Perkin 1 Abstracts: Natural Product Synthesis

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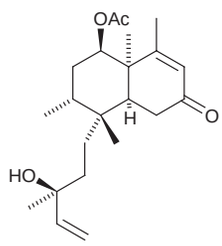
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*

(±)-6β-Acetoxy-2-Oxokolavenool

Biological activity: this Clerodane diterpenoid is isolated from several Mexican *Stevia* species. The biological activity is not reported.

Key steps: face-selective Diels-Alder reaction of an activated 4,4-disubstituted cyclohexenone.

H.-J. Liu and K.-S. Shia, *Tetrahedron*, 1998, **54**, 13449.

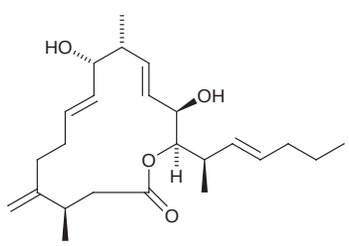


(+)-Amphidinolide J

Biological activity: antitumour agent.

Key steps: (a) asymmetric conjugate addition to an *N*-crotonoyl oxazolidinone; (b) Pd(0)-catalysed coupling between an iodoalkene and an alkylzinc reagent; (c) diastereoselective addition of an alkenylzinc reagent to an aldehyde; (d) Yamaguchi macrolactonisation.

D. R. Williams and W. S. Kissel, *J. Am. Chem. Soc.*, 1998, **120**, 11198.

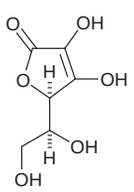


L-Ascorbic acid (vitamin C)

Biological activity: (a) reducing agent involved in the production of collagen; (b) considered important in the prevention of cancer, cerebral apoplexy, diabetes, atopic dermatitis, myocardial infarction and AIDS.

Key steps: enantiopure *cis*-1,2-dihydrocatechol is obtained from microbial oxidation of chlorobenzene and converted to vitamin C *via* 3,5-*O*-benzylidene -L-gulonolactone.

M. Banwell, S. Blakey, G. Harfoot and R. Longmore, *J. Chem. Soc., Perkin Trans. 1*, 1998, 3141.

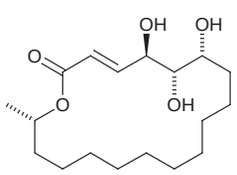


(+)-Aspicilin

Biological activity: not reported.

Key steps: conversion of 2-substituted furans into 4-oxygenated 2-enoic acids.

Y. Kobayashi, M. Nakano, G. B. Kumar and K. Kishihara, *J. Org. Chem.*, 1998, **63**, 7505.

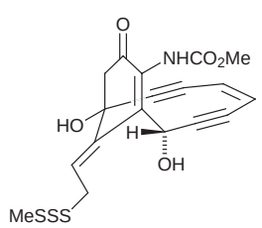


(±)-Calicheamicinone

Biological activity: the title compound, the aglycone of calicheamicin γ_1 isolated from the fermentation broth of *Micromonospora echinospora* sp. calichensis, exhibits potent antitumour activity.

Key steps: (a) appendage of an intact enediyne unit to an *o*-quinone monoketal; (b) generation of the bicyclo[7.3.0]tridecyne system *via* intramolecular addition of an alkynyllithium to an aldehyde. The synthesis was accomplished in 28 steps (2% overall) from 5-methoxysalicylic acid.

I. Churcher, D. Hallett and P. Magnus, *J. Am. Chem. Soc.*, 1998, **120**, 10350.

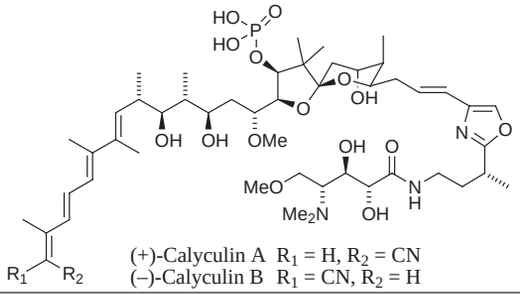


(+)-Calyculin A and (–)-Calyculin B

Biological activity: potent serine-threonine protein phosphatase (PP1 and PP2A) inhibitors endowed with remarkable cell membrane permeability.

