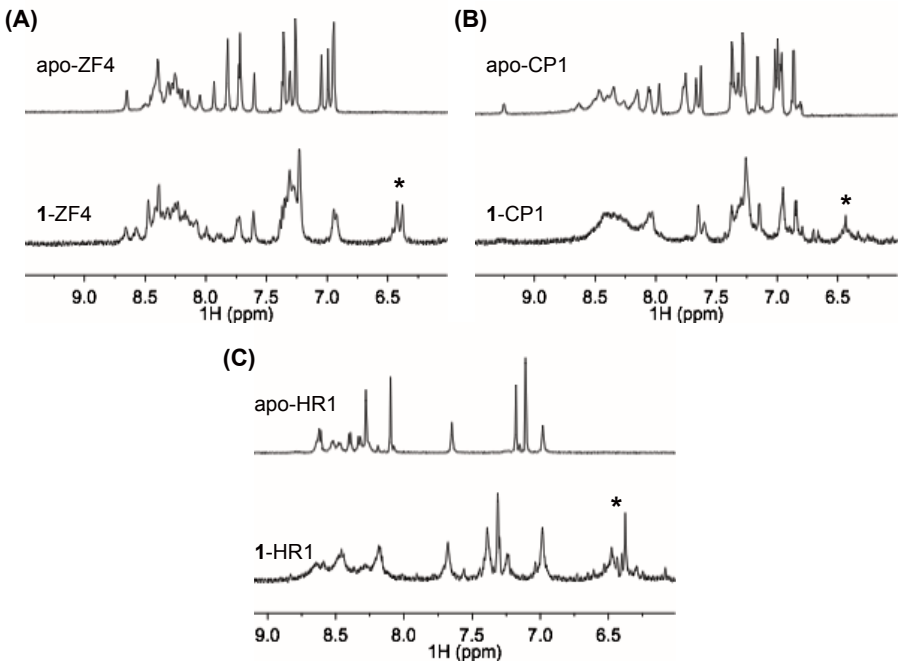
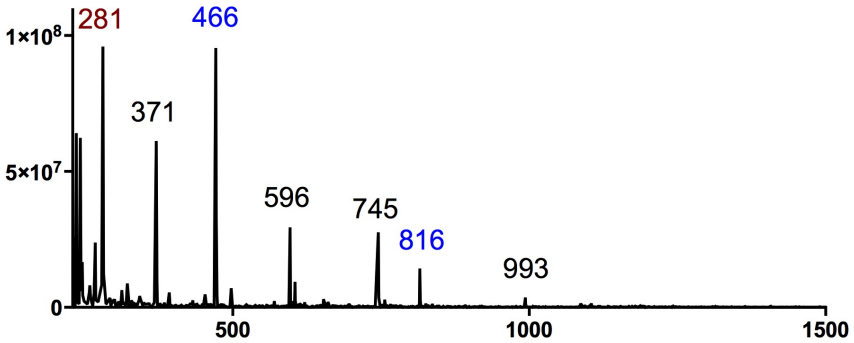
Supporting Information



SI Figure 1: Aromatic and backbone NH region of the ^{1}H NMR of (A) ZF4 and (B) CP1 at 15 ºC (1.5 mM) and (C) HR1 at 10 ºC (5 mM) in the absence (top spectra) or presence (bottom spectra) of **1**. The histidine H2 and H5 protons shift upfield in the presence of **1**. The shifted H5 protons in the **1**-Peptide spectra are marked by asterisks (*). The H2 protons are obscured by the backbone NH peaks and can be more clearly observed in the 2D ^{1}H-^{1}H TOCSY spectra (Figure 1).



SI Figure 2: ESI-MS of ZF4 (expected mass = 2977) in the presence of 1.0 molar equivalents of **1** in positive mode. The m/z peaks [993 (z = 3), 745 (z = 4), 596 (z = 5), 371 (z = 8)] of ZF4 alone are labeled in black. The m/z peak of **1** without axial ligands (m/z = 281) is labeled in red. The m/z of **1**-ZF4 peaks [816 (z = 4), 466 (z = 7)] are labeled in blue. The spectra is representative of the mass detection at t_R = 23 minutes of a reverse-phase HPLC method with a linear gradient of 0.01% aqueous formic acid and acetonitrile from 0 to 70% aqueous mobile phase over 30 minutes.

SI Table 1: Chemical shifts of amino acid ^{1}H of HR1 either A) with 1 or B) free at 10 ºC. Amino acids were classified with ^{1}H-^{1}H TOCSY spectra and sequential assignments were made with ^{1}H-^{1}H NOESY spectra.

A) Chemical Shifts of the Assigned ^{1}H NMR Resonances of 1-HR1 at pH 7.0

	Chemical Shifts at 15 ºC (ppm)			
Residue	NH	CHα	CHβ	Other
R1		3.83	1.75, 1.83	CHγ 1.65; CHδ 3.22
A2	8.60	4.13	1.33	
H3	8.46	4.67	3.00, 3.08	CH5 6.40; CH2 7.29
L4	8.38	4.27	1.60	CHγ 1.55 ; CHδ 0.91, 0.84
Q5	8.67	4.45	1.99, 2.11	CHγ 2.39; NHδ 7.01, 7.67
T6	8.31	4.33	4.18	CHγ 1.16
H7	8.51	4.61	3.09, 3.09	CH5 6.37; CH2 7.32
S8	8.47	4.44	3.83	
D9	8.19	4.4	2.60, 2.72	
V10	---	---	---	

B) Chemical Shifts of the Assigned ^{1}H NMR Resonances of Free HR1 at pH 7.0

	Chemical Shifts at 15 ºC (ppm)			
Residue	NH	CHα	CHβ	Other
R1		4.03	1.73, 1.91	CHγ 1.61; CHδ 3.24
A2	8.85	4.36	1.37	
H3	8.75	4.63	3.15, 3.30	CH5 7.17; CH2 8.26
L4	8.49	4.33	1.61	CHγ 1.54 ; CHδ 0.96, 0.86
Q5	8.63	4.35	2.02, 2.09	CHγ 2.40; NHδ 6.98, 7.66
T6	8.17	4.31	4.25	CHγ 1.19
H7	8.39	4.74	3.18, 3.26	CH5 7.05; CH2 8.10
S8	8.53	4.52	3.84	
D9	8.29	4.52	2.65, 2.86	
V10	---	---	---	

SI Table 2: Chemical shifts of amino acid ^{1}H of ZF4 A) in the presence or B) absence of **1** at 15 ºC. Amino acids were classified with ^{1}H-^{1}H TOCSY spectra and sequential assignments were made with ^{1}H-^{1}H NOESY spectra.

