Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

SUPPORTING INFORMATION

Chlorinated metabolites from an Australian *Streptomyces* sp. highlight the role of biosynthetic mosaics and superclusters in the evolution of chemical diversity

Mahmud T. Morshed,[a] Ernest Lacey,[a,b] Daniel Vuong,[b] Alastair E. Lacey,[b]
Soo Sum Lean,[c] Stephen A. Moggach,[c] Peter Karuso,[a] Yit-Heng Chooi,[c]
Thomas J. Booth[c]* and Andrew M. Piggott[a]*

[a]*Department of Molecular Sciences, Macquarie University, NSW 2109, Australia*
[b]*Microbial Screening Technologies, Smithfield, NSW 2164, Australia*
[c]*School of Molecular Sciences, University of Western Australia, Perth, WA 6009, Australia*

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1. General experimental details

Optical rotations were acquired in $CHCl_3$ on a Jasco P-1010 polarimeter in a 10 × 10 mm cell. UV–vis spectra were acquired in MeOH on a Varian Cary 4000 spectrophotometer or a Jasco V-760 spectrophotometer in a 10 × 10 mm quartz cuvette. ECD spectra were acquired on a Jasco J-810 spectropolarimeter. Analytical HPLC was performed on a gradient Agilent 1260 Infinity quaternary HPLC system consisting of a G4212B diode array detector. The column was an Agilent Poroshell 120 EC-C_{18} (4.6 × 50 mm, 2.7 μm) eluted with a 1 mL min^{-1} gradient of 10–100% acetonitrile/water (0.1% TFA) over 8.33 min. Semi-preparative HPLC was performed on a gradient Agilent 1260 Infinity quaternary HPLC system coupled to a G4212B diode array detector. The column was an Agilent Zorbax SB-C_{18} (9.4 × 250 mm, 5 μm) eluted with a 4.18 mL min^{-1} gradient of 10–100% acetonitrile/water (0.1% TFA) over 40 min.

Preparative HPLC was performed on a gradient Shimadzu HPLC system comprising two LC-20AP preparative liquid pumps with static mixer, SPD-M20A diode array detector and CBM-20A/20Alite system controller with a 7725i Rheodyne injection port. The columns used in the purification of the metabolites were selected from either an Agilent Zorbax SB-C_{18} column (21.2 × 250 mm, 7 μm) or an Agilent Zorbax SB-C_{18} column (50 × 150 mm, 5 μm) eluted isocratically with acetonitrile/water mixtures containing 0.05% TFA modifier. LCMS was performed on an Agilent 1260 Infinity series UHPLC equipped with an Agilent 6130B single quadrupole mass detector in both positive and negative ion modes. High resolution electrospray ionisation mass spectra (HRESIMS) were obtained on a Q Exactive Plus hybrid quadrupole-Orbitrap mass spectrometer (Thermo Fisher Scientific, Bremen, Germany) by direct infusion. ^{1}H NMR and ^{13}C NMR spectra were recorded in 5 mm Pyrex tubes (Wilmad, USA) on either a Bruker Avance II DRX-600K 600 MHz or Bruker Avance III HD 500 MHz spectrometer. All spectra were obtained at 25 °C, processed using Bruker Topspin 3.5 software and referenced to residual solvent signals (DMSO-d_6 δ_H 2.49/δ_C 39.5 or $CDCl_3$ δ_H 7.26/δ_C 77.1).

Molecular modelling: Models of ABX-K and ABX-G were built in Molecular Operating Environment 2019 (MOE2019.01; Chemical Computing Group) and were energy-minimized (MMFF94x)[1]. A comprehensive conformational search using low-mode molecular dynamics was used to identify the global minimum energy structures. All structures within 2.5 kcal mol^{-1} of the global minimum were then minimised using density functional theory (DFT BP86/def2-SV(P) followed by DFT PBE0-D3(BJ)/def2-SV(P)) in DMSO (COSMO) using Turbomole 7.1.1 (Cosmologic, GmbH & Co)[2] ECD calculations were performed at the same level of theory (TDDFT PBE0-D3(BJ)/def2-SV(P)-COSMO (DMSO)) and blue-shifted by 5 nm to compensate for systematic basis set errors.

2. Cultivation and extraction of *Streptomyces* sp. MST-144321

Streptomyces sp. MST-144321 was isolated from soil collected 4.2 km south of Yass, New South Wales, Australia in 1997. Optimisation of cultivation conditions for maximum metabolite production was undertaken on a range of agar- and grain-based media. The agars (ISP2, oatmeal, nutrient, NZ-amine and casein glycerol) were prepared according to the recipes in Table S25. The grains (barley, jasmine rice, basmati race and cracked wheat) were hydrated (30 mL water per 50 g grain) and sterilised at 121 °C for 40 min. Each of the agars and grains were inoculated with a suspension of MST-144321 and were incubated at 28 °C for 10 days. Cultures were sampled (1 g), extracted with methanol (2 mL) for 1 h on a wrist shaker, centrifuged (15,700 × *g* for 3 min) and analysed by HPLC.

Morphologically the strain was unremarkable in pigmentation, growth patterns, media or temperature optima. A crude methanolic extract of the confluent growth on ISP2 agar at 28 °C, 7 days was active against bacteria (*Bacillus subtilis* and *Staphylococcus aureus*) and nematodes (*Haemonchus contortus*), with weak activity against fungi (*Saccharomyces cerevisiae* and *Candida albicans*). DAD-HPLC analysis and dereplication identified the strain as containing no metabolites previously observed in our standards library, not corresponding to the metabolite profile of any of the 2,500 type and patent strains in our collection and only a single partial replicate (MST-123216) isolated from

Wellington, NSW. The UV-vis spectra of the dominant metabolites possessed unusual maxima, some similar to rebeccamycin. LCMS analysis indicated that despite the dissimilarity of the UV-vis spectra, most of the major metabolites showed isotopic clusters characteristic of the presence one or more chlorine atoms. This pattern of bioassay activity, UV spectra and isotopic patterns had not been found in our library previously. MST-144321 grew readily on a wide variety of agar, liquids and grains with consistently high production of secondary metabolites on all media (Figure S2).

Based on the optimisation results, barley was selected for large-scale cultivation of *Streptomyces* sp. MST-144321. The barley was hydrated and sterilised in 40 Erlenmeyer flasks (250 mL, each containing 50 g of barley with 30 mL water), inoculated with a spore suspension made from culture grown on ISP2 for 7 days, and incubated at 28 °C for 10 days, by which time the culture had reached maximal metabolite productivity. The grains were then pooled, extracted with acetone (2 × 6 L), and the combined extract was concentrated *in vacuo* to give an aqueous residue (99 g in 1600 mL). The aqueous concentrate was partitioned against EtOAc (2 × 2 L) and the organic layer was dried under reduce pressure to give an oily residue (46 g), with additional insoluble material at the solvent interface collected separately (4.1 g). The aqueous phase was lyophilised to a solid residue (41 g).

3. Isolation and purification of metabolites

A portion of the crude extract (4 g) was dissolved in MeOH (500 mL) and partitioned against hexane (2 × 400 mL) to remove fats, providing an enriched extract (958 mg). The enriched extract was dissolved in MeOH (20 mL) and evaporated onto 20 g of silica gel under reduced pressure. The silica was dry-loaded onto a silica gel column (55 g; 300 × 30 mm) and the column was washed once with hexane (400 mL), and then eluted with 50% hexane/$CHCl_3$ (400 mL) and $CHCl_3$ (400 mL), followed by a stepwise gradient of 1, 2, 4, 8, 16 and 100% MeOH (400 mL each step) yielding nine fractions (Fr. 1–9). Fr. 2 (74 mg) was purified by semi-preparative HPLC (Agilent Zorbax SB-C_{18}, isocratic 80% MeCN/H_2O containing 0.1% TFA, 4.18 mL min^{-1}) to yield (–)-ABX-D (**13**) (t_R = 11.1 min; 1.3

mg) and (–)BABX (**15**) (t_R = 14.2 min; 31 mg). Fr. 3 (419 mg) was purified by preparative HPLC (Agilent Zorbax C_{18}, isocratic 75% MeCN/H_2O containing 0.05% TFA, 20 mL min^{-1}) to yield (–)-ABX-C (**12**) (t_R = 14.6 min; 3.3 mg) and (–)-ABX-B (**11**) (t_R = 16.9 min; 26 mg). Fr. 4 (135 mg) was further fractioned by C_{18} SPE (2 g) using a stepwise gradient of 20, 30, 40, 50, 60% MeCN/H_2O and 100% MeCN (50 mL per fraction), yielding 6 fractions (Fr. 4A–4F). Fr. 4C (45 mg) was purified by semi-preparative HPLC (Agilent Zorbax SB-C_{18}, isocratic 55% MeCN/H_2O containing 0.1% TFA, 4.18 mL min^{-1}) to yield borregomycin C (**7**) (t_R = 8.8 min; 1.7 mg), (–)-ABX-A (**10**) (t_R = 14.0 min; 3.8 mg), (+)-ABX-G (**8**) (t_R = 18.3 min; 1.7 mg), (–)-ABX-K (**9**) (t_R = 21.3 min; 4.0 mg) and borregomycin B (**6**) (t_R = 24.2 min; 4.3 mg). Fr. 4D was purified by semi-preparative HPLC (Agilent Zorbax SB-C_{18}, isocratic 65% MeCN/H_2O containing 0.1% TFA, 4.18 mL min^{-1}) to yield (–)-ABX-E (**14**) (t_R = 23.0 min; 3.6 mg) and borregomycin E (**4**) (t_R = 28.4 min; 3.9 mg). Fr. 5 (88 mg) was further fractioned by C_{18} SPE (2 g) using stepwise gradient of 20, 40, 60 % MeCN/H_2O and 100% MeCN (50 mL per fraction), yielding four fractions (Fr. 5A–5D). Fr. 5C (18.7 mg) was purified by semi-preparative HPLC (Agilent Zorbax SB-C_{18}, isocratic 85% MeOH/H_2O containing 0.1% TFA, 4.18 mL min^{-1}) to yield borregomycin F (**5**) (t_R = 8.7 min; 1.0 mg). Fr. 6 (85 mg) was purified by semi-preparative HPLC (Agilent Zorbax SB-C_{18}, isocratic 25% MeCN/H_2O containing 0.1% TFA, 4.18 mL min^{-1}) to yield deschlorosvetamycin A (**1**) (t_R = 9.5 min; 2.5 mg) and svetamycin A (**3**) (t_R = 16.7 min; 9.6 mg).

The crude aqueous extract (12 g) was triturated with methanol (20 mL) to provide an enriched extract (2.0 g). The enriched extract was fractionated on by C_{18} SPE (10 g) using a stepwise gradient of 1, 2, 4, 8, 16% MeOH/H_2O and 100% MeOH (200 mL per fraction), yielding six fractions (Fr. 1–6). Fr. 6 (265 mg) was further purified by C_{18} SPE (10 g) using a stepwise gradient of 10, 15, 20, 30 and 100% MeOH (120 mL per fraction), yielding 5 fractions (Fr. A–E). Fraction B was purified by semi-preparative HPLC (Agilent Zorbax SB-C_{18}, isocratic 15% MeCN/H_2O containing 0.01% TFA, 4.18 mL min^{-1}) to yield svetamycin H (**2**) (t_R = 29.0 min; 6.5 mg).

The insoluble material (4.1 g) was triturated with 50% DMSO in MeOH (50 mL) and the solid residue (920 mg) was dissolved in MeOH + 0.1% TFA (10 mL) and purified by preparative HPLC (Agilent Zorbax SB-C_{18}, isocratic 35% MeCN/H_2O containing 0.1% TFA, 60 mL min^{-1}) to yield additional deschlorosvetamycin A (**1**) (t_R = 7.3 min; 4.6 mg) and svetamycin A (**3**) (t_R = 10.85 min; 11.5 mg).

4. Characterisation of compounds

Deschlorosvetamycin A (**1**): Colourless amorphous powder; $[\alpha]_D^{23}$ –31 (*c* 0.024, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 204.4 (4.92), 242.8 (4.60); IR (ATR) ν_{max} 3263, 2936, 2351, 1676, 1528, 1424, 1249, 1128 cm^{-1}; NMR (600 MHz, DMSO-d_6) see Table S1; HR-ESI(+)MS *m/z* 597.2623 $[M + H]^+$ (calculated for $C_{24}H_{37}N_8O_{10}^+$, 597.2627).

Svetamycin H (**2**): White amorphous powder; $[\alpha]_D^{23}$ –21 (*c* 0.027, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ϵ) 205.6 (4.94), 245.0 (4.42), 292.0 (3.72); IR (ATR) ν_{max} 2975, 2351, 1682, 1520, 1052 cm^{-1}; NMR (600 MHz, DMSO-d_6) see Table S2; HR-ESI(–)MS *m/z* 647.2196 $[M - H]^-$ (calculated for $C_{24}H_{36}N_8{}^{35}ClO_{11}^-$, 647.2197).

Borregomycin E (**4**): Greenish black powder, UV ($CHCl_3$) λ_{max} (log ϵ) 212.6 (4.12), 274.8 (4.12), 331.8 (3.98), 368.6 (3.44); IR (ATR) ν_{max} 3327, 2927, 2856, 2352, 1665, 1613, 1446, 1373, 1297, 1192 cm^{-1}; NMR (600 MHz, DMSO-d_6) see Table S4; HR-ESI(–)MS *m/z* 383.0356 $[M - H]^-$ (calculated for $C_{20}H_{13}{}^{35}Cl_2N_2O_2^-$, 383.0359).

Borregomycin F (**5**): Yellow amorphous powder, UV ($CHCl_3$) λ_{max} (log ϵ) 237.0 (4.01), 320.8 (4.18), 400.0 (3.15); IR (ATR) ν_{max} 2933, 1684, 1406, 1197, 1141 cm^{-1}; NMR (600 MHz, DMSO-d_6) see Table S5; HR-ESI(–)MS *m/z* 391.9996 $[M - H]^-$ (calculated for $C_{20}H_8{}^{35}Cl_2N_3O_2^-$, 391.9999).

(+)-ABX-G (**8**): Yellow amorphous powder, $[\alpha]_D^{23}$ +19 (*c* 0.034 $CHCl_3$), UV ($CHCl_3$) λ_{max} (log ϵ) 207 (4.49), 227 (4.25), 269 (3.82), 387 (4.00); ECD (MeOH) λ_{max} ($\Delta\epsilon$) 242 (+18.3), 279 (+4.3), 309 (–1.6), 380 (+0.86); IR (ATR) ν_{max} 2898, 2351, 1686, 1203, 1059 cm^{-1}; NMR (600 MHz, DMSO-d_6) see Table S8; HR-ESI(+)MS *m/z* 525.1303 $[M + H]^+$ (calculated for $C_{28}H_{26}{}^{35}ClO_8^+$, 525.1310).

(–)-ABX-K (**9**): Yellow powder, $[\alpha]_D^{23}$ –80 (*c* 0.097 $CHCl_3$), UV ($CHCl_3$) λ_{max} (log ϵ) 204 (5.00), 226 (4.70), 277 (4.29), 406 (4.45); ECD (MeOH) λ_{max} ($\Delta\epsilon$) 242 (–37.2), 280 (–8.3), 307 (+6.2), 371 (–1.6); IR (ATR) ν_{max} 2936, 2352, 1681, 1600, 1417, 1359, 1249, 1157 cm^{-1}; NMR (600 MHz, DMSO-d_6) see Table S9; HR-ESI(+)MS *m/z* 495.1198 $[M + H]^+$ (calculated for $C_{27}H_{24}{}^{35}ClO_7^+$, 495.1205).

5. Biological screening

Purified metabolites were dissolved in DMSO to provide stock solutions (10,000 μg mL^{-1} or 1,000 μg mL^{-1} depending on the amount of material available). An aliquot of each stock solution was transferred to the first lane of Rows B to G in a 96-well microtitre plate and two-fold serially diluted with DMSO across the 12 lanes of the plate to provide a 2,048-fold concentration gradient. Bioassay medium was added to an aliquot of each test solution to provide a 100-fold dilution into the final bioassay, thus yielding a test range of 100 to 0.05 μg mL^{-1} in 1% DMSO. Row A contained no test compound (as a reference for no inhibition) and Row H was uninoculated (as a reference for complete inhibition).

NS-1 (ATCC TIB-18) mouse myeloma cells were used as indicator of antitumour actives. NS-1 cells were inoculated in 96-well microtitre plates (190 μL) at 50,000 cells mL^{-1} in DMEM (Dulbecco's Modified Eagle Medium) + 10% fetal bovine serum (FBS) + 1% penicillin/streptomycin (10,000 U mL^{-1} / 10,000 μg mL^{-1}, Life Technologies Cat. No. 15140122) with resazurin (250 μg mL^{-1}; 10 μL)

and incubated in 37 °C (5% CO_2) incubator. The plates were incubated for 96 h during which time the positive control wells change colour from a blue to pink colour. The absorbance of each well was measured at 605 nm using a Spectromax plate reader (Molecular Devices).

Bacillus subtilis (ATCC 6633) and *Staphylococcus aureus* (ATCC 25923) were used as indicative species for Gram-positive bacteria, and *Escherichia coli* (ATCC 25922) was used as an indicative species for Gram-negative bacteria. A bacterial suspension (50 mL in 250 mL flask) was prepared in nutrient media by cultivation for 24 h at 250 rpm, 28 °C. The suspension was diluted to an absorbance of 0.01 absorbance units per mL, and 10 μL aliquots were added to the wells of a 96-well microtitre plate, which contained the test compounds dispersed in nutrient broth (Amyl) with resazurin (12.5 μg mL). The plates were incubated at 28 °C for 48 h during which time the positive control wells change colour from a blue to light pink colour. MIC end points were determined visually. The absorbance was measured using Spectromax plate reader (Molecular Devices) at 605 nm and the IC_{50} values determined graphically.

The yeasts *Candida albicans* (ATCC 10231) and *Saccharomyces cerevisiae* (ATCC 9763) were used as indicative species for antifungal activity. A yeast suspension (50 mL in 250 mL flask) was prepared in 1% malt extract broth by cultivation for 24 h at 250 rpm, 24 °C. The suspension was diluted to an absorbance of 0.005 and 0.03 absorbance units per mL for *C. albicans* and S. *cerevisiae*, respectively. Aliquots (20 μL and 30 μL) *of C. albicans* and S. *cerevisiae,* respectively were applied to the wells of a 96-well microtitre plate, which contained the test compounds dispersed in malt extract agar containing bromocresol green (50 μg/mL). The plates were incubated at 24 °C for 48 h during which time the positive control wells change colour from a blue to yellow colour. MIC end points were determined visually. The absorbance was measured using Spectromax plate reader (Molecular Devices) at 620 nm and the IC_{50} determined graphically.

Tritrichomonas foetus was used as an indicative species for inhibitors of animal protozoan pathogen. *T. foetus* (strain KV-1) was inoculated in 96-well microtitre plates (200 µL) at 4×10^4 cells mL^{-1} in *T. foetus* medium (0.2% tryptone, Oxoid; 0.1% yeast extract, Difco; 0.25% glucose; 0.1% L-cysteine; 0.1% K_2HPO_4; 0.1% KH_2PO_4; 0.1% ascorbic acid; 0.01% $FeSO_4.7H_2O$; 1% penicillin/streptomycin (10,000 U mL^{-1} / 10,000 µg mL^{-1}, Life Technologies Cat. No. 15140122); 10% new born calf serum, (NBCS, Life Technologies). The plates were incubated in anaerobic jars (Oxoid AG25) containing an Anaerogen satchet (Oxoid AN25) in 37 °C (5% CO_2) incubator. At 72 h, *T. foetus* proliferation was counted and % inhibition graphed to determine the IC_{50} values.

6. Extraction and sequencing of genomic DNA

Genomic DNA was extracted from *Streptomyces* sp. MST-144321 using a Sigma GenElute Bacterial Genomic DNA Kit. Briefly, a plate culture of MST-144321 was scraped to harvest the cells, which were resuspended in lysozyme solution (200 µL). The resuspended cells were then incubated at 37 °C for 30 min before adding RNase A solution (20 µL) and incubating at room temperature for 2 min. Proteinase K (20 µL) and lysis solution (200 µL) were then added, followed by incubation at 55 °C for 10 min. The homogeneous mixture was diluted with absolute ethanol (200 µL) and vortexed. The mixture was then transferred to the binding column and centrifuged at 6500 × *g* for 1 min. Finally, the column was washed with wash solution (500 µL) and centrifuged at 6500 × *g* for 1 min. Elution buffer (200 µL) was added to the centre of the column to elute the genomic DNA.

DNA was sequenced at the Beijing Genome Institute (BGI). Genome sequences of MST-144321 was produced from 150 bp paired-end sequencing on Illumina platform. Poor quality reads were removed using FastQC.[3]. The draft genome was assembled and polishing using Unicycler.[4] Biosynthetic Gene Clusters (BGCs) were predicted by antiSMASH version 5.1.1.[5] and further analysed using BLASTP and cblaster.[6] Sequence alignments were generated using Clustal Omega[7] and phylogenetic trees were generated using RAxML version 8[8] and FastTree.[9] Trees were visualised in FigTree.[10]

7. Genomic Features of MST-144321

A draft genome of MST-144321 was acquired *via* Illumina sequencing consisting of 49 contigs with an N50 of 530,408. This represents ~6.7 Mb of genomic DNA. Analysis with plasmidSPADES[11] and Bandage[12] did not indicate the presence of plasmids. Multilocus Sequence Typing (MLST)[13, 14] of the strain showed a unique combination in its six housekeeping genes (16S = 27, *atp*D = 14, *gyr*B = 91, *rec*A = 15, *rpo*B = 15 and *trp*B =15), which suggested MST-144321 is a novel strain belonging to the genus *Streptomyces*. Further analysis using autoMLST[15] confirmed this result and revealing that MST-144321 was most closely related to *Streptomyces luteocolor* NBRC 13826 (Figure S73).

8. Single-crystal X-ray diffraction analysis

Crystals of svetamycin A (**3**) were obtained by slow evaporation of a solution of **3** in 1:1 MeOH/MeCN. A clear light colourless block-shaped crystal with dimensions 0.16 × 0.14 × 0.05 mm^3 was mounted. Data were collected using a XtaLAB Synergy, Single source at home/near, HyPix diffractometer operating at T = 100.00(10) K. Data were measured using w scans using Cu K_α radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program CrysAlisPro (Rigaku, V1.171.41.103a, 2021).[16] The maximum resolution that was achieved was Q = 75.702° (0.80 Å). The unit cell was refined using on 22921 reflections, 51% of the observed reflections. Data reduction, scaling and absorption corrections were also performed using CrysAlisPro. The final completeness is 100.00% out to 75.702° in Q. A Gaussian absorption correction was performed based on Gaussian integration over a multifaceted crystal model using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm. The absorption coefficient m of this material is 1.780 mm^{-1} at this wavelength (λ = 1.54184 Å) and the minimum and maximum transmissions are 0.844 and 1.000.

The structure was solved and the space group $P2_12_12_1$ (# 19) determined by the ShelXT 2018/2 structure solution program[17] using dual methods and refined by full matrix least squares minimisation on $\boldsymbol{F^2}$ using version 2018/3 of XL.[18] All non-hydrogen atoms were refined anisotropically. Hydrogen

atom positions were calculated geometrically and refined using the riding model. There is a single molecule in the asymmetric unit, which is represented by the reported sum formula. Z is 4 and Z′ is 1. The Flack parameter was refined to 0.000(7). Determination of absolute structure using Bayesian statistics on Bijvoet differences using the Olex2[19] results in 0.006(6). This provides absolute configuration of the molecule. All crystallographic data have been deposited with the CCDC (2087152) and can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (fax +441223336033; email deposit@ccdc.cam.ac.uk).

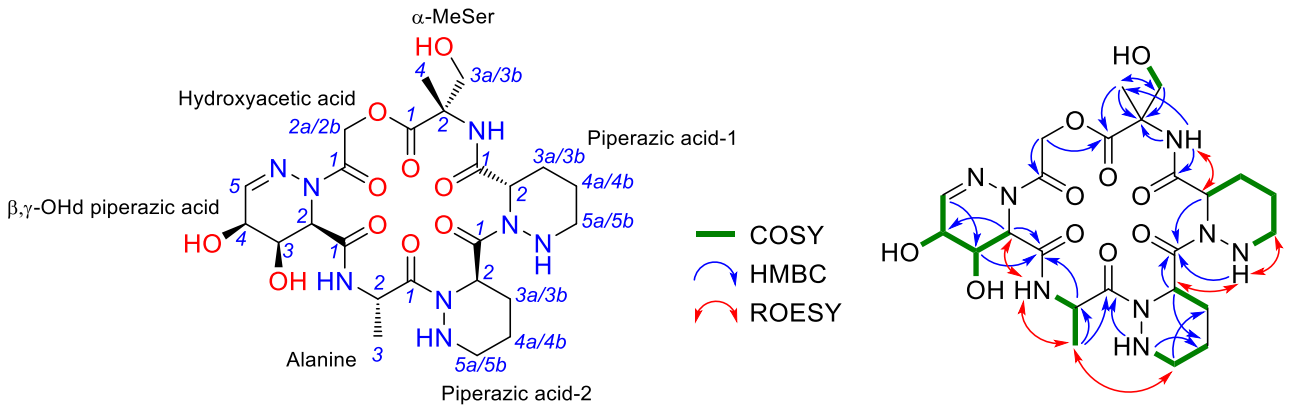


Table S1. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for deschlorosvetamycin A (**1**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	COSY	ROESY
α-Methyl Serine (α-MeSer)					
1		172.3			
2		61.0			
3a	3.77, dd (11.3, 9.1)	63.7	1, 4	3-OH	4
3b	3.85, dd (11.3, 5.3)		1, 4	3-OH	4
4	1.46, s	19.3	1, 2, 3		
2-NH	7.42, s		1, 2, 4, 1_{pip-1}		
3-OH	4.08, dd (9.1, 5.3)			3a/b	
Piperazic acid-1 (Pip-1)					
1		169.7			
2	4.91, br d (5.6)	50.5	1, 3, 4, 1_{pip-2}	3a/b	3a/b, 2-$NH_{α-MeSer}$
3a	1.64, m	23.6	1	2, 4a	2, 4a
3b	2.08, m			2	2
4a	1.36, m	20.3		3a	5b
4b	1.79, m			5a/b	5b
5a	2.60, dddd (15.9, 13.0, 10.5, 3.0)	46.5		4b, 5-NH	
5b	3.01, m			4b	5-NH
5-NH	4.47, br d (15.9)		1_{pip-2}	5a	4b, 5b, 2_{pip-2}
Piperazic acid-2 (Pip-2)					
1		173.3			
2	5.55, d (5.5)	47.6	1, 3, 4	3a/b	3ab, 5-NH_{Pip-1}
3a	1.75, m	24.7	1, 2, 4, 5	2	5a
3b	1.92, m			2	
4a	1.50, m	21.0			5a/b
4b	1.56, m				5a/b
5a	2.60, dddd, (15.9, 13.0, 10.5, 3.1)	46.8	3, 4	4a/b	3_{Ala}
5b	3.01, m		3, 4	4a/b	5-NH
5-NH	4.94, br d (12.7)		4, 1_{Ala}	5a/b	4b, 5b
Alanine (Ala)					
1		172.5			
2	5.16, dq (7.3, 6.8)	44.3	3, $1_{β,γ-OHdPip}$	3, 2-NH	3, 2-NH
3	1.16, d (6.8)	18.3	1, 2	2	2, 2-NH
2-NH	8.02, d (7.3)		$1_{β,γ-OHdPip}$	2	3, $2_{β,γ-OHdPip}$
β,γ-OHd piperazic acid (β,γ-OHdPip)					
1		166.5			
2	4.86, br d (5.8)	56.2	1, 3, 4	3	3, 4, 2-NH_{Ala}
3	4.02, ddd (5.8, 4.2, 4.0)	63.4	1	2, 4, 3-OH	2, 4, 3-OH
4	3.90, ddd (9.5, 4.0, 2.9)	61.7	3	3, 5, 4-OH	3, 5, 4-OH
5	7.02, d (2.9)	146.7	3, 4	4	4, 4-OH
3-OH	5.37, d (4.2)		2	3	3
4-OH	6.06, d (9.5)		3, 4	4	4
Hydroxyacetic acid (Haa)					
1		166.9			
2a	4.76, d (15.9)	62.3	1, $1_{α-MeSer}$		
2b	5.23, d (15.9)		1, $1_{α-MeSer}$		

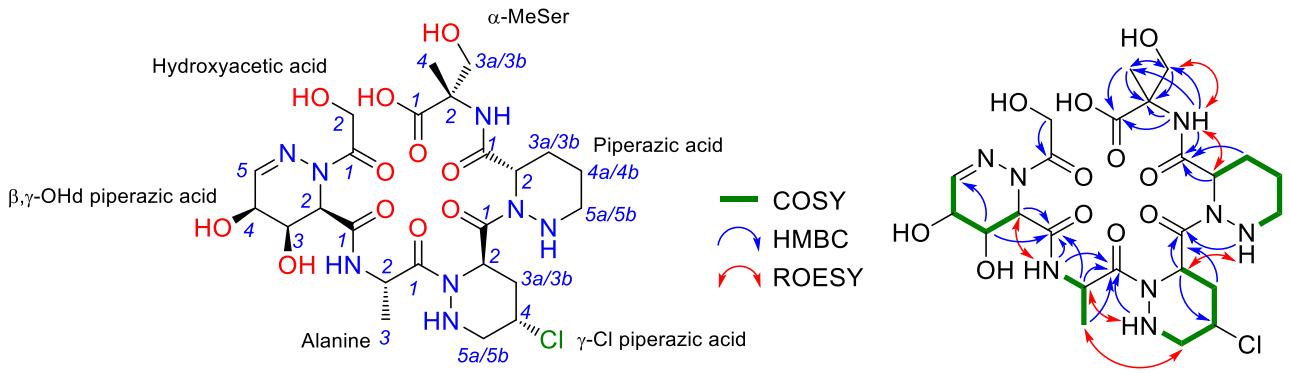


Table S2. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for svetamycin H (**2**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	COSY	ROESY
α-Methyl Serine (α-MeSer)					
1		173.6			
2		60.0			
3a	3.54[a], d (10.5)	64.9	1, 2, 4		4, 2-NH
3b	3.61, d (10.5)		1, 2, 4		4, 2-NH
4	1.34, s	19.8	1, 2, 3		3a/b, 2-NH
2-NH	8.04, s		1, 2, 3, 4, 1_{Pip}		3a/b, 4, 2_{Pip}, $3b_{Pip}$
1-OH	12.35, br s				
3-OH	[b]				
Piperazic acid (Pip)					
1		170.6			
2	4.93, dd (5.4, 1.4)	50.1	1, 3, 4	3a/b	3ab, 2-$NH_{α\text{-}MeSer}$
3a	1.82, m	26.8	1	2, 4b	2, 4a
3b	2.08, m			2, 4a	2, 4a/b, 2-$NH_{α\text{-}MeSer}$
4a	1.46, m	20.5		3b	3a/b, 5ab
4b	1.55, m			3a, 5a	3b, 5b, 5-NH
5a	2.59, m	46.6		4b, 5-NH	4a
5b	3.01, m			5-NH	4ab, 5-NH
5-NH	5.08, dd (11.0, 1.9)		$1_{γ\text{-}ClPip}$	5a/b	4b, 5b, $2_{γ\text{-}ClPip}$
γ-ClPiperazic acid (γ-ClPip)					
1		171.0			
2	5.70, dd (6.5, 2.2)	50.2	1, 3, 4	3a/b	3ab, 5-NH_{Pip}
3a	2.02, ddd (13.0, 13.0, 6.5)	35.3	1, 2, 4	2, 4	2, 5a
3b	2.44, ddd (13.0, 4.4, 2.2)			2, 4	2, 4
4	4.11, dddd (13.0, 10.7, 4.4, 4.4)	52.7		3a/b, 5a/b	3b, 5b, 5-NH
5a	2.65, ddd (12.5, 10.7, 2.2)	53.8	4	4, 5-NH	3a, 3_{Ala}
5b	3.32, m		4	4, 5-NH	4, 5-NH
5-NH	5.47, dd (12.5, 1.8)		1_{Ala}	5a/b	4, 5b, 2_{Ala}
Alanine (Ala)					
1		173.1			
2	5.05, dq (8.4, 6.8)	45.4	1, 3, $1_{β,γ\text{-}OHdPip}$	3, 2-NH	3, 2-NH, 5-$NH_{γ\text{-}ClPip}$
3	1.15, d (6.8)	18.1	1, 2	2	2, 2-NH, $5a_{γ\text{-}ClPip}$
2-NH	7.61, d (8.4)		1, $1_{β,γ\text{-}OHdPip}$	2	2, 3, $2_{β,γ\text{-}OHdPip}$
β,γ-OHd piperazic acid (β,γ-OHdPip)					
1		165.5			
2	4.71, br d (5.3)	55.4	1, 3, 4	3	3, 2-NH_{Ala}
3	3.99, dd (5.3, 1.0)	65.3	1, 5	2, 4	2
4	3.95, dd (2.9, 1.0)	62.5	5	3, 5	2, 5
5	6.84, d (2.9)	144.6	3, 4	4	4
3-OH	[b]				
4-OH	[b]				
Hydroxyacetic acid (Haa)					
1		172.6			
2a	4.29, d (17.3)	60.2	1		
2b	4.34, d (17.3)				
2-OH	[b]				

[a] resonance obscured by water peak; [b] not observed

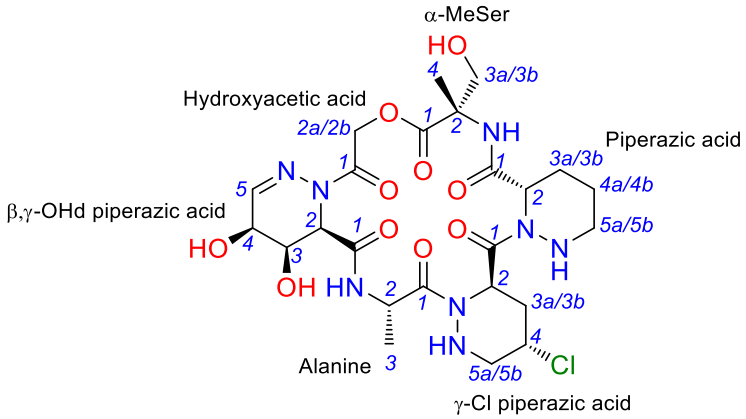


Table S3. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for svetamycin A (**3**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	COSY	ROESY
α-Methyl Serine (α-MeSer)					
1		171.8			
2		60.5			
3a	3.67, d (11.0)	64.2	1, 2, 4		4
3b	3.78, d (11.0)		1, 2, 4		4
4	1.41, s	19.6	1, 2, 3		
2-NH	7.59, s		1, 2, 3, 4, 1_{pip}		4, 3_{ab}, 2_{pip}, $3b_{pip}$
3-OH					
Piperazic acid (Pip)					
1		168.9			
2	4.89, br d, (2.6)	51.2	1, 3, 4	3a/b, 4a/b	3a/b, 4b, 2-$NH_{α\text{-MeSer}}$
3a	1.71[a], m	24.3	1, 5	2, 4a/b	2, 4a,
3b	2.18, m			2, 4a/b	2, 2-$NH_{α\text{-MeSer}}$
4a	1.33, m	20.3	2	3a/b	3b, 4b, 5a/b,
4b	1.71[a], m			3a/b	2, 3b, 4a, 5b
5a	2.60[b], m	46.5		4a/b	4a, 5b,
5b	2.93, br d (12.9)		3	4a/b, 3b	4a/b, 5a, 5-NH
5-NH	4.61[c]				3a, 5b
γ-Cl piperazic acid (γ-ClPip)					
1		171.4			
2	5.71, dd (5.4, 2.4)	50.1	1, 3, 4	3a/b	3a/b, 5-NH_{pip}
3a	1.86, td (12.7, 6.1)	34.9	1, 2, 4, 5	2, 4	3b
3b	2.40, ddd, (12.7, 4.4, 2.4)			2, 4	2, 3a, 4
4	4.35, tt, (11.3, 4.5)	52.6		3a/b, 5a/b,	3b, 5b
5a	2.65[b]	54.3	3, 4	4	5b
5b	3.35[e]		3, 4	4	4, 5a, NH-5
5-NH	5.20, d (12.5)		1_{Ala}	5ab	4, 5b
Alanine (Ala)					
1		172.3			
2	5.32[d], dq (8.1, 7.0)	43.2	1, 3, $1_{β,γ\text{-OHdPip}}$	3, 2-NH	3, 2-NH
3	1.16, d (7.0)	18.1	1, 2	2	2, 5b, 2-NH
2-NH	8.11, d (8.1)		1, 2, $1_{β,γ\text{-OHdPip}}$	2	3, $2_{β,γ\text{-OHdPip}}$
β,γ-OHd piperazic acid (β,γ-OHdPip)					
1		166.5			
2	4.71, d (5.3)	56.9	1, 3, 4	3	3, 4, 2-NH_{Ala}
3	4.03, dd, (5.3, 4.6)	63.8	1, 4, 5		2, 4
4	3.91, dd (4.6, 2.4)	62.6	2, 3, 5		2, 3, 5
5	6.95, d (2.4)	147.0	3, 4	4	4
3-OH					
4-OH					
Hydroxyacetic acid (Haa)					
1		166.7			
2a	4.61[c]	61.7	1, $1_{α\text{-MeSer}}$		
2b	5.32[d]		1, $1_{α\text{-MeSer}}$		

[a–d] resonances overlapping; [e] resonance obscured by water peak

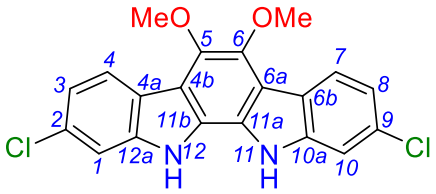
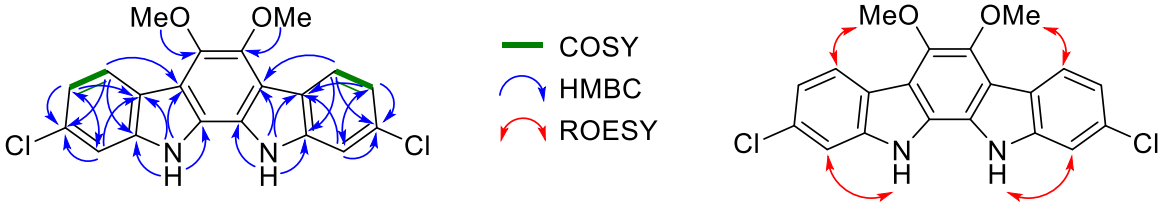


Table S4. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for borregomycin E (**4**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	COSY	ROESY
1/10	7.76, d (1.8)	111.2	2/9, 3/8, 4a/6b		11/12-NH
2/9		129.0			
3/8	7.21, dd (8.3, 1.8)	119.2	1/10, 2/9, 4a/6b	4/7	4/7
4/7	8.15, d (8.3)	122.6[a]	2/9, 4b/6a, 10a/12a	3/8	3/8, 5/6-OMe
4a/6b		121.2			
4b/6a		114.0			
5/6		140.1			
10a/12a		139.7			
11/12-NH	11.27, s		4a/6b, 4b/6a, 11b/11a, 10a/12a		1/10
11a/11b		122.6[a]			
5/6-OMe	4.05, s	60.7	5/6		4/7

[a] resonances overlapping



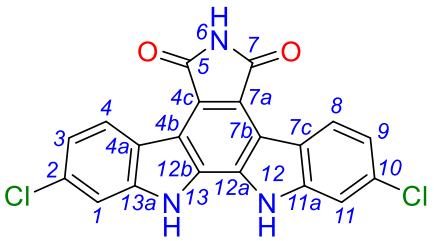
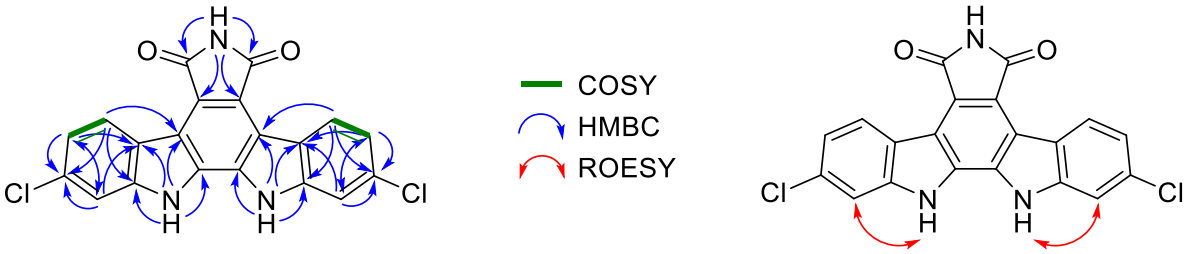


Table S5. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for borregomycin F (**5**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	COSY	ROESY
1/11	7.94, d (1.9)	111.9	2/10, 3/9, 4a/7c		12/13-NH
2/10		131.3			
3/9	7.39, dd (8.4, 1.9)	120.6	1/11, 2/10, 4a/7c	4/8	4/8
4/8	8.93, d (8.4)	125.4	2/10, 4b/7b, 11a/13a	3/9	3/9
4a/7c		120.3			
4b/7b		115.1			
4c/7a		120.1			
5/7		171.0			
11a/13a		140.8			
12a/12b		129.3			
12/13-NH	11.93, s		4a/7c, 4b/7b, 12a/b, 11a/13a		1/11
6-NH	11.07, s		5/7, 4c/7a		



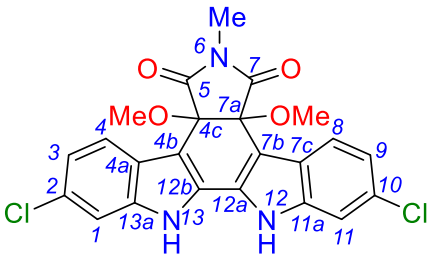


Table S6. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for borregomycin B (**6**) in DMSO-d_6

Pos.	**δ_H, mult (*J* in Hz)**	**δ_C**	**^{1}H-^{13}C HMBC**	**COSY**	**ROESY**
1/11	7.67, d (1.9)	111.8	2, 3, 4a		12/13-NH
2/10		127.0			
3/9	7.15, dd (8.5, 1.9)	120.9	1, 4a	4	4
4/8	7.92, d (8.5)	122.3	2, 13a	3	3, 4c-OMe
4a/7c		124.8			
4b/7b		106.1			
4c/7a		80.5			
5/7		173.1			
11a/13a		137.3			
12a/12b		128.3			
12/13-NH	11.60, s		4a, 4b, 12b, 13a		1
6-NMe	2.93, s	25.0	5		
4c/7a-OMe	3.28, s	53.9	4c		4

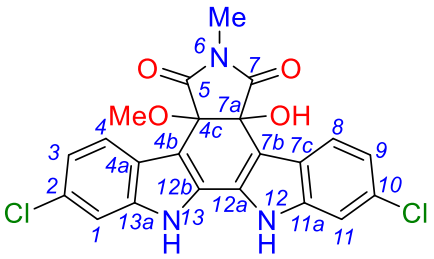


Table S7. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for borregomycin C (**7**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	COSY	ROESY
1	7.64, d (1.9)	111.6	2, 3, 4a		13-NH
2		126.9			
3	7.12, dd (8.5, 1.9)	120.4	1, 4a	4	4
4	7.96, d (8.5)	122.0	2, 13a	3	3, 4c-OMe
4a		125.3			
4b		104.2			
4c		80.0			
5		174.2			
7		174.6			
7a		76.4			
7b		109.9			
7c		125.0			
8	7.99, d (8.5)	122.8	10, 7b, 11b	9	
9	7.14, dd (8.5, 1.9)	120.9	7c, 11	8	
10		126.8			
11	7.66, d (1.9)	111.8	7c, 9		12-NH
11a		137.2			
12a		130.1			
12b		126.2			
12-NH	11.61, s		4a, 4b, 12b, 13a		11
13-NH	11.42, s		7b, 7c, 11a, 12a		1
13a		137.3			
6-NMe	2.84, s	24.9	5		
4c-OMe	2.96, s	52.3	4c		4

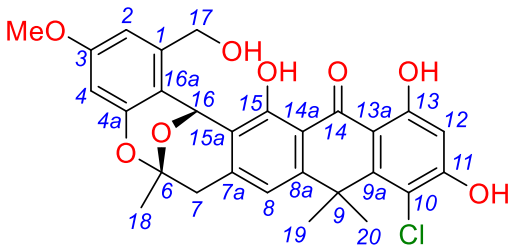
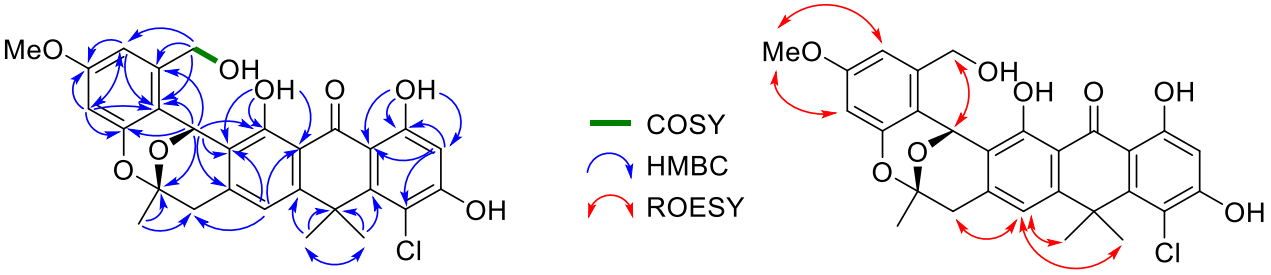


Table S8. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for (+)-ABX-G (**8**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	COSY	ROESY
1		140.6			
2	6.61, d (2.6)	105.5	3, 4, 16a		3-OMe
3		159.3			
3-OMe	3.66, s	55.0			2, 4
4	6.28, d (2.6)	99.9	2, 3, 4a, 16a		3-OMe
4a		151.9			
6		98.0			
7	3.11, d (18.9) 3.35, d (18.9)	39.9			8
7a		142.2			
8	7.14, s	118.2	7, 14a, 15a		7, 19, 20
8a		148.6			
9		39.5			
9a		152.5			
10		112.0			
11		162.4			
12	6.54, s	102.4	10, 13, 13a		
13		163.7			
13-OH	13.26, s		12, 13, 13a		
13a		107.6			
14		190.4			
14a		109.7			
15		156.1			
15-OH	13.20, s		14a, 15, 15a		
15a		122.1			
16	6.24, s	64.6	1, 4a, 6, 7a, 15, 15a, 16a		17b
16a		113.0			
17a	4.54, dd (14.4, 5.7)	59.7	1, 2, 16a	17-OH	
17b	4.91, dd (14.4, 5.7)		1, 2, 16a	17-OH	16
17-OH	5.09, t (5.7)			17a/b	
18	1.63, s	27.3	6, 7		
19	1.90, s	27.9	8a, 9, 9a, 20		8
20	1.83, s	28.1	8a, 9, 9a, 19		8



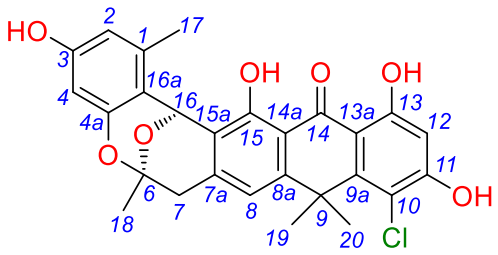
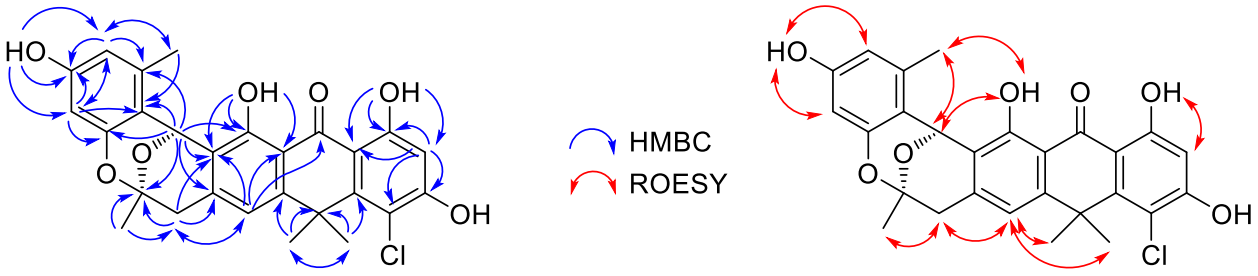


Table S9. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for (–)-ABX-K (**9**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	ROESY
1		135.7		
2	6.15, d (2.4)	110.0	1, 3, 4, 17	3-OH
3		157.0		
3-OH	9.26, s		2, 3, 4	2, 4
4	6.04, d (2.4)	100.6	2, 3, 4a, 16a	3-OH
4a		151.9		
6		97.6		
7	3.06, d (18.9)	39.9	6, 7a, 8, 15a	8, 18
	3.32, d (18.9)			
7a		142.4		
8	7.13, s	118.1	7, 14, 14a, 15a	7, 19, 20
8a		148.6		
9		39.4		
9a		152.4		
10		111.9		
11		162.0		
11-OH	11.75, br s			
12	6.55, s	102.3	10, 11, 13, 13a, 14	13-OH
13		163.7		
13-OH	13.27, s		12, 13, 13a	12
13a		107.5		
14		190.3		
14a		109.6		
15		156.1		
15-OH	13.17, s		14a, 15, 15a	16, 17
15a		122.6		
16	6.14, s	64.3	1, 4a, 6, 7a, 15, 15a, 16a	15-OH, 17
16a		113.0		
17	2.33, s	18.8	1, 2, 16a	15-OH, 16
18	1.60, s	27.3	6, 7	7
19	1.90, s	27.8	8a, 9, 9a, 20	8
20	1.83, s	28.1	8a, 9, 9a, 19	8