Key steps: (a) diastereoselective IBr-induced iodocarbonate cyclisation; (b) dithiane-epoxide coupling tactic to construct a masked aldol; (c) olefin σ-bond construction *via* a Suzuki one-pot three-component triene synthesis; (d) Peterson olefination

A. B. Smith III, G. K. Friestad, J. J.-W. Duan, J. Barbosa, K. G. Hull, M. Iwashima, Y. Qiu, P. G. Spoors, E. Bertounesque and B. A. Salvatore, *J. Org. Chem.*, 1998, **63**, 7596.



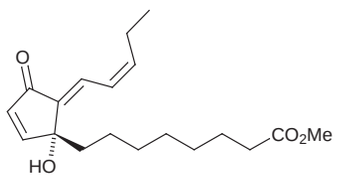
(+)-Calyculin A R_1 = H, R_2 = CN
(–)-Calyculin B R_1 = CN, R_2 = H

Chromomoric Acid D-I Methyl Ester

Biological activity: the acid is a metabolite of linolemic acid isolated from *Chromolaena morii*. The biological activity is not yet determined.

Key steps: (a) addition of an organolithium reagent to an epoxy ketone; (b) regio- and stereospecific reductive ring opening; (c) a crossed aldol condensation.

Z.-Y. Liu and X.-J. Chu, *Tetrahedron*, 1998, **54**, 12561.

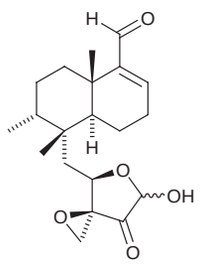


Clerocidin

Biological activity: (a) antibiotic; (b) antitumor.

Key steps: enantioselective homoallenylboration.

A. X. Xiang, D. A. Watson, T. Ling and E. A. Theodorakis, *J. Org. Chem.*, 1998, **63**, 6774.

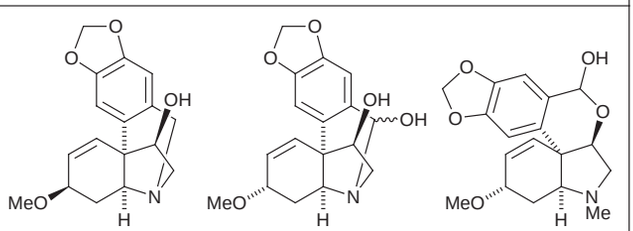


(+)-Crinamine, (–)-Haemanthidine, (+)-Pretazettine

Biological activity: not reported.

Key steps: enantioselective synthesis of the cyclohexenylamine intermediate using Pd_2dba_3•$CHCl_3$ and (*S*)-BINAPO.

T. Nishimata and M. Mori, *J. Org. Chem.*, 1998, **63**, 7586.



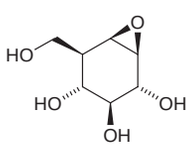
(+)-Crinamine (–)-Haemanthidine (+)-Pretazettine

(+)-Cyclophellitol

Biological activity: sub-microgram inhibitor of β-glucosidase.

Key steps: Grubbs' ring closure methathesis.

F. E. Ziegler and Y. Wang, *J. Org. Chem.*, 1998, **63**, 7920.

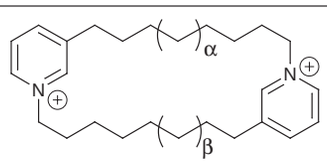


Cyclostellettamines A-F

Biological activity: effective inhibitor of methyl quinuclidinyl benzylate binding to muscarinic acetylcholine receptors.

Key steps: (a) use of pyridine-*N*-oxide as a protected form of pyridine; (b) a one-pot deprotection and activation with PBr_3.

J. E. Baldwin, D. R. Spring, C. E. Atkinson and V. Lee, *Tetrahedron*, 1998, **54**, 13655.



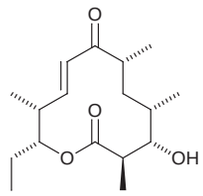
Cyclostellettamine A : α = 5, β = 5
Cyclostellettamine B : α = 5, β = 6
Cyclostellettamine C : α = 6, β = 6
Cyclostellettamine D : α = 5, β = 7
Cyclostellettamine E : α = 6, β = 7
Cyclostellettamine F : α = 7, β = 7

10-Deoxymethymycin

Biological activity: antibiotic.

Key steps: intramolecular Nozaki-Hiyama-Kishi coupling reaction to construct a 12-membered lactone.

