Supporting Information

Nostosin G and Spiroidesin B from the Cyanobacterium *Dolichospermum* sp. NIES-1697

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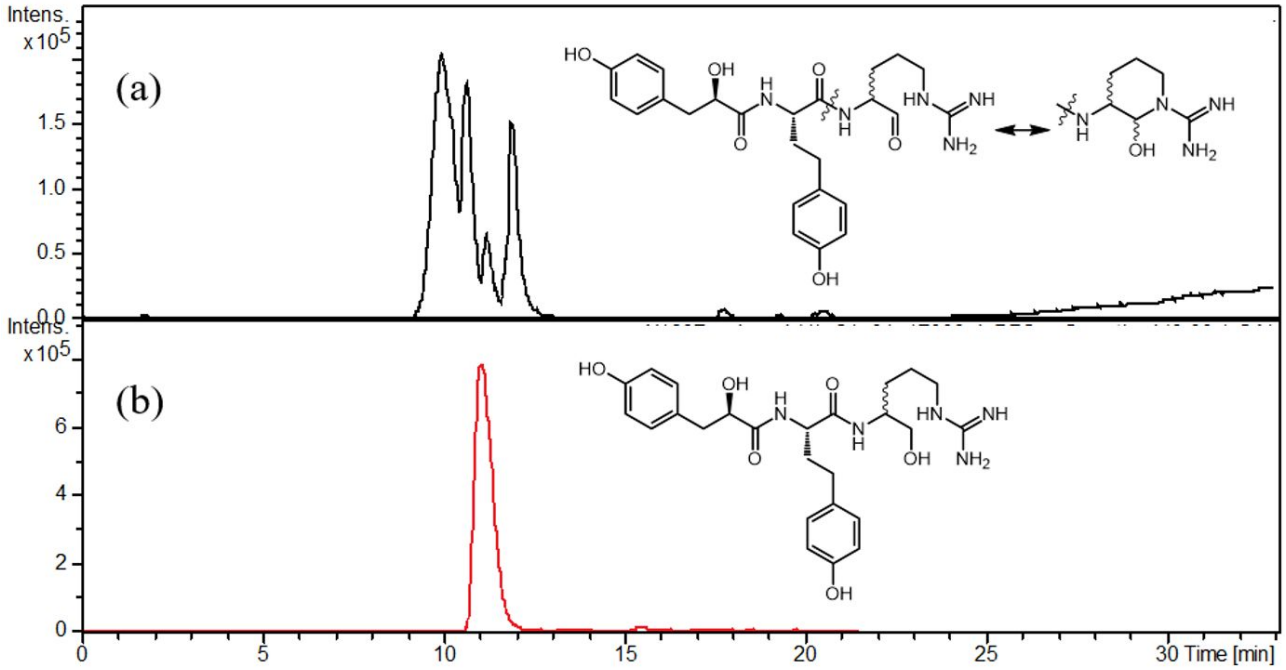

Figure S1. LC-MS chromatogram of **1** before $NaBH_4$ reduction (a) and **5** after $NaBH_4$ reduction (b)

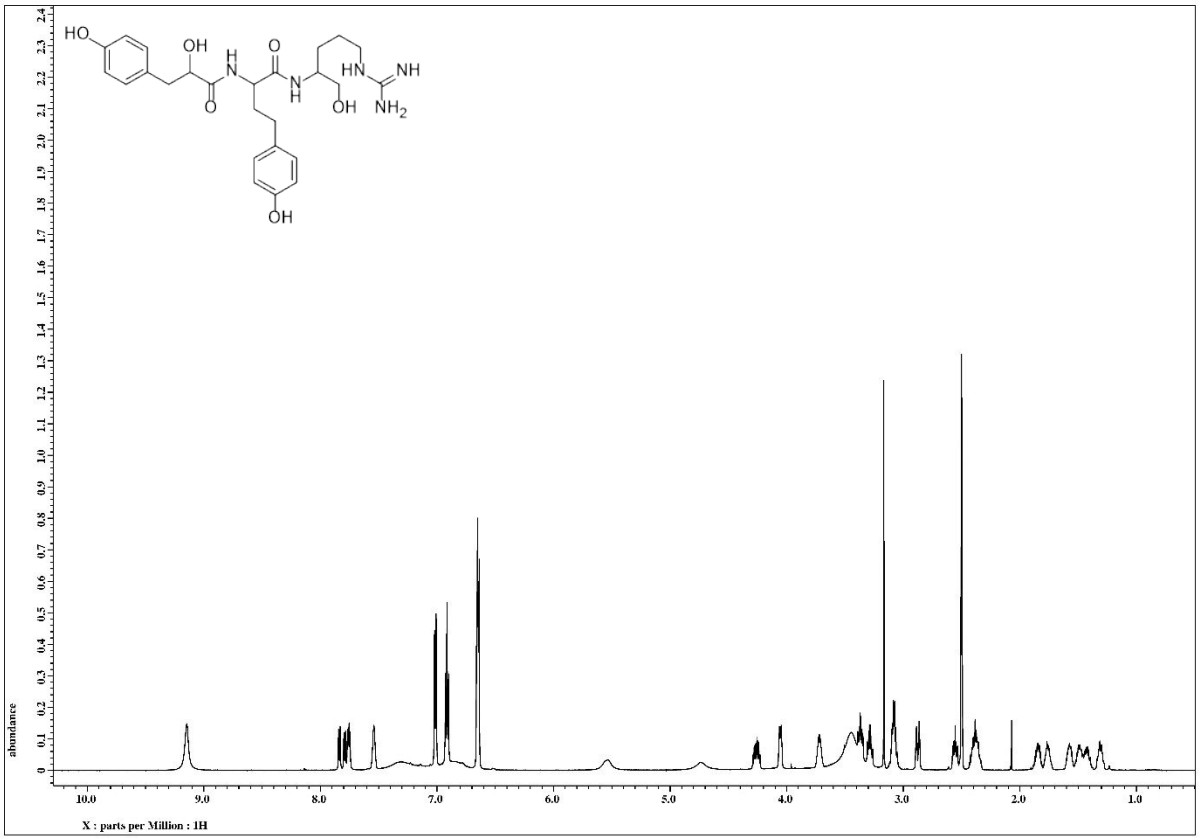

Figure S2. ^{1}H NMR (600 MHz) spectrum of **5** (reduced form of **1**) in DMSO-d_6

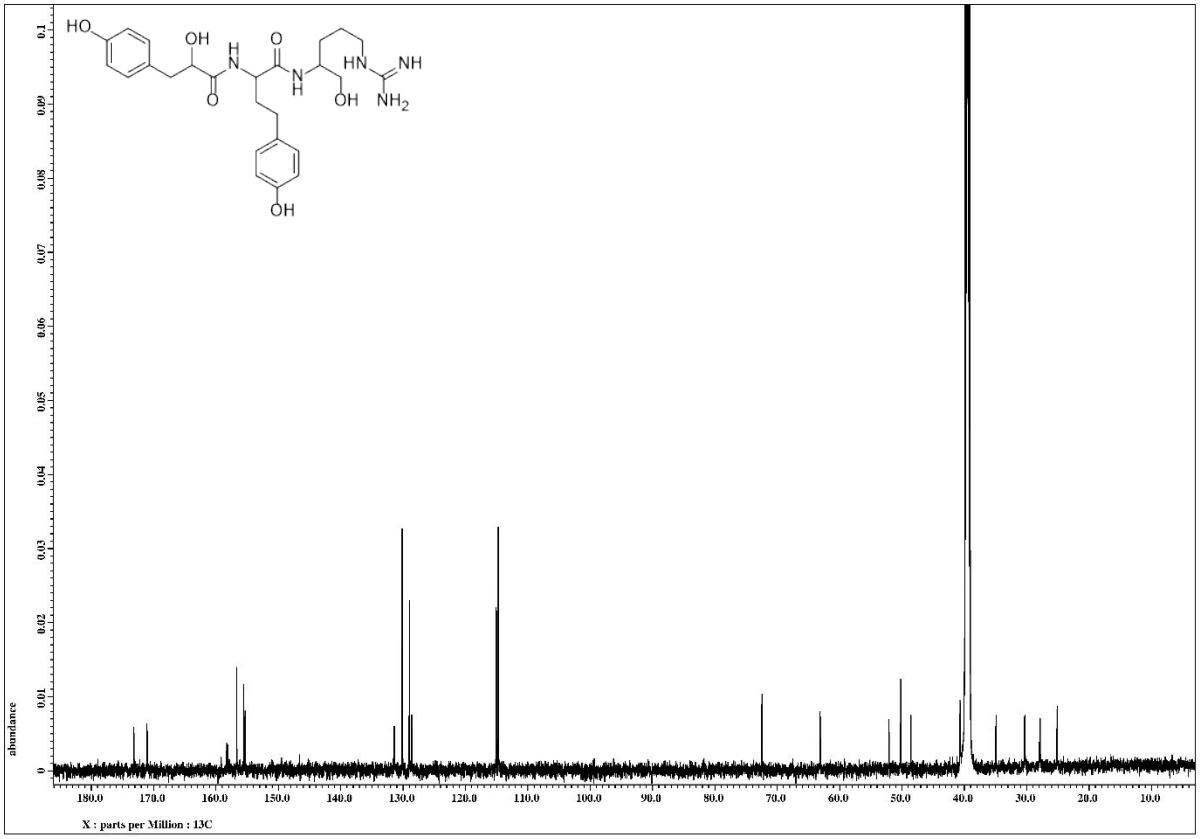

Figure S3. ^{13}C NMR (150 MHz) spectrum of **5** (reduced form of **1**) in DMSO-d_6