A) Chemical Shifts of the Assigned ^{1}H NMR Resonances of 1-ZF4 at pH 7.0

	Chemical Shifts at 15 ºC (ppm)			
Residue	NH	CHα	CHβ	Other
K1	8.38	4.30	1.78, 1.83	CHγ 1.46; CHδ 1.68; CHε 2.99
S2	8.48	4.42	3.85	
C3	8.66	4.87	3.30, 3.30	
P4		4.31	1.99, 2.28	CHδ 3.65, 3.72
H5	8.35	4.62	2.98, 3.17	CH5 6.38; CH2 7.38
C6	7.88	4.57	3.10, 3.49	
S7	8.30	4.42	3.84	
R8	8.32	4.30	1.76, 1.87	CHγ 1.63; CHδ 3.19; NHε 7.27
A9	8.28	4.24	1.29	
F10	8.15	4.49	3.04, 3.15	CH2,6 7.23; CH5 7.26; CH3,5 7.31
A11	8.22	4.24	1.36	
D12	8.07	4.60	2.69, 2.79	
R13	8.36	4.26	1.81, 1.94	CHγ 1.67; CHδ 3.17; NHε 7.25
S14	8.42	4.33	3.87	
N15	8.31	4.72	2.78, 2.86	NHγ 6.97, 7.73
L16	8.09	4.22	1.67	CHδ 0.85, 0.92; CHγ 1.64
R17	8.26	4.23	1.80, 1.89	CHγ 1.62; CHδ 3.20; NHε 7.29
A18	8.00	4.14	1.30	
H19	8.25	4.51	2.97, 3.12	CH5 6.42; CH2 7.36
L20	8.19	4.30	1.67	CHδ 0.87, 0.93; CHγ 1.59
Q21	8.46	4.37	2.03, 2.15	CHγ 2.43; NHδ 6.94, 7.60
T22	8.13	4.33	4.21	CHγ 1.18
H23	8.43	4.58	3.00, 3.12	CH5 6.46; CH2 7.36
S24	8.38	4.48	3.84	
D25	8.57	4.69	2.67, 2.78	
V26	7.73	4.08	2.10	CHγ 0.86, 0.89

B) Chemical Shifts of the Assigned ^{1}H NMR Resonances of Free ZF4 at pH 7.0

	Chemical Shifts at 15 ºC (ppm)			
Residue	NH	CHα	CHβ	Other
K1	8.41	4.29	1.82, 1.84	CHγ 1.45; CHδ 1.72; CHε 3.01
S2	8.51	4.39	3.85	
C3	8.73	4.27	3.04, 3.36	
P4		4.32	2.12, 2.33	CHδ 3.67, 3.78
H5	8.27	4.57	3.12, 3.22	CH5 6.98; CH2 7.84
C6	7.71	4.53	2.99, 3.38	
S7	8.42	4.37	3.92	
R8	8.28	4.33	1.74, 1.85	CHγ 1.61; CHδ 3.28
A9	8.32	4.24	1.30	
F10	8.20	4.56	3.09, 3.20	CH2,6 7.27; CH5 7.32; CH3,5 7.36
A11	8.25	4.23	1.37	
D12	8.27	4.56	2.68, 2.77	
R13	8.38	4.32	1.78, 1.94	CHγ 1.64; CHδ 3.19
S14	8.46	4.39	3.91	
N15	8.42	4.71	2.77, 2.86	NHγ 6.94, 7.73
L16	8.15	4.29	1.67	CHδ 0.87, 0.94; CHγ 1.59
R17	8.29	4.50	1.73, 1.85	CHγ 1.63; CHδ 3.21
A18	8.20	4.21	1.36	
H19	8.32	4.50	3.15, 3.22	CH5 6.93; CH2 7.84
L20	8.06	4.30	1.60	CHδ 0.84, 0.91; CHγ 1.53
Q21	8.41	4.36	1.99, 2.10	CHγ 2.35; NHδ 6.93, 7.61
T22	8.27	4.33	4.21	CHγ 1.18
H23	8.42	4.66	3.13, 3.21	CH5 7.02; CH2 7.96
S24	8.30	4.50	3.84	
D25	8.66	4.68	2.62, 2.75	
V26	7.73	4.05	2.09	CHγ 0.86, 0.89

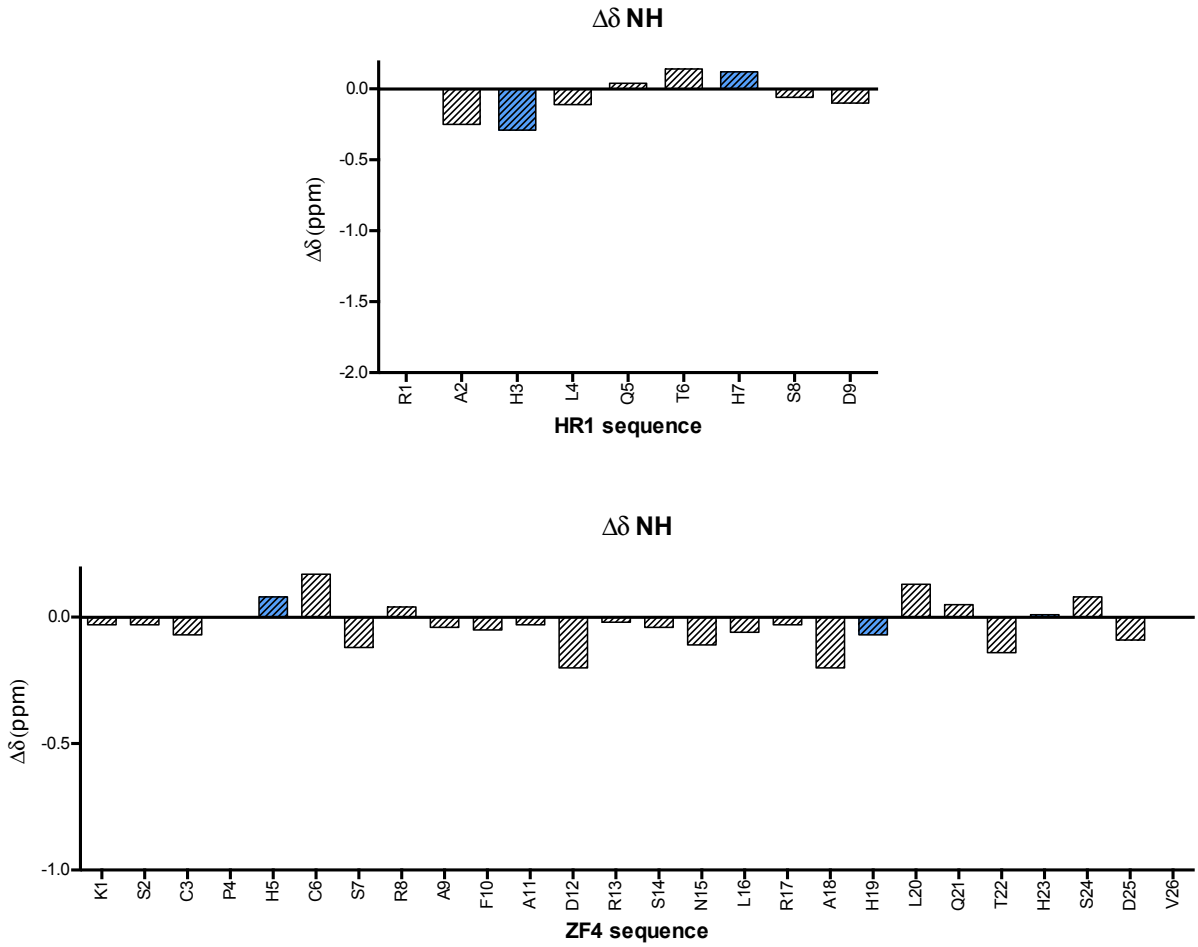
SI Table 3: Changes of ^{1}H chemical shifts, $\Delta\delta$, = δ(**1**-Peptide) – δ(Free Peptide), of A) ZF4 at 15 ºC, (B) HR1 at 10ºC.

