Perkin 1 Abstracts: Natural Product Synthesis

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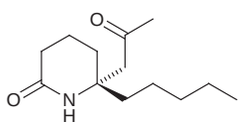
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*

(±)-Adalinine

Biological activity: alkaloid extracted from the ladybird beetles *Adalia bipunctata* and *A. decempunctata*; activity not reported.

Key steps: allylation of the cylic *N*-acyl *N*,*O*-acetals using a combination of Lewis acid and allyltrimethylsilane.

N. Yamazaki, T. Ito and C. Kibayashi, *Synlett*, 1999, 37; N. Yamazaki, T. Ito and C. Kibayashi, *Tetrahedron Lett*., 1999, **40**, 739.

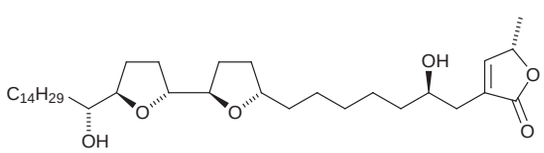


Asimilobin

Biological activity: cytoxicity comparable with adriamycin against six human solid tumour cell lines.

Key steps: (a) Sharpless AD reaction; (b) Wittig olefination.

Z-M. Wang, S-K. Tian and M. Shi, *Tetrahedron Lett*., 1999, **40**, 977.

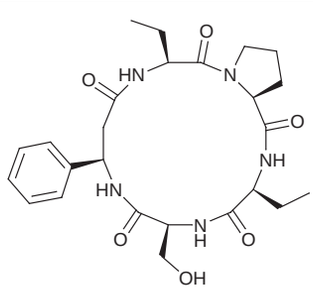


Astin G

Biological activity: antitumour activity but with a fraction of the hepatatoxicity shown by the related cyclochlorotine and islanditoxin.

Key steps: FDPP (pentafluorophenyl diphenylphosphinate) and BOP (benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate) coupling strategies are employed in the synthesis.

K. K. Schumacher, D. B. Hauze, J. Jiang, J. Szewczyk, R. E. Reddy, F. A. Davis and M. M. Joullié, *Tetrahedron Lett*., 1999, **40**, 455.

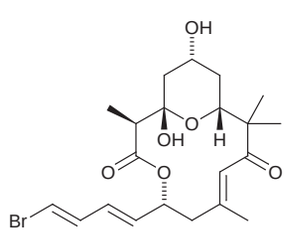


Aglycon of Aurisides A and B

Biological activity: (a) isolated from the Japanese sea hare *Dolabella auricularia*; (b) exhibit cytotoxicities against HeLa S_3 cells (IC_{50} =0.17 and 1.2 μg mL^{-1} for Auriside A and B respectively).

Key steps: (a) Nozaki reaction; (b) Yamaguchi macrolactonisation.

H. Sone, K. Suenaga, Y. Bessho, T. Kondo, H. Kigoshi and K. Yamada, *Chem. Lett*., 1998, 85.

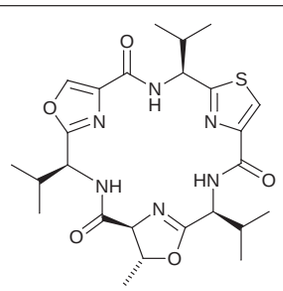


(–)-Bistratamide D

Biological activity: induces depressant effects in mice when administered by intracerebral injection.

Key steps: assembly of enantiomerically pure oxazole, thiazole and oxazoline segments derived from amino acids.

S. V. Downing, E. Agular and A. I. Meyers, *J. Org. Chem.*, 1999, **64**, 826.

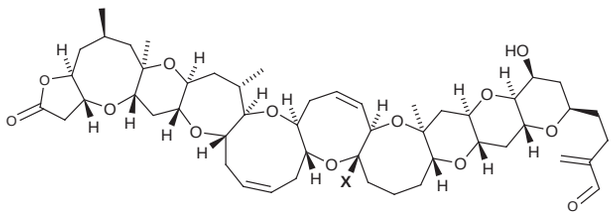


(+)-Brevetoxin A

Biological activity: a cytotoxin from the dinoflagellate *Ptychodiscus brevis* which binds strongly to neuronal sodium channels.

