Supplementary Information

Article

Cinnamides target *Leishmania amazonensis* arginase selectively

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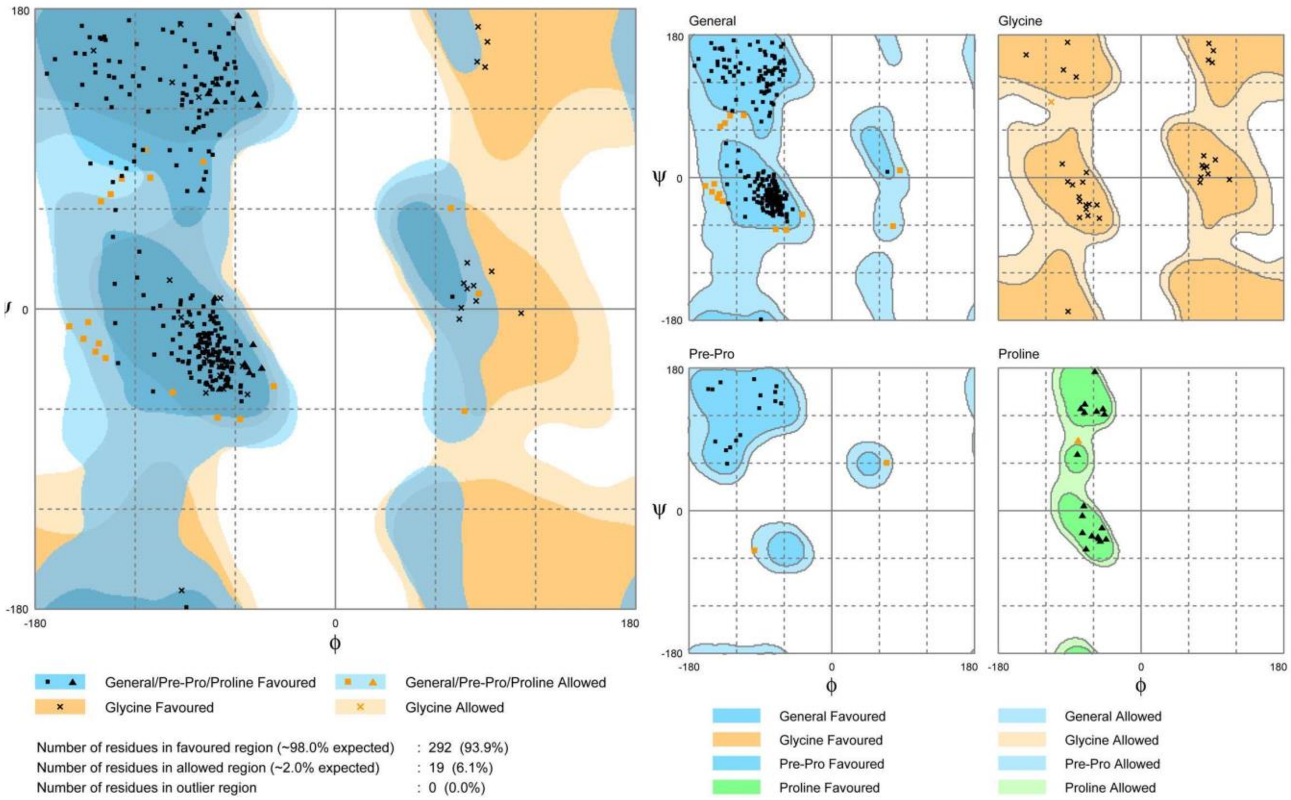

Figure S1. Ramachandran plot analysis of the modeled bovine arginase. (Right): general panel; (Left): representation of the placement of residues in homology modeled bovine arginase for general Gly, Pre-Pro, and Pro, obtained by means of RAMPAGE web server (http://mordred.bioc.cam.ac.uk/~rapper/rampage.php).

