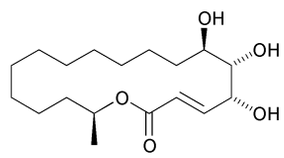
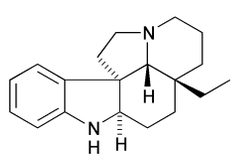
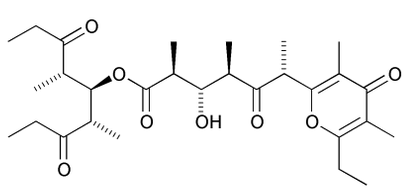
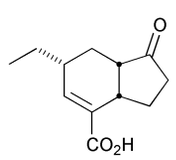
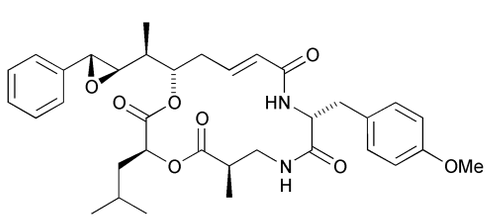
Perkin 1 Abstracts: Natural Product Synthesis

Jacqueline E. Milne,[a] Marcel de Puit[a] and Duncan McArthur[b]

[a] *Department of Chemistry, Leeds University, Leeds, UK LS2 9JT*
[b] *Department of Chemistry, Glasgow University, Glasgow, UK G12 8QQ*

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*.

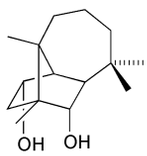
(+)-Aspicilin *Biological activity*: (a) isolated from a lichen *Aspicilia Gibbosa*; (b) biological activity not reported. *Key steps*: (a) asymmetric desymmetrisation of a *meso*-erythritol derivative using a C_2-symmetric bis-sulfoxide; (b) chelation-controlled addition of a Grignard reagent; (c) Horner–Wadsworth–Emmons reaction. N. Maezaki, Y.-X. Li, K. Ohkubo, S. Goda, C. Iwata and T. Tanaka, *Tetrahedron*, 2000, **56**, 4405.	
(+)-Aspidospermidine *Biological activity*: not reported. *Key steps*: intramolecular regioselective Schmidt reaction. R. Iyengar, K. Schildknegt and J. Aubé, *Org. Lett.*, 2000, **2**, 1625.	
(–)-Baconipyrone C *Biological activity*: isolated from *Siphonaria baconi* collected from intertidal rock platforms near Melbourne, Australia. *Key steps*: boron- and tin(II)-mediated aldol additions. I. Paterson, D. Yu-Kai Chen, J. L. Aceña and A. S. Franklin, *Org. Lett.*, 2000, **2**, 1513.	
Coronafacic acid *Biological activity*: (a) isolated from the culture broth of *Pseudomonas syringae*; (b) biological activity not reported. *Key steps*: 6-*endo*-*trig* mode cyclisation reaction of an enone-aldehyde with samarium(II) iodide. M. Sono, A. Hashimoto, K. Nakashima and M. Tori, *Tetrahedron Lett.*, 2000, **41**, 5115.	
(+)-Cryptophycin B *Biological activity*: (a) a potent cytotoxic agent; (b) IC_{50} value of 7 pg/ml against KB cells; (c) equally effective against drug-sensitive and drug-resistant tumour cells. *Key steps*: ester-derived titanium-enolate-mediated *syn*-aldol reaction. A. K. Ghosh and A. Bischoff, *Org. Lett.*, 2000, **2**, 1573.	

(±)-Culmorin

Biological activity: (a) (–)-culmorin was isolated as a metabolite of *Fusarium culmorum*; (b) antifungal.

Key steps: intramolecular double Michael addition.

K. Takasu, S. Mizutani, M. Noguchi, K. Makita and M. Ihara, *J. Org. Chem.*, 2000, **65**, 4112.

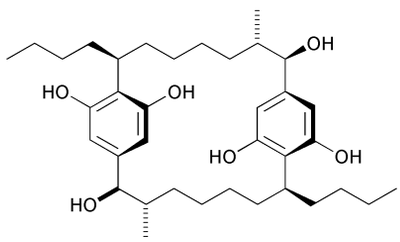


(–)-Cylindrocyclophane A

Biological activity: (a) isolated from the blue green alga, *Cylindrospermum licheniforme* Kützing (ATTC 29204); (b) cytotoxic.

Key steps: double Horner–Wadsworth–Emmons macrocyclisation.

T. R. Hoye, P. E. Humpal and B. Moon, *J. Am. Chem. Soc.*, 2000, **122**, 4982.

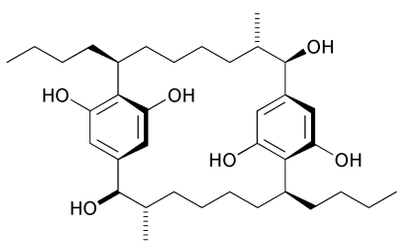


(–)-Cylindrocyclophane A

Biological activity: (a) isolated from the blue green alga, *Cylindrospermum licheniforme* Kützing (ATTC 29204); (b) cytotoxic.