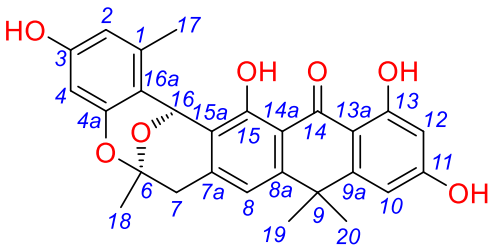


Table S10. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for (–)-ABX-A (**10**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	ROESY
1		135.6		
2	6.15, d (2.4)	110.0	1, 3, 4, 16a, 17	3-OH
3		157.0		
3-OH	9.24, s		2, 3, 4	2, 4
4	6.04, d (2.4)	100.6	2, 3, 4a, 16a	3-OH
4a		151.9		
6		97.6		
7	3.05, d (18.7) 3.30, d (18.7)	39.9		8
7a		141.7		
8	7.14, s	117.7	7, 14, 14a, 15a	7, 19, 20
8a		150.1		
9		38.3		
9a		154.7		
10	6.66, d (2.2)	106.7	9, 11, 12, 13a, 14	11-OH, 9, 20
11		165.7		
11-OH	10.91, s		10, 11, 12	10, 12
12	6.24, d (2.2)	100.9	10, 11, 13a	11-OH
13		164.8		
13-OH	12.65, s		12, 13, 13a	
13a		106.5		
14		190.0		
14a		110.8		
15		156.8		
15-OH	13.36, s		14a, 15, 15a	17
15a		123.0		
16	6.14, s	64.4	1, 4a, 6, 7a, 15, 15a, 16a	17
16a		113.0		
17	2.33, s	18.8	1, 2, 16a	15-OH, 16
18	1.60, s	27.3	6, 7	
19	1.59, s	33.3	8a, 9, 9a, 20	8, 10
20	1.52, s	33.5	8a, 9, 9a, 19	8, 10

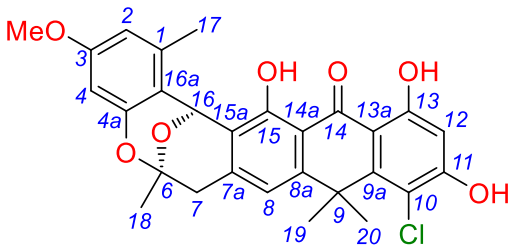


Table S11. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for (–)-ABX-B (**11**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	ROESY
1		135.8		
2	6.31, d (2.5)	108.8	3, 4, 16a, 17	3-OMe, 17
3		158.9		
3-OMe	3.64, s	54.9	3	2, 4
4	6.23, d (2.5)	99.1	2, 3, 4a, 16a	3-OMe
4a		152.0		
6		97.9		
7	3.09, d (18.4) 3.34, d (18.4)	39.9	6, 7a, 8, 15a	8
7a		142.2		
8	7.13, s	118.2	7, 14, 14a, 15a	7, 19, 20
8a		148.6		
9		39.4		
9a		152.5		
10		111.8		
11		161.9		
11-OH	11.75, br s			
12	6.54, s	102.3	10, 11, 13, 13a	
13		163.7		
13-OH	13.27, s		12, 13, 13a	
13a		107.5		
14		190.3		
14a		109.6		
15		156.2		
15-OH	13.19, s		14a, 15, 15a	17
15a		122.2		
16	6.19, s	64.3	1, 4a, 6, 7a, 15, 15a, 16a	17
16a		114.5		
17	2.40, s	18.9	1, 2, 16a	2, 15-OH, 16
18	1.62, s	27.3	6, 7,	
19	1.90, s	27.8	8a, 9, 9a, 20	8
20	1.83, s	28.1	8a, 9, 9a, 19	8

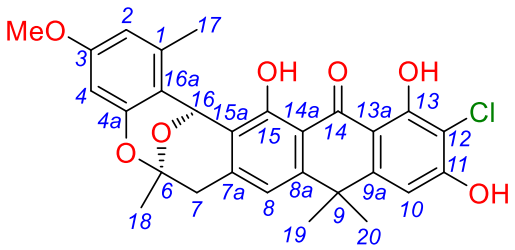


Table S12. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for (–)-ABX-C (**12**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	ROESY
1		135.8		
2	6.32, d (2.3)	108.8	3, 4, 16a ,17	3-OMe, 17
3		158.9		
3-OMe	3.64, s	54.9	3	2, 4
4	6.23, d (2.3)	99.1	2, 3, 4a, 16a	3-OMe
4a		152.0		
6		97.9		
7	3.09, d (18.4) 3.34, d (18.4)	39.9	6, 7a, 8, 15a	8
7a		142.2		
8	7.17, s	117.8	7, 14, 14a, 15a	7, 19, 20
8a		150.0		
9		38.2		
9a		151.8		
10	6.84, s	106.2	9, 11, 12, 13a, 14	11-OH,19, 20
11		160.9		
11-OH	11.64, br s			10
12		105.1		
13		159.8		
13-OH	13.31, s		12, 13, 13a	
13a		107.0		
14		190.0		
14a		110.8		
15		156.9		
15-OH	13.16, s		14a, 15, 15a	17
15a		122.8		
16	6.20, s	64.3	1, 4a, 6, 7a, 15, 15a, 16a	
16a		114.6		17
17	2.41, s	18.9	1, 2, 16a	2, 15-OH, 16a
18	1.62, s	27.2	6, 7	
19	1.59, s	33.4	8a, 9, 9a, 20	8, 10
20	1.52, s	33.2	8a, 9, 9a, 19	8, 10

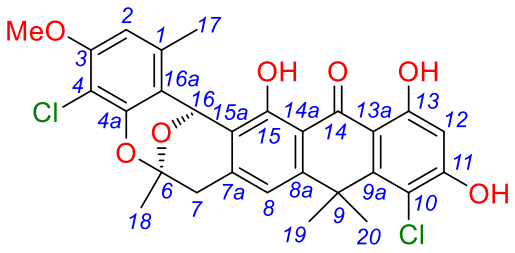


Table S13. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for (–)-ABX-D (**13**) in $CDCl_3$

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	ROESY
1		133.1		
2	6.38, s	105.7	3, 4, 16a, 17	3-OMe, 17
3		154.2		
3-OMe	3.85, s	55.7	3	2
4		106.9		
4a		148.0[a]		
6		99.2		
7	3.25, s	39.9	6, 7a, 8, 15a	8, 18
7a		141.5		
8	6.84, s	117.3	7, 14, 14a, 15a	7, 19, 20
8a		148.0[a]		
9		39.1		
9a		152.0		
10		110.3		
11		158.4		
11-OH				
12	6.65, s	102.7	10, 11, 13, 13a	
13		164.4		
13-OH	13.41, s		12, 13, 13a	
13a		108.9		
14		190.7		
14a		109.9		
15		157.3		
15-OH	13.22, s		14a, 15, 15a	17
15a		121.3		
16	6.31, s	65.2	1, 4a, 6, 7a, 15, 15a, 16a	17
16a		116.9		
17	2.57, s	18.8	1, 2, 16a	15-OH, 2, 16
18	1.78, s	26.9	6, 7	7
19	1.94, s	28.3	8a, 9, 9a, 20	8
20	1.86, s	28.5	8a, 9a, 9, 19	8

[a] resonances overlapping

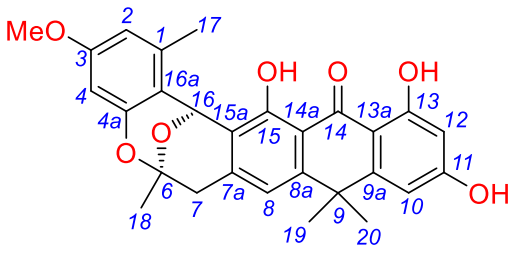


Table S14. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for (–)-ABX-E (**14**) in DMSO-d_6

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	ROESY
1		135.9		
2	6.31, d (2.5)	108.8	1, 3, 4, 16a, 17	3-OMe, 17
3		159.0		
3-OMe	3.64, s	55.0	3	2, 4
4	6.23, d (2.5)	99.2	2, 3, 4a, 16a	3-OMe
4a		152.1		
6		98.0		
7	3.08, d (18.9) 3.32, d (18.9)	39.9	6, 7a, 8, 15a	8
7a		141.6		
8	7.14, s	117.7	7, 14, 14a, 15a	7, 19, 20
8a		150.2		
9		38.4		
9a		154.7		
10	6.66, d (2.1)	106.8	9, 11, 12, 13a, 14	11-OH, 19, 20
11		165.7		
11-OH	10.93, s		10, 11, 12	10, 12
12	6.24, d (2.1)	101.0	10, 11, 13a	11-OH
13		164.9		
13-OH	12.64, s		12, 13, 13a	
13a		106.5		
14		190.0		
14a		110.9		
15		156.9		
15-OH	13.38, s		15, 14a, 15a	
15a		122.7		
16	6.19, s	64.4	1, 4a, 6, 7a, 15, 15a, 16a	17
16a		114.7		
17	2.40, s	18.9	1, 2, 16a	2, 16
18	1.62, s	27.3	6, 7	
19	1.59, s	33.3	8a, 9, 9a, 20	8, 10
20	1.52, s	33.5	8a, 9, 9a, 19	8, 10

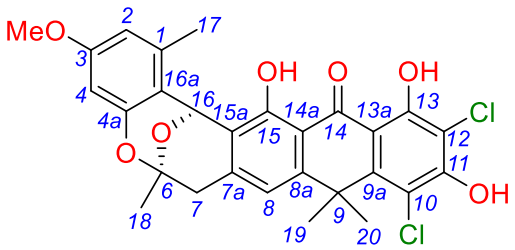


Table S15. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for (–)-BABX (**15**) in $CDCl_3$

Pos.	δ_H, mult (*J* in Hz)	δ_C	^{1}H-^{13}C HMBC	ROESY
1		136.1		
2	6.35, d (2.5)	108.8	3, 4, 16a, 17	3-OMe, 17
3		159.0		
3-OMe	3.73, s	54.7	3	2
4	6.28, d (2.5)	99.0	2, 3, 4a, 16a	
4a		151.9		
6		97.6		
7	3.18, d (17.8) 3.25, d (17.8)	40.2	6, 7a, 8, 15a	8, 18
7a		142.6		
8	6.85, s	117.4	7, 14, 14a, 15a	7, 19, 20
8a		146.2		
9		39.2		
9a		152.1		
10		110.7		
11		154.6		
11-OH				
12		108.7		
13		159.4		
13-OH	14.24, s		12, 13, 13a	
13a		107.3		
14		190.7		
14a		109.7		
15		157.3		
15-OH	12.99, s		14a, 15, 15a	17
15a		122.9		
16	6.33, s	64.8	1, 4a, 6, 7a, 15, 15a, 16a	17
16a		114.4		
17	2.51, s	18.9	1, 2, 16a	2, 15-OH, 16
18	1.74, s	27.1	6, 7	7
19	1.95, s	28.3	8a, 9, 9a, 20	8
20	1.87, s	28.5	8a, 9, 9a, 19	8

Table S16. XYZ coordinates for geometry-optimised (DFT-D3(BJ)/PBE0/def2-SV(P)-COSMO(MeCN)) ground-state structure of (6*R*,16*R*)-ABX-G

```
62

C -0.891064  0.336325 -2.497511
C -0.541856  1.728376 -2.564059
C -0.934388  2.421388 -3.722658
C -1.647123  1.792219 -4.795506
C -1.975917  0.438760 -4.714049
H -2.521867 -0.047093 -5.534499
C -1.608009 -0.302125 -3.581632
C -0.541557 -0.472895 -1.342992
C  0.163207  0.105867 -0.210418
C  0.557969  1.469025 -0.232137
C  0.229875  2.407261 -1.407833
C  0.467980 -0.717456  0.927831
C  1.173849 -0.193739  2.034905
C  1.590237  1.149297  1.980509
C  1.270852  1.959718  0.868829
H  1.609753  3.007131  0.890761
C  1.504090 -1.070490  3.244145
H  1.828152 -2.068374  2.891577
O  2.639646 -0.528347  3.957584
C  2.431470  0.808552  4.336166
C  2.440248  1.715616  3.097010
H  2.089442  2.731721  3.378611
H  3.491181  1.817749  2.739935
C  0.374145 -1.177178  4.255985
C -0.483800 -2.274314  4.482617
C -1.488148 -2.180967  5.473188
H -2.166173 -3.036672  5.605111
C -1.613143 -1.026580  6.269858
C -0.705995  0.040592  6.104705
H -0.763974  0.926172  6.753685
C  0.272303 -0.046562  5.108938
O  1.128217  1.011683  4.971508
C  3.498385  1.165733  5.365655
H  3.400187  0.491837  6.241882
H  3.368744  2.216059  5.700234
H  4.512154  1.041112  4.930359
C -0.438298 -3.560628  3.665033
H -0.633887 -4.418235  4.344125
H  0.579440 -3.717377  3.230884
O -1.446219 -3.617292  2.667637
H -1.199613 -2.917906  2.016893
O -2.554357 -0.856170  7.243763
C -3.491621 -1.894060  7.470451
H -4.155718 -1.536645  8.283596
H -2.994714 -2.839002  7.796600
H -4.106705 -2.103598  6.563005
O  0.105162 -2.015481  0.946424
H -0.325549 -2.191888  0.018693
O -0.854896 -1.723051 -1.316091
O -1.942046 -1.592048 -3.547583
H -1.589248 -1.951973 -2.654919
O -2.015626  2.471911 -5.897063
H -1.704566  3.408802 -5.789931
C  1.591327  2.936405 -1.956845
H  2.225157  2.087178 -2.291369
H  2.144015  3.483367 -1.164421
H  1.453100  3.627676 -2.810631
C -0.651021  3.554757 -0.821829
H -0.101734  4.093190 -0.021397
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Cl-0.618265  4.146175 -4.038325
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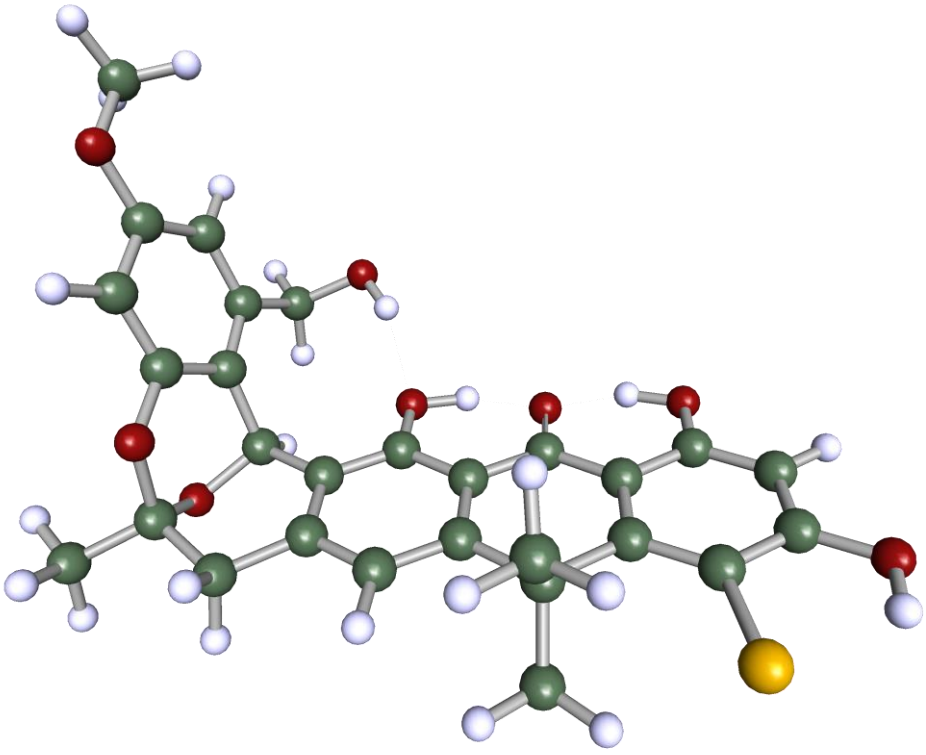

Table S17. XYZ coordinates for geometry-optimised (DFT-D3(BJ)/PBE0/def2-SV(P)-COSMO(MeCN)) ground-state structure of (6*S*,16*S*)-ABX-G

```
62

C -0.31205 -1.24697 -2.42036
C  0.54961 -0.42634 -3.18968
C  0.67519 -0.72731 -4.54092
C -0.02020 -1.80412 -5.13024
C -0.85599 -2.59582 -4.37271
H -1.38763 -3.41981 -4.83050
C -1.01108 -2.32748 -3.02801
C -0.50618 -1.01650 -1.01020
C  0.19861  0.04621 -0.33576
C  1.03936  0.89942 -1.05777
C  1.29509  0.74005 -2.54692
C  0.02295  0.23619  1.05625
C  0.67446  1.26722  1.72601
C  1.47375  2.12836  0.98513
C  1.65732  1.93379 -0.38009
H  2.29801  2.62998 -0.90646
C  0.49144  1.47369  3.21336
H -0.54868  1.28984  3.47792
O  0.73955  2.83822  3.55752
C  2.00561  3.26565  3.15337
C  2.09441  3.32000  1.64168
H  1.57268  4.21858  1.29696
H  3.13929  3.42630  1.34328
C  1.42671  0.64842  4.05614
C  1.12893 -0.51839  4.75400
C  2.12172 -1.16823  5.48871
H  1.86289 -2.07606  6.01753
C  3.40740 -0.64774  5.54992
C  3.69876  0.55594  4.91572
H  4.68323  0.99938  5.00319
C  2.71065  1.19074  4.18781
O  3.04079  2.36873  3.61204
C  2.26464  4.60062  3.80209
H  3.24776  4.96916  3.50771
H  2.23174  4.49170  4.88665
H  1.50758  5.31981  3.48773
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H -1.01242 -0.41404  4.51076
H -0.45048 -1.50386  5.77631
O -0.32998 -2.27642  3.91633
H -0.33332 -1.92397  3.01572
O  4.42705 -1.21930  6.22850
C  4.17892 -2.45478  6.87370
H  5.12499 -2.75977  7.31613
H  3.84904 -3.21412  6.15903
H  3.42796 -2.34635  7.66165
O -0.79572 -0.56108  1.75391
H -1.20783 -1.17612  1.07735
O -1.29987 -1.74817 -0.35181
O -1.83115 -3.11689 -2.34111
H -1.82755 -2.77687 -1.40579
O  0.09654 -2.09814 -6.42528
H  0.70786 -1.47393 -6.84787
C  2.81408  0.51247 -2.69307
H  3.10393 -0.40129 -2.17005
H  3.35891  1.34517 -2.24935
H  3.12007  0.42831 -3.73163
C  0.83301  2.05412 -3.20981
H -0.23253  2.20649 -3.02632
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H  1.37573  2.89835 -2.78563
Cl 1.67024  0.14411 -5.67266
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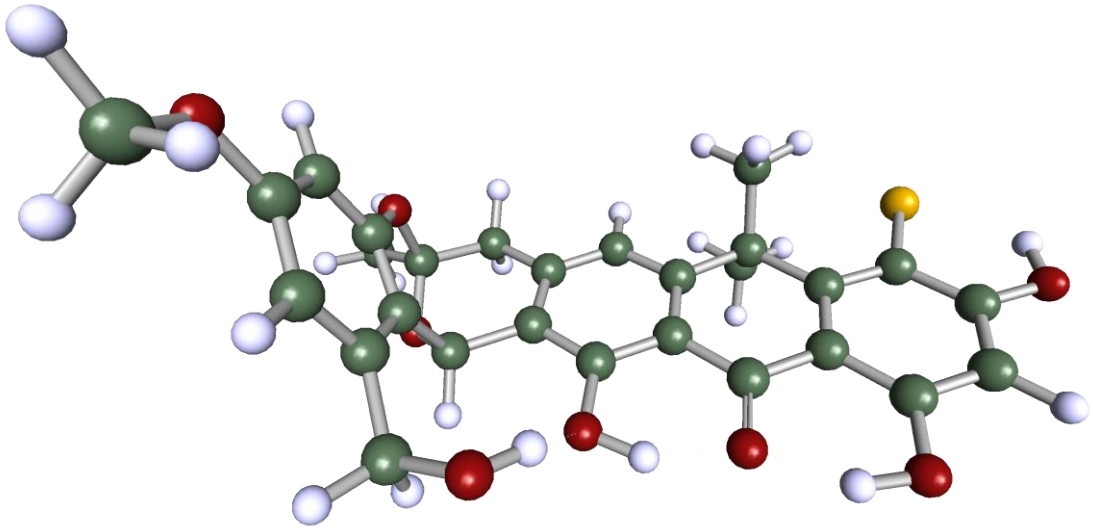

Table S18. XYZ coordinates for geometry-optimised (DFT-D3(BJ)/PBE0/def2-SV(P)-COSMO(MeCN)) ground-state structure of (6*R*,16*R*)-ABX-K

```
58

C  2.726134  0.138723 -0.943023
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C  4.898451 -1.367447 -1.865259
C  5.020258  0.010872 -1.778857
H  5.953819  0.495808 -2.068258
C  3.951051  0.773145 -1.323603
C  1.644497  0.980927 -0.472920
C  0.384307  0.396203 -0.066993
C  0.190877 -0.996311 -0.138206
C  1.273093 -1.956227 -0.621589
C -0.659539  1.243272  0.404191
C -1.889062  0.702078  0.805292
C -2.072072 -0.677831  0.710016
C -1.041661 -1.507229  0.249604
H -1.237628 -2.580608  0.203847
C -2.991926  1.604270  1.329404
H -3.071527  2.495226  0.691704
O -4.252405  0.941190  1.246502
C -4.237821 -0.300990  1.877157
C -3.400245 -1.276942  1.070324
H -3.263549 -2.211344  1.637852
H -3.950164 -1.532395  0.146814
C -2.819944  1.981801  2.779295
C -2.449171  3.234371  3.296841
C -2.361269  3.391691  4.683244
H -2.062941  4.352426  5.111382
C -2.670793  2.339423  5.553431
C -3.113180  1.116966  5.046176
H -3.406566  0.294686  5.704564
C -3.188923  0.959007  3.662105
O -3.622610 -0.228386  3.184205
C -5.670522 -0.739642  2.068759
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H -6.198203  0.003130  2.688927
H -5.699795 -1.719234  2.571116
C -2.179259  4.411712  2.402791
H -1.972324  5.314281  2.999317
H -3.050421  4.624922  1.756966
H -1.324311  4.220198  1.736473
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H -2.804882  1.772474  7.378532
O -0.505080  2.560815  0.465564
H  0.423275  2.760478  0.135761
O  1.798173  2.234038 -0.413925
O  4.114454  2.086417 -1.259010
H  3.250872  2.468917 -0.913521
O  5.946638 -2.057931 -2.306485
H  5.732871 -3.013370 -2.321206
C  0.690810 -2.684098 -1.855134
H  0.425330 -1.948780 -2.633307
H -0.220895 -3.236208 -1.577989
H  1.401720 -3.403602 -2.283526
C  1.553829 -2.918969  0.555318
H  0.638068 -3.467900  0.825801
H  1.885207 -2.345738  1.437560
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Cl 3.735691 -3.741208 -1.675062
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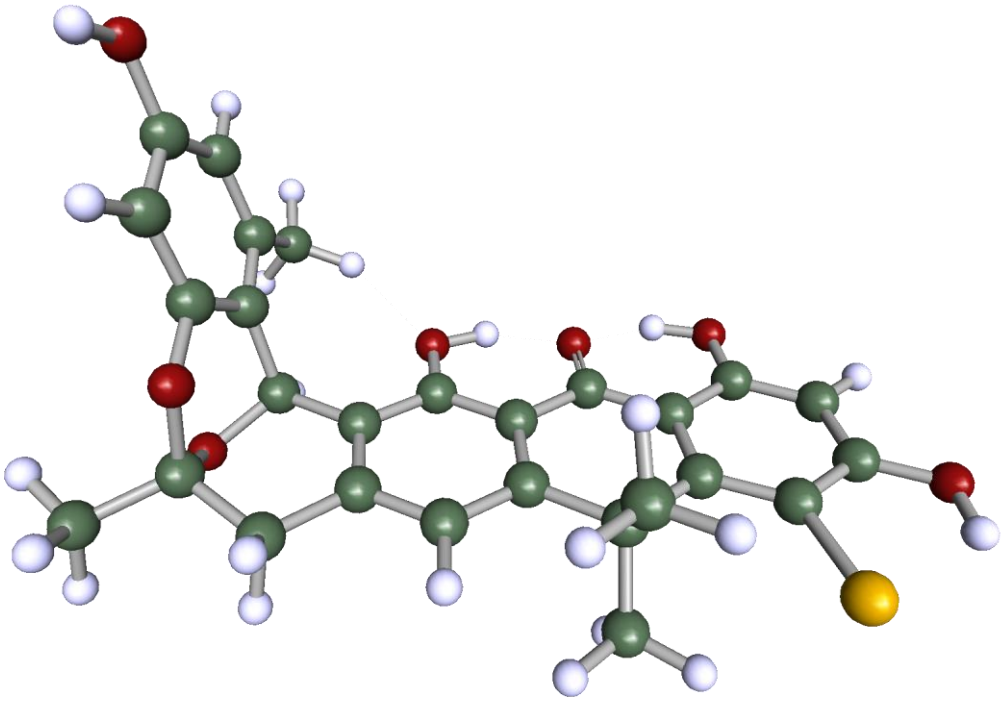


Table S19. XYZ coordinates for geometry-optimised (DFT-D3(BJ)/PBE0/def2-SV(P)-COSMO(MeCN)) ground-state structure of (6*S*,16*S*)-ABX-K