```
Q6TUJ5 Q6TUJ5_LEIME          1     MEHVQQYKFYKEKKMSIVLAPFSGGQPHSGVELGPDYLLKQGLQQDMEKLGWDTRLERVF     60
Q2KJ64 ARGI1_BOVIN           1     -------MSSKPQSIGVIGAPFSKGQPRGGVEEGPTVLRKAGLLEKLKELECDVKDYGD-     52
                                             * :.:.:: **** ***:.*** **  * * ** :.:::*  *.:

Q6TUJ5 Q6TUJ5_LEIME         61     DGKVVEARKASDNGDRIGRVKRPRLTAECTEKIYKCVRRVAEQGRFPLTIGGDHSIALGT    120
Q2KJ64 ARGI1_BOVIN          53     ---LSFAD--NLDDSPFQIVKNPRCVGKASEKLADVVAEVKKTGRISLVLGGDHSLAIGS    107
                                      :  *   . :.. :  **.** ..:.:**: . * .* : **: *.:*****:*:*:

Q6TUJ5 Q6TUJ5_LEIME        121     VAGVLSVHPDAGVIWVDAHADINTMSGTVSGNLHGCPLSILLGLDRENIPE--CFSWVPQ    178
Q2KJ64 ARGI1_BOVIN         108     ISGHARVHPDLCVIWVDAHTDINTPLTTKTGNLHGQPVSFLLKELKEKMPEVPGFYWVAP    167
                                   ::*   ****  *******:****   * :***** *:*:**   :*::**   * **

Q6TUJ5 Q6TUJ5_LEIME        179     VLKPNKIAYIGLRAVDDEEKKILHDLNIAAFSMHHVDRYGIDKVVSMAIEAVSPKGTEPV    238
Q2KJ64 ARGI1_BOVIN         168     CISAKDIVYIGLRDVDPGEHYILKTLGIKYFSMTEVDKLGIGKVMEETFSYLLGRKKRPI    227
                                    :. :.*.***** **  *: **: *.*  *** .**: **.**:. ::. :  : ..*:

Q6TUJ5 Q6TUJ5_LEIME        239     MVSYDVDTIDPLYVPATGTPVRGGLSFREALFLCERIAECGRLVALDVVECNPLLAATES    298
Q2KJ64 ARGI1_BOVIN         228     HLSFDVDGLDPSFTPATGTPVQGGLTYREGLYITEEIYKTGLLSGLDIMEVNPSLGKTPE    287
                                    :*:*** :** :.*******:***::**.*:: *.* : * * .**::* ** *. * .

Q6TUJ5 Q6TUJ5_LEIME        299     HVNDTISVGCAIARCMMGETLLYTPHTSSKL----                             329
