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Solution Structure and Constrained Molecular Dynamics Study of Vitamin B_{12} Conjugates of the Anorectic Peptide PYY(3–36)

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Vitamin B_{12}–peptide conjugates have considerable therapeutic potential through improved pharmacokinetic and/or pharmacodynamic properties imparted on the peptide upon covalent attachment to vitamin B_{12} (B_{12}). There remains a lack of structural studies investigating the effects of B_{12} conjugation on peptide secondary structure. Determining the solution structure of a B_{12}–peptide conjugate or conjugates and measuring functions of the conjugate(s) at the target peptide receptor may offer considerable insight concerning the future design of fully optimized conjugates. This methodology is especially useful in tandem with constrained molecular dynamics (MD) studies, such that predictions may be made about conjugates not yet synthesized. Focusing on two B_{12} conjugates of the anorectic peptide PYY(3–36), one of which was previously demonstrated to have improved food intake reduction compared with PYY(3–36), we performed NMR structural analyses and used the information to conduct MD simulations. The study provides rare structural insight into vitamin B_{12} conjugates and validates the fact that B_{12} can be conjugated to a peptide without markedly affecting peptide secondary structure.

Introduction

Peptide YY (PYY), a member of the pancreatic polypeptide family,[1–8] was first isolated from porcine intestinal tissue extracts in 1980[9] and was later shown to be a critical enteroendocrine hormone involved in appetite regulation.[10–12] PYY has two main circulating forms: PYY(1–36) and a truncated form, PYY(3–36).[13] PYY(1–36) is released in concert with caloric intake or exercise and is cleaved by dipeptidyl peptidase IV (DPP-IV)[14] in the gut to produce PYY(3–36). PYY(1–36) has an appetite-stimulating effect through activation of the orexigenic Y1 receptor (Y1-R) located in the intestines, blood vessels, and brain.[15] The two-amino-acid N-terminal (Tyr-Pro) truncation to PYY(3–36) results in an approximate 100-fold decrease in activity at the Y1-R,[5,16] and generates an agonist of the anorexigenic Y2 receptor (Y2-R) located in the intestines (vagal afferent sensory neuron signaling)[17,18] and brain,[19,20] which exerts a G-protein-coupled receptor (GPCR) G_i-mediated anorectic effect.

We recently reported a B_{12}–PYY(3–36) conjugate that demonstrated similar activity to native PYY(3–36) at the Y2-R in vitro, but improved function over PYY(3–36) upon subcutaneous (s.c.) administration in vivo in a lean rat model (conjugate **3** as described herein below).[21] In earlier work, we focused on conjugating to B_{12} through the ribose hydroxy group, as it is well established in the field that this is an optimal site for such conjugation, as it does not hinder recognition of B_{12} by its carrier proteins.[22–25] Likewise, we focused on an N-terminal region of PYY(3–36) for conjugation (specifically the K_4 residue), because again it has been well documented that modifications at (or indeed complete loss of) this area do not significantly affect Y2-R agonism.[26–28] These assumptions bore out, as the EC_{50} values at the Y2-R obtained for the conjugate produced (and noted as conjugate **3** herein) were similar to that of unconjugated PYY(3–36) used for comparison. These were established using a Fura-2 assay that monitors intracellular Ca^{2+} mobilization under conditions in which the Y2-R signals through a promiscuous G_q GTP binding protein.[21] Questions that remained from this work, however, were what affect, if any, does B_{12} conjugation actually have on the PYY(3–36) secondary structure and whether MD simulations could be used to better understand, and possibly predict, any structural modifications observed. To investigate these questions, two conjugates located at the same coupling sites (ribose on B_{12} and K_4 on PYY(3–36)

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but with a slightly varying spacer length (one methylene unit difference) were assayed for agonism of the Y2-R using a new fluorescence resonance energy transfer (FRET)-based assay that faithfully reports the normal signal transduction process by which the Y2-R signals through G_i proteins to lower levels of intracellular cyclic adenosine monophosphate (cAMP).[29] NMR structures were solved for these conjugates, and their in-solution NMR structures were compared with those previously reported by Keire et al.[30] and Nygaard et al.[7] Subsequent unconstrained and NMR constrained MD simulations were then also performed.

Results and Discussion

In vitro evaluation of conjugates 3 and 4

All assays were performed *at least* in triplicate. Conjugates **3** and **4** were tested for their abilities to lower cAMP levels. Figure 1 shows the dose–response relationships for **3** and **4** relative to K_4PYY, showing both conjugates are less active than K_4PYY and that **4** is more active than **3**. Both conjugates are, however, within one-half log order of K_4PYY.

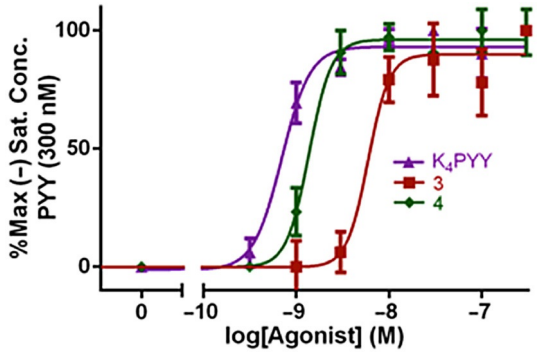


Figure 1. Dose–response curves monitored as percent inhibition of Ex-4 action at AKAR3 by K_4PYY and conjugates **3** and **4** at the Y2-R. EC_{50} values: K_4PYY: 1±0.2 nM, **3**: 6±2 nM, **4**: 2±0.2 nM. EC_{50} values are the average ±SEM.

This difference in EC_{50} values in comparing conjugates with K_4PYY was initially presumed to be a compromise between steric hindrance and/or unfavorable flexibility resulting in modifications/interactions that negatively affect the peptide structure–activity profile. At this point we decided to pursue NMR and molecular dynamics (MD) studies to further explore these in vitro observations.

NMR analysis of 3 and 4

Proton chemical shifts for **3** were assigned by analyzing TOCSY, DQF-COSY, and 2D NOE spectra at 25 °C. The experiments were also performed at 20 and 30 °C, at which slight shifts of some proton signals resolved overlapping peaks. The NMR spectra of **3** have some similarity to those of PYY(3–36), such as line broadening of many signals,[7] indicating increased dynamics, and a decrease in the chemical shift range of the backbone amide protons relative to full-length PYY. All backbone amide protons were assigned with the exception of Leu24, which could not be definitely determined due to overlap. Figure S17 (Supporting Information) shows the proton chemical shift difference between **3** and PYY(3–36). There are chemical shift differences for residue Lys4, which is not surprising, as this is the attachment site for B_{12}. Figure 2 shows an overlay of **3** after

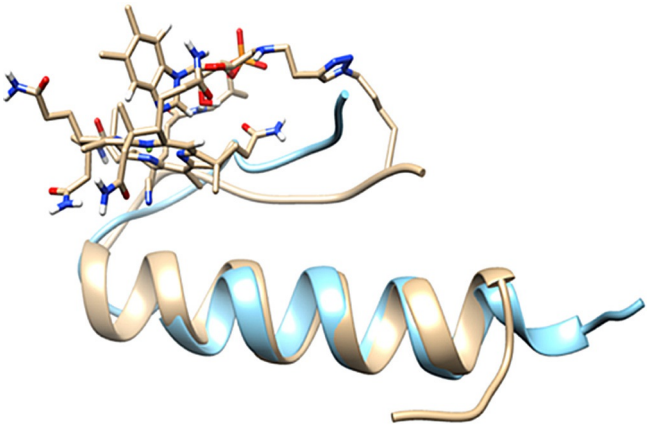


Figure 2. Overlay of PYY(3–36) (blue) versus **3** (tan). The structure of PYY(3–36) was obtained from the RCSB Protein Data Bank (www.pdb.org); PDB ID: 2DF0. The program Chimera (UCSF; www.cgl.ucsf.edu/chimera/)[31] was used to display the image.

MD calculations and PYY(3–36). The first chemical shift difference to consider is that for the methyl and α protons of Ala7. In PYY(3–36), the methyl group of residue Ala7 is pointing toward the α helix, whereas in conjugate **3** the methyl group is oriented away from the α helix. A 2D NOE cross-peak between the Ala7 methyl group and the ring protons of Tyr20 was observed in PYY(3–36),[7] but in **3** only a very weak cross-peak was observed in the longest mixing time 2D NOE experiment. This difference in orientation would also put the Ala7 α proton in distinct environments. The backbone amide protons have different chemical shifts for the β turn residues and residues in the N-terminal side of the α helix, specifically residues Gly9, Ala12, Ser13, Glu15, Leu17, and Arg19. This can be explained by the unraveling of the α helix and increased dynamics at the N-terminal side in the PYY(3–36) structure. Conjugate **3** maintains an α-helical structure similar to that of full-length PYY, and the residue with the largest chemical shift difference for the amide proton, Leu17, has a chemical shift value closer to that of the full-length peptide: PYY Leu17 NH 8.40 ppm,[7] **3** Leu17 NH 8.36 ppm, PYY(3–36) 7.95 ppm.[7] Nygaard et al. suggest that the Pro2–Tyr27 interaction is important for the stability of the PP fold, and that loss of this interaction in PYY(3–36) creates both conformational and dynamic changes in the structure, especially around the turn region.[7] Close inspection of **3** indicates possible hydrogen bonds from Glu6 to Tyr27 and Ser23, which may stabilize the PP fold in the conjugate.[7]

To elaborate on the structural studies, we decided to also investigate the solution structure of **4** to allow a direct comparison with **3**. Based on the NMR spectra, the conjugate structures appear very similar with only minor differences in the proton chemical shift assignments (Supporting Information Figure S18) and greater than 95% similarity in the 2D NOE spectra (Supporting Information Figure S19).

The major difference observed between **3** and **4** is the proton chemical shift change at B7 and B2 on the dimethylbenzimidazole (DMB) ligand (see Supporting Information Figure S12 for B_{12} atom numbering scheme). The C20 methyl protons are closer to the B4 and B2 protons in **4** based on the presence of a weak cross-peak between the C20 methyl protons and B2, which is only seen in the longest mixing time 2D NOE spectra of **3**, and a cross-peak between the methyl protons and B4, which is stronger for **4**. Weak cross-peaks are observed in **4** between a propionamide proton of the *g* side chain of B_{12} (Supporting Information Figure S12) and the Hα of D11 as well as the methyl protons of A12. The α helix motif as a whole is critical for association and subsequent agonism.[26] This is consistent with reported Y2-R interactions, as the C-terminal pentapeptide region is well established as the critical region, or "address", of the main interactions with Y2-R, while the α helix is considered the "message", indicating that both areas are critical in Y2-R agonism.[26]

NMR constrained MD studies of 3 and 4

Molecular dynamics simulations of **3** and **4** were performed both with and without the NMR constraints defined for **3** to consider differences in behavior and potential alternative structures in the simulations. The observed structural changes across the simulations identified intra-PYY(3–36) interactions that might, through their stabilization in the isolated conjugate, promote the decreased activity of **3** relative to **4**. The unconstrained MD simulation data then provide an additional set of structures for considering accessible geometries beyond the restrained set. The average structures from representative MD time ranges for **3** and **4** are shown in Figures 3 (front/side view) and 4 (top view). Apparent from these views, and the full simulations in general, are the persistence of 1) much of the α helical structure and 2) localization of the B_{12} fragment itself to the unstructured region approaching the loop into the α helix (in the images, this loop is at the base of all structures, including residues Glu10, Asp11, and Ala12). Across all of the simulations, several hydrogen bonding motifs are found to persist at the onset of the simulations and over the time evolution of the structure dynamics that serve to effectively anchor the B_{12} at this loop region. Those which specifically anchor the B_{12} to this region in all simulations are shown in Figure 5, visualizing the two most persistent motifs for these structures: a pair of hydrogen bonds from a single B_{12} amide side chain to Pro8 and Glu16 (left, Motif 1) and an amide side chain to Pro8 hydrogen bond and coordination of a hydroxy group H atom on Ser13 to the B_{12} cyano nitrogen atom (right, Motif 2). The structural basis for preservation of the loop region itself across all simulations is evident in Figure 6, which shows that (left) Glu16 is engaged in several persistent hydrogen bonding interactions with Gly9, Glu10, and Asp11, whereas at the far end of the loop (right), Glu6 is in close proximity to hydrogen bond acceptors on Tyr27 and Ser23. The NMR distance lists, ranges, and time-averaged MD structures for **3** and **4** are provided in the Supporting Information.

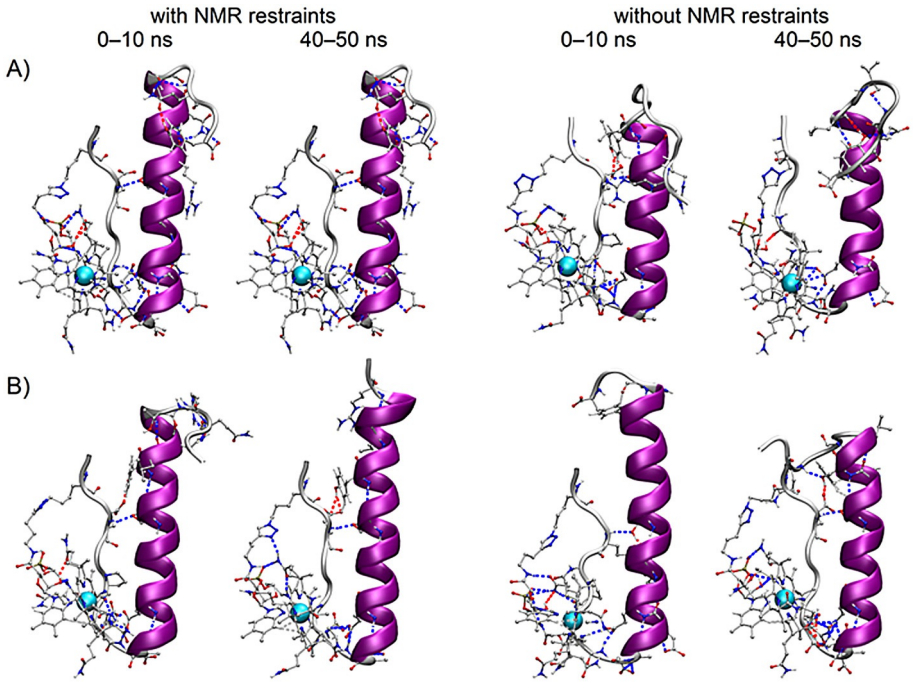


Figure 3. Side-on views (aligned along the α helix) of RMSD average structures (across 10 ns sampling increments) for restrained (left) and unrestrained (right) MD simulations of A) **3** and B) **4**.

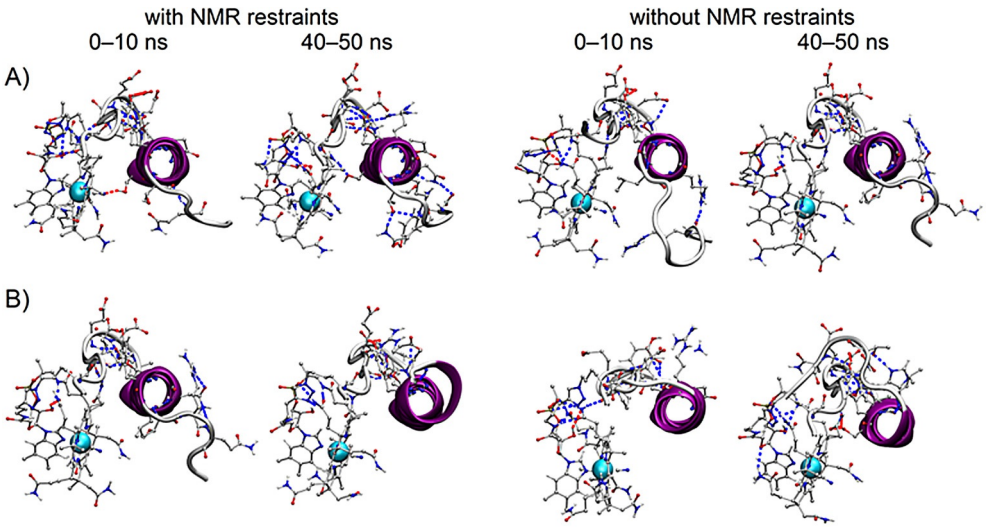


Figure 4. Top-down views (aligned along the α helix) of RMSD average structures (across 10 ns sampling increments) for restrained (left) and unrestrained (right) MD simulations of A) **3** and B) **4**.

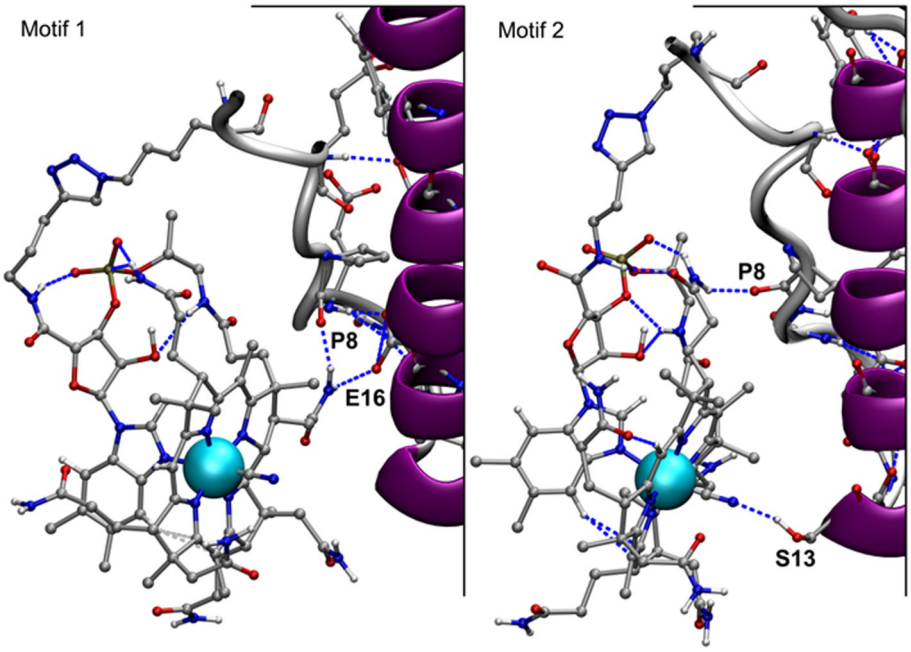


Figure 5. Two persistent hydrogen bonding interaction motifs between the B_{12} and PYY(3–36) unstructured region (residues 3–10) across all simulations.

The differences between structures **3** and **4**, both with and without NMR constraints, are largely localized to the C-terminal side of the α helix and occur to varying degrees in all of the simulations. With the B_{12} largely predicted to be confined to the PYY(3–36) loop due to several strong hydrogen bonding interactions, and with the well-known attenuation of PYY(3–36) activity with modifications to or removal of the C-terminal region, the most logical explanation for any change in behavior to come from these single conjugate simulations is some structural change at the C-terminal region of PYY(3–36). This may occur from B_{12} binding-induced conformational changes at the PYY N terminus, causing changes in activity, meaning any observed interactions between the B_{12} binding-constrained N terminus and concomitantly proximal C-terminal regions are of great interest. Despite the small change in tether length for these two cases, RMSD analyses and average structure generation produced two distinct structures that, for each case, revealed binding interactions deemed consistent with the trends in activity.

MD simulations of **3** and **4** highlight hydrogen bonding interactions that may govern the differences observed in Y2-R agonism and subsequent calcium mobilization and inhibitory cAMP effects. PYY(3–36) does not tolerate any interaction at the C terminus with respect to Y2-R stimulation.[32] If the

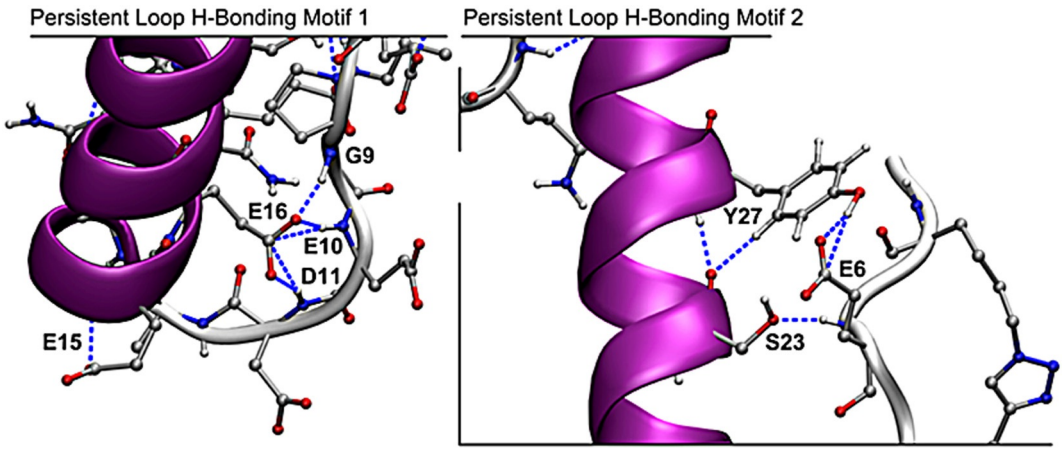


Figure 6. Two persistent hydrogen bonding motifs that define the PYY(3–36) loop region (left) and stabilizing interactions between the unstructured N-terminal region and the α helix.

answer to the decreased activity of **3** lies solely on some response internal to the conjugate, one might argue from the MD simulations that the shortened tether length enhances the stiffness of the unstructured region (residues 3–9) by decreasing its conformational flexibility upon hydrogen bonding between the B_{12} and the near-loop region. This result would provide a less flexible N-terminal region and a more persistent hydrogen bonding pocket for the C-terminal region with which to interact. By the loss of flexibility, necessary at the C-terminal region for biological activity, reduced activity would be predicted (and is observed). Kaiser et al. recently reported data showing that unwinding of C-terminal residues of neuropeptide Y (NPY) is critical for Y2 receptor binding and activation.[32] Solution NMR experiments showed that the ligand is tethered to the second extracellular loop by hydrophobic contacts and revealed NPY to undergo remarkable structural changes within the C terminus. The C-terminal pentapeptide plays a role in extensive and susceptible interactions in NPY; a network that is also relevant for PYY(3–36) in regards to Y2-R agonism. Changes in the C-terminal amino acids can easily disturb receptor binding or switch receptor selectivity for both NPY and PYY(3–36) as observed in numerous earlier structure-activity studies.[33] The ultimate conclusion from Kaiser et al. directly relates to our work, as the binding mode of NPY [and in our case, B_{12} conjugates of PYY(3–36)] might have more general implications for peptide binding GPCR systems.

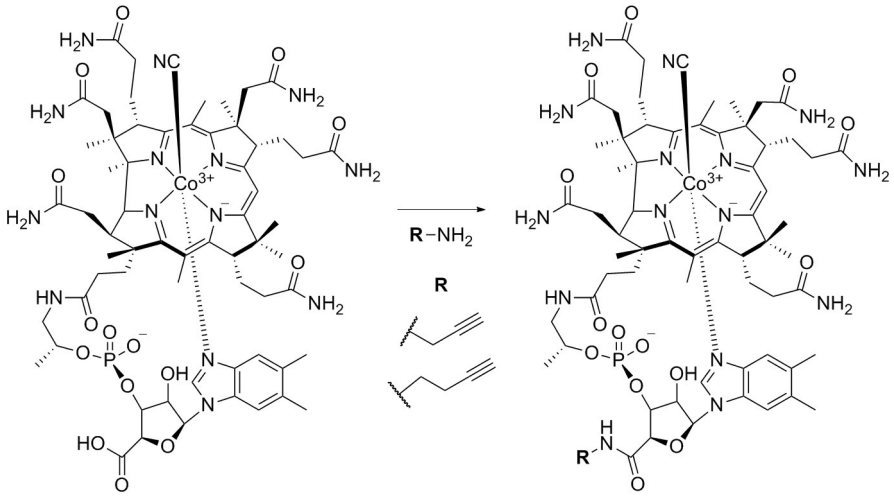
The MD simulations from this study do indicate that if the origin of the decreased activity of **3** is entirely due to factors internal to the B_{12}–PYY(3–36) conjugate itself, then constraint of the C-terminal region by hydrogen bonding interactions with the N-terminal region could explain it—and that this kind of internal mechanism may have its origin in the reduction of tether length.

Conclusions

B_{12}–PYY(3–36) conjugates **3** and **4** with various methylene spacer lengths between the B_{12} and PYY(3–36) show similar Y2-R agonism to that of PYY(3–36). Both intra- and intermolecular interactions between B_{12} and the peptide and small changes in the secondary structure of the peptide brought on by conjugation were observed. Based on the information collected from the NMR constrained MD studies, it would have been possible to offer a detailed assessment of the potential function of both conjugates. These observations suggest that MD could be used a priori to guide conjugate rational design and minimize the number of conjugates that would need to be screened—information of considerable benefit in development terms. Conjugates and modifications of B_{12} have garnered much interest in recent years for their clinical and medicinal applicability.[34] Based on the studies described herein, an ideal B_{12}–peptide conjugate would be one with an appropriate linker length to allow optimal function of both the peptide and B_{12}, which could be predicted by MD via inter- and intramolecular interactions that are known to be useful and/or harmful to the overall function of each component.

