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Supporting Information

Solution Observation of Dimerization and Helix Handedness Induction in a Human Carbonic Anhydrase–Helical Aromatic Amide Foldamer Complex

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Supporting Information

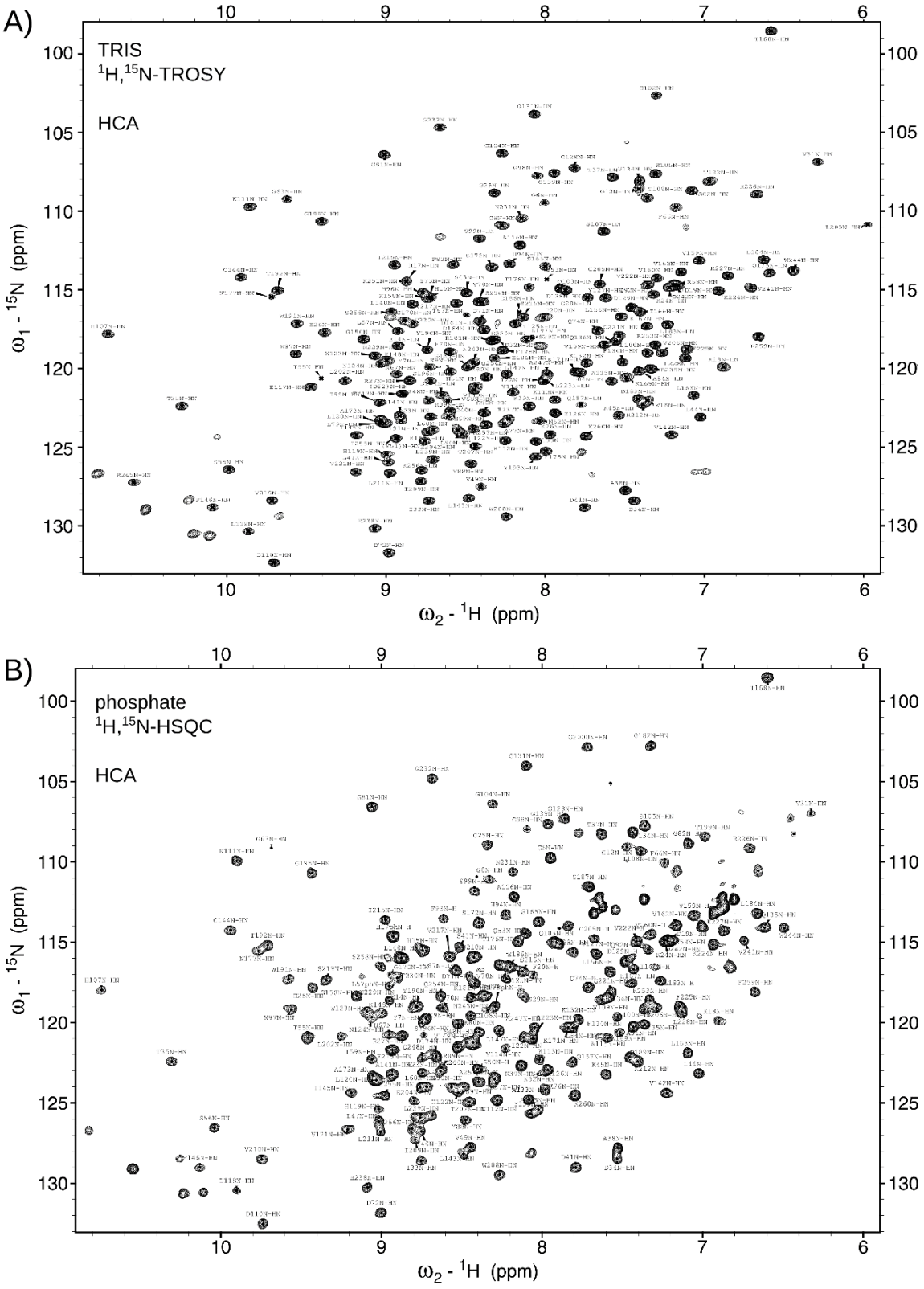


Figure S1. NMR spectra of HCA in TRIS and phosphate. A) ^{1}H,^{15}N TROSY of 300 µM [^{15}N]-HCA in 50 mM TRIS pH 7.4. B) ^{1}H,^{15}N-HSQC of 500 µM [^{15}N]-HCA in 50 mM sodium phosphate pH 7.4. In both spectra the backbone amide crosspeaks are annotated with residue type and sequence number.

