Perkin 1 Abstracts: Natural Product Synthesis

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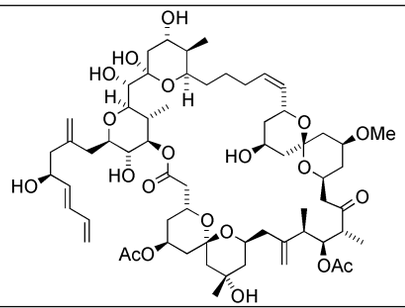
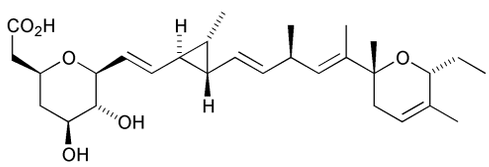
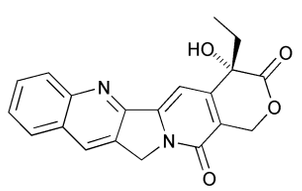
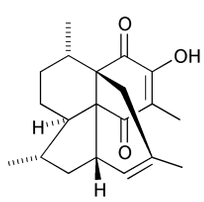
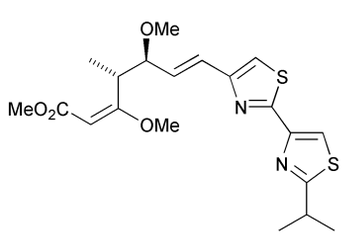
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

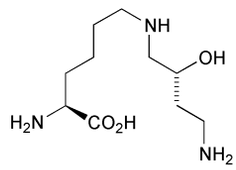
(+)-Altohyrtin A (Spongistatin 1) *Biological activity*: (a) *in vitro* antitumor activity; (b) IC_{50} = 0.03 nM; (c) inhibits tubulin polymerisation. *Key steps*: various boron-mediated aldol condensations. I. Paterson, D. Y.-K. Chen, M. J. Coster, J. L. Aceña, J. Bach, K. R. Gibson, L. E. Keown, R. M. Oballa, T. Trieselmann, D. J. Wallace, A. P. Hodgson and R. D. Norcross, *Angew. Chem., Int. Ed.*, 2001, **40**, 4055.	
(+)-Ambruticin S *Biological activity*: antifungal. *Key steps*: (a) asymmetric cyclopropanation; (b) Kocienski–Julia olefination; (c) ring closing metathesis reaction; (d) 2,3-sigmatropic rearrangement of an allyloxymethyllithium reagent; classical Julia olefination. T. A. Kirkland, J. Colucci, L. S. Geraci, M. A. Marx, M. Schneider, D. A. Kaelin and S. F. Martin, *J. Am. Chem. Soc.*, 2001, **123**, 12432.	
(*S*)-Camptothecin *Biological activity*: (a) isolated from *Camptotheca acuminata*; (b) important lead compound for the preparation of selective anticancer drugs; (c) cytotoxicity attributed to a mechanism of action involving DNA and topoisomerase I. *Key steps*: Heck reaction. D. L. Comins and J. M. Nolan, *Org. Lett.*, 2001, **3**, 4255.	
(–)-Colombiasin A *Biological activity*: not reported. *Key steps*: (a) two *p*-quinone Diels–Alder reactions one of which is asymmetric, being based on an (*S*)-BINOL–$TiCl_2$ catalyst; (b) *C*-allylation of an enolate under Pd(0) catalysis. K. C. Nicolaou, G. Vassilikogiannakis, W. Mägerlein and R. Kranich, *Chem. Eur. J.*, 2001, **7**, 5359.	
Cystothiazole A *Biological activity*: (a) isolated from the myxobacterium culture broth of *Cystobacter fuscus*; (b) antifungal activity against the phytopathogenic fungus *Phytophthora capsici*; (c) exhibits no effect on bacterial growth; (d) *in vitro* cytotoxicity towards human colon carcinoma HCT-116 and human leukemia K562. *Key steps*: (a) (*E*)-selective Horner–Emmons olefination; (b) asymmetric Evans aldol reaction. D. R. Williams, S. Patnaik and M. P. Clark, *J. Org. Chem.*, 2001, **66**, 8463.	