Experimental Section

Synthesis of alkyne precursors (1 and 2) and conjugates (3 and 4): Two B_{12}–alkyne precursors were prepared by activation of a B_{12}–carboxylic acid (B_{12}-CA) derivative[35] with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) and hydroxybenzotriazole (HOBt) in anhydrous DMSO under argon (Scheme 1). Full characterization of the alkyne precursor **1** and **2**, including RP-HPLC, MALDI-ToF MS, and NMR can be found in the Supporting Information (Figure S1–11, Table S1). For conjugate synthesis, click chemistry[36] was implemented using a copper iodide (CuI) and tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA) method, adapted from Gryko et al.[37,38] Copper(I)-catalyzed alkyne–azide cycloaddition (CuAAC) synthesis of conjugates **3** and **4** via the alkyne precursors **1** and **2** and a K_4-azido PYY(3–36) (K_4PYY) is described in Scheme 2 (spacer length $n = 2, 3$ for precursors 1 and 2). K_4PYY was initially tested against PYY(3–36) amide (Sigma–Aldrich), and there was no observed difference in Y2-R agonism. Subsequently, K_4PYY was used as the control for all assays. Characterization of the B_{12}-PYY(3–36) conjugates **3** and **4**, including HPLC and MALDI-ToF MS, can be found in the Supporting Information (Figure S13–16).



Scheme 1. Synthesis of B_{12}–alkyne precursors **1** and **2**. *Reagents and conditions*: EDC, HOBt, anhydrous DMSO; reactions carried out under argon for 16 h at RT.

In vitro assay of 3 and 4 at the Y2 receptor coupled to G_i: Conjugates **3** and **4** were tested for their abilities to lower levels of cAMP in an in vitro assay using HEK293 cell monolayers (Figure 7).[29] These cells were engineered so that they stably express the human GLP-1 receptor (GLP-1R), while also transiently expressing the human Y2-R. Furthermore, these cells were virally transduced with the genetically encoded FRET reporter AKAR3, which is used to monitor cAMP-dependent protein kinase (PKA) activation intracellularly. This assay is unique in that it allows FRET-based detection of the ability of PYY(3–36) to counteract the action of a GLP-1R agonist (Exendin-4; Ex-4) to raise levels of cAMP. When the cells are first treated with Ex-4 (33 pM; injection 1) so that levels of cAMP are elevated, AKAR3 exhibits increased FRET, measured as a decrease in the 485/535 nm emission ratio (Figure 7). This change of FRET occurs after an approximate lag time of 50 s. If PYY(3–36) is then applied at the 180 s time point (injection 2), a functional antagonism of the action of Ex-4 is measured so that the change of FRET is decreased. Note that no change of FRET is measured in response to the administration of a negative control standard extracellular saline (SES; Figure 7). By varying the concentration of added conjugate, it is possible to determine dose–response relationships, and to also determine EC_{50} values describing inhibitory actions of PYY(3–36) conjugates versus 33 pM Ex-4 in this assay. Figure 7 illustrates these responses to the first injection of either Ex-4 or SES, and the second injection of K_4PYY or SES. To normalize these raw data for subsequent dose–response analysis, "end-point" values of FRET were measured during the last 10 sample intervals (Figure 7). As illustrated in Figure 1, the dose-dependent inhibitory actions of PYY(3–36) conjugates are then quantified relative to a value of 100% that corresponds to the maximal inhibitory effect measured when testing 300 nM PYY(3–36) in this assay.

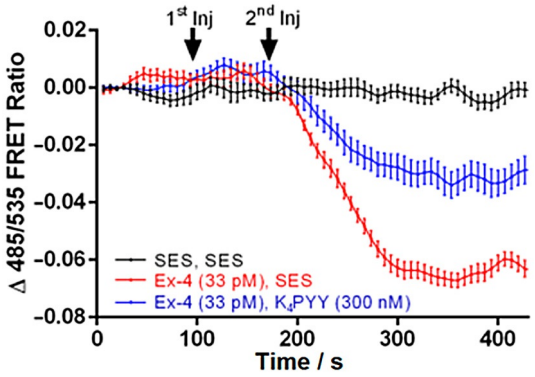
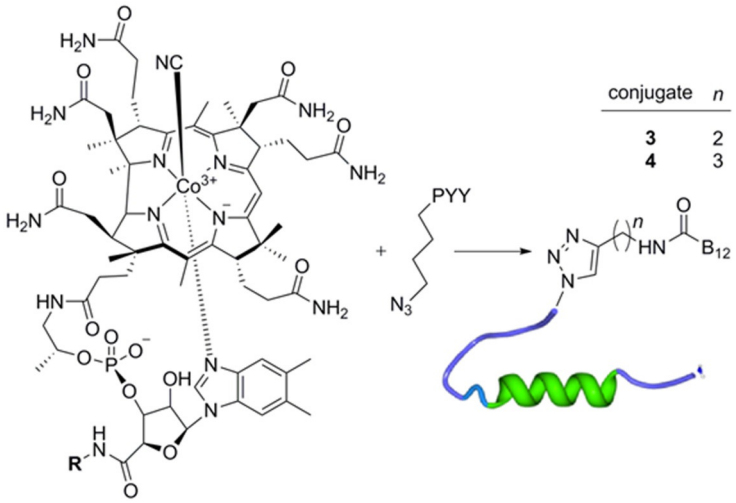


Figure 7. Δ485/535 FRET ratio through the course of a run. The first injection occurs at 100 s followed by a second injection at 180 s.



Scheme 2. Copper(I) alkyne–azide cycloaddition synthesis of B_{12}–PYY(3–36) conjugates **3** and **4** via alkyne precursors **1** and **2** with a two- or three-methylene-unit spacer between the 5′-amide on B_{12} and the triazole linkage to K_4PYY. *Reagents and conditions*: Cu^I, TBTA; reactions were carried out for 16 h at RT. PYY(3–36) adapted from PDB ID: 2DF0.

NMR studies of 3 and 4: NMR studies were executed initially to observe any structural differences between the conjugates and free peptide in solution. Because in vivo studies had previously established in vivo function for **3**, extensive structural studies were first performed with **3** and a direct comparison made to published PYY(3–36).[7] Full NMR studies of **4** were then completed to serve as

a comparison with **3**. Full descriptions of methods and conditions are provided in the Supporting Information.

MD studies of 3 and 4: To complement the NMR studies, MD simulations of **3** and **4** were completed in attempts to explain the minor differences of Y2-R agonism between the two conjugates. These MD studies took the form of 50 ns simulations to probe the potential variation in simulation geometries and time-averaged structures that arise from different tether lengths. MD simulations were performed using the GROMACS (ver. 5.0.4)[39] software package. The NMR distance lists, ranges, and tabulated distances from the time-averaged MD structure for **3** are provided in the Supporting Information.

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Keywords: GPCR · molecular dynamics · NMR spectroscopy · PYY(3–36) · vitamin B_{12}

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1. Synthesis of B_{12}-Alkyne Precursors (1-2)

1.1 B_{12}-Amino Butyne (1)

B_{12}-CA (10 mg, 0.007 mmol), EDC (14 mg, 0.07 mmol), and HOBt (19.7 mg, 0.15 mmol) were mixed in 5 mL anhydrous DMSO for 30 min under argon. To this activated mixture, 1-amino-3-butyne (5.99 μL, 0.07 mmol) was added, and the reaction mixture was stirred for 16 h at rt. The crude product was precipitated out of DMSO using diethyl ether and centrifuged at 4000*g* for 5 min. The pellet was redissolved in ddH_2O for purification by RP-HPLC. The crude reaction was purified via RP-HPLC with a C_{18} analytical column using a gradient of 10% MeCN, 90% H_2O/0.1% TFA, increased to 27% MeCN over 17 min, with a flow rate of 1.0 mL/min and UV detection at 360 nm; t_R of **1** = 12.1 min. Yield was 79-80%. Compound **1** was analyzed via MALDI-ToF MS using a CHCA matrix with a 1:1 sample/matrix ratio. MALDI-ToF MS: $[M-CN]^+$ expected 1395 *m/z*, found 1395.004 *m/z*. ^{1}H NMR was used to confirm the purity of the final product. ^{1}H NMR (400 MHz, D_2O): δ 7.219 (s, 1H), δ 7.002 (s, 1H), δ 6.920 (s, 2H), δ 5.998 (s, 1H). 2D NMR (HSQC/HMBC) was used to confirm the methylene and alkyne protons: ^{1}H NMR (500 MHz, D_2O): δ 3.482 (t, $1H_{a1}$), δ 3.406 (t, $1H_{a2}$), δ 2.489 (t, $2H_b$), δ 2.406 (s, $1H_c$). ^{13}C NMR (500 MHz, D_2O): δ 41.1 (C_a), δ 21.6 (C_b), δ 73.8 (C_c). See Table S1 for labeling schematic.

1.2 B_{12}-Amino Pentyne (2)

B_{12}-CA (10 mg, 0.007 mmol), EDC (14 mg, 0.07 mmol), and HOBt (19.7 mg, 0.1462 mmol) were mixed in 5 mL anhydrous DMSO for 30 min under argon. To this activated mixture, 1-amino-4-pentyne (7.1 μL, 0.07 mmol) was added, and the reaction mixture was stirred for 16 h at rt. The crude product was precipitated out of DMSO using diethyl ether and centrifuged at 4000*g* for 5 min. The pellet was redissolved in ddH_2O for purification by RP-

HPLC. The crude reaction was purified via RP-HPLC with a C_{18} analytical column using a gradient of 10% MeCN and 90% H_2O/0.1% TFA, increased to 27% MeCN over 17 min with flow rate of 1.0 mL/min and UV detection at 360 nm; t_R of **2** = 13.1 min. Yield was 77-81%. Compound **2** was analyzed via MALDI-ToF MS with a 1:1 sample/matrix ratio using a CHCA matrix. MALDI-ToF MS: $[M\text{-}CN]^+$ expected 1409 *m/z*, found 1408.949 *m/z*. ^1H NMR was used to confirm the purity of the final product. ^1H NMR (400 MHz, D_2O): δ 7.281 (s, 1H), δ 7.040 (s, 1H), δ 6.480 (s, 2H), δ 6.058 (s, 1H). 2D NMR (HSQC/HMBC) was used to confirm the methylene and alkyne protons: ^1H NMR (500 MHz, D_2O): δ 3.407 (t, $1H_a$), δ 1.809 (m, $2H_b$), δ 2.315 (t, $2H_c$), δ 2.340 (s, $1H_d$). ^{13}C NMR (500 MHz, D_2O): δ 41.7 (C_a), δ 30.1 (C_b), δ 18.2 (C_c), δ 72.7 (C_d). See Table S1 for labeling schematic.

2. Synthesis and Characterization of B_{12}-PYY_{3-36} Conjugates (3-4)

2.1 Synthesis of 3

CuI (1 mg, 0.005 mmol) and tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine (TBTA) (2.2 mg, 0.004 mmol) were mixed DMF and H_2O (4:1 v/v, 0.5 mL) for 20 min at rt or until a yellow color change occurred. K_4PYY (1 mg, 0.25 μmol) and **2** (3 mg, 0.002 mmol) were added to the mixture and stirred for 16 h. The crude reaction was centrifuged at 4000*g* for 10 min to remove the catalyst/TBTA. Crude product was purified via RP-HPLC with a C_{18} analytical column using a gradient of 20% MeCN, 80% H_2O/0.1% TFA, increased to 35% MeCN over 4 min then increased to 37 % MeCN over 10 min; t_R of **3** = 6.12 min. Yield for **3** was 95-98%. Compound **3** was characterized via MALDI-ToF MS using a CHCA matrix plated in a 1:1 sample/matrix ratio. MALDI-ToF MS: $[M\text{-}CN]^+$ expected 5470 *m/z*, found 5469.603 *m/z*.

2.2 Synthesis of 4

CuI (1 mg, 0.005 mmol) and TBTA (2.2 mg, 0.004 mmol) were mixed DMF and H_2O (4:1 v/v, 0.5 mL) for 20 min at rt or until a yellow color change occurred. K_4PYY (1 mg, 0.25 μmol) and **3** (3 mg, 0.002 mmol) were added to the mixture and stirred for 16 h. The crude reaction was centrifuged at 4000*g* for 10 min to remove the catalyst/TBTA. Crude product was purified via RP-HPLC with a C_{18} analytical column using a gradient of 20% MeCN, 80% H_2O/0.1% TFA, increased to 35% MeCN over 4 min then increased to 37 % MeCN over 10 min; t_R of **4** = 6.15 min. Yield for **4** was 90-95%. Compound **4** was characterized via MALDI-ToF MS using a CHCA matrix plated in a 1:1 sample/matrix ratio. MALDI-ToF MS: $[M\text{-}CN]^+$ expected 5484 *m/z*, found 5484.821 *m/z*.

3. Characterization of B_{12}-Alkyne Precursors 1-2

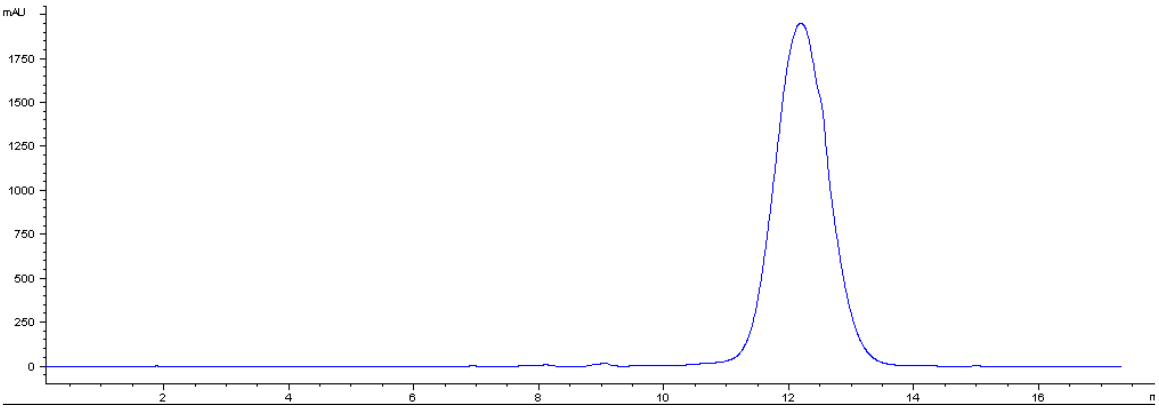


Figure S1. RP-HPLC of **1**; t_R = 12.1 min. UV detection is at 360 nm on a C_{18} column.

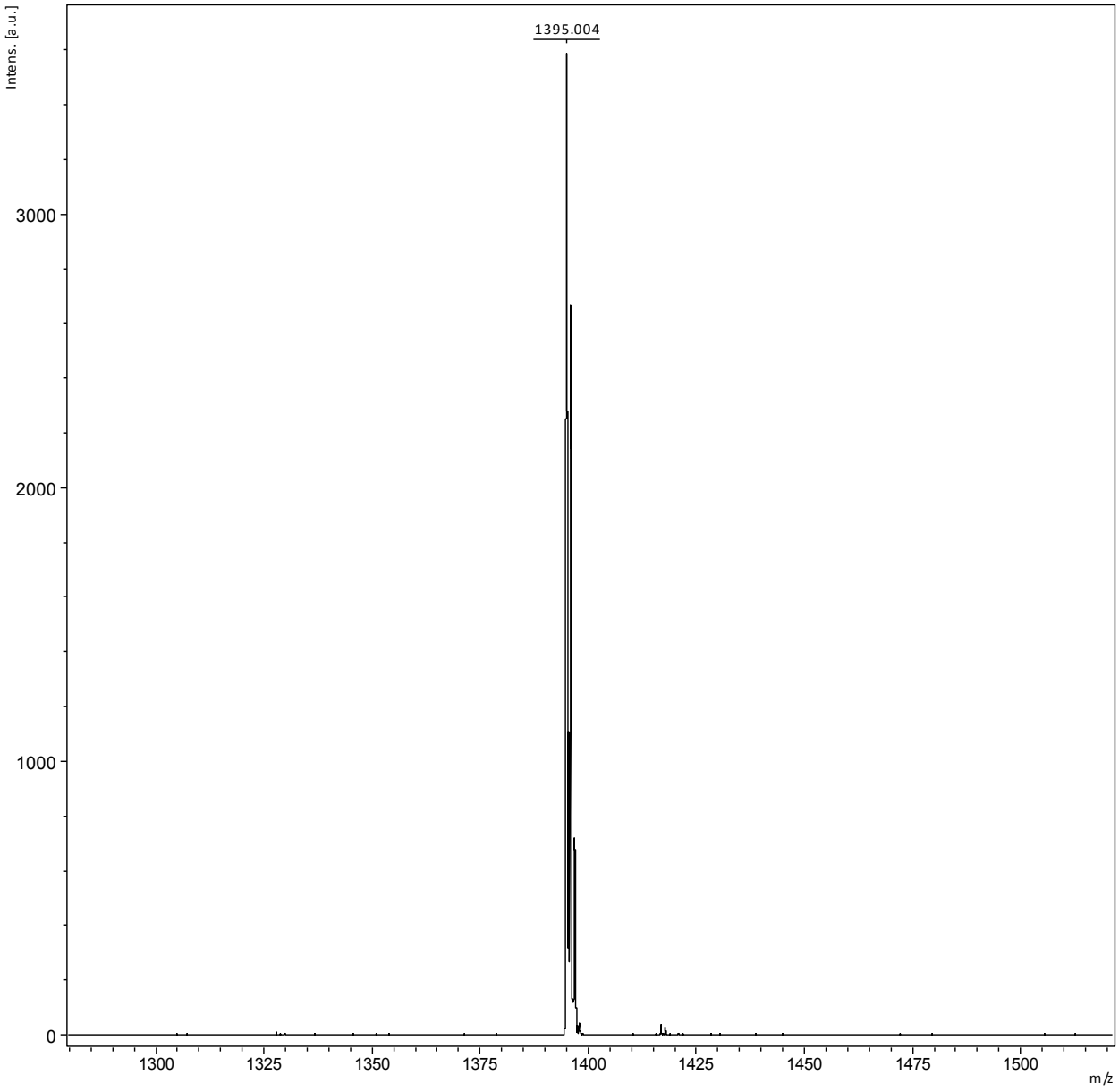
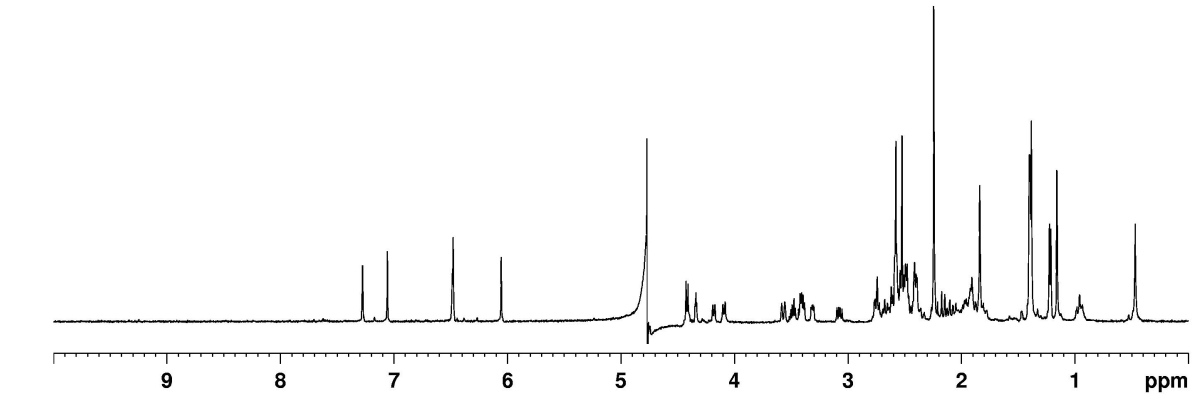
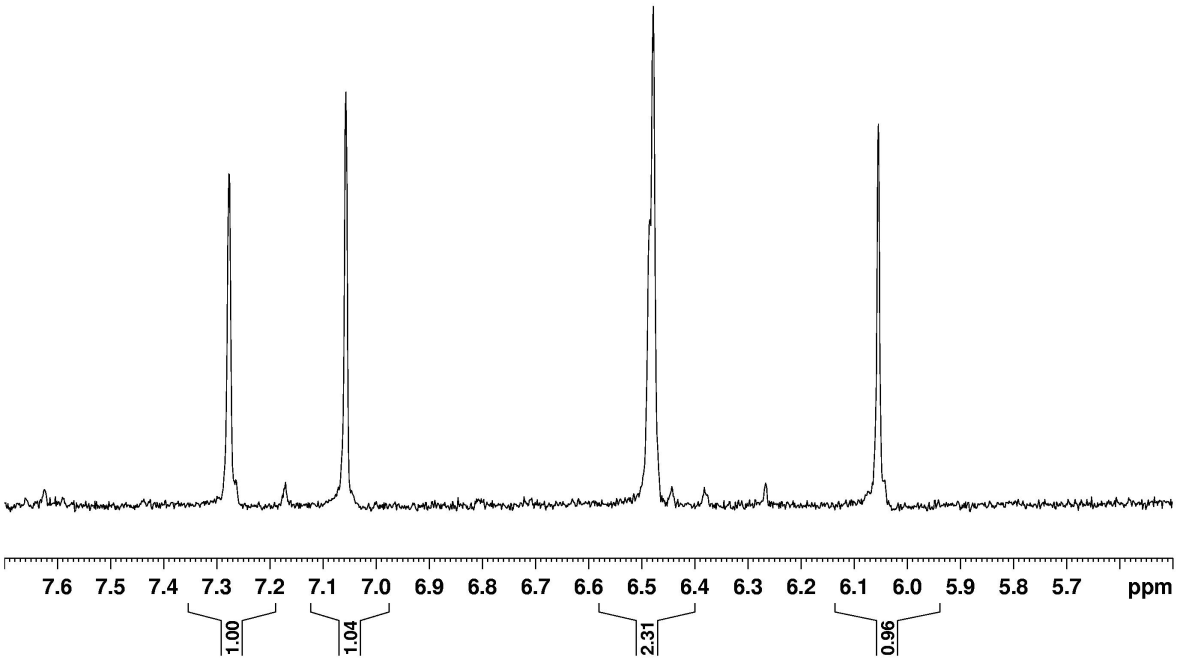


Figure S2. MALDI-ToF mass spectrum of **1**. Expected peak highlighted as $[M\text{-}CN]^+$ = 1395.004 *m/z*.



A



B

Figure S3. ^{1}H NMR of spectrum **1** in D_2O on a 400 MHz spectrometer. The five peaks from 6.0-7.3 ppm are characteristic of protons on the ribose ring, corrin ring, and DMB ligand of B_{12} (**A**). Key diagnostic protons between 6-8 ppm with appropriate integration highlighted (**B**).

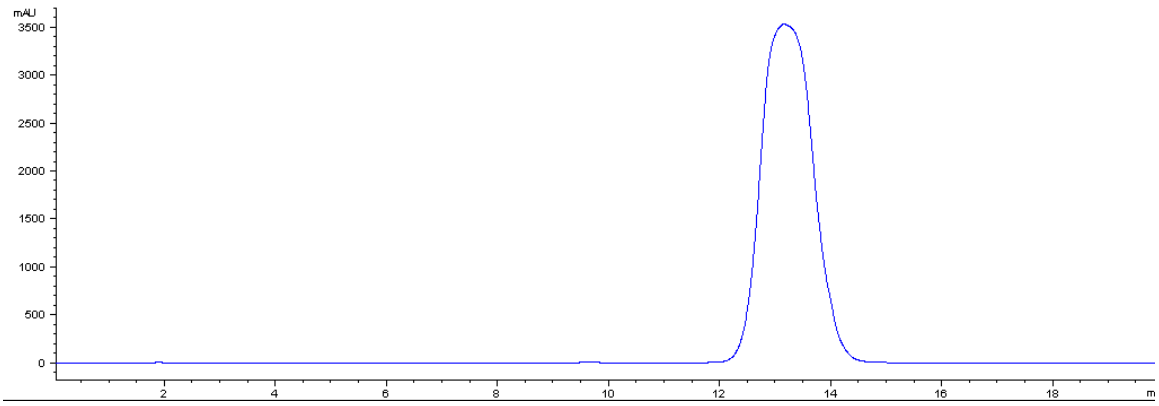


Figure S4. RP-HPLC of **2**; t_R = 13.1 min. UV detection is at 360 nm on a C_{18} column.