R. A. Pilli, C. K. Z. de Andrade, C. R. O. Souto and A. Meijere, *J. Org. Chem.*, 1998, **63**, 7811.

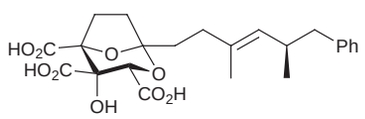


6,7-Dideoxysqualestatin H5

Biological activity: inhibits farnesyl transferase.

Key steps: intramolecular vinylogous aldol reaction of a 5-substituted-2-furoate.

S. F. Martin and S. Naito, *J. Org. Chem.*, 1998, **63**, 7592.

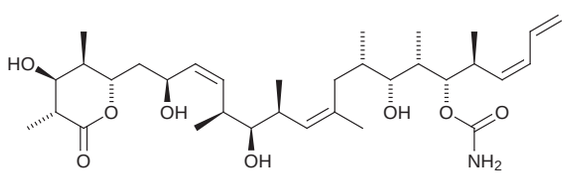


(+)-Discodermolide

Biological activity: (a) potent immunosuppressant; (b) potential antitumor activity.

Key steps: (a) assemblage of three key stereotriad subunits through addition of nonracemic allenyltin, -indium, and -zinc reagents to (*S*)-3-silyloxy-2-methylpropanal derivatives; (b) Suzuki coupling.

J. A. Marshall and B. A. Johns, *J. Org. Chem.*, 1998, **63**, 7885.

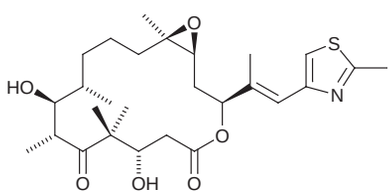


Epothilone B

Biological activity: (a) shows potent *in vitro* antitumour properties; (b) functions through a paclitaxel-like (taxol-like) mechanism as inhibitors of microtubule disassembly.

Key steps: (a) formation of a (*Z*)-lithium enolate; (b) addition of an enolate to a readily available (*S*)-aldehyde providing the C7-C8 *anti* relationship with good diastereoface selectivity in conjunction with the expected C6-C7 *syn* relationship; (c) a B-alkyl Suzuki coupling.

A. Balog, C. Harris, K. Savin, X.-G. Zhang, T. C. Chou and S. J. Danishefsky, *Angew. Chem. Int. Ed.*, 1998, **37**, 2675.

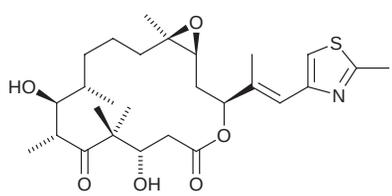


Epothilone B

Biological activity: see above.

Key steps: (a) enantioselective Mukaiyama aldol reaction; (b) (*E*)- and (*Z*)-selective olefinations; (c) sulfone alkylation. The synthesis was accomplished in 23 steps overall (longest linear sequence 18 steps).

J. Mulzer, A. Mantoulidis and E. Öhler, *Tetrahedron Lett.*, 1998, **39**, 8633.

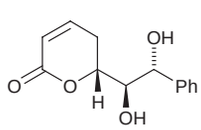


(+)-Gondiodiol

Biological activity: potent and selective cytotoxic acivity against A-549 human lung carcinoma.

Key steps: a diastereoselective oxygen-to-carbon rearrangement of an anomerically linked silyl enol ether.

D. J. Dixon, S. V. Ley and E. W. Tate, *J. Chem. Soc., Perkin Trans.1*, 1998, 3125.

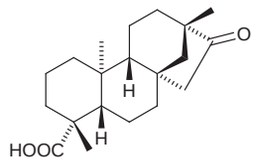


(±)-Isosteviol and (±)-Beyer-15-ene-3β,19-diol

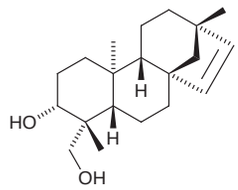
Biological activity: not reported.

Key steps: Manganese(III)-based oxidative quadruple free-radical cyclisation.

B. B. Snider, J. Y. Kiselgof and B. M. Foxman, *J. Org. Chem.*, 1998, **63**, 7945.



Isosteviol



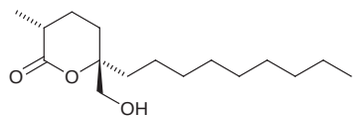
Beyer-15-ene-3,19-diol

(–)-Malyngolide

Biological activity: marine antibiotic isolated from the blue-green alga *Lyngbya majuscula*.

