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A Class of 3*S*-2-Aminoacyltetrahydro-β-carboline-3-carboxylic Acids: Their Facile Synthesis, Inhibition for Platelet Activation, and High in Vivo Anti-Thrombotic Potency

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3S-Tetrahydro-β-carboline-3-carboxylic acid (TCCA) effectively inhibits ADP-induced platelet activation. This paper used TCCA as a lead, modified its 2-position with amino acids, and provided 20 novel 3S-2-aminoacyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acids (**5a**−**t**). With the in vitro assay, it was demonstrated that this modification diminished the IC_{50} values from 701 nM of TCCA to 10 nM of **5a**−**t**. With the in vivo assay, it was demonstrated that this modification reduced the efficacious dose from 5.0 μmol/kg of TCCA to 0.1 μmol/kg of **5a**−**t**. Comparing the Cerius^2 based conformation of them with that of their analogues, the 3-position modified TCCA, it was suggested that the comparatively unfolded conformation was one of the important factors of enhancing the in vivo antithrombotic potency.

Introduction

Intravascular thrombosis is implicated in the most frequent cardiovascular events, such as deep vein thrombosis, pulmonary embolism, myocardial infarction, and stroke, and it is one of the most prominent causes of morbidity and mortality all over the world.[1] Once vascular endothelium of the injured blood vessel is damaged, platelets adhere to the exposed extracellular matrix.[2] Adhesion of platelets following endothelial injury is the primary event usually associated with uncontrolled platelet activation culminating into intravascular thrombosis.[3] The suppression of platelet function, particularly through targeting such secondary regulatory mechanisms, has proven effective in the prevention of inappropriate platelet activation that results in thrombosis.[4] Antiplatelet therapy has an established role in the treatment of this cardiovascular event.[5] Since the most commonly used antiplatelet drugs lack clinical efficacy, in the past decades, continuous efforts have been made to discover new compounds capable of inhibiting platelet uncontrolled activation.

Natural and synthetic β-carbolines and tetrahydro-β-carbolines possess a variety of pharmacologic functions. So far, a wide spectrum of pharmacological actions has been investigated, such as trypanocidal action,[6,7] inhibiting mitogen activated protein kinase-activated protein kinase 2,[8] inhibiting cyclin-dependent kinases 4,[9,10] antimalarial action,[11,12] cytotoxic action,[13−17] cardiovascular effects,[18] neuroprotective and neuron-differentiating actions,[19] inhibiting human monoamine oxidase,[20] improving object recognition memory,[21] antiviral action,[22] binding to imidazoline receptors,[23,24] inhibiting mitotic kinesin Eg5,[25] interacting toward DNA,[26,27] binding to MGluR1 receptor,[28] antileishmanial action,[29] blocking the activity of topoisomerases,[30] stimulating insulin secretion,[31] binding to 5-HT_2 serotonin receptors,[32] inhibiting bacterial enoyl acyl carrier protein reductase,[33] and inhibiting acetyl- and butyryl-cholinesterases[34] as well as binding to benzodiazepine receptor.[35]

A series of β-carbolines such as harmalol, harmaline, norharmane, harmol, harmine, and harmane were used as the leads of the platelet activation inhibitors, but these compounds were capable of inhibiting collagen-induced platelet aggregation only, and the IC_{50} values were more than 130 μM.[36] In a previous paper, we revealed that 3*S*-tetrahydro-β-carboline-3-carboxylic acid (TCCA[a]) may effectively inhibit platelet-activating factor (PAF), adenosine diphosphate (ADP), and arachidonic acid (AA) as well as thrombin (TH) induced platelet aggregation, and the IC_{50} values were less than 1 μM.[37] In this study, we used amino acids modifying the 2-position of TCCA, prepared 20 novel derivatives, evaluated the in vitro antiplatelet aggregation and in vivo antithrombotic activities, and demonstrated the effect of Cerius^2 based conformation on the antithrombotic activity.

Results and Discussion

Facile Synthesis of 5a−t. A facile synthesis of 3*S*-2-aminoacyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acids (**5a**−**t**) was performed by using a five-step route depicted in Scheme 1. The esterification of TCAA from Pictet−Spengler condensation of L-Trp and formaldehyde provided the methylester (**2**, 92% yield). In the presence of DCC, HOBt, and NMM, **2** was conjugated with 20 amino acids to give

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[a] Abbreviations: TCCA, 3*S*-tetrahydro-β-carboline-3-carboxylic acid; ADP, adenosine diphosphate; AA, arachidonic acid; PAF, platelet-activating factor; TH, thrombin; NS, normal saline; Boc, *tert*-butyloxylcarbonyl; HOBt, *N*-hydroxybenzotriazole; DCC, dicyclohexylcarbodiimide; NMM, *N*-methyl morpholine; EtOAc, ethyl acetate; Et_3N, triethylamine; PRP, platelet rich plasma; PPP, platelet poor plasma; TLC, thin layer chromatography; MGluR1, metabotropic glutamate receptor-subtype 1; 5-TH 5-hydroxytryptamine.

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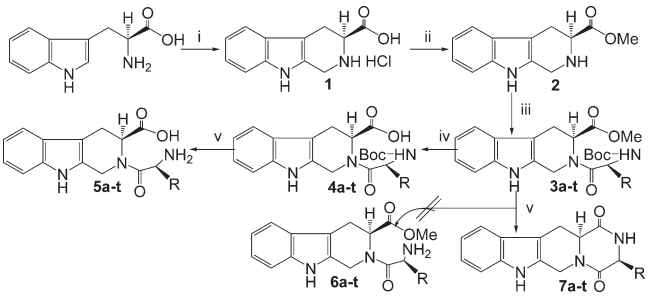
Scheme 1. Five-Step Procedure for Preparing 3*S*-2-Ammonoacyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acids[a]



[a] (i) Formaldehyde and H_2SO_4; (ii) methanol and thionyl chloride, rt, 92% yield; (iii) Boc-AA-OH, DCC and NMM; (iv) aqueous NaOH (2N) and hydrochloric acid; (v) hydrogen chloride in ethyl acetate (4 mol/L) and aqueous NaOH. In **3a**, **4a**, **5a**; $R_1 = CH_3$; **3b**, **4b**, **5b** R = $CH_2C_6H_5$; **3c**, **4c**, **5c** R = $CH(CH_3)_2$; **3d**, **4d**, **5d** R = CH_2OH; **3e**, **4e**, **5e** R = $CH(OH)CH_3$; **3f**, **4f**, **5f** R = $CH_2C_6H_4$-OH-p; **3g**, **4g**, **5g** R = tetrahydropyrrol-2-yl; **3h**, **4h**, **5h** R = CH_2SH; **3i**, **4i** , **5i** R = $CH_2CH_2SCH_3$; **3j** R = $CH_2CH_2CO_2CH_3$; **4j**, **5j** R = $CH_2CH_2CO_2H$; **3k** R = $CH_2CO_2CH_2C_6H_5$; **4k**, **5k** R = CH_2CO_2H; **3l**, **4l**, **5l** R = 1,3-imidazol-5-methylene; **3m**, **4m**, **5m** R = indol-3-yl-methylene; **3n**, **4n**, **5n** R = $CH_2(CH_2)_2NHC(NH_2)$=NH; **3o**, **4o**, **5o** R = H; **3p**, **4p** R = $CH_2(CH_2)_3NHZ$; **5p** R = $CH_2(CH_2)_3NH_2$; **3q**, **4q**, **5q** R = $CH_2CH_2CONH_2$; **2r**, **4r**, **5r** R = CH_2CONH_2; **3s**, **4s**, **5s** R = $CH_2CH(CH_3)_2$; **3t**, **4t**, **5t** R = $CH(CH_3)CH_2CH_3$.

3*S*-*N*-(Boc-aminoacyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid methylesters (**3a**−**t**, 86−95% yield). The saponification of **3a**−**t** provided 3*S*-2-(Boc-aminoacyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acids (**4a**−**t**, 78−95% yield). Removing Boc groups from **4a**−**t** resulted in **5a**−**t** (81−95% yield). These data suggest that the reaction conditions are mild and the yield of the individual reaction is acceptable. Therefore the present synthetic route is suitable for the introduction of amino acids into 2 position of TCCA.

It is worth indicating that the removal of the methylester group occurs prior to the removal of the Boc group and the saponification products of **3a**−**t** adjusted to pH 7 are critical for the formation of **5a**−**t**. Once the removal of the Boc group occurs prior to the removal of the methylester group, the intramolecular cyclization spontaneously proceed to form **7a**−**t** instead of the Boc-removed products **6a**−**t**. Similarly, once the saponification products are adjusted to pH less than 7, the intramolecular cyclization also spontaneously proceed to form **7a**−**t** instead of the Boc-removed products **6a**−**t**.

5a−**t Inhibiting ADP-, AA-, PAF-, and TH-Mediated Platelet Activation.** To evaluate the effect of 2-amino acid modification of TCCA on the in vitro platelet aggregation induced by different aggregators, the in vitro antiplatelet aggregation assays of **5a**−**t** were performed by following a general procedure and using four aggregators, adenosine diphosphate (ADP, final concentration 10 μM), arachidonic acid (AA, final concentration 350 μM), platelet-activating factor (PAF, final concentration 0.1 μM), and thrombin (TH, final concentration 0.1 U/mL). The IC_{50} values were listed in Table 1.

The IC_{50} values of **5a**−**t** against ADP-, AA-, PAF-, and TH-mediated platelet activation are 6.50−11.12, 23.52−30.11, 12.45−18.98, and 25.31−34.10 nM, respectively. The IC_{50} values of **5a**−**t** against ADP-mediated platelet activation are 2.7−3.6-, 1.7−1.9-, and 3.1−3.9- fold lower than those against AA-, PAF-, and TH-mediated platelet activation, respectively. Thus to a certain degree, **5a**−**t** show higher inhibition on platelet activation induced by ADP than the other aggregators. Interestingly, the IC_{50} value of TCCA against ADP-mediated platelet activation is 701 nM and 63−108-fold higher than those of **5a**−**t**. Thus the 2-amino acid modification leads the potency of TCCA inhibiting ADP-mediated platelet activation to increase by 63−108-fold.

Table 1. IC_{50} of **5a**−**t** Inhibiting Platelet Aggregation Induced by Four Aggregators[a]

	inhibition of platelet aggregation IC_{50} (nM)			
compd	ADP	AA	PAF	TH
1	701.01 ± 3.28	866.14 ± 2.39	752.28 ± 2.28	981.52 ± 3.55
5a	6.71 ± 0.54	24.60 ± 1.55	13.60 ± 1.10	27.41 ± 1.62
5b	9.80 ± 0.59	28.62 ± 1.60	18.98 ± 1.55	30.16 ± 1.80
5c	7.80 ± 0.65	27.26 ± 1.60	17.70 ± 1.50	32.52 ± 1.87
5d	8.66 ± 0.63	26.22 ± 1.52	16.10 ± 1.45	30.75 ± 1.90
5e	7.81 ± 0.59	24.55 ± 1.51	14.77 ± 1.48	27.80 ± 1.70
5f	7.76 ± 0.62	25.17 ± 1.55	15.11 ± 1.51	28.40 ± 1.68
5g	9.40 ± 0.66	25.70 ± 1.60	16.66 ± 1.61	30.09 ± 1.76
5h	7.10 ± 0.64	24.44 ± 1.49	14.68 ± 1.47	27.60 ± 1.59
5i	6.50 ± 0.50	23.52 ± 1.56	12.45 ± 1.41	25.31 ± 1.55
5j	10.25 ± 0.70	29.61 ± 1.64	14.75 ± 1.50	30.85 ± 1.83
5k	6.62 ± 0.64	23.98 ± 1.46	13.14 ± 1.35	26.65 ± 1.63
5l	7.31 ± 0.62	24.86 ± 1.62	15.47 ± 1.60	28.96 ± 1.70
5m	10.40 ± 0.69	27.94 ± 1.69	16.82 ± 1.65	29.60 ± 1.80
5n	9.47 ± 0.72	27.52 ± 1.51	18.25 ± 1.59	29.70 ± 1.78
5o	8.56 ± 0.68	26.50 ± 1.62	16.80 ± 1.60	31.95 ± 1.81
5p	11.12 ± 0.72	30.11 ± 1.72	17.04 ± 1.64	33.40 ± 1.85
5q	7.70 ± 0.65	28.20 ± 1.58	17.18 ± 1.61	30.10 ± 1.81
5r	9.19 ± 0.69	28.95 ± 1.64	16.20 ± 1.53	30.00 ± 1.78
5s	8.70 ± 0.59	26.77 ± 1.56	16.95 ± 1.59	34.10 ± 1.86
5t	6.56 ± 0.67	23.86 ± 1.57	12.60 ± 1.45	26.96 ± 1.73

[a] IC_{50} is represented by mean ± SD nM, $n = 6$

Table 2. Thrombus Weights of Intravenous **5a**−**t** Treated Rats[a]

compd	thrombus weight	compd	thrombus weight
NS	24.47 ± 3.21	**5j**	16.60 ± 2.47[b]
aspirin	15.21 ± 2.35	**5k**	14.40 ± 2.32[b]
TCCA	18.79 ± 2.01[b]	**5l**	15.89 ± 2.84[b]
5a	14.61 ± 1.84[b]	**5m**	18.43 ± 1.98[b]
5b	17.25 ± 2.06[b]	**5n**	16.68 ± 2.69[b]
5c	18.56 ± 1.83[b]	**5o**	19.29 ± 2.48[b]
5d	16.25 ± 2.28[b]	**5p**	16.54 ± 2.46[b]
5e	15.72 ± 2.47[b]	**5q**	17.30 ± 2.38[b]
5f	15.49 ± 2.66[b]	**5r**	16.34 ± 2.51[b]
5g	17.24 ± 2.23[b]	**5s**	25.26 ± 3.67[d]
5h	15.25 ± 2.85[b]	**5t**	13.74 ± 2.25[c]
5i	13.00 ± 2.17[c]		

[a] Thrombus weight is represented by mean ± SD mg, NS = vehicle, $n = 12$; Aspirin dose = 167 μmol/kg; TCCA dose = 5 μmol/kg; **5a**−**t** dose = 100 nmol/kg. [b] Compared to NS and **5s** $p < 0.01$. [c] Compared to NS and **5b**,**c**,**g**,**m**,**o**,**q**,**s** $p < 0.01$. [d] At 1 μmol/kg of dose, the thrombus weight is 10.55 ± 1.70 mg and compared to NS $p < 0.01$.

