# *Perkin 1 Abstracts:* Natural Product Synthesis

**Robert Narquizian and Jens Kaufmann**

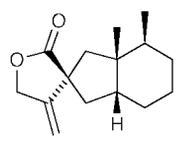
*Department of Chemistry, University of Glasgow, Glasgow, UK G12 8QQ*

*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*

### (±)-Bakkenolide A

*Biological activity*: (a) cytotoxicity toward several carcinoma cell lines; (b) effective insect antifeedant.

*Key steps*: intramolecular Diels-Alder reaction.

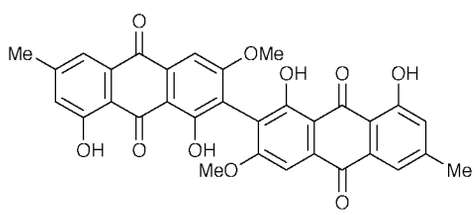


T. G. Back and J. E. Payne, *Org. Lett.*, 1999, **1**, 663.

### (±)-Biphyscion

*Biological activity*: not reported.

*Key steps*: symmetrical biphenyl construction *via* Ullman coupling.

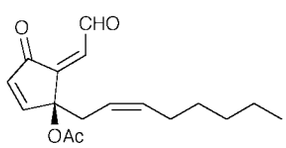


F. M. Hauser and P. J. F. Gauan, *Org. Lett.*, 1999, **1**, 671.

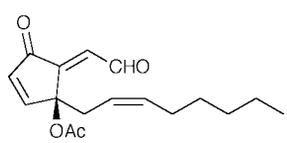
### Clavirin I and II

*Biological activity*: growth-inhibitory activity towards HeLa S3 at 1 μg mL$^{-1}$.

*Key steps*: (a) stereoselective Claisen condensation; (b) Wittig olefination; (c) aldol coupling.



Clavirin I



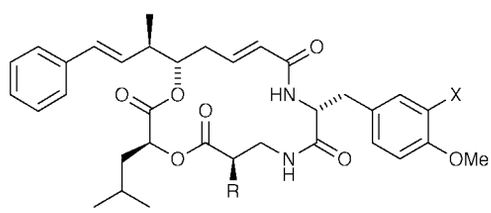
Clavirin II

M. Iwashima, K. Okamoto and K. Iguchi, *Tetrahedron Lett.*, 1999, **40**, 6455.

### Cryptophycins-1, -3, -4, -24 and -29

*Biological activity*: Cryptophycin-1 has an $IC_{50}$ = 20 pM against SKOV3 human ovarian carcinoma; excellent activity against solid tumours implanted in mice including a drug-resistant tumour.

*Key steps*: (a) allylation of an α-homochiral aldehyde; (b) asymmetric crotylation of an aldehyde; (c) Stille coupling; (d) Wadsworth-Emmons condensation.



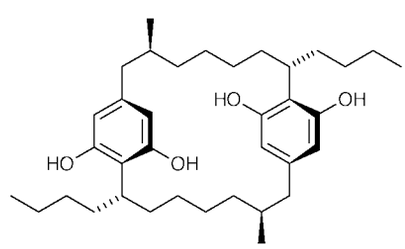
R = Me, X = Cl Cryptophycin-3
R = Me, X = H Cryptophycin-4
R = H, X = Cl Cryptophycin-29

J. D. White, J. Hong and L. A. Robarge, *J. Org. Chem.*, 1999, **64**, 6206.

### (–)-Cyclindrocyclophane F

*Biological activity*: *in vitro* cytotoxicity towards KB and LoVo tumour cell lines. The cyclindrocyclophanes are the first natural cyclophanes to be identified.

*Key steps*: (a) thermal reaction of a cyclobutenone with an ynol silyl ether to generate the resorcinol (Dannheiser benzannulation); (b) fragment linkage by reaction of an organolithium with an *N*-silyl tosylhydrazone to generate an alkane bridge between the two rings; (c) ring closing metathesis using Grubbs' catalyst.



