

## Supporting Information

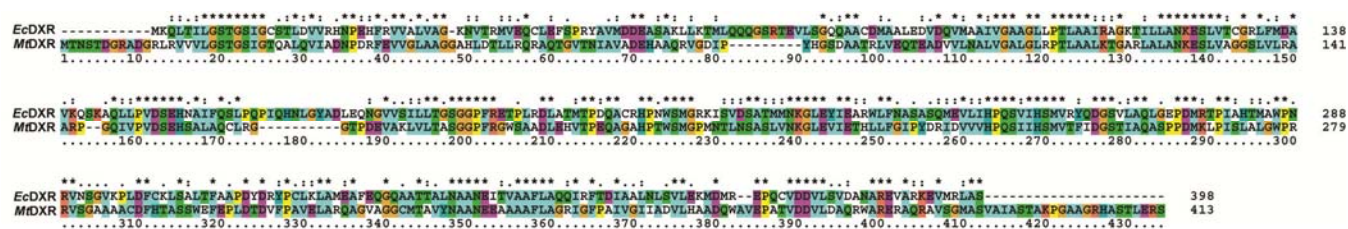
# Inhibition of 1-Deoxy-*D*-Xylulose-5-Phosphate Reductoisomerase by Lipophilic Phosphonates: SAR, QSAR and Crystallographic Studies

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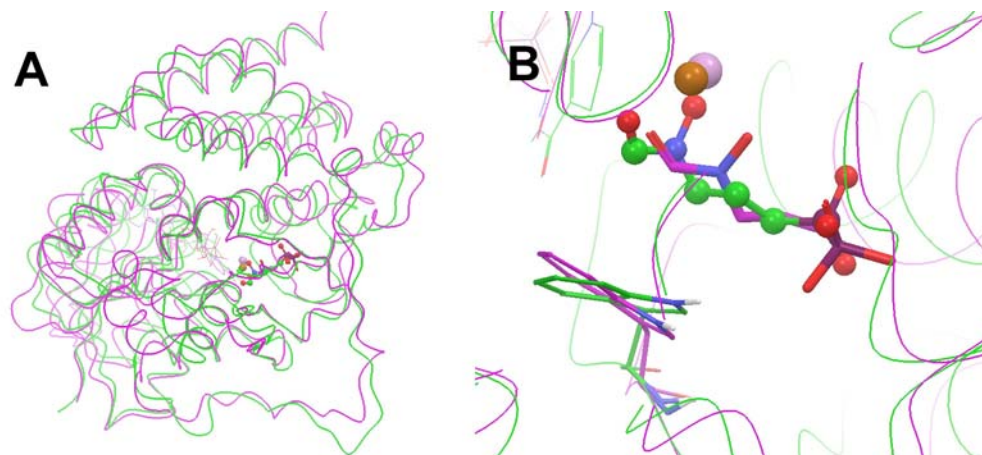
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### Table of Contents:

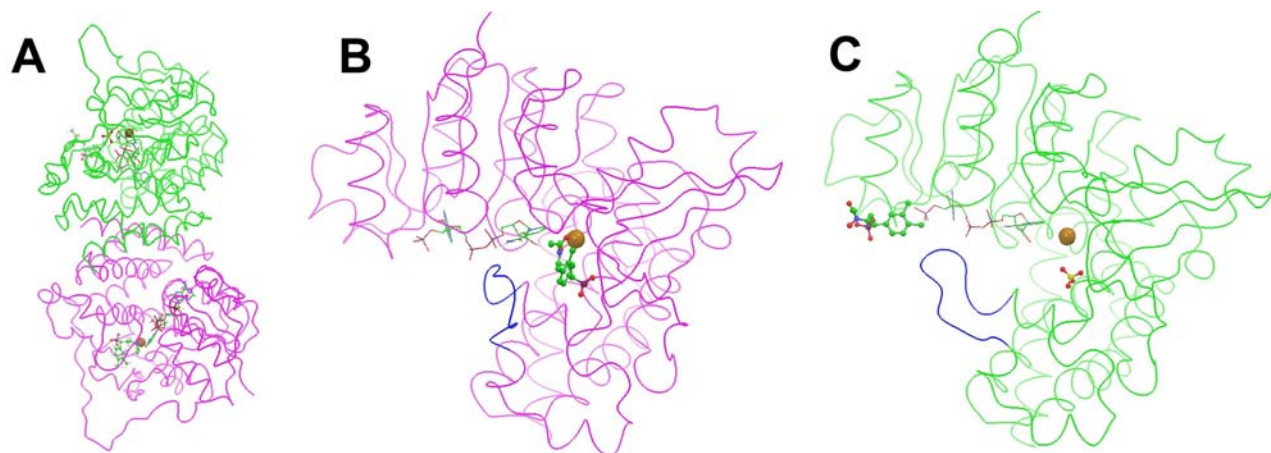
Figure S1	Page S2
Figure S2	Page S3
Figure S3	Page S4
Figure S4	Page S5
Figure S5	Page S6