5a−**t Possess High in Vivo Antithrombotic Potency.** The in vivo antithrombotic activities of **5a**−**t** were assayed on an extracorporeal circulation of arterioveinos cannula model of rats. The individual stock solution of aspirin (positive control) and **5a**−**t** in normal saline (NS) was administered intravenously, the thrombus was weighed, and the data are listed in Table 2. The thrombus weights of the rats receiving 100 nmol/kg of **5a**−**t** range from 13.00 (**5i**) to 19.29 mg (**5o**) and are significantly lower than that (24.47 mg) of the rats receiving NS ($p < 0.01$). Though 100 nmol/kg of **5s** possessed no antithrombotic action at the dose of 1 μmol/kg, the thrombus weight dropped to 10.55 ± 1.70 mg (compared to NS, $p < 0.01$). Table 2 further indicates that the efficacious

dose of TCCA is 5 μmol/kg. This dose is 5- and 50-fold higher than that of **5s** and **5a**−**r**,**t**, respectively. Thus 2-amino acid modification leads the potency of TCCA to increase by 5−50-fold.

Dose Dependence of in Vivo Antithrombotic Action of 5i and 5t. To clarify the effect of the dose on the in vivo antithrombotic activities, 100, 10, and 1 nmol/kg of the most potent **5i** and **5t** were assayed. The data (Table 3) indicate that the antithrombotic potency of 100 nmol/kg dose is significantly higher than that of 10 nmol/kg dose, while the antithrombotic potency of 10 nmol/kg dose is significantly higher than that of 1 nmol/kg dose. These comparisons demonstrate that **5i** and **5t** dose-dependently inhibit the thrombosis of the treated rats.

In Vivo Antithrombotic Activity of Oral 5i and 5t. To explore the possibility of **5a**−**t** as oral antithrombotic agents, the oral antithrombotic effects of **5i** and **5t** were investigated.

Table 3. Effect of Dose of **5i**,**t** on the Thrombus Weight of Intravenously Treated Rats[a]

	thrombus weight at the following doses		
compd	100 nmol/kg	10 nmol/kg	1 nmol/kg
5i	13.00 ± 2.17[b]	17.67 ± 2.65[c]	22.59 ± 2.82
5t	13.74 ± 2.25[b]	18.12 ± 2.77[c]	25.43 ± 3.34

[a] Thrombus weight is represented by mean ± SD mg, n = 12. [b] Compared to 10 nmol/kg $p < 0.01$. [c] Compared to 1 nmol/kg $p < 0.01$.

Table 4. Effect of Oral **5i**,**t** on Thrombus Weight of the Treated Rats[a]

compd	thrombus weight	compd	thrombus weight
NS	25.02 ± 3.01	aspirin	17.90 ± 2.50[b]
5i	13.49 ± 2.07[b]	**5t**	13.88 ± 2.22[b]

[a] Weight of wet thrombus is represented by $X \pm$ SD mg, NS = vehicle, n = 12; Dose of **5i**,**t** = 100 nmol/kg; dose of aspirin = 167 μmol/kg. [b] Compared to NS, $p < 0.01$.

In an extracorporeal circulation of arterioveinos cannula model, the rats were orally treated with NS (negative control), the individual stock solution of aspirin (positive control), and **5i** or **5t** in NS, and the data are listed in Table 4. The evaluation explores that the thrombus weights of the rats orally receiving 100 nmol/kg of **5i** and **5t** are significantly lower than that of the rats receiving NS. The evaluation further indicates that the thrombus weights of the intravenously and orally treated rats gave no significant difference. These results imply that **5i** and **5t** may be potent oral antithrombotic agents due to the similarity between the intravenous and oral potency of them.

Effect of Conformation on the in Vivo Antithrombotic Activities of 5a−**t.** In a previous paper, we demonstrated that at a dose of 5 μmol/kg, the 3-amino acid modified TCCA, 3*S*-1,2,3,4-tetrahydro-β-carboline-3-carboxylamino acids, may successfully inhibit the thrombosis of the treated rats.[37] Herein we explored the hypothesis that the effective dose of 2-amino acid modified TCCA, 3*S*-2-aminoacyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acids, is 100 nmol/kg. To understand this position isomerism-induced huge change of the in vivo antithrombotic potency, the conformations of 2- and 3-amino acid modified TCCA were analyzed. Using TCCA as the template of Cerius[2] based alignment, the distinct stereoview for these two kinds of position isomers could be described as shown in Figure 1. The stereoview-represented conformation explores the idea that 3*S*-1,2,3,4-tetrahydro-β-carboline-3-carboxylamino acids (A in Figure 1) have their amino acid residues over the carboline ring, while 3*S*-2-aminoacyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acids (B in Figure 1) have their amino acid residues aside the carboline ring. This means a comparatively stretched conformation is particularly important for the high in vivo antithrombotic activity. This conformational requirement also explains the difference between the in vivo antithrombotic activities

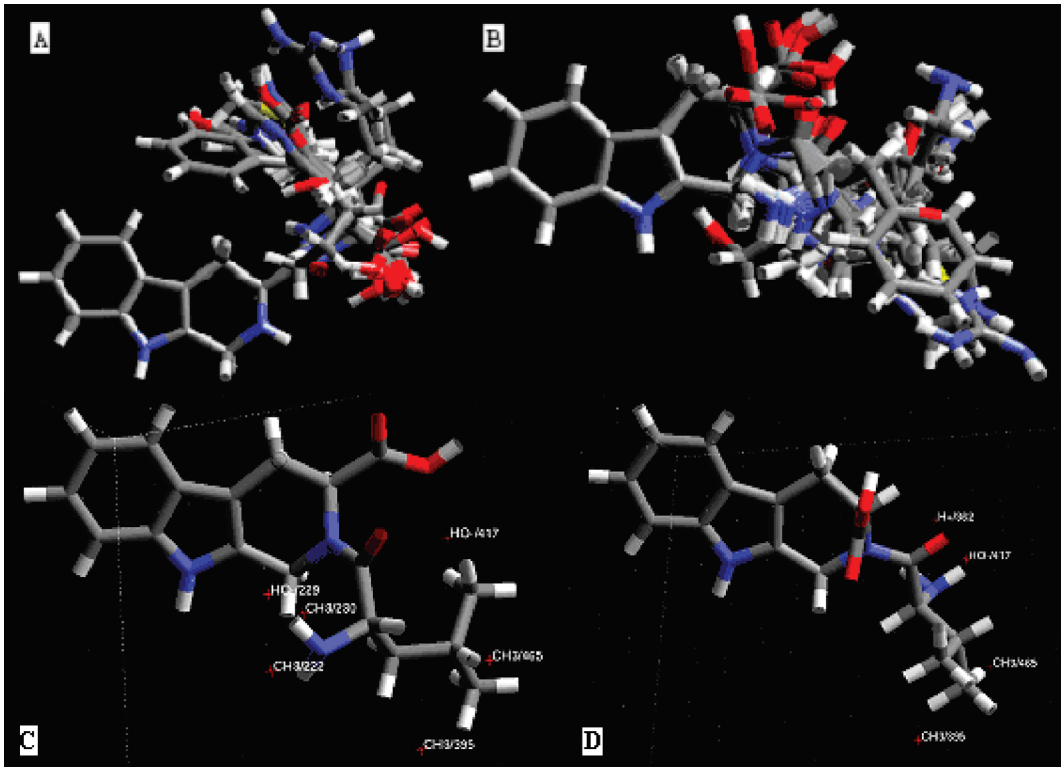


Figure 1. Stereoview of 3- and 2-amino acid modified TCCAs, (A) and (B); **5c** (C); **5s** (D).

of the structurally similar **5c** (C in Figure 1) and **5s** (D in Figure 1).

Conclusions

In conclusion, comparing with 3-amino acid modified TCCA, the 2-position isomers, 3*S*-2-aminoacyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acids, more effectively inhibit ADP-, AA-, PAF-, and TH-induced in vitro platelet aggregation and highly inhibit the in vivo thrombosis of the intravenously treated rats. The Cerius[2] based alignment resulted in a comparatively unfolded conformation for the present 2-amino acid modified TCCA. The fact that the efficacious dose of the in vivo antithrombotic action of the 3-position isomers is 50-fold higher than that of the 2-position isomers suggests that the comparatively unfolded conformation could be used as a criterion in the design of the derivatives having high in vivo antithrombotic potency. The fact that the oral and the intravenous in vivo antithrombotic potencies of the most potent **5i** and **5t** are close to each other suggests that **5a**−**t** could be the oral antithrombotic agents.

Experimental Section

General. The protected amino acids with L-configuration were purchased from Sigma Chemical Co. All coupling and deprotective reactions were carried out under anhydrous conditions. Chromatography was performed on Qingdao silica gel H. The purity (>97%) of the intermediates and the final products was confirmed on both TLC (Merck silica gel plates of type 60 F_{254}, 0.25 mm layer thickness) and HPLC (Waters, C_{18} column 4.6 mm × 150 mm). ^{1}H NMR spectra were recorded on Bruker Advance 500 spectrometers. FAB-MS was determined by VG-ZAB-MS high resolution GC/MS/DS and HP ES-5989x. Optical rotations were determined with a Schmidt+ Haensch Polartromic D instrument. The statistical analysis of all the biological data was performed by ANOVA test with $p < 0.05$ cutoff.

3*S*-1,2,3,4-Tetrahydro-β-carboline-3-carboxylic Acid (1). To a mixture of 5.0 g (24.5 mmol) of L-tryptophan, 25 mL of H_2SO_4 (1 mol/L), and 80 mL of water, 8 mL of formaldehyde (36−38%) were added. The reaction mixture was stirred at room temperature for 2 h and adjusted to pH 6−7 with concentrated ammonia liquor. The mixture obtained was kept at 0 °C for 12 h, and the formed precipitates were collected by filtration. After recrystallization, 3.97 g (75%) of the title compound were obtained as a colorless powder; mp 280−282 °C. ESI/MS: 217 $[M + H]^+$. IR (KBr): 3450, 3200, 3000, 2950, 2850, 1700, 1601, 1452, 1070, 900 cm^{-1}. ^{1}H NMR (BHSC-500, DMSO-d_6): δ 10.99 (s, 1 H), 9.89 (s, 1 H), 7.30 (t, J = 7.5 Hz, 1 H), 7.22 (t, J = 8.0 Hz, 1 H), 7.01 (d, J = 8.0 Hz, 1 H), 6.81 (d, J = 7.5 Hz, 1 H), 4.01 (t, J = 4.8 Hz, 1 H), 3.75 (dd, J = 10.5 Hz, J = 5.0 Hz, 1 H), 3.64 (dd, J = 10.5 Hz, J = 2.4 Hz, 1 H), 2.91 (d, J = 10.5 Hz, 2 H), 2.86 (s, 1 H).

3*S*-1,2,3,4-Tetrahydro-β-carboline-3-carboxylic Acid Methylester (2). At 0 °C, 10 mL of thionyl chloride was added dropwise to 50 mL of methanol, after which 5.0 g (23.1 mmol) of 3S-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid was added. The reaction mixture was stirred at room temperature for 15 h and then TLC (ethyl acetate/petroleum, 5:12) was used to indicate the completion of the reaction. The excess methanol and thionyl chloride were removed by evaporation. The residue was dissolved in 30 mL of ethyl acetate and washed successively with saturated $NaCO_3$ in water (3 × 30 mL) and saturated NaCl in water (3 × 30 mL). The separated ethyl acetate layer was dried with anhydrous $MgSO_4$, evaporated, and purified with flash chromatography ($CHCl_3$/CH_3OH, 30:1) to provide 4.9 g (92%) of the title compound as a colorless powder; mp 143−145 °C. ESI$^+$/MS: 231 $[M + H]^+$. ^{1}H NMR (BHSC-500, DMSO-d_6): δ 9.79 (s, 1H), 7.28 (t, J = 7.5 Hz, 1 H), 7.18 (t, J = 7.5 Hz, 1 H), 7.01 (t, J = 7.5 Hz, 1 H), 6.99 (t, J = 7.5 Hz, 1 H), 4.22 (d, J = 4.8 Hz, 2 H), 3.69 (dd, J = 10.5 Hz, J = 5.0 Hz, 1 H), 3.56 (s, 3 H), 3.14 (dd, J = 10.5 Hz, J = 2.4 Hz, 1 H), 2.83 (ddd, J = 10.5 Hz, J = 5.0 Hz, J = 2.4 Hz, 1 H), 2.66 (s, 1 H).

General Procedure for the Preparation of 3*S*-2-(Boc-aminoacyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3a−t). At 0 °C, to the solution of (2.2 mmol) Boc-L-amino acids in 30 mL of anhydrous THF, 300 mg (2.2 mmol) of HOBt were added. After 10 min, 490 mg (2.4 mmol) of DCC were then added. The suspension of 500 mg (2.17 mmol) of 3*S*-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid methylester in 3 mL of anhydrous THF was adjusted to pH 8−9 with *N*-methylmorpholine and stirred at room temperature for another 20 min. This suspension was then added to the solution of Boc-L-amino acids, and the reaction mixture was stirred at 0 °C for 2 h and at room temperature for 16 h. On evaporation, the residue was dissolved in 30 mL of ethyl acetate. The solution was washed successively with saturated sodium bicarbonate, 5% citric acid, and saturated sodium chloride, and the organic phase was separated and dried over anhydrous sodium sulfate. After filtration and evaporation under reduced pressure, the title compound was obtained as powder.

