Perkin 1 Abstracts: Natural Product Synthesis

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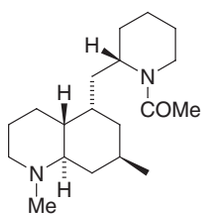
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*

N_a-Acetyl-N_b-methylphlegmarine

Biological activity: not reported.

Key steps: diastereoselective alkylation of a 1-acylpyridinium.

D. L. Comins, A. H. Libby, R. S. Al-awar, and C. J. Foti, *J. Org. Chem.*, 1999, **64**, 2184.

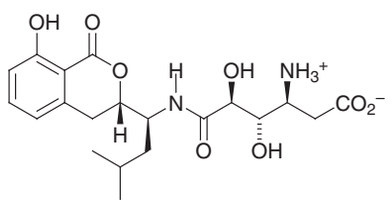


AI-77-B

Biological activity: (a) shows activity against stress ulcers in rats; (b) it is non-central suppressive, non-anticholinergic, non-antihistaminergic.

Key steps: (a) Wittig reaction; (b) dihydroxylation reactions using OsO_4 and NMO; (c) oxazoline-promoted lactone formation.

S. D. Broady, J. E. Rexhausen, and E. J. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1083.

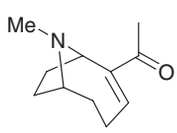


(–)-Anatoxin-a

Biological activity: (a) is often referred to as "very fast death factor"; (b) exerts its action by depolarising the post-synaptic acetylcholine receptors.

Key steps: (a) metathesis reaction to form the cycloheptene; (b) a palladium-catalysed asymmetric cyclisation to form the bicyclic ring system.

B. M. Trost and J. D. Oslob, *J. Am. Chem. Soc.*, 1999, **121**, 3057.

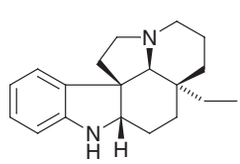


(±)-Aspidospermidine

Biological activity: related compounds vinblastine and vincristine are used as anticancer agents.

Key steps: a tetrathiafulvalene-induced 'radical-polar crossover' reaction.

O. Callaghan, C. Lampard, A. R. Kennedy, and J. A. Murphy, *J. Chem. Soc., Perkin Trans. 1*, 1999, 995.

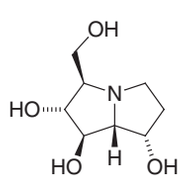


(+)-Australine and (+)-Castanospermine

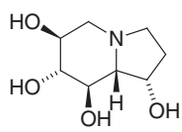
Biological activity: Castanospermine is a powerful inhibitor of both α- and β-D-glucosidases.

Key steps: asymmetric tandem [4+2]/[3+2] cycloaddition between a silaketal nitro olefin and a chiral vinyl ether.

S. E. Denmark and E. A. Martinborough, *J. Am. Chem. Soc.*, 1999, **121**, 3046.



(+)-Australine



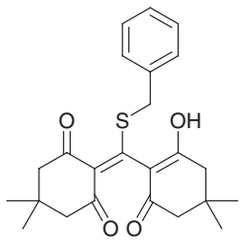
(+)-Castanospermine

Benzylthiocrellidone

Biological activity: (a) isolated from the sponge *Crella spinulata*; (b) has a possible role in protection of the sponge from UV radiation.

Key steps: a Michael addition-elimination.

H. W. Lam, P. A. Cooke, G. Pattenden, W. M. Bandaranayake, and W. A. Wickramasinghe, *J. Chem. Soc., Perkin Trans. 1*, 1999, 847.

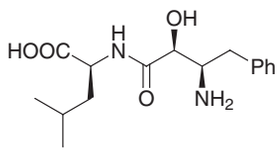


(–)-Bestatin

Biological activity: (a) aminopeptidase inhibitor; (b) exhibits immunostimulatory activity; (c) cytotoxic activity; (d) is used clinically as an anticancer agent.