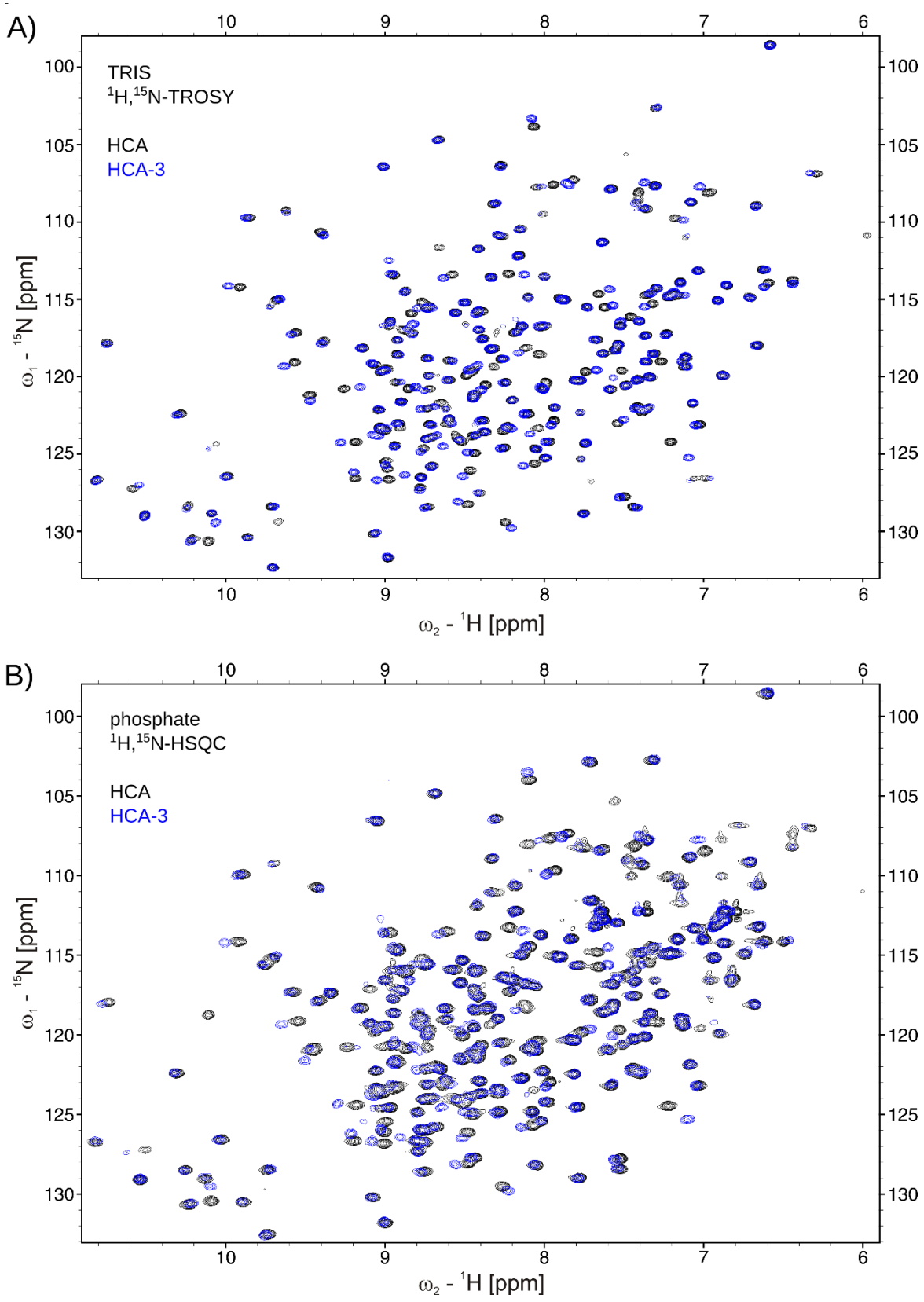


Figure S2. NMR spectra of HCA-**3** in TRIS and phosphate compared to HCA. A) ^{1}H,^{15}N TROSY of 300 µM [^{15}N]-HCA in 50 mM TRIS pH 8.0 without (black) and with (blue) 1.3 molar equivalents of compound **3**. B) ^{1}H,^{15}N-HSQC of 500 µM [^{15}N]-HCA in 50 mM sodium phosphate pH 7.4 without (black) and with (blue) 1.3 molar equivalents of compound **3**.