Key steps: olefin metathesis dimerisation.

A. B. Smith III, S. A. Kozmin, C. M. Adams and D. V. Paone, *J. Am. Chem. Soc.*, 2000, **122**, 4984.

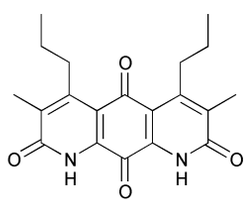


Diazaquinomycin A

Biological activity: (a) antibiotic; (b) inhibitor of thimidylate synthase.

Key steps: hetero Diels–Alder reaction between 2-methylhex-2-enal dimethylhydrazone and 3-methyl-4-propyl-2*H*-quinoline-2,5,8-trione.

J. M. Pérez, P. López-Alvarado, E. Pascual-Alfonso, C. Avendaño and J. C. Menéndez, *Tetrahedron*, 2000, **56**, 4575.

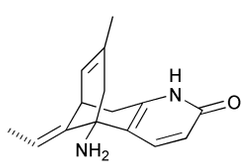


rac-Huperzine A

Biological activity: (a) isolated from the club moss *Huperzia serrata*; (b) potent and selective reversible acetylcholinesterase (AChE) inhibitor.

Key steps: elaboration of the pyridone ring in a late stage, by reaction of an intermediate pyrrolidine enamine with propiolamide (mixture of regioisomers).

P. Camps, J. Contreras, R. El Achab, J. Morral, D. Muñoz-Torrero, M. Font-Bardia, X. Solans, A. Badia and N. M. Vivas, *Tetrahedron*, 2000, **56**, 4541.

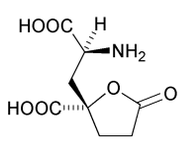


(+)-Lycoperdic acid

Biological activity: (a) a non-proteinogenic α-amino acid isolated from the mushroom *Lycoperdon perlatum*; (b) biological activity unknown but it is expected to possess neuroexcitatory activity because of structural similarity with glutamic acid.

Key steps: palladium-catalysed cross-coupling reaction of an alkenyl iodide with an organozinc reagent.

H. Masaki, T. Mizozoe, T. Esumi, Y. Iwabuchi and S. Hatakeyama, *Tetrahedron Lett.*, 2000, **41**, 4801.

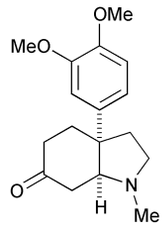


(±)-Mesembrine

Biological activity: not reported.

Key steps: [4 + 1] cycloaddition of a bis(alkylthio)carbene with a functionalised vinyl isocyanate.

J. H. Rigby and W. Dong, *Org. Lett.*, 2000, **2**, 1673.

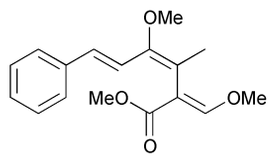


9-Methoxystrobilurin A

Biological activity: (a) antifungal; (b) cytostatic; (c) inhibited the growth of HeLa S3 cell line (IC_{50} = 8.5 nM) without showing significant cytotoxicity.

Key steps: (a) Heck reaction between a bromoarene and an enone; (b) Claisen condensation.

H. Uchiro, K. Nagasawa, Y. Aiba and S. Kobayashi, *Tetrahedron Lett.*, 2000, **41**, 4165.

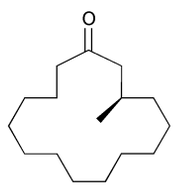


(*R*)-(–)-Muscone

Biological activity: (a) isolated from the male musk deer *Moschus moschiferus*; (b) rare and classical perfumery compound.

Key steps: ring closing olefin metathesis.

V. P. Kamat, H. Hagiwara, T. Katsumi, T. Hoshi, T. Suzuki and M. Ando, *Tetrahedron*, 2000, **56**, 4397.

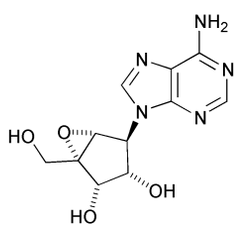


(–)-Neplanocin C

Biological activity: (a) isolated from *Ampullariela regularis*; (b) antibiotic; (c) lead drug for the design of several conformationally constrained nucleosides analogues.

Key steps: (a) intramoleculer Horner–Wadsworth–Emmons; (b) Mitsunobu reaction between a cyclopentenol and 6-chloropurine.

M. J. Comin and J. B. Rodriquez, *Tetrahedron*, 2000, **56**, 4639.

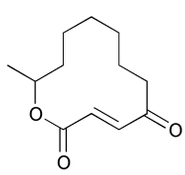


Patulolides A and B

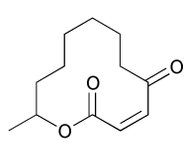
Biological activity: (a) isolated from *Penicillium urticae* mutant S11R59; (b) antifungal; (c) antibacterial; (d) antiinflammatory.

