Supplementary Information

Reprogramming *Escherichia coli* for the production of prenylated indole diketopiperazine alkaloids

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Supplementary Table S1. Sequence data of synthetic PT genes.

РТ	Sequence of synthetic gene†
AnaPT	CCATGGCCAGCCCGCTGAGCATGCAGACCGATAGCGTGCAAGGTACAGCAGAGAATAAAAGCTTAGAGACCAATGGCACCAGCAATGACCAGCAACGCGCGTGGGAAAGTGCTGGGCAAAATCTTTAGGTTTAC CTACCATCGAGCAAGAGCAGTATTGGCTGAACACCGCACCGTACTTCAACAATTACTGATCCAGTGGGGCTATGATGTTCACCAGCAGCAGCAGTACCAGCAGTGCTGCCGCCATGTTTACCGGGGCGCGAGGGTGGGGGGGG
BrePT	CCATGCCCACACACCACCACACACACACACACACACACAC
CdpC2PT	CATGGCCGCAATTAATAGCCGTTGCGGTCTGGCTTGTAAACGCCATAGCGAGAGCGGCGAAGCCGCAAGCCGAATATACCAATCGCGTTACTTTAAGCCCGATCGAAGCACTGGCCCGCTACTGGACCAGTCCGACCGA
CdpC3PT	CCATGGCCACAGTGAGCAGTACCGCAGTTGAAGCCAGCGCACCGTGTGCCGAGATGGGCCATGATATCCCGTATCGTACTTTAAGCCGCAGCATGATTTTTGCCAATTTAGATCAGTACCAGTATTGGCACCAGG ATCGGCCCGGTGCTGGGCAAAATGCTGGTGGACGGCGAGTATAGCATCCACCGCCAGTATGAGTATTATCTTTATTTGCCCATCTGATCATTCCGAAGCTGGGCCCGTTCCCTAGTCCGGGTGGACCAGGACATCTAT CGTTGTTTACTGGGCAATATCGGTGGTCCGTTCGAACTGAGCCAGAATTTCCAGCGCTGGGTAGGACCAGGCACGGCCGCTTGGCCTTTGAGCCTACCAGTTATCTGGCAAGCACAGCGCCGATCCGTTTAACCGTCAC GCAGTTCATGCAACTTTAGCCGAGTTACGATCGACCGGCAGCCGGCGCGGCGGCGGCGGCGCGCGC

†The NcoI and XhoI cloning sites are highlighted in yellow and cyan, respectively; the stop codons are highlighted in green.

Supplementary Table S1 (continued).

РТ	Sequence of synthetic gene ⁺
CdpC7PT	CCATGGCCGCAAACCGCGTGAGCAATGACCCGGACGCCGTTAGCCAGAATGAAGTTCAAGCTGCCAAACGTCCGGACATTGCCCAGAACACCGACAATGTGGACAGCACCCCGTATCGCATTCTGACCCAGTT TCGACCTTTCCGGACGAAGCACACAAGAAGGGTTGGTGGGAAGATAGCGGCAGTTTACTGACGCGCTTTACTGCAAGTTGCCCGTTATGACGTGCATCAGTACGCAACTTTACTGTTCTGTACAAGCATTTAAT TCCGTTTATGGGCCCGTACCCGCAGCGCGCGCGCGCGCGC
CdpNPT	CCATGGCCGATGGCGAAATGACCGCCAGTCCGCCGGATATTAGCGCTTGTGACACCAGTGCAGTTGACGAACAGACTGGTCAAAGTGGCCAGAGCCAAGCTCCGATCCCGAAAGATATCGCCTATCACACTTTA ACCAAAGCTTTACTGTTCCCGGACATTGACCAGTATCAGCATTGGCACCACGTGGCACCTATGCTGGCAACAGACTGGTGATGGCAAGGCACCAGCAGCACCCGCAGCAGAACATTTATGTTTATGTTTATTCGCACAG CTGGTGGCCCCCGTTCTGGCCCCTACCCGAGTCCGGGTCGTGATGTGTATCGCTGTACTTTAGGTGGCAACATGACAGTGGCAAGTGACAACACGCAAACCTCCACCGAGCAGCAACACCCGCATCGCCCTTGAA CCGGTGCCCCCGTTCTGGCCCCTACCCGAGTCGGGCTCGTGAATGGTATGGCTGTACTTTAGGTGGCAACATGACAGTGGAACTGGACCAAACGCGACATGCGAGCGCACAACCCGCATCGCCCTTTGAA CCGGTGCCCCAAGGTGACGCCAAGGTGGCCACGGCATCGGCCCACGCGCGGCGCGCGC
СТгрРТ	CCATGG CAACCACCTATACTTTAAGTAAGGGCAGCGATCGCCCGCAAACAAGTGGCGATACCGATGGTCCGCAGCCGTATGATGTGCTGAGCAAATATTTACGTTTCCCGGACTTTGACCAAGATCAGTGGCGCGACACCGGACACCGGATCCAGCGCGACACCGGACATCAGCGCGACACCGCGACACCGCGACACCGGCGACACCGGCGACACCGGCGACACCGGCGACACCGGCGACGGCGACGGCGACGGCGACGGCGACGGCGACGGCGACGGCGACGGCGG
EchPT1	CCATGG CATCG CACCGAGCGAGGTGCTGACCAGCTATTACGATTACCGACCCATGACCAAGAAGCATGGTGGCGTGATACCGGTCCTCTGTTTGGCCGCTTTCTGAAAGGCGCTGGTTACGACGTTCACACACA