Key steps: a nucleophilic cleavage of a bicyclic acetal using $TiCl_4$ and allyltrimethylsilane resulting in the stereoselective formation of the key 2,2,5-trisubstituted tetrahydrofuran part of the molecule.

N. Maezaki, Y. Matsumori, T. Shogaki, M. Soejima, H. Ohishi, T. Tanaka and C. Iwata, *Tetrahedron*, 1998, **54**, 13087.

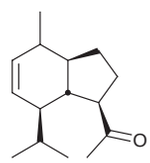


(±)-α-Oplopenone

Biological activity: not reported.

Key steps: (a) internal Diels-Alder cycloaddition with a (*Z*)-dienophile; Wolff rearrangement.

D. F. Taber, S. Kong and S. C. Malcolm, *J. Org. Chem.*, 1998, **63**, 7953.

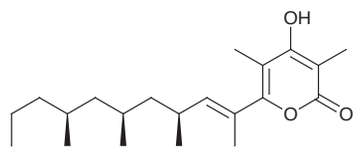


(+)-Pectinatone

Biological activity: (a) antibacterial; (b) antifungal; (c) cytotoxic activity.

Key steps: formation of the 1,3-dimethyl stereocentres using iterative alkylation of propanal SAMP-hydrazone with β-branched iodides.

A. A. Birkbeck and D. Enders, *Tetrahedron Lett.*, 1998, **39**, 7823.

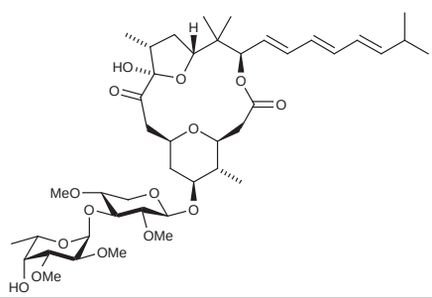


(–)-Polycavernoside A

Biological activity: toxic agent of the red alga *Polycavernosa tsudai*.

Key steps: (a) fragment linkage *via* a metallated dithioacetal mono-*S*-oxide; (b) Yamaguchi macrolactonisation; (c) triene synthesis *via* Pd(0)-catalysed coupling of an iodoalkene with a dienyl mercury derivative.

K. Fujiwara, A. Murai, M. Yotsu-Yamashita, and T. Yasumoto, *J. Am. Chem. Soc.*, 1998, **120**, 10770.

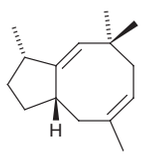


(±)-Precapnelladiene

Biological activity: not reported.

Key steps: Tandem anionic oxy-Cope/transannular ring closure reaction.

J. M. MacDougall, V. J. Santora, S. K. Verma, P. Turnbull, C. R. Hernandez and H. W. Moore, *J. Org. Chem.*, 1998, **63**, 6905.

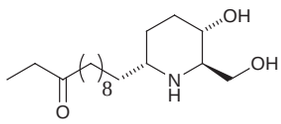


(+)-Prosopinine and (–)-Deoxoprosophylline

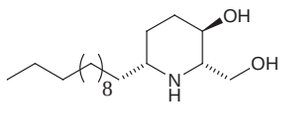
Biological activity: (a) antibiotic; (b) anesthetic.

Key steps: Rh-BIPHEPHOS complex-catalysed cyclohydrocarbonylation.

I. Ojima and E. S. Vidal, *J. Org. Chem.*, 1998, **63**, 7999.



(+)-Prosopinine



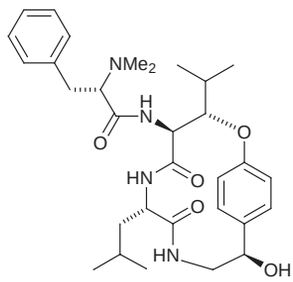
(–)-Deoxoprosophylline

Sanjoinine G1

Biological activity: (a) isolated from the seeds of *Zizphus Vulgaris* var. *spinosus* (Sanjoin); (b) the biologial activity is not reported.

Key steps: (a) an S_NAr reaction with 4-fluorobenzonitrile to form a key alkyl-aryl ether linkage; (b) macrocyclisation using a modified Schmidt protocol that involves an activated pentafluorophenyl ester.

