# *Perkin 1 Abstracts:* Natural Product Synthesis

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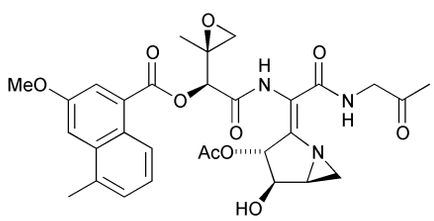
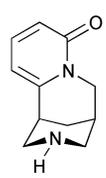
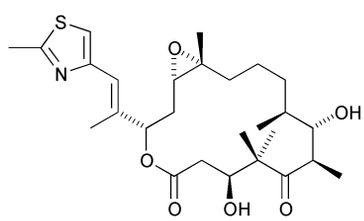
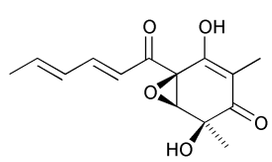
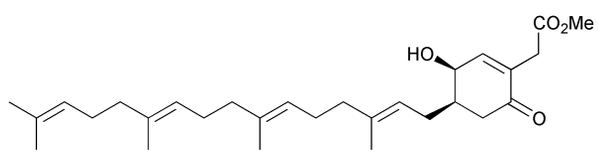
*Perkin 1 Abstracts: Natural Product Synthesis* aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

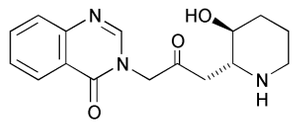
| | |
|---|---|
| **Azinomycin A**<br>*Biological activity*: antitumour activity resulting from DNA binding in the major groove and covalent cross-linking.<br>*Key steps*: generation of the aziridino[1,2-*a*]pyrrolidine ring system by intramolecular addition–elimination of an aziridine onto a β-bromoacrylate system.<br>R. S. Coleman, J. Li and A. Navarro, *Angew. Chem., Int. Ed.*, 2001, **40**, 1736. |  |
| **(±)-Cytisine**<br>*Biological activity*: (a) high affinity partial agonist at neuronal nicotinic receptors ($EC_{50}$ = 1 μM); (b) important probe in nicotinic acetylcholine receptor research; (c) potential therapeutic agent in the treatment of addiction, provided efficacy can be improved.<br>*Key steps*: intramolecular Heck cyclisation of activated glutarimide-derived ketene aminals to construct the tricyclic carbon skeleton.<br>J. W. Coe, *Org. Lett.*, 2000, **2**, 4205. |  |
| **Epothilone B**<br>*Biological activity*: anticancer.<br>*Key steps*: (*a*) stereoselective intermolecular cycloaddition of a nitrile oxide with (*R*)but-3-en-2-ol; (b) (*E*)-selective Roush–Masamune modified Horner–Wadsworth–Emmons olefination; (c) selective reduction of a conjugated isoxazoline to a β-hydroxy ketone using $SmI_2$; (d) one-pot desilylation, stereoselective epoxidation and loss of $SO_2$.<br>J. W. Bode and E. M. Carreira, *J. Am. Chem. Soc.*, 2001, **123**, 3611. |  |
| **(±)-Epxoysorbicillinol**<br>*Biological activity*: not reported.<br>*Key steps*: 1,3-dipolar cycloaddition between an α-diazo ketone and a propiolate ester.<br>J. L. Wood, B. D. Thompson, N. Yusuff, D. A. Pflum and M. S. P. Matthäus, *J. Am. Chem. Soc.*, 2001, **123**, 2097. |  |
| **(+)-Eunicenone A**<br>*Biological activity*: not reported.<br>*Key steps*: (a) asymmetric Diels–Alder reaction of achiral components using a chiral catalyst; (b) Cu(I)-catalysed allylic substitution using a silylcuprate; (c) Pd(0)-catalysed methoxycarbonylation of a 1,2-epoxy-1,3-diene; (d) 1,3-diene synthesis involving a Pd(0)-catalysed coupling of an iodoalkene and an alkenylzirconium reagent.<br>T. W. Lee and E. J. Corey, *J. Am. Chem. Soc.*, 2001, **123**, 1872. |  |

## (+)-Febrifugine

*Biological activity*: (a) isolated from the roots of *Dichroa febrifuga* and related hydrangea plants; (b) antimalarial.

