Perkin 1 Abstracts: Natural Product Synthesis

Robert Narquizian and Jens Kaufmann

Department of Chemistry, University of Glasgow, Glasgow, UK G12 8QQ

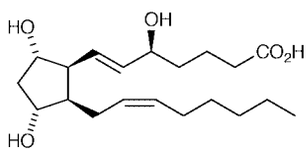
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*

5-F_{2t}-Isoprostane

Biological activity: hormonal activity.

Key steps: syntheses of the four enantiomerically pure diastereoisomers of the target were achieved using a lipase-catalysed resolution of a racemic diol.

D. F. Taber, K. Kanai and R. Pina, *J. Am. Chem. Soc.*, 1999, **121**, 7773.

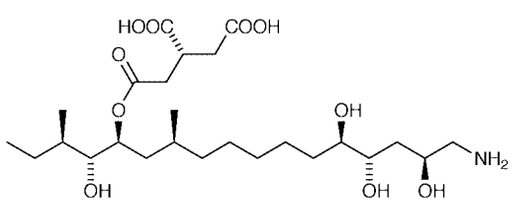


AAL-toxin TA_1

Biological activity: (a) a host-specific toxin from *Alternaria alternata* f. sp. *lycopersici*, a causal fungus of tomato stem canker; (b) reproduces similar symptoms to those of the disease for susceptible genotypes of tomato leaves in concentrations less than 10 ng mL^{-1}.

Key steps: (a) Sharpless asymmetric epoxidation; (b) condensation of a lactone with an acetylide; (c) palladium-catalysed deoxygenation.

H. Oikawa, D. Yamawaki, T. Kagawa and A. Ichihara, *Tetrahedron Lett.*, 1999, **40**, 6621.

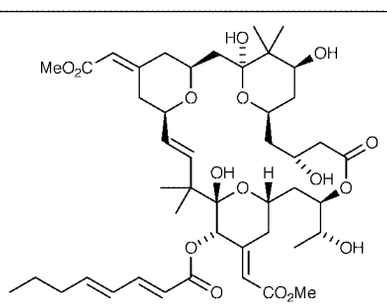


Bryostatin 2

Biological activity: antitumour agent, stimulation of T-cells, activation of protein kinase C, disruption of phorbol ester-induced tumour promotion.

Key steps: (a) aldol and directed reduction steps construct key *anti*-1,3-diol arrays; (b) asymmetric Horner–Wadsworth–Emmons condensation.

D. A. Evans, P. H. Carter, E. M. Carreira, A. B. Charette, J. A. Prunet and M. Lautens, *J. Am. Chem. Soc.*, 1999, **121**, 7540.

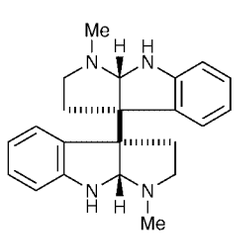


meso- and (–)-Chimonanthine and (+)-Calycanthine

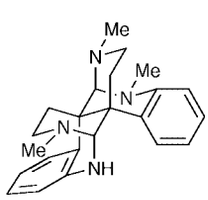
Biological activity: not reported.

Key steps: a double Heck cyclisation creates two vicinal quaternary centres with complete stereocontrol.

L. E. Overman, D. V. Paone and B. A. Stearns, *J. Am. Chem. Soc.*, 1999, **121**, 7702.



(–)-Chimonanthine



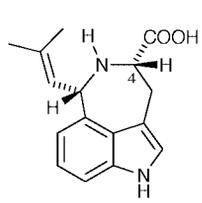
(+)-Calycanthine

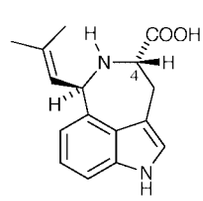
(–)-*cis* and (–)-*trans*-Clavicipitic Acids

Biological activity: isolated from culture of *Claviceps* strain SD58 or *Claviceps fusiformis* 139/2/1G; biological activity not reported.

