Supplemental Material

for

Design of an Active Ultra-Stable Single-Chain Insulin Analog. SYNTHESIS, STRUCTURE, AND THERAPEUTIC IMPLICATIONS

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Purpose of Supplement

This supplement describes our synthetic methods in detail and contains five additional figures and six archival tables. In Figure S1 are shown 1D ¹H-NMR spectra of SCI-57, 2CA, and the well-characterized engineered insulin monomer DKP-insulin. Figure S2 contains representative 2D-NMR spectra of SCI-57 and 2CA under two conditions (pD 7.6 at 32 °C and pD 7.0 at 25 °C). In Figure S3 are shown initial TOCSY spectra of SCI-57 and 2CA, obtained just after dissolving the proteins in 80% D₂O and 20% deuterioacetic acid; the two spectra exhibit similar patterns of protected amide resonances. Summaries of sequential assignment for SCI-57 and 2CA are provided in Figures S4 and S5. The six supplemental tables provide a summary of selected NMR NOEs (Tables S1 and S2), resonance assignments and chemical shifts (Tables S3 and S4), differences in chemical shifts between SCI-57 and 2CA (Table S5), and restraint information and statistical parameters related to the DG/RMD structure of SCI-57.

Experimental Procedures

Materials. Human insulin was provided by Novo-Nordisk (Copenhagen, DK). 9-Fluorenylmethoxycarbonyl (Fmoc) amino acids were obtained from AnaSpec, Inc. (San Jose, CA) and Novabiochem (Darmstadt, Germany); 1,2-diisopropycarbodiimide and N-hydroxybenzotriazole (recrystallized from 95% ethanol) were obtained from Sigma-Aldrich (St. Louis, MO). Chromatography resins were pre-swollen microgranular carboxymethylcellulose (CM-cellulose; CM52), diethylaminoethyl-cellulose (DE53; both from Whatman, Clifton, NJ) and Cellex E (Ecteola cellulose; Sigma-Aldrich, St. Louis, MO). Columns for reverse-phase (rp) high-performance liquid chromatography (HPLC) were semi-preparative C4 and C8 (dimensions 2.2 x 25 cm; Vydac, Inc., Hesperia, CA) and analytical C18 (dimensions 0.5 x 25 cm; Vydac). Solvents were HPLC grade.

Synthesis of Insulin Chains. To obtain the two-chain control analog 2CA, its component A- and B-chains (21 and 30 residues, respectively) were individually prepared by the solid-phase method using an automated peptide synthesizer (Omega model 396, Advanced Chem Tech, Louisville, KY) using Fmoc chemistry with standard sidechain protecting groups. Syntheses were performed by coupling amino-acid esters of 1-hydroxybenzotriazole (HOBt) using 1,3 diisopropylcarbodiimide (DIPC) as coupling agent. A three- or six-fold excess of N^{α} -Fmoc amino-acid esters of HOBt in N,N-dimethylformamide (DMF) was employed at each step with a 1:1 ratio of amino acid to DIPC. Deprotection of the Fmoc group was effected by 25% piperidine in DMF twice (5 min and 25 min). After completion of the syntheses, the peptides were cleaved from the solid support and de-protected using a modified reagent K® cocktail consisting of 88% trifluroacetic acid (TFA), 3% thioanisole, 5% ethanedithiole, 2% water and 2% phenol. The cleavage cocktail (4 ml) was added to the dried peptide-resins in a 15-ml glass vial blanketed with nitrogen; cleavage was carried out for 2.5 hrs with gentle magnetic stirring. Following cleavage, the mixture was filtered on a Quick-Snap column (IsoLabs Inc., Akron, OH). The filtrate was collected in 20-ml ice-cold butane ether. The peptides were allowed to precipitate for an hour at -20 °C, centrifuged, and washed twice with ice-cold methyl-tert-butyl ether. The precipitate was dissolved in 25% acetonitrile and lyophilized. The crude peptides were analyzed by analytical rp-HPLC (Beckman, System Gold HPLC) and mass spectrometry (MS) as determined by matrix-assisted laser-desorption ionization time-of-flight (MALDI-TOF; Applied Biosystem model 4800; Foster City, CA). Sulfitolysis of the crude peptides was in each case accomplished by dissolving the material (typically 100-300 mg) in 25 ml of a buffer consisting of 0.1 M 2amino-2-hydroxymethyl-1,3-propanediol (Tris·HCl; pH 8.8), 8 M guanidine hydrochloride to which was added 500 mg of sodium tetrathionate dihydrate ($Na_2O_6S_4$) and 750 mg of anhydrous sodium sulfite (Na_2SO_3). The solution was allowed to react for 3.5 hr at room temperature, dialyzed against distilled deionized water (ddH₂O) for 24 hours, and lyophilized.

 His^{A8} -A-chain Analog. Fmoc-Asn(Trt) Wang resin; (Novabiochem, Gibbstown, NJ) was used as solid support. After deblocking and sulfitolysis, the S-sulfonated chain was purified by chromatography on a Cellex E column (1.5 x 47 cm) equilibrated with 0.1 M Tris·HCl (pH 7.0). After application of the crude A-chain and an initial wash with 100 mL of the above buffer, elution was carried out with a linear NaCl gradient (from 0-1M) using 0.1

M Tris-HCl (250 mL) and 1 M NaCl in the above buffer (250 mL). The eluted sulfonated A-chain was dialyzed against ddH_2O and lyophilized. 61 mg of the A-chain analog were obtained from 143 mg of the crude S-sulfonated material.

 $[Asp^{B10}, Asp^{B28}, Pro^{B29}]$ -B-chain Analog. Fmoc-L-Thr (tBu-protected) Wang resin (AnaSpec Inc., San Jose, CA) was used as solid support. After deblocking and sulfitolysis, the crude S-sulfonated B-chain analog was purified by chromatography on a cellulose DE52 column (1.5 cm x 47 cm) equilibrated with 0.1 M Tris·HCl (pH 7.5). Elution was carried out with a linear NaCl gradient formed by adding to the above buffer (250 ml) 0.8 M NaCl in the same buffer (250 ml). The effluent corresponding to the major peak was collected, dialyzed against ddH₂O (four changes over 24 hrs) and lyophilized. 117 mg of the B-chain analog were obtained from 124 mg of the crude S-sulfonated material.

Synthesis of [His^{A8}, *Asp*^{B10}, *Asp*^{B28}, *Pro*^{B29}]-*Insulin*. To obtain 2CA, chain combination (1) was effected by interaction of the S-sulfonated derivative of the A-chain analog (30 mg) and B-chain analog (15 mg) in 0.1 M glycine buffer (pH 10.6, 10 ml) in the presence of dithiothreitol (5.2 mg) as described (2,3). CM-52 cellulose chromatography of each combination mixture enabled partial isolation of the hydrochloride form of the protein contaminated by free B-chain (combined weight 4.3 mg). Final purification was accomplished by C18 rp-HPLC, yielding 2.8 mg of the insulin analog. Re-chromatography by analytical rp-HPLC gave a single peak; its predicted molecular mass (5808.5 Da) was verified (5807.6 Da) by MALDI-TOF MS. The overall yield of 2CA was similar to that obtained in control syntheses of wild-type human insulin.

Synthesis of single-chain insulin analog. SCI-57 was synthesized by native chemical ligation (4) of three peptides: segment I (B1-B6; polypeptide residues 1-6), segment II (B7-A6; polypeptide residues 7-42), and segment III (A7-A21; polypeptide residues 43-57). Segments III and II were first ligated; their product was then ligated to segment I to yield the reduced and unfolded 57-residue polypeptide. This synthetic scheme, exploiting cysteines at positions B7 and A7 as ligation sites, thus employs peptides of nominal lengths 6, 36, and 15 residues exclusive of C-terminal thioester extensions (segments I and II; see below). Assembly of peptide segments I and II employed t-Boc chemistry and an *in situ* neutralization protocol as described (5); peptide III was assembled by Fmoc chemistry on polyethylene glycol-polystylene graft polymer (PEG-PS). Each segment was synthesized by a manual solid-phase protocol as described in turn below. Analyses of purity by rp-HPLC (C4 or C18, 2.1 x 50 mm, Microsorb, packed in-house) from Varian, (Palo Alto, CA) and subsequent verification of peptide masses were performed using an Agilent 1100 liquid chromatography/mass spectrometry (LC/MS) system. Preparative HPLC was performed using C4 or C8 columns (1.0 x 25 cm or 2.2 x 25 cm) from Vydac Inc. (Hesperia, CA).

Synthesis of Segment I. Segment I was synthesized as a thioester containing a C-terminal 3-mercaptopropionyl-Leu (BMp-Leu) extension. The synthesis was started from t-Boc-Leu-phenylacetamido-methyl (PAM) resin (0.66 g; 0.5 mmol; Applied Biosystems; Foster City, CA), and the peptide chain was extended stepwise to the Nterminal residue. The Boc group was treated with neat TFA 3 times (each for 1 min), washed twice with DMF, and condensed with S-trityl-BMp (0.75 mmol) dissolved in 0.5M 2-(1H-benzotriazole-1-yl)-1,1,3,3tetramethyluronium hexafluoro-phosphate (HBTU/DMF; 0.675 mmol) and diisopropylethylamine (DIEA; 1.5 mmol). After 20 min with occasional mixing, the solvent was drained, and the resin was washed once with DMF. To remove the S-trityl group, a mixture of TFA/water/triisopropyl silane (95:2.5:2.5 v/v/v) was applied 3 times (each for 1 min) followed by 2 washes with DMF. The next Boc-amino acid (2 mmol), activated with 0.5 M-HBTU (1.9 mmol) and DIEA (2.6 mmol; prepared 1 min before addition), was then added. After 30 min, another portion of DIEA (2.6 mmol) was added and the mixture was left for another 30 min. Removal of the Boc group by neat TFA and subsequent coupling reactions were repeated until the last residue, but the coupling reaction time was reduced to 10 min. The N-terminal Boc group was removed, and the peptidyl resin (dried from dichloromethane; DCM) was treated with anhydrous hydrofluoric acid (HF), with 10% p-cresole (v/v) added as scavenger, at 0 °C for 60 min. HF was evaporated in vacuo, and the residue was washed 4 times with diethyl ether. The peptide was extracted with a mixture of acetonitrile/water/TFA (50:50:0.1 v/v/v) and freeze-dried (wt 465 mg). A portion of crude peptide (150 mg) was purified by preparative C8 rp-HPLC in a solvent system of water with 0.1% TFA (solvent A) and acetonitrile with 0.08% TFA (solvent B). A linear elution gradient (10-35%, solvent B) was applied over 50 min at the flow rate of 10 ml/min with optical detection of peptide bonds at 215 nm. Purified segment I thus obtained was 73 mg (over-all yield, 47%). MS gave a single compound with molecular mass 958.0 Da (calculated 958.2 Da).

Synthesis of Segment II. Boc-Gly-OCH₂-Pam resin (0.64g; 0.5 mmol) was used for the synthesis of segment II, a β Mp-thioester containing C-terminal extension Arg-Arg-Gly. This charged moiety enhanced the solubility of the segment prior to its ligation. The N-terminal amino acid of segment II (Cys^{B7}) was protected as 1,3-thiazolidine-4-carboxylic acid (thioproline; Thz) as described (6,7). The peptide chain was elongated as above to the N-terminal Thz and cleaved by anhydrous HF (crude weight 544 mg). A portion (136 mg) was purified by preparative rp-HPLC using a C4 column in a solvent system of A/B (see above) from 20-35% solvent B in 45 min at the flow rate of 10 ml/min. The yield of purified peptide was 29.7 mg (16.4% relative to the starting Gly-OCH₂-Pam resin). MS gave an observed molecular mass (4335.9 Da) similar to that predicted (4335.96 Da).

Synthesis of Segment III. Fmoc-Asn(trityl)-PEG-PS resin (0.5 mmol, 2.94 g; PerSeptive Biosystems, Framingham, MA), solvated in DMF, was treated with 20% piperidine in DMF for 20 min. After 3 DMF washings, the next Fmoc-amino acid (2 mmol) was activated with 0.5 M HBTU/DMF (3.8 ml), and DIEA (0.35 ml; 2 mmol) was added. The mixture was allowed to react for 20 min. An aliquot was tested for negative ninhydrin reaction prior to the subsequent step. After 3 washes with DMF, the same procedure was repeated at each cycle. The completed peptide on resin was dried from DCM after removal of the final Fmoc group (resin weight 2.12 g). A portion (1.09 g) was stirred with a cleavage mixture of 95% TFA, 2.5% water, and 2.5% ethanedithiol (v/v/v) (8 ml) at 0 °C for 5 min and then at room temp for 2 hr. The reaction mixture was filtered into diethyl ether (140 ml); the peptide precipitate was separated by centrifugation and washed twice more with diethyl ether. After drying in vacuo, 190 mg of crude segment III was obtained. This material was purified by preparative rp-HPLC using a C4 column at the flow rate of 10 ml/min; the linear gradient used was 10-25% (solvent B) over 45 min. Segment III thus obtained was 70 mg (overall yield 31.3%). MS demonstrated that the observed molecular mass (1789.3 Da) was in accord the predicted molecular mass (1790.02 Da).