Q2KJ64 ARGI1_BOVIN         288     EVTRTVNTTVAITMACFGVAREGNHKPIDYLSPPK                             322
                                   .*. *:..  **: . :* :   . :  . *
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Figure S2. *L. mexicana arginase* and bovine arginase sequence alignment as performed by means of the Clustal Omega program accessible via the UniprotKB web server (http://www.uniprot.org/align). *Consensus sequence

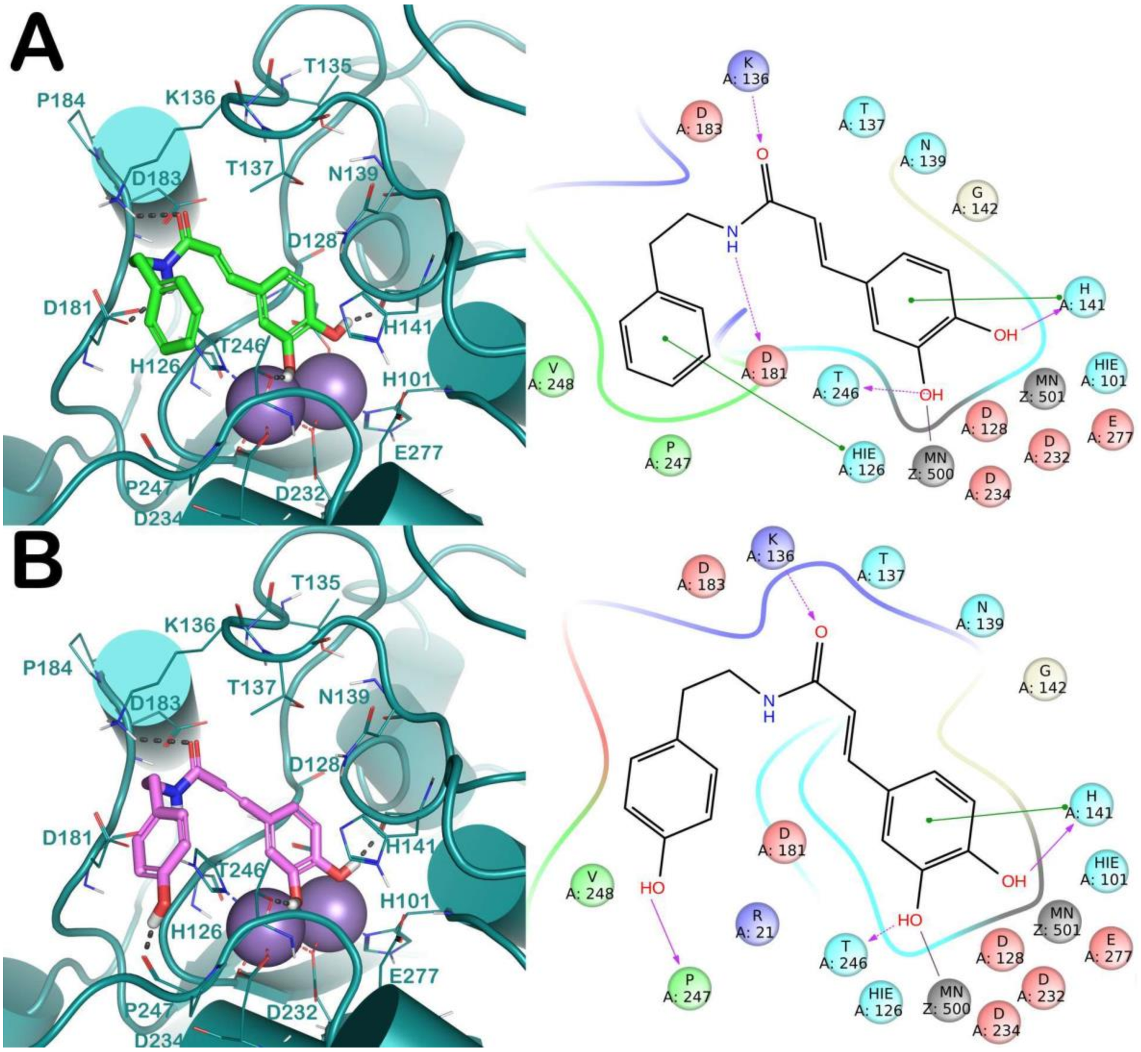

Figure S3. (A) Putative binding mode of CAPA (green sticks) into bovine arginase binding site (deep green cartoon) as found by Glide software. Metals are represented as gray spheres. Key residues of the binding site are represented by lines. H-bonds are represented as black dotted lines, while the metal coordination bonds are represented by colored dotted lines. On the right panel is reported the ligand interaction diagram. (B) Putative binding mode of compound **6** (pink sticks) into bovine arginase binding site (deep green cartoon) as found by Glide software. Metals are represented as gray spheres. Key residues of the binding site are represented by lines. H-bonds are represented as black dotted lines, while the metal coordination bonds are represented by colored dotted lines. On the right panel is reported the ligand interaction diagram The picture was generated by means of PyMOL (The PyMOL Molecular Graphics System, v1.8; Schrodinger, LLC, New York, 2015), while the ligand interaction diagram was generated by Maestro (Maestro, Schrödinger, LLC, New York, NY, 2016).