Key steps: medium-ring oxacycle construction via (a) macrolactonisation and (b) cyclisation of hydroxy groups onto dithioacetals.

K. C. Nicolaou, J. L. Gunzer, G.-q. Shi, K. A. Agrios, P. Gärtner and Z. Yang, *Chem. Eur. J.*, 1999, **5**, 646; K. C. Nicolaou, G.-q. Shi, J. L. Gunzer, P. Gärtner, P. A. Wallace, M. A. Ouellette, S. Shi, M. E. Bunnage, K. A. Agrios, C. A. Veale, C.-K. Hwang, J. Hutchinson, C. V. C. Prasad, W. W. Ogilvie and Z. Yang, *Chem. Eur. J.*, 1999, **5**, 628.

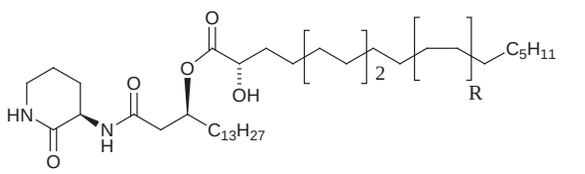


Cepaciamides A and B

Biological activity: (a) novel fungitoxins active against *Botrytis cinerea* and *Penicillium expansum*.

Key steps: (a) formation of a (*Z*)-olefin by means of partial reduction of an acetylene; (b) esterification of fatty acid segments and amide fragment using DCC/DMA.

H. Toshima, K. Maru, M. Saito and A. Ichihara, *Tetrahedron Lett*., 1999, **40**, 939.



Cepaciamide A, R = 

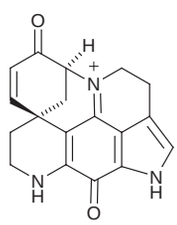
Cepaciamide B, R = 

Dethiadiscorhabdin D and Discorhabdins C and E

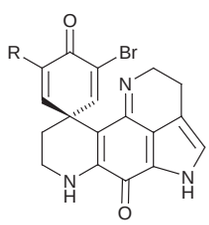
Biological activity: (a) extracted from the sponges of the genus *Latrunculia* du Bocage along the New Zealand coast; (b) antitumor activity.

Key steps: (a) intramolecular Michael addition; (b) Heck cyclisation.

K. M. Aubart and C. H. Heathcock, *J. Org. Chem.*, 1999, **64**, 16.



Dethiadiscorhabdin D



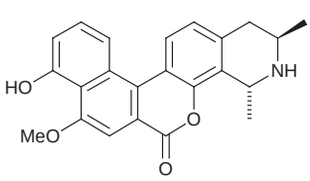
R = Br Discorhabdin C
R = H Discorhabdin E

Dioncolactone A and Dioncopeltine A

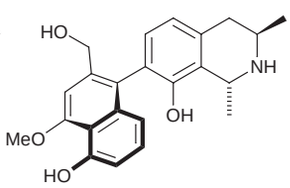
Biological activity: antimalarial activity.

Key steps: regio- and stereoselective construction of the biaryl axes *via* intramolecular coupling and atropo-diastereoselective cleavage of a lactone auxiliary bridge.

G. Bringmann, W. Saeb, and M. Rübenacker, *Tetrahedron*, 1999, **55**, 423.



Dioncolactone A



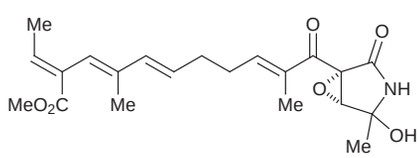
Dioncopeltine A

Epolactaene

Biological activity: effects neurite outgrowth of a human neuroblastoma cell line (SH-SY5Y cells).

Key steps: (a) Griffith-Ley oxidation; (b) Horner-Emmons reaction; (c) Knoevenagel condensation.

