Web alert

Microbial β-lactone natural products

An annotated selection of World Wide Web sites relevant to the topics in microbial biotechnology.

Obafluorin and related antibiotics
http://pubs.acs.org/doi/abs/10.1021/jo00092a025
Obafluorin is an antimicrobial β-lactone compound produced by the bacterium Pseudomonas fluorescens. In this study, the compound was synthesized, analysed chemically and tested for biological activity.

Triene β-lactone antibiotics: Triedimycins
https://www.ncbi.nlm.nih.gov/pubmed/1903377
The triedimycins are a class of spiro β-lactones. They are not potent as antibiotics but show substantial in vitro antitumor activity against murine leukaemia cells.

β-Lactone natural products inactivate homoserine transacetylase
http://www.nature.com/ja/journal/v64/n7/abs/ja201137a.html
The β-lactone ebelactone A served as a lead compound to find potent inhibitors that inactivated homoserine transacetylase. Inhibition against that enzyme makes for a useful antimicrobial substance against pathogens, such as Haemophilus influenzae.

Hymeglusin antifungal agent
http://www.abcam.com/rr-hymeglusin-ab144274.html
This commercial website contains useful information on the β-lactone antibiotic and antifungal agent, (R,R)-hymeglusin.

β-Lactones as antibacterial agents: Patents
https://www.google.com/patents/EP2254574A1?cl=en
This patent builds off a knowledge of β-lactone natural products. Novel hydrophobic β-lactone structures with alkenyl, alkynyl and phenyl groups were synthesized to test as novel antimicrobial substances.

4-Methylene oxetanone
http://webbook.nist.gov/cgi/cbook.cgi?ID=C674828&Mask=8
Methylene-substituted β-lactones are intermediates in the synthesis of mimics of β-lactone natural products. The general characteristics of a simple methylene β-lactone are available here.

(-)-Lipstatin: Pubchem
https://pubchem.ncbi.nlm.nih.gov/compound/71749817
Tetrahydrolipstatin is a β-lactone antiobesity drug, currently available with or without prescription. The Pubchem website for this compound has information on chemical properties, biological assays and commercial availability.

Fermentative production of lipstatin: Patent
https://www.google.com/patents/EP2019869A1?cl=en
Lipstatin is the β-lactone natural product produced by a Streptomyces species that can be reduced to make the drug tetrahydrolipstatin. The patent was filed to protect certain aspects of the fermentative production of the compound.

β-Lactones as synthetic intermediates for natural products
http://oaktrust.library.tamu.edu/handle/1969.1/ETD-TAMU-2011-12-10494
The β-lactone functional group is described here in this thesis for its value in the synthesis of natural products.

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Many of the natural products are not themselves β-lactones, but the versatile reactivity of β-lactones makes them useful as synthetic vehicles.

**(-)-Belactosin C: Pubchem**
https://pubchem.ncbi.nlm.nih.gov/compound/10666031#section=Top

This is the Pubchem page for the β-lactone (-)-belactosin which has been tested for anticancer, antiviral and antimicrobial activity.

**Omuralide: Pubchem**
https://pubchem.ncbi.nlm.nih.gov/compound/Omuralide#section=Top

Omuralide has a β-lactone ring fused to a second five-membered ring. The compound has been shown to inhibit cysteine endopeptidases.

**Synthesis of the proteasome inhibitors salinosporamide A, omuralide and lactacystin**
http://www.organic-chemistry.org/Highlights/2005/28November.shtml

This page contains a general description of compounds containing β-lactone and β-lactam rings.

**Omuralide and vibralactone as different proteasome inhibitors**
http://onlinelibrary.wiley.com/doi/10.1002/anie.201308567/abstract

This study shows that minor structural differences can have a large impact on the biological targets of β-lactone natural products.

**Proteasome mutant in complex with omuralide**
http://www.rcsb.org/pdb/explore.do?structureId=4r00

This link is to a Protein DataBank page. The depositories conducted a study on the binding of different drugs to a yeast mutant proteasome, and one of the compounds tested was the β-lactone omuralide.

**Salinosporamide A: Wikipedia**
https://en.wikipedia.org/wiki/Salinosporamide_A

This natural product is produced by a marine bacterium. It contains a γ-lactam-β-lactone bicyclic core structure. It is being used in early stage clinical trials to treat myeloma.

**β-Lactone inhibitors of fatty acid synthase**
https://www.ncbi.nlm.nih.gov/pubmed/18710210

In this study, the hydrophobic β-lactone natural products with alkyl chains were used as models for synthesizing 28 novel congeners to test for biological activity.

**β-Lactone inhibitors of phospholipase a2: Patent**
https://www.google.com/patents/WO2016128131A1?cl=nl

This patent describes the synthesis of novel β-lactones for the purpose of finding new inhibitors of phospholipase a2.

**Function-oriented synthesis of β-lactone proteosome inhibitors**
http://pubs.acs.org/doi/abs/10.1021/jm901098m

This study combined chemical synthesis and metabolic engineering to generate a series of salinosporamide analogues. Salinosporamide is natural product β-lactone produced by a marine bacterium that acts as a proteosome inhibitor.

**Ebelactone gene cluster**
https://www.researchgate.net/figure/242017149_fig2_Figure-6-Ebelactone-gene-cluster-of-S-aburaviensis-ATCC-31-860-Shown-are-the-putative

This site shows figures that include a gene cluster map depicting the genes encoding the biosynthesis of the β-lactone natural product ebelactone, produced by a Streptomyces species.

**Obafluorin produced by Pseudomonas fluorescens**
https://www.jstage.jst.go.jp/article/antibiotics1968/37/7/37_7_802/_article

This is the original paper describing the discovery of the β-lactone natural product obafluorin.

**Distribution of β-lactam and β-lactone producing bacteria**
https://www.ncbi.nlm.nih.gov/pubmed/7174535

This broadscale screening study, conducted in the pregenomic era, discovered a large number of β-lactam and β-lactone natural products produced by soil bacteria.
β-Lactones inhibiting bacterial virulence factors

https://www.ncbi.nlm.nih.gov/pubmed/19206121

This study highlights the potential for β-lactones to inhibit the central virulence regulator of bacterial pathogens, which could provide for an important new antibiotic mechanism.

β-Lactones for labelling active sites of bacterial enzymes

http://onlinelibrary.wiley.com/store/10.1002/anie.200705768/asset/4600_ftp.pdf?v=1&l=iwlcf2zq&s=67ab989d840aa33b3af90bd8ffc311c07537d230

This communication illustrates the wide range of different bacterial enzymes inhibited by β-lactone natural products.

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