A) $\Delta\delta$ of the Assigned ^{1}H NMR Resonances of ZF4 at pH 7.0

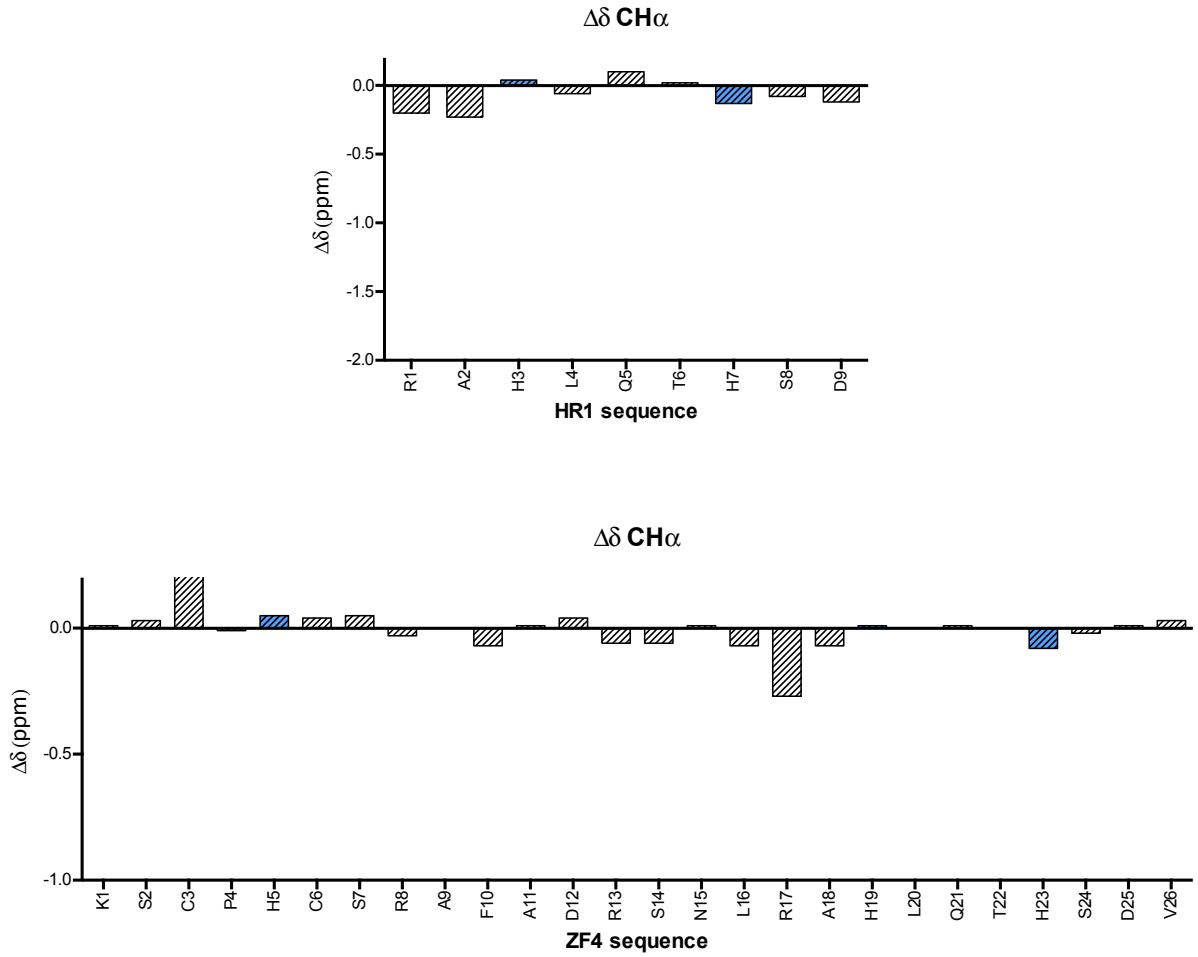
	$\Delta\delta$ = δ(**1**-ZF4) - δ(Free ZF4) 15 ºC (ppm)			
Residue	NH	CHα	CHβ	Other
K1	-0.03	0.01	-0.04, -0.01	CHγ 0.01; CHδ -0.04; CHε -0.02
S2	-0.03	0.03	0.00	
C3	-0.07	0.60	-0.06, -0.06	
P4		-0.01	-0.13, 00.05	CHδ -0.02, -0.06
H5	0.08	0.05	-0.14, -0.05	CH5 -0.60; CH2 -0.46
C6	0.17	0.04	0.11, 0.11	
S7	-0.12	0.05	-0.08	
R8	0.04	-0.03	0.02, 0.02	CHγ 0.02; CHδ -0.09;
A9	-0.04	0.00	-0.01	
F10	-0.05	-0.07	-0.05, -0.05	CH2,6 -0.04; CH5 -0.06; CH3,5 -0.05
A11	-0.03	0.01	-0.01	
D12	-0.20	0.04	0.01, 0.02	
R13	0.02	-0.06	0.03, 0.00	CHγ 0.03; CHδ -0.02
S14	0.04	-0.06	-0.04	
N15	-0.11	0.01	0.01, 0.00	NHγ 0.03, 0.00
L16	-0.06	-0.07	0.00	CHδ -0.02, -0.02; CHγ 0.05
R17	0.03	-0.27	0.07, 0.04	CHγ -0.001 CHδ -0.01
A18	-0.20	-0.07	-0.06	
H19	-0.07	0.01	-0.18, -0.10	CH5 -0.51; CH2 0.48
L20	0.13	0.00	0.00	CHδ 0.00, -0.01; CHγ 0.00
Q21	0.05	0.01	0.04, 0.05	CHγ 0.08; NHδ 0.01, -0.01
T22	-0.14	0.00	0.00	CHγ 0.00
H23	0.01	-0.08	-0.13, -0.09	CH5 -0.56; CH2 -0.60
S24	0.08	-0.02	0.00	
D25	-0.09	0.01	0.05, 0.03	
V26	0.00	0.03	0.01	CHγ 0.00, 0.00

B) *Δδ* of the Assigned ^{1}H NMR Resonances of HR1 at pH 7.0

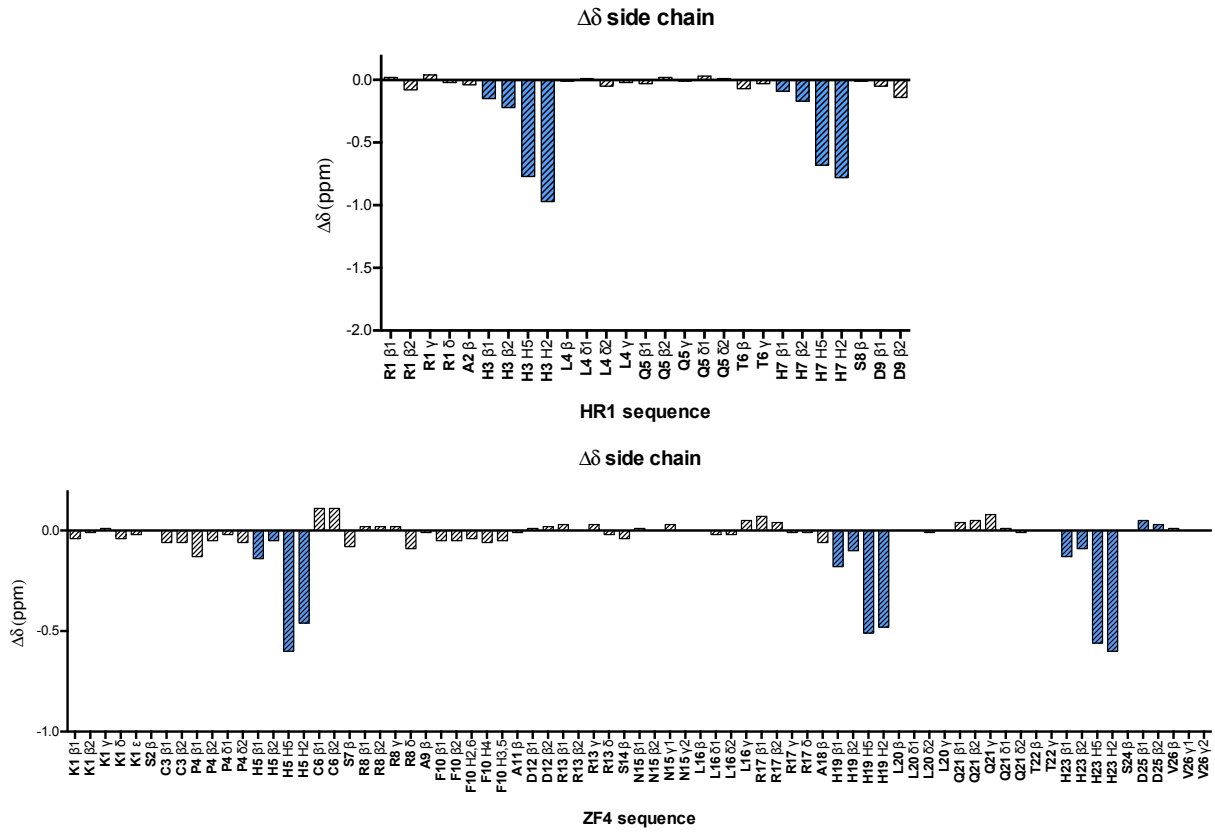
	Δδ = *δ*(**1**-HR1) - *δ*(Free HR1) 15 ºC (ppm)			
Residue	NH	CHα	CHβ	Other
R1		-0.13	0.02, -0.08	CHγ 0.04; CH*δ* -0.02
A2	-0.25	-0.2	-0.04	
H3	-0.29	-0.01	0.15, -0.22	CH5 -0.77; CH2 -0.97
L4	-0.11	-0.1	-0.01	CHγ 0.01 ; CH*δ* -0.05, -0.02
Q5	0.04	0.01	-0.03, 0.02	CHγ -0.01; NH*δ* 0.03, 0.01
T6	0.14	-0.03	-0.07	CHγ -0.03
H7	0.12	-0.17	-0.09, -0.17	CH5 -0.68; CH2 -0.78
S8	-0.06	-0.1	-0.01	
D9	-0.10	-0.05	0.05, -0.14	
V10	---	---	---	



