Perkin 1 Abstracts: Natural Product Synthesis

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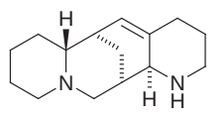
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*

(+)-Aloperine

Biological activity: (a) inhibits inflammatory and allergic responses in rats; (b) inhibits experimental heart arrhythmias in rats, rabbits, and guinea pigs; (c) effects contraction of isolated guinea pig ileum; (d) elicits additional immunological effects.

Key steps: intramolecular Diels-Alder reaction in which the cycloaddends are tethered by an *N*-silylamine linkage.

A. D. Brosius, L. E. Overman and L. Schwink, *J. Am. Chem. Soc.*, 1999, **121**, 700.

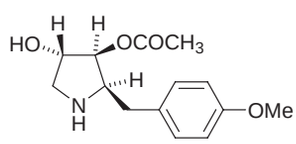


(–)-Anisomycin

Biological activity: (a) antibiotic; (b) possesses strong and selective activity against pathogenic protozoa and fungi and has clinically been used with success in the treatment of vaginitis due to *Trichomonas vaginilis* and for amoebic dysentery.

Key steps: asymmetric 2+2 cycloaddition between dichloroketene and a chiral enol ether.

P. Delair, E. Brot, A. Kanazawa and A. E. Greene, *J. Org. Chem.*, 1999, **64**, 1383.

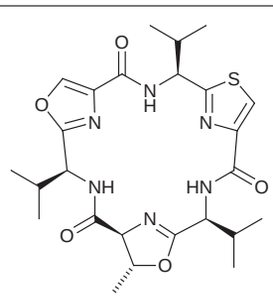


Bistratamide D

Biological activity: (a) cytotoxic; (b) induces depressant effects in mice when administered by intracerebral injection.

Key steps: (a) macrocyclisation using HATU [*O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate].

S. V. Downing, E. Aguilar and A. I. Meyers, *J. Org. Chem.*, 1999, **64**, 826.

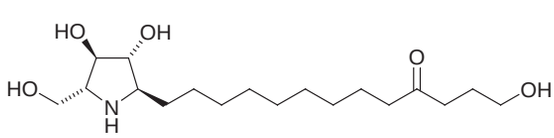


Broussonetine C

Biological activity: exhibits unique β-galactosidase and β-mannosidase inhibitory activities. The natural product is isolated from *Broussonetia kazinoki* SIEB., a plant whose leaves have been used in Chinese folk medicine as a diuretic, a tonic, and a suppressant for edema.

Key steps: Lewis acid-promoted reductive stereoselective deoxygenation of a C_2-imine.

H. Yoda, T. Shimojo and K. Takabe, *Tetrahedron Lett.*, 1999, **40**, 1335.

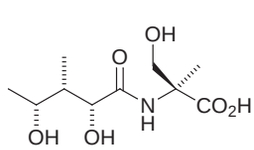


(+)-Conagenin

Biological activity: (a) acts as an immunomodulator by stimulating activated T-cells; (b) acts as a chemoprotector against myelosuppression and thus improves the efficiency of antitumour agents given to tumour carrying mice.

Key steps: asymmetric [2,3]-Wittig rearrangement.

D. Enders, M. Bartsch and J. Runsink, *Synthesis*, 1999, 243.

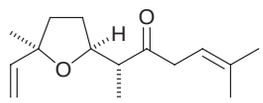


(±)-Davanone

Biological activity: not reported.

Key steps: Lewis acid catalysed [3+4] annulation reaction of 1,4-pentanedione with a bis(trimethylsilyl) enol ether.

G. A. Molander and J. Haas, *Tetrahedron*, 1999, **55**, 617.

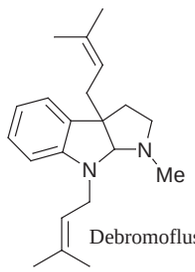


Debromoflustramines A and B

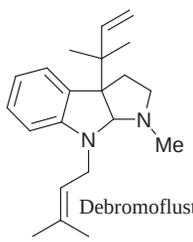
Biological activity: extracted from the marine bryozoan *Flustra foliacea*; biological activity not reported.

Key steps: addition of 3-methyl-2-butenylmagnesium bromide to 2-hydroxyindolenines providing access to a range of functionalised 2-oxofuro[2,3-*b*]indoles.

M. S. Morales-Ríos, O. R. Suárez-Castillo and P. Joseph-Nathan, *J. Org. Chem.*, 1999, **64**, 1086.



Debromoflustramine A



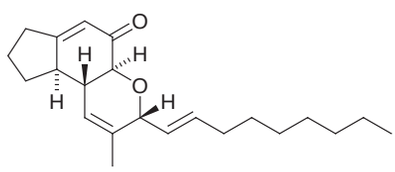
Debromoflustramine B

(±)-Deoxypenostatin A

Biological activity: cytotoxic.

