Supporting Information

Detailed Mechanistic Study of the Non-enzymatic Formation of the Discoipyrrole Family of Natural Products

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Experimental Details

General Procedures. 1H and 2D NMR spectral data were recorded at 600 MHz in DMSO-<i>d</i><sub>6</sub> on a Varian System spectrometer, and chemical shifts were referenced to the corresponding residual solvent signals (δ<sub>H</sub> 2.50/δ<sub>C</sub> 39.51). 13C NMR spectra were acquired at 400 MHz on a Varian System spectrometer. High resolution ESI-TOF mass spectra were provided by The Scripps Research Institute, La Jolla, CA. Low-resolution LC/ESI-MS data were measured using an Agilent 1200 series LC/MS system with a reversed-phase C<sub>18</sub> column (Phenomenex Kinetix, 150 mm × 4.6 mm, 2.5 µm) at a flow rate of 1.0 mL/min. Preparative HPLC was performed on an Agilent 1200 series instrument with a DAD detector, using a reversed-phase C<sub>18</sub> column (Phenomenex Luna, 250 × 10.0 mm, 5 µm) or a phenyl-hexyl column (Phenomenex Luna, 250 × 10.0 mm, 5 µm).

Collection and Phylogenetic Analysis of Strain SNA-048. Bacillus hunanensis strain SNA-048 was isolated from Little San Salvador, Bahamas. The sediment was dissociated and pasted onto agar plates using gauze 1 acidic media (10 g starch, 1 g NaNO<sub>3</sub>, 0.5 g K<sub>2</sub>HPO<sub>4</sub>, 0.5 g MgSO<sub>4</sub>, 0.5 g NaCl, 0.01 g FeSO<sub>4</sub>, 1 L seawater, 15 g agar, adjust pH to 5.3 with phosphate buffer). Bacterial colonies were selected and streaked to purity using the same agar media. Analysis of the strain by 16S rRNA revealed 99.9% identity to Bacillus hunanensis. The sequence is deposited in GenBank under accession no. KC247801.

Cultivation and Extraction of SNA-048 Cultures. Bacterium SNA-048 was cultured in 10 × 2.8 L Fernbach flasks each containing 1 L of a seawater-based medium (10 g starch, 4 g yeast extract, 2 g peptone, 1 g CaCO<sub>3</sub>), 40mg Fe<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>·4H<sub>2</sub>O, 100 mg KBr) and shaken at 200 rpm at 27 °C. After seven days of cultivation, sterilized XAD-7-HP resin (20 g/L) was added to adsorb the organic products, and the culture and resin were shaken at 200 rpm for 2 h. The resin was filtered through cheesecloth, washed with deionized water, and eluted with acetone. The acetone-soluble fraction was dried in vacuo.

Precursor Feeding Studies. Feeding studies with various amino acids (Cambridge Isotopes, Sigma) at indicated concentrations (S1, S4, S5) were carried out in triplicate in 125 mL flasks containing 50 mL of the seawater-based medium. Cultures were each inoculated with 5 mL turbid SNA-048. After 7 days, cultures were spun down at 4,800 rpm (Beckman J25.2 Rotor) and the supernatant was removed, extracted with ethyl acetate and dried in vacuo. The cell pellets were weighed and used to normalize between fermentation cultures. Dried extracts were resuspended in 2 mLs methanol and spun down. Supernatant was analyzed using an Agilent 1200 series LC/MS system with a reversed-phase C<sub>18</sub> column (Phenomenex Luna, 150 mm × 4.6 mm, 5 µm) at a flow rate of 0.7 mL/min. 4: Integration of AUC UV absorbance, λ = 280 nm (τ<sub>R</sub> = 11.5 min). 5: Integration of AUC UV absorbance, λ = 330 nm (τ<sub>R</sub> = 8.3 min). 6: Integration of AUC [M – H] m/z 121.1 (τ<sub>R</sub> = 7.8 min). Values were normalized to cell pellet mass and compiled using Graphpad Prism.