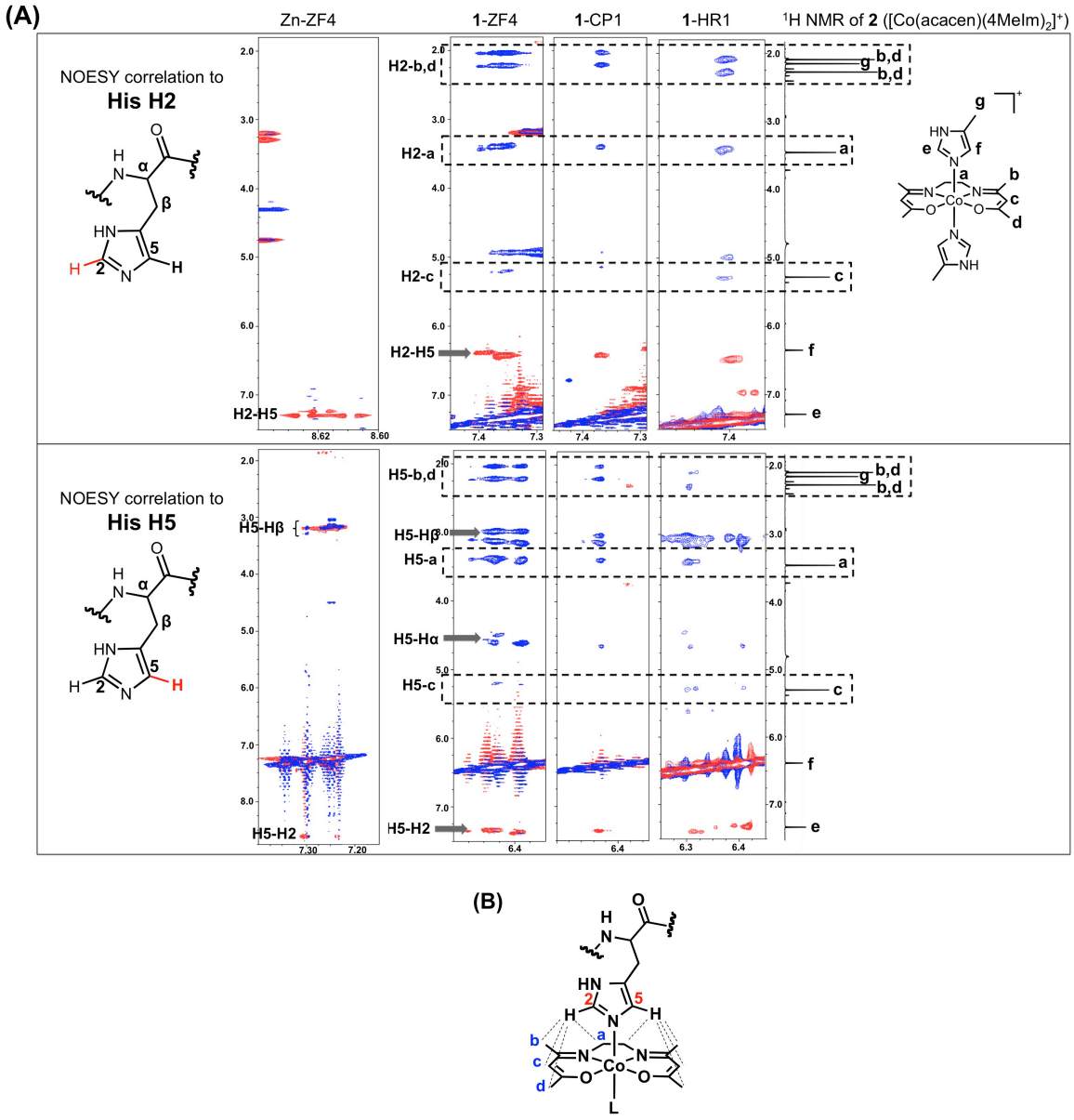
SI Figure 3: The *Δδ* (*δ*(**1**-Peptide) – *δ*(apo-Peptide)) of amino acid NH ^{1}H chemical shifts (in ppm) plotted against peptide sequence of HR1 at 10 ºC and ZF4 at 15 ºC. *Δδ* of His NH protons are highlighted in blue. No significant deviations for specific amino acid NH are observed, indicating chemical shift changes arise from structural changes.