(+)-Hypusine

Biological activity: (a) isolated from extracts of bovine brain; (b) precursor protein of eukaryotic initiation factor 5A (eIF-5A) undergoes posttranslational modification in growing cells to form hypusine; (c) eIF-5A plays a key role in the replication of HIV-1.

Key steps: Wittig reaction of (triphenylphosphoranylidene)acetonitrile with a lactone carbonyl group.

R. P. Jain, B. K. Albrecht, D. E. DeMong and R. M. Williams, *Org. Lett.*, 2001, **3**, 4287.

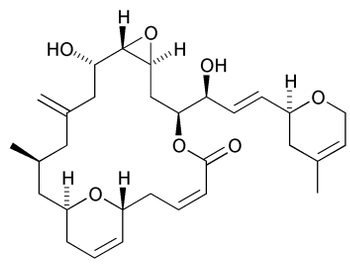


(–)-Laulimalide

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) Sharpless asymmetric epoxidation; (d) intramolecular electrophilic addition of an allylstannane to an oxonium ion generated from an aldehyde acetal derived from (*R,R*)-(+)-pentane-2,4-diol.

V. S. Enev, H. Kaehlig and J. Mulzer, *J. Am. Chem. Soc.*, 2001, **123**, 10764.

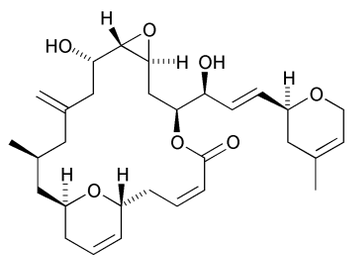


(–)-Laulimalide

Biological activity: (a) isolated from the marine sponge *Cacospongia mycofijiensis*, the Indonesian sponge *Hyattella* sp. and the Okinawan sponge *Fasciospongia rimosa*; (b) antitumour activity against numerous NCI cell lines, P388, A549, HT29, MEL28 and KB cell lines (IC_{50} = 10–50 ng mL^{-1}); (c) highly potent against the multidrug resistant cell line SKVLB-1 (IC_{50} = 1.2 μM).

Key steps: (a) two Julia olefination reactions; (b) intramolecular Horner–Emmons olefination; (c) Yamaguchi macrolactonisation; (d) ring-closing olefin metathesis to construct both dihydropyran rings.

A. K. Ghosh, Y. Wang and J. T. Kim, *J. Org. Chem.*, 2001, **66**, 8973.

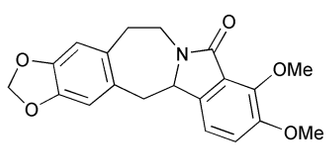


(±)-Lennoxamine

Biological activity: not reported.

Key steps: intramolecular electrophilic aromatic substitution reaction of a 2-amidoacrolein.

J. R. Fuchs and R. L. Funk, *Org. Lett.*, 2001, **3**, 3923.

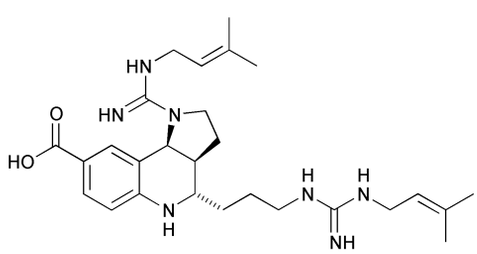


(±)-Martinellic acid

Biological activity: (a) isolated from *Martinella iquitosensis* roots; (b) non-peptide antagonists for the bradykinin B_1 and B_2 receptors.

Key steps: (a) reaction of an aniline with a Meldrum's acid-activated vinylcyclopropane to give a vinyl pyrrolidinone; (b) condensation of an aldehyde with *N*-benzylglycine to form an azomethine ylide that cyclises to give a tetracyclic lactam; (c) selective reduction of a tetracyclic lactam to an amino alcohol with $LiBH_4$ and MeOH; (d) reaction of a cyanamide with 3-methylbut-2-en-1-amine in hexafluoropropan-2-ol to form a guanidine.

