Perkin 1 Abstracts: Natural Product Synthesis

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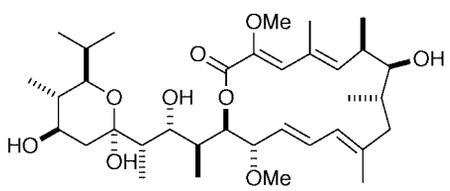
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*

(–)-Bafilomycin A_1

Biological activity: vacuolar ATPase inhibitor.

Key steps: (a) diastereoselective crotylboration; (b) methyl ketone aldol reactions.

K. A. Scheidt, A. Tasaka, T. D. Bannister, M. D. Wendt and W. R. Roush, *Angew. Chem., Int. Ed.*, 1999, **38**, 1652.

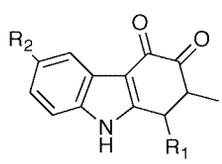


Carbazoquinocin C and (±)-Carquinostatin A

Biological activity: antioxidative activity.

Key steps: palladium-mediated oxidative coupling of arylamines and substituted 1,2-benzoquinones.

H.-J. Knölker and K. R. Reddy, *Synlett*, 1999, 596.



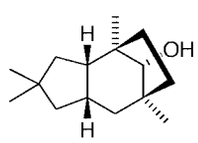
Carbazoquinocin C $R_1 = C_7H_{15}$, $R_2 = H$
Carquinostatin A $R_1 = CH_2CH(OH)CH_3$, $R_2 = CH_2CH{=}C(CH_3)_2$

(±)-Cerapicol

Biological activity: isolated as a metabolite of the fungus *ceratocystis piceae*; biological activity not reported.

Key steps: rearrangement of a cyclobutyl methanol.

N. El-Hachach, M. Fischbach, R. Gerke and L. Fitjer, *Tetrahedron*, 1999, **55**, 6119.

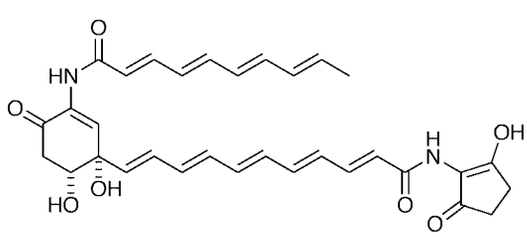


(±)-Colabomycin D

Biological activity: antibiotic.

Key steps: Stille coupling of a vinylstannane with a highly functionalised bromodiene to construct the lower side chain.

X. Wei, J. J. Conjé Grové and R. J. K. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1143.

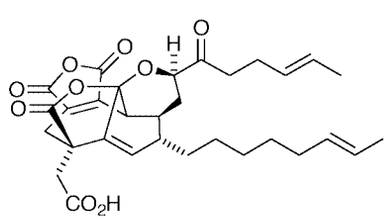


CP-262,114

Biological activity: (a) cholesterol lowering properties through inhibition of squalene synthase; (b) farnesyl transferase inhibitor.

Key steps: (a) construction of the bicylco[4.3.1]decadiene system *via* an intramolecular Diels-Alder reaction; (b) Pd(0)-catalysed methoxycarbonylation of an alkenyl triflate; (c) Wolff rearrangement to homologate a carboxylic acid; (d) oxidation of an *N*-acyl dihydroindole to a hydrolytically labile *N*-acyl indole by chloranil oxidation.

K. C. Nicolaou, P. S. Baran, Y.-L. Zhong, K. C. Fong, Y. He, W. H. Yoon and H.-S. Choi, *Angew. Chem., Int. Ed.*, 1999, **38**, 1676.

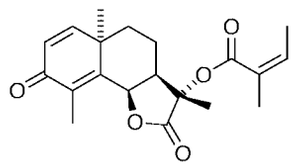


(±)-Decipienin

Biological activity: isolated from *Melanoselinum decipiens*.