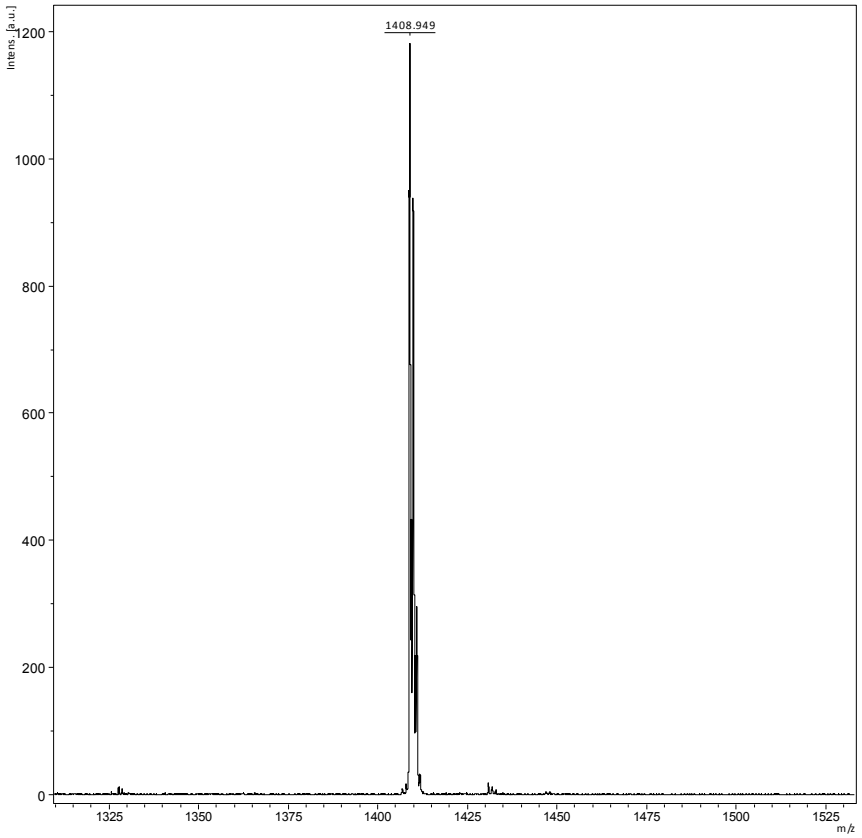
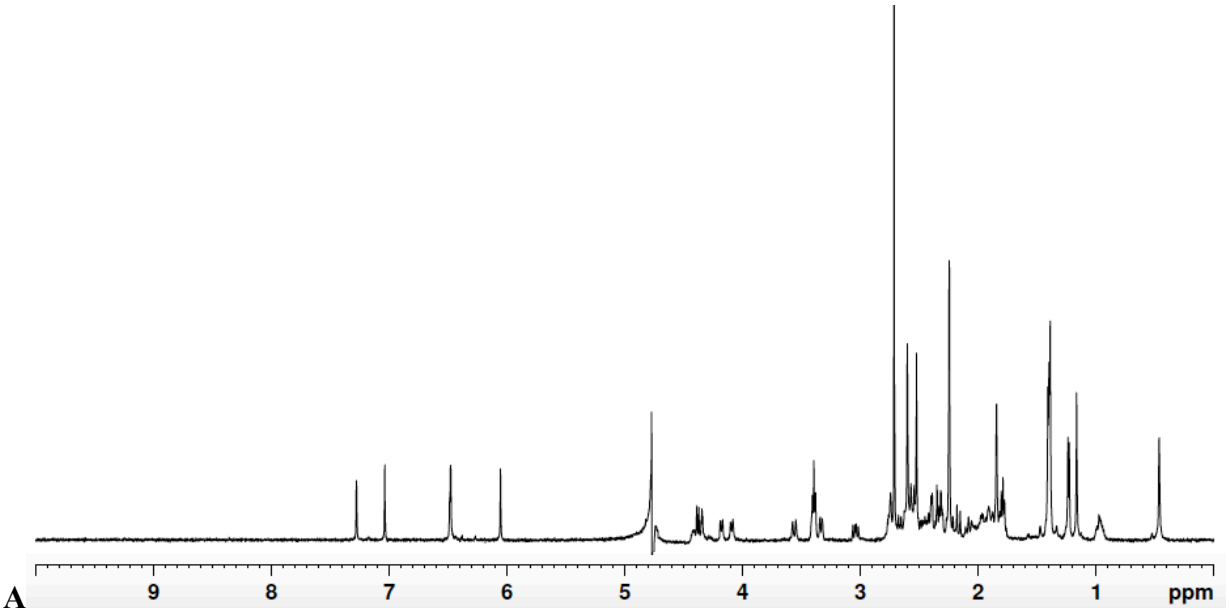
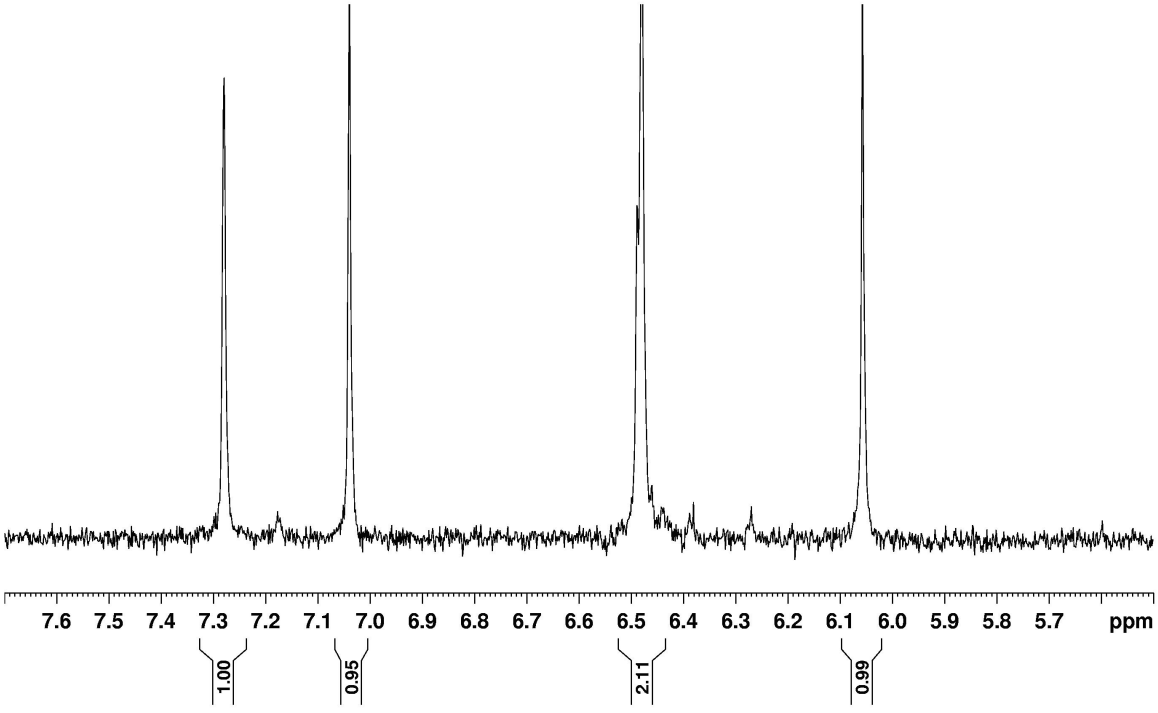


Figure S5. MALDI-ToF mass spectrum of **2**. Expected peak highlighted as $[M\text{-}CN]^+$ = 1408.949 *m/z*.



A



B

Figure S6. ^{1}H NMR spectrum of **2** in D_2O on a 500 MHz spectrometer. The five peaks from 6.0-7.3 ppm are characteristic of protons on the ribose ring, corrin ring, and DMB ligand of B_{12} (**A**). Key diagnostic protons between 6-8 ppm with appropriate integration highlighted (**B**).

4. 2D NMR Spectra of 1-2 and B_{12} NMR Numbering Scheme

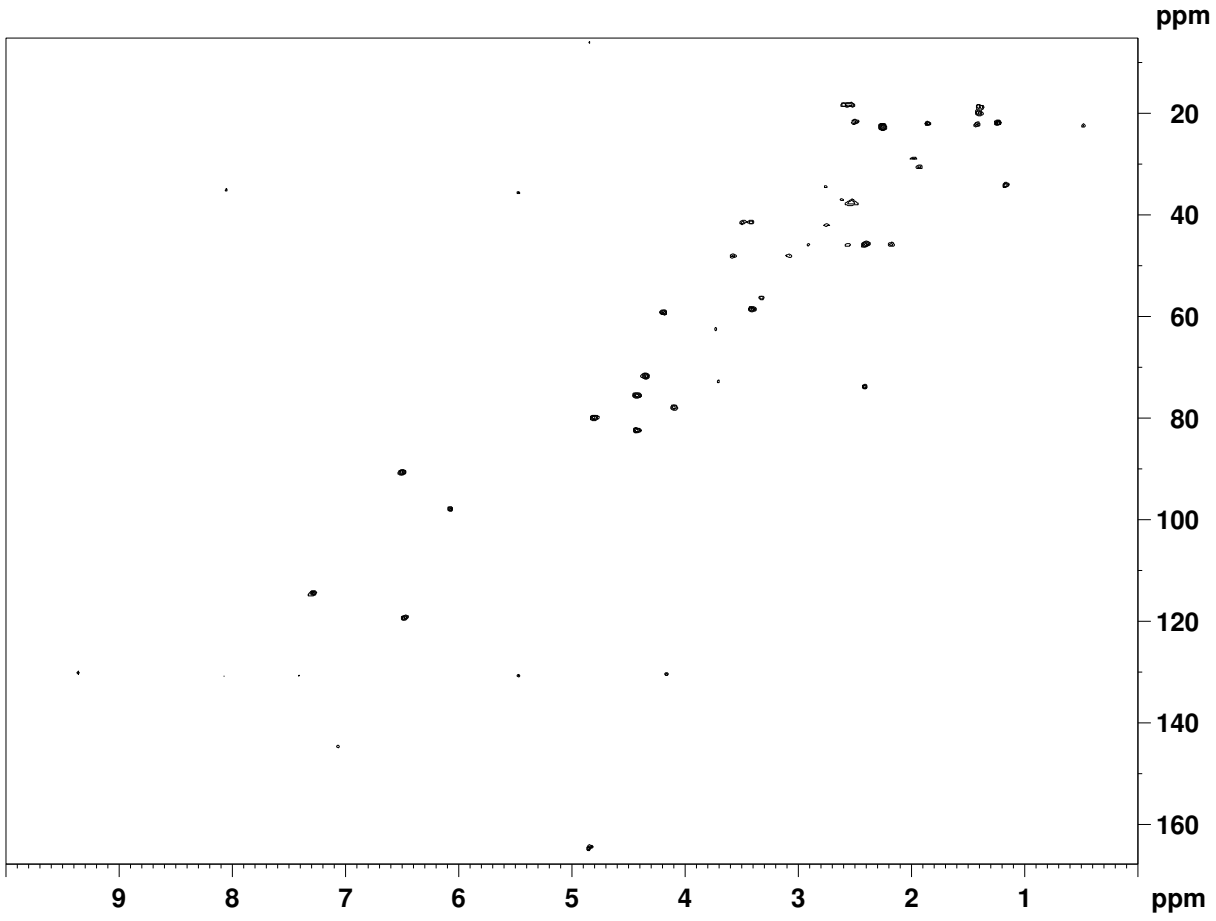


Figure S7. HSQC of **1** in D_2O on a 500 MHz spectrometer.

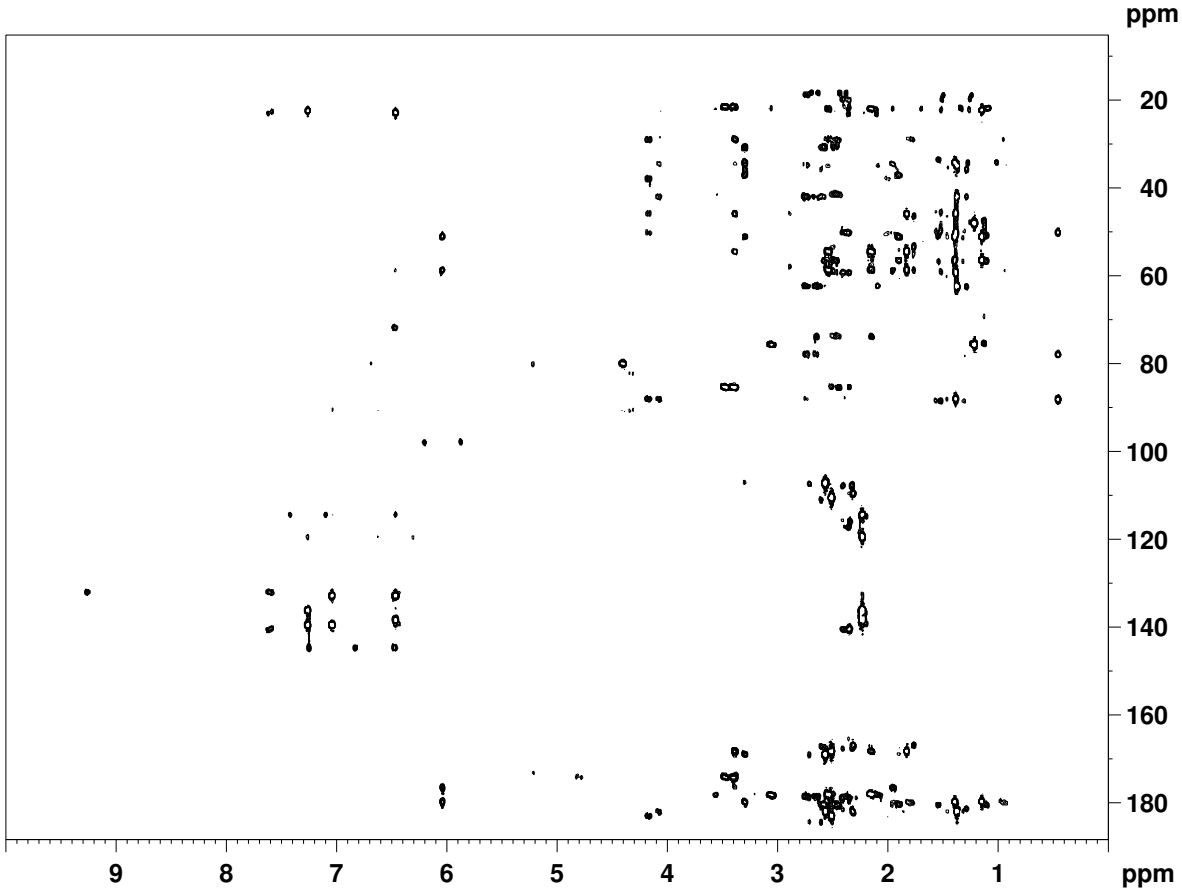


Figure S8. HMBC of **1** in D_2O on a 500 MHz spectrometer.

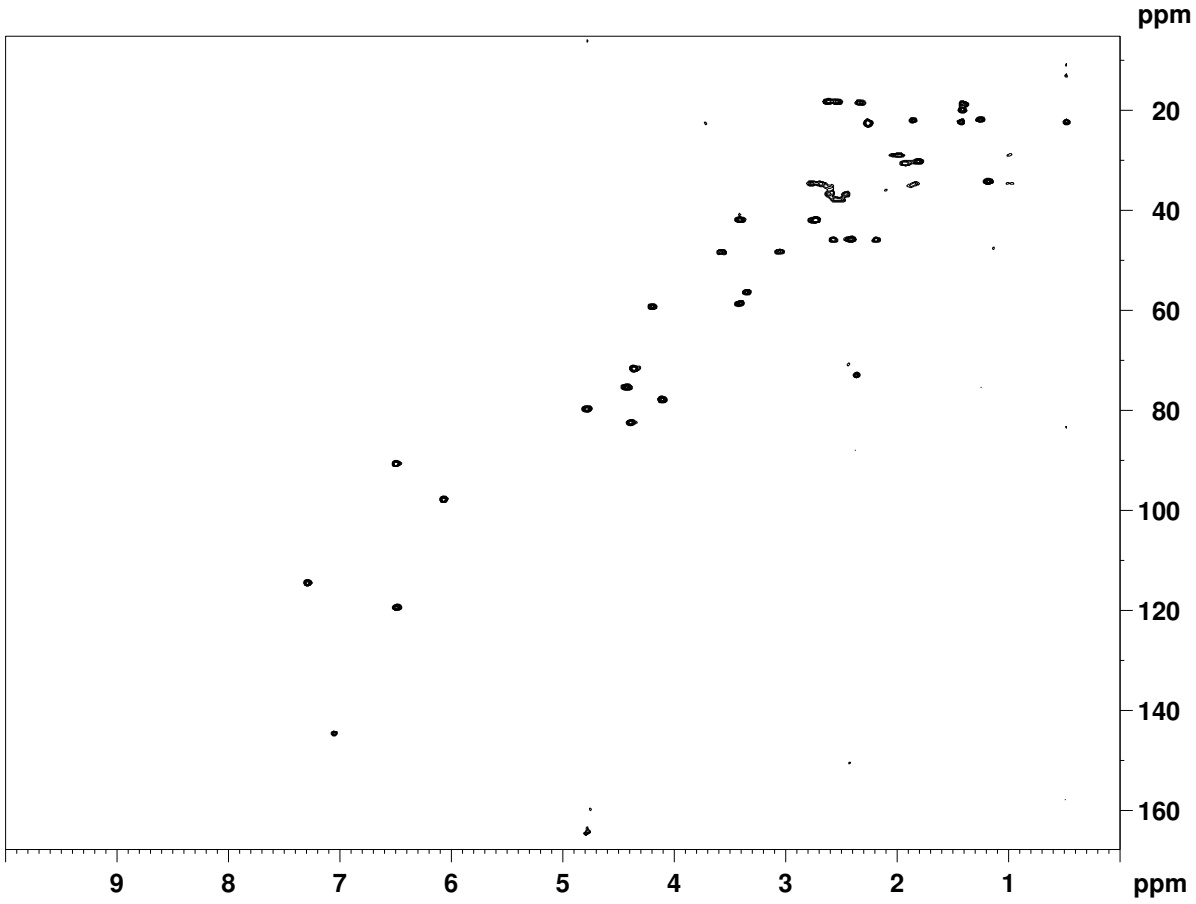


Figure S9. HSQC of **2** in D_2O on a 500 MHz spectrometer.

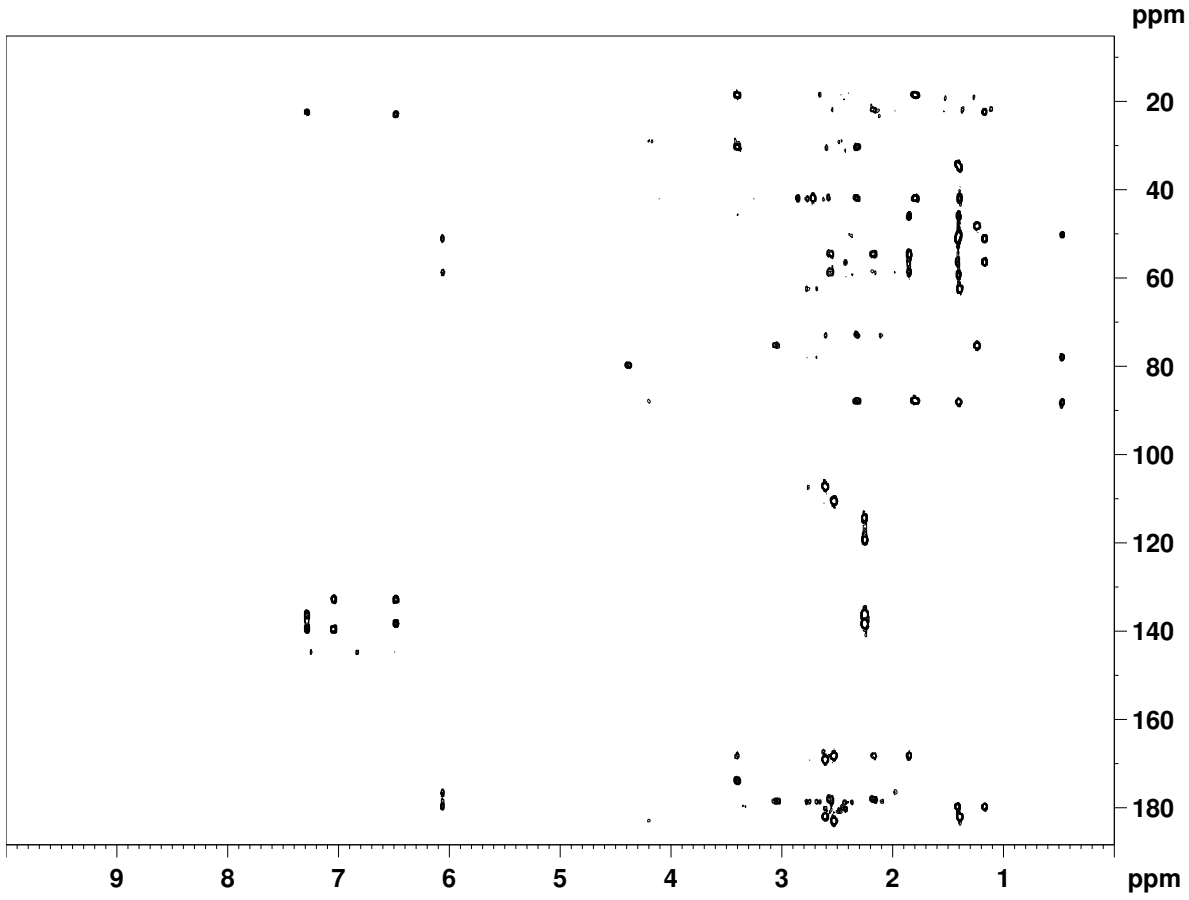


Figure S10. HMBC of **2** in D_2O on a 500 MHz spectrometer.

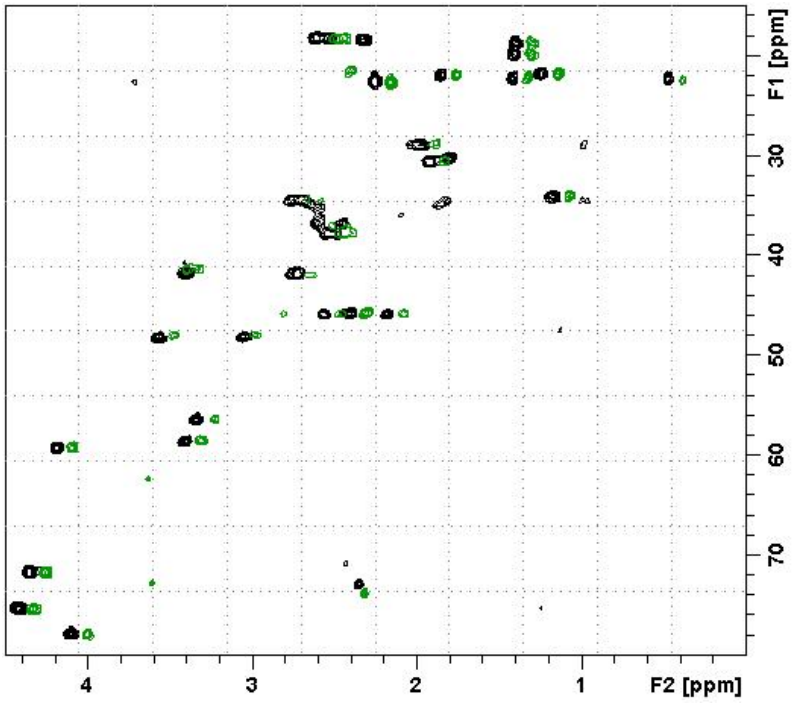


Figure S11. HSQC Overlay of **1** and **2** to display shifts on a 500 MHz spectrometer. The black represents conjugate **2** and the green is conjugate **1**, shifted right to show differences in ppm. **Table S1** outlines the assignments of key protons and carbons to of **1** and **2**.

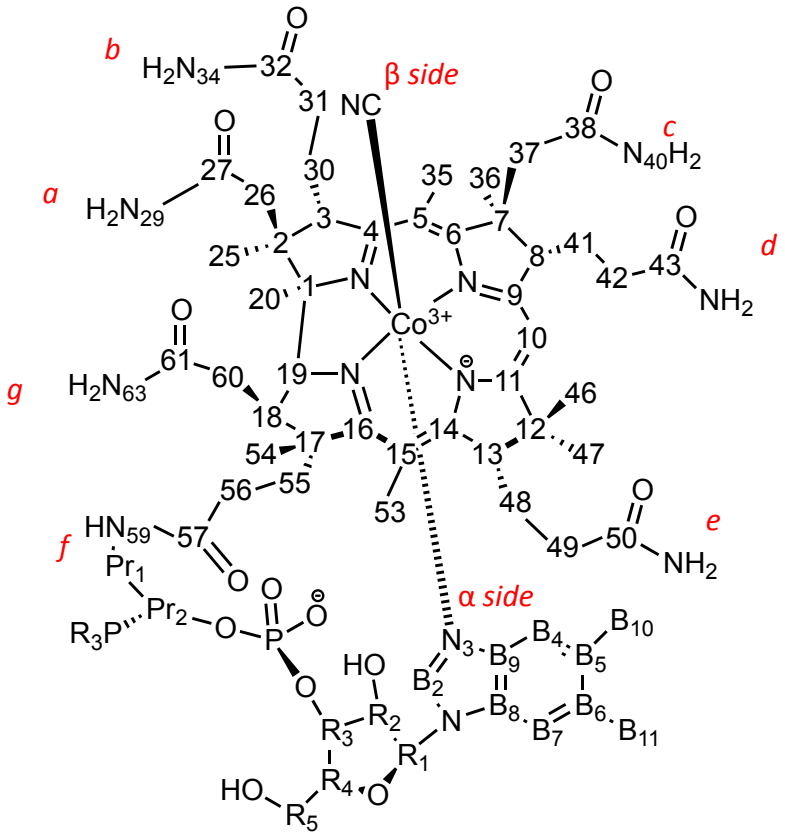
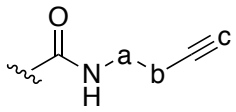
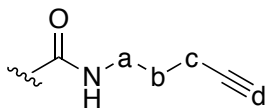


Figure S12. Numbering Scheme for B_{12} NMR.

Table S1. ^{1}H-^{13}C Correlations of New Protons on Derivatives **1-2** as Determined via HSQC/HMBC.

