Perkin 1 Abstracts: Natural Product Synthesis

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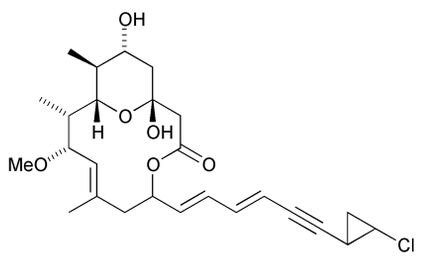
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

Callipeltoside aglycon

Biological activity: (a) the callipeltosides are isolated from the shallow-water lithistid sponge *Callipelta* sp.; (b) biological activity not reported.

Key steps: (a) Yamamoto's vinylogous aldol reaction promoted by an aluminium Lewis Acid; (b) boron-mediated aldol reaction; (c) Sonogashira coupling.

I. Paterson, R. D. M. Davies and R. Marquez, *Angew. Chem., Int. Ed.*, 2001, **40**, 603.

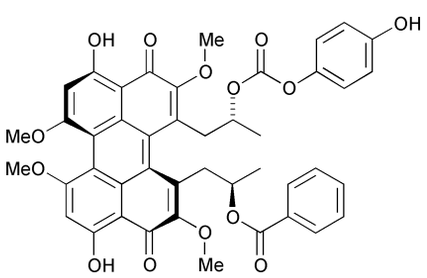


Calphostin C

Biological activity: (a) isolated from *Cladosporium cladosporioides*; (b) a potent and selective inhibitor of protein kinase C, which is a phosphorylation enzyme that plays a central role in signal transduction; (c) a potential agent for anticancer therapy.

Key steps: (a) aminobenzannulation reaction of an enantiopure chromium Fischer carbene complex; (b) selective thermally controlled epimerisation of an atropisomeric mixture of perylenequinones.

C. A. Merlic, C. C. Aldrich, J. Albaneze-Walker, A. Saghatelian and J. Mammen, *J. Org. Chem.*, 2001, **66**, 1297.

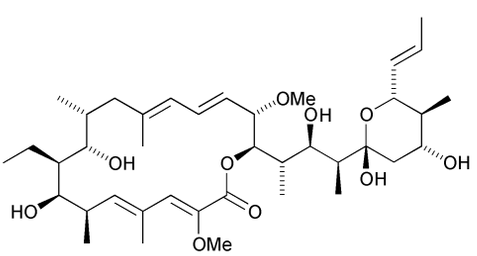


Concanamycin F

Biological activity: (a) antibiotic; (b) potent and specific inhibitor of vacuolar H^+-ATPase.

Key steps: (a) intra- and intermolecular Stille couplings; (b) stereoselective aldol condensation of an 18-membered macrolactonic aldehyde and a ketone.

K. Toshima, T. Jyojima, N. Miyamoto, M. Katohno, M. Nakata and S. Matsumura, *J. Org. Chem.*, 2001, **66**, 1708.

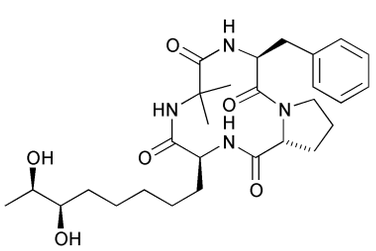


(–)-Diheteropeptin

Biological activity: (a) isolated from the fermentation broth of *Diheterospora chlamydospora* Q 58044; (b) exhibits transforming growth factor β (TGF-β) like properties; regulating immune function, cell proliferation, cell differentiation and extra-cellular matrix production.

Key steps: (a) Schöllkopf amino acid synthesis; (b) Sharpless asymmetric dihydroxylation.

P. Durand, P. Peralba, V. Derain, S. Komesli and P. Renaut, *Tetrahedron Lett.*, 2001, **42**, 2121.

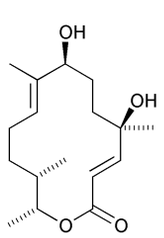


5,6-Dihydrocineromycin B

Biological activity: (a) isolated from *Streptomyces* sp. Gö 40/10; (b) displays antibiotic activity against *staphylococci.*

Key steps: generation of an enantiomerically pure tertiary alcohol by selective allylation of a ketone.

