Perkin 1 Abstracts: Natural Product Synthesis

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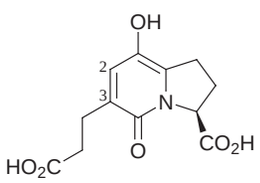
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*

(–)-A58365A and (–)-A58365B

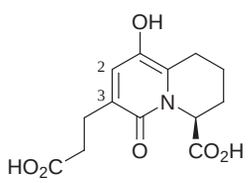
Biological activity: inhibitors of angiotensin-converting enzyme with potential for the treatment of high blood pressure.

Key steps: introduction of the C2-C3 double bond in the disguised form of spirolactones.

D. L. J. Clive, D. M. Coltart, and Y. Zhou, *J. Org. Chem.*, 1999, **64**, 1447.



(–)-A58365A



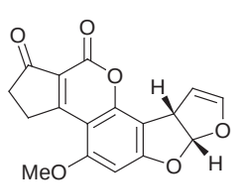
(–)-A58365B

(–)-Aflatoxin B Lactone

Biological activity: potent mycotoxin

Key steps: (a) Pd(0)-catalysed asymmetric alkylation of an *o*-bromophenol by a γ-alkoxybutenolide using a chiral phosphine; (b) reductive Heck cyclisation.

B. M. Trost and F. D. Toste, *J. Am. Chem. Soc.*, 1999, **121**, 3542.

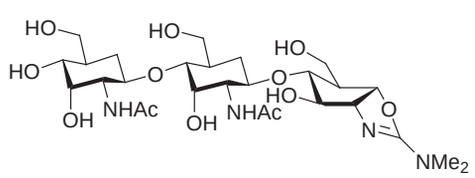


(–)-Allosamidin

Biological activity: (a) chitinase inhibitor; (b) potential insecticide and fungicide.

Key steps: asymmetric ring opening of *meso*-epoxides using $TMSN_3$ and (salen)-Cr^{III} complexes.

D. J. Kassab and B. Ganem, *J. Org. Chem.*, 1999, **64**, 1782.

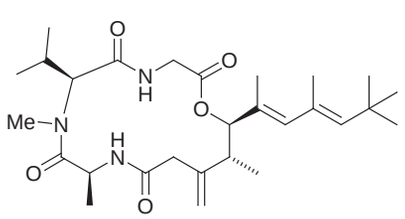


Antillatoxin

Biological activity: highly ichthyotoxic.

Key steps: *anti*-selective boron-mediated asymmetric aldol reaction.

F. Yokokawa, H. Fujiwara and T. Shioiri, *Tetrahedron Lett.*, 1999, **40**, 1915.

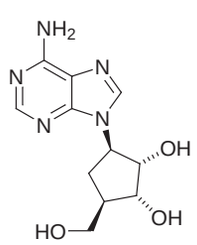


(–)-Aristeromycin

Biological activity: antibiotic.

Key steps: A 2-furyl group was used as a synthetic equivalent of the CH_2OH group; stereoselective dihydroxylation of a cyclopentene possessing the furyl group.

Y. Tokoro and Y. Kobayashi, *Chem. Commun.*, 1999, 807.

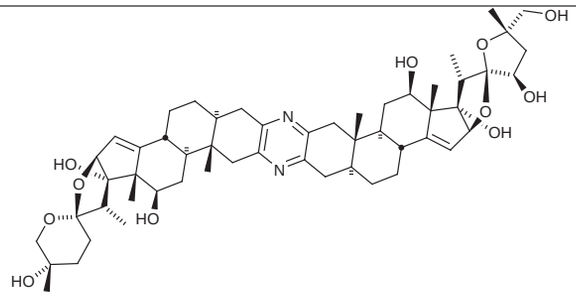


(+)-Cephalostatin 7, (+)-Cephahlostatin 12, (+)-Ritterazine K

Biological activity: extremely potent inhibition of human tumour cells.

Key steps: (a) synthesis of subunits from hecogenin acetate; (b) synthesis of the pyrazine *via* NaHTe reduction of α-azidoketones.