General synthetic model of discoipyrrole formation. 1-(4-methoxyphenyl)-5-methylhexane-2,3-dione, 7, (1 mol equivalent) was dissolved in 0.25 mL DMSO at room temperature. To this solution was added anthranilic acid, 5, (2 mol equivalent) in 0.25 mL DMSO and 4-hydroxybenzaldehyde, 6, (2 molar equivalent) in 0.25 mL DMSO. Then, 4-(dimethylamino)pyridine (3 mol equivalents) in 0.25 mL DMSO was added to the reaction flask. The reaction was stirred at room temperature for indicated amount of time. If formation of 1 was desired, 1% TFA was added after 24 hours and stirred for 12 hours. Scale of reaction varied from 5-100 µmol. 7. Generally, reaction products were purified by adding NH<sub>4</sub>Cl (aq) and direct loading of crude reaction onto reversed phase HPLC (RediSep Rf Gold® 30 g C18, 35 ml/min) using a gradient system from 10% to 100% H<sub>2</sub>O:CH<sub>3</sub>CN with monitoring at UV λ = 254, 330, and 280 nm.

Investigation of biosynthetic genes. Sequence analyses of the annotated SNA-048 genome with the amino acid sequence of Thz1050<sup>1</sup> were performed with the NCBI<sup>2</sup> and SEED<sup>3</sup> databases and the RAST<sup>4</sup> server, using PSI-BLAST. Multiple sequence alignments were performed with CLUSTALW<sup>5</sup>. Genome sequencing of B. hunanensis SNA048 was performed using an Illumina MiSeq. Reads were assembled using SPAdes 3.5<sup>6</sup> with read-pair merging using FLASH<sup>7</sup>.

General <sup>15</sup>N HMBC Monitoring. <sup>15</sup>N-anthranilic acid, 5, (Cambridge Isotopes) and 4-(dimethylamino)pyridine was added to 700 µL of DMSO-<i>d</i><sub>6</sub> in a 5 mm thin wall, 8 inch NMR tube (Wilmad) and inserted into 600 MHz
magnet (Varian). Instrument was tuned, locked, and shimmed. Then, the sample was removed and used to solubilize 7 and 6, before being inserted into the magnet. NMR experiments were then queued to run in the following order: 1X ¹H NMR experiment (32 scans taking 50 seconds) followed by 4X ¹H-¹³N HMBC (4 scans of 128 increments taking 30 minutes). Therefore, a single 1H NMR spectrum was collected once every 2 hours with 4 HMBC spectra collected in between. This was run constantly for 24 hours (until III appeared in isolation), at which point to the sample 1% TFA was added, followed by continued NMR data collection. For subsequent experiments in which alternative 2D experiments were run, a similar method was used albeit with intermittent COSY, HSQC, and HMBC experiments performed.

**Isolation and characterization of III.** 1-(4-methoxyphenyl)-5-methylhexane-2,3-dione,7, (9 mg, 38 μmol) was dissolved in 0.25 mL DMSO-d6 at room temperature. To this solution was added anthranilic acid, 5, (10.6 mg, 77 μmol) in 0.25 mL DMSO and 4-hydroxybenzaldehyde, 6, (9 mg, 76 μmol) in 0.25 mL DMSO. Then, 4-[(dimethylamino)pyridine (14 mg, 116 μmol) in 0.25 mL DMSO was added to the reaction flask. The reaction was stirred for 48 hours. The reaction was then subject to preparative HPLC (Phenomenex Luna, C18, 250 × 10.0 mm, 5 μm, 2.5 mL/min) using an isocratic solvent system at 17% CH₃CN:H₂O over 25 min to afford compound III (10.4 mg, tₑ = 18.0 min)

**III:** yellow oil, UV (MeOH) λₘₐₓ 225, 240, 265, 330, 390 nm; ¹H and ¹³C NMR, see Table S1; HRESIMS [M + H]⁺ m/z 475.1881 (calcd for C₂₆H₂₇¹⁵NO₆, [M + H]+ m/z = 475.1881).

