Perkin 1 Abstracts: Natural Product Synthesis

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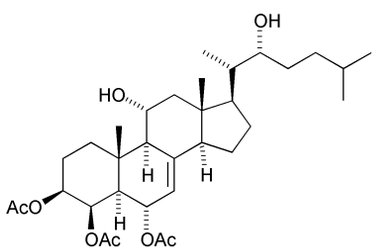
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

Agosterol A

Biological activity: (a) isolated from the marine sponge *Spongia* sp.; (b) a potent modulator of multidrug resistance (MDR) mediated by P-gp and MRP1.

Key steps: (a) regioselective, reductive epoxy-cleavage reaction; (b) regioselective dehydroxylation.

N. Murakami, M. Sugimoto, M. Morita and M. Kobayashi, *Chem. Eur. J.*, 2001, **7**, 2663.

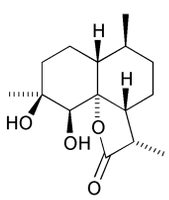


(+)-Arteanniun M

Biological activity: (a) isolated from *Artemisia annua L.* (compositae); (b) biological activity not reported.

Key steps: (a) tandem oxy-Cope/transannular ene reaction; (b) diastereoselective hydrogenation reaction using Crabtree's catalyst.

L. Barriault and D. H. Deon, *Org. Lett.*, 2001, **3**, 1925.

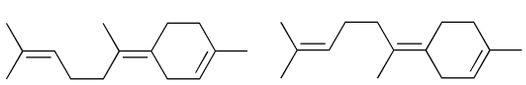


(*Z*)- and (*E*)-γ-Bisabolenes

Biological activity: not reported.

Key steps: (a) Cu-catalysed allylmagnesiation; (b) Pd-catalysed alkylation; (c) Ru-catalysed ring-closing metathesis.

L. Anastasia, Y. R. Dumond and E. Negishi, *Eur. J. Org. Chem.*, 2001, 3039.

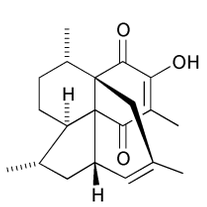


Colombiasin A

Biological activity: not reported

Key steps: two Diels–Alder reactions using benzoquinone derivatives as dienophiles.

K. C. Nicolaou, G. Vassilikogiannakis, W. Mägerlein and R. Kranich, *Angew. Chem., Int. Ed.*, 2001, **40**, 2482.

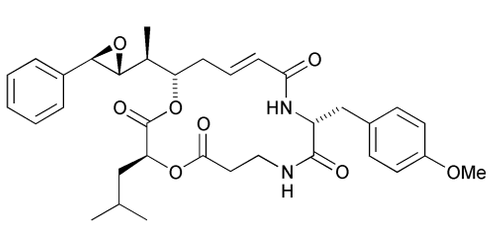


Cryptophycin 24

Biological activity: the cryptophycin macrolides stabilise microtubule dynamics at low concentration.

Key steps: (a) Heck reaction for appendage of an arene to a terminal alkene; (b) macrocyclisation *via* intramolecular opening of an *N*-acyl β-lactam by valinol.

M. Eggen, S. K. Nair and G. I. Georg, *Org. Lett.*, 2001, **3**, 1813.

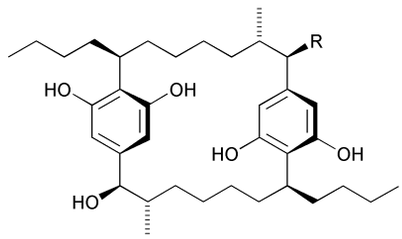


(–)-Cylindrocyclophanes A and F

Biological activity: cytotoxic components of the terrestial blue-green algae *Cylindrospermum lichenforme*.

Key steps: (a) reaction of a cyclobutenone with a siloxyalkyne to generate the resorcinol ring; (b) creation of the macrocycle by double metathesis using the Schrock Mo catalyst.

