Perkin 1 Abstracts: Natural Product Synthesis

Robert Narquizian and Jacqueline Milne

Department of Chemistry, University of Glasgow, Glasgow, UK G12 8QQ

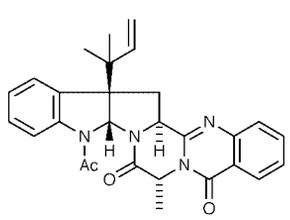
Perkin 1 Abstracts: Natural Product Synthesis aims to highlight syntheses that have been recently published. It includes brief descriptions of *biological activity* and *key steps*. A more comprehensive list of Natural Product syntheses and isolations can be found in *Natural Product Updates*.

5-*N*-Acetylardeemin and Amaurominc

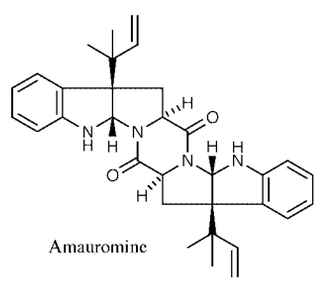
Biological activity: multidrug resistance reversal agents.

Key steps: (a) *N*-phenylselenophthalimide-induced phenyl selenocyclisation of a tryptophan derivative to generate the pyrrolo[2,3-*b*]indole system; (b) substitution of a phenylseleno group by a prenylstannane using methyl triflate activation.

K. M. DePew, S. P. Marsden, D. Zatorska, A. Zatorski, W. G. Bornmann and S. J. Danishefsky, *J. Am. Chem. Soc.*, 1999, **121**, 11953.



5-*N*-Acetylardeemin



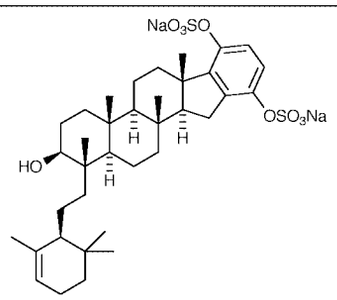
Amaurominc

(–)-Adociasulfate 1

Biological activity: kinensin motor protein inhibitor isolated from extracts of a sponge of the genus *Haliclona*.

Key steps: biomimetic tetracyclisation triggered by an epoxide and terminated by an arene triether.

M. Bogenstätter, A. Limberg, L. E. Overman and A. L. Tomasi, *J. Am. Chem. Soc.*, 1999, **121**, 12206.

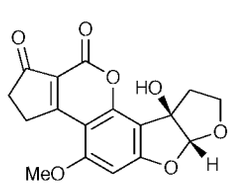


Aflatoxin M_2

Biological activity: potent carcinogen.

Key steps: addition of dichloromethyllithium to a dihydroxy ketone.

G. A. Kraus and X. Wang, *Tetrahedron Lett.*, 1999, **40**, 8513.

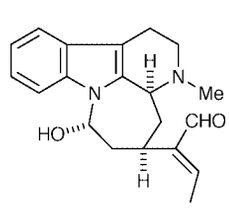


(±)-Akagerine and (±)-Geissoschizine

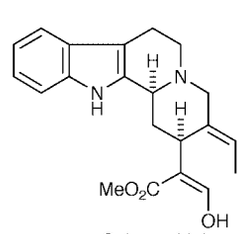
Biological activity: Geissoschizine is an intermediate in indole alkaloid biosynthesis.

Key steps: (a) nucleophilic addition of the enolate derived from 1-acetylindole to a pyridinium salt; (b) acid-induced cyclisation of a 1,4-dihydropyridine; (c) Pummerer reaction.

M.-L. Bennasar, J.-M. Jiménez, B. Vidal, B. A. Sufi and J. Bosch, *J. Org. Chem.*, 1999, **64**, 9605.



Akagerine



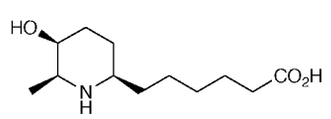
Geissoschizine

(+)-Azimic acid

Biological activity: not reported.

Key steps: chelation-controlled addition of Grignard reagents to chiral α-amino aldehydes.

