Topological constraints placed on short fragments of DNA change the disorder found in chain molecules randomly decorated by nonspecific, architectural proteins into tightly organized three-dimensional structures. The bacterial protein HU builds up, counter to expectations, in greater quantities and at particular sites along simulated DNA minicircles and loops. The many ways in which the protein induces nearly the same closed circular configuration point to the statistical advantage of its nonspecificity. The rotational settings imposed on DNA by the repressor proteins, by contrast, introduce sequential specificity in HU placement, with the nonspecific protein accumulating at particular loci on the constrained duplex. Thus, an architectural protein with no discernable DNA sequence-recognizing features becomes site-specific and potentially assumes a functional role upon loop formation. The locations of HU on the closed DNA reflect long-range mechanical correlations. The protein responds to DNA shape and deformability rather than unique features of the constituent base pairs. The structures of the simulated loops suggest that HU architecture may influence repressor-operator interactions in the context of the bacterial nucleoid. (Received August 25, 2014)