**¹⁸O Labeling Experiment.** DMSO-d6 was degassed and charged with ¹⁸O₂ gas (Sigma) by purging 10 mL DMSO-d6 with N₂ for 10 minutes, followed by purging with ¹⁸O₂ for several minutes. 1-(4-methoxyphenyl)-5-methylhexane-2,3-dione,7, (45 mg, 192 μmol) was dissolved in 0.5 mL DMSO-d6 at room temperature. To this solution was added anthranilic acid, 5, (53 mg, 387 μmol) in 0.5 mL DMSO and 4-hydroxybenzaldehyde, 6, (46 mg, 380 μmol) in 0.5 mL DMSO. Then, 4-[(dimethylamino)pyridine (70 mg, 578 μmol) in 0.5 mL DMSO was added to the reaction flask. The reaction flask was purged with ¹⁸O₂ and stirred at room temperature under an atmosphere of ¹⁸O₂ for 24 hours. Analysis of sample was performed by subjecting aliquots to LC/MS. After completion, an aliquot of the reaction was purified directly (Phenomenex Luna, C18, 250 × 10.0 mm, 5 μm, 2.5 mL/min) using an isocratic solvent system at 17% CH₃CN:H₂O over 25 min to afford compound 8 (6.5, tₑ = 18.0 min). As a control, this experimental design was used albeit with ¹⁸O₂. To induce closure of 8, 1% TFA was added and the reaction stirred for 12 hours. After completion, an aliquot of the reaction was subject to reversed phase chromatography (RediSep Rf Gold® 30 g C18, 35 ml/min) using a gradient solvent system from 10-100% CH₃CN:H₂O over 35 min (2.5 mg, tₑ = 22 min).

**Interrogation of Pathway 1.**

![Diagram](pathway1)

**Synthesis of 9.** ¹⁵N-anthranilic acid (2.5 mg, 18 μmol) was dissolved in 0.2 mL DMSO-d6 at room temperature. To this solution was added 4-hydroxybenzaldehyde, 6, (2.4 mg, 20 μmol) in 0.2 mL DMSO. Then, 4-[(dimethylamino)pyridine (4.2 mg, 34 μmol) in 0.3 mL DMSO was added to the NMR tube. The reaction was stirred for 48 hours with constant ¹H-¹³N HMBC monitoring as described above.

**Synthesis of 10.** ¹⁵N-anilne (1.8 mg, 20 μmol) was dissolved in 0.2 mL DMSO-d6 at room temperature. To this solution was added 4-hydroxybenzaldehyde, 6, (2.3 mg, 19 μmol) in 0.2 mL DMSO. Then, 4-[(dimethylamino)pyridine (4.6 mg, 40 μmol) in 0.3 mL DMSO was added to the NMR tube. The reaction was stirred for 48 hours with constant ¹H-¹³N HMBC monitoring as described above.

**Interrogation of Pathway 2.**
[1-\textsuperscript{13}C]-6 (3.6 mg, 30 \mu mol) was dissolved in 0.2 mL DMSO-\texttextit{d}\textsubscript{6} at room temperature. To this solution was added 7 (3.5 mg, 15 \mu mol) in 0.2 mL DMSO-\texttextit{d}\textsubscript{6}. Then, 4-(dimethylamino)pyridine (5.6 mg, 45 \mu mol) in 0.3 mL DMSO-\texttextit{d}\textsubscript{6} was added to the NMR tube. Reaction was monitored by constant \textsuperscript{1}H-\textsuperscript{13}C HMBC for 48 hours. Aliquots were subjected to LC/MS analysis. After 72 hours, the reaction was heated to 60\degree C and monitored by LC/MS for several days.

7 (13 mg, 55 \mu mol) was dissolved in 1 mL EtOH at room temperature. To this solution was added 6 (10 mg, 83 \mu mol) in 0.5 mL EtOH. Then, NaOH (25 mg, 625 \mu mol) was added to the round bottom flask and the reaction was stirred at room temperature for several days. Aliquots were removed and subjected to LC/MS analysis.

\textbf{Interrogation of Pathway 3}.

7, (12 mg, 51 \mu mol) was dissolved in 0.33 mL DMSO-\texttextit{d}\textsubscript{6} at room temperature. To this solution was added \textsuperscript{15}N-anthranilic acid, 5, (15 mg, 109 \mu mol) in 0.33 mL DMSO-\texttextit{d}\textsubscript{6} and 4-(dimethylamino)pyridine (25 mg, 205 \mu mol) in 0.33 mL DMSO-\texttextit{d}\textsubscript{6}. The reaction was stirred at room temperature for 48 hours.

4, (17 mg, 77 \mu mol) was dissolved in 0.33 mL DMSO-\texttextit{d}\textsubscript{6} at room temperature. To this solution was added \textsuperscript{15}N-anthranilic acid, 5, (21 mg, 154 \mu mol) in 0.33 mL DMSO-\texttextit{d}\textsubscript{6} and 4-(dimethylamino)pyridine (30 mg, 245 \mu mol) in 0.33 mL DMSO-\texttextit{d}\textsubscript{6}. The reaction was stirred at room temperature for 48 hours. After 48 hours, the reaction was heated to 60\degree C for several days.