```
58

C   2.489198   1.058014 -1.378293
C   2.507188  -0.236831 -1.967205
C   3.531927  -0.508927 -2.876757
C   4.519392   0.455106 -3.209285
C   4.487713   1.712228 -2.625619
H   5.247397   2.452412 -2.881457
C   3.486802   2.027306 -1.714354
C   1.466772   1.440570 -0.425190
C   0.426614   0.505901 -0.052219
C   0.406619  -0.791069 -0.599034
C   1.442781  -1.277854 -1.606842
C  -0.576259   0.910002  0.875140
C  -1.596045   0.024617  1.251477
C  -1.589391  -1.264408  0.717624
C  -0.603338  -1.656273 -0.196591
H  -0.652321  -2.674151 -0.589183
C  -2.679360   0.466079  2.219155
H  -2.224808   1.021529  3.050777
O  -3.315018  -0.671357  2.800087
C  -3.793079  -1.558082  1.837765
C  -2.628752  -2.254534  1.156123
H  -2.178142  -2.966868  1.870315
H  -2.993856  -2.840394  0.297409
C  -3.779238   1.263398  1.563985
C  -4.021177   2.642357  1.683643
C  -5.110507   3.197173  1.005323
H  -5.313544   4.269388  1.071849
C  -5.975271   2.399031  0.246810
C  -5.783725   1.018086  0.187379
H  -6.471223   0.366164 -0.358578
C  -4.689308   0.468526  0.855705
O  -4.518163  -0.870466  0.792248
C  -4.755844  -2.503323  2.517045
H  -4.240689  -3.058332  3.317215
H  -5.160381  -3.218778  1.784003
H  -5.584661  -1.924500  2.956129
C  -3.162161   3.525309  2.544299
H  -2.124206   3.552152  2.178909
H  -3.128535   3.151847  3.583885
H  -3.559686   4.552338  2.567032
O  -6.998921   3.011149 -0.386699
H  -7.533759   2.356585 -0.866654
O  -0.568588   2.122922  1.415818
H   0.228382   2.604857  1.037606
O   1.478342   2.596808  0.085123
O   3.497942   3.240887 -1.182677
H   2.713048   3.289458 -0.555762
O   5.495046   0.196330 -4.076072
H   5.405314  -0.718247 -4.414107
C   0.658379  -1.653084 -2.885421
H  -0.074366  -2.445134 -2.664421
H   1.318848  -2.019311 -3.683031
H   0.110790  -0.772324 -3.261204
C   2.139678  -2.497717 -0.961216
H   2.610163  -2.199877 -0.009023
H   2.913471  -2.924228 -1.613832
H   1.404458  -3.289734 -0.749031
Cl  3.752060  -2.029722 -3.719122
```

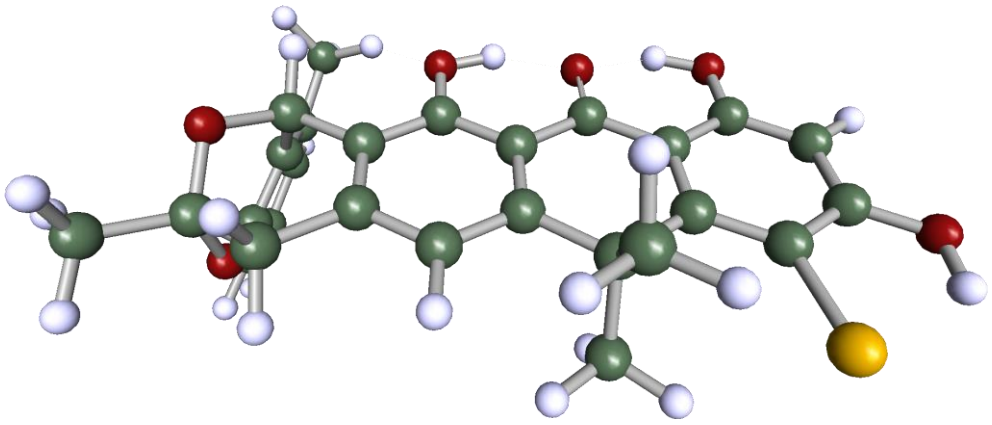


Table S20. Genes encoding the svetamycin (*sve*) biosynthetic gene cluster and their closest known homologues.

Gene	Start	End	Length (nt)	Strand	Known Homologue	BLASTP hit	Coverage	Identity	Putative Role
orf-6	4010	4621	612	forward	*tpdN*	dihydrofolate reductase family protein [*Streptomyces* sp. BA2]	99%	86.70%	-
orf-5	4625	6043	1419	reverse	*SCO2445, xanB3*	acetyl-CoA carboxylase [*Streptomyces* sp. BA2]	95%	84.43%	-
orf-4	6036	7499	1464	reverse	*SCO2444*	AMP-binding protein [*Streptomyces* sp. BA2]	95%	88.79%	-
orf-3	7590	8837	1248	reverse	*SCO2443*	TPA: hypothetical protein [*Streptomyces* sp.]	99%	85.89%	-
orf-2	9066	9806	741	forward	*SCO2442*	FadR family transcriptional regulator [*Streptomyces niveus*]	95%	86.38%	-
orf-1	9931	11052	1122	forward	-	YncE family protein [*Streptomyces* sp. CB02058]	97%	71.15%	-
sveR1	11185	12054	870	forward	-	metalloregulator ArsR/SmtB family transcription factor [*Actinophytocola* sp.]	98%	84.56%	Regulatory
sveB	12051	12662	612	forward	-	dihydrofolate reductase family protein [*Streptomyces scabiei*]	99%	85.22%	Unknown
sveT1	12687	13994	1308	reverse	*dacR3, hex15*	MULTISPECIES: cation:proton antiporter [unclassified *Streptomyces*]	99%	88.74%	Transporter
sveC	13954	14715	762	reverse	-	alpha/beta fold hydrolase [*Streptomyces* sp. DvalAA-43]	99%	81.82%	Unknown
sveD	14744	15703	960	reverse	*barB1, ktzD, kthP*	chlorinating enzyme [*Streptomyces griseus*]	97%	89.46%	Chlorination
sveE	15717	16004	288	reverse	-	MULTISPECIES: acyl carrier protein [unclassified *Streptomyces*]	98%	85.26%	Accessory Protein
sveF	16465	16683	219	forward	*cdeL, ktzJ*	MULTISPECIES: MbtH family protein [unclassified *Streptomyces*]	98%	94.44%	Accessory Protein
sveG1	16725	17678	954	forward	*qcn7, napB*	thiamine pyrophosphate-dependent dehydrogenase E1 component subunit alpha [*Streptomyces griseus*]	99%	85.49%	Glycolic acid biosynthesis and incorporation
sveG2	17675	17905	231	forward	*qcn8, napC*	acyl carrier protein [*Streptomyces griseus*]	98%	84.21%	Glycolic acid biosynthesis and incorporation
sveG3	17902	20001	2100	forward	*qcn9, napD*	MULTISPECIES: 2-oxo acid dehydrogenase subunit E2 [unclassified *Streptomyces*]	99%	83.33%	Glycolic acid biosynthesis and incorporation
sveG4	20001	20996	996	forward	*qcn10, napE*	3-oxoacyl-[acyl-carrier-protein] synthase-3 [*Streptomyces* sp. DvalAA-43]	99%	87.88%	Glycolic acid biosynthesis and incorporation
sveH	21020	22327	1308	reverse	-	tetratricopeptide repeat protein [*Streptomyces griseus*]	99%	80.73%	Accessory Protein
sveR2	23114	23713	600	forward	*hmtD, ktz(orf10), plyB*	MULTISPECIES: LmbU family transcriptional regulator [unclassified *Streptomyces*]	99%	87.94%	Regulation
sveP1	23877	24548	672	reverse	*hmtC, ktz(orf4), mfnJ*	MULTISPECIES: FMN-binding negative transcriptional regulator [unclassified *Streptomyces*]	95%	82.79%	Piperazic acid biosynthesis and incorporation
sveP2	24839	26185	1347	forward	*hmtM, ktzI, mfnI*	MULTISPECIES: lysine N(6)-hydroxylase/L-ornithine N(5)-oxygenase family protein [unclassified *Streptomyces*]	99%	89.06%	Piperazic acid biosynthesis and incorporation
sveP3	26283	27887	1605	forward	*mfnK*	Plipastatin synthase subunit D [*Streptomyces* sp. YIM 121038]\	98%	83.71%	Piperazic acid biosynthesis and incorporation
sveP4	27953	28231	279	forward	-	MULTISPECIES: hypothetical protein [unclassified *Streptomyces*]	97%	91.21%	Piperazic acid biosynthesis and incorporation
sveI	28228	28998	771	forward	*ktzF, plyY*	thioesterase [*Streptomyces* sp. DvalAA-43]	99%	77.34%	Accessory Protein
sveJ	29011	30987	1977	forward	*ktz(orf7), cysS, cmmK*	cobalamin B12-binding domain-containing protein [*Streptomyces griseus*]	99%	91.03%	Methylserine biosynthesis
sveK	31057	32439	1383	forward	*amiS, fmoH, asmD*	serine hydroxymethyltransferase [*Streptomyces griseus*]	98%	85.93%	Serine biosynthesis
sveA1	32521	38031	5511	reverse	*cdeI, cdeJ, hmtL, plyG*	MULTISPECIES: non-ribosomal peptide synthetase [unclassified *Streptomyces*]	99%	75.98%	Non-ribosomal peptide synthesis
sveA2	38462	54790	16329	forward	-	amino acid adenylation domain-containing protein [*Streptomyces tsukubensis*]	99%	78.89%	Non-ribosomal peptide synthesis
sveO1	54866	56074	1209	reverse	*mfnN, sceD*	MULTISPECIES: cytochrome P450 [unclassified *Streptomyces*]	99%	91.50%	Hydroxylation
sveO2	56147	56326	180	reverse	*sceC*	ferredoxin [*Streptomyces griseus*]	93%	78.95%	Hydroxylation
sveO3	56360	57568	1209	reverse	*sceE*	MULTISPECIES: cytochrome P450 [unclassified *Streptomyces*]	99%	91.79%	Hydroxylation
sveL	57882	58658	777	forward	*ulm24*	MULTISPECIES: amidinotransferase [unclassified *Streptomyces*]	99%	91.09%	ornithine biosynthesis
sveM	58715	60808	2094	forward	*cdeI, hmtL, ktzH, mfnC*	MULTISPECIES: amino acid adenylation domain-containing protein [unclassified *Streptomyces*]	99%	73.03%	Unknown
sveN	60816	62228	1413	reverse	*dsaJ, ullm16*	CubicO group peptidase, beta-lactamase class C family [*Streptomyces* sp. DvalAA-43]	99%	90.64%	Unknown
sveT2	62373	63164	792	reverse	*pylK*	MULTISPECIES: ABC transporter permease [unclassified *Streptomyces*]	99%	97.34%	Transport
