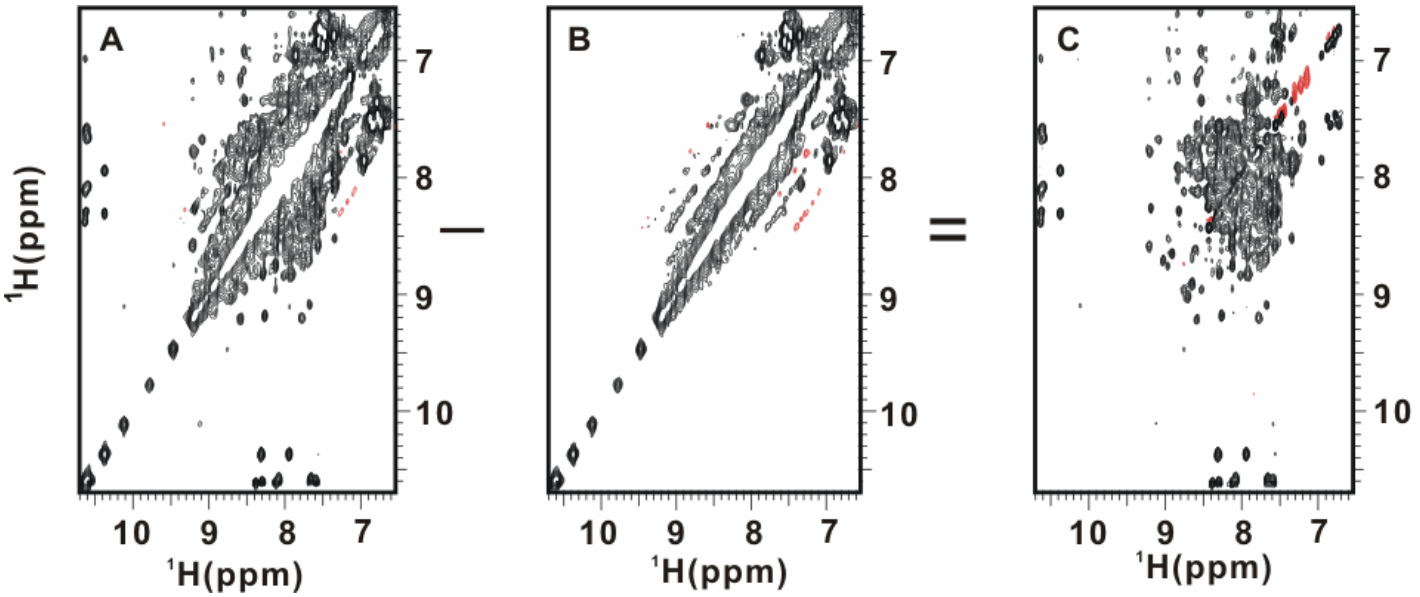


Figure S1. The first 2D $^1$H-$^1$H planes obtained from the first data set (A) and second data set (B) of the 3D $^{15}$N-edited NOESY-HSQC experiment with the pulse scheme shown in Figure 1 in the main text. The experiment was recorded with uniformly $^{15}$N-labeled calmodulin in $^1H_2O$:$^2H_2O$ (90:10) solution (protein concentration 1 mM, 5 mM $CaCl_2$, pH 6.5, 25 ºC) on a Bruker Avance 500 MHz spectrometer equipped with a cryoprobe. 128($t_1$)× 512($t_3$) complex points were collected with spectral widths of 5500 ($^1$H) and 8012 Hz ($^1$H) by setting $t_2$ = 0. An interscan delay of 1 s with 32 scans per increment was used, resulting in a total experimental time of 2.7 h for each data set. The mixing times were: $\tau_{mix}$ = 80 ms and $\tau'_{mix}$ = 74 ms. The scaling factor was 0.99 for the second data set. The two data sets were acquired in an interleaved manner. Figure C is the difference spectrum and C = A - B*0.99. Signals in black represent opposite sign with respect to those in red. Artifacts parallel to the strong diagonals can be observed in both A and B. These are suppressed in the difference spectrum C. Relatively strong negative peaks at ~ 7.2 ppm result from some $NH_2$ groups in which the protons undergo fast chemical exchange with water protons, giving rise to rapid decays of magnetizations $H_zN_z$ and $H_z$. For these $NH_2$ groups, $R(N_z)/R(H_zN_z) < (R(N_z)/R(H_zN_z))_{AV}$ and negative residual diagonal peaks are expected.