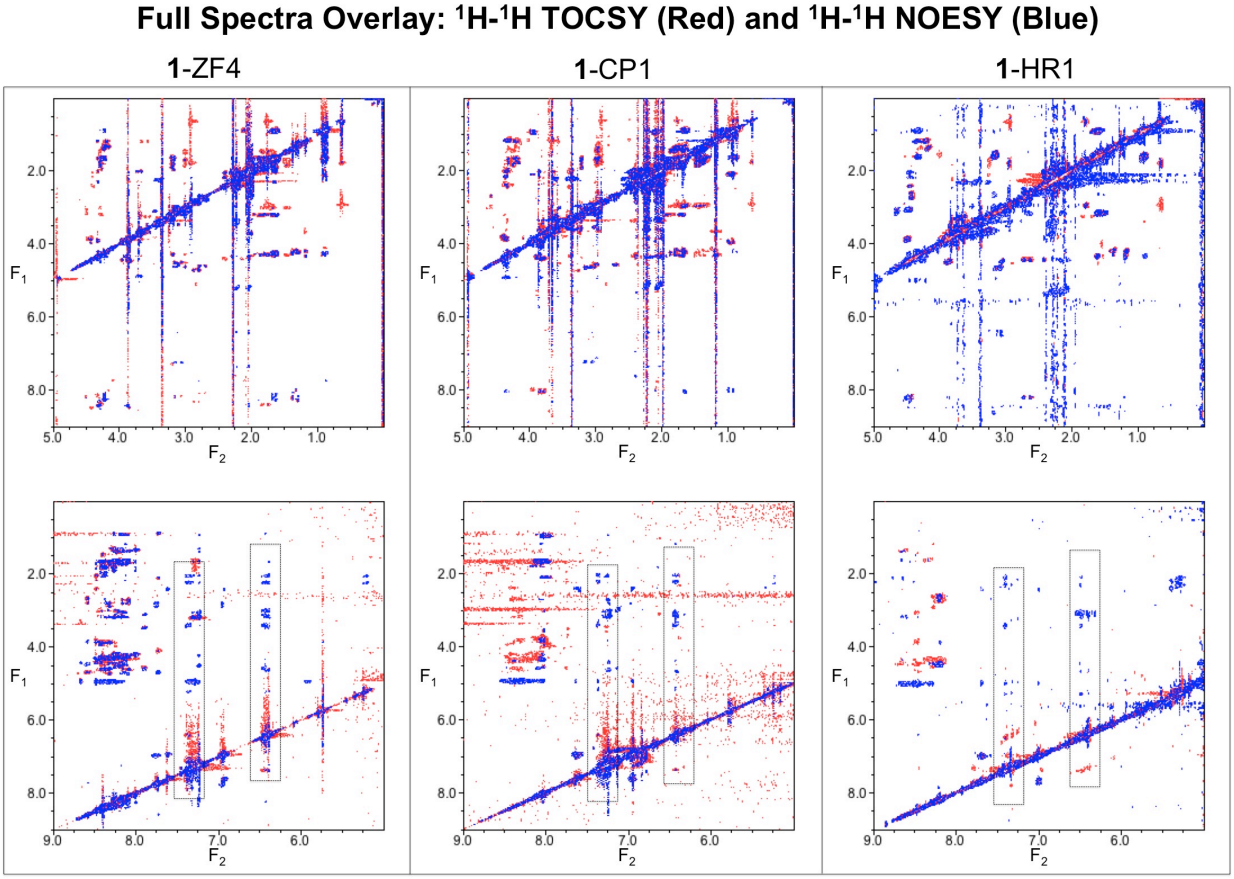
SI Figure 4: The *Δδ* (*δ*(**1**-Peptide) – *δ*(apo-Peptide)) of amino acid CHα ^{1}H chemical shifts (in ppm) plotted against peptide sequence of HR1 at 10 ºC and ZF4 at 15 ºC. *Δδ* of His CHα protons are highlighted in blue. No significant deviations for specific amino acid CHα are observed, indicating chemical shift changes arise from structural changes.



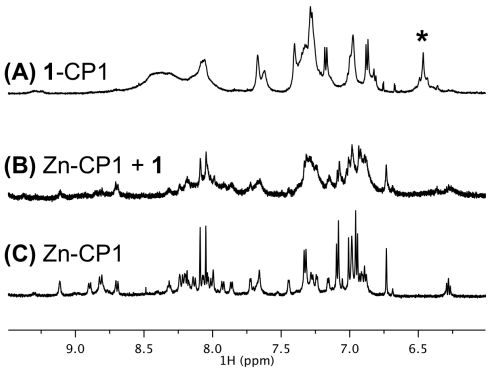
SI Figure 5: The $\Delta\delta$ (δ(**1**-Peptide) – δ(apo-Peptide)) of amino acid side chain proton 1H chemical shifts (in ppm) plotted against peptide sequence of HR1 at 10 ºC and ZF4 at 15 ºC. $\Delta\delta$ of His side chain protons are highlighted in blue. In contrast to Figure 3 in the body, complete labels for each proton are in the x-axis.



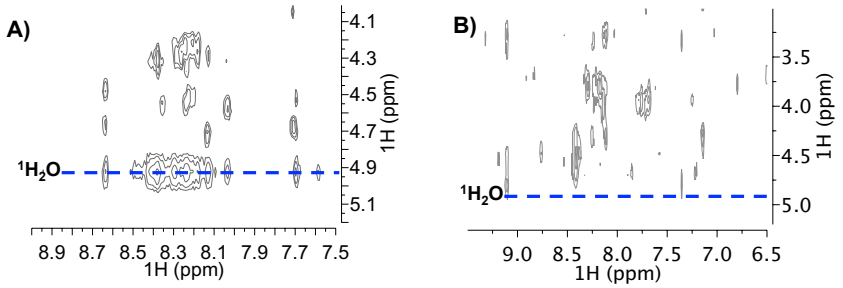
SI Figure 6: (A) Overlays of the ^{1}H-^{1}H NOESY spectra (blue) and ^{1}H-^{1}H TOCSY spectra (red) of His H2 (top panel) and H5 (bottom panel) protons of Zn-ZF4, **1**-ZF4 and **1**-CP1 at 15 ºC and **1**-HR1 at 10 ºC. For comparison, the 1D ^{1}H NMR spectrum of **2**, a small molecule model of **1** coordinated to two His, at 10 ºC is included. The intra-residue TOCSY and NOESY correlations of the His residues are labeled in all spectra and indicated by arrows in the **1**-Peptide spectra. In addition to the intra-residue correlations, NOE correlations are present in the **1**-Peptide spectra with resonances that correspond to the of protons in the acacen ligand of $[Co(acacen)(L)_2]^+$. These correlations are absent in the Zn-ZF4 spectra. These NOEs are indicated by dashed boxes that are inclusive of the homologous NMR peaks of **2**. (B) Schematic of proposed NOE interactions between the acacen protons of **1** and the His imidazole protons.



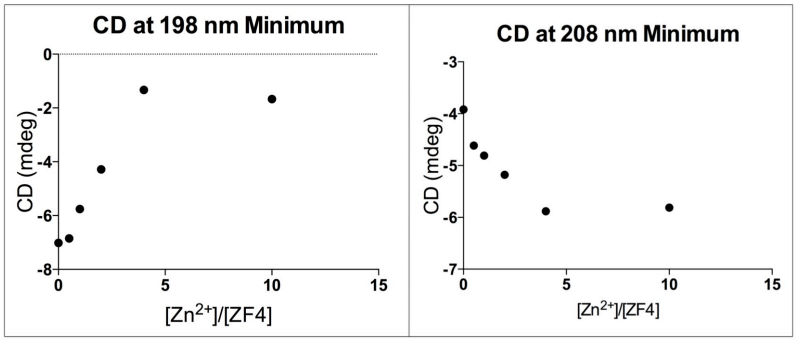
SI Figure 7: Overlay of full ^{1}H-^{1}H TOCSY and ^{1}H-^{1}H NOESY spectra of ZF4 and CP1 at 15 ºC (1.5 µM) and HR1 at 10 ºC (5 mM). The upper panels show the upfield regions (0.0-5.0 ppm) and the lower panels show the downfield regions (5.0-9.0 ppm) of the direct dimensions. The full spectra (0.0-9.0 ppm) in the indirect dimension are shown on both upper and lower panels. The NOESY correlations to H2 and H5 of the His Im protons are boxed in black. No other NOE connectivities to the acacen protons of **1** were observed in the remaining spectra, implying that **1** selectively binds to histidines over other amino acids.



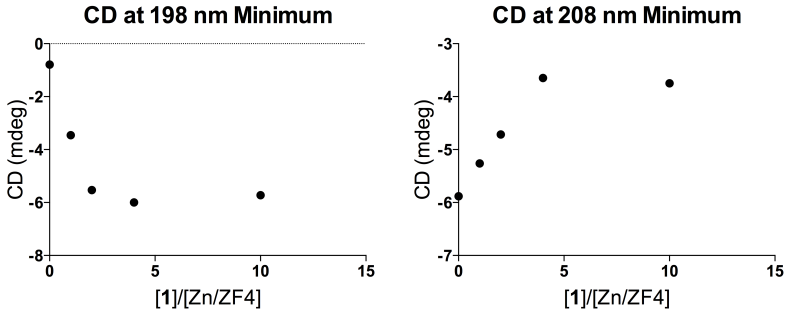
SI Figure 8: ^{1}H NMR of the backbone NH of (A) **1**-CP1 (B) Zn-CP1 challenged with **1** and (C) Zn-CP1. Addition of **1** to Zn-CP1 leads to a loss in signal indicating perturbation by 1, though not to the same degree as is observed in **Figure 7**.