†The NcoI and XhoI cloning sites are highlighted in yellow and cyan, respectively; the stop codons are highlighted in green.

Supplementary Table S1 (continued).

РТ	Sequence of synthetic gene†
FtmPT1	CCATGG CATCGCCACCGCCGCACCTCCGGATCAGAAACCGTGTCATCAGCTGCAGCCGGCACCGTACCGTGCACTGAGCGAAAGCATTTATTT
NotF	CCATGGCAACCGCCCCGGAACTGCGCGTTGACACCTTTCGTGCACCCGAAGATGCACCGAAGAACCGAGCGCACAGCAGCGCGCGC
RoqD	CCATGG CAACCGTTAGCAGCACCGTTCAACCGCTGAAAGCTTGTGTGCCGGAAGCAACCGAGGCAGCAGCAGATATGCCGCATCACACTTTAAGCAAAAGCATGACCTTCGCAAATTTAGACCAGTATCAATATTG GCATGCCGTGGGTCCGATGCTGGGCCGTATGCTGAGCAACGGCAGTTACAGCATCATAAGCAATATGAGTATCTGTGTTTATTCGCCCACGTGATCATTCCGAAGCTGGGCCCGGTTGCCGTCCGGGCGCGCGGCGCGCGGTGGCCGCGGTGCCGCGGCACCGGTGGCCGGGCGCGGGCGCGCGGCGCGCGGCGCGCGGCG

†The *NcoI* and *XhoI* cloning sites are highlighted in yellow and cyan, respectively; the stop codons are highlighted in green.

Supplementary Table S2. Sequence data of recombinant PTs.