A. B. Smith III, C. M. Adams, S. A. Kozmin and D. V. Paone, *J. Am. Chem. Soc.*, 2001, **123**, 5925.



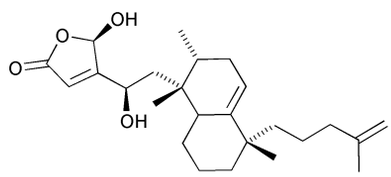
(–)-Cylindrocyclophane A (R = OH)
(–)-Cylindrocyclophane F (R = H)

(–)-Dysidiolide

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

Key steps: intermolecular Diels–Alder reaction of an allene ester and a silyloxydiene.

M. E. Jung and N. Nishimura, *Org. Lett.*, 2001, **3**, 2113.

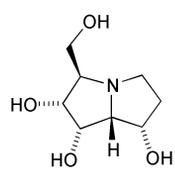


(+)-1-Epiaustraline

Biological activity: (a) isolated from the plant *Castanospermum australae*; (b) an inhibitor of several glycosidases including α-glucosidase, amyloglucosidase (IC_{50} = 26 μM) and yeast α-glucosidase (IC_{50} = 270 μM).

Key steps: tandem intramolecular [4+2]/intermolecular [3+2] nitroalkene cycloaddition.

S. E. Denmark and J. J. Cottell, *J. Org. Chem.*, 2001, **66**, 4276.

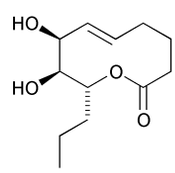


Herbarumin I

Biological activity: (a) isolated from a culture broth of the fungus *Phoma herbarum*; (b) exhibits phytotoxic effects in an assay monitoring the radicle elongation of *Amaranthus hypochondriacus* seedlings (IC_{50} = 5.43 μM).

Key steps: (*E*)-selective ring-closing metathesis reaction.

A. Fürstner and K. Radkowski, *Chem. Commun.*, 2001, 671.

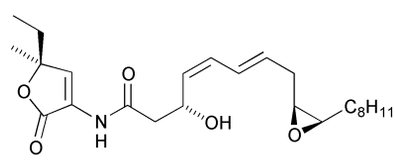


Korormicin

Biological activity: (a) isolated from the bacterium *Pseudoalteromonas* sp. F-420; (b) an inhibitor of the growth of marine Gram-negative bacteria.

Key steps: (a) Ni(0)-catalysed coupling reaction of a boronate ester and an alkenyl halide; (b) kinetic resolution using Sharpless's reagent; (c) Sharpless asymmetric dihydroxylation; (c) Suzuki–Miyaura reaction.

Y. Kobayashi, S. Yoshida, and Y. Nakayama, *Eur. J. Org. Chem.*, 2001, 1873.

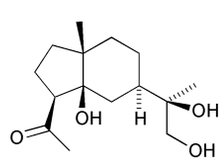


Lucinone

Biological activity: isolated from the aerial parts of *Jasonia glutinosa*, an annual medicinal plant traditionally used as an antispasmodic drug.

Key steps: tandem conjugate reduction/aldol cyclisation using Stryker's reagent.

P. Chiu, C. P. Szeto, Z. Geng and K. F. Cheng, *Tetrahedron Lett.*, 2001, **42**, 4091.

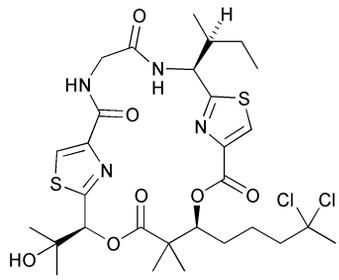


Lyngbyabellin A

Biological activity: (a) isolated from the marine cyanobacterium *Lyngbya majuscula*; (b) cytotoxic towards the human cancer cell lines; (c) potent disrupter of the cellular microfilament network.

Key steps: (a) titanium(IV)-mediated tandem deprotection/dehydrocyclisation; (b) Sharpless asymmetric dihydroxylation; (c) asymmetric aldol reaction.

