Perkin 1 Abstracts: Natural Product Synthesis

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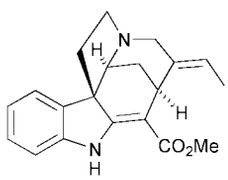
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

(±)-Akuammicine

Biological activity: (a) isolated from the seeds of *Picralima klaineana*; (b) biological activity not reported.

Key steps: (a) tandem vinylogous Mannich addition; (b) intramolecular hetero Diels–Alder reaction; (c) sequential oxidation and base-induced skeletal reorganisation.

M. Ito, C. W. Clark, M. Mortimore, J. B. Goh and S. F. Martin, *J. Am. Chem. Soc.*, 2001, **123**, 8003.

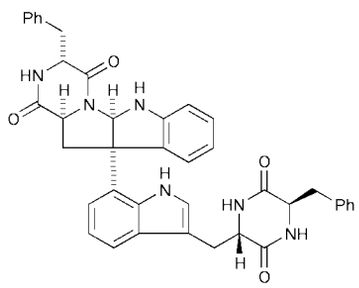


(+)-Asperazine

Biological activity: cytotoxic towards leukemia cell lines.

Key steps: intramolecular Heck reaction to construct a highly congested quaternary centre.

S. P. Govek and L. E. Overman, *J. Am. Chem. Soc.*, 2001, **123**, 9468.

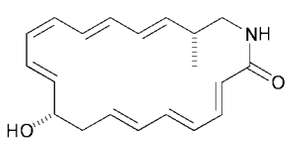


(9*S*,18*R*)-Cyclamenol A

Biological activity: inhibits leukocyte adhesion to endothelial cells.

Key steps: (a) Wittig olefination reaction; (b) macrocyclic ring formation *via* a vanadium-mediated pinacolisation reaction; (c) Corey–Hopkins sequence.

M. Nazaré and H. Waldmann, *Chem. Eur. J.*, 2001, **7**, 3363.

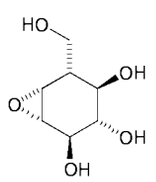


(+)- and (–)-Cyclophellitol

Biological activity: (a) isolated from the mushroom *Phellinus* sp.; (b) inactivator of β-glucosidase; (c) HIV inhibitor.

Key steps: Pd(0)-catalysed dynamic kinetic asymmetric allylic alkylation of racemic conduritol tetraesters.

B. M. Trost, D. E. Patterson, and E. J. Hembre, *Chem. Eur. J.*, 2001, **7**, 3768.



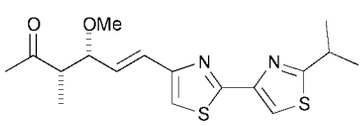
(+)-Cyclophellitol

(–)-Cystothiazole E

Biological activity: (a) isolated from a culture broth of the myxobacterium *Cystobacter fuscus* AJ-13278; (b) antiinfective; (c) cytotoxic.

Key steps: Suzuki cross-coupling.

T. Bach and S. Heuser, *Angew. Chem., Int. Ed.*, 2001, **40**, 3184.

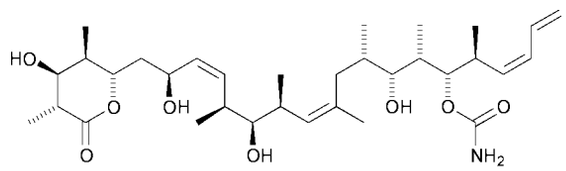


(+)-Discodermolide

Biological activity: (a) immunosuppressant; (b) stabilises microtubules and promotes polymerisation of tubulin.

Key steps: A 23-step synthesis (longest linear sequence) based on substrate-controlled boron-mediated *anti*-selective aldol reactions of chiral ethyl ketones and (+)-diisopinylcampheylboron chloride-mediated aldol reaction of a methyl ketone.

I. Paterson, G. J. Florence, K. Gerlach, J. P. Scott and N. Sereinig, *Angew. Chem., Int. Ed.*, 2000, **39**, 377.

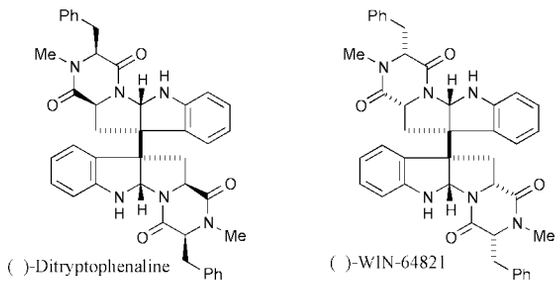


(–)-Ditryptophenaline and (–)-WIN 64821

Biological activity: substance P antagonist, cholecystokinin type-B receptor antagonist.

Key steps: oxidative cleavage of a readily available C_2-symmetric cyclohexane-1,2-diol.