3*S*-2-(Boc-L-alanyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3a). Yield 93%; mp 148−150 °C. ESI/MS: 402 $[M + H]^+$. IR (KBr): 3340, 3006, 2953, 2840, 1748, 1642, 1605, 1450, 1391, 1072, 902 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.93 (s, 1 H), 8.03 (s, 1 H), 7.28 (t, J = 7.5 Hz, 1 H), 7.18 (t, J = 7.5 Hz, 1 H), 6.97 (t, J = 7.5 Hz, 1 H), 6.94 (t, J = 7.5 Hz, 1 H), 4.76 (t, J = 5.8 Hz, 1 H), 4.66 (m, J = 5.3 Hz, 1 H), 3.84 (s, 2 H), 3.62 (dd, J = 10.2 Hz, J = 5.2 Hz, 1 H), 3.61 (s, 3 H), 3.20 (dd, J = 10.2 Hz, J = 2.8 Hz, 1 H), 1.48 (d, J = 5.3 Hz, 3 H), 1.45 (s, 9 H). Anal. Calcd for $C_{21}H_{27}N_3O_5$: C, 62.83; H, 6.78; N, 10.47. Found: C, 62.66; H, 6.61; N, 10.29.

3*S*-2-(Boc-L-phenylalanyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3b). Yield 90%; mp 147−149 °C. ESI/MS: 478 $[M + H]^+$. IR (KBr): 3338, 3010, 2943, 2840, 1752, 1640, 1602, 1458, 1390, 1070, 902 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.97 (s, 1 H), 7.89 (s, 1 H), 7.27 (t, J = 7.4 Hz, 1 H), 7.20 (t, J = 7.8 Hz, 2 H), 7.16 (t, J = 7.4 Hz, 1 H), 7.11 (d, J = 7.8 Hz, 2 H), 7.07 (t, J = 7.8 Hz, 1H), 6.99 (t, J = 7.4 Hz, 1 H), 6.95 (t, J = 7.4 Hz, 1 H), 5.01 (t, J = 5.6 Hz, 1 H), 4.79 (t, J = 5.6 Hz, 1 H), 3.88 (s, 2 H), 3.64 (dd, J = 10.0 Hz, J = 5.1 Hz, 1 H), 3.63 (s, 3 H), 3.26 (dd, J = 10.0 Hz, J = 2.9 Hz, 1 H), 3.06 (d, J = 5.6 Hz, 2 H), 1.46 (s, 9H).; Anal. Calcd for $C_{27}H_{31}N_3O_5$: C, 67.91; H, 6.54; N, 8.80. Found: C, 67.73; H, 6.70; N, 9.00.

3*S*-2-(Boc-L-valinyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3c). Yield 87%; mp 137−139 °C. ESI/MS: 430 $[M + H]^+$. IR (KBr): 3343, 3000, 2952, 2845, 1743, 1640, 1605, 1455, 1391, 1375, 1070, 900 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.92 (s, 1 H), 8.00 (s, 1 H), 7.25 (t, J = 7.2 Hz, 1 H), 7.13 (t, J = 7.2 Hz, 1 H), 6.95 (t, J = 7.2 Hz, 1 H), 6.91 (t, J = 7.2 Hz, 1 H), 4.73 (t, J = 5.6 Hz, 1 H), 4.52 (d, J = 5.2 Hz, 1 H), 3.86 (s, 2 H), 3.62 (dd, J = 10.3 Hz, J = 5.1 Hz, 1 H), 3.64 (s, 3 H), 3.22 (dd, J = 10.3 Hz, J = 3.2 Hz, 1 H), 2.66 (m, J = 5.2 Hz, 1 H), 1.45 (s, 9 H), 1.03 (d, J = 5.4 Hz, 6 H). Anal. Calcd for $C_{23}H_{31}N_3O_5$: C, 64.32; H, 7.27; N, 9.78. Found: C, 64.16; H, 7.20; N, 9.92.

3*S*-2-(Boc-L-serinyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3d). Yield 93%; mp 155−157 °C. ESI/MS: 418 $[M + H]^+$. IR (KBr): 3339, 3006, 2945, 2842, 1750, 1643, 1605, 1459, 1391, 1072, 900 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.01 (s, 1 H), 8.03 (s, 1 H), 7.29 (t, J = 7.6 Hz, 1 H), 7.19 (t, J = 7.6 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1 H), 6.90 (t, J = 7.6 Hz, 1 H), 4.78 (t, J = 5.7 Hz, 1 H), 4.65 (t, J = 5.5 Hz, 1 H), 4.05 (d, J = 5.5 Hz, 1 H), 3.91 (s, 2 H), 3.62 (dd, J = 10.1 Hz, J = 5.0 Hz, 1 H), 3.60 (s, 3 H), 3.28 (dd, J = 10.1 Hz, J = 2.7 Hz, 1 H), 3.08 (d, J = 5.5 Hz, 2 H), 1.48 (s, 9 H). Anal. Calcd for $C_{21}H_{27}N_3O_6$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.60; H, 6.71; N, 9.88.

3*S*-2-(Boc-L-threoninyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3e). Yield 90%; mp 128−130 °C. ESI/MS: 432 $[M + H]^+$. IR (KBr): 3433, 3205, 3000, 2955, 2841,

1730, 1643, 1605, 1452, 1390, 1372, 1060, 904 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 10.02 (s, 1 H), 7.89 (s, 1 H), 7.30 (t, J = 7.3 Hz, 1 H), 7.22 (t, J = 7.3 Hz, 1 H), 6.90 (d, J = 7.4 Hz, 1 H), 6.70 (d, J = 7.3 Hz, 1 H), 4.82 (t, J = 5.3 Hz, 1 H), 4.63 (m, J = 5.3 Hz, 1 H), 4.44 (t, J = 5.3 Hz, 1 H), 4.03 (m, J = 5.2 Hz, 2 H), 3.62 (s, 3 H), 2.95 (d, J = 5.4 Hz, 2 H), 2.21 (d, J = 3.6 Hz, 1 H), 1.45 (s, 9 H), 1.21 (d, J = 5.6 Hz, 3 H). Anal. Calcd for $C_{22}H_{29}N_3O_6$: C, 61.24; H, 6.77; N, 9.74. Found: C, 61.11; H, 6.65; N, 9.89.

3*S*-2-(Boc-L-tyrosinyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3f). Yield 87%; mp 145−147 °C. ESI/MS: 494 $[M + H]^+$. IR (KBr): 3337, 3004, 2945, 2845, 1752, 1641, 1600, 1452, 1390, 1070, 903 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 10.02 (s, 1 H), 8.00 (s, 1 H), 7.27 (t, J = 7.5 Hz, 1 H), 7.19 (t, J = 7.5 Hz, 1 H), 6.96 (d, J = 7.6 Hz, 2 H), 6.89 (d, J = 7.5 Hz, 1 H), 6.88 (d, J = 7.5 Hz, 1 H), 6.68 (d, J = 7.6 Hz, 2 H), 5.02 (s, 1 H), 4.94 (t, J = 5.4 Hz, 1 H), 4.83 (t, J = 5.4 Hz, 1H), 3.93 (s, 2 H), 3.64 (dd, J = 10.0 Hz, J = 5.1 Hz, 1 H), 3.63 (s, 3 H), 3.31 (dd, J = 10.0 Hz, J = 2.7 Hz, 1 H), 3.07 (d, J = 5.4 Hz, 2 H), 1.46 (s, 9 H). Anal. Calcd for $C_{27}H_{31}N_3O_6$: C, 65.71; H, 6.33; N, 8.51. Found: C, 65.54; H, 6.46; N, 8.70.

3*S*-2-(Boc-L-prolinyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3g). Yield 92%; mp 118−120 °C. ESI/MS: 428 $[M + H]^+$. IR (KBr): 3431, 3206, 3003, 2954, 2842, 1730, 1643, 1605, 1456, 1394, 1370, 1065, 904 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 9.97 (s, 1 H), 7.32 (t, J = 7.2 Hz, 1 H), 7.22 (t, J = 7.4 Hz, 1H), 7.03 (d, J = 7.4 Hz, 1H), 6.93 (d, J = 7.2 Hz, 1 H), 4.85 (t, J = 5.3 Hz, 1 H), 4.31 (t, J = 5.5 Hz, 1 H), 4.25 (d, J = 5.4 Hz, 2 H), 3.62 (s, 3 H), 3.44 (t, J = 5.5 Hz, 2 H), 2.97 (d, J = 5.5 Hz, 2 H), 2.25 (d, J = 5.4 Hz, 2 H), 1.95 (t, J = 5.1 Hz, 2 H), 1.47 (s, 9 H). Anal. Calcd for $C_{23}H_{29}N_3O_5$: C, 64.62; H, 6.84; N, 9.83. Found: C, 64.75; H, 6.92; N, 9.97.

3*S*-2-(Boc-L-cysteinyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3h). Yield 93%; mp 133−135 °C. ESI/MS: 434 $[M + H]^+$. IR (KBr): 3441, 3205, 3004, 2940, 2842, 1734, 1640, 1605, 1450, 1392, 1370, 1064, 900 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 10.02 (s, 1 H), 7.99 (s, 1 H), 7.30 (t, J = 7.3 Hz, 1 H), 7.20 (t, J = 7.5 Hz, 1 H), 7.03 (d, J = 7.5 Hz, 1 H), 6.85 (d, J = 7.3 Hz, 1 H), 4.90 (t, J = 5.1 Hz, 1H), 4.73 (t, J = 5.3 Hz, 1H), 4.23 (d, J = 5.4 Hz, 2 H), 3.63 (s, 3 H), 3.13 (d, J = 5.2 Hz, 2H), 2.99 (d, J = 5.3 Hz, 2 H), 1.47 (s, 9 H), 1.64 (s, 1 H). Anal. Calcd for $C_{21}H_{27}N_3O_5S$: C, 58.18; H, 6.28; N, 9.69. Found: C, 58.25; H, 6.38; N, 9.86.

3*S*-2-(Boc-L-methioninyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3i). Yield 91%; mp 133−135 °C. ESI/MS: 462 $[M + H]^+$. IR (KBr): 3443, 3205, 3007, 2950, 2844, 1730, 1645, 1602, 1455, 1392, 1375, 1064, 902 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 10.01 (s, 1 H), 7.99 (s, 1 H), 7.30 (t, J = 7.3 Hz, 1 H), 7.20 (t, J = 7.5 Hz, 1H), 6.97 (d, J = 7.5 Hz, 1 H), 6.83 (d, J = 7.3 Hz, 1 H), 4.83 (t, J = 5.2 Hz, 1H), 4.47 (t, J = 5.3 Hz, 1 H), 4.27 (d, J = 5.3 Hz, 2 H), 3.66 (s, 3 H), 2.95 (d, J = 5.4 Hz, 2H), 2.45 (t, J = 5.3 Hz, 2 H), 2.25 (d, J = 5.3 Hz, 2 H), 2.11 (s, 3 H), 1.47 (s, 9 H). Anal. Calcd for $C_{23}H_{31}N_3O_5S$: C, 59.85; H, 6.77; N, 9.10. Found: C, 59.69; H, 6.85; N, 9.26.

3*S*-2-[Boc-L-glutamyl(OMe)]-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3j). Yield 91%; mp 122−124 °C. ESI/MS: 474 $[M + H]^+$. IR (KBr): 3443, 3205, 3004, 2940, 2834, 1735, 1642, 1601, 1452, 1395, 1370, 1063, 901 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 9.92 (s, 1 H), 8.01 (s, 1 H), 7.35 (t, J = 7.2 Hz, 1 H), 7.26 (t, J = 7.2 Hz, 1 H), 7.00 (d, J = 7.5 Hz, 1 H), 6.86 (d, J = 7.3 Hz, 1 H), 4.87 (d, J = 5.3 Hz, 1 H), 4.45 (t, J = 5.5 Hz, 1 H), 4.24 (d, J = 5.4 Hz, 2 H), 3.67 (s, 3 H), 3.65 (s, 3 H), 2.97 (d, J = 5.3 Hz, 2 H), 2.29 (t, J = 5.4 Hz, 2 H), 2.23 (t, J = 5.5 Hz, 2 H), 1.47 (s, 9 H). Anal. Calcd for $C_{24}H_{31}N_3O_7$: C, 60.88; H, 6.60; N, 8.87. Found: C, 60.75; H, 6.47; N, 9.05.

3*S*-2-[Boc-L-Aspartyl(OBzl)]-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3k). Yield 92%; mp 144−146 °C. ESI/MS: 536 $[M + H]^+$. IR (KBr): 3340, 3004, 2948, 2845, 1748, 1642, 1600, 1455, 1391, 1072, 904 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 9.95 (s, 1 H), 8.02 (s, 1 H), 7.29 (t, J = 7.6 Hz, 1 H), 7.22 (t, J = 7.2 Hz, 2 H), 7.20 (d, J = 7.2 Hz, 2 H), 7.18 (t, J = 7.5 Hz, 1 H), 7.16 (t, J = 7.2 Hz, 1H), 6.97 (t, J = 7.5 Hz, 1 H), 6.93 (t, J = 7.5 Hz, 1 H), 5.36 (s, 2 H), 5.14 (t, J = 5.5 Hz, 1H), 4.77 (t, J = 5.7 Hz, 1 H), 3.62 (dd, J = 10.2 Hz, J = 5.1 Hz, 1 H), 3.64 (s, 3 H), 3.24 (dd, J = 10.2 Hz, J = 2.7 Hz, 1 H), 3.06 (d, J = 5.6 Hz, 2 H), 2.75 (d, J = 5.5 Hz, 2 H), 1.46 (s, 9 H). Anal. Calcd for $C_{29}H_{33}N_3O_7$: C, 65.03; H, 6.21; N, 7.85. Found: C, 65.18; H, 6.06; N, 7.99.

