Riboswitches are structural motifs located in the 5'-untranslated regions of some messenger RNAs that can bind to cellular metabolites and regulate gene expression. These microbial-specific elements are believed to regulate over 3% of bacterial genes, and having been found in several human pathogens, are potential new antibiotic targets. Among riboswitches, the preQ₁ (a precursor of quenosine) aptamer is notable for being only 34 nucleotides long, less than one-half as long as functionally similar riboswitches. In this Paper of the Week, Robert Spitalé and colleagues determine the structure of preQ₁ in complex with its precursor metabolite preQ₀ at 2.75 Å, revealing how it does so much with so little. The preQ₁ structure is highly compact and holds the metabolite within a deep pocket via Watson-Crick pairing of cytosine 15; the interaction also provides a platform to allow pairing between cytosine 9 of preQ₁ and the first base of the ribosomal binding site, suggesting a mechanism of translational arrest. This work revealing this “minimalist” switch could lend insight into many other metabolite binding sites and increase our knowledge of bacterial gene regulation.

† See referenced article, J. Biol. Chem. 2009, 284, 11012–11016