L. E. Overman and D. V. Paone, *J. Am. Chem. Soc.*, 2001, **123**, 9465.

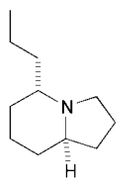


(+)-5-Epiindolizidine 167B

Biological activity: not reported.

Key steps: asymmetric intramolecular Heck cyclisation of an endocyclic enamide to yield an indolizidone.

K. Kiewel, M. Tallant and G. A. Sulikowski, *Tetrahedron Lett.*, 2001, **42**, 6621.

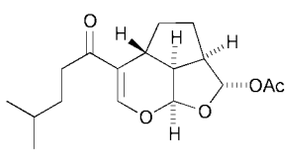


(±)-Euplotin A

Biological activity: cytotoxin.

Key steps: (a) Paterno Büchi reaction; retro-Diels Alder reaction to construct a 2-acylpropenal; (c) intramolecular Diels–Alder reaction of a dihydrofuran and a 2-acylpropenal to construct the tricyclic framework.

R. A. Aungst and R. L. Funk, *J. Am. Chem. Soc.*, 2001, **123**, 9455.

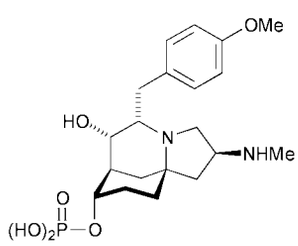


FR901483

Biological activity: (a) immunosuppressant; (b) inhibitor of the biosynthesis of purines.

Key steps: oxidative cyclisation of a phenolic oxazoline using iodobenzene diacetate to form a spirolactam.

M. Ousmer, N. A. Braun, C. Bavoux, M. Perrin and M. A. Ciufolini, *J. Am. Chem. Soc.*, 2001, **123**, 7534.

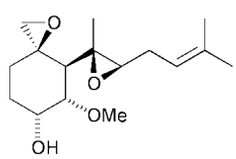


(–)-Fumagillol

Biological activity: (a) antiangiogenic; (b) irreversible inhibitor of methionine aminopeptidase 2.

Key steps: (a) Evans aldol reaction; (b) ring-closing metathesis.

J.-G. Boiteau, P. Van de Weghe and J. Eustache, *Org. Lett.*, 2001, **3**, 2737.

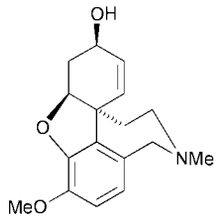


(–)-Galanthamine

Biological activity: (a) isolated from the *Amaryllidaceae* family; (b) used in the treatment of Alzheimer's disease; (c) selective acetylcholinesterase inhibitor.

Key steps: phenolic oxidative coupling reaction using phenyliodine(III) bis(trifluoroacetate) as the oxidant.

M. Node, S. Kodama, Y. Hamashima, T. Baba, N. Hamamichi and K. Nishide, *Angew. Chem., Int. Ed.*, 2001, **40**, 3060.

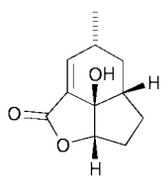


(+)-Galiellalactone

Biological activity: (a) isolated from *Galiella rufa*; (b) selective inhibitor of interleukin-6 signalling in HepG2 cells (IC_{50} – 250 nM); (c) inhibits gibberillic acid-induced synthesis of α-amylase.

Key steps: (a) diastereoselective Pd-catalysed hydrogenation; (b) intramolecular aldol reaction.

M. Johansson and O. Sterner, *Org. Lett.*, 2001, **3**, 2843.

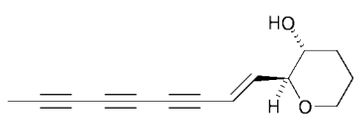


(–)-Ichthyothereol

Biological activity: (a) isolated from *Dahlia coccinea* and *Ichthyotherterminals*; (b) toxin.

Key steps: (a) stereoselective formation of a tetrahydropyran ring *via* a $Co_2(CO)_8$-mediated *endo* mode cyclisation of an epoxy-alkyne derivative; (b) Stille coupling.

C. Mukai, N. Miyakoshi and M. Hanaoka, *J. Org. Chem.*, 2001, **66**, 5875.

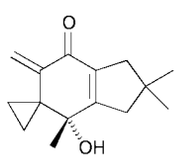


(±)-Illudin C

Biological activity: (a) isolated from several fungi; (b) displays antimicrobial activity against methicillin-resistant *Staphylococcus aureus*; (c) cytotoxic in a mammalian cell culture system.

Key steps: intramolecular nitrile oxide olefin cycloaddition.

R. A. Aungst, Jr., C. Chan and R. L. Funk, *Org. Lett.*, 2001, **3**, 2611.

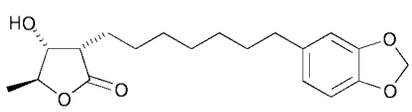


(+)-Juruenolide C

Biological activity: (a) isolated from seedlings and micropropagated leaves of *Virola surinamensis*; (b) antifungal.

