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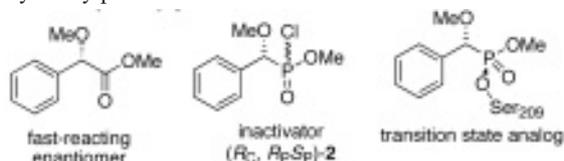
X-Ray Structure of a Bound Phosphonate Transition State Analog and Enantioselectivity of *Candida rugosa* lipase toward Chiral Carboxylic Acids

P. Grochulski^a, I.J. Colton^b, R.J. Kazlauskas^c

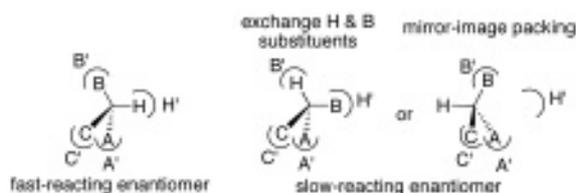
^aCanadian Light Source, University of Saskatchewan, 101 Perimeter Road, Saskatoon SK S7N 0X4 Canada; ^bMcGill University, Department of Chemistry, 801 Sherbrooke Street West, Montréal, QC H3A 2K6 Canada; ^cUniversity of Minnesota, Department of Biochemistry, Molecular Biology & Biophysics & The Biotechnology Institute, 1479 Gortner Avenue, Saint Paul, MN 55108 USA E-mail: pawel.grochulski@lightsource.ca

Keywords: protein-ligand complexes, enzyme catalysis, chirality

Candida rugosa lipase (CRL) resolves chiral aryloxy- and arylpropionic acids with moderate to high enantioselectivity [1]. To understand how CRL distinguishes between enantiomers, we determined the X-ray crystal structure of a transition state analog for a typical enantiomer of a chiral carboxylic acid ester, methyl α -methoxyphenyl acetate, **1**, covalently linked to CRL. Purified CRL shows moderate enantioselectivity ($E = 23$) toward this chiral acid favoring the (*S*)-enantiomer. To prepare a transition state analog that mimics reaction of the fast reacting enantiomer, we prepared inactivator (R_C, R_P, S_P)-**2**. An X-ray crystal structure of CRL containing the covalently linked transition state analog shows the phenyl ring in the hydrophobic tunnel of the lipase, as proposed previously based on molecular modeling [1]. Phe344 and Ph415 crowd the region near the substrate stereocenter, suggesting that shape of the active site prevents binding the slow-reacting enantiomer in a catalytically productive orientation.



Previous x-ray crystal structures of enantiomers bound to enzymes show that their relative orientation is either an exchange of two substituent positions or, more commonly, a mirror image orientation [2]. Modeling will test both of these possibilities for the slow enantiomer of **1**.



[1] Ahmed, S. N.; Kazlauskas, R. J.; Morinville, A. H.; Grochulski, P.; Schrag, J. D.; Cygler, M. *Biocatalysis*, 1994, 9, 209-225.

[2] Mezzetti, A.; Schrag, J. D.; Cheong, C. S.; Kazlauskas, R. J. *Chem. Biol.* 2005, 12, 427-437.

m09.p08

SdsA1 from *P. aeruginosa*, defines a new mechanistic class of sulfatases

Gregor Hagelueken^a, Thorsten M. Adams^b, Lutz Wiehlmann^b, Ute Widow^a, Harald Kolmar^c, Burkhard Tümmler^b, Dirk W. Heinz^a, Wolf-Dieter Schubert^a

^aDivision of Structural Biology, German Research Centre for Biotechnology, Mascheroder Weg 1, D-38124 Braunschweig, Germany. ^bKlinische Forschergruppe OE 6711, Medizinische Hochschule Hannover, Carl-Neuberg-Strasse 1, D-30625 Hannover, Germany ^cClemens-Schoepf-Institute for Organic Chemistry and Biochemistry, Darmstadt University of Technology, Petersenstrasse 22, D-64287, Darmstadt, Germany. E-mail: wds@gbf.de

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Pseudomonas aeruginosa exhibits a remarkable metabolic versatility allowing it to occupy a multitude of ecological niches. Strikingly, it is able to degrade and utilize biocidal sodium dodecyl-sulfate (SDS), the detergent of most commercial personal hygiene products. We identify SdsA1 of *P. aeruginosa* as a secreted SDS-hydrolase that allows the bacterium to utilize primary sulfates such as SDS as sole carbon or sulfur source. The crystal structure of SdsA1 reveals three distinct domains. The N-terminal catalytic domain with a binuclear Zn^{2+} cluster is a new member of the metallo- β -lactamase fold family, the central dimerization domain ensures resistance to high concentrations of SDS, while the C-terminal domain provides a hydrophobic groove, presumably to recruit long aliphatic substrates. Crystal structures of apo-SdsA1, and complexes with a substrate-analog and products, indicate a novel enzymatic mechanism involving a water molecule indirectly activated by the Zn^{2+} cluster.