**Supplementary Figure 3.** Alternative FC45 mini-aptamer structures support the proposed structure of the FC45 mini-aptamer. Alternative secondary structures proposed by mfold for the FC45 mini-aptamer sequence were examined by stabilizing the base stems of these structures with an extension of two GC base-pairs as illustrated in (A) and (B). SPR assays demonstrated that these stabilized alternative structures did not exhibit significant codeine-binding affinities and therefore do not allow for the formation of the correct codeine-binding pocket. (C) Formation of a small hairpin by the 3' constant terminus proposed by mfold.