sveQ	63161	64237	1077	reverse	*cdeD, hmtL, ktzH, mfnC, pylG, pylF*	ATP-binding cassette domain-containing protein [*Streptomyces tsukubensis*]	99%	90.50%	Transport
sveR3	64752	67886	3135	reverse	*hmt(orf+2) pylL*	MULTISPECIES: LuxR family transcriptional regulator [unclassified *Streptomyces*]	99%	90.23%	Regulation
sveS	68026	68547	522	forward	-	MULTISPECIES: chloramphenicol phosphotransferase CPT [unclassified *Streptomyces*]	98%	81.40%	Putative self-resistance
sveT	68584	69252	669	forward	-	haloacid dehalogenase type II [*Streptomyces* sp. MZ04]	99%	83.78%	Putative self-resistance
sveR4	69198	69881	684	reverse	-	TetR/AcrR family transcriptional regulator [*Nonomuraea solani*]	89%	75.86%	Regulation
orf+1	69986	70930	945	forward	-	chlorophyllase [*Streptomyces aurantiacus*]	99%	81.41%	-
orf+2	71045	72382	1338	reverse	-	hypothetical protein [*Streptomyces* sp. MZ04]	99%	85.20%	-

Table S21. cblaster analysis of the svetamycin (*sve*) BGC showing hits against the MIBiG database.

Scaffold	Major Product	–6	–5	–4	–3	–2	–1	R1	B	T1	C	D	E	F	G1	G2	G3	G4	H	R2	P1	P2	P3	P4	I	J	K	A1	A2	O1	O2	O3	L	M	N	T2	Q	R3	S	T	R4	+1	+2	Count
BGC0001968	cadaside	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	1	2	0	0	0	0	2	0	0	0	0	0	0	0	0	0	8
BGC0000378	kutzneride	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1	1	0	0	0	1	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	8
BGC0001036	polyoxypeptin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0	0	0	2	0	1	1	1	0	0	0	0	0	8
BGC0001117	himastatin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	1	1	0	0	0	0	1	0	0	0	1	0	0	0	0	0	7
BGC0001519	aurantimycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	2	0	1	1	0	0	0	0	0	0	6
BGC0000429	skyllamycin	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	0	0	1	0	0	0	0	0	0	5
BGC0001214	marfomycin	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5
BGC0001975	atratumycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	2	0	0	1	0	0	0	0	0	0	5
BGC0000595	SCO-2138	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4
BGC0000296	actinomycin D	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4
BGC0000336	daptomycin	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	1	0	0	0	0	0	0	0	4
BGC0000439	taromycin A	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	1	0	0	0	0	0	0	0	0	0	4
BGC0000414	qinocarcin	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4
BGC0000394	naphithyridinomycin	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4
BGC0001770	clostridiolysin S	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0	4
BGC0001908	sceliphrolactam	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0	4
BGC0000596	SL2138	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0000333	cyclomarin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	3
BGC0001582	ecumicin	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0001297	WS9326	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0001443	azanigerone	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0001042	sanglifehrin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	3
BGC0001752	qinchelins	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0000434	SW-163C	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	3

Table S22. Genes encoding the borregomycin/anthrabenzoxocinone (*bab*) biosynthetic super cluster and their closest known homologues.

Gene	Start	End	Length (nt)	Strand	*abx/bor Homologue*	BLAST hit	Cover	Identity	Putative Role
orf-4	534	1,343	810	forward	—	hypothetical protein [*Streptomyces* sp. NRRL S-237]	99%	62.54%	—
orf-3	1,340	2,407	1,068	forward	—	hypothetical protein ACS04_32320 [*Streptomyces roseus*]	99%	52.04%	—
orf-2	2,563	3,744	1,182	forward	—	hypothetical protein [*Streptomyces indicus*]	92%	73.22%	—
orf-1	3,790	4,545	756	forward	—	L,D-transpeptidase [*Streptomyces indicus*]	93%	80.51%	—
babR1	4,742	6,301	1,560	forward	—	sigma-70 family RNA polymerase sigma factor [*Streptomyces* sp. MZ04]	99%	88.02%	Regulation
babR2	6,329	7,399	1,071	reverse	—	AsnC family transcriptional regulator [*Streptomyces* sp. CB01635]	93%	81.25%	Regulation
babT1	7,584	8,975	1,392	forward	—	MFS transporter [*Streptomyces atratus*]	99%	81.21%	Transport
babA	8,972	10,183	1,212	forward	—	amidohydrolase [*Streptomyces* sp. AcE210]	95%	78.65%	Unknown
babR3	10,203	10,988	786	forward	—	DeoR/GlpR transcriptional regulator [*Streptomyces* sp. MZ04]	99%	93.87%	Regulation
babB	11,022	11,399	378	forward	—	hypothetical protein [*Nonomuraea* sp. NBRC 110462]	99%	85.60%	Unknown
babC	11,396	12,064	669	forward	—	NUDIX domain-containing protein [*Streptomyces* sp. or43]	97%	85.71%	Unknown
babD	12,091	12,969	879	forward	—	NAD(P)-dependent oxidoreductase [*Streptomyces* sp. MZ04]	99%	88.70%	Unknown
babO1	12,991	14,208	1,218	reverse	*borX3*	cytochrome P450 [*Streptomyces albulus*]	96%	62.50%	Rubottom-like oxidation
babO2	14,262	15,881	1,620	reverse	*borC*	FAD-binding monooxygenase [*Streptomyces* sp. NRRL B-1568]	97%	60.57%	Oxygenation
babM1	16,199	16,933	735	forward	*AbxJ, AbxQ, BorM1*	methyltransferase [*Streptomyces* sp.]	99%	89.34%	*N*-methyltransfer
babO3	16,963	18,594	1,632	reverse	*abxL, borX1*	FAD-dependent monooxygenase [*Streptomyces* sp.]	99%	87.93%	Hydroxylation
babM2	18,594	19,340	747	reverse	*abxJ, abxQ, borM1, borM2*	methyltransferase [*Streptomyces* sp.]	99%	94.33%	*O*-methyltransfer
babR4	19,897	20,487	591	reverse	*abxI, abxR1*	TetR family transcriptional regulator [*Streptomyces* sp.]	96%	97.37%	Regulation
babT2	20,568	22,160	1,593	forward	*abxA, abxG*	MFS transporter [*Streptomyces* sp.]	99%	91.34%	Transport
babE	22,600	23,340	741	forward	*abxF*	glyoxalase [*Streptomyces* sp.]	99%	77.14%	Unknown
babM3	23,412	24,446	1,035	reverse	*abxM*	*O*-methyltransferase [*Streptomyces* sp.]	99%	93.29%	*O*-methyltransfer
babF	24,511	25,209	699	reverse	*abxE*	3-oxoacyl-(acyl-carrier protein) reductase [*Streptomyces* sp.]	99%	90.52%	Polyketide reduction
babT3	25,193	26,530	1,338	reverse	*abxB*	potassium transporter [*Streptomyces* sp.]	99%	89.62%	Transport
babH1	26,530	27,807	1,278	reverse	*abxH*	halogenase [*Streptomyces* sp.]	99%	91.29%	Halogenation
babG	27,851	28,207	357	reverse	*abxD*	cyclase [*Streptomyces* sp.]	94%	94.64%	Polyketide cyclisation
babI	28,204	28,695	492	reverse	*abxC*	polyketide cyclase [*Streptomyces* sp.]	99%	87.73%	Polyketide cyclisation
babJ	28,692	28,931	240	reverse	*abxS*	putative acyl carrier protein [*Streptomyces* sp.]	98%	91.14%	Polyketide biosynthesis
babK	28,968	30,227	1,260	reverse	*abxK*	keto-acyl synthase beta [*Streptomyces* sp.]	96%	92.36%	Polyketide biosynthesis
babL	30,224	31,489	1,266	reverse	*abxP*	putative polyketide beta-ketoacyl synthase alpha [*Streptomyces* sp.]	96%	95.10%	Polyketide biosynthesis
babN	31,486	31,887	402	reverse	*abxR*	polyketide WhiE II [*Streptomyces* sp.]	99%	91.73%	Polyketide cyclisation
babP	31,884	32,561	678	reverse	*abxO*	WhiE ORF I SchA/CurD like domain protein [*Streptomyces* sp.]	99%	79.57%	Polyketide oxidation
babT4	32,680	34,155	1,476	reverse	*abxA*	MFS transporter [*Streptomyces* sp.]	99%	90.02%	Transport
babR5	34,270	34,935	666	forward	*abxI, abxR1*	transcriptional regulator TetR family [*Streptomyces* sp.]	99%	89.59%	Regulation