Key steps: intramolecular acylnitrene-mediated aziridination to generate a bicyclic aziridine.

S. C. Bergmeier and D. M. Stanchina, *J. Org. Chem.*, 1999, **64**, 2852.

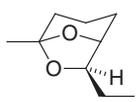


(+)-*exo*-Brevicomin

Biological activity: component of the sex attracting pheromone system of several bark beetle species belonging to genera *Dendroctonus* and *Dryocoetes.*

Key steps: *cis*-vinyl epoxide obtained *via* chloroallylboration.

S. Hu, S. Jayaraman, and A. C. Oehlschlager, *J. Org. Chem.*, 1999, **64**, 2524.

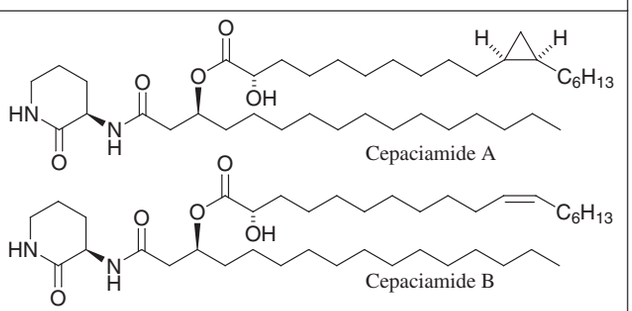


Cepaciamides A and B

Biological activity: fungitoxic against *Botrytis cinerea* and *Penicillium expansum*.

Key steps: Sharpless asymmetric dihydroxylation.

H. Toshima, K. Maru, M. Saito, and A. Ichihara, *Tetrahedron*, 1999, **55**, 5793.

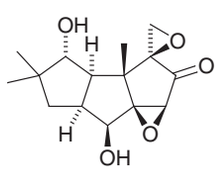


(–)-Coriolin

Biological activity: not reported.

Key steps: (a) [3+2] cycloaddition reaction of a 1-(methylthio)-2-siloxyallyl cationic species and vinyl sulfides; (b) C7 hydroxy group introduced by epoxidation of a dienol silyl ether; (c) diastereocontrolled construction of the spiro epoxide moiety was accomplished on the basis of a Darzens-type reaction.

H. Mizuno, K. Domon, K. Masuya, K. Tanino, and I. Kuwajima, *J. Org. Chem.*, 1999, **64**, 2648.

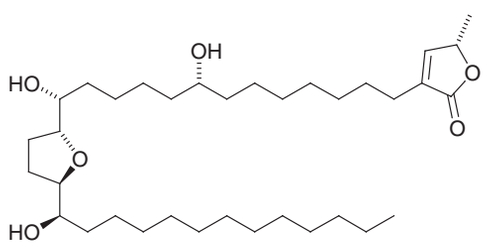


Corossolin

Biological activity: *in vitro* cytotoxicity against B16BL6 cell line (GI_{50} 0.042 μg mL^{-1}, LC_{50} = 7 μg mL^{-1}).

Key steps: (a) Wittig reaction; (b) Sharpless asymmetric epoxidation; (c) coupling of the lithium salt of an alkyne with an epoxide in the presence of boron trifluoride.

Q. Yu, Z.-J. Yao, X.-G. Chen, and Y.-L. Wu, *J. Org. Chem.*, 1999, **64**, 2440.

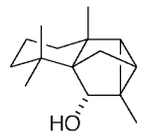


(+)-Cyclomyltaylan-5α-ol

Biological activity: Isolated from *Reboulia hemisphaerica*, activity not reported.

Key steps: SmI_2-promoted reductive cyclisation.

