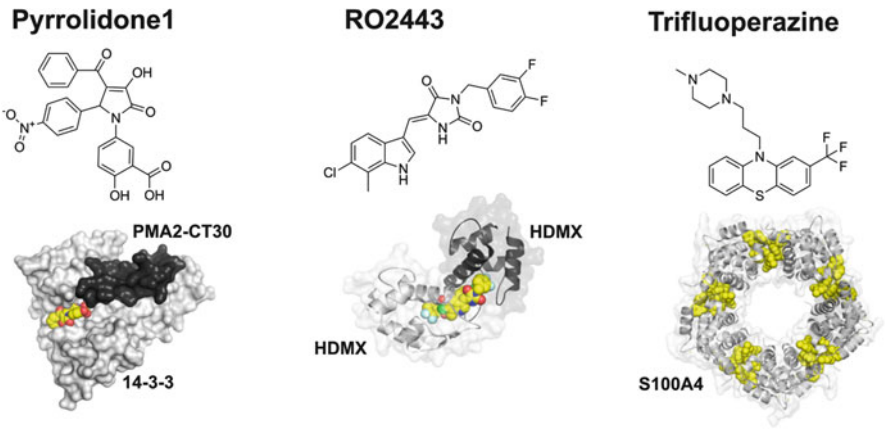

Fig. 5 Small-molecule stabilizers of 14-3-3's interaction with PMA2-CT30 (plasma membrane ATPase 2-C-terminus 30), HDMX's (human double minute X) homodimerization, and S100A4 oligomer. The PDB codes of the crystal structures are 3M51, 3U15, and 3K0O, respectively

thus inhibiting its function (Classen et al. 2003); and **tafamidis** works as a stabilizer of the tetrameric form of transthyretin (Bulawa et al. 2012). Another heterodimeric complex-stabilizing compound is the surprisingly simple molecule **NS309** that enhances the affinity of calmodulin (CaM) to the respective binding domain (CaMBD) of the SK potassium channel (Fig. 6) (Zhang et al. 2013).

5 Conclusions and Outlook

In this chapter, a number of success examples of inhibition as well as stabilization of PPIs illustrate the feasibility of this approach in drug development. With an estimated number between 130,000 and 650,000 PPIs in the human body, in principle it is plausible to identify a "druggable" PPI for every disease or pathological condition. Since nature itself regulates protein function very often by controlling interactions among proteins, the strategy to modulate PPIs with small molecules is a promising concept to complement more classical approaches of pharmacological intervention. As reviewed here, inhibition of PPIs is by far the prevalent strategy, clearly favored by the beautiful successes of molecules like tirofiban, navitoclax, nutlins, or bromodomain inhibitors. However, PPI-stabilizing compounds display a number of generally advantageous features that make them ideal complements to active site inhibitors and disruptors of PPIs. One important characteristic is their uncompetitive nature. As far as we know, PPI stabilizers don't have to compete neither with a small molecule nor another biomacromolecule (protein, complex carbohydrate, DNA, or RNA) for their binding pocket. Especially in the immensely crowded intracellular environment, this is helpful for achieving a physiologically significant activity on their targets. Related to this, a