Key steps: (a) C-4 selective functionalisation of an indole ring *via* directed lithiation of 1-(triisopropylsilyl)gramine; (b) stereoselective alkylation of Schöllkopf's bislactim ether; (c) PPTS-catalysed dehydrative cyclisation to azepinoindoles.

H. Shinohara, T. Fukuda and M. Iwao, *Tetrahedron*, 1999, **55**, 10989.



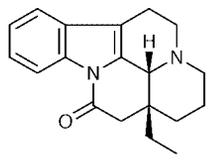


(±)-Eburnamonine

Biological activity: not reported.

Key steps: intramolecular Diels–Alder reaction of a cyclic imine to a 3-vinyl indole generates the pentacyclic skeleton in one step. The cycloaddition is catalysed by Florisil (magnesium polysilicate).

P. A. Grieco and M. D. Kaufman, *J. Org. Chem.*, 1999, **64**, 7586.

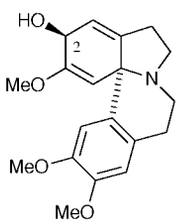


(±)-2-*epi*-Erythrinitol

Biological activity: alkaloid isolated from extracts of *Erythrina variegata* flowers.

Key steps: (a) [1+4] vinyl isocyanate-isocyanide cycloaddition; (b) intramolecular Heck reaction.

J. H. Rigby, C. Deur and M. J. Heeg, *Tetrahedron Lett.*, 1999, **40**, 6887.

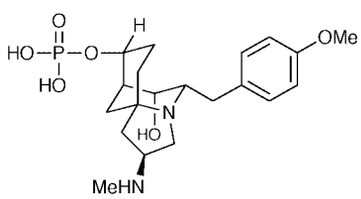


(–)-FR901483

Biological activity: immunosuppressant isolated from the fermentation broth of *Cladobotrym* sp. No. 11231 which acts by inhibition of purine nucleotide biosynthesis.

Key steps: a 1,3-dipolar cycloaddition generates a spirocyclic isoxazolidine which is hydrogenated to give an azaspirolactam.

B. B. Snider and H. Lin, *J. Am. Chem. Soc.*, 1999, **121**, 7778.

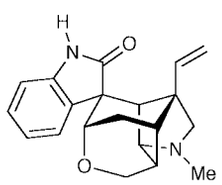


(±)-Gelsemine

Biological activity: not reported.

Key steps: (a) aza-Cope rearrangement; (b) Mannich cyclisation; (c) intramolecular Heck reaction.

A. Madin, C. J. O'Donnell, T. Oh, D. W. Old, L. E. Overman and M. J. Sharp, *Angew. Chem., Int. Ed.*, 1999, **38**, 2934.

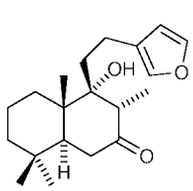


(–)-Hispanolone and Prehispanolone

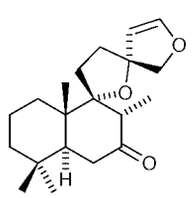
Biological activity: (a) PAF receptor antagonist; (b) inhibits ^{3}H-platelet activating factor binding to rabbit platelet membranes ($IC_{50} = 4 \times 10^{-6}$M).

Key steps: (a) Pd(0)-catalysed Sonogashira cross-coupling reaction; (b) intramolecular Michael addition.

W. S. Cheung and H. N. C. Wong, *Tetrahedron*, 1999, **55**, 11001.



(-)-Hispanolone



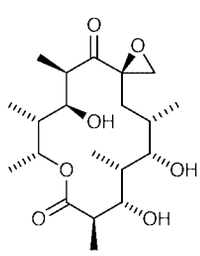
Prehispanolone

Oleandolide

Biological activity: Oleandomycin inhibits bacterial RNA-dependent protein synthesis by binding to the 50–S ribosomal subunit and blocking either translocation and or transpeptidation.

Key steps: (a) asymmetric *anti*-crotylation of aldehydes mediated by $TiCl_4$ using scalemic crotylsilanes as nucleophiles; (b) Pd(0)-catalysed fragment coupling of an organozinc reagent with an enol triflate.