Alkyne Derivative					
1			**2**		
					
Proton	**^{1}H (ppm)**	**^{13}C (ppm)**	**Proton**	**^{1}H (ppm)**	**^{13}C (ppm)**
a_1	3.482	41.1	**a**	3.407	41.7
a_2	3.406	41.1	**b**	1.809	30.1
b	2.489	21.6	**c**	2.315	18.2
c	2.406	73.8	**d**	2.345	72.7

5. Characterization of B_{12}-PYY_{3-36} Conjugates 3-4

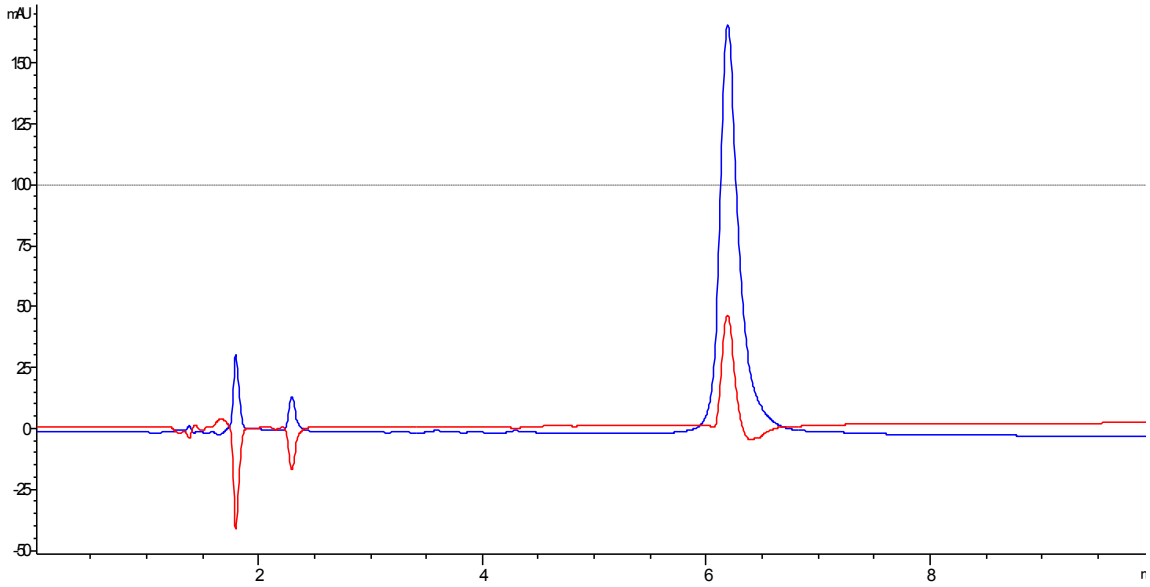


Figure S13. RP-HPLC of **3** at > 98% purity; t_R = 6.12 min. UV detection is at 280 (blue) and 360 (red) nm on a C_{18} column.

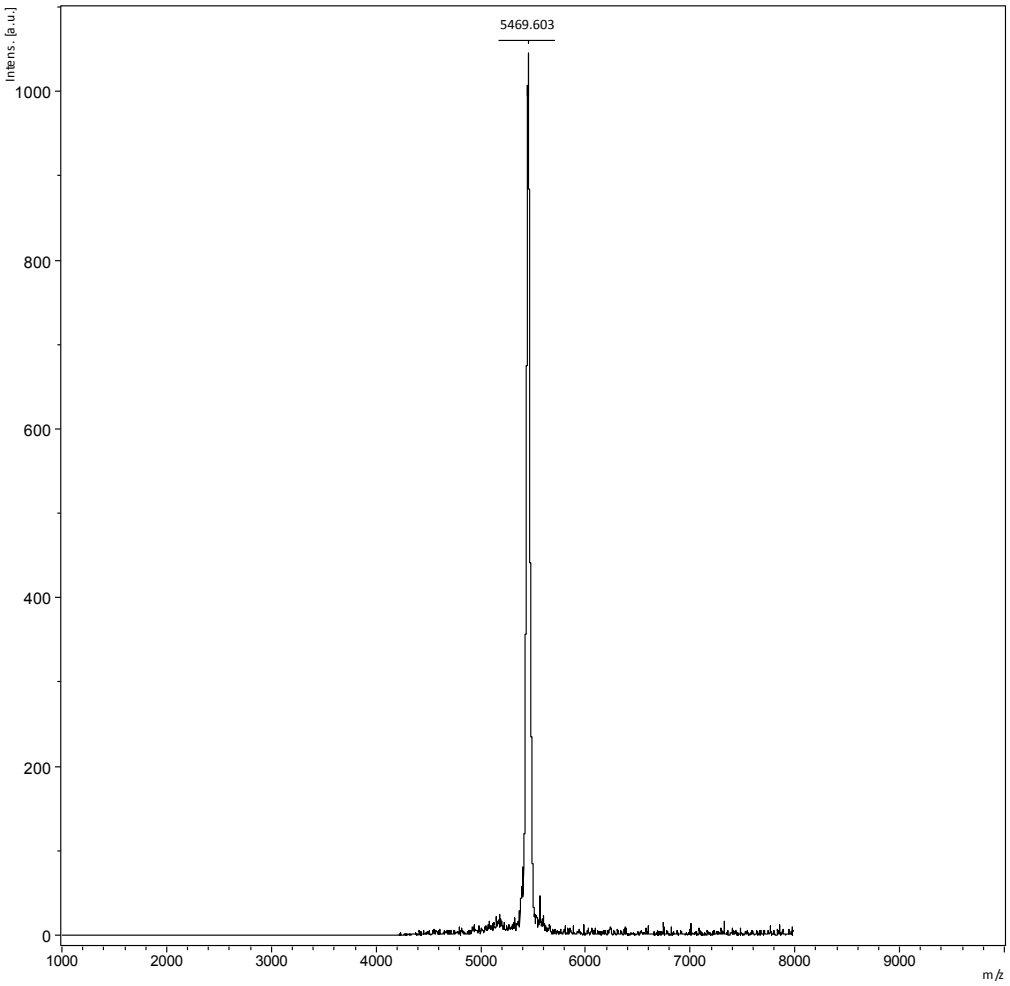


Figure S14. MALDI ToF mass spectrum of **3**. Expected peak highlighted as $[M\text{-}CN]^+$ = 5469.603 *m/z*.

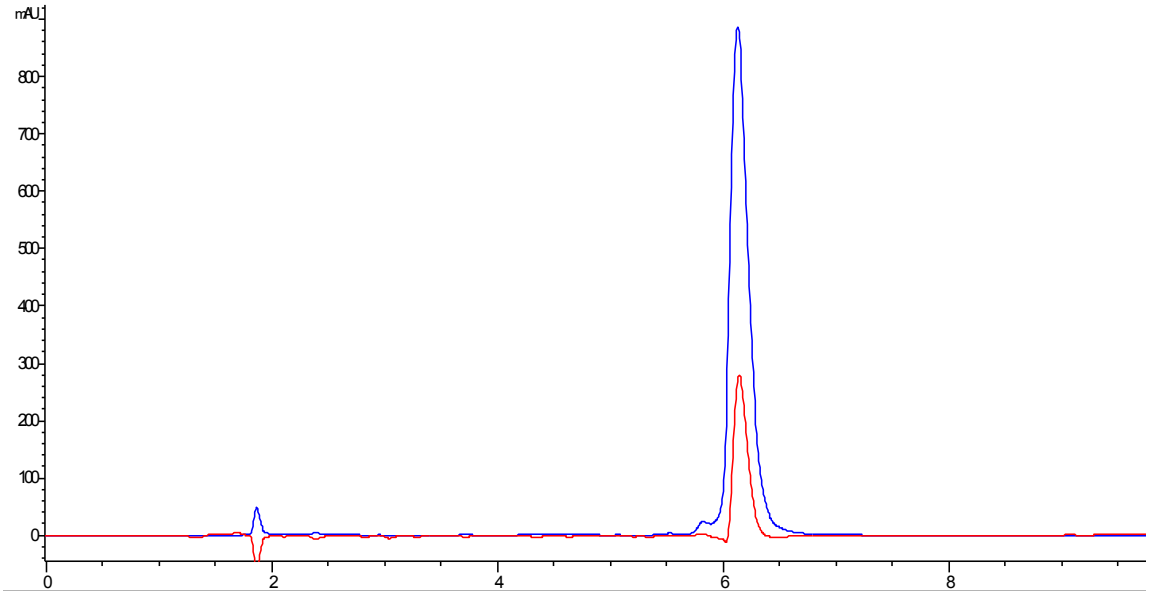


Figure S15. RP-HPLC of **4** at > 98% purity; t_R = 6.15 min. UV detection is at 280 (blue) and 360 (red) nm on a C_{18} column.

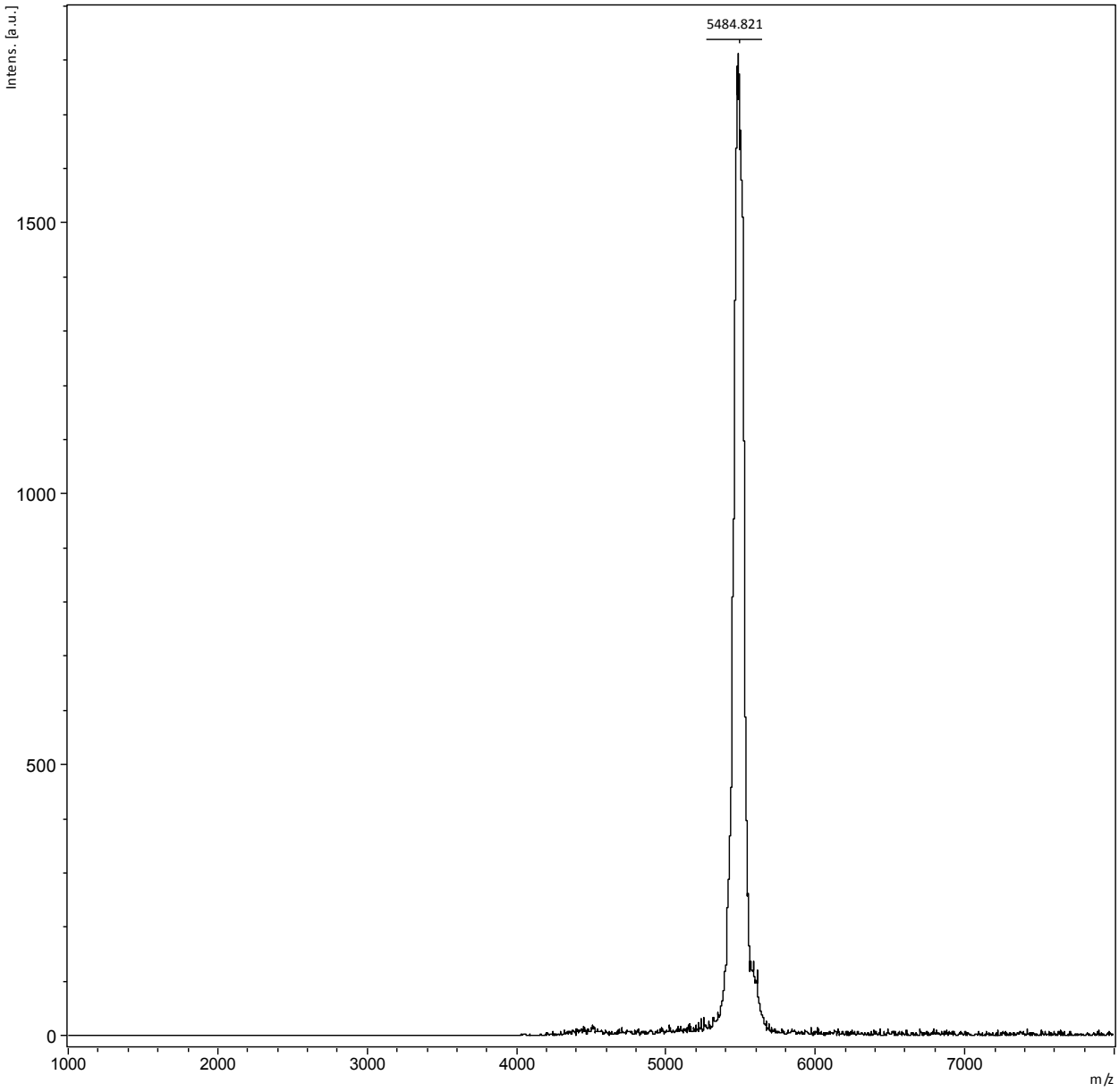


Figure S16. MALDI ToF-MS of **4**. Expected peak highlighted as $[M\text{-}CN]^+$ = 5484.821 *m/z*.

6. NMR Methods and Conditions

NMR experiments were performed on a Bruker DRX500 Advance spectrometer equipped with a 5 mm inverse detection probe. The NMR samples were prepared at a concentration of 1 mM in 90% H_2O/10% D_2O, pH adjusted to 5.5. Both 1- and 2D NMR were acquired with a spectral width of 5518 Hz using excitation sculpting[33] for water suppression. Proton chemical shifts were referenced based on the HDO signal. For chemical shift assignment of conjugate **3** and **4**, TOSCY (total correlation spectroscopy) and DQFCOSY (double-quantum-filtered correlation spectroscopy) experiments were performed at temperature of 20, 25, and 30 °C. TOCSY experiments were run with mixing times of 60 or 90 ms and a relaxation delay of 2 s. 2D nuclear Overhauser effect (NOE) spectra were acquired at the three different temperatures with mixing times of 100, 200 and 300 ms and a relaxation delay of 5 s. For all 2D experiments, 2k points were collected in t2 and 512 points in t1 with 96 scans per t1 increment. The data was processed using a cosine squared function along both dimensions and zero filled to give a final dimension of 1k X 1K. The 2D NOE cross peaks were categorized as strong, medium or weak and proton distance ranges were set to 1.8 – 3.5, 1.8 – 4.5, 1.8 – 6 Å, respectively.

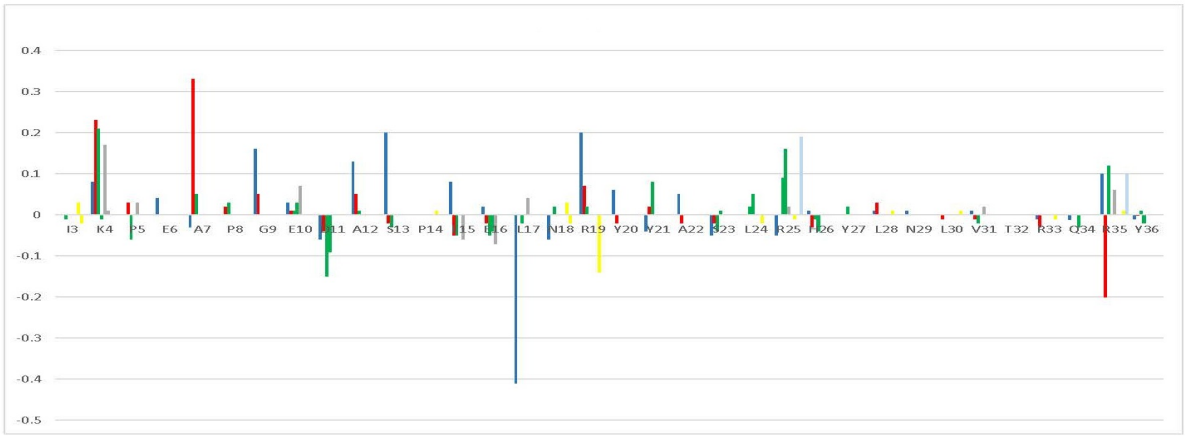


Figure S17. Highlighted differences (ppm) in the assigned proton chemical shift between PYY(3-36) and the **3**. The chemical shifts for the PYY(3-36) were obtained from the Biological Magnetic Resonance Bank (www.bmrb.wisc.edu). The backbone amide protons are represented by blue lines, α protons by red, β protons by green, γ protons by gray, δ by yellow and ε by light blue.

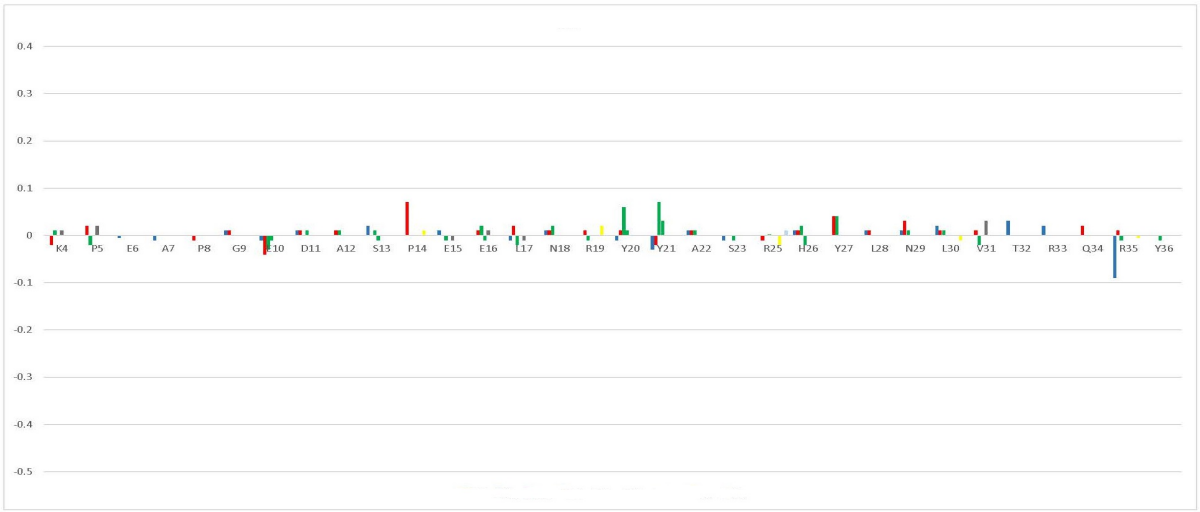


Figure S18. Highlighted differences (ppm) in the assigned proton chemical shift between conjugate **3** and **4**. The backbone amide protons are represented by blue lines, α protons by red, β protons by green, γ protons by gray, δ by yellow, and ε by light blue.

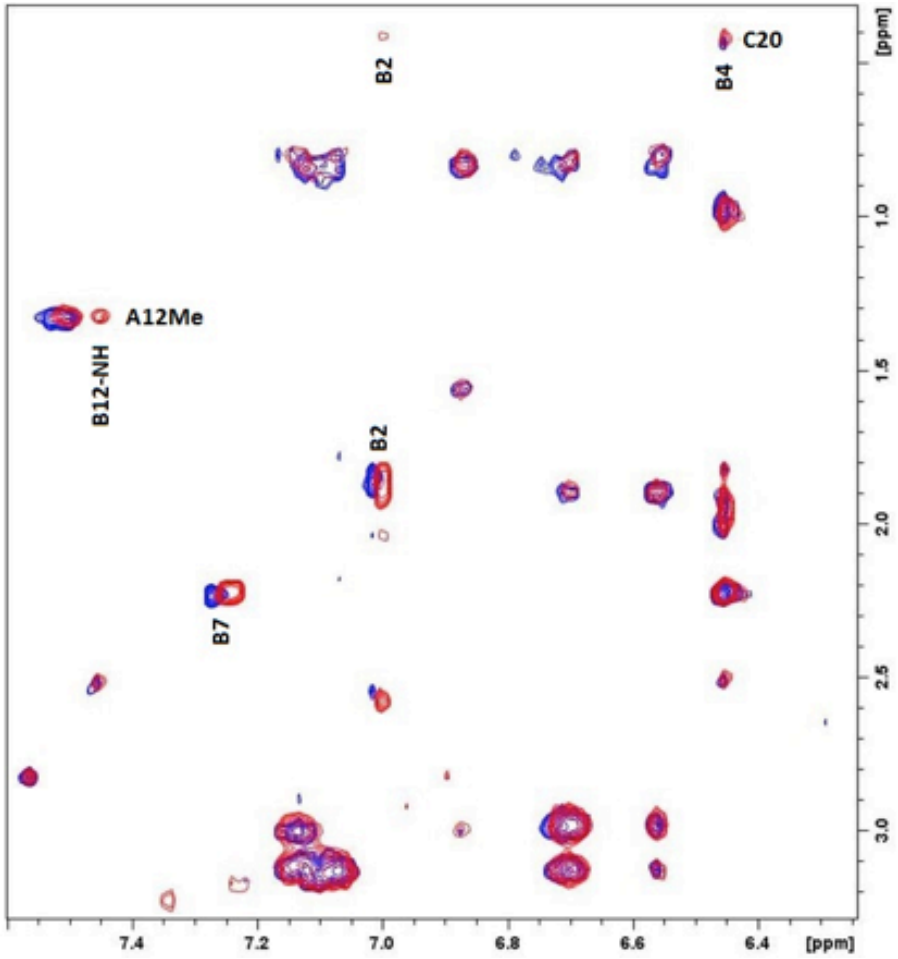


Figure S19. Overlay of 2D NOE spectra for **3** in blue and **4** in red. The spectra were acquired at 25 ºC with conjugate concentration of 1 mM concentration and pH of 5.5.