Synthesis of SCI (1-57) by Native Chemical Ligation. Segment II, as a C-terminal-extended thioester ((Thz⁷-42)βMp-RRG; 18.5 mg (4 μmoles)), segment III (an unmodified peptide, 7.7 mg (4 μmol)), and tris-(2carboxyethyl)-phosphine hydrochloride (TCEP·HCl; 12 mg (0.04 mmole)) were dissolved in 1.8 ml of a ligation buffer consisting of 0.1 M sodium phosphate (pH 6.9) and 6 M guanidine HCl. After dissolution, the pH of the solution was re-adjusted to 7.0 with 2 M sodium hydroxide (NaOH), and an aliquot of ligation buffer was added to a final volume of 2.0 ml. Argon was flushed through the solution for 1 min, and thiophenol (10 μ l, 0.5% v/v) was added. The solution was tightly capped, stirred vigorously until the mixture became cloudy, placed on a shaker, and gently mixed at room temperature. After 8 hrs, additional aliquots of segment II (2 mg) and thiophenol (5 µl) were added, and the pH of the mixture was re-adjusted to 7.0. After 12 hrs, CH₃ONH₂·HCl (49 mg) was added to a final concentration of 0.2 M (6,7) and the solution was kept for 9 hrs. The reaction mixture was transferred to a dialysis tube (Spectra/Por membrane with molecular-weight cut-off 1,000 Da; Fisher Scientific, Pittsburg, PA) and dialyzed against water (1 L x 5) for 1 day at room temperature. The dialyzed mixture containing precipitates was lyophilized. The dried powder was dissolved in the same ligation buffer (2 ml) and mixed with thioester peptide segment I ((1-6)- β Mp-Leu; 4.2 mg (4.3 μ mol)) and TCEP·HCl (17.2 mg); the pH was re-adjusted to 6.9; argon was flushed, and thiophenol (15 µl) was added (total volume, 3ml). After 20 hr, additional segment I (3.2 mg) was added; the pH was re-adjusted to 6.9, and additional thiophenol (5 µl) was added. The reaction was continued for 8 more hrs, yielding a clear solution.

Redox-Coupled Protein Folding. To the above solution was added an oxidation-reduction-coupled (redox) buffer (0.4 ml) consisting of 100 mM reduced glutathione (GSH) and 10 mM oxidized glutathione (GSSG); the pH was adjusted to 8.6 with 2 N NaOH. This solution was immediately diluted with ddH₂O to 40 ml. Soon after, precipitates appeared, which after 16 hr were centrifuged and separated from the supernatant (*folding mixture 1*).

The precipitate was dissolved in the same ligation buffer containing redox mixture (4 ml); the pH was adjusted to 8.6, and ddH₂O was added to a final volume of 40 ml. Precipitates again appeared, and the mixture was centrifuged to separate the supernatant (*folding mixture 2*). Precipitates were once more dissolved, and the above procedure repeated to generate *folding mixture 3*. Each folding mixture was gently stirred for 1-2 days at room temperature. The extent of folding was periodically monitored by LC/MS. When almost no further folding was observed, the mixture was acidified to pH 2 with 10% TFA, and acetonitrile was added to a final concentration of 10% (v/v). The solutions were subjected to rp-HPLC using a C4 column (1 x 25cm); a gradient elution was applied from 15-35% (solvent B) over 40 min at the flow rate of 4 ml/min. Pure fractions corresponding to SCI-57 were pooled and lyophilized. In total, 6.6 mg was obtained, representing an overall yield of 24.4 % for the 2-step ligation procedure, subsequent folding, and purification. MS of the final product gave an observed molecular mass (6370.8 Da) in accord with the predicted molecular mass (6371.2 Da)

Supplemental Abbreviations

βMp, 3-mercaptopropionyl; Boc, butoxycarbonyl; ddH₂O, distilled de-ionized water; Da, Daltons; DCM, dichloromethane; DIPC, diisopropylcarbodiimide; DIEA, diisopropylethylamine; DMF, N,N-dimethylformamide; Fmoc, fluorenylmethoxycarbonyl; GSH, reduced glutathione; GSSG, oxidized glutathione; HBTU, 1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluoro-phosphate; HOBt, 1-hydroxybenzotriazole; HPLC, high-performance liquid chromatography; kDa, kilo-dalton of mass; LC/MS, liquid chromatography coupled MS; MALDI-TOF, matrix-assisted laser-desorption ionization time-of-flight; MS, mass spectrometry; PAM, phenylacetamido-methyl resin; PEG-PS, polyethylene glycol-polystylene graft polymer; pI, isoelectric point; rp-HPLC, reverse-phase HPLC; TCEP·HCl, tris-(2-carboxyethyl)-phosphine hydrochloride; TFA, trifluroacetic acid; Thz, thiazolidine-4-carboxylic acid (thioproline); and Wang resin, *p*-benzyloxybenzyl alcohol resin.

Supplemental References

- 1. Chance, R. E., Hoffman, J. A., Kroeff, E. P., Johnson, M. G., Schirmer, W. E., and Bormer, W. W. (1981) The production of human insulin using recombinant DNA technology and a new chain recombination procedure. In: Rich, D. H., and Gross, E. (eds). *Peptides: Synthesis, Structure and Function; Proceedings* of the Seventh American Peptide Symposium, Pierce Chemical Co., Rockford, IL
- Hu, S. Q., Burke, G. T., Schwartz, G. P., Ferderigos, N., Ross, J. B., and Katsoyannis, P. G. (1993) Biochemistry 32, 2631-2635
- 3. Hua, Q. X., Hu, S. Q., Frank, B. H., Jia, W., Chu, Y. C., Wang, S. H., Burke, G. T., Katsoyannis, P. G., and Weiss, M. A. (1996) *J. Mol. Biol.* **264**, 390-403
- 4. Dawson, P. E., and Kent, S. B. H. (2000) Annu. Rev. Biochem. 69, 923-960
- 5. Schnolzer, M., Alewood, P., Jones, A., Alewood, D., and Kent, S. B. (1992) Int. J. Pept. Protein Res. 40, 180-193
- 6. Villain, J., Vizzavona, K., and Rose, K. (2001) Chem. Biol. 8, 673-679
- 7. Bang, D., and Kent, S. B. (2004) Angew. Chem. Int. Ed. Engl. 43, 2534-2538

Figure S1. **Comparison of NMR spectra.** 1D ¹H-NMR spectra of SCI-57 (*A*), its two-chain analog 2CA (*B*) and standard engineered monomer DKP-insulin (*C*). Single-chain analog retains favorable line widths and chemical-shift dispersion. Spectra were obtained at 700 MHz in D_2O at pD 7.6 (direct meter reading) and 32 °C.





Figure S2. **2D-NMR studies of SCI-57 and 2CA in D₂O under two conditions.** (*A* and *B*) NMR studies of SCI-57. (*C* and *D*) NMR studies of 2CA. In each panel (boxed) the TOCSY spectrum of the aromatic region is shown at left, and the NOESY spectrum of aromatic-aliphatic contacts is shown at right; TOCSY and NOESY mixing times were 55 and 200 ms, respectively. Spectra in panels *A* and *C* were acquired at pD 7.6 (direct meter reading) and 32 °C whereas spectra in panels *B* and *D* were acquired at pD 7.0 and 25 °C. Selected assignments are as labeled. Corresponding long-range NOEs from the H₈ of His^{A8} to A3 γ 1,2-CH3 are labeled a and b (panels *A* and *C*) or a' and b' (panels *B* and *D*).



Figure S3. **SCI-57 and 2CA exhibit corresponding sites of amide proton protection in D₂O.** TOCSY spectra of SCI-57 (*A*) and its two-chain analog 2CA (*B*) obtained within two hours after sample dissolved in 20% (v/v) deuterioacetic acid at 25 °C. The sample was first dissolved in H₂O and then lyophilized as powder. 1D spectra, obtained within five minutes of initial idssolution in the deuterated solvent, provide evidence for additional sites of subglobal protection, including in each case Cys^{A11} and Leu^{B6} (sites of inter-chain or inter-domain hydrogen bonds in crystallographic T-state protomers, data not shown).



Figure S4. **Summary of sequential assignment in Wuthrich format for SCI-57.** NOE intensities are represented in schematic fashion by line thickness. Open circle indicate site of slowly exchanging amide resonances in D_2O . The residue numbering is 1 - 30 for B-domain (residues B1-B30 in insulin), 31 - 36 for C-domain (C1-C6), and 37 - 57 for A-domain (A1-A21).



Figure S5. Summary of sequential assignment in Wuthrich format for two-chain analog 2CA. NOE intensities and protected amide protons are represented as in Figure S3.

		u = 01 H	
A8 proton	SCI-57	2CA	
A8 H _N	A4 Hα	A4 Hα	
	Α5 Ηα	A5 Hα	
Α8 Ηα	A4 Hα		
		B5 Hα	
Α8 Ηβ	Α4 Ηα	A4 Hα	
	A4 H _Y		
	Α5 Η α, Η β		
A8 H₀	A3 H _Y	A3 H _Y	
	Α4 Ηα, Ηβ	A4 Hα	
	Α5 Η α, Η β		
A8 Hε		A3 H _Y	
		A4 H_{β} , H_{γ}	

Table S1. His^{A8}-related NOEs in SCI-57 and 2CA.

Table S2.NOE comparison between SCI-57 and 2CA

A, Additional NOEs in SCI-57

helix-related NOEs		long-range NOEs	inter-chain NOEs		
A1 HN -	$A4 H_{\beta}$	A6 HN - A10 H_{γ}	Α6 Ηα - Β5 Ηβ		
A1 HN -	Α5 Ηβ	A9 HN - A6 Hα	Α7 Ηα - Β5 Ηβ		
A5 Hn -	A2 Ha	Α11 Ηβ - Α5 Ηβ	A11 Hn - B5 Hα		
A7 Hn -	A4 Ha	B6 Hα - B14 Hβ	A21 HN - B19 Hα		
A15 Hn -	Α12 Ηα	B23 Hn - B19 Hβ	A21 Hn - B19 Hβ		
A15 Hn -	Α12 Ηβ	B4 Hε - A13 H · 1, 2			
A19 HE -	Α15 Ηβ	B8 Hn - A7 Hβ			
A20 Hn -	Α17 Ηα	B14 H α - A13 H · 1, 2			
B11 Hγ -	B15 H \cdot 1, 2	B18 H γ - A16 H · 1, 2			
$B11\ H\cdot$ 1, 2 -	B15 H \cdot 1, 2	B19 Hα - A17 Hα			
B12 HN -	B9 Hα	B25 Hn - A19 Hβ			
B14 Hn -	B10 Hα				
B15 Н• -	B11 H • 1, 2				
B17 Hn -	B14 Hβ				
B. Additional	NOEs in 2CA				

helix-related	NOE	long-ran	ige NOE	inter-ch	ain NOE
none		<u>A3 Hγ2</u>	- Α19 Ηε	A21 Hδ	- B23 Hα

Table S3-A. Chemical shifts of ¹H-NMR resonances of SCI-57 (pH 7.4 and 25 ^oC)

Residue	NH	C-H	<u>с.н</u>	others
Residue R1 Phe	INFI	<u> </u>	<u> </u>	C26H 7 18 C35H 7 31
B2 Val	8 18	4.00	1 02	CvH2 0 70 0 70
B3 Asn	8.62	4.00	2 82 2 73	Cyris 0.79,0.79
B4 Gln	8.37	4.50	2 09 1 93	CvH2 2 20 2 15
B5 His	8 4 5	4.31	3 44 3 04	C2H C4H 6 89
Belou	0.45	4.60	1 75 0 86	CVH 1 66 C8H2 0 74 0 71
B7 Cvs	8.80	4.00	3 20 2 96	C ¥11 1.00, CONS 0.74, 0.71
B8 Glv	0.00	3 98 3 86	0.20, 2.00	
B9 Ser	9 16	3.99	4 02 3 90	
B10 Asp	7.92	4 38	2 99 2 63	
B11 Leu	6.88	3 89	1 83 1 13	СуН 1 22. СбН₃ 0 75. 0 65
B12 Val	6.96	3 12	2 03	$C_VH_3 0.94 0.78$
B13 Glu	7 98	4 04	2 13 2 06	$C_{VH_2} = 2.43 + 2.30$
B14 Ala	7.54	4.02	CBH: 1 34	0 112 2.43, 2.30
B15 Lou	7.04	3.62	1 00 0 07	
B16 Tyr	8 10	J.00 1 33	3 14 3 14	$C_{0.0}H = 7.27$ $C_{0.0}H = 6.82$
B17 Lou	7.64	4.04	1 08 1 37	CVH 1 75 CAH 0 05 0 05
B17 Leu B18 Vol	0.04	4.04	1.90, 1.57	
B10 Val	0.44	3.73	3 26 2 00	Сүпз 0.96, 0.64
B19 Cys	0.00 7.70	4.00	3.20, 2.90	
B20 Gly	0.16	J.90, J.0J 4 16	2 18 2 04	
DZI GIU D22 Ara	9.10	4.10	2.16, 2.04	
BZZ AIY	0.13	4.10	2.10, 2.04	CγΠ2 1.65, C0Π2 5.56, 5.52
B24 Dho	7.31	4.12, 3.03	3 3 2 2 9 7	
B25 Dho	8 50	1.09	3.18	$C_{2,6}$ 10.72, $C_{3,5}$ 10.80, C_{4} 10.85
B26 Tyr	0.50	4.60	2 94 2 94	$C_{2,611}$ 7.25, $C_{3,511}$ 7.51
B27 Thr	8 10	4.00	4.04	CvH2 1 06
B28 Asn	8 50	4.35	2 76 2 61	Cy113 1.00
B20 Pro	0.00	4.70	2 25 1 97	
B20 Thr	8 33	4.32	4 20	
	0.55	4.52	4.29	GY115 1.22
32 Gly				
33 Gly	8 26	4 10		
34 Pro	0.20	4 29	2 10 1 96	
35 Ara	8 37	4.28	1 90 1 82	CVH2 1.66, 1.62, CAH2 3.13, 3.07
36 Arg	0.57	4.20	1.88, 1.68	CVH2 1.68 CAH2 3.19
		4.22	1.00, 1.00	Cyriz 1.00, Coriz 5.15
		3 82	0.96	
	7 09	3.50	1.04	$C_{VH_{2}} = 0.04, 0.66$
	7.90	4.03	2 12 2 13	$C_{VH_{2}} = 2.40, 2.30$
		4.03	2.13, 2.13	Cylla 2 22
	0.00	5.95	2.11	ΟγΗ2 2.32
AU Cys	8.20	1.88	3 78 3 16	
AR Uys	8.00	4.56	3 34 3 20	C2H 6 82 C4H
AQ Ser	7 32	4.50	3 96 3 83	62110.02, 0411
	7.80	4.03	1 52	
	7.00	4.27	1.52	CY112 1.01, 0.22, CY113 0.02, C0113 0.40
A11 Cys	9.98	5.18	3.22	
A12 Ser	8.59	4.62	4.20, 4.02	
	8.75 7.67	3.90	1.44, 1.44	
	1.0/	4.31	3.UZ, Z.98	
A15 GIN	7.49	3.94	2.21, 2.03	CγH2 2.40, 2.34, NEH2 /.5/,/.05
A16 Leu	7.91	4.12	1.98, 1.40	Сүн 1.74, Сонз 0.74, 0.74
A17 Glu	8.12	4.16	2.05, 1.98	СүН2 2.36, 2.19
A18 Asn	7.31	4.46	2.61, 2.52	NδH₂ 7.21, 6.52
A19 Tyr	7.96	4.36	3.32, 2.89	C _{2,6} H 7.26, C _{3,5} H 6.75
A20 Cys	7.37	5.06	3.31, 2.84	
A21 Asn	8.12	4.48	2.80, 2.67	NõH2 7.48, 6.42

