Perkin 1 Abstracts: Natural Product Synthesis

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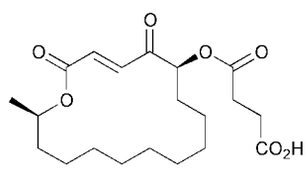
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

(–)-A26771B

Biological activity: antibiotic.

Key steps: (a) kinetic resolution of a racemic furfuryl alcohol with *t*-BuOOH/Ti(O-*i*-Pr)$_4$ and DIPT; (b) oxidation of a 2-substituted furan to a γ-oxo-α,β-unsaturated carboxylic acid using NBS.

Y. Kobayashi and H. Okui, *J. Org. Chem.*, 2000, **65**, 612.

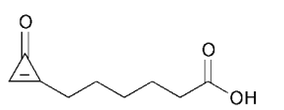


Alutacenoic Acids A and B

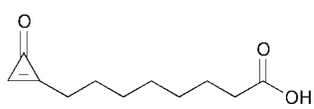
Biological activity: inhibit factor XIIIa, a plasma transglutaminase which acts on the final step in the blood coagulation cascade.

Key steps: metallation alkylation of an acetal-protected cyclopropenone.

H. Kogen, T. Kiho, K. Tago, S. Miyamoto, T. Fujioka, N. Otsuka, K. Suzuki-Konagai and T. Ogita, *J. Am. Chem. Soc.*, 2000, **122**, 1842.



Alutacenoic Acid A



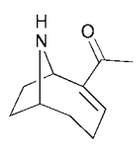
Alutacenoic Acid B

(±)-Anatoxin-a

Biological activity: (a) poison; (b) potent agonist for the nicotinic acetylcholine receptor nAChR. Its resistance to degradation by acetylcholine esterase results in overstimulation of muscle tissue, thus respiratory paralysis and ultimately death.

Key steps: β-lactam ring opening transannular cyclisation sequence.

P. J. Parsons, N. P. Camp, N. Edwards, and L. R. Sumorecah, *Tetrahedron*, 2000, **56**, 309.

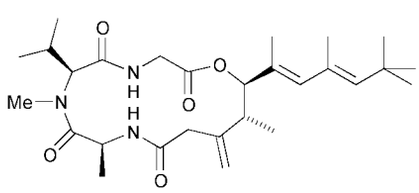


(–)-Antillatoxin

Biological activity: potent ichthyotoxin.

Key steps: (a) Abiko Masamune anti-aldol reaction. The correct stereochemistry of the natural product was established by total synthesis.

F. Yokokawa, H. Fujiwara and T. Shioiri, *Tetrahedron*, 2000, **56**, 1759.

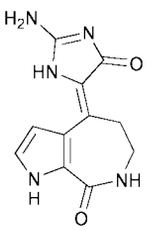


(*Z*)-Debromohymenialdisine

Biological activity: (a) protein kinase C modulator; (b) proinflammatory transcription factor, nuclear factor κB (NFκB).

Key steps: (a) electrophilic cyclisation of an acetal to a pyrrole to generate the 7-membered ring; (b) bromine oxidation of a 2-amino imidazole to an α,β-unsaturated aminoimidazolidinone.

A. C. B. Sosa, K. Yakushijin and D. A. Horne, *J. Org. Chem.*, 2000, **65**, 610.

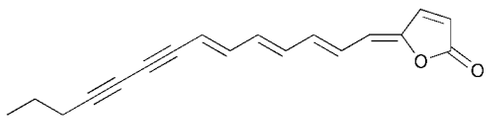


Dihydroxerulin

Biological activity: potent noncytotoxic inhibitor of cholesterol biosynthesis.

Key steps: (a) Wittig reaction between (*Z*)-5-[(*E*)-3-formyl-2-propenylidene]-5*H*-furan-2-one and the phosphonium ylide derived from [(*E*)dec-2-ene-4,6-diyn-1-yl]triphenylphosphonium bromide; (b) Stille coupling.

R. Rossi, F. Bellina, A. Catanese, L. Mannina and D. Valensin, *Tetrahedron*, 2000, **56**, 479.

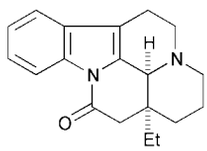


(–)-Eburnamonine

Biological activity: not described.

Key steps: Rh(II) carbenoid mediated tertiary C-H insertion reaction of a chiral non-racemic diazomalonate.

A. G. H. Wee and Q. Yu, *Tetrahedron Lett.*, 2000, **41**, 587.

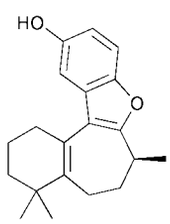


Frondosin B

Biological activity: inhibits binding of interleukin-8 to its receptor.

Key steps: starting with a benzofuran, the 7-membered ring was generated by an intramolecular Friedel–Crafts acylation and the 6-membered ring by a Diels–Alder reaction.

M. Inoue, A. J. Frontier and S. J. Danishefsky, *Angew. Chem., Int. Ed.*, 2000, **39**, 761.

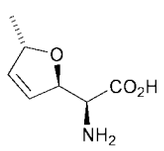


L-(+)-Furanomycin

Biological activity: antibiotic.