*Key steps*: 1,3-dipolar cycloaddition of a nitrone with allyl alcohol.

H. Ooi, A. Urushibara, T. Esumi, Y. Iwabuchi and S. Hatakeyama, *Org. Lett.*, 2001, **3**, 953.

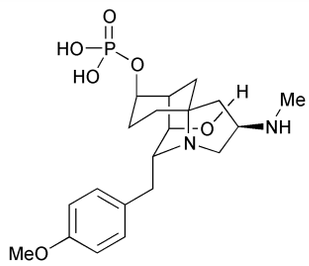


## FR901483

*Biological activity*: (a) isolated from the fermentation broth of a fungal strain *Cladobotryum* sp. No. 11231; (b) suppresses the antiproliferative activity of tacrolimus; (c) potent immunosuppressant; (d) prolongs graft survival in the rat skin allograft model.

*Key steps*: (a) intermolecular Diels–Alder cycloaddition; (b) two sequential aldol cyclisations.

J.-H. Maeng and R. L. Funk, *Org. Lett.*, 2001, **3**, 1125.

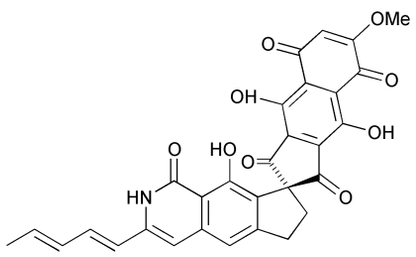


## (*S*)-Fredericamycin A

*Biological activity*: (a) isolated from *Streptomyces griseus*; (b) inhibitor of topoisomerases I and II; (c) exhibits potent antitumour activity against P388 leukemia, B16 melanoma and CD8F mammary carcinoma; (d) exhibits no mutagenic properties in the Ames test.

*Key steps*: construction of the chiral spiro[cyclopentane-1,1′-indane]-2,5-dione system *via* a stereospecific rearrangement of the optically active benzofused-*trans*-2,3-epoxy acylates using a Lewis acid.

Y. Kita, K. Higuchi, Y. Yoshida, K. Iio, S. Kitagaki, K. Ueda, S. Akai and H. Fujioka, *J. Am. Chem. Soc.*, 2001, **123**, 3214.

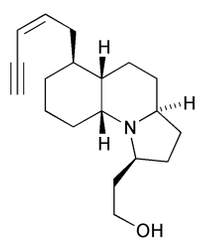


## (+)-Gephyrotoxin

*Biological activity*: neurotoxin.

*Key steps*: formal intramolecular [3+3] cycloaddition of a vinylogous amide with an α,β-unsaturated aldehyde.

L.-L. Wei, R. P. Hsung, H. M. Sklenicka and A. I. Gerasyuto, *Angew. Chem., Int. Ed.*, 2001, **40**, 1516.

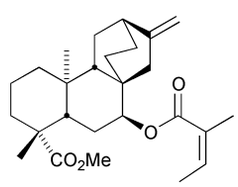


## (±)-Gummiferolic acid, methyl ester

*Biological activity*: plant growth regulator.

*Key steps*: homoallyl–homoallyl radical rearrangement to generate the bicyclo[2.2.2]octane ring system.

M. Toyota, M. Yokota and M. Ohara, *J. Am. Chem. Soc.*, 2001, **123**, 1856.

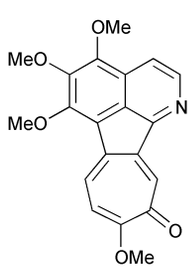


## Imerubrine

*Biological activity*: (a) isolated from the plants *Abuta imene* and *Abuta refescens* of the *Menispermacae* family; (b) biological activity not reported.

*Key steps*: (a) intramolecular Diels–Alder reaction of an acetylene-tethered oxazole; (b) [4+3] cycloaddition of an oxyallyl.

J. C. Lee and J. K. Cha, *J. Am. Chem. Soc.*, 2001, **123**, 3243.

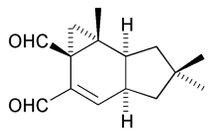


## (+)-Isovelleral

*Biological activity*: (a) isolated from *Lactarius vellereus*; (b) biological activity not reported.

*Key steps*: $MgI_2$-catalysed tandem rearrangement–cyclopropanation sequence.

