Perkin 1 Abstracts: Natural Product Synthesis

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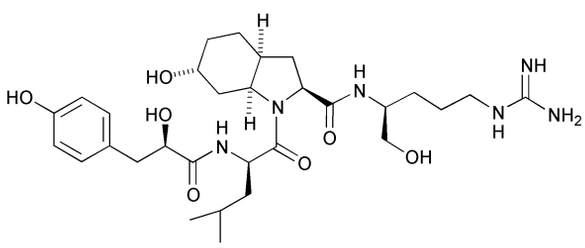
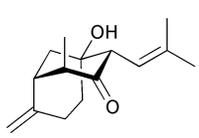
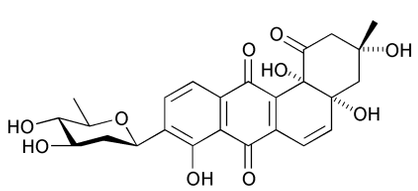
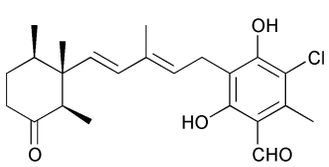
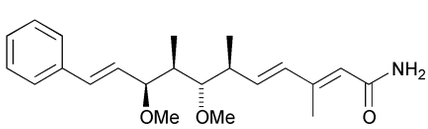
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

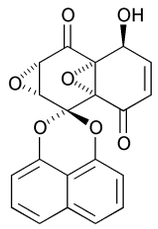
Aeruginosin 298-A *Biological activity*: protease inhibitor. *Key steps*: elaboration of tyrosine to give the octahydroindolone. N. Valls, M. López-Canet, M. Vallribera and J. Bonloch, *J. Am. Chem. Soc.*, 2000, **122**, 11248.	
(±)-AM6898A *Biological activity*: (a) isolated from *Pseudallescheria* sp.; (b) inhibitor of IgE production. *Key steps*: stereoselective aldol cyclisation. Y Fukuda, M. Sakurai and Y. Okamoto, *Tetrahedron Lett.*, 2000, **41**, 8505.	
Aquayamycin *Biological activity*: angucycline antibiotic. *Key steps*: (a) Hauser reaction; (b) intramolecular pinacol coupling. T. Matsumoto, H. Yamaguchi, M. Tanabe, Y. Yasui and K. Suzuki, *Tetrahedron Lett.*, 2000, **41**, 8393.	
(–)-Ascochlorin *Biological activity*: (a) antiviral; (b) antibiotic; (c) antitumour. *Key steps*: (a) Resorcinol benzannulation using a cascade involving a 1-alkoxyalkyne and an α-chlorocyclobutenone; (b) Pd(0)-catalysed Stille coupling to generate the diene. G. B. Dudley, K. S. Takaki, D. D. Cha and R. L. Danheiser, *Org. Lett.*, 2000, **2**, 3407.	
(+)-Crocacin C *Biological activity*: (a) isolated from *Chondromyces crocatus*; (b) moderate inhibitor of the growth of some Gram-positive bacteria; (c) potent inhibitor of animal cell cultures and several yeasts and fungi (MIC = 100 μg mL^{-1} against the fungus *Saccharmyces cerevisiae*). *Key steps*: (a) stereoselective Stille cross-coupling to afford the (*E,E*)-dienamide moiety; (b) substrate-controlled asymmetric *syn*-aldol reaction. J. T. Feutrill, M. J. Lilly and M. A. Rizzacasa, *Org. Lett.*, 2000, **2**, 3365.	

(+)-Diepoxin σ

Biological activity: antitumour agent.

Key steps: (a) Ullmann coupling; (b) biomimetic oxidative spirocyclisation; (c) retro-Diels–Alder reaction to unmask a reactive enone; (d) boron-mediated asymmetric Diels–Alder reaction.

