Perkin 1 Abstracts: Natural Product Synthesis

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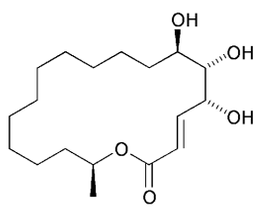
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

(+)-Aspicilin

Biological activity: (a) isolated from a lichen of the *Lecanoraceae* family; (b) no significant biological activity.

Key steps: (a) whole-cell-mediated dihydroxylation of chlorobenzene using a genetically engineered strain of *Echerichia coli* [JM109 (pDTG601)]; (b) Wadsworth–Emmons reaction; (c) ring-closing metathesis reaction.

M. G. Banwell and K. J. McRae, *Org. Lett.*, 2000, **2**, 3583.

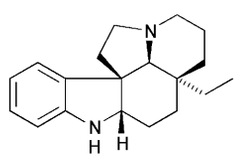


(±)-Aspidospermidine

Biological activity: not reported.

Key steps: iodoazide radical cascade cyclisation.

B. Patro and J. A. Murphy, *Org. Lett.*, 2000, **2**, 3599.

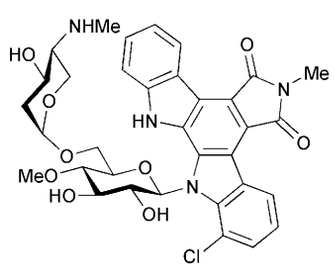


AT2433-A1

Biological activity: (a) antitumour; (b) antibiotic.

Key steps: (a) Mannich cyclisation; (b) glycosylation.

J. D. Chisholm and D. L. Van Vranken, *J. Org. Chem.*, 2000, **65**, 7541.

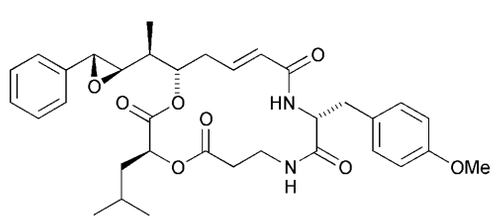


Cryptophycin-24 (Arenastatin A)

Biological activity: (a) isolated from the Okinawan marine sponge *Dysidea arenaria*; (b) cytotoxic.

Key steps: Yamaguchi coupling.

M. Eggen, C. J. Mossman, S. B. Buck, S. K. Nair, L. Bhat, S. M. Ali, E. A. Reiff, T. C. Boge and G. I. Georg, *J. Org. Chem.*, 2000, **65**, 7792.

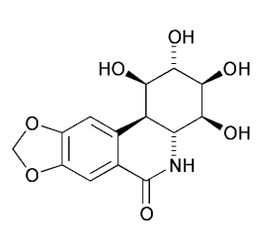


(+)-7-Deoxypancratistatin

Biological activity: (a) isolated from extracts of the *Amaryllidaceous* plant species; (b) antineoplasic; (c) growth regulator; (d) mitogenic; (e) antimitotic.

Key steps: (a) ring opening of an enantiomerically pure 7-oxanorbornenic system; (b) intramolecular lactonisation with concomitant oxirane opening.

J. L. Aceña, O. Arjona, M. L. León and J. Plumet, *Org. Lett.*, 2000, **2**, 3683.

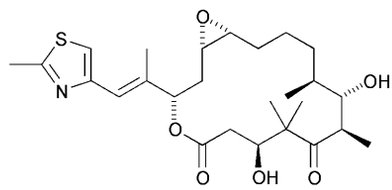


Epothilone A

Biological activity: (a) isolated from the myxobacteria of the genus *Sorangium*; (b) potent antitumour activity by binding and stabilising microtubules.

Key steps: (a) catalytic asymmetric cyanosilylation; (b) catalytic asymmetric aldol reaction; (c) catalytic asymmetric protonation in the conjugate addition of a thiol to an α,β-unsaturated thioester; (d) Suzuki cross-coupling; (e) Yamaguchi lactonisation.

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

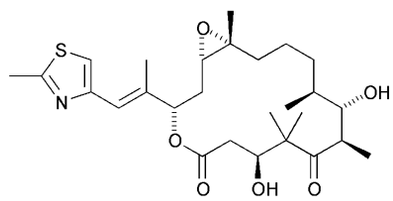


Epothilone B

Biological activity: microtubule stabilising antitumour drug.

Key steps: (a) Horner–Wadsworth–Emmons olefination; (b) enantioselective Mukaiyama aldol addition; (c) a sulfone anion allyl iodide alkylation.

J. Mulzer, A. Mantoulidis and E. Öhler, *J. Org. Chem.*, 2000, **65**, 7456.

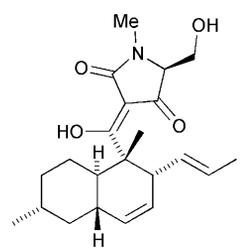


Equisetin

Biological activity: (a) fungal metabolite isolated from the white mold *Fusarium equiseti*; (b) antibiotic; (c) HIV inhibitor; (d) cytotoxic; (e) mammalian DNA binder.

Key steps: stereoselective lithium perchlorate mediated intramolecular Diels–Alder reaction of a fully conjugated *E,E,E*-triene with a trisubstituted γ,δ-unsaturated β-ketothioester.

L. T. Burke, D. J. Dixon, S. V. Ley and F. Rodríguez, *Org. Lett.*, 2000, **2**, 3611.

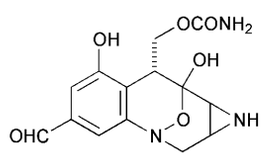


(+)-FR900482

Biological activity: (a) isolated from the fermentation broth of *Streptomyces sandaensis* No.6897; (b) antitumour; (c) antibiotic.