РТ	Sequence of expressed recombinant PT	MW (kDa)
AnaPT	MASPLSMQTDSVQGTAENKSLETNGTSNDQQLPWKVLGKSLGLPTIEQEQYWLNTAPYFNNLLIQCGYDVHQQYQYLAFYHRHVLPVLGPFIRSSAEAN YISGFSAEGYPMELSVNYQASKATVRLGCEPVGEFAGTSQDPMNQFMTREVLGRLSRLDPTFDLRLFDYFDSQFSLTTSEANLAASKLIKQRRQSKVIAFD LKDGAIIPKAYFFLKGKSLASGIPVQDVAFNAIESIAPKQIESPLRVLRTFVTKLFSKPTVTSDVFILAVDCIVPEKSRIKLYVADSQLSLATLREFWTLGGSV TDSATMKGLEIAEELWRILQYDDAVCSHSNMDQLPLVVNYELSSGSATPKPQLYLPLHGRNDEAMANALTKFWDYLGWKGLAAQYKKDLYANNPCR NLAETTTVQRWVAFSYTESGGAYLTVYFHAVGGMKGNL	48.9
BrePT	MATAPELRAPAGHPQEPPARSSPAQALSSYHHFPTSDQERWYQETGSLCSRFLEAGQYGLHQQYQFMFFFMHHLIPALGPYPQKWRSTISRSGLPIEFSL NFQKGSHRLLRIGFEPVNFLSGSSQDPFNRIPIADLLAQLARLQLRGFDTQCFQQLLTRFQLSLDEVRQLPPDDQPLKSQGAFGFDFNPDGAILVKGYVF PYLKAKAAGVPVATLIAESVRAIDADRNQFMHAFSLINDYMQESTGYNEYTFLSCDLVEMSRQRVKIYGAHTEVTWAKIAEMWTLGGRLIEEPEIMEGL ARLKQIWSLLQIGEGSRAFKGGFDYGKASATDQIPSPIIWNYEISPGSSFPVPKFYLPVHGENDLRVARSLAQFWDSLGWSEHACAYPDMLQQLYPDLDV SRTSRLQSWISYSYTAKKGVYMSVYFHSQSTYLWEED	49.6
CdpC2PT	MAAINSRCGLACKRHSESGEAEYTNRVTLSPIEALARYWTSPTEHHTQWQNDTAPLFSRLLEAAQYDVHDQYQYLLFMFGHIIPSLGPYPQRWKSTMTTL GIPLEFSINYQKHGKETVRVALEPVSVVSGTDEDPFNLITTRKFMSDIANLGLESFDMELHDYLINAFFPSANEIRDLQASGYGKRGGEQKSPSAFGFDL KAGGCITVKGYCHLLLKHLATGTPVSDIVREPLVRLCRQMTCSAAFDLMHDYLTKSSGYIKHTFLSWDYVPKEKSRLKVYSGSTSISLEKAEEVWSLGGR VQGEEISEGIKLIKQLWKTLGLKSCTDNTAQPVELEFDVNEEAQQKFQPPLTWNYELQPGISHPLTKLYFPVHGMNDLKVAEALSKFFHFLGWHDQAESY LSVLRDLYPEEDISKCTQLQSWISLAYTSQKGAYISVYYRSAKRSL	50.6
