Perkin 1 Abstracts: Natural Product Synthesis

Andrew Gunn,[a] Jacqueline E. Milne,[a] Marcel de Puit[a] and Duncan McArthur[b]

[a] *Department of Chemistry, Leeds University, Leeds, UK LS2 9JT*
[b] *Department of Chemistry, Glasgow University, Glasgow, UK G12 8QQ*

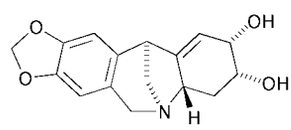
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

(–)-Brunsvigine

Biological activity: not reported.

Key steps: (a) Mitsunobu reaction; (b) anionic cyclisation of a Weinreb amide to yield an azabicyclic enone.

C.-K. Sha, A.-W. Hong and C.-M. Huang, *Org. Lett.*, 2001, **3**, 2177.

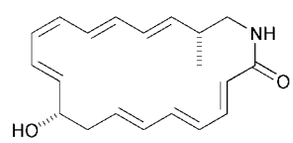


Cyclamenol A

Biological activity: inhibits leukocyte adhesion to endothelial cells

Key steps: (a) assembly of the linear polyene by Wittig and Horner olefinations; (b) ring closure *via* vanadium-mediated pinacolisation.

M. Nazaré and H. Waldmann, *Chem. Eur. J.*, 2001, **7**, 3363.

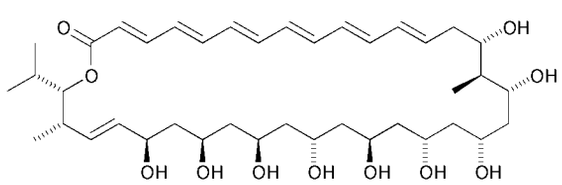


Dermostatin A

Biological activity: antifungal polyene macrolide from *Streptomyces viridogriseus* used clinically to combat deep vein mycoses. Antiproliferative activity against HIV in H9 cells.

Key steps: (a) connection of 1,3-diol motifs *via* alkylation of metallated cyano acetonides; (b) macrocyclisation *via* Wadsworth–Horner–Emmons reaction; (c) polyene construction *via* Stille coupling.

C. J. Sinz and S. D. Rychnovsky, *Angew. Chem., Int. Ed.*, 2001, **40**, 3224.

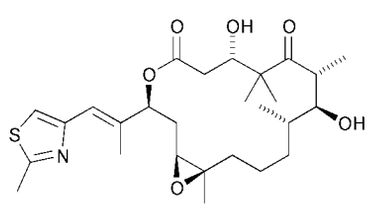


Epothilone B

Biological activity: anticancer agent.

Key steps: (a) Nozaki–Hiyama–Kishi coupling of a vinyl iodide with an aldehyde; (b) stereoselective thionyl chloride induced allylic rearrangement.

R. E. Taylor and Y. Chen, *Org. Lett.*, 2001, **3**, 2221.

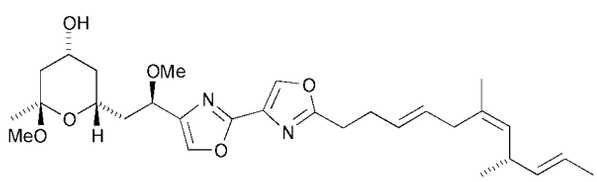


(–)-Hennoxazole A

Biological activity: (a) isolated from the marine sponge *Polyfibrospongia* sp.; (b) active against herpes simplex virus type 1 (IC_{50} = 0.6 μg mL^{-1}).

Key steps: (a) Mukaiyama aldol reaction; (b) chelation-controlled 1,3-*syn* reduction; (c) modified Wacker oxidation; (d) acid catalysed intramolecular ketalisation.

F. Yokokawa, T. Asano and T. Shioiri, *Tetrahedron*, 2001, **57**, 6311.

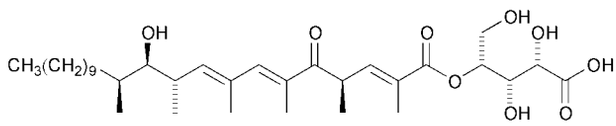


Khafrefungin

Biological activity: (a) isolated from the fermentation culture MF6020; (b) inhibitor of IPC synthase.