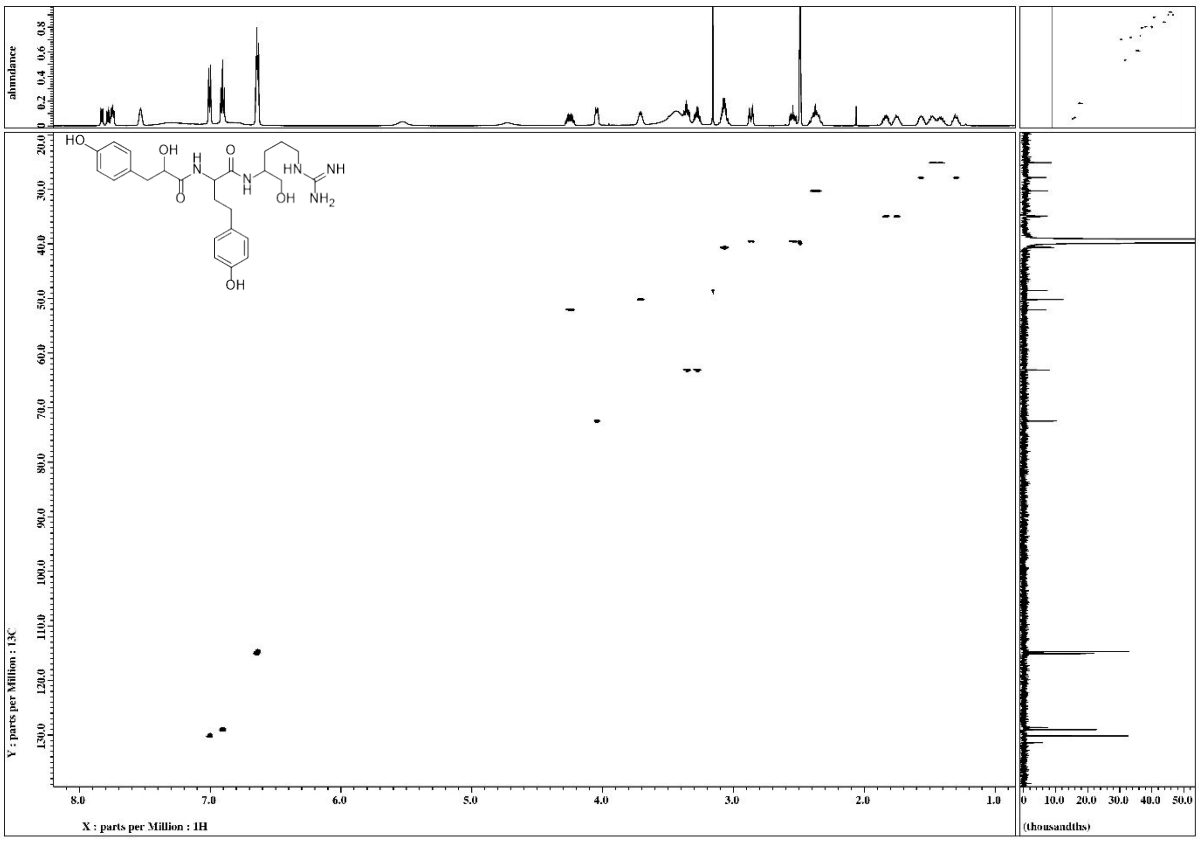

Figure S4. HSQC spectrum of **5** (reduced form of **1**) in DMSO-d_6

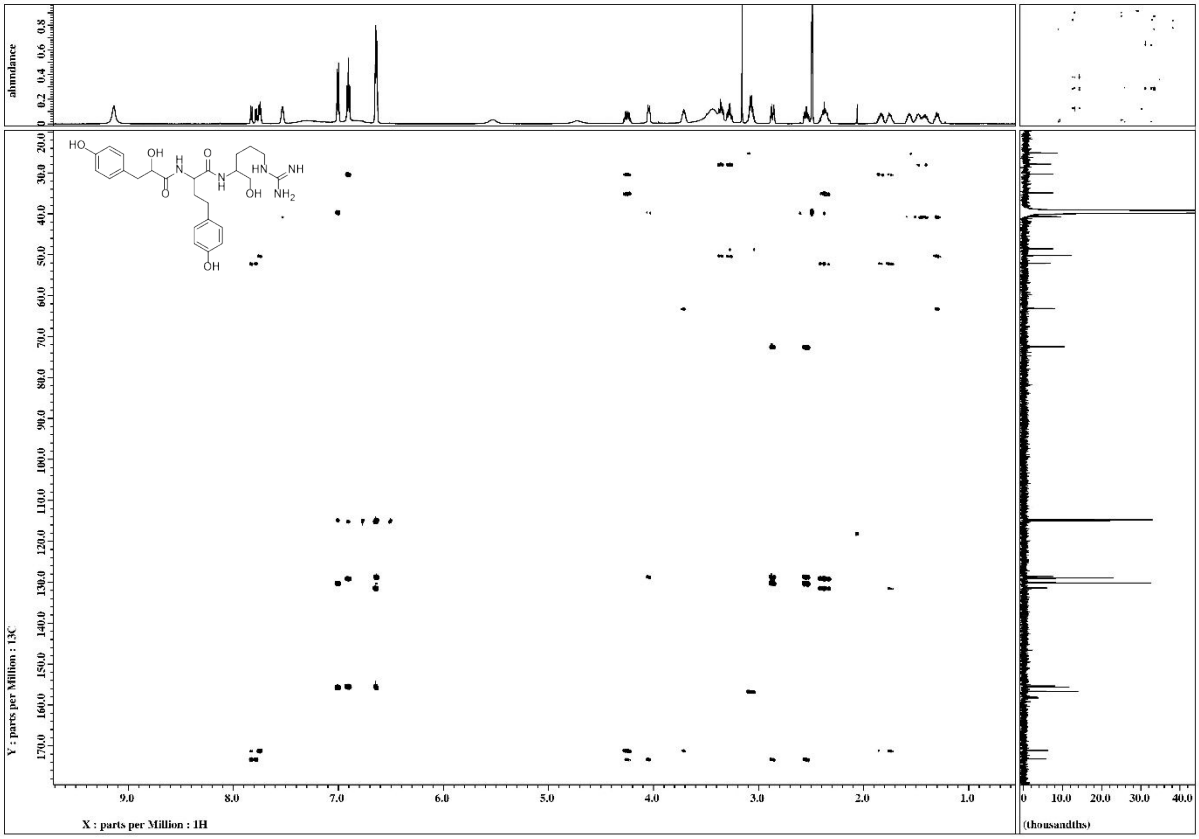

Figure S5. HMBC spectrum of **5** (reduced form of **1**) in DMSO-d_6

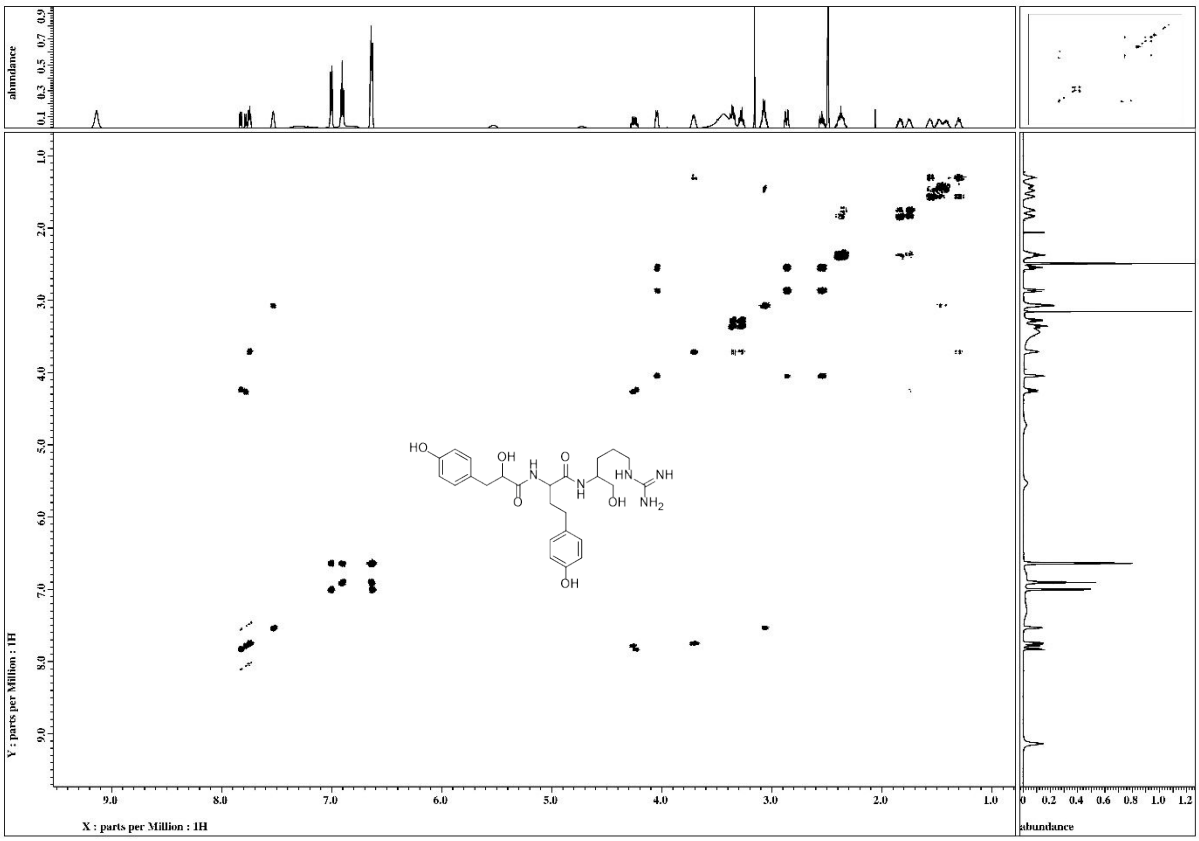

Figure S6. ^{1}H-^{1}H DQF COSY spectrum of **5** (reduced form of **1**) in DMSO-d_6