Key steps: sequential 5-*exo*-*digonal* radical cyclisation, 1,5-intramolecular hydrogen transfer and 5-*endo*-*trigonal* cyclisation.

D. L. J. Clive and E.-S. Ardelean, *J. Org. Chem.*, 2001, **66**, 4841.

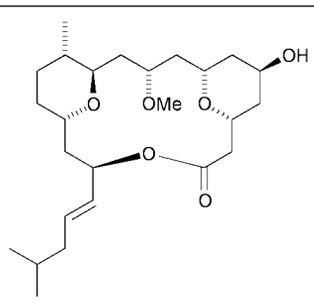


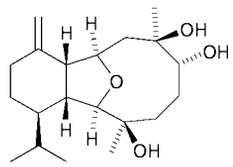
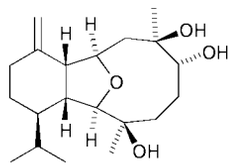
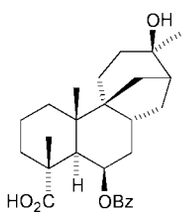
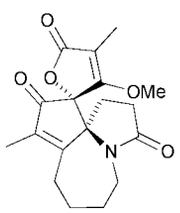
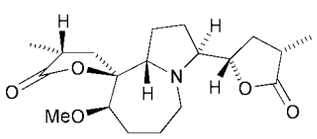
Leucascandrolide A Macrolide

Biological activity: (a) isolated from the sponge *Leucascandra caveolata*; (b) shows potent cytotoxicity against P388 cancer cells.

Key steps: Mukaiyama aldol Prins cyclisation cascade reaction.

D. J. Kopecky and S. D. Rychnovsky, *J. Am. Chem. Soc.*, 2001, **123**, 8420.



(–)-Sclerophytin A *Biological activity*: cytotoxic to L1210 cells at 1 ng ml $^{-1}$ *Key steps*: (a) Prins-pinacol reaction; (b) Nozaki–Hiyama–Kishi cyclisation to construct the oxacyclononane ring; (c) hydroxy-directed epoxidation; (d) oxymercuration to generate the tetrahydrofuran ring. D. W. C. Macmillan, L. E. Overman and L. D. Pennington, *J. Am. Chem. Soc.*, 2001, **123**, 9033.	
(–)-Sclerophytin A *Biological activity*: cytotoxic to L1210 at 1 ng ml $^{-1}$ *Key steps*: (a) tandem Tebbe–Claisen ring expansion; (b) asymmetric Diels–Alder reaction using a chiral auxiliary. P. Bernardelli, O. M. Moradei, D. Friedrich, J. Yang, F. Gallou, B. P. Dyck, R. W. Doskotch, T. Lange and L. A. Paquette, *J. Am. Chem. Soc.*, 2001, **123**, 9021.	
(±)-Scopadulin *Biological activity*: (a) antiviral; (b) cytotoxic. *Key steps*: (a) intramolecular aldol condensation; (b) conversion of a primary aliphatic amine into a primary alcohol; (c) chemo- and stereoselective methylation using $MeTi(O\text{-}i\text{-}Pr)_3$. S. M. A. Rahman, H. Ohno, T. Murata, H. Yoshino, N. Satoh, K. Murakami, D. Patra, C. Iwata, N. Maezaki and T. Tanaka, *J. Org. Chem.*, 2001, **66**, 4831.	
(±)-Stemonamide *Biological activity*: (a) isolated from the roots of *Stemona japonica*; (b) biological activity not reported. *Key steps*: (a) reaction between a silyloxyfuran and an *N*-acyliminium ion; (b) intramolecular aldol spirocyclisation. A. S. Kende, J. I. M. Hernando and J. B. J. Milbank, *Org. Lett.*, 2001, **3**, 2505.	
(–)-Stemospironine *Biological activity*: (a) isolated from the leaves of *Stemona japonica*; (b) biological activity not reported. *Key steps*: (a) Staudinger reaction; (b) aza-Wittig ring closure; (c) stereoselective intramolecular capture of an aziridinium salt to form a vicinal pyrrolidine butyrolactone. D. R. Williams, M. G. Fromhold and J. D. Earley, *Org. Lett.*, 2001, **3**, 2721.	
(±)-Strychnine *Biological activity*: mild stimulatory tonic, appetite enhancer, rodenticide, human poison. *Key steps*: (a) cobalt-mediated [2+2+2] cycloaddition of an enynoylindole with acetylene; (b) formal 1,8-conjugate addition of an amine; (c) Pd- Ni- and radical mediated cyclisation. M. J. Eichberg, R. L. Dorta, D. B. Grotjahn, K. Lamottke, M. Schmidt and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, 2001, **123**.