Key steps: (a) Zr(IV)-catalysed asymmetric aldol reaction; (b) Suzuki coupling; (c) Keck esterification.

S. Kobayashi, K. Mori, T. Wakabayashi, S. Yasuda and K. Hanada, *J. Org. Chem.*, 2001, **66**, 5580.

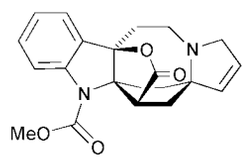


(±)-Lapidilectine B

Biological activity: (a) isolated from the leaves of the tree *Kopsia lapidilecta*; (b) biological activity not reported.

Key steps: (a) cycloaddition of a 2-azaallyllithium with phenyl vinyl sulfide to form a pyrroline ring; (b) formation of a 1,2-dihydro-3*H*-indol-3-one *via* an intramolecular cyclisation of an azido enolate.

W. H. Pearson, Y. Mi, I. Y. Lee and P. Stoy, *J. Am. Chem. Soc.*, 2001, **123**, 6724.

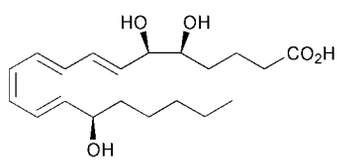


15-*epi*-Lipoxin A_4

Biological activity: (a) identified in the bronchoalveolar lavage fluid of humans with lung disease; (b) anti-inflammatory agent.

Key steps: (a) Sharpless catalytic asymmetric epoxidation; (b) stereospecific (*Z*)-reduction of a conjugated trienyne to a tetraene using Zn(Cu/Ag) in aqueous methanol.

A. R. Rodriguez and B. W. Spur, *Tetrahedron Lett.*, 2001, **42**, 6057.

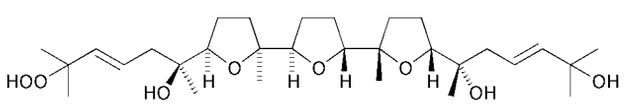


(–)-Longilene peroxide

Biological activity: (a) isolated from the wood of *Eurycoma longifolia*; (b) cytotoxic against KB cells (IC_{50} = 5.3 μg mL $^{-1}$).

Key steps: Shi's asymmetric epoxidation.

Y. Morimoto, T. Iwai and T. Kinoshita, *Tetrahedron Lett.*, 2001, **42**, 6307.

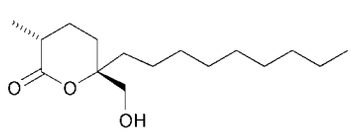


(–)-Malyngolide

Biological activity: antibiotic activity against *Streptococcus pyogenes* and *Mycobacterium smegmatis*.

Key steps: chiral bis(oxazoline) metal complex catalysed asymmetric hetero Diels–Alder reaction.

A. K. Ghosh and M. Shirai, *Tetrahedron Lett.*, 2001, **42**, 6231.

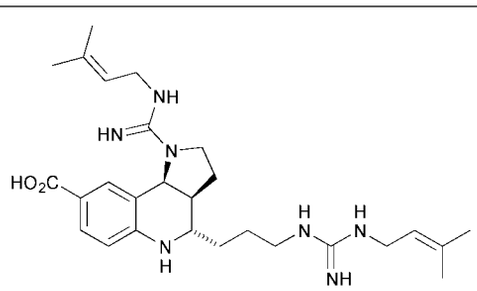


Martinellic acid

Biological activity: (a) isolated from the organic extract of the roots of *Martinella iquitosensis*; (b) potent antagonist of bradykinin (BK) B1 and B2 receptors.

Key steps: (a) CuI-catalysed coupling reaction of a β-amino ester with 1,4-diiodobenzene; (b) guanylation reaction of a secondary amine.

D. Ma, C. Xia, J. Jiang and J. Zhang, *Org. Lett.*, 2001, **3**, 2189.

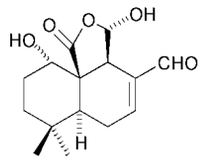


(–)-Mniopetal F

Biological activity: (a) isolated from the fermentation broth of Canadian *Mniopetalum* sp. 87256; (b) inhibitor of RNA-directed DNA-polymerases (RT, reverse transcriptases) of (HIV)-1, AMV and MMuLV.