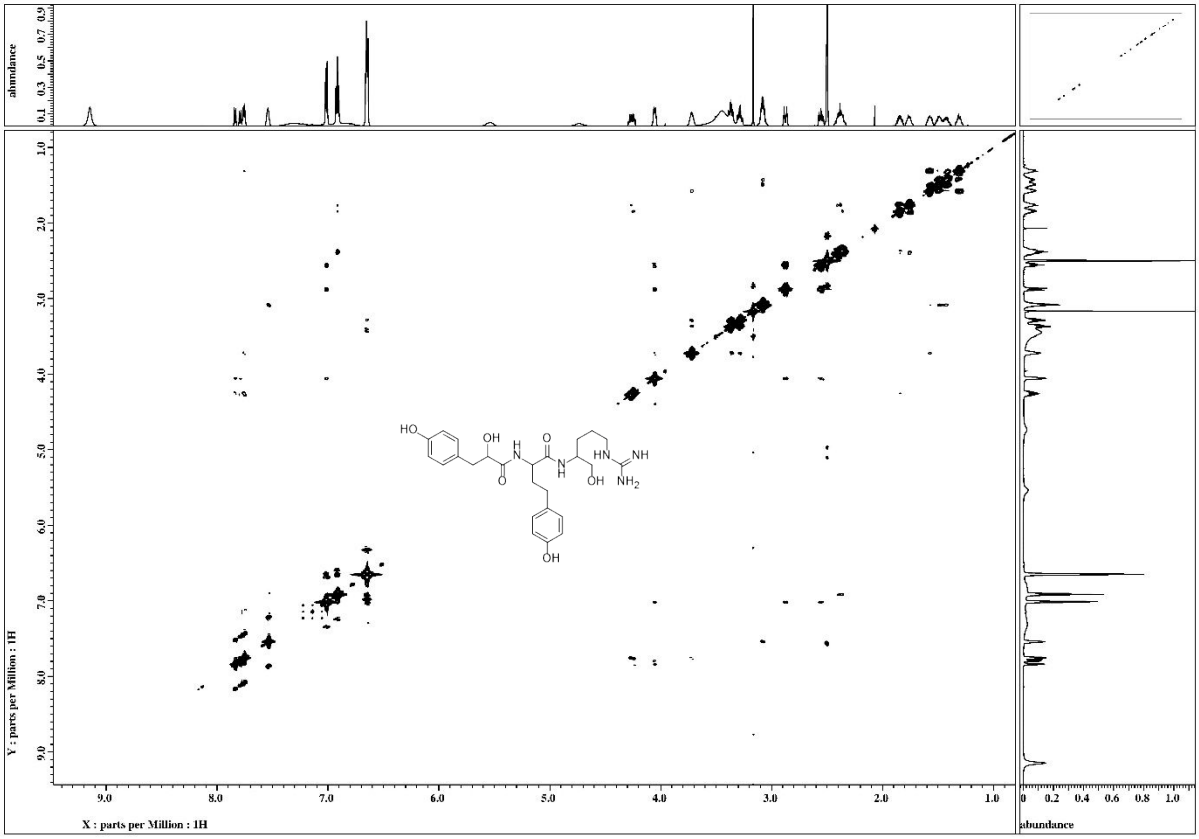

Figure S7. ROESY spectrum of **5** (reduced form of **1**) in DMSO-d_6

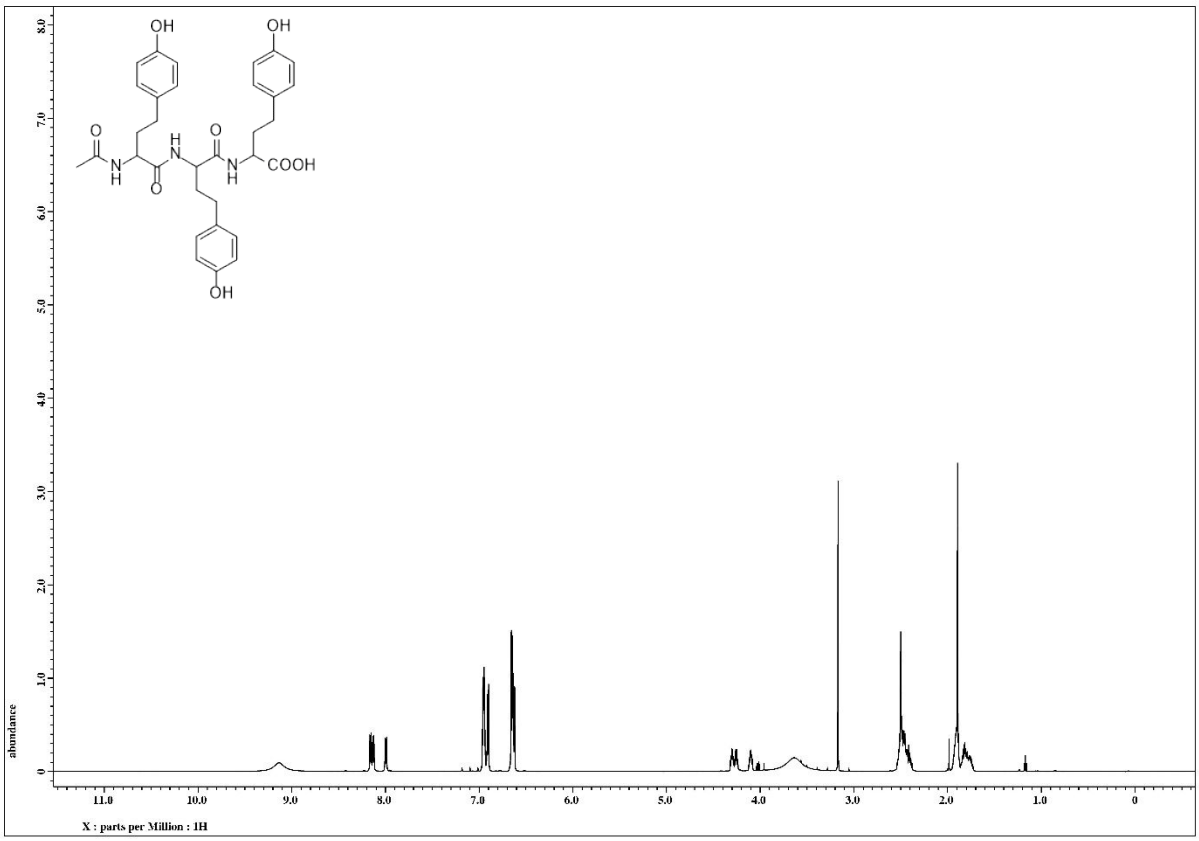

Figure S8. ^{1}H NMR (600 MHz) spectrum of **2** in DMSO-d_6

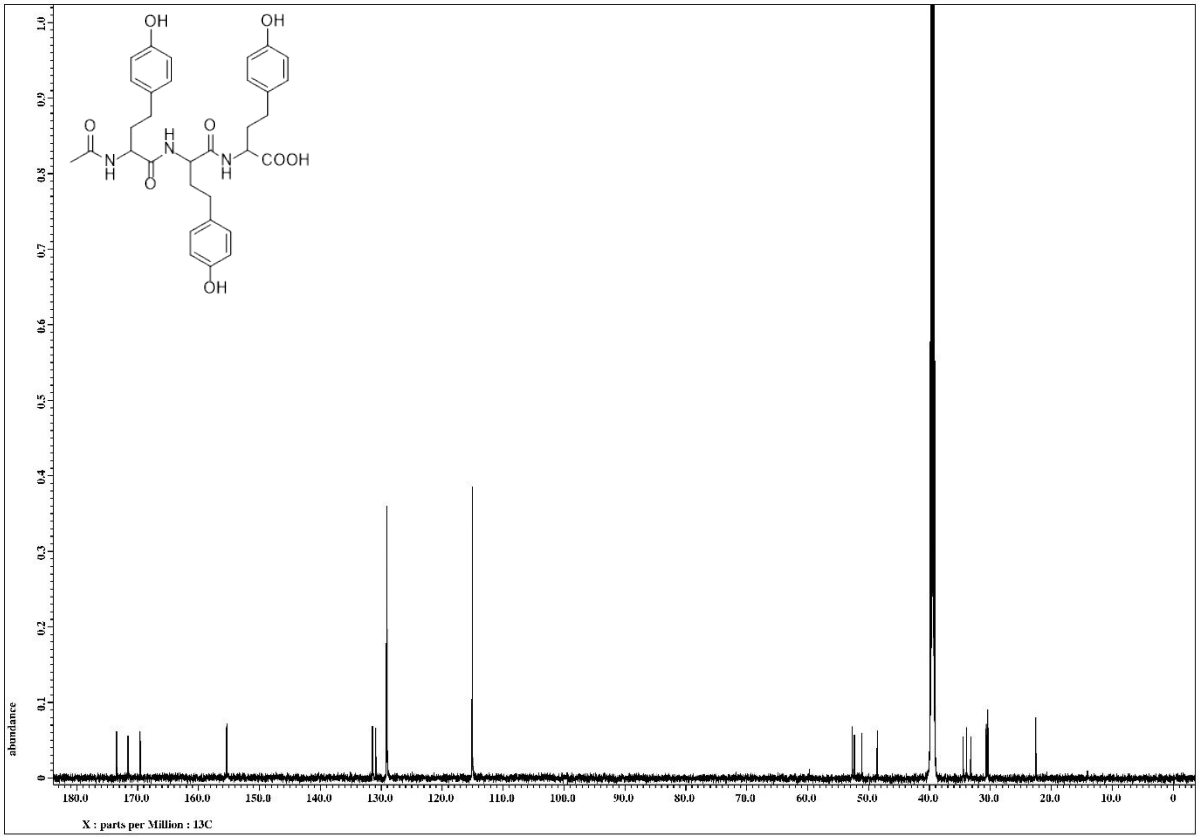

Figure S9. ^{13}C NMR (150 MHz) spectrum of **2** in DMSO-d_6

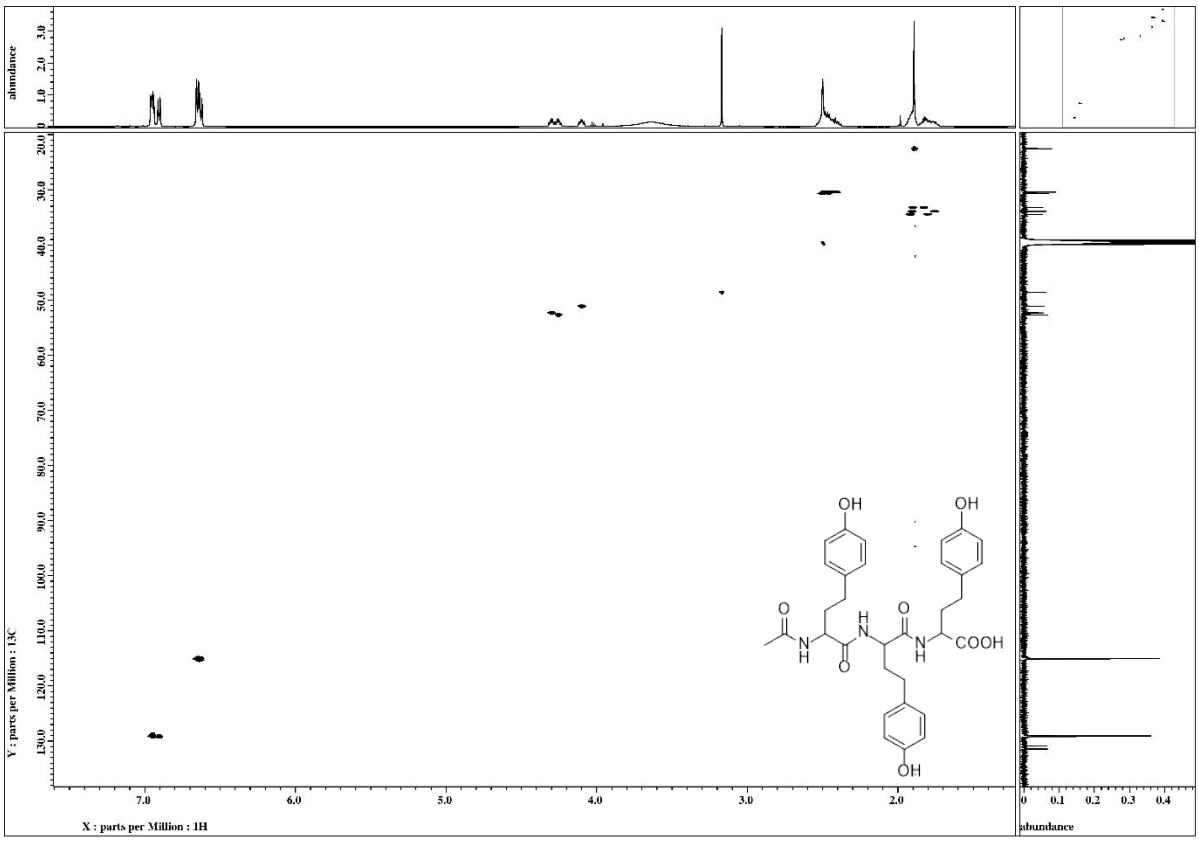