7. Average Structures For 3-4 From MD Simulations

Geometry For 3

```
ATOM      1  N    ILE     1       3.910   8.456   6.261  1.00  0.00
ATOM      2  H1   ILE     1       3.198   9.227   6.363  1.00  0.00
ATOM      3  H2   ILE     1       3.390   7.702   6.716  1.00  0.00
ATOM      4  H3   ILE     1       4.779   8.752   6.745  1.00  0.00
ATOM      5  CA   ILE     1       4.060   8.165   4.826  1.00  0.00
ATOM      6  CB   ILE     1       5.120   7.111   4.517  1.00  0.00
ATOM      7  CG1  ILE     1       6.427   7.532   5.176  1.00  0.00
ATOM      8  CG2  ILE     1       5.479   7.005   3.069  1.00  0.00
ATOM      9  CD   ILE     1       7.425   6.455   5.478  1.00  0.00
ATOM     10  C    ILE     1       2.693   7.679   4.284  1.00  0.00
ATOM     11  O    ILE     1       2.384   6.555   4.687  1.00  0.00
ATOM     12  C27  LP2     2      -9.013  -9.596   2.385  1.00  0.00
ATOM     13  O28  LP2     2      -9.978 -10.047   1.771  1.00  0.00
ATOM     14  N29  LP2     2      -8.032 -10.333   2.958  1.00  0.00
ATOM     15  HAE  LP2     2      -7.299  -9.859   3.433  1.00  0.00
ATOM     16  HAD  LP2     2      -8.075 -11.293   3.006  1.00  0.00
```

```
ATOM     17  C32 LP2     2     -11.875  -9.769   7.734  1.00  0.00
ATOM     18  O34 LP2     2     -11.541  -9.397   8.826  1.00  0.00
ATOM     19  N33 LP2     2     -12.969 -10.527   7.667  1.00  0.00
ATOM     20  HAG LP2     2     -13.266 -11.099   6.885  1.00  0.00
ATOM     21  HAF LP2     2     -13.398 -10.841   8.480  1.00  0.00
ATOM     22  C38 LP2     2      -4.352  -9.102   7.820  1.00  0.00
ATOM     23  O39 LP2     2      -4.144  -8.745   6.665  1.00  0.00
ATOM     24  N40 LP2     2      -4.085 -10.337   8.182  1.00  0.00
ATOM     25  HAI LP2     2      -4.341 -10.716   9.081  1.00  0.00
ATOM     26  HAH LP2     2      -3.591 -10.863   7.511  1.00  0.00
ATOM     27  C43 LP2     2      -5.568  -2.592  10.094  1.00  0.00
ATOM     28  O44 LP2     2      -5.046  -2.096   9.100  1.00  0.00
ATOM     29  N45 LP2     2      -6.574  -1.987  10.595  1.00  0.00
ATOM     30  HAK LP2     2      -7.164  -2.310  11.336  1.00  0.00
ATOM     31  HAJ LP2     2      -6.820  -1.095  10.111  1.00  0.00
ATOM     32  C50 LP2     2      -4.884   1.958   3.343  1.00  0.00
ATOM     33  O51 LP2     2      -6.019   2.012   2.901  1.00  0.00
ATOM     34  N52 LP2     2      -4.214   3.028   3.670  1.00  0.00
ATOM     35  HAM LP2     2      -3.330   2.792   4.101  1.00  0.00
ATOM     36  HAL LP2     2      -4.652   3.917   3.495  1.00  0.00
ATOM     37  C61 LP2     2     -11.516  -4.876   0.823  1.00  0.00
ATOM     38  O63 LP2     2     -12.238  -5.003   1.866  1.00  0.00
ATOM     39  N62 LP2     2     -12.122  -4.864  -0.377  1.00  0.00
ATOM     40  HAO LP2     2     -11.688  -4.665  -1.229  1.00  0.00
ATOM     41  HAN LP2     2     -13.091  -4.945  -0.478  1.00  0.00
ATOM     42  C20 LP2     2     -10.343  -5.036   4.615  1.00  0.00
ATOM     43  C25 LP2     2     -11.235  -7.535   3.225  1.00  0.00
ATOM     44  C36 LP2     2      -7.033  -7.210   9.772  1.00  0.00
ATOM     45  C46 LP2     2      -2.310  -3.378   5.141  1.00  0.00
ATOM     46  C47 LP2     2      -3.108  -1.352   6.512  1.00  0.00
ATOM     47  C54 LP2     2      -7.501  -4.298   0.047  1.00  0.00
ATOM     48  C26 LP2     2      -8.887  -8.107   2.728  1.00  0.00
ATOM     49  C30 LP2     2     -10.805  -8.183   6.077  1.00  0.00
ATOM     50  C31 LP2     2     -11.172  -9.597   6.390  1.00  0.00
ATOM     51  C37 LP2     2      -5.034  -8.314   8.982  1.00  0.00
ATOM     52  C41 LP2     2      -5.954  -5.050  10.035  1.00  0.00
ATOM     53  C42 LP2     2      -5.284  -3.922  10.711  1.00  0.00
ATOM     54  C48 LP2     2      -4.501  -0.332   4.543  1.00  0.00
ATOM     55  C49 LP2     2      -4.113   0.610   3.367  1.00  0.00
ATOM     56  C56 LP2     2      -9.515  -1.456   1.791  1.00  0.00
ATOM     57  C55 LP2     2      -8.577  -2.234   0.836  1.00  0.00
ATOM     58  C60 LP2     2      -9.981  -4.976   0.814  1.00  0.00
ATOM     59  C2R LP2     2      -8.922   0.497   5.257  1.00  0.00
ATOM     60  O7R LP2     2      -8.066   0.049   4.220  1.00  0.00
ATOM     61  HAA LP2     2      -7.567   0.952   4.022  1.00  0.00
ATOM     62  C1R LP2     2      -8.695  -0.213   6.628  1.00  0.00
ATOM     63  O6R LP2     2      -7.575   0.451   7.313  1.00  0.00
ATOM     64  C4R LP2     2      -7.469   1.759   6.649  1.00  0.00
ATOM     65  C3R LP2     2      -8.617   1.917   5.668  1.00  0.00
ATOM     66  C5R LP2     2      -7.069   3.070   7.326  1.00  0.00
ATOM     67  P   LP2     2      -9.088   4.070   4.199  1.00  0.00
ATOM     68  O2P LP2     2      -8.328   2.656   4.483  1.00  0.00
ATOM     69  O4  LP2     2     -10.027   4.473   5.322  1.00  0.00
ATOM     70  O5  LP2     2      -8.047   5.105   3.938  1.00  0.00
ATOM     71  O3  LP2     2     -10.011   3.802   2.947  1.00  0.00
ATOM     72  C2P LP2     2      -9.152   3.465   1.845  1.00  0.00
ATOM     73  C3P LP2     2      -9.016   4.629   0.843  1.00  0.00
ATOM     74  C1P LP2     2      -9.424   2.192   1.049  1.00  0.00
ATOM     75  N59 LP2     2      -9.404   0.986   1.612  1.00  0.00
ATOM     76  HAC LP2     2      -8.947   0.904   2.479  1.00  0.00
ATOM     77  C57 LP2     2     -10.093  -0.104   1.224  1.00  0.00
ATOM     78  O58 LP2     2     -11.226  -0.081   0.726  1.00  0.00
ATOM     79  C5B LP2     2      -9.921  -4.671   9.102  1.00  0.00
ATOM     80  C5M LP2     2     -10.556  -6.002   9.549  1.00  0.00
ATOM     81  C6B LP2     2     -10.483  -3.436   9.446  1.00  0.00
ATOM     82  C6M LP2     2     -11.613  -3.370  10.465  1.00  0.00
ATOM     83  C4B LP2     2      -8.893  -4.742   8.124  1.00  0.00
ATOM     84  H4B LP2     2      -8.358  -5.620   8.034  1.00  0.00
ATOM     85  C7B LP2     2     -10.054  -2.309   8.745  1.00  0.00
ATOM     86  H7B LP2     2     -10.230  -1.303   9.127  1.00  0.00
ATOM     87  N3B LP2     2      -7.754  -3.525   6.277  1.00  0.00
ATOM     88  C9B LP2     2      -8.558  -3.661   7.333  1.00  0.00
ATOM     89  N1B LP2     2      -8.665  -1.644   6.811  1.00  0.00
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ATOM     90  C8B LP2     2      -9.148  -2.431   7.692  1.00  0.00
ATOM     91  C2B LP2     2      -7.811  -2.260   5.988  1.00  0.00
ATOM     92  H2B LP2     2      -7.112  -1.685   5.373  1.00  0.00
ATOM     93  C5  LP2     2      -7.594  -7.810   6.799  1.00  0.00
ATOM     94  C35 LP2     2      -7.661  -9.311   7.174  1.00  0.00
ATOM     95  C15 LP2     2      -5.876  -2.803   2.684  1.00  0.00
ATOM     96  C53 LP2     2      -5.219  -2.061   1.475  1.00  0.00
ATOM     97  FE  LP2     2      -6.851  -5.012   5.027  1.00  0.00
ATOM     98  N21 LP2     2      -8.235  -6.177   5.072  1.00  0.00
ATOM     99  N22 LP2     2      -6.148  -5.778   6.630  1.00  0.00
ATOM    100  N23 LP2     2      -5.525  -3.678   5.037  1.00  0.00
ATOM    101  N24 LP2     2      -7.362  -4.563   3.394  1.00  0.00
ATOM    102  C1  LP2     2      -9.271  -5.973   4.080  1.00  0.00
ATOM    103  C2  LP2     2      -9.791  -7.438   3.829  1.00  0.00
ATOM    104  C3  LP2     2      -9.596  -8.166   5.157  1.00  0.00
ATOM    105  C4  LP2     2      -8.415  -7.364   5.751  1.00  0.00
ATOM    106  C6  LP2     2      -6.530  -6.976   7.269  1.00  0.00
ATOM    107  C7  LP2     2      -5.924  -7.130   8.682  1.00  0.00
ATOM    108  C8  LP2     2      -5.121  -5.810   8.924  1.00  0.00
ATOM    109  C9  LP2     2      -5.149  -5.250   7.452  1.00  0.00
ATOM    110  C16 LP2     2      -7.009  -3.628   2.472  1.00  0.00
ATOM    111  C17 LP2     2      -8.031  -3.560   1.277  1.00  0.00
ATOM    112  C18 LP2     2      -9.170  -4.325   1.889  1.00  0.00
ATOM    113  C19 LP2     2      -8.530  -5.289   2.884  1.00  0.00
ATOM    114  C11 LP2     2      -4.567  -3.347   5.935  1.00  0.00
ATOM    115  C12 LP2     2      -3.425  -2.450   5.471  1.00  0.00
ATOM    116  C13 LP2     2      -4.041  -1.760   4.233  1.00  0.00
ATOM    117  C14 LP2     2      -5.151  -2.856   3.948  1.00  0.00
ATOM    118  C10 LP2     2      -4.391  -4.082   7.104  1.00  0.00
ATOM    119  H10 LP2     2      -3.721  -3.604   7.787  1.00  0.00
ATOM    120  N   LP2     2       1.900   8.473   3.531  1.00  0.00
ATOM    121  H   LP2     2       2.308   9.273   3.035  1.00  0.00
ATOM    122  CA  LP2     2       0.494   8.172   3.223  1.00  0.00
ATOM    123  CB  LP2     2      -0.182   9.554   3.396  1.00  0.00
ATOM    124  CG  LP2     2      -1.569   9.338   3.944  1.00  0.00
ATOM    125  CD  LP2     2      -1.581   8.659   5.352  1.00  0.00
ATOM    126  CE  LP2     2      -3.043   8.499   5.715  1.00  0.00
ATOM    127  C   LP2     2       0.340   7.502   1.851  1.00  0.00
ATOM    128  O   LP2     2       0.103   8.263   0.871  1.00  0.00
ATOM    129  OLB LP2     2      -7.189   4.392   6.565  1.00  0.00
ATOM    130  C1N LP2     2      -5.501  -6.030   4.469  1.00  0.00
ATOM    131  N1C LP2     2      -4.628  -6.618   4.071  1.00  0.00
ATOM    132  CZ  LP2     2      -5.363   4.174   8.575  1.00  0.00
ATOM    133  CY  LP2     2      -4.182   3.998   7.633  1.00  0.00
ATOM    134  CT1 LP2     2      -3.498   5.323   7.469  1.00  0.00
ATOM    135  CT2 LP2     2      -3.676   6.128   6.397  1.00  0.00
ATOM    136  NT1 LP2     2      -3.329   7.339   6.721  1.00  0.00
ATOM    137  NT2 LP2     2      -2.944   7.352   8.022  1.00  0.00
ATOM    138  NT3 LP2     2      -3.037   6.098   8.419  1.00  0.00
ATOM    139  NZ2 LP2     2      -6.186   3.008   8.363  1.00  0.00
ATOM    140  HZ2 LP2     2      -5.785   2.121   8.685  1.00  0.00
ATOM    141  N   PRO     3       0.186   6.155   1.734  1.00  0.00
ATOM    142  CA  PRO     3       0.103   5.540   0.434  1.00  0.00
ATOM    143  CB  PRO     3       0.057   4.001   0.771  1.00  0.00
ATOM    144  CG  PRO     3       0.588   3.923   2.183  1.00  0.00
ATOM    145  CD  PRO     3       0.191   5.236   2.846  1.00  0.00
ATOM    146  C   PRO     3      -1.003   6.010  -0.500  1.00  0.00
ATOM    147  O   PRO     3      -1.954   6.502   0.007  1.00  0.00
ATOM    148  N   GLU     4      -0.825   5.858  -1.851  1.00  0.00
ATOM    149  H   GLU     4      -0.149   5.227  -2.301  1.00  0.00
ATOM    150  CA  GLU     4      -2.116   6.025  -2.593  1.00  0.00
ATOM    151  CB  GLU     4      -1.865   6.750  -3.932  1.00  0.00
ATOM    152  CG  GLU     4      -1.616   8.225  -3.711  1.00  0.00
ATOM    153  CD  GLU     4      -0.941   8.923  -4.895  1.00  0.00
ATOM    154  OE1 GLU     4      -1.673   9.539  -5.750  1.00  0.00
ATOM    155  OE2 GLU     4       0.217   8.572  -5.088  1.00  0.00
ATOM    156  C   GLU     4      -2.886   4.764  -2.759  1.00  0.00
ATOM    157  O   GLU     4      -2.679   3.900  -3.647  1.00  0.00
ATOM    158  N   ALA     5      -3.860   4.609  -1.891  1.00  0.00
ATOM    159  H   ALA     5      -4.143   5.364  -1.338  1.00  0.00
ATOM    160  CA  ALA     5      -4.496   3.283  -1.544  1.00  0.00
ATOM    161  CB  ALA     5      -4.920   3.301  -0.088  1.00  0.00
ATOM    162  C   ALA     5      -5.765   2.910  -2.333  1.00  0.00
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ATOM    163  O   ALA     5      -6.654   3.771  -2.337  1.00  0.00
ATOM    164  N   PRO     6      -5.712   1.826  -3.148  1.00  0.00
ATOM    165  CA  PRO     6      -6.941   1.182  -3.770  1.00  0.00
ATOM    166  CB  PRO     6      -6.409   0.268  -4.828  1.00  0.00
ATOM    167  CG  PRO     6      -5.004  -0.058  -4.316  1.00  0.00
ATOM    168  CD  PRO     6      -4.529   1.322  -3.812  1.00  0.00
ATOM    169  C   PRO     6      -7.681   0.320  -2.737  1.00  0.00
ATOM    170  O   PRO     6      -7.310   0.256  -1.569  1.00  0.00
ATOM    171  N   GLY     7      -8.600  -0.477  -3.284  1.00  0.00
ATOM    172  H   GLY     7      -8.725  -0.567  -4.280  1.00  0.00
ATOM    173  CA  GLY     7      -9.523  -1.252  -2.416  1.00  0.00
ATOM    174  C   GLY     7     -10.953  -1.170  -2.829  1.00  0.00
ATOM    175  O   GLY     7     -11.736  -0.613  -2.077  1.00  0.00
ATOM    176  N   GLU     8     -11.348  -1.739  -3.958  1.00  0.00
ATOM    177  H   GLU     8     -10.698  -2.233  -4.602  1.00  0.00
ATOM    178  CA  GLU     8     -12.518  -1.285  -4.725  1.00  0.00
ATOM    179  CB  GLU     8     -12.465   0.169  -5.292  1.00  0.00
ATOM    180  CG  GLU     8     -11.398   0.508  -6.353  1.00  0.00
ATOM    181  CD  GLU     8     -11.660   1.884  -7.017  1.00  0.00
ATOM    182  OE1 GLU     8     -12.182   1.997  -8.138  1.00  0.00
ATOM    183  OE2 GLU     8     -11.285   2.863  -6.327  1.00  0.00
ATOM    184  C   GLU     8     -12.962  -2.272  -5.846  1.00  0.00
ATOM    185  O   GLU     8     -14.131  -2.212  -6.211  1.00  0.00
ATOM    186  N   ASP     9     -12.101  -3.160  -6.360  1.00  0.00
ATOM    187  H   ASP     9     -11.167  -3.123  -6.064  1.00  0.00
ATOM    188  CA  ASP     9     -12.346  -4.072  -7.510  1.00  0.00
ATOM    189  CB  ASP     9     -11.809  -3.567  -8.823  1.00  0.00
ATOM    190  CG  ASP     9     -12.256  -4.431  -9.944  1.00  0.00
ATOM    191  OD1 ASP     9     -11.451  -5.240 -10.342  1.00  0.00
ATOM    192  OD2 ASP     9     -13.395  -4.277 -10.500  1.00  0.00
ATOM    193  C   ASP     9     -11.779  -5.513  -7.185  1.00  0.00
ATOM    194  O   ASP     9     -12.665  -6.338  -7.016  1.00  0.00
ATOM    195  N   ALA    10     -10.454  -5.734  -6.918  1.00  0.00
ATOM    196  H   ALA    10      -9.774  -5.003  -6.901  1.00  0.00
ATOM    197  CA  ALA    10      -9.869  -7.079  -6.646  1.00  0.00
ATOM    198  CB  ALA    10      -9.145  -7.651  -7.858  1.00  0.00
ATOM    199  C   ALA    10      -8.929  -7.020  -5.424  1.00  0.00
ATOM    200  O   ALA    10      -7.759  -6.694  -5.616  1.00  0.00
ATOM    201  N   SER    11      -9.297  -7.743  -4.369  1.00  0.00
ATOM    202  H   SER    11     -10.122  -8.282  -4.401  1.00  0.00
ATOM    203  CA  SER    11      -8.612  -7.558  -3.079  1.00  0.00
ATOM    204  CB  SER    11      -9.377  -8.042  -1.887  1.00  0.00
ATOM    205  OG  SER    11      -9.455  -9.483  -1.923  1.00  0.00
ATOM    206  HG  SER    11     -10.087  -9.847  -2.659  1.00  0.00
ATOM    207  C   SER    11      -7.145  -8.087  -3.018  1.00  0.00
ATOM    208  O   SER    11      -6.321  -7.286  -2.614  1.00  0.00
ATOM    209  N   PRO    12      -6.753  -9.197  -3.703  1.00  0.00
ATOM    210  CA  PRO    12      -5.355  -9.590  -3.830  1.00  0.00
ATOM    211  CB  PRO    12      -5.351 -11.063  -4.299  1.00  0.00
ATOM    212  CG  PRO    12      -6.648 -11.588  -3.744  1.00  0.00
ATOM    213  CD  PRO    12      -7.608 -10.352  -3.969  1.00  0.00
ATOM    214  C   PRO    12      -4.467  -8.601  -4.666  1.00  0.00
ATOM    215  O   PRO    12      -3.437  -8.195  -4.142  1.00  0.00
ATOM    216  N   GLU    13      -5.035  -8.066  -5.705  1.00  0.00
ATOM    217  H   GLU    13      -5.996  -8.207  -5.977  1.00  0.00
ATOM    218  CA  GLU    13      -4.259  -7.248  -6.608  1.00  0.00
ATOM    219  CB  GLU    13      -4.567  -7.451  -8.122  1.00  0.00
ATOM    220  CG  GLU    13      -4.368  -8.892  -8.662  1.00  0.00
ATOM    221  CD  GLU    13      -5.201  -9.170  -9.913  1.00  0.00
ATOM    222  OE1 GLU    13      -6.414  -9.208  -9.712  1.00  0.00
ATOM    223  OE2 GLU    13      -4.623  -9.498 -10.980  1.00  0.00
ATOM    224  C   GLU    13      -4.215  -5.701  -6.309  1.00  0.00
ATOM    225  O   GLU    13      -3.213  -5.039  -6.481  1.00  0.00
ATOM    226  N   GLU    14      -5.276  -5.270  -5.643  1.00  0.00
ATOM    227  H   GLU    14      -6.176  -5.715  -5.702  1.00  0.00
ATOM    228  CA  GLU    14      -5.323  -3.980  -4.878  1.00  0.00
ATOM    229  CB  GLU    14      -6.789  -3.690  -4.621  1.00  0.00
ATOM    230  CG  GLU    14      -7.499  -3.289  -5.957  1.00  0.00
ATOM    231  CD  GLU    14      -8.970  -2.953  -5.786  1.00  0.00
ATOM    232  OE1 GLU    14      -9.319  -1.857  -6.287  1.00  0.00
ATOM    233  OE2 GLU    14      -9.620  -3.681  -5.059  1.00  0.00
ATOM    234  C   GLU    14      -4.482  -4.068  -3.554  1.00  0.00
ATOM    235  O   GLU    14      -3.786  -3.103  -3.328  1.00  0.00
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ATOM    236  N   LEU    15      -4.403  -5.241  -2.903  1.00  0.00
ATOM    237  H   LEU    15      -5.161  -6.002  -2.895  1.00  0.00
ATOM    238  CA  LEU    15      -3.399  -5.487  -1.914  1.00  0.00
ATOM    239  CB  LEU    15      -3.686  -6.836  -1.260  1.00  0.00
ATOM    240  CG  LEU    15      -3.792  -6.753   0.281  1.00  0.00
ATOM    241  CD1 LEU    15      -4.138  -8.155   0.845  1.00  0.00
ATOM    242  CD2 LEU    15      -2.553  -6.283   1.065  1.00  0.00
ATOM    243  C   LEU    15      -1.981  -5.320  -2.470  1.00  0.00
ATOM    244  O   LEU    15      -1.351  -4.370  -1.920  1.00  0.00
ATOM    245  N   ASN    16      -1.661  -5.803  -3.662  1.00  0.00
ATOM    246  H   ASN    16      -2.121  -6.673  -3.931  1.00  0.00
ATOM    247  CA  ASN    16      -0.341  -5.567  -4.292  1.00  0.00
ATOM    248  CB  ASN    16       0.133  -6.628  -5.307  1.00  0.00
ATOM    249  CG  ASN    16      -0.122  -8.115  -4.991  1.00  0.00
ATOM    250  OD1 ASN    16      -0.242  -8.447  -3.819  1.00  0.00
ATOM    251  ND2 ASN    16      -0.146  -8.910  -6.036  1.00  0.00
ATOM    252 1HD2 ASN    16       0.027  -8.632  -7.055  1.00  0.00
ATOM    253 2HD2 ASN    16      -0.088  -9.915  -5.811  1.00  0.00
ATOM    254  C   ASN    16      -0.114  -4.175  -4.851  1.00  0.00
ATOM    255  O   ASN    16       1.019  -3.761  -5.157  1.00  0.00
ATOM    256  N   ARG    17      -1.198  -3.552  -5.265  1.00  0.00
ATOM    257  H   ARG    17      -2.018  -4.052  -5.433  1.00  0.00
ATOM    258  CA  ARG    17      -1.203  -2.109  -5.605  1.00  0.00
ATOM    259  CB  ARG    17      -2.455  -1.884  -6.407  1.00  0.00
ATOM    260  CG  ARG    17      -2.047  -0.841  -7.453  1.00  0.00
ATOM    261  CD  ARG    17      -2.973  -0.458  -8.603  1.00  0.00
ATOM    262  NE  ARG    17      -4.260   0.123  -8.120  1.00  0.00
ATOM    263  HE  ARG    17      -4.080   1.076  -7.777  1.00  0.00
ATOM    264  CZ  ARG    17      -5.495  -0.477  -8.205  1.00  0.00
ATOM    265  NH1 ARG    17      -5.648  -1.692  -8.668  1.00  0.00
ATOM    266 1HH1 ARG    17      -4.979  -2.309  -9.103  1.00  0.00
ATOM    267 2HH1 ARG    17      -6.478  -2.192  -8.422  1.00  0.00
ATOM    268  NH2 ARG    17      -6.602   0.172  -7.985  1.00  0.00
ATOM    269 1HH2 ARG    17      -6.491   1.127  -7.823  1.00  0.00
ATOM    270 2HH2 ARG    17      -7.548  -0.244  -8.229  1.00  0.00
ATOM    271  C   ARG    17      -0.875  -1.164  -4.477  1.00  0.00
ATOM    272  O   ARG    17       0.003  -0.307  -4.599  1.00  0.00
ATOM    273  N   TYR    18      -1.447  -1.567  -3.304  1.00  0.00
ATOM    274  H   TYR    18      -2.202  -2.224  -3.295  1.00  0.00
ATOM    275  CA  TYR    18      -1.023  -1.038  -1.959  1.00  0.00
ATOM    276  CB  TYR    18      -2.038  -1.474  -0.950  1.00  0.00
ATOM    277  CG  TYR    18      -1.699  -1.112   0.556  1.00  0.00
ATOM    278  CD1 TYR    18      -1.063  -2.179   1.291  1.00  0.00
ATOM    279  HD1 TYR    18      -1.076  -3.233   1.004  1.00  0.00
ATOM    280  CD2 TYR    18      -1.622   0.226   0.932  1.00  0.00
ATOM    281  HD2 TYR    18      -1.807   1.043   0.197  1.00  0.00
ATOM    282  CE1 TYR    18      -0.301  -1.751   2.317  1.00  0.00
ATOM    283  HE1 TYR    18       0.433  -2.429   2.746  1.00  0.00
ATOM    284  CE2 TYR    18      -0.884   0.578   2.064  1.00  0.00
ATOM    285  HE2 TYR    18      -1.083   1.476   2.587  1.00  0.00
ATOM    286  CZ  TYR    18      -0.238  -0.404   2.760  1.00  0.00
ATOM    287  OH  TYR    18       0.406  -0.190   3.945  1.00  0.00
ATOM    288  HH  TYR    18       0.411  -1.016   4.578  1.00  0.00
ATOM    289  C   TYR    18       0.396  -1.225  -1.582  1.00  0.00
ATOM    290  O   TYR    18       1.116  -0.217  -1.454  1.00  0.00
ATOM    291  N   TYR    19       0.866  -2.516  -1.580  1.00  0.00
ATOM    292  H   TYR    19       0.250  -3.284  -1.712  1.00  0.00
ATOM    293  CA  TYR    19       2.330  -2.798  -1.523  1.00  0.00
ATOM    294  CB  TYR    19       2.772  -4.255  -1.291  1.00  0.00
ATOM    295  CG  TYR    19       2.282  -4.788   0.017  1.00  0.00
ATOM    296  CD1 TYR    19       1.261  -5.699   0.201  1.00  0.00
ATOM    297  HD1 TYR    19       1.043  -6.282  -0.646  1.00  0.00
ATOM    298  CD2 TYR    19       2.846  -4.221   1.101  1.00  0.00
ATOM    299  HD2 TYR    19       3.776  -3.690   0.892  1.00  0.00
ATOM    300  CE1 TYR    19       0.888  -6.056   1.500  1.00  0.00
ATOM    301  HE1 TYR    19       0.145  -6.837   1.646  1.00  0.00
ATOM    302  CE2 TYR    19       2.458  -4.456   2.453  1.00  0.00
ATOM    303  HE2 TYR    19       2.747  -3.762   3.256  1.00  0.00
ATOM    304  CZ  TYR    19       1.483  -5.431   2.568  1.00  0.00
ATOM    305  OH  TYR    19       1.085  -6.015   3.720  1.00  0.00
ATOM    306  HH  TYR    19       0.091  -6.081   3.716  1.00  0.00
ATOM    307  C   TYR    19       3.199  -1.989  -2.542  1.00  0.00
ATOM    308  O   TYR    19       4.104  -1.333  -2.128  1.00  0.00
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ATOM    309  N   ALA    20       2.943  -2.156  -3.818  1.00  0.00
ATOM    310  H   ALA    20       2.229  -2.750  -4.160  1.00  0.00
ATOM    311  CA  ALA    20       3.626  -1.393  -4.894  1.00  0.00
ATOM    312  CB  ALA    20       2.846  -1.586  -6.124  1.00  0.00
ATOM    313  C   ALA    20       3.656   0.133  -4.584  1.00  0.00
ATOM    314  O   ALA    20       4.756   0.697  -4.549  1.00  0.00
ATOM    315  N   SER    21       2.576   0.730  -4.093  1.00  0.00
ATOM    316  H   SER    21       1.842   0.132  -4.006  1.00  0.00
ATOM    317  CA  SER    21       2.452   2.172  -3.692  1.00  0.00
ATOM    318  CB  SER    21       1.004   2.642  -3.470  1.00  0.00
ATOM    319  OG  SER    21       0.980   3.986  -3.062  1.00  0.00
ATOM    320  HG  SER    21       1.135   4.516  -3.943  1.00  0.00
ATOM    321  C   SER    21       3.308   2.599  -2.473  1.00  0.00
ATOM    322  O   SER    21       4.190   3.411  -2.544  1.00  0.00
ATOM    323  N   LEU    22       3.169   1.753  -1.410  1.00  0.00
ATOM    324  H   LEU    22       2.740   0.852  -1.521  1.00  0.00
ATOM    325  CA  LEU    22       3.926   1.843  -0.139  1.00  0.00
ATOM    326  CB  LEU    22       3.449   0.693   0.694  1.00  0.00
ATOM    327  CG  LEU    22       4.088   0.485   2.015  1.00  0.00
ATOM    328  CD1 LEU    22       4.142   1.753   2.835  1.00  0.00
