Secondary Metabolites from Microorganisms Isolated by the HPFiedler Group

AG Mikrobiologie/Antibiotika

EBERHARD KARLS
UNIVERSITÄT
TÜBINGEN

Edited in June 2008

by

Hans-Peter Fiedler

4th Revision, July 2013

Dedicated to late Professor Hans Zähner

I. Introduction

A more than 20-years period in the search for secondary metabolites from microorganisms provides the opportunity of looking back to the beginning of the research and summarizing an overview on the discovered and published novel natural compounds. First of all, I wish to acknowledge my appreciation of the outstanding work of my doctoral father and mentor Professor Hans Zähner, who founded in 1964 the Institute of Microbiology at the University of Tübingen. Both my diploma thesis in 1972 and my doctoral thesis in 1974 were performed under his supervision. The stimulating atmosphere in his huge team and the excellent technical facilities contributed mainly to the success of my own research. Hans Zähner's retirement in 1994 was an encouragement to continue his fascinating scientific work in screening and discovery of novel biologically active secondary metabolites produced by new isolated members of the bacterial order *Actinomycetales*.

Looking back to the late 1980s, it was a promising decision to establish a natural product library based on high-performance liquid chromatography and diode-array monitoring (HPLC-DAD) with the aim to identify or to characterize secondary metabolite profiles of freshly isolated actinomycetes strains in culture filtrates and crude extracts. In 1984 the first fully automated HPLC systems equipped with a diode array monitoring system was introduced to the market. Hewlett-Packard (Waldbronn, Germany) was our main partner in optimizing hardware and software suitable for routine HPLC analysis. At the late 1980s, a first fast computing Pascal Workstation and hard disks having capacities of 10-20 MB (!) were available, even at an exorbitant price compared to the current market situation. This 'high-tech' equipment permitted us to create an efficient data base on natural products which was built up in my group starting in 1988 (Fiedler, 1993). At this time no further coupling techniques with more efficient monitoring devices, e.g. mass spectrometry, were imaginable. Therefore, *ortho*-phosphoric acid was chosen as the most suitable acidic modifier added to the mobile phase, having optimal properties in separation selectivity and UV transmission. The separation was performed by a standardized linear gradient system from 0.1% aqueous *ortho*-phosphoric acid to 100% acetonitrile within 15 minutes. Nucleosil-100 C_{18} reversed-phase material (5-µm particles; Macherey & Nagel, Germany) was selected as stationary phase because of its less adsorptive properties, high resolution and stability of retention times. This system continued to work excellently today.

New secondary metabolites from *Streptomyces* Tü strains

During the years 1988-1998 the research of my group was mainly sponsored by the Ministry of Research BMBF, who provided most of the fermentation and HPLC equipment. This period was the beginning of establishing my own group for isolating new actinomycetes strains from soil samples which were collected at various sites

throughout the world, and resulted in the discovery of following new secondary metabolites in strains of the genus *Streptomyces*:

- **Arylomycin A and B series:** lipopeptide antibiotics produced by *Streptomyces* sp. Tü 6075, antibacterial active, novel inhibitors of bacterial signal peptidase (Schimana *et al*., 2004).
- **Bagremycins A and B:** produced by *Streptomyces* sp. Tü 4128, antibacterial and antifungal active (Bertasso *et al*., 2001).
- **Decadienoic acid** and **decatrienoic acid:** produced by *Streptomyces viridochromogenes* Tü 6105, herbicidal active (Maier *et al*., 1999).
- **Dioxolides A, B and D:** produced by *Streptomyces tendae* Tü 4042; no biological activity was found (Blum *et al*., 1995).
- **Echinoserine:** a quinoxaline antibiotic produced by *Streptomyces tendae* Tü 4031, antibacterial active (Blum *et al*., 1995).
- **Kanchanamycins A, C and D:** 36-membered polyene macrolide antibiotics produced by *Streptomyces olivaceus* Tü 4018 with antibacterial and antifungal activities (Fiedler *et al*., 1996).
- **Naphthgeranine F:** a naphthoquinone antibiotic produced by *Streptomyces violaceus* Tü 3556 with antibacterial and antifungal activities (Hartjen *et al*., 1995).
- **Nataxazole:** a benzoxazole antibiotic produced by *Streptomyces* sp. Tü 6176, antitumor active (Sommer *et al*., 2008)
- **Phenalinolactones A–D:** terpenoglycoside antibiotics produced by *Streptomyces* sp. Tü 6071, active against Gram-positive bacteria (Gebhardt et al., 2011).
- **Ripromycin:** a macrolactame antibiotic produced by *Streptomyces* sp. Tü 6239, antibacterial and antitumor active (Bertasso *et al*., 2003).
- **Simocyclinones A–D:** angucyclinone antibiotics produced by *Streptomyces antibioticus* Tü 6040, antibacterial and antitumor active, novel potent inhibitors of bacterial gyrase (Schimana *et al*., 2000, 2001; Holzenkämpfer *et al*., 2002).
- **Spiridionic Acid:** produced by *Streptomyces* sp. Tü 6077, no biological activity was found (Textor *et al*., 2007).
- **Spirofungin:** a polyketide-spiroketal antibiotic produced by *Streptomyces violaceus-niger* Tü 4113, antifungal active (Höltzel *et al*., 1998).
- **Streptocidins A–D:** cyclic decapeptide antibiotics produced by *Streptomyces* sp. Tü 6071, antibacterial active (Gebhardt *et al*., 2001; Höltzel *et al*., 2001).

New secondary metabolites from *Micromonospora* strain Tü 6368

From a novel species of the genus *Micromonospora*, strain Tü 6368, the following new secondary metabolites were isolated and their structures elucidated (Antal *et al*., 2005; Ströch *et al*., 2005):

- **Galtamycin B:** an anthracycline antibiotic with antitumor activity;
- **Retymicin:** a xanthone antibiotic with antitumor activity;
- **Ribofuranosyl-lumichrome:** a new lumichrome derivative; no biological activity was found;
- **Saquayamycin Z:** an angucycline antibiotic, antibacterial and antitumor active.

New secondary metabolites from strains of the families *Streptosporangiaceae* and *Micromonosporaceae*

Within a scientific project funded by Novo Nordisk A/S, Denmark, specific attention was given to the actinomycete families *Streptosporangiaceae* and *Micromonosporaceae*. It was the beginning of a new area in the isolation and screening of less investigated actinomycete genera in my group with the aim to detect novel secondary metabolites. This work resulted in the discovery of:

- **(*E*)-4-Oxonon-2-enoic acid:** a fatty acid produced by *Streptomyces olivaceus* Tü 4018, antibacterial active (Pfefferle *et al*., 1996).
- **1-Hydroxy-4-methoxy-2-naphthoic acid:** a naphthalene antibiotic produced by *Streptosporangium cinnabarinum* NNO 29536 and herbicidal active (Pfefferle *et al.*, 1997).
- **Kyanomycin:** an anthracycline antibiotic produced by a novel species of *Nonomuria*, strain NNO 22303. A blue-coloured compound with an unusual anthracycline-phosphatidylethanolamine hybrid structure exhibiting an antibacterial activity (Pfefferle *et al*., 2000).
- **Tigloside:** a tigloylated tetrasaccharide produced by a novel species of *Amycolatopsis*, strain NNO 21702; no biological activity was found (Breinholt *et al*., 1998).

New secondary metabolites from symbiotic microorganisms associated with arthropods

BMBF and BASF AG (Ludwigshafen, Germany) funded a 6-year research project to investigate symbiotic microorganisms from arthropods as a source of novel bioactive secondary metabolites. The results were not very promising, but led to the discovery of the following novel antibiotics:

- **Aspochalamins A-D and aspochalasin Z:** cytochalasan antibiotics produced by *Aspergillus niveus*, antibacterial and antitumor active (Gebhardt *et al*., 2004, Höltzel *et al*., 2004).

- **Endophenazines A–D:** phenazine antibiotics produced by various endosymbiotic isolates of *Streptomyces anulatus* with antibacterial, antifungal and herbicidal activities (Gebhardt *et al*., 2002; Krastel *et al*., 2002).

In addition, a multitude of partial novel natural products deriving from the primary metabolism were isolated and characterized, such as **3-hydroxyphenylacetic acid methylester**, **malonic acid phenylester**, ***N*-acetyl-phenylalanine** and ***N*-acetyl-tryptophan**.

Screening with actinomycetes from extreme terrestrial and marine habitats

A very stimulating and successful collaboration was started in 2000 together with the groups of Professor Michael Goodfellow from the University of Newcastle upon Tyne and Professor Alan T. Bull from the University of Kent (UK) that continued till my retirement in 2013. Both groups provided me with a huge series of dereplicated actinomycetes strains which were isolated from unique terrestrial and marine habitats including sediments of deep-sea trenches located in the Pacific and Atlantic Oceans. All strains were taxonomically characterised to the genus level that permitted an individual submerged cultivation in the screening stage, applying genus-adapted cultivation media. This collaboration resulted in the discovery of following metabolites:

- **Abyssomicins B, C, D, G and H, and atrop-Abyssomicin C:** polycyclic polyketide antibiotics with an unusual pharmacophore produced by the marine strain *Verrucosispora maris* AB-18-032 with antibacterial activity against Gram-positive bacteria including MRSA and vancomycin-resistant strains. Abyssomicin C and atrop-Abyssomicin C are novel inhibitors of *para*-aminobenzoic acid biosynthesis (Riedlinger *et al*., 2004; Bister *et al*., 2004; Keller *et al*., 2007).
- **Atacamycins A–C:** 22-membered macrolactone antibiotics produced by *Streptomyces* sp. C38 which was isolated from a hyper-arid soil from the Atacama Desert, North Chile, showing an antitumor and phosphodiesterase inhibitoring activity (Nachtigall *et al*., 2011).
- **Bhimamycins F, H and I:** aromatic octaketide antibiotics produced by alkaliphilic strain *Streptomyces* sp. AK 671 with antibacterial and enzyme inhibitory activities (Jetter *et al*., 2013).
- **Dermacozines A–L:** phenazine antibiotics produced by the deep-sea strains *Dermacoccus abyssi* MT1.1 and MT1.2, investigated in close collaboration with Professor Marcel Jaspars from the Aberdeen University. The novel phenazine-type compounds exhibit a free radical scavenging activity, antitumor and antiparasitic activities (Abdel-Mageed *et al.*, 2010).
- **Elaiomycins B and C:** alkylhydrazide antibiotics produced by *Streptomyces* sp. BK 190 with antibacterial, phosphodiesterase and acetylcholinesterase inhibitoring activity (Kim *et al*., 2011; Helaly *et al.*, 2011).

- **Genoketides A1 and A2, prechrysophanol glucuronide and chrysophanol glucuronide:** aromatic octaketides produced by alkaliphilic strain *Streptomyces* sp. AK 671, antitumor active (Fiedler *et al*., 2008).
- **Lactonamycin Z:** produced by *Streptomyces sanglieri* AK 623, antibacterial and antitumor active (Höltzel *et al*., 2003).
- **Proximicins A–C:** aminofuran antibiotics produced by the marine strain *Verrucosispora fiedleri* MG-37. Proximicin A was also isolated from the abyssomicin producer *Verrucosispora maris* AB-18-032. The metabolites show a weak antibacterial but a strong antitumor activity (Fiedler *et al*., 2008; Keller *et al*., 2008).
- **Pyrocoll:** a diketopiperazine antibiotic produced by alkaliphilic strain *Streptomyces* sp. AK 409, antibacterial, anti-parasitic and antitumor active (Dieter *et al*., 2003).

NTK screening project with marine and extremophilic terrestrial actinomycetes

The promising results coming out of the collaboration with Professor Goodfellow and Professor Bull were the fundamentals that our consortium was funded by Boehringer Ingelheim Pharma (Biberach, Germany) in a 3-years scientific project, starting from 2002 till 2004. The goal of the collaboration was to screen extracts from unique marine and some extremophilic terrestrial members of the families *Streptomycetaceae*, *Micromonosporaceae* and *Pseudonocardiaceae*, and from selected members of mycolata as *Nocardia*, *Rhodococcus, Gordonia* and *Tsukamurella* for activities in various HTS assays. The first secondary metabolites coming out of this collaboration were:

- **Frigocyclinone:** an angucyclinone antibiotic produced by *Streptomyces griseus* NTK 97 from a soil sample collected at Antarctica, antibacterial active (Bruntner *et al*., 2005).
- **Gephyromycin:** an angucyclinone antibiotic produced by *Streptomyces griseus* NTK 14, glutaminergic active towards neuronal cells (Bringmann *et al*., 2005).

Unfortunatelly, the Boehringer-Ingelheim Company decided in 2004 to drop their activities in natural products completely, and therefore, the planned second phase of the proposed project in metabolite isolation and structure elucidation of the numerous hit strains was not possible. Only a few of these strains could be investigated later on in my group by undergraduated students, resulting in following new metabolites:

- **Albidopyrone:** a pyrone antibiotic produced by *Streptomyces* strain NTK 227, isolated from a sediment which was collected in the North-Atlantic Ocean. Albidopyrone showed an inhibitory activity against protein-tyrosin phosphokinase 1B (Hohmann *et al*., 2009).

- **Benzoxacystol:** a 1,4-benzoxazine-type antibiotic produced by the marine strain *Streptomyces* sp. NTK 935, isolated from the same Canary Basin sediment as caboxamycin producer NTK 937. The metabolite has inhibitory activity against the enzymes glycogen synthase kinase 3β and acetylcholinesterase (Nachtigall *et al*., 2011)
- **Caboxamycin:** a benzoxazol antibiotic produced by *Streptomyces* strain NTK 937, isolated from a sediment which was collected in the Canary Basin at -3814 m. The metabolite showed antibacterial, antitumor and phosphodiesterase inhibitory activities (Hohmann *et al*., 2009).

Project ACTAPHARM

Parallel to the NTK project sponsored by a pharmaceutical company, a further project was established with the aim to discover novel bioactive secondary metabolites from actinomycetes for clinical applications. Project ACTAPHARM was funded by the European Commission within the 5th framework program from 2001 till 2004, for a collaboration of the groups of Professor Liz Wellington (University of Warwick, UK), Professor Michael Goodfellow and Dr. Alan Ward (University of Newcastle, UK), Professor Lubbert Dujikhuizen (University of Groningen, The Netherlands), PD Dr. Joachim Vater (Technische Universität Berlin, Germany), Professor Amalia Karagouni (University of Athens, Greece), Dr. Flavia Marinelli (Biosearch Italia, Gerenzano, Italy), and Dr. Fotinos (Lavipharm Group, Athens, Greece) and my own group. Until today, the following new secondary metabolites have been described:

- **Aurachins Q and R:** new members of the aurachin family produced by *Rhodococcus* sp. Acta 2259 with inhibitory activity against glycogen synthase kinase 3β (Nachtigall *et al.*, 2010).
- **Bendigoles A–C:** new steroid metabolites produced by *Gordonia australis* Acta 2299 (Schneider *et al*., 2008).
- **Elloxazinones A and B:** aminophenoxazinone antibiotics produced by *Streptomyces* sp. Acta 2871 showing potent and selective antitumor activities (Graf *et al*., 2006).
- **Fluostatins C, D and E:** fluorenone antibiotics produced by *Streptomyces* sp. Acta 1383 exhibiting an antitumor activity (fluostatin C) (Baur *et al*., 2006; Schneider *et al*., 2006).
- **Gombapyrones A–D:** α-pyrone antibiotics produced by *Streptomyces griseoruber* Acta 3662 with inhibitory activity against protein tyrosine phosphatase 1B and glycogen synthase kinase 3β (Helaly *et al.*, 2009)
- **Grecocyclines A and B:** angucycline antibiotics from *Streptomyces* sp Acta 1362 with cytotoxic activity and inhibitory activity against protein tyrosine phosphatase 1B (Paululat *et al.*, 2010).

- **Grecoketides A and B:** glycosilated naphthoquinones produced by *Streptomyces* sp. Acta 1362 (Paululat *et al*., 2008).
- **Nocardichelins A and B:** new type of siderophores produced by *Nocardia* sp. Acta 3026 with iron-chelating properties (Schneider *et al*., 2006).
- **Langkocyclines A1, A2, A3, B1 and B2:** angucycline antibiotics produced by *Streptomyces* sp. Acta 3034 with antibacterial and antitumor activities (Kalyon *et al*., 2013).
- **Langkolide:** a 32-membered macrolactone antibiotic produced by *Streptomyces* sp. Acta 3062 with antibacterial and antiproliferative activities (Helaly *et al*., 2012).
- **Lipocarbazoles A1–A4:** carbazole-type metabolites produced by *Tsukamurella pseudospumae* Acta 1857 acting as free radical scavengers and showing antioxidative activity (Schneider *et al.*, 2009).
- **Phenelfamycins G and H:** antibiotics belonging to the elfamycin family related to phenelfamycins E and F, produced by *Streptomyces albospinus* Acta 3619 (Brötz *et al.*, 2011).
- **Skyllamycins A and B:** depsipeptide antibiotics produced by *Streptomyces* sp. Acta 2897. Skyllamycin A is identical with Antibiotic RP-1776, skyllamycin B is a new demethyl derivative of A. The compounds show an antibacterial activity (Pohle *et al.*, 2011).
- **Warkmycin:** an angucycline antibiotic produced by *Streptomyces* sp. Acta 2930 with antibacterial and antitumor activity (Helaly *et al.*, 2013).

Interactions of streptomycetes in the rhizosphere

A new research field was started in 2002 to investigate the interaction of soil streptomycetes with symbiotic fungi, pathogenic fungi and plants in the rhizosphere. The project was funded till 2010 by the Deutsche Forschungsgemeinschaft within the Graduate College 'Infectious Biology' at the University of Tübingen and was treated in close collaboration with the group of Professor Hampp, Institute of Physiological Ecology of Plants. The aim of our research was to characterize and identify the metabolites which act as signals in the communication between the different organisms. New metabolites coming out of this research were:

- **Aranciamycin Anhydride:** an anthracycline antibiotic from *Streptomyces* sp. Tü 6384 with antitumor activity (Nachtigall *et al.*, 2010).
- **Auxofuran:** a furan-type metabolite produced by the mycorrhiza helper bacterium *Streptomyces* sp. AcH 505 which act as a growth-stimulating factor for *Amanita muscaria* (fly acaric), and induces resistence against plant pathogenic fungi in plants (Riedlinger *et al*., 2006).
- **Elaiomycins K and L:** azoxy-type antibiotics produced by *Streptomyces* sp. Tü 6399, exhibiting an antibacterial activity (Manderscheid *et al*., 2013).

- **Fomannoxin Acids DFA, MFA-1 and MFA-2:** inactive conversion products of the fungal phytotoxin fomannoxin produced by *Heterobasidion* sp., converted by the rhizospheric strain *Streptomyces* sp. AcH 505.
- **Piceamycin:** a 23-membered macrolactam polyketide antibiotic produced by *Streptomyces* sp. GB 4-2 with inhibitory activity against Gram-positive bacteria, human tumor cell lines, and protein tyrosine phosphatase 1B (Schulz *et al*., 2009).
- **Silvalactam:** a 24-membered macrolactam antibiotic produced by *Streptomyces* sp. Tü 6392 with antitumor activity (Schulz *et al*., 2012).

National and international activities with strains and secondary metabolites discovered by the HP Fiedler Group

Some of the discovered new secondary metabolites which showed an unusual structure or structural elements were attractive for various groups involved in the genetics of the biosynthetic pathways. The following metabolites were investigated regarding their biosynthetic gene cluster and mode of action:

Abyssomicins: The characterization of the biosynthetic gene cluster in *Verrucosispora* sp. AB-18-032 is still in progress by the groups of Professor Roderich Süssmuth, Technische Universität Berlin, and Dr. JEM Stach, University of Newcastle, UK.

Gottardi, E.M.; J.M. Krawczyk, H. von Suchodoletz, S. Schadt, A. Mühlenweg, G.C. Uguru, S. Pelzer, H.-P. Fiedler, M.J. Bibb, J.E.M. Stach & R.D. Süssmuth: Abyssomicin biosynthesis: formation of an unusual polyketide, antibiotic-feeding studies and genetic analysis. ChemBioChem 12: 1401-1410, 2011.

Arylomycins: The biosynthetic gene cluster of these lipopeptide antibiotics produced by *Streptomyces* sp. Tü 6075 is under investigation in the group of Professor Stephanie Grond, Universität Tübingen. Studies for organic syntheses with biaryl-coupling enzymes are topic in the group of Dr. Tobias Gulder, Universität Bonn.

Caboxamycin and **Nataxazole**: The biosynthetic gene clusters of these carboxazole antibiotics produced by *Streptomyces* sp. NTK 937 and *Streptomyces* sp. Tü 6176, respectively, are investigated in the group of Professor José Salas, Universidad de Oviedo, Spain.

Endophenazines: The characterization of the biosynthetic gene cluster in *Streptomyces anulatus* 9958 with specific consideration of the origin of the prenyl side-chain was investigated in the group of Professor Lutz Heide, Universität Tübingen.

Saleh, O.; B. Gust, B. Boll, H.-P. Fiedler & L. Heide: Aromatic prenylation in the phenazine biosynthesis: dihydrophenazine-1-carboxylate dimethylallyltransferase from *Streptomyces anulatus*. J. Biol. Chem. 284: 14439-14447, 2009.

Frigocyclinone: The biosynthetic gene cluster of the angucyclinone antibiotic frigocyclinone produced by *Streptomyces griseus* NTK 97 is under investigation in the group of Professor Huizhan Zhang, East China University of Science and Technology, Shanghai, P.R. China.

Genoketides A1and **A2:** The biosynthetic gene cluster of chrysophanol glucuronide and its biosynthetic intermediates genoketide A1 and A2 and pre-chrysophanol glucuronide is under investigation in the group of Professor Tom Simpson, University of Bristol, UK.

Grecocyclines and **Grecoketides:** The biosynthetic gene cluster of both novel angucycline and naphthoquinone antibiotics, respectively, is under investigation by Dr. Andriy Luzhetskyy, Universität des Saarlandes.

Lactonamycin Z: The characterization of the biosynthetic gene cluster in *Streptomyces sanglieri* AK 623 was described by the group of Professor Ron Parry, Rice University, Houston, Texas, USA.

Zhang, X.; L.B. Alemany, H.-P. Fiedler, M. Goodfellow & R.P. Parry: Biosynthetic investigations of lactonamycin and lactonamycin Z: cloning of the biosynthetic gene clusters and discovery of an unusual starter unit. Antimicrob. Agents Chemother. 52: 574-585, 2008.

Kanchanamycins: The producing strain *Streptomyces olivaceus* Tü 4018 is used as a host for heterologous expression experiments in the group of Dr. Andriy Luzhetskyy, Universität des Saarlandes.

Phenalinolactones: The biosynthetic gene cluster in *Streptomyces* sp. Tü 6071 was described by the group of Professor Andreas Bechthold, Universität Freiburg. The strain is under investigation in the group of Professor Pieter Dorrestein, University of California, San Diego, USA.

Dürr, C.; H.-J. Schnell, A. Luzhetskyy, R. Murillo, M. Weber, K. Welzel, A. Vente & A. Bechthold: Biosynthesis of terpene phenalinolactone in *Streptomyces* sp. Tü6071: analysis of the gene cluster and generation of derivatives. Chem. Biol. 13: 365-377, 2006.

Polyketomycin: The characterization of the biosynthetic gene cluster in *Streptomyces diastatochromogenes* Tü 6028 was done in the group of Professor Andreas Bechthold, Universität Freiburg.

Daum, M.; I. Peintner, A. Frerich, M. Weber, T. Paululat & A. Bechthold: Organisation of the biosynthetic gene cluster and tailoring enzymes in the biosynthesis of the tetracyclic quinone glycoside antibiotic polyketomycin. ChemBioChem 10: 1073-1083, 2009.