Key steps: (a) decalin system obtained by the addition of 5-methyl-2-furyllithium to 3-ethoxycyclohex-2-enone and acidic treatment; (b) α-hydroxy-γ-lactone moiety obtained by condensation of the appropriate decalone with methyl pyruvate and subsequent Luche reduction.

F. J. Moreno-Dorado, F. M. Guerra, F. J. Aladro, J. M. Bustamante, Z. D. Jorge and G. M. Massanet, *Tetrahedron*, 1999, **55**, 6997.

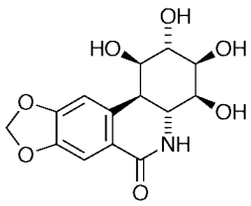


7-Deoxypancratistatin

Biological activity: anticancer and antiviral. The 7-deoxy compound is less toxic than pancratistatin itself.

Key steps: intramolecular 6-*exo*-*trig* addition of a benzyl radical to an *O*-benzyloxime ether.

G. E. Keck, S. F. McHardy and J. A. Murray, *J. Org. Chem.*, 1999, **64**, 4465.

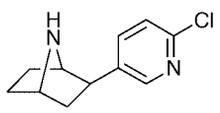


(±)-Epibatidine

Biological activity: potent analgesic.

Key steps: multi-step sequence of polymer supported reagents.

J. Habermann, S. V. Ley and J. S. Scott, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1253.

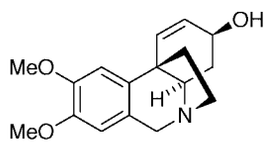


(±)-Epimaritidine and (±)-oxomaritidine

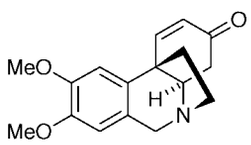
Biological activity: not reported.

Key steps: multi-step sequence of polymer supported reagents.

S. V. Ley, O. Schucht, A. W. Thomas and P. J. Murray, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1251.



(±)-Epimaritidine



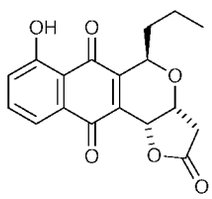
(±)-Oxomaritidine

(±)-Frenolicin B

Biological activity: antibiotic.

Key steps: intramolecular palladium-catalysed aryloxycarbonylation of 2-allyl-1-naphthol derivatives to give tricyclic γ-lactones.

P. Contant, M. Haess, J. Riegl, M. Scalone and M. Visnick, *Synthesis*, 1999, 821.

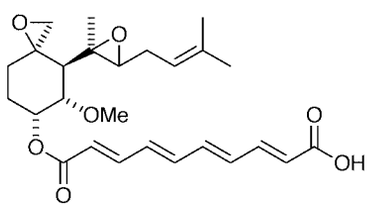


(–)-Fumagillin

Biological activity: inhibits methionine aminopeptidase; inhibits angiogenesis.

Key steps: (a) intramolecular insertion of a vinylidene carbene into a C–H bond to generate a spirocyclic cyclopentene; (b) conjugate addition of an alkenyl cuprate to a cyclohexenone; (c) Rubottom oxidation of an enol silane; (d) sulfoxonium ylide epoxidation of a ketone.

D. F. Taber, T. E. Christos, A. L. Rheingold and I. A. Guzei, *J. Am. Chem. Soc.*, 1999, **121**, 5589.

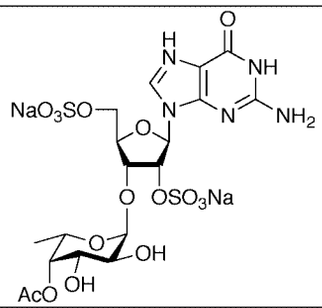


HF-7 Spider Toxin

Biological activity: blocks kainate receptors and L-type calcium channels (weakly). The target may be used in treating global ischemia arising after cardiac arrest.

Key steps: stepwise introduction of the *O*- and *N*-glycosidic linkages, followed by sulfation and deprotection.