H. Sakai, H. Hagiwara, Y. Ito, T. Hoshi, T. Suzuki, and M. Ando, *Tetrahedron Lett.*, 1999, **40**, 2965.

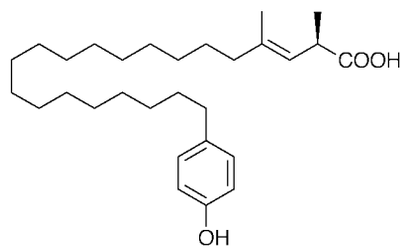


Elenic acid

Biological activity: (a) cytotoxicity with an IC_{50} of 5 μg mL^{-1} in P-388, A-549, and MEL-28 bioassays; (b) inhibitor of topoisomerase II, an indicator enzyme in the treatment of lung cancer at 0.1 μg mL^{-1}.

Key steps: (a) novel zipper reaction of a 1-arylalkyne; (b) one-pot elaboration of a terminal alkyne to an (*E*)-β,γ-unsaturated ester containing an α-stereocenter.

R. C. Hoye, A. S. Baigorria, M. E. Danielson, A. A. Pragman, and H. A. Rajapakse, *J. Org. Chem.*, 1999, **64**, 2450.

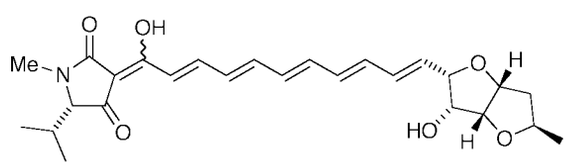


Erythroskyrine

Biological activity: a mycotoxin, exhibits antibiotic activity against several *Staphylococcus* species.

Key steps: (a) Pd(II) catalysed oxycarbonylation of a tetraol derived from D-galactose; (b) Stille coupling.

D. J. Dixon, S. V. Ley, T. Gracza, and P. Szolcsanyi, *J. Chem. Soc., Perkin Trans. 1*, 1999, 839.

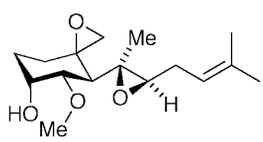


Fumagillol

Biological activity: (a) shows potent antiparasitic properties; (b) the related TNP-470 inhibits the proliferation of endothelial cells *in vitro* and tumor-induced angiogenesis *in vivo*.

Key steps: (a) selective Upjohn dihydroxylation; (b) regio- and diastereoselective addition of an organocuprate to an enal; (c) mild hydrolysis of an α-acetoxy-*N*-cyclohexamine; (d) $VO(acac)_2$ epoxidation.

D. A. Vosburg, S. Weiler, and E. J. Sorensen, *Angew. Chem., Int. Ed.*, 1999, **38**, 971.

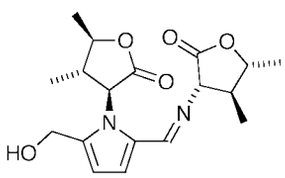


(±)-Funebrine

Biological activity: not reported.

Key steps: new variation of the Paal-Knorr condensation to construct the pyrrole lactone moiety.

Y. Dong, N. N. Pai, S. L. Ablaza, S.-X. Yu, S. Bolvig, D. A. Forsyth, and P. W. Le Quesne, *J. Org. Chem.*, 1999, **64**, 2657.

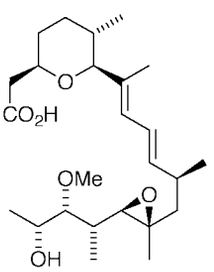


Herboxidiene

Biological activity: displays exceptional phytotoxicity against oilseed rape, wild buckwheat and hemp sesbania; innocuous towards wheat.

Key steps: (a) a modified Julia olefination based on the benzothiazole sulfone activator; (b) an intramolecular addition of an alkoxide to an α,β-unsaturated ester; (c) a directed aldol reaction; (d) an Ireland-Claisen rearrangement; (e) a hydroxy-directed epoxidation.