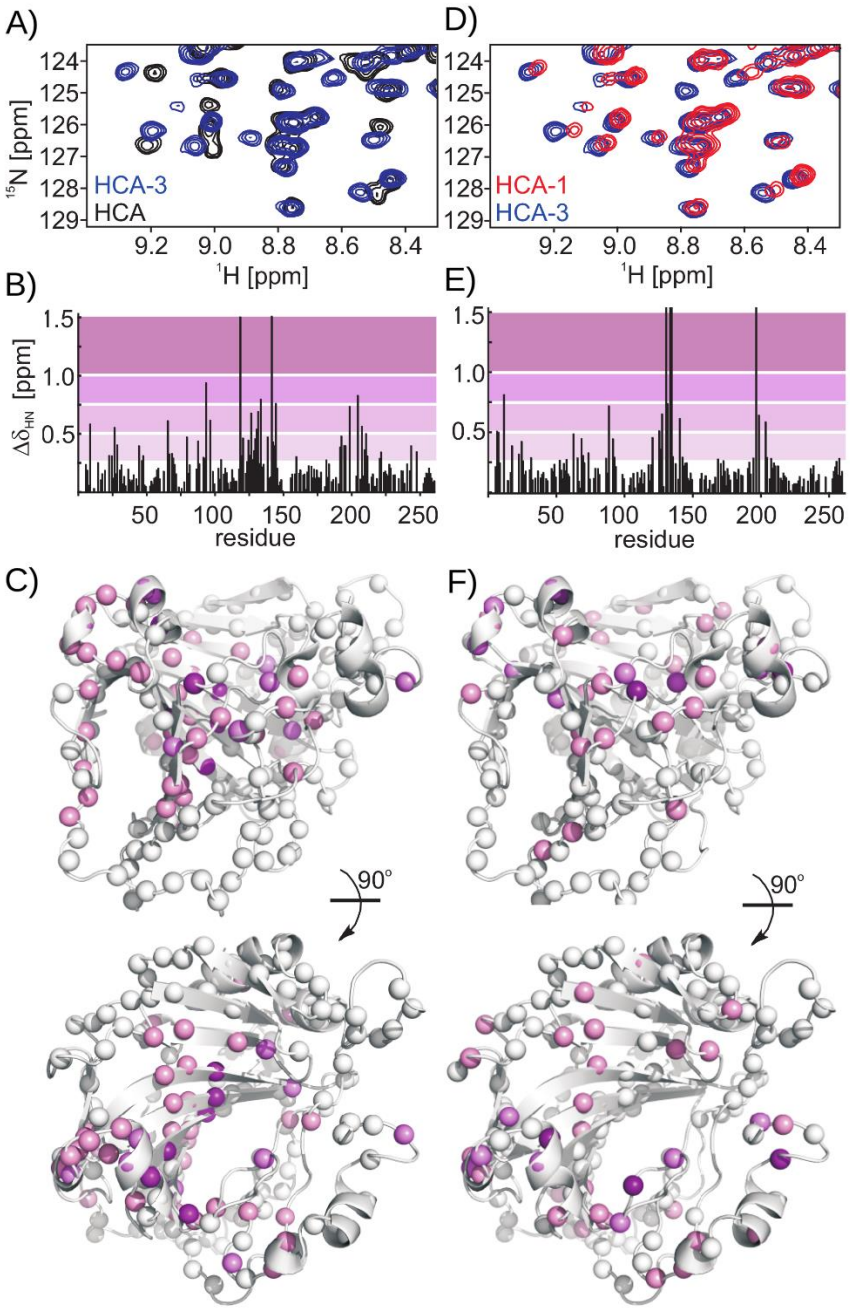


Figure S3. Intermolecular contacts in phosphate for HCA and HCA-**1** identified by NMR spectroscopy**.** A) Region of ^{1}H,^{15}N-HSQC spectra (Figure S2B) from samples of unbound 300 μM [^{15}N]-HCA in phosphate without (black) and with (blue) 1.3 molar equivalents of added compound **3**. Selected crosspeaks have been annotated. B) $\Delta\delta_{H,N}$ of HCA-**3** compared to HCA, calculated as the root mean square deviation, $((\Delta\delta_H/0.14)^2+(\Delta\delta_N)2)^{0.5}$. C) Each observed amide nitrogen atom in the ^{1}H,^{15}N-HSQC is represented as a sphere on the structure of HCA (chain A from PDB ID 4LP6) and colored as in (B). The top orientation is the same as the green HCA protein in Figure 1A. D) Region of ^{1}H,^{15}N-TROSY spectra overlay (Figure S4B) of HCA-**1** (red) and the ^{1}H^{15}N-HSQC of HCA-**3** (blue) in phosphate buffer. E) $\Delta\delta_{H,N}$ of HCA-**1** compared to HCA-**3**, calculated as in (B). F) Each observed amide is represented as a sphere on the structure of HCA and colored as in (E).