Saquayamycin Z: The characterization of the biosynthetic gene cluster in *Micromonospora* sp. Tü 6368 is still in work by the group of Professor Andreas Bechthold, University of Freiburg, and Professor Rongson Pongdee, University of Sewanee, Sewanee, TN, USA.

Erb, A.; A. Luzhetskyy, U. Hardter & A. Bechthold: Cloning and sequencing of biosynthetic gene cluster for saquayamycin Z and galtamycin B and the elucidation of the assembly of their saccharide chains. ChemBioChem 10: 1392-1401, 2009.

Simocyclinones: The complete biosynthetic gene cluster in *Streptomyces antibioticus* Tü 6040 was described by the groups of Professor Lutz Heide, Universität Tübingen, and Professor Andreas Bechthold, Universität Freiburg.

Galm, U.; J. Schimana, H.-P. Fiedler, J. Schmidt, S.-M. Li & L. Heide: Cloning and analysis of the simocyclinone biosynthetic gene cluster of *Streptomyces antibioticus* Tü 6040. Arch. Microbiol. 178: 102-114, 2002.

Trefzer, A.; S. Pelzer, J. Schimana, S. Stockert, C. Bihlmaier, H.-P. Fiedler, K. Welzel, A. Vente & A. Bechthold: Biosynthetic gene cluster of simocyclinone, a natural multihybrid antibiotic. Antimicrob. Agents Chemother. 46: 1174-1182, 2002.

The mode of action of simocyclinones is extensively studied by the groups of Professor Tony Maxwell and Professor Mark J. Buttner (John Innes Centre, Norwich, UK) and Dr. Keith C. Ellis (University of Kansas, USA).

Flatman, R.H.; A.J. Howells, L. Heide, H.-P. Fiedler & A. Maxwell: Simocyclinone D8: an inhibitor of DNA gyrase with a novel mode of action. Antimicrob. Agents Chemother. 49: 1093-1100, 2005.

Le, T.B.K.; H.-P. Fiedler, C.D. den Hengst, S.K. Ahn, A. Maxwell & M.J. Buttner: Coupling of the biosynthesis and export of the DNA gyrase inhibitor simocyclinone in *Streptomyces antibioticus*. Molec. Microbiol. 72: 1462-1474, 2009.

Oppegard, L.M.; B.L. Hamann, K.R. Streck, K.C. Ellis, H.-P. Fiedler, A.B. Khodursky & H. Hiasa: *In vivo* and *in vitro* patterns of the activity of simocyclinone D8, an angucyclinone antibiotic from *Streptomyces antibioticus*. Antimicrob. Agents Chemother. 53:2110-2119, 2009.

Edwards, M.J.; R.H. Flatman, L.A. Mitchenall, C.E.M. Stevenson, T.B.K. Le, T.A. Clarke, A.R. McKay, H.-P. Fiedler, M.J. Buttner, D.M. Lawson & A. Maxwell: A crystal structure of the bifunctional antibiotic, simocyclinone D8, bound to DNA gyrase. Science 326: 1415-1417, 2009.

Le, T.B.K.; C.E.M. Stevenson, H.-P. Fiedler, A. Maxwell, D.M. Lawson & M.J. Buttner: Structures of the TetR-like simocyclinone efflux pump repressor, SimR, and the mechanism of ligand-mediated derepression. J. Molec. Biol. 408: 40-56, 2011.

The simocyclinone producing strain *Streptomyces antibioticus* Tü 6040 is investigated in the group of Professor Justin Nodwell, McMaster University, Hamilton, Canada, regarding TetR-like proteins.

Skyllamycin: The biosynthetic gene cluster of the NRPS cyclodepsipeptide is investigated in the group of Professor Roderich Süssmuth, Technische Universität Berlin.

Pohle, S.; C. Appelt, M. Roux, H.-P. Fiedler & R.D. Süssmuth: Biosynthetic gene cluster of the non-ribosomally synthesized cyclodepsipeptide skyllamycin: deciphering unprecendented ways of unusual hydroxylation reactions. J. Am. Chem. Soc. 133: 6194-6205, 2011.

Spirodionic Acid: The characterization of the biosynthetic gene cluster in *Streptomyces* sp. Tü 6077 is under investigation in the group of Professor Stephanie Grond, Universität Tübingen.

Spirofungin: Investigations on the organization of PKS genes of *Streptomyces violaceusniger* Tü 4113 are in progress in the group of Dr. Leonard Katz, SynBERC, University of California, Emeryville, USA.

The spirofungin producing strain *Streptomyces violaceusniger* Tü 4113 is investigared regarding volatiles in the group of Dr. Jeroen Dickschat, TU Braunschweig.

Some of our secondary metabolites with interesting and unusual structural elements were subject for chemical total synthesis:

Abyssomicins

Rath, J.-P.; S. Kinast & M.E. Maier: Synthesis of the fully functionalized core structure of the antibiotic abyssomicin C. Org. Lett. 7: 3089-3092, 2005.

Zografos, A.L.; A. Yiotakis & D. Georgiadis: Rapid access to the tricyclic spirotetronic core of abyssomicins. Org. Lett. 7: 4515-4518, 2005

Snider, B.B. & Y. Zou: Synthesis of the carbocyclic skeletonof abyssomicins C and D. Org. Lett. 7, 4939-4941, 2005

Zapf, C.W.; B.A. Harrison, C. Drahl & E.J. Sorensen: A Diels-Alder macrocyclization enables an efficient asymmetric synthesis of the antibacterial natural product abyssomicin C. Angew. Chem. Int. Ed. 44: 6533-6537, 2005.

Nicolaou, K.C. & S.T. Harrison: Total synthesis of abyssomicin and atrop-abyssomicin C. Angew. Chem. Int. Ed. 45: 3256-3260, 2006.

Couladouros, E.A.; E.A. Bouzas & A.D. Magos: Formal synthesis of abyssomicin C. Tetrahedron 62: 5272-5279, 2006.

Arylomycins

Roberts, T.C.; P.A. Smith, R.T. Cirz & F.E. Romersberg: Structural and initial biological analysis of synthetic arylomycin A2. J. Am. Chem. Soc. 129: 15830-15838, 2007.

Fluostatin

Yu, M. & S.J. Danishefsky: A direct route to fluostatin C by a fascinating Diels-Alder reaction. J. Am. Chem. Soc. 130: 2783-2785, 2008.

Lactonamycin Z

Adachi, S.; K. Watanabe, Y. Iwata, S. Kameda, Y. Miyaoka, M. Onozuka, R. Mitusi, Y. Saikawa & M. Nakata: Total synthesis of lactonamycin and lactonamycin Z with late-stage A-ring formation and glycosylation. Angew. Chem. Int. Ed. 52: 2087-2091, 2013.

Spirofungin

Shimizu, Y.; H. Kiyota & T. Oritani: Synthesis of the spiroacetal parts of spirofungin A and B. Tetrahedr. Lett. 41: 3141-3144, 2000.

Zanatta, S.D.; J.M. White & M.A. Rizzacasa: Total synthesis of the proposed structure for spirofungin B: a reassignment of the stereochemistry. Org. Lett. 6: 1041-1044, 2004.

Shimizu, T.; T. Satoh, K. Murakoshi & M. Sodeoka: Asymmetric total synthesis of (-)-spirofungin A and (+)-sprirofungin B. Org. Lett. 7: 5573-5576, 2005.

Marjanovic, J. & S.A. Kozmin: Spirofungin A; stereoselective synthesis and inhibition of isoleucyl-tRNA synthetase. Angew. Chem. Int. Ed. 46: 8854-8857, 2007.

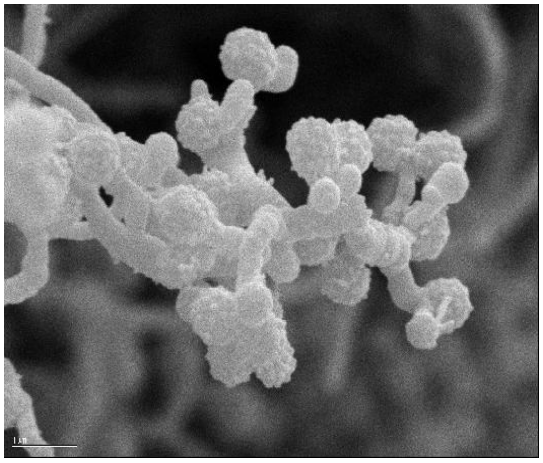
Crimmins, M.T. & E.A. O'Bryan: Enantioselective total synthesis of spirofungins A and B. Org. Lett. 12: 4416-4419, 2010.

Neumaier, J. & M.E. Maier: Synthesis of the spirofungin A core via a domino strategy consisting of olefinic ester ring-closing metathesis and iodospiroacetalization. Synlett 2011, 2, 187-190.

II. Isolated Metabolites

Abyssomicins B, C, atrop C, D, G and H

Producing organism: *Verrucosispora maris* AB-18-032

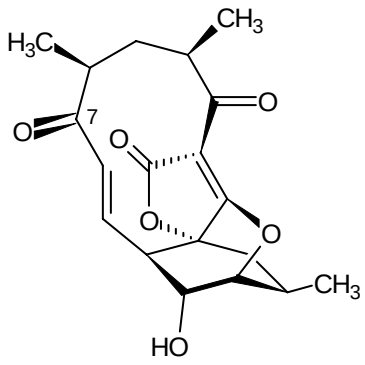


Habitat: marine; Sea of Japan, sediment –289 m

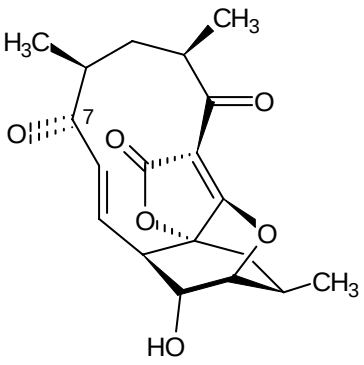
Screening method: inhibition of *para*-aminobenzoic acid biosynthesis

Biological activity: antibacterial, inhibitior of *para*-aminobenzoic acid and folic acid biosynthesis (abyssomicin C, atrop-abyssomicin C)

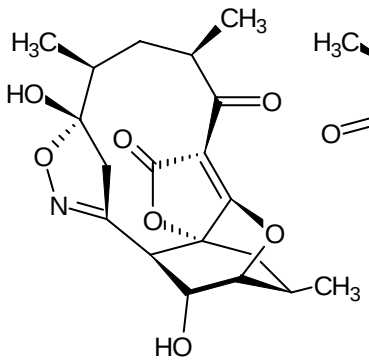
Structures:



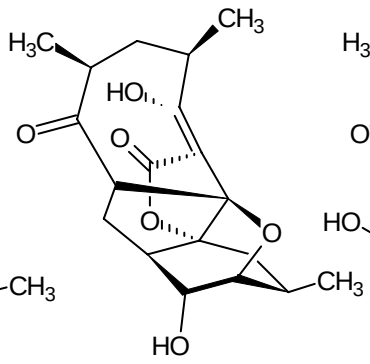
C



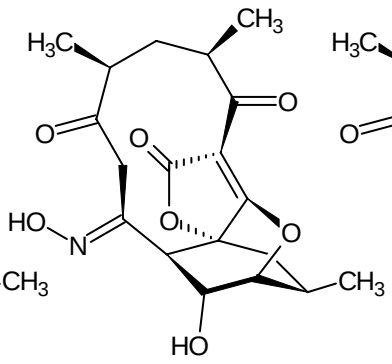
atrop C



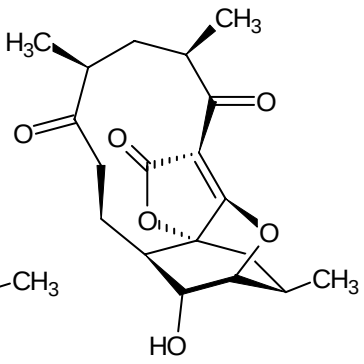
B



D



G



H

Abyssomicins B, C, atrop C, D, G and H

References:

Riedlinger, J.; A. Reicke, H. Zähner, B. Krismer, A.T. Bull, L.A. Maldonado, A.C. Ward, M. Goodfellow, B. Bister, D. Bischoff, R. Süssmuth & H.-P. Fiedler. J. Antibiotics 57: 271-279, 2004

Bister, B.; D. Bischoff, M. Ströbele, J. Riedlinger, A. Reicke, F. Wolter, A.T. Bull, H. Zähner, H.-P. Fiedler & R.D.Süssmuth. Angew. Chem. Int. Ed. 43: 2574-2576, 2004

Keller, S.; G. Nicholson, C. Drahl, E. Sorensen, H.-P. Fiedler & R.D. Süssmuth. J. Antibiotics 60: 391-394, 2007

Gottardi, E.M.; J.M. Krawczyk, H. von Suchodoletz, S. Schadt, A. Mühlenweg, G.C. Uguru, S. Pelzer, H.-P. Fiedler, M.J. Bibb, J.E.M. Stach & R.D. Süssmuth: ChemBioChem 12: 1401-1410, 2011

Goodfellow, M.; J.E.M. Stach, R. Brown, A.N.V. Bonda, A.L. Jones, J. Mexson, H.-P. Fiedler, T.D. Zucchi & A.T. Bull. Antonie van Leeuwenhoeck 101: 185-193, 2012.

Albidopyrone

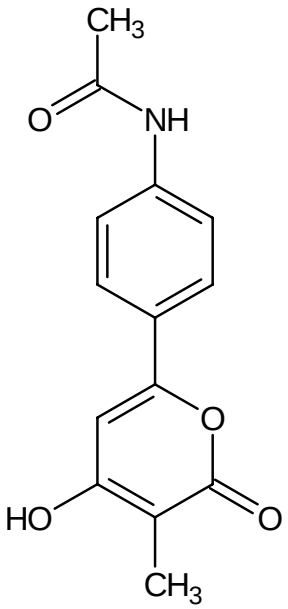
Producing organism: *Streptomyces* sp. NTK 227

Habitat: marine; sediment –158 m, North Atlantic Ocean

Screening method: HPLC-DAD

Biological activity: inhibitor of protein-tyrosin phosphokinase 1B

Structure:



Reference:

Hohmann, C.; K. Schneider, C. Bruntner, R. Brown, A.L. Jones, M. Goodfellow, M. Krämer, J.F. Imhoff, G. Nicholson, H.-P. Fiedler & R.D.Süssmuth. J. Antibiotics 62: 75-79, 2009

Aranciamycin Anhydride

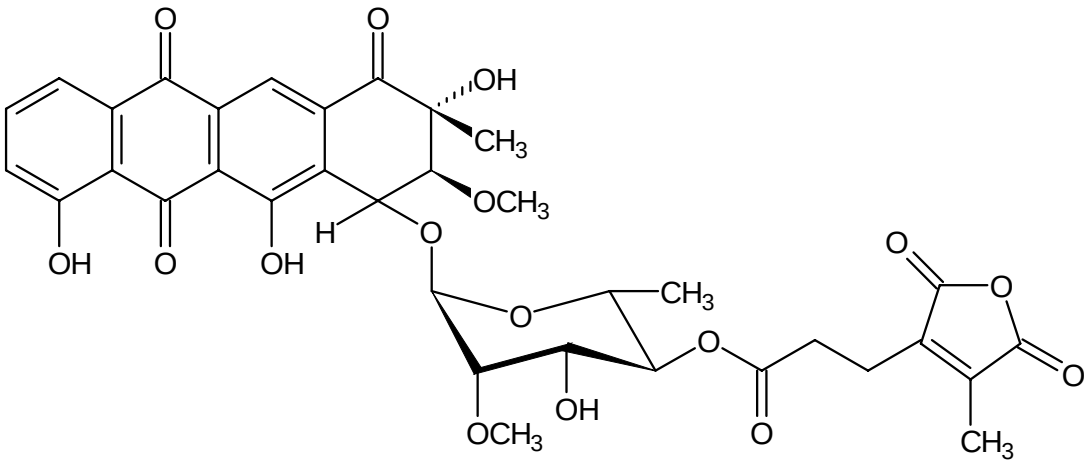
Producing organism: *Streptomyces* sp. Tü 6384

Habitat: terrestrial; rhizosphere of Norway spruce, Rammert Forest, Tübingen, Germany

Screening method: HPLC-DAD

Biological activity: antitumor

Structure:

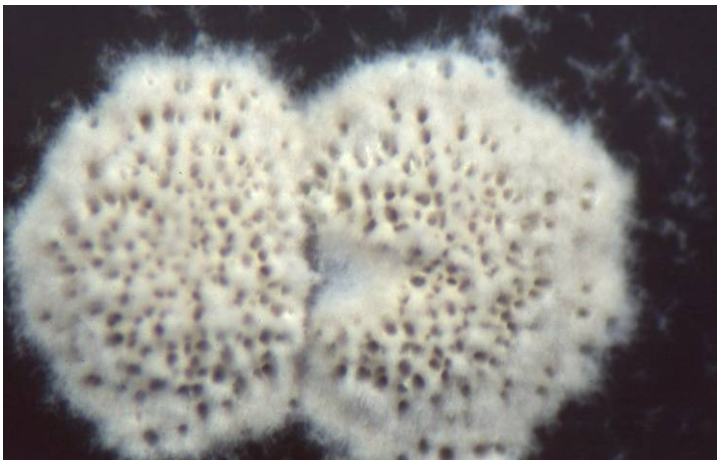


Reference:

Nachtigall, J.; D. Schulz, W. Beil, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics 63: 397-399, 2010

Arylomycins A and B

Producing organism: *Streptomyces* sp. Tü 6075



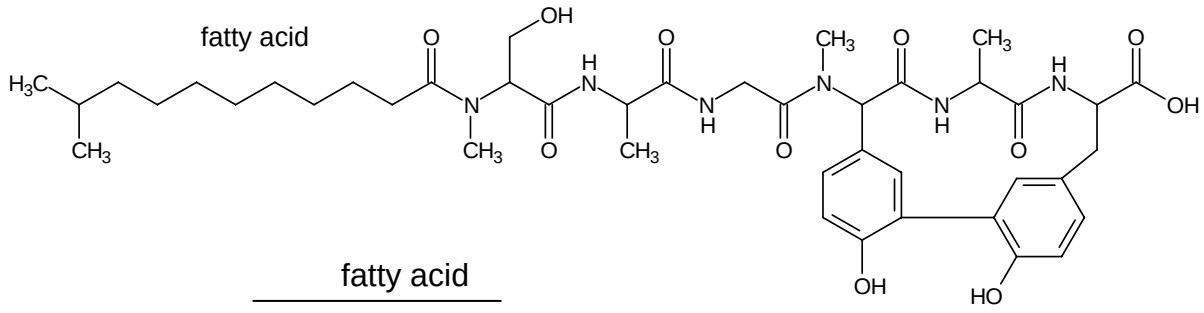
Habitat: terrestrial; Cape Coast, Ghana

Screening method: HPLC-DAD

Biological activity: antibacterial, inhibitors of bacterial signal peptidase

Structures:

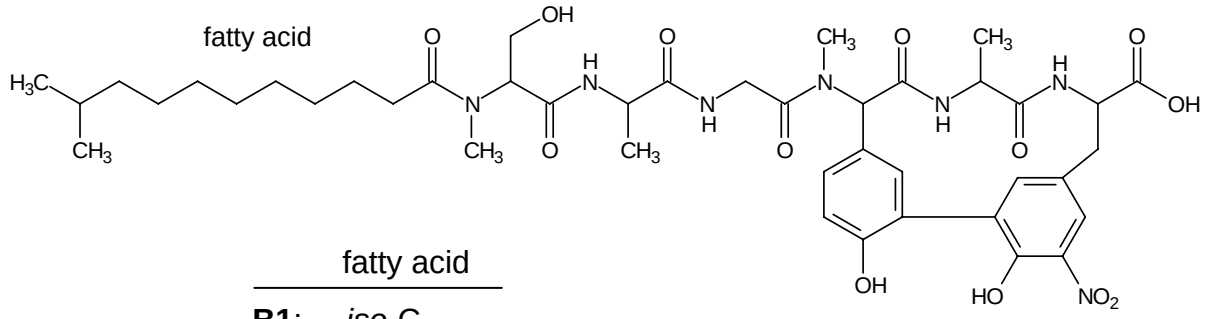
Arylomycin A series



fatty acid	
A1:	*iso*-C_{11}
A2:	*iso*-C_{12}
A3:	*n*-C_{12}
A4:	*anteiso*-C_{13}
A6:	*iso*-C_{14}

Arylomycins A and B

Arylomycin B series



fatty acid	
B1:	*iso*-C_{11}
B2:	*iso*-C_{12}
B3:	*n*-C_{12}
B4:	*anteiso*-C_{13}
B6:	*iso*-C_{14}
B7:	*anteiso*-C_{16}

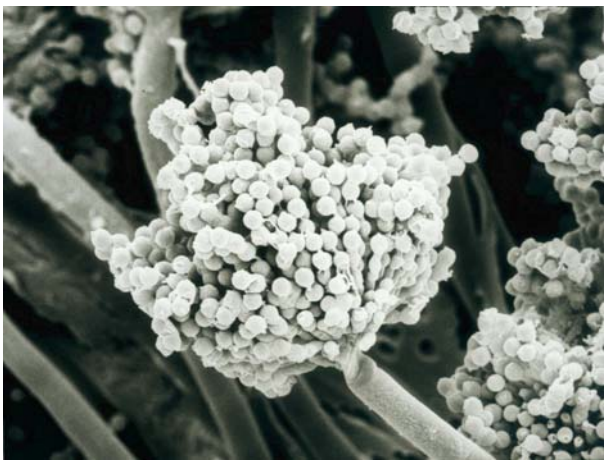
References:

Schimana, J.; K. Gebhardt, J. Müller, A. Höltzel, D.G. Schmid, R. Süssmuth, R. Pukall & H.-P. Fiedler. J. Antibiotics 55: 565-570, 2002

Höltzel, A.; D.G. Schmid, G.J. Nicholson, S. Stevanovic, J. Schimana, K. Gebhardt, H.-P. Fiedler & G. Jung. J. Antibiotics 55: 571-577, 2002

Aspochalamins A–D

Producing organism: *Aspergillus niveus* LU 9575

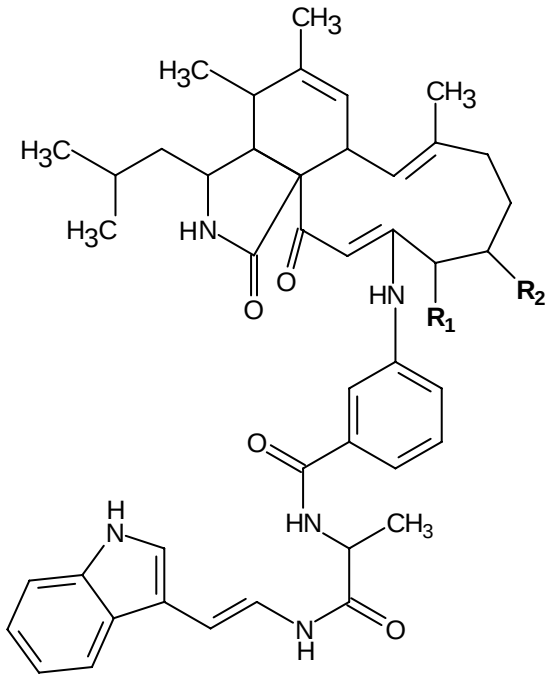


Habitat: endosymbiotic; gut from a *Trichoniscidae*

Screening method: HPLC-DAD

Biological activity: antitumor, antibacterial

Structures:



A: $R_1 = R_2 = OH$
B: $R_1 = R_2 = OH$
C: $R_1 = H$; $R_2 = OH$
D: $R_1 = R_2 = H$

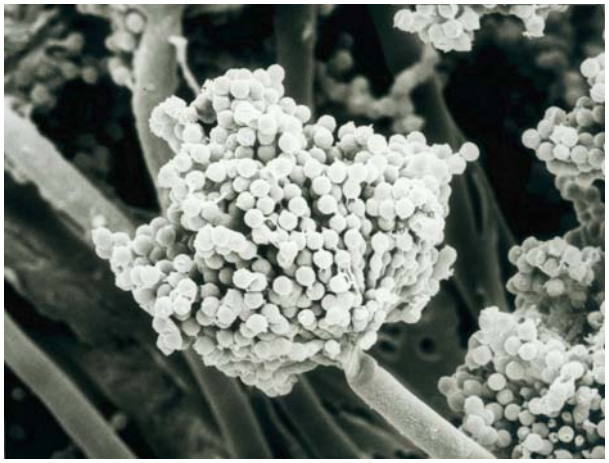
References:

Gebhardt, K.; J. Schimana, A. Höltzel, K. Dettner, S. Draeger, W. Beil, J. Rheinheimer & H.-P. Fiedler. J. Antibiotics 57: 707-714, 2004

Höltzel, A.; D.G. Schmid, G.J. Nicholson, P. Krastel, A. Zeeck, K. Gebhardt, H.-P. Fiedler & G. Jung. J. Antibiotics 57: 715-720, 2004

Aspochalasin Z

Producing organism: *Aspergillus niveus* LU 9575

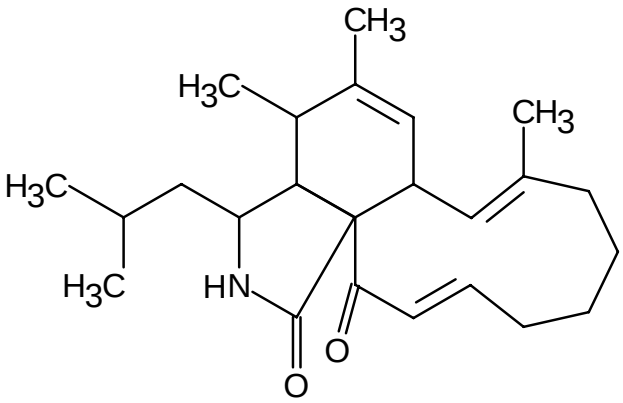


Habitat: endosymbiotic; gut from a *Trichoniscidae*

Screening method: HPLC-DAD

Biological activity: antitumor

Structure:



References:

Gebhardt, K.; J. Schimana, A. Höltzel, K. Dettner, S. Draeger, W. Beil, J. Rheinheimer & H.-P. Fiedler. J. Antibiotics 57: 707-714, 2004

Höltzel, A.; D.G. Schmid, G.J. Nicholson, P. Krastel, A. Zeeck, K. Gebhardt, H.-P. Fiedler & G. Jung. J. Antibiotics 57: 715-720, 2004

Atacamycins A–C

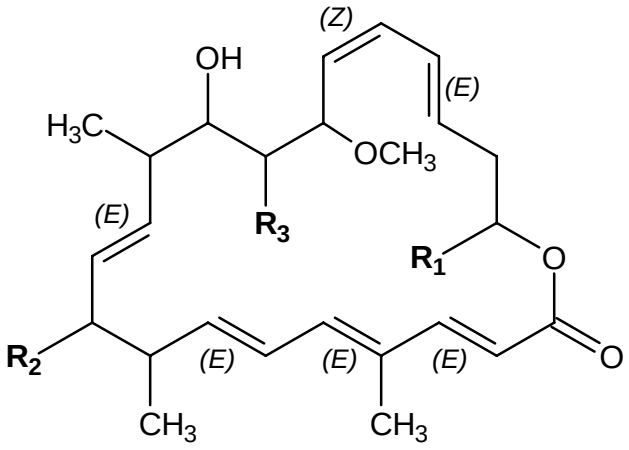
Producing organism: *Streptomyces* sp. C38

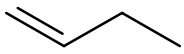
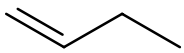
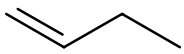
Habitat: terrestrial; hyper-arid soil from the Atacama Desert, Salar de Atacama, Chile

Screening method: HPLC-DAD

Biological activity: antitumor, inhibitors of phosphodieserase

Structures:



	R_1	R_2	R_3
A		OCH_3	OH
B		H	OH
C		H	H

Reference:

Nachtigall, J.; A. Kulik, S. Helaly, A.T. Bull, M. Goodfellow, J.A. Asenjo, A. Maier, J. Wiese, J.F. Imhoff, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics 64: 775-780, 2011

Aurachines Q and R

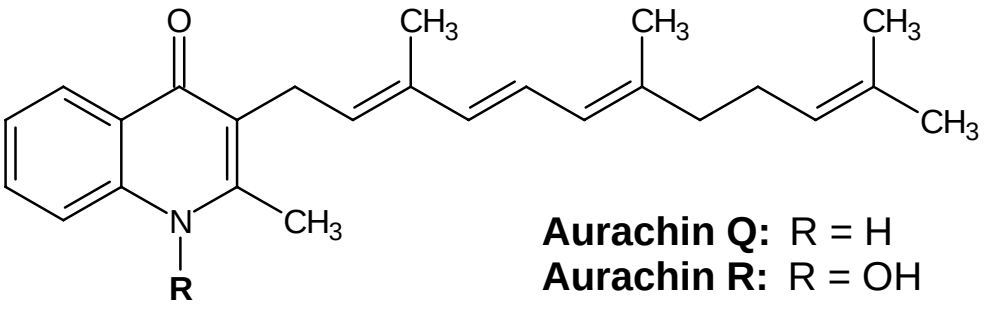
Producing organism: *Rhodococcus* sp. Acta 2259

Habitat: activated sludge; Milcote Pilot Sewage Treatment Plant, Stratford-upon-Avon, UK

Screening method: HPLC-DAD

Biological activity: inhibitor of glycogen synthase kinase 3-beta

Structures:

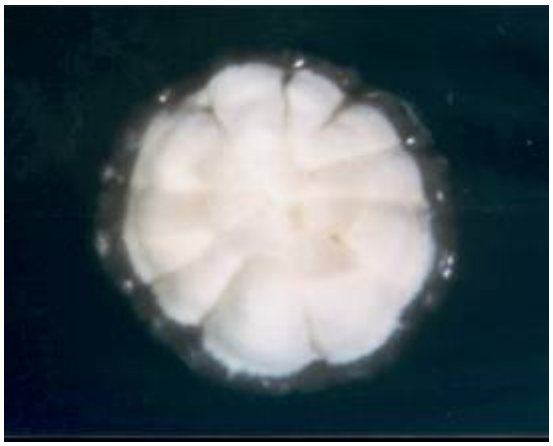


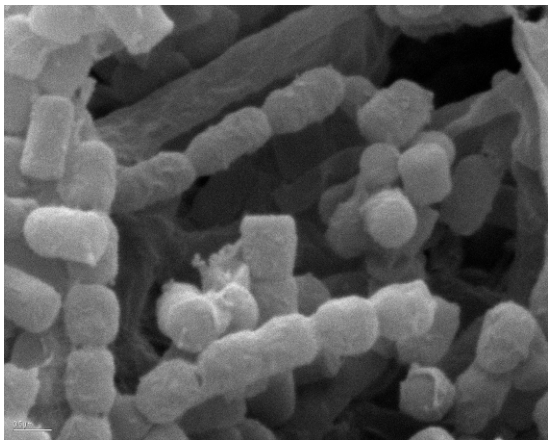
Reference:

Nachtigall, J.; K. Schneider, G. Nicholson, M. Goodfellow, H. Zinecker, J.F. Imhoff, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics 63: 567-569, 2010

Auxofuran

Producing organism: *Streptomyces* sp.AcH 505



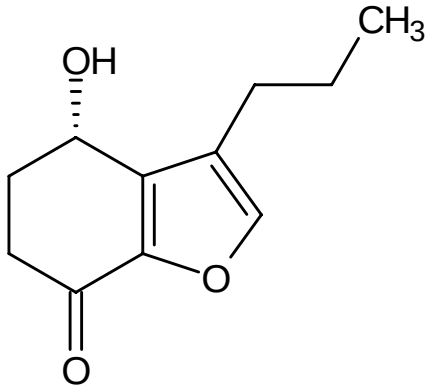


Habitat: terrestrial; rhizosphere of Norway spruce, Haigerloch, Germany

Screening method: HPLC-DAD

Biological activity: growth stimulating factor for symbiotic fungi

Structure:

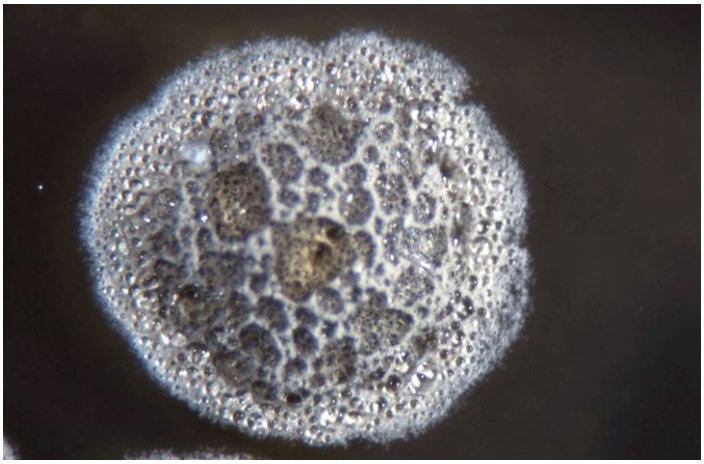


Reference:

Riedlinger, J.; S.D. Schrey, M.T. Tarkka, R. Hampp, M. Kapur & H.-P. Fiedler. Appl. Environ. Microbiol. 72: 3550-3557, 2006

Bagremycins A and B

Producing organism: *Streptomyces* sp. Tü 4128

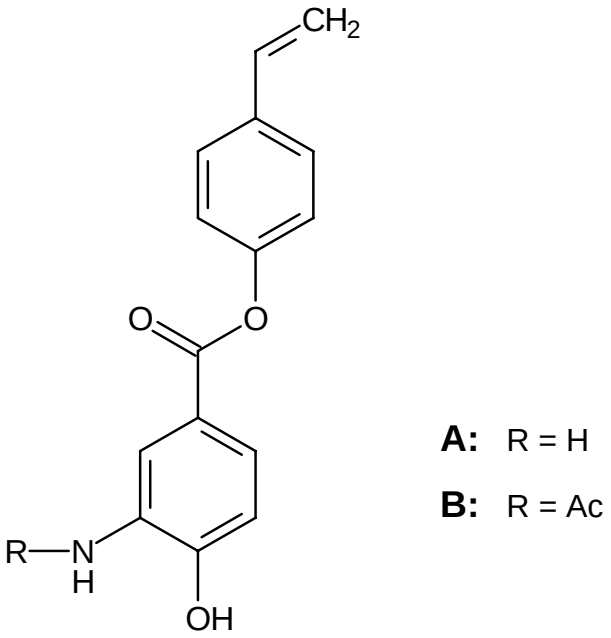


Habitat: terrestrial; Java, Indonesia

Screening method: HPLC-DAD

Biological activity: antibacterial, antifungal

Structures:



A: R = H

B: R = Ac

Reference:

Bertasso, M.; M. Holzenkämpfer, A. Zeeck, F. Dall'Antonia & H.-P. Fiedler. J. Antibiotics 54: 730-736, 2001

Bendigoles A–C

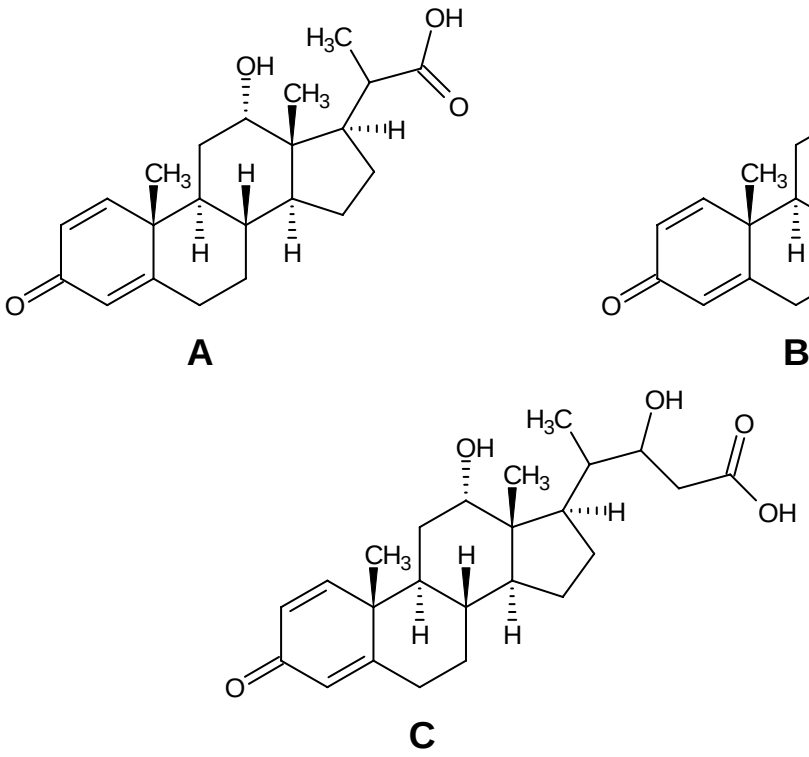
Producing organism: *Gordonia australis* Acta 2299

Habitat: activated sludge; Bendigo, Australia

Screening method: HPLC-DAD

Biological activity: binding activity to human progesterone and androgen receptor

Structures:

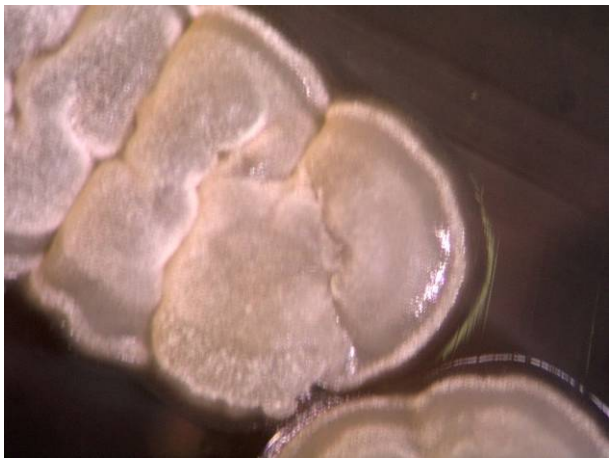


Reference:

Schneider, K.; E. Graf, E. Irran, G. Nicholson, F.M. Stainsby, M. Goodfellow, S.A. Borden, S. Keller, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics 61: 356-364, 2008

Benzoxacystol

Producing organism: *Streptomyces* sp. NTK 935

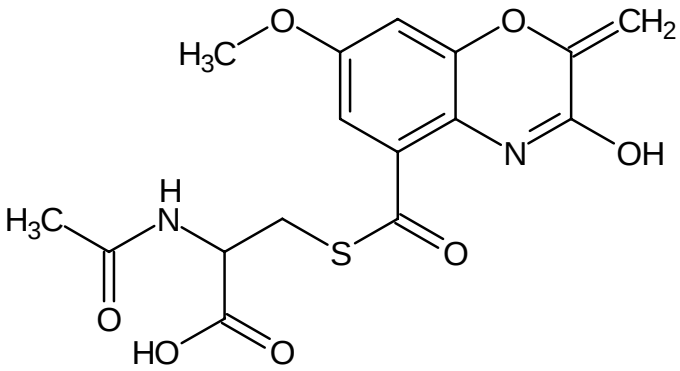


Habitat: marine; sediment –3814 m, Canary Basin, Atlantic Ocean

Screening method: HPLC-DAD

Biological activity: inhibitor of glycogen synthase kinase 3β and acetylcholin esterase

Structure:

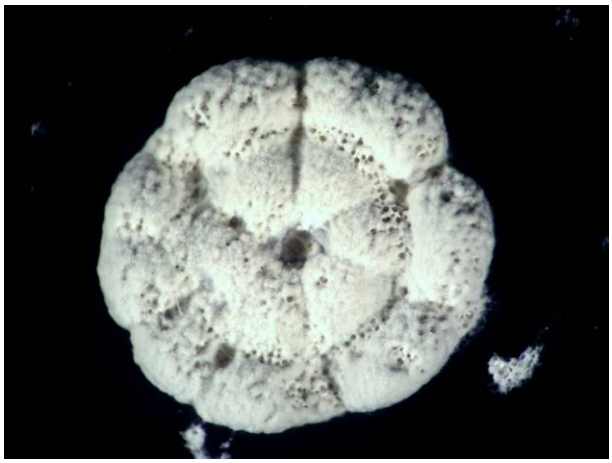


Reference:

Nachtigall, J.; K. Schneider, C. Bruntner, A.T. Bull, M. Goodfellow, H. Zinecker, J.F. Imhoff, G. Nicholson, E. Irran, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics 64: 453-457, 2011

Bhimamycins F, H and I

Producing organism: *Streptomyces* sp. AK 671

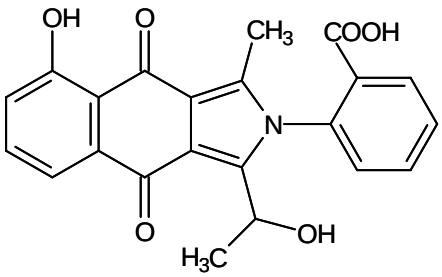


Habitat: terrestrial; Hamsterley Forest, Northumberland, UK

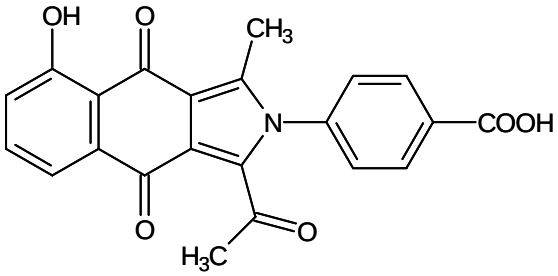
Screening method: HPLC-DAD

Biological activity: antibacterial (H, I), inhibitors of phosphodiesterase 4 (H, I) and glycogen synthase kinase-3β (H)

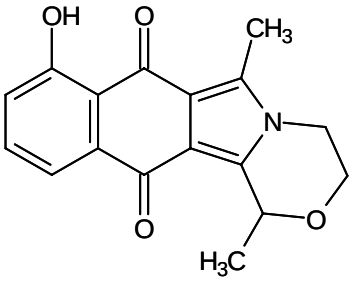
Structures:



Bhimamycin F



Bhimamycin H



Bhimamycin I

Reference:

Jetter, P.; C. Steinert, M. Knauer, G. Zhang, T. Bruhn, J. Wiese, J.F. Imhoff, H.-P. Fiedler & G. Bringmann. J. Antibiotics in press, 2013

Caboxamycin

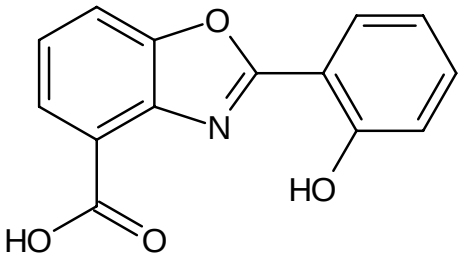
Producing organism: *Streptomyces* sp. NTK 937

Habitat: marine; sediment –3814 m, Canary Basin, Atlantic Ocean

Screening method: HPLC-DAD

Biological activity: antibacterial, antitumor, phosphodiesterase inhibitor

Structure:



Reference:

Hohmann, C.; K. Schneider, C. Bruntner, E. Irran, G. Nicholson, A.T. Bull, A.L. Jones, R. Brown, J.E.M. Stach, M. Goodfellow, W. Beil, M. Krämer, J.F. Imhoff, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics 62: 99-104, 2009

Dermacozines A–L

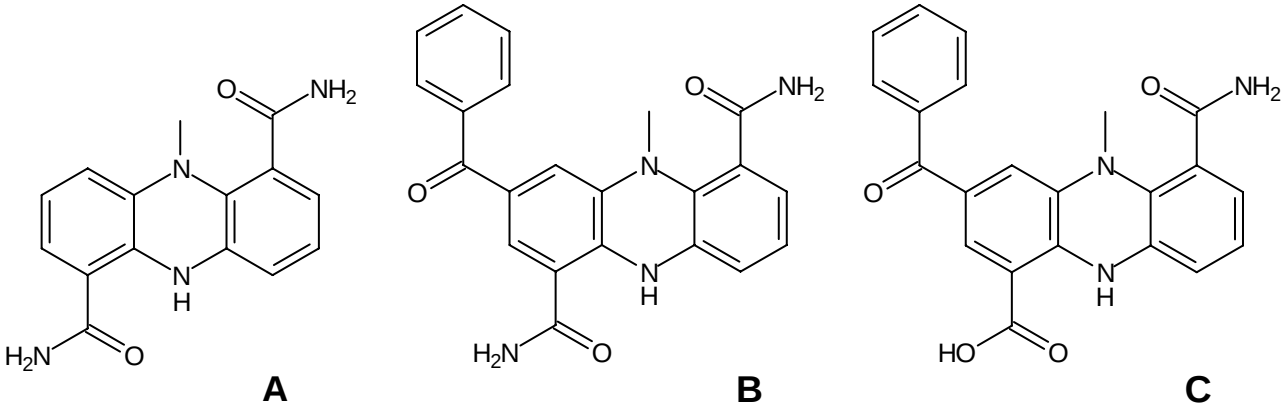
Producing organism: *Dermacoccus abyssi* MT1.1, *Dermacoccus* sp. MT1.2

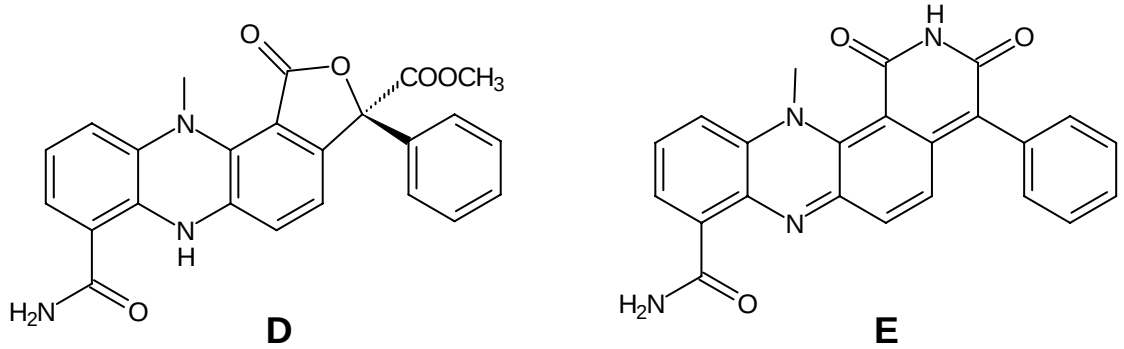
Habitat: marine; sediment –11,898 m, Challenger Deep, Mariana Trench, Pacific Ocean

Screening method: HPLC-DAD

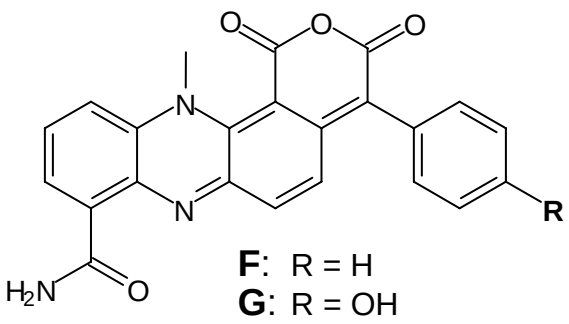
Biological activity: antioxidant

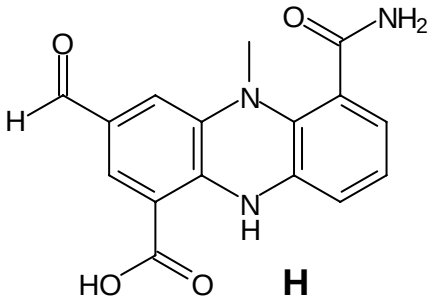
Structures:



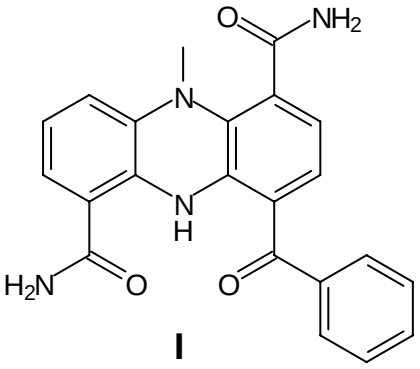


Dermacozines A–L

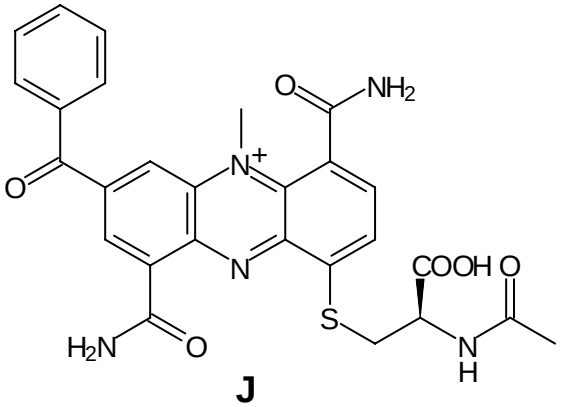




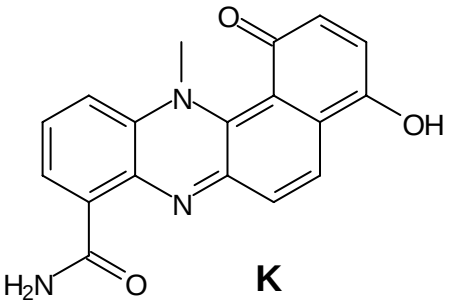
H



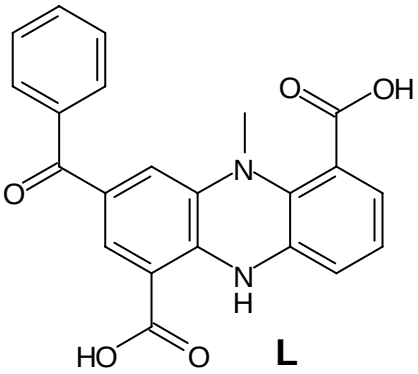
I



J



K



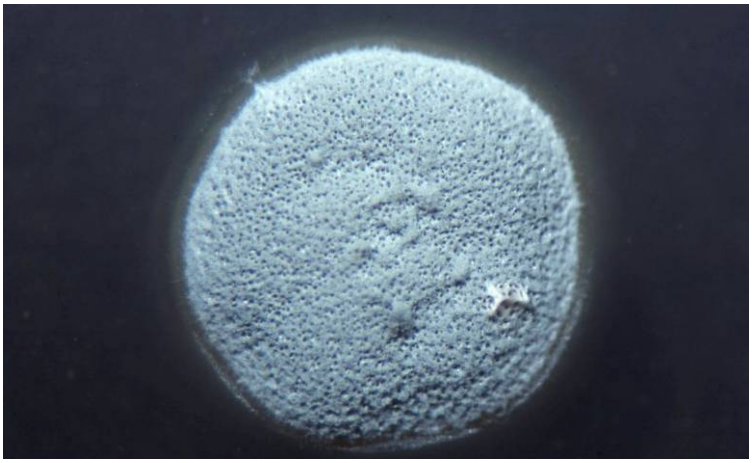
L

Reference:

Abdel-Mageed, W.M.; B.F. Milne, M. Wagner, M. Schumacher, P. Sandor, W. Pathom-aree, M. Goodfellow, A.T. Bull, K. Horikoshi, R. Ebel, M. Diedrich, H.-P. Fiedler & M. Jaspars. Org. Biomol. Chem. 8: 2352-2362, 2010

(2*E*,4*Z*)-Decadienoic Acid
(2*E*,4*Z*,7*Z*)-Decatrienoic Acid

Producing organism: *Streptomyces viridochromogenes* Tü 6105

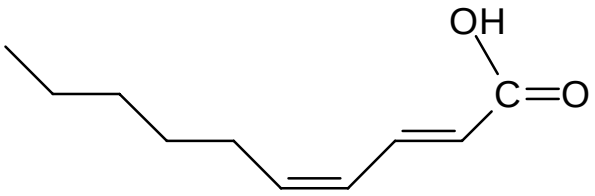


Habitat: terrestrial; Cape Coast, Ghana

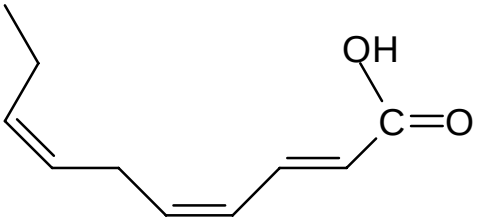
Screening method: HPLC-DAD

Biological activity: herbicidal

Structures:



2*E*,4*Z*-Decadienoic acid



2*E*,4*Z*,7*Z*-Decatrienoic acid

Reference:

Maier, A.; J. Müller, P. Schneider, H.-P. Fiedler, I. Groth, F.S.K. Tayman, F. Teltschik, C. Günther & G. Bringmann. Pestic. Science 55: 733-739, 1999

Dioxolides

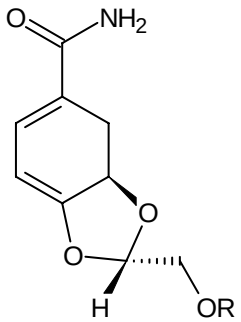
Producing organism: *Streptomyces tendae* Tü 4042

Habitat: terrestrial; Alice Springs, Australia

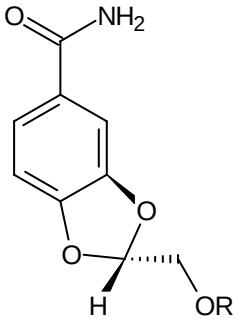
Screening method: HPLC-DAD

Biological activity: none

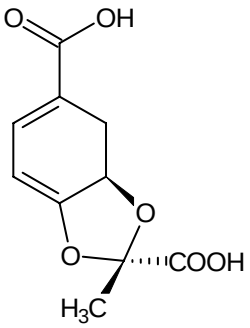
Structures:



Dioxolide A R = H
Dioxolide B R = $COCH_3$



Dehydrodioxolide A R = H
Dehydrodioxolide B R = $COCH_3$



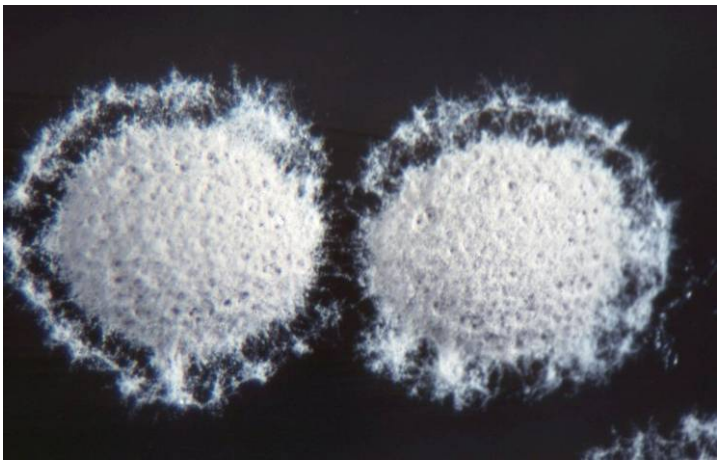
Dioxolide D

Reference:

Blum, S.; I. Groth, J. Rohr & H.-P. Fiedler. J. Basic Microbiol. 36: 19-25, 1996

Echinoserine

Producing organism: *Streptomyces tendae* Tü 4031

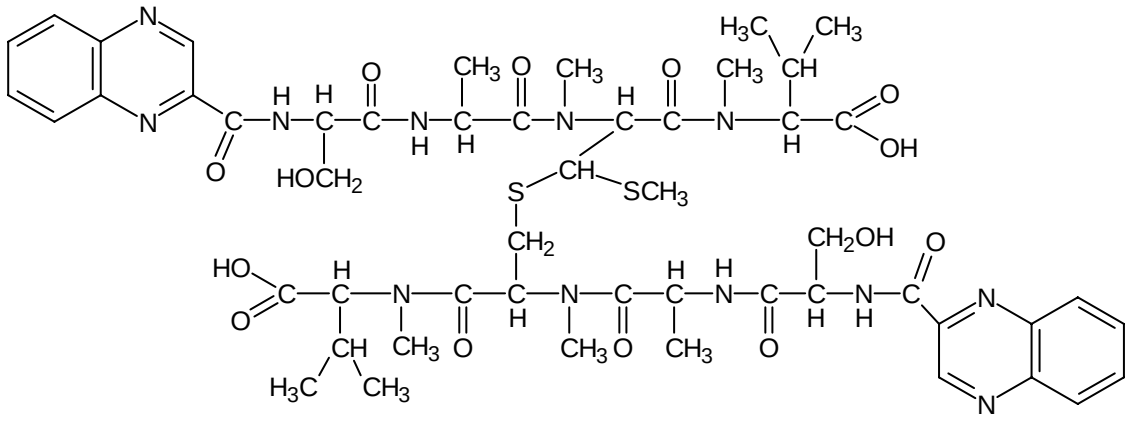


Habitat: terrestrial; Alice Springs, Australia

Screening method: HPLC-DAD

Biological activity: antibacterial

Structure:



Reference:

Blum, S.; H.-P. Fiedler, I. Groth, C. Kempter, H. Stephan, G. Nicholson, J.W. Metzger & G. Jung. J. Antibiotics 48: 619-625, 1995

Elaiomycins B and C

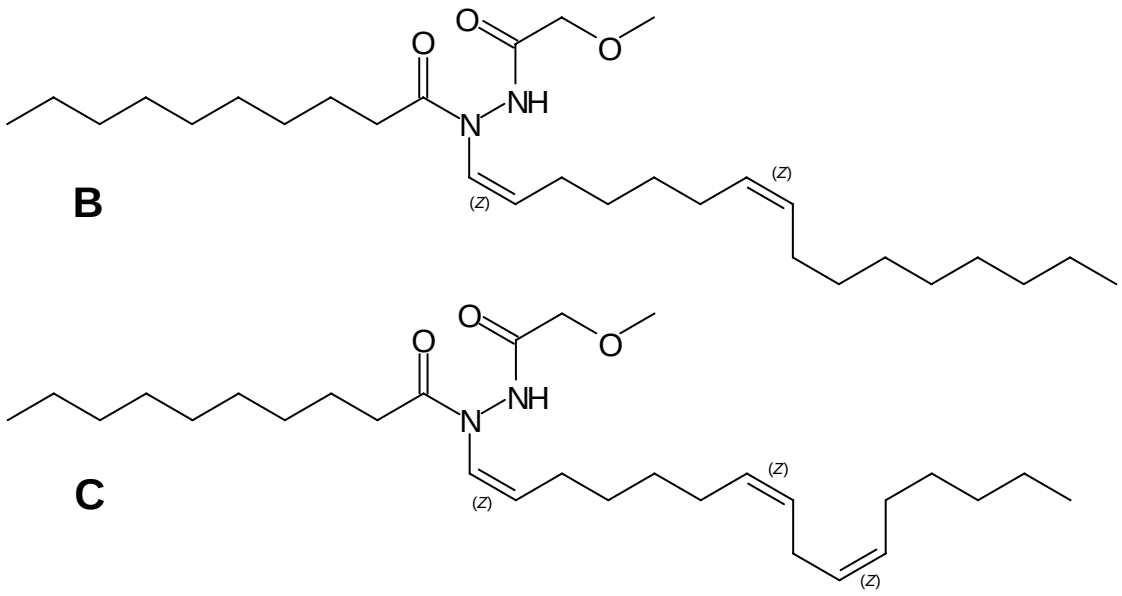
Producing organism: *Streptomyces* sp. BK 190

Habitat: terrestrial; hay meadow soil, Cockle Park, Northumberland, UK

Screening method: HPLC-DAD

Biological activity: antibacterial, inhibitors of phosphodiesterase and acetylcholinesterase

Structures:



References:

Kim, B.-Y.; S. Willbold, A. Kulik, S.E. Helaly, H. Zinecker, J. Wiese, J.F. Imhoff, M. Goodfellow, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics 64: 595-597, 2011

Helaly, S.E.; A. Pesic, H.-P. Fiedler & R.D. Süssmuth. Org. Lett. 13: 1052-1054, 2011

Elaiomycins K and L

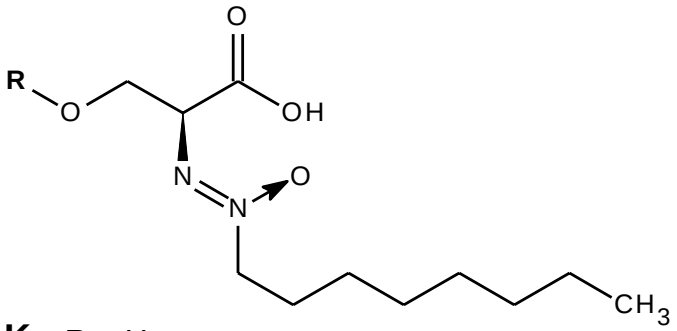
Producing organism: *Streptomyces* sp. Tü 6399

Habitat: terrestrial; rhizosphere of Norway spruce, Rammert Forest, Germany

Screening method: HPLC-DAD

Biological activity: antibacterial

Structures:



K: R = H

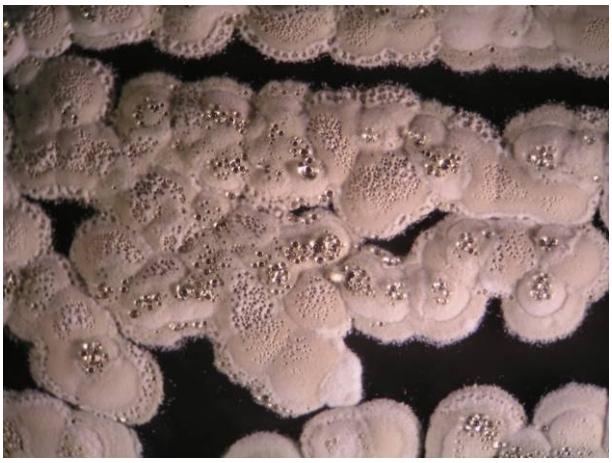
L: R = CH_3

References:

Manderscheid, N.; S.E. Helaly, A. Kulik, J. Wiese, J.F. Imhoff, H.-P. Fiedler & R.D. Süssmuth. J. Antibiotics 66: 85-88, 2013

Elloxazinones A and B

Producing organism: *Streptomyces griseus* Acta 2871

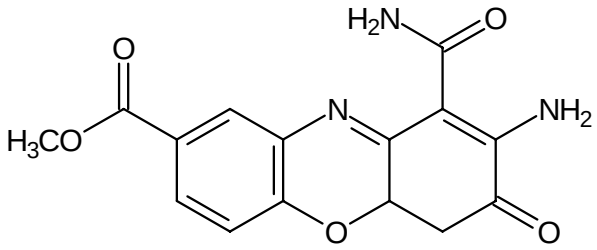


Habitat: terrestrial; steel waste tip soil, Consett, UK

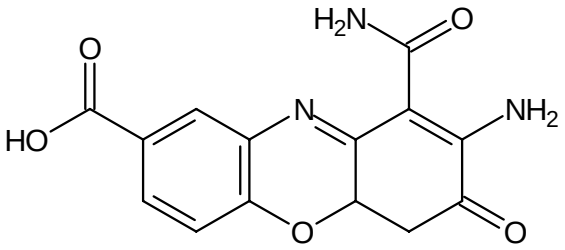
Screening method: HPLC-DAD

Biological activity: antitumor

Structures:



A



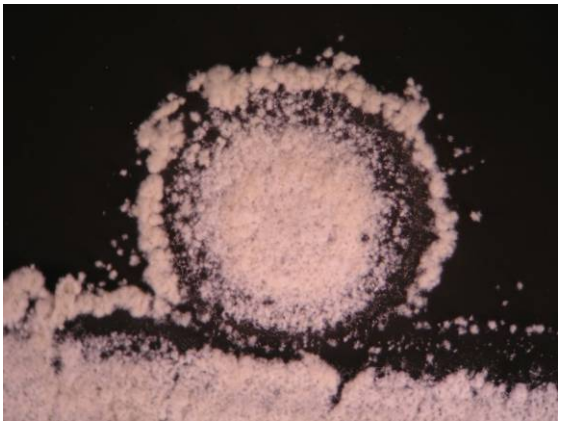
B

Reference:

Graf, E.; K. Schneider, G. Nicholson, M. Ströbele, A.L. Jones, M. Goodfellow, W. Beil, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics 60: 277-284, 2007

Endophenazines A–D

Producing organism: *Streptomyces anulatus* LU 9663, LU 9843, LU 9958, LU 10099

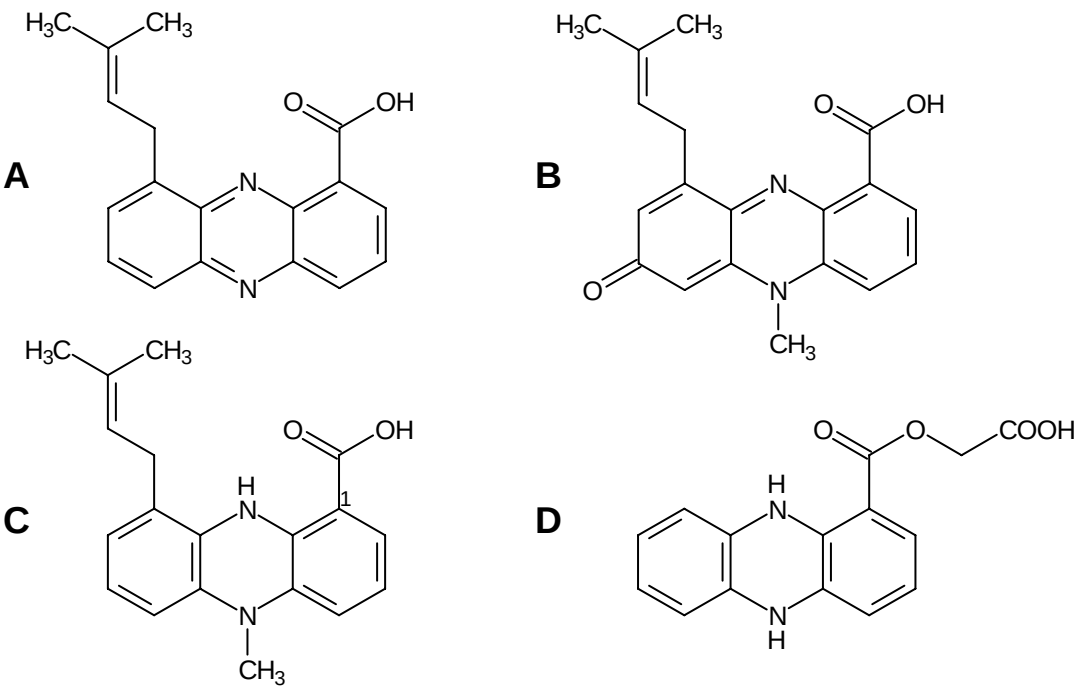


Habitat: endosymbiotic; gut of wood-louse Gen. spec. (LU 9663), gut of leaf-beatle *Exosoma lusitanica* (LU 9843), gut of millipede *Glomeris* spec. (LU 9958), gut of wood-louse *Armadillidium* sp. (LU 10099)

Screening method: HPLC-DAD

Biological activity: antibacterial, antifungal, herbicidal

Structures:



References:

Gebhardt, K.; J. Schimana, P. Krastel, K. Dettner, J. Rheinheimer, A. Zeeck & H.-P. Fiedler: J. Antibiotics 55: 794-800, 2002.

Krastel, P.; A. Zeeck, K. Gebhardt, H.-P. Fiedler & J. Rheinheimer. J. Antibiotics 55: 801-806, 2002

Fluostatins C–E

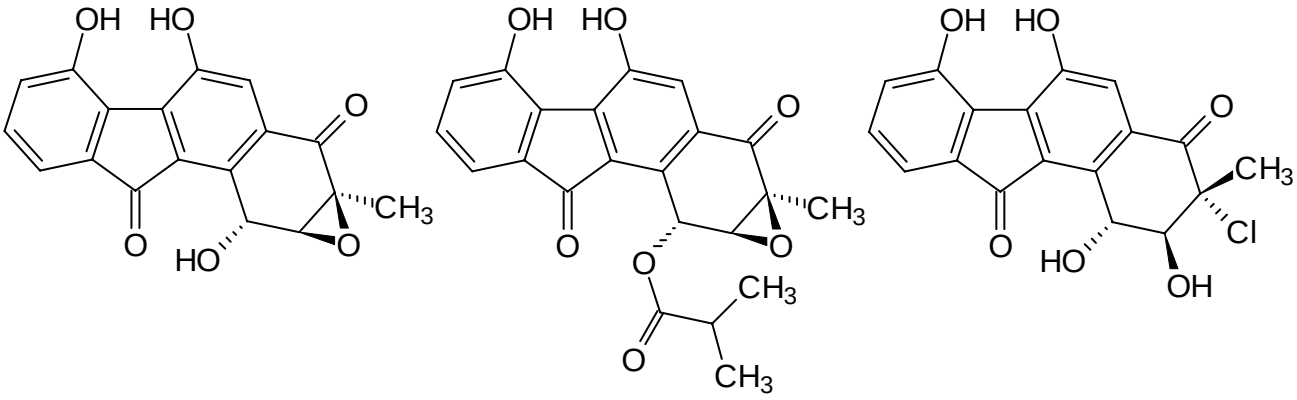
Producing organism: *Streptomyces lavendulae* Acta 1383

Habitat: terrestrial, rhizosphere; Kaisariani area, Greece

Screening method: HPLC-DAD

Biological activity: antitumor

Structures:



C **D** **E**

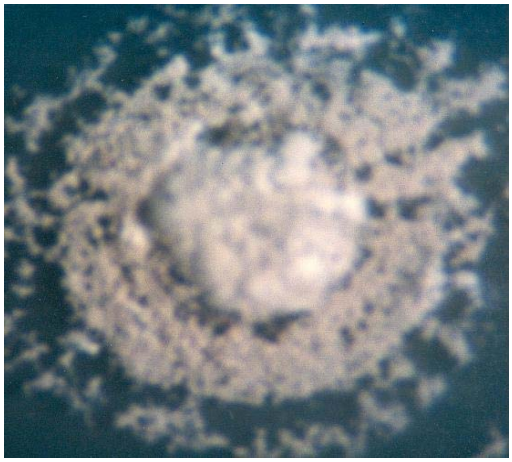
References:

Baur, S.; J. Niehaus, A.D. Karagouni, E.A. Katsifas, K. Chalkou, C. Meintanis, A. Jones, M. Goodfellow, A.C. Ward, W. Beil, K. Schneider, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics 59: 293-297, 2006

Schneider, K.; G. Nicholson, M. Ströbele, S. Baur, J. Niehaus, H.-P. Fiedler & R.D. Süssmuth. J. Antibiotics 59: 105-109, 2006

Fogacin

Producing organism: *Streptomyces* sp. Tü 6319

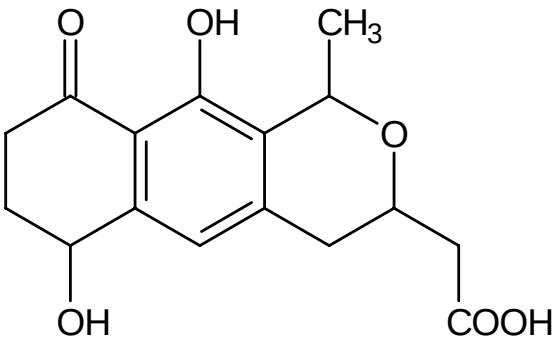


Habitat: terrestrial; Fogaras, Romania

Screening method: HPLC-DAD

Biological activity: antitumor

Structure:



Reference:

Radzom, M.; A. Zeeck, N. Antal & H.-P. Fiedler: J. Antibiotics 59: 315-317, 2006

Fomannoxin Acids DFA, MFA-1 and MFA-2

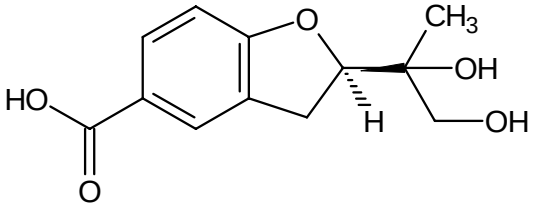
Producing organism: *Streptomyces* sp. AcH 505

Habitat: terrestrial; rhizospheric soil, Schönbuch Forest, Germany

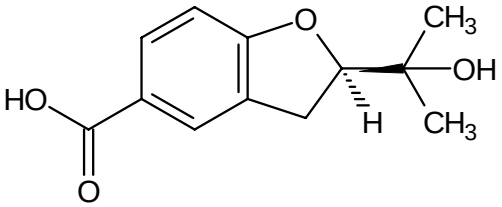
Screening method: HPLC-DAD

Biological activity: inactive conversion products of the fungal phytotoxin fomannoxin from *Heterobasidion* sp.