Key steps: asymmetric 1,3-dipolar cycloaddition of a nitrile oxide to 2-methylfuran to give a furo[2,3-*d*]isoxazoline.

P. J. Zimmermann, I. Blanarikova and V. Jäger, *Angew. Chem., Int. Ed.*, 2000, **39**, 910.

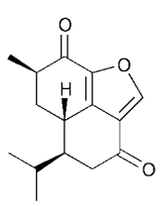


(±)-Hibiscone C

Biological activity: not reported.

Key steps: Swern oxidation of a triol directly to a furan.

G. A. Kraus and Z. Wan, *Synlett*, 2000, 363.

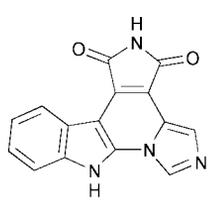


Isogranulatimide

Biological activity: cell cycle inhibitor at the G2 checkpoint.

Key steps: condensation cyclisation of didemnimide A by irradiation (MeCN, medium-pressure mercury lamp) in the presence of Pd black.

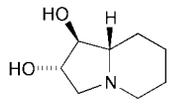
E. Piers, R. Britton and R. J. Andersen, *J. Org. Chem.*, 2000, **65**, 530.



(+)-Lentiginosine

Biological activity: not reported.

Key steps: samarium diiodide-promoted reductive cyclisation of *N*-(ω-iodoalkyl) cyclic imides in the presence of catalytic amounts of tris(dibenzoylmethido)iron (III) [$Fe(DBM)_3$].

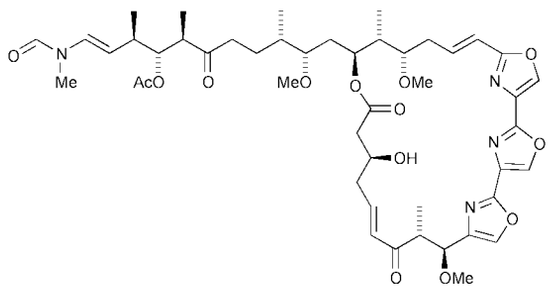


D.-C. Ha, C.-S. Yun and Y. Lee, *J. Org. Chem.*, 2000, **65**, 621.

(–)-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 polymerising agent.

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

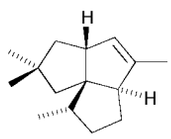


P. Liu and J. S. Panek, *J. Am. Chem. Soc.*, 2000, **122**, 1235.

Pentalenene

Biological activity: antibiotic.

Key steps: sequential 5-*exo*-*trig* and 5-*exo*-*dig* radical cyclisations involving ketene intermediates produced from an α,β-unsaturated acyl radical precursor.

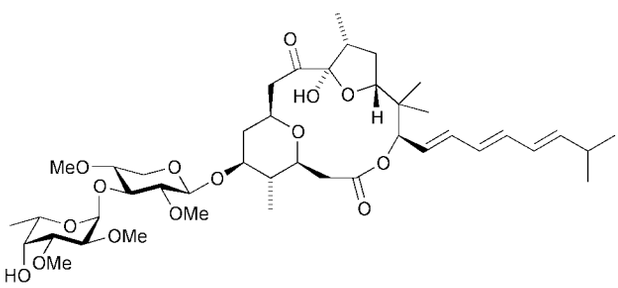


N. M. Harrington-Frost and G. Pattenden, *Tetrahedron Lett.*, 2000, **41**, 403.

(–)-Polycavernoside A

Biological activity: toxin isolated from the frequently ingested red alga *Polycavernosa tsudai*.

Key steps: (a) sulfonyl anion addition to an aldehyde; (b) macrolactonisation under modified Yamaguchi conditions; (c) NBS-promoted glycosidaton; (d) Stille coupling.

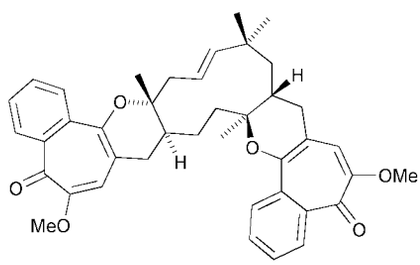


L. A. Paquette, L. Barriault, D. Pissarnitski and J. A. Johnston, *J. Am. Chem. Soc.*, 2000, **122**, 619.

Pycnidione analogue

Biological activity: (a) induces erythropoietin gene expression; (b) potential treatment of patients with anemia due to chronic renal failure; (c) inhibition of stromelysine, an enzyme postulated to cause cartilage degradation.

Key steps: tandem retro-hetero Diels–Alder/hetero Diels–Alder reaction.

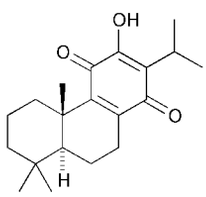


J. E. Baldwin, A. V. W. Mayweg, K. Neumann and G. J. Pritchard, *Org. Lett.*, 1999, **1**, 1933.

(+)-Royleanone

Biological activity: (a) used in the Himalaya region as an insecticide and disinfectant; (b) modest antitumour activity.