S. P. East, F. Shao, L. Williams and M. M. Joullié, *Tetrahedron*, 1998, **54**, 13371.

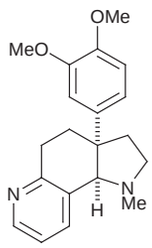


(+)-Sceletium A-4

Biological activity: not reported.

Key steps: three different methods for producing the enantiomerically pure intermediate 2-(3,4-dimethoxyphenyl)cyclohex-2-en-1-ol.

O. Yamada and K. Ogasawara, *Tetrahedron Lett.*, 1998, **39**, 7747.

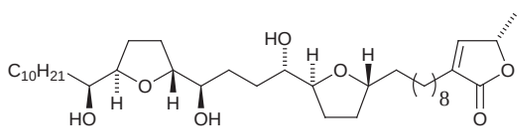


Squamostatin-D

Biological activity: cytotoxicity toward human tumor cell lines.

Key steps: (a) enantioselective addition of chiral oxygenated allylic tin and indium reagents to aldehydes; (b) addition of a functionalised organozinc reagent to an aldehyde in the presence of a chiral bis-sulfonamide-titanium catalyst.

J. A. Marshall and H. Jiang, *J. Org. Chem.*, 1998, **63**, 7066.

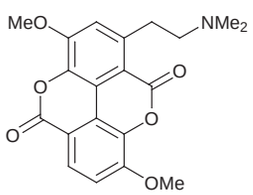


Taspine

Biological activity: (a) active ingredient in the sap of the *Croton lechleri* tree used by the Jivaro Indians of Peru to promote wound healing and to treat various maladies; (b) anti-inflammatory; (c) anti-ulcer; (d) cytotoxic activity; (e) inhibits viral DNA polymerase.

Key steps: (a) Ullmann coupling reaction ; (b) Stille coupling.

T. R. Kelly and R. L. Xie, *J. Org. Chem.*, 1998, **63**, 8045.

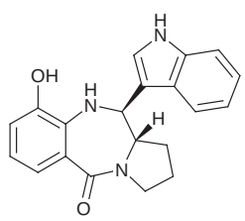


Tilivalline

Biological activity: cytotoxicity toward mouse leukemia L1210.

Key steps: (a) modified Curtius reaction; (b) stereoselective introduction of indole.

T. Nagasaka and Y. Koseki, *J. Org. Chem.*, 1998, **63**, 6797.

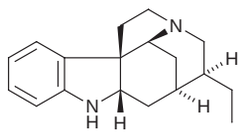


Tubifolidine

Biological activity: not reported.

Key steps: (a) asymmetric Michael addition using the heterobimetallic asymmetric catalyst (ALB-KO-*t*-Bu-MS 4Å); (b) one pot construction of the tetracyclic synthetic intermediates from the tricyclic intermediates using DDQ.

S. Shimizu, K. Ohori, T. Arai, H. Sasai and M. Shibasaki, *J. Org. Chem.*, 1998, **63**, 7547.

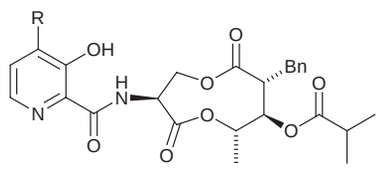


UK-2A and UK-3A

Biological activity: (a) strongly inhibit the growth of various types of yeast and filamentous fungi; (b) show very weak cytotoxic activity against several kinds of mammalian cells.

Key steps: (a) Evans aldol reaction; (b) an intramolecular Mitsunobu reaction.

M. Shimano, N. Kamei, T. Shibata, K. Inoguchi, N. Itoh, T. Ikari and H. Senda, *Tetrahedron*, 1998, **54**, 12745.



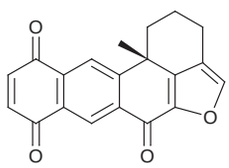
UK-2A : R = OMe
UK-3A : R = H

(+) -Xestoquinone

Biological activity: not reported.

Key steps: cascade-type asymmetric Heck reaction. Investigations carried out into the effect of the amount of silver salt required to produce the product in high yield and ee.

F. Miyazaki, K. Uotsu and M. Shibasaki, *Tetrahedron*, 1998, **54**, 13073.



(*S*)-Zearalenone

Biological activity: not reported.

Key steps: solid phase synthesis for the formation of macrocycles by a novel cyclorelease mechanism that employs the Stille coupling.

K. C. Nicalaou, N. Winssinger, J. Pastor and F. Murphy, *Angew. Chem. Int. Ed.*, 1998, **37**, 2534.