J. U. Jeong, C. Guo and P. L. Fuchs, *J. Am. Chem. Soc.*, 1999, **121**, 2071.

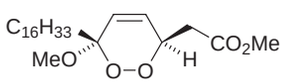


Chondrillin and Plakorin

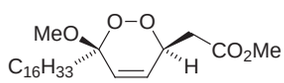
Biological activity: (a) potent activator of sarcoplasmic reticulum calcium-ATPase; (b) anticancer agents.

Key steps: (a) hydroxy-directed addition of $^1O_2$ to *Z*-allylic alcohols; (b) stereoselective radical rearrangement to form 4-hydroperoxy-2-alkenols.

P. H. Dussault, C. T. Eary and K. R. Woller, *J. Org. Chem.*, 1999, **64**, 1789.



Chondrillin



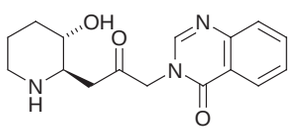
Plakorin

Febrifugine and Isofebrifugine

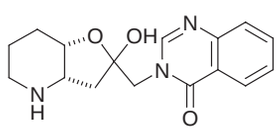
Biological activity: powerful antimalarial activity.

Key steps: (a) tin(II)-catalysed asymmetric aldol reaction; (b) Mannich-type adduct synthesised *via* a lanthanide-catalysed aqueous three-component reaction.

K. Kobayashi, M. Ueno, R. Suzuki and H. Ishitani, *Tetrahedron Lett.*, 1999, **40**, 2175.



Febrifugine



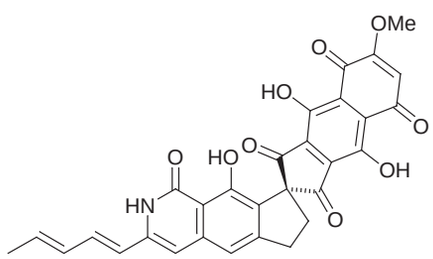
Isofebrifugine

Fredericamycin A

Biological activity: potent *in vivo* antitumour activity against a variety of tumour models (e.g. P388 leukaemia, B16 melanoma and CD8F mammary) and does not show mutagenicity in the Ames test.

Key steps: (a) stereoselective rearrangement of the epoxy acylate; (b) regiocontrolled base-induced intramolecular [4+2] cycloaddition of a functionalised homophthalic anhydride to an optically pure dienophile.

Y. Kita, K. Higuchi, Y. Yoshida, K. Iio, S. Kitagaki, S. Akai and H. Fujioka, *Angew. Chem. Int. Ed.*, 1999, **38**, 683.

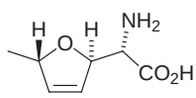


(+)-Furanomycin

Biological activity: (a) competitive antagonist of L-isoleucine; (b) inhibits the growth of T-even coliphage.

Key steps: radical cyclisation.

J. Zhang and D. L. J. Clive, *J. Org. Chem.*, 1999, **64**, 1754.

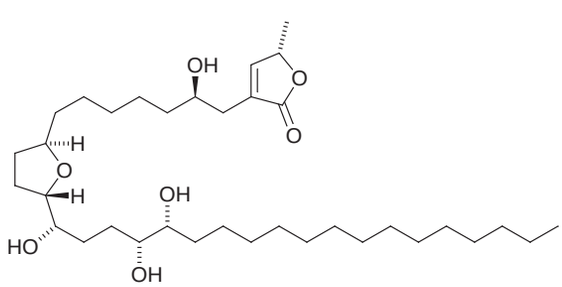


(+)-Gigantetrocin A

Biological activity: selective cytotoxicity towards cultured human tumour cells.

Key steps: (a) Sharpless asymmetric dihydroxylation; (b) $Co(modp)_2$-mediated cyclisation of a hydroxy group onto a terminal alkene to generate the tetrahydrofuran ring. The synthesis required 19 steps from *trans*-1,4-dichlorobut-2-ene.

Z-M. Wang, S.-K. Tian and M. Shi, *Tetrahedron: Asymmetry*, 1999, **10**, 667.