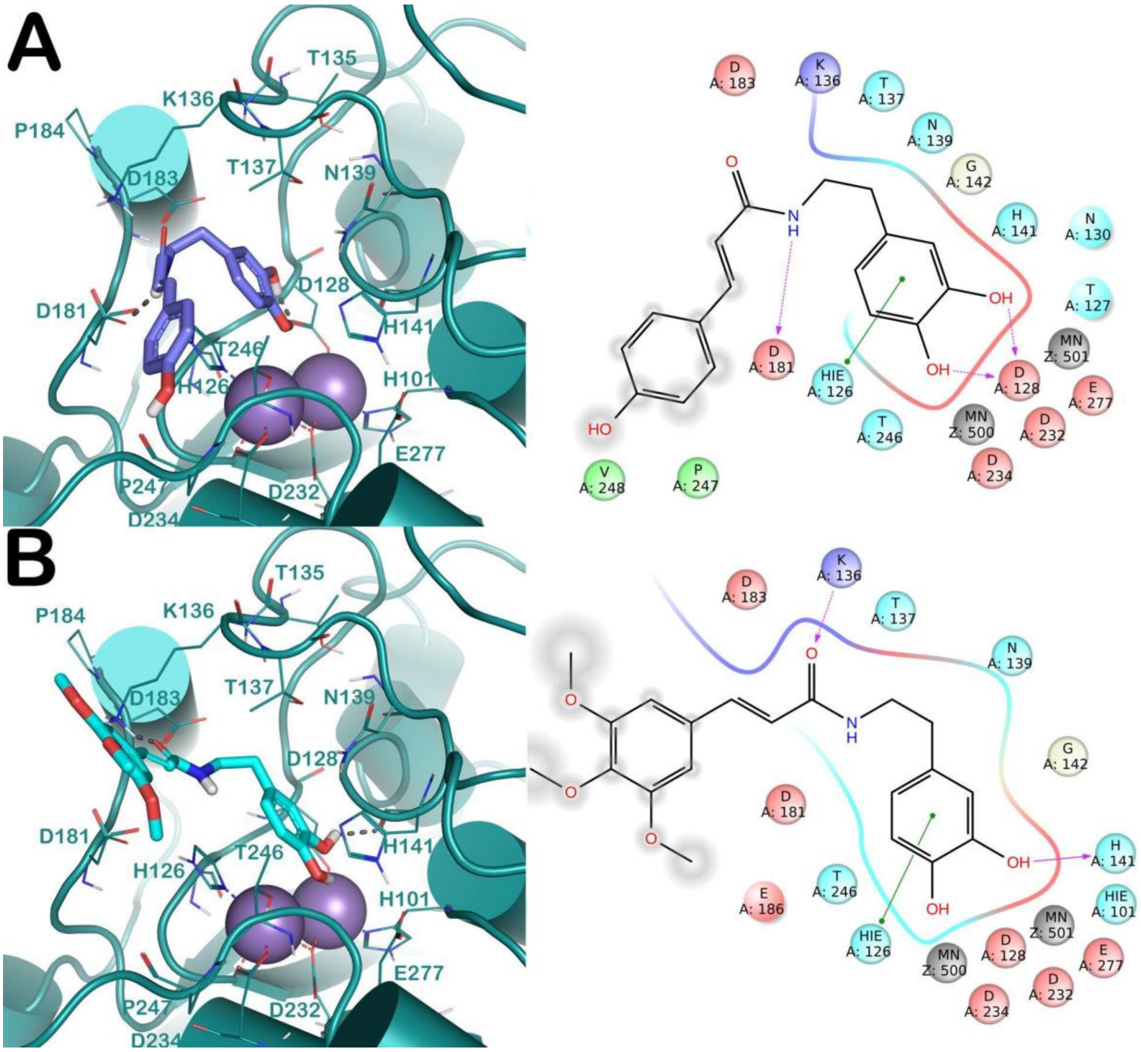

Figure S4. (A) Putative binding mode of compound **13** (blue sticks) into bovine arginase binding site (deep green cartoon) as found by Glide software. Metals are represented as gray spheres. Key residues of the binding site are represented by lines. H-bonds are represented as black dotted lines, while the metal coordination bonds are represented by colored dotted lines. On the right panel is reported the ligand interaction diagram. (B) Putative binding mode of compound **14** (cyan sticks) into bovine arginase binding site (deep green cartoon) as found by Glide software. Metals are represented as gray spheres. Key residues of the binding site are represented by lines. H-bonds are represented as black dotted lines, while the metal coordination bonds are represented by colored dotted lines. On the right panel is reported the ligand interaction diagram The picture was generated by means of PyMOL (The PyMOL Molecular Graphics System, v1.8; Schrodinger, LLC, New York, 2015), while the ligand interaction diagram was generated by Maestro (Maestro, Schrödinger, LLC, New York, NY, 2016).