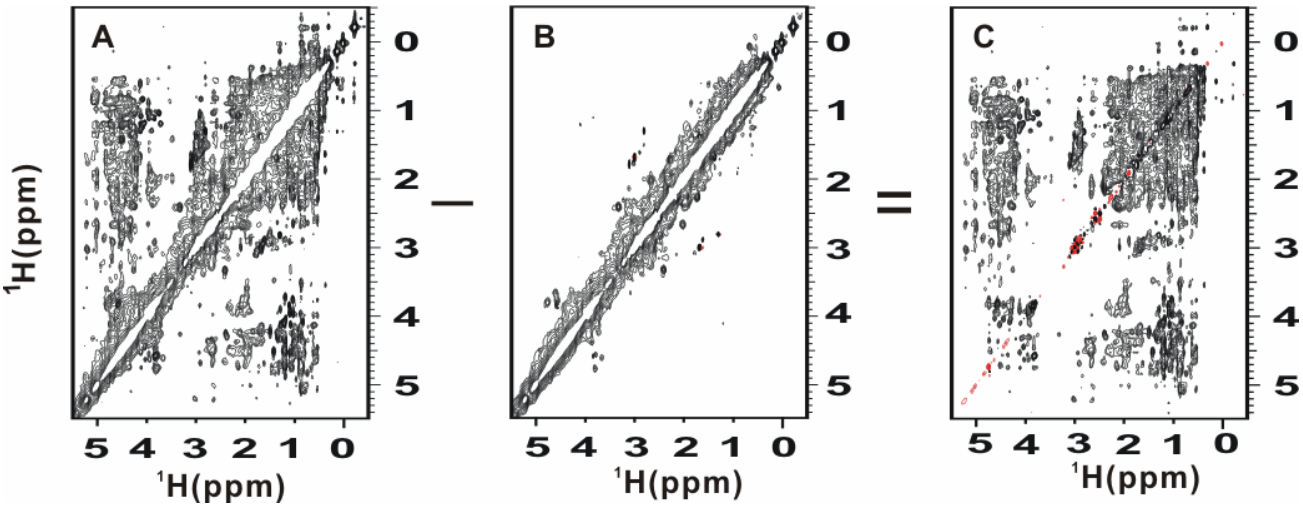


Figure S2. The first 2D $^1$H-$^1$H planes obtained from the first data set (A) and second data set (B) of the 3D $^{13}$C-edited NOESY-HSQC experiment. The experiment was recorded with uniformly $^{13}$C-labeled DdCAD-1 (24 kDa) in $^2H_2O$ solution (protein concentration 0.8 mM, 20 mM $Na_3PO_4$, pH 6.6, 30 ºC) on a Bruker Avance 500 MHz spectrometer equipped with a cryoprobe. 128($t_1$)× 512($t_3$) complex points were collected with spectral widths of 5500 ($^1$H) and 8012 Hz ($^1$H) by setting $t_2$ = 0. An interscan delay of 1 s with 8 scans per increment was used, resulting in a total experimental time of 40 minutes for each data set. The mixing times were: $\tau_{mix}$ = 80 ms and $\tau'_{mix}$ = 64 ms. The scaling factor was 0.98 for the second data set. The two data sets were acquired in an interleaved manner. Figure C is the difference spectrum and C = A - B*0.98. Signals in red represent opposite sign with respect to those in black.