4, (27 mg, 122 \mu mol) was dissolved in 1 mL anhydrous dichloroethane (DCE) at room temperature. To this solution was added \textsuperscript{15}N-anthranilic acid, 5, (8.4 mg, 61 \mu mol) in 1 mL anhydrous DCE, sodium triacetyoxyborohydride (25 mg, 118 \mu mol) and glacial acetic acid (AcOH, 7 \mu l). The reaction was stirred at room temperature for 16 hours. (Figure S10) After completion, the reaction was quenched with NH\textsubscript{4}Cl (aq), extracted three times with EtOAc, and the organic layer was subject to reversed phase chromatography (RediSep Rf Gold\textsuperscript{\textregistered} 30 g C18, 35 ml/min) using a gradient solvent system from 10-100\% CH\textsubscript{3}CN:H\textsubscript{2}O over 35 min (13 mg, \textit{t}_R = 10 min).
Investigation of Enzymatic Routes to DP Precursors

Anthranilic acid (5): 5 is a compound ubiquitous in primary metabolism, namely amino acid catabolism and anabolism (KEGG Compound C00108) 8. Specifically, anthranilic acid can be produced by the enzymatic breakdown of tryptophan through various mechanisms, most of which involve indole intermediates 9. Preliminary feeding of SNA-048 cultures with L-tryptophan (1 g/L) provided a 22 fold increase in excreted anthranilic acid (SI Figure 1) suggesting that indeed tryptophan was a source for anthranilic acid in this bacteria. Based on the objective observation that SNA-048 seemed to produce high quantities of anthranilic acid compared to other Bacillus bacteria in our soil microbe library, we hypothesized that a supplemental mechanism might be driving the anthranilic acid production. Uncommon in bacteria, anthranilic acid can be produced directly from L-tryptophan via the oxidative kynurenine pathway in three steps, similar to mammalian systems [4]. Analysis of our annotated SNA-048 genome indicated that the kynurenine gene cluster was present, suggesting this as a potential explanation for the increased source of excreted anthranilic acid.

4-hydroxsattabacin (4): Decarboxylative condensation of amino acid pyruvates result in an acyloin conjugated dimer is a well-studied biosynthetic mechanism for the construction of simple alkaloids including the circumcins, kurasoins, sattabacins, soraphinol C, and xenocycoins (SI Figure 2) [1, 10]. These compounds have also been implicated as intermediates in more complex natural product biosynthesis as in the case of the UV-protectant scytominen A by cyanobacteria [11]. In several bacterial systems, the TPP dependent decarboxylase, or acyloin synthase, capable of performing these condensations has been cloned, purified, and tested in vitro [1, 11-12]. Recently, Park et al. thoroughly characterized the protein Thzk1050 from the thermophile Thermosporothrix hazakensis that produces sattabacin (SI Figure 2) from phenylalanine and leucine in vitro [1]. Our DP precursor 4, differs from sattabacin only by the aromatic hydroxyl substitution. We hypothesized that a homologous enzyme in our Bacillus hunanensis SNA-048 could carry out this reaction by using tyrosine instead of phenylalanine. Using the published gene sequences of TPP dependent decarboxylases (kdcA, scyA, and thzk1050) [1, 11-13] we performed PSI-BLAST analysis of the annotated genome of B. hunanensis SNA-048 for such genes. This led us to the discovery of three genes which showed high sequence homology to TPP dependent decarboxylases (SI Figure 3). To affirm incorporation of these amino acids into 4 [2-13C]-L-leucine and [2,13C]-L-tyrosine were fed into B. hunanensis SNA-048 cultures. Indeed, LC/MS and subsequent 13C NMR studies confirmed incorporation of the isotope at the correct position (SI Figure 4). These studies confirmed that B. hunanensis SNA-048 could produce 4-hydroxsattabacin from L-tyrosine and L-leucine, likely through the acyloin synthases found in our genomic analysis.