3*S*-2-(Boc-L-histidinyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3l). Yield 92%; mp 140−142 °C. ESI/MS: 468 $[M + H]^+$. IR (KBr): 3445, 3203, 3005, 2944, 2837, 1731, 1645, 1602, 1451, 1393, 1370, 1060, 900 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 12.95 (s, 1 H), 9.98 (s, 1 H), 8.02 (s, 1 H), 7.45 (s, 1 H), 7.32 (t, J = 7.2 Hz, 1 H), 7.18 (t, J = 7.5 Hz, 1 H), 7.18 (d, J = 7.5 Hz, 1 H), 6.99 (t, J = 7.2 Hz, 1 H), 6.87 (s, 1 H), 4.94 (t, J = 5.1 Hz, 1 H), 4.81 (t, J = 5.3 Hz, 1 H), 4.23 (d, J = 5.1 Hz, 2 H), 3.67 (s, 3 H), 3.17 (d, J = 5.2 Hz, 2 H), 2.95 (d, J = 5.1 Hz, 2 H), 1.47 (s, 9 H). Anal. Calcd for $C_{24}H_{29}N_5O_5$: C, 61.66; H, 6.25; N, 14.98. Found: C, 61.79; H, 6.34; N, 14.82.

3*S*-2-(Boc-L-tryptophanyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3m). Yield 89%; mp 126−128 °C. ESI/MS: 517 $[M + H]^+$. IR (KBr): 3335, 3009, 2942, 2842, 1750, 1643, 1604, 1453, 1391, 1072, 900 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 9.99 (s, 1 H), 9.96 (s, 1 H), 8.02 (s, 1 H), 7.29 (t, J = 7.6 Hz, 1 H), 7.21 (t, J = 7.4 Hz, 1 H), 7.19 (t, J = 7.4 Hz, 1 H), 7.18 (t, J = 7.4 Hz, 1 H), 7.17 (t, J = 7.4 Hz, 1 H), 7.16 (t, J = 7.6 Hz, 1 H), 7.01 (t, J = 7.6 Hz, 1H), 6.89 (t, J = 7.6 Hz, 1 H), 6.82 (s, 1 H), 4.90 (t, J = 5.5 Hz, 1 H), 4.85 (t, J = 5.4 Hz, 1 H), 3.92 (s, 2 H), 3.62 (dd, J = 10.1 Hz, J = 5.0 Hz, 1 H), 3.65 (s, 3 H), 3.32 (dd, J = 10.1 Hz, J = 2.9 Hz, 1 H), 2.92 (t, J = 5.5 Hz, 2 H), 1.48 (s, 9H). Anal. Calcd for $C_{29}H_{32}N_4O_5$: C, 67.43; H, 6.24; N, 10.85. Found: C, 67.59; H, 6.40; N, 10.72.

3*S*-2-(Boc-L-argininyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3n). Yield 88%; mp 137−139 °C. ESI/MS: 487 $[M + H]^+$. IR (KBr): 3445, 3209, 3004, 2945, 2840, 1733, 1642, 1600, 1451, 1392, 1370, 1064, 900 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 10.20 (s, 1 H), 8.43 (s, 2 H), 8.25 (s, 1 H), 8.20 (s, 1 H), 8.03 (s, 1 H), 7.27 (t, J = 7.4 Hz, 1 H), 7.17 (t, J = 7.5 Hz, 1 H), 7.01 (d, J = 7.5 Hz, 1 H), 6.93 (d, J = 7.4 Hz, 1 H), 4.91 (d, J = 5.1 Hz, 1 H), 4.40 (t, J = 4.3 Hz, 1 H), 4.27 (d, J = 5.1 Hz, 2 H), 3.67 (s, 3 H), 2.92 (d, J = 4.3 Hz, 2 H), 2.66 (t, J = 5.5 Hz, 2 H), 1.93 (m, J = 5.3 Hz, 2 H), 1.57 (m, J = 5.4 Hz, 2 H), 1.55 (s, 9 H). Anal. Calcd for $C_{24}H_{34}N_6O_5$: C, 59.24; H, 7.04; N, 17.27. Found: C, 59.10; H, 6.95; N, 17.40.

3*S*-2-(Boc-glycyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3o). Yield 95%; mp 150−152 °C. ESI/MS: 388 $[M + H]^+$. IR (KBr): 3342, 3003, 2950, 2844, 1745, 1645, 1603, 1452, 1390, 1070, 900 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 9.91 (s, 1 H), 8.11 (s, 1 H), 7.29 (t, J = 7.6 Hz, 1 H), 7.16 (t, J = 7.6 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1 H), 6.97 (t, J = 7.6 Hz, 1 H), 4.76 (t, J = 5.6 Hz, 2 H), 4.52 (d, J = 4.9 Hz, 2 H), 3.87 (s, 2 H), 3.65 (dd, J = 10.5 Hz, J = 5.0 Hz, 1 H), 3.58 (s, 3 H), 3.17 (dd, J = 10.5 Hz, J = 2.4 Hz, 1 H), 1.44 (s, 9 H). Anal. Calcd for $C_{20}H_{25}N_3O_5$: C, 62.00; H, 6.50; N, 10.85. Found: C, 62.18; H, 6.34; N, 10.67.

3*S*-2-[Boc-L-lysinyl(*Z*)]-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid Methylester (3p). Yield 92%; mp 95−97 °C. ESI/MS: 593 $[M + H]^+$. IR (KBr): 3342, 3003, 2940, 2845, 1752, 1641, 1602, 1456, 1390, 1070, 902 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 9.97 (s, 1 H), 8.05 (s, 1 H), 8.00 (s, 1 H), 7.27 (t, J = 7.5 Hz, 1 H), 7.22 (t, J = 7.2 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1 H), 7.15 (d, J = 7.2 Hz, 2H), 7.13 (t, J = 7.2 Hz, 2 H), 7.00 (t, J = 7.5 Hz, 1H), 6.88 (t, J = 7.5 Hz, 1 H), 5.36 (s, 2 H), 4.76 (t, J = 5.6 Hz, 1H), 4.55 (t, J = 5.6 Hz, 1H), 3.63 (dd, J = 10.2 Hz, J = 5.1 Hz, 1 H), 3.64 (s, 3 H), 3.30 (dd, J = 10.1 Hz, J = 2.7 Hz, 1 H), 3.08 (d, J = 5.5 Hz, 2 H), 2.95 (t, J = 5.4 Hz, 2 H), 1.75 (t, J = 5.5 Hz, 2 H), 1.58 (t, J = 5.3 Hz, 2 H), 1.48 (s, 9 H), 1.27 (m, J = 5.6 Hz, 2 H). Anal. Calcd for $C_{32}H_{40}N_4O_7$: C, 64.85; H, 6.80; N, 9.45. Found: C, 64.69; H, 6.71; N, 9.62.

3*S*-2-(Boc-L-glutaminyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid Methylester (3q). Yield 86%; mp 145−147 °C. ESI/MS: 459 $[M + H]^+$. IR (KBr): 3342, 3011, 2949, 2844, 1750, 1640, 1603, 1456, 1391, 1072, 905 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 10.00 (s, 1 H), 8.02 (s, 1 H), 7.29 (t, J = 7.6 Hz, 1 H), 7.17 (t, J = 7.6 Hz, 1 H), 6.86 (d, J = 7.6 Hz, 1 H), 6.83 (d, J = 7.6 Hz, 1 H), 6.12 (s, 2 H), 4.90 (t, J = 5.4 Hz, 1 H), 4.55 (t, J = 5.4 Hz, 1 H), 3.95 (s, 2 H), 3.62 (dd, J = 10.2 Hz, J = 5.0 Hz, 1 H), 3.60 (s, 3 H), 3.32 (dd, J = 10.1 Hz, J = 2.9 Hz, 1 H), 2.19 (t, J = 4.9 Hz, 2 H), 2.01 (m, J = 4.9 Hz, 2 H), 1.42 (s, 9 H). Anal. Calcd for $C_{23}H_{30}N_4O_6$: C, 60.25; H, 6.59; N, 12.22. Found: C, 60.38; H, 6.77; N, 12.37.

3*S*-2-(Boc-L-asparaginyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid Methylester (3r). Yield 91%; mp 137−139 °C. ESI/MS: 445 $[M + H]^+$. IR (KBr): 3443, 3205, 3001, 2932, 2833, 1734, 1630, 1604, 1457, 1391, 1370, 1061, 900 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 9.97 (s, 1 H), 8.01 (s, 1 H), 7.22 (t, J = 7.3 Hz, 1 H), 7.14 (t, J = 7.1 Hz, 1 H), 7.01 (d, J = 7.3 Hz, 1 H), 6.85 (d, J = 7.3 Hz, 1 H), 6.03 (s, 2 H), 4.91 (d, J = 5.3 Hz, 1 H), 4.41 (t, J = 5.3 Hz, 1 H), 4.24 (d, J = 5.3 Hz, 2 H), 3.65 (s, 3 H), 2.92 (d, J = 5.1 Hz, 2 H), 2.55 (t, J = 5.3 Hz, 2 H), 1.49 (s, 9 H). Anal. Calcd for $C_{22}H_{28}N_4O_6$: C, 59.45; H, 6.35; N, 12.60. Found: C, 59.62; H, 6.44; N, 12.43.

3*S*-2-(Boc-L-leucyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid Methylester (3s). Yield 87%; mp 135−137 °C. ESI/MS: 444 $[M + H]^+$. IR (KBr): 3344, 3002, 2950, 2842, 1745, 1640, 1603, 1452, 1390, 1070, 900 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 9.87 (s, 1H), 8.00 (s, 1H), 7.27 (t, J = 7.4 Hz, 1 H), 7.15 (t, J = 7.4 Hz, 1 H), 6.99 (t, J = 7.4 Hz, 1 H), 6.96 (t, J = 7.4 Hz, 1 H), 4.75 (t, J = 5.9 Hz, 1 H), 4.55 (d, J = 5.4 Hz, 1 H), 3.88 (s, 2 H), 3.60 (dd, J = 10.0 Hz, J = 5.0 Hz, 1 H), 3.62 (s, 3 H), 3.22 (dd, J = 10.0 Hz, J = 2.9 Hz, 1 H), 1.88 (m, J = 5.4 Hz, 1 H), 1.78 (t, J = 5.0 Hz, 2 H), 1.46 (s, 9 H), 1.03 (d, J = 5.4 Hz, 6 H). Anal. Calcd for $C_{24}H_{33}N_3O_5$: C, 64.99; H, 7.50; N, 9.47. Found: C, 65.16; H, 7.63; N, 9.32.

3*S*-2-(Boc-L-isoleucyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid Methylester (3t). Yield 88%; mp 130−132 °C. ESI/MS: 444 $[M + H]^+$. IR (KBr): 3344, 3002, 2950, 2842, 1745, 1640, 1603, 1452, 1390, 1070, 900 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 9.89 (s, 1 H), 8.03 (s, 1 H), 7.27 (t, J = 7.4 Hz, 1 H), 7.15 (t, J = 7.4 Hz, 1H), 6.99 (t, J = 7.4 Hz, 1 H), 6.96 (t, J = 7.4 Hz, 1 H), 4.75 (t, J = 5.9 Hz, 1 H), 4.55 (d, J = 5.4 Hz, 1 H), 3.88 (s, 2 H), 3.60 (dd, J = 10.0 Hz, J = 5.0 Hz, 1 H), 3.62 (s, 3 H), 3.22 (dd, J = 10.0 Hz, J = 2.9 Hz, 1 H), 2.48 (m, J = 5.4 Hz, 1 H), 1.33 (m, J = 5.0 Hz, 2 H), 1.46 (s, 9 H), 1.06 (d, J = 5.4 Hz, 3 H), 1.00 (t, J = 5.0 Hz, 3 H). Anal. Calcd for $C_{24}H_{33}N_3O_5$: C, 64.99; H, 7.50; N, 9.47. Found: C, 65.16; H, 7.63; N, 9.32.

General Procedure for Preparation of 4a−t. At 0 °C, to the solution of 0.50 g (1.25 mmol) of **3a−t** in 4 mL of methanol and 2 mL of chloroform, 0.24 g (6.00 mmol) of NaOH was added. The reaction mixture was stirred at 0 °C for 60 min. TLC analysis (chloroform/methanol, 30:1) indicated a complete disappearance of **3a−t**. After evaporation, the residue was dissolved in 30 mL of water, and the solution was adjusted to pH 7 with dilute hydrochloric acid and extracted with ethyl acetate (3 × 20 mL). The organic phase was washed successively with 5% sodium bicarbonate and saturated sodium chloride. The solution was then dried over anhydrous sodium sulfate. Compounds **4a−t** was obtained after filtration and evaporation under reduced pressure.

3*S*-2-(Boc-L-alanyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (4a). Yield 81%; mp 175−177 °C. ESI/MS: 388 $[M + H]^+$. IR (KBr): 3340, 3006, 2953, 2840, 1748, 1642, 1605, 1450, 1391, 1072, 902 cm^{-1}; $[\alpha]_D^{20}$ = −67 (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.99 (s, 1 H), 10.01 (s, 1 H), 7.95 (s, 1 H), 7.27 (d, J = 7.5 Hz, 1 H), 7.18 (d, J = 7.5 Hz, 1 H), 6.98 (t, J = 7.5 Hz, 1 H), 6.88 (t, J = 7.5 Hz, 1 H), 4.58 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.46 (m, 1 H), 4.25 (d, J = 13.0 Hz, 1 H), 3.83 (d, J = 13.0 Hz, 1 H), 2.97 (m, 1 H), 2.57 (t, 1 H), 1.47 (d, J = 5.4 Hz, 3 H), 1.41 (s, 9 H). Anal. Calcd for $C_{20}H_{25}N_3O_5$: C, 62.00; H, 6.50; N, 10.85. Found: C, 62.18; H, 6.64; N, 10.62.

