

Chlorinated Glycopeptide Antibiotic peptide precursors improve Cytochrome P450-catalyzed cyclization cascade efficiency

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Supporting Information

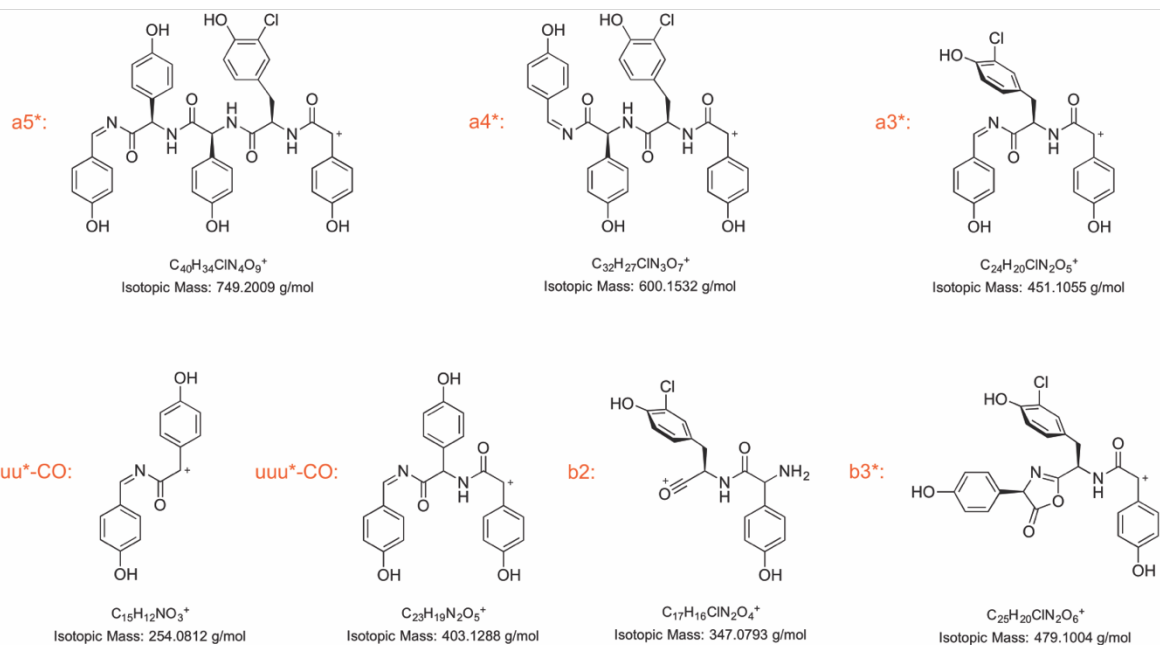
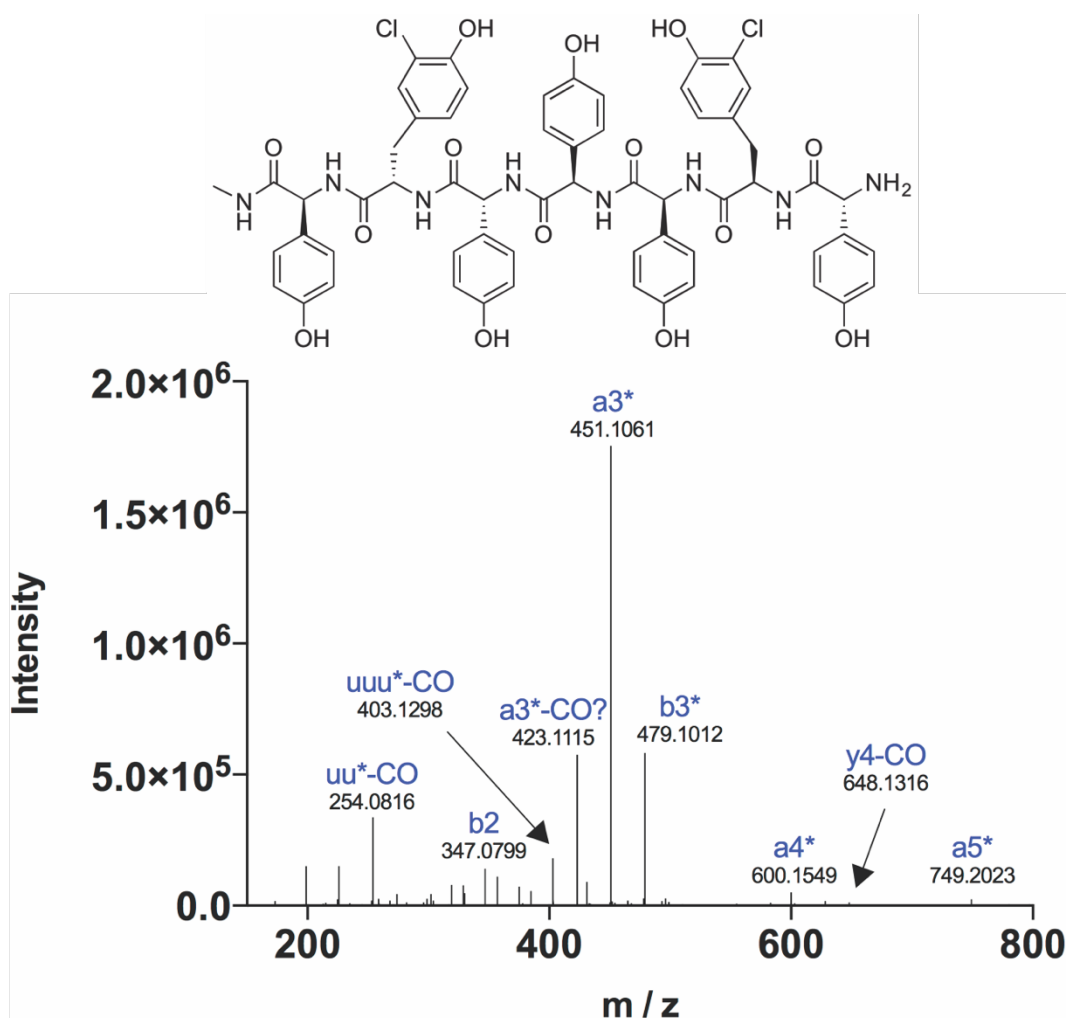