4-hydroxybenzaldehyde (6): 6 can be derived from oxidative degradation of metabolites such as L-tyrosine and toluene (KEGG Compound C00633) [8]. It has been found in bacteria, fungus, and algae as a byproduct of primary and secondary metabolism 14. In addition 6 can be produced from degradation of oxidized 4 when left at ambient temperature for a period of time. Feeding of varying doses of L-tyrosine drastically increased levels of 6 in B. hunanensis SNA-04 fermentations (SI Figure 5), however this cannot be attributed specifically to the catabolism of L-tyrosine or the increased presence of labile 4.
Figure S1. Anthranilic acid biogenesis. Left) SNA-048 cultures were fed with different amino acids and their media was extracted after 5 days fermentation. Extracts were subject to LC/MS analysis to compare levels of anthranilic acid production via integration of absorbance at $\lambda = 280$ nm ($t_R = 8.3$ min). Top right) Kynurenine pathway of tryptophan degradation (Tryptophan 2,3-dioxygenase (TDO), Bacterial kynurenine formamidase (KFA), Kynureninase (KYN)) Bottom Right) Organization of kynurenine pathway locus (4.6 kbp) as found in SNA-048.

Figure S2. Acyloin containing amino acid dimers. Reported alkaloid dimers with acyloin linkage.
Figure S3. Investigations of acyloin synthases in SNA-048. PSI-BLAST of the SNA-048 genome with protein sequence of thzk1050, the known sattabacin producing enzyme in Thermosporothrix hazakensis' reveals three top hits. B. Sequence alignment of candidate gene peg.3401 with sequences of known acyloin synthases. Conserved residues involved in catalytic function and substrate binding are signaled with asterisks (*).
Figure S4. 4-hydroxysattabacin feeding studies. a) Feeding of putative 4-hydroxysattabacin precursors leads to increased production of 4-hydroxysattabacin. SNA-048 cultures were fed with amino acid and their media was extracted after 5 days of fermentation. Extracts were subject to LC/MS analysis and production was calculated via integration of absorbance at $\lambda = 280$ nm ($t_R = 11.5$ min). b) Structures of 4-hydroxysattabacin analogs with incorporated 13C isotopes. c) Mass spectra (negative ion mode) of different SNA-048 feeding conditions as indicated by titles.
Figure S5. 4-hydroxybenzaldehyde feeding studies. SNA-048 cultures were fed with amino acid and their media was extracted after 5 days of fermentation. Extracts were subject to LC/MS analysis and production was calculated via integration of monoisotopic mass at [M – H] m/z 121.1 (t_R = 7.8 min).

Figure S6. $^{15}$N NMR chemical shifts. Common chemical shifts (ppm) of different $^{15}$N containing functional groups.$^{15}$
Figure S7. HRMS data of 9. Expected [M + H]$^+$ $m/z = 477.1923$

Figure S8. HRMS data of $^{16}$O 9. HRMS of isolated $^{16}$O control reaction (estimated [M + H]$^+$ $m/z = 475.1881$).
Figure S9. HRMS data of 10. Expected [M + H]^+ m/z = 457.1776).
Figure S10. LC/MS trace of imine trapping via reductive amination. LC/MS trace (Phenomenex Kinetix C18, 10% hold for 1', 10-99% in 13', 99% flush for 6'). Asterisk indicates $^{15}$N anthranilic acid starting material. No 4-hydroxysattabacin starting material was present. (Top) Chromatogram of LC run observing UV absorbance at 254 nm. (Bottom Left) Mass spectrum of diol side product ($t_R = 6.4$ min) [M – H]$^{-}$ m/z 223.2. (Bottom Right) Mass spectrum of amination product ($t_R = 9.3$ min) [M – H]$^{-}$ m/z 343.2.
**Supplementary Table 1**

| No. | δ\(^\text{H}\), mult (\(J\) in Hz) | COSY | HMBC |
|-----|-----------------------------------|------|------|
| 1   | -92.30 -13, 14                     |      |      |
| 2   | -199.5 -13                         |      |      |
| 3   | -110.0 -10, 10'                    |      |      |
| 4   | -172.2 -6, 6'                      |      |      |
| 5   | -121.2 -7, 7', 6, 6'               |      |      |
| 6   | 6.85, d (8.7) 131                 | 4, 6, 6', 8 |
| 7   | 6.45, d (8.7) 114.7               | 5, 6, 6', 8 |
| 8   | -158.2 -6, 6', 7, 7'              |      |      |
| 9   | -125.5 -11, 11'                   |      |      |
| 10  | 6.92, d (6.8) 129.6               | 3, 11, 11', 12 |
| 11  | 6.71, d (6.8) 112.9               | 9, 10, 10', 12 |
| 12  | -156.9 -10, 10', 11, 11'         |      |      |
| 13  | 1.69, d (4.6) 44.5               | 1, 2, 14, 15, 16 |
| 14  | 1.92, m 23.6                       | 13, 15, 16 |
| 15  | 1.04, d (6.7) 24.4               | 14 |
| 16  | 0.79, d (6.7) 23.8               | 13, 14, 15 |