Figure S10. HSQC spectrum of **2** in DMSO-d_6

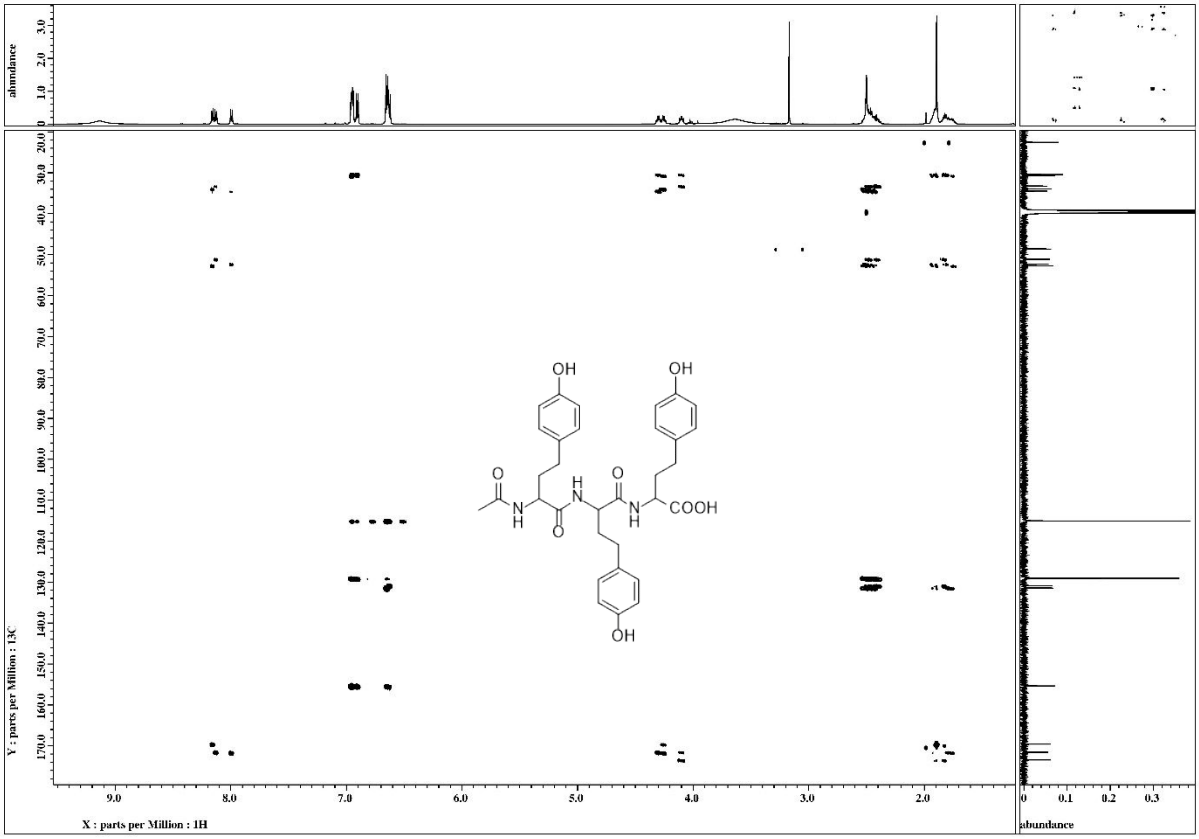

Figure S11. HMBC spectrum of **2** in DMSO-d_6

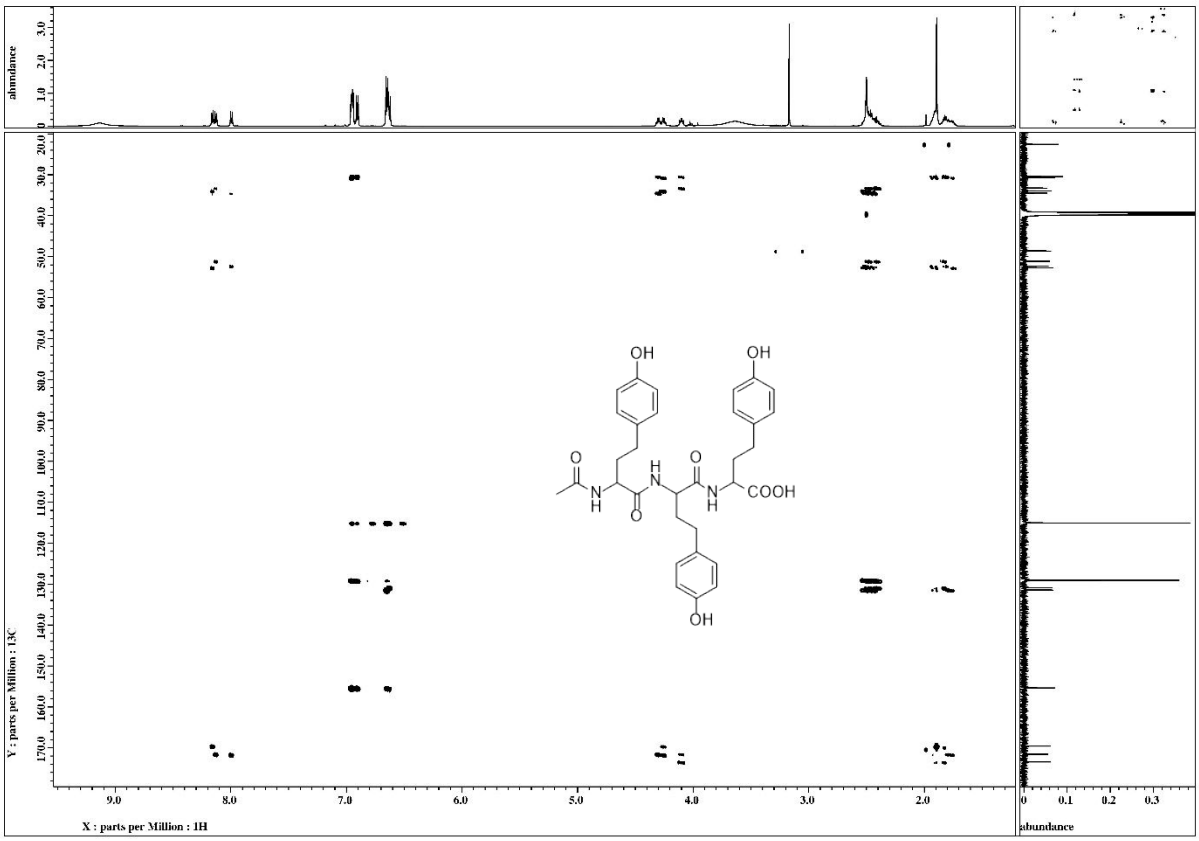

Figure S12. ^{1}H-^{1}H DQF COSY spectrum of **2** in DMSO-d_6

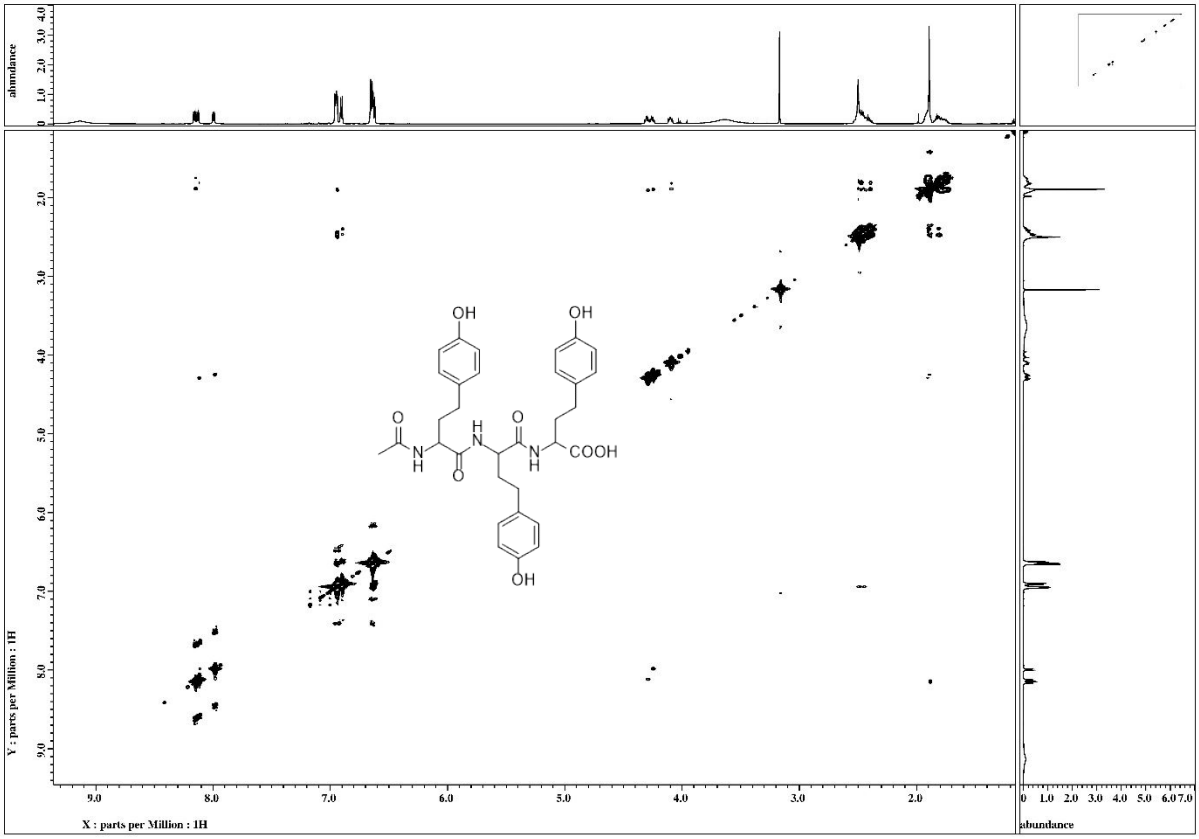

Figure S13. ROESY spectrum of **2** in DMSO-d_6