CdpC3PT	MATVSSTAVEASAPCAEMGHDIPYRTLSRSMIFANLDQYQYWHQIGPVLGKMLVDGEYSIHRQYEYLSLFAHLIIPKLGPFPSPGRDIYRCLLGNIGGPF ELSQNFQRLGSTARLAFEPTSYLASTSADPFNRHAVHATLAELRMTGSATVDLELHHALAADLTLTDRNEQLLTAELAKTNWKSQILLALDLNKTGITVK EYFYPALKAAATGHSVAELCFSAIRKVDVQGRLAAPCKAIEAHMQRQTQTDIHFLSVDLVEPGTTRFKLYLMELEVTLAKLEEHWTLGGTLTDKETMRGL QMIRELWVDLEIVDGKRAEPQRPSLPGDPLSIVPFFMNYEITPGQPLPKPKFYFPLIGIPELKIANVLAAFFERHGMHDLARVYPENLQSYYPGEDLAIA TDRQAWLSISYTEEKGPYLTMYYH	47.7
CdpC7PT	MAANRVSNDPDAVSQNEVQAAKRPDIAQNTDNVDSTPYRILTQFLTFPDEAQKGWWEDSGSLLSRLLQVARYDVHDQYATLLFLYKHLIPFMGPYPQRR RCVFEPYGAPIEYSINFQENKKEILRIVLDLVSIPYCTKDNPSHLDCVAAFESTLGQISPKVYNRDLYKHFADDLLPTKKDDEELTLHEMITDSNSLPAVA LWGFVLEEGGDVTIKGYINPQPNAKAVGASPRERLNESLQKLDSMVDYSDSLKLVREYTMEGSWHTGDQLVSWDYGPPEVSRIKMYGAAPENVSPATIR DVWTLGGRVDKETSRKGLELAIKLWELIHMQMESPPMDRKREFLMHGMLWHYEVWPGAQYPVPKIYLPAAGTNDGRVAETISKFFYSLGWKERAESYP QMLKDIFPDVDLSQSSRLQTWISFSYTEQGGAYSTVYYQAATRSTEFLAE	51.1
CdpNPT	MADGEMTASPPDISACDTSAVDEQTGQSGQSQAPIPKDIAYHTLTKALLFPDIDQYQHWHHVAPMLAKMLVDGKYSIHQQYEYLCLFAQLVAPVLGPYP SPGRDVYRCTLGGNMTVELSQNFQRSGSTTRIAFEPVRYQASVGHDRFNRTSVNAFFSQLQLLVKSVNIELHHLLSEHLTLTAKDERNLNEEQLTKYLTNF QVKTQYVVALDLRKTGIVAKEYFFPGIKCAATGQTGSNACFGAIRAVDKDGHLDSLCQLIEAHFQQSKIDDAFLCCDLVDPAHTRFKVYIADPLVTLARA EEHWTLGGRLTDEDAAVGLEIIRGLWSELGIIQGPLEPSAMMEKGLLPIMLNYEMKAGQRLPKPKLYMPLTGIPETKIARIMTAFFQRHDMPEQAEVFME NLQAYYEGKNLEEATRYQAWLSFAYTKEKGPYLSIYYFWPE	49.8
CTrpPT	MATTYTLSKGSDRPQTSGDTDGPQPYDVLSKYLRFPDFDQDQWWQNTAPMLGKLLSQCKYNVHQQYQHLCLYGLHVIPFLGPWPDIQRSKLYKSVLSG LGSLEFSQNFTKTGKTVRMGFEPTTFIASTSRDVCNRHCLGKVLNRFKQLDIKLDLQLYHQLVNEVSLTDQEENTLLERAILDDEPAKSQSLLALDFNKDD VTVKLYLYPQLKSLATGIPRTQLMFSAVRNVDKTRAFSESMNMIEEYFTSVRANAAPYWISCDLVEPNKTRFKIYIALFQVNFENAVSMWTLGNRITDPET MRGLAMVRDLWNSFDIQDGLREQKNRPGNPGDPSNIVPMLFNLEILPGKAYPQPKIYFPTTGMNDLDVAKVMVEFFKRHGLHEHAQSYIDNLASYVPHM DLNDCTDLQAWISFSYSDATGPYITVYYH	49.1