Y. Hayashi and K. Narasaka, *Chem. Lett.*, 1998, 313.

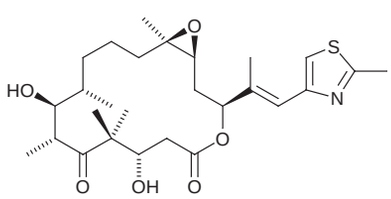


Epothilone B

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

Key steps: the Wittig reaction is used twice to link fragments and the macrocyclisation is accomplished with a Yamaguchi reaction.

J. D. White, R. G. Garter, and K. F. Sundermann, *J. Org. Chem.*, 1999, **64**, 684.

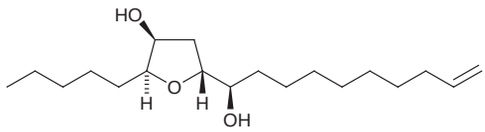


(6*S*,7*S*,9*R*,10*R*)-6,9-Epoxynonadec-18-ene-7,10-diol

Biological activity: isolated from the Australian marine brown alga *Notheia anomala*; activity not reported.

Key steps: formation of the key 2,3,5-trisubstituted tetrahydrofuran unit *via* alkylation of a sulfonyl-stablised oxiranyl anion followed by 5-*endo* cyclisation.

Y. Mori, T. Sawada and H. Furukawa, *Tetrahedron Lett*., 1999, **40**, 731.

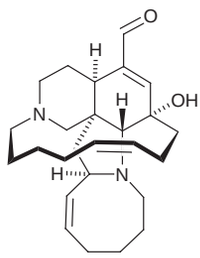


(+)-Ircinal

Biological activity: related compounds (e.g. manzamine) have antitumour activity.

Key steps: (a) a Stille/Diels-Alder domino reaction; (b) two sequential ring closing metathesis reactions to generate the 8- and 13-membered rings.

S. F. Martin, J. M. Humphrey, A. Ali, and M. C. Hillier, *J. Am. Chem. Soc.*, 1999, **121**, 866.

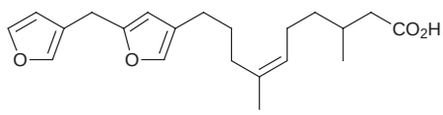


Ircinin-4

Biological activity: one member of the ircinin family acts as a selective inhibitor of phospholipase A.

Key steps: (a) condensation of a sulfur ylide with aldehydes; (b) Pd-catalysed opening of a vinyloxirane; (c) oxidative cyclisation of a furan ring.

A. Fürstner, T. Gastner and J. Rust, *Synlett*, 1999, 29.

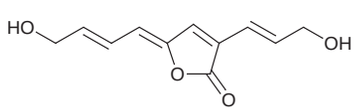


Lissoclinolide

Biological activity: active against Gram negative bacteria.

Key steps: (a) hydrogen transfer hydrozirconation of TBS-protected propargyl alcohol with *i*BuZrCp$_2$Cl; (b) Pd-catalysed *trans*-selective cross-coupling of the hydrozirconation product with a 1,1-dibromo alkene; (c) Ag-catalysed lactonisation of a trienynoic acid precursor.

C. Xu and E.-i. Negishi, *Tetrahedron Lett*., 1999, **40**, 431.

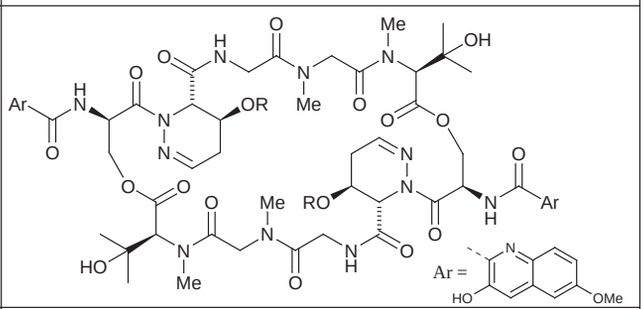


Luzopeptins A-C

Biological activity: inhibit HIV reverse transcriptase at non-cytotoxic concentrations.

Key steps: closure of the 32-membered ring by macrolactamisation using a carbodiimde. (EDCI).