R. P. L. Bell, J. B. P. A. Wijnberg, and A. de Groot, *J. Org. Chem.*, 2001, **66**, 2350.

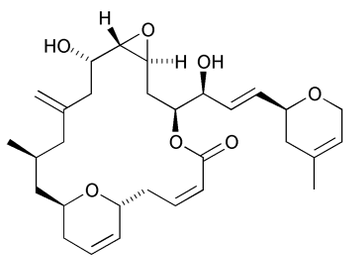



## (–)-Laulimalide

*Biological activity*: (a) isolated from the Indonesian sponge *Hyattella* sp. and the Okinawan sponge *Fasciospongia rimosa*; (b) displays antitumour activity against numerous NCI cell lines; (c) exhibits cytotoxicity against the KB, P388, A549, HT29 and MEL28 cell lines ($IC_{50}$ = 10–50 ng $mL^{-1}$); (d) microtubule-stabilizing agent; (e) inhibits the P-glycoprotein responsible for multiple-drug resistance in tumour cells.

*Key steps*: (a) (*E*)-selective Julia olefination; (b) alkylation of a dibromo olefin derived alkynyl anion; (c) Yamaguchi macrolactonisation.

A. K. Ghosh and Y. Wang, *Tetrahedron Lett.*, 2001, **42**, 3399.

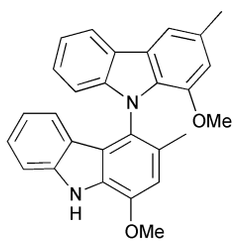



## Murrastifoline-F

*Biological activity*: not reported.

*Key steps*: biomimetic oxidative coupling of murrayafoline-A with $Pb(OAc)_4$.

G. Bringmann, S. Tasler, H. Endress, J. Kraus, K. Messer, M. Wohlfarth and W. Lobin, *J. Am. Chem. Soc.*, 2001, **123**, 2703.

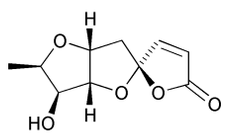



## (+)-Pyrenolide D

*Biological activity*: cytotoxic towards HeLa cells

*Key steps*: oxidative ring contraction of a glycal with dimethoxyiodosylbenzene generated *in situ* to give a tetrahydrofuran ring.

K. M. Engstrom, M. R. Mendoza, M. Navarro-Villalobos and D. Y. Gin, *Angew. Chem., Int. Ed.*, 2001, **40**, 1128.

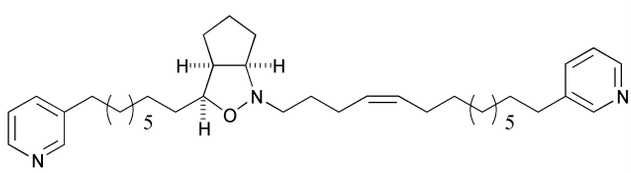



## Pyrinodemin A

*Biological activity*: (a) isolated from the marine sponge *Amphimedon* sp.; (b) cytotoxic against murine leukaemia L1210 and KB epidermoid carcinoma cells.

*Key steps*: intramolecular nitrone/double bond cycloaddition.

J. E. Baldwin, S. P. Romeril, V. Lee and T. D. W. Claridge, *Org. Lett.*, 2001, **3**, 1145.

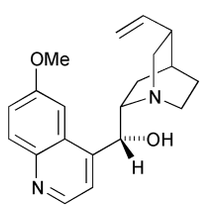



## Quinine

*Biological activity*: remedy for the treatment of malaria.

*Key steps*: (a) intramolecular Staudinger reaction to form a tetrahydropyridine ring; (b) stereospecific reduction of a tetrahydropyridine ring to yield a piperidine ring.

G. Stork, D. Niu, A. Fujimoto, E. R. Koft, J. M. Balkovec, J. R. Tata and G. R. Dake, *J. Am. Chem. Soc.*, 2001, **123**, 3239.