<u>Table S3-B.</u>	Chemical shifts of 1	H-NMR resonances of	<u>SCI-57 (20% deuter</u>	ioacetic acid and 25 °C)
Residue	NH	<u>C</u> αH	<u>С</u> β <u>Н</u>	others
B1 Phe		4.31	3.20, 3.20	C _{2, 6} H 7.25, C _{3, 5} H 7.38
B2 Val	8.22	4.14	1.94	СүН₃ 0.88, 0.88
B3 Asn	8.52	4.73	2.76, 2.70	NδH ₂ 7.59, 6.97
B4 Gln	8.43	4.48	2.11, 1.92	CγH ₂ 2.26, 2.20, NεH ₂ 7.35, 6.85
B5 His	8.61	4.58	3.57, 3.27	C2H 8.50, C4H 7.40
B6 Leu	8.82	4.58	1.72, 0.98	СүН 1.60, СठН₃ 0.90, 0.77
B7 Cys	8.37	4.92	3.22, 2.98	
B8 Gly	9.08	4.02, 3.89		
B9 Ser	9.05	4.17	3.97, 3.97	
B10 Asp	8.24	4.52	3.22, 2.86	
B11 Leu	7.12	4.00	1.93, 1.22	СүН 1.34, СठН₃ 0.84, 0.75
B12 Val	7.17	3.30	2.10	СүН₃ 0.95, 0.95
B13 Glu	8.03	4.15	2.20, 2.11	СүН₂ 2.55
B14 Ala	7.80	4.08	CβH₃ 1.48	
B15 Leu	8.02	3.83	1.29, 0.55	СүН 1.45, СठН₃ 0.65, 0.42
B16 Tyr	8.24	4.28	3.16, 3.16	C _{2,6} H 7.16, C _{3,5} H 6.80
B17 Leu	7.98	4.08	1.97, 1.66	СүН 1.90, СठН₃ 0.95, 0.95
B18 Val	8.55	3.86	2.09	CyH₃ 1.04, 0.88
B19 Cys	8.76	4.84	3.26, 2.97	•
B20 Gly	7.77	4.01, 3.89		
B21 Glu	8.70	4.19	2.22, 2.12	CyH₂ 2.56
B22 Arg	8.06	4.22	2.02, 1.83	CyH2 1.80, CδH2 3.32, NεH2 7.14
B23 Gly	7.52	4.07, 3.86		
B24 Phe	7.72	4.94	3.22, 2.97	C _{2,6} H 6.90, C _{3,5} H 7.04, C ₄ H 7.06
B25 Phe	8.41	4.71	3.14, 3.08	C _{2,6} H 7.23, C _{3,5} H 7.28
B26 Tyr	8.03	4.63	2.95, 2.95	C _{2, 6} H 7.07, C _{3, 5} H 6.78
B27 Thr	7.74	4.37	4.16	СүН₃ 1.14
B28 Asp	8.31	4.92	2.96, 2.76	
B29 Pro		4.47	2.27, 2.06	CγH₂ 2.02, CδH₂ 3.84
B30 Thr	7.92	4.40	4.37	CyH3 1.22
31 Gly	8.14	4.06, 4.01		•
32 Gly	8.22	4.03, 4.03		
33 Gly	8.25	4.21, 4.08		
34 Pro		4.47	2.26, 2.00	СүН₂ 1.92, СбН₂ 3.69, 3.63
35 Arg	8.34	4.31	1.94, 1.84	СγН₂ 1.72, 1.64, СδН₂ 3.19, №Н₂ 7.21
36 Arg	8.19	4.32	1.92, 1.85	CγH₂ 1.70, 1.68, CδH₂ 3.22, NεH₂ 7.24
A1 Gly	8.46	4.09, 4.09		
A2 lle	7.83	3.87	1.17	СүН₂ 1.38, 0.82, Сү'Н₃ 0.76, СठН₃ 0.62
A3 Val	7.80	3.59	2.05	СүН₃ 0.96, 0.86
A4 Glu	8.18	4.08	2.14, 2.14	CyH₂ 2.53, 2.53
A5 Gln	8.28	4.09	2.16, 2.12	CγH ₂ 2.49, 2.44, NεH ₂ 7.53,6.94
A6 Cys	8.37	4.94	3.37, 2.91	• • • •
A7 Cys	8.00	4.82	3.73, 3.14	
A8 His	8.13	4.58	3.55, 3.36	C2H 8.70, C4H 7.30
A9 Ser	7.49	4.78	4.14, 3.94	
A10 lle	7.91	4.47	1.63	СүН₂ 1.20, Сү'Н₃ 0.69, СठН₃ 0.57
A11 Cvs	9.69		3.16	
A12 Ser	8.77	4.64	4.34, 4.03	
A13 leu	8.68	3.89	1.40, 1.40	CvH 1.46. CδH₃ 0.85. 0.79
A14 Tyr	7.57	4.18	3.00, 2.93	C _{2,6} H 7.09, C _{3,5} H 6.86
A15 GÍn	7.59	4.00	2.05	CyH2 2.47, 2.40, NEH2 7.55, 7.00
A16 Leu	8.05	4.14	1.96. 1.52	CyH 1.77, CōH₃ 0.88. 0.83
A17 Glu	8.15	4.18	2.14, 2.05	CvH ₂ 2.59, 2.39
A18 Asn	7.46	4.51	2.66, 2.60	NõH2 7.26, 6.53
A19 Tvr	7.95	4.44	3.38, 2.99	C _{2.6} H 7.31, C _{3.5} H 6.80
A20 Cvs	7.42	4.97	3.28, 2.87	<u>e_, arr r.or</u> , <u>e</u> , arr 0.00
A21 Asn	8.27	4.72	2.88, 2.73	NδH ₂ 7.52, 6.57

Table S3-B. Chemical shifts of ¹H-NMR resonances of SCI-57 (20% deuterioacetic acid and 25 ^oC)

Table S4-A. Chemical shifts of ¹H-NMR resonances of 2CA (pH 7.4 and 25^oC)