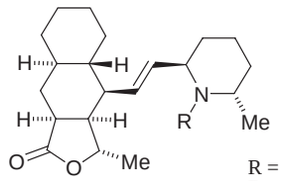


(+)-Himbacine and (+)-Himbeline

Biological activity: potent inhibitor of muscarinic receptors of the M_2 subtype; (b) lead for the treatment of Alzheimer's disease.

Key steps: intramolecular Diels-Alder reaction.

S. Chackalamannil, R. J. Davies, Y. Wang, T. Asberom, D. Doller, J. Wong, D. Leone and A. T. McPhail, *J. Org. Chem.*, 1999, **64**, 1932.



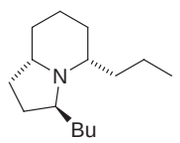
R = Me Himbacine
R = H Himbeline

(+)-Indolizidine 223AB and (–)-Pinidine

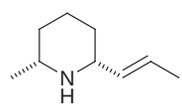
Biological activity: not reported.

Key steps: (a) asymmetric enolisation using Koga's lithium amide; (b) stereoselective cyclopropanation; (c) hypervalent λ^n-iodane-mediated fragmentation of tertiary cyclopropanol systems.

M. Kirihara, T. Nishio, S. Yokoyama, H. Kakuda and T. Momose, *Tetrahedron*, 1999, **55**, 2911.



(+)-Indolizidine 223AB



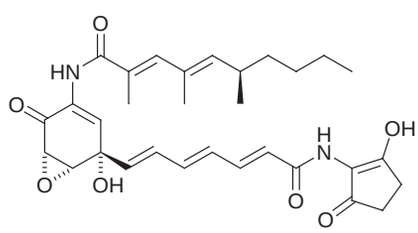
(–)-Pinidine

(+)-Manumycin A

Biological activity: (a) Manumycins A-C act as selective inhibitors of the enzyme Ras protein farnesyl transferase and thus show potential anticancer activity; (b) the manumycin family also show antibacterial, insecticidal, antifungal and anticoccidial activity.

Key steps: (a) Wynberg's chiral phase transfer epoxidation; (b) Stille cross-coupling reaction.

L. Alcaraz, G. Macdonald, J. Ragot, N. J. Lewis and R. J. K. Taylor, *Tetrahedron*, 1999, **55**, 3707.

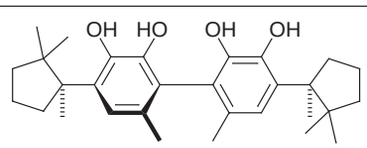


(–)-Mastigophorene A and B

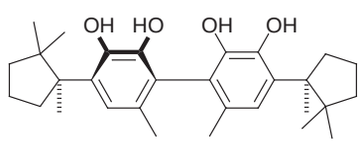
Biological activity: not reported.

Key steps: (a) use of a bicyclic lactam to construct the chiral cyclopentane; (b) a highly atroposelective oxazoline-mediated Ullmann coupling to establish chirality about the biaryl axis.

A. P. Degnan and A. I. Meyers, *J. Am. Chem. Soc.*, 1999, **121**, 2762.



(–)-Mastigophorene A



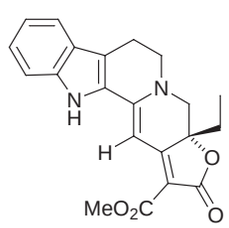
(–)-Mastigophorene B

(–)-Mitralactonine

Biological activity: extracted from the leaves of *Mitragyna speciosa* Korth. which produce narcotic-like actions when smoked or chewed.

Key steps: (a) construction of piperidinone ring *via* condensation of an epoxyketone with 3,4-dihydro-β-carboline; (b) reduction of an enone using a chiral oxazaborolidine catalyst; (c) Sharpless asymmetric epoxidation under kinetic resolution conditions.

H. Takayama, M. Kurihara, M. Kitajima, I. M. Said and N. Aimi, *J. Org. Chem.*, 1999, **64**, 1772.

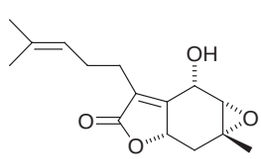


Paniculide A

Biological activity: Sesquiterpene observed from callus cultures derived from *Andrographis paniculate* - no activity reported.