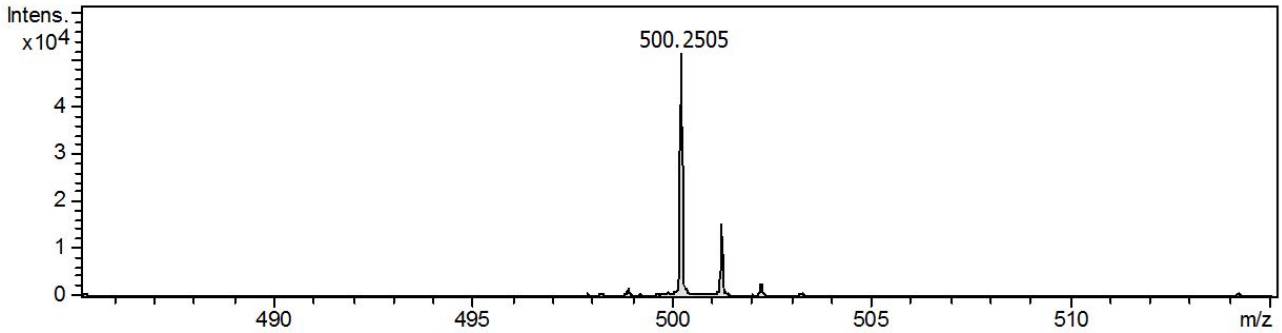

Figure S14. HRESI(-) mass spectrum of **5** (reduced form of **1**)

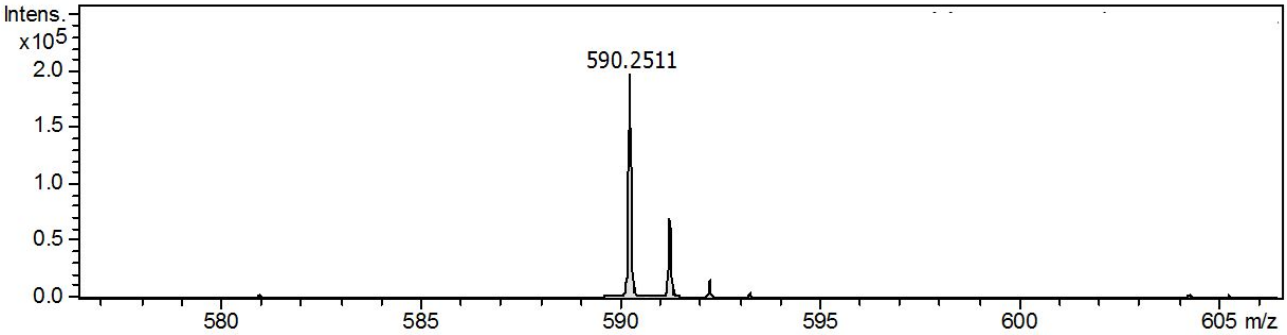

Figure S15. HRESI(-) mass spectrum of **2**

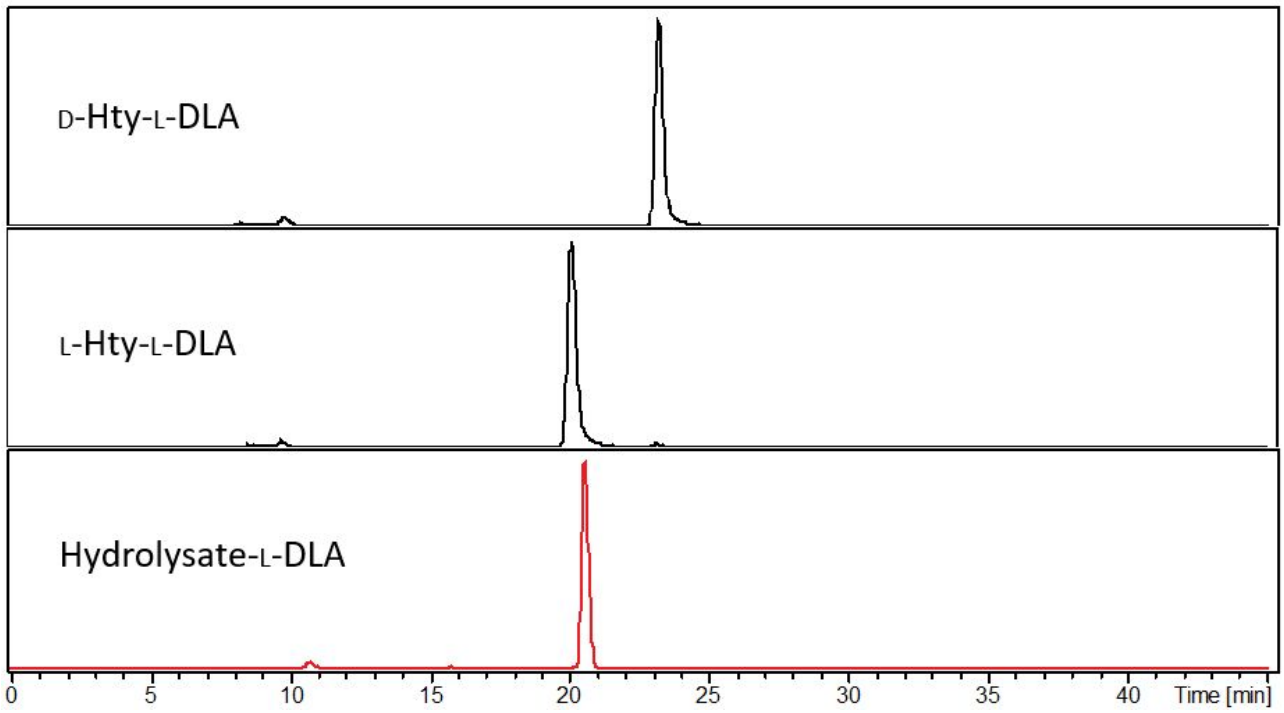

Figure S16. LC-MS chromatogram of Marfey's analysis of hydrolysate **1** (non-reduced), and standards D-Hty and L-Hty.