P. Wipf and J.-K. Jung, *J. Org. Chem.*, 2000, **65**, 6319.

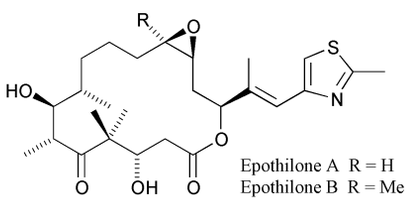


Epothilone A and B

Biological activity: potent microtubule binding, stabilizing abilities and antitumor properties; selective cytotoxicity against certain drug-resistant tumor cell lines.

Key steps: (a) asymmetric cyanosilylation of an aldehyde; (b) asymmetric aldol reaction of a ketone to an aldehyde; (c) asymmetric conjugate addition of a thiol to an α,β-unsaturated ester.

D. Sawada, M. Kanai and M. Shibasaki, *J. Am. Chem. Soc.*, 2000, **122**, 10521.

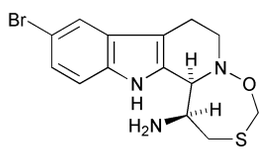


(–)-Eudistomin L

Biological activity: antiviral.

Key steps: (a) Pictet-Spengler reaction; (b) modified Pummerer reaction.

J.-J. Liu, T. Hino, A. Tsuruoka, N. Harada and M. Nakagawa, *J. Chem. Soc., Perkin Trans. 1*, 2000, 3487.

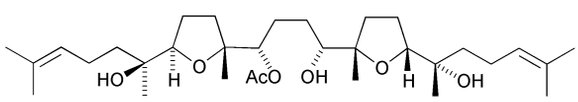


(+)-Eurylene

Biological activity: cytotoxic agent isolated from the wood of *Eurycoma longifolia*.

Key steps: two Sharpless asymmetric epoxidations; (b) oxidative cyclisations promoted by Re(VII) and Cr(VI) to generate the two tetrahydrofuran rings.

Y. Morimoto, K. Muragaki, T. Iwai, Y. Morishita and T. Kinoshita, *Angew. Chem., Int. Ed.*, 2000, **39**, 4082.

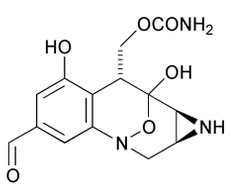


(+)-FR900482

Biological activity: anticancer agent.

Key steps: (a) enzymatic desymmetrisation of a 1,3-diester; (b) ring closing metathesis to generate a benzazocine ring. The present synthesis intersects with an earlier route by Fukuyama.

I. M. Fellows, D. E. Kaelin and S. F. Martin, *J. Am. Chem. Soc.*, 2000, **122**, 10781.

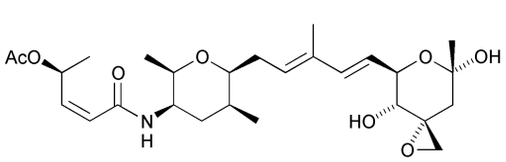


FR901464

Biological activity: (a) induces G_1 and G_2/M phase arrest in tumour cells; (b) causes changes in chromatin structure; (c) strongly differentiated transcriptional regulation.

Key steps: (a) two highly enantio- and diastereo-selective chromium-catalysed hetero-Diels–Alder reactions; (b) Noyori Ru-catalysed asymmetric hydrogenation of a β-keto ester; (c) hydrozirconation of an alkyne followed by Negishi Pd(0)-catalysed coupling with an iodoalkene to generate a conjugated diene.

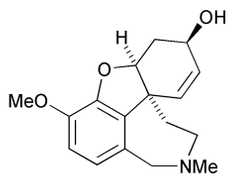
C. F. Thompson, T. F. Jamison and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2000, **122**, 10482.



(–)-Galanthamine

Biological activity: selective acetylcholinesterase inhibitor with potential for treatment of Alzheimer's disease.

Key steps: (a) Pd(0)-catalysed asymmetric allylic alkylation using a phenol as the nucleophile; (b) intramolecular Heck reaction to generate the oxacycle and a quaternary centre simultaneously.