D. L. Boger, M. W. Jedeboer and M. Kume, *J. Am. Chem. Soc.*, 1999, **121**, 1098.

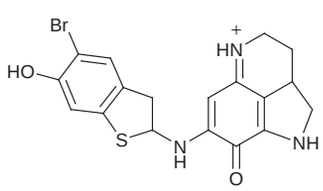


(±)-Makaluvamine F

Biological activity: (a) cytotoxicity towards the human colon tumor cell-line HCT-116 (IC_{50} = 0.17 μM); (b) inhibitor of topoisomerase II.

Key steps: use of hypervalent iodine(III)-induced reactions.

Y. Kita, M. Egi and H. Tohma, *Chem. Commun.*, 1999, 143.

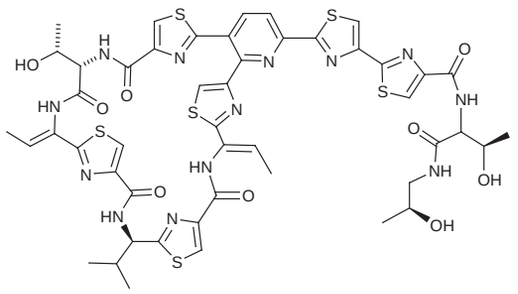


Micrococcin P

Biological activity: antibiotic.

Key steps: synthesis of various dehydropeptide derivatives and their thiazolation.

C.-g. Shin, K. Okumura, M. Shigekuni, and Y. Nakamura, *Chem. Lett.*, 1998, 139.

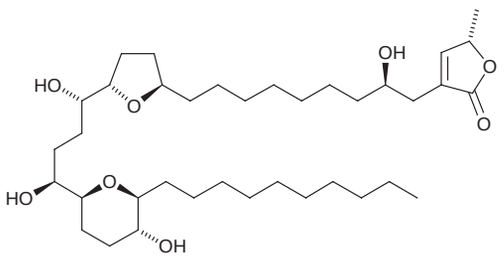


Mucocin

Biological activity: anticancer agent

Key steps: (a) lactone formation *via* Bu_3SnH-mediated radical cyclisation; (b) Pd-catalysed cross-coupling reaction.

S. Takahashi and T Nakata, *Tetrahedron Lett*., 1999, **40**, 723 and 727.

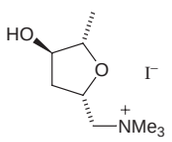


(+)-Muscarine

Biological activity: acetylcholine agonist isolated from the poisonous mushroom *Amanita muscaria*.

Key steps: Standard transformations were used to convert glucose to the target in >15 steps.

V. Popasavin, O. Beric, L. Radic, M. Popasavin, V. Cirin-Novta and D. Miljkovic, *Collect. Czech. Chem. Commun.*, 1998, **63**, 1522.

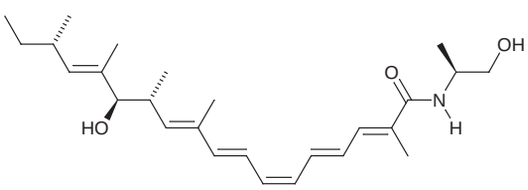


Myxalamide A

Biological activity: antibiotic.

Key steps: (a) Evans asymmetric aldol reaction; (b) enolate Claisen rearrangement; (c) Evans-Mislow allyl sulfoxide rearrangement; (d) Suzuki coupling.

A. K. Mapp and C. H. Heathcock, *J. Org. Chem.*, 1999, **64**, 23.

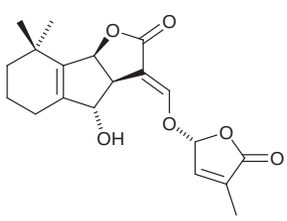


Orobanchol

Biological activity: a germination stimulant for the parasitic weed *Orobanche minor*.

Key steps: Mitsunobu reaction.

K. Mori, J. Matsui, T. Yokota, H. Sakai, M. Bando and Y. Takeuchi, *Tetrahedron Lett*., 1999, **40**, 943.

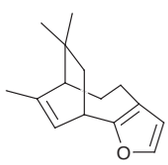


(±)-Pallescensin B

Biological activity: not reported.