3*S*-2-(Boc-L-phenylalanyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (4b). Yield 89%; mp 125−127 °C. ESI/MS: 464 $[M + H]^+$. IR (KBr): 3338, 3010, 2943, 2840, 1752, 1640, 1602, 1458, 1390, 1070, 902 cm^{-1}; $[\alpha]_D^{20}$ = −42 (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.99 (s, 1 H), 9.98 (s, 1 H), 7.98 (s, 1 H), 7.28 (d, J = 7.5 Hz, 1 H), 7.18 (m, 6 H), 6.96 (t, J = 7.5 Hz, 1 H), 6.81 (t, J = 7.5 Hz, 1 H), 4.53 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.36 (m, 1 H), 4.27 (d, J = 13.0 Hz, 1 H), 3.79 (d, J = 13.0 Hz, 1 H), 2.95 (m, 3 H), 2.58 (t, 1 H), 1.41 (s, 9 H). Anal. Calcd for $C_{26}H_{29}N_3O_5$: C, 67.37; H, 6.31; N, 9.07. Found: C, 67.18; H, 6.16; N, 9.31.

3*S*-2-(Boc-L-valinyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (4c). Yield 92%; mp 135−137 °C. ESI/MS: 416 $[M + H]^+$. IR (KBr): 3343, 3000, 2952, 2845, 1743, 1640, 1605, 1455, 1391, 1375, 1070, 900 cm^{-1}; $[\alpha]_D^{20}$ = −94 (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 11.01 (s, 1 H), 9.99 (s, 1 H), 7.96 (s, 1 H), 7.30 (d, J = 7.5 Hz, 1 H), 7.18 (d, J = 7.5 Hz, 1 H), 6.98 (t, J = 7.5 Hz, 1 H), 6.79 (t, J = 7.5 Hz, 1 H), 4.55 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.37 (m, 1 H), 4.19 (d, J = 13.0 Hz, 1 H), 3.78 (d, J = 13.0 Hz, 1 H), 2.92 (m, 1 H), 2.72 (m, J = 4.5 Hz, 1 H), 2.54 (t, 1 H), 1.41 (s, 9 H), 1.15 (d, J = 5.6 Hz, 6 H). Anal. Calcd for $C_{22}H_{29}N_3O_5$: C, 63.60; H, 7.04; N, 10.11. Found: C, 63.79; H, 6.90; N, 9.80.

3*S*-2-(Boc-L-serinyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (4d). Yield 89%; mp 123−125 °C. ESI/MS: 404 $[M + H]^+$. IR (KBr): 3339, 3006, 2945, 2842, 1750, 1643, 1605, 1459, 1391, 1072, 900 cm^{-1}; $[\alpha]_D^{20}$ = −81 (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.95 (s, 1 H), 9.95 (s, 1 H), 7.97 (s, 1 H), 7.29 (d, J = 7.5 Hz, 1 H), 7.17 (d, J = 7.5 Hz, 1 H), 7.02 (t, J = 7.5 Hz, 1 H), 6.88 (t, J = 7.5 Hz, 1 H), 4.52 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.35 (m, 1 H), 4.14 (d, J = 13.0 Hz, 1 H), 4.05 (m, 2 H), 3.82 (d, J = 13.0 Hz, 1 H), 2.93 (m, 1 H), 2.51 (t, 1 H), 1.44 (s, 9 H). Anal. Calcd for $C_{20}H_{25}N_3O_6$: C, 59.54; H, 6.25; N, 10.42. Found: C, 59.72; H, 6.10; N, 10.65.

3*S*-2-(Boc-L-threoninyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (4e). Yield 87%; mp 148−150 °C. ESI/MS: 418 $[M + H]^+$. IR (KBr): 3433, 3205, 3000, 2955, 2841, 1730, 1643, 1605, 1452, 1390, 1372, 1060, 904 cm^{-1}; $[\alpha]_D^{20}$ = −60 (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.96 (s, 1 H), 9.92 (s, 1 H), 7.95 (s, 1 H), 7.29 (d, J = 7.5 Hz, 1 H), 7.16 (d, J = 7.5 Hz, 1 H), 7.06 (t, J = 7.5 Hz, 1 H), 6.95 (t, J = 7.5 Hz, 1 H), 4.58 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.33 (m, 1 H), 4.20 (m, 3 H), 3.85 (d, J = 13.0 Hz, 1 H), 2.95 (m, 1 H), 2.52 (t, 1 H), 1.41 (s, 9 H), 1.25 (d, J = 5.2 Hz, 3 H). Anal. Calcd for $C_{21}H_{27}N_3O_6$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.64; H, 6.68; N, 9.83.

3*S*-2-(Boc-L-tyrosinyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (4f). Yield 90%; mp 144−145 °C. ESI/MS: 480 $[M + H]^+$. IR (KBr): 3337, 3004, 2945, 2845, 1752, 1641, 1600, 1452, 1390, 1070, 903 cm^{-1}; $[\alpha]_D^{20}$ = −66 (c = 0.5, CH_3OH).; ^1H NMR (500 MHz, DMSO-d_6): δ 10.97 (s, 1 H), 9.90 (s, 1 H), 8.05 (s, 1 H), 7.32 (d, J = 7.5 Hz, 1 H), 7.15 (d, J = 7.5 Hz, 1 H), 7.02 (t, J = 7.5 Hz, 1 H), 6.90 (t, J = 7.5 Hz, 1 H), 6.94 (d, J = 7.2 Hz, 2 H), 6.88 (d, J = 7.2 Hz, 2 H), 4.54 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.34 (m, 1 H), 4.07 (d, J = 13.0 Hz, 1 H), 3.82 (d, J = 13.0 Hz, 1 H), 3.05 (m, 3 H), 2.52 (t, 1 H), 1.42 (s, 9 H). Anal. Calcd for $C_{26}H_{29}N_3O_6$: C, 65.12; H, 6.10; N, 8.76. Found: C, 65.33; H, 5.85; N, 9.00.

3*S*-2-(Boc-L-prolinyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (4g). Yield 93%; mp 131−133 °C. ESI/MS: 414 $[M + H]^+$. IR (KBr): 3431, 3206, 3003, 2954, 2842, 1730, 1643, 1605, 1456, 1394, 1370, 1065, 904 cm^{-1}; $[\alpha]_D^{20}$ = −60 (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.95 (s, 1 H), 9.90 (s, 1 H), 7.35 (d, J = 7.5 Hz, 1 H), 7.16 (d, J = 7.5 Hz, 1 H), 7.06 (t, J = 7.5 Hz, 1 H), 6.86 (t, J = 7.5 Hz, 1 H), 4.52 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.26 (m, 1 H), 4.12 (d, J = 13.0 Hz, 1 H), 3.98 (d, J = 13.0 Hz, 1 H), 3.37 (t, J = 5.2 Hz, 2 H), 2.96 (m, 1 H), 2.50 (t, 1 H), 1.84 (m, 2 H), 1.62 (m, 2 H), 1.41 (s, 9 H). Anal. Calcd for $C_{22}H_{27}N_3O_5$: C, 63.91; H, 6.58; N, 10.16. Found: C, 63.70; H, 6.42; N, 9.93.

3*S*-2-(Boc-L-cysteinyl)-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (4h). Yield 78%; mp 142−144 °C. ESI/MS: 420 $[M + H]^+$. IR

(KBr): 3441, 3205, 3004, 2940, 2842, 1734, 1640, 1605, 1450, 1392, 1370, 1064, 900 cm^{-1}; $[\alpha]_D^{20} = -51$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.97 (s, 1 H), 9.92 (s, 1 H), 7.85 (s, 1 H), 7.35 (d, J = 7.5 Hz, 1 H), 7.12 (d, J = 7.5 Hz, 1 H), 7.02 (t, J = 7.5 Hz, 1 H), 6.92 (t, J = 7.5 Hz, 1 H), 4.52 (dd, J = 10.5 Hz, J = 4.2 Hz, 1 H), 4.25 (m, 1 H), 4.14 (d, J = 13.0 Hz, 1 H), 3.88 (d, J = 13.0 Hz, 1 H), 3.02 (m, 3 H), 2.58 (t, 1 H), 1.42 (s, 9 H). Anal. Calcd for $C_{20}H_{25}N_3O_5S$: C, 57.26; H, 6.01; N, 10.02. Found: C, 57.04; H, 6.16; N, 9.80.

3*S*-2-(Boc-L-methioninyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4i). Yield 87%; mp 120−122 °C. ESI/MS: 448 $[M + H]^+$. IR (KBr): 3443, 3205, 3007, 2950, 2844, 1730, 1645, 1602, 1455, 1392, 1375, 1064, 902 cm^{-1}; $[\alpha]_D^{20} = -35$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 11.00 (s, 1 H), 9.90 (s, 1 H), 7.83 (s, 1 H), 7.36 (d, J = 7.5 Hz, 1 H), 7.14 (d, J = 7.5 Hz, 1 H), 6.98 (t, J = 7.5 Hz, 1 H), 6.82 (t, J = 7.5 Hz, 1 H), 4.52 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.20 (m, 1 H), 4.05 (d, J = 13.0 Hz, 1 H), 3.89 (d, J = 13.0 Hz, 1 H), 2.98 (m, 1 H), 2.53 (t, 1 H), 2.35 (m, 2 H), 2.10 (m, 5 H), 1.41 (s, 9 H). Anal. Calcd for $C_{22}H_{29}N_3O_5S$: C, 59.04; H, 6.53; N, 9.39. Found: C, 59.26; H, 6.69; N, 9.15.

3*S*-2-(Boc-L-glutamyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4j). Yield 86%; mp 168−170 °C. ESI/MS: 446 $[M + H]^+$. IR (KBr): 3443, 3205, 3007, 2950, 2844, 1730, 1645, 1602, 1455, 1392, 1375, 1064, 902 cm^{-1}; $[\alpha]_D^{20} = -55$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 11.00 (s, 1 H), 9.89 (s, 2 H), 7.85 (s, 1 H), 7.36 (d, J = 7.5 Hz, 1 H), 7.15 (d, J = 7.5 Hz, 1 H), 6.97 (t, J = 7.5 Hz, 1 H), 6.82 (t, J = 7.5 Hz, 1 H), 4.55 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.28 (m, 1 H), 4.12 (d, J = 13.0 Hz, 1 H), 3.85 (d, J = 13.0 Hz, 1 H), 3.09 (m, 1 H), 2.52 (t, 1 H), 2.20 (t, 2 H), 2.15 (m, 1 H), 2.03 (m, 1 H), 1.42 (s, 9 H). Anal. Calcd for $C_{22}H_{27}N_3O_7$: C, 59.32; H, 6.11; N, 9.43. Found: C, 59.55; H, 6.27; N, 9.20.

3*S*-2-(Boc-L-aspartyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4k). Yield 91%; mp 133−135 °C. ESI/MS: 432 $[M + H]^+$. IR (KBr): 3340, 3004, 2948, 2845, 1748, 1642, 1600, 1455, 1391, 1072, 904 cm^{-1}; $[\alpha]_D^{20} = -54$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 11.02 (s, 1 H), 9.90 (s, 2 H), 7.85 (s, 1 H), 7.35 (d, J = 7.5 Hz, 1 H), 7.15 (d, J = 7.5 Hz, 1 H), 6.99 (t, J = 7.5 Hz, 1 H), 6.83 (t, J = 7.5 Hz, 1 H), 4.54 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.32 (m, 1 H), 4.16 (d, J = 13.0 Hz, 1 H), 3.88 (d, J = 13.0 Hz, 1 H), 3.06 (m, 1 H), 2.72(m, 1 H), 2.53 (m, 2 H), 1.42 (s, 9 H). Anal. Calcd for $C_{21}H_{25}N_3O_7$: C, 58.46; H, 5.84; N, 9.74. Found: C, 58.55; H, 6.02; N, 9.91. Found: C, 58.77; H, 6.19; N, 10.15.

3*S*-2-(Boc-L-histidinyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4l). Yield 89%; mp 160−162 °C. ESI/MS: 454 $[M + H]^+$. IR (KBr): 3445, 3203, 3005, 2944, 2837, 1731, 1645, 1602, 1451, 1393, 1370, 1060, 900 cm^{-1}; $[\alpha]_D^{20} = -72$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 11.00 (s, 1 H), 9.95 (s, 1 H), 7.87 (s, 1 H), 7.45 (s, 1 H), 7.32 (d, J = 7.5 Hz, 1 H), 7.15 (d, J = 7.5 Hz, 1 H), 6.99 (t, J = 7.5 Hz, 1 H), 6.88(s, 1 H), 6.82 (t, J = 7.5 Hz, 1 H), 4.50 (dd, J = 10.5, 4.5 Hz, 1 H), 4.35 (m, 1 H), 4.24 (d, J = 13.0 Hz, 1 H), 3.94 (d, J = 13.0 Hz, 1 H), 3.03 (m, 3 H), 2.52 (t, 1 H), 1.44 (s, 9 H). Anal. Calcd for $C_{23}H_{27}N_5O_5$: C, 60.92; H, 6.00; N, 15.44. Found: C, 60.71; H, 6.15; N, 15.66.

3*S*-2-(Boc-L-tryptophanyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4m). Yield 90%; mp 140−142 °C. ESI/MS: 503 $[M + H]$.; IR (KBr): 3335, 3009, 2942, 2842, 1750, 1643, 1604, 1453, 1391, 1072, 900 cm^{-1}; $[\alpha]_D^{20} = -52$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 11.00 (s, 1 H), 10.03 (s, 1 H), 9.97 (s, 1 H), 7.90 (s, 1 H), 7.56 (d, J = 7.5 Hz, 1 H), 7.42 (d, J = 7.5 Hz, 1 H), 7.28 (d, J = 7.5 Hz, 1 H), 7.15 (d, J = 7.5 Hz, 1 H), 7.01 (s, 1 H), 6.88 (m, 4 H), 4.52 (dd, J = 10.5 Hz, J = 4.2 Hz, 1 H), 4.38 (m, 1 H), 4.20 (d, J = 13.0 Hz, 1 H), 3.89 (d, J = 13.0 Hz, 1 H), 3.01 (m, 3 H), 2.50 (t, 1 H), 1.42 (s, 9 H). Anal. Calcd for $C_{28}H_{30}N_4O_5$: C, 66.92; H, 6.02; N, 11.15. Found: C, 66.73; H, 6.18; N, 11.38.