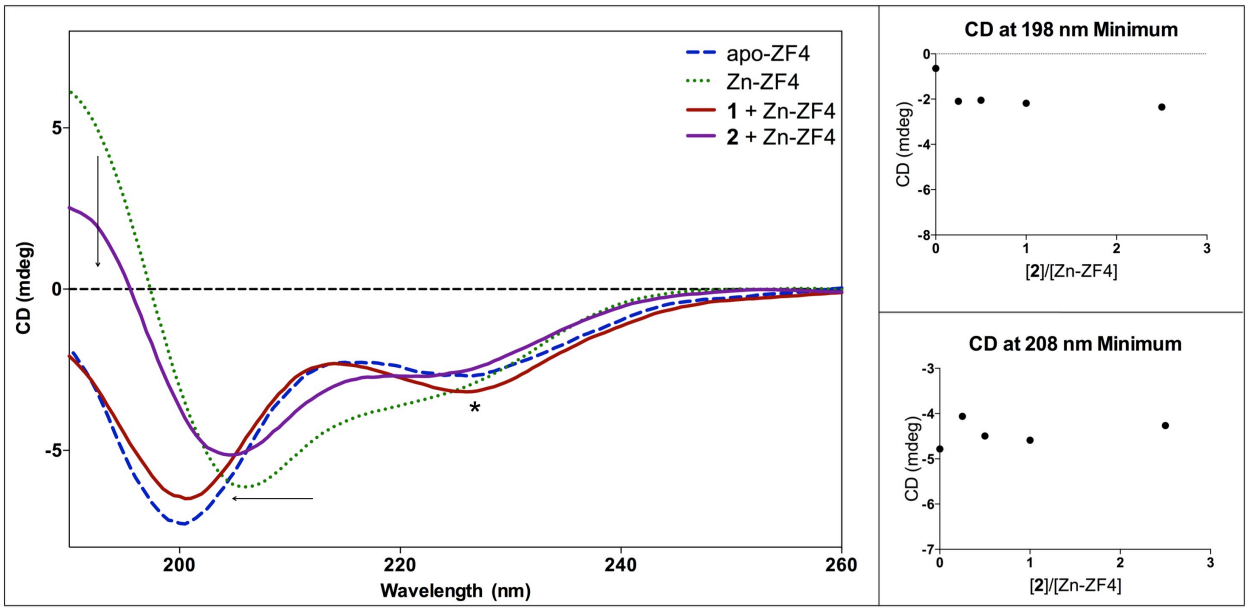
SI Figure 9: ^{1}H-^{1}H NOESY with 150 ms mixing time at 15 ºC in the backbone NH-CHα region of (A) apo-ZF4 or (B) Zn-ZF4. Rate of chemical exchange of backbone NH protons with water protons (δ ^{1}H2O = 4.9 ppm, 15 ºC) was used to evaluate the degree of hydrogen bonding and consequently, structure. This figure was evaluated in conjunction with **Figure 8** in the main text. Peaks from the backbone NH of apo-ZF4 (as with **1**-ZF4) exhibit detectable chemical exchange with water in comparison to those of Zn-ZF4. The position of the water peak is indicated by the blue dotted line.



SI Figure 10: CD signal of ZF4 with Zn^{II} titration at 25 ºC. Increasing concentrations of Zn^{II} shifts the spectra from a random coil to a ββα motif signal, indicated by loss of the random coil minimum at 198 nm and growth in the ββα minimum at 208 nm.

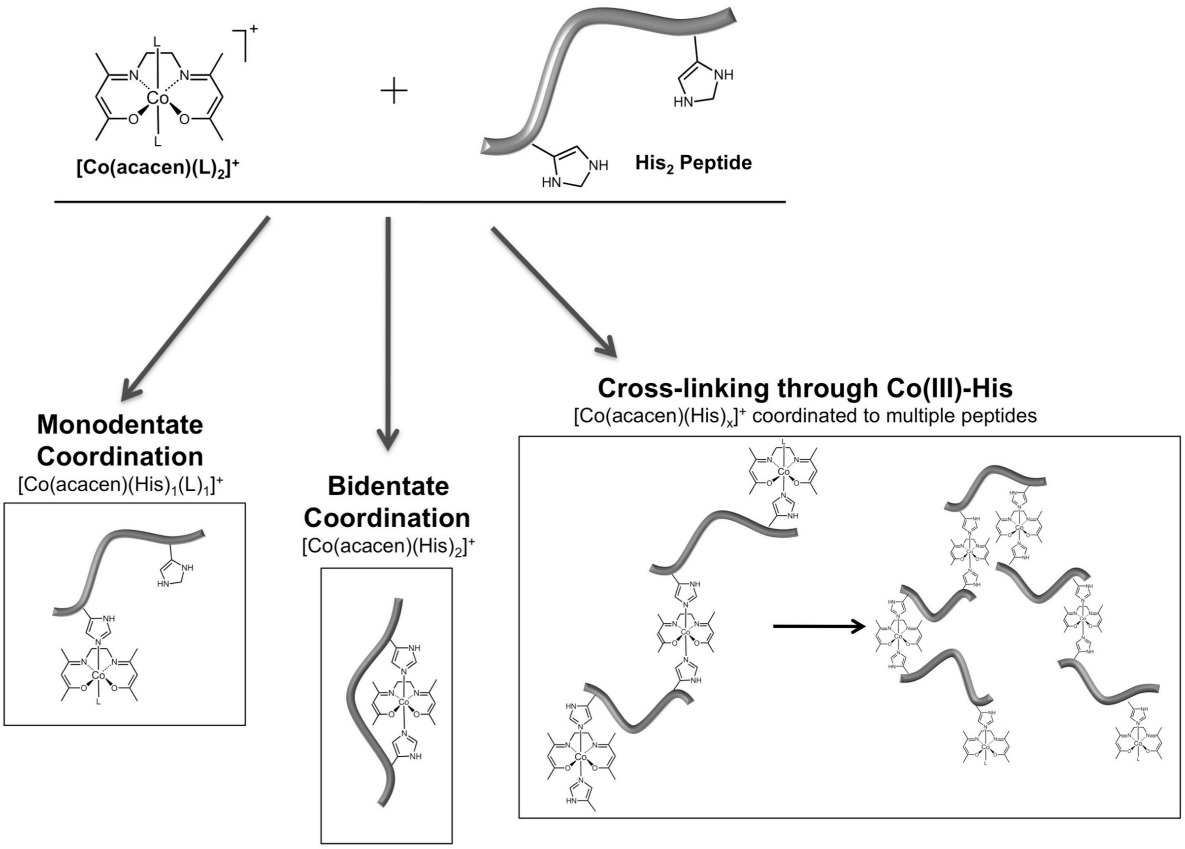


SI Figure 11: CD signal of Zn-ZF4 with titration of **1** at 25 ºC. Addition of **1** to Zn-ZF4 disrupts the ββα motif in a concentration-dependent



SI Figure 12: CD of **2** + Zn-ZF4 as compared to apo-ZF4 (free), Zn-ZF4, and **1** + Zn-ZF4 at 25 ºC. In contrast to the concentration-dependent shift of the **1** + Zn-ZF4 CD spectra toward a random coil singal, 2 does not induce the same concentration-dependent loss of the ββα 208 minimum and a shift towards the random coil 198 nm minimum. Although a slight shift from the Zn-ZF4 spectra is observed, the resulting spectra of 2 + Zn-ZF4 more closely resembles the ββα Zn-ZF4 than the random coil apo-ZF4.

