NMR spin relaxation studies are a powerful and site-specific probe of conformational disorder and dynamics in biological macromolecules. In RNA, dynamics are critical in such molecular functions as ribozyme catalysis and RNA-protein recognition. $^{13}$C relaxation dispersion studies in solution on nucleotide base groups have allowed considerable insight into these processes. Along the polynucleotide backbone, however, spin relaxation analysis has been hampered by strong $^{13}$C-$^{13}$C magnetic interactions within the ribose ring. We have recently (1,2) introduced a specific isotope labeling scheme that takes advantage of bacterial metabolic pathways to produce an alternate-site ($^{12}$C-$^{13}$C-$^{12}$C-$^{13}$C-$^{12}$C) pattern within the ribose ring, permitting analysis of backbone dynamics using $^{13}$C2’ and $^{13}$C4’ as probes. We have now applied this scheme to relaxation dispersion studies in the GNRA RNA tetraloop, a fundamental building block of higher-order RNA structure. Seven of eight sites probed display relaxation dispersion effects, indicating extensive conformational exchange on the $\mu$s-ms timescale. These data can be analyzed in terms of the nature, timescale, and activation energy for conversions between sugar pucker conformations within the tetraloop. Both correlated and independent dynamics are observed at different sites in the tetraloop.

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