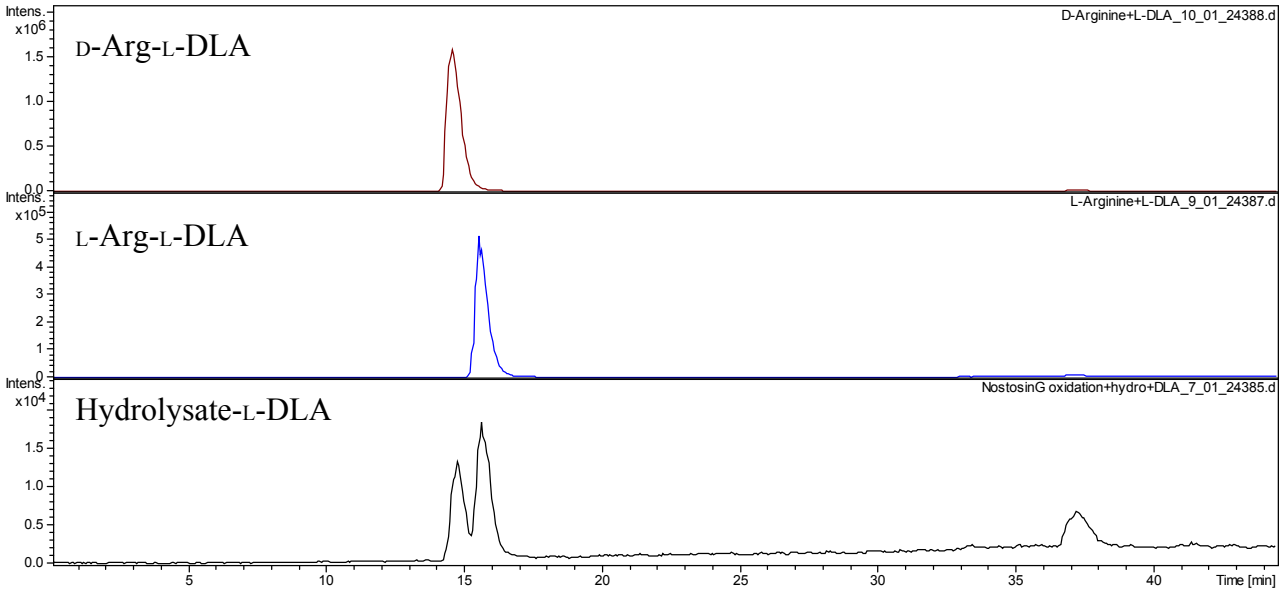

Figure S17. LC-MS chromatogram of Marfey's analysis of hydrolysate **1** (non-reduced), and standards D-Arg and L-Arg.

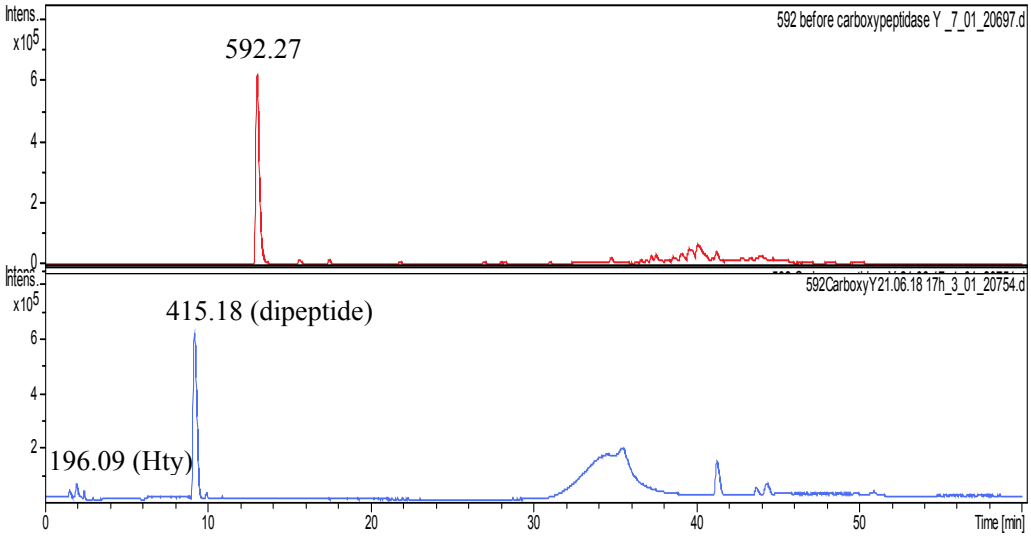

Figure S18. Enzymatic hydrolysis of **2** using carboxypeptidase Y.

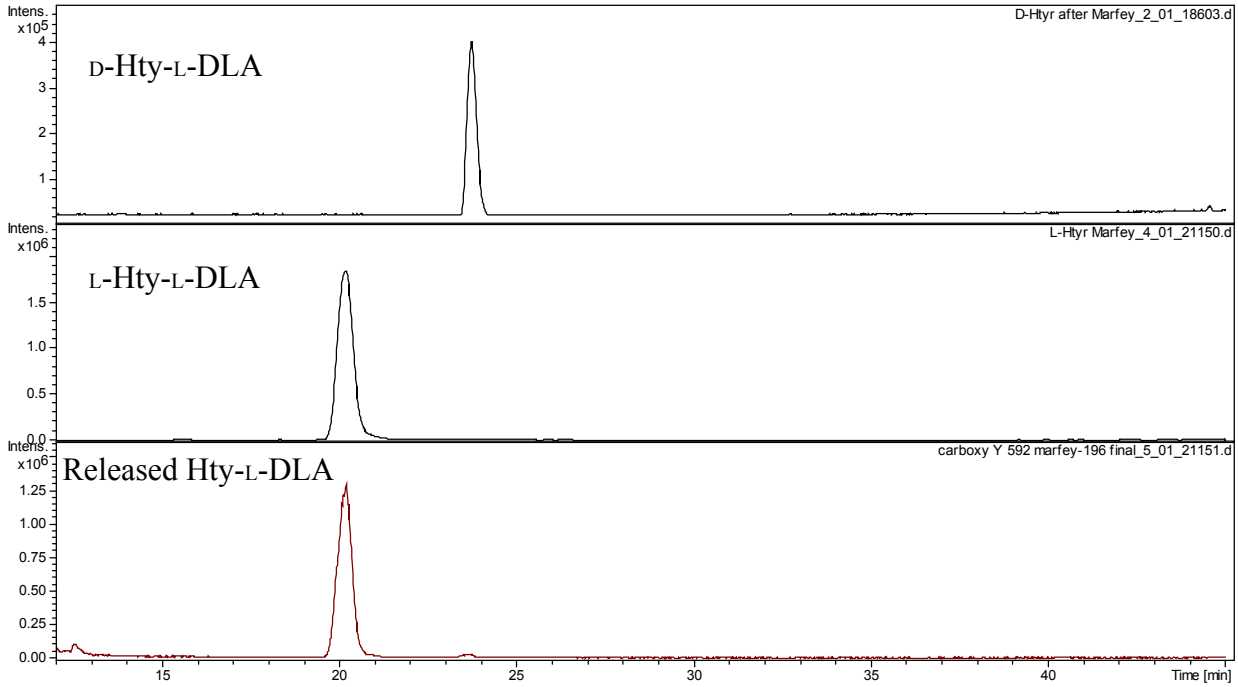

Figure S19. LC-MS chromatogram of Marfey's analysis of released Hty from **2** after hydrolysis with carboxypeptidase Y.

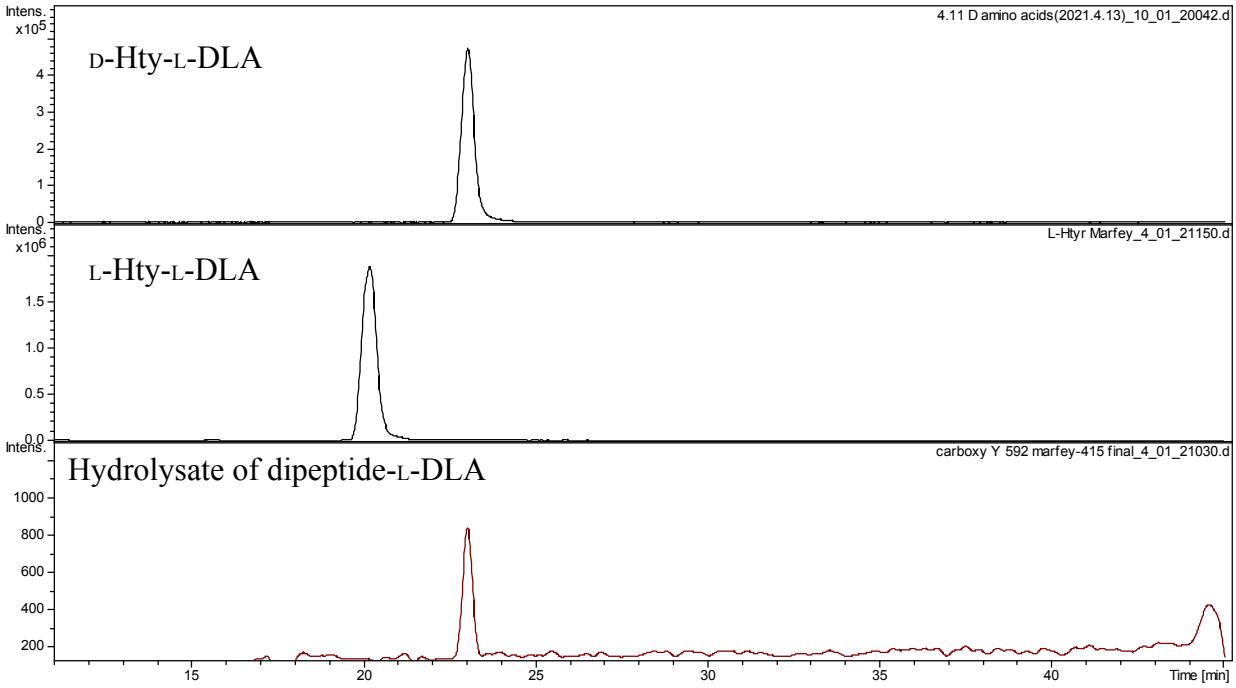

Figure S20. LC-MS chromatogram of Marfey's analysis of hydrolysates of dipeptide from **2** after hydrolysis with carboxypeptidase Y.