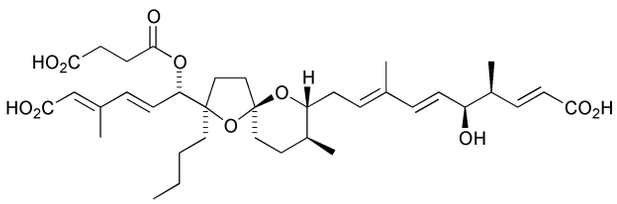


## (–)-Reveromycin B

*Biological activity*: (a) isolated from a soil actinomycete belonging to the *Streptomyces* genus; (b) inhibits the mitogenic activity of epidermal growth factor ($IC_{50}$ = 6.0 μg $mL^{-1}$).

*Key steps*: (a) hetero-Diels–Alder reaction; (b) epoxidation-acid induced ring contraction sequence; (c) tin-mediated asymmetric aldol reaction; (d) Stille cross coupling reaction.

A. N. Cuzzupe, C. A. Hutton, M. J. Lilly, R. K. Mann, K. J. McRae, S. C. Zammit and M. A. Rizzacasa, *J. Org. Chem.*, 2001, **66**, 2382.

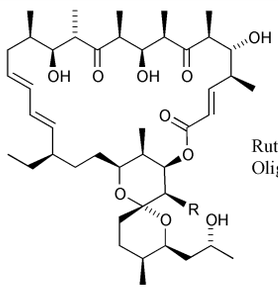



## Rutamycin B and oligomycin C

*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) regioselective and enantiofacial selective $S_E2'$ reactions on scalemic crotylsilanes; (b) alkylation of an *N,N*-dimethylhydrazone; (c) Mukaiyama directed aldol reactions (3 times), (d) intermolecular Stille coupling; (e) Yamaguchi macrolactonisation.

J. S. Panek and N. P. Jain, *J. Org. Chem.*, 2001, **66**, 2747.



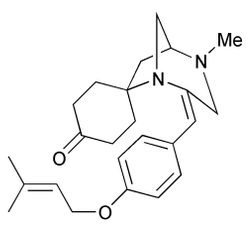

Rutamycin C R = H
Oligomycin C R = Me

## (–)-TAN1251A

*Biological activity*: (a) isolated from *Penicillium thomii* RA-89; (b) selective and potent muscarinic $M_1$ receptor antagonist; (c) inhibits the acetylcholine-induced contraction of Guinea-pig ileum ($ED_{50}$ = 8.0 nM).

*Key steps*: *N*-methoxy-*N*-acylnitrenium ion-induced spirocyclisation.

D. J. Wardrop and A. Basak, *Org. Lett.*, 2001, **3**, 1053.

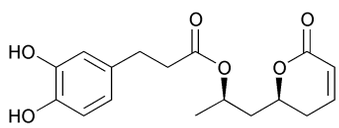



## (–)-Tarchonanthuslactone

*Biological activity*: (a) isolated from the compositae *Tarchonanthus trilobus*; (b) biological activity not reported.

*Key steps*: (a) asymmetric allylboration; (b) ring-closing metathesis.

M. V. R. Reddy, A. J. Yucel and P. V. Ramachandran, *J. Org. Chem.*, 2001, **66**, 2512.

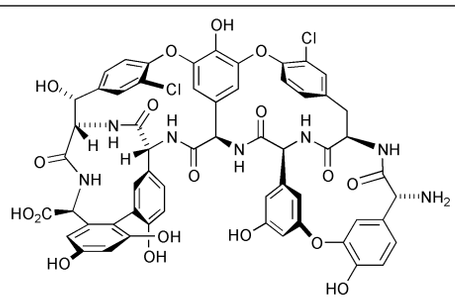



## Teicoplanin aglycone

*Biological activity*: antibiotic with greater potency and lower toxicity than vancomycin.

*Key steps*: (a) nucleophilic substitution macrocyclisation using an *o*-fluoronitroarene to generate a 16-membered biaryl ether ring; (b) macrolactamisation to construct a 12-membered biaryl ether ring.

D. L. Boger, S. H. Kim, Y. Mori, J.-H. Weng, O. Rogel, S. L. Castle and J. J. McAtee, *J. Am. Chem. Soc.*, 2001, **123**, 1862.




## (–)-Tetrazomine

*Biological activity*: antitumour and antibiotic agent that damages DNA by superoxides generated in the auto-redox disproportionation of the oxazolidine.

*Key steps*: 1,3-dipolar cycloaddition of an azomethine ylide.

J. D. Scott and R. M. Williams, *Angew. Chem., Int. Ed.*, 2001, **40**, 1463.