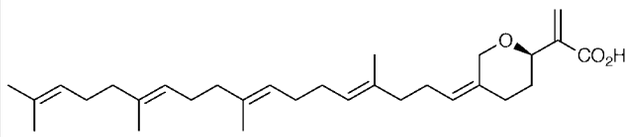
A. B. Smith, S. A. Kozmin and D. V. Paone, *J. Am. Chem. Soc.*, 1999, **121**, 7423.

**(±)-Hippospongic acid A**

*Biological activity*: inhibitory activity against gastrulation of starfish embryos.

*Key steps*: (a) Claisen rearrangement; (b) Knoevenagel reaction; (c) intramolecular Michael addition.

H. Takikawa, J. Koizumi, Y. Kato and K. Mori, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2271.

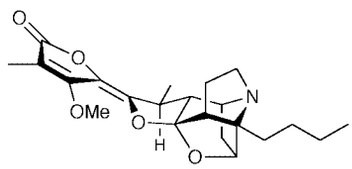



**(±)-Isostemofoline**

*Biological activity*: not reported.

*Key steps*: synthesis of the nortropinone ring system *via* [4+3] cycloaddition of an α-diazo ester to a pyrrole.

A. S. Kende, T. I. Smalley and H. Huang, *J. Am. Chem. Soc.*, 1999, **121**, 7431.

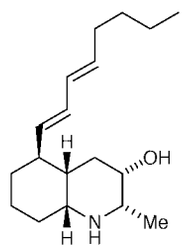



**(–)-Lepadin B**

*Biological activity*: not reported.

*Key steps*: (a) intramolecular aldol cyclisation; (b) Julia olefination.

N. Toyooka, M. Okumura, H. Takahata and H. Nemoto, *Tetrahedron*, 1999, **55**, 10673.

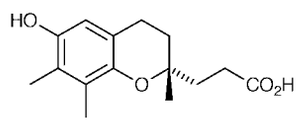



**LLU-α**

*Biological activity*: endogenous natriuretic and eukaluretic agent.

*Key steps*: (a) Sharpless asymmetric epoxidation; (b) Gassman-Sato process; (c) acid-catalysed cyclisation to afford the dihydrobenzopyran (chroman) ring system.

M. E. Jung and J. M. MacDougall, *Tetrahedron Lett.*, 1999, **40**, 6339.

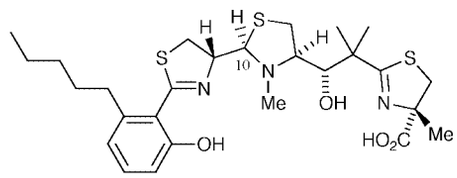



**Micacocidin**

*Biological activity*: antimycoplasma antibiotic.

*Key steps*: (a) phosphorus pentachloride-mediated cyclisation of *N*-acylcysteamine derivatives to construct thiazoline rings; (b) Wittig reaction; (c) isomerisation of unnatural C10 center through formation of a Zn-complex.

A. Ino, Y. Hasegawa and A. Murabayashi, *Tetrahedron*, 1999, **55**, 10271 and 10283.

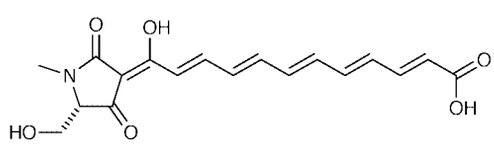



**Physarorubinic acid**

*Biological activity*: not reported.

*Key steps*: (a) Stille coupling; (b) aminolysis of a pentaene thioester mediated by silver trifluoroacetate; (c) Lacey-Dieckmann cyclisation.