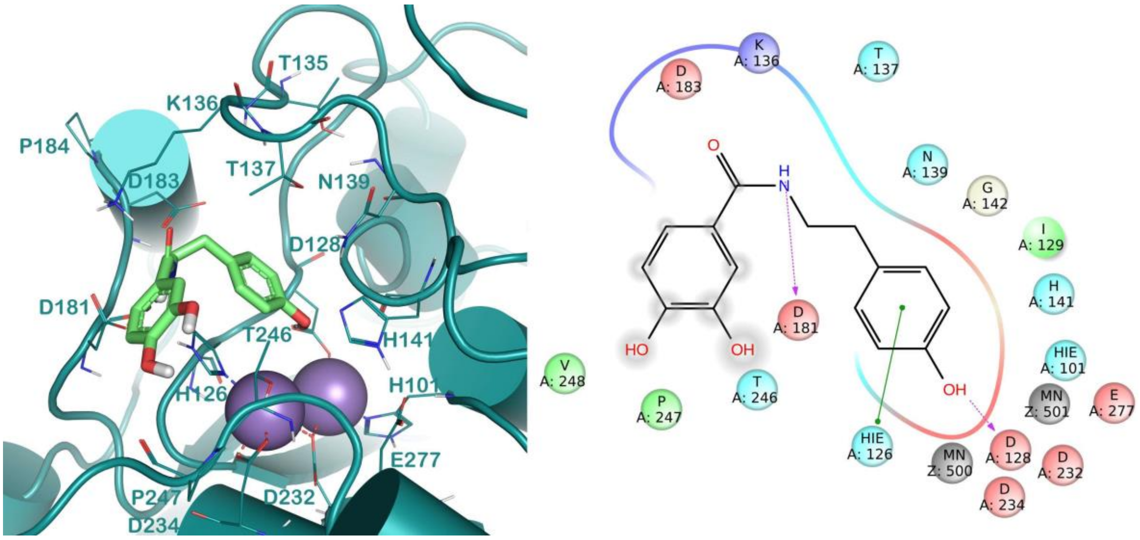

Figure S5. Putative binding mode of compound **17** (light green sticks) into bovine arginase binding site (deep green cartoon) as found by Glide software. Metals are represented as gray spheres. Key residues of the binding site are represented by lines. H-bonds are represented as black dotted lines, while the metal coordination bonds are represented by colored dotted lines. On the right panel is reported the ligand interaction diagram The picture was generated by means of PyMOL (The PyMOL Molecular Graphics System, v1.8; Schrodinger, LLC, New York, 2015), while the ligand interaction diagram was generated by Maestro (Maestro, Schrödinger, LLC, New York, NY, 2016).