A1 Gly A2 lie 3.69 0.90 $Cy+b 0.70, 0.59, Cy+b 0.50, C0+b 0.34$ A3 Val 8.34 3.40 1.82 $Cy+b 0.90, 0.60$ A4 Glu 8.46 3.85 2.16 2.16 $Cy+b 2.82, 2.29$ A5 Gln 8.04 4.03 2.07 $Cy+b 2.53, 2.42$ A6 Cys 8.17 4.86 3.81 3.21 A8 His 8.10 4.52 3.81 3.21 A8 His 8.10 4.52 3.81 3.21 A8 His 8.10 4.52 3.81 3.21 A10 lie 7.76 4.38 1.50 $Cy+b 1.05, Cy+b 0.48, C5+b 0.28$ A11 Cys 9.92 A12 Ser 4.61 4.17, 3.99 A13 leu 8.73 3.88 1.44, 1.44 $Cy+h 1.51, C5+b 0.81, 0.76$ A14 Tyr 7.64 4.32 3.02, 2.98 $C_{24}H 7.11, C_{34}H 8.65$ A15 Gln 7.47 3.94 2.21, 2.02 $Cy+b 2.32, 2.34, Nb+7, 57, 7.07$ A16 Leu 7.87 4.11 1.94, 1.44 $Cy+H 1.72, C3+b 0.81, 0.76$ A17 Glu 8.01 4.19 2.04, 1.98 $Cy+b 2.36, 2.21$ A18 Asn 7.30 4.44 2.60, 2.49 Nobt 7.13, 6.54 A19 Tyr 7.96 4.35 3.31, 2.81 A20 Cys 7.32 5.13 3.31, 2.81 A21 Asn 8.13 4.48 2.76, 2.49 Nobt 7.13, 6.54 A19 Tyr 7.96 4.35 3.31, 2.81 A22 Cys 7.32 5.13 3.31, 2.81 A24 Asn 8.13 4.48 2.76, 2.49 Nobt 7.13, 6.54 A19 Tyr 7.96 4.35 3.31, 2.81 A22 Cys 7.32 5.13 3.31, 2.81 A24 Asn 8.57 4.59 2.51, 2.72 B Gln 4.49 1.94, 1.94 Cy+h 2.16, 2.16 B 1 Phe 4.11 1.91 Cy+h 0.83, 0.83 B Cya 7.32 5.13 3.31, 2.81 B Cya 8.84 4.229 3.46, 3.06 C2H 7.24, C3H 7.33 B Cya 8.72 5.00 3.30, 2.39 B Cya 9.75 3.98, 3.86 B Lie 9.12 4.57 7.07 6.44 6.35 B Cym 1.75 4.08 0.040 B Ty Asn 7.55 4.08 0.041, 0.81 0.244 6.32, 0.340, 3.32 B Cyh 9.55 3.98, 3.86 0.91, 0.02 0.944 1.13, 0.084 B Ty Asn 7.55 4.08 0.91, 0.02 0.944 1.13, 0.084 B Ty Asn 7.55 4.08 0.91, 0.02 0.944 1.30, 0.364 B Ty Asn 7.55 4.29 4.08 0.944 0.317, 3.	Residue	NH	<u>С</u> а <u>Н</u>	<u>C</u> βH	others
A2 lie 3.69 0.90 CyHe 0.70, 0.59, CyHe 0.50, C6He 0.34 A3 Val 8.34 3.40 1.82 CyHe 0.70, 0.59, CyHe 0.50, C6He 0.34 A4 Glu 8.46 3.85 2.16, 2.16 CyHe 2.58, 2.29 A5 Gin 8.04 4.03 2.07 CyHe 2.53, 2.42 A6 Cys 8.10 4.52 3.48, 3.31 C2H 6.83, C4H 7.84 A8 His 8.10 4.52 3.48, 3.31 C2H 6.83, C4H 7.84 A9 Ser 7.16 4.71 4.05, 3.87 A11 Cys 9.92	A1 Gly				
A3 Val 8.34 3.40 1.82 CyHb 0.90, 0.60 A4 Glu 8.46 3.85 2.16, 2.16 CyHb 2.53, 2.42 A5 Gin 8.04 4.03 2.07 CyHb 2.53, 2.42 A6 Cys 8.17 4.86 3.81, 3.21 C2H 6.83, C4H 7.84 A9 Ser 7.16 4.71 4.05, 3.87 C2H 6.83, C4H 7.84 A9 Ser 7.16 4.71 4.05, 3.87 C2H 6.83, C4H 7.84 A10 10 7.76 4.38 1.50 CyHb 1.01, 0.65, CyHb 0.48, C6Hb 0.28 A11 QyB 9.92	A2 lle		3.69	0.90	СүН₂ 0.70, 0.59, Сү'Н₃ 0.50, СठН₃ 0.34
A4 Glu 8.46 3.85 2.16, 2.16 CyHz 2.58, 2.29 A5 Gin 3.21, 2.79 CyHz 2.53, 2.42 A6 CyS 8.30 5.01 3.21, 2.79 A7 CyS 8.17 4.86 3.31, 3.21 A8 His 8.10 4.52 3.48, 3.31 C2H 6.83, C4H 7.84 A9 Ser 7.16 4.38 1.50 CyHz 1.01, 0.65, CyHz 0.48, C5Hz 0.28 A11 CyS 9.92	A3 Val	8.34	3.40	1.82	СүН₃ 0.90, 0.60
A5 Gin 8.04 4.03 2.07 $CYH_2 2.53, 2.42$ A6 Cys 8.17 4.86 3.21, 2.79 $CYH_2 2.53, 2.42$ A7 Cys 8.17 4.86 3.81, 3.21 A8 His 8.10 4.52 3.48, 3.31 C2H 6.83, C4H 7.84 A9 Ser 7.16 4.71 4.05, 3.87 A10 lie 7.76 4.38 1.50 C/H 1.01, 0.65, CYH_3.0.48, C5H; 0.28 A11 Cys 9.92 - 4.61 4.17, 3.99 A12 Ser 4.61 4.17, 3.99 - A14 Tyr 7.64 4.32 3.02, 2.98 CxH 7.11, CxH 6.85 A14 Tyr 7.64 4.32 3.02, 2.99 CyH 1.22, 0.241, NEE, 75.7, 07 A16 Leu 7.87 4.11 1.94, 1.44 CyH 1.72, C5H 5.0.77, 071 A17 Giu 8.01 4.19 2.04, 1.98 CyH 2.39, 234, NEE, 75.7, 071 A17 Giu 8.01 4.19 2.04, 1.93 CyH 1.72, C5H 5.0.71, 071 A17 Giu 8.01 4.19 2.04, 2.02 CyH 1.72, C5H 5.0.7, 071 A17 Giu 8.01<	A4 Glu	8.46	3.85	2.16, 2.16	CyH ₂ 2.58, 2.29
A6 Cys 8.30 5.01 3.21, 2.79 A7 Cys 8.17 4.86 3.81, 3.21 A8 His 8.10 4.52 3.48, 3.31 C2H 6.83, C4H 7.84 A9 Ser 7.16 4.38 1.50 CyHz 1.01, 0.65, CyHz 0.48, C5Hz 0.28 A11 Cys 9.92 - - - CyHz 1.01, 0.65, CyHz 0.48, C5Hz 0.28 A13 Isu 8.73 3.88 1.44, 1.44 CyH 1.51, C6Hz 0.81, 0.76 - A13 Isu 8.73 3.88 1.44, 1.44 CyH 1.72, C6Hz 0.77, 0.71 - A16 Leu 7.87 4.11 1.94, 1.44 CyH 1.72, C6Hz 0.77, 0.71 - A17 Glu 8.01 4.19 2.04, 1.98 CyHz 2.39, 2.34, NEHz 7.57, 7.07 - A17 Glu 8.01 4.11 1.94, 1.44 CyH 1.72, C6Hz 0.77, 0.71 - - A17 Glu 8.13 4.44 2.60, 2.49 NöHz 7.34, 6.54 - - A17 Glu 8.13 4.48 2.76, 2.64 NöHz 7.34, 6.26 - - - B1 Phe 4.11 3.12, 3.12	A5 Gln	8.04	4.03	2.07	CvH ₂ 2.53, 2.42
A7 Cys 8.17 4.86 3.81 3.21 A8 His 8.10 4.52 3.48 3.31 C2H 6.83, C4H 7.84 A9 Ser 7.16 4.71 4.05, 3.87 A10 Ile 7.76 4.38 1.50 CyHz 1.01, 0.65, CyHz 0.48, C5Hz 0.28 A11 Cys 9.92 - - - - A12 Ser 4.61 4.17, 3.99 - - - A13 Ieu 8.73 3.88 1.44, 1.44 CyH 1.51, C5Hz 0.81, 0.76 - A14 Tyr 7.64 4.32 3.02, 2.98 CzaH 7.11, CasH 6.85 - A15 Gin 7.47 3.94 2.21, 2.02 CyHz 2.39, 2.34, NEHz 7.57, 7.07 - A16 Leu 7.87 4.11 1.94, 1.44 CyH 1.72, C6Hz 0.77, 0.71 - - A17 Glu 8.01 4.19 2.04, 1.98 CyHz 2.39, 2.34, NEHz 7.57, 7.07 - A17 Glu 8.01 4.19 2.06, 2.04 NöHz 7.44, 6.26 - - B17 Pre 4.11 3.12, 2.12 CasH 7.32, CasH 7.33, CasH 7.32 -<	A6 Cys	8.30	5.01	3.21, 2.79	•
A8 His 8.10 4.52 3.48, 3.31 C2H 6.83, C4H 7.84 A9 Ser 7.16 4.71 4.05, 3.87 A10 lle 7.76 4.38 1.50 CyH_2 1.01, 0.65, CyH_3 0.48, C5H 5 0.28 A11 Cys 9.92 6.11 4.17, 3.99 A13 leu 8.73 3.88 1.44, 1.44 CyH 1.51, C6H 5 0.81, 0.76 A14 Tyr 7.44 4.32 3.02, 2.98 C2aH 7.11, C3aH 6.85 A15 Gin 7.47 3.94 2.21, 2.02 CyHz 2.39, 2.34, NeH 7.57, 7.07 A16 Leu 7.87 4.11 1.94, 1.44 CyHz 2.36, 2.21 A17 Giu 8.01 4.19 2.04, 1.98 CyHz 2.36, 2.21 A18 Asn 7.30 4.44 2.60, 2.49 N6Hz 7.34, 6.54 A19 Tyr 7.96 4.35 3.31, 2.81 C2H 7.23, 2.34, NeH 3.75, 7.07 A20 Cys 7.32 5.13 3.31, 2.81 C2H 7.31, C3aH 6.76 A21 Asn 8.15 3.44, 2.80 2.46 N5Hz 7.44, 6.26 B1 Phe 4.11 3.12, 3.12 Cys 7.46, 6.26 B1 San	A7 Cys	8.17	4.86	3.81, 3.21	
A9 Ser 7.16 4.71 4.05, 3.87 A10 lie 7.76 4.38 1.50 CyHz 1.01, 0.65, CyHz 0.48, CöHz 0.28 A11 Cys 9.92	A8 His	8.10	4.52	3.48, 3.31	C2H 6.83, C4H 7.84
A10 lie 7.76 4.38 1.50 CyH± 1.01, 0.65, CyH± 0.48, C6H± 0.28 A11 Cys 9.92	A9 Ser	7.16	4.71	4.05, 3.87	
A11 Cys9.92A12 Ser4.614.17, 3.99A13 leu8.733.881.44, 1.44CyH1.75, CoH 0.81, 0.76A14 Tyr7.644.323.02, 2.98Call7.473.942.21, CoH 0.23, 2.34, Neb 7.57, 07A16 Leu7.874.111.94, 1.44CyH 2.23, 2.34, Neb 7.57, 07A17 Glu8.014.192.04, 1.98A17 Glu8.014.192.04, 1.98CyHz 2.36, 2.21A.1442.60, 2.49Nobit; 7.13, 6.54A19 Tyr7.964.353.41, 2.81Call Cys7.325.133.31, 2.81A21 Asn8.134.482.76, 2.64A21 Asn8.134.482.76, 2.64A21 Asn8.134.482.76, 2.64B3 Asn8.574.592.81, 2.72B4 Gln4.491.94, 1.94CyHz 2.16, 2.16B5 His8.444.293.46, 3.06B7 Cys8.725.003.20, 2.92B8 Gly9.553.98, 3.86B9 Ser9.184.183.99, 3.99B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.65Cyth 2.12, Chb 0.60, 0.60CyHz 2.47, 2.31B14 Ala7.554.08CyHz 2.47, 2.31B14 Ala7.553.660.91, 0.02Cyth 1.10, CoHs 0.50, 0.191.91B15 Leu7.953.66D91, 0.02Cyth 1.19, CoHs 0.50, 0.19B16 Tyr8.20	A10 lle	7.76	4.38	1.50	СүН₂ 1.01, 0.65, Сү'Н₃ 0.48, СठН₃ 0.28
A12 Ser 4.61 4.17, 3.99 A13 leu 8.73 3.88 1.44, 1.44 CyH 1.51, C5H: 0.81, 0.76 A14 Tyr 7.64 4.32 3.02, 2.98 Cs.eH 7.11, Cs.eH 6.85 A15 Gin 7.47 3.94 2.21, 2.02 CyHz 2.39, 2.34, Neth 7.57, 7.07 A16 Leu 7.87 4.11 1.94, 1.44 CyH 1.72, C5H 50, 0.77, 0.71 A17 Glu 8.01 4.19 2.04, 1.98 CyHz 2.36, 2.21 A18 Asn 7.30 4.44 2.60, 2.49 NHz 7.31, 6.54 A19 Tyr 7.96 4.35 3.41, 2.81 Cs.eH 7.31, Cs.eH 6.76 A20 Cys 7.32 5.13 3.31, 2.81 Cs.eH 7.22, Cs.eH 7.33 A21 Asn 8.13 4.48 2.76, 2.64 N6Hz 7.44, 6.26 B1 Phe 4.01 1.91 CyHz 2.16, 2.16 CS B3 Asn 8.57 4.59 2.61, 2.72 Cs.eH 6.95 CS B4 Gin 4.49 1.94, 1.94 CyHz 2.16, 2.16 CS CS B5 His 8.44 4.29 3.46, 3.06 C2H 1.12, C6H 0.60, 0.60 CS CS CH 1.12, C6H 0.6	A11 Cvs	9.92			
A13 leu8.733.881.441.44 C_{YH} 1.51, $C\delta H_{0}$ 0.81 0.76A14 Tyr7.644.323.02, 2.98 $C_{28}H$ 7.11, $C_{38}H$ 0.85A15 Gin7.473.942.21, 2.02 C_{YH} 2.39, 2.34, NeH 7.57, 7.07A16 Leu7.874.111.94, 1.44 C_{YH} 1.72, $C\delta H_{5}$ 0.77, 0.71A17 Glu8.014.192.04, 1.98 C_{YH} 2.36, 2.24, NeH 7.57, 7.07A18 Asn7.304.442.60, 2.49NOH 2.13, 6.54A19 Tyr7.964.353.41, 2.81C_{28}H 7.31, C_{38}H 6.76A20 Cys7.325.133.13, 2.81A21 Asn8.134.482.76, 2.64NOH 2.74, 6.26B1 Phe4.113.12, 3.12C_{28}H 7.22, C_{58}H 7.33B2 Val4.011.91C/H 5.083.083B3 Asn8.574.592.81, 2.72B4 Gln4.491.94, 1.94C/H 2.16, 2.16B5 His8.444.293.46, 3.06C2H , C4H 6.95B6 Leu9.124.571.74, 0.81C/H 1.12, C\delta H_5 0.60, 0.60B7 Cys8.725.003.20, 2.92B8 Gly9.553.98, 3.86B11 Leu6.883.871.83, 1.05B12 Val7.904.383.03, 2.63B14 Ala7.554.08Cβ H_5 1.36B14 Ala7.554.08Cβ H_5 1.36B15 Leu7.953.660.91, 0.02CyH 1.19, C\delta H_5 0.50, 0.192.14, 1.73, 3.17B14 Ala7.554.08 </td <td>A12 Ser</td> <td></td> <td>4.61</td> <td>4.17.3.99</td> <td></td>	A12 Ser		4.61	4.17.3.99	
A14 Tyr 7.64 4.32 $3.02, 2.98$ $C_{24}H 7.11, C_{34}H 6.85$ A15 Gin 7.47 3.94 $2.21, 2.02$ $CYHz 2.39, 2.34, NeHz 7.57, 7.07$ A16 Leu 7.87 4.11 $1.94, 1.44$ $CYH 1.72, CSH 0.77, 0.71$ A17 Glu 8.01 4.19 $2.04, 1.98$ $CYHz 2.36, 2.21$ A18 Leu 7.30 4.44 $2.60, 2.49$ $NSHz 7.31, 6.54$ A19 Tyr 7.96 4.35 $3.11, 2.81$ $C_{24}H 7.21, C_{34}H 6.76$ A20 Cys 7.32 5.13 $3.31, 2.81$ $C_{24}H 7.22, C_{35}H 7.33$ B1 Phe 4.11 $3.12, 3.12$ $C_{24}H 7.22, C_{35}H 7.33$ B2 Val 4.01 1.91 $CYHz 0.83, 0.83$ B3 Asn 8.57 4.59 $2.81, 2.72$ B4 Gin 4.49 $1.94, 1.94$ $CYHz 2.16, 2.16$ B5 His 8.44 4.29 $3.46, 3.06$ $C2H$ $C_{2.0.68}$ B7 Cys 8.72 5.00 $3.20, 2.92$ $2.06, 2.08$ $CYH 1.12, CSHs 0.60, 0.60$ B6 Isi 8.14 2.99 $3.99, 3.99$ 3.9	A13 leu	8.73	3.88	1.44, 1.44	CvH 1.51. CδH3 0.81.0.76
A15 C 7.47 3.94 2.21, 2.02 C C V $2.39, 2.34, NEH_2 7.57, 7.07$ A16 Leu 7.87 4.11 1.94, 1.44 C C V $2.23, 2.21$ A17 Glu 8.01 4.19 2.04, 1.98 C V $2.36, 2.21$ A18 Asn 7.30 4.44 2.60, 2.49 N N $7.36, 5.4$ A19 Tyr 7.96 4.35 3.41, 2.81 $C_{24H} 7.31, C_{34H} 6.76$ A20 Cys 7.32 5.13 3.31, 2.81 A21 Asn 8.13 4.48 2.76, 2.64 N N $7.47, 0.33$ $2.81, 7.22, C_{34H} 7.23, C_{34H} 7.33$ B2 Val 4.01 1.91 C V $2.81, 7.22, C_{34H} 7.23, C_{34H} 7.33$ B4 Gin 4.49 1.94, 1.94 C C $2.16, 2.16$ B5 His 8.44 4.29 3.46, 3.06 C2H C C C C C R C R C R C R R R R R R R R	A14 Tyr	7.64	4.32	3.02, 2.98	C _{2.6} H 7.11, C _{3.5} H 6.85
A16 Leu 7.87 4.11 1.94, 1.44 $CYH 1.72, C\deltaH_5 0.77, 0.71$ A17 Glu 8.01 4.19 2.04, 1.98 $CYH 2.236, 2.21$ A18 Asn 7.30 4.44 2.60, 2.49 NoHz 7.13, 6.54 A19 Tyr 7.96 4.35 3.41, 2.81 $C_{2xH} 7.31, C_{3xH} 6.76$ A20 Cys 7.32 5.13 3.31, 2.81 $C_{2xH} 7.22, C_{3xH} 7.23, C_{3xH} 7.23$ B1 Phe 4.11 3.12, 3.12 $C_{2xH} 7.22, C_{3xH} 7.33$ $C_{2xH} 7.22, C_{3xH} 7.23, C_{3xH} 7.23$ B2 Val 4.01 1.91 $CYH_2 2.16, 2.16$ $C_{2H} - C_{2H} 2.272, C_{2H} 7.23, C_{3xH} 7.33$ B3 Asn 8.57 4.59 2.81, 2.72 $C_{2H} - C_{2H} 2.2, 0.68$ $C_{2H} - C_{2H} 2.2, 0.68$ B4 Gin 4.49 1.94, 1.94 $CYH_2 2.16, 2.16$ $C_{2H} - C_{2H} 3.06, 0.60$ B5 His 8.44 4.29 3.46, 3.06 C2H - $C_{2H} + 3.02, 0.28$ $C_{2H} + 3.02, 0.28$ B6 Leu 9.12 4.57 1.74, 0.81 $C_{YH} 1.12, C\deltaH_3 0.60, 0.60$ $C_{2H} - 2.37$ B10 Asp 7.90 4.38 3.03, 2.63 $C_{2H} + 1.02, 0.92$ $C_{2H} + 7.2, 2.31$	A15 GIn	7.47	3.94	2.21, 2.02	CvH ₂ 2.39, 2.34, ΝεH ₂ 7.57,7,07
A17 Glu8.014.192.04, 1.98 $CYHz 236, 2.21$ A18 Asn7.304.442.60, 2.49Nöht-7.13, 6.54A19 Tyr7.964.353.41, 2.81 $C_{2xH} 7.31, C_{3xH} 6.76$ A20 Cys7.325.133.31, 2.81A21 Asn8.134.482.76, 2.64Nöht-7.42, C_{3xH} 7.33B2 Val4.011.91 $CYHz 0.83, 0.83$ B3 Asn8.574.592.81, 2.72B4 Gln4.491.94, 1.94 $CYHz 2.16, 2.16$ B5 His8.444.293.46, 3.06C2H , C4H 6.95B6 Leu9.124.571.74, 0.81CYH 1.64, C5Hz 0.72, 0.68B7 Cys8.725.003.20, 2.92B8 Gly9.553.98, 3.86B9 Ser9.184.183.99, 3.99B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.05CYH 1.12, C5Hz 0.60, 0.60B12 Val7.033.182.07CYHz 1.02, 0.92B13 Glu7.974.092.08, 2.08CYH 1.24, C5Hz 0.50, 0.19B15 Leu7.953.660.91, 0.02CYH 1.19, C5Hz 0.50, 0.19B16 Tyr8.204.403.17, 3.17C2xH 7.30, C3xH 6.85B17 Leu7.684.081.91, 1.78CYHz 1.00, 0.86B18 Val8.433.771.97Cycle 2.47, 2.37B22 Arg8.134.122.16, 2.08CYHz 1.00, 0.86B17 Leu7.684.083.29, 2.92B16 Tyr8.20	A16 Leu	7 87	4 11	1 94 1 44	CvH 1 72 CδH ₃ 0 77 0 71