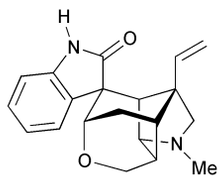


(+)-Gelsemine

Biological activity: not reported.

Key steps: (a) chiral auxiliary controlled asymmetric Diels–Alder reaction of a β-chloroacryloyl oxazolidinone with cyclopentadienyldimethylsilane to generate a bicyclo[2.2.1]heptene system; (b) divinylcyclopropane rearrangement to control the stereochemistry of the spiroindolinone system. This is the first enantiospecific synthesis of gelsemine.

S. Yokoshima, H. Tokuyama and T. Fukuyama, *Angew. Chem., Int. Ed.*, 2000, **39**, 4073.

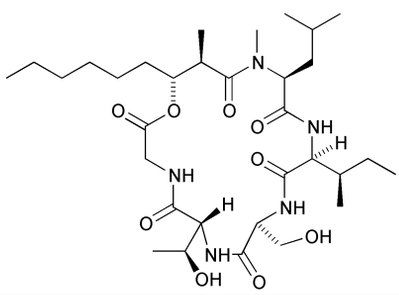


Globomycin

Biological activity: (a) antibiotic against Gram-negative bacteria; (b) specific inhibitor of signal peptidase II; (c) causes the accumulation of the acylated forms of lipoprotein in the cytoplasmic membrane resulting in cell death; (d) MIC = 0.2 μg mL^{-1}).

Key steps: (a) *anti*-selective asymmetric boron-mediated aldol reaction; (b) macrolactamisation.

H. Kogen, T. Kiho, M. Nakayama, Y. Furukawa, T. Kinoshita and M. Inukai, *J. Am. Chem. Soc.*, 2000, **122**, 10214.

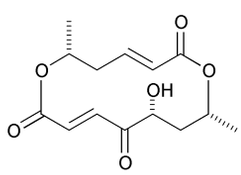


Grahamimycin A

Biological activity: (a) isolated from the medium used for the aerobic fermentation of cultures of *Cytospora* sp. ATCC 20502; (b) antibacterial; (c) antifungal.

Key steps: (a) Wittig reaction; (b) oxidative conversion of a 2-alkylfuran into a *trans* 4-oxoalk-2-enoic acid; (c) Yamaguchi macrocyclisation.

Y. Kobayashi and M. Matsuumi, *J. Org. Chem.*, 2000, **65**, 7221.

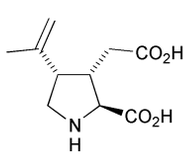


(–)-Kainic Acid

Biological activity: (a) isolated from the marine algae *Digenea simplex*; (b) anthelmintic; (c) exhibits excitatory neurotransmitting activity.

Key steps: concurrent Chugaev *syn*-elimination and intramolecular ene reaction.

H. Nakagawa, T. Sugahara and K. Ogasawara, *Org. Lett.*, 2000, **2**, 3181.

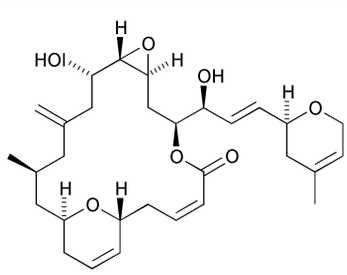


(–)-Laulimalide

Biological activity: cytotoxicity against several human tumour cell lines with IC_{50} 10–50 ng ml^{-1}.

Key steps: (a) ring closing metathesis to generate both dihydropyran rings; (b) Julia olefination to generate exocyclic methylene.

A. K. Ghosh and Y. Wang, *J. Am. Chem. Soc.*, 2000, **122**, 11027.

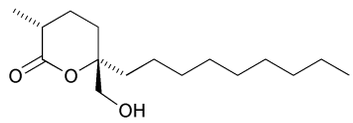


(–)-Malyngolide

Biological activity: antibiotic.

Key steps: (a) asymmetric [2+2] cycloaddition of a ketene onto a propynal to generate a β-lactone; (b) Cu(I)-catalysed S_N2' reaction of a Grignard reagent with an acetylenic β-lactone to generate an allene.