L. F. Tietze and L. Völkel, *Angew. Chem., Int. Ed.*, 2001, **40**, 901.

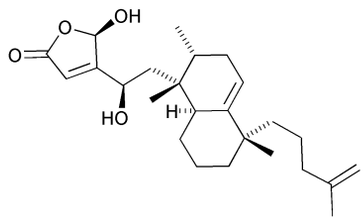


(–)-Dysidiolide

Biological activity: (a) isolated from the Caribbean sponge *Dysidea etheria* de Laubenfels; (b) inhibitor of the protein phosphatase cdc25A (IC_{50} = 9.4 μM), which is essential for cell proliferation; (c) inhibits the growth of A-549 human lung carcinoma (IC_{50} = 4.7 μM) and P388 murine leukemia cells (IC_{50} = 1.5 μM).

Key steps: intramolecular Diels–Alder reaction.

H. Miyaoka, Y. Kajiwara, Y. Hara and Y. Yamada, *J. Org. Chem.*, 2001, **66**, 1429.

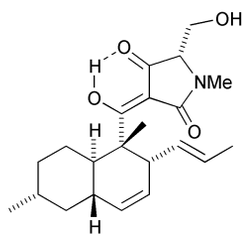


(–)-Equisetin

Biological activity: (a) isolated from the extracts of the active fungal broths *Fusarium heterosporum* and *Phoma* sp.; (b) inhibits the *in vitro* recombinant integrase enzyme (IC_{50} = 7-20 μM); (c) prevents the integration reactions catalysed by preintegration complexes isolated from HIV-1 infected cells.

Key steps: (a) Suzuki coupling; (b) (*E*)-selective Wittig olefination; (c) diastereoselective Me_3Al-mediated intramolecular Diels–Alder reaction; (d) (*E*)-selective Takai-olefination.

K. Yuki, M. Shindo and K. Shishido, *Tetrahedron Lett.*, 2001, **42**, 2517.

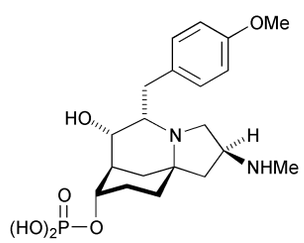


FR901483

Biological activity: (a) isolated from a *Cladobotryum* species; (b) immunosuppressant.

Key steps: cyclisation involving the oxidative dearomatisation of a phenolic oxazoline to a spirolactam.

M. Ousmer, N. A. Braun and M. A. Ciufolini, *Org. Lett.*, 2001, **3**, 765.

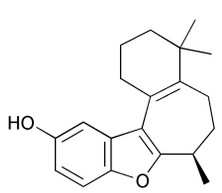


(+)-Frondosin B

Biological activity: interleukin-8 receptor antagonist.

Key steps: (a) Friedel–Crafts reaction to construct the 7-membered ring; (b) cationic cyclisation of a vinylogous benzofuran to generate a 6-membered ring; (c) Diels–Alder reaction. Two routes to the racemic product are reported as well as a scalemic route that established the absolute configuration.

M. Inoue, M. W. Carson, A. J. Frontier and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2001, **39**, 1878.

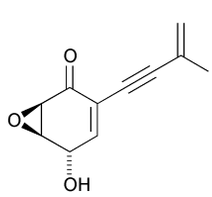


(+)-Harveynone

Biological activity: phytotoxin isolated from the tea gray blight fungus *Pestalotiopsis theae*.

Key steps: Stille cross-coupling.

M. T. Barros, C. D. Maycock and M. R. Ventura, *Chem. Eur. J.*, 2000, **6**, 3991.

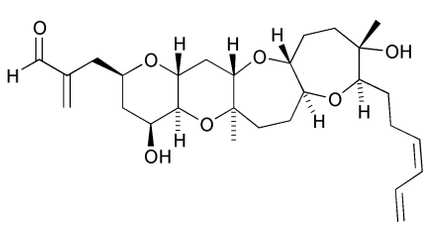


(±)-Hemibrevetoxin B

Biological activity: a member of a family of red tide toxins possessing properties including neurotoxicity and antimicrobial activity.

Key steps: (a) hetero-Diels–Alder reaction; (b) ring-closing metathesis; (c) acid-mediated annulation.

J. D. Rainier, S. P. Allwein and J. M. Cox, *J. Org. Chem.*, 2001, **66**, 1380.

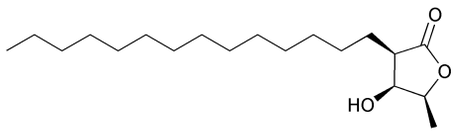


(2*R*,3*S*,4*S*)-3-Hydroxy-4-methyl-2-(1′-*n*-tetradecyl)butanolide

Biological activity: (a) isolated from the fruit of *Trichilia claussenii*; (b) biological activity not reported.