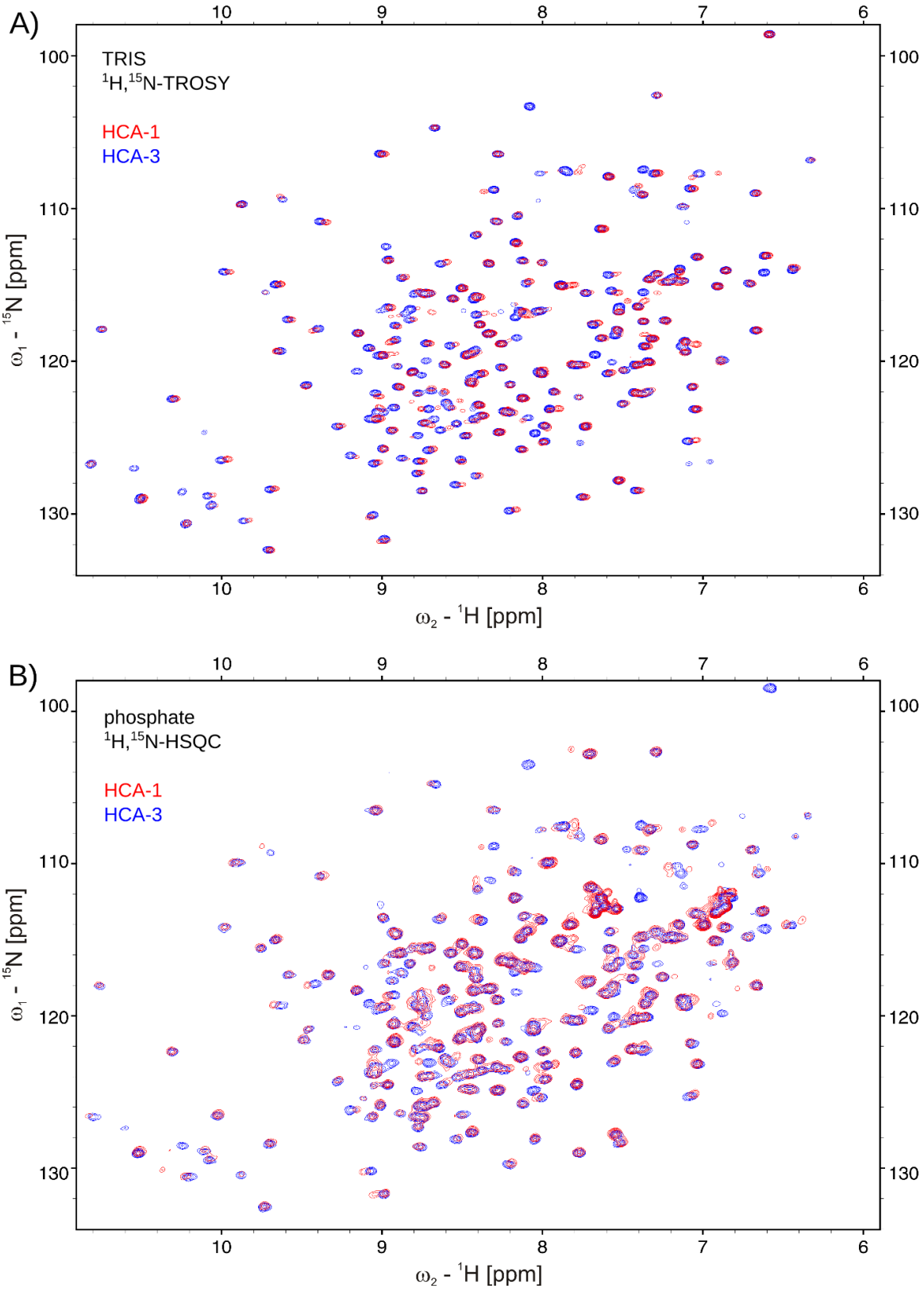


Figure S4 NMR spectra of HCA-**1** in TRIS and phosphate compared to HCA-**3**. A) ^{1}H,^{15}N TROSY of 300 µM [^{15}N]-HCA in 50 mM TRIS pH 8.0 with 1.3 molar equivalents of compound **1** (red) or compound **3** (blue). B) ^{1}H,^{15}N-HSQC of 270 µM [^{15}N]-HCA in 50 mM sodium phosphate pH 7.4 with 1.3 molar equivalents of compound **1** (red) or compound **3** (blue).