D. J. Dixon, S. V. Ley and D. A. Longbottom, *J. Chem . Soc., Perkin Trans. 1*, 1999, 2231.

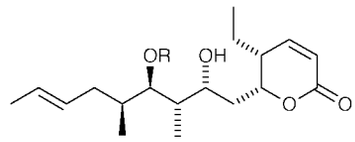


## Pironetin and NK10958P

*Biological activity*: (a) plant growth regulatory activity; (b) immunosuppressive activity; (c) antitumour activity.

*Key steps*: epoxide opening with the anion of a 1,3-dithiane.

H. Watanabe, H. Watanabe, M. Bando, M. Kido and T. Kitahara, *Tetrahedron*, 1999, **55**, 9755.



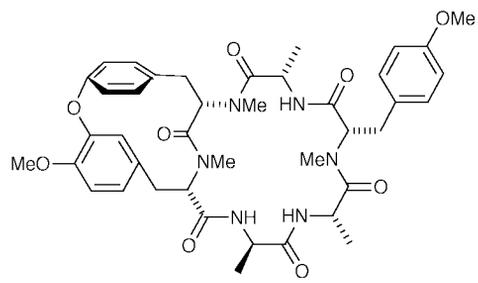

R = Me, Pironetin (PA-48153C)
R = H, NK10958P

## RA-VII

*Biological activity*: potent antitumour activity owing to inhibition of protein synthesis through eukaryotic 80S ribosomal binding.

*Key steps*: intramolecular $S_NAr$-based cycloetherification reaction.

A. Bigot, M. E. Tran Huu Dau and J. Zhu, *J. Org. Chem.*, 1999, **64**, 6283.

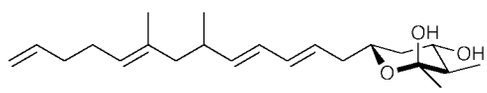



## (+)-Rottnestol

*Biological activity*: possible antibiotic activity.

*Key steps*: (a) Brown crotylmetallation; (b) Stille coupling; (c) Ireland-Claisen rearrangement.

I. R. Czuba and M. A. Rizzacasa, *Chem. Commun.*, 1999, 1419.

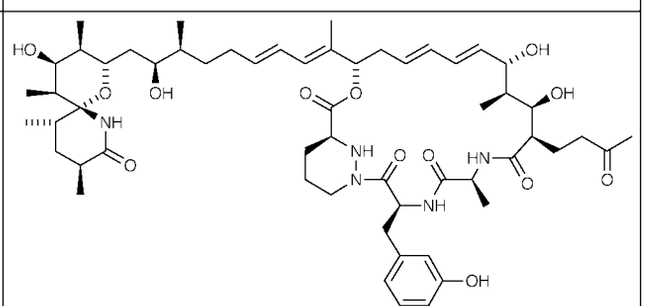



## Sanglifehrin A

*Biological activity*: immunosuppressant.

*Key steps*: double Stille coupling to generate the two conjugated diene units.

K. C. Nicolaou, J. Xu, F. Murphy, S. Barluenga, O. Baudoin, H.-x. Wei, D. L. F. Gray and T. Ohshima, *Angew. Chem., Int. Ed.*, 1999, **38**, 2447.

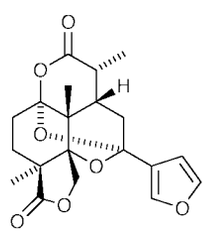



## (±)-Saudin

*Biological activity*: potent hypoglycemic activity.

*Key steps*: intramolecular dioxenone photocycloaddition.

J. D. Winkler and E. M. Doherty, *J. Am. Chem. Soc.*, 1999, **121**, 7425.

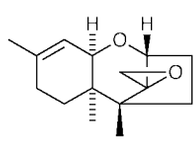



## (±)-Scirpene

*Biological activity*: not reported

*Key steps*: (a) oxidative ring expansion of a vinylidene cyclopropane to a cyclobutanone; (b) Pd(II)-catalysed ring expansion of a vinylcyclobutanol to an α-methylene cyclopentanone.