Supplementary Table S2 (continued).

РТ	Sequence of expressed recombinant PT				
EchPT1	MAPSEVLTSYYDYPTHDQEAWWRDTGPLFGRFLKGAGYDVHTQYQYLVFFIKNILPSLGPYPARWRSTITPTGLPIEYSLNFQLNSRPLLRIGFEPLSRF SGTPQDPYNKIAAADLLNQLSKLQLHEFDTQLFNHFTNEFELSKSESESLQKQGGINGKSTVRSQTAFGFDLKGGRVAVKGYAFAGLKNRATGTPVGQL ISNSIRNLEPQMHCWDSFSILNSYMEESDGWNEYSFVSWDCVDIERSRLKLYGVHNAVTWDKVKEMWTLGGRIENNATIKTGLELLQHMWSLLQINEG DRDYKGGFAADNGGKTLPIIWNYELNKGSPHPAPKFYFPVHGENDLQVSKSISEFFTHLGWQDHARQYPHLLRQIYPNQNISQTERLQAWISFAYNERT GPYLSVYYYSAERPPWGSDQVK	48.0			
FtmPT1	MAPPAPPDQKPCHQLQPAPYRALSESILFGSVDEERWWHSTAPILSRLLISSNYDVDVQYKYLSLYRHLVLPALGPYPQRDPETGIIATQWRSGMVLTGL PIEFSNNVARALIRIGVDPVTADSGTAQDPFNTTRPKVYLETAARLLPGVDLTRFYEFETELVITKAEEAVLQANPDLFRSPWKSQILTAMDLQKSGTVL VKAYFYPQPKSAVTGRSTEDLLVNAIRKVDREGRFETQLANLQRYIERRRRGLHVPGVTADKPPATAADKAFDACSFFPHFLSTDLVEPGKSRVKFYASE RHVNLQMVEDIWTFGGLRRDPDALRGLELLRHFWADIQMREGYYTMPRGFCELGKSSAGFEAPMMFHFHLDGSQSPFPDPQMYVCVFGMNSRKLVEG LTTFYRRVGWEEMASHYQGNFLANYPDEDFEKAAHLCAYVSFAYKNGGAYVTLYNHSFNPVGDVSFPN	52.7			
NotF	MATAPELRVDTFRAPEDAPKEPSAQQPRLPSSPSPAQALASYHHFPTNDQERWWEETGSLFSRFLEAGQYGLPQQYQFMFFFMHHLIPALGPYPQKWRST ISRSGLPIEFSLNFQKGSHRLLRIGFEPVSFLSGSSQDPFNRIPITDLLNRLSKLQLSNFDTPFFQHLLSKFQLSLSEVRQLQKQGSGPDAHPLKSQAAF GFDFNPDGAILVKGYVFPYLKAKAADVPVGTLIAEAVRTIDVERNQFTHAFGLINDYMQESTGYNEYTFLSCDFVETSEQRLKIYGAHTEVTWAKIAEMW TLGGRLIEEPEIIAGLARLKQIWSLLQIGEGSRAFKGGFDYDKSSATDQIASPIIWNYEIHPGSRFPVPKFYLPVHGENDLHVARALAQFWDSLGWPEHA CAYPDTLQQLYPDQDISQTTRLQSWISYSYTAKRGVYMSVYHSQSTYLWEED	51.7			
RoqD	MATVSSTVQPLKACVPEATEAADMPHHTLSKSMTFANLDQYQYWHAVGPMLGRMLSNGSYSIHKQYEYLCLFAHVIIPKLGPFPGGRDIYKCLLGGTGSV ELSQNVQKLGLTARVAFEPTSYIASTGVDPLNRHTVHATLVELRAIGSASIDMELHQMLVNELTLTDREERLMSPEAISGTAWKTQILLALDLGQTGITI KEYFYPALKASVTGQSVAKLCFSAIRKVDKQGRFEPASKAIETYMKTQSQTDLYFLSCDLVDPAATRIKLYLMELDMRLAKVEEHWTMGGKLNDEETLLG LKMLQELWVEFGIIEGMRNEPERPSLPGDPDTIVPFIMNYEMSPGEALPKPKFYFPLVGIPELKIANVLTAFFERYGMPEQAAVYRNNLQTPSKDLVIAT DHQAWLSFSYTKKKGPYLTMYYH	47.4			

Supplementary Table S3. Identification of recombinant PTs by PMF and peptide sequencing.

Sample	Best hit with PMF Mascot search			Summary of PMF results			Summary of peptide sequencing results		
	Accession number	Name	Organism	Mascot score	Peptide mass values matched	Protein sequence coverage (%)	Identified peptide sequences	Scores (min-max) for sequenced peptides	Protein sequence coverage (%)
AnaPT	XP_001258078	Dimethylallyl tryptophan synthase	Aspergillus fischeri NRRL 181	103	19	53	8	49-139	28
BrePT	I4AY86	Brevianamide F reverse prenyltransferase	Aspergillus versicolor	127	22	57	12	43-115	38
CdpC3PT	XP_001259405	Dimethylallyl tryptophan synthase	Aspergillus fischeri NRRL 181	139	23	68	5	56-128	20
CdpC7PT	XP_001213396	Predicted protein	Aspergillus terreus NIH2624	77	20	47	9	59-112	34
CdpNPT	ABR14712	Cyclic dipeptide N- prenyltransferase	Aspergillus fumigatus	162	27	57	6	42-91	15
CTrpPT	ADI60056	cyclo-L-Trp-L-Trp prenyltransferase	Aspergillus oryzae	114	28	53	9	50-131	39
FtmPT1	AAX56314	Brevianamide F prenyltransferase	Aspergillus fumigatus	198	29	62	12	40-80	35
NotF	ADM34132	Reverse prenyltransferase	Aspergillus sp. MF297-2	155	24	59	16	7-129	56
RoqD	XP_002568553	Pc21g15430	Penicillium rubens Wisconsin 54-1255	61	17	40	6	32-72	23



Supplementary Figure S1. Analysis of recombinant PT expression by SDS-PAGE. Bacteria BL21AI grown in M9 minimal medium were collected after 48-hour expression of various PTs. Whole-cell fractions (a), soluble fractions (b), and insoluble fractions (c) were prepared and analysed by 12% SDS-PAGE and Coomassie-blue staining. The corresponding overexpressed PT and CDPS are indicated for each lane. The sizes of the proteins of the protein standard (PageRulerTM Prestained Protein Ladder; ThermoScientific) are indicated in kDa. Red arrows in a and b indicate the presence of additional protein bands for which molecular weight corresponds to that of the expected PTs.