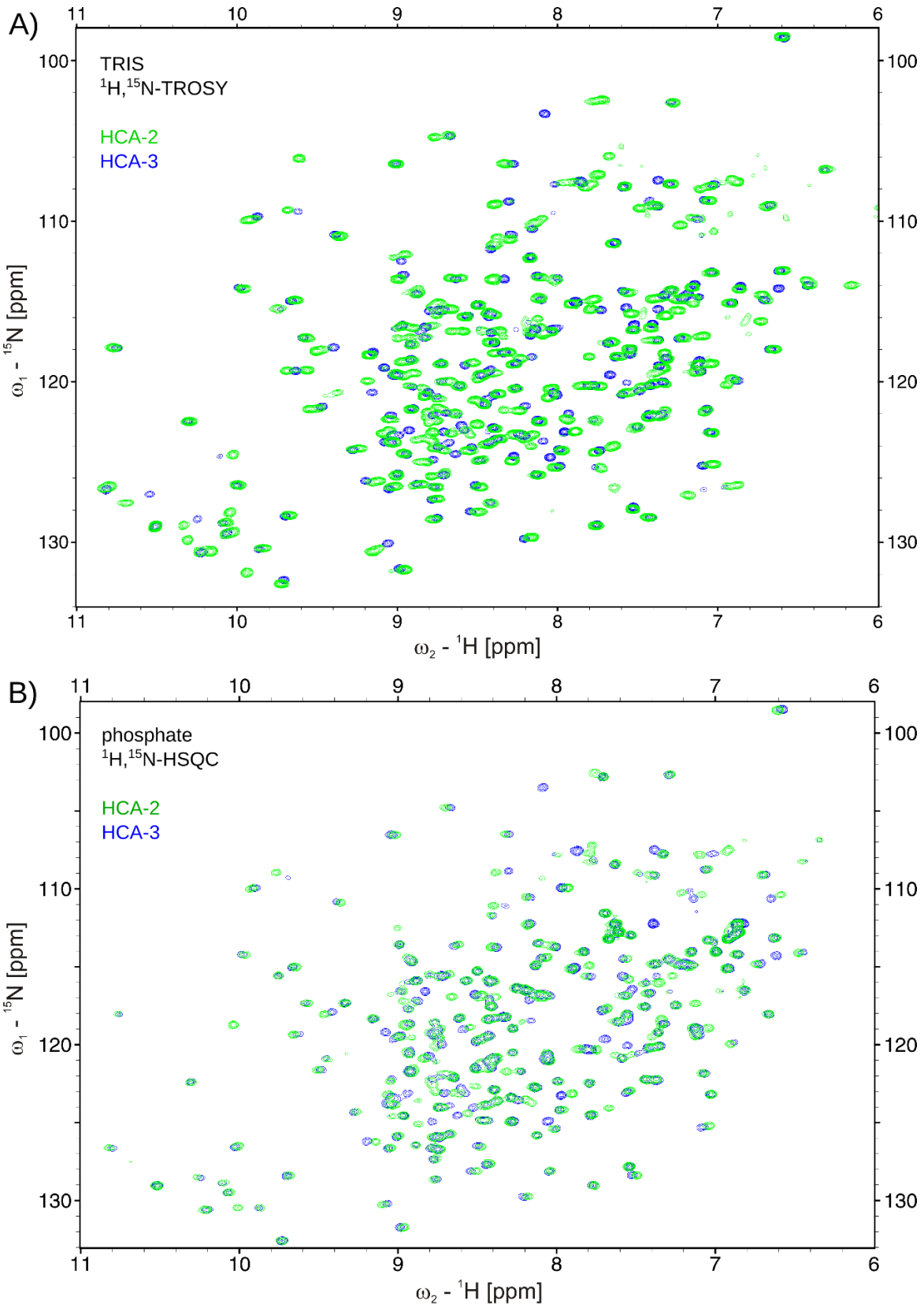


Figure S5. NMR spectra of HCA-**2** in TRIS and phosphate compared to HCA-**3.** A) ^{1}H,^{15}N TROSY of 300 µM [^{15}N]-HCA in 50 mM TRIS pH 8.0 with 1.3 molar equivalents of compound **2** (green) or compound **3** (blue). B) ^{1}H,^{15}N-HSQC of 500 µM [^{15}N]-HCA in 50 mM sodium phosphate pH 7.4 with 1.3 molar equivalents of compound **2** (green) or compound **2** (blue).