Figure S1. MS² fragmentation spectra and assignment of methylamine cleaved chlorinated, linear teicoplanin-like peptide **1**. MS² spectra are derived from the initial peptide with doubly ^{35}Cl labeling (isotopic mass: 1170.3293 g/mol).

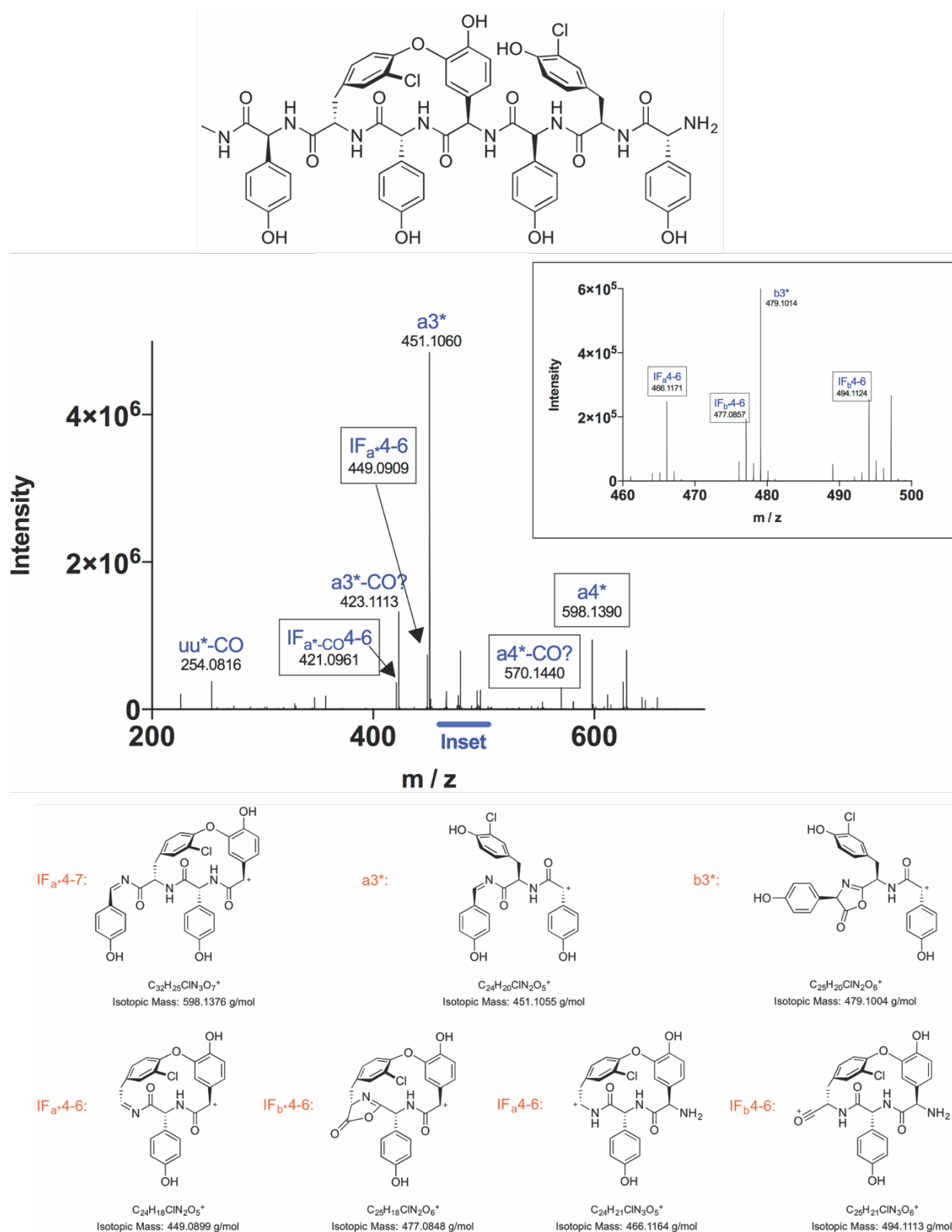


Figure S2. MS² fragmentation spectra and assignment of methylamine cleaved chlorinated, monocyclic teicoplanin-like peptide **1**; MS² spectra are derived from the initial peptide with doubly ³⁵Cl labeling (isotopic mass: 1168.3137 g/mol). Spectra clearly indicate the presence of the C-O-D ring installed by OxyB_{tei}.