Z. Wan and S. G. Nelson, *J. Am. Chem. Soc.*, 2000, **122**, 10470.

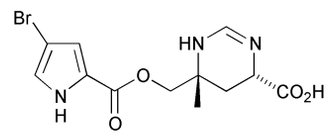


Manzacidin A

Biological activity: not reported.

Key steps: Strecker synthesis of an amino ketone.

K. Namba, T. Shinada, T. Teramoto and Y. Ohfune, *J. Am. Chem. Soc.*, 2000, **122**, 10708.

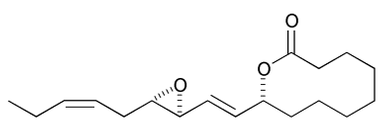


Mueggelone

Biological activity: (a) isolated from a bloom-forming strain of *Aphanizomenon flos-aquae*; (b) an inhibitor of fish development; (c) a concentration of 10 μg mL^{-1} caused 45% mortality of zebra fish larvae; surviving larvae showed edema in the heart region and thrombosis.

Key steps: (a) Horner–Wadsworth–Emmons reaction; (b) asymmetric reduction of an enone using CBS-reagent and borane–THF complex; (c) macrolactonisation.

K. Ishigami, H. Motoyoshi and T. Kitahara, *Tetrahedron Lett.*, 2000, **41**, 8897.

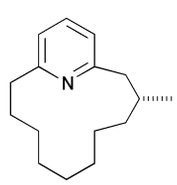


(*R*)-(+)-Muscopyridine

Biological activity: (a) isolated from the musk gland of male musk deers *Moschus moschiferus*; (b) natural perfumery ingredient.

Key steps: ring closing metathesis macrocyclisation of a 1,16-diene.

H. Hagiwara, T. Katsumi, V. P. Kamat, T. Hoshi, T. Suzuki and M. Ando, *J. Org. Chem.*, 2000, **65**, 7231.

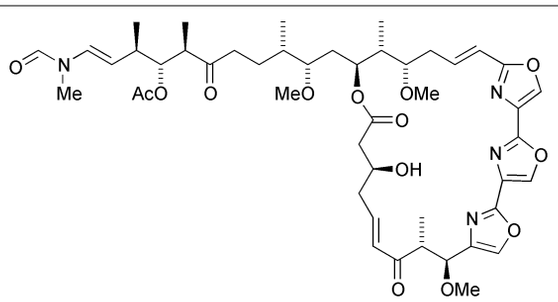


(–)-Mycalolide A

Biological activity: (a) antifungal activity; (b) cytotoxicity towards B16 melanoma (IC_{50} 0.5 ng ml^{-1}); (c) specifically inhibits actinomycin Mg^{2+}-ATPase; (d) actin depolymerising agent.

Key steps: Lewis-acid induced crotylmetallation using a homochiral allyl silane; (b) epoxide kinetic resolution using Co-salen complex; (c) Kishi-Nozaki coupling.

J. S. Panek and P. Liu, *J. Am. Chem. Soc.*, 2000, **122**, 11090.

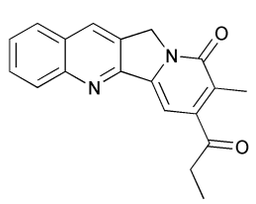


Nothapodytine B

Biological activity: (a) isolated from *Nothapodytes foetida*; (b) exhibits cytotoxic activity in the human KB cell line; (c) antiviral agent with selective activities against HSV-1 and HSV-2.

Key steps: (a) intramolecular hetero Diels–Alder reaction of a 1-azadienyne; (b) palladium-catalysed Sonogashira coupling of a 2-chloroquinoline with trimethylsilylacetylene.

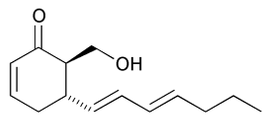
M. Toyota, C. Komori and M. Ihara, *J. Org. Chem.*, 2000, **65**, 7110.