F. Yokokawa, H. Sameshima and T. Shioiri, *Tetrahedron Lett.*, 2001, **42**, 4171.

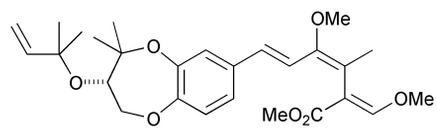


9-Methoxystrobilurin K

Biological activity: (a) isolated from a mycelial culture of the *Favolaschia*; (b) exhibits strong antifungal activities by specific binding to the Qo-centre of cytochrome b and inhibiting mitochondrial respiration; (c) cytostatic towards human-derived tumour cell lines without significant cytotoxicity.

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

H. Uchiro, K. Nagasawa, Y. Aiba, T. Kotake, D. Hasegawa and S. Kobayashi, *Tetrahedron Lett.*, 2001, **42**, 4531.

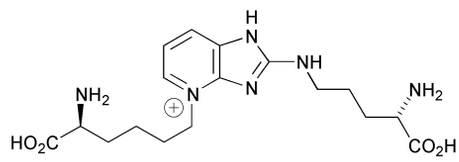


Pentosidine

Biological activity: (a) a fluorescent protein crosslink isolated from the human extracellular matrix; (b) a clinically useful marker for diabetic complications.

Key steps: (a) asymmetric alkylation of a chiral Schiff base with an allyl iodide; (b) mercury salt mediated intramolecular guanylation of an amino thiourea.

F. Yokokawa, H. Sugiyama, T. Shioiri, N. Katagiri, O. Oda and H. Ogawa, *Tetrahedron*, 2001, **57**, 4759.

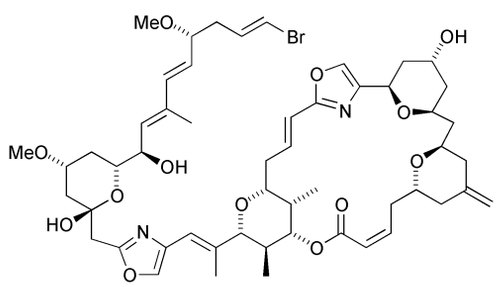


(+)-Phorboxazole

Biological activity: antimitotic agent; arrests the cell cycle at the S phase and does not affect tubulin.

Key steps: (a) Petasis–Ferrier rearrangement to construct two *cis*-tetrahydropyran rings; (b) two Stille couplings: one to construct the conjugated diene and the other to append an alkene to an oxazole ring.

A. B. Smith, P. R. Verhoest, K. B. Minbiole and M. Schelhaas, *J. Am. Chem. Soc.*, 2001, **123**, 4834.

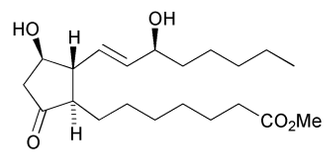


Prostaglandin E methyl ester

Biological activity: not reported.

Key steps: asymmetric Cu(II)-catalysed conjugate addition of a dialkylzinc reagent meditated by phosphoramidite ligands

L. A. Arnold, R. Naasz, A. J. Minnaard and B. L. Feringa, *J. Am. Chem. Soc.*, 2001, **123**, 5841.

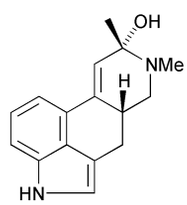


Rugulovasines A and B, Setoclavine

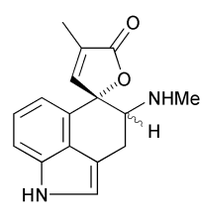
Biological activity: not reported in this paper.

Key steps: (a) inter- and intra-molecular vinylogous Mannich reactions; intramolecular $S_{RN}1$ reaction of a butenolide enolate onto a 4-bromoindole derivative to generate a six-membered ring.