Key steps: (a) asymmetric dihydroxylation of an enyne with AD-mix-α; (b) reaction of an alkynyltungsten complex with an alkynyl aldehyde and BF_3•Et_2O to yield an oxacarbenium salt that gave an α-alkylidene-γ-lactone upon demetallation.

B. Liu, M.-J. Chen, C.-Y. Lo and R.-S. Liu, *Tetrahedron Lett.*, 2001, **42**, 2533.

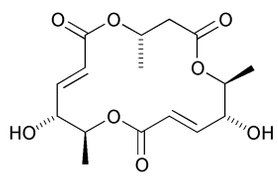


Macrosphelide A

Biological activity: (a) isolated from *Microsphaeropsis* sp. FO-5050; (b) strong inhibitor of the adhesion of human leukemia HL-60 cells to human-umbilical-vein endothelial cells.

Key steps: (a) oxidation of a 2-substituted furan ring to yield a 4-oxo-2-alkenoic acid; (b) Yamaguchi lactonisation.

Y. Kobayashi, G. B. Kumar, T. Kurachi, H. P. Acharya, T. Yamazaki, and T. Kitazume, *J. Org. Chem.*, 2001, **66**, 2011.

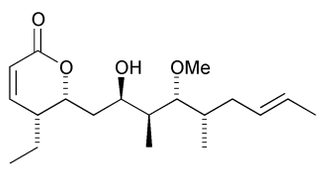


(–)-Pironetin

Biological activity: (a) isolated from the fermentation broth of *Streptomyces prunicolor* PA-48153; (b) immunosuppressant.

Key steps: (a) diastereoselective Lewis acid mediated addition of a crotylstannane to an aldehyde; (b) Lewis acid promoted Mukaiyama aldol reaction; (c) *anti*-selective SmI_2 reduction of a β-hydroxyketone; (d) lactone annulation reaction.

G. E. Keck, C. E. Knutson and S. A. Wiles, *Org. Lett.*, 2001, **3**, 707.

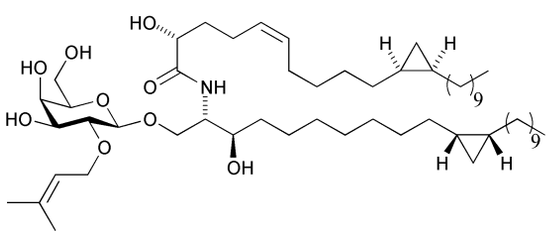


(+)-Plakoside A

Biological activity: (a) isolated from the Caribbean sponge *Plakortis simplex*; (b) strong immunosuppressive activity without cytotoxicity.

Key steps: (a) stereoselective enzymatic acetylation of a *meso*-diol with vinyl acetate in the presence of lipase AK; (b) two (*Z*)-selective Wittig olefinations; (c) stereoselective coupling of an alkyne with the Garner aldehyde derived from (*S*)-serine; (d) β-selective Königs–Knorr glycosidation.

M. Seki, A. Kayo and K. Mori, *Tetrahedron Lett.*, 2001, **42**, 2357.

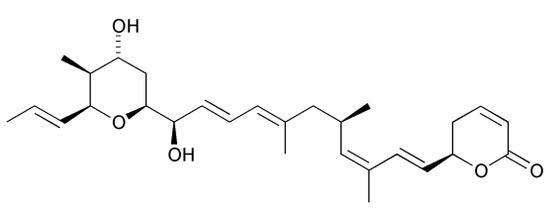


(+)-Ratjadone

Biological activity: (a) isolated from *Sorangium cellulosum* (So ce360); (b) cytotoxic against cultured mouse cell lines (L929)(IC_{50} = 50 pg mL^{-1}); (c) inhibits growth of the HeLa cell line (KB 3.1) at 40 pg mL^{-1}; (d) antifungal (MIC = 0.04 - 0.6 μg mL^{-1}).

Key steps: (a) asymmetric hetero-Diels–Alder reaction; (b) Wittig olefination; (c) Heck reaction.

U. Bhatt, M. Christmann, M. Quitschalle, E. Claus and M. Kalesse, *J. Org. Chem.*, 2001, **66**, 1885.

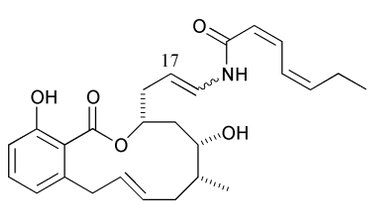


Salicylihalamides A and B

Biological activity: cytotoxin.