Key steps: tandem asymmetric Diels–Alder reaction/pyrolytic sulfoxide elimination.



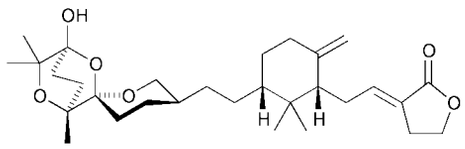
M. C. Carreño, J. L. García Ruano and M. A. Toledo, *Chem. Eur. J.*, 2000, **6**, 288.

(+)-Saponaceolide B

Biological activity: antitumour activity against leukemia K-562, nonsmall cell lung NCI-H23, melanoma LOX-IMVI, and SK-MEL-5.

Key steps: (a) palladium-catalysed cycloisomerisation of enynes; (b) silver-promoted Heck cyclisation; (c) alkylation of a sulfone-stabilised anion using an iodide; (d) Wittig reactions.

B. M. Trost, J. R. Corte and M. S. Gudiksen, *Angew. Chem., Int. Ed.*, 1999, **38**, 3662 and B. M. Trost and J. R. Corte, *Angew. Chem., Int. Ed.*, 1999, **38**, 3664.

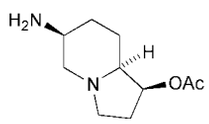


(–)-Slaframine

Biological activity: (a) causes excessive salivation in animals; (b) clinically useful for the treatment of disease arising from cholinergic dysfunctions; (c) possible drug for the treatment of the symptoms of cystic fibrosis sufferers.

Key steps: (a) highly stereoselective phenylselenocyclocarbamation reaction; (b) chemoselective reduction of a 1,2-bromovinyl triflate to provide a vinyl bromide; (c) the use of CuOAc to convert a vinyl bromide to a vinyl acetate.

D. L. Comins and A. B. Fulp, *Org. Lett.*, 1999, **1**, 1941.

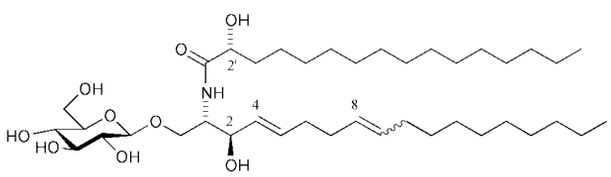


Sphingadiene-type glucocerebrosides

Biological activity: ionophoretic property for Ca^{2-} ion; the (8*Z*)-isomer shows higher binding activity than the (8*E*)-isomer.

Key steps: use of a vinylepoxide derived from D-glucosamine as a key intermediate of the sphingadiene moiety by (a) reaction with dodec-2-enyl cyanocuprate; (b) allylic bromide allylic sulfone coupling followed by desulfonylation; (c) S_N2'-type addition of di(cyanomethyl)copper-lithium followed by Wittig reaction.

T. Murakami, T. Shimizu and K. Taguchi, *Tetrahedron*, 2000, **56**, 533.



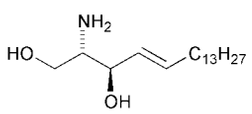
A: (2*S*,3*R*,4*E*,8*E*,2'*R*)
B: (2*S*,3*R*,4*E*,8*Z*,2'*R*)

D-*erythro*-Sphingosine and L-*lyxo*-Phytosphingosine

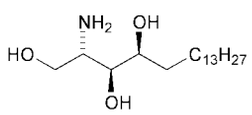
Biological activity: (a) potent inhibitory activity against protein kinase C; (b) implicated in intracellular signaling along with other secondary messenger molecules.

Key steps: Chiral β-lactam ring opening by treatment with *n*-tetradecyl toluene-*p*-sulfonate and *n*-BuLi.

T. Nakamura and M. Shiozaki, *Tetrahedron Lett.*, 1999, **40**, 9063.



D-*erythro*-sphingosine



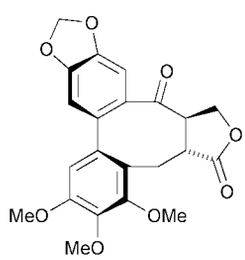
L-*lyxo*-phytosphingosine

(–)-Steganone

Biological activity: Some natural and synthetic congeners of steganone inhibit tubulin polymerisation *in vivo* and *in vitro*.

Key steps: (a) intramolecular Sm(II) iodide-promoted 8-*endo* ketyl-olefin coupling; (b) use of an enantiopure planar chiral arene chromium tricarbonyl complex to control and protect stereochemistry; (b) Pd(0)-catalysed biaryl coupling.

L.G. Monovich, Y. LeHuérou, M. Rönn and G.A. Molander, *J. Am. Chem. Soc.*, **122**, 2000, 52.



VM55599

Biological activity: not reported.

Key steps: intramolecular Diels Alder cycloaddition of a reverse isoprene across an azadiene system.

E. M. Stocking, J. F. Sanz-Cervera and R. M. Williams, *J. Am. Chem. Soc.*, 2000, **122**, 1675.