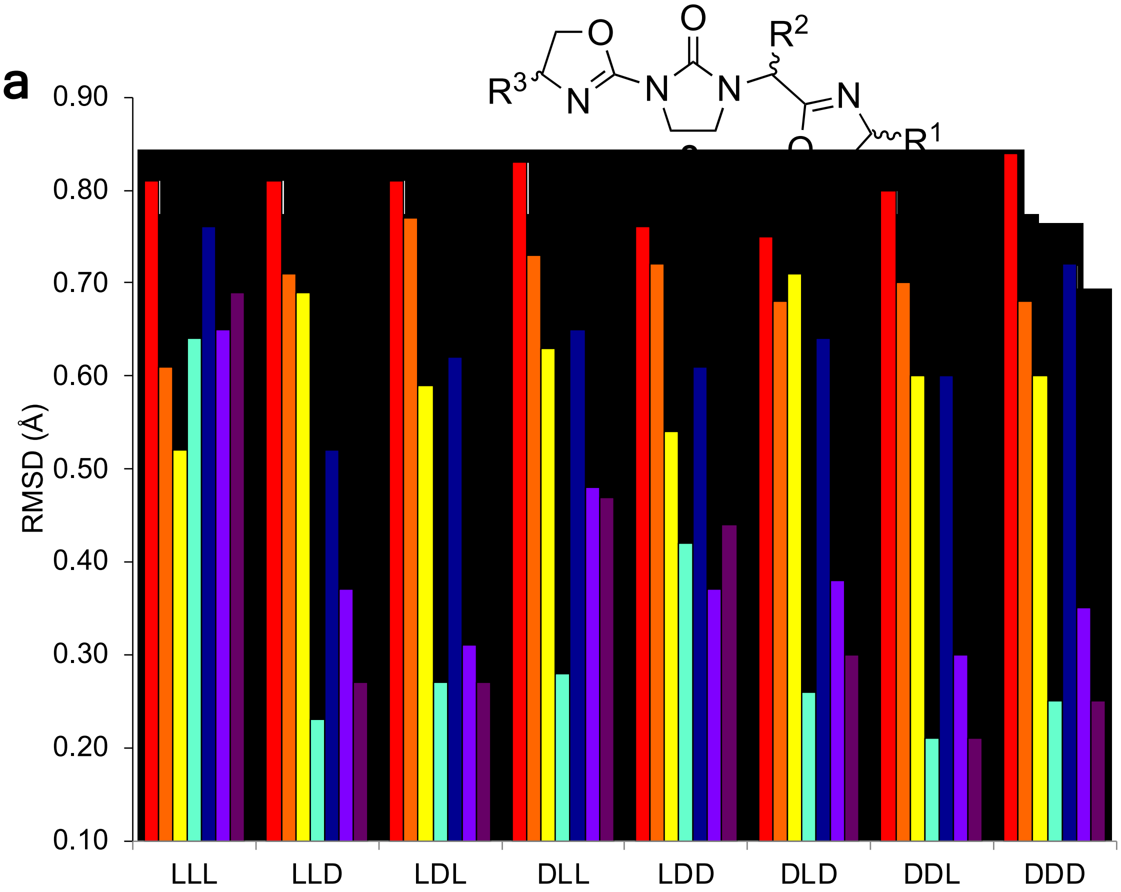


Figure S1. (**a**) RMSD (Å) of the overlays of mimics **2** on each of the ideal secondary structures, organized by stereochemistry. Statistical distribution of secondary structures at PPI interfaces derived by DSSP and STRIDE calculations; (**b**) the best 115 overlays of DDD-**2**; and, (**c**) 287 overlays of LDD-**2**.

C. EKOS, EKO, and DSSP/STRIDE data for chemotype 3

■ 3_{10}-helix
■ α-helix
■ π-helix
■ γ-turn
■ inverse γ-turn
■ strand-turn strand
■ β-strand
■ parallel β-sheet
■ antiparallel β-sheet