B. B. Snider, Y. Ahn and S. M. O'Hare, *Org. Lett.*, 2001, **3**, 4217.

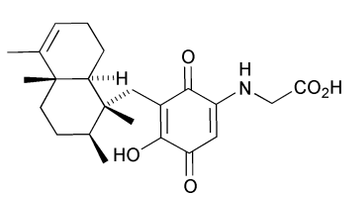


Nakijiquinone A

Biological activity: (a) cytotoxic against L 1210 murine leukemia cells and KB human epidermoid carcinoma cells; (b) inhibitor of the Her-2/Neu receptor tyrosine kinase.

Key steps: (a) reductive alkylation of a Wieland–Miescher-type enone with a tetramethoxyaryl bromide; (b) oxidative conversion of an aryl ring into a *p*-quinoid system; (c) regioselective saponification of one of two vinylogous esters.

P. Stahl, L. Kissau, R. Mazitschek, A. Huwe, P. Furet, A. Giannis and H. Waldmann, *J. Am. Chem. Soc.*, 2001, **123**, 11586.

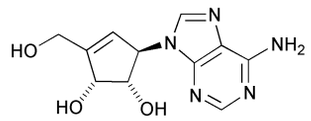


(–)-Neplanocin A

Biological activity: (a) isolated from *Ampullariella regularis*; (b) exhibits *S*-adenosylhomocystein hydrolase inhibitory activity.

Key steps: (a) (*E*)-selective Horner–Emmons olefination; (b) lithium thiolate-initiated stereoselective intramolecular Michael–aldol tandem cyclisation.

M. Ono, K. Nishimura, H. Tsubouchi, Y. Nagaoka and K. Tomioka, *J. Org. Chem.*, 2001, **66**, 8199.

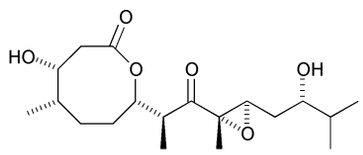


(–)-Octalactin A

Biological activity: (a) anticancer agent; (b) potent toxicity against certain human colon cancer cell lines.

Key steps: ring-closing metathesis.

K. R. Buszek, N. Sato and Y. Jeong, *Tetrahedron Lett.*, 2002, **43**, 181.

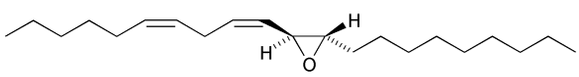


(11*S*,12*S*)-Posticlure

Biological activity: (a) isolated from the tussock moth *Orgyia postica*; (b) female sex pheromone.

Key steps: Sharpless asymmetric dihydroxylation.

S. Muto and K. Mori, *Eur. J. Org. Chem.*, 2001, 4635.

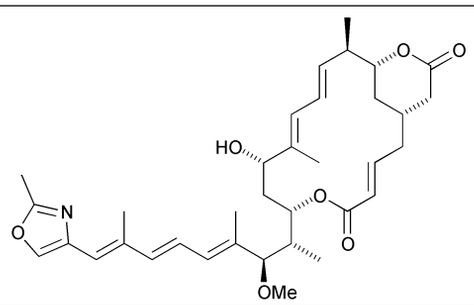


Rhizoxin D

Biological activity: (a) isolated from *Rhizopus chinensis*; (b) exhibits antitumour activity.

Key steps: (a) Horner–Wadsworth–Emmons olefination; (b) intramolecular Stille reaction.

I. S. Mitchell, G. Pattenden and J. P. Stonehouse, *Tetrahedron Lett.*, 2002, **43**, 493.

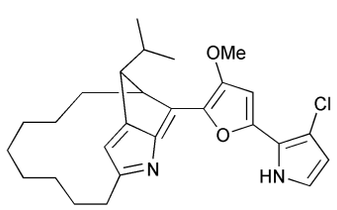


ent-(–)-Roseophilin

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.

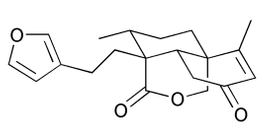


(±)-Sacacarin

Biological activity: isolated from the bark of a Brazilian tree used in folk medicine for the treatment of digestive upset.

Key steps: (a) double Michael reaction; (b) Pinner reaction; (c) Dieckmann reaction.