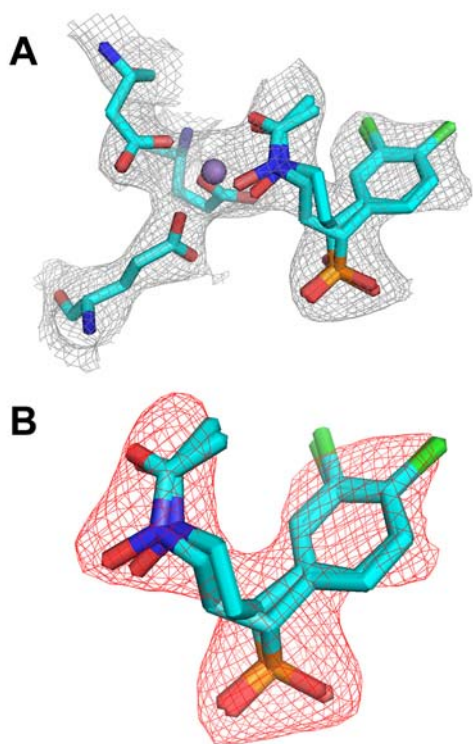
**Figure S1.** Sequence alignment for *EcDXR* and *MtDXR*, showing ~40% identity and 69% similarity.



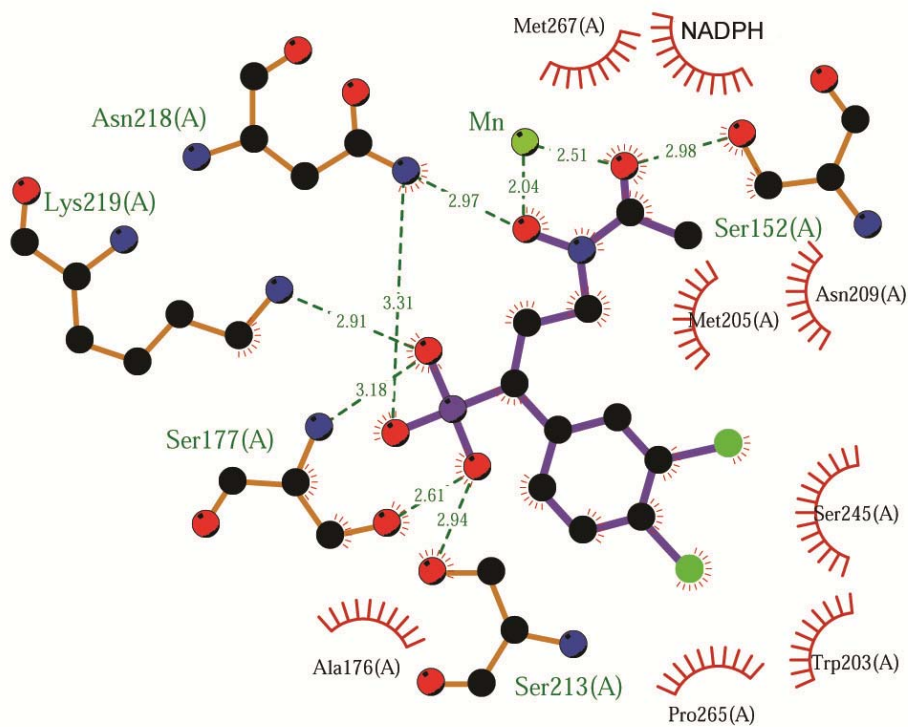
**Figure S2.** (A) Aligned crystal structures of *Ec*DXR:1 (PDB code: 2EGH, in purple) and *Mt*DXR:1 (PDB code: 2JCV, in green); (B) Close-up view of the superimposed active sites.  $Mg^{2+}$  is shown as a pink and  $Mn^{2+}$  as a brown sphere.



**Figure S3.** (A) The overall structure of the *MtDXR:4* complex as a homodimer; (B) Monomer A containing **4** (ball & stick model), Mn<sup>2+</sup> (brown sphere) and NADPH in the active site, with a “closed” flexible loop (residues 198-208) highlighted as a blue curved line; (C) Monomer B containing SO<sub>4</sub><sup>2-</sup> (ball & stick model), Mn<sup>2+</sup> (brown sphere) and NADPH in the active site, with an “open” flexible loop shown in blue. There is one molecule of **4** non-specifically bound on the surface of monomer B.



**Figure S4.** (A) The 2F<sub>o</sub>-F<sub>c</sub> electron density map of (*R*)- and (*S*)-**4**, Mn<sup>2+</sup>, and three metal-coordinating residues Asp151, Glu153 and Glu222, contoured at 1σ; (B) The F<sub>o</sub>-F<sub>c</sub> omit map of (*R*)- and (*S*)-**4**, contoured at 3σ.



**Figure S5.** Ligplot interaction diagram for (R)-4 in MtDXR.