Key steps: double bond formation to construct the 12-membered macrocycle from a bisdiazocarbonyl compound *via* catalytic "carbene dimer" formation.

M. P. Doyle, W. Hu, I. M. Phillips and A. G. H. Wee, *Org. Lett.*, 2000, **2**, 1777.



Patulolide A



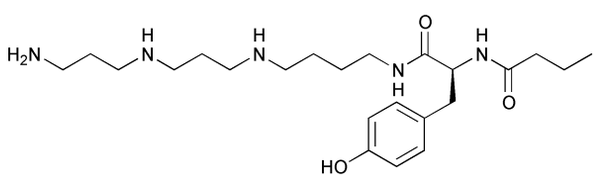
Patulolide B

PhTX-433

Biological activity: (a) isolated from the venoms of the female digger wasp *Philanthus triangulum* (bee wolf); (b) antagonist of ionotropic glutamate and nictotinic acetylcholine receptors present in neuromuscular junction; (c) inhibits signal transmission in the central nervous system of mammalians.

Key steps: mild oxidative workup protocol for the borane-promoted reduction of a polyamide.

F. Wang, S. Manku and D. G. Hall, *Org. Lett.*, 2000, **2**, 1581.

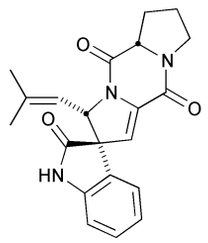


(–)-Spirotryprostatin B

Biological activity: (a) isolated from *Aspergillus fumigatus*; (b) inhibits G2/M progression of mammalian tsFT210 cells.

Key steps: intramolecular Mannich reaction to generate a spirocyclic pyrrolidine intermediate.

F. von Nussbaum and S. J. Danishefsky, *Angew. Chem., Int. Ed.*, 2000, **39**, 2175.

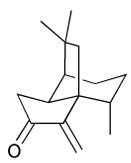


(±)-Suberosenone

Biological activity: potent and differential cytotoxicity toward various cancer cell lines.

Key steps: tandem free radical cyclisation–rearrangement sequence, mediated by tin hydride, to produce a tricyclo[4.3.2.0]undecane from a cyclopentene.

H.-Y. Lee and B. G. Kim, *Org. Lett.*, 2000, **2**, 1951.

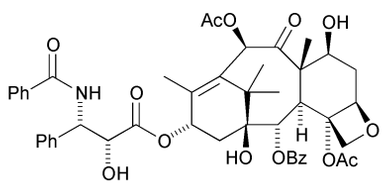


(–)-Taxol

Biological activity: antitumour agent

Key steps: (a) cyclooctane ring generated by an intramolecular directed aldol reaction; (b) introduction of the C-19 angular methyl group by reductive cleavage of a cyclopropyl ketone.

H. Kusama, R. Hara, S. Kawahara, T. Nishimori, H. Kashima, N. Nakamura, K. Morihira and I. Kuwajima, *J. Am. Chem. Soc.*, 2000, **122**, 3811.

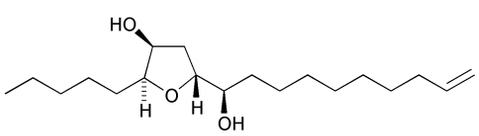


(2*S*,3*S*,5*R*)-5-[(1*R*)-1-Hydroxydec-9-enyl]-2-pentyltetrahydrofuran-3-ol

Biological activity: (a) isolated from the marine brown alga *Notheia anomala,* a member of the Notheiaceae family; (b) potent and selective inhibitors of larval development in parasitic nematodes.

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

C. García, M. A. Soler and V. S. Martín, *Tetrahedron Lett.*, 2000, **41**, 4127.

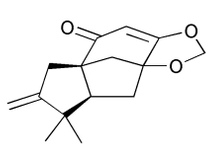


(±)-Tricycloillicinone

Biological activity: potential treatment of Alzheimer's disease owing to induction of choline acetyltransferase.

Key steps: (a) two ortho Claisen rearrangements; (b) Corey–Snider oxidative cyclisation of a β-diketone onto two alkenes to generate two cyclopentane rings; (c) Barton–McCombie deoxygenation.

T. R. R. Pettus, M. Inoue, X.-T. Chen and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2000, **122**, 6160.



(–)-Vindoline

Biological activity: (a) major alkaloid of *Catharanthus roseus* G. Don; (b) biosynthetic precursor of the antitumour agents vinblastine and vincristine.

Key steps: (a) phosphine-free Heck reaction of acrolein with an aryl iodide; (b) Stille coupling of methyl 2-tri-*n*-butylstannylacrylate with an *N*-Boc-2-iodoindole; (c) Mitsunobu reaction.

S. Kobayashi, T. Ueda and T. Fukuyama, *Synlett*, 2000, **6**, 883.