ABSTRACT: The conformation of telomerase changes as the multicomponent ribonucleoprotein complex is assembled and reverse transcription proceeds. The conformational changes associated with the RNA, DNA, and protein components of telomerase assembly and activity are poorly understood. Previously, even the secondary structure and base pairing configuration of individual nucleotides within the telomerase RNA subunit were not accurately identified. To overcome this limitation, I have used a novel combination of results from several low-resolution structural techniques to generate models of telomerase during assemblage and catalysis. I have combined secondary structural constraints determined by SHAPE and tertiary constraints generated from reported FRET experiments of telomerase RNA with homology modeling of the reverse transcriptase. This combination of low-resolution structural data enabled observation of major telomerase RNA structural changes associated with binding an accessory protein, p65, and the catalytic reverse transcriptase. It appears that binding of p65 does not change the secondary structure of telomerase RNA but it does increase the dynamism of key residues and this facilitates assembly into the active complex. The resulting models explain how the assemblage of the telomerase ribonucleoprotein allows this molecular machine to perform its function.