J. McCormick, Y. Li, K. McCormick, H. I. Duynstee, A. K. van Engen, G. A. van der Marel, B. Ganem, J. H. van Boom and J. Meinwald, *J. Am. Chem. Soc.*, 1999, **121**, 5661.

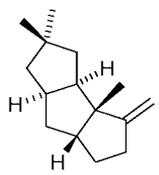


Hirsutene

Biological activity: not reported.

Key steps: a lithium amide mediated spiro-epoxide fragmentation reaction.

J. Leonard, L. Bennett and A. Mahmood, *Tetrahedron Lett.*, 1999, **40**, 3965.

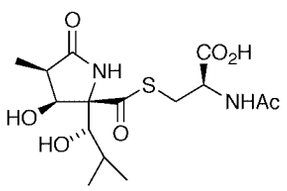


(+)-Lactacystin

Biological activity: (a) exhibits significant neurotrophilic activity; (b) potent proteosome inhibitor.

Key steps: (a) asymmetric Sharpless aminohydroxylation; (b) *anti*-selective crotylmetallation.

J. S. Panek and C. E. Masse, *Angew. Chem., Int. Ed.*, 1999, **38**, 1093.

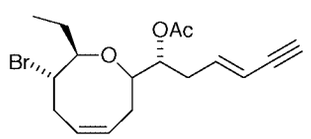


(+)-Laurencin

Biological activity: none reported.

Key steps: (a) asymmetric aldol addition of a glycolate enolate; (b) ring closing metathesis to generate an oxocene ring. This is a formal total synthesis which intersects with the synthesis of A. B. Holmes and co-workers.

M. T. Crimmins and A. L. Choy, *J. Am. Chem. Soc.*, 1999, **121**, 5653.

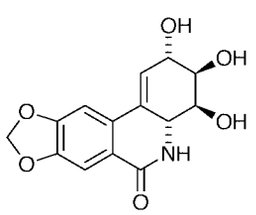


(+)-Lycoricidine and (+)-Narciclasine

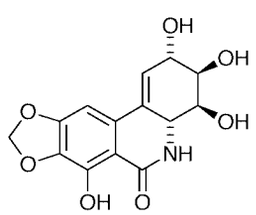
Biological activity: not specified.

Key steps: (a) regioselective addition of a thiyl radical to an alkyne followed by stereoselective 6-*exo* radical cyclisation of the vinyl radical to an *O*-benzyloxime; (b) direct conversion of a hindered benzamide to an ester; (c) use of a tosylate as an electron-withdrawing protecting group for a phenolic hydroxy and its deblocking with samarium diiodide.

G. E. Keck, T. T. Wager and J. F. D. Rodriguez, *J. Am. Chem. Soc.*, 1999, **121**, 5176.



(+)-Lycoricidine



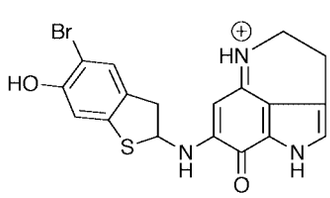
(+)-Narciclasine

(±)-Makaluvamine F

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

Key steps: intramolecular nucleophilic substitution reactions of phenol ethers using activated hypervalent iodine species.

Y. Kita, M. Egi, T. Takada and H. Tohma, *Synthesis*, 1999, 885.

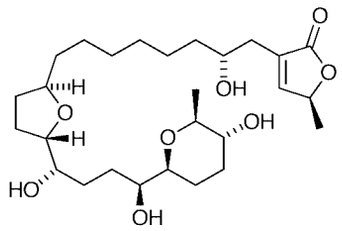


(–)-Mucocin

Biological activity: selective inhibitor of A-549 (lung cancer) and PACA-2 (pancreatic cancer) cell lines with a selectivity up to 10 000 times that of adriamycin.

Key steps: (a) Sharpless epoxidation; (b) Wittig reaction; (c) acid-catalysed intramolecular 6-*endo* attack on an alkenyl epoxide of an acetonide; (d) coupling reaction between a metallated iodide and an aldehyde.