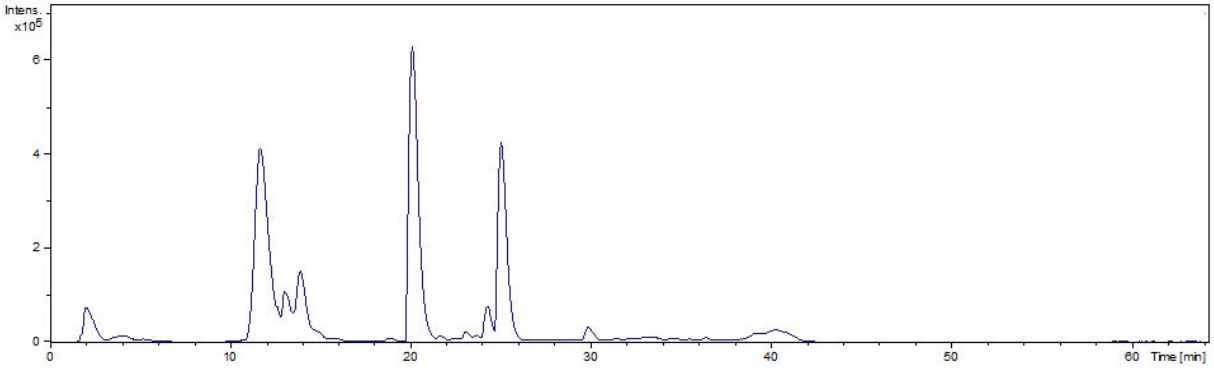

Figure S21. LC-MS chromatogram of water fraction of *Dolichospermum* sp. NIES-1697.

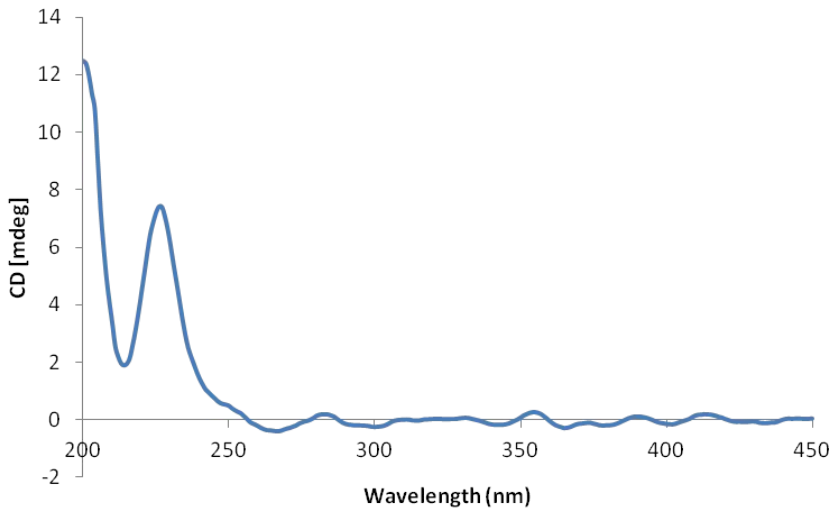

Figure S22. ECD spectrum of reduced form of nostosin G (**5**).

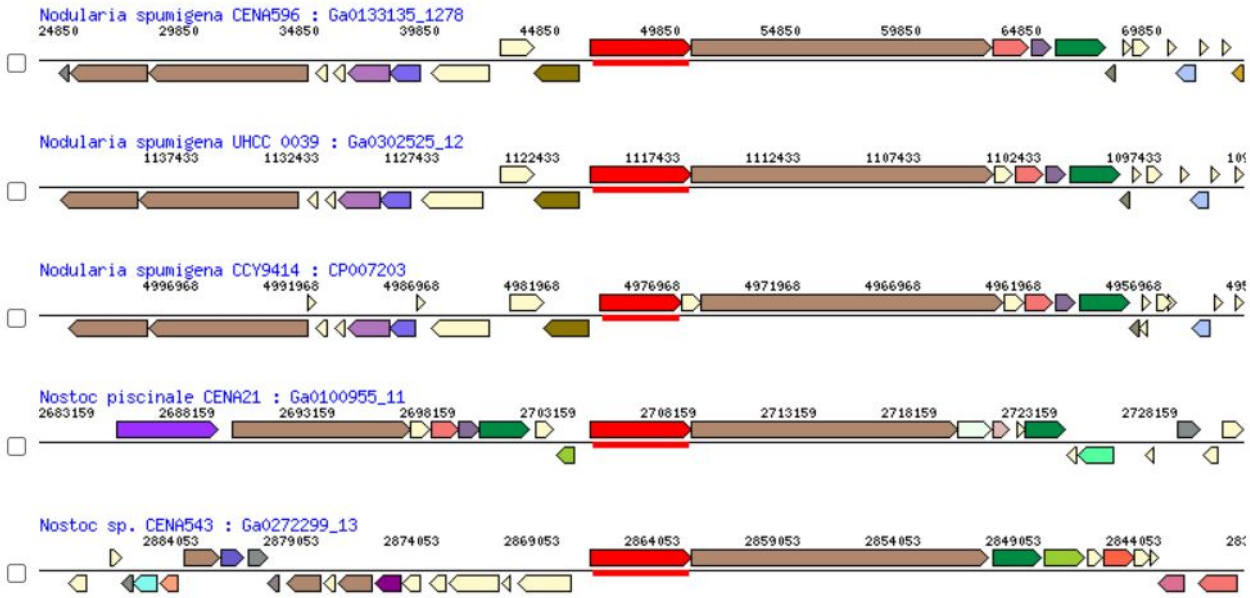

Figure S23. The homolog analysis was carried out on the Integrated Microbial Genomes and Microbiomes (IMG/M) System using NstA as query found five homolog genes (indicated as red color).

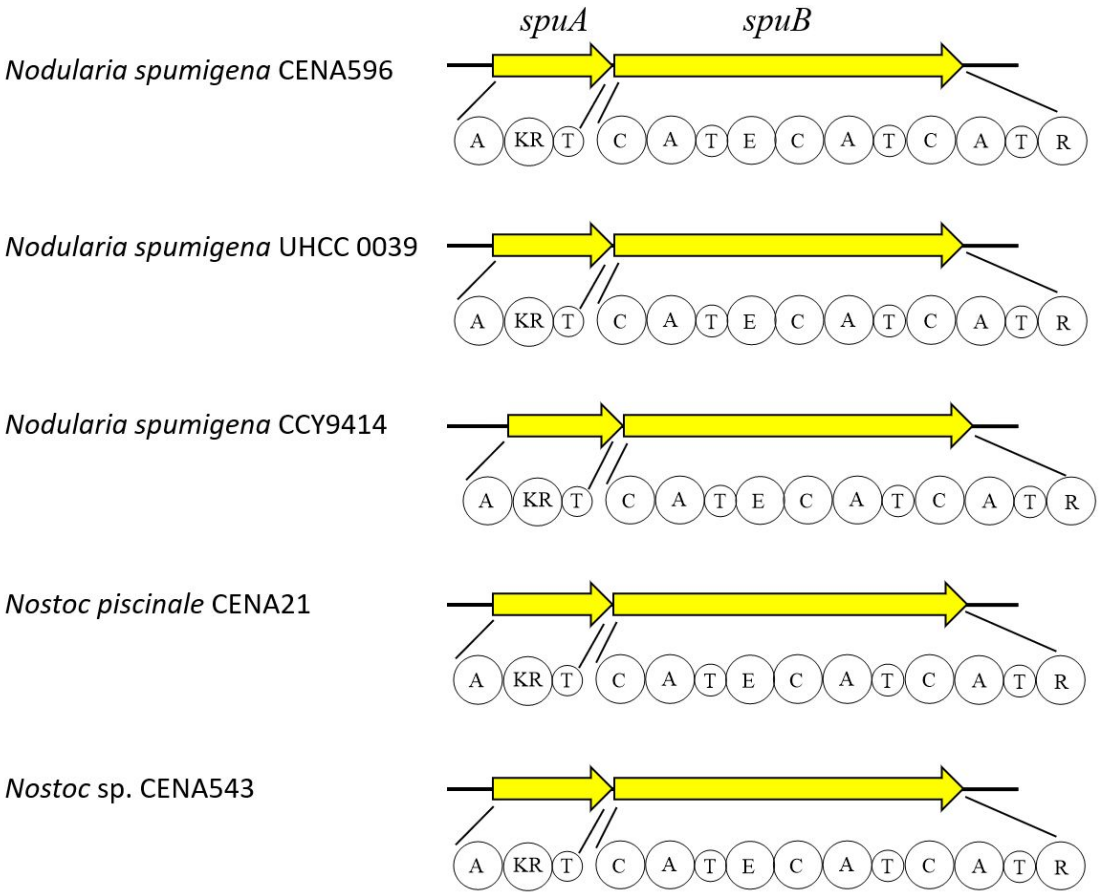

Figure S24. NstA shares homology 89.2% to SpuA (IMG Gene ID: 2745817816, *Nodularia spumigena* CENA596), 90.2% to SpuA (IMG Gene ID: 2813300686, *Nodularia spumigena* UHCC 0039), 89.4% to SpuA (IMG Gene ID: 2563163931 and 2563163930, *Nodularia spumigena* CCY9414), 75.9% to SpuA (IMG Gene ID: 2651623386, *Nostoc piscinale* CENA21) and 76.6% to SpuA (IMG Gene ID: 2791298690, *Nostoc sp.* CENA543). The domain structures of SpuA and SpuB (four residues spumigin biosynthesis) shared similarity to NstA and NstB except their genetic organization.

Table S1. Comparison of the AptC A_2 domain binding pockets for Hty or Hph residue in cyanobacteria.