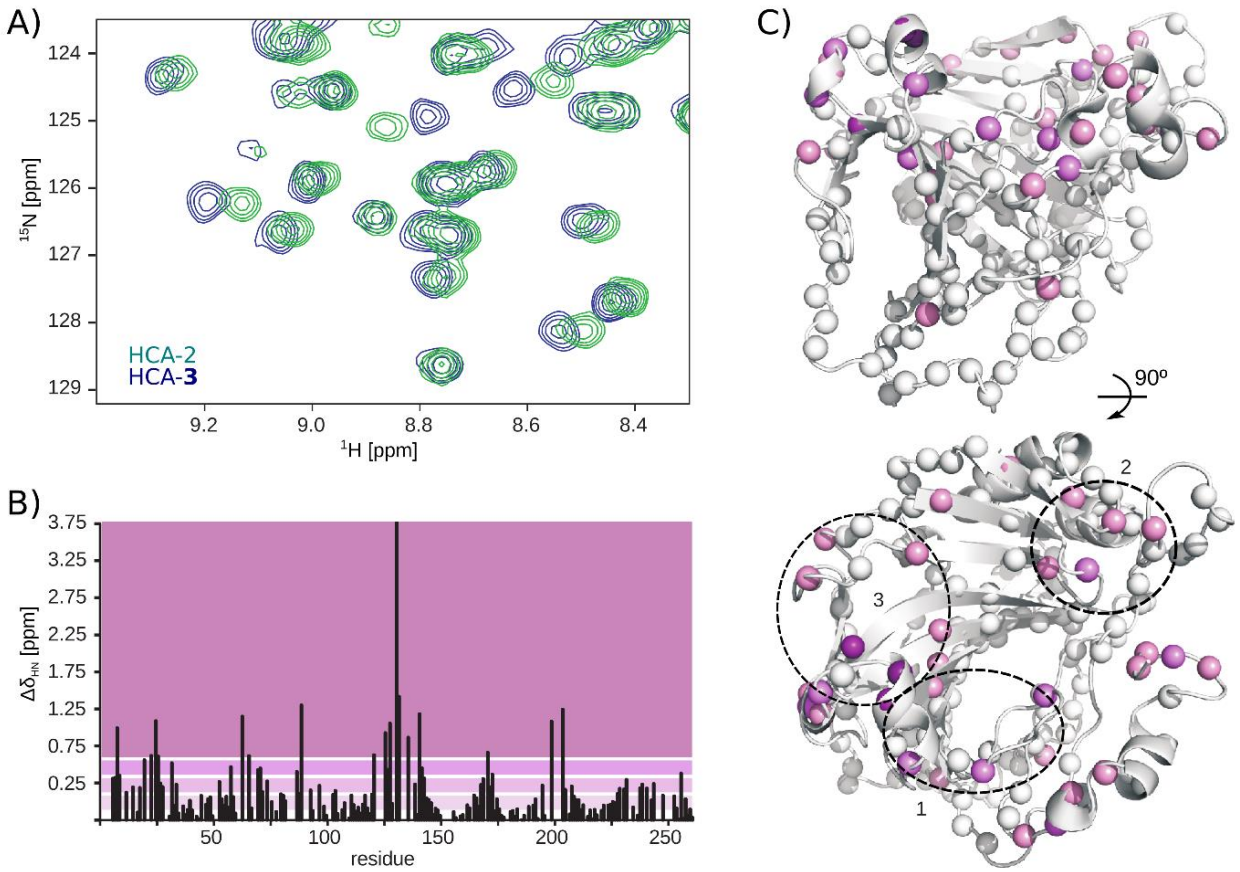
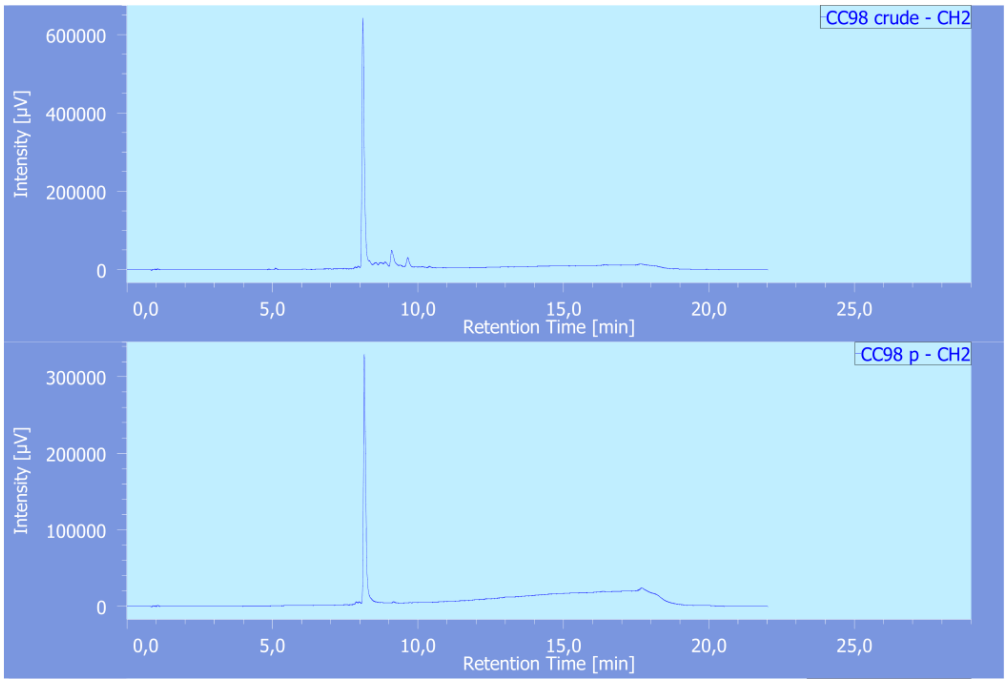