Key steps: stereoselective intramolecular Diels–Alder reaction.

Y. Suzuki, A. Ohara, K. Sugaya, K. Takao and K. Tadano, *Tetrahedron*, 2001, **57**, 7291.

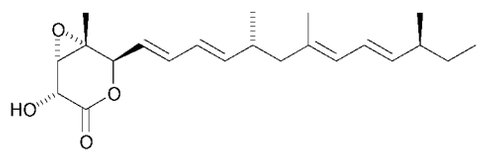


Nafuredin

Biological activity: (a) isolated from the fermentation broth of the fungal strain *Aspergillus niger* FT-0554; (b) inhibitor of NADH-fumarate reductase of *Ascaris suum* (IC_{50} = 12 nM); (c) exerts anthelmintic activity against *Haemonchus contortus* in *in vivo* trials with sheep.

Key steps: Julia olefination.

D. Takano, T. Nagamitsu, H. Ui, K. Shiomi, Y. Yamaguchi, R. Masuma, I. Kuwajima and S. Omura, *Org. Lett.*, 2001, **3**, 2289.

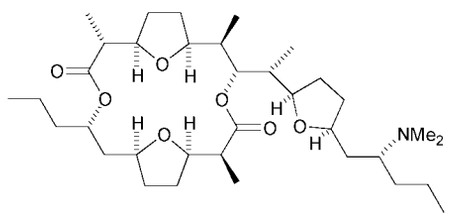


Pamamycin 607

Biological activity: (a) isolated from *Streptomyces alboniger*; (b) antifungal activity.

Key steps: (a) tin(IV) chloride-promoted reaction between an aldehyde and an allylstannane; (b) phenylselenenyl-induced cyclisation.

O. Germay, N. Kumar and E. J. Thomas, *Tetrahedron Lett.*, 2001, **42**, 4969.

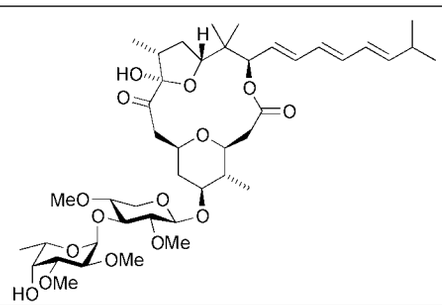


(–)-Polycavernoside A

Biological activity: toxic agent of the red alga *Polycavernosa tsudai*.

Key steps: (a) fragment linkage *via* Nozaki–Hiyama–Kishi Ni/Cr-mediated coupling; (b) asymmetric allylation; (c) triene synthesis *via* Stille coupling.

J. D. White, P. R. Blakemore, C. C. Browder, J. Hong, C. M. Lincoln, P. A. Nagornyy, L. A. Robarge and D. J. Wardrop, *J. Am. Chem. Soc.*, 2001, **123**, 8593.

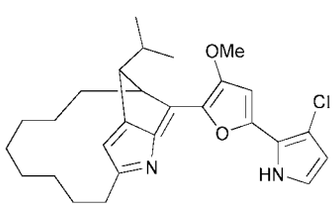


ent-(–)-Roseophilin

Biological activity: antitumour agent isolated from *Streptomyces griseoviridis*. The enantiomer of the natural product was synthesised. It was 2–10 fold more potent than natural (+)-roseophilin.

Key steps: (a) azadiene inverse demand Diels–Alder reaction to form a 1,2-diazine followed by reductive ring contraction to generate the pyrrole; (b) ring closing metathesis to generate the macrocycle; (c) 5-*exo*-*trig* acyl radical-alkene cyclisation reaction to construct a fused pyrrole.

D. L. Boger and J. Hong, *J. Am. Chem. Soc.*, 2001, **123**, 8515.



(+)-Roseophilin

Biological activity: antitumour agent.

Key steps: (a) asymmetric Nazarov cyclisation; (b) ring closing metathesis to generate the macrocycle; Paal–Knorr reaction to construct a fused pyrrole. This synthesis establishes the absolute configuration of the natural product.

P. E. Harrington and M. A. Tius, *J. Am. Chem. Soc.*, 2001, **123**, 8509.