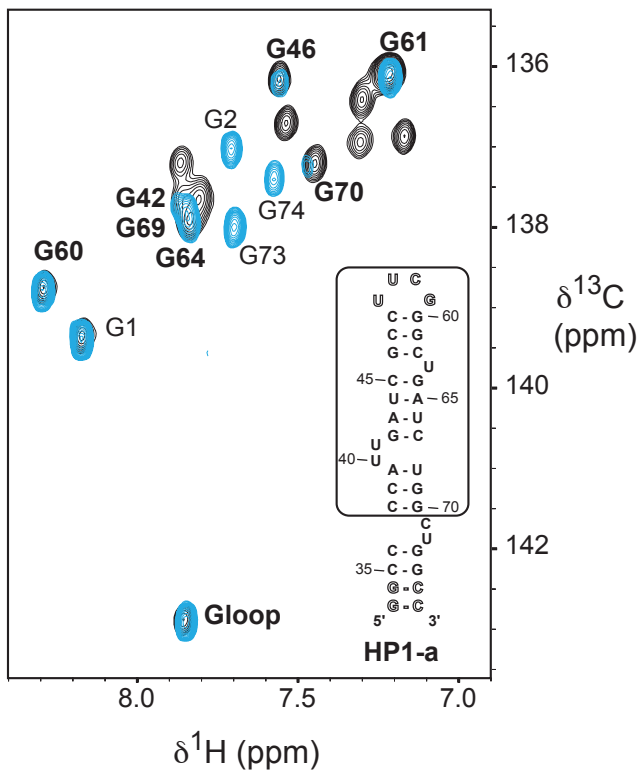
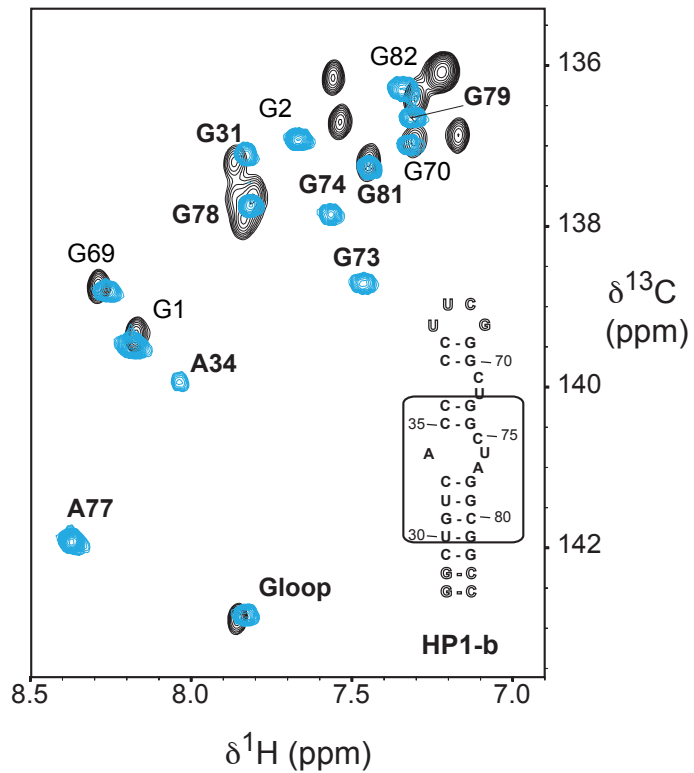
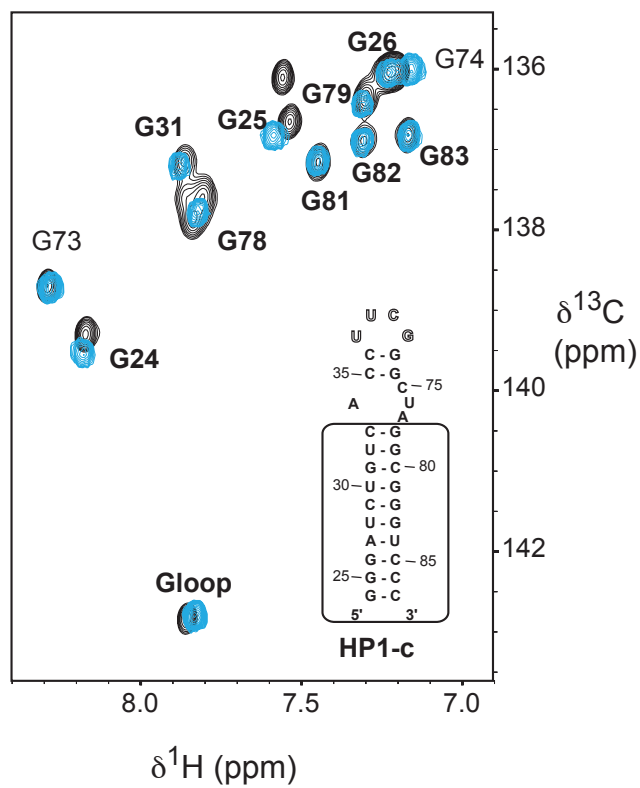
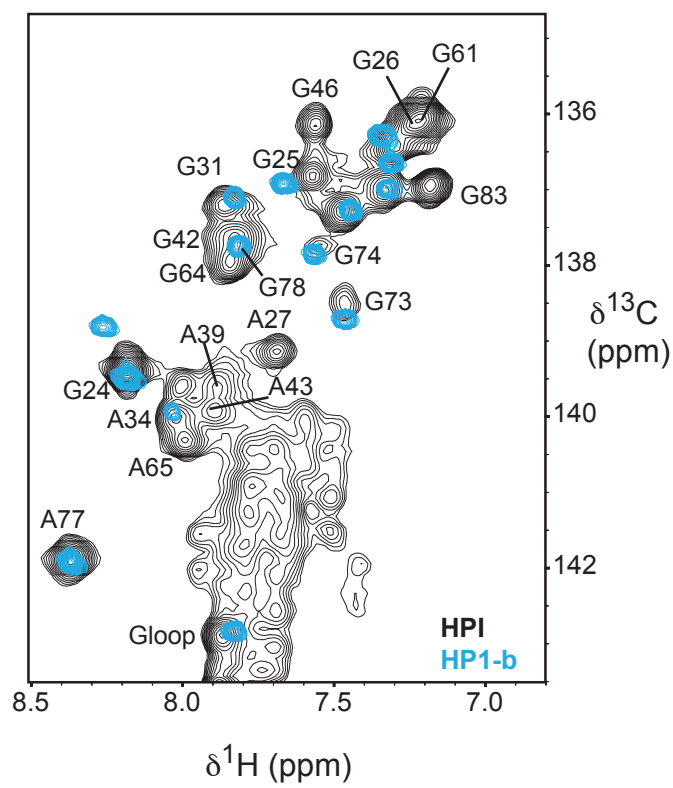