A18 Asn 7.30 4.44 2.60, 2.49 NöH: 7.13, 6.54 A19 Tyr 7.96 4.35 3.41, 2.81 CasH 7.31, CasH 6.76 A20 Cys 7.32 5.13 3.31, 2.81 CasH 7.31, CasH 6.76 A21 Asn 8.13 4.48 2.76, 2.64 NöH: 7.44, 6.26 B1 Phe 4.11 3.12, 2.31 CasH 7.22, CasH 7.33 B2 Val 4.01 1.91 CyH: 0.83, 0.83 B3 Asn 8.57 4.59 2.81, 2.72 B4 Gln 4.49 1.94, 1.94 CyH: 2.16, 2.16 B5 His 8.44 4.29 3.46, 3.06 C2H , CAH 6.95 B6 Leu 9.12 4.57 1.74, 0.81 CyH 1.64, C6Hs 0.72, 0.68 B7 Cys 8.72 5.00 3.20, 2.92 B8 Gly 9.55 3.98, 3.86 B9 Ser 9.18 4.18 3.99, 3.99 B11 Leu 6.88 3.87 1.83, 1.05 CyH 1.12, C6Hs 0.60, 0.60 B10 Asp 7.90 4.38 3.03, 2.63 CH1 1.12, C6Hs 0.50, 0.19 B13 Glu 7.97 4.09 2.08, 2.08 CyH 1.19, C6Hs 0.50, 0.19 <	A17 Glu	8 01	4 19	2 04 1 98	CvH ₂ 2 36 2 21
A19 Tyr7.964.353.41, 2.81 C_{2xH} 7.31, C_{3xH} 6.76A20 Cys7.325.133.31, 2.81A21 Asn8.134.482.76, 2.64NõHz 7.44, 6.26B1 Phe4.113.12, 3.12 C_{2xH} 7.22, C_{3xH} 7.33B2 Val4.011.91 CYH_{9} 0.83, 0.83B3 Asn8.574.592.81, 2.72B4 Gln4.491.94, 1.94 CYH_{2} 2.16, 2.16B5 His8.444.293.46, 3.06C2HB6 Leu9.124.571.74, 0.81CYH 1.64, CõH ₃ 0.72, 0.68B7 Cys8.725.003.20, 2.92B8 Gly9.553.99, 3.86B9 Ser9.184.183.09, 3.09B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.05CYH 1.12, CõH ₃ 0.60, 0.60B12 Val7.033.182.07CYH 1.12, CõH ₃ 0.60, 0.60B13 Glu7.974.092.08, 2.08CYH 2.47, 2.31B14 Ala7.554.08CβH ₃ 1.36B15 Leu7.684.081.91, 1.78B16 Tyr8.204.403.17, 3.17Cz ₄ H 7.30, Ca ₃ H 6.851.97B17 Leu7.684.0819 Cys8.884.883.29, 2.92B20 Gly7.753.99, 3.85B21 Glu9.184.182.02, 2.05CYH 2.37B22 Arg8.134.122.16, 2.08CYH ₂ 2.37B22 Arg8.134.1	A18 Asn	7.30	4 44	2 60 2 49	NδH ₂ 7 13 6 54
A20 Cys7.325.133.31 2.81ControlA21 Asn8.134.482.76, 2.64N6H ₂ 7.44, 6.26B1 Phe4.113.12, 3.12C2aH 7.22, C3aH 7.33B2 Val4.011.91CyH ₂ 0.83, 0.83B3 Asn8.574.592.81, 2.72B4 Gln4.491.94, 1.94CyH ₂ 2.16, 2.16B5 His8.444.293.46, 3.06C2HB6 Leu9.124.571.74, 0.81CyH 1.64, C6H ₃ 0.72, 0.68B7 Cys8.725.003.20, 2.92B8 Gly9.553.98, 3.86B9 Ser9.184.183.99, 3.99B10 Asp7.904.383.05B11 Leu6.883.871.83, 1.05CyH 1.12, C6H ₃ 0.60, 0.60B12 Val7.033.182.07CyH ₃ 1.02, 0.92B13 Glu7.974.092.08, 2.08CyH ₂ 2.47, 2.31B14 Ala7.554.08C9H ₃ 1.36B17 Leu7.684.081.91, 1.78CyH 1.19, C6H ₃ 0.50, 0.192.16, 2.08CyH ₂ 1.72, C3H ₄ 3.09, 3.92B13 Clu7.953.660.91, 0.02CyH 1.19, C6H ₃ 0.50, 0.19B15 Leu7.953.660.91, 0.02CyH 1.19, C6H ₃ 0.50, 0.19B16 Tyr8.204.403.17, 3.17C2aH 7.30, CsH ₄ 6.85B17 Leu7.684.081.91, 1.78CYH 1.78, C6H ₃ 3.40, 3.32B20 Gly7.753.98, 3.85B22B21 Glu9.184.182.20, 2.05CyH ₂	A19 Tvr	7.96	4 35	3 41 2 81	$C_{26}H 7 31 C_{35}H 6 76$
A21 Asn B1 PheB134.482.762.64NöH2 7.44,6.26B1 Phe4.113.123.12CzaH 7.22GzaH 7.33B2 Val4.011.91CyH3 0.83,0.83B3 Asn8.574.592.81, 2.72B4 Gin4.491.94, 1.94CyH2 2.16, 2.16B5 His8.444.293.46, 3.06C2HB6 Leu9.124.571.74, 0.81CyH1 0.64, 0.72, 0.68B7 Cys8.725.003.20, 2.92B8 Giy9.553.98, 3.86B9 Ser9.184.183.99, 3.99B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.05CyH 1.12, CöH5 0.60, 0.60B12 Val7.033.182.07CyH3 1.02, 0.92B13 Glu7.974.092.08, 2.08CyH2 2.47, 2.31B14 Ala7.554.08CgH3 1.36B15 Leu7.953.660.91, 0.02CyH 1.19, CöH5 0.50, 0.19B16 Tyr8.204.403.17, 3.17CzaH 7.30, CasH 6.85B17 Leu7.684.081.91, 1.78CyH3 1.00, 0.86B19 Cys8.884.883.29, 2.92B20 Giy7.753.98, 3.85B21 Glu9.184.182.20, 2.05CyH2 1.89, CöH2 3.40, 3.32B22 Giy7.553.98, 3.85B23 Gily7.314.10, 3.80B24 Phe7.525.143.38, 2.91CzaH 6.75, C3aH 6.92, CaH 6.94B25 Phe8.694.873.21	A20 Cvs	7 32	5 13	3 31 2 81	
B1 Phe4.113.12, 3.12CzeH 7.22, CasH 7.33B2 Val4.011.91 $CyH_3 0.83 0.83$ B3 Asn8.574.592.81, 2.72B4 Gin4.491.94, 1.94 $CyH_2 2.16, 2.16$ B5 His8.444.293.46, 3.06 $C2H$, $C4H 6.95$ B6 Leu9.124.571.74, 0.81 $CyH_1 0.46, C5H_5 0.72, 0.68$ B7 Cys8.725.003.20, 2.92B8 Gly9.553.98, 3.86B9 Ser9.184.183.09, 3.99B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.05 $CyH 1.12, C5H_5 0.60, 0.60$ B12 Val7.033.182.07 $CyH_2 2.47, 2.31$ B14 Ala7.554.08 $C6H_3 1.36$ B15 Leu7.953.660.91, 0.02 $CyH 1.19, C5H_5 0.50, 0.19$ B16 Tyr8.204.403.17, 3.17 $C_28H 7.30, C_{3.5H} 6.85$ B17 Leu7.684.081.91, 1.78 $CyH_1 1.78, C3H 6.85$ B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $CyH_2 2.37$ B22 Arg8.134.122.16, 2.08 $CyH_2 3.40, 3.32$ B23 Gly7.314.10, 3.80E24 Phe7.525.14B24 Phe7.525.143.38, 2.91C2aH 6.75, Ca_5H 6.92, C4H 6.94B25 Phe8.694.873.29, 2.89C2aH 7.28, Ca_5H 7.32B26 Tyr8.184.61 <td< td=""><td>A21 Asn</td><td>8 13</td><td>4 48</td><td>2 76 2 64</td><td>NδH₂ 7 44 6 26</td></td<>	A21 Asn	8 13	4 48	2 76 2 64	NδH₂ 7 44 6 26
B2 Val4.011.91CyH0.13,0.83B3 Asn8.574.592.81, 2.72B4 Gln4.491.94,1.94CyH2 2.16, 2.16B5 His8.444.293.46, 3.06C2HB7 Cys8.725.003.20, 2.92B8 Gly9.553.98, 3.86B9 Ser9.184.183.99, 3.99B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.05CVH 1.12, CõH3 0.60, 0.606.00B12 Val7.033.182.07CVH 1.12, CõH3 0.60, 0.60B14 Ala7.554.08CPH3 1.36B15 Leu7.953.660.91, 0.02CVH 1.19, CõH3 0.50, 0.19B16 Tyr8.204.403.17, 3.17C2aH 7.30, C3aH 6.85B17 Leu7.684.081.91, 1.78CYH 1.19, CõH3 0.50, 0.19B16 Tyr8.204.403.17, 3.17C2aH 7.30, C3aH 6.85B17 Leu7.684.081.91, 1.78CYH 1.18, CõH3 0.94, 0.94B18 Val8.433.771.97CYH2 2.37B22 Arg8.134.103.80B24 Phe7.525.143.38, 2.91C2aH 6.52, C3aH 6.92, C4H 6.94B25 Phy8.694.873.21, 3.18C2aH 7.28, C3aH 7.32B24 Phe7.525.143.38, 2.91C2aH 7.28, C3aH 6.92, C4H 6.94B	B1 Phe	00	4 11	3 12 3 12	$C_{26}H 7 22 C_{35}H 7 33$
Ba Asn8.574.592.81, 2.720, 10, 05, 050, 050B4 Gln4.491.94, 1.94 CYH_2 2.16, 2.16B5 His8.444.293.46, 3.06C2HB6 Leu9.124.571.74, 0.81CYH 1.64, C8H ₃ 0.72, 0.68B7 Cys8.725.003.20, 2.92B8 Gly9.553.98, 3.86B9 Ser9.184.183.99, 3.99B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.05CYH 1.12, C6H ₃ 0.60, 0.600.60B12 Val7.033.182.07CYH 3 1.02, 0.92B13 Glu7.974.092.08, 2.08CYH 1.12, C6H ₃ 0.50, 0.19B16 Tyr8.204.403.17B16 Tyr8.204.403.17B17 Leu7.684.081.91, 1.78CYH 1.78, C6H ₃ 0.94, 0.941.94B19 Cys8.884.883.29, 2.922.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05CYHz 2.37B22 Arg8.134.122.16, 2.08C2+H 6.75, C3+H 6.92, C4H 6.94B25 Phe8.694.87B26 Tyr8.184.612.99, 2.89C2+H 6.92, C3+H 6.63B27 Thr7.564.294.08CYHz 2.37B28 Asp8.214.842.74, 2.47B29 Pro4.502.02, 044.09CYHz 1.73	B2 Val		4 01	1.91	CvH ₃ 0 83 0 83
B4 Gin4.491.94, 1.94 $CYH_2 2.16, 2.16$ B5 His8.444.293.46, 3.06 $C2H$, $C4H 6.95$ B6 Leu9.124.571.74, 0.81 $CYH 1.64, C5H_3 0.72, 0.68$ B7 Cys8.725.003.20, 2.92B8 Gly9.553.98, 3.86B9 Ser9.184.183.99, 3.99B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.05 $CYH 1.12, C5H_3 0.60, 0.60$ B12 Val7.033.182.07 $CYH_3 1.02, 0.92$ B13 Glu7.974.092.08, 2.08 $CYH_2 2.47, 2.31$ B14 Ala7.554.08 $C9H_3 1.36$ B15 Leu7.953.660.91, 0.02 $CYH 1.19, C5H_3 0.50, 0.19$ B16 Tyr8.204.403.17, 3.17 $C_{2.8H} 7.30, C_{3.5H} 6.85$ B17 Leu7.684.081.91, 1.78 $CYH_3 1.00, 0.86$ B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $CYH_2 2.37$ B22 Arg8.134.122.16, 2.08 $CYH_2 1.89, C5H_2 3.40, 3.32$ B22 Arg8.134.122.16, 2.08 $CYH_2 1.89, C5H_2 3.40, 3.32$ B22 Arg8.134.122.16, 2.08 $CYH_2 1.89, C5H_4 6.92, C_4H 6.94$ B25 Phe7.564.294.08 $CYH_3 1.13$ B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $CYH_2 1.94, C5H_2 3.79$ B30 Th	B3 Asn	8.57	4.59	2.81. 2.72	
B5 His8.444.293.46, 3.06C2H, C4H 6.95B6 Leu9.124.571.74, 0.81CyH 1.64, CõH ₃ 0.72, 0.68B7 Cys8.725.003.20, 2.92B8 Gly9.553.98, 3.86B9 Ser9.184.183.99, 3.99B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.05CyH 1.12, CõH ₃ 0.60, 0.60B12 Val7.033.182.07CyH ₃ 1.02, 0.92B13 Glu7.974.092.08, 2.08CyH ₂ 2.47, 2.31B14 Ala7.554.08CβH ₃ 1.36B15 Leu7.953.660.91, 0.02CyH 1.19, CõH ₃ 0.50, 0.19B16 Tyr8.204.403.17, 3.17C _{2.6H} 7.30, Ca _{3.6H} 6.85B17 Leu7.684.081.91, 1.78CyH 1.32, CõH ₃ 0.94, 0.94B18 Val8.433.771.97CyH ₃ 1.00, 0.86B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05CyH ₂ 2.37B22 Arg8.134.122.16, 2.08CyH ₂ 1.89, CõH ₂ 3.40, 3.32B23 Gly7.314.10, 3.80B24H.675, Ca _{3.6H} 6.92, C4H 6.94B25 Phe8.694.873.21, 3.18C _{2.6H} 6.75, Ca _{3.6H} 6.63B27 Thr7.564.294.08CyH ₃ 1.13B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04CyH ₂ 1.94, CõH ₂ 3.79B30 T	B4 Gln		4 49	1 94 1 94	CvH2 2 16 2 16
B6 Leu9.124.571.74, 0.81 $CYH 1.64, C6H_3 0.72, 0.68$ B7 Cys8.725.003.20, 2.92B8 Gly9.553.98, 3.86B9 Ser9.184.183.99, 3.99B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.05 $CYH 1.12, C5H_5 0.60, 0.60$ B12 Val7.033.182.07 $CYH_3 1.02, 0.92$ B13 Glu7.974.092.08, 2.08 $CYH_2 2.47, 2.31$ B14 Ala7.554.08 $CGH_3 1.36$ B15 Leu7.953.660.91, 0.02 $CYH 1.19, C5H_3 0.50, 0.19$ B16 Tyr8.204.403.17, 3.17 $C_2eH 7.30, C_{3.5H} 6.85$ B17 Leu7.684.081.91, 1.78 $CYH_3 1.00, 0.86$ B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $CYH_2 2.37$ B22 Arg8.134.122.16, 2.08 $CYH_2 1.39, C5H_2 3.40, 3.32$ B23 Gly7.314.10, 3.80 $C_{2.6H} 6.75, C_{3.6H} 6.92, C_{4H} 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2.6H} 6.75, C_{3.6H} 7.32$ B26 Tyr8.184.612.99, 2.89C_{2.6H} 6.92, C_{3.6H} 7.32B26 Tyr8.184.612.99, 2.89C_{2.6H} 6.92, C_{3.6H} 7.32B26 Tyr8.184.612.99, 2.89C_{2.6H} 6.92, C_{3.6H} 6.63B27 Thr7.564.294.08 $CYH_3 1.13$ B28 Asp8.214.	B5 His	8.44	4.29	3.46. 3.06	C2H C4H 6.95
B7 Cys8.725.00 $3.20, 2.92$ B8 Gly9.55 $3.98, 3.86$ B9 Ser9.184.18 $3.99, 3.99$ B10 Asp7.90 4.38 $3.03, 2.63$ B11 Leu6.88 3.87 $1.83, 1.05$ $C\gamma H 1.12, C\delta H_3 0.60, 0.60$ B12 Val7.03 3.18 2.07 $C\gamma H_3 1.02, 0.92$ B13 Glu7.97 4.09 $2.08, 2.08$ $C\gamma H_2 2.47, 2.31$ B14 Ala7.55 4.08 $C\beta H_3 1.36$ B15 Leu7.95 3.66 $0.91, 0.02$ $C\gamma H 1.19, C\delta H_3 0.50, 0.19$ B16 Tyr 8.20 4.40 $3.17, 3.17$ $C_{2.6H} 7.30, C_{3.5H} 6.85$ B17 Leu7.68 4.08 $1.91, 1.78$ $C\gamma H_3 1.00, 0.86$ B19 Cys 8.88 4.88 $3.29, 2.92$ B20 Gly 7.75 $3.98, 3.85$ $8.220, 2.05$ $C\gamma H_2 2.37$ B22 Arg 8.13 4.12 $2.16, 2.08$ $C\gamma H_2 1.89, C\delta H_2 3.40, 3.32$ B23 Gly 7.31 $4.10, 3.80$ 8.291 $C_{2.6H} 6.75, C_{3.6H} 6.92, C_{4H} 6.94$ B25 Phe 8.69 4.87 $3.21, 3.18$ $C_{2.6H} 7.28, C_{3.6H} 7.32$ B26 Tyr 8.18 4.61 $2.99, 2.89$ $C_{2.6H} 6.75, C_{3.6H} 6.92, C_{4H} 6.94$ B27 Thr 7.56 4.29 4.08 $C\gamma H_3 1.13$ B28 Asp 8.21 4.84 $2.74, 2.47$ B29 Pro 4.50 $2.20, 2.04$ $C\gamma H_2 1.94, C\delta H_2 3.79$ B30 Thr 7.90 4.22 4.09 $C\gamma H3 1.18$	B6 Leu	9 12	4 57	1 74 0 81	CvH 1 64 CδH ₃ 0 72 0 68
B8 Gly9.553.98, 3.86B9 Ser9.184.183.99, 3.99B10 Asp7.904.383.03, 2.63B11 Leu6.883.871.83, 1.05 $CYH 1.12, C\deltaH_3 0.60, 0.60$ B12 Val7.033.182.07 $CYH_3 1.02, 0.92$ B13 Glu7.974.092.08, 2.08 $CYH_2 2.47, 2.31$ B14 Ala7.554.08 $C\betaH_3 1.36$ B15 Leu7.953.660.91, 0.02 $CYH 1.19, C\deltaH_3 0.50, 0.19$ B16 Tyr8.204.403.17, 3.17 $C_{2.6H} 7.30, C_{3.6H} 6.85$ B17 Leu7.684.081.91, 1.78 $CYH 1.78, C\deltaH_3 0.94, 0.94$ B18 Val8.433.771.97 $CYH_3 1.00, 0.86$ B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $CYH_2 1.89, C\deltaH_2 3.40, 3.32$ B22 Arg8.134.122.16, 2.08 $CYH_2 1.89, C\deltaH_2 3.40, 3.32$ B24 Phe7.525.143.38, 2.91 $C_{2.6H} 6.75, C_{3.6H} 6.92, C_{4H} 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2.6H} 7.28, C_{3.6H} 7.32$ B26 Tyr8.184.612.99, 2.89 $C_{2.6H} 6.92, C_{3.6H} 6.63$ B27 Thr7.564.294.08 $CYH_3 1.13$ B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $CYH_3 1.18$	B7 Cvs	8.72	5.00	3.20, 2.92	
B9 Ser9.184.18 $3.99, 3.99$ B10 Asp7.904.38 $3.03, 2.63$ B11 Leu6.88 3.87 $1.83, 1.05$ $CYH 1.12, C\deltaH_3 0.60, 0.60$ B12 Val7.03 3.18 2.07 $CYH_3 1.02, 0.92$ B13 Glu7.974.09 $2.08, 2.08$ $CYH_2 2.47, 2.31$ B14 Ala7.55 4.08 $CGH_3 1.36$ B15 Leu7.95 3.66 $0.91, 0.02$ $CYH 1.19, C\deltaH_3 0.50, 0.19$ B16 Tyr 8.20 4.40 $3.17, 3.17$ $C_{2.6H} 7.30, C_{3.6H} 6.85$ B17 Leu7.68 4.08 $1.91, 1.78$ $CYH 1.78, C\deltaH_3 0.94, 0.94$ B18 Val 8.43 3.77 1.97 $CYH_3 1.00, 0.86$ B19 Cys 8.88 4.88 $3.29, 2.92$ B20 Gly 7.75 $3.98, 3.85$ 8.20 $CYH_2 2.37$ B22 Arg 8.13 4.12 $2.16, 2.08$ $CYH_2 1.89, C\deltaH_2 3.40, 3.32$ B23 Gly 7.31 $4.10, 3.80$ $8.29, 12.24$ $6.26H 6.75, C_{3.6H} 6.92, C_{4H} 6.94$ B25 Phe 8.69 4.87 $3.21, 3.18$ $C_{2.6H} 7.28, C_{3.6H} 7.32$ B26 Tyr 8.18 4.61 $2.99, 2.89$ $C_{2.6H} 6.92, C_{3.6H} 6.63$ B27 Thr 7.56 4.29 4.08 $CYH_3 1.13$ B28 Asp 8.21 4.84 $2.74, 2.47$ B29 Pro 4.50 $2.02, 2.04$ $CYH_3 1.18$	B8 Glv	9.55	3.98. 3.86		