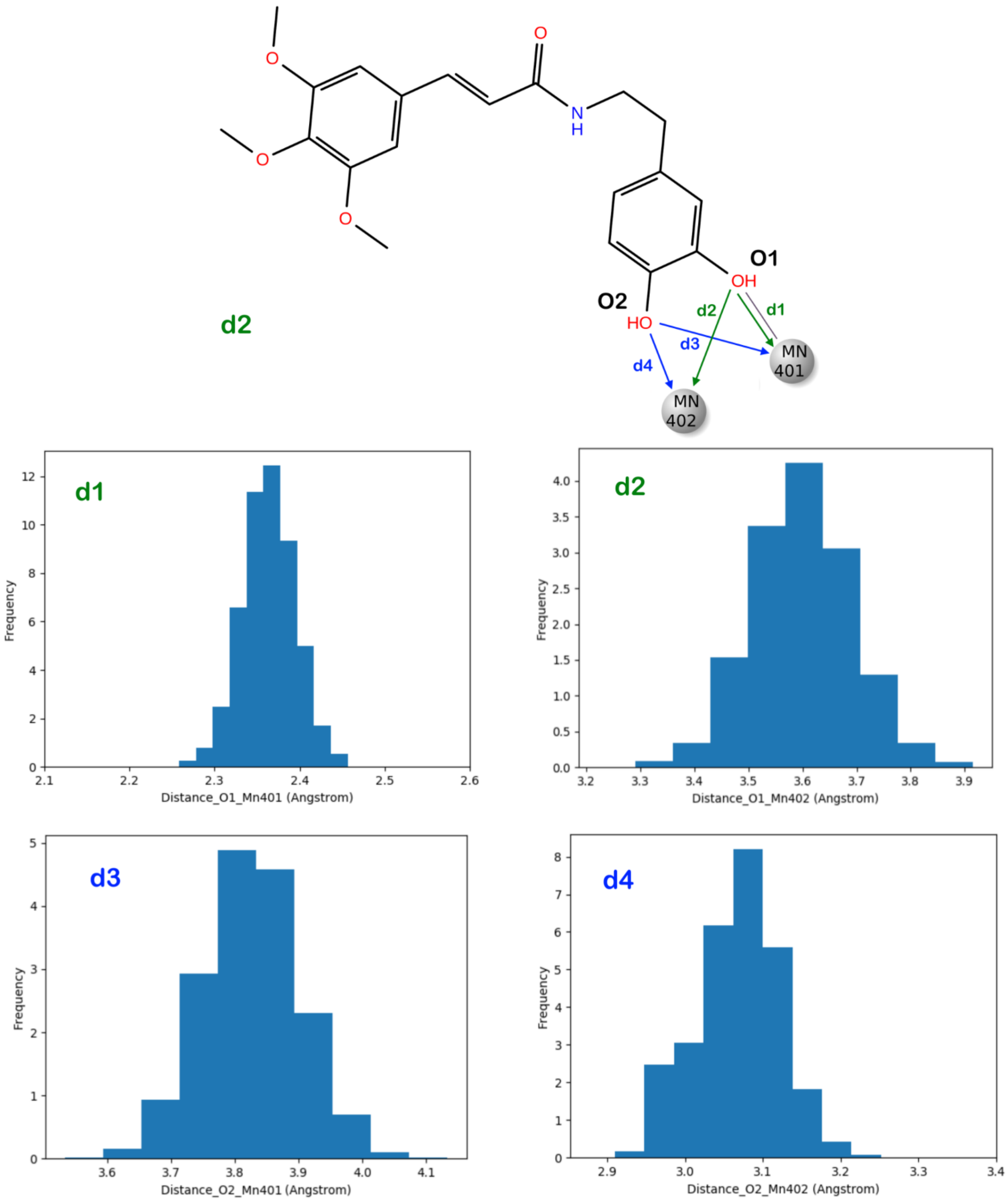

Figure S6. Plots for the selected distances measured during 200 ns of MD simulation of the complex compound **14**/L-ARG.