Key steps: (a) intramolecular Diels-Alder reaction of a masked *o*-benzoquinone; (b) anionic [1,3]-rearrangement of a vinylbicyclo[2.2.2]octenol; (c) intramolecular hetero-Michael addition of a hydroxy enone.

W.-C. Liu and C.-C. Liao, *Chem. Commun.*, 1999, 117.

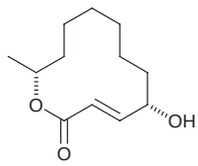


(±)-Patulolide C

Biological activity: not reported.

Key steps: 1,8-stereocontrol by 1,5-induction using an allylstannane followed by an Ireland-Claisen rearrangement.

E. K. Dorling and E. J. Thomas, *Tetrahedron Lett.*, 1999, **40**, 471.

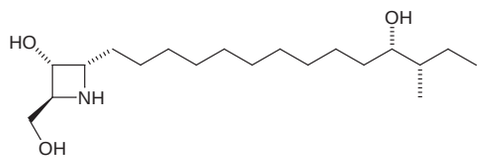


Penaresidin A

Biological activity: exhibits potent actomyocin ATPase-activating.

Key steps: (a) cyclisation under Mitsunobu conditions; (b) coupling of two key fragments using a Wittig olefination.

D-G. Liu and G-Q. Lin, *Tetrahedron Lett.*, 1999, **40**, 337.

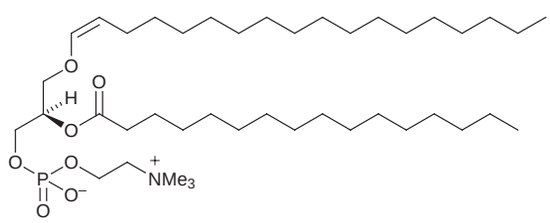


Plasmalogen

Biological activity: Plasmalogens (phospholipids with a *cis*-*O*-vinyl ether at the *sn*-1 position of the glycerol backbone) are the major phospholipids in membranes of the heart and brain. They may act as peroxy radical scavengers.

Key steps: Lindlar reduction of an alkynyl ether generates the *cis*-*O*-vinyl ether.

D. Qin, H.-S. Byun and R. Bittman, *J. Am. Chem. Soc.*, 1999, **121**, 662.

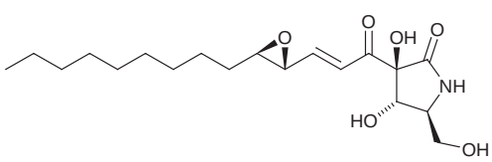


(+)-Pramanicin

Biological activity: antifungal activity towards *Candida albicans*, *Candida parapsilosis* and *Cryptococcus neoformans* (responsible for meningitis infection in AIDS).

Key steps: "one pot" Michael addition of an aminosilyl zincate species to an α,β-unsaturated lactam and quenching of the resultant enolate with an α,β-unsaturated γ,δ-epoxy aldehyde.

A. G. M. Barrett, J. Head, M. L. Smith and N. S. Stock, *Chem. Commun.*, 1999, 133.

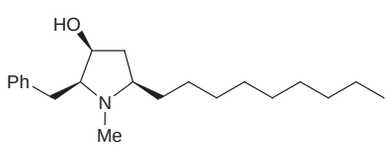


(+)-Preussin

Biological activity: antifungal.

Key steps: Paternò-Büchi reaction.

T. Bach and H. Brummerhop, *Angew. Chem. Int. Ed.*, 1998, **37**, 3400.

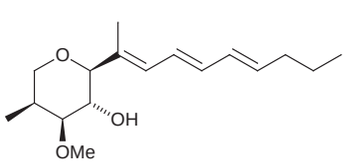


Restrictinol

Biological activity: (a) isolated from the fermentation broth of *Penicillium sp.* NR6564; (b) the related compounds restricticin and lanomycin exhibit potent antifungal activity through inhibition of cytochrome P_{450} lanosterol demethylase. Restrictinol itself is not antifungal.

Key steps: (a) Brown allylboration; (b) Suzuki coupling reaction.