(A)**(B)****(C)****(D)****Supplemental Figure S3**

Supplemental Figure S3: Analysis of non-exchangeable protons for the “Divide and Conquer approach”

Overlays of regions of ^1H - ^{13}C HSQC spectra showing the aromatic H8-C8 of HPI and the three sub-domains HPI-a, HPI-b and HPI-c, at 30°C. **(A)** ^1H - ^{13}C HSQC spectra showing the aromatic H8-C8 of selectively labeled [$^{13}\text{C}/^{15}\text{N}$ -G] HPI (black) and [$^{13}\text{C}/^{15}\text{N}$ -G] HPI-a (blue), recorded at 30°C. **(B)** ^1H - ^{13}C HSQC spectra showing the aromatic H8-C8 of selectively labeled [$^{13}\text{C}/^{15}\text{N}$ -G] HPI (black) and [$^{13}\text{C}/^{15}\text{N}$ -G/A] HPI-b (blue), recorded at 30°C. **(C)** ^1H - ^{13}C HSQC spectra showing the aromatic H8-C8 of selectively labeled [$^{13}\text{C}/^{15}\text{N}$ -G] HPI (black) and [$^{13}\text{C}/^{15}\text{N}$ -G] HPI-c (blue), recorded at 30°C. **(D)** ^1H - ^{13}C TROSY-HSQC spectra showing the aromatic H8-C8 of fully labeled $^{13}\text{C}/^{15}\text{N}$ HPI (black) and selectively labeled [$^{13}\text{C}/^{15}\text{N}$ -A/G] HPI-b (blue), recorded at 30°C. It is worth noting that G73 and G74 that were not visible in the ^1H - ^{13}C HSQC spectrum (B), show up and exhibit chemical shifts similar to those observed in HPI-b. In addition, chemical shifts of A34 and A77 are identical in HPI-b and HPI.