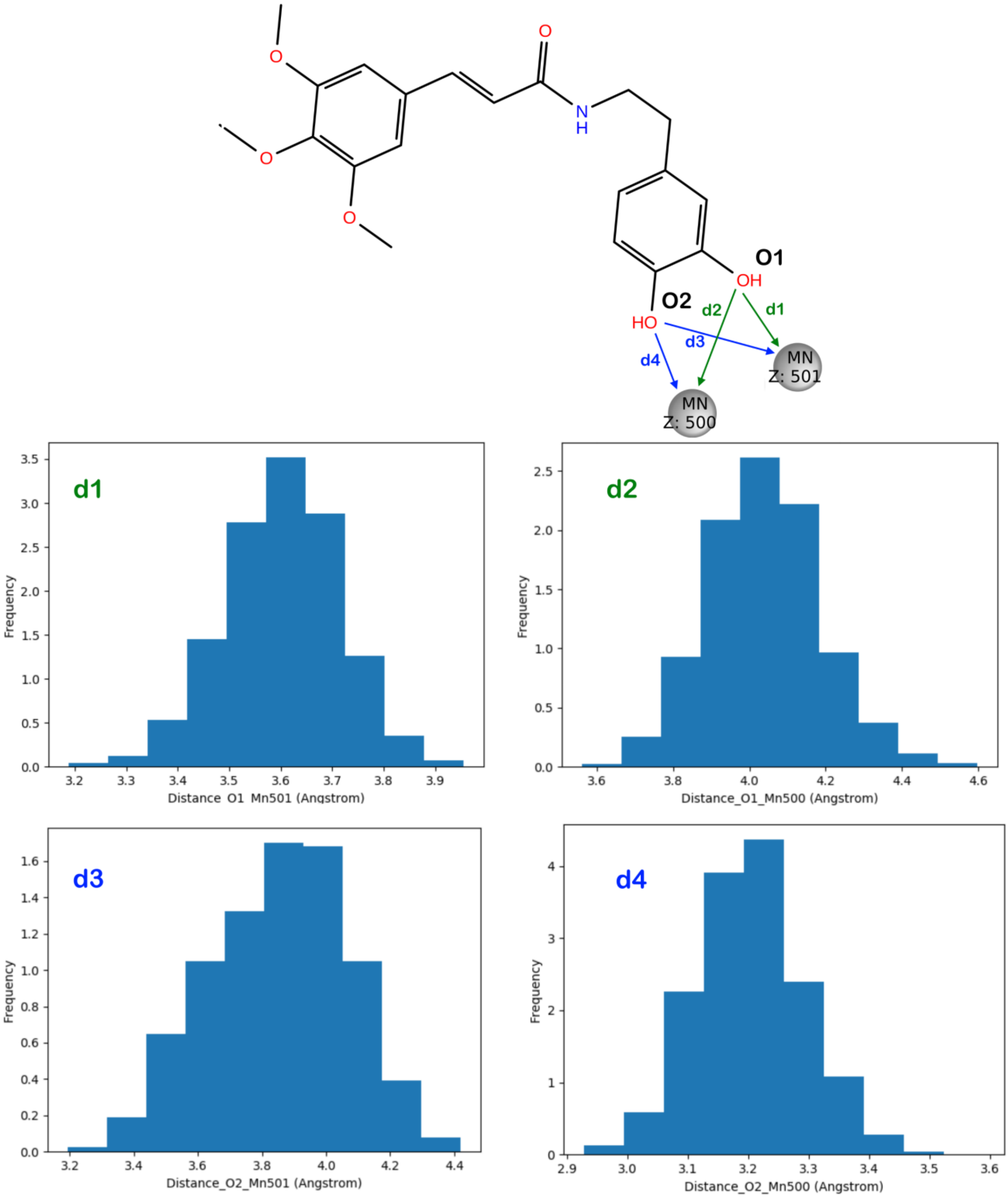

Figure S7. Plots for the selected distances measured during 200 ns of MD simulation of the complex compound **14**/B-ARG.