Key steps: catalytic Ferrier carbocyclisation.

S. Amano, N. Takemura, M. Ohtsuka, S. Ogawa and N. Chida, *Tetrahedron*, 1999, **55**, 3855.

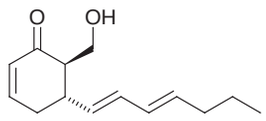


(–)-Penienone and (+)-Penihydrone

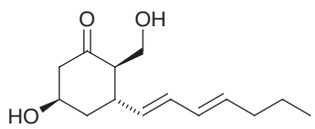
Biological activity: plant growth regulators isolated from a *Penicillium* fungus.

Key steps: (a) Ti(II)-mediated intramolecular nucleophilic acyl substitution to generate a 1-hydroxybicyclo[3.1.0]hexane; (b) $FeCl_3$-mediated ring expansion of a 1-hydroxybicyclo[3.1.0]hexane to generate a 3-chlorocyclohexanone.

G. Hareau, M. Koiwa, S. Hikichi and F. Sato, *J. Am. Chem. Soc.*, 1999, **121**, 3640.



(–)-Penienone



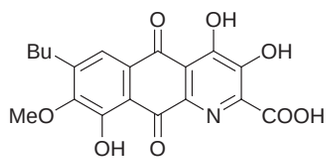
(+)-Penihydrone

Phomazarin

Biological activity: cytotoxic.

Key steps: (a) heterocyclic azadiene inverse electron demand Diels-Alder reaction using a 1,2,4-triazine as a precursor of the pyridine ring; (b) Friedel-Crafts ring closure.

D. L. Boger, J. Hong, M. Hikota and M. Ishida, *J. Am. Chem. Soc.*, 1999, **121**, 2471.

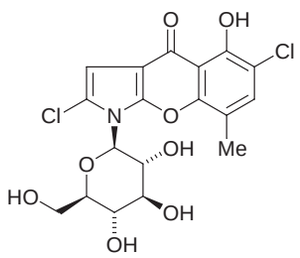


Pyralomicin 2C

Biological activity: novel antibiotic.

Key steps: *N*-glucosylation using Mitsunobu conditions.

K. Tatsuta, M. Takahashi and N. Tanaka, *Tetrahedron Lett.*, 1999, **40**, 1929.

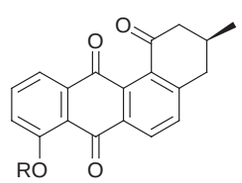


(+)-Rubiginone B_2 and (+)-Ochromycinone

Biological activity: antibiotic.

Key steps: Diels–Alder reaction between a racemic vinyl cyclohexene and (*S*)-5-methoxy-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone.

M. C. Carreño, A. Urbano and C. D. Vitta, *Chem. Commun.*, 1999, 817.



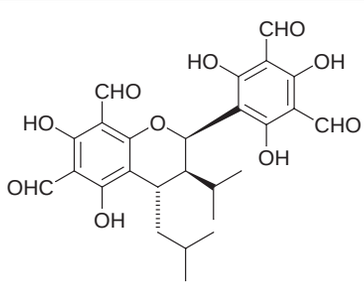
(+)-Ochromycinone (R = H)
(+)-Rubiginone B_2 (R = Me)

Sideroxylonal B

Biological activity: shows biological activities against Gram-positive bacteria, HeLa S-3 cells and aldose reductase.

Key steps: a hetero Diels–Alder reaction.

K. Tatsuta, T. Tamura and T. Mase, *Tetrahedron Lett.*, 1999, **40**, 1925.

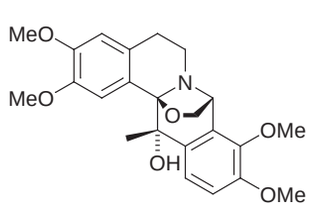


(±)-Solidaline

Biological activity: not reported.

Key steps: a single electron transfer photoaddition reaction.