Key steps: intramolecular Diels-Alder reaction of a hydrated glyoxylate ester catalysed by $Yb(OTf)_3$.

B. B. Snider and T. Liu, *J. Org. Chem.*, 1999, **64**, 1088.

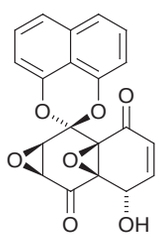


(±)-Diepoxin σ

Biological activity: (a) antifungal activity and MIC's against a panel of selected bacteria in the range of 4-32μg/mL; (b) potent *in vitro* activity in the antitumor invasion assay (IC_{50} = 0.75μM against HT 1080 human fibrosarcoma cells; (c) *in vivo*, this compound demonstrated a significant reduction in the size of primary tumors and the number of metastases.

Key steps: asymmetric version of the Diels-Alder reaction of *O*-methylnaphthazarin and cyclopentadiene.

P. Wipf and J.-K. Jung, *J. Org. Chem.*, 1999, **64**, 1092.

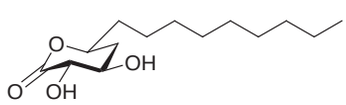


(2*R*,3*R*,5*S*)-(–)-2,3-Dihydroxytetradecan-5-olide

Biological activity: tree pathogen, causes the resinous canker disease of *Chamaecyparis obtusa* Sieb. et Zycc (Hinoki).

Key steps: Sharpless AD reaction.

H. Toshima, H. Sato, and A. Ichihara, *Tetrahedron*, 1999, **55**, 2581.

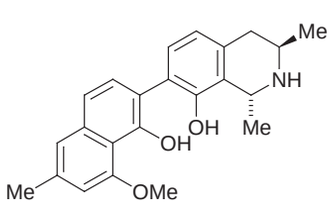


Dioncophylline B

Biological activity: shows high antimalarial and fungicidal activities.

Key steps: regioselective intermolecular biaryl Stille coupling of a modified naphthalene and an isoquinoline, with MOM-functionalised oxygen substituents next to the coupling sites.

G. Bringmann and C. Günther, *Synlett*, 1999, 216.

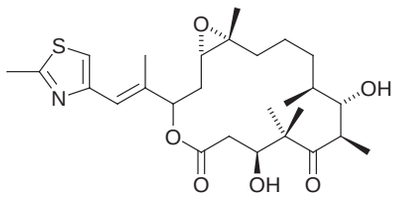


Epothilone B

Biological activity: (a) antifungal; (b) exhibits a high level of cytotoxicity.

Key steps: (a) Horner-Emmons condensation; (b) removal of a THP protecting group using magnesium bromide; (c) Wittig coupling; (d) macrolactonisation under Yamaguchi's conditions.

J. D. White, R. G. Carter, and K. F. Sundermann, *J. Org. Chem.*, 1999, **64**, 684.

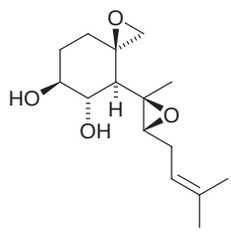


FR65814

Biological activity: potent immunosuppressive activity.

Key steps: (a) Ferrier's carbocyclisation; (b) Claisen rearrangement; (c) Stille coupling; (d) bis-epoxide function stereoselectively constructed by sulfur ylide chemistry and vanadium-catalysed epoxidation of a homoallyl alcohol derivative.

S. Amano, N. Ogawa, M. Ohtsuka and N. Chida, *Tetrahedron*, 1999, **55**, 2205.

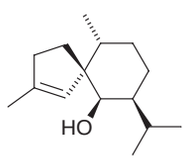


(–)-Gleenol

Biological activity: not reported.

Key steps: (a) Curtius rearrangement; (b) C-H insertion reaction of a vinylidene carbene to generate the spirocycle.

S. Ohira, N. Yoshihara and T. Hasegawa, *Chem. Lett.*, 1998, 739.

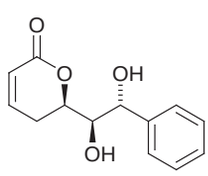


(+)-Goniodiol and (+)-Goniopypyrone

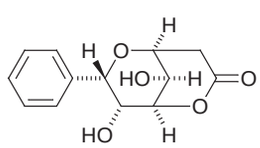
Biological activity: several styryl lactones have been synthesised and they exhibit cytotoxicity against human tumour cells (IC_{50} against P388 Murine Leukemia cells 0.39-15μg/ml).

Key steps: (a) chemoselective reactions of triisopropoxyphenyltitanium with aldehydes; (b) the same methodology has been used to form five related lactones.