S. Liras, C. l. Lynch, A. M. Fryer, B. T. Vu and S. F. Martin, *J. Am. Chem. Soc.*, 2001, **123**, 5918.



Setoclavine



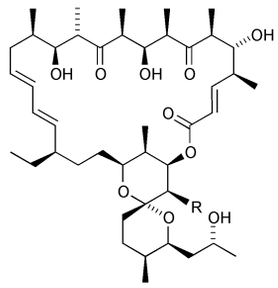
β-H Rugulovasine A
α-H Rugulovasine B

Rutamycin B

Biological activity: cytotoxin that inhibits oxidative phosphorylation in mitochondria by preventing ATP synthesis; decoupling of the F0 and F1 factors that facilitate proton transfer through the inner mitochondria membrane.

Key steps: (a) Julia coupling reaction; (b) Wadsworth-Emmons reaction; (c) Suzuki coupling.

J. D. White, R. Hanselmann, R. W. Jackson, W. J. Porter, Y. Ohba, T. Tiller and S. Wang, *J. Org. Chem.*, 2001, **66**, 5217.

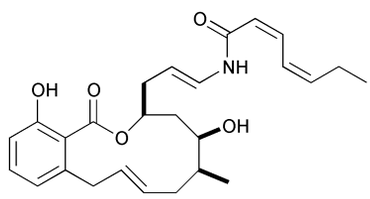


(–)-Salicylihalamides A

Biological activity: differential cytotoxicity in the NCI 60-cell line screen. The mean GI_{50} concentration was *ca.* 15 nM with a range of differential sensitivity of 10^3. Melanoma cell lines show highest sensitivity.

Key steps: (a) carbocupration of an alkyne; (b) ring-closing metathesis; (c) Cu(II)-catalysed asymmetric aldol reaction of a β-ketoester equivalent

B. B. Snider and F. Song, *Org. Lett.*, 2001, **3**, 1817.

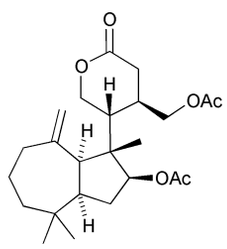


(+)-Shahamin K

Biological activity: not reported.

Key steps: (a) kinetic resultion of a cyclohexanone using the Corey oxazaborolidine reduction; (b) Prins-pinacol annulation to construct the hydroazulene skeleton; (c) conjugate addition of a cyclopentanone enolate onto an α-phenylsulfonyl cyclopentenone.

A. D. Lebsack, L. E. Overman and R. D. Valentekovich, *J. Am. Chem. Soc.*, 2001, **123**, 4851.

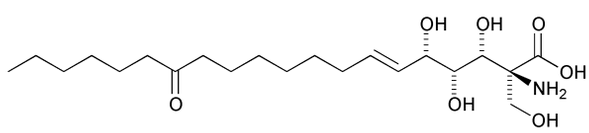


Sphingofungin E

Biological activity: inhibits serine palmitoyltransferase; antifungal activity against human pathogenic fungi.

Key steps: (a) substrate-controlled asymmetric dihydroxylation; (b) Baylis-Hillman reaction.

B. Wand, X.-m. Xu and G.-q. Lin, *Synlett*, 2001, 904

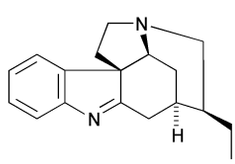


(–)-Tubifoline

Biological activity: not reported.

Key steps: (a) palladium-catalysed asymmetric allylic substitution; (b) intramolecular Heck reaction.

M. Mori, M. Nakanishi, D. Kajishima, and Y. Sato, *Org. Lett.*, 2001, **3**, 1913.



Uvaricin

Biological activity: annonaceous acetogenin.

Key steps: (a) palladium-mediated, ligand-controlled double cyclisation reaction of a diol bis(allylic acetate); (b) Sharpless asymmetric dihydroxylation reaction.

S. D. Burke and L. Jiang, *Org. Lett.*, 2001, **3**, 1953.