R. B. Grossman and R. M. Rasne, *Org. Lett.*, 2001, **3**, 4027.

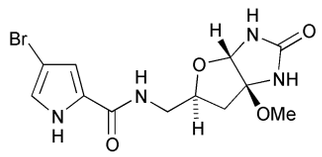


Slagenin B

Biological activity: (a) isolated from the Okinawan sponge *Agelas nakamurai*; (b) preliminary biological tests have shown that slagenins exhibit pharmacologically useful activities.

Key steps: preparation of the *cis*-fused tetrahydrofuro[2,3-*d*]imidazolidin-2-one skeleton *via* condensation of a glyoxal hydrate and urea.

B. Jiang, J.-F. Liu and S.-Y. Zhao, *Org. Lett.*, 2001, **3**, 4011.

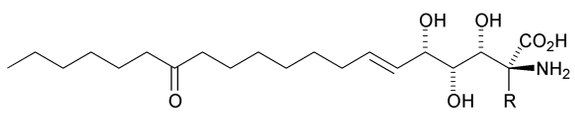


Sphingofungins E and F

Biological activity: (a) isolated from the fermentation of *Paecilomyces variotii*; (b) antifungal; (c) block the biosynthesis of sphingolipids, leading to apoptosis in both yeast and mammalian cells.

Key steps: Pd(0)-catalysed asymmetric allylic alkylation of a *gem*-diacetate with a silylazlactone.

B. M. Trost and C. Lee, *J. Am. Chem. Soc.*, 2001, **123**, 12191.



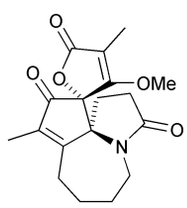
Sphingofungin E; R = CH_2OH
Sphingofungin F; R = CH_3

(±)-Stemonamide

Biological activity: (a) isolated from the roots of *Stemona japonica*; (b) alkaloids from *Stemona* plants have been used in Chinese and Japanese folk medicine as cough-relief agents and insecticides.

Key steps: (a) addition of a silyloxyfuran to an *N*-acyliminium ion; (b) aldol spirocyclisation.

A. S. Kende, J. I. M. Hernando and J. B. J. Milbank, *Tetrahedron*, 2002, **58**, 61.

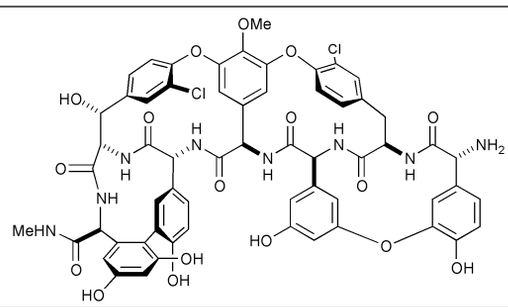


Teichoplanin aglycone

Biological activity: antibiotic

Key steps:(a) asymmetric catalytic hydrogenation; (b) $Cu(OAc)_2$ mediated diaryl ether synthesis from a phenol and an arylboronic acid; (c) diaryl ether synthesis *via* cyclisation of a phenol onto an *o*-fluoronitroarene

D. A. Evans, J. L. Katz, G. S. Peterson and T. Hintermann, *J. Am. Chem. Soc.*, 2001, **123**, 12411.

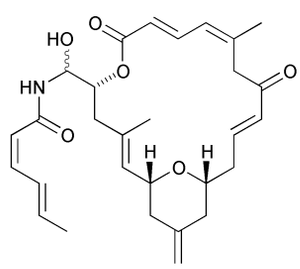


(+)-Zampanolide

Biological activity: cytotoxic against several human cancer lines.

Key steps: (a) asymmetric allylboration; (b) Petasis–Ferrier rearrangement to generate the oxacycle; (c) Kocienski–Julia olefination; (c) Curtius rearrangement to generate the *N*-acyl aminal.

A. B. Smith, I. G. Safonov and R. M. Corbett, *J. Am. Chem. Soc.*, 2001, **123**, 12426.



(*S*)-Zearalane

Biological activity: (a) estrogenic; (b) anabolic; (c) anthelminthic; (d) immunomodulator.

Key steps: Pd-catalysed cross-coupling of an arene trifluoromethanesulfonate with a 9-alkyl-9-borabicyclo[3.3.1]nonane derivative.

F. Bracher and J. Krauβ, *Eur. J. Org. Chem.*, 2001, 4701.