K. K. Kumar and A. Datta, *Tetrahedron*, 1999, **55**, 13899.

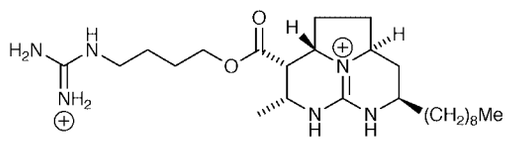


Batzelladine D

Biological activity: (a) Batzelladines A and B are micromolecular inhibitors of binding of the HIV envelope protein gp-120 to the human CD4 receptor; (b) Batzelladines F-I induce dissociation of the protein kinase called $p56^{lck}$ from CD4; (c) biological activity of Batzelladine D is not reported.

Key steps: tethered Biginelli condensation of a guanidine aldehyde and an acetoacetic ester to generate a 7-substituted-1-iminohexahydropyrrolo-[1,2-*c*]pyrimidine intermediate having the *anti* stereochemistry of the methine hydrogens flanking the pyrrolidine nitrogen.

F. Cohen, L. E. Overman and S. K. Ly Sakata, *Org. Lett.*, 1999, **1**, 2169.

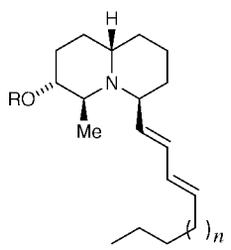


Clavepictines A, B and Pictamine

Biological activity: inhibition of growth of murine leukaemia and human solid tumour cell lines (P-388, A-539, U-251 and SN12K1) at IC_{50} = 1.8–8.5 μg mL^{-1}.

Key steps: stereocontrolled intramolecular Michael-type ring closure of a conformationally constrained piperidine ring system.

N. Toyooka, Y. Yotsui, Y. Yoshida, T. Momose and H. Nemoto, *Tetrahedron*, 1999, **55**, 15209.



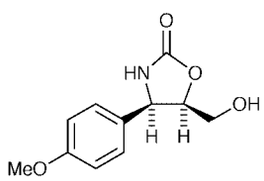
Clavepictine A: R=Ac
n =3
Clavepictine B: R=H
n =3
Pictamine: R=Ac
n =1

(–)-Cytoxazone

Biological activity: cytokine-modulating activity due to the inhibition of the signaling pathway of Th2 cells.

Key steps: imino 1,2-Wittig rearrangement.

O. Miyata, H. Asai and T. Naito, *Synlett*, 1999, 1915.

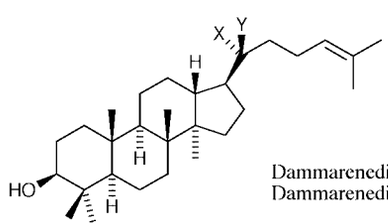


Dammarenediol I and II

Biological activity: modest *in vitro* antiviral activity against *Herpes simplex*.

Key steps: nonenzymatic biomimetic polyene tetracyclisation of a substrate containing a tetramethylallylic alcohol initiator, an allyltrimethylsilane terminating group, and a fluorine atom to serve as a cation-stabilising (C-S) auxiliary controlling the stereochemistry of the C/D ring juncture.

W. S. Johnson, W. R. Bartlett, B. A. Czeskis, A. Gautier, C. H. Lee, R. Lemoine, E. J. Leopold G. R. Luedtke and K. J. Bancroft, *J. Org. Chem.*, 1999, **64**, 9587.



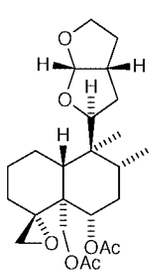
Dammarenediol I: X=OH, Y=Me
Dammarenediol II: X=Me, Y=OH

Dihydroclerodin

Biological activity: insect-antifeedant.

Key steps: (a) Mukaiyama reaction; (b) catalytic hydrogenation of an enone; (c) Chugaev elimination to give an exocyclic double bond.

T. M. Meulemans, G. A. Stork, F. Z. Macaev, B. J. M. Jansen and A. de Groot, *J. Org. Chem.*, 1999, **64**, 9178.

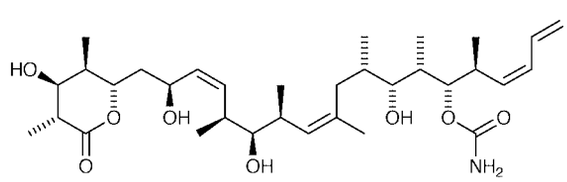


(+)-Discodermolide

Biological activity: (a) immunosuppressant; (b) stabilises microtubules and promotes polymerisation of tubulin.