babM4	34,898	35,953	1,056	forward	*abxN*	methyltransferase protein [*Streptomyces* sp.]	99%	91.14%	Gem-dimethylation
babR6	35,979	38,822	2,844	reverse	*borR*	LuxR family transcriptional regulator [*Streptomyces* sp. A1499]	96%	53.56%	Regulation
babR7	38,979	40,880	1,902	reverse	—	AfsR/SARP family transcriptional regulator [*Streptomyces sparsogenes*]	95%	63.10%	Regulation
babO4	41,031	42,299	1,269	reverse	*borP, borX3*	RebP-like cytochrome P450 [uncultured bacterium]	97%	54.00%	C-C bond formation
babQ	42,324	45,542	3,219	reverse	*borD*	MULTISPECIES: VioB - polyketide synthase [unclassified *Streptomyces*]	99%	67.92%	Chromopyrrolic acid biosynthesis
babS	45,539	47,002	1,464	reverse	*borO*	FAD-dependent oxidoreductase [*Streptomyces* sp. PT12]	94%	67.67%	Chromopyrollic acid biosynthesis
babH2	47,245	48,834	1,590	forward	*borH*	MULTISPECIES: tryptophan 7-halogenase [unclassified *Streptomyces*]	99%	74.10%	Halogenation
babU	48,831	49,358	528	forward	—	flavin reductase family protein [*Streptomyces* sp. PT12]	92%	61.59%	Unknown
babV	49,364	50,047	684	reverse	—	alpha/beta hydrolase [*Kribbella* sp. VKM Ac-2575]	99%	77.97%	Unknown
babW	50,044	50,532	489	reverse	—	SnoaL-like domain-containing protein [*Microtetraspora niveoalba*]	90%	78.38%	Unknown
babX	50,594	51,541	948	reverse	—	zinc-binding dehydrogenase [*Streptomyces* sp. Tu 3180]	98%	84.62%	Unknown
babR8	51,677	52,309	633	reverse	—	TetR family transcriptional regulator [*Streptomyces* sp. Tu 3180]	99%	84.29%	Regulation
orf+1	52,608	52,967	360	forward	—	hypothetical protein [*Streptomyces* sp. BA2]	94%	73.33%	—
orf+2	53,002	53,220	219	forward	—	hypothetical protein [*Streptomyces* sp. CB01635]	93%	62.32%	—

Table S23. cblaster analysis of the borregomycin/anthrabenzoxocinone (*bab*) biosynthetic super cluster showing hits against the MIBiG database.

Scaffold	Major Product	*R1*	*R2*	*T1*	*A*	*R3*	*B*	*C*	*D*	*O1*	*O2*	*M1*	*O3*	*M2*	*R4*	*T2*	*E*	*M3*	*F*	*T3*	*H1*	*G*	*I*	*J*	*K*	*L*	*N*	*P*	*T4*	*R5*	*M4*	*R6*	*R7*	*O4*	*Q*	*S*	*H2*	*U*	*V*	*W*	*X*	*R8*	Count
BGC0001512	BE-24566B	0	0	0	0	0	0	0	0	0	0	2	1	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	0	0	0	0	0	0	0	0	0	0	0	24
BGC0001335	borregomycin	0	0	0	0	0	0	0	0	0	1	2	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	0	0	0	0	0	11
BGC0001366	BE-24566B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1	1	1	1	1	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	11
BGC0001333	BE-54017	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	0	0	10
BGC0001334	caldoniamide	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	0	0	10
BGC0001337	lazarimide	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	2	1	0	0	0	0	10
BGC0001376	hexaricin	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	1	1	1	1	1	1	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	10
BGC0001513	anthrabenzoxocinone	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	1	1	1	1	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	10
BGC0000266	colinomycin	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	2	0	0	1	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8
BGC0000230	griseorhodin A	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	0	0	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	8
BGC0000242	lysolipin	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	1	1	0	1	1	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	8
BGC0000222	FD-594	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2	0	0	1	1	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	8
BGC0000821	rebeccamycin	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	0	0	7
BGC0000822	rebeccamycin	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	0	0	7
BGC0000823	rebeccamycin	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	0	0	7
BGC0000198	arenimycin	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
BGC0000809	AT2433-A1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	0	0	0	0	0	6
BGC0000200	arixanthomycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	1	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
BGC0000279	xantholipin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
BGC0001590	formicamycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
BGC0001782	spiroindimicin A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	0	0	6
BGC0000814	K-252a	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	0	0	0	0	0	0	5
BGC0000825	staurosporine	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	0	0	0	0	0	0	5
BGC0000826	staurosporine	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	0	0	0	0	0	0	5
BGC0000827	staurosporine	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	0	0	0	0	0	0	5
BGC0001730	paramagnetoquinone	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5
BGC0000256	pradimicin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5
BGC0001062	TLN-05220	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5
BGC0000238	lactonomycin	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	4
BGC0001223	hydroxysporine	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	4
BGC0000209	chloroteteracycline	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	4
BGC0000224	fredericamycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4
BGC0000236	kinamycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	4
BGC0001061	polyketomycin	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	4
BGC0001675	murayaquinone	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	4
BGC0000813	K-252a	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	3
BGC0000130	pyrrolomycin	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	3
BGC0000190	A-74528	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0000204	benastatin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	3
BGC0000210	chromomycin A3	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	3
BGC0000215	curamycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0000268	Sch-47554	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0000271	spore pigment	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0000274	tetarimycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0000275	tetracenomycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0000439	taromycin A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0	0	0	3
BGC0000652	napyradiomycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0001079	napyradiomycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0001224	reductasporine	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	3
BGC0001336	erdasporine	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	3
BGC0001368	JBIR-126	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	3
BGC0001439	cervimycin	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0001500	allocyclinone	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0001661	mayamycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
BGC0001819	venemycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	3
BGC0001922	isoindolomycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	3
BGC0002016	lugdunomycin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	3