3*S*-2-(Boc-L-argininyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4n). Yield 88%; mp 148−150 °C. ESI/MS: 473 $[M + H]^+$. IR (KBr): 3445, 3209, 3004, 2945, 2840, 1733, 1642, 1600, 1451, 1392, 1370, 1064, 900 cm^{-1}; $[\alpha]_D^{20} = -84$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.97 (s, 1 H), 9.85 (s, 1 H), 7.85 (s, 1 H), 7.31 (d, J = 7.5 Hz, 1 H), 7.14 (d, J = 7.5 Hz, 1 H), 6.97 (t, J = 7.5 Hz, 1H), 6.81 (t, J = 7.5 Hz, 1 H), 4.62 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.26 (m, 1 H), 4.11 (d, J = 13.0 Hz, 1 H), 3.86 (d, J = 13.0 Hz, 1 H), 3.12 (m, 1 H), 2.58 (m, 3 H), 1.87 (m, 1 H), 1.71 (m, 1 H), 1.53 (m, 2 H), 1.40 (s, 9 H). Anal. Calcd for $C_{23}H_{32}N_6O_5$: C, 58.46; H, 6.83; N, 17.78. Found: C, 58.69; H, 6.97; N, 17.55.

3*S*-2-(Boc-glycyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4o). Yield 95%; mp 142−144 °C. ESI/MS: 374 $[M + H]^+$. IR (KBr): 3342, 3003, 2950, 2844, 1745, 1645, 1603, 1452, 1390, 1070, 900 cm^{-1}; $[\alpha]_D^{20} = -64$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.99 (s, 1 H), 10.00 (s, 1 H), 7.95 (s, 1 H), 7.26 (d, J = 7.5 Hz, 1 H), 7.16 (d, J = 7.5 Hz, 1 H), 6.95 (t, J = 7.5 Hz, 1 H), 6.86 (t, J = 7.5 Hz, 1 H), 4.56 (dd, J = 10.5 Hz, J = 4.2 Hz, 1 H), 4.20 (d, J = 13.0 Hz, 1H), 4.12 (d, 2 H), 3.77 (d, J = 13.0 Hz, 1 H), 2.99 (m, 1 H), 2.54 (m, 1 H), 1.43 (s, 9 H). Anal. Calcd for $C_{19}H_{23}N_3O_5$: C, 61.11; H, 6.21; N, 11.25. Found: C, 61.33; H, 6.38; N, 11.48.

3*S*-2-[Boc-L-lysinyl(*Z*)]-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4p). Yield 92%; mp 151−153 °C. ESI/MS: 579 $[M + H]^+$. IR (KBr): 3342, 3003, 2940, 2845, 1752, 1641, 1602, 1456, 1390, 1070, 902 cm^{-1}; $[\alpha]_D^{20} = -50$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.96 (s, 1 H), 9.94 (s, 1 H), 8.04 (s, 1 H), 7.97 (s, 1 H), 7.32 (d, J = 7.5 Hz, 1 H), 7.18 (m, 6 H), 6.98 (t, J = 7.5 Hz, 1 H), 6.82 (t, J = 7.5 Hz, 1 H), 5.32 (s, 2 H), 4.62 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.42 (t, J = 4.5 Hz, 1 H), 4.14 (d, J = 13.0 Hz, 1 H), 3.88 (d, J = 13.0 Hz, 1 H), 2.95 (m, 3 H), 2.54 (m, 1 H), 1.82 (m, 2 H), 1.55 (m, 2 H), 1.43 (s, 9 H), 1.25 (m, 2 H). Anal. Calcd for $C_{31}H_{38}N_4O_7$: C, 64.34; H, 6.62; N, 9.68. Found: C, 64.11; H, 6.45; N, 9.94.

3*S*-2-(Boc-L-glutaminyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4q). Yield 85%; mp 134−136 °C. ESI/MS: 445 $[M + H]^+$. IR (KBr): 3342, 3011, 2949, 2844, 1750, 1640, 1603, 1456, 1391, 1072, 905 cm^{-1}; $[\alpha]_D^{20} = -67$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 11.00 (s, 1 H), 9.89 (s, 1 H), 7.85 (s, 1 H), 7.35 (d, J = 7.5 Hz, 1 H), 7.18 (d, J = 7.5 Hz, 1 H), 6.97 (t, J = 7.5 Hz, 1 H), 6.83 (t, J = 7.5 Hz, 1 H), 6.34 (s, 2 H), 4.53 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.26 (m, 1H), 4.08 (d, J = 13.0 Hz, 1 H), 3.84 (d, J = 13.0 Hz, 1 H), 2.96 (m, 1 H), 2.50 (m, 1 H), 2.18 (m, 2 H), 2.11 (m, 1 H), 1.98 (m, 1 H), 1.42 (s, 9 H). Anal. Calcd for $C_{22}H_{28}N_4O_6$: C, 59.45; H, 6.35; N, 12.60. Found: C, 59.22; H, 6.20; N, 12.38.

3*S*-2-(Boc-L-asparaginyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4r). Yield 83%; mp 139−141 °C. ESI/MS: 431 $[M + H]^+$. IR (KBr): 3443, 3205, 3001, 2932, 2833, 1734, 1630, 1604, 1457, 1391, 1370, 1061, 900 cm^{-1}; $[\alpha]_D^{20} = -58$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.95 (s, 2 H), 9.87 (s, 1 H), 7.91 (s, 1 H), 7.32 (d, J = 7.5 Hz, 1 H), 7.15 (d, J = 7.5 Hz, 1 H), 6.98 (t, J = 7.5 Hz, 1 H), 6.82 (t, J = 7.5 Hz, 1 H), 6.20 (s, 2 H), 4.50 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.34 (m, 1 H), 4.15 (d, J = 13.0 Hz, 1 H), 3.89 (d, J = 13.0 Hz, 1H), 2.98 (m, 1 H), 2.77 (m, 1 H), 2.59 (m, 1 H), 2.52 (m, 1 H), 1.41 (s, 9 H). Anal. Calcd for $C_{21}H_{26}N_4O_6$: C, 58.59; H, 6.09; N, 13.02. Found: C, 58.36; H, 5.91; N, 13.27.

3*S*-2-(Boc-L-leucyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4s). Yield 94%; mp 138−140 °C. ESI/MS: 430 $[M + H]^+$. IR (KBr): 3344, 3002, 2950, 2842, 1745, 1640, 1603, 1452, 1390, 1070, 900 cm^{-1}; $[\alpha]_D^{20} = -77$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.89 (s, 1 H), 9.95 (s, 1 H), 7.93 (s, 1 H), 7.29 (d, J = 7.5 Hz, 1 H), 7.16 (d, J = 7.5 Hz, 1 H), 6.96 (t, J = 7.5 Hz, 1 H), 6.78 (t, J = 7.5 Hz, 1 H), 4.58 (dd, J = 10.5 Hz, J = 4.5 Hz, 1H), 4.39 (m, 1 H), 4.22 (d, J = 13.0 Hz, 1 H), 3.81 (d, J = 13.0 Hz, 1 H), 2.92 (m, 1 H), 2.53 (m, 1 H), 1.85 (m, 1 H), 1.78 (m, 1 H), 1.66 (m, 1 H), 1.41 (s, 9 H), 1.08 (d, J = 5.6 Hz, 6H). Anal. Calcd for $C_{23}H_{31}N_3O_5$: C, 64.32; H, 7.27; N, 9.78. Found: C, 64.10; H, 7.10; N, 9.54.

3*S*-2-(Boc-L-isoleucyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (4t). Yield 90%; mp 134−136 °C. ESI/MS: 430 $[M + H]^+$. IR (KBr): 3344, 3002, 2950, 2842, 1745, 1640, 1603, 1452, 1390, 1070, 900 cm^{-1}; $[\alpha]_D^{20} = -67$ (c = 0.5, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.92 (s, 1 H), 9.90 (s, 1 H), 7.93 (s, 1 H), 7.28 (d,

J = 7.5 Hz, 1 H), 7.14 (d, J = 7.5 Hz, 1 H), 6.96 (t, J = 7.5 Hz, 1 H), 6.78 (t, J = 7.5 Hz, 1 H), 4.57 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.32 (m, 1 H), 4.22 (d, J = 13.0 Hz, 1 H), 3.80 (d, J = 13.0 Hz, 1 H), 2.91 (m, 1 H), 2.53 (m, 2 H), 1.49 (m, 2 H), 1.41 (s, 9 H), 0.92 (d, J = 6.6 Hz, 3 H), 0.86 (t, 3 H). Anal. Calcd for $C_{23}H_{31}N_3O_5$: C, 64.32; H, 7.27; N, 9.78. Found: C, 64.11; H, 7.13; N, 9.54.

General Procedure for Preparation of 5a−t. At 0 °C, solution of 0.5 g (1.28 mmol) of **4a−t** in 8 mL of hydrogen chloride/ethyl acetate (4 mol/L) was stirred for 1 h and TLC analysis (chloroform/methanol, 5:1) indicated complete disappearance of **4a−t**. Upon evaporation, the residue was dissolved in ethyl acetate (3 × 10 mL) and evaporated under reduced pressure to remove hydrogen chloride. At 0 °C, the residue was dissolved in 2 mL of water and titrated with the solution of sodium hydroxide (0.32 mmol/L, 4 mL). The formed precipitates were collected by filtration and dried to provide **5a−t**.

3*S*-2-L-Alanyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (5a). Yield 93%; mp 175−177 °C. ESI/MS: 288 $[M + H]^+$; $[\alpha]_D^{20}$ = −89 (c = 0.35, CH_3OH). IR (KBr): 3340, 3006, 2953, 2840, 1748, 1642, 1605, 1450, 1391, 1072, 902 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 11.02 (s, 1 H), 7.69 (d, J = 7.5 Hz, 2 H), 7.28 (d, J = 7.5 Hz, 1 H), 7.18 (d, J = 7.5 Hz, 1 H), 6.97 (t, J = 7.5 Hz, 1 H), 6.86 (t, J = 7.5 Hz, 1 H), 4.58 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.42 (m, 1 H), 4.27 (d, J = 13.0 Hz, 1 H), 3.84 (d, J = 13.0 Hz, 1 H), 2.98 (m, 1 H), 2.56 (m, 1 H), 1.47 (d, J = 5.4 Hz, 3 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.8, 129.8, 126.7, 121.6, 119.1, 118.1, 111.6, 105.3, 54.9, 51.2, 47.1, 23.6. Anal. Calcd for $C_{15}H_{17}N_3O_3$: C, 62.71; H, 5.96; N, 14.63. Found: C, 62.89; H, 6.10; N, 14.40.

3*S*-2-L-Phenylalanyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (5b). Yield 93%; mp 171−173 °C. ESI/MS: 364 $[M + H]^+$. $[\alpha]_D^{20}$ = −96 (c = 0.36, CH_3OH). IR (KBr): 3338, 3010, 2943, 2840, 1752, 1640, 1602, 1458, 1390, 1070, 902 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 10.96 (s, 1 H), 7.85 (d, J = 7.5 Hz, 2 H), 7.27 (d, J = 7.5 Hz, 1 H), 7.18 (m, 6 H), 6.97 (t, J = 7.5 Hz, 1 H), 6.83 (t, J = 7.5 Hz, 1 H), 4.54 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.47 (m, 1 H), 4.26 (d, J = 13.0 Hz, 1 H), 3.79 (d, J = 13.0 Hz, 1 H), 2.94 (m, 3 H), 2.52 (m, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.1, 170.8, 136.6, 129.8, 128.7, 127.8, 126.7, 126.0, 121.6, 119.1, 118.1, 111.6, 105.3, 54.9, 51.2, 47.1, 23.6. Anal. Calcd for $C_{21}H_{21}N_3O_3$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.22; H, 5.67; N, 11.31.

3*S*-2-L-Valinyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (5c). Yield 87%; mp 165−167 °C. ESI/MS: 316 $[M + H]^+$. $[\alpha]_D^{20}$ = −92 (c = 0.32, CH_3OH). IR (KBr): 3343, 3000, 2952, 2845, 1743, 1640, 1605, 1455, 1391, 1375, 1070, 900 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 10.98 (s, 1 H), 7.74 (d, J = 7.5 Hz, 2 H), 7.31 (d, J = 7.5 Hz, 1 H), 7.18 (d, J = 7.5 Hz, 1 H), 6.98 (t, J = 7.5 Hz, 1 H), 6.79 (t, J = 7.5 Hz, 1 H), 4.56 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.48 (m, 1 H), 4.20 (d, J = 13.0 Hz, 1 H), 3.79 (d, J = 13.0 Hz, 1 H), 2.92 (m, 1 H), 2.73 (m, J = 4.5 Hz, 1 H), 2.52 (m, 1 H), 1.13 (d, J = 5.5 Hz, 6 H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 173.2, 171.6, 135.8, 129.6, 126.5, 121.6, 119.1, 118.1, 111.6, 105.3, 59.4, 57.8, 35.2, 34.1, 23.6, 17.6. Anal. Calcd for $C_{17}H_{21}N_3O_3$: C, 64.74; H, 6.71; N, 13.32. Found: C, 64.51; H, 6.57; N, 13.10.

3*S*-2-L-Serinyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (5d). Yield 93%; mp 161−163 °C. ESI/MS: 304 $[M + H]^+$. IR (KBr): 3339, 3006, 2945, 2842, 1750, 1643, 1605, 1459, 1391, 1072, 900 cm^{-1}; $[\alpha]_D^{20}$ = −68 (c = 0.35, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.94 (s, 1 H), 7.57 (d, J = 7.5 Hz, 2 H), 7.28 (d, J = 7.5 Hz, 1 H), 7.17 (d, J = 7.5 Hz, 1 H), 7.02 (t, J = 7.5 Hz, 1 H), 6.86 (t, J = 7.5 Hz, 1 H), 4.52 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.39 (m 1 H), 4.13 (d, J = 13.0 Hz, 1 H), 4.01 (m, 2 H), 3.82 (d, J = 13.0 Hz, 1 H), 2.95 (m, 1 H), 2.52 (m, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.8, 129.8, 126.7, 121.8, 119.5, 118.0, 111.4, 105.3, 64.9, 54.9, 51.2, 37.1, 23.6. Anal. Calcd for $C_{15}H_{17}N_3O_4$: C, 59.40; H, 5.65; N, 13.85. Found: C, 59.59; H, 5.70; N, 13.61.