T. Hu, N. Takenaka and J. S. Panek, *J. Am. Chem. Soc.*, 1999, **121**, 9229.

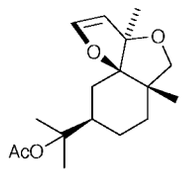


Phytuberin

Biological activity: (a) metabolite induced by stress on potato stems and tobacco leaves; (b) modest antifungal activity.

Key steps: (a) alkoxide-directed addition of dichloromethyllithium; (b) alkoxide-mediated hydrolysis of a dichloromethyl alcohol.

G. A. Kraus and X. Wang, *Synlett*, 1999, **9**, 1395.

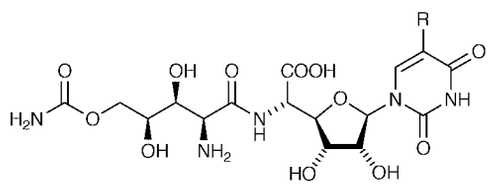


(+)-Polyoxin J and (+)-Polyoxin L

Biological activity: (a) antibiotic; (b) specific action against phytopathogenic fungi and human fungal pathogens.

Key steps: addition of vinylmagnesium bromide to an L-threose derivative.

K. Uchida, K. Kato and H. Akita, *Synthesis*, 1999, **9**, 1678.



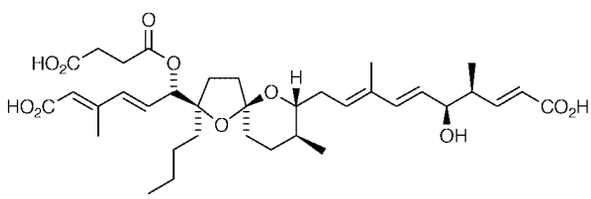
R=Me Polyoxin J
R=H Polyoxin L

Reveromycin B

Biological activity: (a) antibiotic; (b) inhibits mitogenic activity induced by the epidermal growth factor (EGF) in a mouse epidermal keratinocyte.

Key steps: (a) one-pot Julia olefination; (b) Wittig reactions; (c) Horner-Wadsworth-Emmons reaction; (d) coupling between a Weinreb amide and an alkyne.

T. Masuda, K. Osako, T. Shimizu and T. Nakata, *Org. Lett.*, 1999, **1**, 941.

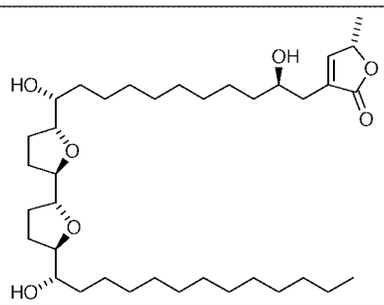


Squamotacin

Biological activity: cytotoxic selectivity for the human prostate tumour cell line.

Key steps: (a) Sharpless asymmetric dihydroxylation reaction; (b) Sharpless asymmetric epoxidation reaction.

S. C. Sinha, S. C. Sinha and E. Keinan, *J. Org. Chem.*, 1999, **64**, 7067.

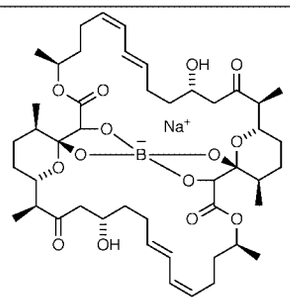


Tartrolon B

Biological activity: broad spectrum antibiotic against Gram-positive bacteria.

Key steps: (a) two aldol connections; (b) esterifications to create first a dimer and then the 42-membered diolide ring.

M. Berger and J. Mulzer, *J. Am. Chem. Soc.*, 1999, **121**, 8393.

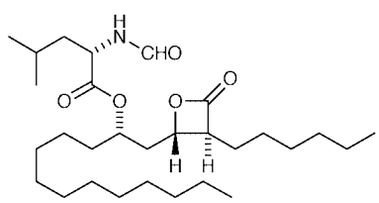


(–)-Tetrahydrolipstatin

Biological activity: potent and irreversible inhibitor of pancreatic lipase.