P. R. Blakemore, P. J. Kocienski, A. Morley, and K. Muir, *J. Chem. Soc., Perkin Trans. 1*, 1999, 955.

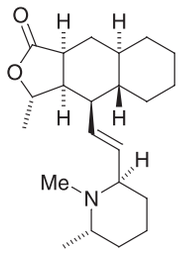


(+)-Himbacine

Biological activity: potent antagonist of the muscarinic receptor of M_2 type with 20-fold selectivity toward the M_1 receptor.

Key steps: an intermolecular Diels-Alder reaction.

M. Takadoi, T. Katoh, A. Ishiwata, and S. Tershima, *Tetrahedron Lett.*, 1999, **40**, 3399.

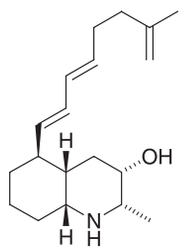


Lepadin B

Biological activity: cytotoxic activity toward a variety of murine and human cancer cell lines.

Key steps: intramolecular aldol cyclisation of a functionalised piperidine.

N. Toyooka, M. Okumura, and H. Takahata, *J. Org. Chem.*, 1999, **64**, 2182.

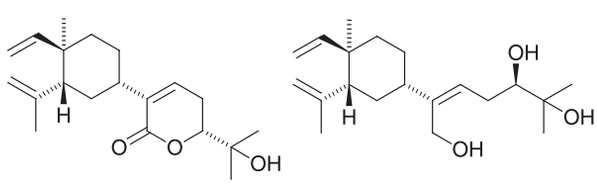


(+)-Lobatrienolide and (+)-Lobatrientriol

Biological activity: related lobane diterpenes which show antiinflammatory activity and selectively inhibit leukotriene synthesis.

Key steps: The scalemic starting material is easily obtained from (+)-nopinone.

M. Kato, H. Kosugi, T. Ichiyanagi, and O. Yamabe, *J. Chem. Soc., Perkin Trans. 1*, 1999, 783.



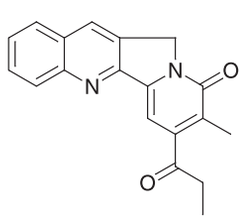
(+)-Lobatrienolide (+)-Lobatrientriol

Mappicine ketone

Biological activity: antiviral agent with selective activites against HSV-1, HSV-2 and human cytomegalovirus (HCMV).

Key steps: (a) Friendlander condensation; (b) periselective Diels-Alder reaction.

J. S. Yadav, S. Sarkar, and S. Chandrasekhar, *Tetrahedron*, 1999, **55**, 5449.

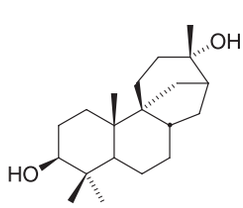


(+)-Maritimol

Biological activity: used in Caribbean folk medicine to treat venereal diseases.

Key steps: (a) Evans Aldol reaction; (b) Horner-Emmons olefinations; (c) an acetylenic ester tandem vicinal difunctionalisation; (d) transannular Diels-Alder reaction.

A. Toró, C.-A. Lemelin, P. Préville, G. Bélanger, and P. Deslongchamps, *Tetrahedron*, 1999, **55**, 4655.

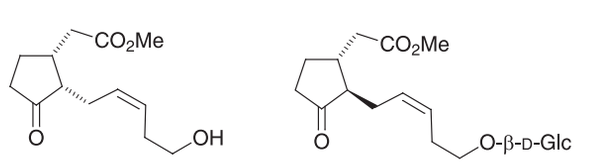


Methyl tuberonate and Methyl β-D-glucopyranosyloxyjasmonate

Biological activity: potential plant growth regulators.

Key steps: (a) Wittig reaction; (b) mild deprotection of trifluoroacetate and dichloroacetate by methanolysis.