ATOM    329  CD2 LEU    22       3.347  -0.480   2.837  1.00  0.00
ATOM    330  C   LEU    22       5.447   1.766  -0.315  1.00  0.00
ATOM    331  O   LEU    22       6.177   2.650   0.145  1.00  0.00
ATOM    332  N   ARG    23       5.930   0.920  -1.235  1.00  0.00
ATOM    333  H   ARG    23       5.356   0.251  -1.674  1.00  0.00
ATOM    334  CA  ARG    23       7.378   0.799  -1.472  1.00  0.00
ATOM    335  CB  ARG    23       7.771  -0.545  -2.083  1.00  0.00
ATOM    336  CG  ARG    23       7.385  -1.706  -1.121  1.00  0.00
ATOM    337  CD  ARG    23       8.047  -3.048  -1.615  1.00  0.00
ATOM    338  NE  ARG    23       7.115  -4.158  -1.458  1.00  0.00
ATOM    339  HE  ARG    23       6.731  -4.311  -0.501  1.00  0.00
ATOM    340  CZ  ARG    23       6.897  -4.991  -2.481  1.00  0.00
ATOM    341  NH1 ARG    23       7.489  -4.995  -3.724  1.00  0.00
ATOM    342 1HH1 ARG    23       8.002  -4.177  -3.999  1.00  0.00
ATOM    343 2HH1 ARG    23       7.401  -5.749  -4.353  1.00  0.00
ATOM    344  NH2 ARG    23       6.042  -5.960  -2.186  1.00  0.00
ATOM    345 1HH2 ARG    23       5.695  -6.075  -1.207  1.00  0.00
ATOM    346 2HH2 ARG    23       5.900  -6.676  -2.876  1.00  0.00
ATOM    347  C   ARG    23       8.075   1.961  -2.253  1.00  0.00
ATOM    348  O   ARG    23       9.190   2.383  -1.925  1.00  0.00
ATOM    349  N   HIS    24       7.285   2.426  -3.211  1.00  0.00
ATOM    350  H   HIS    24       6.464   1.868  -3.468  1.00  0.00
ATOM    351  CA  HIS    24       7.392   3.703  -3.926  1.00  0.00
ATOM    352  CB  HIS    24       6.219   3.784  -4.934  1.00  0.00
ATOM    353  CG  HIS    24       6.061   5.154  -5.678  1.00  0.00
ATOM    354  ND1 HIS    24       6.732   5.490  -6.805  1.00  0.00
ATOM    355  CD2 HIS    24       5.185   6.115  -5.400  1.00  0.00
ATOM    356  HD2 HIS    24       4.537   6.235  -4.535  1.00  0.00
ATOM    357  CE1 HIS    24       6.221   6.621  -7.283  1.00  0.00
ATOM    358  HE1 HIS    24       6.495   7.100  -8.233  1.00  0.00
ATOM    359  NE2 HIS    24       5.261   7.043  -6.383  1.00  0.00
ATOM    360  HE2 HIS    24       4.508   7.689  -6.522  1.00  0.00
ATOM    361  C   HIS    24       7.360   4.900  -2.925  1.00  0.00
ATOM    362  O   HIS    24       8.392   5.544  -2.756  1.00  0.00
ATOM    363  N   TYR    25       6.307   5.031  -2.132  1.00  0.00
ATOM    364  H   TYR    25       5.625   4.231  -2.043  1.00  0.00
ATOM    365  CA  TYR    25       6.208   6.091  -1.080  1.00  0.00
ATOM    366  CB  TYR    25       4.828   5.904  -0.434  1.00  0.00
ATOM    367  CG  TYR    25       3.876   6.944  -1.048  1.00  0.00
ATOM    368  CD1 TYR    25       3.213   6.550  -2.231  1.00  0.00
ATOM    369  HD1 TYR    25       3.203   5.459  -2.464  1.00  0.00
ATOM    370  CD2 TYR    25       3.563   8.136  -0.445  1.00  0.00
ATOM    371  HD2 TYR    25       3.975   8.396   0.559  1.00  0.00
ATOM    372  CE1 TYR    25       2.281   7.405  -2.846  1.00  0.00
ATOM    373  HE1 TYR    25       1.832   7.114  -3.802  1.00  0.00
ATOM    374  CE2 TYR    25       2.630   9.006  -1.041  1.00  0.00
ATOM    375  HE2 TYR    25       2.391   9.918  -0.496  1.00  0.00
ATOM    376  CZ  TYR    25       1.925   8.645  -2.226  1.00  0.00
ATOM    377  OH  TYR    25       1.117   9.531  -2.824  1.00  0.00
ATOM    378  HH  TYR    25       0.764   9.259  -3.802  1.00  0.00
ATOM    379  C   TYR    25       7.460   6.004  -0.151  1.00  0.00
ATOM    380  O   TYR    25       8.010   7.063   0.095  1.00  0.00
ATOM    381  N   LEU    26       7.869   4.792   0.256  1.00  0.00
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ATOM    382  H   LEU    26       7.206   4.024   0.225  1.00  0.00
ATOM    383  CA  LEU    26       9.172   4.569   1.002  1.00  0.00
ATOM    384  CB  LEU    26       9.459   3.065   1.403  1.00  0.00
ATOM    385  CG  LEU    26       8.875   2.539   2.689  1.00  0.00
ATOM    386  CD1 LEU    26       9.281   1.082   2.992  1.00  0.00
ATOM    387  CD2 LEU    26       9.073   3.486   3.902  1.00  0.00
ATOM    388  C   LEU    26      10.367   5.193   0.280  1.00  0.00
ATOM    389  O   LEU    26      10.861   6.184   0.823  1.00  0.00
ATOM    390  N   ASN    27      10.729   4.663  -0.920  1.00  0.00
ATOM    391  H   ASN    27      10.160   3.899  -1.328  1.00  0.00
ATOM    392  CA  ASN    27      11.869   5.184  -1.721  1.00  0.00
ATOM    393  CB  ASN    27      11.839   4.498  -3.084  1.00  0.00
ATOM    394  CG  ASN    27      13.282   4.280  -3.586  1.00  0.00
ATOM    395  OD1 ASN    27      14.148   5.108  -3.544  1.00  0.00
ATOM    396  ND2 ASN    27      13.463   3.117  -4.177  1.00  0.00
ATOM    397 1HD2 ASN    27      12.856   2.295  -4.231  1.00  0.00
ATOM    398 2HD2 ASN    27      14.285   3.160  -4.721  1.00  0.00
ATOM    399  C   ASN    27      11.810   6.690  -2.021  1.00  0.00
ATOM    400  O   ASN    27      12.874   7.319  -1.921  1.00  0.00
ATOM    401  N   LEU    28      10.614   7.222  -2.203  1.00  0.00
ATOM    402  H   LEU    28       9.838   6.592  -2.396  1.00  0.00
ATOM    403  CA  LEU    28      10.371   8.661  -2.358  1.00  0.00
ATOM    404  CB  LEU    28       8.915   8.899  -2.798  1.00  0.00
ATOM    405  CG  LEU    28       8.561   8.702  -4.270  1.00  0.00
ATOM    406  CD1 LEU    28       7.101   9.264  -4.591  1.00  0.00
ATOM    407  CD2 LEU    28       9.615   9.167  -5.276  1.00  0.00
ATOM    408  C   LEU    28      10.703   9.562  -1.123  1.00  0.00
ATOM    409  O   LEU    28      11.368  10.552  -1.393  1.00  0.00
ATOM    410  N   VAL    29      10.488   9.024   0.097  1.00  0.00
ATOM    411  H   VAL    29      10.101   8.113   0.208  1.00  0.00
ATOM    412  CA  VAL    29      10.813   9.850   1.278  1.00  0.00
ATOM    413  CB  VAL    29       9.532   9.786   2.109  1.00  0.00
ATOM    414  CG1 VAL    29       9.154   8.488   2.838  1.00  0.00
ATOM    415  CG2 VAL    29       9.501  10.994   3.075  1.00  0.00
ATOM    416  C   VAL    29      12.146   9.373   2.035  1.00  0.00
ATOM    417  O   VAL    29      12.844  10.254   2.515  1.00  0.00
ATOM    418  N   THR    30      12.345   8.029   2.050  1.00  0.00
ATOM    419  H   THR    30      11.732   7.305   1.695  1.00  0.00
ATOM    420  CA  THR    30      13.574   7.494   2.626  1.00  0.00
ATOM    421  CB  THR    30      13.163   6.653   3.881  1.00  0.00
ATOM    422  OG1 THR    30      12.366   7.461   4.657  1.00  0.00
ATOM    423  HG1 THR    30      11.739   6.882   5.178  1.00  0.00
ATOM    424  CG2 THR    30      14.440   6.319   4.645  1.00  0.00
ATOM    425  C   THR    30      14.302   6.576   1.649  1.00  0.00
ATOM    426  O   THR    30      13.826   5.515   1.305  1.00  0.00
ATOM    427  N   ARG    31      15.618   6.889   1.444  1.00  0.00
ATOM    428  H   ARG    31      16.132   7.348   2.167  1.00  0.00
ATOM    429  CA  ARG    31      16.356   6.342   0.270  1.00  0.00
ATOM    430  CB  ARG    31      17.622   7.150   0.192  1.00  0.00
ATOM    431  CG  ARG    31      18.439   6.795  -1.057  1.00  0.00
ATOM    432  CD  ARG    31      17.831   7.287  -2.377  1.00  0.00
ATOM    433  NE  ARG    31      18.626   6.906  -3.571  1.00  0.00
ATOM    434  HE  ARG    31      19.570   7.039  -3.485  1.00  0.00
ATOM    435  CZ  ARG    31      18.156   6.835  -4.843  1.00  0.00
ATOM    436  NH1 ARG    31      16.944   7.119  -5.223  1.00  0.00
ATOM    437 1HH1 ARG    31      16.227   7.438  -4.621  1.00  0.00
ATOM    438 2HH1 ARG    31      16.796   6.999  -6.156  1.00  0.00
ATOM    439  NH2 ARG    31      19.024   6.587  -5.807  1.00  0.00
ATOM    440 1HH2 ARG    31      19.992   6.425  -5.592  1.00  0.00
ATOM    441 2HH2 ARG    31      18.674   6.275  -6.642  1.00  0.00
ATOM    442  C   ARG    31      16.504   4.777   0.164  1.00  0.00
ATOM    443  O   ARG    31      17.313   4.103   0.818  1.00  0.00
ATOM    444  N   GLN    32      15.680   4.216  -0.745  1.00  0.00
ATOM    445  H   GLN    32      15.075   4.806  -1.274  1.00  0.00
ATOM    446  CA  GLN    32      15.658   2.800  -1.129  1.00  0.00
ATOM    447  CB  GLN    32      16.605   2.332  -2.266  1.00  0.00
ATOM    448  CG  GLN    32      18.007   3.013  -2.371  1.00  0.00
ATOM    449  CD  GLN    32      18.738   2.927  -3.719  1.00  0.00
ATOM    450  OE1 GLN    32      18.558   3.682  -4.677  1.00  0.00
ATOM    451  NE2 GLN    32      19.655   2.075  -3.896  1.00  0.00
ATOM    452 1HE2 GLN    32      19.919   1.425  -3.216  1.00  0.00
ATOM    453 2HE2 GLN    32      19.862   1.927  -4.870  1.00  0.00
ATOM    454  C   GLN    32      15.668   1.786   0.074  1.00  0.00
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ATOM    455  O   GLN    32      16.392   0.846   0.145  1.00  0.00
ATOM    456  N   ARG    33      14.878   2.167   1.080  1.00  0.00
ATOM    457  H   ARG    33      14.489   3.137   1.078  1.00  0.00
ATOM    458  CA  ARG    33      14.591   1.357   2.273  1.00  0.00
ATOM    459  CB  ARG    33      14.503   2.278   3.491  1.00  0.00
ATOM    460  CG  ARG    33      15.839   2.750   4.001  1.00  0.00
ATOM    461  CD  ARG    33      16.499   1.549   4.836  1.00  0.00
ATOM    462  NE  ARG    33      15.597   1.265   5.978  1.00  0.00
ATOM    463  HE  ARG    33      15.182   0.320   5.914  1.00  0.00
ATOM    464  CZ  ARG    33      15.498   2.049   7.049  1.00  0.00
ATOM    465  NH1 ARG    33      16.289   3.047   7.383  1.00  0.00
ATOM    466 1HH1 ARG    33      17.072   3.377   6.831  1.00  0.00
ATOM    467 2HH1 ARG    33      16.233   3.486   8.254  1.00  0.00
ATOM    468  NH2 ARG    33      14.618   1.713   8.002  1.00  0.00
ATOM    469 1HH2 ARG    33      14.150   0.865   7.985  1.00  0.00
ATOM    470 2HH2 ARG    33      14.418   2.399   8.683  1.00  0.00
ATOM    471  C   ARG    33      13.359   0.466   2.131  1.00  0.00
ATOM    472  O   ARG    33      12.313   0.728   2.631  1.00  0.00
ATOM    473  N   TYR    34      13.605  -0.716   1.605  1.00  0.00
ATOM    474  H   TYR    34      14.403  -0.844   0.995  1.00  0.00
ATOM    475  CA  TYR    34      12.749  -1.946   1.566  1.00  0.00
ATOM    476  CB  TYR    34      11.631  -1.880   0.511  1.00  0.00
ATOM    477  CG  TYR    34      11.949  -1.226  -0.823  1.00  0.00
ATOM    478  CD1 TYR    34      11.712   0.137  -0.900  1.00  0.00
ATOM    479  HD1 TYR    34      11.325   0.677  -0.031  1.00  0.00
ATOM    480  CD2 TYR    34      12.280  -1.987  -1.945  1.00  0.00
ATOM    481  HD2 TYR    34      12.577  -3.016  -1.801  1.00  0.00
ATOM    482  CE1 TYR    34      11.889   0.744  -2.171  1.00  0.00
ATOM    483  HE1 TYR    34      11.395   1.661  -2.334  1.00  0.00
ATOM    484  CE2 TYR    34      12.404  -1.392  -3.203  1.00  0.00
ATOM    485  HE2 TYR    34      12.797  -2.002  -3.988  1.00  0.00
ATOM    486  CZ  TYR    34      12.233   0.035  -3.312  1.00  0.00
ATOM    487  OH  TYR    34      12.208   0.685  -4.464  1.00  0.00
ATOM    488  HH  TYR    34      12.730   0.140  -5.199  1.00  0.00
ATOM    489  C   TYR    34      13.559  -3.195   1.349  1.00  0.00
ATOM    490  O1  TYR    34      14.683  -3.093   0.903  1.00  0.00
ATOM    491  O2  TYR    34      13.029  -4.229   1.695  1.00  0.00
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Geometry For 4

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ATOM      1  N    ILE     1       8.017  10.417   4.295  1.00  0.00
ATOM      2  H1   ILE     1       8.453  11.259   3.837  1.00  0.00
ATOM      3  H2   ILE     1       7.751  10.662   5.217  1.00  0.00
ATOM      4  H3   ILE     1       8.693   9.703   4.341  1.00  0.00
ATOM      5  CA   ILE     1       6.843   9.843   3.603  1.00  0.00
ATOM      6  CB   ILE     1       6.856  10.040   2.105  1.00  0.00
ATOM      7  CG1  ILE     1       5.589   9.642   1.400  1.00  0.00
ATOM      8  CG2  ILE     1       8.042   9.479   1.377  1.00  0.00
ATOM      9  CD   ILE     1       4.333  10.040   2.098  1.00  0.00
ATOM     10  C    ILE     1       6.696   8.348   3.996  1.00  0.00
ATOM     11  O    ILE     1       7.698   7.641   4.023  1.00  0.00
ATOM     12  C27  LP3     2      -8.434 -10.538   6.420  1.00  0.00
ATOM     13  O28  LP3     2      -8.468 -11.685   6.789  1.00  0.00
ATOM     14  N29  LP3     2      -9.582  -9.955   6.077  1.00  0.00
ATOM     15  HAE  LP3     2      -9.771  -8.954   6.035  1.00  0.00
ATOM     16  HAD  LP3     2     -10.338 -10.635   5.941  1.00  0.00
ATOM     17  C32  LP3     2      -4.390 -14.367   4.184  1.00  0.00
ATOM     18  O34  LP3     2      -4.514 -14.786   3.073  1.00  0.00
ATOM     19  N33  LP3     2      -3.285 -14.650   4.868  1.00  0.00
ATOM     20  HAG  LP3     2      -3.347 -14.696   5.884  1.00  0.00
ATOM     21  HAF  LP3     2      -2.503 -14.937   4.314  1.00  0.00
ATOM     22  C38  LP3     2      -9.230  -9.155  -1.243  1.00  0.00
ATOM     23  O39  LP3     2      -9.027  -9.983  -2.148  1.00  0.00
ATOM     24  N40  LP3     2     -10.383  -8.463  -1.389  1.00  0.00
ATOM     25  HAI  LP3     2     -10.929  -8.162  -0.590  1.00  0.00
ATOM     26  HAH  LP3     2     -10.696  -8.409  -2.337  1.00  0.00
ATOM     27  C43  LP3     2      -5.101  -6.610  -3.448  1.00  0.00
ATOM     28  O44  LP3     2      -4.052  -6.341  -2.948  1.00  0.00
ATOM     29  N45  LP3     2      -5.231  -6.734  -4.781  1.00  0.00
ATOM     30  HAK  LP3     2      -6.090  -7.067  -5.280  1.00  0.00
ATOM     31  HAJ  LP3     2      -4.549  -6.313  -5.300  1.00  0.00
ATOM     32  C50  LP3     2      -2.143  -0.344   3.220  1.00  0.00
ATOM     33  O51  LP3     2      -1.455   0.107   2.312  1.00  0.00
ATOM     34  N52  LP3     2      -1.715  -0.364   4.473  1.00  0.00
ATOM     35  HAM  LP3     2      -2.386  -0.396   5.277  1.00  0.00
ATOM     36  HAL  LP3     2      -0.831  -0.285   4.680  1.00  0.00
ATOM     37  C61  LP3     2      -4.953  -7.831  10.175  1.00  0.00
ATOM     38  O63  LP3     2      -4.721  -8.995  10.082  1.00  0.00
ATOM     39  N62  LP3     2      -4.737  -7.145  11.216  1.00  0.00
ATOM     40  HAO  LP3     2      -5.006  -6.185  11.354  1.00  0.00
ATOM     41  HAN  LP3     2      -4.335  -7.712  11.962  1.00  0.00
ATOM     42  C20  LP3     2      -3.472  -8.998   5.785  1.00  0.00
ATOM     43  C25  LP3     2      -5.205 -10.811   7.410  1.00  0.00
ATOM     44  C36  LP3     2      -6.269 -10.171  -0.682  1.00  0.00
ATOM     45  C46  LP3     2      -7.376  -2.873   1.900  1.00  0.00
ATOM     46  C47  LP3     2      -5.436  -2.707   0.350  1.00  0.00
ATOM     47  C54  LP3     2      -5.868  -4.819   8.327  1.00  0.00
ATOM     48  C26  LP3     2      -7.246  -9.604   6.559  1.00  0.00
ATOM     49  C30  LP3     2      -4.808 -12.096   4.775  1.00  0.00
ATOM     50  C31  LP3     2      -5.378 -13.501   4.908  1.00  0.00
ATOM     51  C37  LP3     2      -8.618  -9.433   0.170  1.00  0.00
ATOM     52  C41  LP3     2      -5.734  -8.001  -1.469  1.00  0.00
ATOM     53  C42  LP3     2      -6.256  -7.257  -2.692  1.00  0.00
ATOM     54  C48  LP3     2      -3.732  -2.249   2.563  1.00  0.00
ATOM     55  C49  LP3     2      -3.602  -0.747   2.920  1.00  0.00
ATOM     56  C56  LP3     2      -3.410  -3.314   8.695  1.00  0.00
ATOM     57  C55  LP3     2      -3.355  -4.757   8.116  1.00  0.00
ATOM     58  C60  LP3     2      -5.597  -7.098   8.917  1.00  0.00
ATOM     59  C2R  LP3     2      -0.218  -4.839   4.688  1.00  0.00
ATOM     60  O7R  LP3     2      -1.454  -4.115   4.899  1.00  0.00
ATOM     61  HAA  LP3     2      -1.128  -3.180   4.653  1.00  0.00
ATOM     62  C1R  LP3     2      -0.167  -5.910   3.523  1.00  0.00
ATOM     63  O6R  LP3     2       0.369  -5.289   2.433  1.00  0.00
ATOM     64  C4R  LP3     2       0.323  -3.912   2.715  1.00  0.00
ATOM     65  C3R  LP3     2       0.698  -3.803   4.176  1.00  0.00
ATOM     66  C5R  LP3     2       1.283  -3.123   1.870  1.00  0.00
ATOM     67  P    LP3     2       1.510  -1.815   5.618  1.00  0.00
ATOM     68  O2P  LP3     2       0.363  -2.518   4.811  1.00  0.00
ATOM     69  O4   LP3     2       2.807  -2.292   5.036  1.00  0.00
ATOM     70  O5   LP3     2       1.136  -0.364   5.662  1.00  0.00
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ATOM     71  O3  LP3     2       1.351  -2.409   7.099  1.00  0.00
ATOM     72  C2P LP3     2       1.008  -1.422   8.050  1.00  0.00
ATOM     73  C3P LP3     2       2.207  -1.082   8.950  1.00  0.00
ATOM     74  C1P LP3     2      -0.056  -1.820   9.052  1.00  0.00
ATOM     75  N59 LP3     2      -1.293  -2.066   8.598  1.00  0.00
ATOM     76  HAC LP3     2      -1.471  -1.851   7.651  1.00  0.00
ATOM     77  C57 LP3     2      -2.043  -2.979   9.267  1.00  0.00
ATOM     78  O58 LP3     2      -1.783  -3.402  10.429  1.00  0.00
ATOM     79  C5B LP3     2      -2.488 -10.021   1.262  1.00  0.00
ATOM     80  C5M LP3     2      -3.022 -11.331   0.657  1.00  0.00
ATOM     81  C6B LP3     2      -1.115  -9.793   1.233  1.00  0.00
ATOM     82  C6M LP3     2      -0.099 -10.771   0.669  1.00  0.00
ATOM     83  C4B LP3     2      -3.358  -9.072   1.760  1.00  0.00
ATOM     84  H4B LP3     2      -4.384  -9.299   1.858  1.00  0.00
ATOM     85  C7B LP3     2      -0.713  -8.590   1.890  1.00  0.00
ATOM     86  H7B LP3     2       0.412  -8.469   1.964  1.00  0.00
ATOM     87  N3B LP3     2      -3.544  -7.032   3.157  1.00  0.00
ATOM     88  C9B LP3     2      -2.987  -7.940   2.381  1.00  0.00
ATOM     89  N1B LP3     2      -1.406  -6.612   3.185  1.00  0.00
ATOM     90  C8B LP3     2      -1.608  -7.645   2.430  1.00  0.00
ATOM     91  C2B LP3     2      -2.605  -6.197   3.623  1.00  0.00
ATOM     92  H2B LP3     2      -2.787  -5.341   4.224  1.00  0.00
ATOM     93  C5  LP3     2      -6.482 -10.114   2.581  1.00  0.00
ATOM     94  C35 LP3     2      -7.133 -11.460   2.257  1.00  0.00
ATOM     95  C15 LP3     2      -4.867  -4.013   5.135  1.00  0.00
ATOM     96  C53 LP3     2      -4.834  -2.609   5.733  1.00  0.00
ATOM     97  FE  LP3     2      -5.448  -7.067   3.698  1.00  0.00
ATOM     98  N21 LP3     2      -5.476  -8.705   4.369  1.00  0.00
ATOM     99  N22 LP3     2      -6.049  -7.732   1.946  1.00  0.00
ATOM    100  N23 LP3     2      -5.386  -5.278   3.025  1.00  0.00
ATOM    101  N24 LP3     2      -5.168  -6.333   5.368  1.00  0.00
ATOM    102  C1  LP3     2      -5.017  -8.785   5.782  1.00  0.00
ATOM    103  C2  LP3     2      -5.828 -10.057   6.192  1.00  0.00
ATOM    104  C3  LP3     2      -5.862 -11.011   4.955  1.00  0.00
ATOM    105  C4  LP3     2      -5.930  -9.955   3.879  1.00  0.00
ATOM    106  C6  LP3     2      -6.533  -9.044   1.647  1.00  0.00
ATOM    107  C7  LP3     2      -7.087  -9.198   0.241  1.00  0.00
ATOM    108  C8  LP3     2      -6.807  -7.829  -0.395  1.00  0.00
ATOM    109  C9  LP3     2      -6.333  -7.006   0.797  1.00  0.00
ATOM    110  C16 LP3     2      -4.880  -5.154   5.997  1.00  0.00
ATOM    111  C17 LP3     2      -4.661  -5.352   7.542  1.00  0.00
ATOM    112  C18 LP3     2      -4.650  -6.869   7.737  1.00  0.00
ATOM    113  C19 LP3     2      -5.382  -7.380   6.428  1.00  0.00
ATOM    114  C11 LP3     2      -5.683  -4.777   1.720  1.00  0.00
ATOM    115  C12 LP3     2      -5.904  -3.267   1.664  1.00  0.00
ATOM    116  C13 LP3     2      -5.114  -2.829   2.937  1.00  0.00
ATOM    117  C14 LP3     2      -5.128  -4.109   3.736  1.00  0.00
ATOM    118  C10 LP3     2      -6.142  -5.598   0.681  1.00  0.00
ATOM    119  H10 LP3     2      -6.444  -5.088  -0.175  1.00  0.00
ATOM    120  N   LP3     2       5.555   8.039   4.655  1.00  0.00
ATOM    121  H   LP3     2       5.029   8.793   4.929  1.00  0.00
ATOM    122  CA  LP3     2       5.166   6.706   5.081  1.00  0.00
ATOM    123  CB  LP3     2       5.341   6.611   6.566  1.00  0.00
ATOM    124  CG  LP3     2       5.510   5.093   6.860  1.00  0.00
ATOM    125  CD  LP3     2       4.248   4.292   7.226  1.00  0.00
ATOM    126  CE  LP3     2       4.414   2.799   7.151  1.00  0.00
ATOM    127  C   LP3     2       3.708   6.360   4.626  1.00  0.00
ATOM    128  O   LP3     2       2.809   7.043   5.127  1.00  0.00
ATOM    129  OLB LP3     2       2.609  -3.707   1.384  1.00  0.00
ATOM    130  C1N LP3     2      -7.015  -6.361   3.927  1.00  0.00
ATOM    131  N1C LP3     2      -8.006  -5.869   4.051  1.00  0.00
ATOM    132  CZ  LP3     2       1.910  -0.826   1.139  1.00  0.00
ATOM    133  CY  LP3     2       3.022  -0.384   2.082  1.00  0.00
ATOM    134  CX  LP3     2       2.409   0.580   3.073  1.00  0.00
ATOM    135  CT1 LP3     2       3.429   1.247   4.004  1.00  0.00
ATOM    136  CT2 LP3     2       3.403   1.356   5.360  1.00  0.00
ATOM    137  NT1 LP3     2       4.317   2.234   5.725  1.00  0.00
ATOM    138  NT2 LP3     2       5.005   2.621   4.685  1.00  0.00
ATOM    139  NT3 LP3     2       4.415   2.040   3.575  1.00  0.00
ATOM    140  NZ2 LP3     2       0.985  -1.839   1.785  1.00  0.00
ATOM    141  HZ2 LP3     2       0.209  -1.440   2.366  1.00  0.00
ATOM    142  N   PRO     3       3.650   5.749   3.461  1.00  0.00
ATOM    143  CA  PRO     3       2.297   5.348   2.911  1.00  0.00
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ATOM    144  CB  PRO     3       2.624   4.491   1.689  1.00  0.00
ATOM    145  CG  PRO     3       3.815   5.211   1.206  1.00  0.00
ATOM    146  CD  PRO     3       4.649   5.466   2.477  1.00  0.00
ATOM    147  C   PRO     3       1.226   4.655   3.733  1.00  0.00
ATOM    148  O   PRO     3       1.325   3.507   4.179  1.00  0.00
ATOM    149  N   GLU     4       0.196   5.412   4.112  1.00  0.00
ATOM    150  H   GLU     4       0.126   6.369   3.790  1.00  0.00
ATOM    151  CA  GLU     4      -0.970   4.821   4.857  1.00  0.00
ATOM    152  CB  GLU     4      -1.145   5.608   6.125  1.00  0.00
ATOM    153  CG  GLU     4       0.089   5.579   7.034  1.00  0.00
ATOM    154  CD  GLU     4      -0.053   6.629   8.137  1.00  0.00
ATOM    155  OE1 GLU     4       0.544   7.730   7.851  1.00  0.00
ATOM    156  OE2 GLU     4      -0.405   6.296   9.271  1.00  0.00
ATOM    157  C   GLU     4      -2.275   4.902   4.009  1.00  0.00
ATOM    158  O   GLU     4      -2.807   5.964   3.764  1.00  0.00
ATOM    159  N   ALA     5      -2.689   3.784   3.449  1.00  0.00
ATOM    160  H   ALA     5      -2.098   2.978   3.391  1.00  0.00
ATOM    161  CA  ALA     5      -3.984   3.710   2.687  1.00  0.00
ATOM    162  CB  ALA     5      -3.612   3.749   1.193  1.00  0.00
ATOM    163  C   ALA     5      -5.006   2.587   3.007  1.00  0.00