B10 Asp7.904.38 $3.03, 2.63$ B11 Leu6.88 3.87 $1.83, 1.05$ $CYH 1.12, C\deltaH_3 0.60, 0.60$ B12 Val7.03 3.18 2.07 $CYH_3 1.02, 0.92$ B13 Glu7.97 4.09 $2.08, 2.08$ $CYH_2 2.47, 2.31$ B14 Ala7.55 4.08 $C\betaH_3 1.36$ B15 Leu7.95 3.66 $0.91, 0.02$ $CYH 1.19, C\deltaH_3 0.50, 0.19$ B16 Tyr 8.20 4.40 $3.17, 3.17$ $C_{2.6H} 7.30, C_{3.5H} 6.85$ B17 Leu7.68 4.08 $1.91, 1.78$ $CYH_3 1.00, 0.86$ B19 Cys 8.88 4.88 $3.29, 2.92$ B20 Gly 7.75 $3.98, 3.85$ B21 Glu 9.18 4.18 $2.20, 2.05$ $CYH_2 2.37$ B22 Arg 8.13 4.12 $2.16, 2.08$ $CYH_2 2.37$ B24 Phe 7.52 5.14 $3.38, 2.91$ $C_{2.6H} 6.75, C_{3.5H} 6.92, C_{4H} 6.94$ B25 Phe 8.69 4.87 $3.21, 3.18$ $C_{2.6H} 7.28, C_{3.5H} 7.32$ B26 Tyr 8.18 4.61 $2.99, 2.89$ $C_{2.6H} 6.92, C_{3.5H} 6.63$ B27 Thr 7.56 4.29 4.08 $CYH_2 1.94, C\deltaH_2 3.79$ B28 Asp 8.21 4.84 $2.74, 2.47$ B29 Pro 4.50 $2.20, 2.04$ $CYH_2 1.94, C\deltaH_2 3.79$ B30 Thr 7.90 4.22 4.09 $CYH_3 1.18$	B9 Ser	9.18	4.18	3.99, 3.99	
B11 Leu6.883.871.83, 1.05 $C\gamma H 1.12, C\delta H_{3} 0.60, 0.60$ B12 Val7.033.182.07 $C\gamma H_{3} 1.02, 0.92$ B13 Glu7.974.092.08, 2.08 $C\gamma H_{2} 2.47, 2.31$ B14 Ala7.554.08 $C\beta H_{3} 1.36$ B15 Leu7.953.660.91, 0.02 $C\gamma H 1.19, C\delta H_{3} 0.50, 0.19$ B16 Tyr8.204.403.17, 3.17 $C_{2,6H} 7.30, C_{3,6H} 6.85$ B17 Leu7.684.081.91, 1.78 $C\gamma H_{3} 1.00, 0.86$ B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $C\gamma H_{2} 2.37$ B22 Arg8.134.122.16 2.08 $C\gamma H_{2} 1.89, C\delta H_{2} 3.40, 3.32$ B23 Gly7.314.10, 3.804.873.21, 3.18 $C_{2,6H} 6.75, C_{3,6H} 6.92, C_{4H} 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2,6H} 6.75, C_{3,6H} 6.92, C_{4H} 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2,6H} 6.92, C_{3,6H} 7.32$ B26 Tyr8.184.612.99, 2.89 $C_{2,6H} 6.92, C_{3,6H} 6.63$ B27 Thr7.564.294.08 $C\gamma H_{3} 1.13$ B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $C\gamma H_{2} 1.94, C\delta H_{2} 3.79$ B30 Thr7.904.224.09 $C\gamma H_{3} 1.18$	B10 Asp	7.90	4.38	3.03, 2.63	
B12 Val7.033.182.07 $CYH_3 1.02, 0.92$ B13 Glu7.974.092.08, 2.08 $CYH_2 2.47, 2.31$ B14 Ala7.554.08 $C\betaH_3 1.36$ B15 Leu7.953.660.91, 0.02 $CYH 1.19, C\deltaH_3 0.50, 0.19$ B16 Tyr8.204.403.17, 3.17 $C_{2.6}H 7.30, C_{3.6}H 6.85$ B17 Leu7.684.081.91, 1.78 $CYH 1.78, C\deltaH_3 0.94, 0.94$ B18 Val8.433.771.97 $CYH_3 1.00, 0.86$ B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $CYH_2 2.37$ B22 Arg8.134.122.16, 2.08 $CYH_2 1.89, C\deltaH_2 3.40, 3.32$ B23 Gly7.314.10, 3.803.28, 2.91 $C_{2.6}H 6.75, C_{3.6}H 6.92, C_4H 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2.6}H 7.28, C_{3.5}H 7.32$ B26 Tyr8.184.612.99, 2.89 $C_{2.6}H 6.92, C_{3.5}H 6.63$ B27 Thr7.564.294.08 $CYH_3 1.13$ B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $CYH_2 1.94, C\delta H_2 3.79$ B30 Thr7.904.224.09 $CYH_3 1.18$	B11 Leu	6.88	3.87	1.83, 1.05	СүН 1.12, СठН₃ 0.60, 0.60
B13 Glu7.974.092.08, 2.08 $CYH_2 2.47$, 2.31B14 Ala7.554.08 $C\betaH_3 1.36$ B15 Leu7.953.660.91, 0.02 $CYH 1.19$, $C\deltaH_3 0.50$, 0.19B16 Tyr8.204.403.17, 3.17 $C_{2.6}H 7.30$, $C_{3.6}H 6.85$ B17 Leu7.684.081.91, 1.78 $CYH 1.78$, $C\deltaH_3 0.94$, 0.94B18 Val8.433.771.97 $CYH_3 1.00$, 0.86B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $CYH_2 2.37$ B22 Arg8.134.122.16, 2.08 $CYH_2 1.89$, $C\deltaH_2 3.40$, 3.32B23 Gly7.314.10, 3.803.82, 2.91 $C_{2.6}H 6.75$, $C_{3.6}H 6.92$, $C_4H 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2.6}H 7.28$, $C_{3.6}H 6.92$, $C_4H 6.94$ B25 Thr7.564.294.08 $CYH_3 1.13$ B26 Tyr8.184.612.99, 2.89 $C_{2.6}H 6.92$, $C_{3.6}H 6.63$ B27 Thr7.564.294.08 $CYH_3 1.13$ B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $CYH_2 1.94$, $C\deltaH_2 3.79$ B30 Thr7.904.224.09 $CYH3 1.18$	B12 Val	7.03	3.18	2.07	CvH ₃ 1.02,0.92
B14 Ala7.554.08 $C\betaH_3 1.36$ B15 Leu7.953.660.91, 0.02 $C\gamma H 1.19$, $C\deltaH_3 0.50$, 0.19B16 Tyr8.204.403.17, 3.17 $C_{2,6}H 7.30$, $C_{3,6}H 6.85$ B17 Leu7.684.081.91, 1.78 $C\gamma H 1.78$, $C\deltaH_3 0.94$, 0.94B18 Val8.433.771.97 $C\gamma H_3 1.00$, 0.86B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $C\gamma H_2 2.37$ B22 Arg8.134.122.16, 2.08 $C\gamma H_2 1.89$, $C\delta H_2 3.40$, 3.32B23 Gly7.314.10, 3.80824B24 Phe7.525.143.38, 2.91 $C_{2,6}H 6.75$, $C_{3,6}H 6.92$, $C_4H 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2,6}H 7.28$, $C_{3,6}H 7.32$ B26 Tyr8.184.612.99, 2.89 $C_{2,6}H 6.92$, $C_{3,6}H 6.63$ B27 Thr7.564.294.08 $C\gamma H_3 1.13$ B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $C\gamma H_2 1.94$, $C\delta H_2 3.79$ B30 Thr7.904.224.09 $C\gamma H3 1.18$	B13 Glu	7.97	4.09	2.08. 2.08	CvH ₂ 2.47, 2.31
B15 Leu7.953.660.91, 0.02 $CYH 1.19, C\deltaH_3 0.50, 0.19$ B16 Tyr8.204.403.17, 3.17 $C_{2,6H} 7.30, C_{3,5H} 6.85$ B17 Leu7.684.081.91, 1.78 $CYH 1.78, C\deltaH_3 0.94, 0.94$ B18 Val8.433.771.97 $CYH_3 1.00, 0.86$ B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $CYH_2 2.37$ B22 Arg8.134.122.16, 2.08 $CYH_2 1.89, C\deltaH_2 3.40, 3.32$ B23 Gly7.314.10, 3.808B24 Phe7.525.143.38, 2.91 $C_{2,6H} 6.75, C_{3,6H} 6.92, C_{4H} 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2,6H} 7.28, C_{3,6H} 7.32$ B26 Tyr8.184.612.99, 2.89 $C_{2,6H} 6.92, C_{3,6H} 6.63$ B27 Thr7.564.294.08 $CYH_3 1.13$ B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $CYH_2 1.94, C\deltaH_2 3.79$ B30 Thr7.904.224.09 $CYH3 1.18$	B14 Ala	7.55	4.08	CBH ₃ 1.36	
B16 Tyr8.204.40 $3.17, 3.17$ $C_{2,6H} 7.30, C_{3,5H} 6.85$ B17 Leu7.684.08 $1.91, 1.78$ $CYH 1.78, C\deltaH_3 0.94, 0.94$ B18 Val8.43 3.77 1.97 $CYH_3 1.00, 0.86$ B19 Cys8.884.88 $3.29, 2.92$ B20 Gly7.75 $3.98, 3.85$ B21 Glu9.184.18 $2.20, 2.05$ $CYH_2 2.37$ B22 Arg8.134.12 $2.16, 2.08$ $CYH_2 1.89, C\deltaH_2 3.40, 3.32$ B23 Gly7.314.10, 3.80824B24 Phe7.52 5.14 $3.38, 2.91$ $C_{2,6H} 6.75, C_{3,6H} 6.92, C_{4H} 6.94$ B25 Phe8.69 4.87 $3.21, 3.18$ $C_{2,6H} 7.28, C_{3,6H} 7.32$ B26 Tyr8.18 4.61 $2.99, 2.89$ $C_{2,6H} 6.92, C_{3,6H} 6.63$ B27 Thr7.56 4.29 4.08 $CYH_3 1.13$ B28 Asp 8.21 4.84 $2.74, 2.47$ B29 Pro 4.50 $2.20, 2.04$ $CYH_2 1.94, C\deltaH_2 3.79$ B30 Thr 7.90 4.22 4.09 $CYH_3 1.18$	B15 Leu	7.95	3.66	0.91. 0.02	CvH 1.19. CδH₃ 0.50. 0.19
B17 Leu7.684.081.91, 1.78 $CYH 1.78, C\deltaH_3 0.94, 0.94$ B18 Val8.433.771.97 $CYH_3 1.00, 0.86$ B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $CYH_2 2.37$ B22 Arg8.134.122.16, 2.08 $CYH_2 1.89, C\deltaH_2 3.40, 3.32$ B23 Gly7.314.10, 3.80B24 Phe7.525.143.38, 2.91 $C_{2.6H} 6.75, C_{3.6H} 6.92, C_{4H} 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2.6H} 6.75, C_{3.6H} 6.92, C_{4H} 6.94$ B26 Tyr8.184.612.99, 2.89 $C_{2.6H} 6.92, C_{3.6H} 6.63$ B27 Thr7.564.294.08 $CYH_3 1.13$ B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $CYH_2 1.94, C\deltaH_2 3.79$ B30 Thr7.904.224.09 $CYH3 1.18$	B16 Tvr	8.20	4.40	3.17. 3.17	C _{2.6} H 7.30. C _{3.5} H 6.85
B18 Val8.433.771.97 $C\gamma$ H3 1.00, 0.86B19 Cys8.884.883.29, 2.92B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $C\gamma$ H2 2.37B22 Arg8.134.122.16, 2.08 $C\gamma$ H2 1.89, $C\delta$ H2 3.40, 3.32B23 Gly7.314.10, 3.80B24 Phe7.525.143.38, 2.91 $C_{2.6}$ H 6.75, $C_{3.6}$ H 6.92, C_{4} H 6.94B25 Phe8.694.873.21, 3.18 $C_{2.6}$ H 7.28, $C_{3.6}$ H 7.32B26 Tyr8.184.612.99, 2.89 $C_{2.6}$ H 6.92, $C_{3.6}$ H 6.63B27 Thr7.564.294.08 $C\gamma$ H3 1.13B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $C\gamma$ H2 1.94, $C\delta$ H2 3.79B30 Thr7.904.224.09 $C\gamma$ H3 1.18	B17 Leu	7.68	4.08	1.91, 1.78	CvH 1.78, CδH ₃ 0.94,0.94
B19 Cys8.884.88 $3.29, 2.92$ B20 Gly7.75 $3.98, 3.85$ B21 Glu9.184.18 $2.20, 2.05$ $C\gamma H_2 2.37$ B22 Arg8.134.12 $2.16, 2.08$ $C\gamma H_2 1.89, C\delta H_2 3.40, 3.32$ B23 Gly7.314.10, 3.80B24 Phe7.52 5.14 $3.38, 2.91$ $C_{2.6H} 6.75, C_{3.5H} 6.92, C4H 6.94$ B25 Phe8.69 4.87 $3.21, 3.18$ $C_{2.6H} 7.28, C_{3.5H} 7.32$ B26 Tyr8.18 4.61 $2.99, 2.89$ $C_{2.6H} 6.92, C_{3.5H} 6.63$ B27 Thr7.56 4.29 4.08 $C\gamma H_3 1.13$ B28 Asp8.21 4.84 $2.74, 2.47$ B29 Pro 4.50 $2.20, 2.04$ $C\gamma H_2 1.94, C\delta H_2 3.79$ B30 Thr7.90 4.22 4.09 $C\gamma H3 1.18$	B18 Val	8 43	3 77	1 97	$C_{VH_3} = 1.00 + 0.86$
B20 Gly7.753.98, 3.85B21 Glu9.184.182.20, 2.05 $C\gamma H_2 2.37$ B22 Arg8.134.122.16, 2.08 $C\gamma H_2 1.89$, $C\delta H_2 3.40$, 3.32B23 Gly7.314.10, 3.80B24 Phe7.525.143.38, 2.91 $C_{2.6H} 6.75$, $C_{3.5H} 6.92$, $C_{4H} 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2.6H} 7.28$, $C_{3.5H} 7.32$ B26 Tyr8.184.612.99, 2.89 $C_{2.6H} 6.92$, $C_{3.5H} 6.63$ B27 Thr7.564.294.08 $C\gamma H_3 1.13$ B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $C\gamma H_2 1.94$, $C\delta H_2 3.79$ B30 Thr7.904.224.09 $C\gamma H3 1.18$	B19 Cvs	8.88	4.88	3.29. 2.92	
B21 Glu9.184.182.20, 2.05 $CYH_2 2.37$ B22 Arg8.134.122.16, 2.08 $CYH_2 1.89$, $C\delta H_2 3.40$, 3.32B23 Gly7.314.10, 3.80B24 Phe7.525.143.38, 2.91 $C_{2.6H} 6.75$, $C_{3.5H} 6.92$, $C4H 6.94$ B25 Phe8.694.873.21, 3.18 $C_{2.6H} 7.28$, $C_{3.5H} 7.32$ B26 Tyr8.184.612.99, 2.89 $C_{2.6H} 6.92$, $C_{3.5H} 6.63$ B27 Thr7.564.294.08 $CYH_3 1.13$ B28 Asp8.214.842.74, 2.47B29 Pro4.502.20, 2.04 $CYH_2 1.94$, $C\delta H_2 3.79$ B30 Thr7.904.224.09 $CYH3 1.18$	B20 Glv	7.75	3.98. 3.85		
B22 Arg 8.13 4.12 2.16, 2.08 CyH2 1.89, CõH2 3.40, 3.32 B23 Gly 7.31 4.10, 3.80	B21 Glu	9.18	4.18	2.20. 2.05	CvH ₂ 2.37
B23 Gly 7.31 4.10, 3.80 B24 Phe 7.52 5.14 3.38, 2.91 C2.6H 6.75, C3.5H 6.92, C4H 6.94 B25 Phe 8.69 4.87 3.21, 3.18 C2.6H 7.28, C3.5H 7.32 B26 Tyr 8.18 4.61 2.99, 2.89 C2.6H 6.92, C3.5H 6.63 B27 Thr 7.56 4.29 4.08 CYH3 1.13 B28 Asp 8.21 4.84 2.74, 2.47 B29 Pro 4.50 2.20, 2.04 CYH2 1.94, C5H2 3.79 B30 Thr 7.90 4.22 4.09 CYH3 1.18	B22 Arg	8 13	4 12	2 16 2 08	CvH ₂ 1 89 CδH ₂ 3 40 3 32
B24 Phe 7.52 5.14 3.38, 2.91 C2.6H 6.75, C3.5H 6.92, C4H 6.94 B25 Phe 8.69 4.87 3.21, 3.18 C2.6H 7.28, C3.5H 7.32 B26 Tyr 8.18 4.61 2.99, 2.89 C2.6H 6.92, C3.5H 6.63 B27 Thr 7.56 4.29 4.08 CYH3 1.13 B28 Asp 8.21 4.84 2.74, 2.47 B29 Pro 4.50 2.20, 2.04 CYH2 1.94, C5H2 3.79 B30 Thr 7.90 4.22 4.09 CYH3 1.18	B23 Glv	7.31	4.10.3.80	,	
B25 Phe 8.69 4.87 3.21, 3.18 C2.6H 7.28, C3.5H 7.32 B26 Tyr 8.18 4.61 2.99, 2.89 C2.6H 6.92, C3.5H 6.63 B27 Thr 7.56 4.29 4.08 CYH3 1.13 B28 Asp 8.21 4.84 2.74, 2.47 B29 Pro 4.50 2.20, 2.04 CYH2 1.94, C5H2 3.79 B30 Thr 7.90 4.22 4.09 CYH3 1.18	B24 Phe	7.52	5.14	3.38. 2.91	C2.6H 6.75. C3.5H 6.92. C4H 6.94
B26 Tyr 8.18 4.61 2.99, 2.89 C2.6H 6.92, C3.5H 6.63 B27 Thr 7.56 4.29 4.08 CYH3 1.13 B28 Asp 8.21 4.84 2.74, 2.47 B29 Pro 4.50 2.20, 2.04 CYH2 1.94, C5H2 3.79 B30 Thr 7.90 4.22 4.09 CYH3 1.18	B25 Phe	8.69	4.87	3.21. 3.18	C _{2.6} H 7.28, C _{3.5} H 7.32
B27 Thr 7.56 4.29 4.08 CγH₃ 1.13 B28 Asp 8.21 4.84 2.74, 2.47 B29 Pro 4.50 2.20, 2.04 CγH₂ 1.94, CõH₂ 3.79 B30 Thr 7.90 4.22 4.09 CγH₃ 1.13	B26 Tyr	8.18	4.61	2.99, 2.89	C _{2,6} H 6.92, C _{3,5} H 6.63
B28 Asp 8.21 4.84 2.74, 2.47 B29 Pro 4.50 2.20, 2.04 CγH₂ 1.94, CõH₂ 3.79 B30 Thr 7.90 4.22 4.09 CγH₃ 1.18	B27 Thr	7.56	4.29	4.08	CyH₃ 1.13
B29 Pro 4.50 2.20, 2.04 CYH2 1.94, CõH2 3.79 B30 Thr 7.90 4.22 4.09 CYH3 1.18	B28 Asp	8.21	4.84	2.74, 2.47	•
B30 Thr 7.90 4.22 4.09 CvH3 1.18	B29 Pro		4.50	2.20, 2.04	CγH₂ 1.94, CδH₂ 3.79
	<u>B30 Thr</u>	7.90	4.22	4.09	СуНЗ 1.18