S. Bäurle, S. Hoppen and U. Koert, *Angew. Chem., Int. Ed.*, 1999, **38**, 1263.

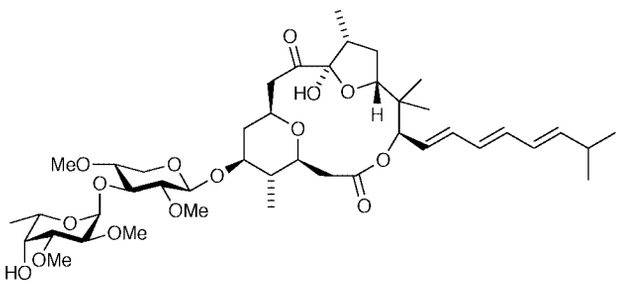


(–)-Polycavernoside A

Biological activity: toxin isolated from a frequently ingested red alga.

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

L. A. Paquette, L. Barriault and D. Pissarnitski, *J. Am. Chem. Soc.*, 1999, **121**, 4542.

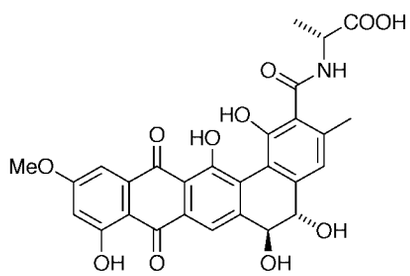


Pradimicinone (Benanomicinone)

Biological activity: (a) antibiotic; (b) antifungal; (c) anti-HIV; (d) activity attributed to the potentially specific binding to oligosaccharides of fungi or viral surfaces.

Key steps: (a) Pd-catalysed internal cyclisation; (b) pinacol-forming reaction; (c) Diels-Alder reaction.

M. Kitamura, K. Ohmori, T. Kawase and K. Suzuki, *Angew. Chem., Int. Ed.*, 1999, **38**, 1229.

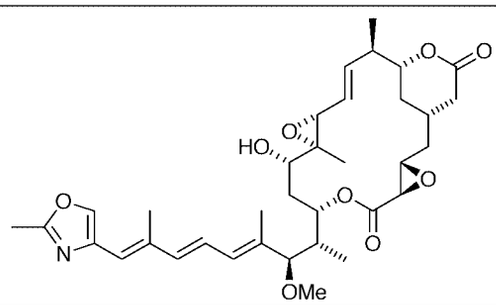


Rhizoxin D

Biological activity: potent antitumor agent.

Key steps: (a) Julia olefination; (b) Horner-Emmons macrocyclisation.

J. A. Lafontaine, D. P. Provencal, C. Gardelli and J. W. Leahy, *Tetrahedron Lett.*, 1999, **40**, 4145.

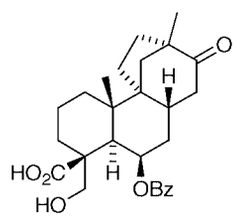


(+)- and (–)-Scopadulcic Acid A

Biological activity: The closely related scopadulcic acid B is antiviral and inhibits tumour promotion by phorbol esters; inhibits H^+,K^+-ATPase; inhibits bone resorbtion by osteoclasts.

Key steps: a cascade intramolecular Heck reaction of a methylene iodide which generates three rings.

M. E. Fox, C. Li, J. P. Marino and L. E. Overman, *J. Am. Chem. Soc.*, 1999, **121**, 5467.



Vibsanol

Biological activity: moderate inhibitory activity toward lipid peroxidation in rat brain homogenates.

Key steps: tandem cyclisation of an *o*-(*tert*-butyldimethylsiloxy)diarylalkyne with tetrabutylammonium fluoride and excess paraformaldehyde.

A. Sakai, T. Aoyama and T. Shioiri, *Tetrahedron Lett.*, 1999, **40**, 4211.