Key steps: (a) Mitsunobu esterification; (b) ring-closing metathesis; (c) Horner–Wadsworth–Emmons coupling.

D. Labrecque, S. Charron, R. Rej, C. Blais and S. Lamothe, *Tetrahedron Lett.*, 2001, **42**, 2645.



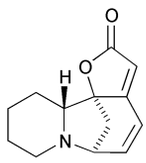
Salicylihalamide A : 17-*E*
Salicylihalamide B : 17-*Z*

(±)-Securinine

Biological activity: GABA receptor antagonist.

Key steps: (a) addition of a silyloxyfuran to an *in situ* generated iminium ion; (b) ring-closing metathesis.

S. Liras, J. E. Davoren and J. Bordner, *Org. Lett.*, 2001, **3**, 703.

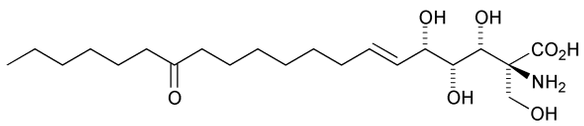


Sphingofungin E

Biological activity: (a) antifungal agent; (b) serinepalmitoyl transferase inhibitor.

Key steps: (a) stereoselective reduction of a ketone using L-Selectride; (b) Suzuki coupling of a vinyl iodide and an organoborane.

T. Nakamura and M. Shiozaki, *Tetrahedron Lett.*, 2001, **42**, 2701.

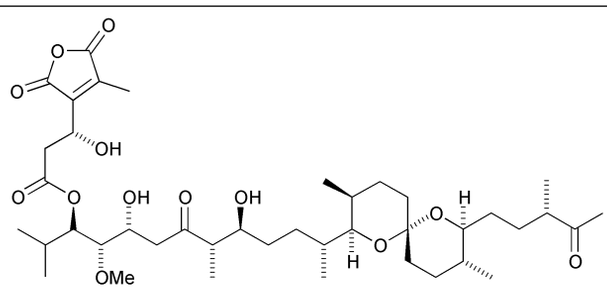


Tautomycin

Biological activity: (a) antifungal soil metabolite; (b) selective inhibitor of protein-serine/threonine phosphatase types 1 and 2A.

Key steps: (a) three separate additions of allenylmetal reagents to appropriate aldehyde segments to yield *syn* or *anti* adducts with high diastereoselectivity; (b) intramolecular hydrosilylation of an alkyne to afford a five-membered siloxane; (c) Tamao oxidation of a siloxane.

J. A. Marshall and M. M. Yanik, *J. Org. Chem.*, 2001, **66**, 1373.

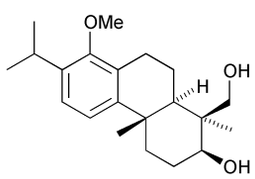


(+)-Triptocallol

Biological activity: isolated from tissue cultures of *Tripterygium wilfordii*.

Key steps: $Mn(OAc)_3$ mediated asymmetric radical cyclisation of a β-keto ester employing a chiral auxiliary.

D. Yang, M. Xu and M.-Y. Bian, *Org. Lett.*, 2001, **3**, 111.

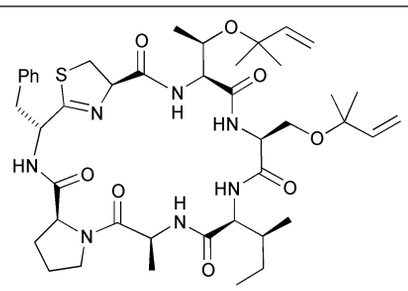


Trunkamide A

Biological activity: (a) isolated from ascidians of the genus *Lissoclinum*; (b) antitumour activity.

Key steps: (a) peptide macrocyclisation; (b) selective epimerisation with methanolic pyridine.

B. McKeever and G. Pattenden, *Tetrahedron Lett.*, 2001, **42**, 2573.



Unsaturated polyazamacrolide

Biological activity: (a) isolated from the pupal defensive secretion of the ladybird beetle *Subcoccinella vigintiquatuorpunctata*; (b) biological activity not reported.

Key steps: nucleophilic opening of a chiral aziridine.

M. R. Gronquist and J. Meinwald, *J. Org. Chem.*, 2001, **66**, 1075.