ATOM    164  O   ALA     5      -5.185   1.680   2.164  1.00  0.00
ATOM    165  N   PRO     6      -5.793   2.823   4.119  1.00  0.00
ATOM    166  CA  PRO     6      -6.665   1.865   4.847  1.00  0.00
ATOM    167  CB  PRO     6      -7.707   2.675   5.490  1.00  0.00
ATOM    168  CG  PRO     6      -7.158   4.049   5.671  1.00  0.00
ATOM    169  CD  PRO     6      -6.186   4.162   4.540  1.00  0.00
ATOM    170  C   PRO     6      -7.458   0.790   3.985  1.00  0.00
ATOM    171  O   PRO     6      -7.374  -0.375   4.251  1.00  0.00
ATOM    172  N   GLY     7      -8.074   1.194   2.884  1.00  0.00
ATOM    173  H   GLY     7      -8.175   2.174   2.644  1.00  0.00
ATOM    174  CA  GLY     7      -9.025   0.316   2.078  1.00  0.00
ATOM    175  C   GLY     7     -10.249  -0.156   2.863  1.00  0.00
ATOM    176  O   GLY     7     -10.127  -1.081   3.663  1.00  0.00
ATOM    177  N   GLU     8     -11.335   0.622   2.819  1.00  0.00
ATOM    178  H   GLU     8     -11.469   1.076   1.916  1.00  0.00
ATOM    179  CA  GLU     8     -12.517   0.371   3.567  1.00  0.00
ATOM    180  CB  GLU     8     -12.675   1.493   4.612  1.00  0.00
ATOM    181  CG  GLU     8     -11.955   1.192   5.918  1.00  0.00
ATOM    182  CD  GLU     8     -12.319   2.054   7.085  1.00  0.00
ATOM    183  OE1 GLU     8     -12.942   1.565   8.030  1.00  0.00
ATOM    184  OE2 GLU     8     -12.020   3.282   6.965  1.00  0.00
ATOM    185  C   GLU     8     -13.815   0.160   2.827  1.00  0.00
ATOM    186  O   GLU     8     -14.660  -0.556   3.393  1.00  0.00
ATOM    187  N   ASP     9     -13.894   0.968   1.762  1.00  0.00
ATOM    188  H   ASP     9     -13.145   1.527   1.476  1.00  0.00
ATOM    189  CA  ASP     9     -15.077   0.983   0.919  1.00  0.00
ATOM    190  CB  ASP     9     -15.661   2.350   1.142  1.00  0.00
ATOM    191  CG  ASP     9     -17.094   2.630   0.900  1.00  0.00
ATOM    192  OD1 ASP     9     -17.518   3.380  -0.049  1.00  0.00
ATOM    193  OD2 ASP     9     -17.848   2.245   1.813  1.00  0.00
ATOM    194  C   ASP     9     -14.939   0.547  -0.526  1.00  0.00
ATOM    195  O   ASP     9     -15.003  -0.666  -0.835  1.00  0.00
ATOM    196  N   ALA    10     -14.689   1.562  -1.405  1.00  0.00
ATOM    197  H   ALA    10     -14.778   2.480  -1.185  1.00  0.00
ATOM    198  CA  ALA    10     -14.592   1.371  -2.865  1.00  0.00
ATOM    199  CB  ALA    10     -15.106   2.557  -3.588  1.00  0.00
ATOM    200  C   ALA    10     -13.205   0.899  -3.299  1.00  0.00
ATOM    201  O   ALA    10     -12.233   1.601  -3.522  1.00  0.00
ATOM    202  N   SER    11     -13.263  -0.374  -3.628  1.00  0.00
ATOM    203  H   SER    11     -14.073  -0.990  -3.449  1.00  0.00
ATOM    204  CA  SER    11     -12.065  -1.091  -4.084  1.00  0.00
ATOM    205  CB  SER    11     -12.237  -2.585  -4.110  1.00  0.00
ATOM    206  OG  SER    11     -12.923  -3.020  -2.930  1.00  0.00
ATOM    207  HG  SER    11     -13.955  -3.080  -3.134  1.00  0.00
ATOM    208  C   SER    11     -11.304  -0.682  -5.392  1.00  0.00
ATOM    209  O   SER    11     -10.055  -0.739  -5.306  1.00  0.00
ATOM    210  N   PRO    12     -11.957  -0.204  -6.479  1.00  0.00
ATOM    211  CA  PRO    12     -11.265   0.408  -7.603  1.00  0.00
ATOM    212  CB  PRO    12     -12.311   0.716  -8.574  1.00  0.00
ATOM    213  CG  PRO    12     -13.206  -0.451  -8.413  1.00  0.00
ATOM    214  CD  PRO    12     -13.273  -0.680  -6.922  1.00  0.00
ATOM    215  C   PRO    12     -10.473   1.648  -7.131  1.00  0.00
ATOM    216  O   PRO    12      -9.263   1.878  -7.421  1.00  0.00
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ATOM    217  N   GLU    13     -11.191   2.495  -6.373  1.00  0.00
ATOM    218  H   GLU    13     -12.129   2.417  -6.303  1.00  0.00
ATOM    219  CA  GLU    13     -10.561   3.650  -5.731  1.00  0.00
ATOM    220  CB  GLU    13     -11.509   4.521  -4.965  1.00  0.00
ATOM    221  CG  GLU    13     -11.184   5.981  -4.913  1.00  0.00
ATOM    222  CD  GLU    13     -11.913   6.721  -3.771  1.00  0.00
ATOM    223  OE1 GLU    13     -11.970   6.206  -2.651  1.00  0.00
ATOM    224  OE2 GLU    13     -12.551   7.732  -4.163  1.00  0.00
ATOM    225  C   GLU    13      -9.311   3.420  -4.886  1.00  0.00
ATOM    226  O   GLU    13      -8.176   3.441  -5.399  1.00  0.00
ATOM    227  N   GLU    14      -9.471   2.835  -3.682  1.00  0.00
ATOM    228  H   GLU    14     -10.380   2.460  -3.354  1.00  0.00
ATOM    229  CA  GLU    14      -8.396   2.624  -2.623  1.00  0.00
ATOM    230  CB  GLU    14      -8.972   1.982  -1.347  1.00  0.00
ATOM    231  CG  GLU    14     -10.096   2.944  -0.904  1.00  0.00
ATOM    232  CD  GLU    14     -11.207   2.201  -0.110  1.00  0.00
ATOM    233  OE1 GLU    14     -11.821   2.957   0.707  1.00  0.00
ATOM    234  OE2 GLU    14     -11.530   0.993  -0.341  1.00  0.00
ATOM    235  C   GLU    14      -7.170   1.825  -3.109  1.00  0.00
ATOM    236  O   GLU    14      -5.993   2.234  -2.847  1.00  0.00
ATOM    237  N   LEU    15      -7.359   0.892  -4.015  1.00  0.00
ATOM    238  H   LEU    15      -8.320   0.641  -4.354  1.00  0.00
ATOM    239  CA  LEU    15      -6.184   0.134  -4.547  1.00  0.00
ATOM    240  CB  LEU    15      -6.794  -1.103  -5.221  1.00  0.00
ATOM    241  CG  LEU    15      -7.072  -2.321  -4.415  1.00  0.00
ATOM    242  CD1 LEU    15      -8.116  -3.215  -4.953  1.00  0.00
ATOM    243  CD2 LEU    15      -5.781  -3.141  -4.160  1.00  0.00
ATOM    244  C   LEU    15      -5.169   0.765  -5.460  1.00  0.00
ATOM    245  O   LEU    15      -4.001   0.352  -5.405  1.00  0.00
ATOM    246  N   ASN    16      -5.612   1.945  -5.987  1.00  0.00
ATOM    247  H   ASN    16      -6.549   2.324  -6.008  1.00  0.00
ATOM    248  CA  ASN    16      -4.660   2.733  -6.836  1.00  0.00
ATOM    249  CB  ASN    16      -5.440   3.824  -7.580  1.00  0.00
ATOM    250  CG  ASN    16      -6.094   3.306  -8.896  1.00  0.00
ATOM    251  OD1 ASN    16      -5.431   2.691  -9.769  1.00  0.00
ATOM    252  ND2 ASN    16      -7.304   3.755  -9.197  1.00  0.00
ATOM    253 1HD2 ASN    16      -7.699   4.617  -8.793  1.00  0.00
ATOM    254 2HD2 ASN    16      -7.968   3.091  -9.513  1.00  0.00
ATOM    255  C   ASN    16      -3.481   3.368  -6.088  1.00  0.00
ATOM    256  O   ASN    16      -2.312   3.356  -6.515  1.00  0.00
ATOM    257  N   ARG    17      -3.864   4.076  -4.991  1.00  0.00
ATOM    258  H   ARG    17      -4.832   4.411  -4.792  1.00  0.00
ATOM    259  CA  ARG    17      -2.897   4.643  -4.027  1.00  0.00
ATOM    260  CB  ARG    17      -3.537   5.503  -2.894  1.00  0.00
ATOM    261  CG  ARG    17      -2.527   6.439  -2.294  1.00  0.00
ATOM    262  CD  ARG    17      -3.318   7.433  -1.383  1.00  0.00
ATOM    263  NE  ARG    17      -4.317   8.214  -2.241  1.00  0.00
ATOM    264  HE  ARG    17      -4.974   7.577  -2.697  1.00  0.00
ATOM    265  CZ  ARG    17      -4.566   9.499  -2.294  1.00  0.00
ATOM    266  NH1 ARG    17      -3.831  10.228  -1.462  1.00  0.00
ATOM    267 1HH1 ARG    17      -3.081   9.852  -0.895  1.00  0.00
ATOM    268 2HH1 ARG    17      -4.028  11.202  -1.329  1.00  0.00
ATOM    269  NH2 ARG    17      -5.535   9.992  -2.992  1.00  0.00
ATOM    270 1HH2 ARG    17      -6.099   9.361  -3.604  1.00  0.00
ATOM    271 2HH2 ARG    17      -5.812  10.945  -2.925  1.00  0.00
ATOM    272  C   ARG    17      -1.993   3.562  -3.365  1.00  0.00
ATOM    273  O   ARG    17      -0.854   3.616  -3.618  1.00  0.00
ATOM    274  N   TYR    18      -2.598   2.413  -2.937  1.00  0.00
ATOM    275  H   TYR    18      -3.594   2.339  -2.889  1.00  0.00
ATOM    276  CA  TYR    18      -1.772   1.225  -2.551  1.00  0.00
ATOM    277  CB  TYR    18      -2.789   0.149  -2.433  1.00  0.00
ATOM    278  CG  TYR    18      -2.254  -1.243  -2.078  1.00  0.00
ATOM    279  CD1 TYR    18      -2.631  -2.166  -3.041  1.00  0.00
ATOM    280  HD1 TYR    18      -2.986  -1.773  -4.034  1.00  0.00
ATOM    281  CD2 TYR    18      -1.918  -1.590  -0.774  1.00  0.00
ATOM    282  HD2 TYR    18      -1.602  -0.872  -0.053  1.00  0.00
ATOM    283  CE1 TYR    18      -2.702  -3.525  -2.748  1.00  0.00
ATOM    284  HE1 TYR    18      -2.958  -4.244  -3.493  1.00  0.00
ATOM    285  CE2 TYR    18      -1.957  -2.935  -0.512  1.00  0.00
ATOM    286  HE2 TYR    18      -1.761  -3.138   0.465  1.00  0.00
ATOM    287  CZ  TYR    18      -2.359  -3.874  -1.432  1.00  0.00
ATOM    288  OH  TYR    18      -2.476  -5.175  -1.102  1.00  0.00
ATOM    289  HH  TYR    18      -2.980  -5.693  -1.844  1.00  0.00
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ATOM    290  C   TYR    18      -0.717   0.833  -3.610  1.00  0.00
ATOM    291  O   TYR    18       0.500   0.881  -3.415  1.00  0.00
ATOM    292  N   TYR    19      -1.252   0.502  -4.796  1.00  0.00
ATOM    293  H   TYR    19      -2.257   0.461  -4.983  1.00  0.00
ATOM    294  CA  TYR    19      -0.487   0.115  -5.984  1.00  0.00
ATOM    295  CB  TYR    19      -1.347  -0.296  -7.114  1.00  0.00
ATOM    296  CG  TYR    19      -1.816  -1.717  -6.943  1.00  0.00
ATOM    297  CD1 TYR    19      -1.181  -2.668  -6.281  1.00  0.00
ATOM    298  HD1 TYR    19      -0.213  -2.509  -5.828  1.00  0.00
ATOM    299  CD2 TYR    19      -3.026  -2.087  -7.592  1.00  0.00
ATOM    300  HD2 TYR    19      -3.679  -1.330  -7.909  1.00  0.00
ATOM    301  CE1 TYR    19      -1.697  -3.940  -6.087  1.00  0.00
ATOM    302  HE1 TYR    19      -1.165  -4.626  -5.393  1.00  0.00
ATOM    303  CE2 TYR    19      -3.515  -3.381  -7.477  1.00  0.00
ATOM    304  HE2 TYR    19      -4.418  -3.597  -8.057  1.00  0.00
ATOM    305  CZ  TYR    19      -2.888  -4.303  -6.654  1.00  0.00
ATOM    306  OH  TYR    19      -3.311  -5.540  -6.377  1.00  0.00
ATOM    307  HH  TYR    19      -2.690  -5.990  -5.768  1.00  0.00
ATOM    308  C   TYR    19       0.587   1.111  -6.368  1.00  0.00
ATOM    309  O   TYR    19       1.770   0.698  -6.409  1.00  0.00
ATOM    310  N   ALA    20       0.243   2.378  -6.422  1.00  0.00
ATOM    311  H   ALA    20      -0.718   2.637  -6.219  1.00  0.00
ATOM    312  CA  ALA    20       1.263   3.428  -6.772  1.00  0.00
ATOM    313  CB  ALA    20       0.408   4.682  -6.855  1.00  0.00
ATOM    314  C   ALA    20       2.347   3.474  -5.755  1.00  0.00
ATOM    315  O   ALA    20       3.520   3.332  -6.209  1.00  0.00
ATOM    316  N   SER    21       2.029   3.574  -4.491  1.00  0.00
ATOM    317  H   SER    21       1.079   3.728  -4.203  1.00  0.00
ATOM    318  CA  SER    21       2.988   3.470  -3.408  1.00  0.00
ATOM    319  CB  SER    21       2.260   3.403  -2.110  1.00  0.00
ATOM    320  OG  SER    21       1.631   4.647  -1.930  1.00  0.00
ATOM    321  HG  SER    21       0.982   4.618  -1.153  1.00  0.00
ATOM    322  C   SER    21       3.944   2.293  -3.434  1.00  0.00
ATOM    323  O   SER    21       5.178   2.460  -3.187  1.00  0.00
ATOM    324  N   LEU    22       3.433   1.106  -3.699  1.00  0.00
ATOM    325  H   LEU    22       2.379   1.017  -3.683  1.00  0.00
ATOM    326  CA  LEU    22       4.209  -0.118  -4.125  1.00  0.00
ATOM    327  CB  LEU    22       3.176  -1.220  -4.406  1.00  0.00
ATOM    328  CG  LEU    22       2.515  -1.892  -3.175  1.00  0.00
ATOM    329  CD1 LEU    22       1.313  -2.715  -3.588  1.00  0.00
ATOM    330  CD2 LEU    22       3.504  -2.761  -2.377  1.00  0.00
ATOM    331  C   LEU    22       5.173   0.189  -5.297  1.00  0.00
ATOM    332  O   LEU    22       6.369   0.413  -5.060  1.00  0.00
ATOM    333  N   ARG    23       4.615   0.424  -6.472  1.00  0.00
ATOM    334  H   ARG    23       3.626   0.298  -6.487  1.00  0.00
ATOM    335  CA  ARG    23       5.338   0.685  -7.705  1.00  0.00
ATOM    336  CB  ARG    23       4.357   1.078  -8.837  1.00  0.00
ATOM    337  CG  ARG    23       3.499  -0.091  -9.290  1.00  0.00
ATOM    338  CD  ARG    23       2.276   0.411 -10.171  1.00  0.00
ATOM    339  NE  ARG    23       1.711  -0.793 -10.824  1.00  0.00
ATOM    340  HE  ARG    23       1.077  -1.360 -10.309  1.00  0.00
ATOM    341  CZ  ARG    23       2.141  -1.212 -12.013  1.00  0.00
ATOM    342  NH1 ARG    23       3.110  -0.598 -12.713  1.00  0.00
ATOM    343 1HH1 ARG    23       3.655   0.185 -12.360  1.00  0.00
ATOM    344 2HH1 ARG    23       3.374  -0.903 -13.631  1.00  0.00
ATOM    345  NH2 ARG    23       1.686  -2.372 -12.473  1.00  0.00
ATOM    346 1HH2 ARG    23       1.120  -2.882 -11.839  1.00  0.00
ATOM    347 2HH2 ARG    23       1.883  -2.605 -13.445  1.00  0.00
ATOM    348  C   ARG    23       6.390   1.809  -7.576  1.00  0.00
ATOM    349  O   ARG    23       7.501   1.619  -8.151  1.00  0.00
ATOM    350  N   HIS    24       6.083   2.819  -6.825  1.00  0.00
ATOM    351  H   HIS    24       5.141   2.795  -6.430  1.00  0.00
ATOM    352  CA  HIS    24       6.797   4.095  -6.673  1.00  0.00
ATOM    353  CB  HIS    24       5.835   5.312  -6.855  1.00  0.00
ATOM    354  CG  HIS    24       6.692   6.656  -6.744  1.00  0.00
ATOM    355  ND1 HIS    24       7.333   7.278  -7.784  1.00  0.00
ATOM    356  CD2 HIS    24       6.981   7.349  -5.645  1.00  0.00
ATOM    357  HD2 HIS    24       6.405   7.286  -4.688  1.00  0.00
ATOM    358  CE1 HIS    24       7.981   8.330  -7.241  1.00  0.00
ATOM    359  HE1 HIS    24       8.696   9.004  -7.764  1.00  0.00
ATOM    360  NE2 HIS    24       7.808   8.361  -5.929  1.00  0.00
ATOM    361  HE2 HIS    24       8.481   8.735  -5.305  1.00  0.00
ATOM    362  C   HIS    24       7.780   4.084  -5.472  1.00  0.00
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ATOM    363  O   HIS    24       8.974   3.823  -5.616  1.00  0.00
ATOM    364  N   TYR    25       7.177   4.184  -4.253  1.00  0.00
ATOM    365  H   TYR    25       6.296   3.801  -4.110  1.00  0.00
ATOM    366  CA  TYR    25       7.993   4.330  -3.014  1.00  0.00
ATOM    367  CB  TYR    25       7.113   4.690  -1.832  1.00  0.00
ATOM    368  CG  TYR    25       6.656   6.132  -1.921  1.00  0.00
ATOM    369  CD1 TYR    25       5.333   6.352  -2.001  1.00  0.00
ATOM    370  HD1 TYR    25       4.685   5.469  -2.169  1.00  0.00
ATOM    371  CD2 TYR    25       7.552   7.168  -1.999  1.00  0.00
ATOM    372  HD2 TYR    25       8.604   7.018  -1.718  1.00  0.00
ATOM    373  CE1 TYR    25       4.861   7.626  -2.316  1.00  0.00
ATOM    374  HE1 TYR    25       3.817   7.710  -2.475  1.00  0.00
ATOM    375  CE2 TYR    25       7.091   8.460  -2.331  1.00  0.00
ATOM    376  HE2 TYR    25       7.781   9.344  -2.396  1.00  0.00
ATOM    377  CZ  TYR    25       5.699   8.728  -2.494  1.00  0.00
ATOM    378  OH  TYR    25       5.319   9.944  -2.749  1.00  0.00
ATOM    379  HH  TYR    25       6.084  10.478  -3.037  1.00  0.00
ATOM    380  C   TYR    25       8.761   3.071  -2.603  1.00  0.00
ATOM    381  O   TYR    25       9.989   3.106  -2.696  1.00  0.00
ATOM    382  N   LEU    26       7.999   1.967  -2.320  1.00  0.00
ATOM    383  H   LEU    26       7.057   2.026  -1.977  1.00  0.00
ATOM    384  CA  LEU    26       8.592   0.658  -1.983  1.00  0.00
ATOM    385  CB  LEU    26       7.507  -0.329  -1.567  1.00  0.00
ATOM    386  CG  LEU    26       6.957   0.082  -0.188  1.00  0.00
ATOM    387  CD1 LEU    26       5.655  -0.705  -0.023  1.00  0.00
ATOM    388  CD2 LEU    26       7.807  -0.301   0.997  1.00  0.00
ATOM    389  C   LEU    26       9.467   0.019  -3.112  1.00  0.00
ATOM    390  O   LEU    26      10.399  -0.654  -2.695  1.00  0.00
ATOM    391  N   ASN    27       8.992  -0.094  -4.345  1.00  0.00
ATOM    392  H   ASN    27       8.023  -0.068  -4.522  1.00  0.00
ATOM    393  CA  ASN    27       9.769  -0.638  -5.458  1.00  0.00
ATOM    394  CB  ASN    27       8.833  -0.860  -6.653  1.00  0.00
ATOM    395  CG  ASN    27       7.907  -2.081  -6.426  1.00  0.00
ATOM    396  OD1 ASN    27       7.083  -2.134  -5.511  1.00  0.00
ATOM    397  ND2 ASN    27       7.908  -2.948  -7.450  1.00  0.00
ATOM    398 1HD2 ASN    27       8.615  -2.688  -8.239  1.00  0.00
ATOM    399 2HD2 ASN    27       7.093  -3.546  -7.740  1.00  0.00
ATOM    400  C   ASN    27      11.122   0.141  -5.824  1.00  0.00
ATOM    401  O   ASN    27      12.121  -0.522  -6.141  1.00  0.00
ATOM    402  N   LEU    28      10.928   1.422  -6.017  1.00  0.00
ATOM    403  H   LEU    28       9.962   1.721  -6.128  1.00  0.00
ATOM    404  CA  LEU    28      12.084   2.275  -6.401  1.00  0.00
ATOM    405  CB  LEU    28      11.741   3.178  -7.577  1.00  0.00
ATOM    406  CG  LEU    28      11.899   2.610  -8.946  1.00  0.00
ATOM    407  CD1 LEU    28      10.936   1.395  -9.210  1.00  0.00
ATOM    408  CD2 LEU    28      11.751   3.716 -10.060  1.00  0.00
ATOM    409  C   LEU    28      12.674   3.171  -5.370  1.00  0.00
ATOM    410  O   LEU    28      13.831   2.922  -5.007  1.00  0.00
ATOM    411  N   VAL    29      11.897   4.218  -4.943  1.00  0.00
ATOM    412  H   VAL    29      11.035   4.482  -5.408  1.00  0.00
ATOM    413  CA  VAL    29      12.496   5.278  -4.097  1.00  0.00
ATOM    414  CB  VAL    29      11.400   6.356  -3.929  1.00  0.00
ATOM    415  CG1 VAL    29      12.002   7.509  -3.035  1.00  0.00
ATOM    416  CG2 VAL    29      10.976   6.903  -5.251  1.00  0.00
ATOM    417  C   VAL    29      13.121   4.906  -2.702  1.00  0.00
ATOM    418  O   VAL    29      14.244   5.320  -2.432  1.00  0.00
ATOM    419  N   THR    30      12.246   4.441  -1.771  1.00  0.00
ATOM    420  H   THR    30      11.286   4.204  -2.083  1.00  0.00
ATOM    421  CA  THR    30      12.442   4.078  -0.312  1.00  0.00
ATOM    422  CB  THR    30      11.679   4.851   0.807  1.00  0.00
ATOM    423  OG1 THR    30      10.682   5.572   0.106  1.00  0.00
ATOM    424  HG1 THR    30       9.932   5.701   0.867  1.00  0.00
ATOM    425  CG2 THR    30      12.657   5.638   1.727  1.00  0.00
ATOM    426  C   THR    30      11.986   2.605   0.009  1.00  0.00
ATOM    427  O   THR    30      10.919   2.247   0.421  1.00  0.00
ATOM    428  N   ARG    31      12.971   1.778  -0.058  1.00  0.00
ATOM    429  H   ARG    31      13.901   2.164  -0.078  1.00  0.00
ATOM    430  CA  ARG    31      12.871   0.345  -0.008  1.00  0.00
ATOM    431  CB  ARG    31      14.103  -0.207  -0.784  1.00  0.00
ATOM    432  CG  ARG    31      13.944  -0.188  -2.301  1.00  0.00
ATOM    433  CD  ARG    31      15.216  -0.732  -3.008  1.00  0.00
ATOM    434  NE  ARG    31      14.933  -0.722  -4.444  1.00  0.00
ATOM    435  HE  ARG    31      14.228  -1.399  -4.779  1.00  0.00
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ATOM    436  CZ  ARG    31      15.574  -0.128  -5.423  1.00  0.00
ATOM    437  NH1 ARG    31      16.654   0.593  -5.206  1.00  0.00
ATOM    438 1HH1 ARG    31      16.956   0.788  -4.201  1.00  0.00
ATOM    439 2HH1 ARG    31      17.334   0.795  -6.030  1.00  0.00
ATOM    440  NH2 ARG    31      15.071  -0.110  -6.647  1.00  0.00
ATOM    441 1HH2 ARG    31      14.168  -0.529  -6.952  1.00  0.00
ATOM    442 2HH2 ARG    31      15.589   0.272  -7.379  1.00  0.00
ATOM    443  C   ARG    31      12.804  -0.226   1.479  1.00  0.00
ATOM    444  O   ARG    31      13.787  -0.053   2.245  1.00  0.00
ATOM    445  N   GLN    32      11.695  -0.854   1.799  1.00  0.00
ATOM    446  H   GLN    32      11.003  -0.831   1.096  1.00  0.00
ATOM    447  CA  GLN    32      11.372  -1.546   3.101  1.00  0.00
ATOM    448  CB  GLN    32      11.367  -3.069   2.975  1.00  0.00
ATOM    449  CG  GLN    32      10.620  -3.595   4.213  1.00  0.00
ATOM    450  CD  GLN    32       9.097  -3.512   3.914  1.00  0.00
ATOM    451  OE1 GLN    32       8.583  -3.979   2.906  1.00  0.00
ATOM    452  NE2 GLN    32       8.390  -2.876   4.772  1.00  0.00
ATOM    453 1HE2 GLN    32       8.841  -2.710   5.614  1.00  0.00
ATOM    454 2HE2 GLN    32       7.498  -2.492   4.470  1.00  0.00
ATOM    455  C   GLN    32      12.121  -0.985   4.352  1.00  0.00
ATOM    456  O   GLN    32      13.140  -1.597   4.727  1.00  0.00
ATOM    457  N   ARG    33      11.730   0.218   4.704  1.00  0.00
ATOM    458  H   ARG    33      11.076   0.702   4.113  1.00  0.00
ATOM    459  CA  ARG    33      12.257   0.921   5.875  1.00  0.00
ATOM    460  CB  ARG    33      12.550   2.407   5.553  1.00  0.00
ATOM    461  CG  ARG    33      13.684   2.588   4.541  1.00  0.00
ATOM    462  CD  ARG    33      14.948   1.790   4.946  1.00  0.00
ATOM    463  NE  ARG    33      16.029   1.979   3.876  1.00  0.00
ATOM    464  HE  ARG    33      15.892   1.853   2.906  1.00  0.00
ATOM    465  CZ  ARG    33      17.244   2.312   4.201  1.00  0.00
ATOM    466  NH1 ARG    33      17.581   2.441   5.465  1.00  0.00
ATOM    467 1HH1 ARG    33      16.900   2.328   6.258  1.00  0.00
ATOM    468 2HH1 ARG    33      18.555   2.565   5.705  1.00  0.00
ATOM    469  NH2 ARG    33      18.274   2.391   3.287  1.00  0.00
ATOM    470 1HH2 ARG    33      18.140   2.153   2.350  1.00  0.00
ATOM    471 2HH2 ARG    33      19.211   2.753   3.544  1.00  0.00
ATOM    472  C   ARG    33      11.248   0.770   7.122  1.00  0.00
ATOM    473  O   ARG    33      11.074   1.734   7.830  1.00  0.00
ATOM    474  N   TYR    34      10.681  -0.407   7.349  1.00  0.00
ATOM    475  H   TYR    34      10.817  -1.177   6.709  1.00  0.00
ATOM    476  CA  TYR    34       9.665  -0.704   8.380  1.00  0.00
ATOM    477  CB  TYR    34       8.329   0.063   8.204  1.00  0.00
ATOM    478  CG  TYR    34       7.326  -0.353   7.095  1.00  0.00
ATOM    479  CD1 TYR    34       7.571   0.075   5.771  1.00  0.00
ATOM    480  HD1 TYR    34       8.427   0.679   5.601  1.00  0.00
ATOM    481  CD2 TYR    34       6.222  -1.112   7.406  1.00  0.00
ATOM    482  HD2 TYR    34       5.965  -1.274   8.471  1.00  0.00
ATOM    483  CE1 TYR    34       6.707  -0.282   4.736  1.00  0.00
ATOM    484  HE1 TYR    34       6.919  -0.022   3.740  1.00  0.00
ATOM    485  CE2 TYR    34       5.354  -1.521   6.385  1.00  0.00
ATOM    486  HE2 TYR    34       4.437  -1.966   6.745  1.00  0.00
ATOM    487  CZ  TYR    34       5.649  -1.163   5.039  1.00  0.00
ATOM    488  OH  TYR    34       5.084  -1.863   4.015  1.00  0.00
ATOM    489  HH  TYR    34       4.206  -2.028   4.442  1.00  0.00
ATOM    490  C   TYR    34       9.412  -2.231   8.434  1.00  0.00
ATOM    491  O1  TYR    34       9.192  -2.876   9.471  1.00  0.00
ATOM    492  O2  TYR    34       9.663  -2.839   7.407  1.00  0.00
```