Figure S6 Intermolecular contacts in phosphate for HCA-**2** identified by NMR spectroscopy. A) Selected region of the superposition of ^{1}H,^{15}N-HSQC spectra of HCA-**2** (green) and HCA-**3** (blue) in phosphate buffer (from Figure S6B). B) $\Delta\delta_{H,N}$ of HCA-**2** compared to HCA-**3**, calculated as in Figure 2B. C) Each observed amide is represented as a sphere on the structure of HCA (chain A from PDB ID 4LP6) and colored as in (B).

A)



B)

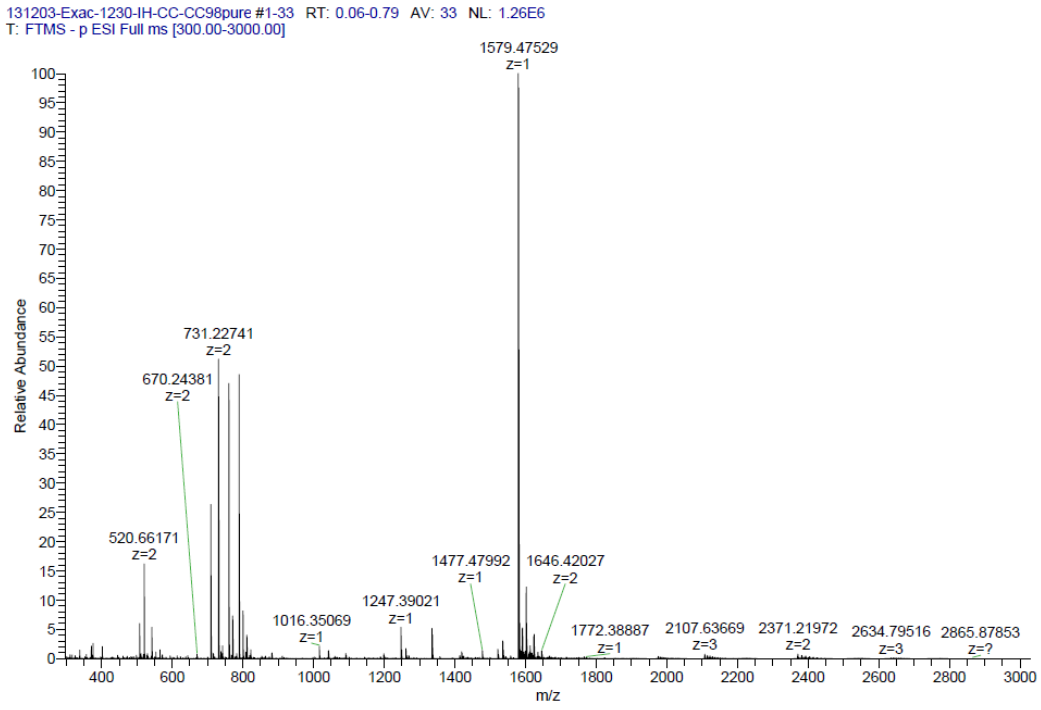


Figure S7 Analysis of compound **2** by HPLC and ESI-MS. A) RP-HPLC (Jasco PU-2089 pump) Macherey–Nagel Nucleodur C18 gravity column (4.6×100 mm, 5µm). The mobile phase was composed of 0.1 % (v/v) TFA/H_2O (solvent A) and 0.1 % TFA/CH_3CN (solvent B) with a 5-100% solvent B gradient over 15 min (t_r =8.2 min). Monitoring was performed by UV detection at 300 nm with a diode array detector (Jasco UV-2077). B) HRMS (Thermo Exactive Orbitrap) in negative mode: m/z calculated for $[C_{80}H_{71}N_{14}O_{20}S]^-$: 1579.4695; found : 1579.4753.