Table S24. Biosynthetic gene clusters in the MST-144321 genome as predicted by AntiSMASH v4.0

Region	Start	End	Cluster Fragment	Cluster Type	Top Hit	Hit
1.1	78,083	102,289	false	terpene	Hopene	92%
1.2	261,832	319,609	false	terpene, NRPS	Griseobactin	52%
1.3	531,379	551,996	false	Linaridin	Formicamycins A-M	18%
1.4	585,905	658,441	false	T2PKS	Resistomycin	55%
2.1	620,926	678,899	false	NRPS, T1PKS	Oxazolomycin	15%
2.2	795,787	836,827	false	T3PKS	Akaeolide	12%
4.1	225,799	246,402	false	Terpene	Ebelactone	8%
4.2	437,486	458,784	false	Terpene	2-methylisoborneol	100%
4.3	476,366	487,178	false	bacteriocin	-	N/A
5.1	172,325	194,967	false	lanthipeptide	SapB	75%
7.1	430,007	440,423	false	Ectoine	Ectoine	100%
8.1	105,937	126,965	false	Terpene	-	N/A
9.1	178,527	241,222	false	NRPS	Streptovaricin	19%
9.2	248,727	348,014	false	T2PKS, indole, butyrolactone, T1PKS	Anthrabenzoxocinone	100%
10.1	371,376	392,383	false	furan	Napyradiomycin	6%
11.1	110,567	122,333	false	siderophore	Desferrioxamine B	83%
13.1	66,041	80,913	false	siderophore	-	N/A
13.2	276,950	288,254	false	bacteriocin	-	N/A
14.1	15,792	26,265	false	melanin	Istamycin	7%
15.1	155,838	166,065	false	bacteriocin	-	N/A
15.2	204,535	219,371	false	siderophore	-	N/A
18.1	73,173	153,980	false	PKS-like, other, NRPS	Kutznerides	24%
19.1	66,076	92,531	false	lanthipeptide	-	N/A
20.1	9,128	30,198	false	Terpene	Albaflavenone	100%
21.1	1	117,825	true	NRPS, T2PKS, T1PKS	Xantholipin	36%
24.1	8,158	36,817	true	T1PKS	Hitachimycin	45%
25.1	1	33,020	true	other	Lavendiol	6%
29.1	1	13,550	true	T1PKS	Hitachimycin	27%
30.1	1	12,247	true	NRPS	-	N/A
34.1	1	4,043	true	T1PKS	Micromonolactam	100%

Table S25. Homologues of proteins encoded by the tjipanazole (*tjp*) BGC in the genome of *Streptomyces* sp. MST-144321

Tjp	Top Hit	Identity	Coverage	Hit Function
1	BabS	41.8%	91.6%	chromopyrolic acid biosynthesis
2	BabQ	42.9%	99.3%	chromopyrolic acid biosynthesis
3	No hit	—	—	—
4	BabM3	35.9%	96.3%	*O*-methyltransferase
5	No hit	—	—	—
6	No hit	—	—	—
7	BabO2	30.7%	72.5%	chromopyrolic acid biosynthesis
8	BabO3	26.1%	84.7%	hydroxylase
9	BabO4	41.1%	96.3%	chromopyrolic acid biosynthesis
10	BabH2	42.0%	91.5%	tryptophan-7-halogenase

Table S26. Media recipes

Agars

Glycerol Casein Agar (CGA)	
Ingredient	*Quantity*
Glycerol (Chem-Supply)	30 g
Casein peptone (Amyl)	2 g
K_2HPO_4(Chem-Supply)	1 g
NaCl (Chem-Supply)	1 g
$MgSO_4.7H_2O$ (AnalaR)	0.5 g
Trace element solution*	5 mL
Distilled H_2O	1000 mL
Bacteriological agar (Amyl)	20 g
Autoclave	

***Trace element solution**	
$CaCl_2.2H_2O$	3 g
$FeC_6O_7H_5$	1 g
$MnSO_4$	0.2 g
$ZnCl_2$	0.1 g
$CuSO_4.5H_2O$	0.025 g
$Na_2B_4O_7.10H_2O$	0.02 g
$CoCl_2$	0.004 g
$Na_2MoO_4.2H_2O$	0.01 g
Distilled H_2O	1000 mL
Filter sterilize	

ISP2 Agar (I2A)	
Ingredient	*Quantity*
Yeast extract (Difco)	4 g
Malt extract (Difco)	10 g
Glucose (Country Brewers)	4 g
Distilled H_2O	1000 mL
Adjust pH to 7.3	
Bacteriological agar (Amyl)	20 g
Autoclave	

N-Z Amine Agar (NZA)	
Ingredient	*Quantity*
Yeast extract (Difco)	4 g
N-Z-Amine (Sigma)	10 g
Glucose (Amyl)	4 g
Distilled H_2O	1000 mL
Bacteriological Agar (Amyl)	20 g
Autoclave	

Nutrient Agar (NA)	
Ingredient	*Quantity*
Nutrient Agar (Amyl)	26 g
Distilled H_2O	1000 mL
Autoclave	

Oatmeal Agar (OMA)	
Ingredient	*Quantity*
Oatmeal Agar (Amyl)	72.5 g
Distilled H_2O	1000 mL
Autoclave	

Grains

Cracked Wheat (BL)	
Ingredient	*Quantity*
Cracked Wheat	46 g
Distilled H_2O	30 mL
Autoclave	

Pearl Barley (PB)	
Ingredient	*Quantity*
Pearl barley	48 g
Distilled H_2O	35 mL
Autoclave	

Jasmine Rice (JR)	
Ingredient	*Quantity*
Jasmine rice	50 g
Distilled H_2O	25 mL
Autoclave	

Basmati rice (BS)	
Ingredient	*Quantity*
Basmati rice	44 g
Distilled H_2O	30 mL
Autoclave	

Table S27. Comparison of composition and abundance of secondary metabolites from methanolic extracts of *Streptomyces* sp. MST-144321 from various media.

Media	AUC 210 nm	AUC 254 nm	Total Peaks	Peaks 90% AUC	Peaks 95% AUC	Peaks 99% AUC	UV Classes	UV Unique	UV Unresolved
CGA	939	207	33	4	8	23	4	16	2
I2A	434	141	17	5	8	14	3	8	0
NA	131	24	11	5	7	9	2	2	1
OMA	320	106	28	10	14	23	5	10	0
Cracked wheat	596	107	58	16	24	45	8	20	5
Basmati rice	1502	213	50	11	15	34	6	18	3
Pearl barley	559	172	51	17	25	41	6	27	4
Jasmine rice	761	179	42	13	18	31	4	16	1

The abundance and numbers of secondary metabolites were used as indices for quantifying the chemical diversity of an extract. Abundance was determined by calculation of the total area under the curve (AUC) at 210 and 254 nm and the positive and negative total ion current (TIC) traces from the mass detector. The higher the AUC the higher the secondary metabolite productivity of the organism on that media. The number of peaks eluting between 0.5 and 11 min were determined using the 210 nm channel and resolved peaks above the baseline were automatically counted. The greater the number of peaks, the greater the secondary metabolite diversity produced by the organism. The distribution of total peaks was further analysed by calculation of the number of peaks constituting 90%, 95% and 99% of the total AUC, respectively. The higher the number in each group, the more chemically diverse the extract. UV classes is the number of classes with two or more related UV spectra; UV unique is the number of peaks where the UV spectra appears once in the trace; UV unresolved is the number of peaks where the UV spectra is not clearly defined or resolved.

Table S28. cblaster search results for svetamycin against the NCBI database

Organism	Scaffold	Start	End	Score	T1	C	D	E	F	G1	G2	G3	G4	H	R2	P1	P2	P3	P4	I	J	K	A1	A2	O1	O2	O3
Pseudonocardia sp. HH130629-09	NZ_CP011868.1	5700061	5753546	20.1383	1	1	1	1	1	0	0	0	0	0	1	1	1	0	0	0	0	1	2	1	1	0	0
Pseudonocardia sp. HH130629-09	CP011868.1	5700061	5753546	17.1211	1	0	1	1	1	0	0	0	0	0	1	1	1	0	0	0	0	1	2	1	1	0	0
Kutzneria buriramensis DSM 45791	NZ_QUNO01000006.1	100638	147810	14.5744	0	1	1	1	1	0	0	0	0	0	1	1	1	0	0	0	0	0	2	1	0	0	0
Kutzneria buriramensis DSM 45791	QUNO01000006.1	100638	147810	14.5744	0	1	1	1	1	0	0	0	0	0	1	1	1	0	0	0	0	0	2	1	0	0	0
Pseudonocardia sp. EC080625-04	NZ_CP010990.1	237106	243317	12.1857	1	1	1	1	1	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0
Nonomuraea sp.	JABFWI010000668.1	3256	29156	9.961	0	0	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	1	2	1	0	0	0
Pseudonocardia sp. EC080625-04	CP010990.1	237106	243317	9.1668	1	0	1	1	1	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0
Actinospica acidiphila SID13773	JAAGLZ010000089.1	17204	48690	8.2167	0	0	0	0	1	0	0	0	0	0	2	1	1	0	0	0	0	0	1	0	0	0	0
Micromonospora sp. M71_S20	RCCV01000001.1	3932533	3950679	8.1133	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	1	0	0	0	0	0	0	0
Micromonospora sp. M71_S20	NZ_RCCV01000001.1	3932533	3950679	8.1132	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	1	0	0	0	0	0	0	0
Pseudonocardia sp. EC080625-04	NZ_CP010990.1	57868	84467	7.9549	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	2	1	1	0	0
Pseudonocardia sp. EC080625-04	CP010990.1	57820	84467	7.9532	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	2	1	1	0	0
Actinomadura sp. 14C53	NZ_VCKW01000026.1	4161	37202	7.6525	0	0	0	0	2	0	0	0	0	0	1	1	1	0	0	0	0	0	1	1	0	0	0