Key steps: ring-closing metathesis of a highly functionalised diene to yield an eight membered ring.

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

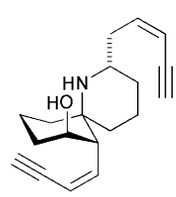


(±)-Histrionicotoxin and (±)-Histrionicotoxin 235A

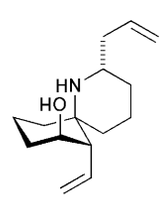
Biological activity: (a) isolated from the skin extracts of the Columbian "poison arrow" frog, *Dendrobates histrionicus*; (b) Histrionicotoxin is a biochemical tool for probing the mechanisms of transsynaptic transmission of neuromuscular impulses.

Key steps: tandem Michael addition/[3+2] cycloaddition.

R. A. Stockman, *Tetrahedron Lett.*, 2000, **41**, 9163.



(±)-Histrionicotoxin



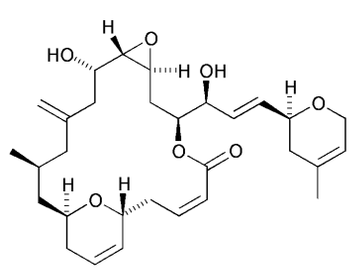
(±)-Histrionicotoxin 235A

(–)-Laulimalide

Biological activity: (a) isolated from the Indonesian sponge *Hyattella* sp. and from the Okinawan sponge *Fasciospongia rimosa*; (b) antitumour; (c) potent cytotoxicity against the KB cell line with an IC_{50} = 15 ng mL^{-1}.

Key steps: (a) Julia olefination; (b) intramolecular Horner–Wadsworth–Emmons; (c) Sharpless epoxidation; (d) ring-closing metathesis.

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

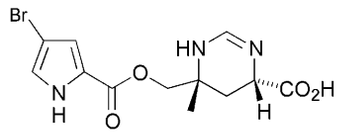


Manzacidin A

Biological activity: (a) isolated from an Okinawan sponge *Hymeniacidon* sp.; (b) exhibits similar biological activities to bromopyrrole alkaloids which are α-adrenoceptor blockers, antagonists of serotonergic receptor and actomyosin ATPase activators.

Key steps: Strecker amino ketone synthesis.

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

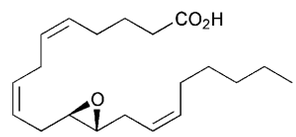


(11*R*,12*S*)-Oxidoarachidonic Acid

Biological activity: (a) formed by the action of the cytochrome P450 isoform CYP2J2 on arachidonic acid in endothelial cells; (b) plays a regulatory role in the TNF-α and NF-κB vascular inflammation signaling pathways by inhibiting the degradation of IκB, thereby blocking the release of NF-κB (IC_{50} = 20 nM).

Key steps: (a) enantioselective Sharpless dihydroxylation; (b) (*Z*)-selective Wittig olefination.

X. Han, S. N. Crane and E. J. Corey, *Org. Lett.*, 2000, **2**, 3437.

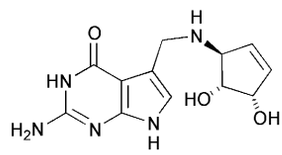


Q Base (Queuine)

Biological activity: (a) found in the tRNA of plants and animals; (b) inhibits growth of tumour cell line in mice.

Key steps: (a) Mitsunobu reaction of a nosyl-protected amine with a cyclopentenol; (b) cyclocondensation reaction of a β-aminobromoaldehyde and 2,4-diamino-6-hydroxypyrimidine.

C. J. Barnett and L. M. Grubb, *Tetrahedron*, 2000, **56**, 9221.

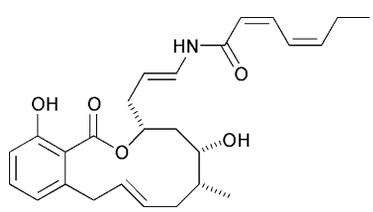


Salicylihalamide A

Biological activity: (a) isolated from extracts of the *Haliclona* genus; (b) a potent cytotoxin with a mean GI_{50} = 15 nM in NCI's 60 cell line human tumour assay.

Key steps: (a) two asymmetric hydrogenations of β-keto esters catalysed by [(*R*)-BINAP•$RuCl_2$]$_2$•NEt_3; (b) a ring-closing metathesis based macrocyclisation catalysed by a ruthenium carbene.

A. Fürstner, O. R. Thiel and G. Blanda, *Org. Lett.*, 2000, **2**, 3731.

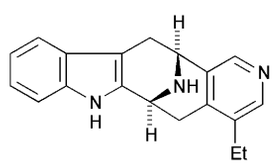


(–)-Suaveoline

Biological activity: not reported.

Key steps: (a) *cis*-selective Pictet–Spengler reaction; (b) one pot Horner–Wadsworth–Emmons; (c) vinylogous Thorpe cyclisation.

P. D. Bailey and K. M. Morgan, *J. Chem. Soc., Perkin Trans. 1*, 2000, 3578.



(*S*)-(–)-Zearalenone

Biological activity: (a) anabolic; (b) estrogenic; (c) antibacterial.

Key steps: ring-closing metathesis using a "second generation" ruthenium carbene catalyst bearing a *N*-heterocyclic carbene ligand.

A. Fürstner, O. R. Thiel, N. Kindler and B. Bartkowska, *J. Org. Chem.*, 2000, **65**, 7990.