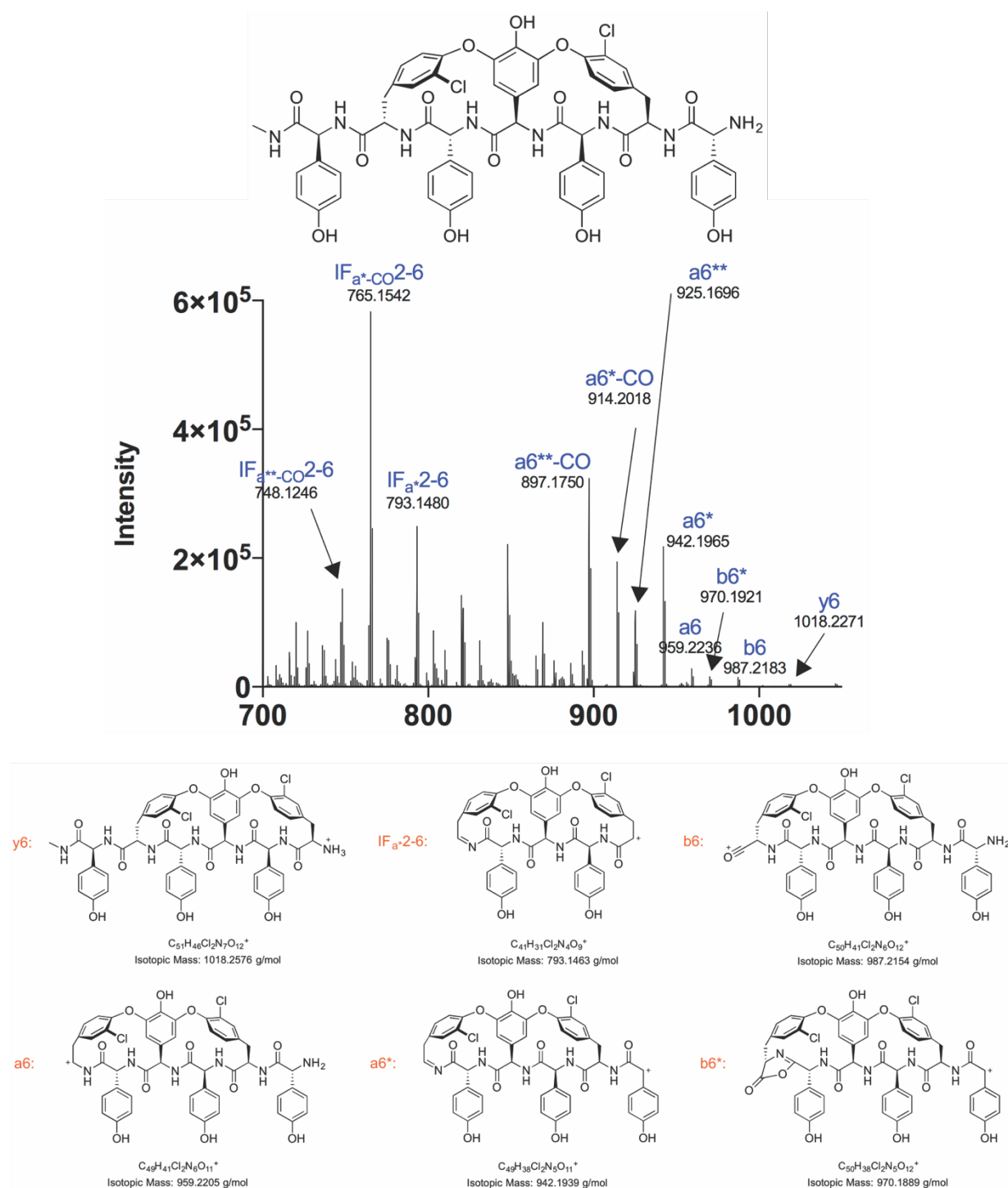


Figure S3. MS2 fragmentation spectra and assignment of methylamine cleaved chlorinated, bicyclic teicoplanin-like peptide **1**; MS² spectra are derived from the initial peptide with doubly ³⁵Cl labeling (isotopic mass: 1166.2980 g/mol). Spectra clearly indicate the presence of both the C-O-D ring installed by OxyB_{tei} and the presence of the D-O-E ring installed by OxyA_{tei}.

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tei      --MFEEINVVRAAELHRRDRFDPVPQLRSLMAEGPLTTLGTEESPGGRTAWLATGYDEIR
dbv      MEVFEEINVVLPGELHWRDRFDPVPQLRSFMAEGPMTELGAEEGPGGRTAWLATGFDEV
          :***:*** .*** *****:*****:* **:**.*****:***:
          :***:***:*****:***:*****:*****:*****:*****:*****:*****:

tei      QVLSSDDFSARLLYGGTAAGITWPGFLTQYDPPEHTRLRRMVAPAFVRRMQKFQPPER
dbv      QVLGSDKFSSRLLYGGTAAGIVFPGFITQYDPPEHTRLRRVSPAFTVRRMERFRPQVDQ
          ***.*.*.*.*****:***:*****:*****:*****:*****:*****:

tei      VVQDSLDAIEALGGPVDFVPRFGWSVATTATCDFLGIPRDDQADLARSLSHASRTERSGKR
dbv      VVEDCLDAIESIGGPLDFVPHFGWSIATTATCDFLGIPRDDQAELSRLHASRSQRAASR
          *:*.*****:***:*****:***:*****:*****:*****:*****:*****:

tei      RTAAGNKFMITYMNKMTARTRRDPGDDMFGVVVREYGD EITDAELTGVAAFVMGAGADQVA
dbv      RGAAGNKFMITYMGQVVARTRRDPGDDMLS VVVREHGDEITDAELTGAAAFVMGAGGDQVA