Cyanobacteria	AptC A_2	Activated residue (peptide)
Sphaerospermopsis torquesreginae ITEP-024	DLGFTGCV	Hty (anabaenopeptin 808)
Anabaena sp. 90	DLGFTGCV	Hty (anabaenopeptin A)
Nodularia spumigena CCY 9414	DLGAIGCV	Hph (nodulapeptin B)
Nostoc punctiforme PCC 73102	DLGTIGCV	Hty (anabaenopeptin NZ 857) Hph (anabaenopeptin NZ 825)
Planktothrix agardhii CYA126/8	DLGFTGCV	Hty (anabaenopeptin 908) Hty (anabaenopeptin 915)

Note: AptC A_2 domain is the adenylation domain of module 4 in anabaenopeptin biosynthetic gene clusters; Hty is homotyrosine; Hph is homophenylalanine; references.[1-3]

Table S2. NstA, SprA, NstB and their amino acid sequences

Genes	Amino acid sequences
NstA	MNLDNHNQILATSTNENFTYQKIEVAIRSSLTVDDCVVIKRQTEKVKQELIAY IVPSGLFAPEQLLSHLQTILPSELTPTAFVPVSTIPLTETGQVDEVALASLEVIKS DLIRDLEKQLESLSEIDQVAVVVEPVVKSISIPPVHLEDLLGETPANPYENNQQ EIQVSTHSQNIENKNYYLSKKLAISHSEPLPYSPDAPKNLVEVLQRASENSNK GIIYIKSDGSETFQSYRKLWQDAQIILAGLRKTGLKPQDKVIFQLEDNQDFICA FWGCVLGGFVPVPVSIAPIYEPANNTASKLKNTWEMLEKPLVLTSGSLAADI DDFARGLNLENFKIVTVDELRQCEADLNIYENQPEDLAILLLTSGSTGIPKCV MLNHRNILSMTTGLILMGHFSSQESVLNWMPLDHVGALVSLSIMAASLGCQ QIHVHTDLIVQKPLHWLDLIDKHQATISWSPNFAFSLICDRAVEINRQQWDLS SMKFIINAGEPIVTKTARNFLKLLSHHGLPTNAIHPAFGMCETSSGITYSDSFSL ESSSDQTSFVELGLPIAGAALRIVDENEQIVTENTIGRLQVKGASVTIGYYQNP QANQEAFTTDGWFNTGDLGFLDQGRLTITGRIKDVIIINGLNYYCHEIEAAVE EMTGVEVSYTGACAVRQPGSNTDKLAIFFNTYLNDDQSLLTLLKEIRACVVN KVRINPDYLIPIDKDIIPKTAIGKIQRSQLSQRFQTGEFKSTIKRVDILLGNSNTIP NWFYRQVWKPKSPITVNSSLTITNTTLVFLDDWGLGDYLCQTLSENKLSYIT VYPGKEFQKISSSHYVVNPEIAKDYQLLIESLAADKIIIGQILHLWTYDKYQEI NNIDSLEKAQAQGIYSLLFLVQALAKVQGTNNYIQLLFISSHIQSIASDDPIAYE KSTVLGLLKTIPQELPKLNCRHIDLPFAEVEKNGFYILQEMQISSKERELAYRN GQRLISRLEQVDFTNTPKSSITFQQEGTYLITGGLGGIGVEVARYLLKHYQAK LLLVGRTPLNSEKHIKLYQELAQLGGEVIYESVDICDLEQLQIIVEKAQFRWG ENLDGILHLAGTFHEQQVLEETQENLAAILCPKLLGAWVLHQLAKENQASIFI NFSSAHGFFGSTAVGGYAAANSFLDSFTHYQNSPNKLTNKLTSYCFSWSMW DDTGMSQGYQMKNLIRAKGSYIMSCSQAISSMLASLHHQQHNLLIGLDGSN QNILRWQSSTFNLQKLTAYFTTNTGEVVKLPGLKVQDNFGNVCIYDSVQLPE MPCLENGEVDRARLIKRSNNQENREQIEPRNEIELKIAQCWQQVLKVTLLGIH DNFFELGGNSLLAGQVISRLREDFSLELSLQRLLQTPTIVGLAQTIAAIQTVTQ SQNTFTETSLQEYEEDYL
SprA	MWFIYQIAPESVAYNIFITVKIDYELKIDVVNRVWQKIIEKHPILRTTYTNHEG KPVQQVNQQENFSVEVIDSKEWSEEQLAKKIYAIADRPFNLEQDSVLRVNLF SRSAEKHILMLTMHHIAGDMWSFDLLLSEFQTLYLREIEQISQEQTETVDYLS EKKSYADFVHWQSEMLSSSQGEKLWQHWQEQLAGELPILNLLPDKPRPAVQ TYQGASYIVKLDEQLTEKLNHLAVASKTSLYQILLTAFYIQLYRYTNQTDILIS SPMRGRRGGNFEEIVGYFVNLTVLRVSVQENATFQEFLAQVSKTVKKAQYH

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NstB	MAIFEFLSLLNNLDIKIWVEDGQLRYRAPKGAMTDEIKQQIKERKAEIIAFLQE AQTATQINYSSLVPVVRDKDLPLSFAQQRMWFLSQLDGESTSYNESFQLRIV GKLSLTALEQSINEIIRRHEVLRTNFPTVEGVPFQVIRPNLTLSIPVINVQEFTEI AVQEIINQEVNKSFDLGTEPLIRATLLQQDPESHLLLITMHHIIIDGWSMGVFF KELEALYPAFIQGKPSPLPELTIQYADFALWQREWLTKEVQDKQLEYWKQQ LAGTPPLLELPTDYPRPPEQSFAGASIEFNIDADLTSQLVTLSQKSGVTLFMTL LTAFAVVLHRYSGQDDICIGSPFANRNRREIDSLIGFFVNTLVLRTQMEGNPR FSQLLEKVRSVVWDAHAHQDIPFEQVVEALKPERSLGYNPLFQVMFVLENFS LDTLELPGISLTPEIVDRGTAKFDLGLSMWQTQQGLIGSWEYNSDIFAPDTIAR MINHFQTLLAGIVKNPEQRIGELPLLTESEKHQLLTEWNDTQVEYPVDKCIHQ LFEEQVEKTPNAIAVVFENEQLTYQQLNSRANQLAHHLQSLGVKPETLVGIC VERSLEMVIGLLGILKAGGAYVPLDPEYPTERLSFMLEDAQVSVLLTQKSLLN QLPLDNREKPCQVICLEQLVLSEVEVNTFNLELTENPNHQNQPENLAYVIYTS GSTGKPKGVTIEHRAIVNLSLTWGQTFQVQNHSRLLQFGSFSFDLSVGEITTA LVTGACLYLGNKVTLLPSQSLVDFLTVNKITHSFLSPSALSVLPKAKLPDLQCI TVGGEACTTELVNQWGTERKFYNCYGPTESTVTATIFHCQPNGKKPAIGKAI SNIRTYILDKNNQLLPPGIPGELCIAGVGLARGYLNRPQATGEKFIEIDINGQV ERIYKTGDLARYLADGNIEYIGRIDNQVKIRGFRIELGEIEAVLNQHPQIQTSC VIVREDNPGQKQLVSYLIPHQHSTVTISEMRQYLKETLPEYMVPHSFVTLETL PITPNGKIDRRALPKPELESTLLEKYVAARNPIEELLTQTWLQVLKVESVGIND NFFELGGHSLIATQIVSRIRNIFQVELPLNKLFAAPTVRELAHIITQLQQDKLEL SADKAPLLLPRAKDADLPMSFAQQRLWFLDQFEANSVVYNMPTALRLLGKL QIAALEQSLQTIIHRHEALRTNFTTIDGQPIQVIREQKAGNKEQGIVSIVDLQHL PKTEQEIAVEQLTQQQMMTGFDLETEALIRVQLILLNETEQVLLVCMHHIVSD GWSMGVFVQELTQLYNAYCQNQPLPLTPLPIQYSDFAIWQRQWLQGDVLQN

	QITYWEQQLKDAPTLLSLPTDRPRPAVQTLVGATHEFALSVELTDKLIKLSQN QGCTLFMTLLAAYDTLLYRYTGQSDILVGSPIANRDRAEIEGLIGLFVNTLVM RTNLADNPRFSELLTRVREVALGAYAHQHLPFEMLVEALQPERDLSHSPLFQ VMFNLQNAPVSELELNGLTVSSVPFKGVTAAFDMTLFMQNTDNGLVGVWE YNTNLFDHSTIERMIGHFVTLLEAVVNNPQERIDKLPILTADEKQKLLIEWNN TQSDYPVGKCLHQLFAQQVELTPDAVAVVFDDQQLTYQQLNTQANQLAHY LQSLGVGAEVLVGIYLERSLSMTVALLAVLKAGGGYVPLDVDYPQQRLTYIS QDSQISVLITQESLLNSLPVEGVKVLVLDQEYEVFNSQSPENPFSEVLPENLAC VLYTSGSTGQPKGVILTHGALVNHSSAISEAFGLTSSDRVLQFAAFGFDVALE EIFPTWFKGGTVVLRPTQMFSSFANFAQFIEQQQLSVLTLTSAYWHEWMVAV SQSYATVPQSLRLLTVGGDTVLPETVAMWQQLVGNRITCLNAYGPTEASVT AIIYDVQNFSSEKTNTVLIGRPVANTEIYILDSNLQAVPMGVKGELYIGGERLA RGYLNRPELTQEKFIAHPFNNPKSQIKNPKLYKTGDLARYLPDGNIEFIGRIDD VVKIRGFRVALGEIESLLIQHPDVICQVVILREDQPGHKQLVAYVVTDNPSLT QNELQSFLKQKLPNYMIPTAFVMMEGLPVTTNGKVDRRALPAPSQEINLSNF VLPNTPTQKLIADIWRSVLVTTQLGIHNNFFDIGGNSLRAMQVMSLLTETLQI DLPLRYLFENPTVAELAAGFDSLLTSQTNTITTSNLDLKAEAVLDPSIQIPNQP FEYNNKPQGIFLTGVTGFLGSHLLYELLQHTQADIYCLIRATNIEQAQQKLQN QLQLYKLWSGVDRKRIIPVVGDLGKNYLGLSTSEFQQLAGQIDAIYHCGAWI NVIYPYSVLKPANVLGTQEIIRLASEIKVKPLHYISTTSVLSAATPNETGLILES DLLEQYQVLENGYVQSKWVAEKLVMQSRDLGLPVAIYRASRITGNTQTGIS NTDDLFCRLVKGCLETRIFPDVQMEDNLTPVDYVSKIIVNLSGQKESLGKAFH LVNPESTTIRDLFHLMHSLGYPVQMIPVEKWHSEISLESQISDTDNLRVLSHIIP KVAVENSPEPQIDYENTINGVGNIDLMYPALDQKLLKTYISYFISSGFIDEQLV TEQMVFENMTN

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