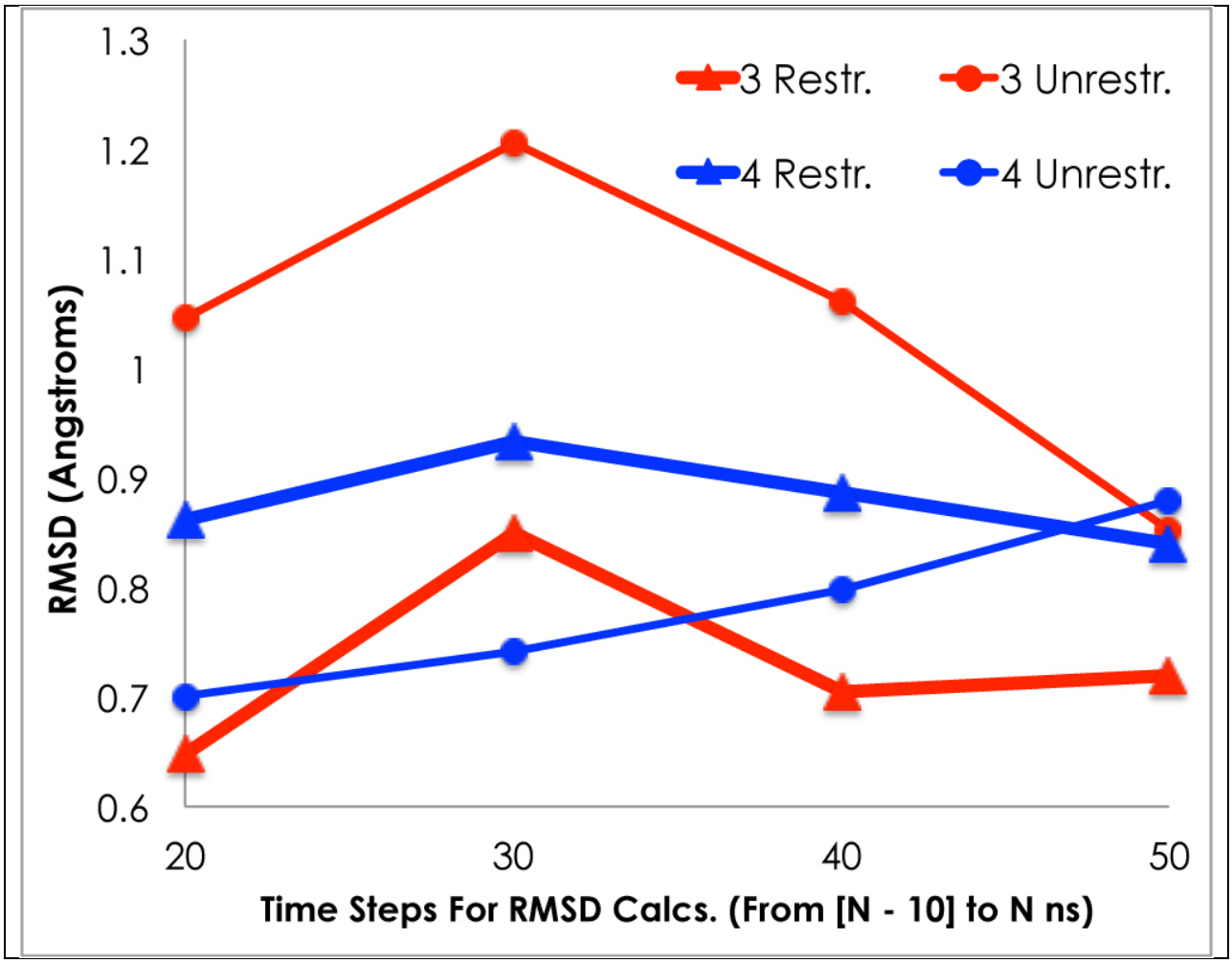

Figure S20. RMSD values for the four simulations, sampling geometries across 10 ns intervals (the 20 ns RMSD values generated from RMSD calculations of structures from 10 to 20 ns, etc.).

8. Molecular Dynamics Simulations: Experimental Details

The GROMOS96[2] (53a6) united-atom force field was used both as the force field set for the defined amino acids and as the basis force field for B_{12}-tether-lysine residues. All simulations were performed as NPT ensembles (X,Y,Z) under periodic boundary conditions. Simulation temperatures were kept constant at 300 K using program option v-rescale thermostats[3] with 0.1 ps coupling time constants for solvent (flexible Simple Point Charge (SPC) water model + neutralizing counter-ions) and solute separately. Simulation pressures were kept constant using

program-option Parrinello-Rahman barostats of 1.0 bar with isotropic coupling (scaling of the pac cell vectors) and a time coupling constant of 2.0 ps.[4] Electrostatic interactions were evaluated by the particle mesh Ewald (PME) method order 4 with a grid spacing of 0.2 nm in the X,Y,Z-directions.[5] The real-space and neighbor-search cut-off were set to 1.0 nm, with non-bonded pair lists updated every 10 steps. MD simulations for all systems were performed with 1.0 fs timesteps for 100 ns.

Parameter generation, topology definitions, and structural data for B_{12}-[tether]-(LYS) residues are an amalgam of quantum chemical, crystallographic, and pre-existing G53a6 force field data, with the majority of the B_{12} terms coming from two previous studies.[6,7] The base structure and heavy atom labeling scheme for the B_{12} topology definition are taken from the human Cbl/TCII crystal structure (PDB 2BB5)[8] as reported in a previous study outlining the parameter generation approach.[7] The geometries and derived charges for the B_{12}-tether structures were generated at a B3LYP[9,10] level of theory with the 6-31G(d) basis set[11] using the program Gaussian09.[12] Averaged geometries for all of the B_{12}-tether-LYS structures are provided as Supplemental Material. All images were rendered with VMD.[13]

9. Tables of NMR Constraints And Distances From The Time-Averaged Simulation of 3

Table S2. Intra-residue NMR Distance Constraints and the Corresponding Simulation Distances

NMR constraints					MD Simulation Distances For **3**			
H1	H2	lower	upper					methyl ave
A12NH	A12me	1.8	3.5		3.23	2.78	3.85	3.29
A12NH	A12Ha	1.8	6		2.78	3.23	3.85	3.29
A22NH	A22Ha	1.8	4.5		2.74			
A22NH	A22me	1.8	3.5		2.43	2.27	3.44	2.71
A7NH	A7Ha	1.8	6		2.92			
A7NH	A7me	1.8	4.5		2.48	3.6	2.6	2.89
D11NH	D11Ha	1.8	3.5		2.94			
D11NH	D11Hb1	1.8	4.5		3.14			
D11NH	D11Hb2	1.8	4.5		2.79			
E10NH	E10Ha	1.8	4.5		2.87			
E15NH	E15Ha	1.8	3.5		2.87			
E15NH	E15Hg	1.8	4.5		2.72	4.01		
E15NH	E15Hb1	1.8	3.5		2.57			
E15NH	E16NH	1.8	3.5		2.51			
E16NH	E16Ha	1.8	3.5		2.83			
E16NH	E16Hg	1.8	4.5		3.46			
E16NH	E16Hb	1.8	4.5		3.44			
G9NH	G9Ha2	1.8	3.5		2.99			
G9NH	G9Ha1	1.8	3.5		2.57			
H26NH	H26Ha	1.8	3.5		2.82			
H26NH	H26Hb	1.8	4.5		2.5	2.27		
K4NH	K4Hb	1.8	6		2.74			
K4NH	K4H	1.8	6		2.36			
L17NH	L17Hb1	1.8	3.5		1.81	3.07		
L17NH	L17Hb2	1.8	3.5		1.81	3.07		
L28NH	L28Hb1	1.8	4.5		2.51	3.72		
L30NH	L30Ha	1.8	4.5		2.79			
L30NH	N29Hb	1.8	4.5		2.5	3.46		
L30NH	L30Hg	1.8	4.5		2.6			
L30NH	L30Hb	1.8	4.5		2.25	3.54		
L30NH	L30me	1.8	6		3.51	4.76	4.36	4.21
N18NH	N18Ha	1.8	3.5		2.73			
N18NH	N18Hb	1.8	4.5		2.95	3.65		
N18NH	L17Hb1	1.8	4.5		2.67	3.43		
N18NH	L17Hb2	1.8	4.5		2.67	3.43		
N18NH	L17me	1.8	6		4.85	4.86	6.11	5.27
N18NH	R19NH	1.8	3.5		3.02			
N29NH	N29Ha	1.8	3.5		2.85			
N29NH	N29Hb	1.8	3.5		2.07	2.98		
Q34NH	Q34Hb	1.8	4.5		3.18	4.03		
R19NH	R19Ha	1.8	3.5		2.78			
R35NH	R35Hb	1.8	4.5		2.22	3.54		
S13NH	S13Hb2	1.8	4.5		3.69			
S13NH	S13Ha	1.8	3.5		2.81			
S23NH	S23Ha	1.8	4.5		2.85			
S23NH	S23Hb2	1.8	4.5		2.64			
S23NH	S23Hb1	1.8	4.5		2.81			
T32NH	T32me	1.8	6		4.57	4.38	4.82	4.59
V31NH	V31Ha	1.8	3.5		2.99			
V31NH	V31Hb	1.8	3.5		2.6			
V31NH	V31me	1.8	4.5		2.18	3.45	3.64	3.09

Y20NH	Y20Ha	1.8	3.5		2.8			
Y20NH	Y20Hb1	1.8	3.5		2.54			
Y20NH	Y20Hb2	1.8	3.5		2.3			
Y21NH	Y21Ha	1.8	4.5		2.78			

Y21NH	Y21Hb1	1.8	4.5		3.77			
Y21NH	Y21Hb2	1.8	3.5		2.68			
Y27NH	Y27Ha	1.8	4.5		2.9			
Y27NH	Y27Hb	1.8	3.5		1.95	3.33		
Y36NH	Y36Ha	1.8	4.5		2.89			
Y36NH	R35Ha	1.8	3.5		2.35			
Y36NH	Y36Hb1	1.8	4.5		3.66			
Y36NH	Y36Hb2	1.8	4.5		3.77			
N29Hd1	N29Hb	1.8	6		2.32	3.44		
N18Hd1	N18Hb	1.8	6		3.67	2.93		
Y21Hd	Y21Hb1	1.8	3.5		2.29			
N18Hd2	N18Hb	1.8	6		2.93	2.39		
N29Hd2	N29Hb	1.8	6		2.32	3.26		
Y21He	Y21Hb2	1.8	6		4.7			
Y21He	Y21Hb1	1.8	6		5.48			
Y21Hd	Y21Ha	1.8	3.5		2.32			
Y21He	Y21Ha	1.8	6		4.1			
Y27he	Y27Ha	1.8	6		4.9			
Y20Hd	Y20Ha	1.8	3.5		2.53			
Y20He	Y20Ha	1.8	6		5.61	4.84		
Y20He	Y21Ha	1.8	6		3.97			
Y20Hd	Y20Hb1	1.8	3.5		2.42			
Y20Hd	Y20Hb2	1.8	3.5		2.77			
Y20He	Y20Hb2	1.8	6		4.7			
Y20He	Y20Hb1	1.8	6		4.78			
I3Ha	I3me	1.8	4.5		3.01	2.46	3.69	3.05
I3Ha	I3Hb	1.8	3.5		3.04			
L17Ha	L17Hg	1.8	3.5		2.41			
A22Ha	A22me	1.8	3.5		2.37	2.51	3.01	
P5Hd	P5Hd	1.8	3.5		1.79			
H26Ha	H26Hb	1.8	3.5		2.42	3.05		
Y36Ha	Y36Hb	1.8	3.5		2.58	2.28		
Y20Ha	Y20Hb1	1.8	3.5		2.96			
Y27Ha	Y27Hb	1.8	3.5		2.77	2.95		
Y20Ha	Y20Hb2	1.8	3.5		2.28			
Y21Ha	Y21Hb	1.8	3.5		2.91			
Y21Ha	Y21Hb	1.8	3.5		2.45			
N29Ha	N29Hb	1.8	3.5		2.71	2.99		
N18Ha	N18Hb	1.8	3.5		2.29	2.98		
E15Ha	E15Hg	1.8	3.5		2.84	2.82		
D11Ha	D11Hb	1.8	3.5		2.46	3.01		
E6Ha	E6Hg	1.8	3.5		2.55	2.53		
P5Ha	P5Hb	1.8	3.5		2.32	3.02		
P14Hg	P14Hd	1.8	3.5		2.43	2.46		
P14Hg	P14Ha	1.8	4.5		2.77	3.82		
P5Hd	P5Hg	1.8	3.5		2.72	2.35		
P5Hd	P5Hg	1.8	3.5		2.35	3.03		
P5Ha	P5Hg	1.8	3.5		3.01			
E15Ha	E15Hb	1.8	3.5		2.46	3.02		
V31Ha	V31Hb	1.8	3.5		2.46			
L30Ha	L30Hb	1.8	3.5		2.62	2.99		
A12Ha	A12me	1.8	3.5		2.46	2.43	3.03	2.64
A7Ha	A7me	1.8	3.5		2.43	3.03	2.48	2.65
I3me	I3Hb	1.8	3.5		3.03	2.47	2.44	2.65
V31me	V31Hb	1.8	3.5		2.38	3.02	2.47	2.62
L24Hb	L24me	1.8	4.5		3.18	2.52	3.7	3.13
L24Hg	L28Hg	1.8	4.5		3.66			
L30Ha	L30me	1.8	4.5		2.32	2.31	3.61	2.75

Table S3. Inter-residue NMR Distance Constraints and the Corresponding Simulation Distance

NMR constraints					MD Simulation Distances For **3**			
H1	H2	lower	upper					methyl ave
A12NH	D11Ha	1.8	4.5		3.82			
A22NH	Y21Ha	1.8	4.5		3.63			
A7NH	E6Hg	1.8	4.5		4.2			
A7NH	E6Hb	1.8	4.5		3.75			
D11NH	E10Ha	1.8	4.5		3.51			
D11NH	E10Hb	1.8	6		4.18			
D11NH	A12NH	1.8	3.5		2.49			
D11NH	E10NH	1.8	3.5		1.79			
E10NH	G9Ha2	1.8	4.5		2.41			
E15NH	P14Hd	1.8	4.5		3.06	4.25		
E15NH	A12me	1.8	6		3.23	4.73	3.35	3.77
E16NH	E15Hb1	1.8	6		3.89			
E16NH	E15Hb2	1.8	4.5		3.03			
E16NH	L17NH	1.8	3.5		3			
E16NH	E15Ha	1.8	4.5		3.58			
E6NH	P5Ha	1.8	3.5		2.59			
G9NH	P8Ha	1.8	3.5		2.74			
H26NH	R25Ha	1.8	3.5		3.45			
H26NH	R25Hb	1.8	4.5		2.7	3.61		
H26NH	Y27NH	1.8	3.5		2.89			
K4NH	I3Ha	1.8	3.5		2.4			
K4NH	I3Hb	1.8	6		4.42			
L17NH	S13Ha	1.8	6		3.41			
L17NH	E16Hb	1.8	4.5		2.86	3.71		
L28NH	Y27Hb	1.8	4.5		3.11	3.01		
L30NH	N29Ha	1.8	4.5		3.59			
N29NH	L28Hb	1.8	3.5		2.64			
N29NH	L28Hb	1.8	4.5		2.98			
N29NH	L28NH	1.8	4.5		3.34			
Q34NH	R33Hd	1.8	4.5		2.96			
R19NH	N18Ha	1.8	4.5		3.48			
R19NH	N18Hb	1.8	4.5		3.01	4.05		
S13NH	E16Hb	1.8	6		4.68			
S13NH	A12me	1.8	4.5		3.51	4.4	4.31	4.07
S23NH	A22me	1.8	4.5		3.36	2.45	3.86	3.22
T32NH	L28Hb	1.8	6		4.52	5.65		
V31NH	L30Hb	1.8	4.5					
V31NH	L30H	1.8	6					
Y21NH	N18Ha	1.8	6		2.94			
Y21NH	Y20NH	1.8	3.5		3.11			

Y27NH	H26Ha	1.8	6		3.68			
Y27NH	H26Hb	1.8	4.5		2.47	3.91		
Y36NH	R35Ha	1.8	3.5		2.35			
A12me	E15Hb	1.8	4.5		2.7	3.59	4.27	3.52
A7me	Y20Hb2	1.8	4.5		4.29	5.02	5.88	5.06
E15Ha	N18Hb	1.8	4.5		3.14			
E15Ha	N18Hb	1.8	3.5		3.14			
G9Ha	B12-56	1.8	4.5		4.14			
H26Hb	S23Hb1	1.8	6		4.95			
H26Hb	S23Hb2	1.8	6		5.28			
L17Ha	Y20Hb2	1.8	4.5		2.58			
L17Ha	Y20Hb1	1.8	4.5		3.75			
L17Ha	Y20Hb1	1.8	4.5		3.75			
L17Ha	Y20Hb2	1.8	4.5		2.58			
P14Ha	L17me	1.8	4.5		3.32	3.96	5	4.09
P8Hd	A7Ha	1.8	3.5		1.92			
P8Hg	Y20Hb	1.8	3.5		3.08			
P8Hg	Y20Hb2	1.8	3.5		3.01			
S23Ha	H26Hb	1.8	6		3.73	2.6		
Y20Hd	L17me	1.8	4.5		3.39	3.81	3.64	3.61
Y20Hd	P5Hg	1.8	4.5		3.78			
Y20Hd	Y21Ha	1.8	6		4.11			
Y20Hd	S23Hb2	1.8	6		3.86	5.34		
Y20He	P5Hg	1.8	4.5		2.02			
Y20He	A7me	1.8	6		4.9	4.17		
Y20He	L17me	1.8	6		4.42	5.37	5.03	4.94
Y20He	Y21He	1.8	6		2.72			
Y21Hd	N18Hb	1.8	6		4.79			
Y21Hd	N18Ha	1.8	4.5		3			
Y21HE	L17me	1.8	3.5		3	2.03	3.04	2.69
Y21He	L17me	1.8	6		4.95			
Y21He	N18Ha	1.8	6		5.26			
Y27Hd	H26Hb	1.8	6		3.42			
Y27He	S23Hb1	1.8	6		4.82			

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