Possible Binding Modes of Co(III) Schiff base Complexes with His_2 Peptides like HR1



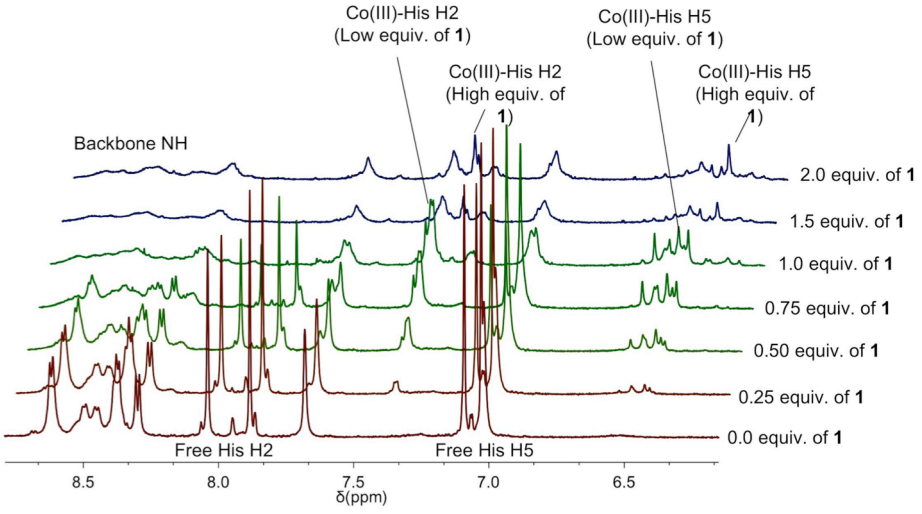
SI Scheme 1: Scheme of possible binding modes of Co^{III} Schiff base complexes with labile ligands (L) such as $[Co(acacen)(NH_3)_2]^+$ (**1**). Co^{III} Schiff base complexes contain two axial sites whereupon His residues can coordinate. Consequently, Co^{III} Schiff base complexes can exhibit multiple possible binding modes with peptides containing two His residues (His_2) such as the model peptide HR1. Some examples are displayed in this scheme. The cross-linking binding mode may result in increased molecular weight and slower tumbling rates.

SI Discussion 1: *Concentration-Dependent NMR of HR1*

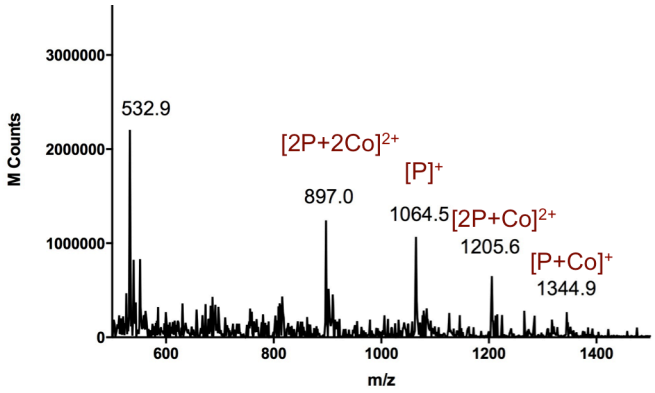
^{1}H NMR spectra of HR1 were acquired at increasing concentrations of **1**; the **1**:HR1 ratio was varied from 0.0 to 2.0. The aromatic and backbone NH regions of the spectra (6.0-9.0 ppm) were analyzed (Accompanying Figure 1). With increasing concentration of **1** up to 0.75 equivalents, a concentration-dependent reduction of signal corresponding to free His protons (His3 H2 8.06ppm, His3 H5 7.10 ppm; His7 H2 7.89 ppm, His7 H5 7.03 ppm) was observed while peaks at 7.45-7.35 ppm and 6.60-6.43 ppm emerged. Based on assignments made by TOCSY and NOESY these new peaks correspond to the H2 and H5 protons of His coordinated to **1** (SI Scheme 1).

A further increase in concentration of **1** (≥1.0 equivalents) resulted in the appearance of peaks at 7.34-7.29 ppm and 6.42-6.32 ppm. While these new peaks are within the region of the expected chemical shifts of Co^{III}-coordinated His protons, the chemical shifts are distinct from the peaks observed at <1.0 equivalents of **1**. These observations indicate the presence of more than one species containing His coordinated to $[Co(acacen)(L)_2]^+$ (Co^{III}-His). The growth of these new resonances coincides with the appearance of visible precipitate in the solution and loss of signal intensity, possibly due to the presence of large molecular weight species with slow tumbling rates.

While the identity of the two different Co^{III}-His species is unclear, free His proton peaks signals are reduced to undetectable intensities with as little as 1.0 equivalent of **1** and replaced with upfield-shifted His H2 and H5 peaks in a concentration-dependent manner. It is possible that at low concentrations (<1.0 equivalents), the HR1 peptide coordinates to **1** with a 1:1 ratio, such as with His_2 binding (SI Scheme 1 illustrates possible binding modes of $[Co(acacen)(L)_2]^+$ complexes to a His_2 peptide). As **1** concentration increases, **1** may coordinate two HR1 peptides (2:1 HR1:**1** ratio) in a cross-linking manner through the two axial sites. Such behavior would result in a species with higher molecular weight and aggregation propensity consistent with experimental observations. ESI-MS confirms the possibility of this scenario (See Accompanying Figure 2) Regardless of the identity of the species formed upon addition of **1**, the complete loss of free His ^{1}H NMR signals at 1:1 HR1/**1** ratios demonstrates high concentration-dependent reactivity of the Co^{III} Schiff base complex with His residues.



Accompanying Figure 1 for SI Discussion 1: NMR of 1-HR1 at varying ratios of 1:HR1 from 0.0 – 2.0. With increasing concentrations of 1, a loss of peaks corresponding to the free His H2 and H5 are observed (8.06, 7.89, 7.10, and 7.03 ppm). The loss of these peaks is accompanied by a rise in new peaks at 7.45-7.29 and 6.60-6.32 ppm, indicating His-coordination to 1 (Co(III)-His) in a concentration-dependent manner. A complete loss of free His peaks is observed at <1.0 eq. of 1. Two Co(III)-His species are observed: one major species increases until <1.0 eq. of 1. At ≥ 1.0 eq. of 1, the signals of this species are reduced while signal for a second species increases. The growth of NMR signals for this new species is accompanied by loss of overall signal intensity and visible aggregation.