(–)-Penienone

Biological activity: regulates plant growth.

Key steps: reaction of the anion of a cyanoenamine with *trans*-hept-2-enal.

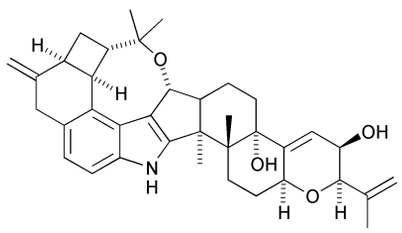


(–)-Penitrem D

Biological activity: environmental toxin produced by ergot fungi that grow on grass.

Key steps: (a) simultaneous union of two principal fragments and construction of the indole ring; (b) $Sc(OTf)_3$ promoted cation cascade to construct the oxocane ring and its pendent cyclopentane.

A. B. Smith, N. Kanoh, H. Ishiyama and R. A. Hartz, *J. Am. Chem. Soc.*, 2000, **122**, 11254.

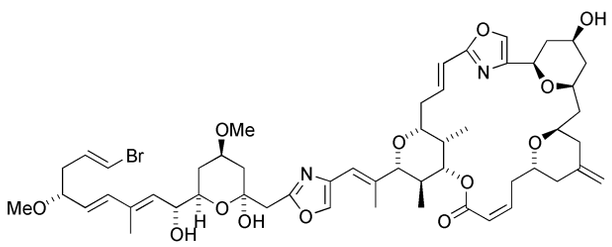


Phorboxazole B

Biological activity: Phorboxazole B isolated from an Indian Ocean sponge is a potent antitmitotic agent which halts progression of the cell cycle during S phase.

Key steps: (a) Cu(II)-catalysed enantioselective aldol reaction using a Pybox ligand; (b) Sn(II)-catalysed enantioselective aldol reaction using a Box ligand; (c) modified Julia olefination; (d) oxazole-stabilised Wittig olefination; (e) metallated oxazole alkylation.

D. A. Evans, D. M. Fitch, T. E. Smith and V. J. Cee, *J. Am. Chem. Soc.*, 2000, **122**, 10033.

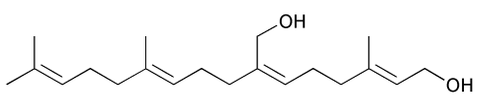


Plaunotol

Biological activity: an antibacterial agent against *Helicobacter pylori*, which is a causative agent of gastric ulcer and gastric adenocarcinoma.

Key steps: (a) an (*E*)-selective Horner–Wadsworth–Emmons reaction to give an (*E*)-α-bromoacrylate derivative; (b) a stereoselective palladium-catalysed Suzuki cross-coupling.

K. Tago and H. Kogen, *Tetrahedron*, 2000, **56**, 8825.

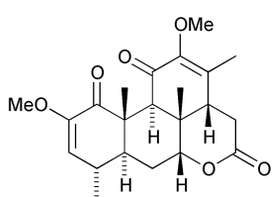


(+)-Quassin

Biological activity: (a) *in vivo* antineoplastic; (b) antiviral; (c) antimalarial; (d) antifeedant; (e) antiamoebic; (f) antituberculosis; (g) insecticidal.

Key steps: (a) stereoselective aldol reaction; (b) an *endo*-selective intramolecular Diels–Alder reaction; (c) intramolecular acylation.

T. K. M. Shing and Q. Jiang, *J. Org. Chem.*, 2000, **65**, 7059.



(–)-Slaframine

Biological activity: (a) isolated from the mold *Rhizoctonia leguminicola*; (b) a toxin that infects members of the *Leguminosae* family; (c) leads to excess salivation ("slobber syndrome"), liver damage and eventual death in ruminants that graze on the contaminated feed.

Key steps: diastereofacially selective 2+2 cycloaddition of dichloroketene with a chiral dienol ether.

M. Pourashraf, P. Delair, M. O. Rasmussen and A. E. Greene, *J. Org. Chem.*, 2000, **65**, 6966.