helical → *extended*



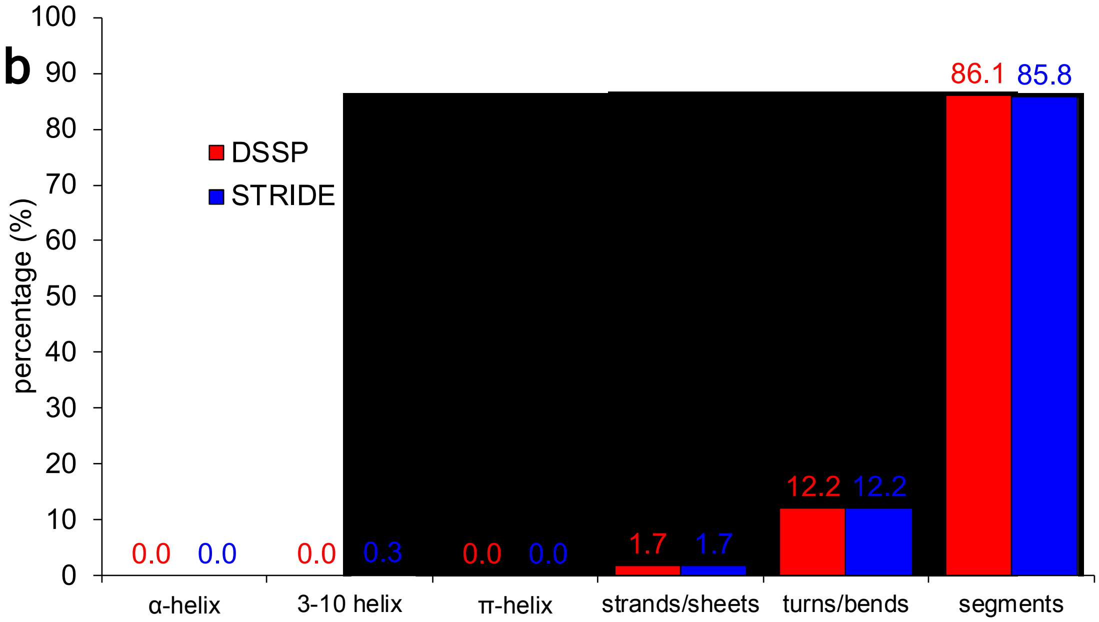


Figure S2. (**a**) RMSD (Å) of the overlays of mimics **3** on each of the ideal secondary structures, organized by stereochemistry. Statistical distribution of secondary structures at PPI interfaces derived by DSSP and STRIDE calculations; (**b**) the best 288 overlays of DDD-**3**.