Key steps: A 27 step synthesis based on boron-mediated *anti*-selective aldol reactions of chiral ketones.

I. Paterson, G. J. Florence, K. Gerlach and J. P. Scott, *Angew. Chem., Int. Ed.*, 2000, **39**, 377.

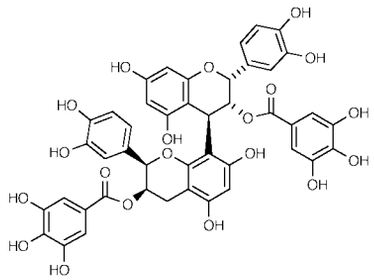


3-*O*-Galloyl-(2*R*,3*R*)-epicatechin-4β,8-[3-*O*-galloyl-(2*R*,3*R*)-epicatechin

Biological activity: the target, a proanthocyanidin derivative found in cocoa, is a protein kinase C inhibitor and cancer cell growth inhibitor.

Key steps: (a) benzylic oxidation with DDQ in ethylene glycol introduces a 2-hydroxyethoxy group; (b) $TiCl_4$-induced arylation of a benzylic cation creates an epicatechin dimer.

W. Tückmantel, A. P. Kozikowski and L. R. Romanczyk, *J. Am. Chem. Soc.*, 1999, **121**, 12073.

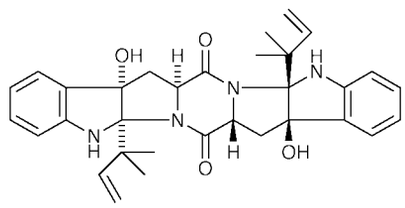


Gypsetin

Biological activity: inhibits acyl CoA:cholesterol acyltransferase.

Key steps: (a) addition of a prenylborane to a chloroindoline; (b) two-fold dimethyldioxirane-induced oxidative ring closure of a tryptophan-derived diketopiperazine derivative. Deoxybrevianamide, brevianamide E and tryprostatin B were also synthesised.

J. M. Schkeryantz, J. C. G. Woo, P. Siliphaivanh, K. M. DePew and S. J. Danishefsky, *J. Am. Chem. Soc.*, 1999, **121**, 11964.

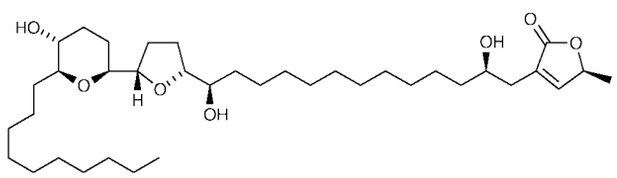


Jimenezin

Biological activity: (a) active against BST assay (IC_{50} = 5.7 ng mL^{-1}); (b) potent cytotoxic activity against six human solid tumour cell lines.

Key steps: (a) efficient construction of the THP-THF fragments through a stereoselective condensation between a pyranyl aldehyde and an acetylene derivative; (b) palladium-catalysed coupling reaction between an alkyne and a terminal butenolide under Hoye's conditions.

S. Takahashi, K. Maeda, S. Hirota and T. Nakata, *Org. Lett.*, 1999, **1**, 2025.

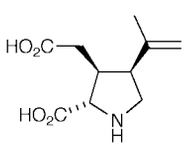


(–)-α–Kainic acid and (+)-α-Allokainic acid

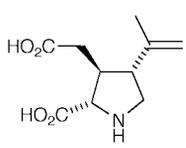
Biological activity: neuroexcitatory properties.

Key steps: (a) from an alkyne precursor, a nickel-catalysed cyclisation and a palladium-catalysed rearrangement were used in the synthesis of (+)-α-allokainic acid; (b) from an allene precursor, a nickel-catalysed cyclisation was used in the synthesis of (–)-α-kainic acid.

M. V. Chevliakov and J. Montgomery, *J. Am. Chem. Soc.*, 1999, **121**, 11139.



(–)-α-Kainic acid



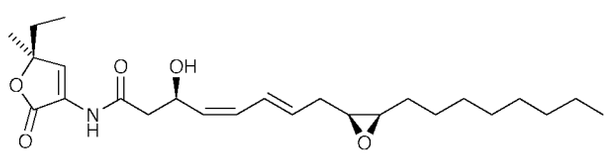
(+)-α-Allokainic acid

Korormicin

Biological activity: inhibits the growth of marine Gram-negative bacteria without affecting terrestrial species.

