



Fig. 6 Small-molecule stabilizers of the INF NP (influenza nucleoprotein) homodimer, topo II (topoisomerase II) homodimer, transthyretin homotetramer, and the complex of SK-CaMBD (small-conductance K channel calmodulin-binding domain) and CaM (calmodulin). The PDB codes of the crystal structures are 4DYB, 1QZR, 3TCT, and 4J9Z, respectively

second advantage is of thermodynamic nature. In general, it can be expected that the amount of binding energy that has to be added by a small-molecule binding event to an already existing and biologically relevant protein complex is much less than the energy that is needed to disrupt a given protein–protein or protein–ligand interaction. This in turn would allow for a weaker overall affinity of the stabilizing ligand in comparison to an inhibitor of an active site or a PPI interface.

In the last 5–10 years, our knowledge on how to target PPIs with small molecules has dramatically increased, thus holding great promises for the clinical application of this kind of compounds.