D. EKOS, EKO, and DSSP/STRIDE data for chemotype 4

🟥 3_{10}-helix

🟧 α-helix

🟨 π-helix

🟩 γ-turn

🟩 inverse γ-turn

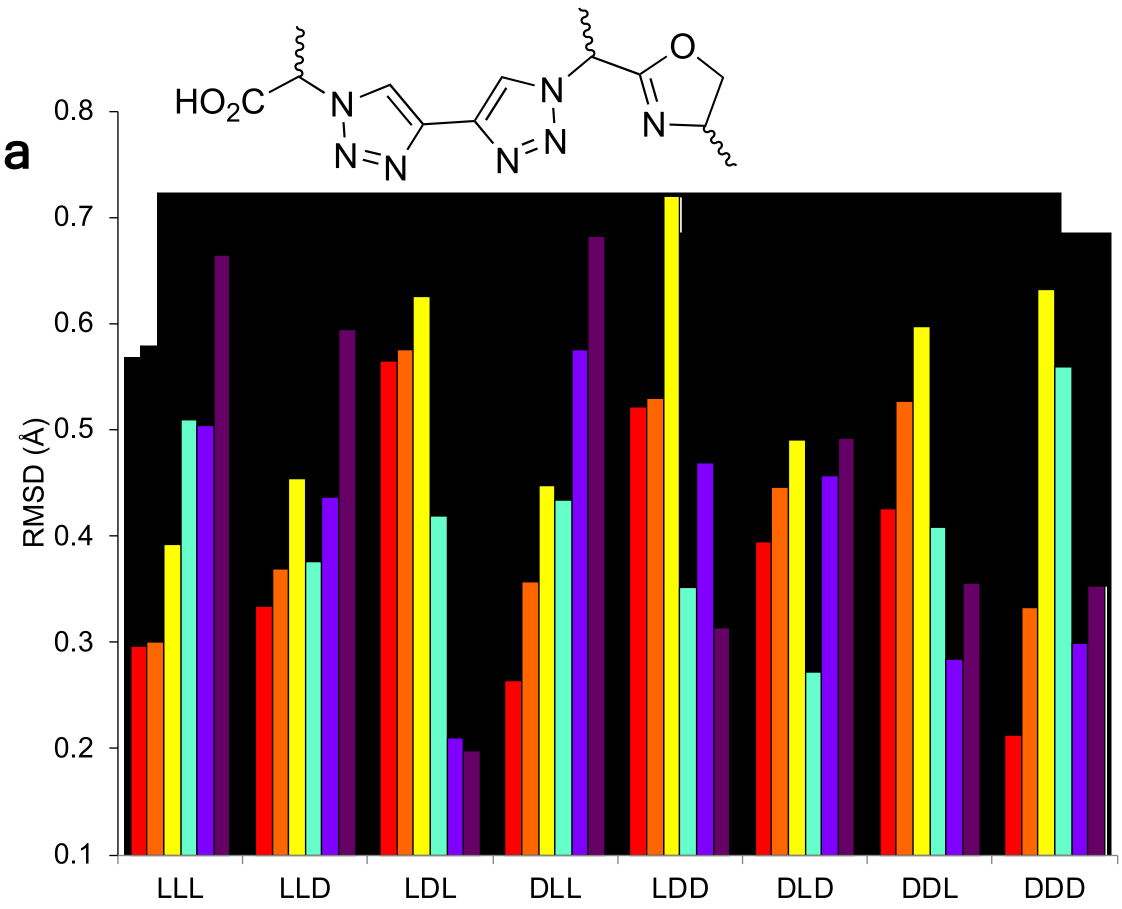
🟦 strand-turn strand

🟦 β-strand

🟪 parallel β-sheet

🟪 antiparallel β-sheet

helical → *extended*



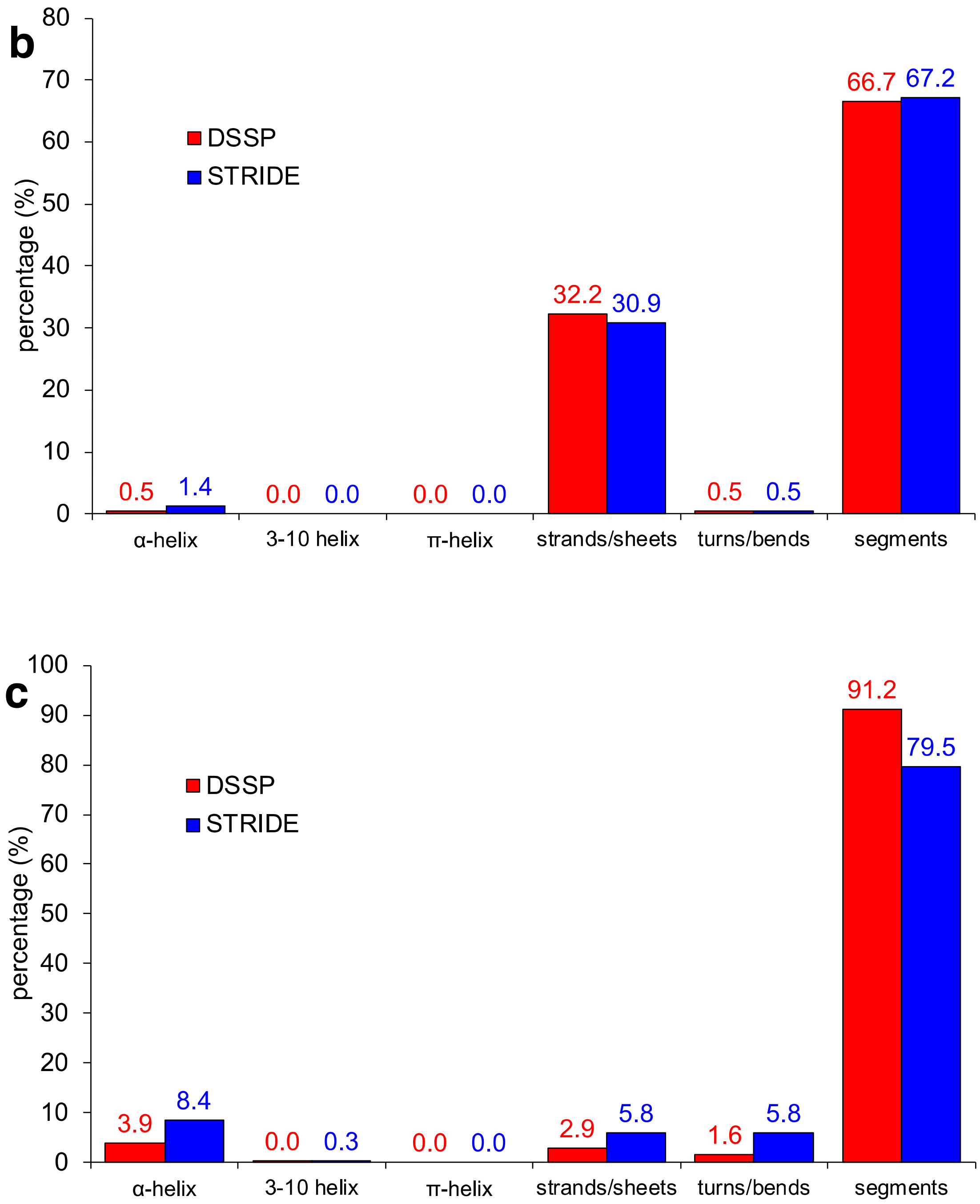


Figure S2. (**a**) RMSD (Å) of the overlays of mimics **4** on each of the ideal secondary structures, organized by stereochemistry. Statistical distribution of secondary structures at PPI interfaces derived by DSSP and STRIDE calculations; (**b**) the best 369 overlays of LDL-**4**; (**c**) the best 308 overlays of LLL-**4**.

E. Reference

1. D. Xin, E. Ko, L. M. Perez, T. R. Ioerger and K. Burgess, *Org. Biomol. Chem.*, 2013, **11**, 7789-7801.
2. D. Xin, L. M. Perez, T. R. Ioerger and K. Burgess, *Angew. Chem. Int. Ed.* , 2014, **53**, 3594-3598.