Spectra collected in DMSO-\(d_6\) on a) 600 MHz spectrometer or b) 400 MHz spectrometer.

Figure S11. Validation of \(^1\)H-\(^{15}\)N HMBC in aqueous solvent. 4-hydroxybenzaldehyde, oxidized 4-methoxysattabacin, and \(^{15}\)N-anthranilate were combined in A1+C media made in D\(_2\)O and placed into an NMR tube. Thirty minute \(^1\)H-\(^{15}\)N HMBC were run constantly for 72 hours. After, the reaction was subject to LC-MS and full NMR analysis to validate the formation of DPA in these conditions. Shown above is a representative \(^1\)H-\(^{15}\)N HMBC spectrum from these experiments demonstrating the correlations of the \(^{15}\)N to protons in the final product.
| No. | δH, mult (J in Hz)a | δC | COSYb | HMBCc |
|-----|---------------------|-----|-------|-------|
| 1   | -                   | 92.3| -     | 13, 14|
| 2   | -                   | 199.5| -     | 13    |
| 3   | -                   | 110.0| -     | 10, 10'|
| 4   | -                   | 172.2| -     | 6, 6' |
| 5   | -                   | 121.2| -     | 7, 7' |
| 6, 6'| 6.85, d (8.7)      | 131 | 7, 7' | 4, 6, 6', 8 |
| 7, 7'| 6.45, d (8.7)      | 114.7| 6, 6' | 5, 6, 6', 8 |
| 8   | -                   | 158.2| -     | 6, 6', 7, 7' |
| 9   | -                   | 125.5| -     | 11, 11'|
| 10, 10'| 6.92, d (6.8)   | 129.9| 11, 11'| 3, 11, 11', 12 |
| 11, 11'| 6.71, d (6.8)   | 113.0| 10, 10' | 9, 10, 10', 12 |
| 12  | -                   | 156.5| -     | 10, 10', 11, 11'|
| 13  | 1.69, d (4.6)      | 44.5 | 14    | 1, 2, 14, 15, 16 |
| 14  | 1.92, m             | 23.2 | 13, 15, 16 |
| 15  | 1.04, d (6.7)      | 24.4 | 14    | 13, 14, 16 |
| 16  | 0.79, d (6.7)      | 23.8 | 14    | 13, 14, 15 |
| 17  | -                   | 169.8| -     | 20, 23 |
| 18  | -                   | 135.9| -     | 20, 21, 22, 23 |
| 19  | -                   | 143.0| -     | 20, 22 |
| 20  | 7.24 d (7.7)       | 130.8| 21    | 17, 22, 135.8, 141.9 |
| 21  | 7.34 t (7.5)       | 128.4| 20, 22 | 23, 135.8 |
| 22  | 7.17 t (7.5)       | 126.9| 21, 23 | 21, 23, 20, 135.8, 141.9 |
| 23  | 7.37 d (7.7)       | 130.3| 22    | 17, 21, 135.8 |
| 24  | 3.67, s            | 54.8 | -     | 12    |
| OH  | 9.76, s            | -    | -     |      |
| OH  | 6.64, s            | -    | -     |      |
| OH  | 10.71, s           | -    | -     |      |

Spectra collected in DMSO-d6 on a) 600 MHz spectrometer or b) 400 MHz spectrometer

Table S1. NMR Table for Compound III.
Figure S12. The $^1$H-NMR spectrum of compound IV
Figure S13. The $^{13}$C-NMR spectrum of compound IV
Figure S14. The COSY-NMR spectrum of compound IV
Figure S15. The HSQC-NMR spectrum of compound IV
Figure S16. The HMBC-NMR spectrum of compound IV
Figure S17. The $^1$H-$^{15}$N HMBC NMR spectrum of compound IV
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