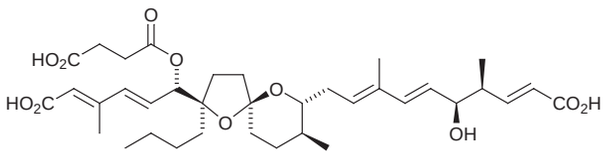
A. G. M. Barrett, A. J. Bennett, S. Menzer, M. L. Smith, A. J. P. White and D. J. Williams, *J. Org. Chem.*, 1999, **64**, 162.



Reveromycin B

Biological activity: inhibits eukaryotic cell growth presumably by interfering with the epidermal growth factor receptor pathway.

Key steps: construction of the diene units in the two side chains using Kishi-Nozaki and modified Negishi couplings.

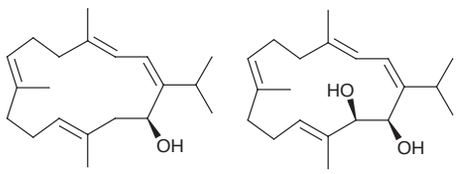


K. E. Drouet and E. A. Theodorakis, *J. Am. Chem. Soc.*, 1999, **121**, 456.

(±)-Sarcophytols A and B

Biological activity: (a) antitumour activity; (b) potent inhibitory activity against various tumour promoters; (c) sarcophytol A appears to show potential for cancer prevention with little toxic effects.

Key steps: low-valent titanium-mediated intramolecular McMurry olefination strategy.



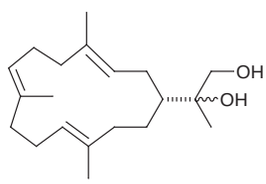
Sarcophytol-A Sarcophytol-B

W-D. Z. Li, Y. Li and Y. Li, *Tetrahedron Lett*., 1999, **40**, 965.

(±)-Sinulariol-B

Biological activity: not reported.

Key steps: (a) coupling of a sulfone and an allylic chloride by sulfone-stabilised carbanionic alkylation; (b) macrocyclisation by intramolecular thioether-stabilised carbanionic alkylation.

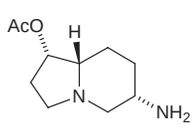


X. Yue, J. Lan, J. Li, Z. Liu and Y. Lin, *Tetrahedron*, 1999, **55**, 133.

(–)-Slaframine

Biological activity: (–)-Slaframine is a neurotoxic alkaloid, thought to be responsible for the excess salivating in ruminants after ingestion of contaminated forages, causing a disease called 'black patch'.

Key steps: (a) kinetic separation of a diastereomer mixture by reaction with Me_3Al; (b) construction of the indolizidine skeleton by intramolecular alkylation of an α-sulfonyl carbanion.

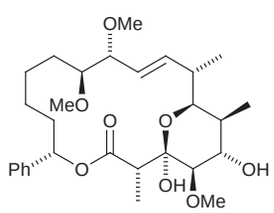


J. C. Carretero and R. G. Arrayás, *Synlett*, 1999, 49.

Soraphen $A_{1\alpha}$

Biological activity: highly potent fungicide which acts as a specific inhibitor of acetyl CoA carboxylase and thus disturbs the lipid synthesis in fungi.

Key steps: (a) Julia olefination; (b) macrolactonisation.

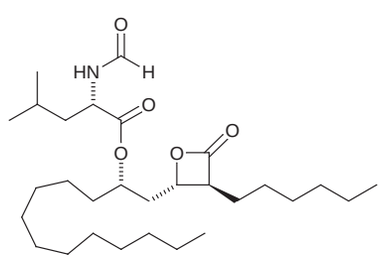


S. Abel, D. Faber, O. Hüter, and B. Giese, *Synthesis*, 1999, 188.

(–)-Tetrahydrolipstatin

Biological activity: potent inhibitor of pancreatic lipase - used clinically as an anti-obesity drug (Xenical).

Key steps: boron-mediated *anti*-selective aldol coupling.



I. Paterson and V. A. Doughty, *Tetrahedron Lett*., 1999, **40**, 393.