Key steps: olefin metathesis of an acrylate ester.

A. K. Ghosh and C. Liu, *Chem. Commun.*, 1999, 1743.

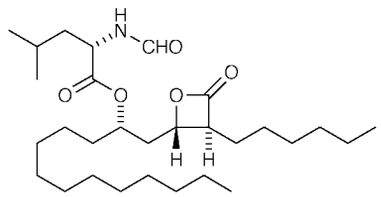


(–)-Tetrahydrolipstatin

Biological activity: potent and irreversible inhibitor of pancreatic lipase.

Key steps: oxazoline *N*-oxide-mediated [2+3] cycloadditions.

O. Dirat, C. Kouklovsky and Y. Langlois, *Org. Lett.*, 1999, **1**, 753.

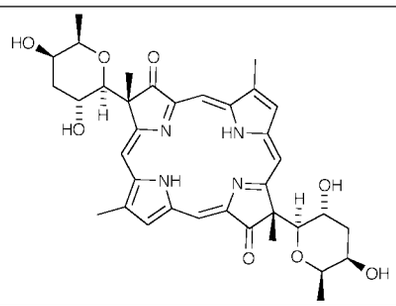


Tolyporhin A

Biological activity: reverses multidrug resistance in a vinblastine-resistant population of human ovarian adenocarcinoma cells.

Key steps: (a) *C*-glycosidation of an acetyl glycoside with a silyl ketene acetal; (b) use of thioamides in the construction of the porphyrin ring system.

W. Wang and Y. Kishi, *Chem. Lett.*, 1999, **1**, 1129.

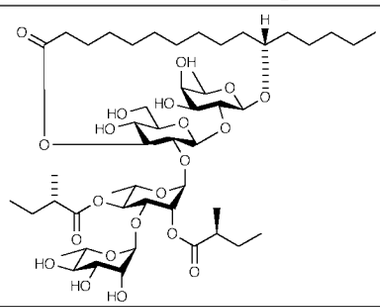


Tricolorin A

Biological activity: weed growth inhibitor and cytotoxic activity against P-388 human breast cancer cells. Tricolorin A was isolated from *Ipomoea tricolor* (convolvulaceae), a plant used in traditional Mexican agriculture as a weed controller.

Key steps: ring-closing metathesis to generate the macrolactone ring. Tricolorin G and jalapinolic acid were also synthesised.

A. Fürstner and T. Müller, *J. Am. Chem. Soc.*, 1999, **121**, 7814.

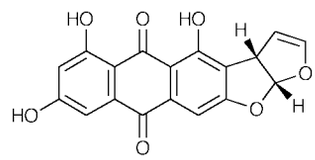


(±)-Versicolorin A

Biological activity: intermediates on the aflatoxin biogenetic pathway.

Key steps: two silyl triflate-mediated cyclisations create the dihydrobisfuran ring.

T. L. Graybill, E. G. Casillas, K. Pal and C. A. Townshend, *J. Am. Chem. Soc.*, 1999, **121**, 7729.

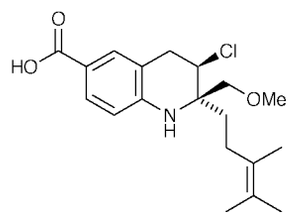


(±)-Virantmycin

Biological activity: antiviral.

Key steps: heterocyclic ring generated by the intramolecular Diels–Alder cycloaddition of a chloroalkene to an *o*-azaxylylene generated by elimination of a 2-chloromethylaniline derivative.

H. Steinhagen and E. J. Corey, *Org. Lett.*, 1999, **1**, 823.



Xerulin

Biological activity: inhibitor of the biosynthesis of cholesterol in HeLa S3 cells (ID_{50} = 1 μg g^{-1}) without being cytotoxic.

Key steps: (a) Fritsch-Buttenberg-Wiechel rearrangement; (b) $Pd(dba)_2$/CuI-catalysed Cadiot-Chodkiewicz reaction; (c) Wittig reaction.

K. Siegel and R. Brückner, *Synlett*, 1999, **8**, 1227.