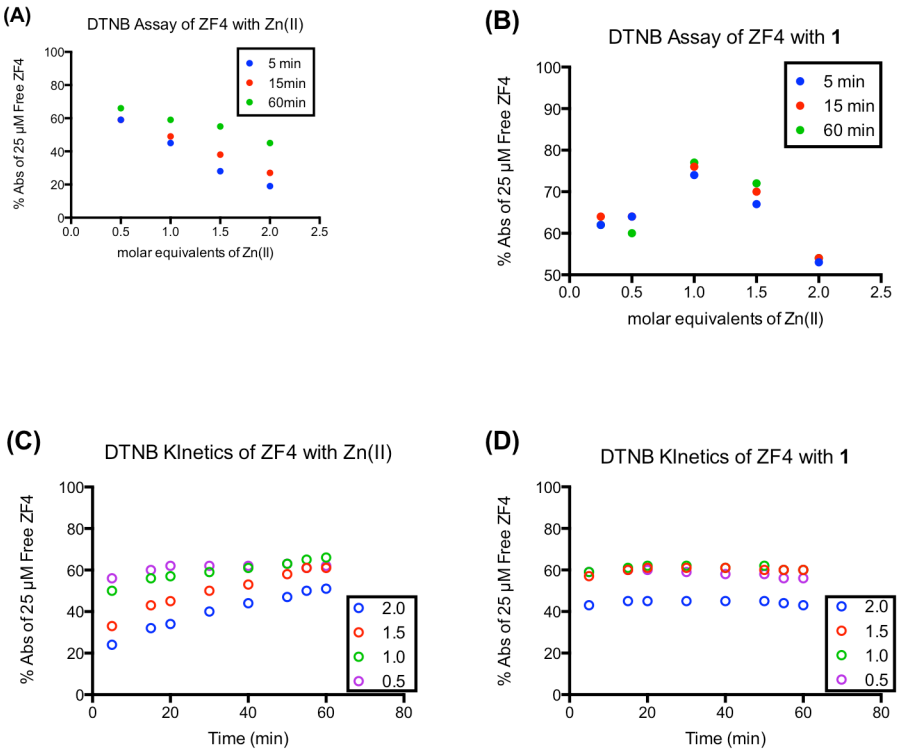
Accompanying Figure 2 for SI Discussion 1: ESI-MS from direct injection of HR1 (expected mass = 1064) in the presence of 1.0 molar equivalents of **1** in positive mode. The m/z peaks are labeled with species identity wherein **P** referes to the HR1 peptide and **Co** refers to **1**. A mixture of adducts with different ratios of HR1 to **1** are observed, suggesting the scenario described in SI Discussion 1.

SI Discussion 2: *Determination of Free Thiols in ZF4*

Ellman's reagent (5,5'-dithiobis-(2-nitrobenzoic acid) or DTNB) was used to evaluate the state of the thiols of the cysteine residues in ZF4 upon treatment with Zn^{II} ($ZnCl_2$) or **1**. ZF4 was incubated with either Zn^{II} or 1 with varying concentrations and evaluated over time for slow- and fast-reacting thiols by the absorbance at 412 nm. Increasing concentrations of Zn^{II} results in a linear reduction of free thiols (decrease in absorbance) due to Zn-coordination (Graph A in the accompanying figure). Over time, the absorbance of the DTNB reaction with the Zn^{II}/ZF4 mixture increases, indicating the presence of slow-reacting thiols (Graph C in the accompanying figure). Slow-reacting thiols are expected of cysteines coordinated to Zn^{II} wherein the DTNB can compete for cysteine access with the coordination bond and react to produce a signal.

The behavior of the cysteines of ZF4 in the presence **1** is more complex. At 0.25 - 0.5 molar equivalents of **1** to ZF4, free thiols are are reduced to 60-65% of apo-ZF4. As **1** is increased to 1.0 molar equivalents, an increase in free thiols are observed to 75-80% of apo-ZF4. However, further increase in **1** leads to a sharp reduction, down to <55% of apo-ZF4 at 2.0 molar equivalents. In contrast to the slow-reactiong thiols of Zn^{II}-treated ZF4, slow-reacting thiols are not detected, as the DTNB not significantly recover over time. This suggests that the consumption of the free thiols occurs through a process that is stable against DTNB reaction competition. Such cysteine consumption can occur through formation of disulfide bonds or tighter coordination to a metal than what occurs in Zn^{II}-cysteine coordination.

The non-linear behavior of the ZF4 cysteine thiols with increasing concentrations of **1** indicates a mechanism that is more complicated than coordination observed with Zn^{II}. One possibility is that the presence of **1** from His coordination can catalyze the oxidation of cysteines and promote disulfide bond formation. The scenario is consistent with the reduction of free thiols and the formation of non-reactive (rather than slow-reacting) species. The non-linear dependence may result from the difference in thiol reactivity of a Co^{III} complex coordinated to one His versus two His residues. However, elucidating the exact interaction with cysteines is beyond the scope of this work. Ongoing work evaluating peptides with varying cysteine and histidine residues by fast analytical techniques, such as ESI-MS and fluorimetry is seeking to address these questions.



Accompanying Figure for SI Discussion 2: DTNB assays of free thiols in ZF4 with increasing concentrations of (A) Zn(II) or (B) **1**. Free thiols in cysteines were evaluated using the absorbance of reacted DTNB at 412 nm. The time-dependence of DTNB reactivity in graph (C) and (D) were used to evaluate the presence of slow-reacting cysteine thiols, such as those coordinated to Zn(II) in zinc fingers.

Supplementary Experimental:

Concentration-Dependent NMR of HR1 (Supplementary Discussion 1)

HR1 was coincubated with 0.0, 0.25, 0.50, 0.75, 1.0, 1.5, and 2.0 molar equivalents of 1 at 37 ºC for at least 1 hour at 37 ºC prior to data acquisition. Data were accumulated on an Bruker Avance III 600 MHz spectrometer using 32k data points with 256 scans for each concentration of 1. The 1D data were processed with TopSpin software and analyzed by MestReNova 7.0.3 software.

Electrospray Ionization Mass Spectrometry (ESI-MS) of Peptides treated with 1

ESI-MS spectra were obtained using a Varian 1200 L single quadrupole spectrometer through sample introduction by either direct injection through a controlled mechanical infuser (HR1) or HPLC (ZF4). For HR1, the the peptide was dissolved in H_2O without buffer and combined with 1.0 molar equivalents of **1** to produce 16 µL of a solution of 500 µM peptide. The sample was incubated for 1 h at 37 ºC and diluted 20x with MeOH and H_2O (50/50 final) for to produce a final volume of 400 uL with 20 µM peptide. The methanolic peptide solution was infused at a rate into the ESI-MS with a flow rate of 50 µL min^{-1}. Mass spectra were obtained in positive mode in the range of 100-1500 *m/z* at a capillary temperature of 200 ºC with a spray voltage of 1.1 kV and capillary voltage of 10 V. For ZF4, the peptide was dissolved in H_2 without buffer and combined with 1.0 molar equivalents of **1** to produce 24 µL of a solution of 500 µM peptide. The sample was incubated for 1 h at 37 ºC and diluted to 60 µL to produce a solution of 200 µM peptide. 50 µL of the prepared peptide/**1** solution was analyzed by an Atlantis T3 analytical HPLC and 0.1% formic acid in H_2O (solvent A) and acetonitrile (B) as the mobile phases, with a linear gradient from 0-70% B over 35 minutes. The sample was eluted from the HPLC column into the ESI-MS analyzer. Mass spectra were obtained in positive mode in the range of 100-1500 m/z at a capillary temperature of 200 ºC with a spray voltage of 1.5 kV and capillary voltage of 40 V. The corresponding ESI-MS spectra corresponding to the HPLC chromatograms were deconvoluted by the expected *m/z* of possible **1**/ZF4 species using the Prostar/Dynamax Varian software.

DTNB Assay of Free Thiols

Varying concentrations of free ZF4 or 25 μM ZF4 with selected molar equivalents of 1 or ZnCl2 (100 mM Phosphate Buffer, pH 7.0) were incubated for 1 h at 37°C (84 μL incubation solution). After the incubation, a DTNB assay solution (per sample, 3.5 μL of saturated DTNB, 14 μL of tris buffer at 100 μM, pH 8.0) was added to each sample in a 96-well plate. The presence of free thiols was monitored through the formation of NTB2- by an absorbance of 412 nm. Absorbance readings were acquired on a Biotek Synergy 4 microplate reader at varying time points from 5 to 60 min. Dithiothreitol (DTT, 0-50 μM) was used a calibration control. The absorbance of varying concentrations of ZF4 was used to determine the expected absorbance of free ZF4 at 25 μM peptide. The absorbances of the ZF4 samples treated with varying concentrations of 1 or ZnCl2 were evaluated in terms of the percentage absorbance of the free peptide at 25 μM.