M. Inoue and T. Kitahara, *Tetrahedron*, 1999, **55**, 4621.



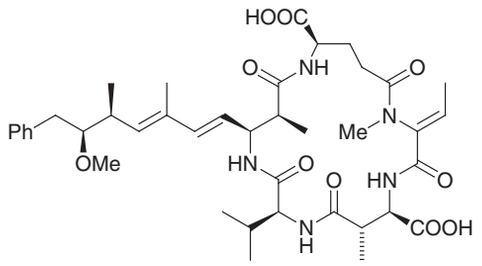
Methyl tuberonate Methyl β-D-glucopyranosyloxyjasmonate

(–)-Motuporin

Biological activity: inhibits the activity of protein phosphotase-1 (PP1) in rat adipocyte lysates with IC_{50} = 4.0 nM.

Key steps: (a) asymmetric crotylation methodology for the introduction of the stereogenic centers; (b) stereoselective azidation of a β-silyl enolate.

T. Hu and J. S. Panek, *J. Org. Chem.*, 1999, **64**, 3000; *cf* .R. Samy, H. Y. Kim, M. Brady, and P. L. Toogood, *J. Org. Chem.*, 1999, **64**, 2711.

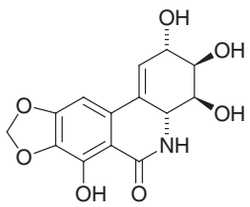


(+)-Narciclasine

Biological activity: antitumor agent.

Key steps: (a) enzymatic dihydroxylation; (b) Suzuki coupling; (c) Bischler-Napieralski type cyclisation.

D. Gonzalez, T. Martinot, and T. Hudlicky, *Tetrahedron Lett.*, 1999, **40**, 3077.

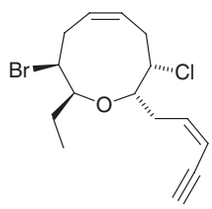


(+)-Obtusenyne

Biological activity: not reported.

Key steps: conversion of a mono-unsaturated nine-membered lactone to dienyl ether *via* ethylation of the corresponding vinyl triflate with an organocopper reagent.

K. Fujiwara, D. Awakura, M. Tsunashima, A. Nakamura, T. Honma, and A. Murai, *J. Org. Chem.*, 1999, **64**, 2616.

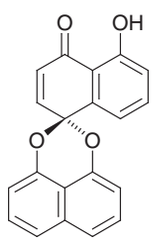


Palmarumycin CP_1, Palmarumycin CP_2, and Deoxypreussomerin A

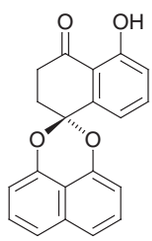
Biological activity: The palmarumycins possess antibiotic, antifungal and antitumour activites, the related CJ-12,371 is a DNA gyrase inhibitor.

Key steps: Triflic acid-catalysed ketone acetalisation to form a key spiroacetal.

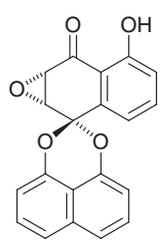
J. P. Ragot, C. Steeneck, M.-L. Alcaraz, and R. J. K. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1073.



Palmarumycin CP_1



Palmarumycin CP_2



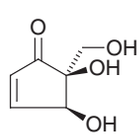
Deoxypreussomerin A

(–)-Pentenomycin I

Biological activity: moderately active against Gram-positive and Gram-negative bacteria.

Key steps: Baylis-Hillman protocol.

T. Sugahara and K. Ogasawara, *Synlett*, 1999, 419.

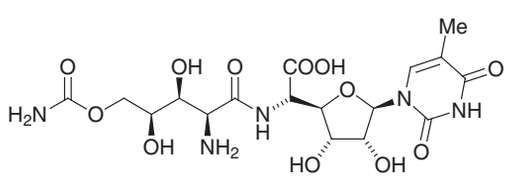


(+)-Polyoxin J

Biological activity: potent inhibitor of chitin synthetase from the medically important human pathogen *Candida albicans*.

Key steps: (a) stereoselective electrophilic epoxidation of ribose-derived allylic alcohol; (b) Sharpless epoxidation followed by regioselective opening of epoxide ring.