Actinomadura sp. 14C53	VCKW01000026.1	4161	37202	7.652	0	0	0	0	2	0	0	0	0	0	1	1	1	0	0	0	0	0	1	1	0	0	0
Amycolatopsis oliviviridis CGMCC 4.7683	NZ_BNAY01000001.1	229211	239905	7.2427	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	0	1	0	0	0	0	0	0
Actinoalloteichus sp. GBA129-24	CP016077.1	3709615	3748979	7.2255	0	0	0	0	1	0	0	0	0	0	0	1	1	0	0	1	0	0	1	0	0	0	1
Amycolatopsis jiangsuensis DSM 45859	JACHMG010000001.1	4186728	4193244	7.1933	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5	1	3
Amycolatopsis jiangsuensis DSM 45859	NZ_JACHMG010000001.1	4187004	4193244	7.193	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5	1	3
Kutzneria sp. 744	NZ_KK037166.1	10094720	10116260	7.1795	0	0	0	0	1	0	0	0	0	0	1	1	1	0	0	1	1	0	0	0	0	0	0
Actinosynnema sp. ALI-1.44	MTQO01000036.1	4495	8703	7.1791	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Actinosynnema sp. ALI-1.44	NZ_MTQO01000036.1	4495	8733	7.179	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Actinocrispum wychmicini DSM 45934	SLWS01000021.1	2232	6447	7.1715	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Actinocrispum wychmicini DSM 45934	NZ_SLWS01000021.1	2232	6294	7.1714	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Kitasatospora aureofaciens NRRL B-1286	NZ_JNWR01000011.1	95621	125008	7.1651	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	1	0	0	0	0	0
Kitasatospora aureofaciens ATCC 10762	JPRF03000028.1	38912	68316	7.1646	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	1	0	0	0	0	0

Results limited to the top 25 of 2,363 hits. Columns T1 – O3 represent Sve protein homologues. Empty cells outside of this region are omitted for clarity. Importantly, homologues of SveG1-G4 are not present in *Pseudonocardia* spp. known to produce gerumycin, indicating that they incorporate their starter units by an alternative mechanism.

Table S29. Single-crystal XRD experimental details for svetamycin A (**3**)

Crystal data	
Chemical formula	$C_{24}H_{35}ClN_8O_{10}$
M_r	631.05
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	100
***a*, *b*, *c* (Å)**	6.7387 (1), 9.5889 (1), 44.6727 (4)
***V* (Å^3)**	2886.60 (6)
Z	4
Radiation type	Cu *K*α
m (mm^{-1})	1.78
Crystal size (mm)	0.16 × 0.14 × 0.05

Data collection	
Diffractometer	XtaLAB Synergy, Single source at home/near, HyPix
Absorption correction	Gaussian *CrysAlis PRO* 1.171.41.103a (Rigaku Oxford Diffraction, 2021) Numerical absorption correction based on Gaussian integration over a multifaceted crystal model Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.
T_{min}, T_{max}	0.844, 1.000
No. of measured, independent and observed [$I > 2s(I)$] reflections	44662, 5890, 5663
R_{int}	0.061
(sin q/l)$_{max}$ (Å^{-1})	0.628

Refinement	
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.033, 0.084, 1.04
No. of reflections	5890
No. of parameters	393
H-atom treatment	H-atom parameters constrained
Dρ$_{max}$, Dρ$_{min}$ (e Å^{-3})	0.21, -0.22
Absolute structure	Flack x determined using 2272 quotients [(I+)−(I−)]/[(I+)+(I−)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
Absolute structure parameter	0.000(7)

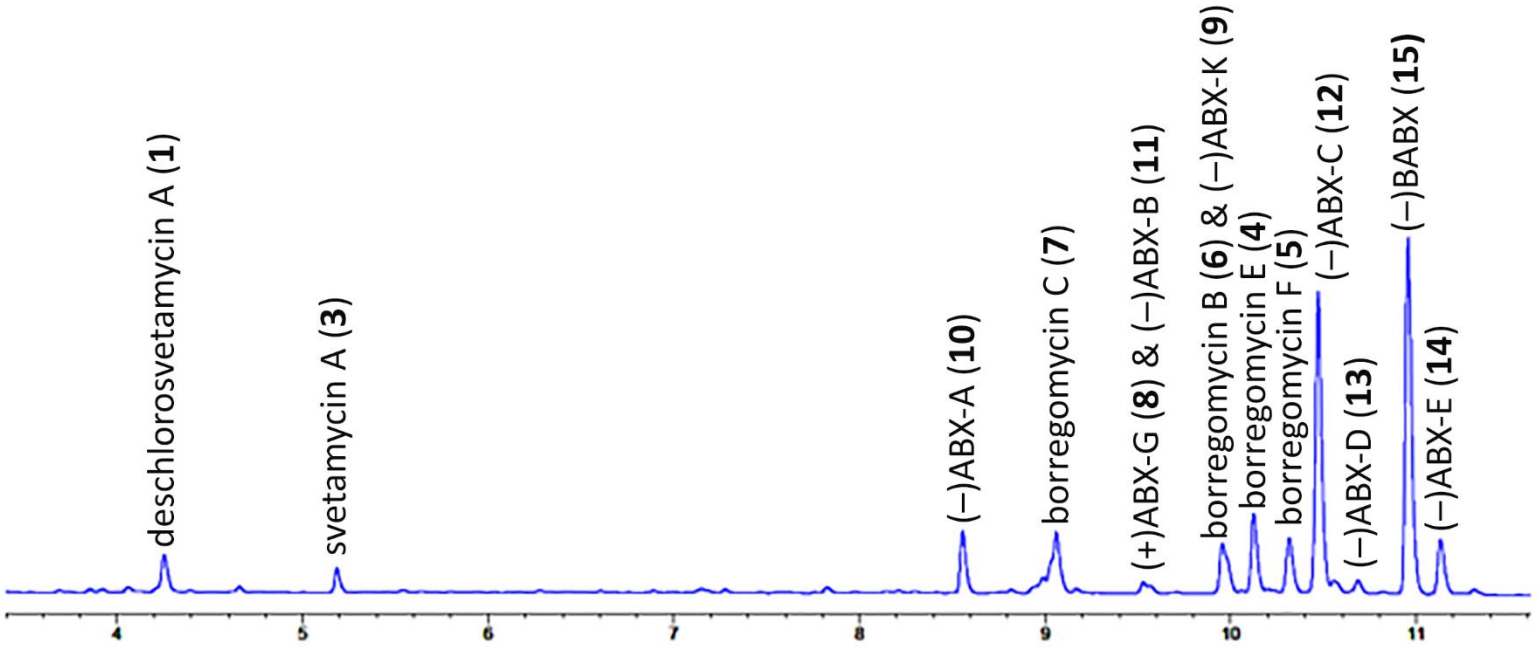
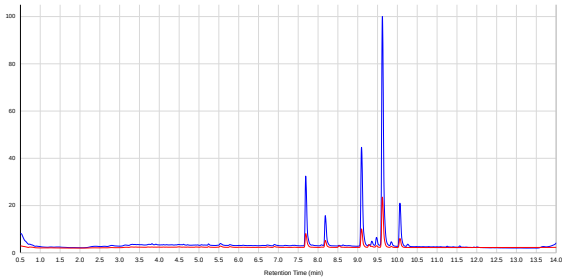
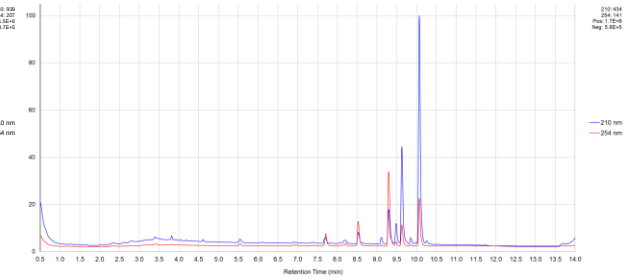


Figure S1. HPLC trace of crude ethyl acetate extract of *Streptomyces* sp. MST-144321 after cultivation on pearl barley media for 10 days

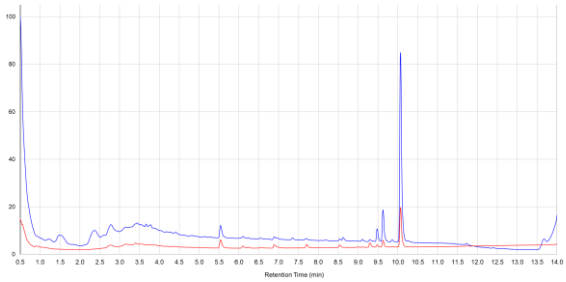
a. CGA



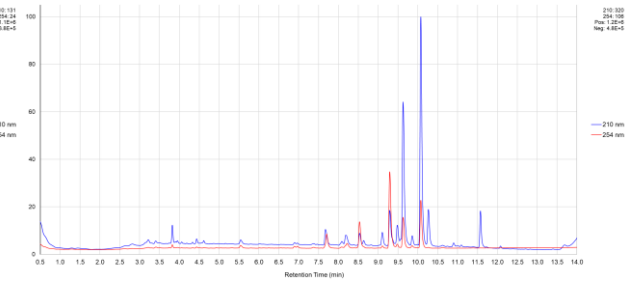
b. ISP2



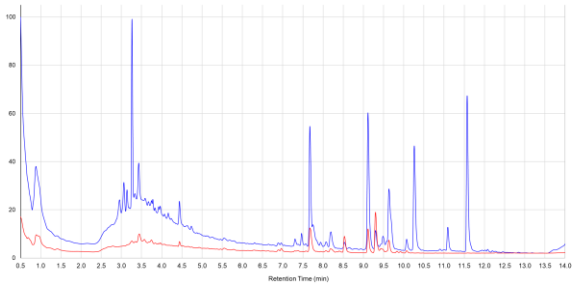
c. NA



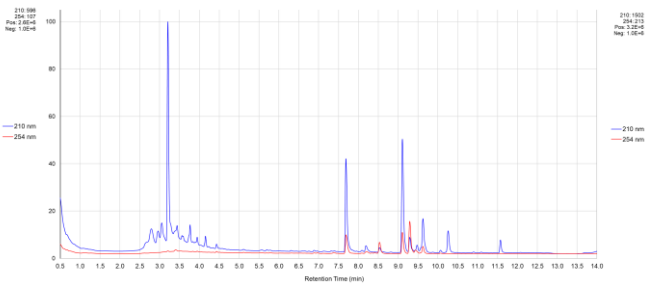
d. OMA



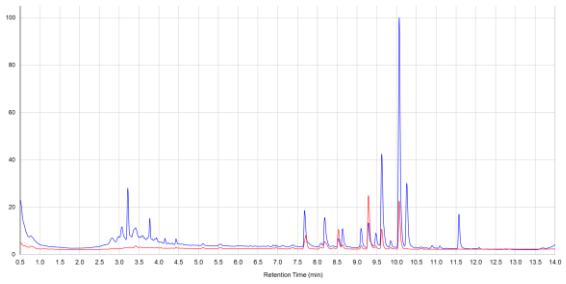
e. Cracked wheat



f. Basmati rice



g. Jasmine rice



h. Pearl barley

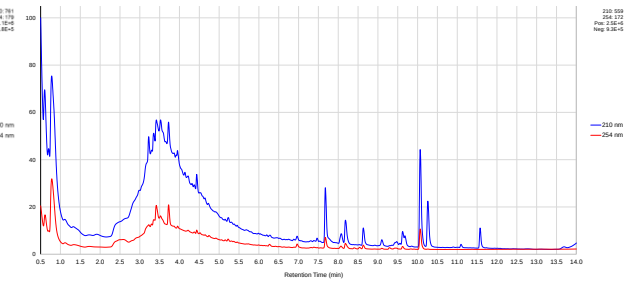


Figure S2. HPLC traces of the methanolic extracts of *Streptomyces sp.* MST-144321 grown on various media for 7 days at 28 °C.

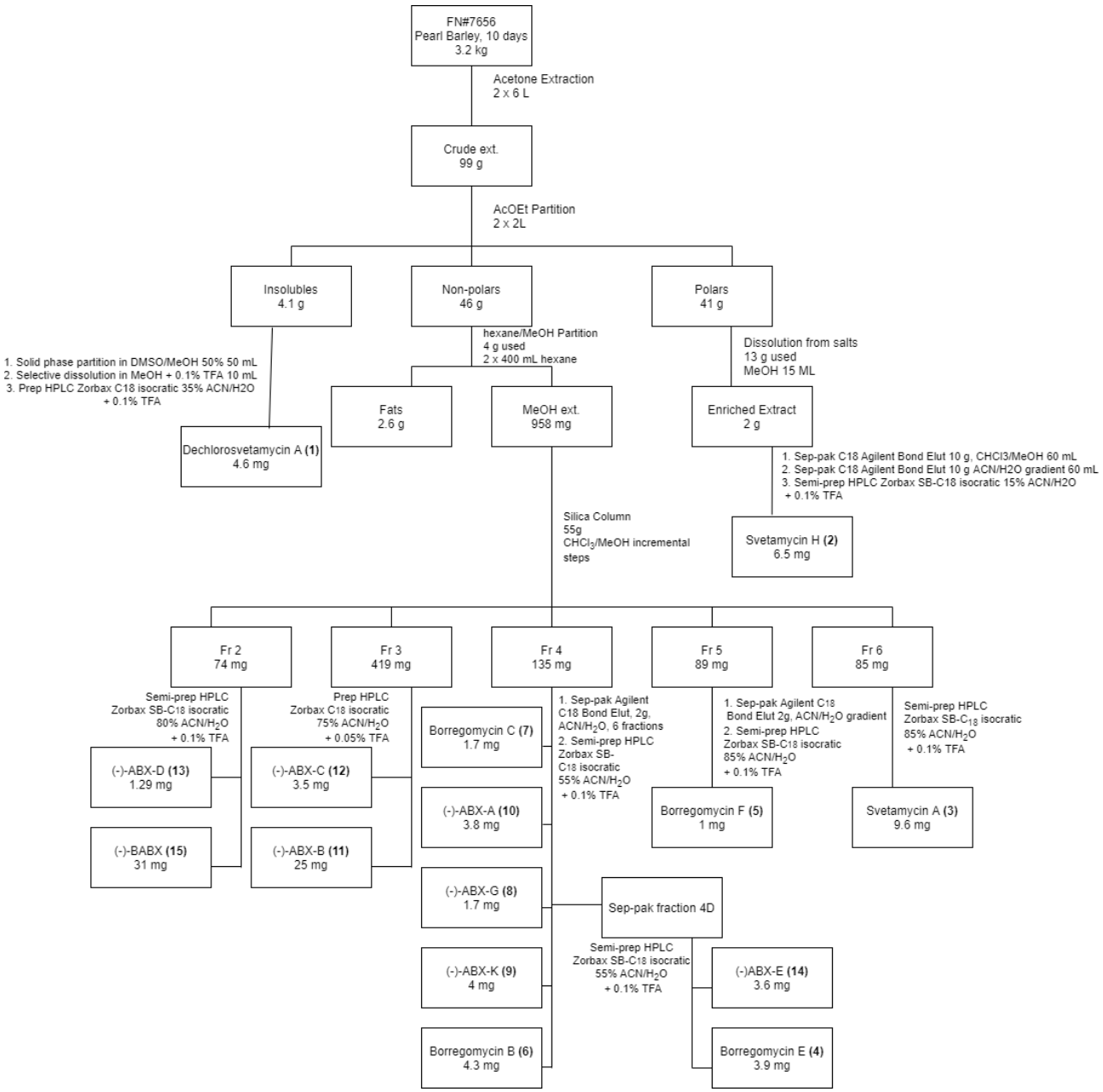


Figure S3. Fractionation of crude ethyl acetate extract of *Streptomyces* sp. MST-144321 after cultivation on pearl barley media for 10 days

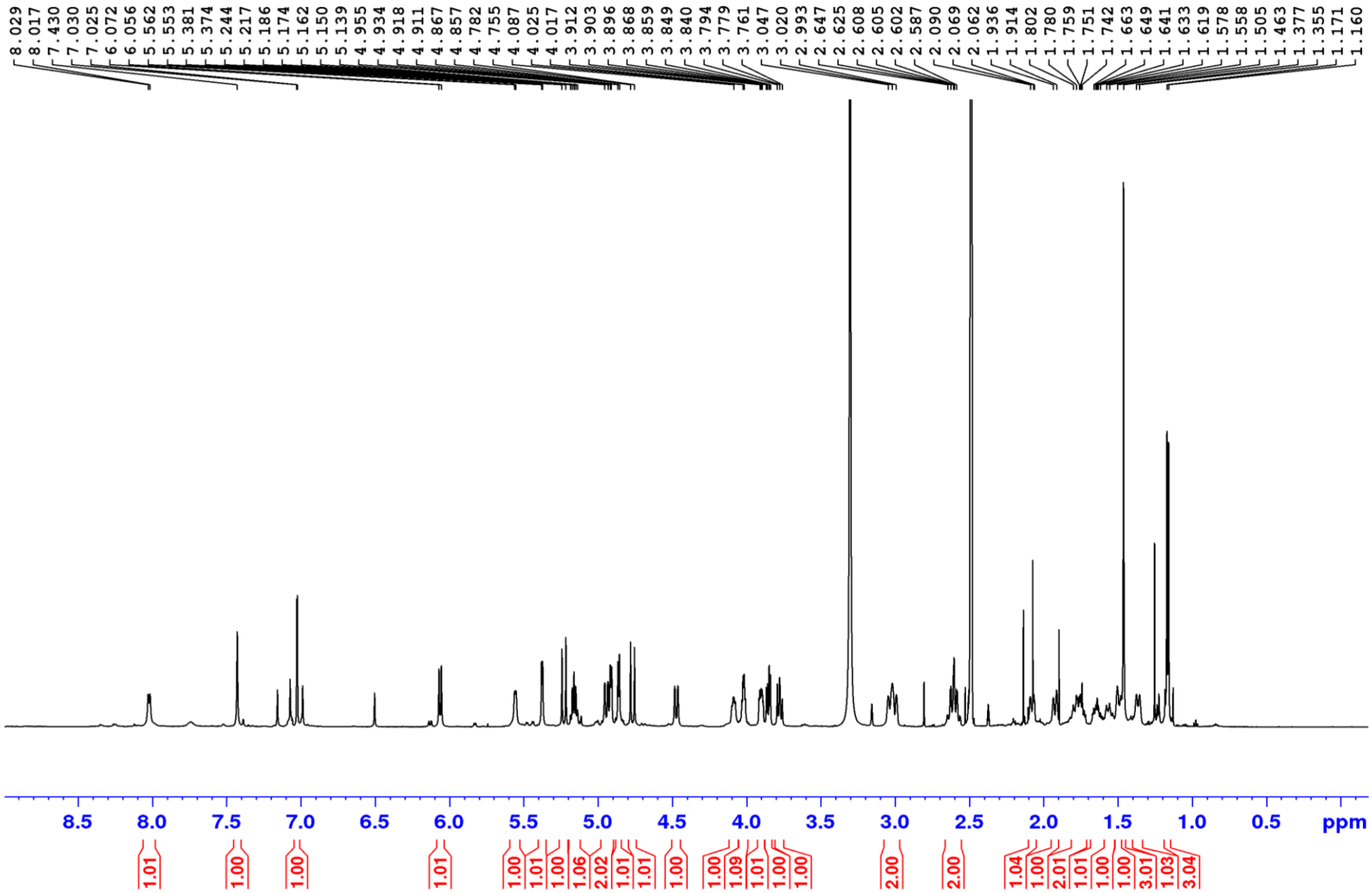


Figure S4. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of deschlorosvetamycin A (**1**)

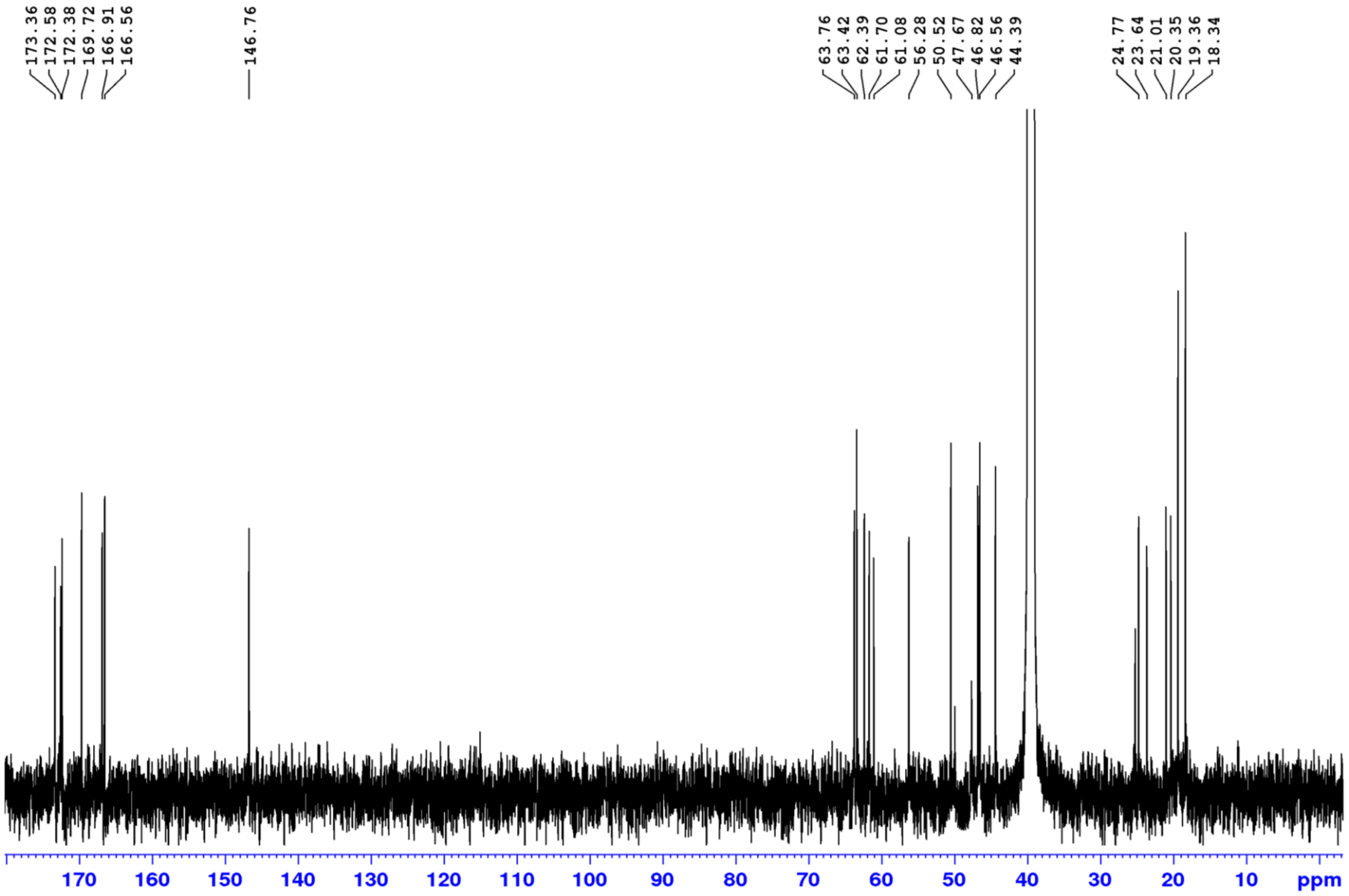


Figure S5. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of deschlorosvetamycin A (**1**)

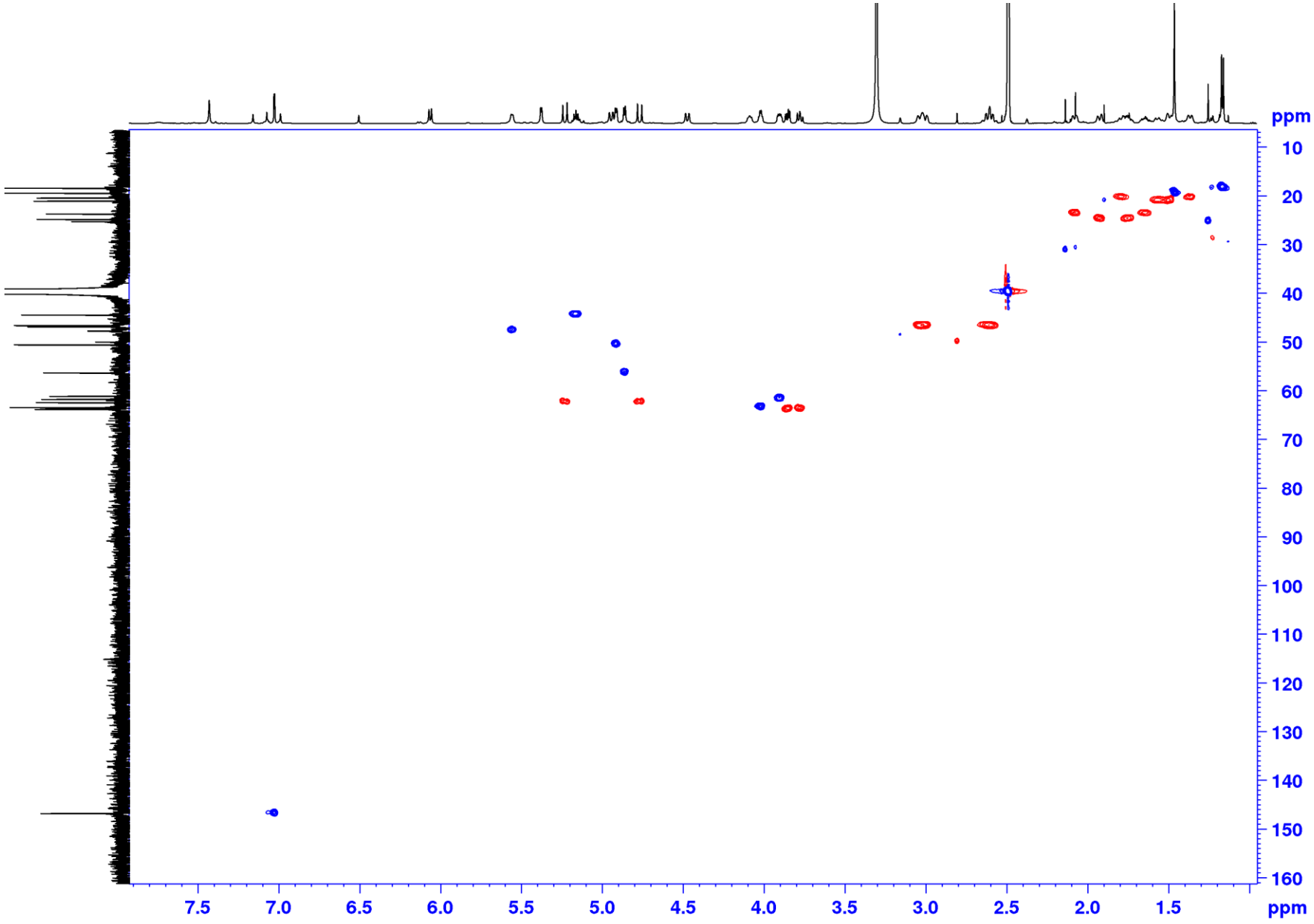


Figure S6. ^{1}H-^{13}C HSQC NMR spectrum (600 MHz, DMSO-d_6) of deschlorosvetamycin A (**1**)

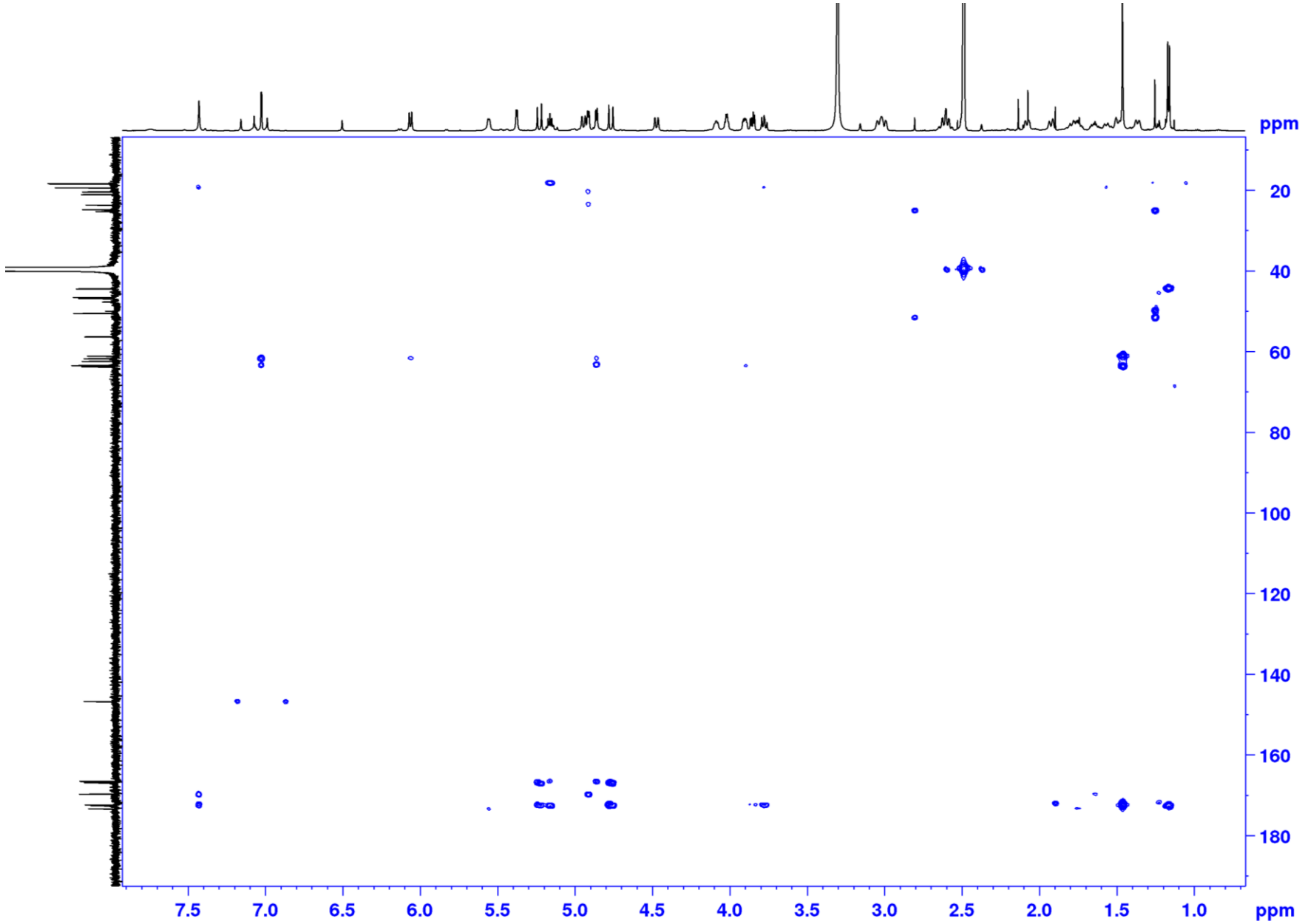


Figure S7. ^{1}H-^{13}C HMBC NMR spectrum (600 MHz, DMSO-d_6) of deschlorosvetamycin A (**1**)

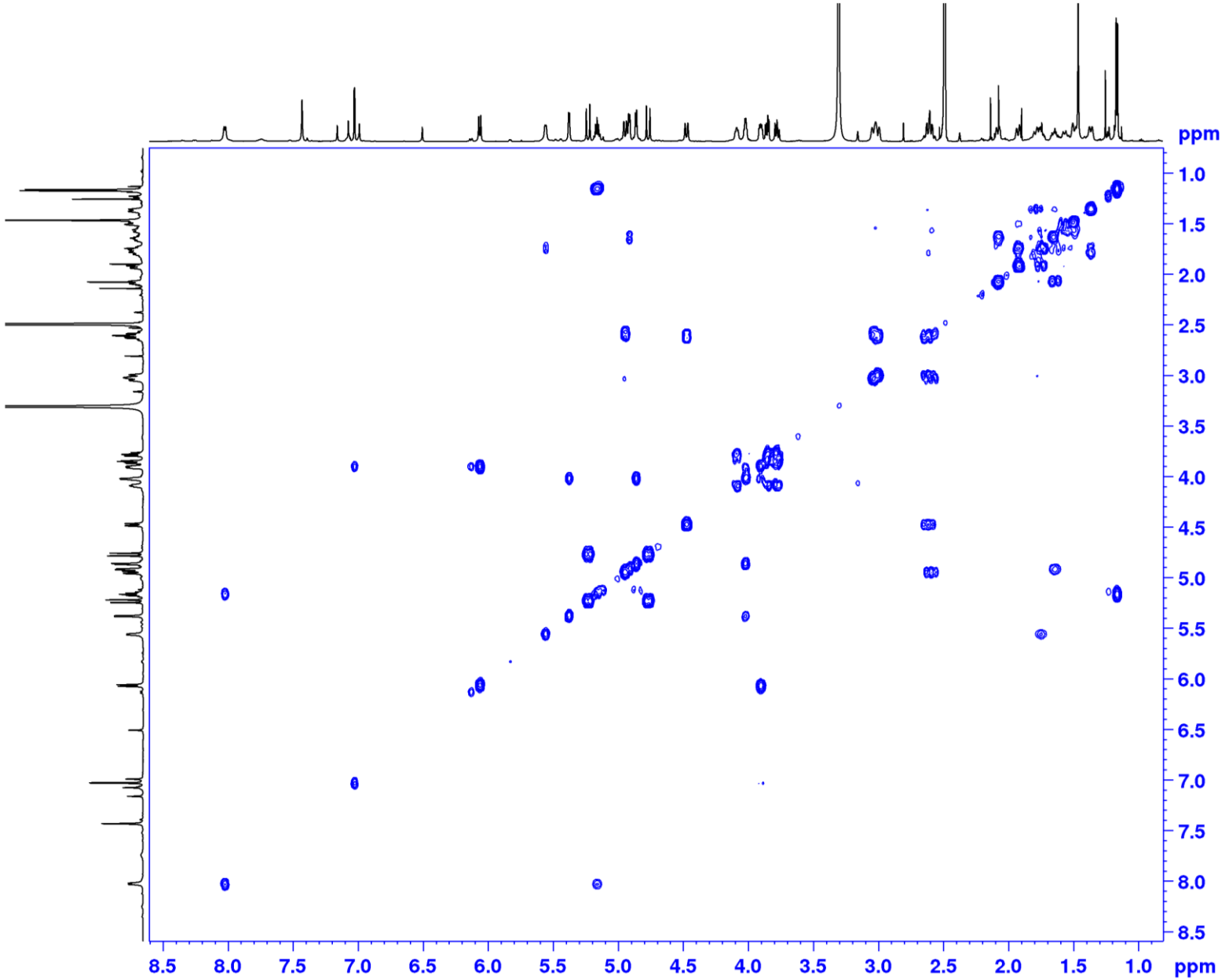


Figure S8. ^{1}H-^{1}H COSY NMR spectrum (600 MHz, DMSO-d_6) of deschlorosvetamycin A (**1**)

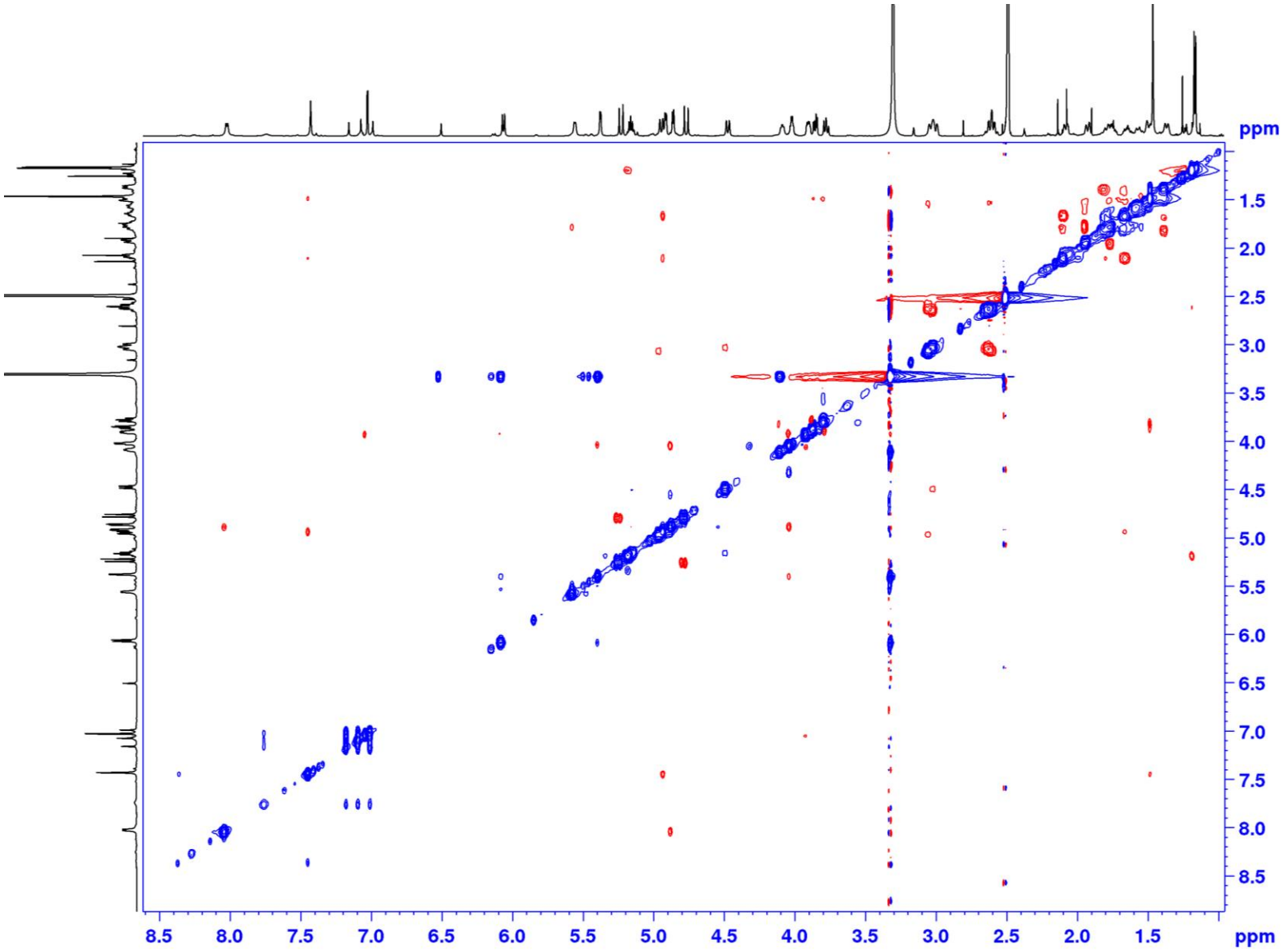


Figure S9. ^{1}H-^{1}H ROESY NMR spectrum (600 MHz, DMSO-d_6) of deschlorosvetamycin A (**1**)

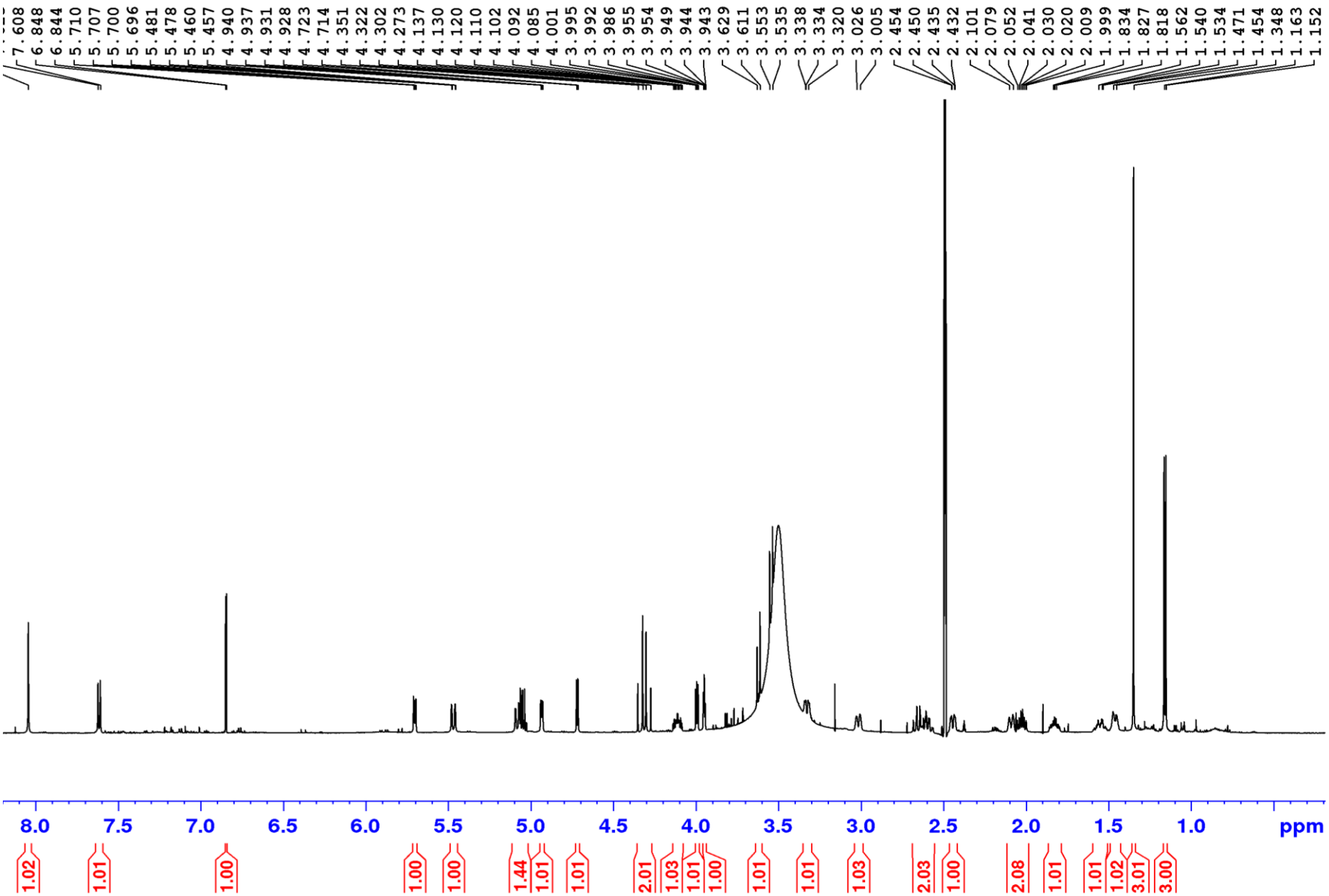


Figure S10. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of svetamycin H (**2**)

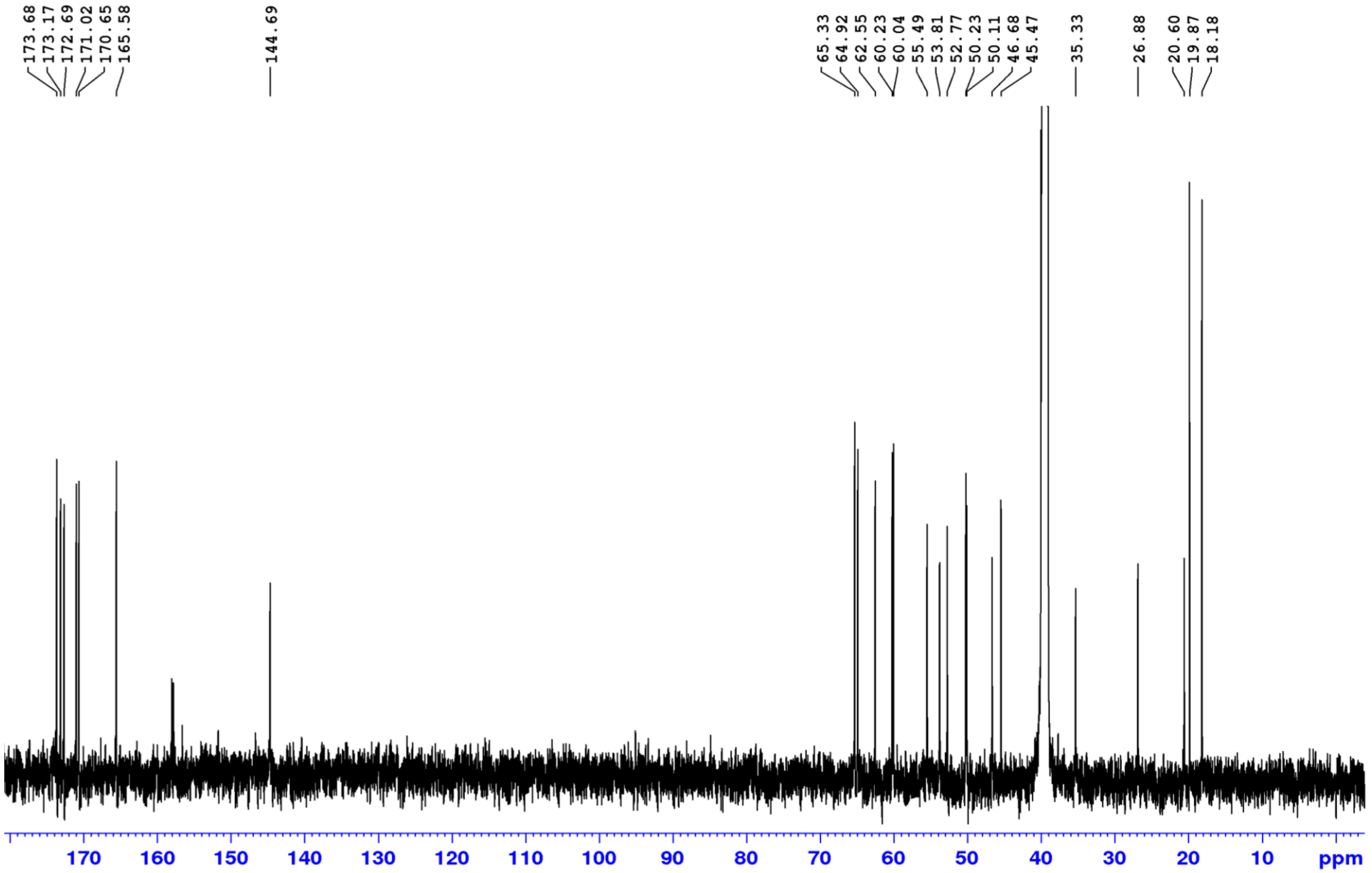


Figure S11. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of svetamycin H (**2**)

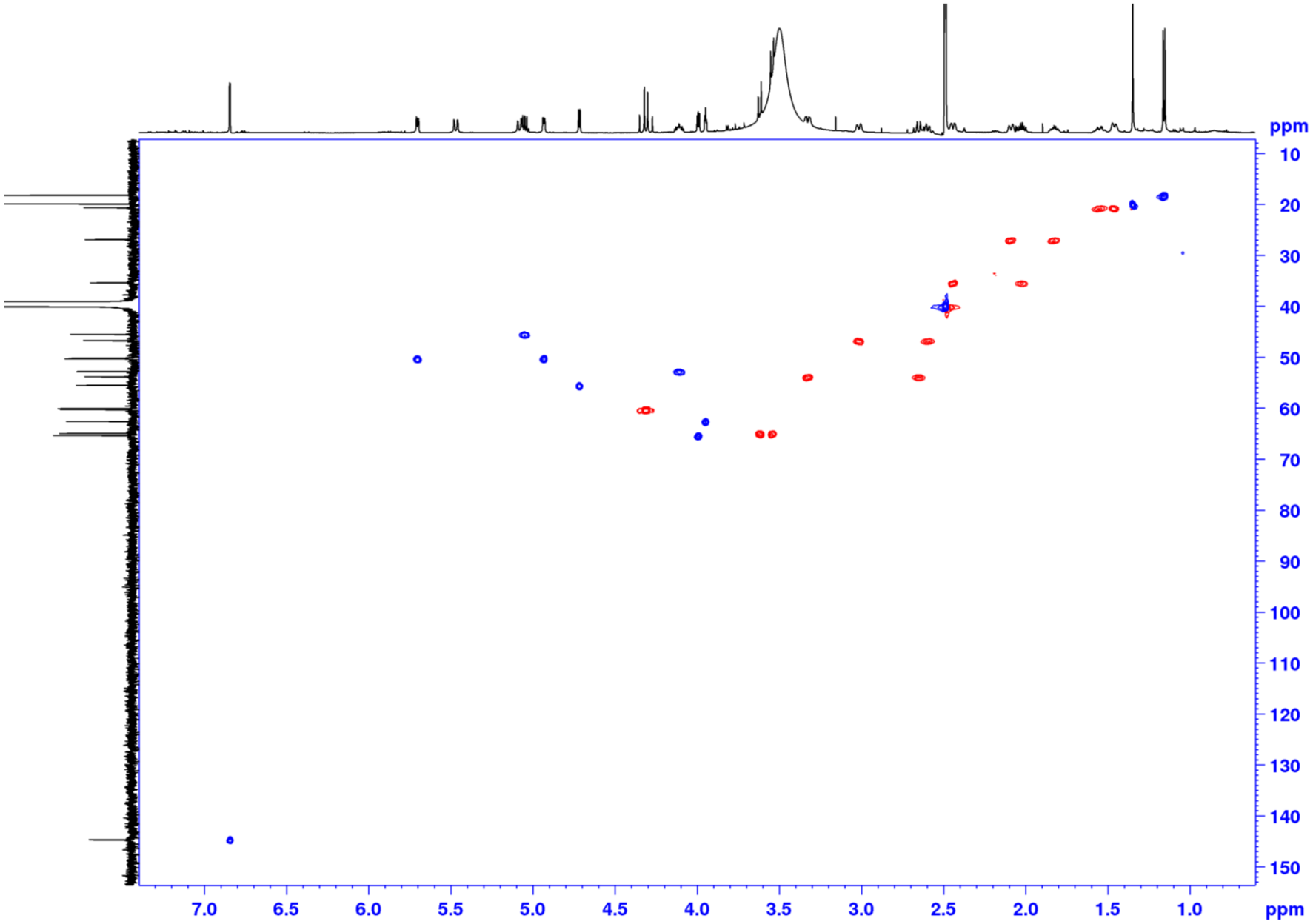


Figure S12. ^{1}H-^{13}C HSQC NMR spectrum (600 MHz, DMSO-d_6) of svetamycin H (**2**)

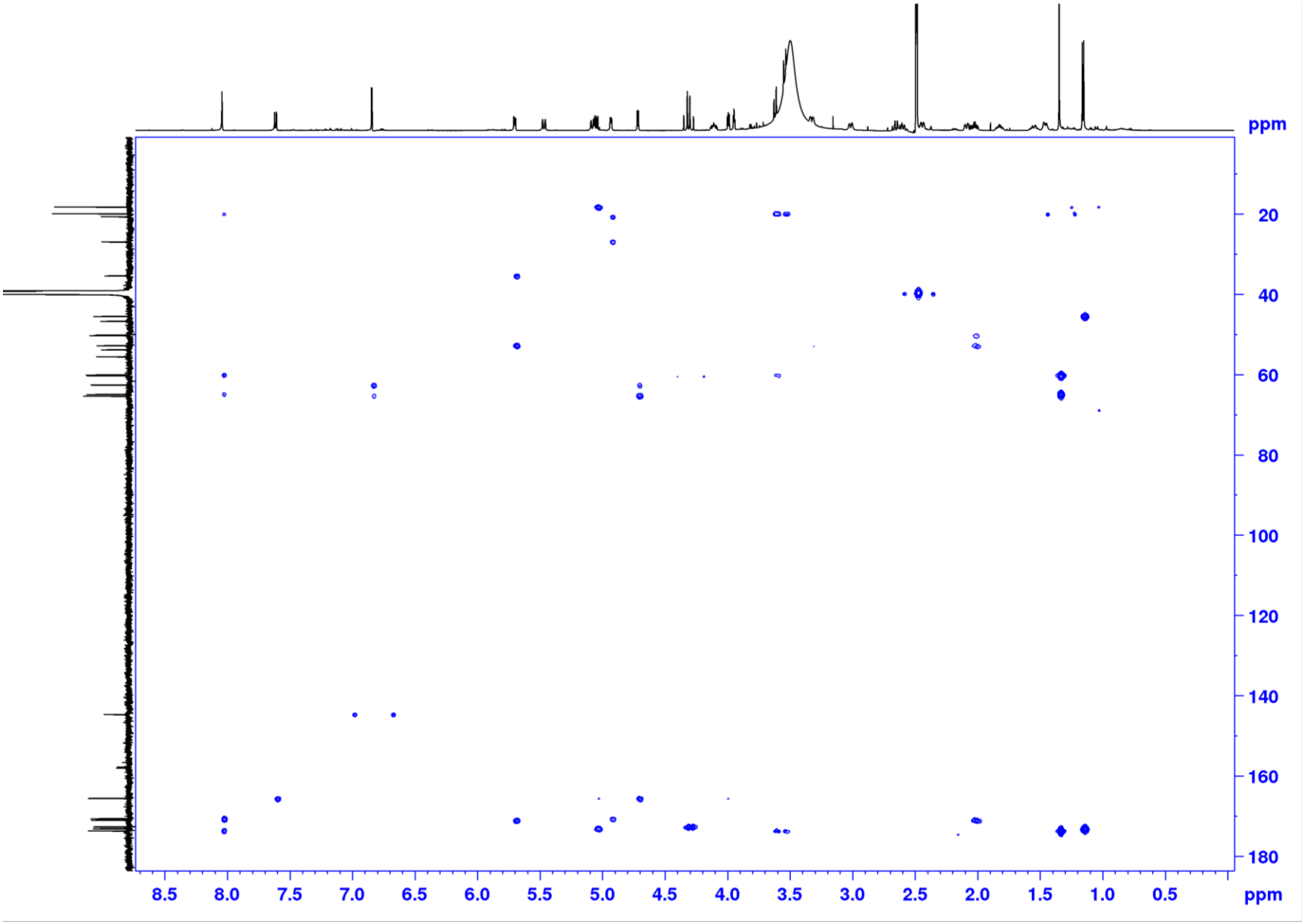


Figure S13. ^{1}H-^{13}C HMBC NMR spectrum (600 MHz, DMSO-d_6) of svetamycin H (**2**)

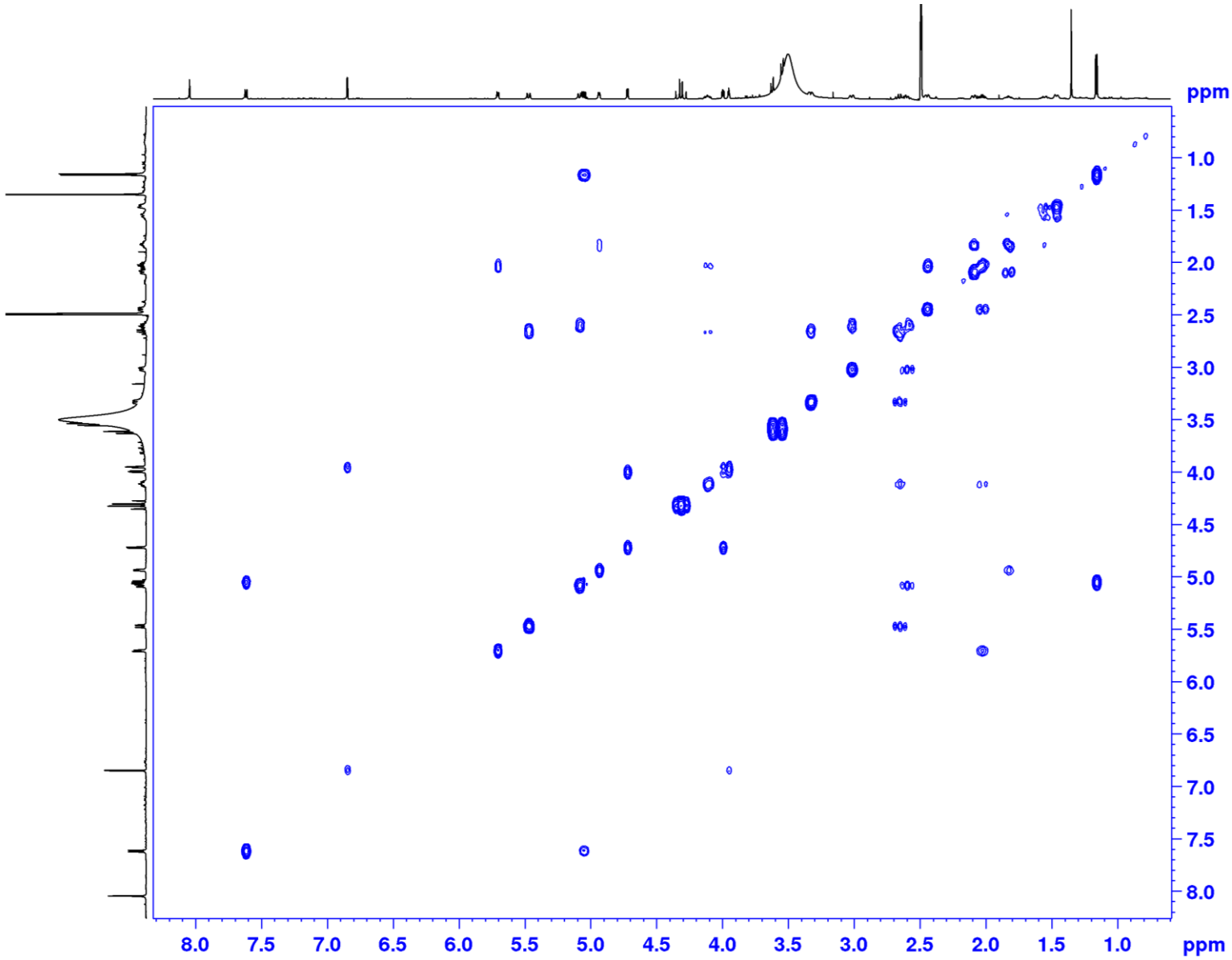


Figure S14. ^{1}H-^{1}H COSY NMR spectrum (600 MHz, DMSO-d_6) of svetamycin H (**2**)

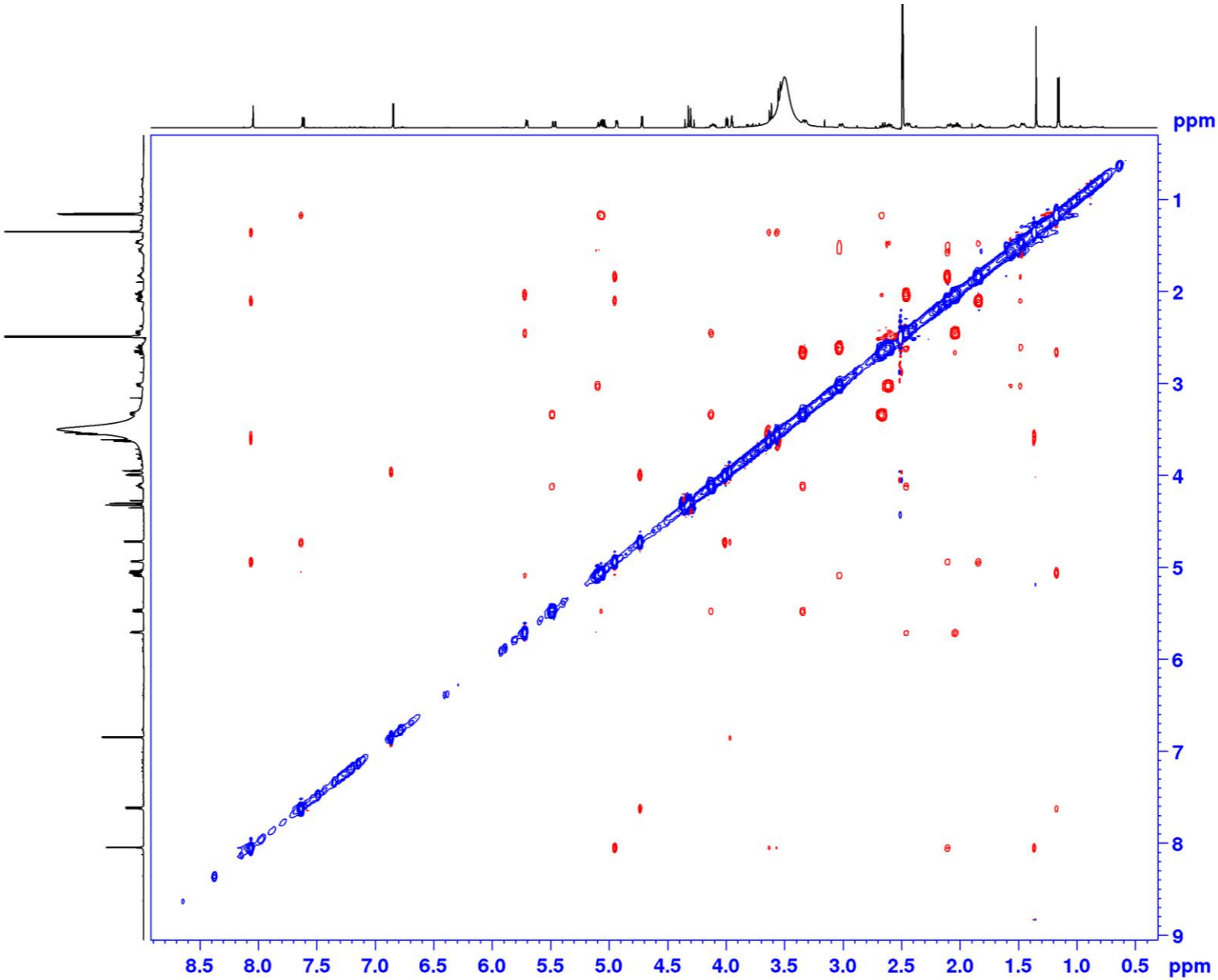


Figure S15. ^{1}H-^{1}H ROESY NMR spectrum (600 MHz, DMSO-d_6) of svetamycin H (**2**)

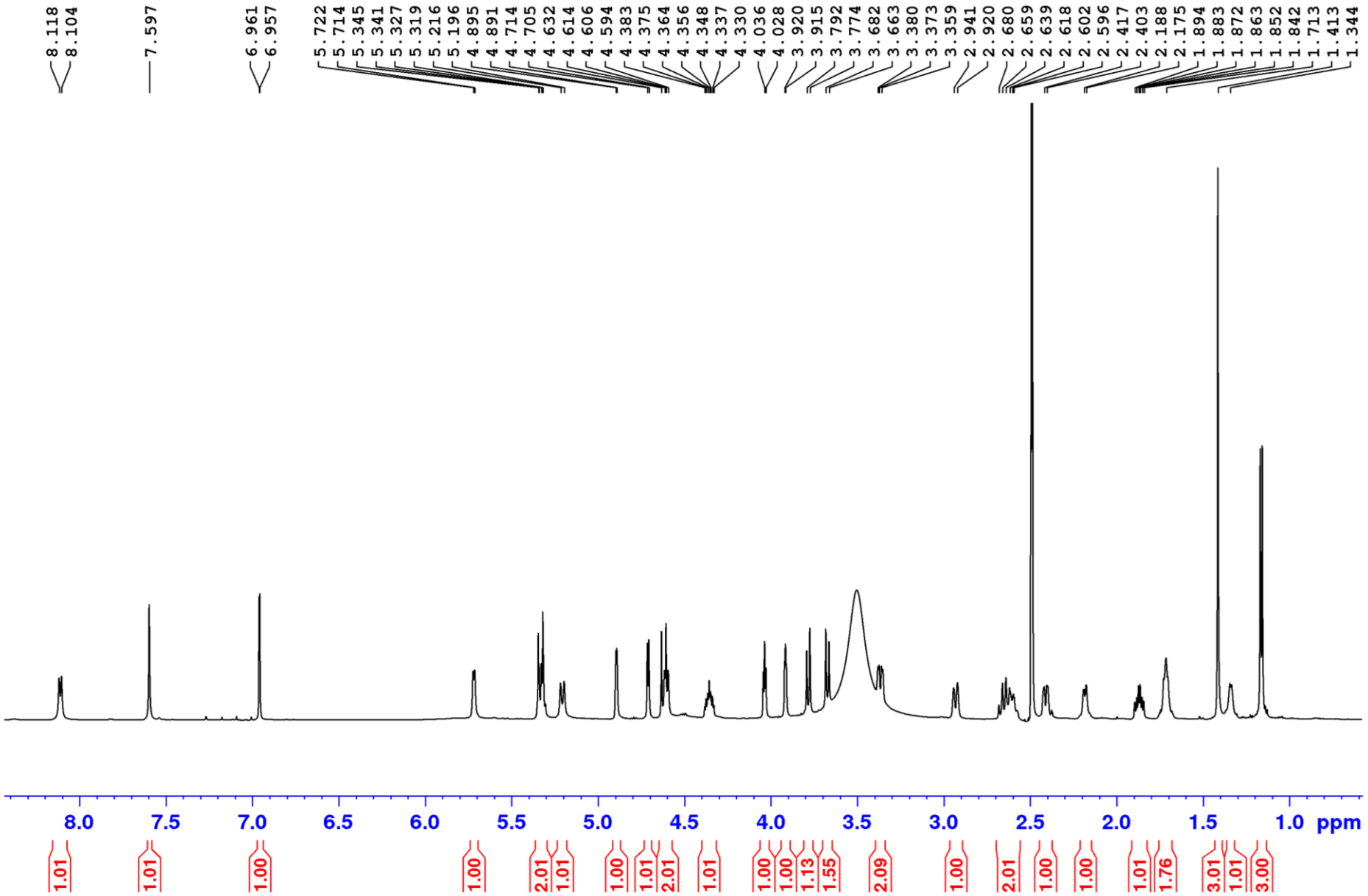


Figure S16. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of svetamycin A (**3**)

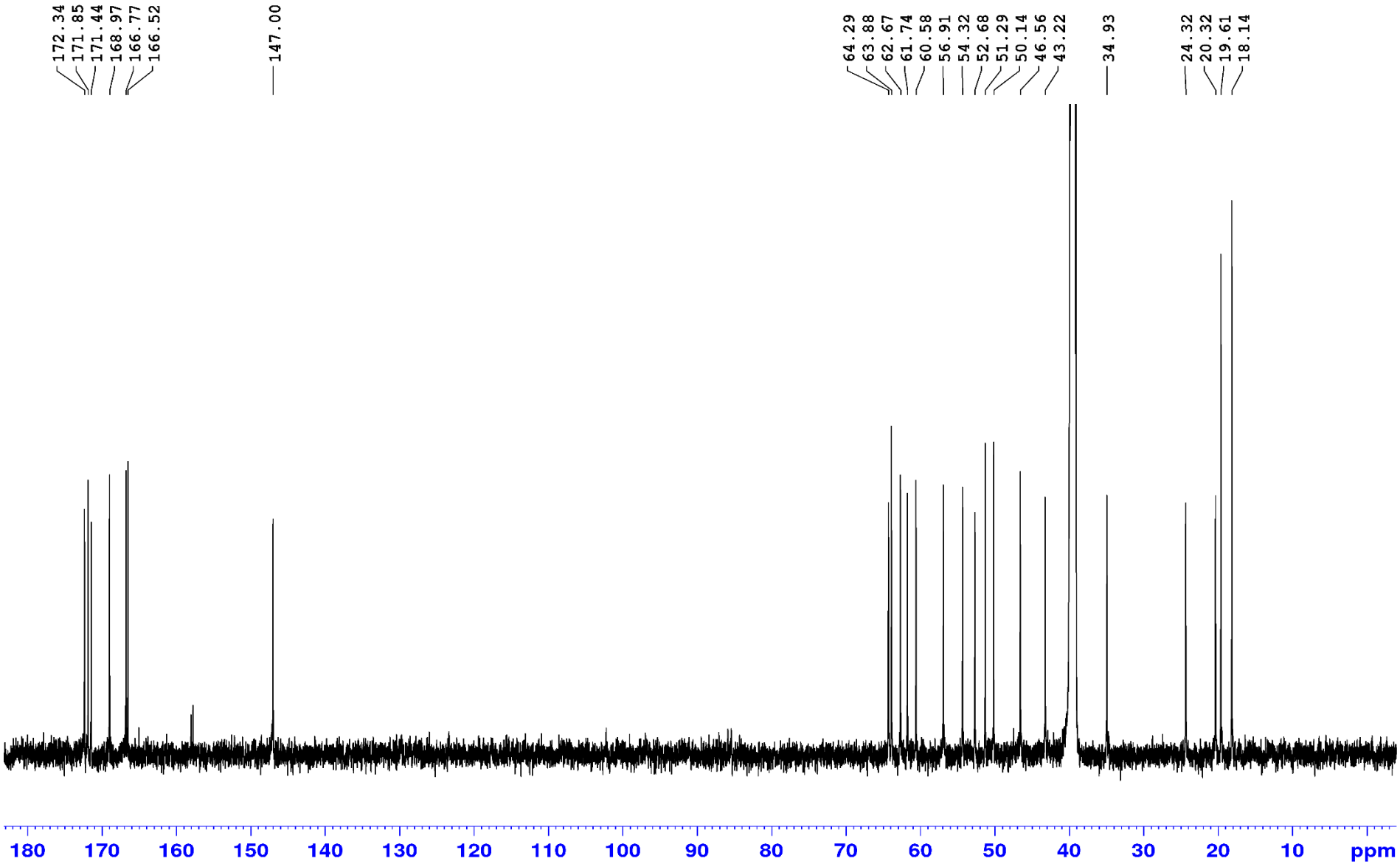


Figure S17. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of svetamycin A (**3**)

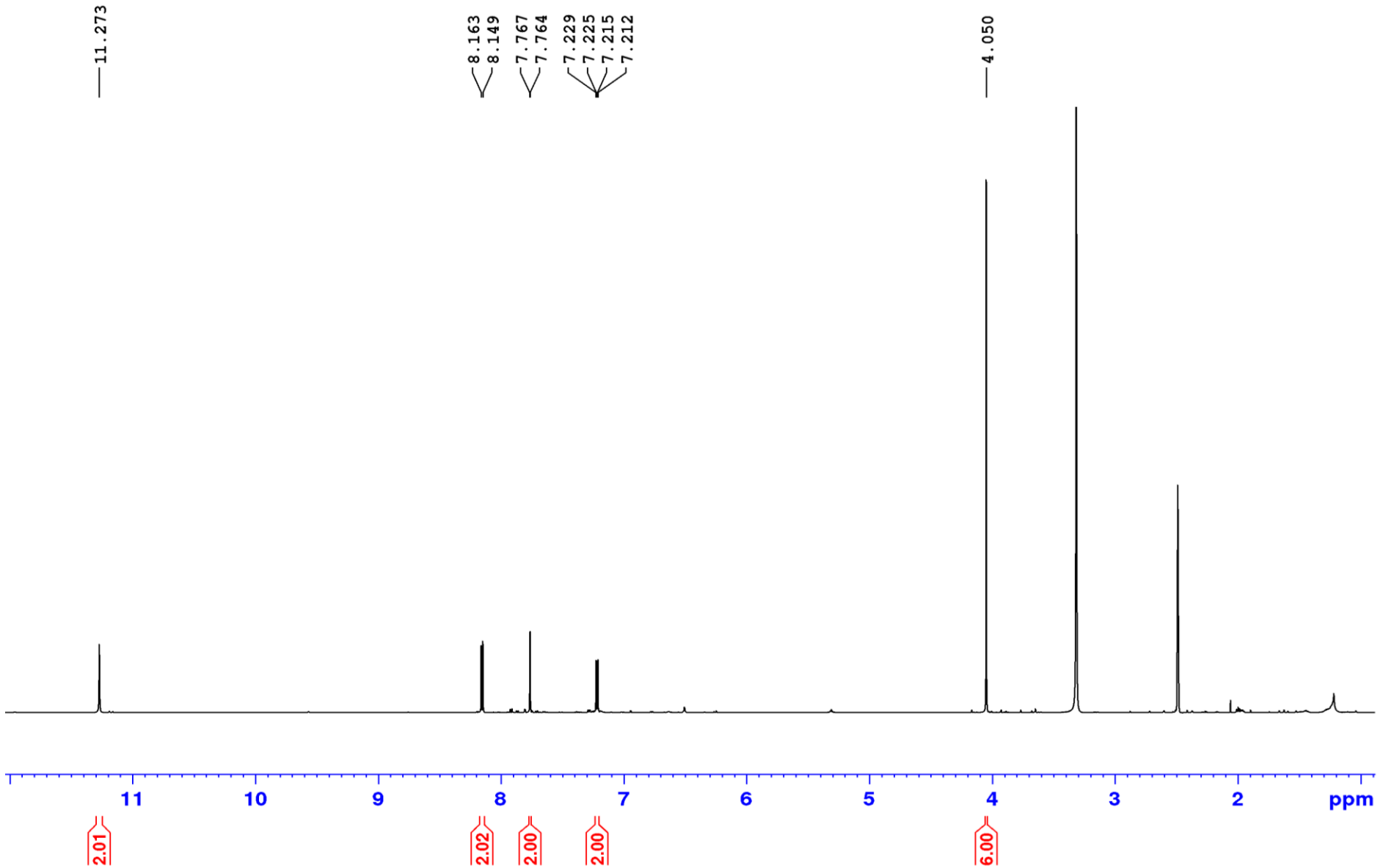


Figure S18. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of borregomycin E (**4**)

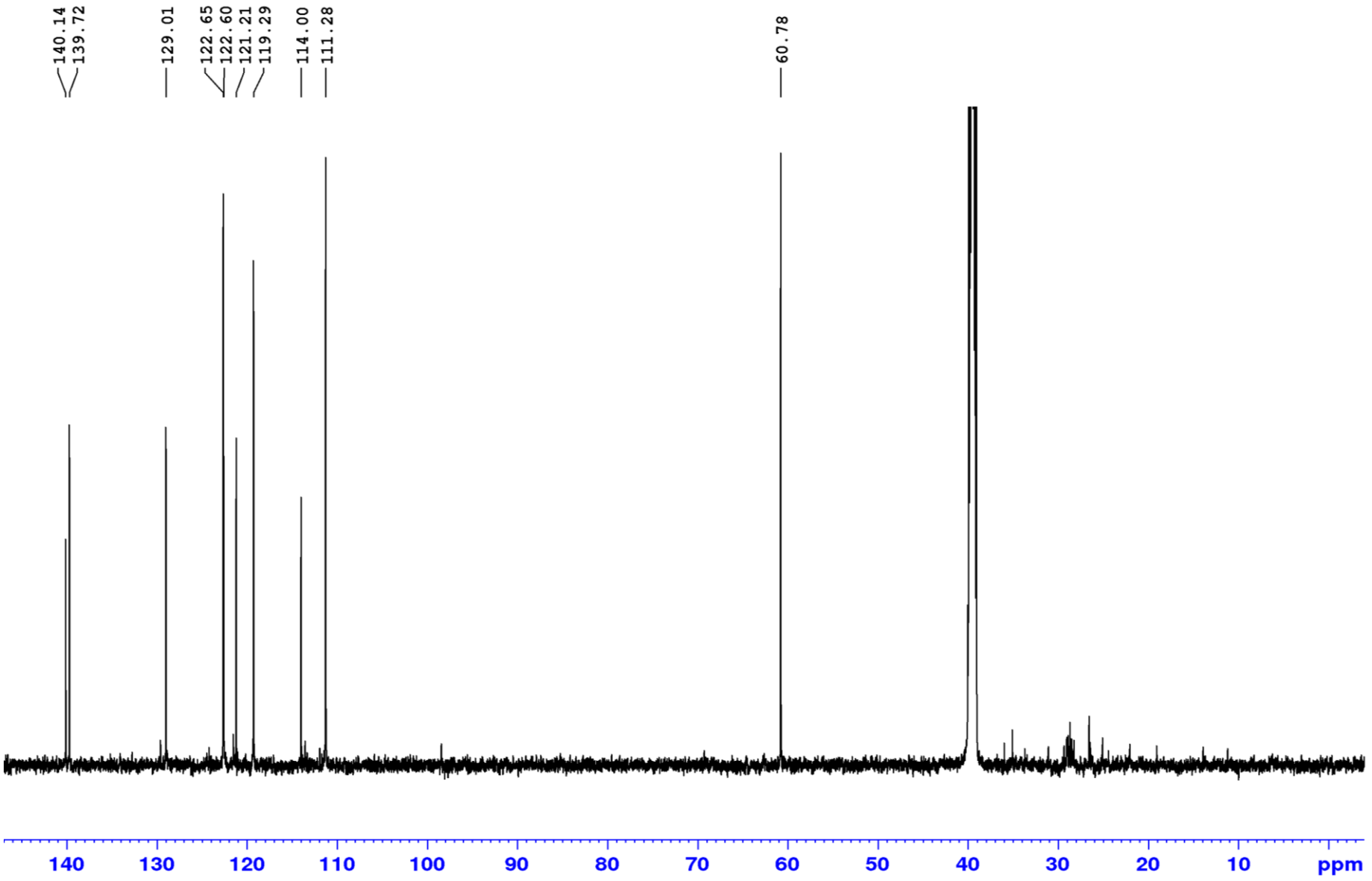


Figure S19. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of borregomycin E (**4**)

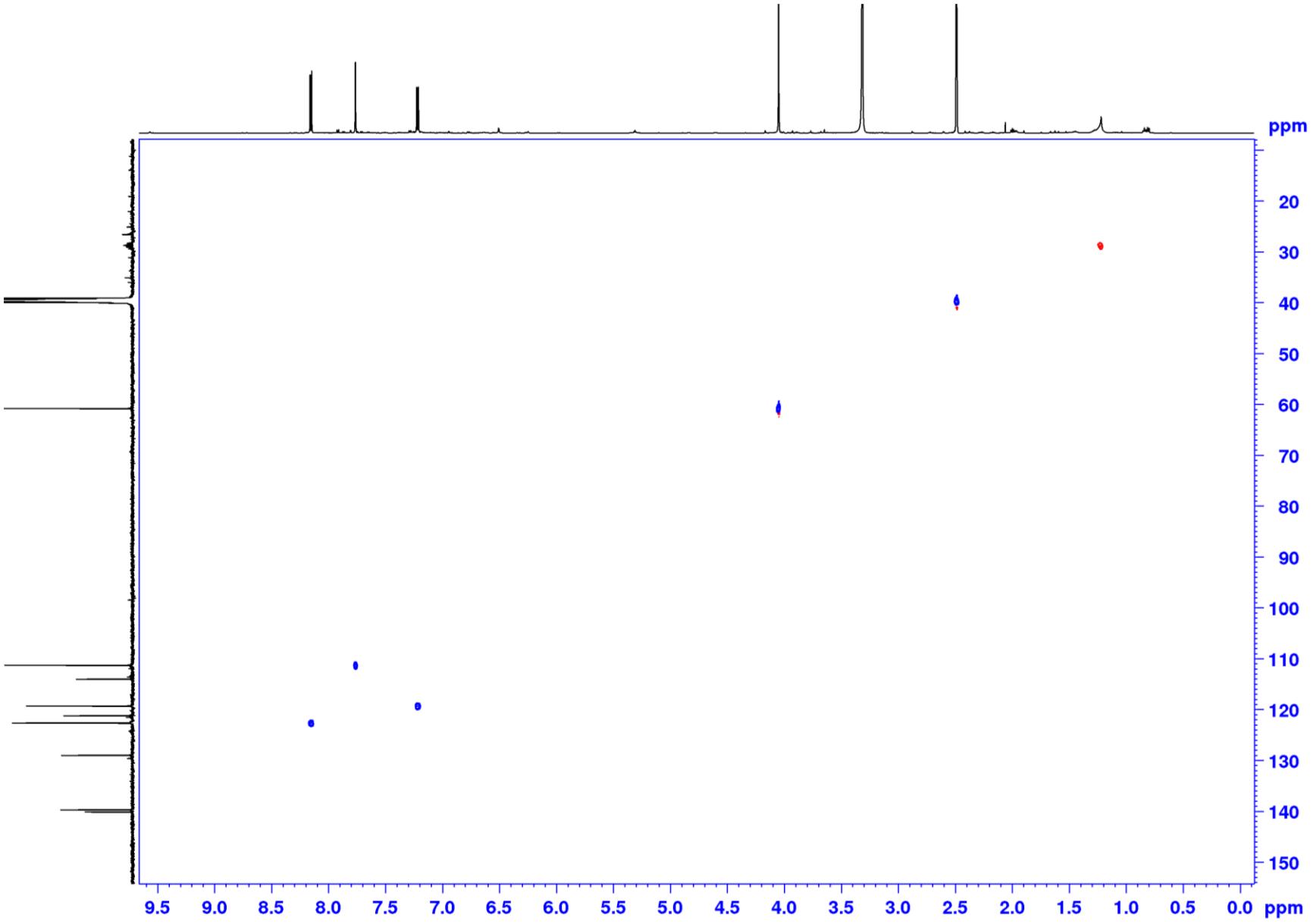


Figure S20. ^{1}H-^{13}C HSQC NMR spectrum (600 MHz, DMSO-d_6) of borregomycin E (**4**)

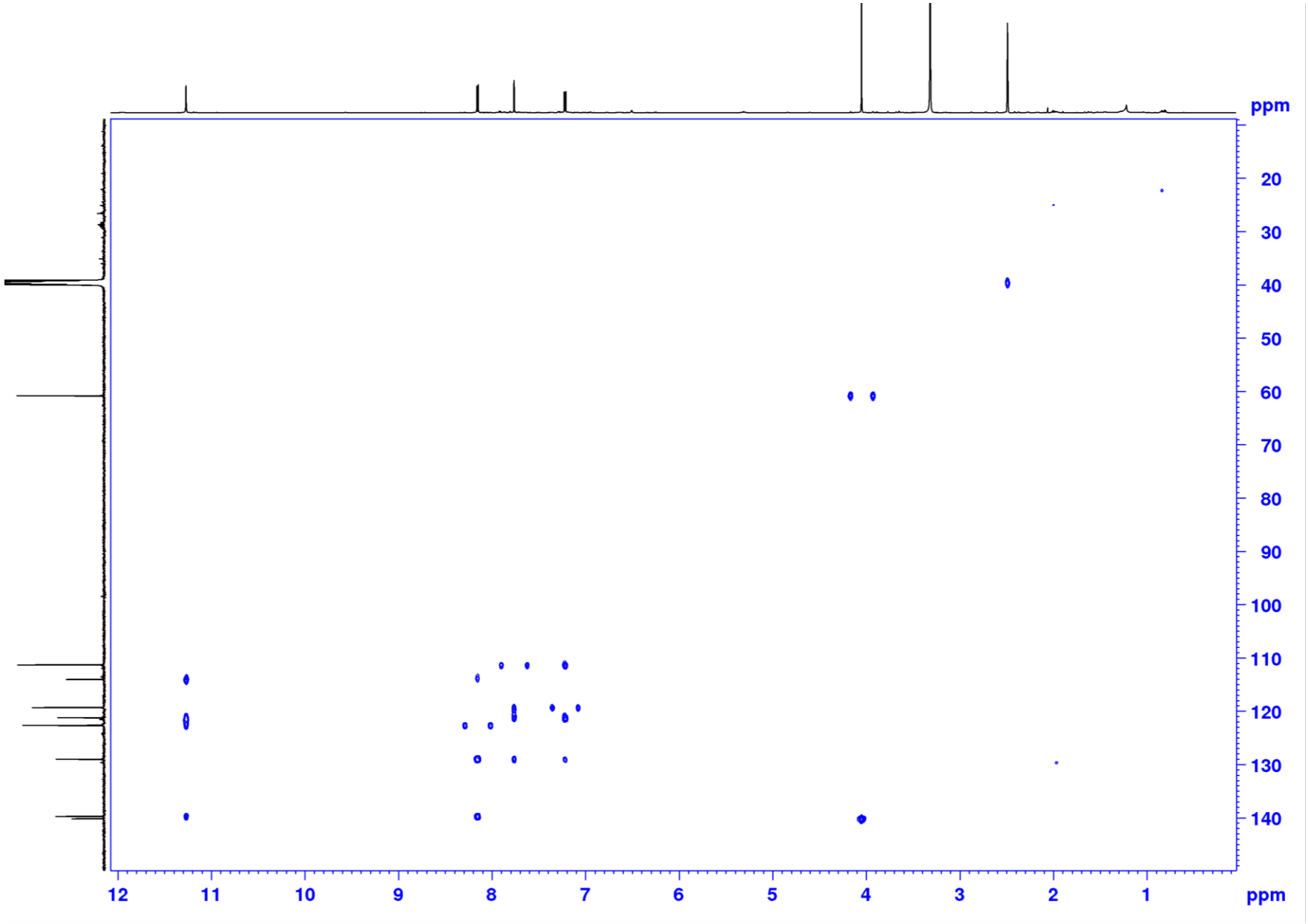


Figure S21. ^{1}H-^{13}C HMBC NMR spectrum (600 MHz, DMSO-d_6) of borregomycin E (**4**)

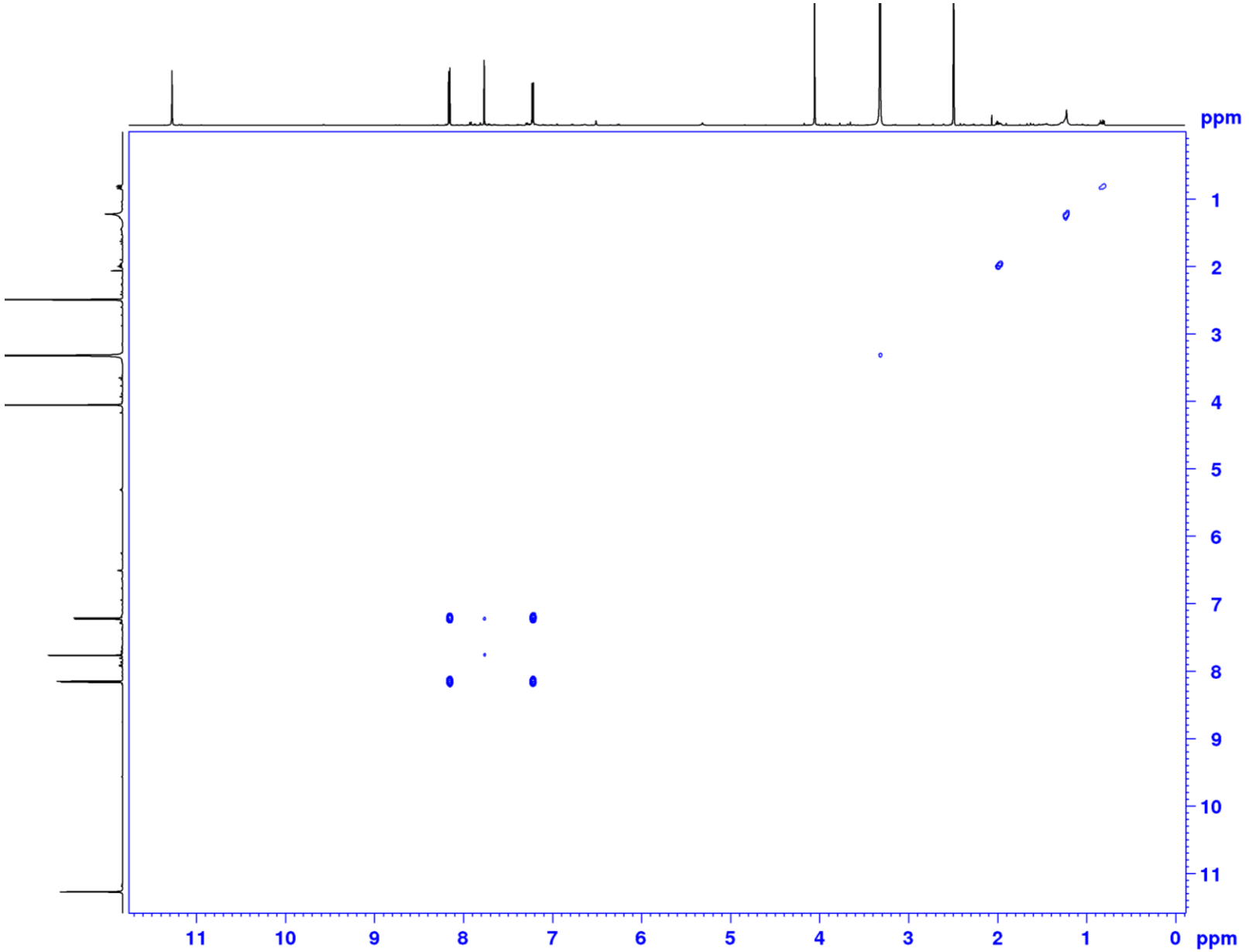


Figure S22. ^{1}H-^{1}H COSY NMR spectrum (600 MHz, DMSO-d_6) of borregomycin E (**4**)

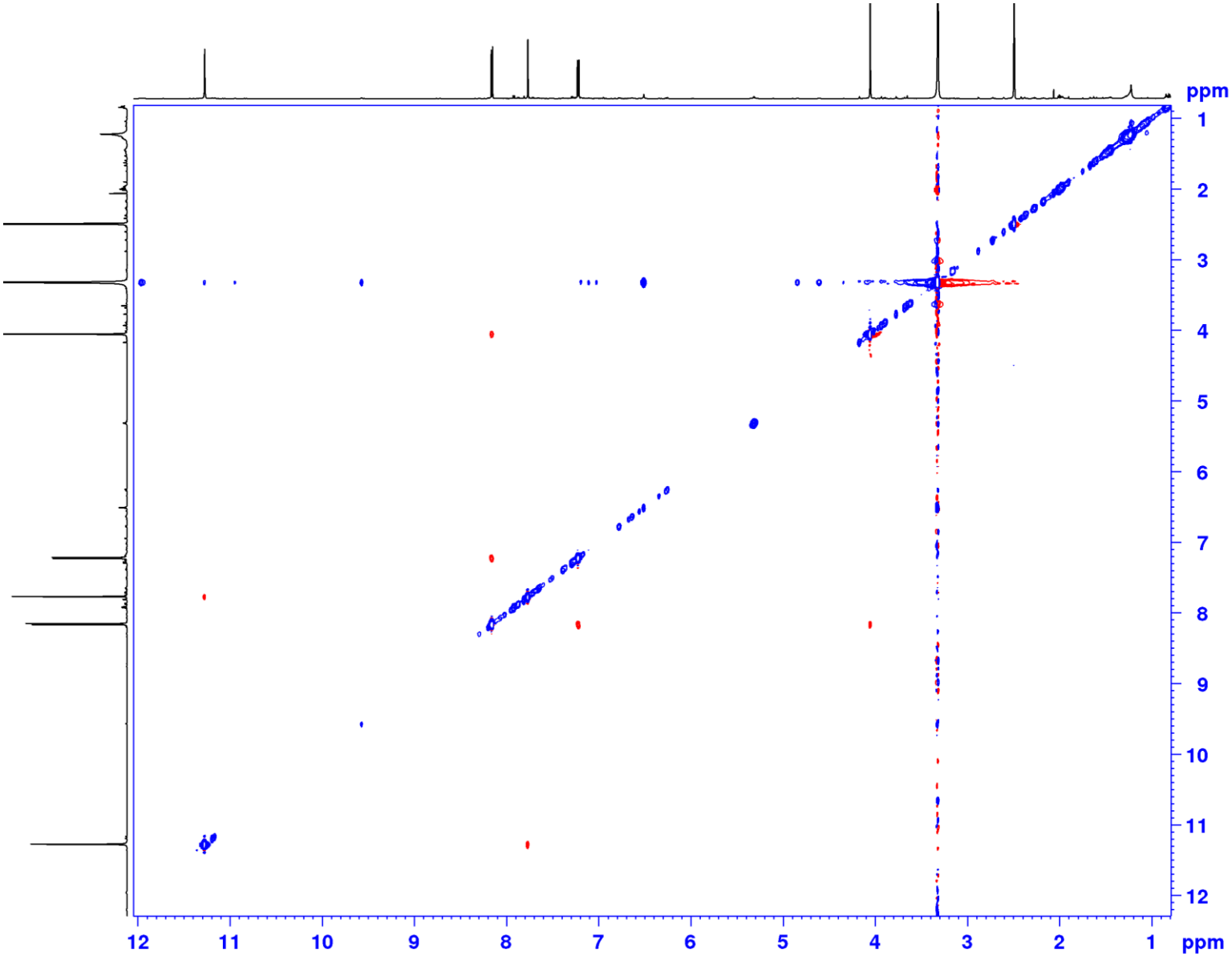


Figure S23. ^{1}H-^{1}H ROESY NMR spectrum (600 MHz, DMSO-d_6) of borregomycin E (**4**)

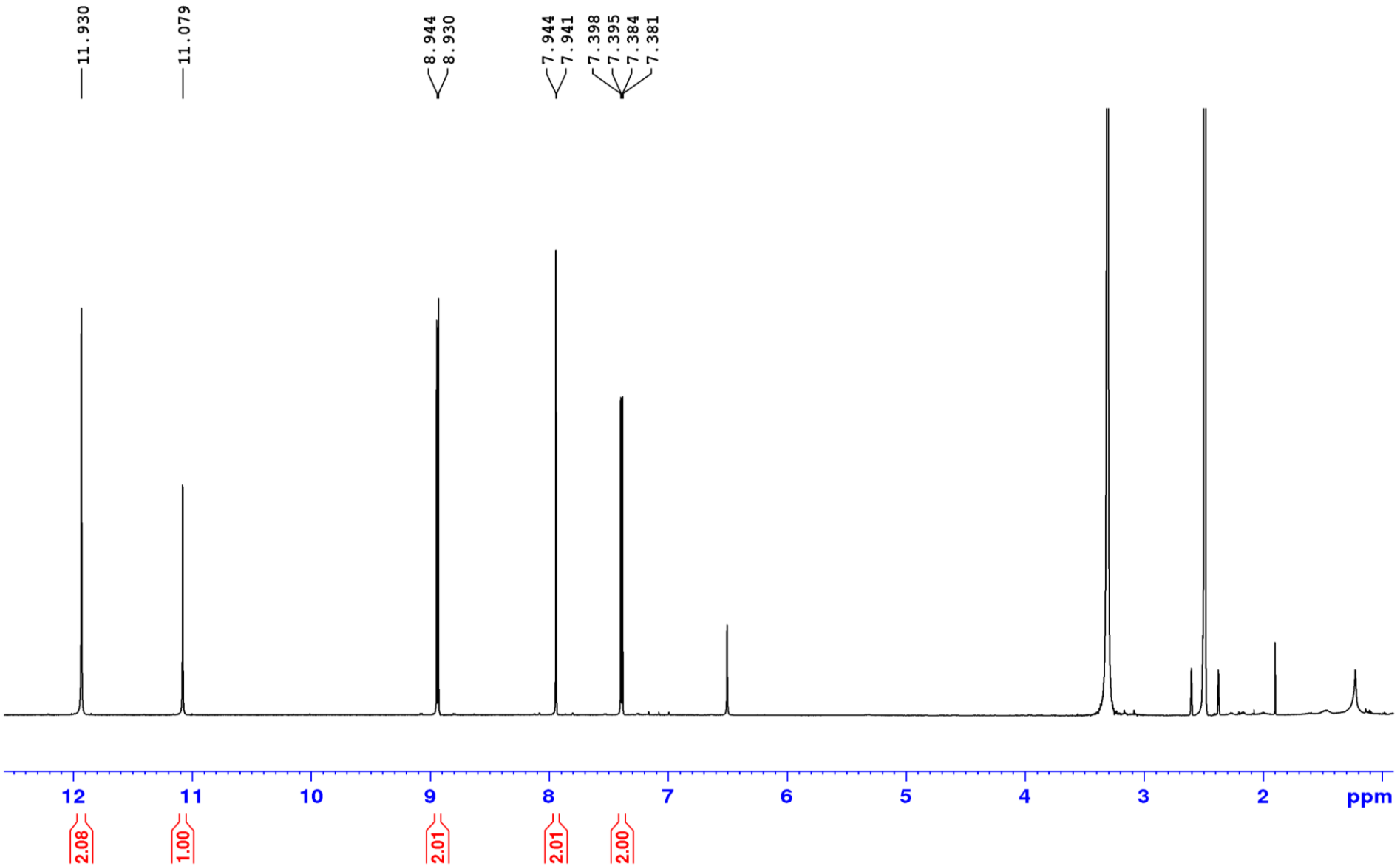


Figure S24. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of borregomycin F (**5**)

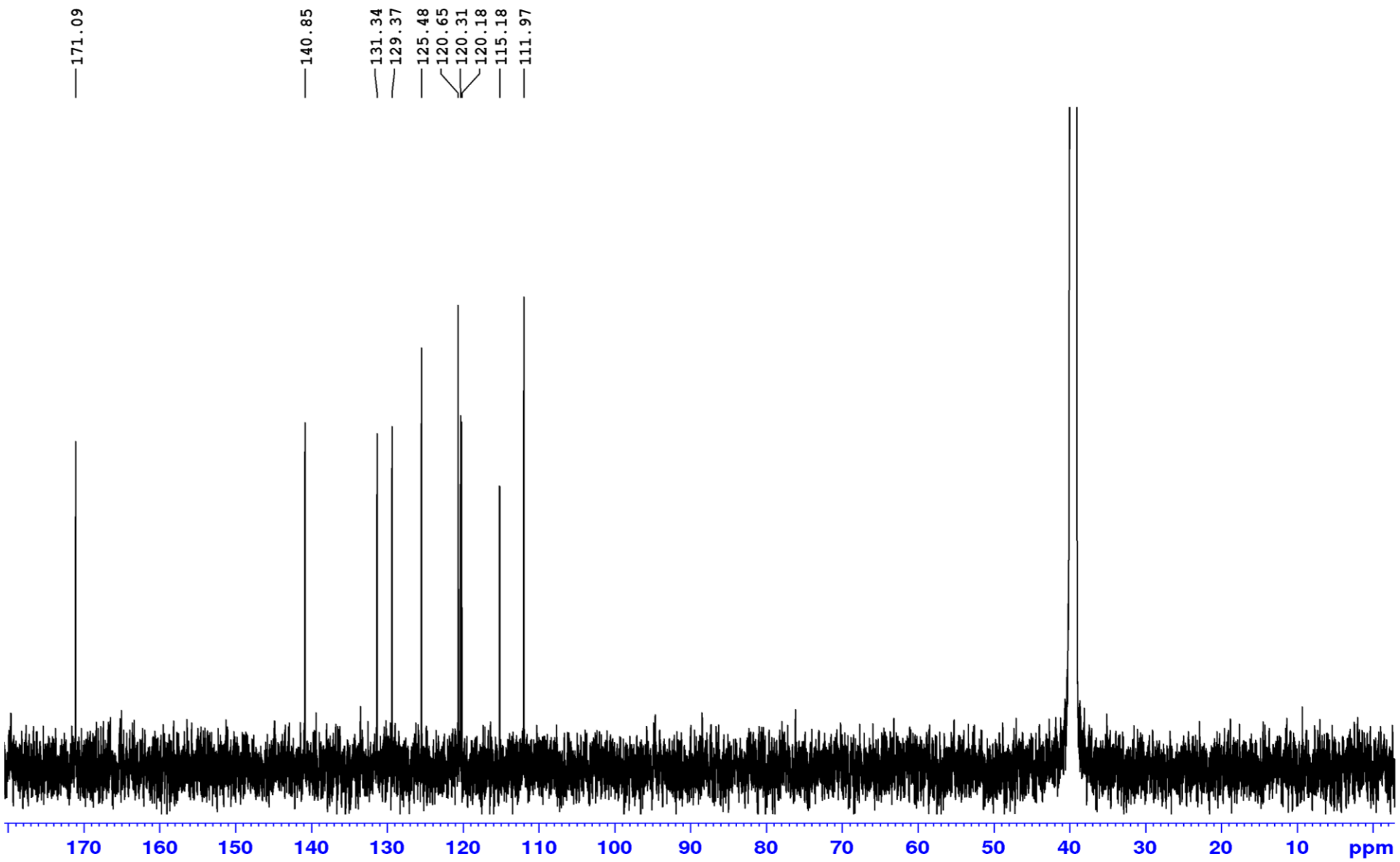


Figure S25. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of borregomycin F (**5**)

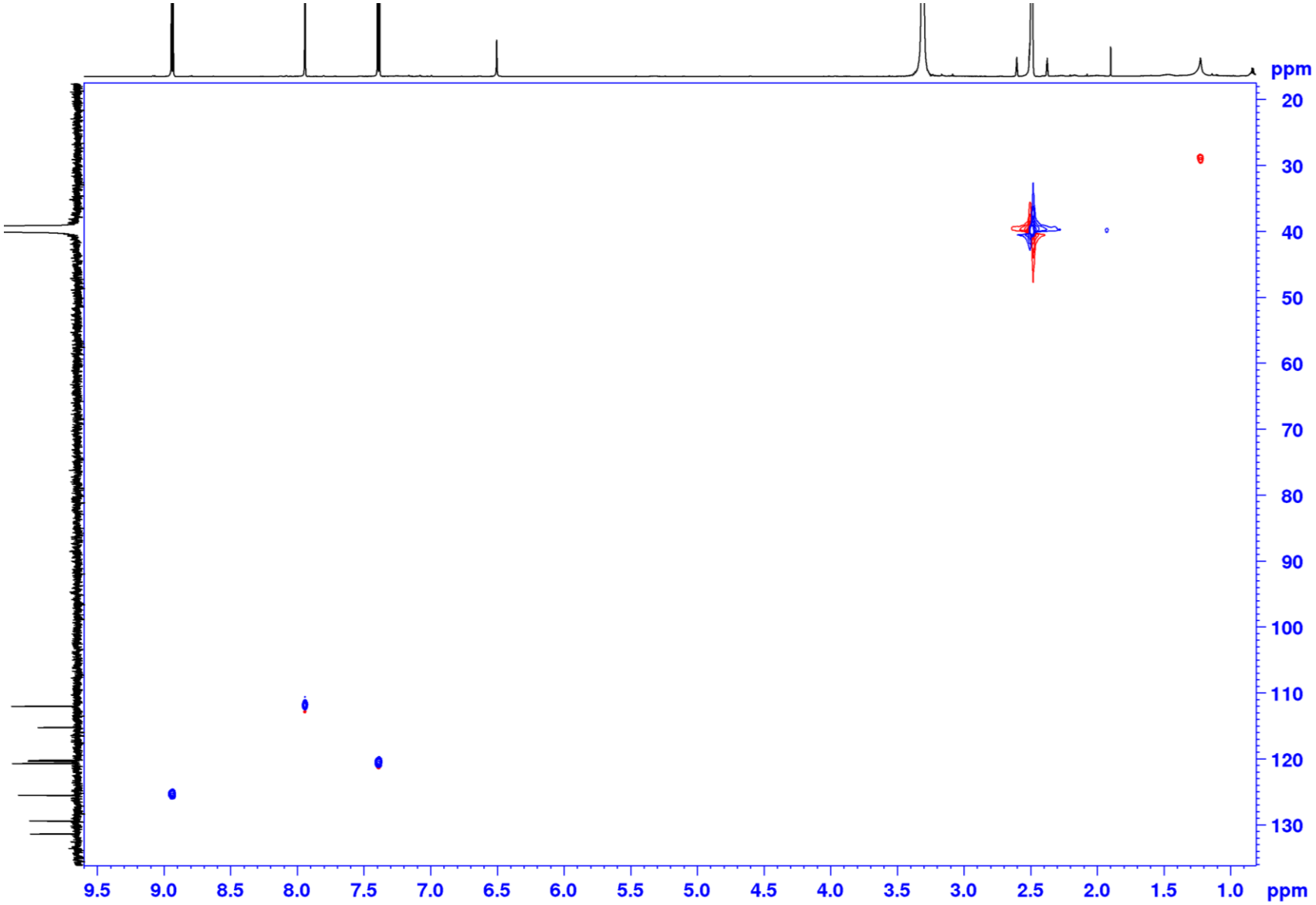


Figure S26. ^{1}H-^{13}C HSQC NMR spectrum (600 MHz, DMSO-d_6) of borregomycin F (**5**)