Supplementary Figure S2. MS2 and MS3 spectra of prenylated cWP produced by recombinant *E. coli* overexpressing CDPS74 and BrePT without DMAPP pathway engineering.



Supplementary Figure S3. MS2 and MS3 spectra of prenylated cWP produced by recombinant *E. coli* overexpressing CDPS74 and EchPT1 without DMAPP pathway engineering.



Supplementary Figure S4. MS2 and MS3 spectra of prenylated cWP produced by recombinant *E. coli* overexpressing CDPS74 and NotF without DMAPP pathway engineering.



Supplementary Figure S5. MS2 spectrum of cWP produced by recombinant *E. coli* expressing CDPS74. The chemical structure of the MH^+ ion at m/z 130 characteristic of the indole ring is shown.



Supplementary Figure S6. MS2 and MS3 spectra of the compound produced by recombinant *E. coli* expressing CDPS68 and CdpC3PT with a retention time of 20.1 min in Fig. 2b.



Supplementary Figure S7. MS2 and MS3 spectra of the compound produced by recombinant *E. coli* expressing CDPS68 and CdpC3PT with a retention time of 21.2 min in Fig. 2b.



Supplementary Figure S8. MS2 and MS3 spectra of the compound produced by recombinant *E. coli* expressing CDPS68 and CdpC3PT with a retention time of 22.9 min in Fig. 2b.



Supplementary Figure S9. MS2 spectrum of cWL produced by recombinant *E. coli* expressing CDPS68. The chemical structure of the MH⁺ ion at m/z 130 characteristic of the indole ring is shown. The chemical structure of the immonium ion characteristic of leucine at m/z 86 is also shown.



Supplementary Figure S10. LC-MSMS analysis of metabolite production by recombinant *E. coli* expressing CDPS14 and PTs. SPE-treated bacterial supernatants of cultures of BL21AI expressing CDPS 14 and AnaPT, CdpC2PT, CdpC7PT, CdpNPT, CTprPT, RoqD or no PT were analysed. UV chromatograms recorded at 220 nm (a) and EIC chromatograms for m/z 441 (b) are shown between 13 and 35 min. The injected volume of SPE eluates corresponded to 50 µl of culture supernatant.



Supplementary Figure S11. MS2 and MS3 spectra of the compound produced by recombinant *E. coli* expressing CDPS74 and FtmPT1 with DMAPP pathway engineering with a retention time of 19.0 min in Fig. 3a.



Supplementary Figure S12. MS2 and MS3 spectra of the compound produced by recombinant *E. coli* expressing CDPS14 and AnaPT with DMAPP pathway engineering with a retention time of 24.6 min in Fig. 3c.



Supplementary Figure S13. MS2 and MS3 spectra of the compound produced by recombinant *E. coli* expressing CDPS14 and CTrpPT with DMAPP pathway engineering with a retention time of 21.4 min in Fig. 3c.



Supplementary Figure S14. MS2 spectrum of cWW produced by recombinant *E. coli* expressing CDPS14 with DMAPP pathway engineering. The chemical structure of the MH^+ ion at m/z 130 characteristic of the indole ring is shown.



Supplementary Figure S15. Recovery of CDPs and prenylated CDPs from different bacterial culture fractions. a) BL21AI bacteria carrying pJBEI3085 and the 11 CDPS/PT combinations tested in our study where grown and induced for prenylated CDPs production. Culture supernatants were treated by SPE as described. Bacteria were lysed by sonication and the lysates extracted with ethyl acetate. Samples corresponding to culture supernatants and bacterial lysate extracts were analysed by LC-MSMS. The injected volumes corresponded to 50 μ l of the original cultures. Peak areas on chromatograms recorded at 220 nm are shown for CDPs (blue) and prenylated CDPs (orange) found in the culture supernatants and in ethyl acetate extracts. When several prenylated CDPs were detected, their peak areas were summed. Blue stars indicate CDPs and orange stars prenylated CDPs that were detected only in EIC traces. b) The experiment was repeated using a chemical lysis protocol to prepare the bacterial lysates. The legend is as in a).