Table S4-B. Chemical shifts of 1H-NMR	resonances of 2CA (20	% deuterioacetic acid and 25°C)

Residue	NH	СαН	CβH	others
A1 Gly				
A2 lle	8.57	3.88	1.13	СγН2 0.94, 0.81, Сү'Н3 0.74, СδН3 0.60
A3 Val	8.14	3.58	1.95	СүН₃ 0.95, 0.83
A4 Glu	8.22	4.04	2.16, 2.16	CγH ₂ 2.56, 2.46
A5 Gln	8.26	4.08	2.12, 2.12	CγH ₂ 2.52, 2.44, ΝεH ₂
A6 Cys	8.42	4.96	3.34, 2.87	
A7 Cys	8.00	4.85	3.78, 3.18	
A8 His	8.19	4.58	3.58, 3.40	C2H 8.73, C6H 7.31
A9 Ser	7.44	4.78	4.14, 3.96	
A10 lle	7.88	4.42	1.61	СүН₂ 1.18, Сү'Н₃ 0.70, СδН₃ 0.58
A11 Cys	9.74			
A12 Ser	8.77	4.64	4.34, 4.03	
A13 leu	8.67	3.89	1.38, 1.38	СүН 1.45, СōН₃ 0.83,0.77
A14 Tyr	7.54	4.19	3.00, 2.92	C _{2,6} H 7.08, C _{3,5} H 6.85
A15 Gln	7.60	4.02	2.05	CγH ₂ 2.49, 2.41, NεH ₂ 7.54,6.98
A16 Leu	8.10	4.17	1.94, 1.62	СүН 1.76, СōН₃ 0.83, 0.81
A17 Glu	8.13	4.21	2.13, 2.06	CγH ₂ 2.59, 2.38
A18 Asn	7.45	4.50	2.62, 2.56	NõH2 7.20, 6.56
A19 Tyr	7.93	4.46	3.38, 2.98	C _{2,6} H 7.34, C _{3,5} H 6.81
A20 Cys	7.44	4.92	3.27, 2.85	
A21 Asn	8.31	4.75	2.89, 2.77	NōH2 7.53,6.66
B1 Phe		4.30	3.15, 3.15	C _{2,6} H 7.24, C _{3,5} H 7.37
B2 Val	8.23	4.15	1.94	СүН₃ 0.88,0.88
B3 Asn	8.52	4.74	2.76, 2.76	NõH2 7.60,6.96
B4 Gln	8.45	4.49	2.10,1.92	CγH ₂ 2.27, 2.20, NεH ₂ 7.36,6.86
B5 His	8.63	4.54	3.56, 3.28	C2H 8.62, C6H 7.41
B6 Leu	8.85	4.59	1.74, 0.95	СүН 1.63,СδН₃ 0.91,0.79
B7 Cys	8.37	4.93	3.21, 2.96	
B8 Gly	9.13	4.03, 3.89		
B9 Ser	9.05	4.18	4.02, 4.02	
B10 Asp	8.22	4.53	3.22, 2.86	
B11 Leu	7.12	4.01	1.91, 1.22	СүН 1.37, СōН₃ 0.82, 0.77
B12 Val	7.19	3.35	2.11	СүН₃ 0.96,0.96
B13 Glu	8.02	4.15	2.20, 2.11	CγH ₂ 2.55
B14 Ala	7.83	4.09	СβН₃ 1.49	
B15 Leu	8.04	3.88	1.34, 0.70	СүН 1.50, СδН₃ 0.70, 0.52
B16 Tyr	8.20	4.28	3.17, 3.17	C _{2,6} H 7.16, C _{3,5} H 6.80
B17 Leu	7.98	4.09	1.94, 1.66	СүН 1.87, СōН₃ 0.95,0.95
B18 Val	8.58	3.88	2.12	СүН₃ 1.04, 0.90
B19 Cys	8.78	4.82	3.28, 2.96	
B20 Gly	7.78	3.96, 3.96		
B21 Glu	8.50	4.24	2.21, 2.11	СүН2 2.53
B22 Arg	8.03	4.24	1.97, 1.82	CγH2 1.76, CδH2 3.28, NεH2 7.15
B23 Gly	7.69	4.04, 3.86		
B24 Phe	7.74	4.85	3.18, 2.94	C _{2,6} H 6.95, C _{3,5} H 7.09, C ₄ H
B25 Phe	8.34	4.70	3.13, 3.04	C _{2,6} H 7.21, C _{3,5} H 7.28
B26 Tyr	8.01	4.64	2.94, 2.94	C _{2,6} H 7.04, C _{3,5} H 6.78
B27 Thr	7.79	4.33	4.12	СүН₃ 1.14
B28 Asp	8.31	4.90	2.96, 2.75	
B29 Pro		4.51	2.26, 2.03	СγН₂ 2.03, СδН₂ 3.81
B30 Thr	7.97	4.49	4.40	СуНЗ 1.22