R. Suau, F. Nájera and R. Rico, *Tetrahedron*, 1999, **55**, 4019.

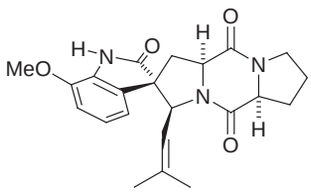


Spirotryprostatin A

Biological activity: inhibits the cell cycle in the G2/M phase with IC_{50} = 197.5 μM.

Key steps: oxidative rearrangement of a β-carboline derivative to an oxindole *via* the action of *N*-bromosuccinimide.

S. Edmondson, S. J. Danishefsky, L. Sepp-Lorenzino and N. Rosen, *J. Am. Chem. Soc.*, 1999, **121**, 2147.

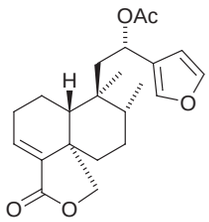


(–)-Tanabalin

Biological activity: potent antifeedant activity against the cotton pest *Pectinophora gossypiella*.

Key steps: construction of the *trans*-octalin skeleton *via* a tandem intermolecular alkylation-intramolecular Robinson annulation.

H. Watanabe, T. Onoda and T. Kitahara, *Tetrahedron Lett.*, 1999, **40**, 2545.

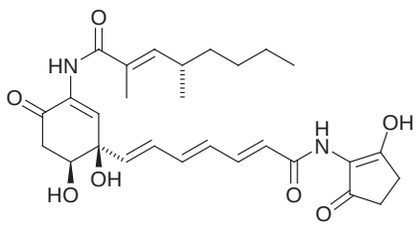


(+)-TMC-1 A

Biological activity: cytotoxic to a range of tumour lines *in vitro*.

Key steps: epoxy ketone reduction using $Na[PhSeB(OEt)_3]$.

J. J. C. Grové, X. Wei and R. J. K. Taylor, *Chem. Commun.*, 1999, 421.

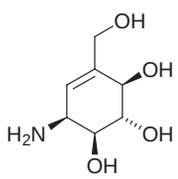


Valienamine and 2-*epi*-Valienamine

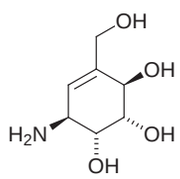
Biological activity: (a) α-glucosidase inhibitor having 50% the activity of maltase and sucrase at a concentration of 0.34 mM and 53 μM respectively; (b) antibiotic activity against *Bacillus* species.

Key steps: regio- and stereo-selective cyclic sulfite opening using azide anion.

T. K. M. Shing, T. Y. Li and H.-L. S. Kok, *J. Org. Chem.*, 1999, **64**, 1941.



Valienamine



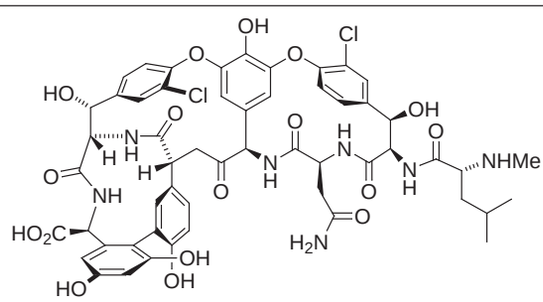
2-*epi*-Valienamine

Vancomycin Aglycone

Biological activity: antibiotic

Key steps: (a) nucleophilic substitution macrocyclisation using an *o*-fluoronitroarene to generate a 16-membered biaryl ether ring; (b) macrolactamisation to construct a 12-membered biaryl ether ring.

D. L. Boger, S. Miyazaki, S. H. Kim, J. H. Wu, O. Loiseleur and S. L. Castle, *J. Am. Chem. Soc.*, 1999, **121**, 3226.



(+)-Xenovenine

Biological activity: not reported

Key steps: intramolecular hydroamination of an allene to generate a pyrrolidine ring catalysed by an organolanthanide.

V. M. Arredondo, S. Tian, F. E. McDonald and T. J. Marks, *J. Am. Chem. Soc.*, 1999, **121**, 3633.