Supplementary Figure S16. Key HMBC and ROE connectivities used to elucidate the structure of compounds **4-11**. ¹H-¹³C HMBC correlations are indicated by plain arrows (from ¹³C to ¹H) and ¹H-¹H ROEs are indicated by dashed arrows.



Supplementary Figure S17. 1D ¹³C DEPTQ spectrum (upper panel) and 1D ¹H spectrum (lower panel) of compound **4** in DMSO-*d*₆.



Supplementary Figure S18. 2D ¹³C-¹H HSQC spectrum (upper panel) and 2D ¹³C-¹H HMBC spectrum (lower panel) of compound **4** in DMSO-*d6*.



Supplementary Figure S19. 2D ¹H-¹H ROESY spectrum of compound 4 in DMSO-*d6*.



Supplementary Figure S20. 1D ¹³C DEPTQ spectrum (upper panel) and 1D ¹H spectrum (lower panel) of compound **5** in DMSO- d_6 .



Supplementary Figure S21. 2D ¹³C-¹H HSQC spectrum (upper panel) and 2D ¹³C-¹H HMBC spectrum (lower panel) of compound **5** in DMSO-*d6*.



Supplementary Figure S22. 2D ¹H-¹H ROESY spectrum of compound 5 in DMSO-*d6*.



Supplementary Figure S23. 1D ¹³C DEPTQ spectrum (upper panel) and 1D ¹H spectrum (lower panel) of compound **6** in DMSO- d_6 .



Supplementary Figure S24. 2D ¹³C-¹H HSQC spectrum (upper panel) and 2D ¹³C-¹H HMBC spectrum (lower panel) of compound **6** in DMSO-*d6*.



Supplementary Figure S25. 2D ¹H-¹H ROESY spectrum of compound 6 in DMSO-*d6*.



Supplementary Figure S26. 1D ¹³C DEPTQ spectrum (upper panel) and 1D ¹H spectrum (lower panel) of compound 7 in DMSO- d_6 .



Supplementary Figure S27. 2D ¹³C-¹H HSQC spectrum (upper panel) and 2D ¹³C-¹H HMBC spectrum (lower panel) of compound 7 in DMSO-*d6*.



Supplementary Figure S28. 2D ¹H-¹H ROESY spectrum of compound 7 in DMSO-*d6*.



Supplementary Figure S29. 1D ¹³C DEPTQ spectrum (upper panel) and 1D ¹H spectrum (lower panel) of compound **8** in DMSO- d_6 .



Supplementary Figure S30. 2D ¹³C-¹H HSQC spectrum (upper panel) and 2D ¹³C-¹H HMBC spectrum (lower panel) of compound **8** in DMSO-*d6*.



Supplementary Figure S31. 2D ¹H-¹H ROESY spectrum of compound **8** in DMSO-*d6*.



Supplementary Figure S32. 1D ¹³C DEPTQ spectrum (upper panel) and 1D ¹H spectrum (lower panel) of compound **9** in DMSO- d_6 .



Supplementary Figure S33. 2D ¹³C-¹H HSQC spectrum (upper panel) and 2D ¹³C-¹H HMBC spectrum (lower panel) of compound **9** in DMSO-*d6*.



Supplementary Figure S34. 2D ¹H-¹H ROESY spectrum of compound **9** in DMSO-*d6*.



Supplementary Figure S35. 1D ¹³C DEPTQ spectrum (upper panel) and 1D ¹H spectrum (lower panel) of compounds **10** and **11** in DMSO-*d*₆.



Supplementary Figure S36. 2D ¹³C-¹H HSQC spectrum (upper panel) and 2D ¹³C-¹H HMBC spectrum (lower panel) of compound **10** and **11** in DMSO-*d6*.



Supplementary Figure S37. 2D ¹H-¹H ROESY spectrum of compound 10 and 11 in DMSO-*d6*.