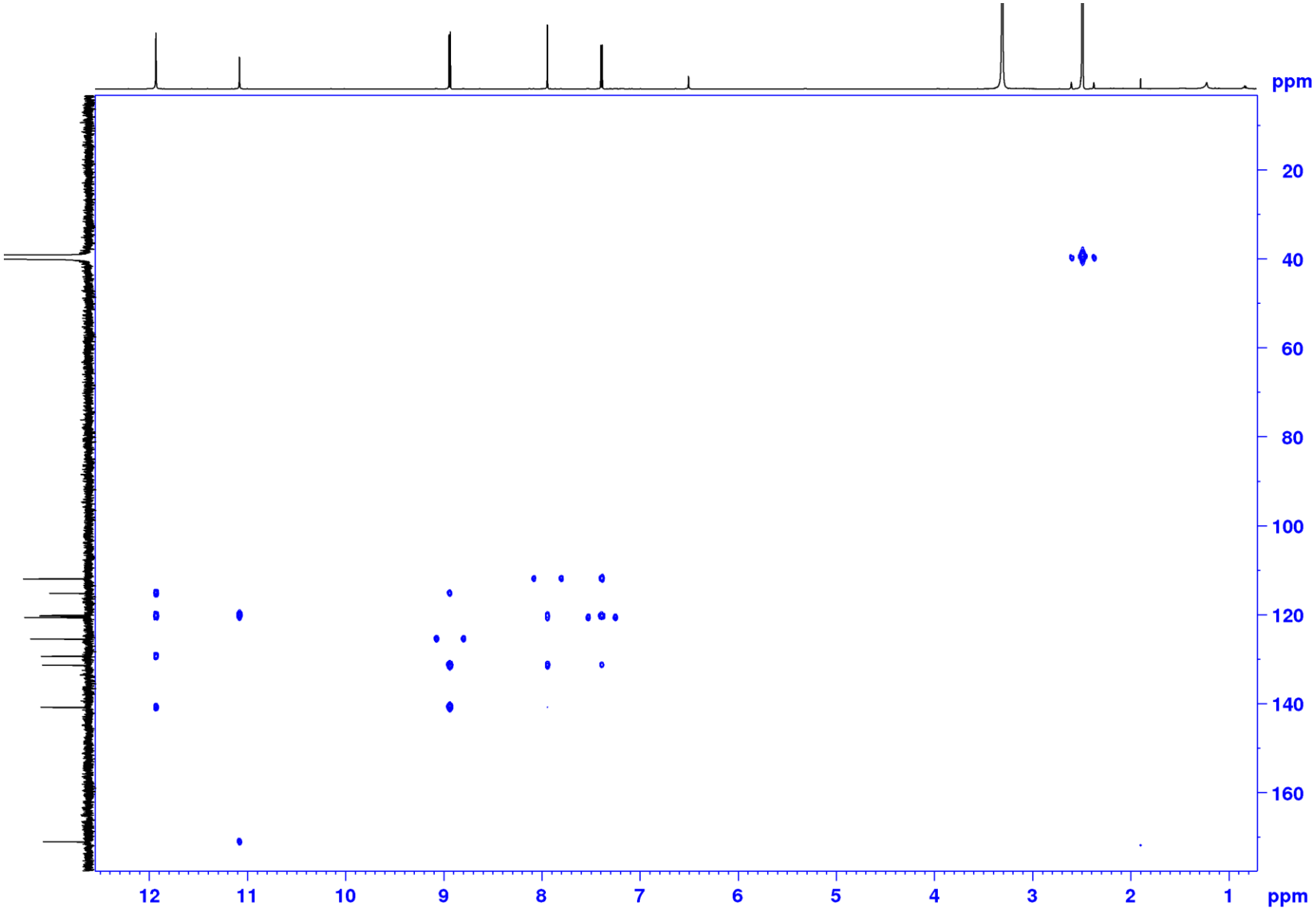


Figure S27. ^{1}H-^{13}C HMBC NMR spectrum (600 MHz, DMSO-d_6) of borregomycin F (**5**)

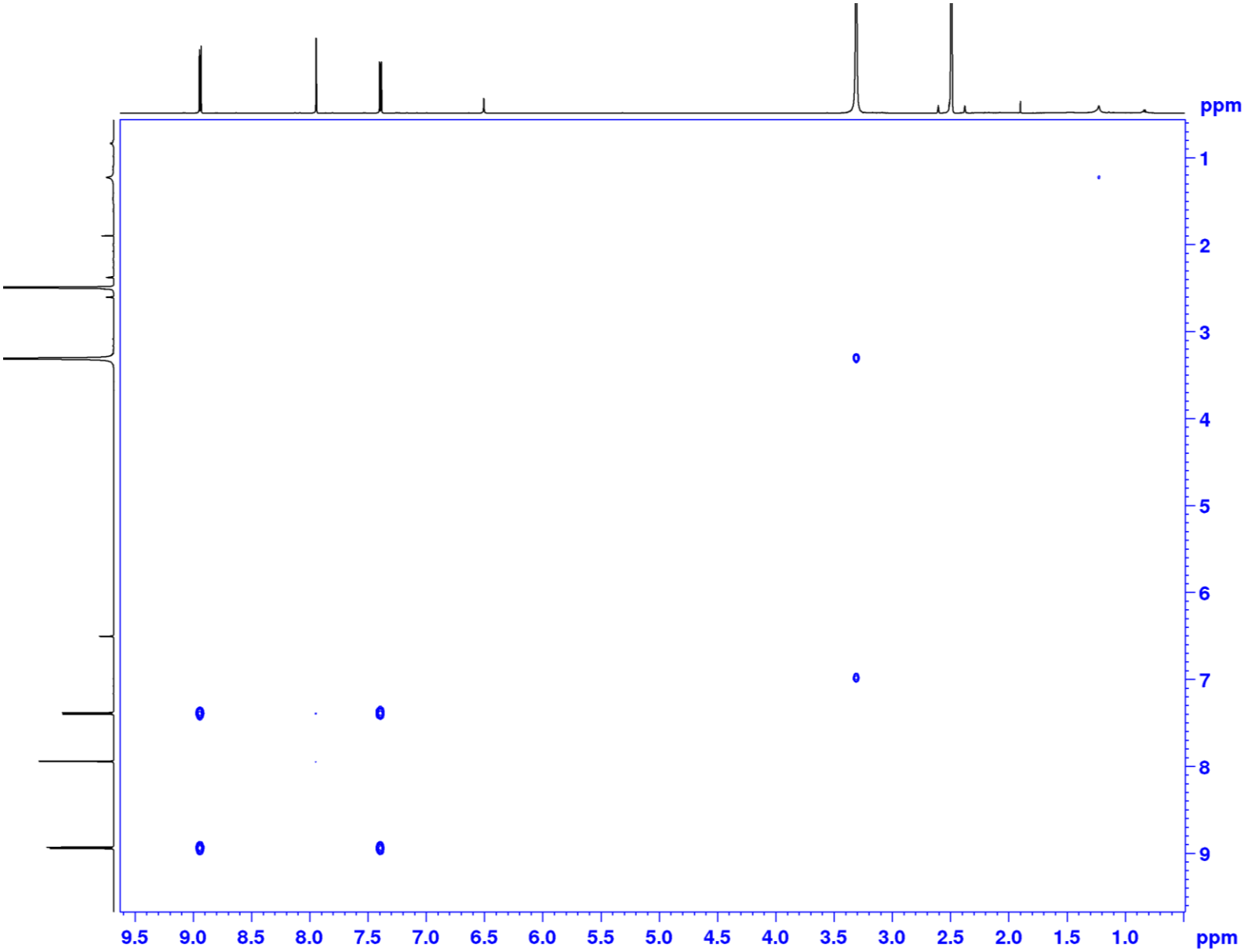


Figure S28. ^{1}H-^{1}H COSY NMR spectrum (600 MHz, DMSO-d_6) of borregomycin F (**5**)

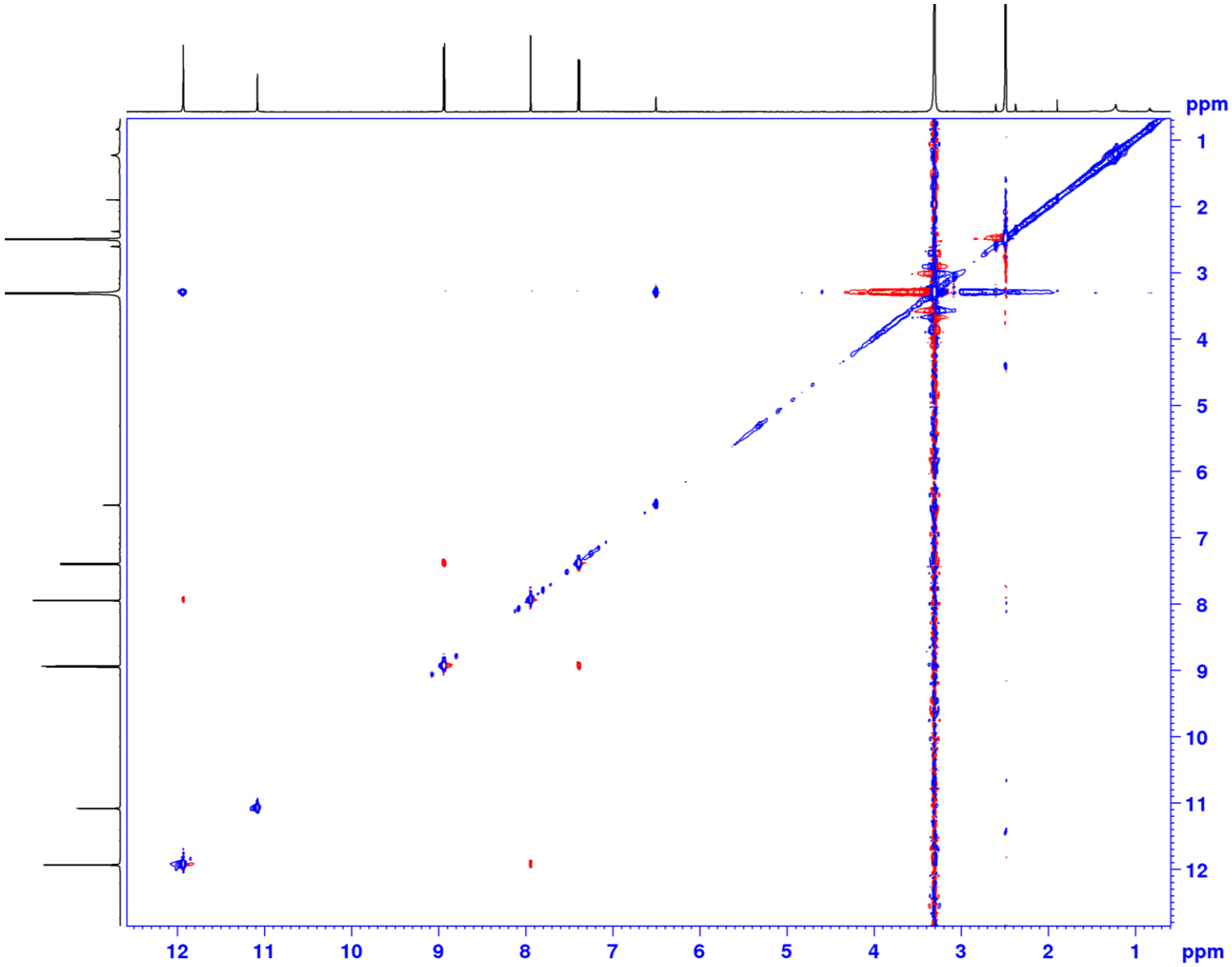


Figure S29. ^{1}H-^{1}H ROESY NMR spectrum (600 MHz, DMSO-d_6) of borregomycin F (**5**)

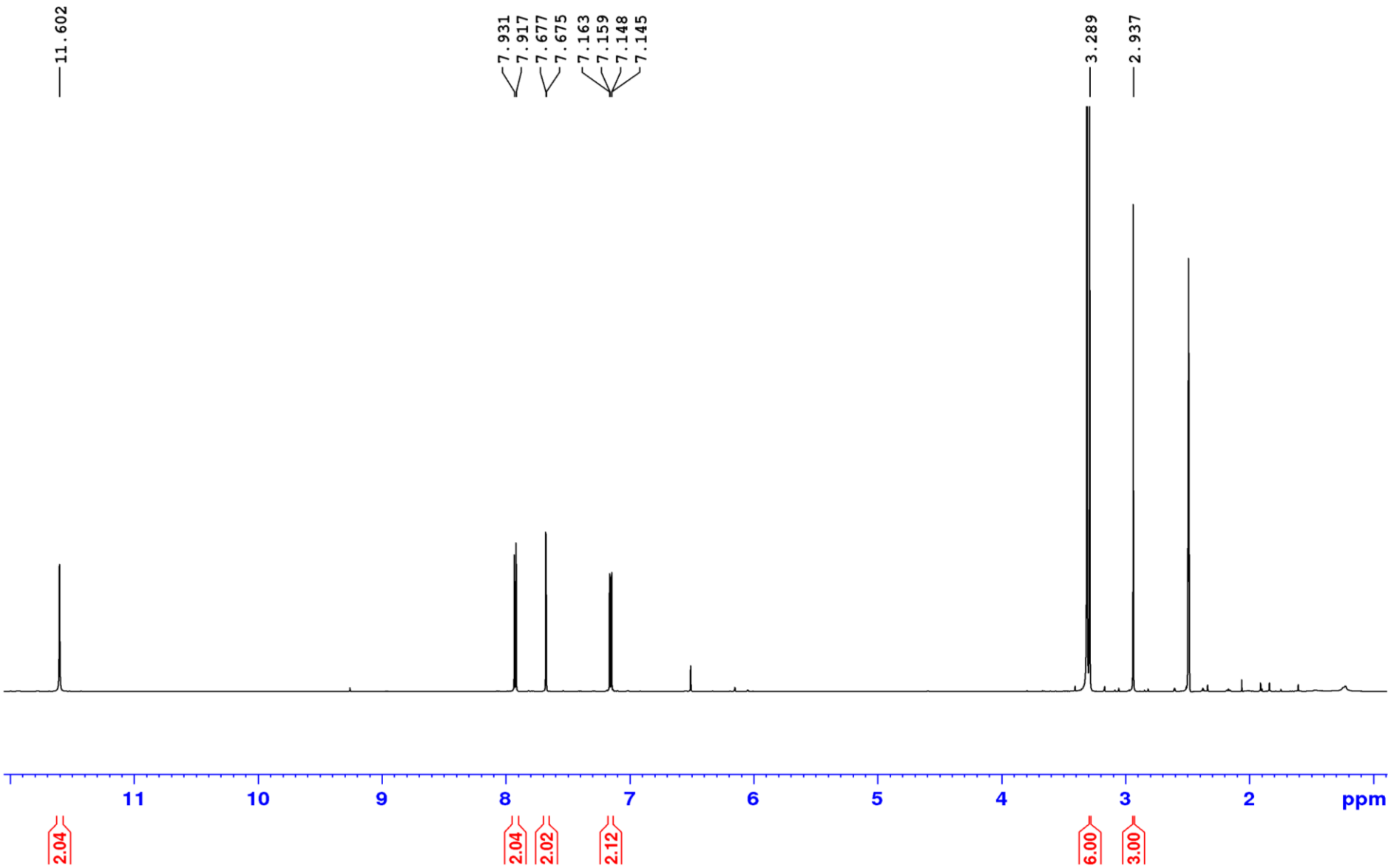


Figure S30. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of borregomycin B (**6**)

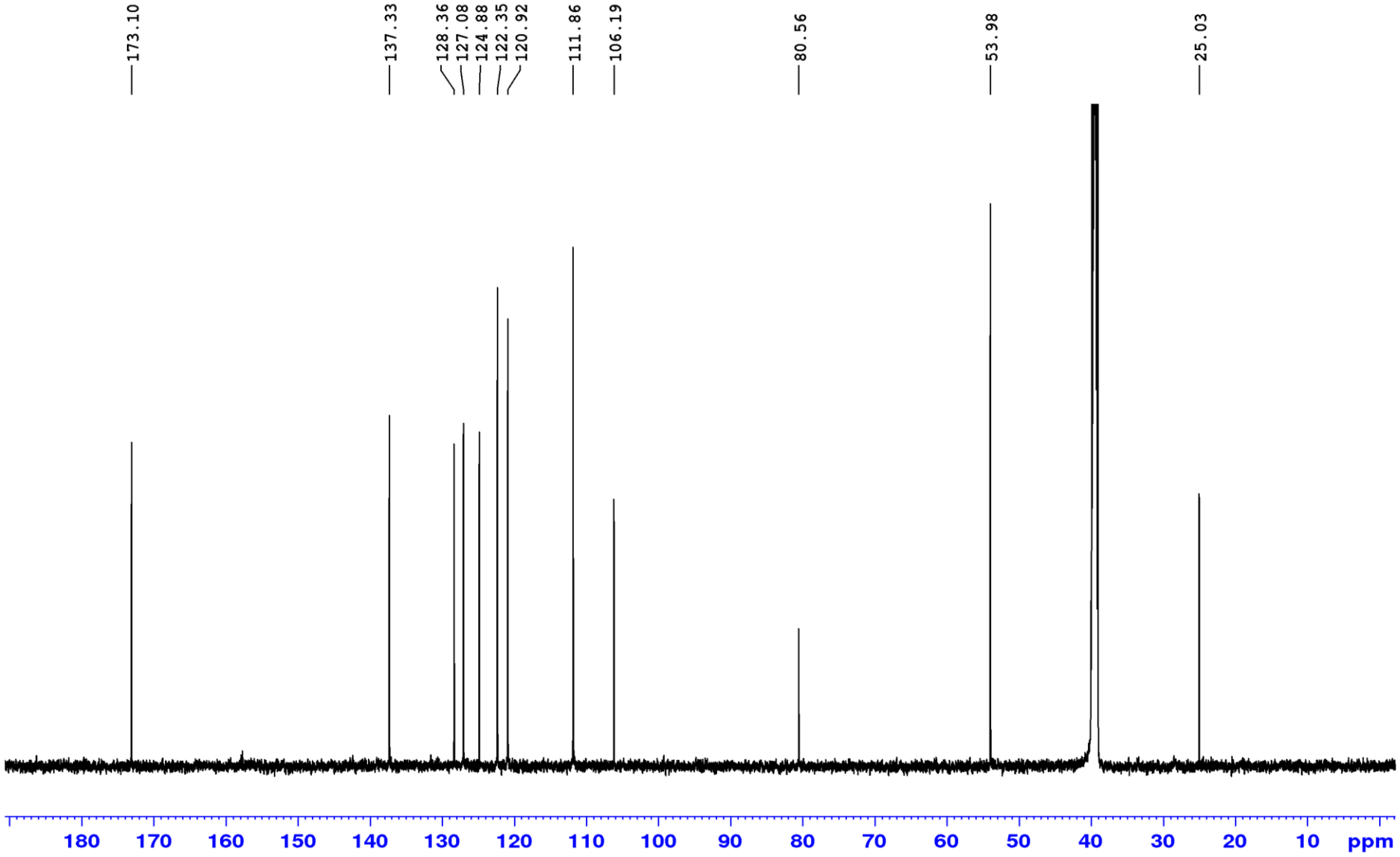


Figure S31. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of borregomycin B (**6**)

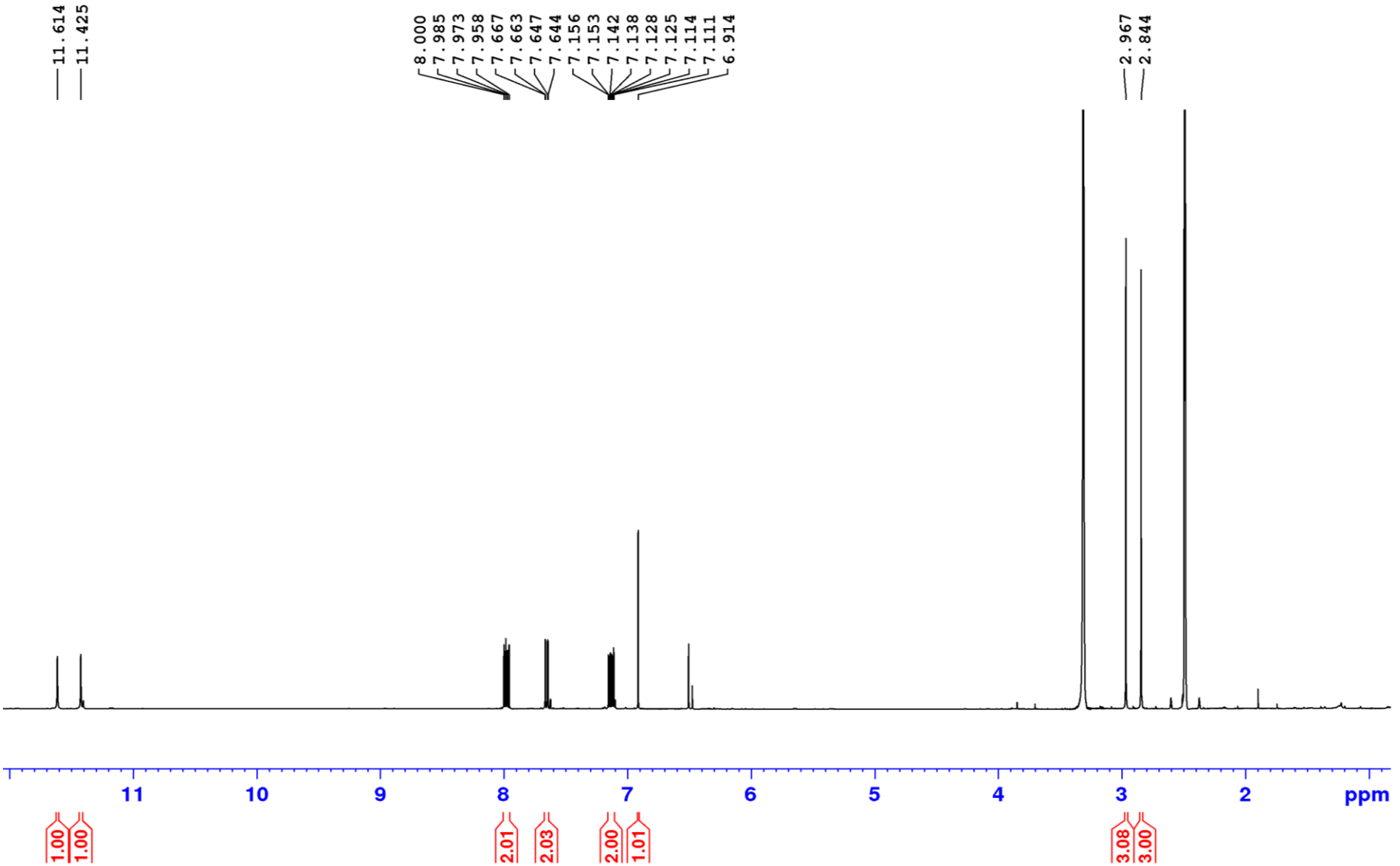


Figure S32. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of borregomycin C (**7**)

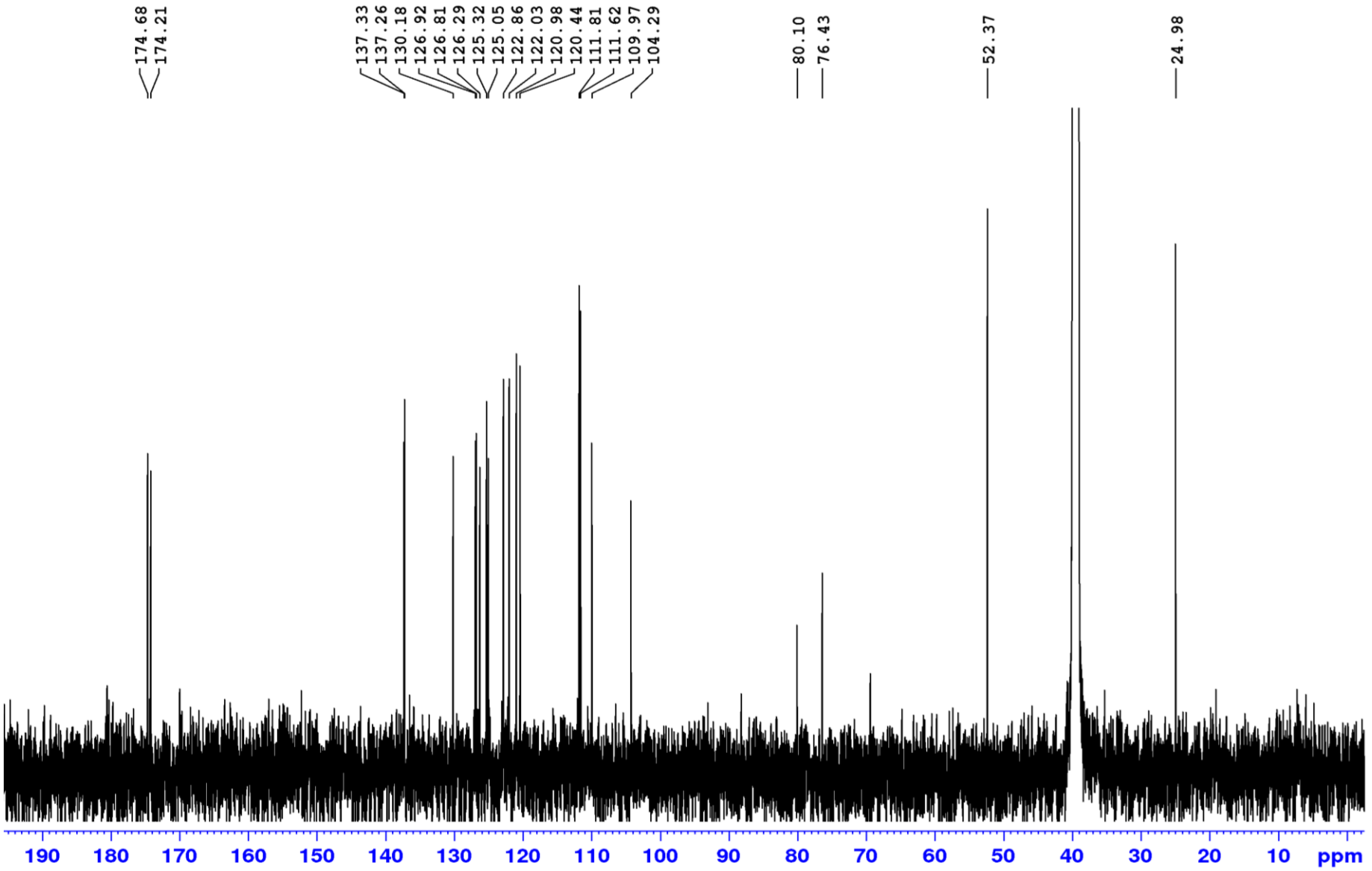


Figure S33. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of borregomycin C (**7**)

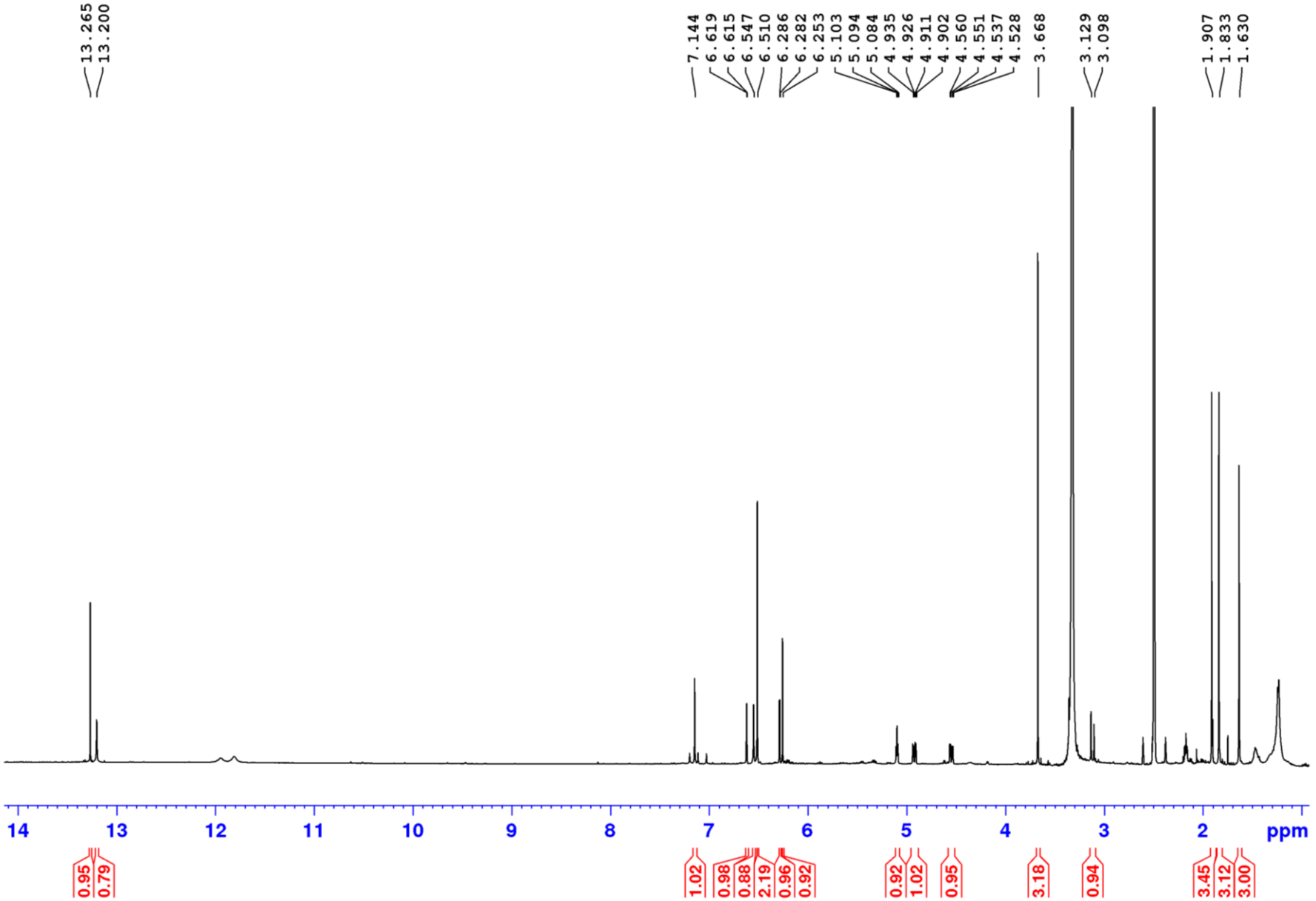


Figure S34. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of (+)-ABX-G (**8**)

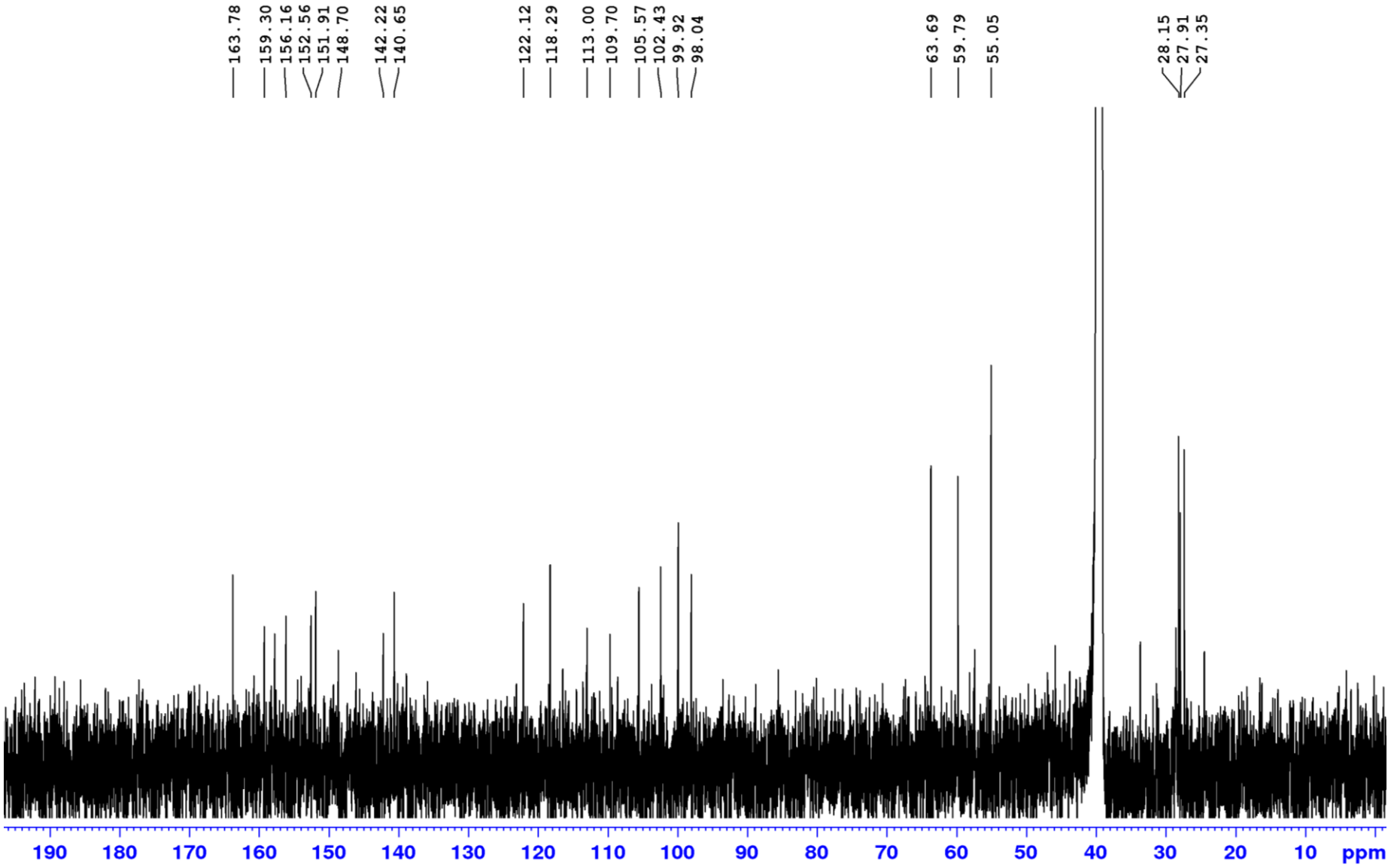


Figure S35. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of (+)-ABX-G (**8**)

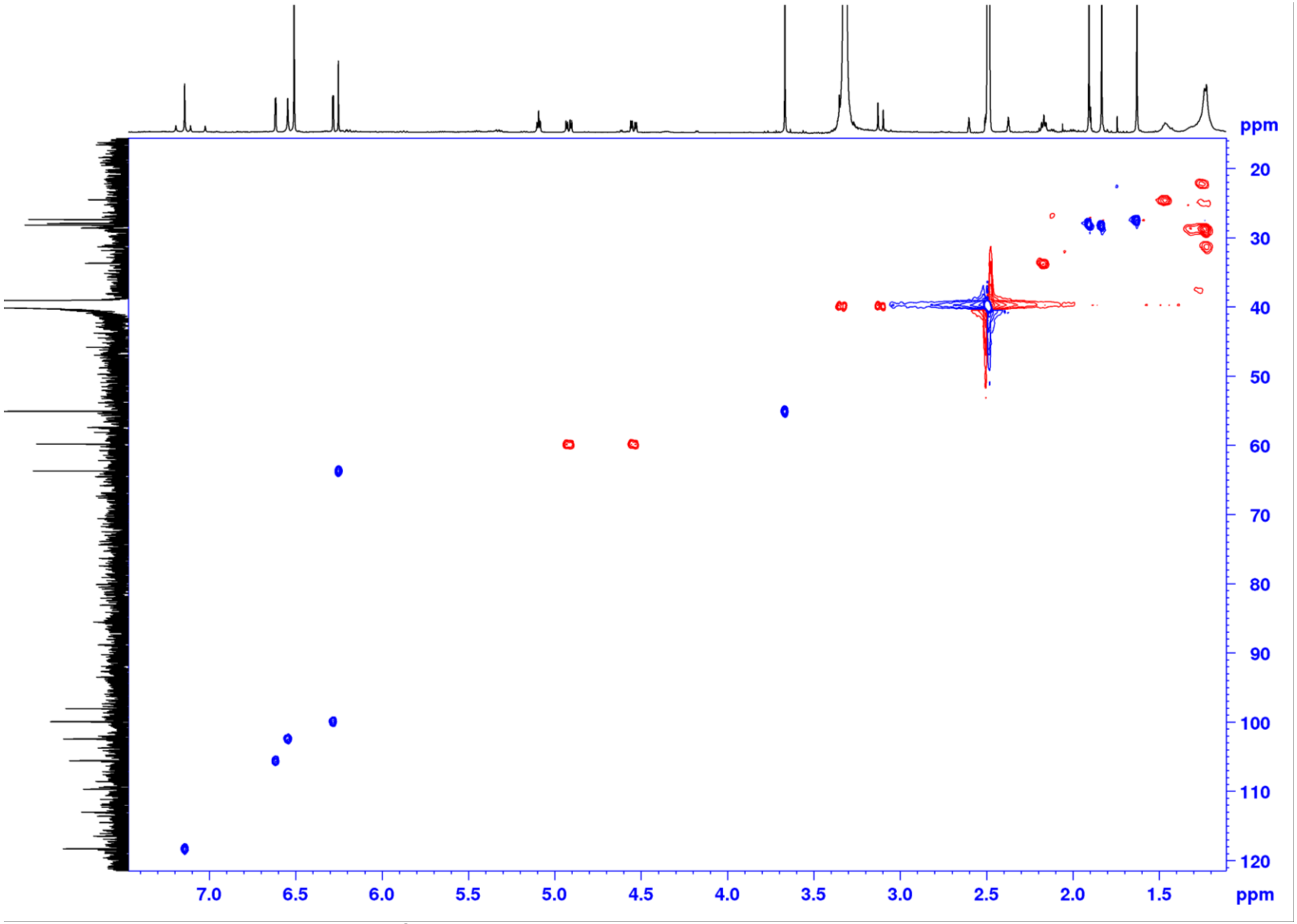


Figure S36. ^{1}H-^{13}C HSQC NMR spectrum (600 MHz, DMSO-d_6) of (+)-ABX-G (**8**)

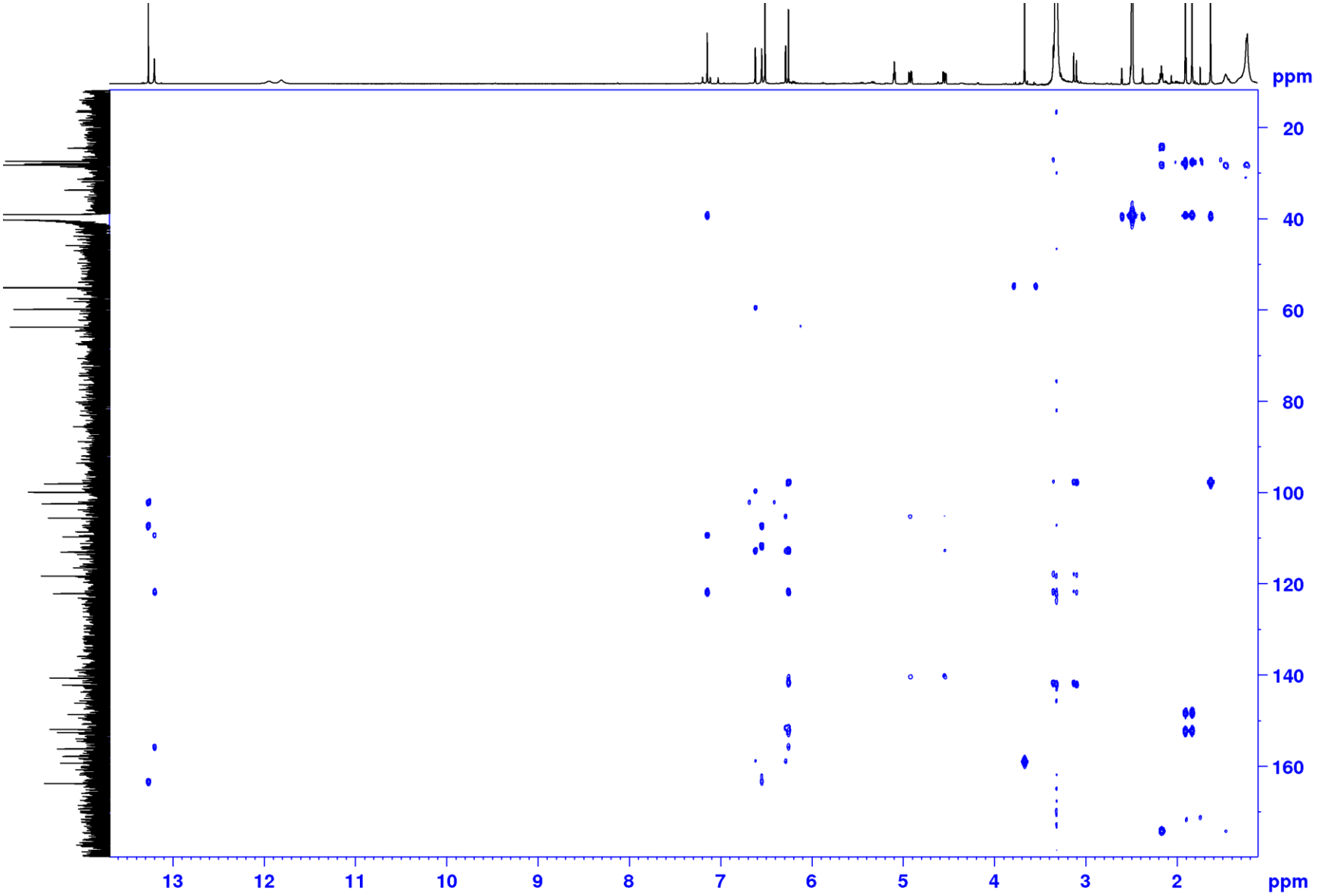


Figure S37. ^{1}H-^{13}C HMBC NMR spectrum (600 MHz, DMSO-d_6) of (+)-ABX-G (**8**)

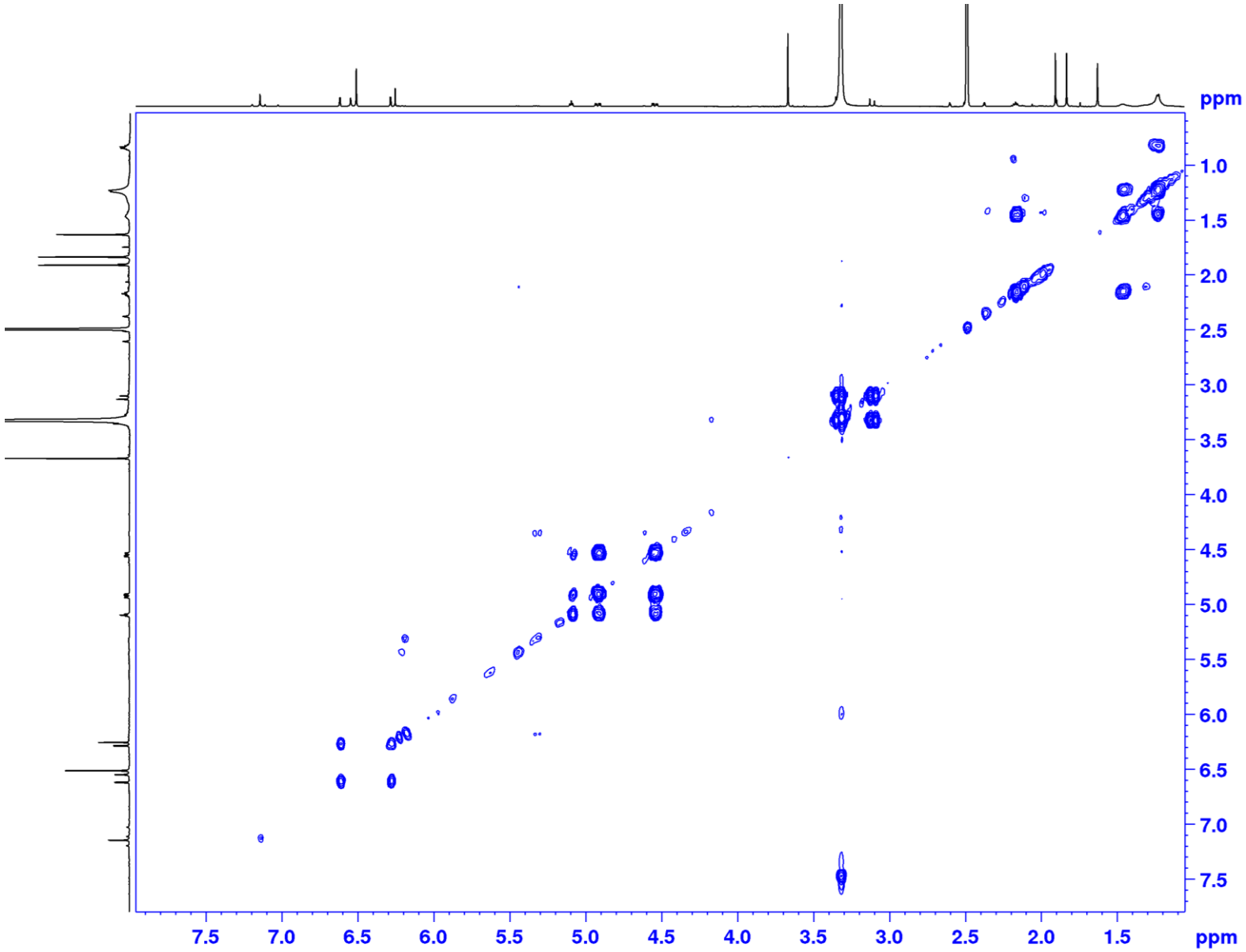


Figure S38. ^{1}H-^{1}H COSY NMR spectrum (600 MHz, DMSO-d_6) of (+)-ABX-G (**8**)

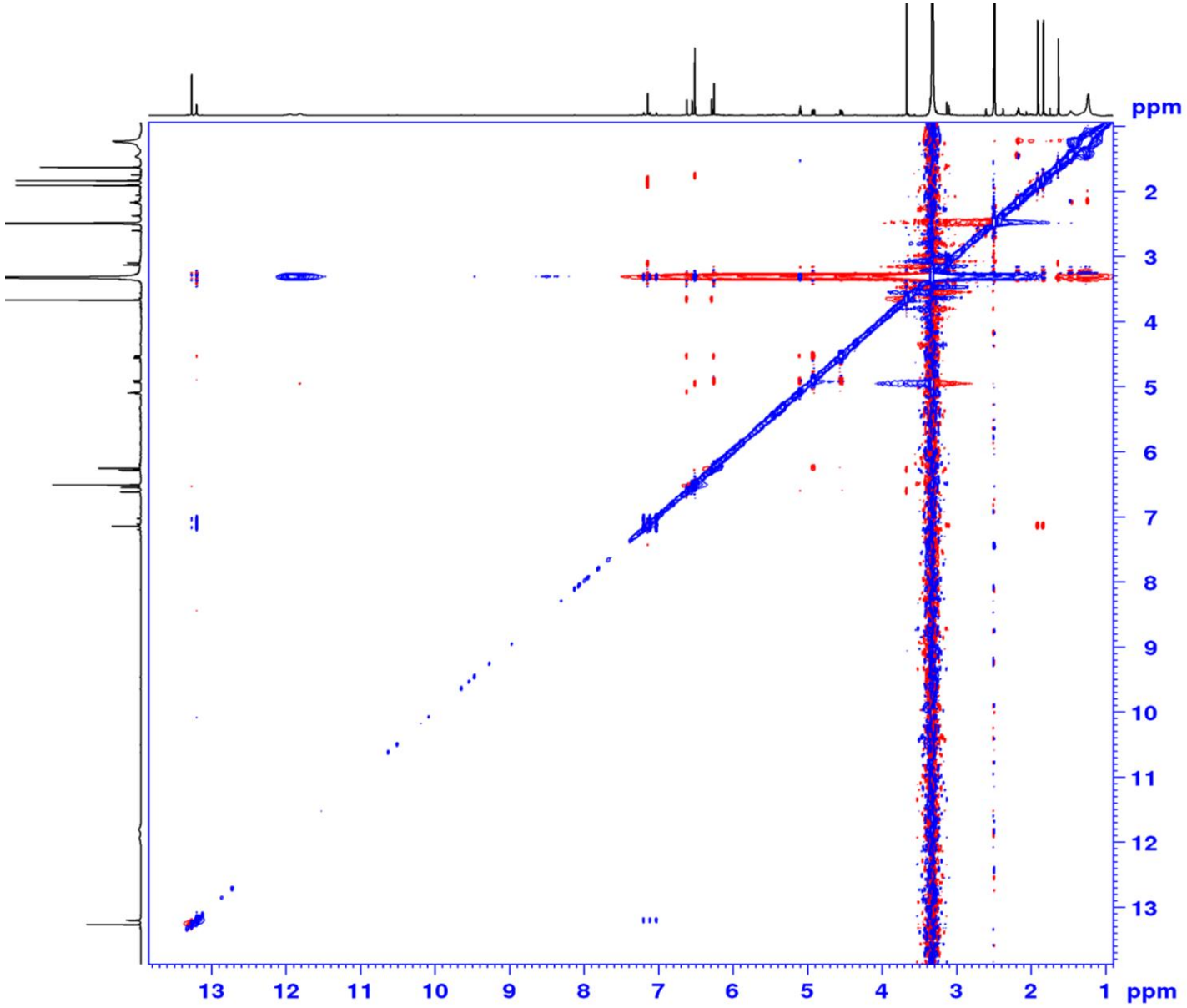


Figure S39. ^{1}H-^{1}H ROESY NMR spectrum (600 MHz, DMSO-d_6) of (+)-ABX-G (**8**)

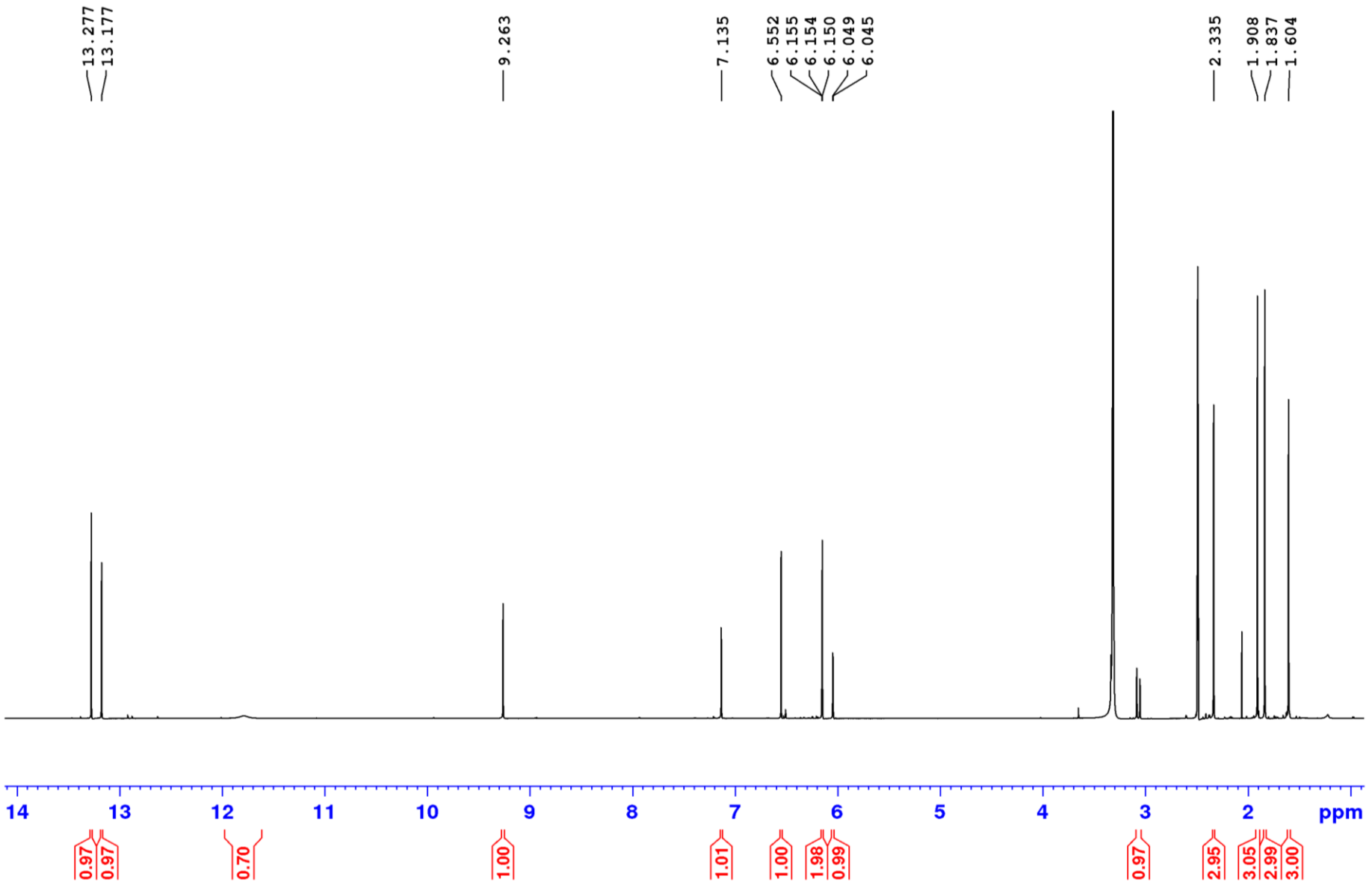


Figure S40. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of (–)-ABX-K (**9**)

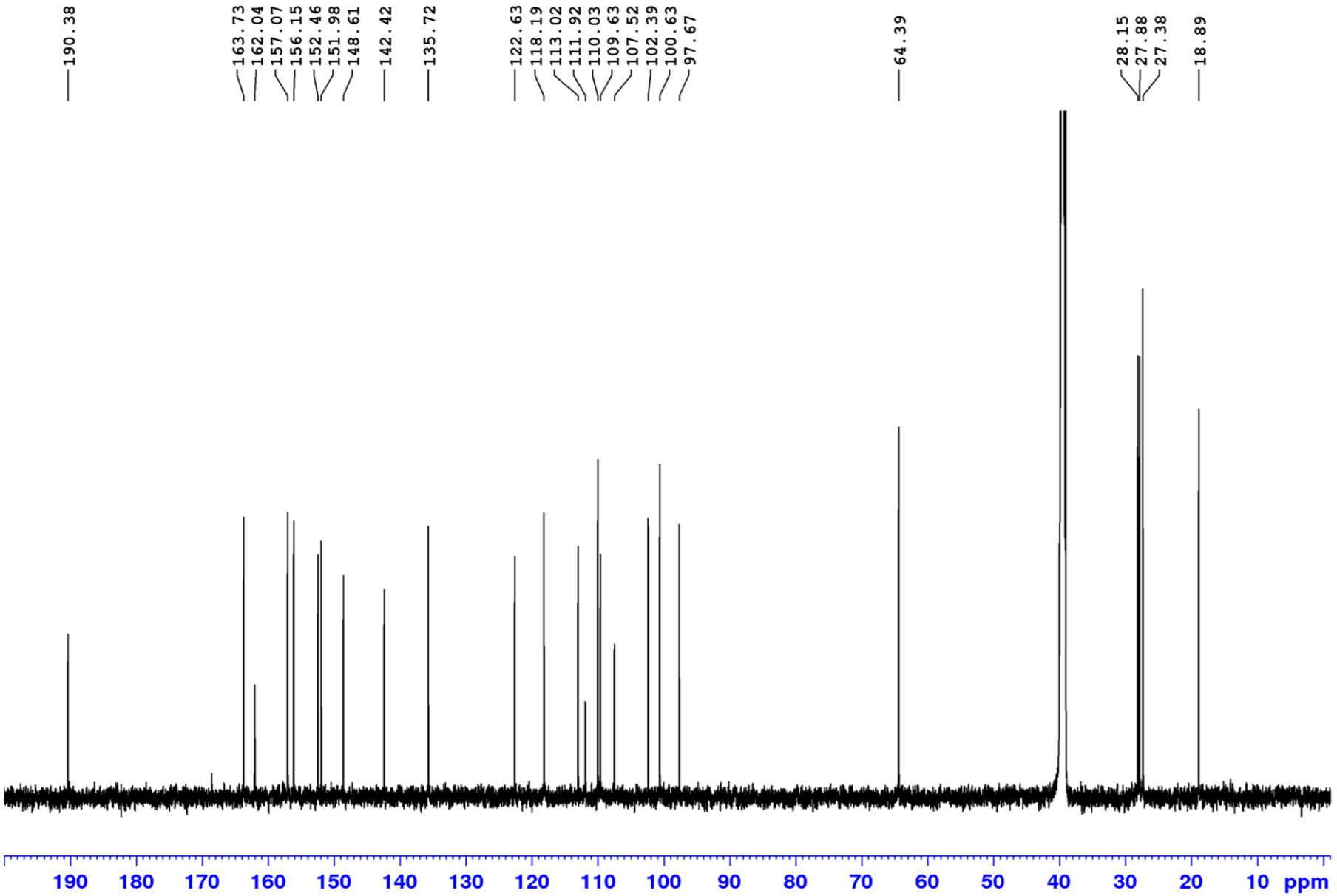


Figure S41. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of (–)-ABX-K (**9**)

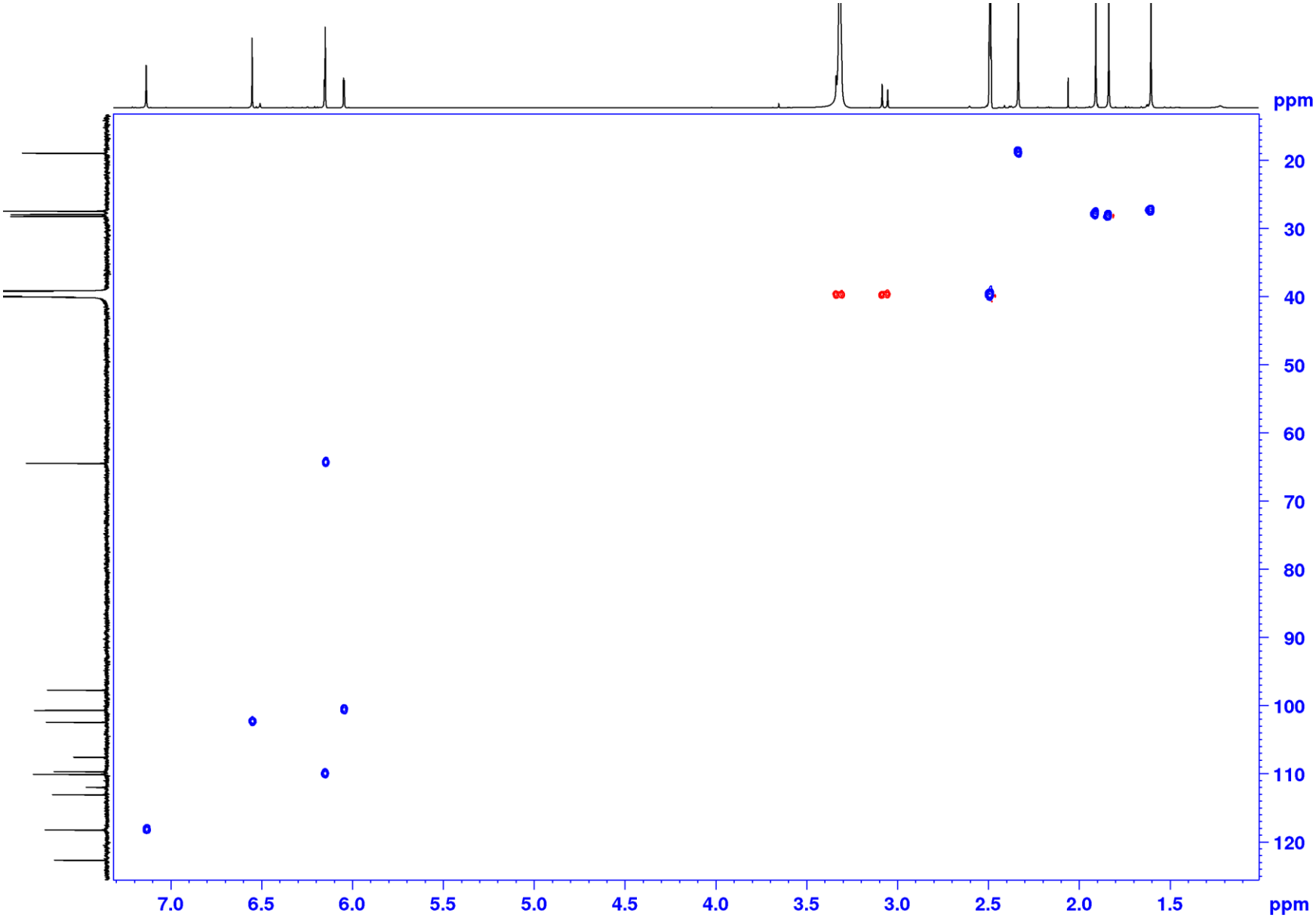


Figure S42. ^{1}H-^{13}C HSQC NMR spectrum (600 MHz, DMSO-d_6) of (–)-ABX-K (**9**)

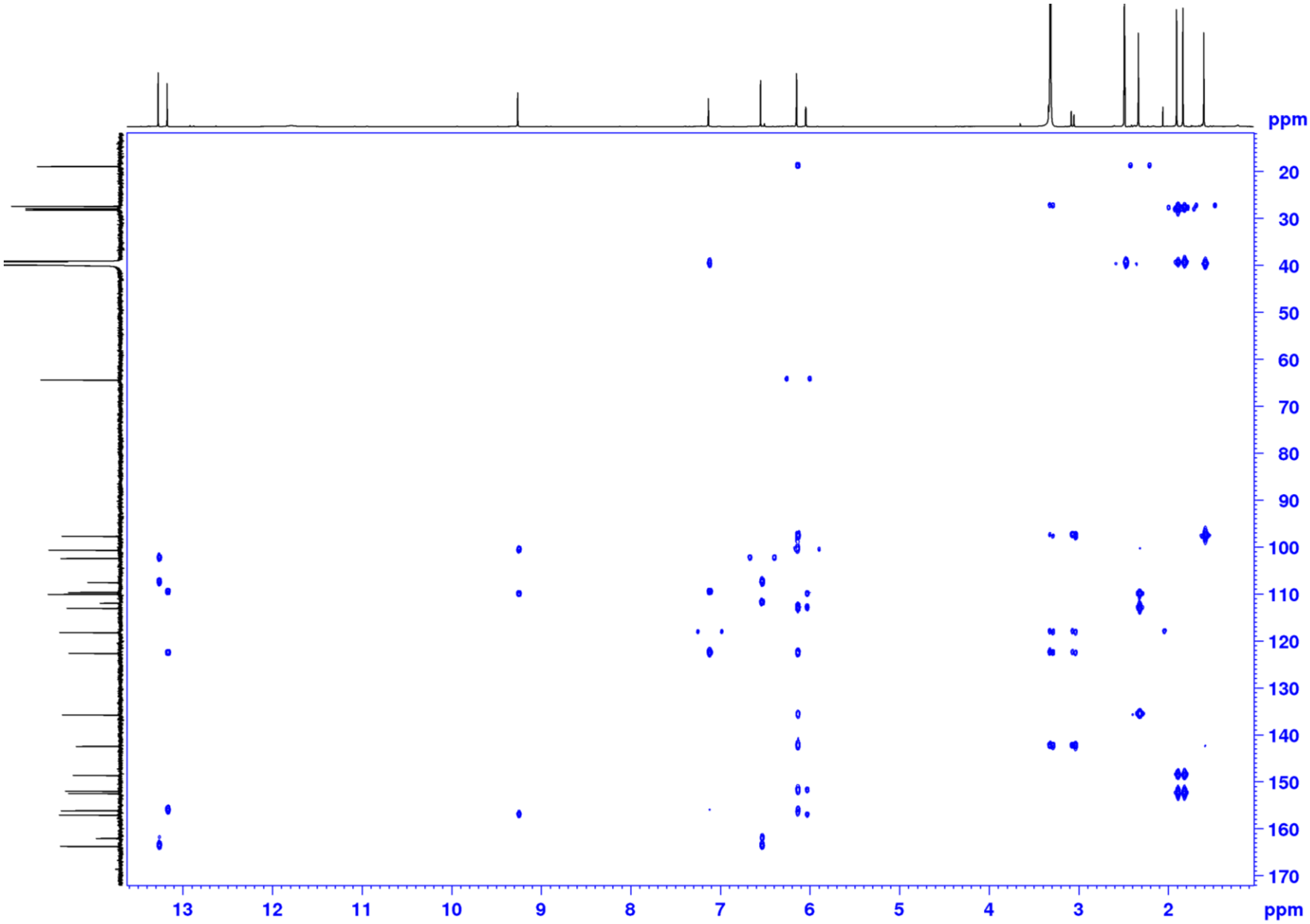


Figure S43. ^{1}H-^{13}C HMBC NMR spectrum (600 MHz, DMSO-d_6) of (–)-ABX-K (**9**)

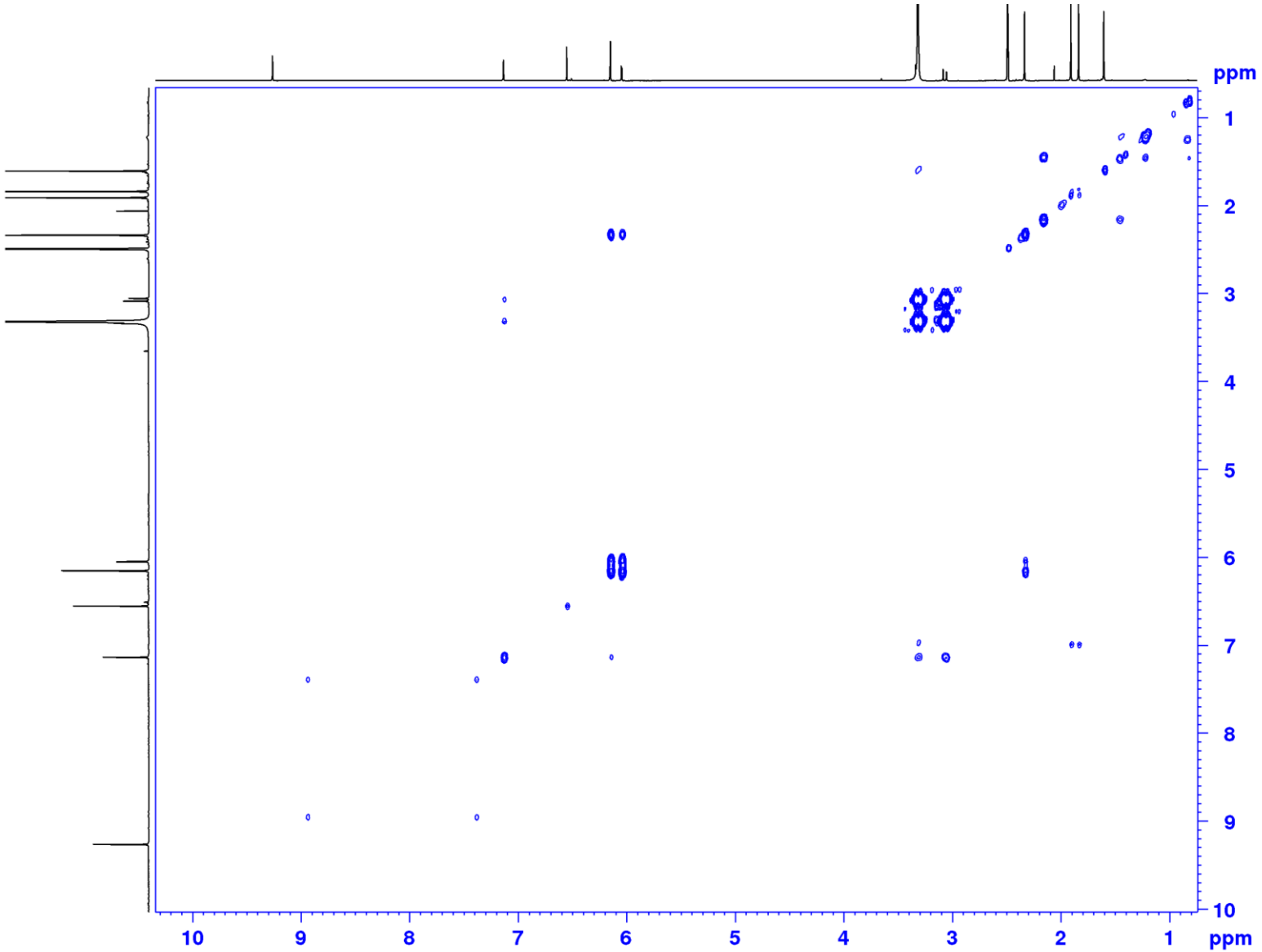


Figure S44. ^{1}H-^{1}H COSY NMR spectrum (600 MHz, DMSO-d_6) of (–)-ABX-K (**9**)

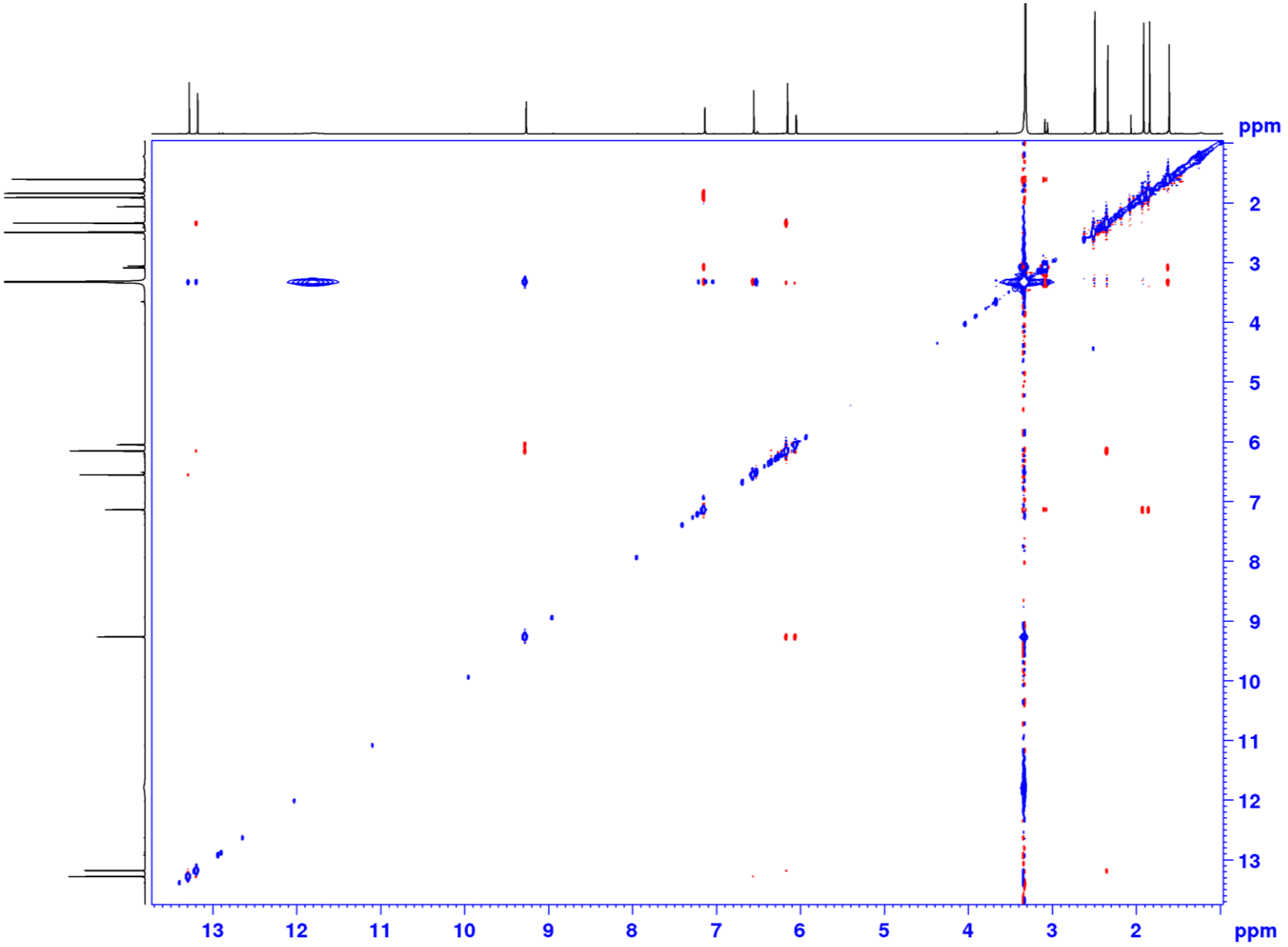


Figure S45. ^{1}H-^{1}H ROESY NMR spectrum (600 MHz, DMSO-d_6) of (–)-ABX-K (**9**)

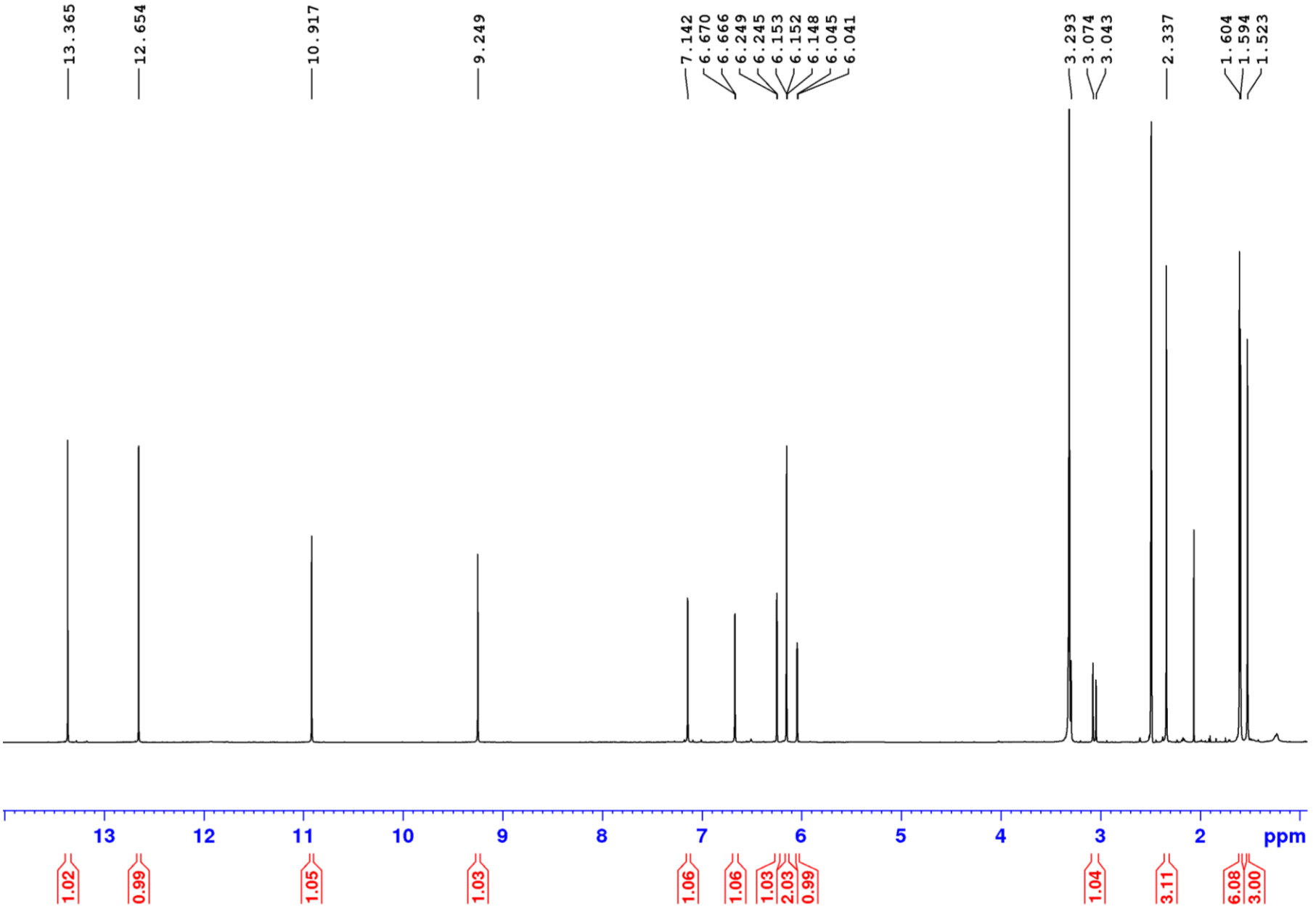


Figure S46. [1]H NMR spectrum (600 MHz, DMSO-d_6) of (–)-ABX-A (**10**)

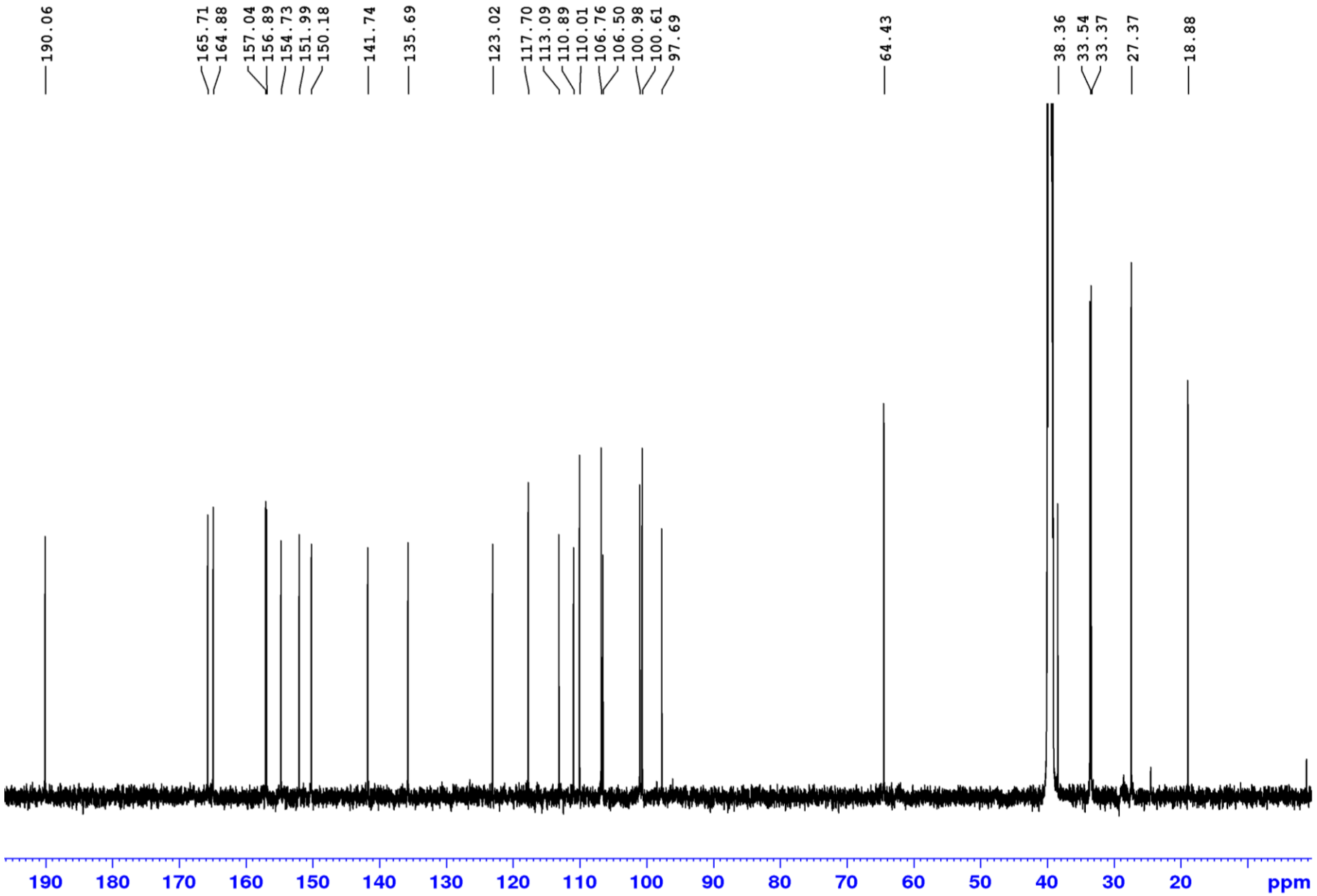


Figure S47. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of (–)-ABX-A (**10**)

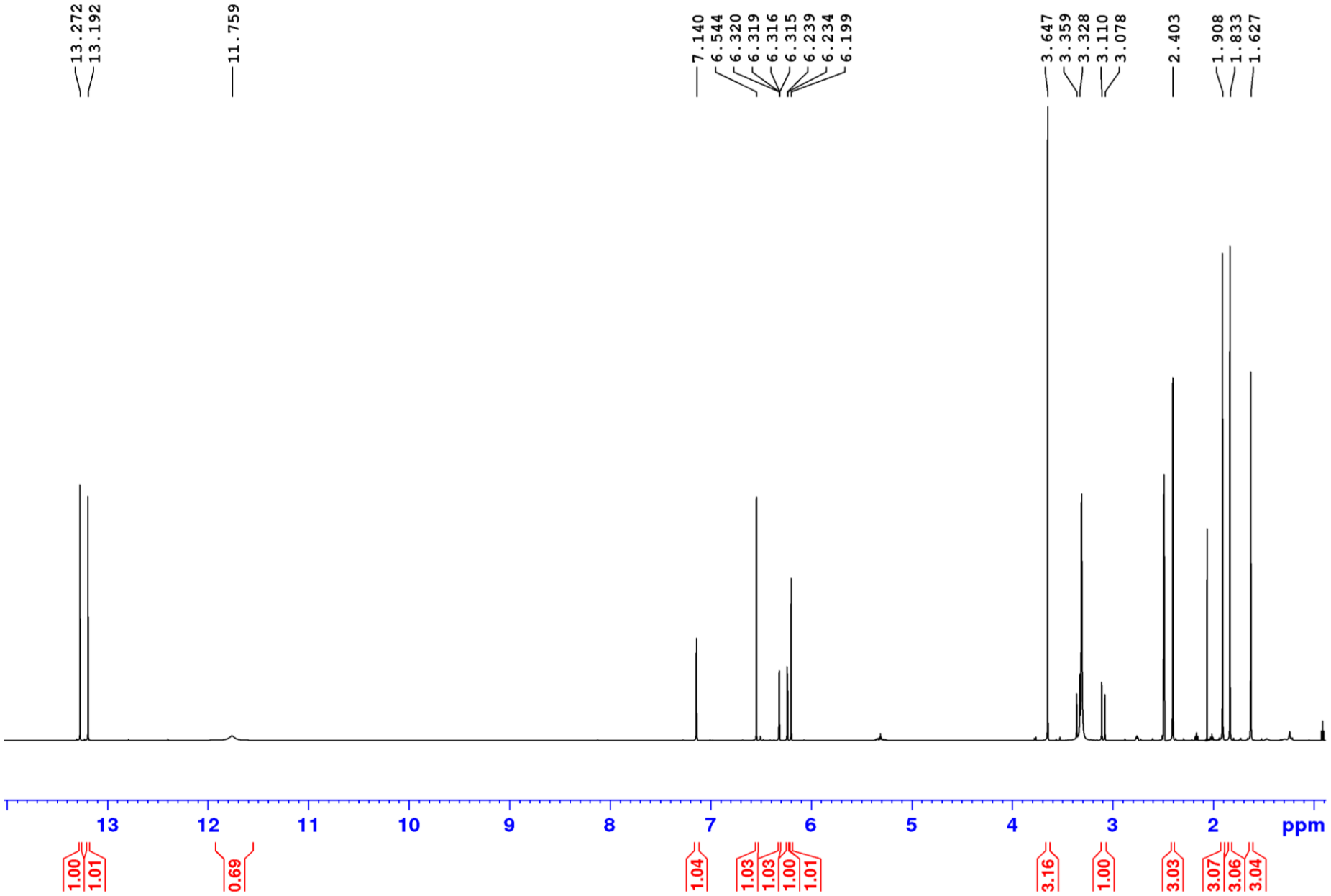


Figure S48. [1]H NMR spectrum (600 MHz, DMSO-d_6) of (–)-ABX-B (**11**)

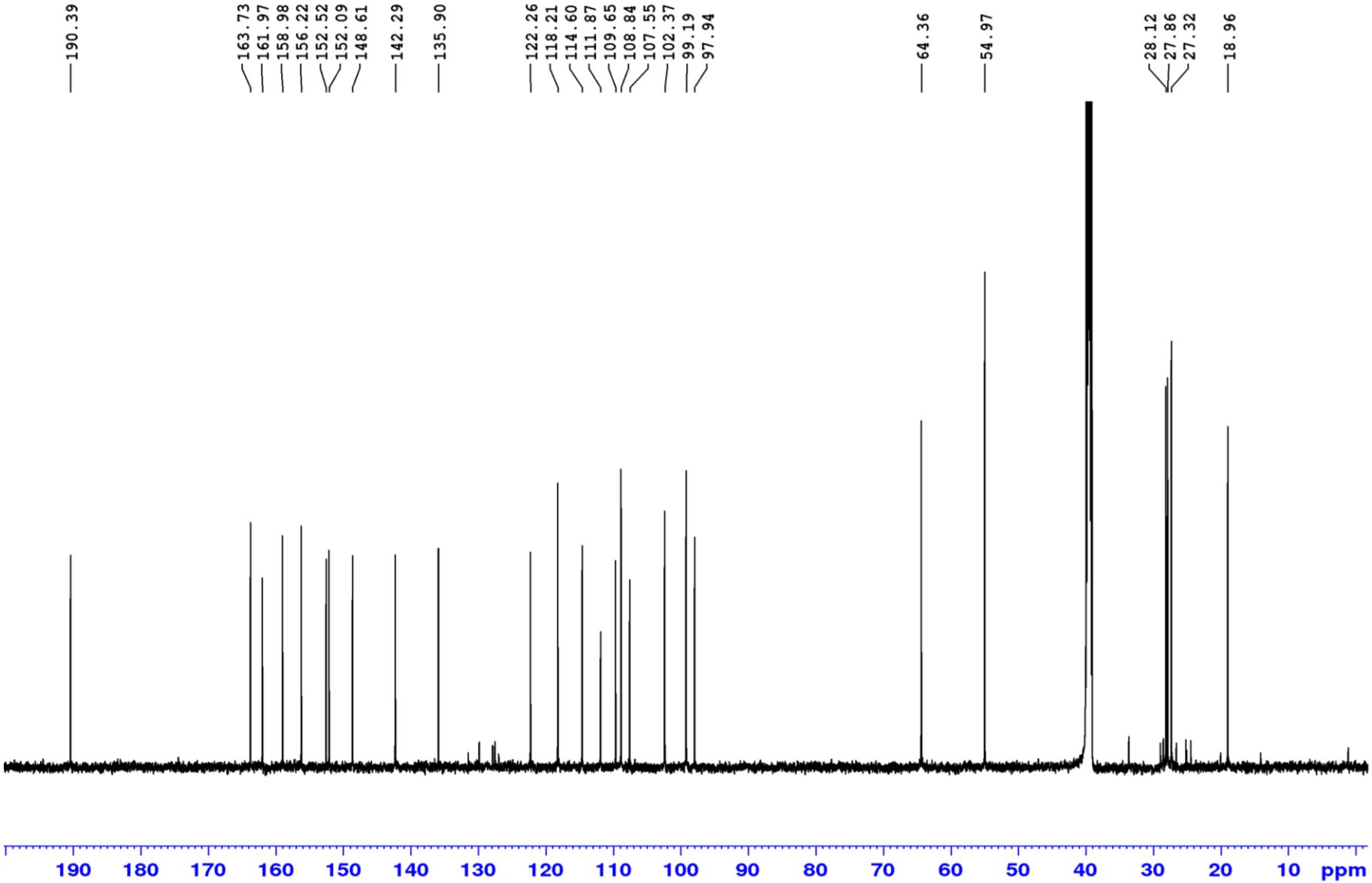


Figure S49. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of (–)-ABX-B (**11**)

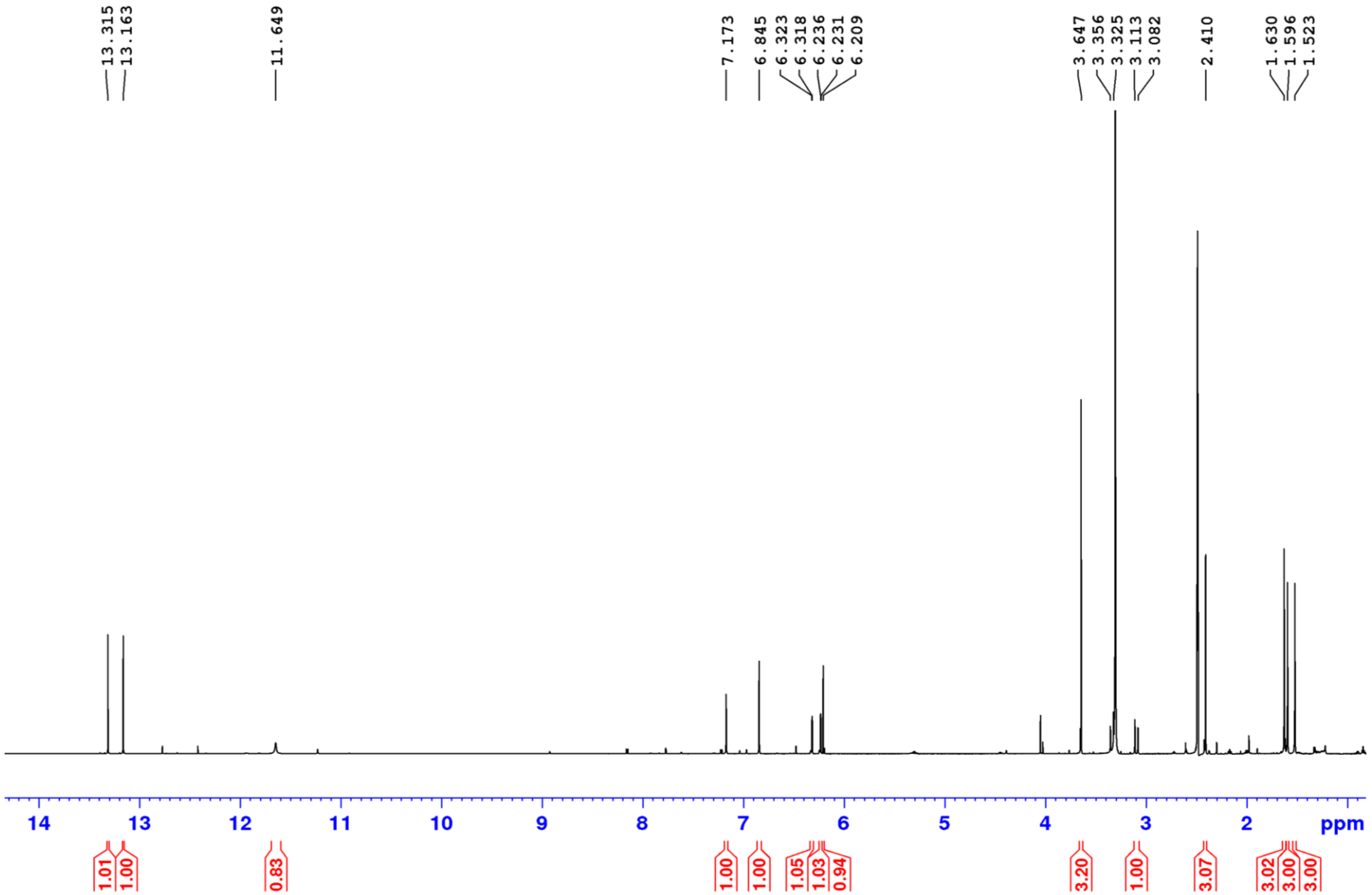


Figure S50. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of (–)-ABX-C (**12**)

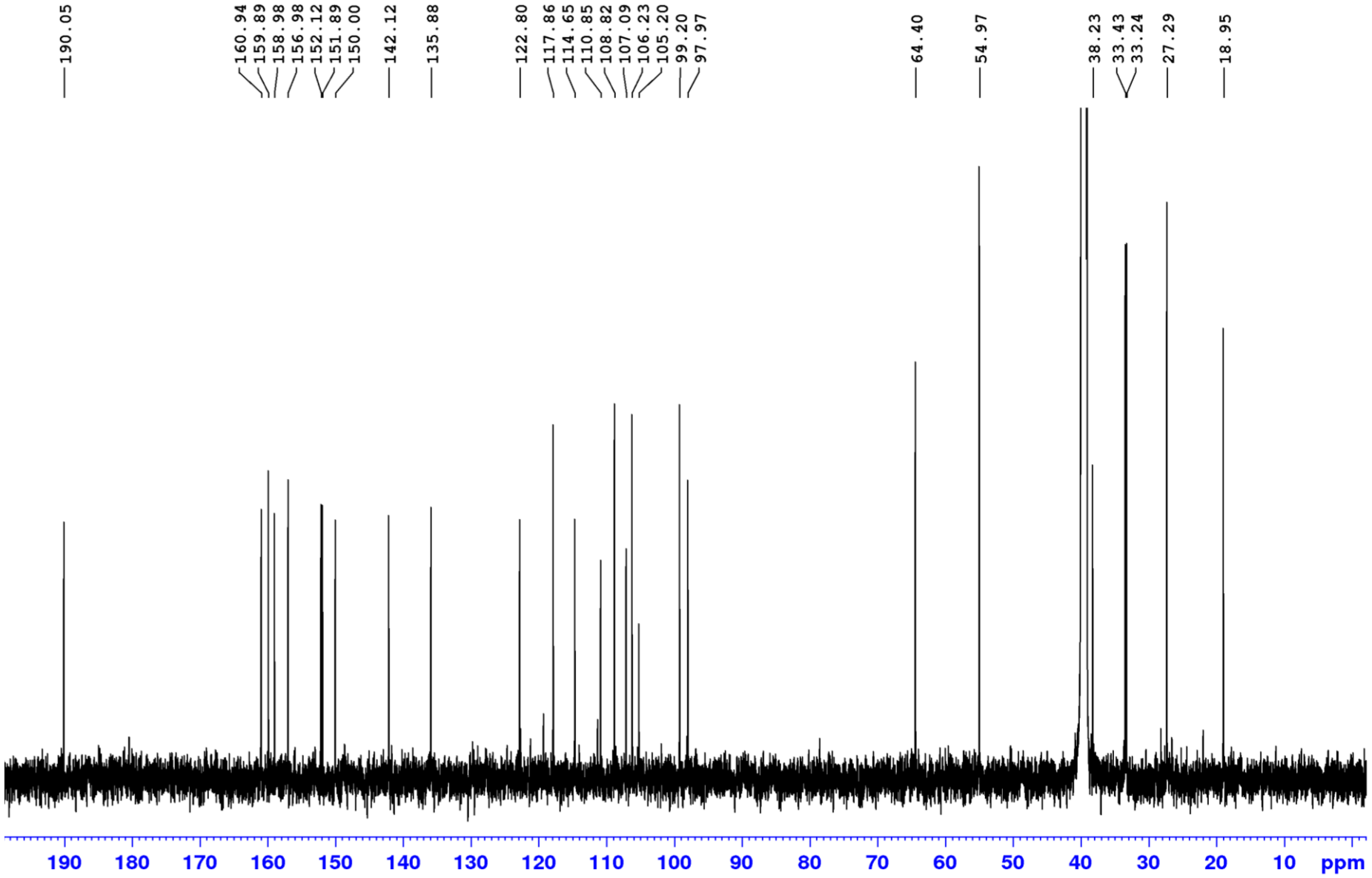


Figure S51. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of (–)-ABX-C (**12**)

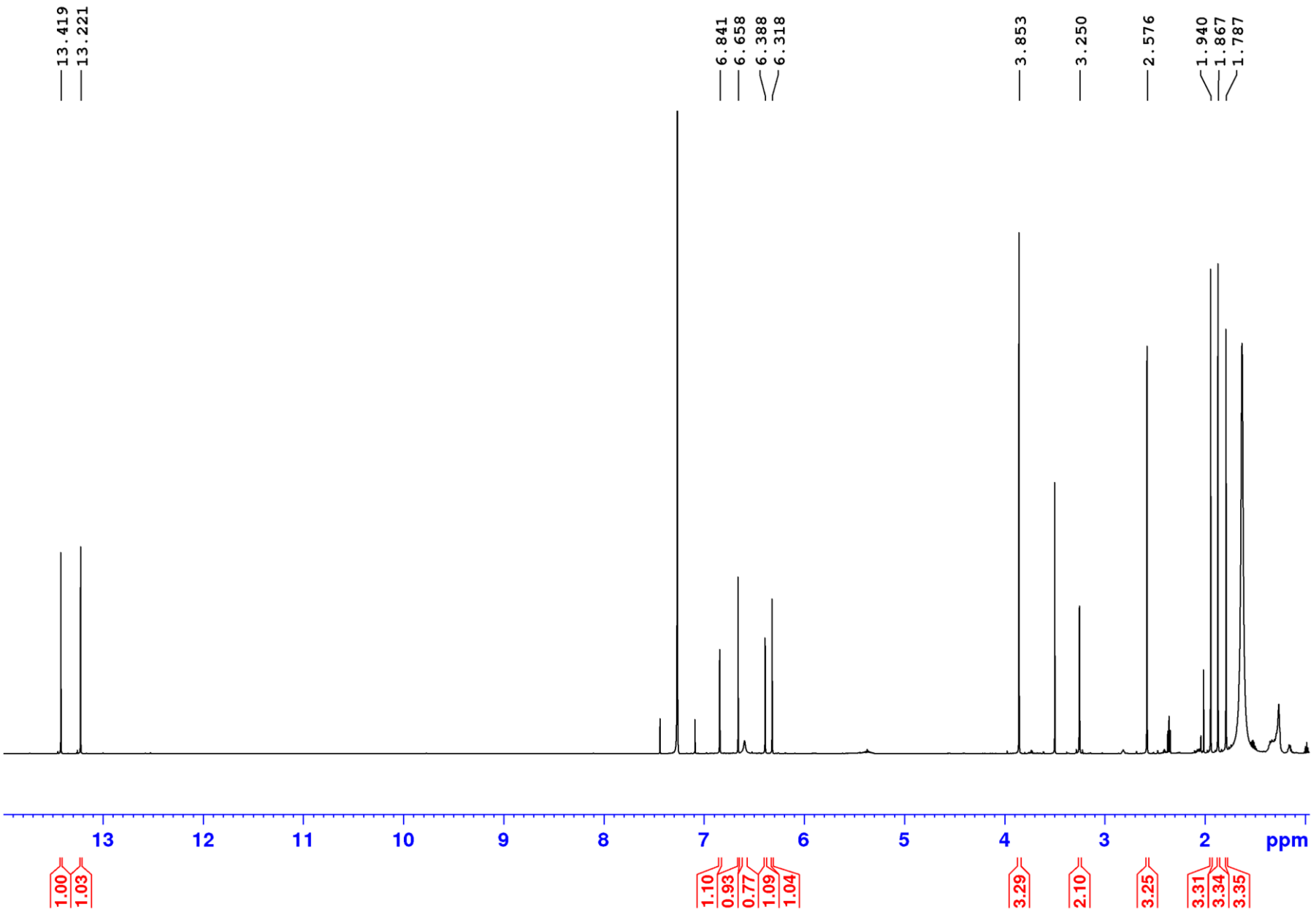


Figure S52. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of (–)-ABX-D (**13**)

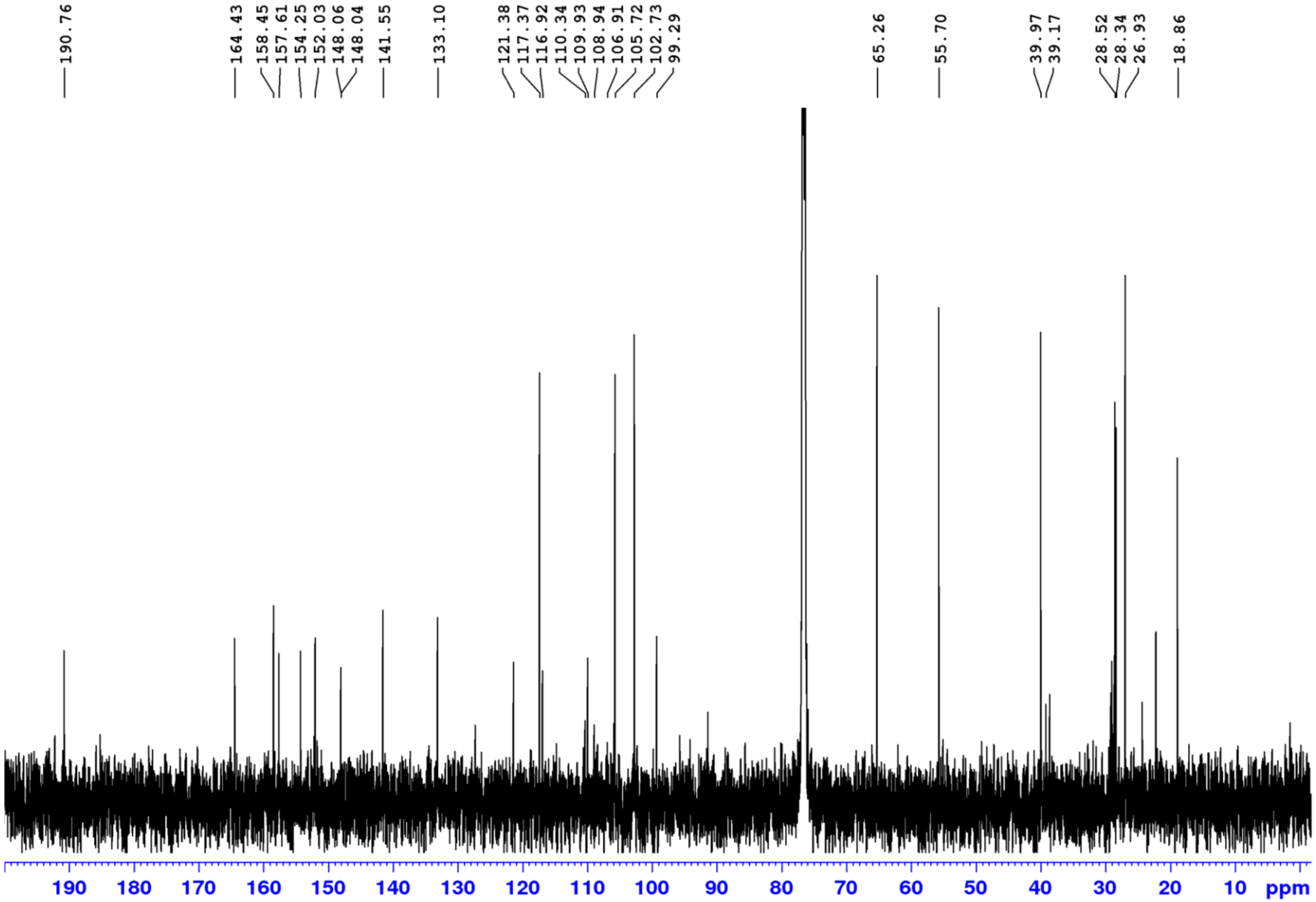


Figure S53. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of (–)-ABX-D (**13**)

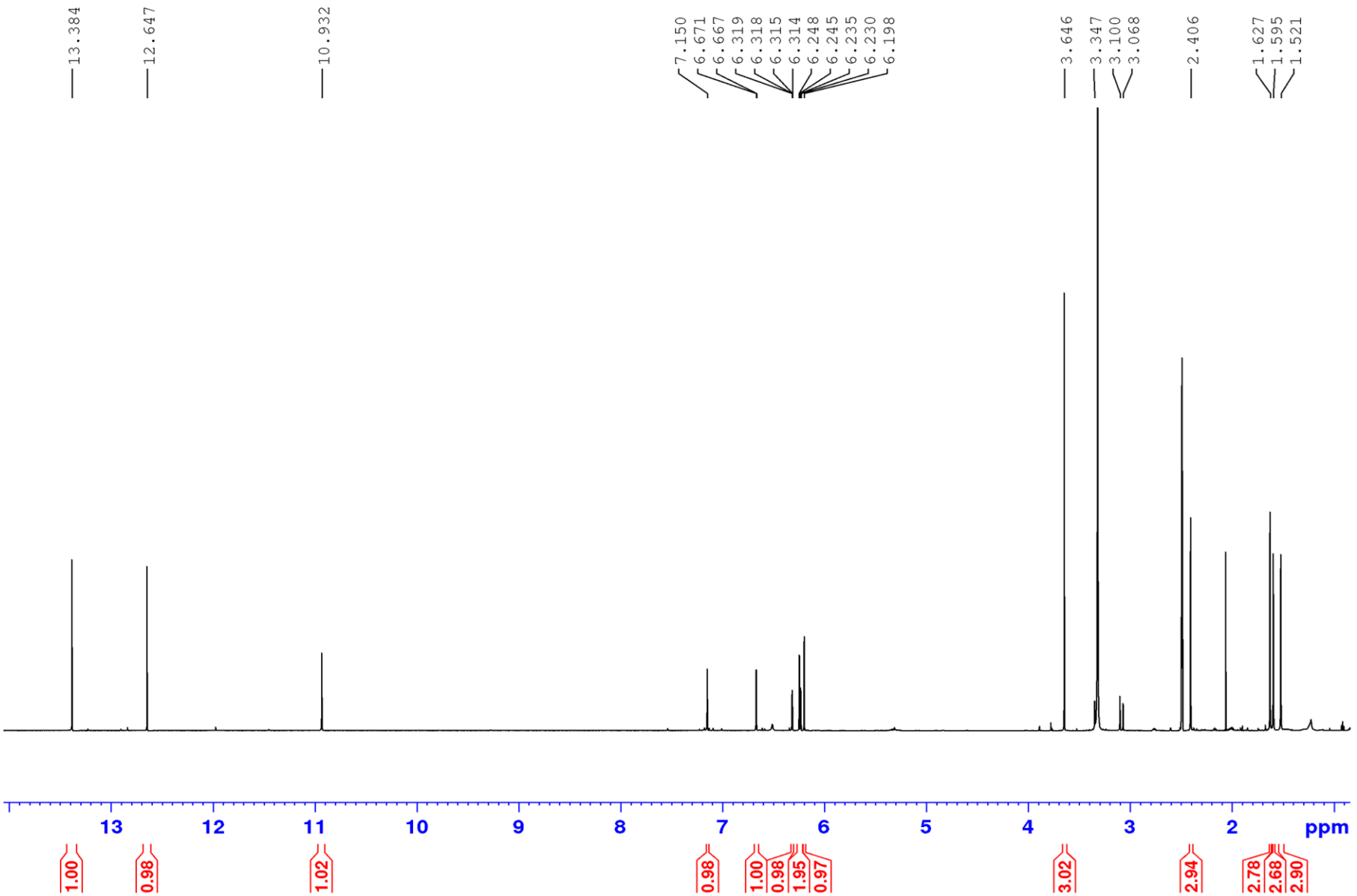


Figure S54. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of (–)-ABX-E (**14**)

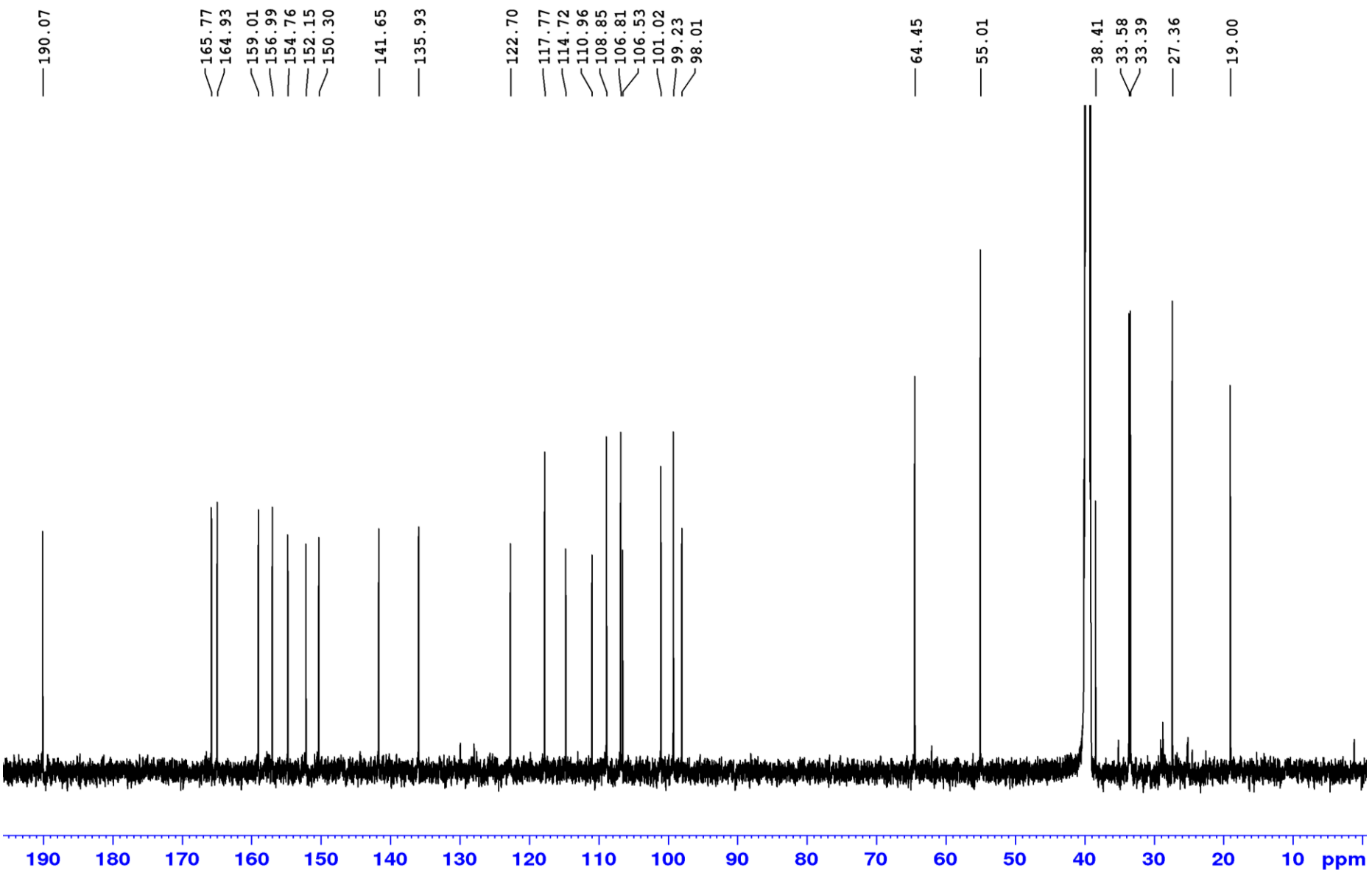


Figure S55. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of (–)-ABX-E (**14**)

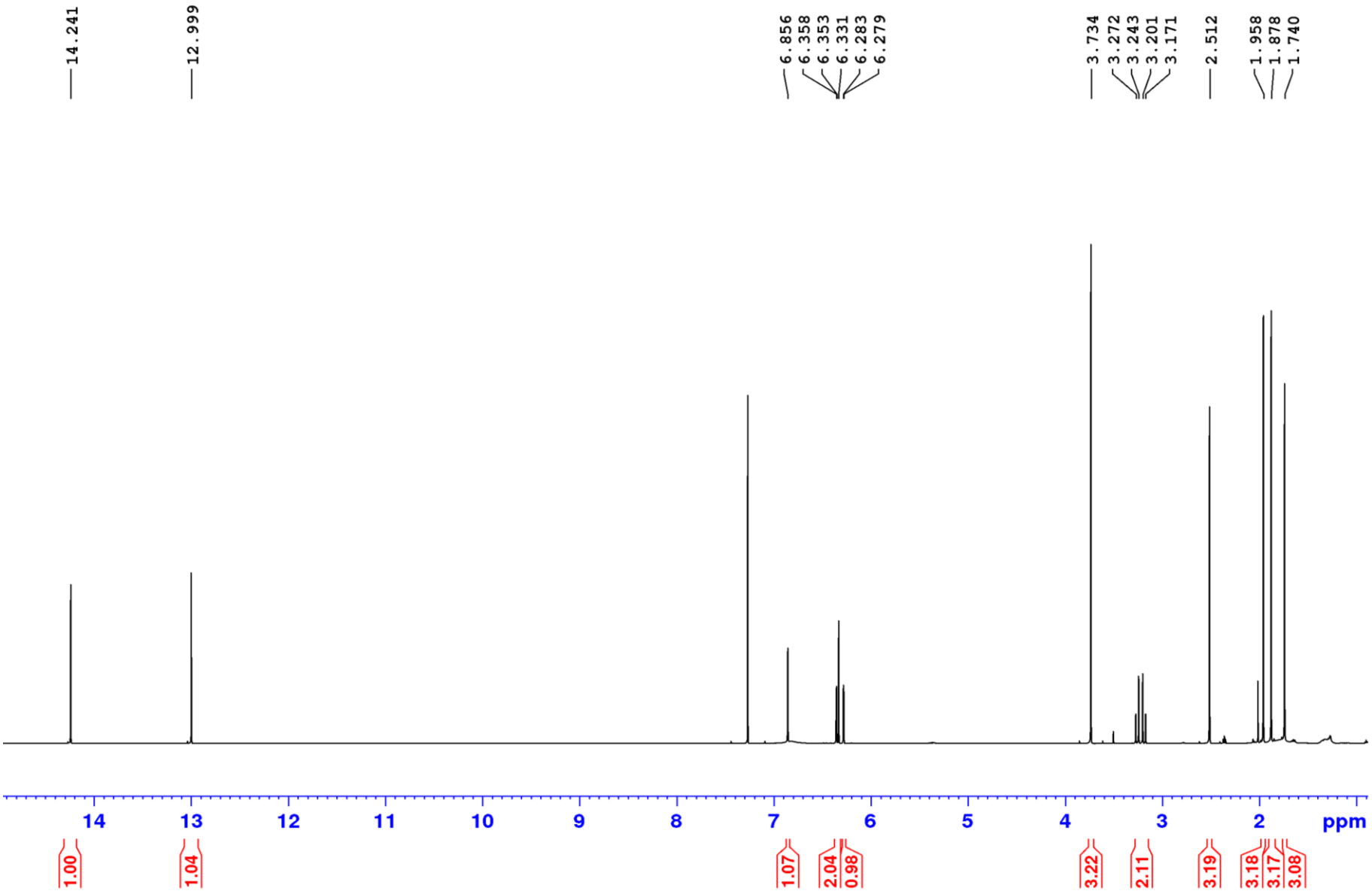


Figure S56. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of (–)-BABX (**15**)

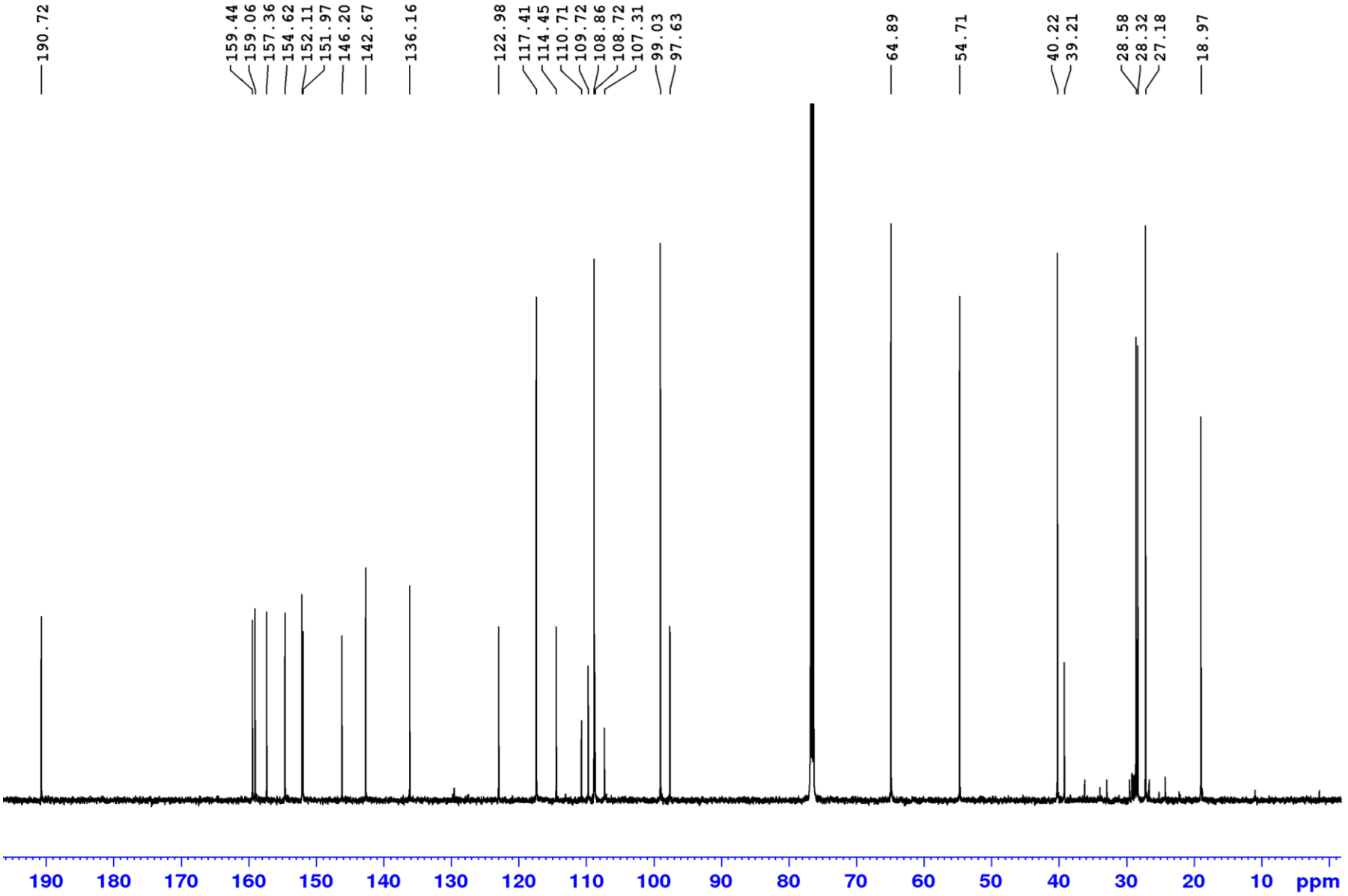


Figure S57. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of (–)-BABX (**15**)

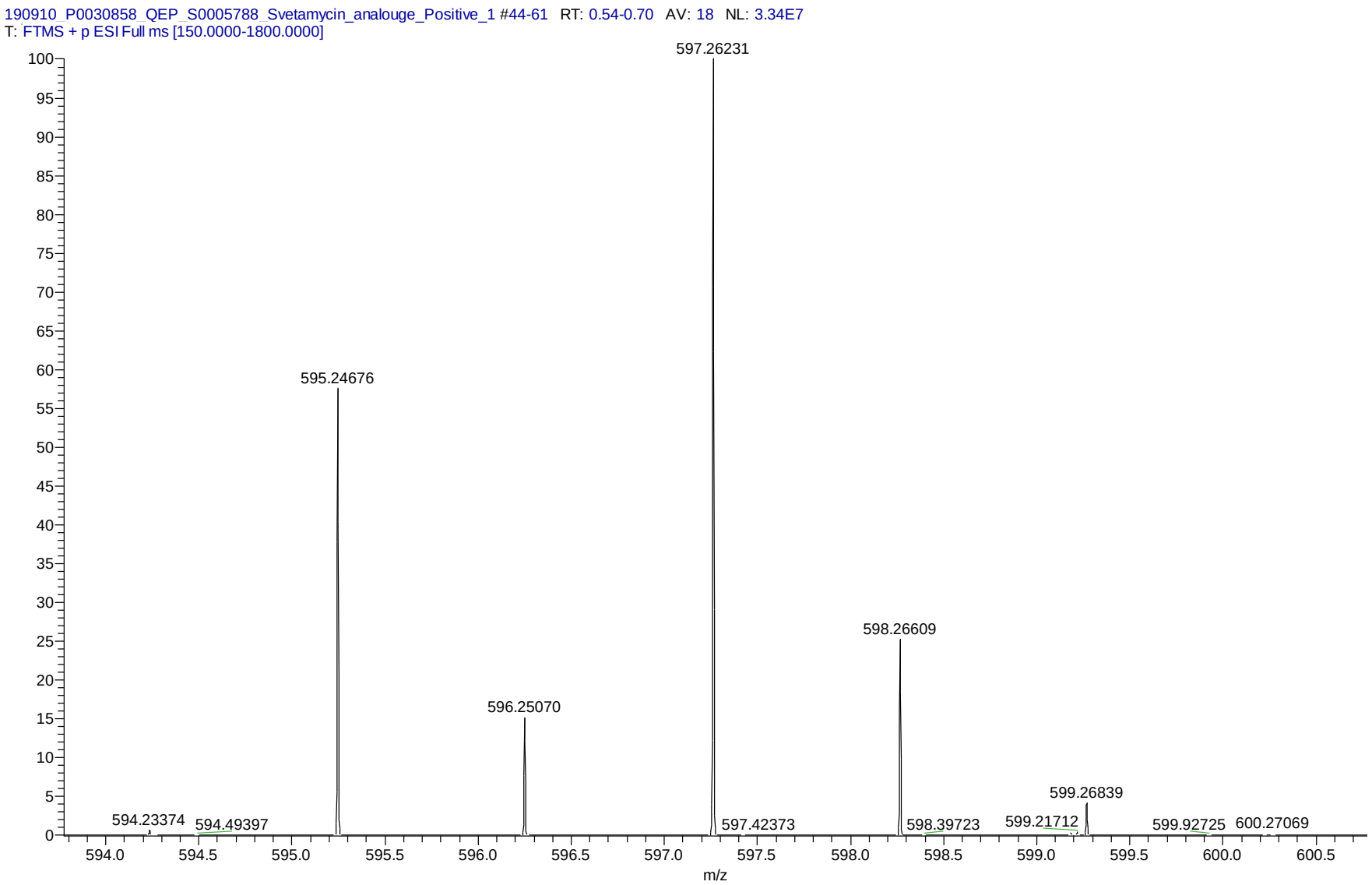


Figure S58. HR-ESI(+)-MS spectrum of deschlorosvetamycin A (**1**)

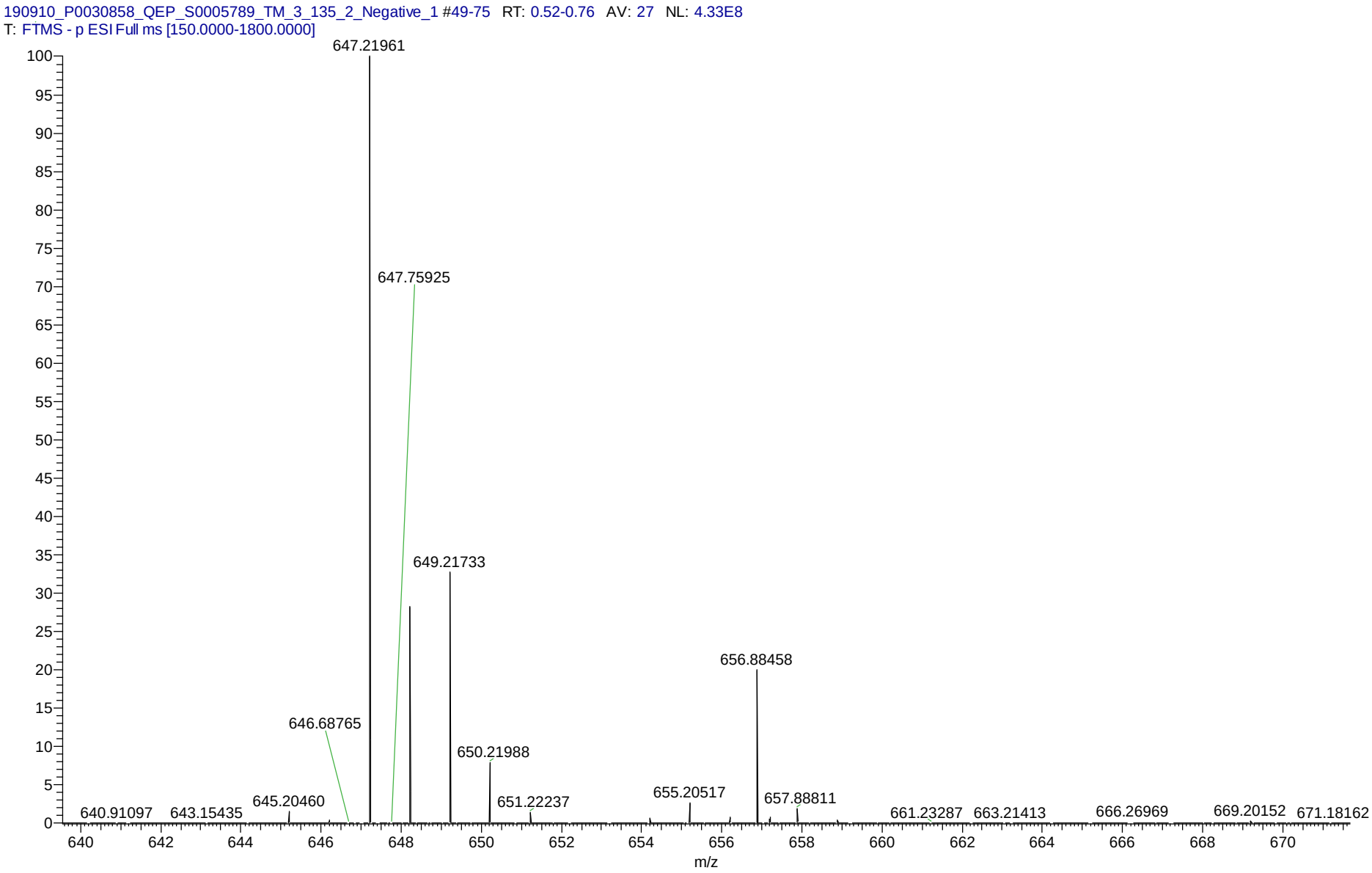


Figure S59. HR-ESI(–)-MS spectrum of svetamycin H (**2**)

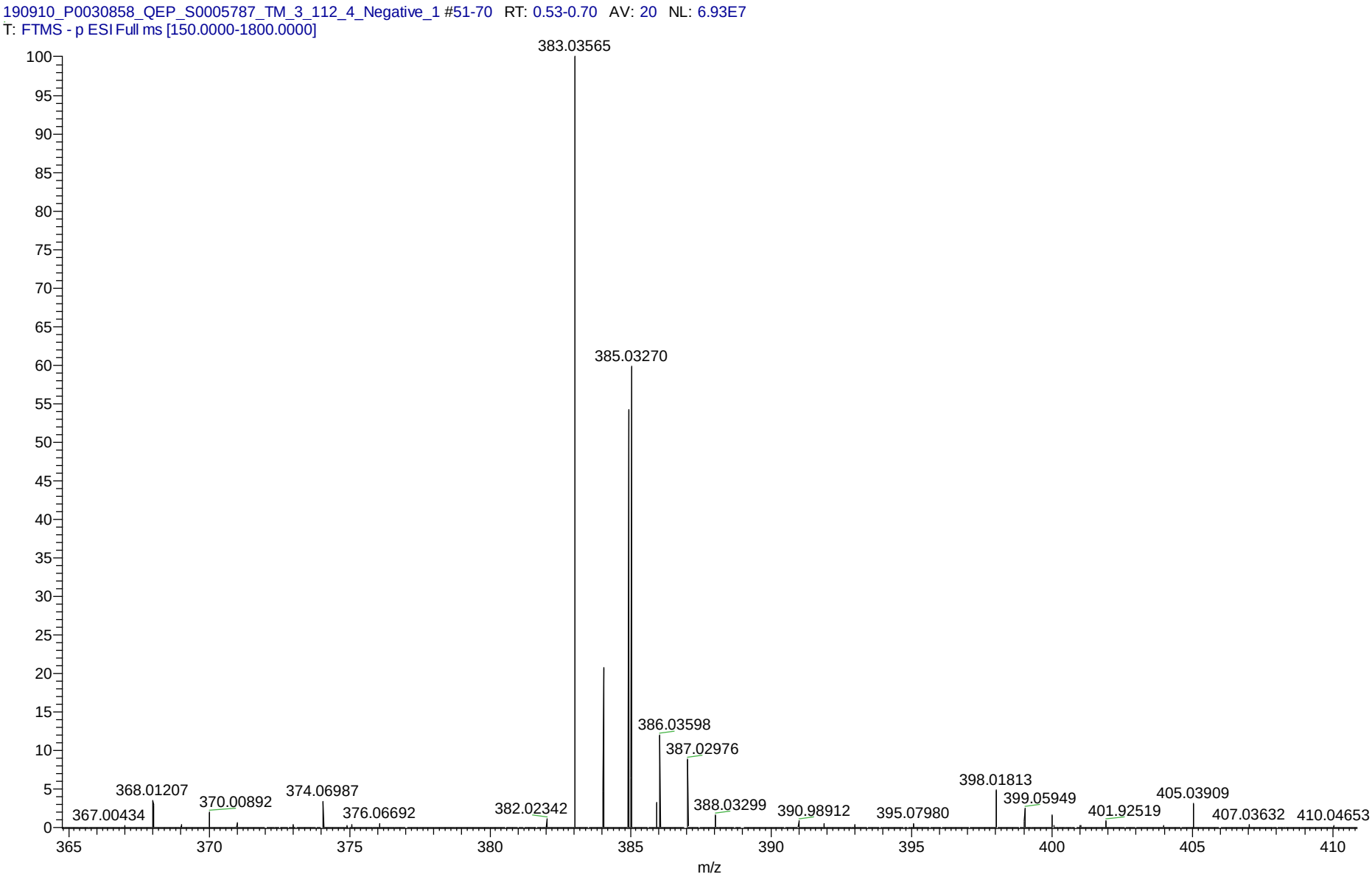


Figure S60. HR-ESI(–)-MS spectrum of borregomycin E (**4**)

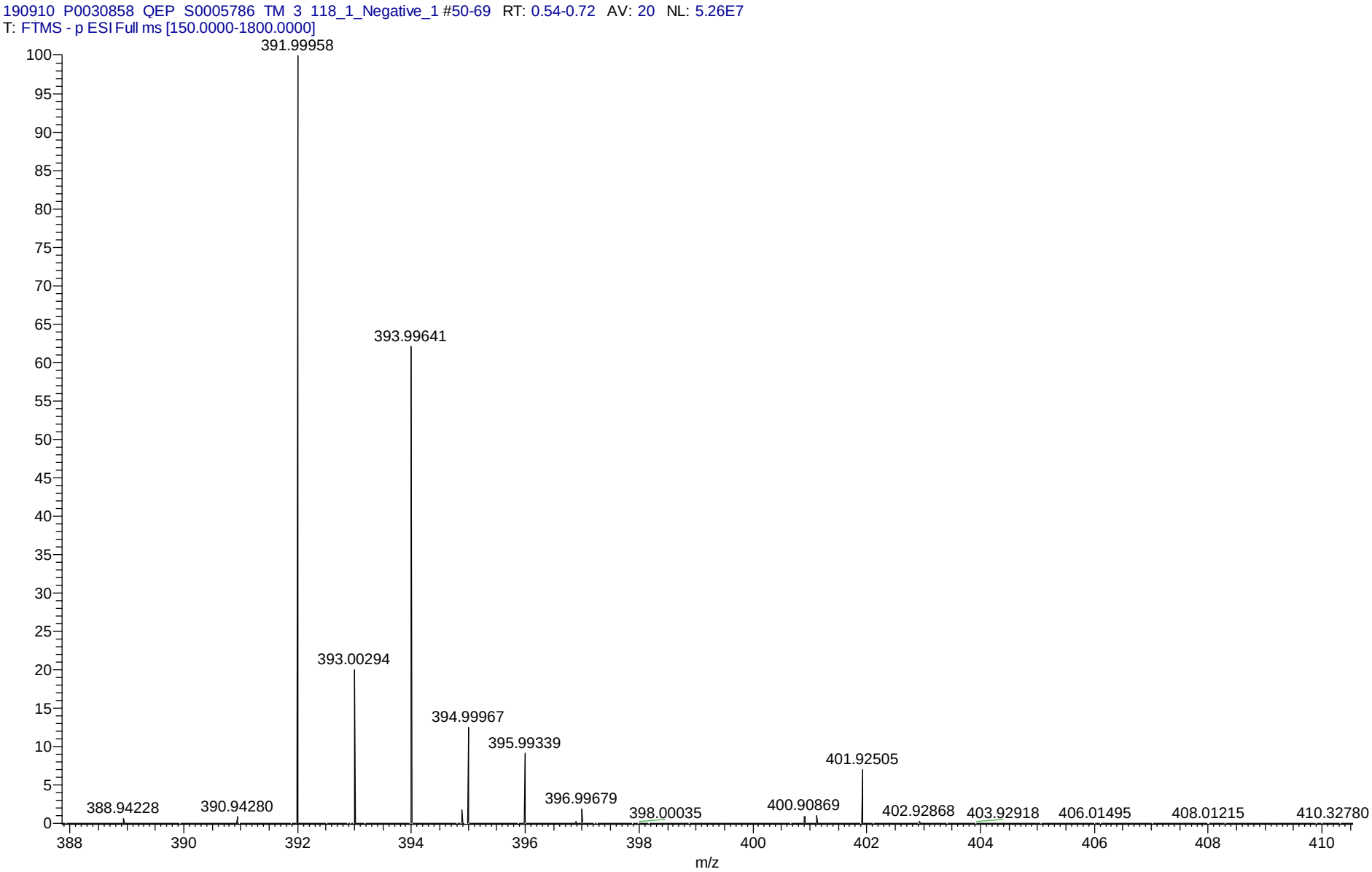


Figure S61. HR-ESI(–)-MS spectrum of borregomycin F (**5**)

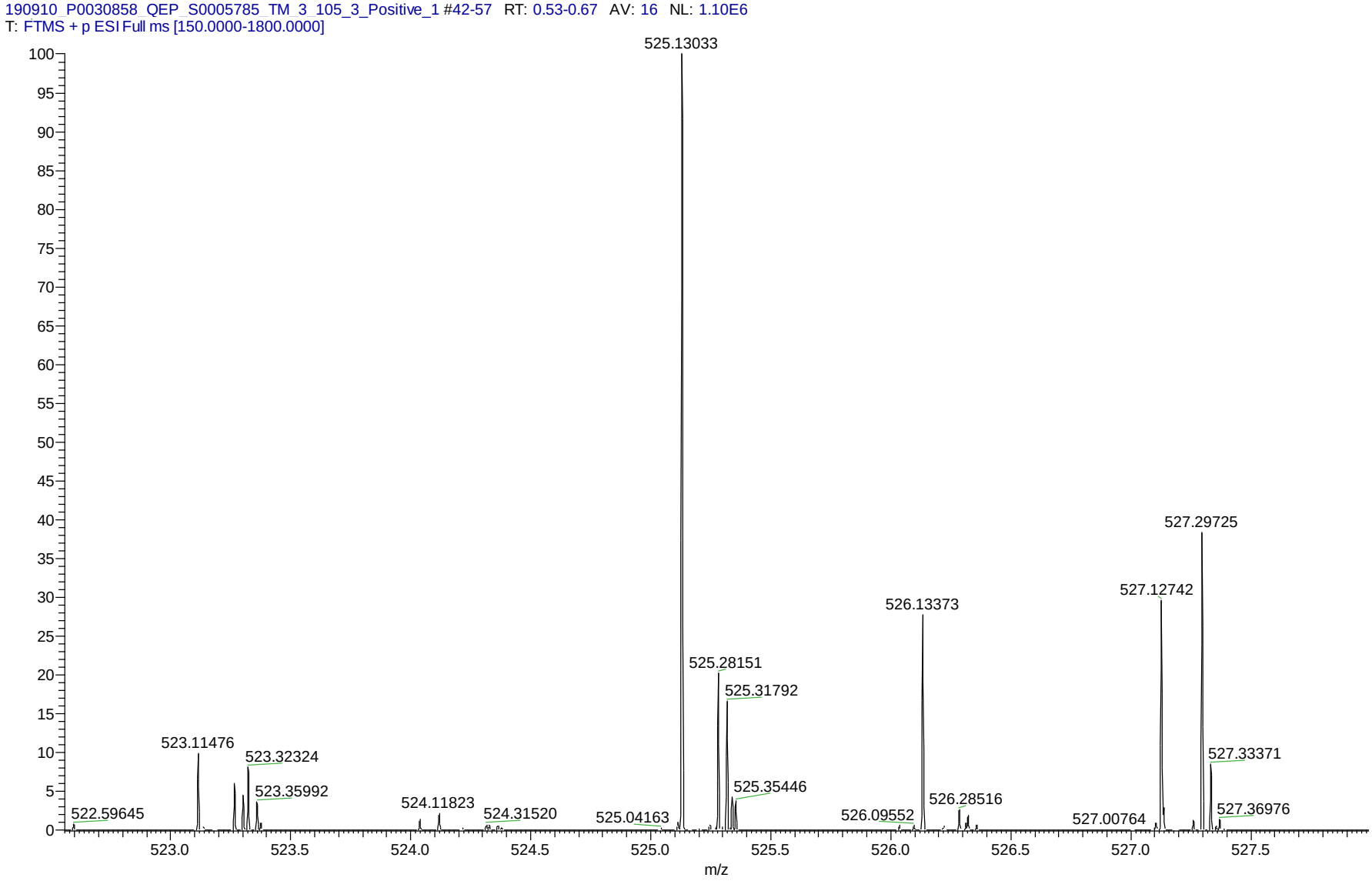


Figure S62. HR-ESI(+)-MS spectrum of (+)-ABX-G (**8**)

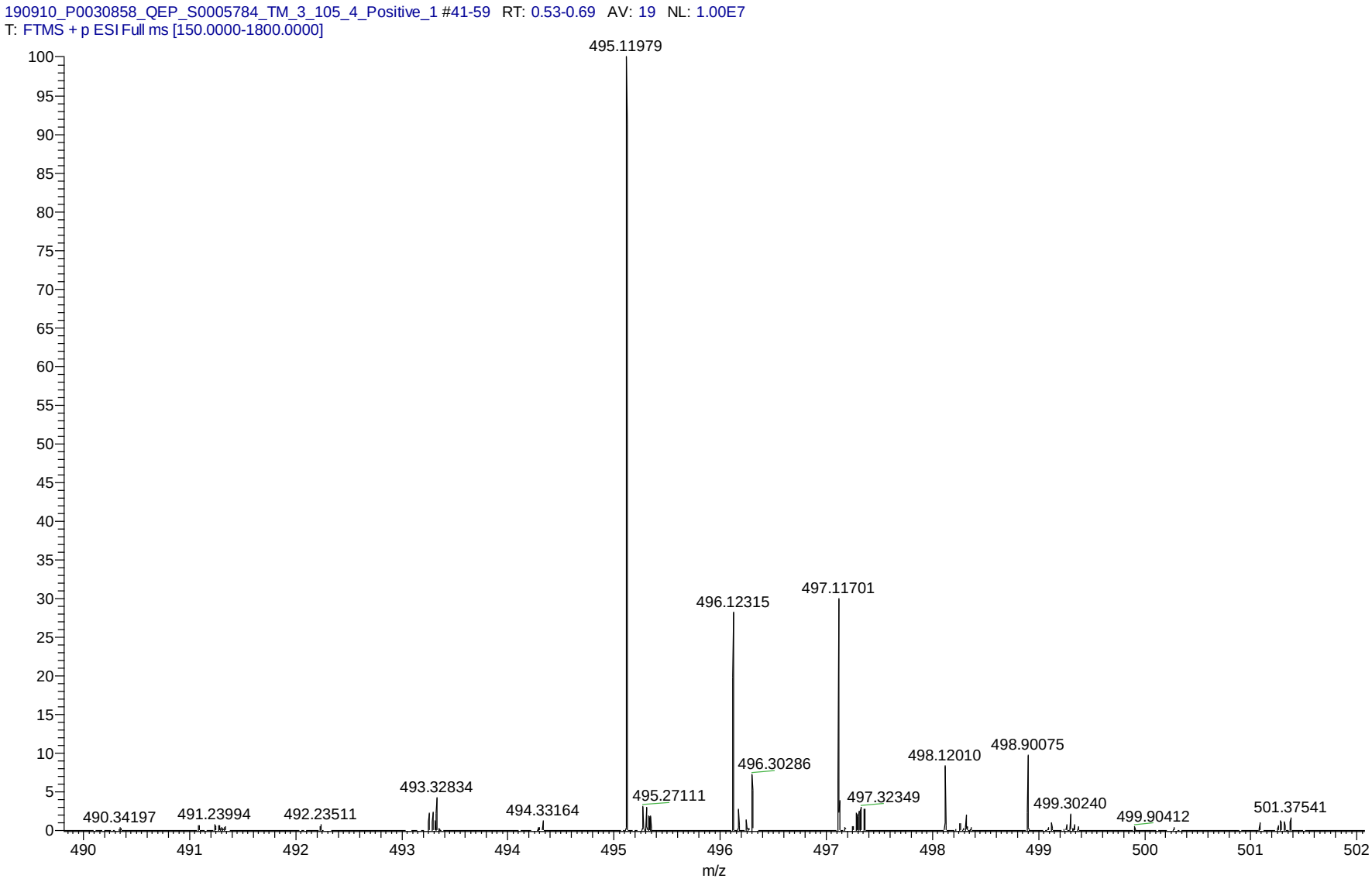


Figure S63. HR-ESI(+)-MS spectrum of (–)-ABX-K (**9**)

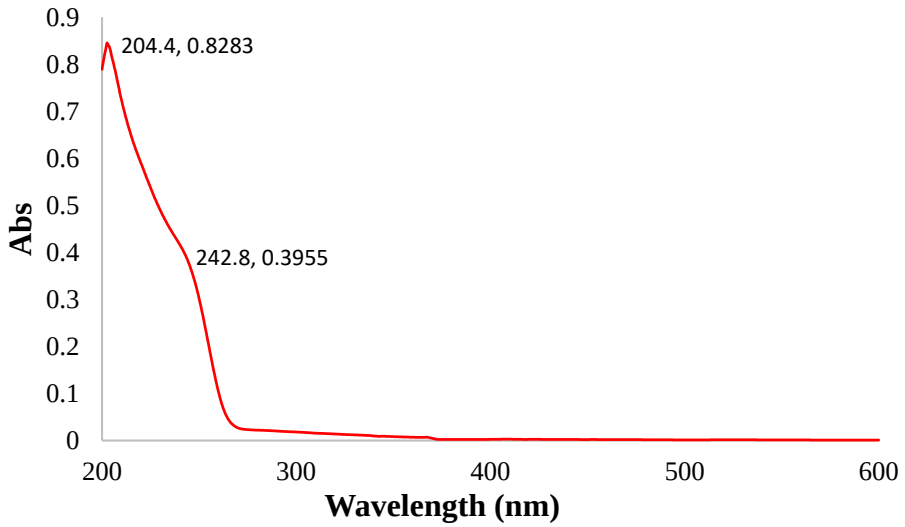


Figure S64. UV-vis spectrum of deschlorosvetamycin A (**1**) in $CHCl_3$

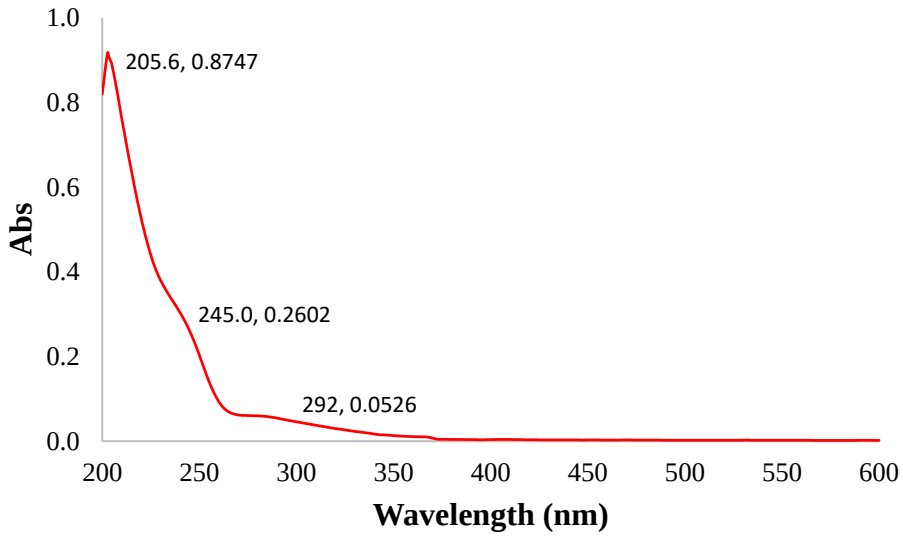


Figure S65. UV-vis spectrum of svetamycin H (**2**) in $CHCl_3$

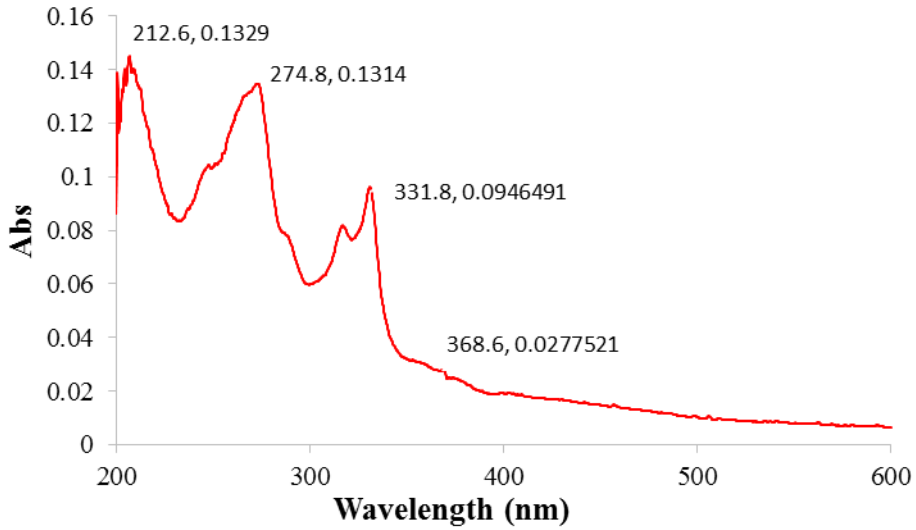


Figure S66. UV-vis spectrum of borregomycin E (**4**) in $CHCl_3$

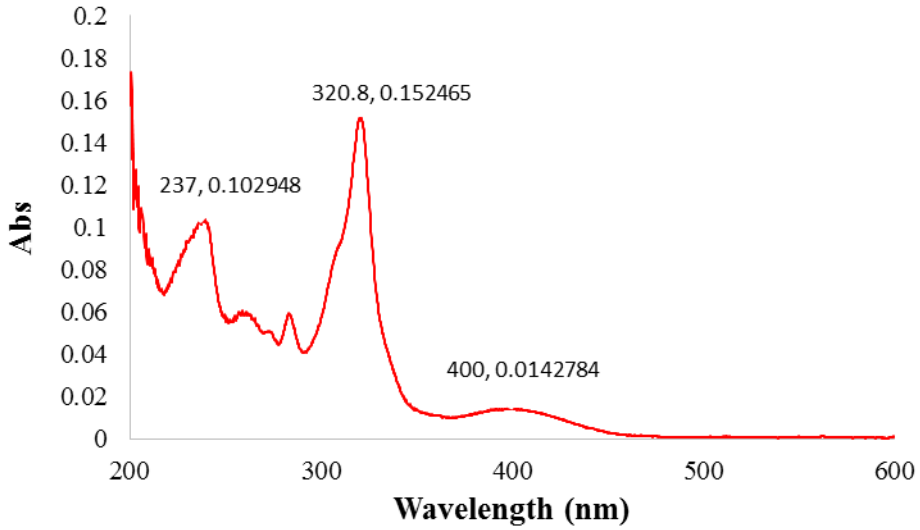


Figure S67. UV-vis spectrum of borregomycin F (**5**) in $CHCl_3$

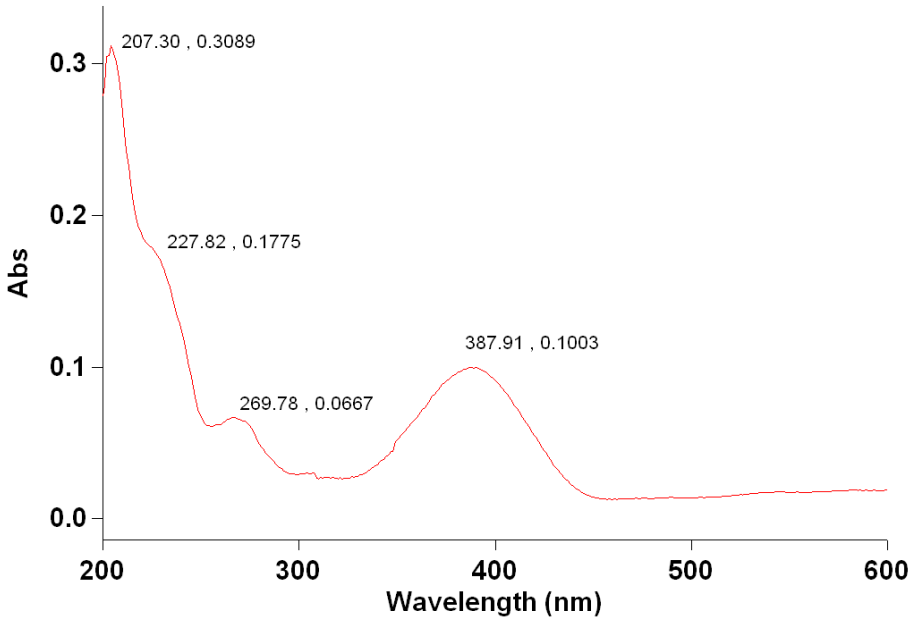


Figure S68. UV-vis spectrum of (+)-ABX-G (**8**) in $CHCl_3$

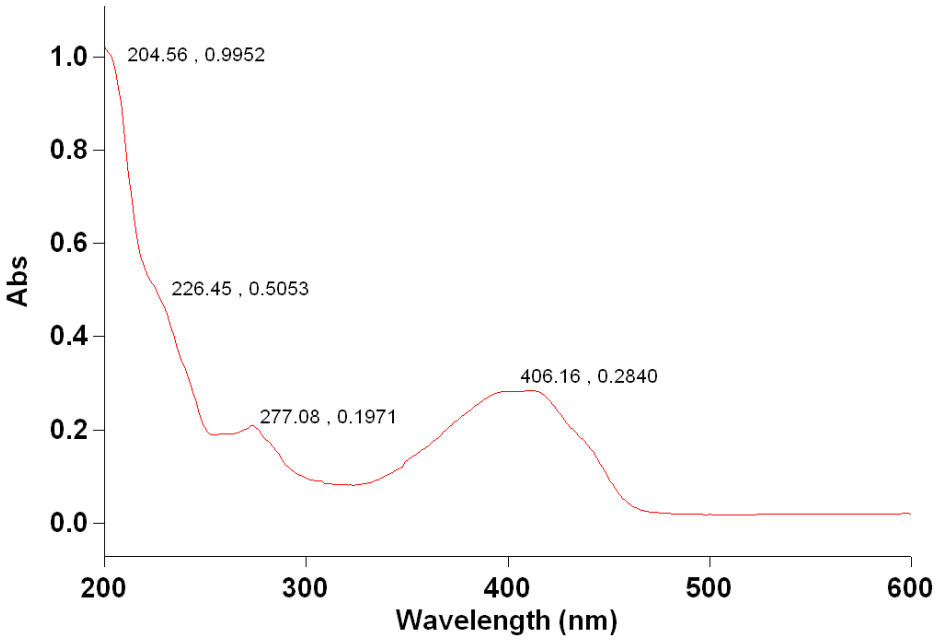


Figure S69. UV-vis spectrum of (–)-ABX-K (**9**) in $CHCl_3$

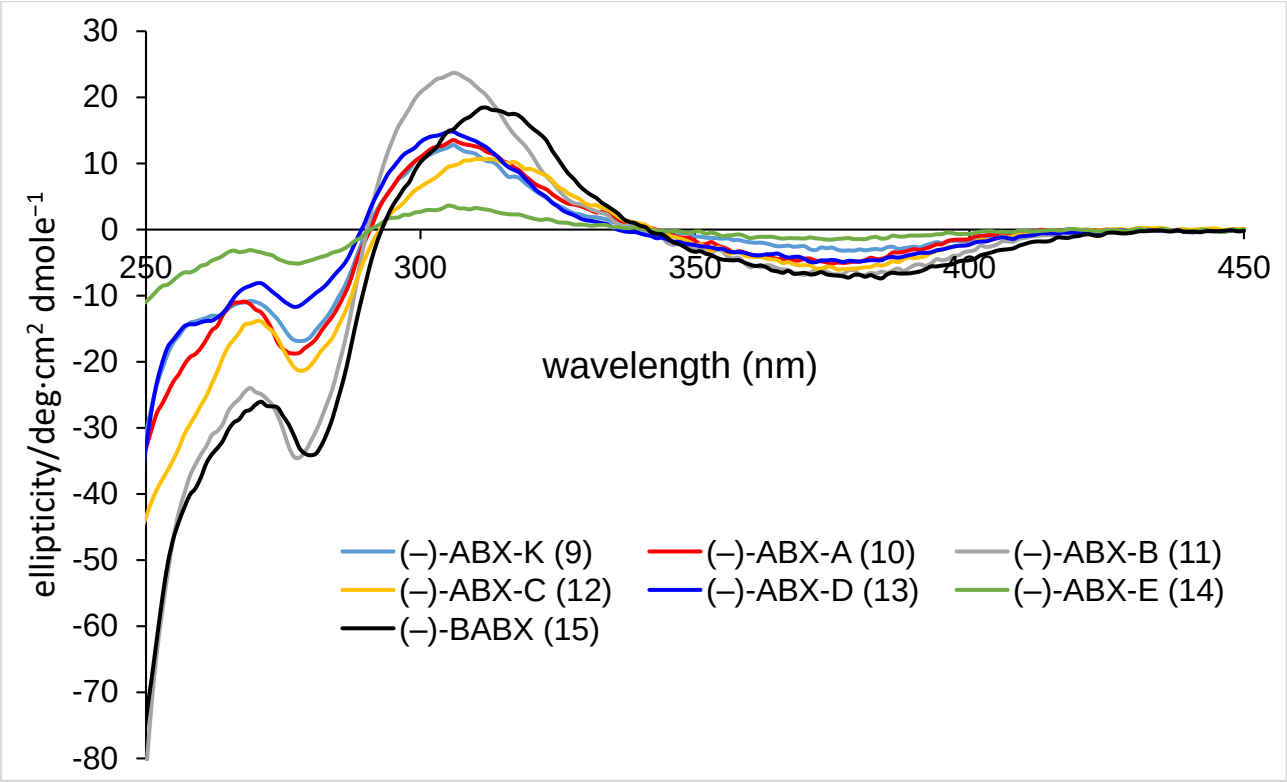


Figure S70. ECD spectra of ABX analogues **9**–**15** in $CHCl_3$

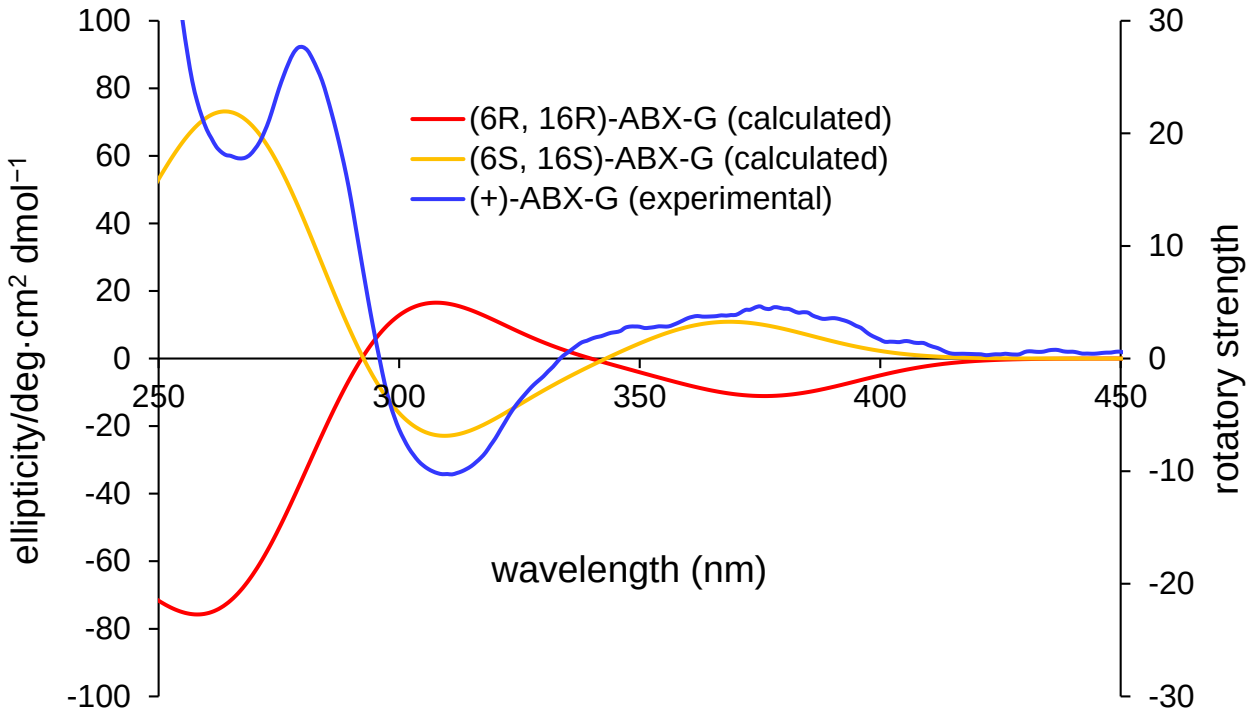


Figure S71. TD-DFT-D3(BJ)/PBE0/def2-SV(P)-COSMO(MeCN) calculated rotatory strengths for (6*R*,16*R*)-ABX-G and (6*S*,16*S*)-ABX-G, blue-shifted by 5 nm and broadened with an 18 nm standard deviation, compared to the experimental ECD spectrum for the natural product (+)-ABX-G (**8**).

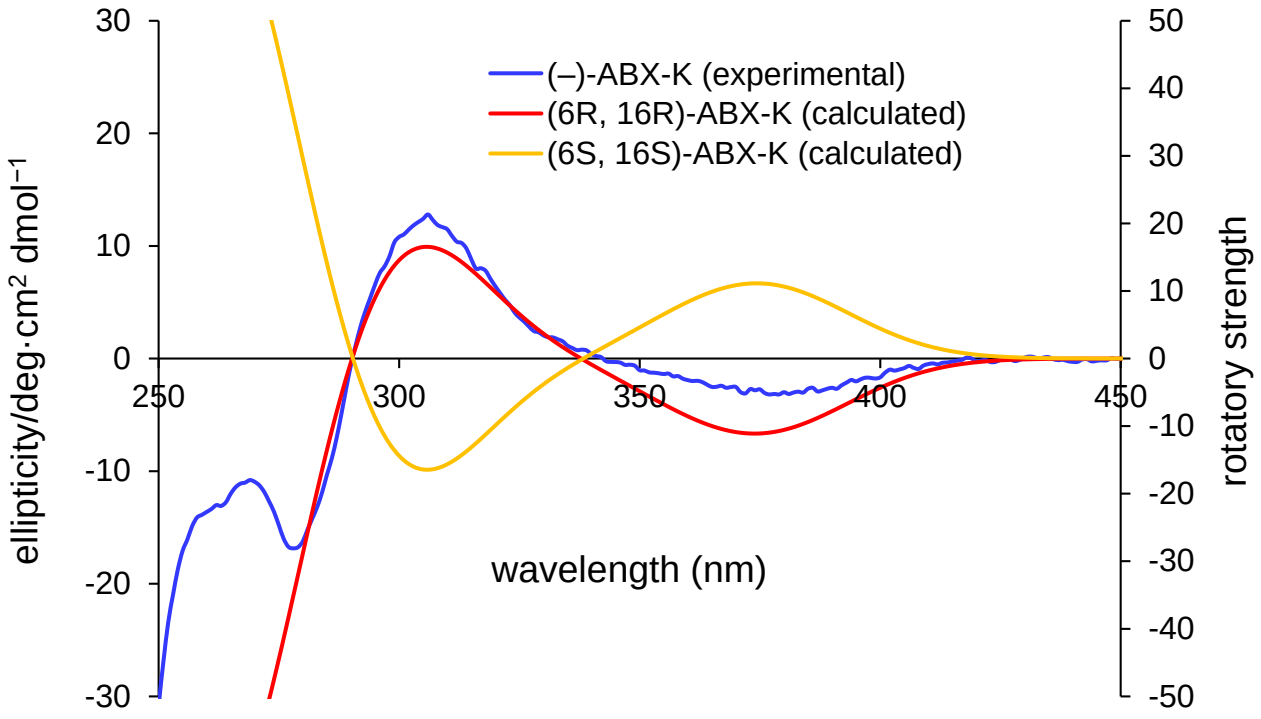


Figure S72. TD-DFT-D3(BJ)/PBE0/def2-SV(P)-COSMO(MeCN) calculated rotatory strengths for (6*R*,16*R*)-ABX-K and (6*S*,16*S*)-ABX-K, broadened with an 18 nm standard deviation, compared to the experimental ECD spectrum for the natural product (–)-ABX-K (**9**).

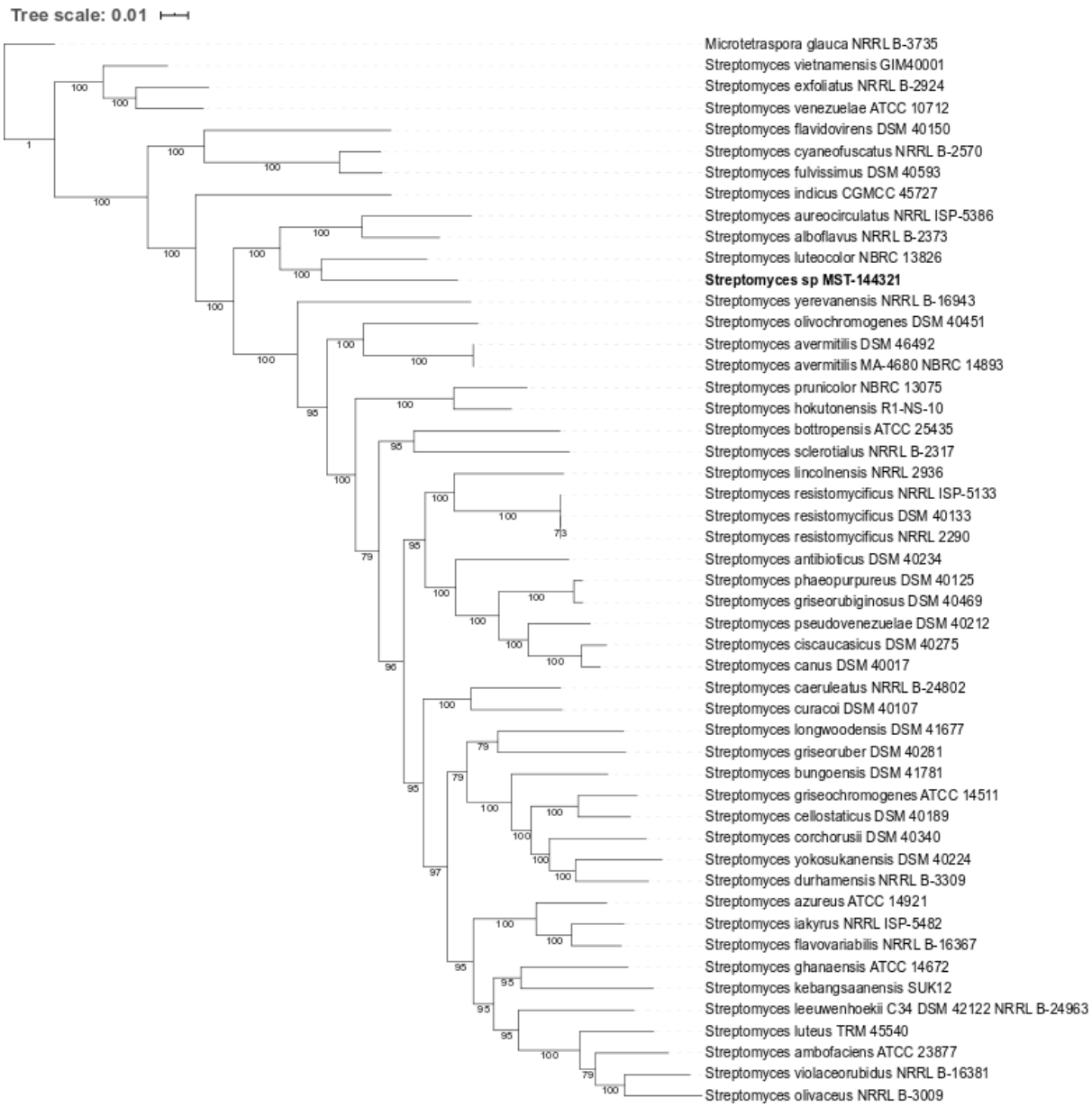


Figure S73. Phylogenetic tree of related *Streptomyces* strains as produced by AutoMLST.

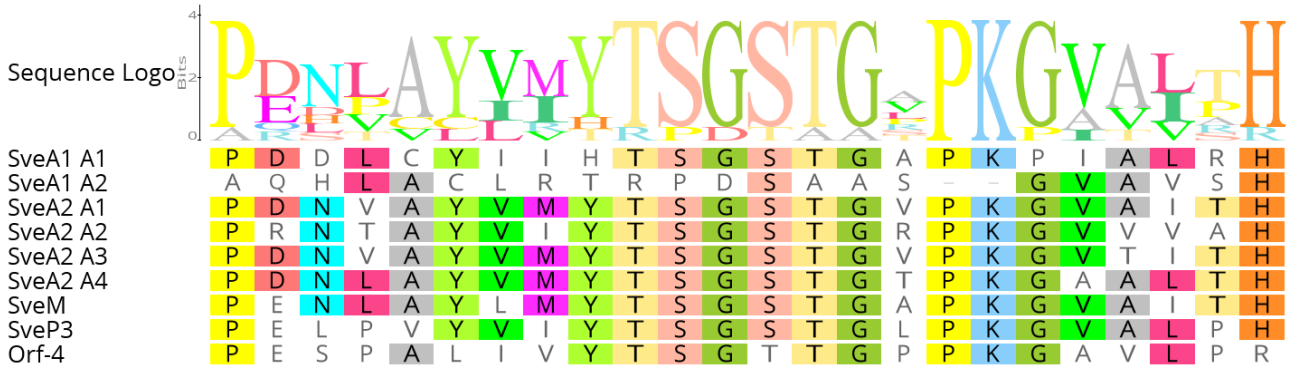


Figure S74. Walker motif of adenylation domains from the svetamycin (*sve*) biosynthetic gene cluster.

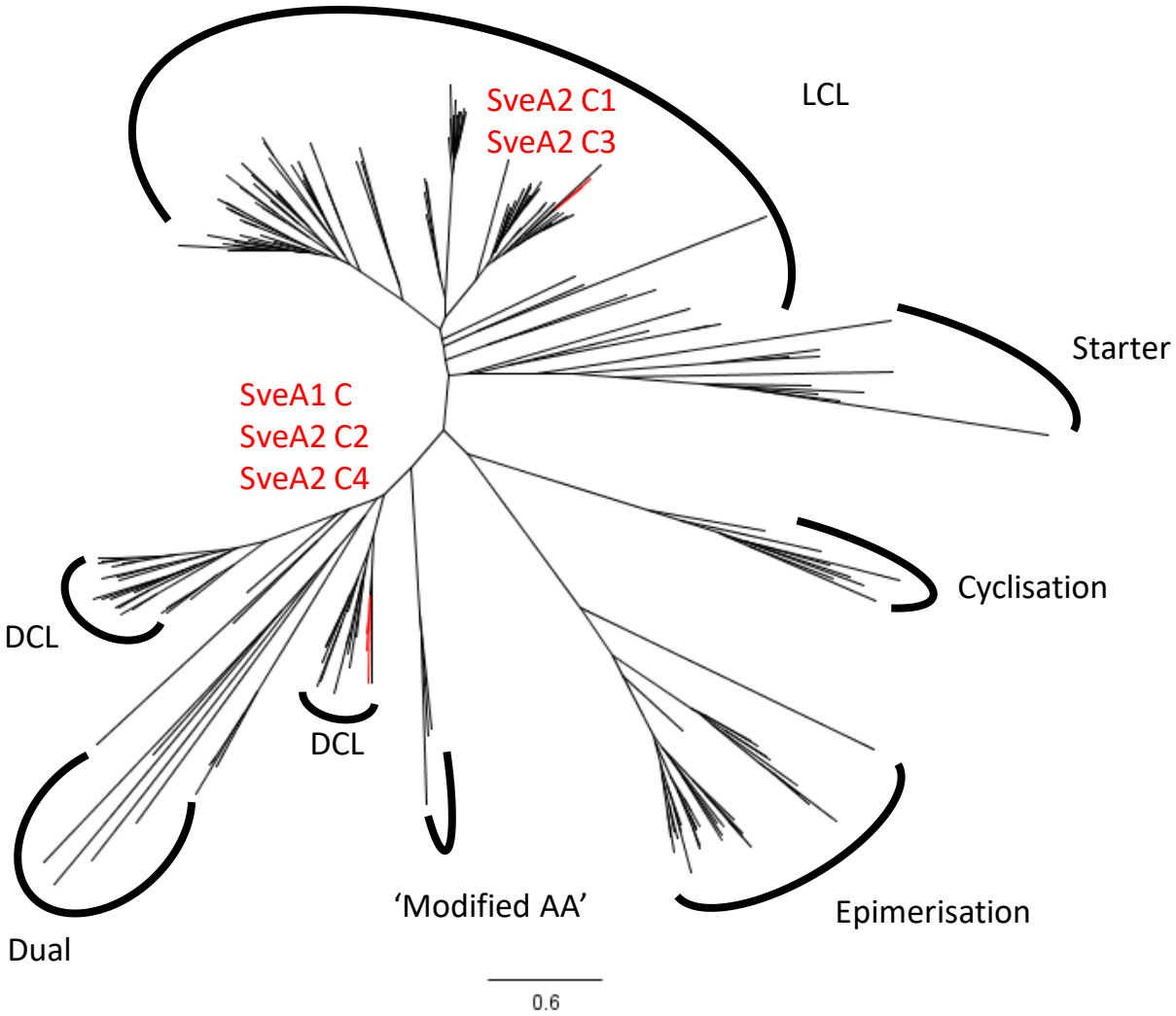


Figure S75. Phylogenetic prediction of condensation domain function generated by NaPDoS.[20]

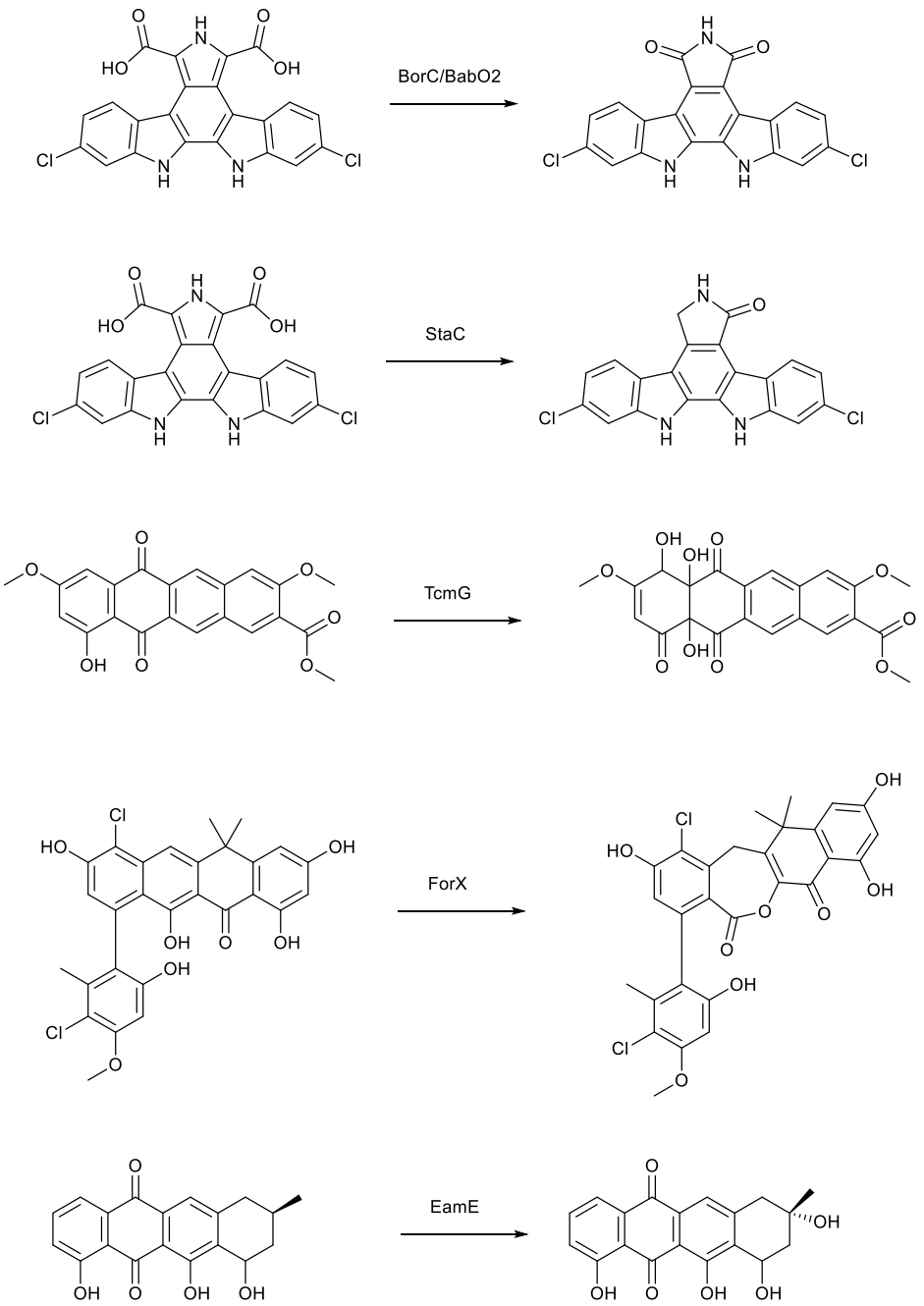


Figure S76. Varied oxidative reactions catalysed by BabO2 homologues.

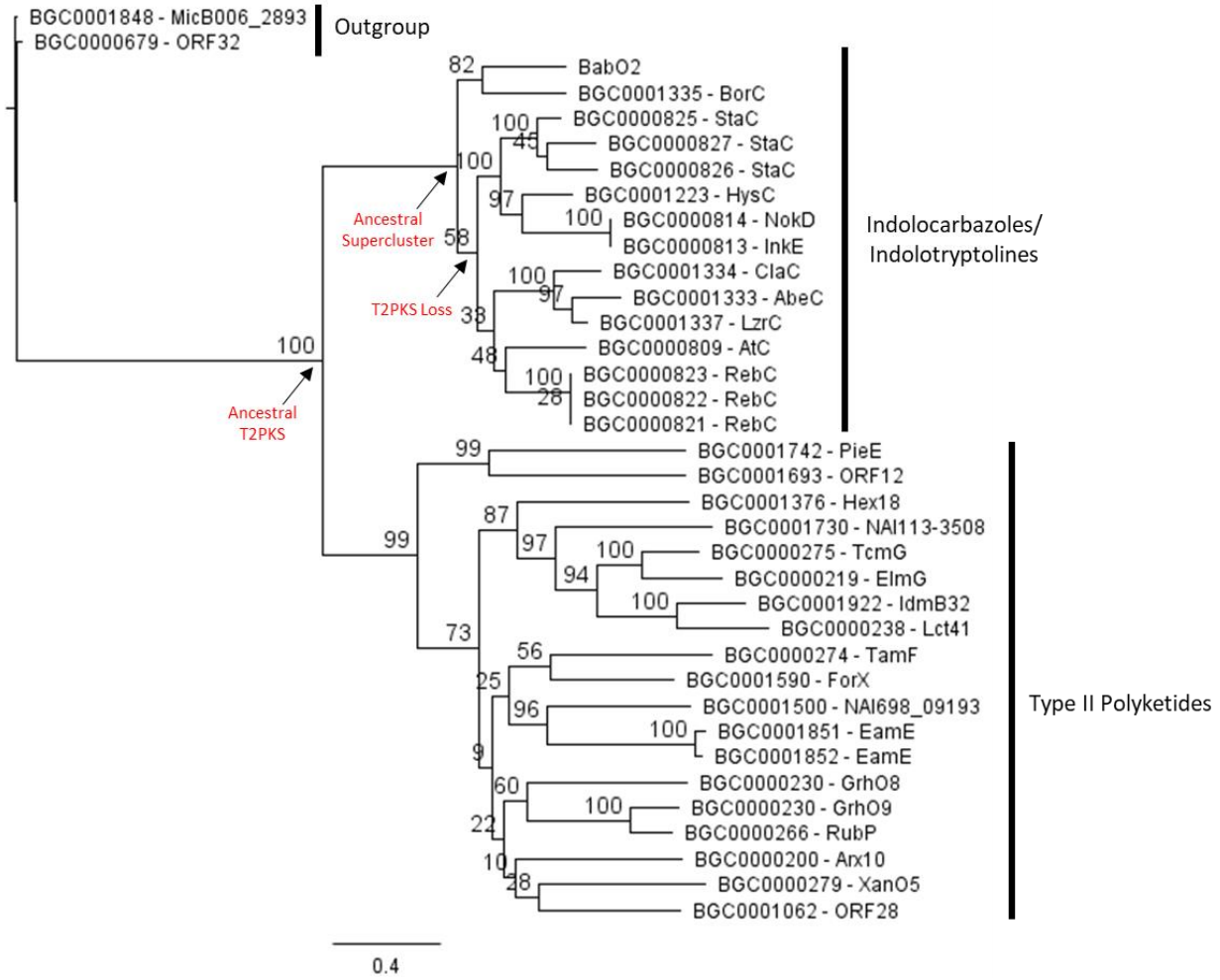


Figure S77. Phylogenetic tree of BabO2 homologues indicating the evolutionary history of the biosynthetic supercluster.

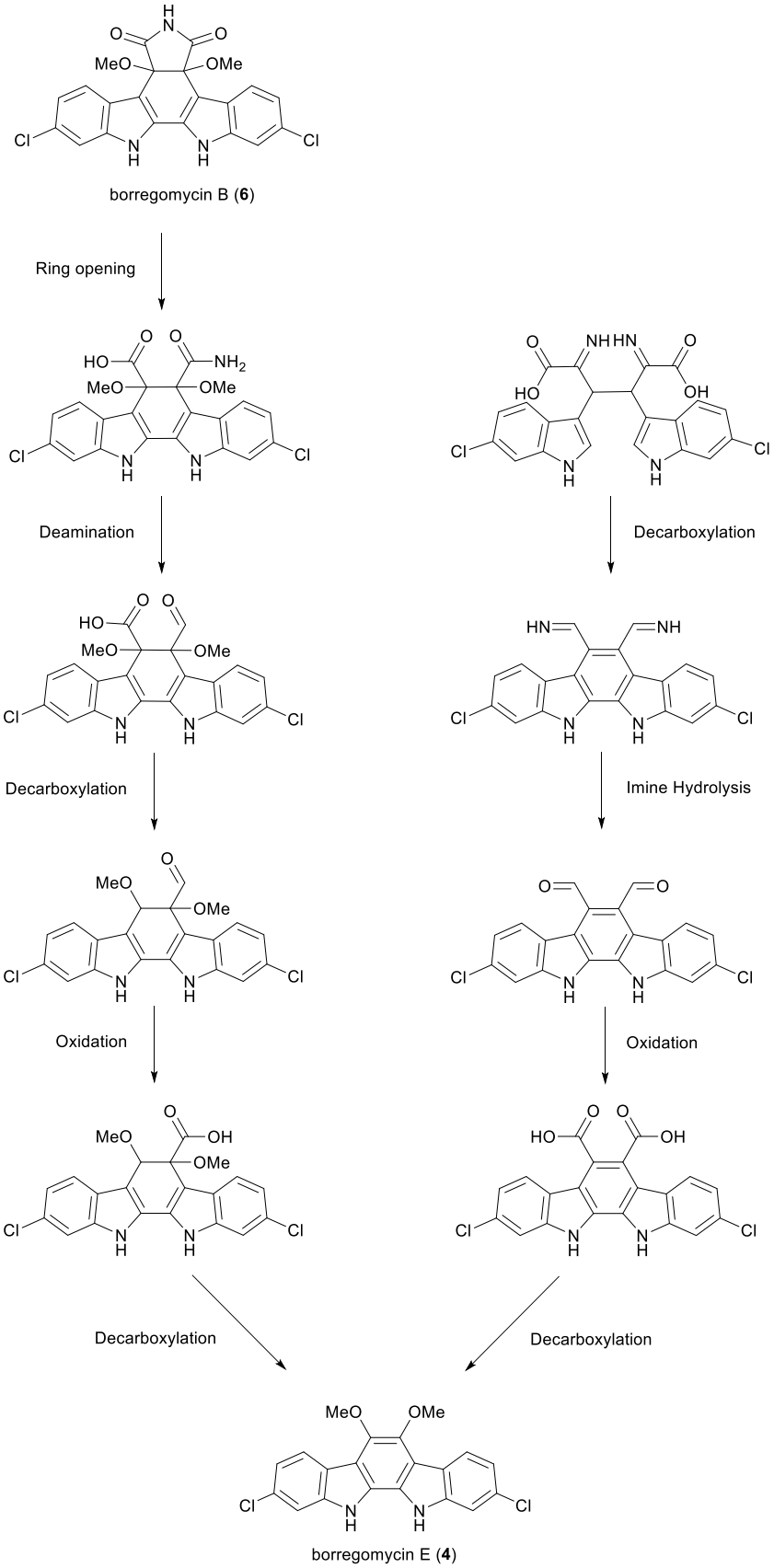


Figure S78. Putative pathways for the biosynthesis of borregomycin E (**4**) adapted from Chilczuk et al., 2020.[21]

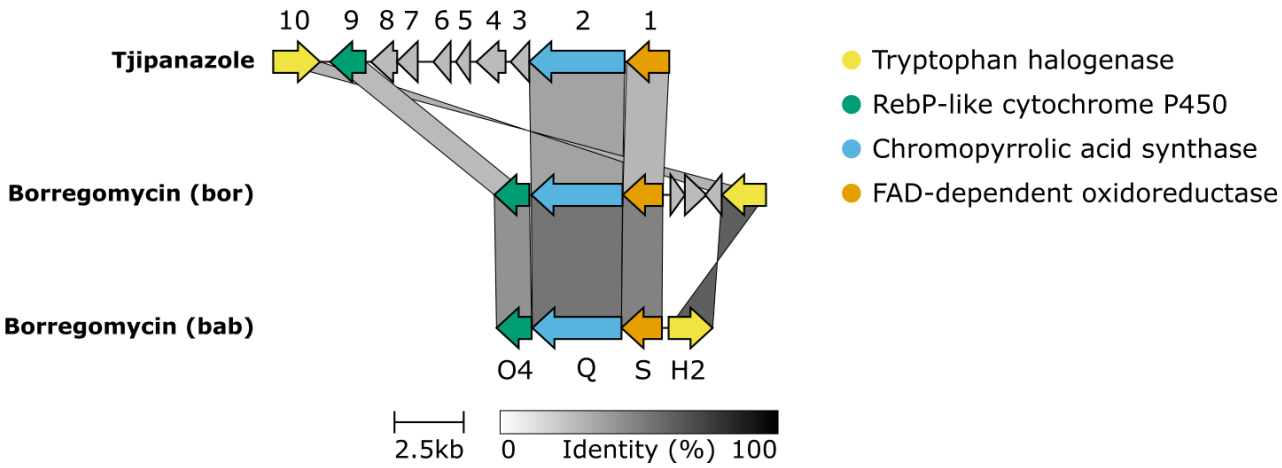


Figure S79. Comparison of borregomycin (*bor* and *bab*) and tjipanazole (*tjp*) BGCs. For simplicity, only regions homologous to tjipanazole biosynthesis are shown. Made using clinker[22]

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