A. K. Ghosh and Y. Wang, *J. Org. Chem.*, 1999, **64**, 2789.

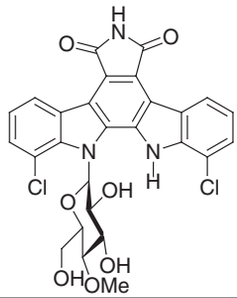


Rebeccamycin

Biological activity: inhibits protein kinase C and topoisomerase activity.

Key steps: synthesis of unsymmetrical bisindolylmaleimides by condensation of methyl indole-3-glyoxylates with indole-3-acetamides.

M. M. Faul, L. L. Winneroski, and C. A. Krumrich, *J. Org. Chem.*, 1999, **64**, 2465.

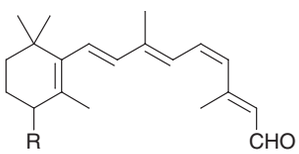


11-*cis*-Retinoids

Biological activity: potential use as a visual chromophore in bioorganic studies.

Key steps: (a) Horner-Wadsworth-Emmons reaction; (b) Michael-type, high order cuprate addition; (c) Semi-hydrogenation of the 11-yne precursor using Cu/Ag-activated Zinc dust.

B. Borhan, M. L. Souto, J. M. Um, B. Zhou, and K. Nakanishi, *Chem. Eur. J.*, 1999, **5**, 1172.



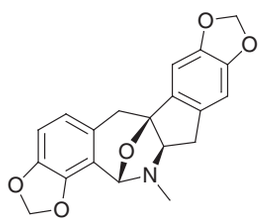
R = H or R = O

(+)-Ribasine

Biological activity: extracted from the plants *Fumeriaceae* and *Papaveraceae*; activity not reported.

Key steps: stereo-controlled addition of a substituted α-lithiated-*o*-toluate to a homochiral *N*-Pf-2-aminoindan-1-one, which is synthesised from an oxazinone using Dellaria's method.

L. Ollero, L. Castedo, and D. Domínguez, *Tetrahedron*, 1999, **55**, 4445.

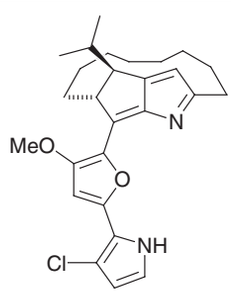


Roseophilin

Biological activity: cytotoxic agent.

Key steps: (a) Pd(0)-catalysed reaction of a vinyloxirane with a sulfone; (b) ring closure metathesis catalysed by Grubbs' reagent.

A. Fürstner, T. Gastner, and H. Weintritt, *J. Org. Chem.*, 1999, **64**, 2361.

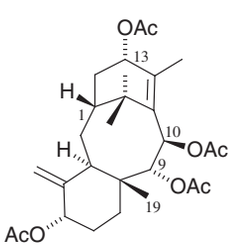


(+)-Taxusin

Biological activity: isolated from yew trees as is the related anticancer drug Taxol®.

Key steps: (a) B-ring cyclisation in the presence of Me_2AlOTf to produce a ABC *endo*-tricarbocycle having C9α, C10β-substituents; (b) installation of the C19 methyl group *via* the Birch reduction of the cyclopropyl ketone followed by enol/keto isomerisation owing to the stereoselective protonation directed by the C13-OH.

R. Hara, T. Furukawa, H. Kashima, H. Kusama, Y. Horiguchi, and I. Kuwajima, *J. Org. Chem.*, 1999, **121**, 3072.



Trilobin

Biological activity: highly cytotoxic agent.

Key steps: (a) Sharpless asymmetric dihydroxylation; (b) Sharpless asymmetric epoxidation.

A. Sinha, S. C. Sinha, S. C. Sinha, and E. Keinan, *J. Org. Chem.*, 1999, **64**, 2381.