H. Nemoto, E. Takahashi and M. Ihara, *Org. Lett.*, 1999, **1**, 517.

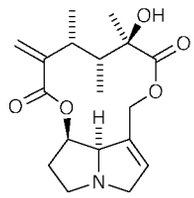


## Senecivernine

*Biological activity*: not reported.

*Key steps*: retro-Diels-Alder reaction.

Z.-Y. Liu and L.-Y. Zhao, *Tetrahedron Lett.*, 1999, **40**, 5593.

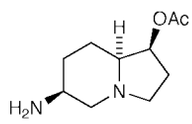


## (–)-Slaframine

*Biological activity*: responsible for excess salivation in cattle when they graze on fungus-infested feeds.

*Key steps*: novel thermolytic annulation of an oxazolidinone to form the six-membered piperidine ring.

M. P. Sibi and J. W. Christensen, *J. Org. Chem.*, 1999, **64**, 6434.

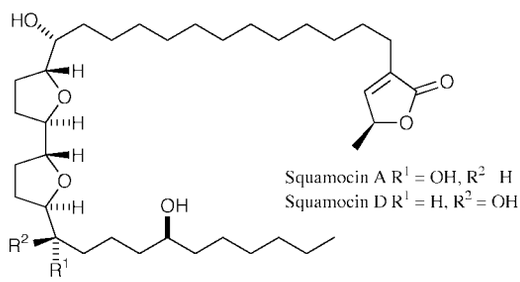


## Squamocin A and D

*Biological activity*: (a) potent cytotoxic activity; (b) blocks the mitochondrial complex I.

*Key steps*: (a) multiple Williamson reaction; (b) coupling of fragments *via* Grignard reagent addition to an aldehyde.

U. Emde and U. Koert, *Tetrahedron Lett.*, 1999, **40**, 5979.

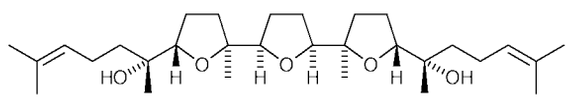



## Teurilene

*Biological activity*: cytotoxic with IC50 = 7.0 mg ml $^{1}$ against KB cells.

*Key steps*: two-directional synthesis strategy using a Re(VII)-promoted *syn* oxidative cyclisation. The synthesis is accomplished in 10 steps from methyl tiglate.

Y. Morimoto, T. Iwai and T. Kinoshita, *J. Am. Chem. Soc.*, 1999, **121**, 6792.

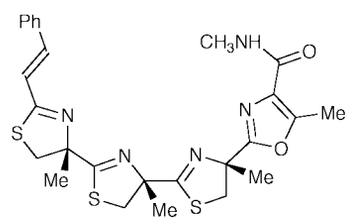


## Thiangazole

*Biological activity*: selective inhibitor of HIV-1 with no cell toxicity even at millimolar levels.

*Key steps*: (a) formation of multiple thiazoline rings mediated by 2-chloro-1,3-dimethylimidazolidium hexafluorophosphate (CIP); (b) Robinson-Gabriel cyclodehydration; (c) Heathcock cyclisation.

K. Akaji and Y. Kiso, *Tetrahedron*, 1999, **55**, 10685.



## Tonkinecin

*Biological activity*: potent cytotoxicity towards Bel 7402 (heptoma), BGC (gastrocarcinoma), HCT-8 (colon adenocarcinoma and HL-60 (leukemia) human tumour cell lines.

*Key steps*: fragment linkage *via* Pd(0)-catalysed cross coupling of a terminal alkyne with an iodoalkene. Stereogenic centres derived from D-xylose, D-glucose L-lactate and Sharpless asymmetric epoxidation.

T.-S. Hu, Q. Yu, Q. Lin, Y.-L. Wu and Y. Wu, *Org. Lett.*, 1999, **1**, 399.