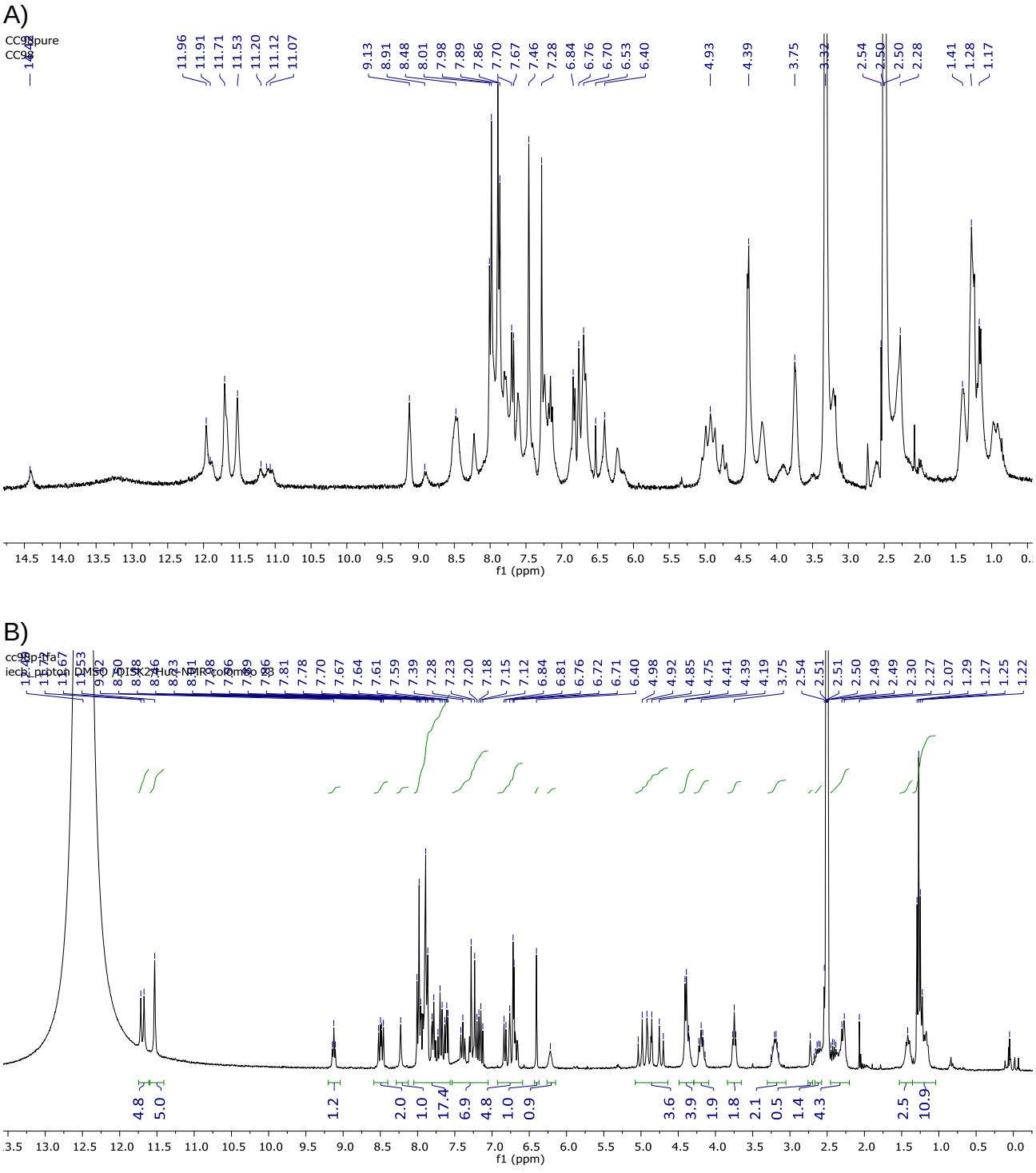


Figure S8 Analysis of compound **2** by ^{1}H NMR. A) 1D ^{1}H NMR of compound **2** in DMSO-d6 at 300 MHz and 298 K. B) 1D ^{1}H NMR of compound **2** in DMSO-d6 with 1% trifluoroacetic acid at 300 MHz and 298 K.