Key steps: (a) aldol condensation of a hydroxy aldehyde with an enolate of a Schiff base glycine ester to form the lactone moiety; (b) Stille coupling; (c) Sharpless epoxidation.

H. Uehara, T. Oishi, K. Yoshikawa, K. Mochida and M. Hirama, *Tetrahedron Lett.*, 1999, **40**, 8641.

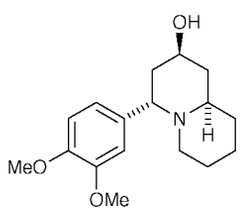


(–)-Lasubine(I)

Biological activity: not reported.

Key steps: (a) formation of an enantiopure planar chiral arylaldehyde tricarbonylchromium complex; (b) highly diastereoselective aza-Diels-Alder cycloaddition; (c) intramolecular radical cyclisation reactions to afford a quinolizidinone intermediate.

H. Ratni and E. P. Kündig, *Org. Lett.*, 1999, **1**, 1997.

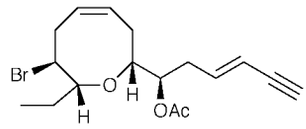


(+)-Laurencin

Biological activity: not reported.

Key steps: asymmetric alkylation-ring-closing metathesis approach to medium ring ethers.

M. T. Crimmins and K. A. Emmitte, *Org. Lett.*, 1999, **1**, 2029.

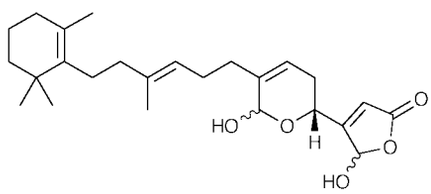


Manoalide

Biological activity: (a) analgesic; (b) anti-inflammatory; (c) inhibition of phospholipase A_2 (PLA_2).

Key steps: enantioselective aldol condensation using a $Ti(OiPr)_4$–(*R*)-(+)-BINOL complex.

A. Soriente, M. De Rosa, A. Apicella, A. Scettri and G. Sodano, *Tetrahedron: Asymmetry*, 1999, **10**, 4481.

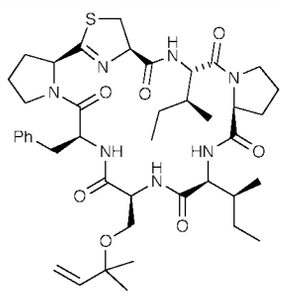


Mollamide

Biological activity: shows cytotoxicity against a range of cell lines with an IC_{50} of 1 μg ml^{-1} for murine leukaemia and 2.5 μg ml^{-1} against human lung carcinoma.

Key steps: macrolactamisation.

B. McKeever and G. Pattenden, *Tetrahedron Lett.*, 1999, **40**, 9317.

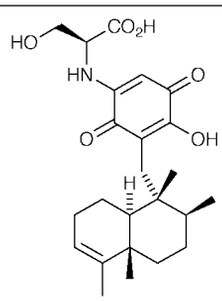


Nakijiquinone C

Biological activity: selective inhibitor of the Her-2/Neu Protooncogene.

Key steps: (a) reductive alkylation of an α,β-unsaturated Wieland-Miescher type enone with a benzyl halide; (b) Wittig reactions.

P. Stahl and H. Waldmann, *Angew. Chem., Int. Ed.*, 1999, **38**, 3710.

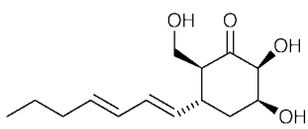


(–)-Palitantine

Biological activity: metabolite isolated from *Penicillium palitans* that exhibits antifungal and antibiotic activities.

Key steps: (a) Sharpless asymmetric dihydroxylation of a dienylsilane; (b) oxidation of C-Si bond.

R. Angelaud, O. Babot, T. Charvat and Y. Landais, *J. Org. Chem.*, 1999, **64**, 9613.



Puupehedione

Biological activity: antitumour activity against cell lines P-388, A-549, HT-29.

Key steps: several strategies were attempted.

A. F. Barrero, E. J. Alvarez-Manzaneda, R. Chahboun, M. Cortés and V. Armstrong, *Tetrahedron*, 1999, **55**, 15181.