residue	NH	C _a H	C _B H	others
B1 Phe		-0.11		
B8 Gly				
B9 Ser		-0.19		
B11 Leu				С _γ Н 0.10, СδН ₃ 0.15
B12 Val				$C_{\gamma}H_{3}$,-0.14
B16 Tyr	-0.10			
B20 Gly	-0.12			
B24 Phe	0.11			
B25 Phe	-0.19			
B27 Thr	0.63			
B28 Asp	0.29		0.14	
B30 Thr	0.43	0.10	0.20	
A2 Ile		0.13		C _γ H ₂ -0.16
A3 Val	-0.36	0.10	0.12	
A4 Glu				$C_{\gamma} H_2$, 0.10
A5 Gln	-0.10			$C_{\gamma} H_2$, -0.10
A6 Cys	-0.10		0.17	
A9 Ser	0.16			
A10 Ile		-0.11		Cγ'H3 0.14, CδH3 0.18
A17 Glu	0.11			

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Table S5-B. Chemical-Shift Differences between SCI-57 and 2CA (20% deuterioacetic acid and 25°C)

residue	NH	C _α H	C _b H	others	*
B5 His		0.10	-	C ₂ H -0.12	
B15 Leu				C _δ H3 -0.10	
B21 Glu	0.20				
B23 Gly	-0.17				
A2 Ile	-0.74			$C_{\gamma}H_{2} 0.44$	
A3 Val	-0.34		0.10	·	

^aChemical Shifts relative to 5,5-dimethylsilapentanesulfonate (0 ppm). Only $\Delta \delta > 0.1$ ppm listed.

NOE restraints:			Average restraint violations	Average restraint violations	
	total	783	NOE-violation	0.038 Å	
	sequential	287	Dihedral angle-violation	1.72°	
	medium	167	C		
	long-range	202			
	Intra-residue	127			
Dihedral angle restraints:		47	Deviations from idea covale	Deviations from idea covalent geometry	
	φ-angles	34	bond length	0.004 Å	
	χ_1 -angles	13	bond angle	0.69°	
H-bonds:		22			
Main chain (RMSD1)		Empirical energy function ³ (kcal/mol)			
	α-helices ² A-domain	0.23 0.33	NOE restrain energy van der Waals	59.18 ± 9.6 29.64 ± 2.77	
	B-domain	0.20	improper dihedral angles	16.76 ± 1.76	
Side chain (RMSD ¹)		constrained dihedral angles	8.59 ± 2.07		
	α-helices ²	0.56	covalent bond lengths	15.09 ± 1.96	
	A-domain P. domain	0.79	bond angles	81.81 ± 6.24	

(1) RMSD were calculated according to C_{α} atoms of residues A1-19 and B5-25.

(2) Helical segments employed in RMSD calculation span residues A2-7, A13-19 and B9-19. (3) NOE and dihedral force constants were 40 kcal A^2 and 40 kcal radian², respectively (1 kcal = 4.18 kJ)