3*S*-2-L-Threoninyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (5e). Yield 90%; mp 156−158 °C. ESI/MS: 318 $[M + H]^+$. IR (KBr): 3433, 3205, 3000, 2955, 2841, 1730, 1643, 1605, 1452, 1390, 1372, 1060, 904 cm^{-1}; $[\alpha]_D^{20}$ = −75 (c = 0.34, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.90 (s, 1 H), 7.59 (d, J = 7.5 Hz, 2 H), 7.28 (d, J = 7.5 Hz, 1 H), 7.16 (d, J = 7.5 Hz, 1 H), 7.06 (t, J = 7.5 Hz, 1 H), 6.94 (t, J = 7.5 Hz, 1 H), 4.57 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.45 (m, 1 H), 4.22 (m, 3 H), 3.84 (d, J = 13.0 Hz, 1 H), 2.95 (m, 1 H), 2.52 (m, 1 H), 1.21 (d, J = 5.0 Hz, 3 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 171.2, 170.1, 136.6, 129.6, 126.5, 121.3, 119.5, 118.0, 111.4, 105.3, 64.8, 54.6, 50.2, 37.5, 23.6, 19.0. Anal. Calcd for $C_{16}H_{19}N_3O_4$: C, 60.56; H, 6.03; N, 13.24. Found: C, 60.75; H, 6.17; N, 13.46.

3*S*-2-L-Tyrosinyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (5f). Yield 87%; mp 155−157 °C. ESI/MS: 380 $[M + H]^+$. IR (KBr): 3337, 3004, 2945, 2845, 1752, 1641, 1600, 1452, 1390, 1070, 903 cm^{-1}; $[\alpha]_D^{20}$ = −84 (c = 0.32, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.91 (s, 1 H), 7.85 (d, J = 7.5 Hz, 2 H), 7.34 (d, J = 7.5 Hz, 1 H), 7.17 (d, J = 7.5 Hz, 1 H), 7.03 (t, J = 7.5 Hz, 1 H), 6.90 (t, J = 7.5 Hz, 1 H), 6.93 (d, J = 7.2 Hz, 2 H), 6.85 (d, J = 7.2 Hz, 2H), 4.54 (dd, J = 10.5, J = 4.5 Hz, 1 H), 4.42 (m, 1 H), 4.10 (d, J = 13.0 Hz, 1H), 3.81 (d, J = 13.0 Hz, 1 H), 3.02 (m, 3 H), 2.53 (m, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.1, 170.8, 155.6, 136.6, 132.2, 129.3, 128.7, 127.8, 126.7, 126.0, 121.6, 119.1, 105.3, 54.9, 51.2, 47.1, 35.2, 23.6. Anal. Calcd for $C_{21}H_{21}N_3O_4$: C, 66.48; H, 5.58; N, 11.08. Found: C, 66.71; H, 5.74; N, 10.89.

3*S*-2-L-Prolinyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (5g). Yield 92%; mp 158−160 °C. ESI/MS: 314 $[M + H]^+$. IR (KBr): 3431, 3206, 3003, 2954, 2842, 1730, 1643, 1605, 1456, 1394, 1370, 1065, 904 cm^{-1}; $[\alpha]_D^{20}$ = −104 (c = 0.38, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.98 (s, 1 H), 7.66 (d, J = 7.5 Hz, 2 H), 7.36 (d, J = 7.5 Hz, 1 H), 7.19 (d, J = 7.5 Hz, 1 H), 7.10 (t, J = 7.5 Hz, 1 H), 6.95 (t, J = 7.5 Hz, 1 H), 4.58 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.39 (m, 1 H), 4.14 (d, J = 13.0 Hz, 1 H), 3.99 (d, J = 13.0 Hz, 1 H), 3.36 (t, J = 5.2 Hz, 2 H), 2.95 (m, 1 H), 2.51 (m, 1 H), 1.87 (m, 2 H), 1.61 (m, 2 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.8, 129.8, 126.7, 121.6, 119.1, 111.6, 105.3, 59.9, 45.2, 35.6, 32.6, 23.6, 19.6. Anal. Calcd for $C_{17}H_{19}N_3O_3$: C, 65.16; H, 6.11; N, 13.41. Found: C, 65.35; H, 6.26; N, 13.62.

3*S*-2-L-Cysteinyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (5h). Yield 93%; mp 145−147 °C; ESI/MS: 320 $[M + H]^+$. IR (KBr): 3441, 3205, 3004, 2940, 2842, 1734, 1640, 1605, 1450, 1392, 1370, 1064, 900 cm^{-1}; $[\alpha]_D^{20}$ = −56 (c = 0.35, CH_3OH). IR (KBr): 3441, 3205, 3004, 2940, 2842, 1734, 1640, 1605, 1450, 1392, 1370, 1064, 900 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ 10.90 (s, 1 H), 7.58 (d, J = 7.5 Hz, 2 H), 7.32 (d, J = 7.5 Hz, 1 H), 7.10 (d, J = 7.5 Hz, 1 H), 6.97 (t, J = 7.5 Hz, 1 H), 6.84 (t, J = 7.5 Hz, 1 H), 4.52 (dd, J = 10.5 Hz, J = 4.2 Hz, 1 H), 4.38 (m, 1 H), 4.13 (d, J = 13.0 Hz, 1 H), 3.88 (d, J = 13.0 Hz, 1 H), 9.97 (m, 3 H), 2.53 (m, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.8, 129.8, 126.7, 121.6, 119.1, 111.6, 105.3, 58.9, 54.1, 35.6, 30.6, 20.6. Anal. Calcd for $C_{15}H_{17}N_3O_3S$: C, 56.41; H, 5.37; N, 13.16. Found: C, 56.59; H, 5.52; N, 13.39.

3*S*-2-L-Methioninyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (5i). Yield 91%; mp 163−165 °C. ESI/MS: 348 $[M + H]^+$. IR (KBr): 3443, 3205, 3007, 2950, 2844, 1730, 1645, 1602, 1455, 1392, 1375, 1064, 902 cm^{-1}; $[\alpha]_D^{20}$ = −88 (c = 0.30, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.91 (s, 1 H), 7.62 (d, J = 7.5 Hz, 2 H), 7.35 (d, J = 7.5 Hz, 1 H), 7.16 (d, J = 7.5 Hz, 1 H), 6.97 (t, J = 7.5 Hz, 1 H), 6.82 (t, J = 7.5 Hz, 1 H), 4.55 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.41 (m, 1 H), 4.02 (d, J = 13.0 Hz, 1 H), 3.86 (d, J = 13.0 Hz, 1 H), 2.98 (m, 1 H), 2.52 (m, 1 H), 2.33 (m, 2 H), 2.11 (m, 5 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 172.2, 170.6, 136.8, 129.8, 126.7, 121.6, 111.6, 105.3, 58.8, 51.1, 35.4, 34.2, 30.6, 20.6, 17.4. Anal. Calcd for $C_{17}H_{21}N_3O_3S$: C, 58.77; H, 6.09; N, 12.09. Found: C, 58.96; H, 6.26; N, 11.88.

3*S*-2-L-Glutamyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (5j). Yield 91%; mp 172−174 °C. ESI/MS: 346 $[M + H]^+$.

IR (KBr): 3443, 3205, 3007, 2950, 2844, 1730, 1645, 1602, 1455, 1392, 1375, 1064, 902 cm^{-1}; $[\alpha]_D^{20} = -84$ ($c = 0.32$, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.89 (s, 1 H), 9.85 (s, 1 H), 7.64 (d, $J = 7.5$ Hz, 2 H), 7.37 (d, $J = 7.5$ Hz, 1 H), 7.18 (d, $J = 7.5$ Hz, 1 H), 6.97 (t, $J = 7.5$ Hz, 1 H), 6.83 (t, $J = 7.5$ Hz, 1 H), 4.58 (dd, $J = 10.5$ Hz, $J = 4.5$ Hz, 1 H), 4.46 (m, 1 H), 4.13 (d, $J = 13.0$ Hz, 1 H), 3.85 (d, $J = 13.0$ Hz, 1 H), 3.06 (m, 1 H), 2.51 (t, 1 H), 2.26 (t, 2 H), 2.10 (m, 2 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.8, 129.8, 126.7, 121.6, 119.1, 111.6, 105.3, 59.9, 51.2, 35.2, 27.1, 20.6. Anal. Calcd for $C_{17}H_{19}N_3O_5$: C, 59.12; H, 5.55; N, 12.17. Found: C, 58.93; H, 5.40; N, 12.41.

3*S*-2-L-Aspartyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (5k). Yield 92%; mp 178−180 °C. ESI/MS: 332 $[M + H]^+$. IR (KBr): 3340, 3004, 2948, 2845, 1748, 1642, 1600, 1455, 1391, 1072, 904 cm^{-1}; $[\alpha]_D^{20} = -98$ ($c = 0.34$, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.92 (s, 1 H), 9.88 (s, 1 H), 7.70 (d, $J = 7.5$ Hz, 2 H), 7.36 (d, $J = 7.5$ Hz, 1 H), 7.15 (d, $J = 7.5$ Hz, 1 H), 6.99 (t, $J = 7.5$ Hz, 1 H), 6.84 (t, $J = 7.5$ Hz, 1 H), 4.57 (dd, $J = 10.5$ Hz, $J = 4.5$ Hz, 1 H), 4.42 (m, 1 H), 4.12 (d, $J = 13.0$ Hz, 1 H), 3.87 (d, $J = 13.0$ Hz, 1 H), 3.05 (m, 1 H), 2.78(m, 1 H), 2.56 (m, 2 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.8, 128.8, 126.7, 122.6, 119.2, 111.6, 105.3, 59.9, 47.2, 43.2, 35.2, 20.6. Anal. Calcd for $C_{16}H_{17}N_3O_5$: C, 58.00; H, 5.17; N, 12.68. Found: C, 58.20; H, 5.34; N, 12.89.

3*S*-2-L-Histidinyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (5l). Yield 92%; mp 159−161 °C. ESI/MS: 354 $[M + H]^+$. IR (KBr): 3445, 3203, 3005, 2944, 2837, 1731, 1645, 1602, 1451, 1393, 1370, 1060, 900 cm^{-1}; $[\alpha]_D^{20} = -72$ ($c = 0.35$, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.96 (s, 1 H), 7.76 (d, $J = 7.5$ Hz, 2 H), 7.43 (s, 1 H), 7.32 (d, $J = 7.5$ Hz, 1 H), 7.14 (d, $J = 7.5$ Hz, 1 H), 6.96 (t, $J = 7.5$ Hz, 1 H), 6.87(s, 1 H), 6.80 (t, $J = 7.5$ Hz, 1 H), 4.51 (dd, $J = 10.5$ Hz, $J = 4.5$ Hz, 1 H), 4.39 (m, 1 H), 4.24 (d, $J = 13.0$ Hz, 1 H), 3.95 (d, $J = 13.0$ Hz, 1 H), 3.09 (m, 3 H), 2.52 (m, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 136.7, 135.5, 133.1, 129.8, 126.5, 121.6, 119.6, 119.0, 111.6, 105.4, 59.9, 51.2, 35.2, 33.1, 20.6. Anal. Calcd for $C_{18}H_{19}N_5O_3$: C, 61.18; H, 5.42; N, 19.82. Found: C, 61.37; H, 5.25; N, 19.60.

3*S*-2-L-Tryptophanyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (5m). Yield 89%; mp 171−173 °C. ESI/MS: 403 $[M + H]^+$. IR (KBr): 3335, 3009, 2942, 2842, 1750, 1643, 1604, 1453, 1391, 1072, 900 cm^{-1}; $[\alpha]_D^{20} = -123$ ($c = 0.30$, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 11.04 (s, 1 H), 10.98 (s, 1 H), 7.82 (d, $J = 7.5$ Hz, 2 H), 7.57 (d, $J = 7.5$ Hz, 1 H), 7.42 (d, $J = 7.5$ Hz, 1 H), 7.28 (d, $J = 7.5$ Hz, 1 H), 7.14 (d, $J = 7.5$ Hz, 1 H), 7.03 (s, 1 H), 6.87 (m, 4 H), 4.60 (dd, $J = 10.5$ Hz, $J = 4.2$ Hz, 1 H), 4.48 (m, 1 H), 4.21 (d, $J = 13.0$ Hz, 1 H), 3.89 (d, $J = 13.0$ Hz, 1 H), 3.06 (m, 3 H), 2.51 (m, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.8, 136.2, 129.8, 127.1, 126.7, 122.3, 121.6, 120.2, 119.1, 111.6, 105.3, 59.9, 53.2, 35.2, 34.1, 20.6. Anal. Calcd for $C_{23}H_{22}N_4O_3$: C, 68.64; H, 5.51; N, 13.92. Found: C, 68.83; H, 5.33; N, 14.16.

3*S*-2-L-Argininyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (5n). Yield 88%; mp 162−164 °C. ESI/MS: 373 $[M + H]^+$. IR (KBr): 3445, 3209, 3004, 2945, 2840, 1733, 1642, 1600, 1451, 1392, 1370, 1064, 900 cm^{-1}; $[\alpha]_D^{20} = -76$ ($c = 0.32$, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.89 (s, 1 H), 7.82 (d, $J = 7.5$ Hz, 2 H), 7.64 (s, 1 H), 7.32 (d, $J = 7.5$ Hz, 1 H), 7.15 (d, $J = 7.5$ Hz, 1 H), 6.97 (t, $J = 7.5$ Hz, 1 H), 6.83 (t, $J = 7.5$ Hz, 1 H), 4.62 (dd, $J = 10.5$ Hz, $J = 4.5$ Hz, 1 H), 4.49 (m, 1 H), 4.12 (d, $J = 13.0$ Hz, 1 H), 3.86 (d, $J = 13.0$ Hz, 1 H), 3.10 (m, 1 H), 2.62 (m, 3 H), 1.88 (m, 1 H), 1.75 (m, 1 H), 1.54 (m, 2 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 158.6, 136.8, 129.8, 126.7, 121.6, 119.1, 111.6, 105.3, 59.2, 51.2, 37.1, 35.2, 32.1, 23.6, 20.4. Anal. Calcd for $C_{18}H_{24}N_6O_3$: C, 58.05; H, 6.50; N, 22.57. Found: C, 57.83; H, 6.34; N, 22.35.

