Synthesis of inhibitor probes against GH116 D-arabinofuranosidase

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D-Arabinan is found in the cell wall component of mycobacteria such as mycolyl arabinogalactan-peptidoglycan complex and lipoarabinomannan. The D-arabinan is a branched polysaccharide with linear alpha-(1,5) linkages of D-arabinofuranoside (Ara*f*) in the backbone, alpha-(1,3) branching linkages and beta-(1,2) linkages at non-reducing terminal. D-Arabinofuranosidases (Ara*f*ases) have been found in*Microbacterium* sp. [1,2] to cleave D-arabinan. As a substrate to study one of the enzymes, beta-D-Ara*f*ase (GH116), *para*-nitrophenyl (*p*NP) beta-D-Ara*f* was synthesized stereoselectively according to the synthesis of *p*NP beta-L-Ara*f*.[3] By enzymatic reactions of the substrate suggested the retention mechanism of action. For further analysis of the enzyme, the inhibitor candidates were prepared for both competitive and covalent inhibitions and were used for the inhibition study.

In the structure of the inhibitor, a substrate motif, D-Ara*f*, was included for the binding efficiency with the enzyme. Hydroxymolactone derivative [4], which can competitively interact with both carboxy groups of two acidic amino acid for acid-base catalytic and nucleophilic residues, and 2-deoxy-2-fluoro derivative that stabilize covalently bonded enzyme-substrate complexes reacted by nucleophilic residues, were designed. Hydroxymolactone derivative was synthesized by applying the synthetic procedure [5] when investigating inhibitors of beta-L-Ara*f*ase previously, and 2-deoxy-2-fluoro derivative was synthesizedfrom a known 2-deoxy-2-fluoro-D-aranbinofuranose derivative.[6] We also would like to report their inhibitory activities against the enzyme.

Bibliographic references:

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