          * *****.:*.:*****:*****:*****:*****:*****:*****:

tei      RFLAAGAWLMADDPEQFALLREKPDTPVDWLDEVIRYLTIDEKTHPRVATDDVRIGDHLI
dbv      RFLAAGAWLMAEVPEQFALLRDKPDVVPDWLEEMVRYLTIDEKLTPIRALEDVRIGDRIV
          *****:*****:***.*****:***:*****:*****:*****:*****:

tei      KAGDVTCSLLAANRRNFPRPEDRFDITRVRPEHLAFGHGIIHCLGRSLAELVFTAIPA
dbv      KAGDVTCSLLGANRRHFPGPDDQFDLTRDAPNVAFGHGIHCLGRPLAELIFRSAIPA
          *****.****:*.*:***:*** * :*:***** *****:***:*****

tei      LAHRFPTRLRLAEPHREIRLGPPFFDVEALLLDW
dbv      LARRFPALRLAEPEQEIRLGPPFFDVKALLLDW
          **:***:*****.:*****:*****

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Figure S4. Sequence alignment of the OxyA homologues from the teicoplanin (tei) and A40926 (dbv) GPA biosynthetic machineries, showing the high degree of overall similarity as well as in the regions of the protein closest to the active site heme moiety. Specific structural regions close to the active site that are specifically indicated include portions of the B-C loop region (highlighted in magenta), the I-helix (highlighted in light blue and containing the conserved P450 catalytic residues essential for enzyme function) and the loop following the K-helix (highlighted in apple green).