3*S*-2-Glycyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (5o). Yield 95%; mp 174−176 °C. ESI/MS: 274 $[M + H]^+$. IR (KBr): 3342, 3003, 2950, 2844, 1745, 1645, 1603, 1452, 1390, 1070, 900 cm^{-1}; $[\alpha]_D^{20} = -54$ ($c = 0.35$, CH_3OH).; ^1H NMR (500 MHz, DMSO-d_6): δ 11.01 (s, 1 H), 7.83 (t, $J = 7.5$ Hz, 2 H), 7.29 (d, $J = 7.5$ Hz, 1 H), 7.15 (d, $J = 7.5$ Hz, 1 H), 6.95 (t, $J = 7.5$ Hz, 1 H), 6.82 (t, $J = 7.5$ Hz, 1 H), 4.56 (dd, $J = 10.5$ Hz, $J = 4.2$ Hz, 1 H), 4.36 (d, 2 H), 4.19 (d, $J = 13.0$ Hz, 1 H), 3.78 (d, $J = 13.0$ Hz, 1H), 2.98 (m, 1 H), 2.53 (m, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.6, 129.8, 126.7, 121.6, 118.1, 111.6, 105.3, 54.9, 51.2, 47.1, 23.6. Anal. Calcd for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53; N, 15.38. Found: C, 61.72; H, 5.69; N, 15.61.

3*S*-2-L-Lysinyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (5p). To the solution of 500 mg (0.86 mmol) of **4p** in 15 mL of methanol, 30 mg of Pd/C (5%) was added. The solution was agitated with hydrogen at room temperature for 24 h. The reaction mixture was filtered and evaporated to give a colorless powder. The powder was treated by use of the procedure same as that used for **4a**, giving 240 mg (81%) of the title compound; mp 159−161 °C. ESI/MS: 345 $[M + H]^+$. IR (KBr): 3342, 3003, 2940, 2845, 1752, 1641, 1602, 1456, 1390, 1070, 902 cm^{-1}; $[\alpha]_D^{20} = -72$ ($c = 0.30$, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.94 (s, 1 H), 7.94−7.86 (m, 4 H), 7.34 (d, $J = 7.5$ Hz, 1 H), 7.19 (d, $J = 7.5$ Hz, 1 H), 6.97 (t, $J = 7.5$ Hz, 1 H), 6.82 (t, $J = 7.5$ Hz, 1 H), 4.66 (dd, $J = 10.5$ Hz, $J = 4.5$ Hz, 1 H), 4.48 (m, 1 H), 4.16 (d, $J = 13.0$ Hz, 1 H), 3.89 (d, $J = 13.0$ Hz, 1 H), 3.02 (m, 3 H), 2.52 (m, 1 H), 1.85 (m, 2 H), 1.60 (m, 2 H), 1.26 (m, 2 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.8, 171.6, 136.5, 129.8, 126.7, 121.6, 118.1, 111.6, 105.3, 54.9, 52.2, 43.1, 35.1, 32.2, 20.6. Anal. Calcd for $C_{18}H_{24}N_4O_3$: C, 62.77; H, 7.02; N, 16.27. Found: C, 62.56; H, 7.20; N, 16.06.

3*S*-2-L-Glutaminyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (5q). Yield 86%; mp 177−179 °C. ESI/MS: 345 $[M + H]^+$. IR (KBr): 3342, 3011, 2949, 2844, 1750, 1640, 1603, 1456, 1391, 1072, 905 cm^{-1}; $[\alpha]_D^{20} = -76$ ($c = 0.34$, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.90 (s, 1 H), 7.68 (d, $J = 7.5$ Hz, 2 H), 7.35 (d, $J = 7.5$ Hz, 1 H), 7.19 (d, $J = 7.5$ Hz, 1 H), 6.98 (t, $J = 7.5$ Hz, 1 H), 6.83 (t, $J = 7.5$ Hz, 1 H), 6.45 (s, 2 H), 4.55 (dd, $J = 10.5$ Hz, $J = 4.5$ Hz, 1 H), 4.43 (m, 1 H), 4.09 (d, $J = 13.0$ Hz, 1 H), 3.84 (d, $J = 13.0$ Hz, 1 H), 2.95 (m, 1 H), 2.51 (m, 1 H), 2.25 (m, 2 H), 2.08 (m, 2 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.6, 129.8, 126.7, 121.6, 118.1, 111.6, 105.3, 54.9, 51.2, 37.1, 32.6, 30.5, 20.6. Anal. Calcd for $C_{17}H_{20}N_4O_4$: C, 59.29; H, 5.85; N, 16.27. Found: C, 59.10; H, 5.69; N, 16.51.

3*S*-2-L-Asparaginyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (5r). Yield 91%; mp 173−175 °C. ESI/MS: 331 $[M + H]^+$. IR (KBr): 3443, 3205, 3001, 2932, 2833, 1734, 1630, 1604, 1457, 1391, 1370, 1061, 900 cm^{-1}; $[\alpha]_D^{20} = -88$ ($c = 0.32$, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.88 (s, 1 H), 7.78 (d, $J = 7.5$ Hz, 2 H), 7.32 (d, $J = 7.5$ Hz, 1 H), 7.16 (d, $J = 7.5$ Hz, 1 H), 6.97 (t, $J = 7.5$ Hz, 1 H), 6.82 (t, $J = 7.5$ Hz, 1 H), 6.29 (s, 2 H), 4.51 (dd, $J = 10.5$ Hz, $J = 4.5$ Hz, 1 H), 4.39 (m, 1 H), 4.14 (d, $J = 13.0$ Hz, 1 H), 3.89 (d, $J = 13.0$ Hz, 1 H), 2.96 (m, 1 H), 2.78 (m, 1 H), 2.62 (m, 1 H), 2.51 (m, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 173.2, 171.6, 136.5, 129.6, 126.5, 121.4, 118.1, 111.8, 105.3, 59.1, 48.1, 40.1, 35.3, 23.6. Anal. Calcd for $C_{16}H_{18}N_4O_4$: C, 58.17; H, 5.49; N, 16.96. Found: C, 58.36; H, 5.65; N, 16.74.

3*S*-2-L-Leucyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (5s). Yield 87%; mp 161−163 °C. ESI/MS: 330 $[M + H]^+$. IR (KBr): 3344, 3002, 2950, 2842, 1745, 1640, 1603, 1452, 1390, 1070, 900 cm^{-1}; $[\alpha]_D^{20} = -90$ ($c = 0.35$, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.95 (s, 1 H), 7.78 (d, $J = 7.5$ Hz, 2 H), 7.31 (d, $J = 7.5$ Hz, 1 H), 7.15 (d, $J = 7.5$ Hz, 1 H), 6.96 (t, $J = 7.5$ Hz, 1 H), 6.79 (t, $J = 7.5$ Hz, 1 H), 4.58 (dd, $J = 10.5$ Hz, $J = 4.5$ Hz, 1 H), 4.44 (m, 1 H), 4.23 (d, $J = 13.0$ Hz, 1 H), 3.82 (d, $J = 13.0$ Hz, 1 H), 2.93 (m, 1 H), 2.52 (m, 1 H), 1.86 (m, 1 H), 1.78 (m, 1 H), 1.64 (m, 1 H), 1.01 (d, $J = 5.6$ Hz, 6 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.6, 129.8, 126.7, 121.6, 118.1, 111.6, 105.3, 59.9, 50.2, 45.1, 35.1, 23.6, 20.4. Anal. Calcd for $C_{18}H_{23}N_3O_3$: C, 65.63; H, 7.04; N, 12.76. Found: C, 65.82; H, 7.21; N, 12.54.

3*S*-2-L-Isoleucyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic Acid (5t). Yield 88%; mp 166−168 °C. ESI/MS: 330 $[M + H]^+$. IR (KBr): 3344, 3002, 2950, 2842, 1745, 1640, 1603, 1452, 1390, 1070, 900 cm^{-1}; $[\alpha]_D^{20} = -85$ ($c = 0.33$, CH_3OH). ^1H NMR (500 MHz, DMSO-d_6): δ 10.92 (s, 1 H), 7.72 (d, $J = 7.5$ Hz, 2 H), 7.29 (d, $J = 7.5$ Hz, 1 H), 7.13 (d, $J = 7.5$ Hz, 1H), 6.98 (t, $J = 7.5$ Hz,

1 H), 6.81 (t, J = 7.5 Hz, 1 H), 4.56 (dd, J = 10.5 Hz, J = 4.5 Hz, 1 H), 4.42 (m, 1 H), 4.20 (d, J = 13.0 Hz, 1 H), 3.80 (d, J = 13.0 Hz, 1 H), 2.92 (m, 1 H), 2.56 (m, 2 H), 1.52 (m, 2 H), 0.91(d, J = 6.6 Hz, 3 H), 0.89 (m, 3 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 170.6, 136.6, 129.8, 126.7, 121.6, 118.1, 111.6, 105.3, 59.9, 55.5, 40.1, 35.1, 23.6, 20.4, 14.2, 11.5. Anal. Calcd for $C_{18}H_{23}N_3O_3$: C, 65.63; H, 7.04; N, 12.76. Found: C, 65.86; H, 7.20; N, 12.99.

In Vitro Antiplatelet Aggregation Activity Assay. An H-10 cell counter was used to determine the platelet count and a two-channel Chronolog aggregometer was used to evaluate platelet aggregation. The pig blood (six pigs, purchased from Animal Center of Peking University) was centrifuged at 1000 rpm for 10 min and the platelet rich plasma (PRP) was collected. The remaining blood was centrifuged for an additional 10 min at 1500g to prepare platelet poor plasma (PPP). The final platelet count of the PRP was adjusted to 2×10^8 platelets/mL with autologous PPP. To an optical aggregometry testing tube, 0.5 mL of the adjusted plasma sample and 5 μL of NS or 5 μL of the solution of **5a**−**t** (in a series of final concentrations of 100, 10, 1, 0.1, 0.01, and 0.001 μM, prepared by diluting 10 mM of stock solutions of **5a**−**t** in DMSO/NS, 1/10(v/v), with NS) was added. After adjustment of the baseline, 5 μL of the solution of PAF (final concentration 0.1 μM, prepared with normal saline) or 5 μL of the solution of ADP (final concentration 10 μM, prepared with normal saline) or 5 μL of the solution of arachidonic acid in NS (AA, final concentration 350 μM, prepared with 1 M sodium carbonate) or 50 μL of the solution of TH (final concentration 0.1 U/mL, prepared with normal saline) was added and aggregation was measured at 37 °C for 5 min. The effects of **5a**−**t** (at a series of concentrations ranging from 100 μM to 1 nM) on PAF or ADP or AA or TH-induced platelet aggregation were observed. All these antiplatelet aggregation tests in sextuplicate tubes were carried out. The maximum platelet aggregation (A_m) of control group (NS) or sample group (**5a**−**t**) was represented by the peak height of aggregation curve (equal to the maximum light transmission). The inhibition rate was calculated according to the following formula: inhibition (%) = [(A_m of NS) − (A_m of **5a**−**t**)]/(A_m of NS) × 100%. A_m of NS is the value of platelet aggregation induced by PAF, ADP, AA, and TH without **5a**−**t** and are 52.30 ± 1.78, 50.16 ± 3.65, 49.62 ± 2.90, and 61.20 ± 2.97, respectively. The concentration vs inhibition rate curve is plotted to determine the IC_{50} values with GWBASIC.EXE program.

In Vivo Antithrombotic Assay of Intravenously Injection of 5a−**t in Rat Model.** The assessments described here were performed based on a protocol reviewed and approved by the ethics committee of Capital Medical University. The committee assures the welfare of the animals was maintained in accordance to the requirements of the Animal Welfare Act and according to the Guide for Care and Use of Laboratory Animals. Aspirin and **5a**−**t** were dissolved in NS before administration and kept in an ice bath. Male Wister rats weighing 250−300 g (purchased from Animal Center of Peking University) were used. The rats were anesthetized with pentobarbital sodium (80.0 mg/kg, ip), and the right carotid artery and left jugular vein were separated. A weighed 6 cm thread was inserted into the middle of a polyethylene tube. The polyethylene tube was filled with heparin sodium (50 IU/mL in NS) and one end was inserted into the left jugular vein. From the other end of the polyethylene tube heparin sodium was injected as anticoagulant, then NS or **5a**−**t** was injected, and this end was inserted into the right carotid artery. Blood was allowed to flow from the right carotid artery to the left jugular vein through the polyethylene tube for 15 min. The thread was removed to obtain the weight of the wet thrombus.

In Vivo Antithrombotic Assay of Orally Administration of 6s in Rat Model. Male Wistar rats were fed with three doses (5, 1, and 0.2 μmol/kg) of **6s** in NS or NS (0.6 mL) alone were fed to Male Wistar rats orally. Then the rats were anesthetized with pentobarbital sodium (80.0 mg/kg, ip). Thirty min later, the right carotid artery and left jugular vein of the rat were separated. A weighed 6 cm thread was inserted into the middle of a polyethylene tube. The polyethylene tube was filled with heparin sodium (50 IU/mL in NS) and one end was inserted into the left jugular vein while another end was inserted into the right carotid artery. Blood flowed from the right carotid artery to the left jugular vein through the polyethylene tube for 15 min. The thread was taken out and the weight of the wet thrombus was recorded.

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