M. Tsubuki, K. Kanai, H. Nagase and T. Honda, *Tetrahedron*, 1999, **55**, 2493.



(+)-Goniodiol



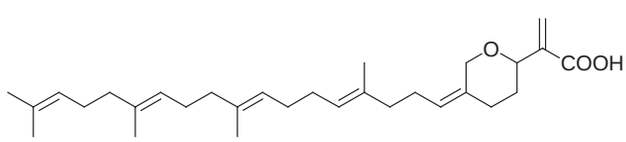
(+)-Goniopypyrone

Hippospongic acid A

Biological activity: inhibits gastrulation of starfish embryos.

Key steps: Wadsworth-Emmons reaction.

M. Tokumasu, H. Ando, Y. Hiraga, S. Kojima and K. Ohkata, *J. Chem. Soc., Perkin Trans. 1*, 1999, 489.

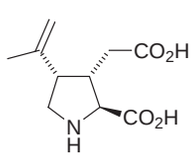


(–)-α-Kainic acid

Biological activity: shows potent neuroexcitatory activity.

Key steps: Titanium-mediated diene metallabicyclisation-elimination-functionalisation for the preparation of *syn*-3,4-disubstituted and *syn,syn*-2,3,4-trisubstituted pyrrolidines.

A. D. Campbell, T. M. Raynham and R. J. K. Taylor, *Chem. Commun.*, 1999, 245.

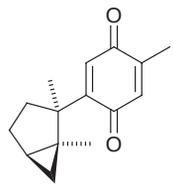


(–)-Laurequinone

Biological activity: potential 5-lipoxygenase inhibitory activity.

Key steps: (a) Heck reaction; (b) insertion of carbene.

H. Takahashi, Y. Tonoi, K. Matsumoto, H. Minami, and Y. Fukuyama, *Chem. Lett.*, 1998, 485.

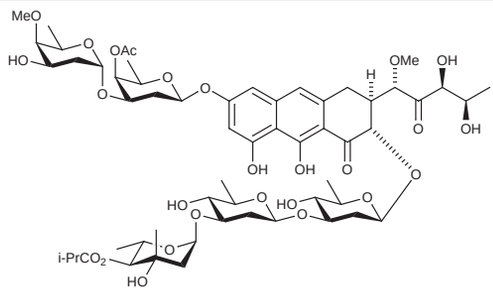


(–)-Olivomycin A

Biological activity: binds to the minor groove of double stranded DNA as 2:1 antibiotic: Mg^{2+} complexes with selectivity for GC-rich sequences.

Key steps: 2-α-phenylthio- or phenylseleno-substituted sugar units are used to control the stereochemistry of three key β-glycosidation reactions *via* trichloroacetimidate activation.

W. R. Roush, R. A. Hartz and D. J. Gustin, *J. Am. Chem. Soc.*, 1999, **121**, 1990.

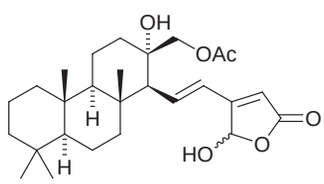


(–)-Spongianolide A

Biological activity: reported to inhibit proliferation of the mammary tumour cell line MCF-7.

Key steps: Wittig reaction using a furanmethylide.

T. Hata, K. Tanaka and S. Katsumura, *Tetrahedron Lett.*, 1999, **40**, 1731.

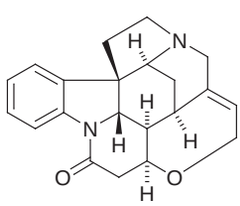


(–)-Strychnine

Biological activity: potent poison.

Key steps: (a) a Pd-catalysed piperidine ring closure incorporating an *E*-double bond; (b) closure of an indoline ring *via* reductive cyclisation of an α-(2-nitrophenyl) ketone.

D. Solé, J. Bonjoch, S. García-Rubio, E. Peidró, and J. Bosch, *Angew. Chem. Int. Ed.*, 1999, **38**, 395.

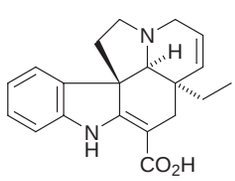


(–)-Tabersonine and (±)-Vincadifformine

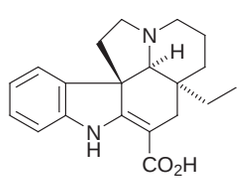
Biological activity: not reported.

Key steps: (a) novel indole synthesis involving a Bu_3SnH-mediated cyclisation of an isonitrile; (b) novel amine protecting protocol by means of 2,4-dinitrobenzenesulfonamides using for the deprotection PhOK in MeCN [(±)-Vincadifformine] or pyrrolidine in MeOH/MeCN [(–)-Tabersonine].

S. Kobayashi, G. Peng and T. Fukuyama, *Tetrahedron Lett.*, 1999, **40**, 1519.



(–)-Tabersonine



(±)-Vincadifformine

Trilobin

Biological activity: highly potent against human breast cancer, lung cancer, colon cancer 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 catalyst.

J. A. Marshall and H. Jiang, *J. Org. Chem.*, 1999, **64**, 971.