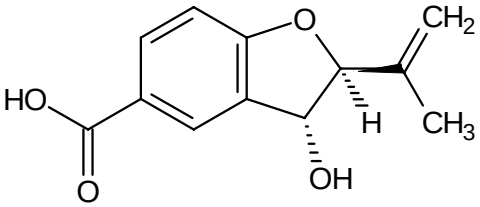
Structures:



DFA
(Dihydroxy-Fomannoxin Acid)



MFA-1
(Monohydroxy-Fomannoxin Acid-1)



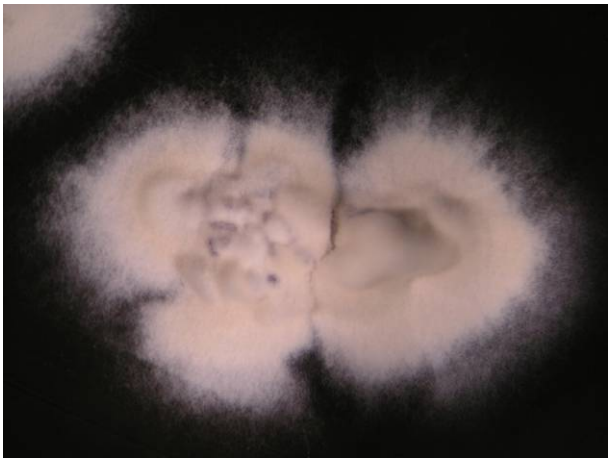
MFA-2
(Monohydroxy-Fomannoxin Acid-2)

Reference:

Horlacher, N.; J. Nachtigall, D. Schulz, R.D. Süssmuth, R. Hampp, H.-P. Fiedler & S. Schrey. J. Chem. Ecol. DOI: 10.1007/s10886-013-0290-3, 2013

Frigocyclinone

Producing organism: *Streptomyces griseus* NTK 97

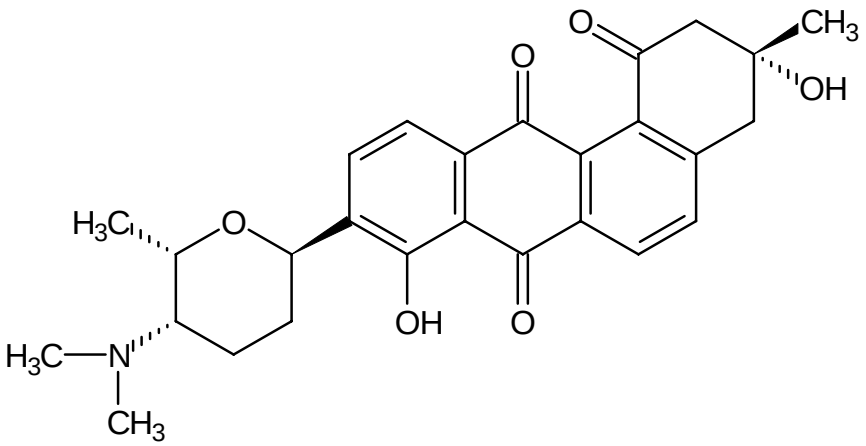


Habitat: terrestrial; Terra Nova Bay, Antarctica

Screening method: HPLC-DAD

Biological activity: antibacterial

Structure:

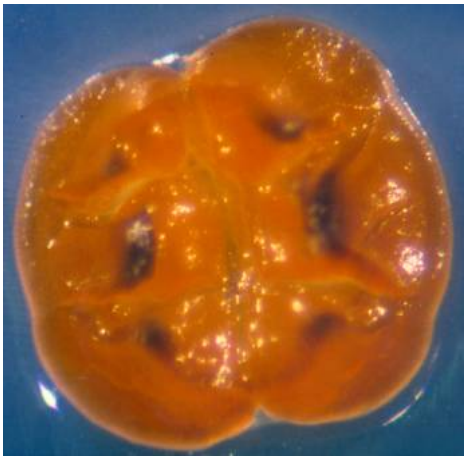


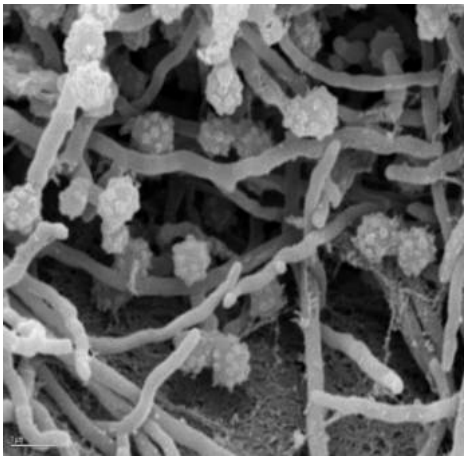
Reference:

Bruntner,C.; T. Binder, W. Pathom-aree, M. Goodfellow, A.T. Bull, O. Potterat, C. Puder, S. Hörer, A. Schmid, W. Bolek, K. Wagner, G. Mihm & H.-P. Fiedler. J. Antibiotics 58: 346-349, 2005

Galtamycin B

Producing organism: *Micromonospora* sp. Tü 6368



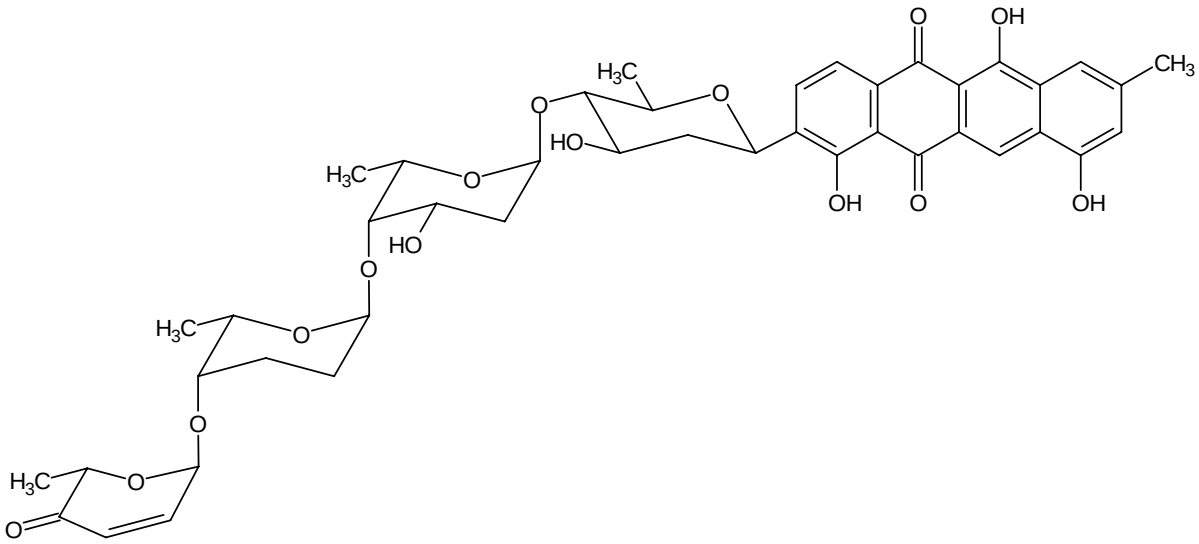


Habitat: terrestrial, Rety, Romania

Screening method: HPLC-DAD

Biological activity: antitumor

Structure:



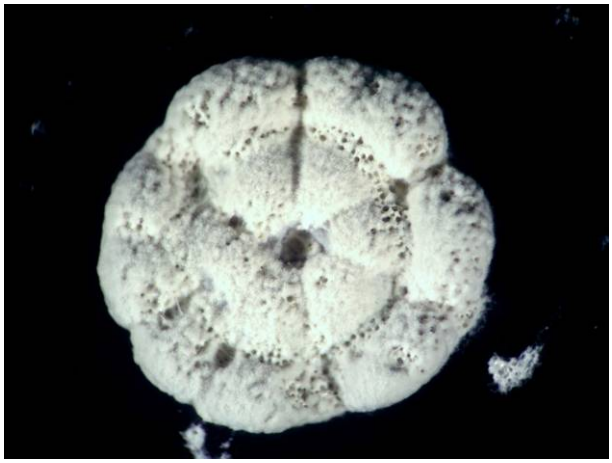
References:

Antal, N.; H.-P. Fiedler, E. Stackebrandt, W. Beil, K. Ströch & A. Zeeck. J. Antibiotics 58: 95-102, 2005

Ströch, K.; A. Zeeck, N. Antal & H.-P. Fiedler. J. Antibiotics 58: 103-110, 2005

Genoketides A1 and A2, Prechrysophanol-Glucuronide and Chrsophanol-Glucuronide

Producing organism: *Streptomyces* sp. AK 671

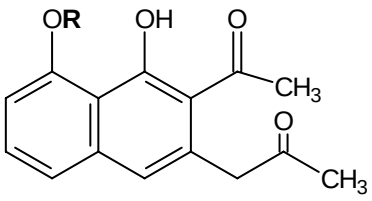


Habitat: terrestrial; Hamsterley Forest, Northumberland, UK

Screening method: HPLC-DAD

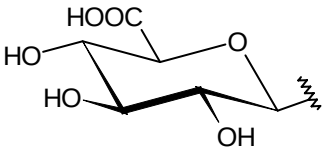
Biological activity: antitumor (genoketetide B2)

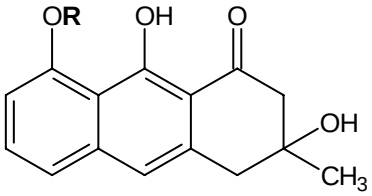
Structures:



Genoketide A1: R = H

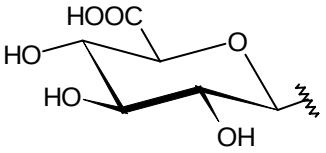
Genoketide A2: R =

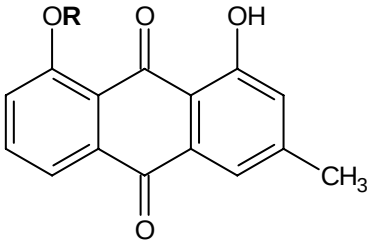




Prechrysophanol-Glucuronide

R =





Chrysophanol-Glucuronide

Reference:

Fiedler, H.-P.; A. Dieter, T.A.M. Gulder, I. Kajahn, A. Hamm, R. Brown, A.L. Jones, M. Goodfellow, W.E.G. Müller & G. Bringmann. J. Antibiotics 61: 464-473, 2008

Gephyromycin

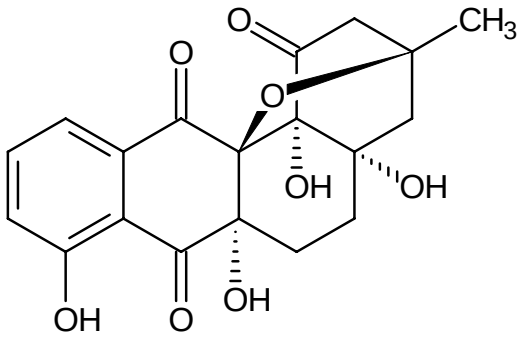
Producing organism: *Streptomyces griseus* NTK 14

Habitat: terrestrial; Terra Nova Bay, Antarctica

Screening method: HPLC-DAD

Biological activity: glutaminergic activity towards neuronal cells

Structure:

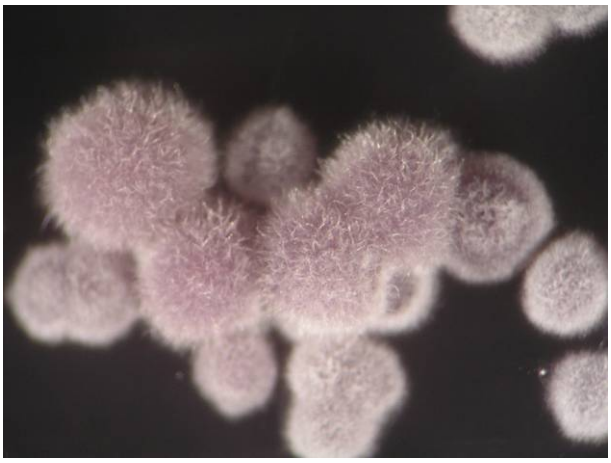


Reference:

Bringmann, G.; G. Lang, K. Maksimenka, A. Hamm, T.A.M. Gulder, A. Dieter, A.T. Bull, J.E.M. Stach, N. Kocher, W.E.G. Müller & H.-P. Fiedler. Phytochemistry 66: 1365-1372, 2005

Gombapyrones A–D

Producing organism: *Streptomyces griseoruber* Acta 3662

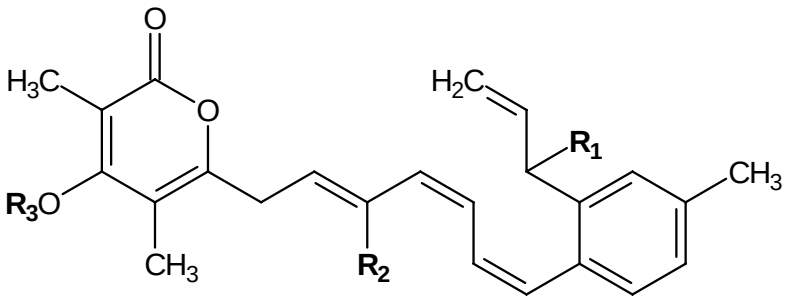


Habitat: terrestrial; rhizosphere of bamboo trees, Gombak, Malaysia

Screening method: HPLC-DAD

Biological activity: inhibitors of protein tyrosine phosphatase 1B and glycogen synthase kinase 3β

Structures:



	R_1	R_2	R_3
A:	OH	CH_3	CH_3
B:	H	CH_3	H
C:	H	H	CH_3
D:	H	CH_3	CH_3

Reference:

Helaly, S.; K. Schneider, J. Nachtigall, S. Vikineswary, G.Y.A. Tan, H. Zinecker, J.F. Imhoff, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics 62: 445-452, 2009

Grecocyclines A and B

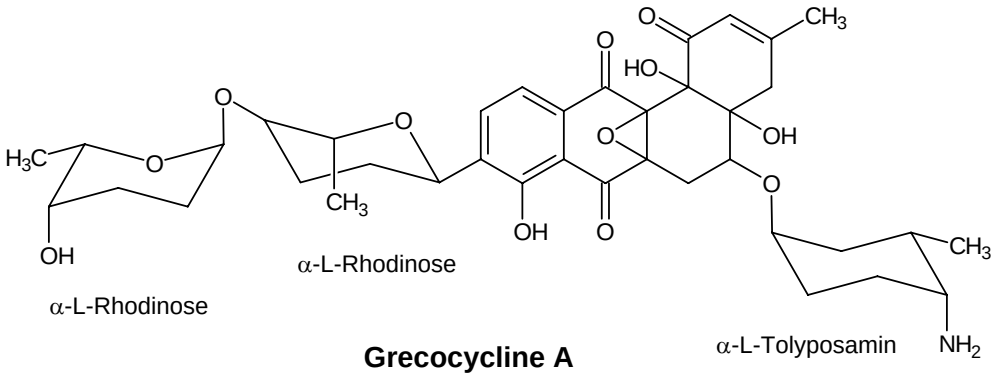
Producing organism: *Streptomyces* sp. Acta 1362

Habitat: terrestrial, rhizosphere; Crete, Greece

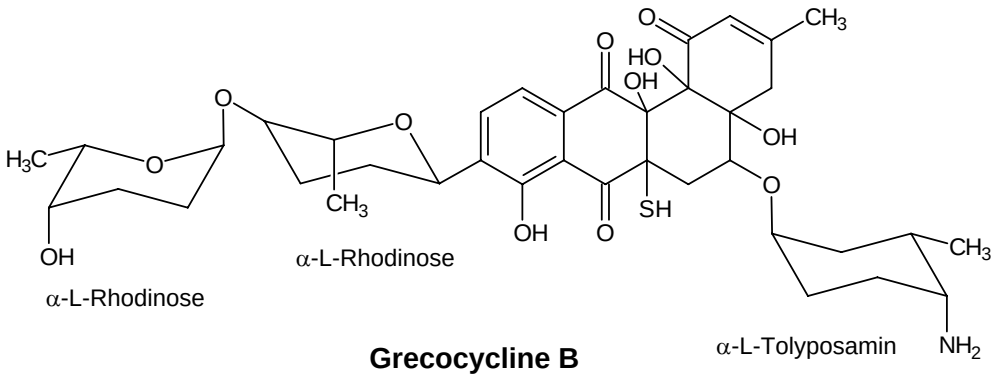
Screening method: HPLC-DAD

Biological activity: cytotoxic (A), protein tyrosine phosphatase 1B inhibiotor (B)

Structures:



Grecocycline A



Grecocycline B

Reference:

Paululat, T.; A. Kulik, H. Hausmann, A.D. Karagouni, H. Zinecker, J.F. Imhoff & H.-P. Fiedler. Eur. J. Org. Chem. 2010: 2344-2350, 2010

Grecoketides A and B

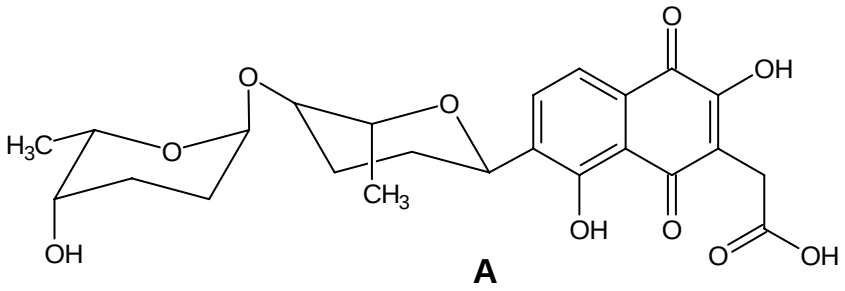
Producing organism: *Streptomyces* sp. Acta 1362

Habitat: terrestrial, rhizosphere; Crete, Greece

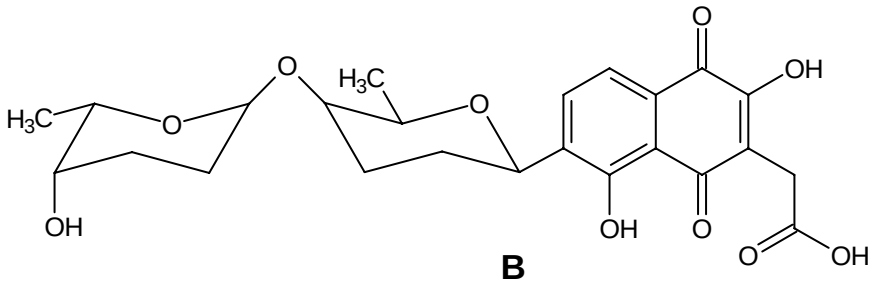
Screening method: HPLC-DAD

Biological activity: none

Structures:



A



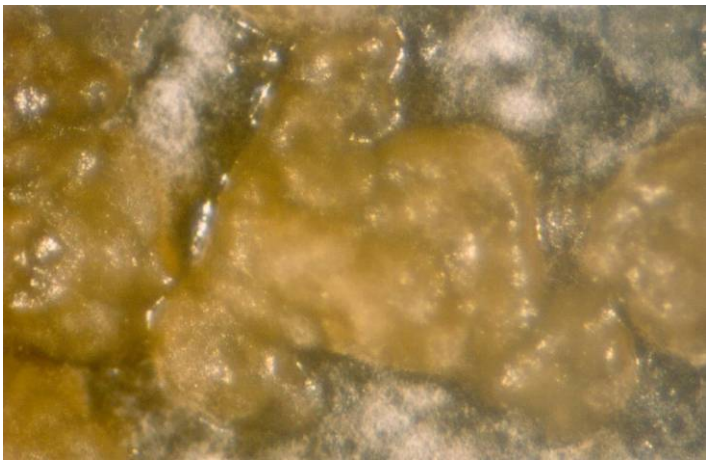
B

Reference:

Paululat, T.; E.A. Katsifas, A.D. Karagouni & H.-P. Fiedler. Eur. J. Org. Chem. 2008: 5283-5288, 2008

1-Hydroxy-4-Methoxy-2-Naphthoic Acid

Producing organism: *Streptosporangium cinnabarinum* NNO 29536

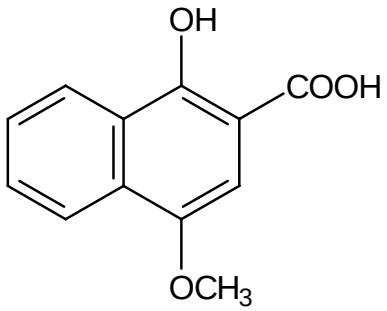


Habitat: terrestrial (ATCC 31213)

Screening method: HPLC-DAD

Biological activity: herbicidal

Structure:

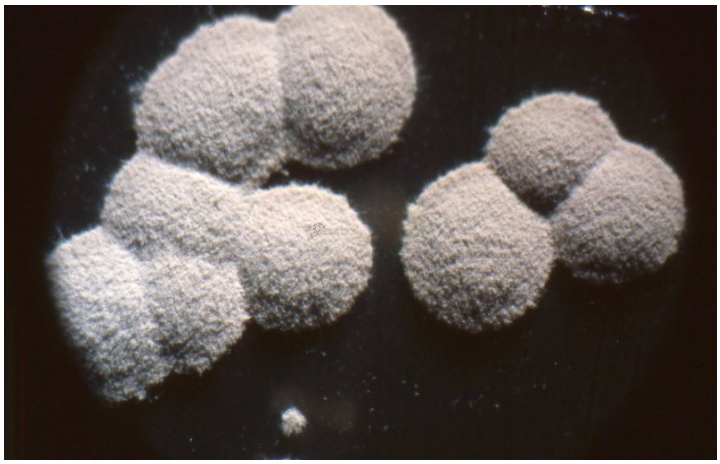


Reference:

Pfefferle, C.; J. Breinholt, H. Gürtler & H.-P. Fiedler. J. Antibiotics 50: 1067-1068, 1997

Juglomycin Z

Producing organism: *Streptomyces tendae* Tü 901

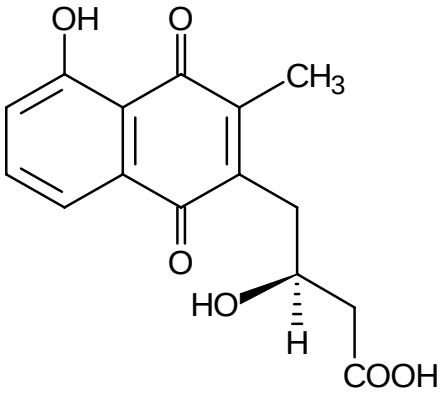


Habitat: terrestrial; Nikko, Japan

Screening method: HPLC-DAD

Biological activity: antibacterial, antifungal

Structure:

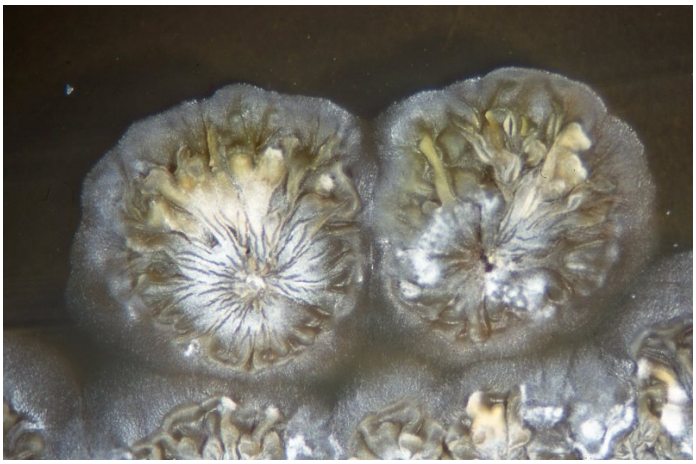


Reference:

Fiedler, H.-P.; A. Kulik, T.C. Schüz, C. Volkmann & A. Zeeck. J. Antibiotics 47: 1116-1122, 1994

Kanchanamycins A, C, D

Producing organism: *Streptomyces olivaceus* Tü 4018

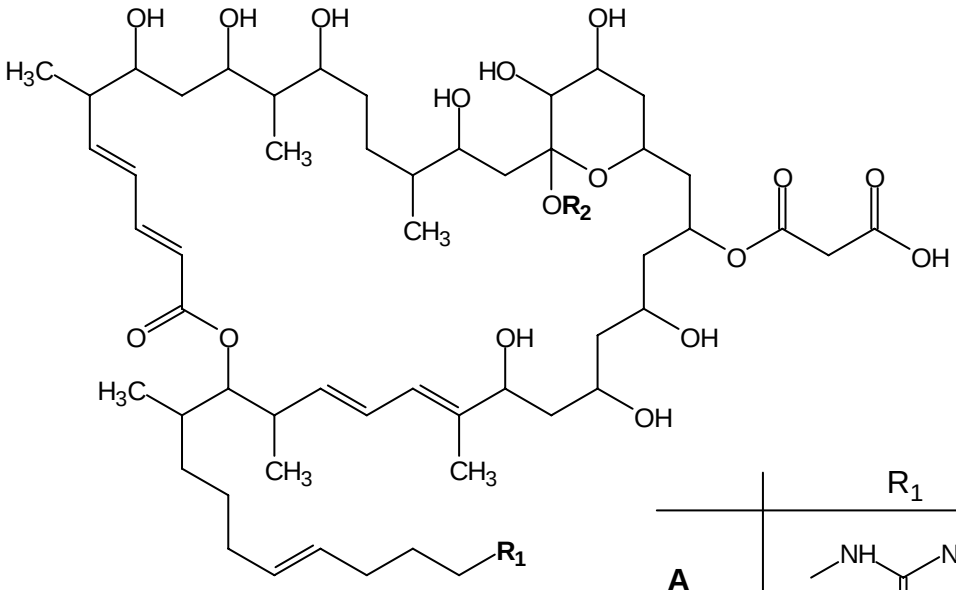


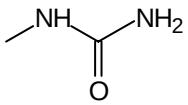
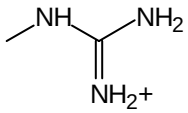
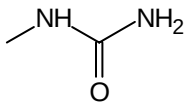
Habitat: terrestrial; Kanchana Buri, Thailand

Screening method: HPLC-DAD

Biological activity: antibacterial, antifungal

Structures:



	R_1	R_2
A		—H
C		—H
D		—CH_3

Kanchanamycins A, C, D

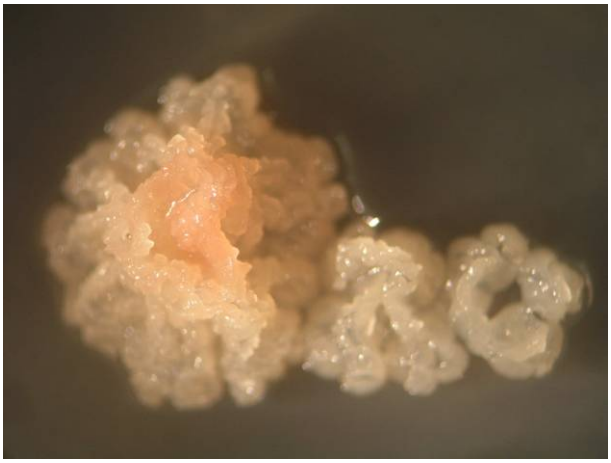
References:

Fiedler, H.-P.; M. Nega, C. Pfefferle, I. Groth, C. Kempter, H. Stephan & J.W. Metzger. J. Antibiotics 49: 101-107, 1996

Stephan, H.; C. Kempter, J.W. Metzger, G. Jung, O. Potterat, C. Pfefferle & H.-P. Fiedler. J. Antibiotics 49: 109-113, 1996

Kyanomycin

Producing organism: *Nonomuria* sp. NN0 22303

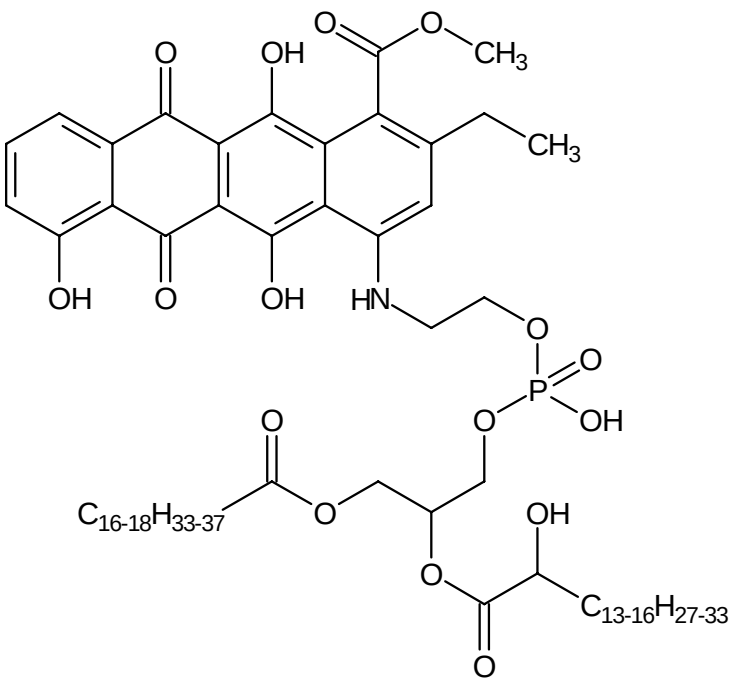


Habitat: terrestrial; India

Screening method: HPLC-DAD

Biological activity: antibacterial

Structure:

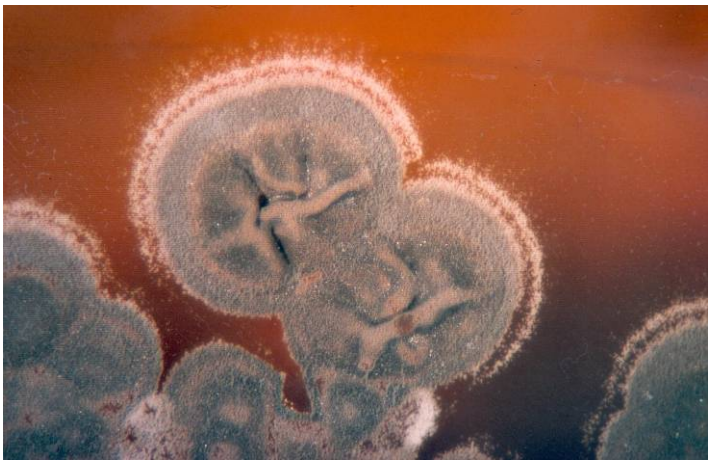


Reference:

Pfefferle, C.; J. Breinholt, C.E. Olsen, R.M. Kroppenstedt, E.M.H. Wellington, H. Gürtler & H.-P. Fiedler. J. Nat. Prod. 63: 295-298, 2000

Lactonamycin Z

Producing organism: *Streptomyces sanglieri* AK 623

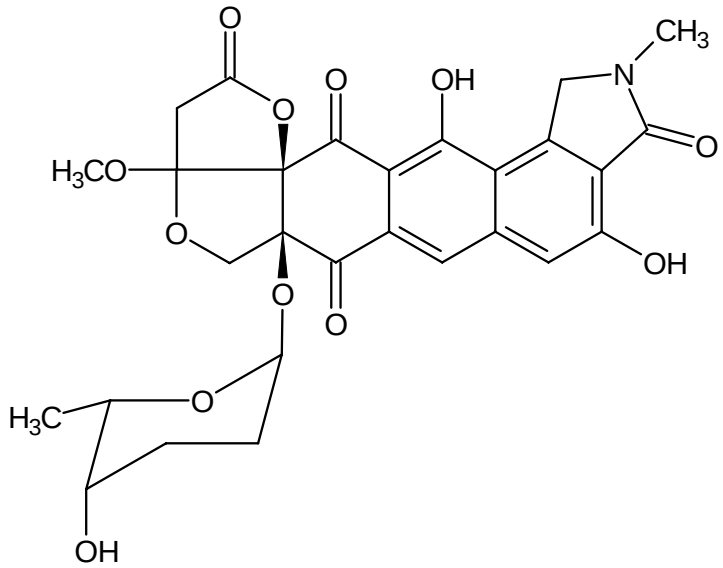


Habitat: terrestrial; Hamsterley Forest, UK

Screening method: HPLC-DAD

Biological activity: antibacterial, antitumor

Structure:



Reference:

Höltzel, A.; A. Dieter, D.G. Schmid, R. Brown, M. Goodfellow, W. Beil, G. Jung & H.-P. Fiedler. J. Antibiotics 56: 1058-1061, 2003

Langkocyclines A1, A2, A3, B1 and B2

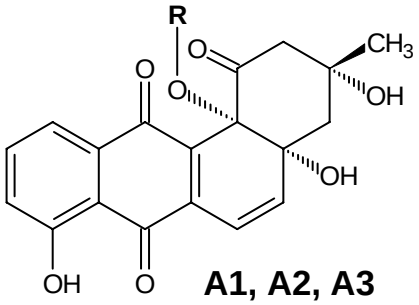
Producing organism: *Streptomyces* sp. Acta 3034

Habitat: terrestrial; rhizospheric soil, Langkawi, Malaysia

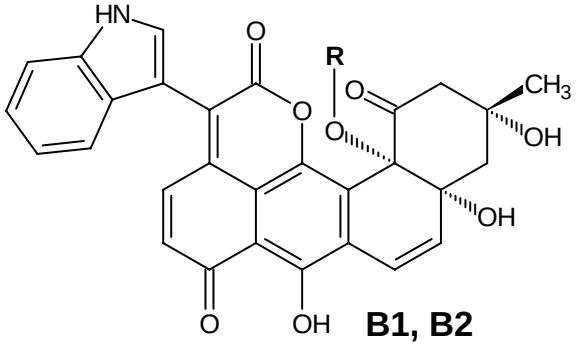
Screening method: HPLC-DAD

Biological activity: antibacterial, antitumor

Structures:

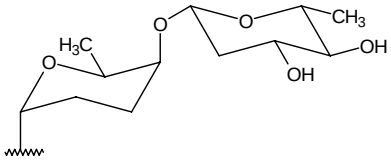


A1, A2, A3

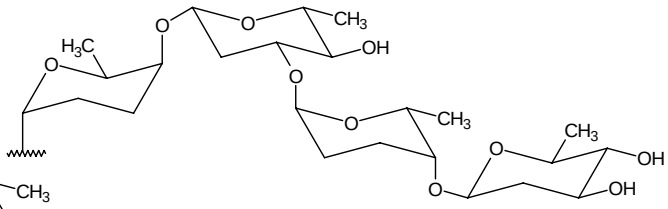


B1, B2

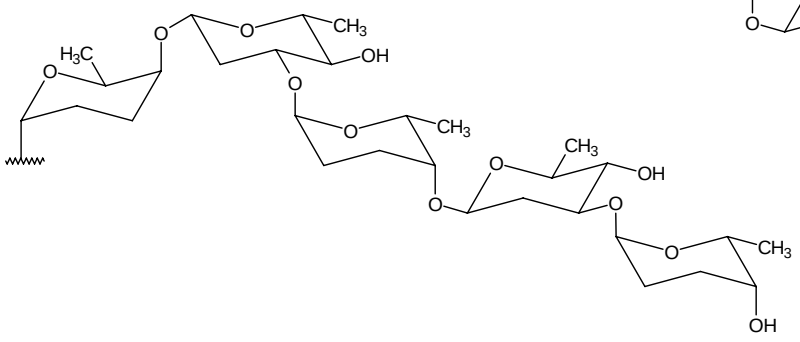
A1: R =



A2: R =
B1: R =



A3: R =
B2: R =



Reference:

Kalyon, B.; G.Y.A. Tan, J.M. Pinto, C.Y. Foo, J. Wiese, J.F. Imhoff, R.D. Süssmuth, V. Sabaratnam & H.-P. Fiedler. J. Antibiotics, DOI:10.1038/ja.2013.53, 2013

Langkolide

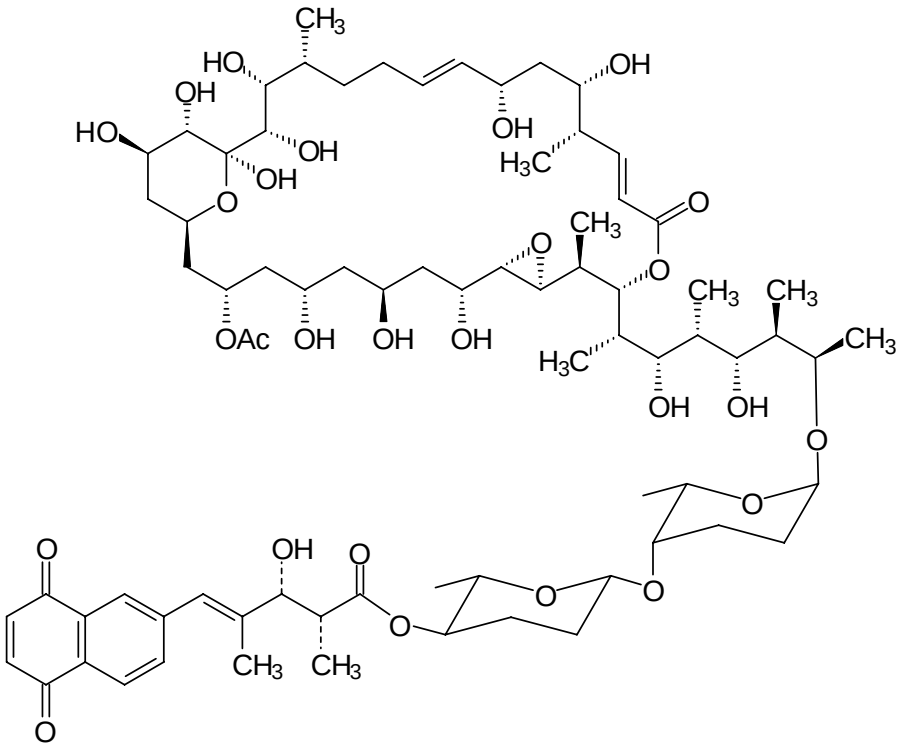
Producing organism: *Streptomyces sp.* Acta 3062

Habitat: terrestrial; rhizospheric soil, Langkawi, Malaysia

Screening method: HPLC-DAD

Biological activity: antifungal, antitumor, inhibitor of phosphodiesterase and glycogen synthase kinase

Structure:

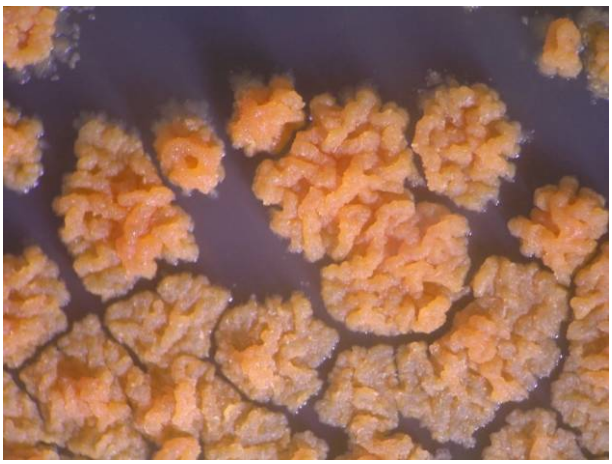


Reference:

Helaly, S.; A. Kulik, H. Zinecker, K. Ramachandaran, G.Y.A. Tan, J.F. Imhoff, R.D. Süssmuth, H.-P. Fiedler & V. Sabaratnam. J. Nat. Prod. 75: 1018-1024, 2012

Lipocarbazoles A1–A4

Producing organism: *Tsukamurella pseudospumae* Acta 1857

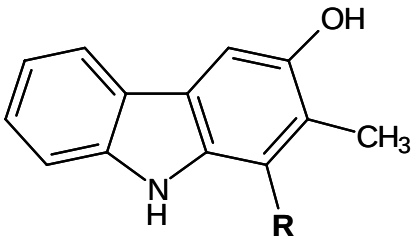


Habitat: activated sludge foam, Stoke Bardolph, UK

Screening method: HPLC-DAD

Biological activity: free radical scavengers, antioxidant

Structures:



A1: R = $(CH_2)_7CH=CHCH_2CH=CHCH_2CH=CHCH_2CH_3$

A2: R = $(CH_2)_7CH=CHCH_2CH=CH(CH_2)_4CH_3$

A3: R = $(CH_2)_7CH=CH(CH_2)_7CH_3$

A4: R = $(CH_2)_{16}CH_3$

Reference:

Schneider, K.; J. Nachtigall, A. Hänchen, G. Nicholson, M. Goodfellow, R.D. Süssmuth & H.-P. Fiedler. J. Nat. Prod. 72: 1768-1772, 2009

Naphthgeranine F

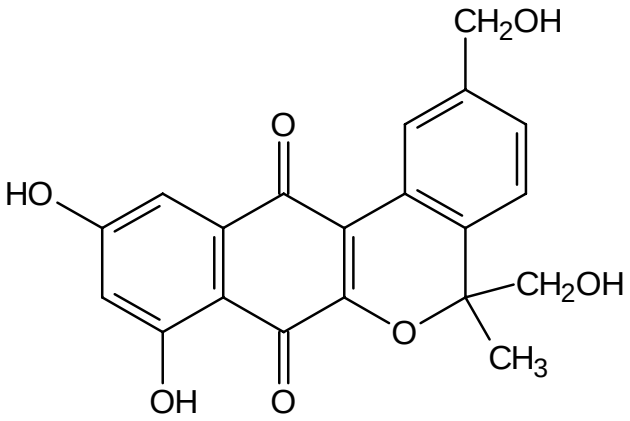
Producing organism: *Streptomyces violaceus* Tü 3556

Habitat: terrestrial; Dakshinkali, Nepal

Screening method: HPLC-DAD

Biological activity: antibacterial, antifungal

Structure:

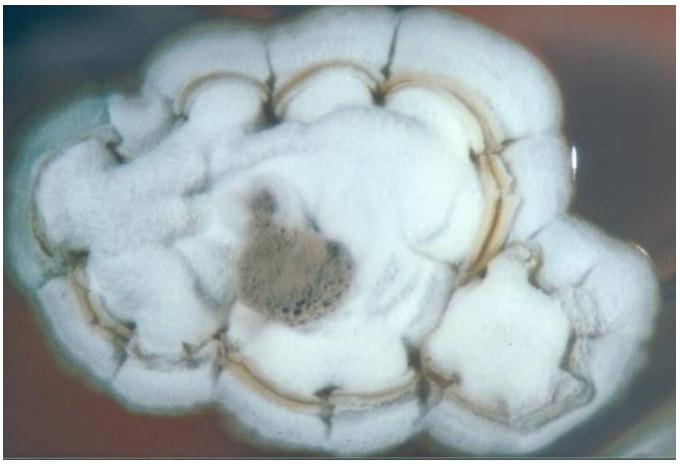


Reference:

Volkmann, C.; U. Hartjen, A. Zeeck & H.-P. Fiedler. J. Antibiotics 48: 522-524, 1995

Nataxazole

Producing organism: *Streptomyces* sp. Tü 6176

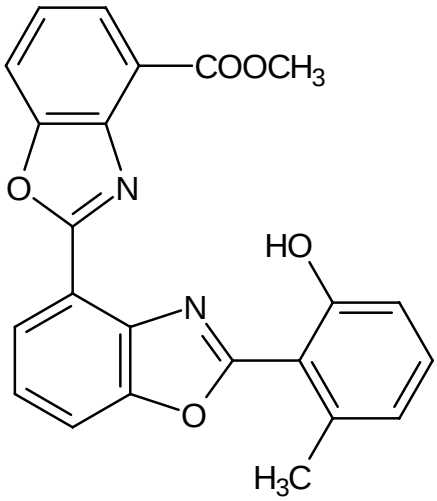


Habitat: terrestrial; Natal, Brazil

Screening method: HPLC-DAD

Biological activity: antitumor

Structure:

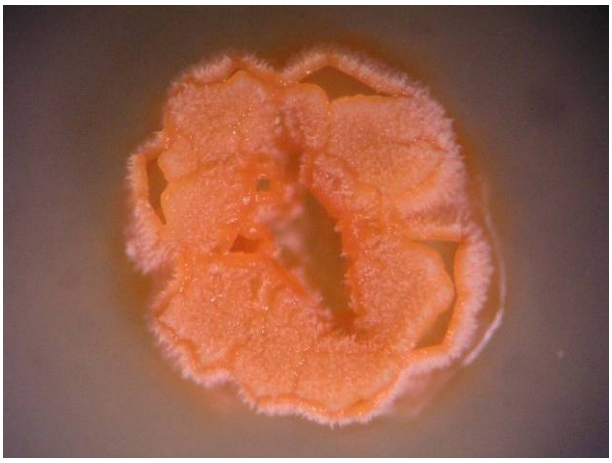


Reference:

Sommer, P.S.M.; R.C. Almeida, K. Schneider, W. Beil, R.D. Süssmuth & H.-P. Fiedler: J. Antibiotics 61: 683-686, 2008

Nocardichelins A and B

Producing organism: *Nocardia* sp. Acta 3026

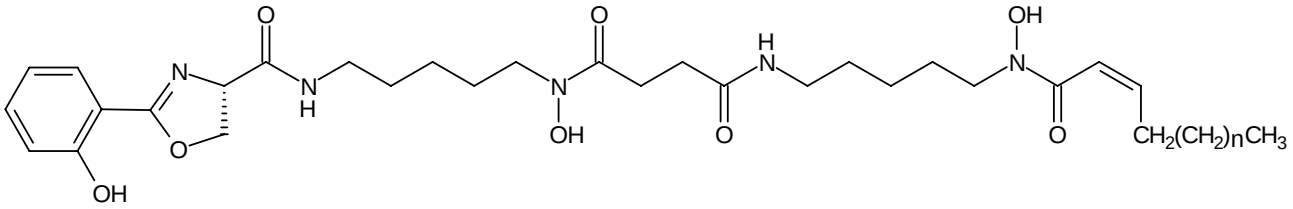


Habitat: terrestrial, rhizosphere; Morib, Selangor, Malaysia

Screening method: HPLC-DAD

Biological activity: siderophor

Structures:



Nocardichelin A: n = 11

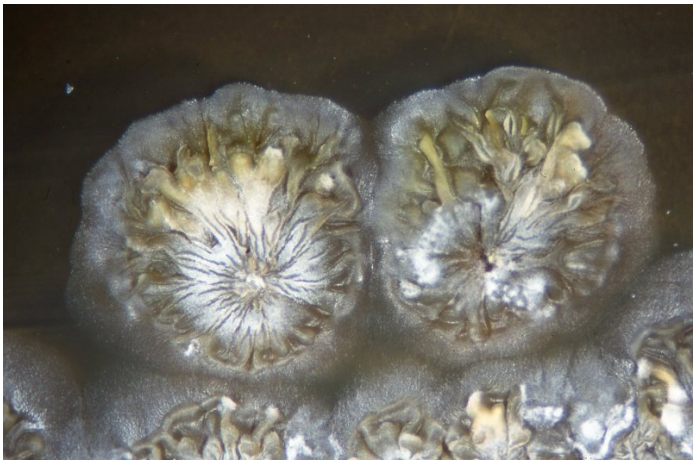
Nocardichelin B: n = 9

Reference:

Schneider, K.; I. Rose, S. Vikineswary, A.L. Jones, M. Goodfellow, G. Nicholson, W. Beil, R. Süssmuth & H.-P. Fiedler. J. Nat. Prod. 70: 932-935, 2007

(*E*)-4-Oxonon-2-Enoic Acid

Producing organism: *Streptomyces olivaceus* Tü 4018

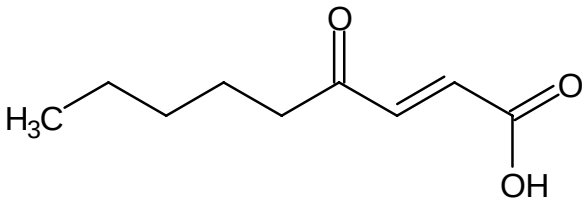


Habitat: terrestrial; Kanchana Buri, Thailand

Screening method: HPLC-DAD

Biological activity: antibacterial

Structure:



Reference:

Pfefferle, C.; C. Kempter, J.W. Metzger & H.-P. Fiedler. J. Antibiotics 49: 826-828, 1996

Phenalinolactones A–D

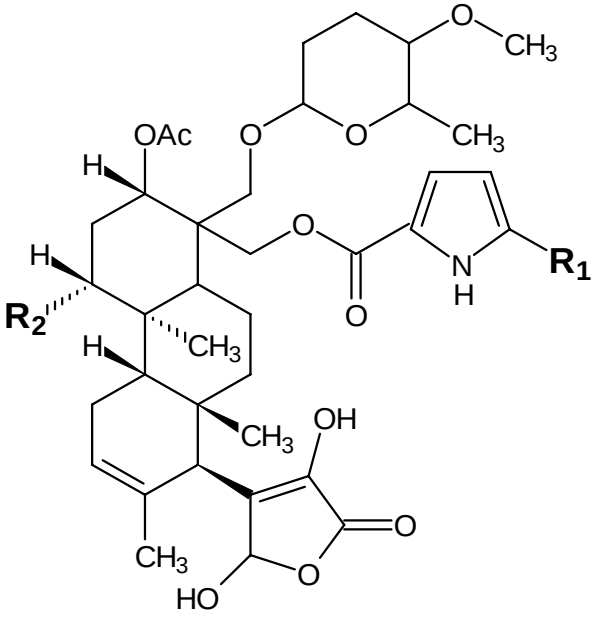
Producing organism: *Streptomyces* sp. Tü 6071

Habitat: terrestrial; Cape Coast, Ghana

Screening method: HPLC-DAD

Biological activity: antibacterial against Gram-positive bacteria

Structures:



Phenalinolactones

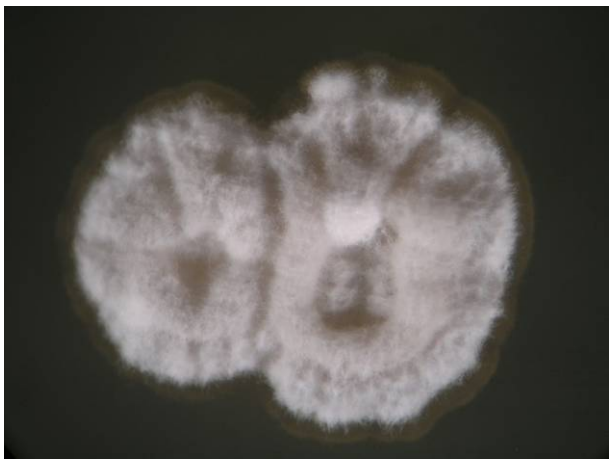
A: $R_1 = CH_3$; $R_2 = OH$
B: $R_1 = H$; $R_2 = OH$
C: $R_1 = CH_2OCH_3$; $R_2 = OH$
D: $R_1 = CH_3$; $R_2 = H$

Reference:

Gebhardt, K.; S.W. Meyer, J. Schinko, G. Bringmann, A. Zeeck & H.-P. Fiedler. J. Antibiotics 64: 229-232, 2011

Phenelfamycins G and H

Producing organism: *Streptomyces albospinus* Acta 3619

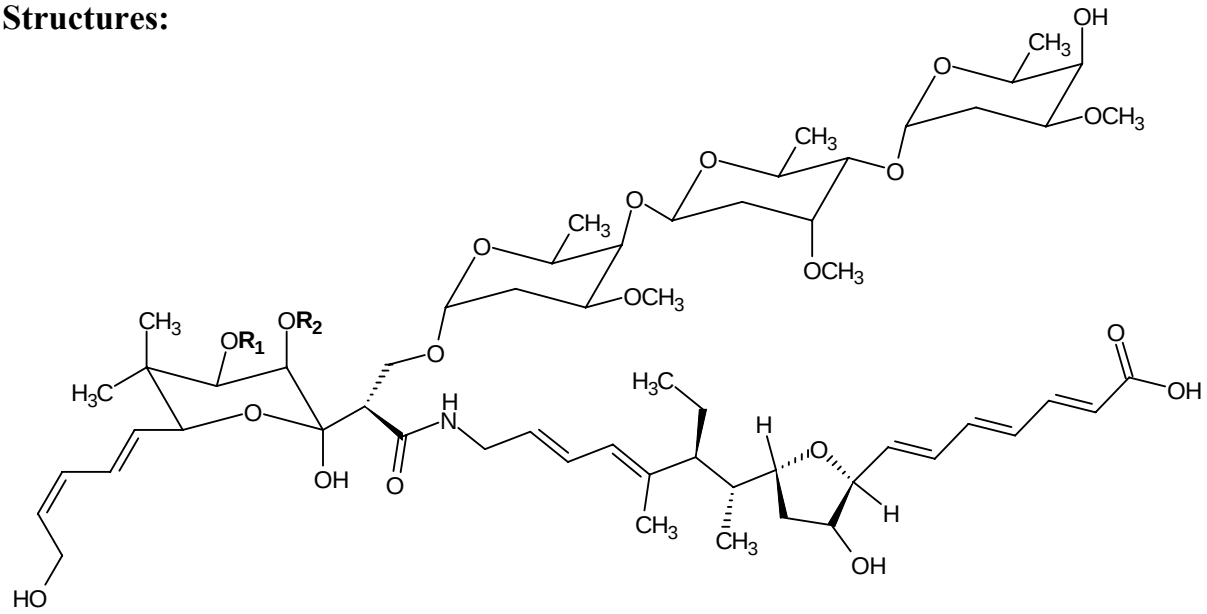


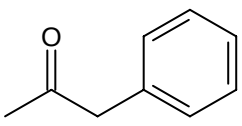
Habitat: terrestrial; rhizospere soil from Gombak, Malaysia

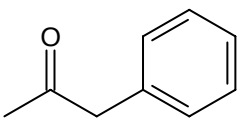
Screening method: HPLC-DAD

Biological activity: narrow antibacterial spectrum

Structures:



G: R_1 = H R_2 = 

H: R_1 =  R_2 = H

Reference:

Brötz, E.; A. Kulik, S. Vikineswary, C.-T. Lim, G.Y.A. Tan, H. Zinecker, J.F. Imhoff, T. Paululat & H.-P. Fiedler. J. Antibiotics 64: 257-266, 2011

Piceamycin

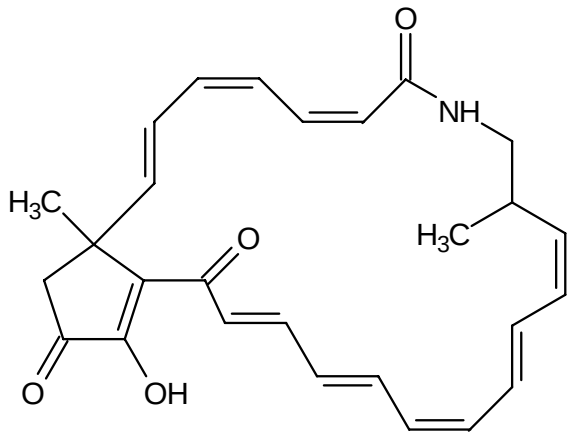
Producing organism: *Streptomyces* sp. GB 4-2

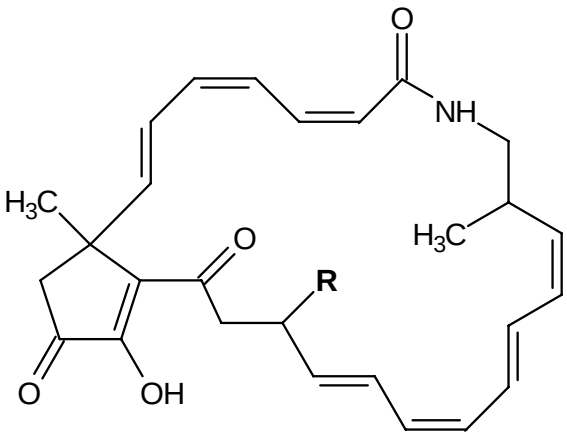
Habitat: terrestrial; rhizosphere of Norway spruce, Schönbuch , Germany

Screening method: HPLC-DAD

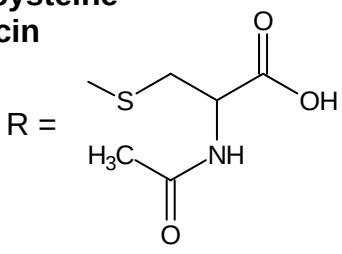
Biological activity: antibacterial, antitumor, inhibitor of protein tyrosine phosphatase 1B

Structures:





***N*-acetylcysteine piceamycin**



Reference:

Schulz, D.; J. Nachtigall, J. Riedlinger, K. Schneider, K. Poralla, J.F. Imhoff, W. Beil, G. Nicholson, H.-P. Fiedler & R.D. Süssmuth. J. Antibiotics 62, 513-518, 2009

Polyketomycin

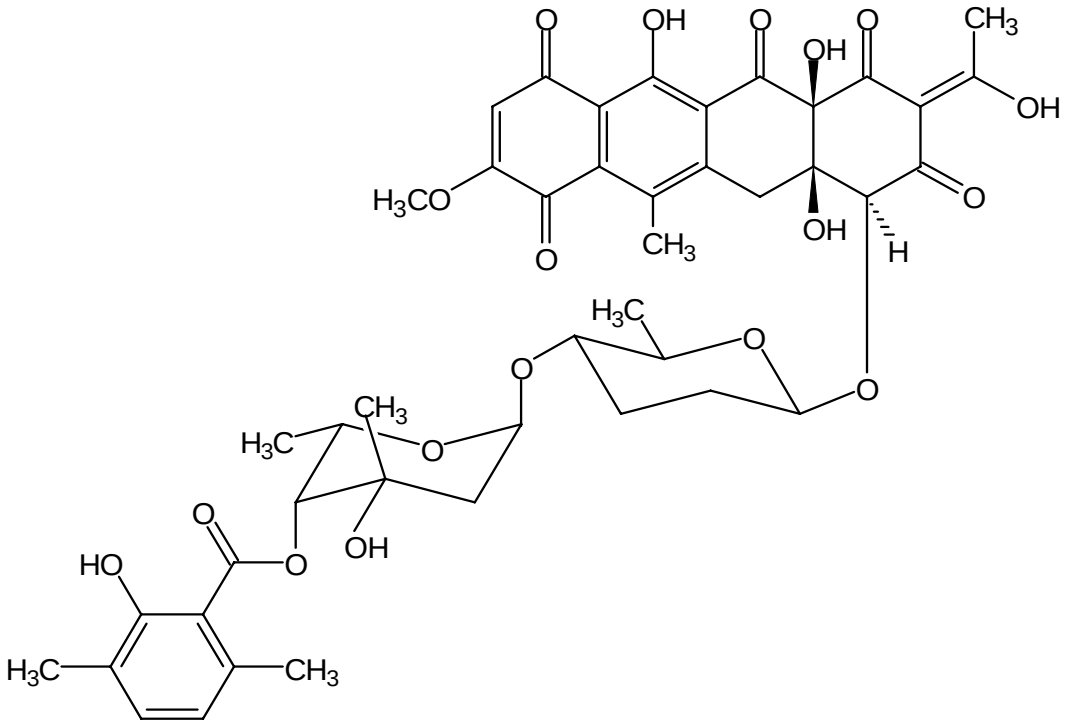
Producing organism: *Streptomyces diastatochromogenes*. Tü 6028

Habitat: terrestrial; Iguaçu, Argentina

Screening method: HPLC-DAD

Biological activity: antibacterial, antitumor

Structure:

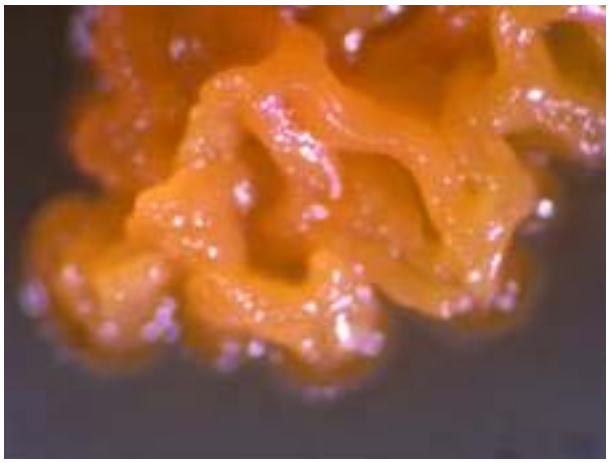


Reference:

Paululat, T.; A. Zeeck, J.M. Gutterer & H.-P. Fiedler. J. Antibiotics 52: 96-101, 1999

Proximicins A–C

Producing organism: *Verrucosispora fiedleri* MG-37



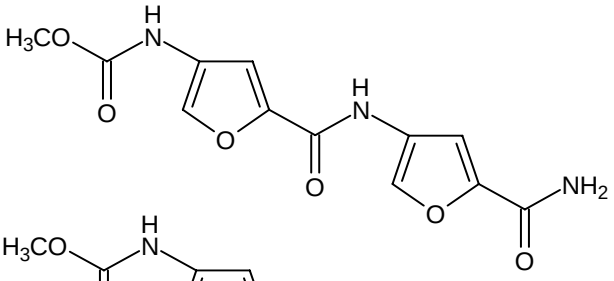
Habitat: marine; sediment –250 m, Raune Fjord, Norway

Screening method: HPLC-DAD

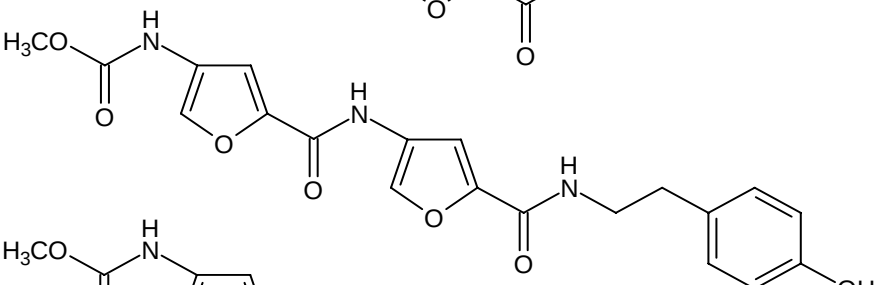
Biological activity: antitumor

Structures:

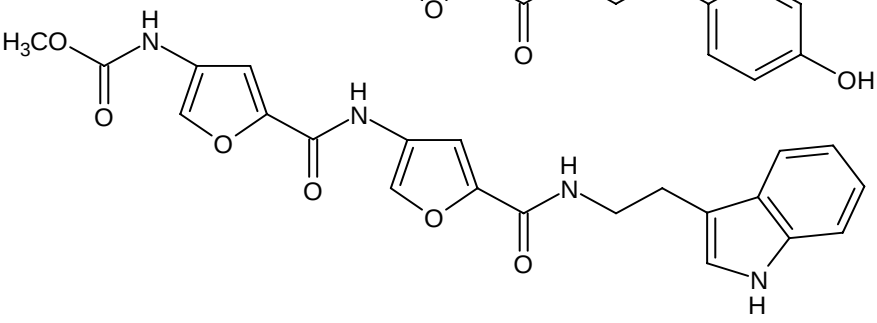
A



B



C



References:

Fiedler, H.-P.; C. Bruntner, J. Riedlinger, A.T. Bull, G. Knutsen, A.L. Jones, M. Goodfellow, W. Beil, K. Schneider, S. Keller & R.D. Süssmuth. J. Antibiotics 61: 158-163, 2008

Schneider, K.; S. Keller, F.E. Wolter, L. Röglin, W. Beil, O. Seitz, G. Nicholson, C. Bruntner, J. Riedlinger, H.-P. Fiedler & R.D. Süssmuth: Angew. Chem. Int. Ed. 47: 3258-3261, 2008

Pyrocoll

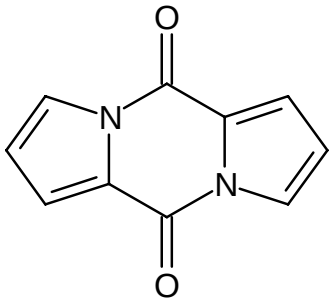
Producing organism: *Streptomyces* sp. AK 409

Habitat: terrestrial; steel waste tip soil, Consett, UK

Screening method: HPLC-DAD

Biological activity: antibacterial, antiparasitic, antitumor

Structure:

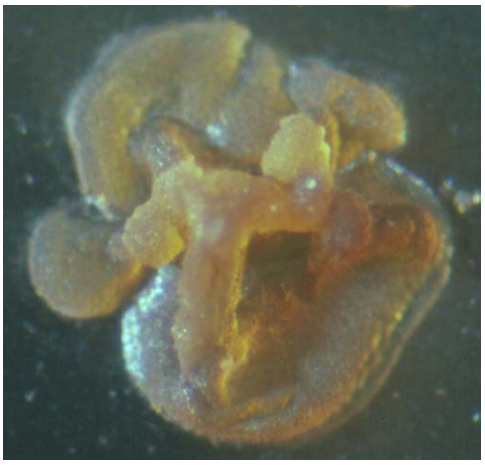


Reference:

Dieter, A.; A. Hamm, H.-P. Fiedler, M. Goodfellow, W.E.G. Müller, R. Brun, W. Beil & G. Bringmann. J. Antibiotics 56: 639-646, 2003

Retymicin

Producing organism: *Micromonospora* sp. Tü 6368

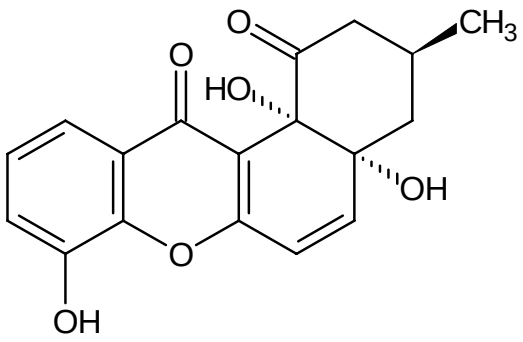


Habitat: terrestrial, Rety, Romania

Screening method: HPLC-DAD

Biological activity: antitumor

Structure:



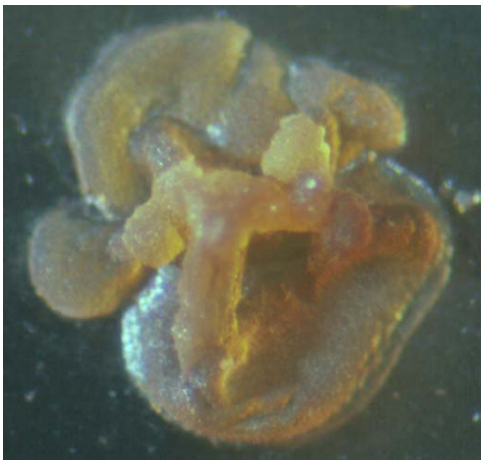
References:

Antal, N.; H.-P. Fiedler, E. Stackebrandt, W. Beil, K. Ströch & A. Zeeck. J. Antibiotics 58: 95-102, 2005

Ströch, K.; A. Zeeck, N. Antal & H.-P. Fiedler. J. Antibiotics 58: 103-110, 2005

1-(α-Ribofuranosyl)-lumichrome

Producing organism: *Micromonospora* sp. Tü 6368

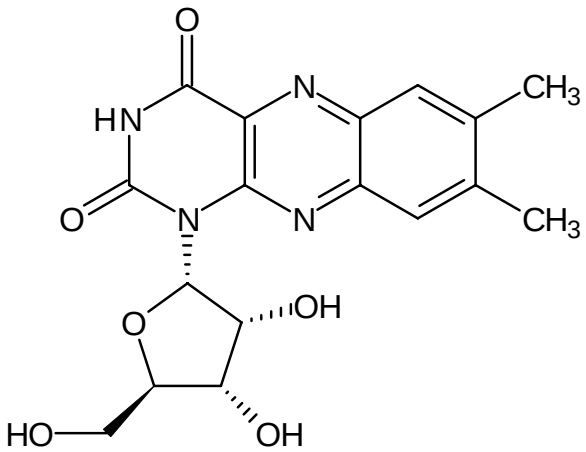


Habitat: terrestrial, Rety, Romania

Screening method: HPLC-DAD

Biological activity: none

Structure:



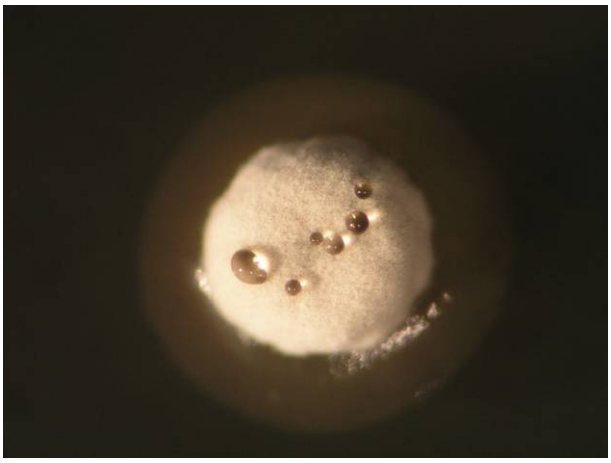
References:

Antal, N.; H.-P. Fiedler, E. Stackebrandt, W. Beil, K. Ströch & A. Zeeck. J. Antibiotics 58: 95-102, 2005

Ströch, K.; A. Zeeck, N. Antal & H.-P. Fiedler. J. Antibiotics 58: 103-110, 2005

Ripromycin

Producing organism: *Streptomyces* sp. Tü 6239

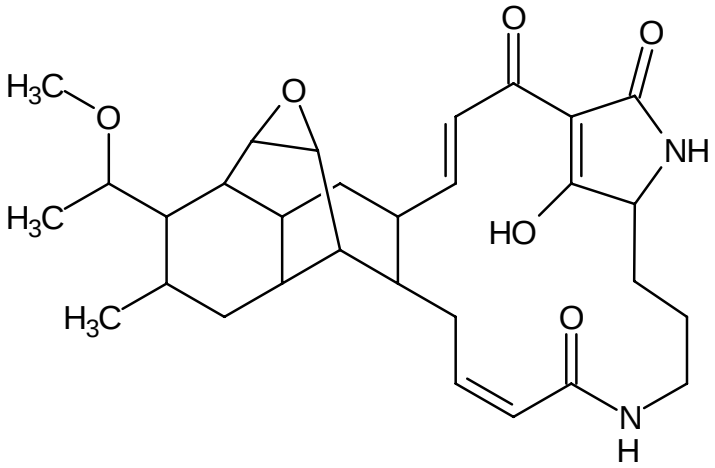


Habitat: terrestrial, São José do Rio Preto, Brazil

Screening method: HPLC-DAD

Biological activity: antibacterial, antitumor

Structure:

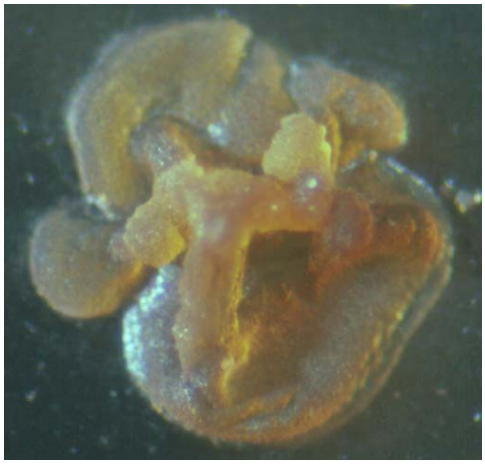


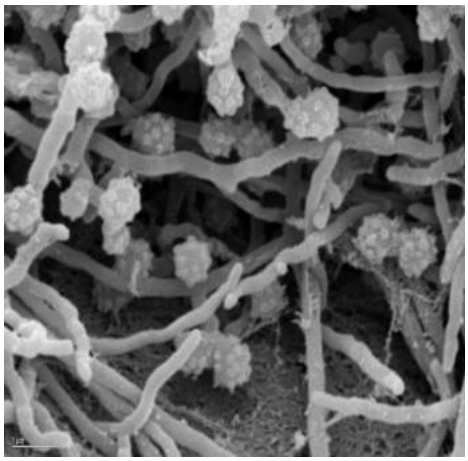
Reference:

Bertasso, M.; M. Holzenkämpfer, A. Zeeck, E. Stackebrandt, W. Beil & H.-P. Fiedler. J. Antibiotics 56: 364-371, 2003

Saquayamycin Z

Producing organism: *Micromonospora* sp. Tü 6368



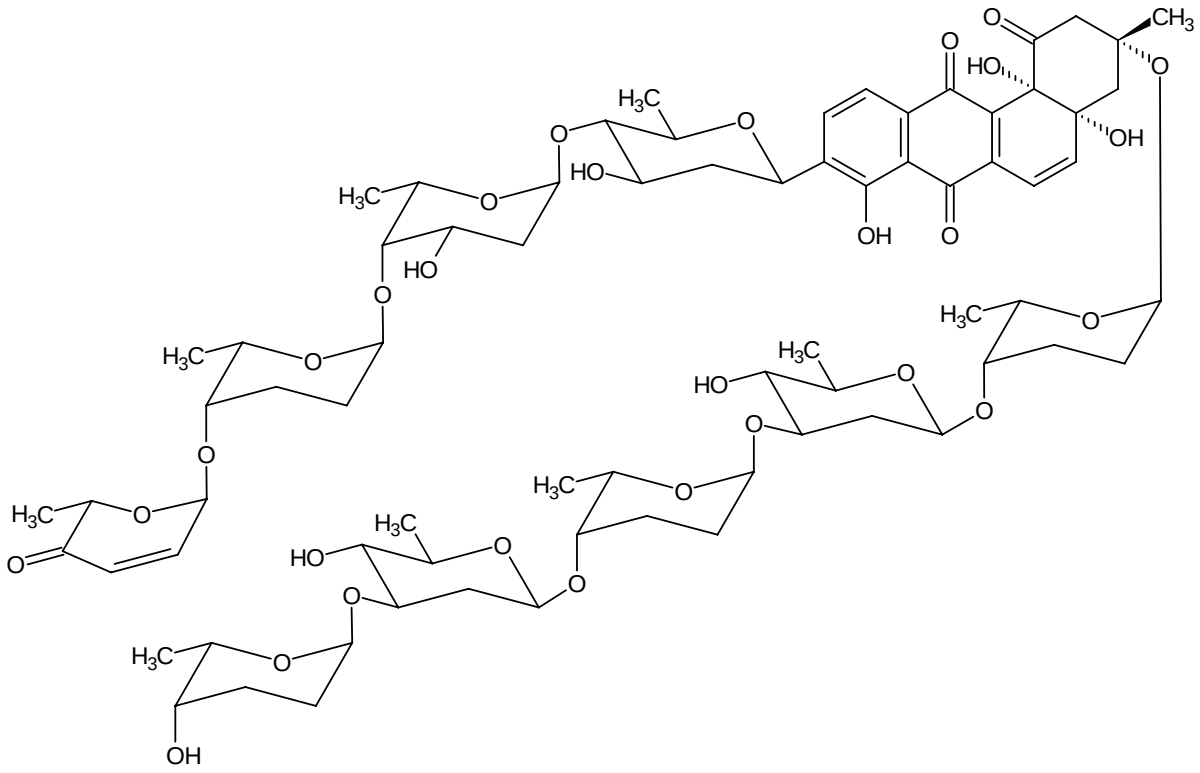


Habitat: terrestrial, Rety, Romania

Screening method: HPLC-DAD

Biological activity: antibacterial, antitumor

Structure:



References:

Antal, N.; H.-P. Fiedler, E. Stackebrandt, W. Beil, K. Ströch & A. Zeeck. J. Antibiotics 58: 95-102, 2005

Ströch, K.; A. Zeeck, N. Antal & H.-P. Fiedler. J. Antibiotics 58: 103-110, 2005

Silvalactam

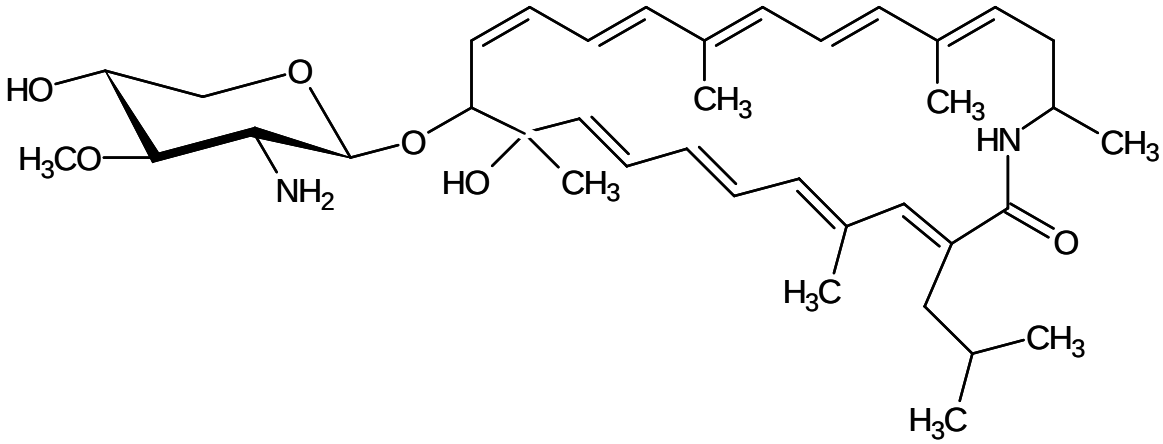
Producing organism: *Streptomyces* sp. Tü 6392

Habitat: terrestrial; rhizosphere of Norway spruce, Rammert Forest, Tübingen, Germany

Screening method: HPLC-DAD

Biological activity: antitumor

Structure:



Reference:

Schulz, D.; J. Nachtigall, U. Geisen, H. Kalthoff, J.F. Imhoff, H.-P. Fiedler & R.D. Süssmuth. J. Antibiotics 65: 369-372, 2012

Simocyclinones A–D

Producing organism: *Streptomyces antibioticus* Tü 6040

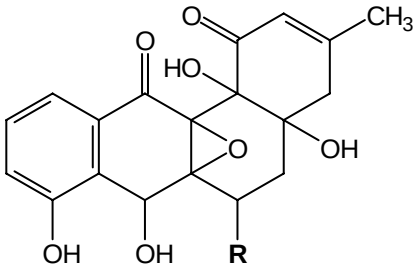
Habitat: terrestrial; Iguaçu Falls, Argentina

Screening method: HPLC-DAD

Biological activity: antibacterial, inhibitors of bacterial gyrase (simocyclinones D); antitumor, inhibitors of protein kinase C (simocyclinones C and D)

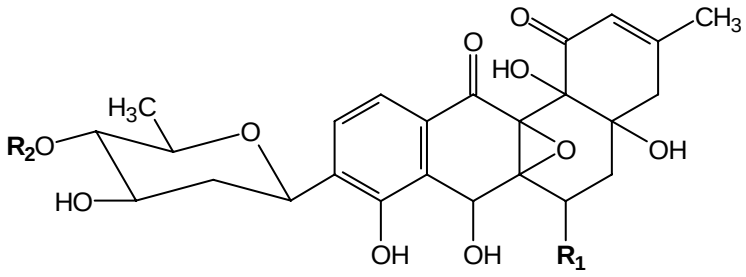
Structures:

Simocyclinones A



A1: R = H
A2: R = OH

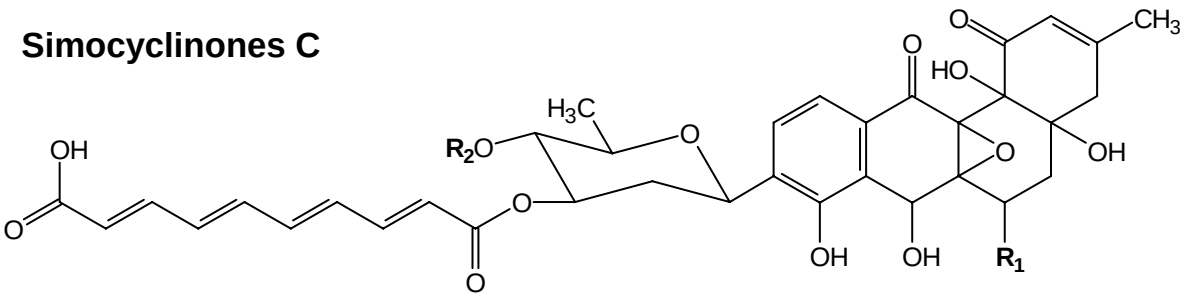
Simocyclinones B



	R_1	R_2
B1:	H	H
B2:	OH	H
B3:	H	$COCH_3$
B4:	OH	$COCH_3$

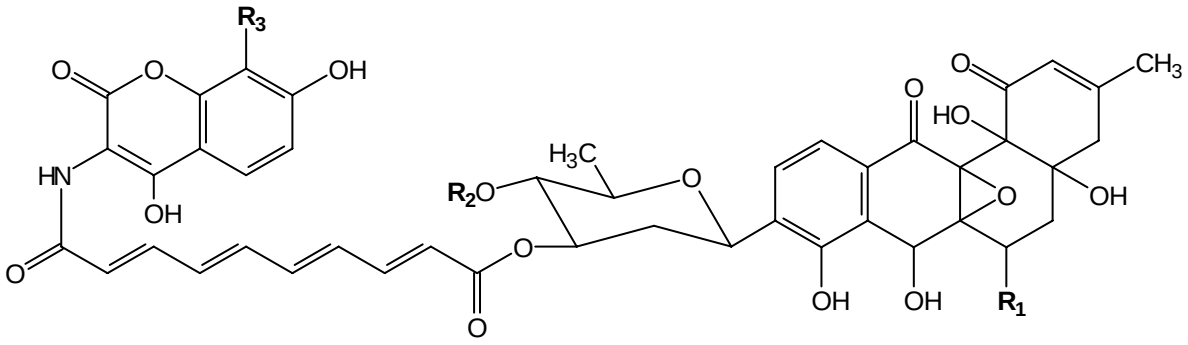
Simocyclinones A–D

Simocyclinones C



	R_1	R_2
C2:	OH	H
C3:	H	$COCH_3$
C4:	OH	$COCH_3$

Simocyclinones D



	R_1	R_2	R_3
D2:	OH	H	H
D3:	H	$COCH_3$	H
D4:	OH	$COCH_3$	H
D6:	OH	H	Cl
D7:	H	$COCH_3$	Cl
D8:	OH	$COCH_3$	Cl

Simocyclinones A–D

References:

Schimana, J.; H.-P. Fiedler, I. Groth, R. Süssmuth, W. Beil, M. Walker & A. Zeeck. J. Antibiotics 53: 779-787, 2000

Theobald, U.; J. Schimana & H.-P. Fiedler. Antonie van Leeuwenhoek 78: 307-313, 2000

Schimana, J.; M. Walker, A. Zeeck & H.-P. Fiedler. J. Ind. Microbiol. Biotechnol. 27: 144-148, 2001

Holzenkämpfer, M.; M. Walker, A. Zeeck, J. Schimana & H.-P. Fiedler. J. Antibiotics 55: 301-307, 2002

Trefzer, A.; S. Pelzer, J. Schimana, S. Stockert, C. Bihlmaier, H.-P. Fiedler, K. Welzel, A. Vente & A. Bechthold. Antimicrob. Agents Chemother. 46: 1174-1182, 2002

Galm, U.; J. Schimana, H.-P. Fiedler, J. Schmidt, S.-M. Li & L. Heide. Arch. Microbiol. 178: 102-114, 2002

Flatman, R.H.; A.J. Howells, L. Heide, H.-P. Fiedler & A. Maxwell. Antimicrob. Agents Chemother. 49: 1093-1100, 2005

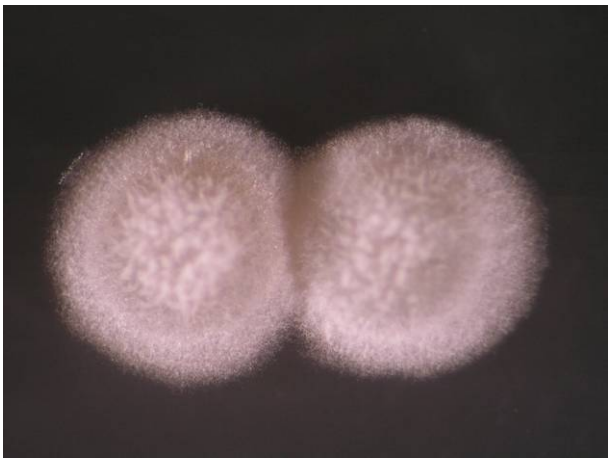
Oppegard, L.M.; B.L. Hamann, K.R. Streck, K.C. Ellis, H.-P. Fiedler, A.B. Khodursky & H. Hiasa. Antimicrob. Agents Chemother. 53:2110-2119, 2009

Le, T.B.K.; H.-P. Fiedler, C.D. den Hengst, S.K. Ahn, A. Maxwell & M.J. Buttner. Molec. Microbiol. 72: 1462-1474, 2009

Edwards, M.J.; R.H. Flatman, L.A. Mitchenall, C.E.M. Stevenson, T.B.K. Le, T.A. Clarke, A.R. McKay, H.-P. Fiedler, M.J. Buttner, D.M. Lawson & A. Maxwell. Science 326: 1415-1417, 2009

Skyllamycins A and B

Producing organism: *Streptomyces* sp. Acta 2897

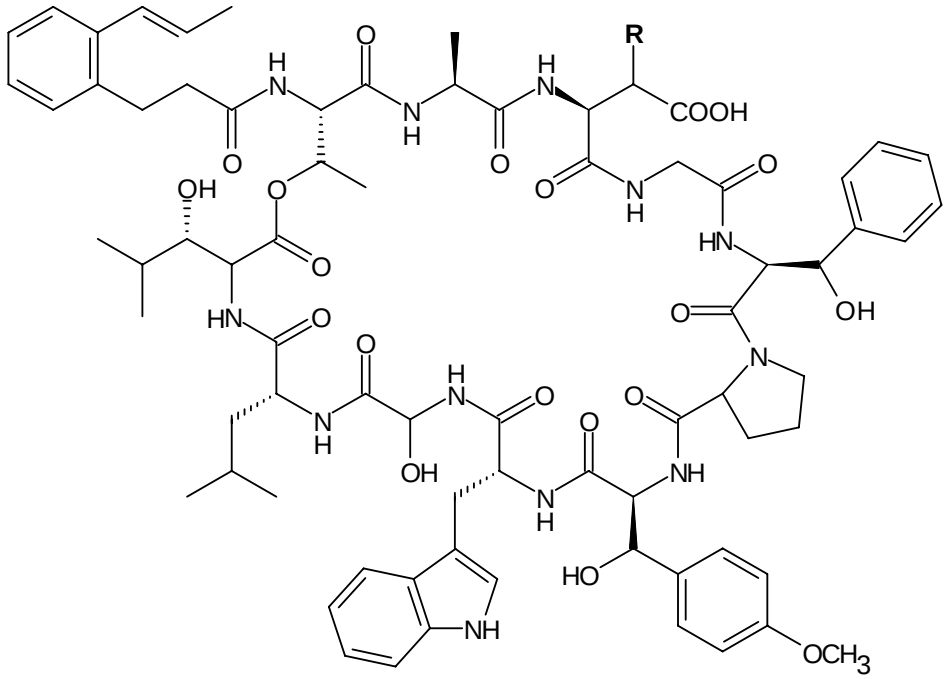


Habitat: terrestrial; Dune Slack, Warkworth, UK

Screening method: HPLC-DAD

Biological activity: antibacterial

Structures:



A: R = CH_3

B: R = H

Reference:

Pohle, S.; C. Appelt, M. Roux, H.-P. Fiedler & R.D. Süssmuth. J. Am. Chem. Soc. 133: 6194-6205, 2011

Spirodionic Acid Tü 6077

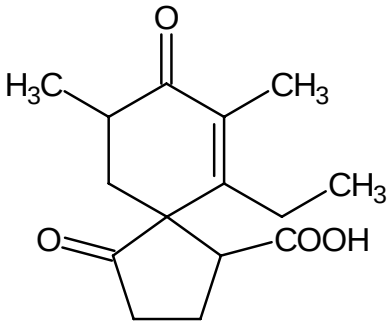
Producing organism: *Streptomyces* sp. Tü 6077

Habitat: terrestrial; Cape Coast, Ghana

Screening method: HPLC-DAD

Biological activity: none

Structure:

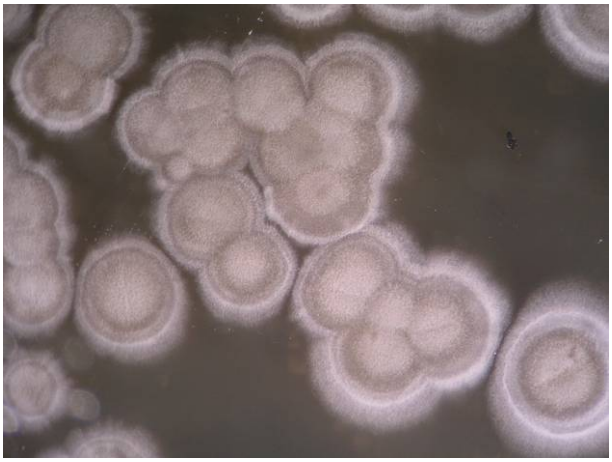


Reference:

Textor, A.; I. Papastavrou, J. Siewert, J. Magull, A. Kulik, H.-P. Fiedler, P. von Zezschwitz & S. Grond. Chem. Eur. J. 13: 7416-7423, 2007

Spirofungin

Producing organism: *Streptomyces violaceusniger* Tü 4113

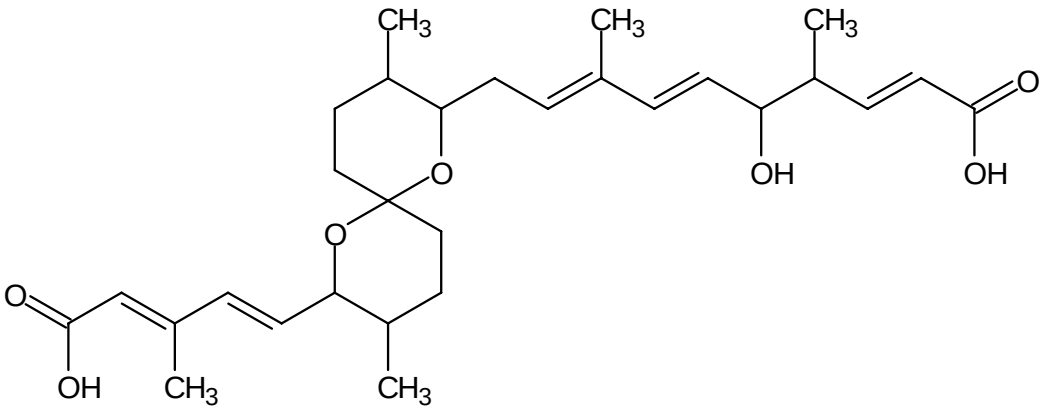


Habitat: terrestrial; Otway National Park, Australia

Screening method: HPLC-DAD

Biological activity: antifungal

Structure:



Reference:

Höltzel, A.; C. Kempter, J.W. Metzger, G. Jung, I. Groth, T. Fritz & H.-P. Fiedler. J. Antibiotics 51: 699-707, 1998

Streptocidins A–D

Producing organism: *Streptomyces* sp. Tü 6071

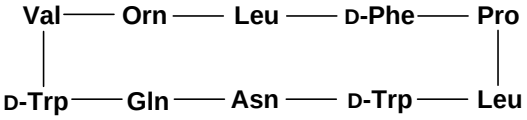
Habitat: terrestrial; Cape Coast, Ghana

Screening method: HPLC-DAD

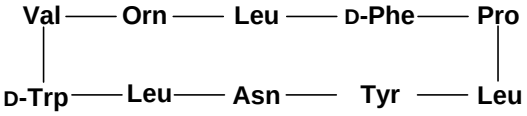
Biological activity: antibacterial

Structures:

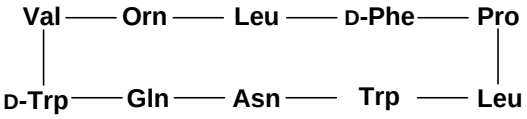
A



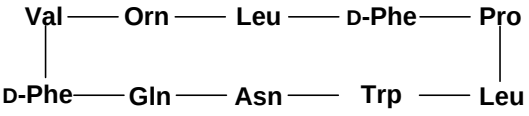
B



C



D



References:

Gebhardt, K.; R. Pukall & H.-P. Fiedler. J. Antibiotics 54: 428-433, 2001

Höltzel, A.; R.D. Süssmuth, R.W. Jack, G.J. Nicholson, K. Gebhardt, H.-P. Fiedler & G. Jung. J. Antibiotics 54: 434-440, 2001

Streptofactin

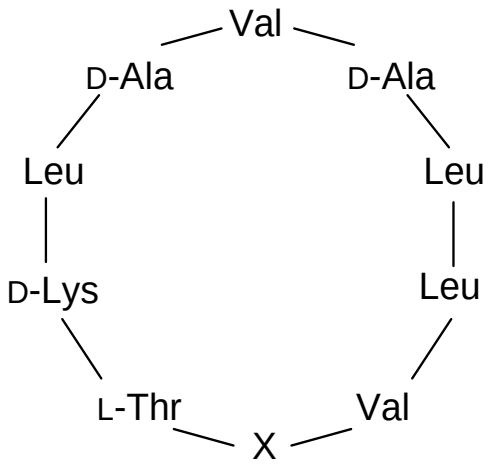
Producing organism: *Streptomyces tendae* Tü 901/8c

Habitat: terrestrial; Nikko, Japan

Screening method: complementation of bald mutants

Biological activity: induction of aerial mycelium

Structure:

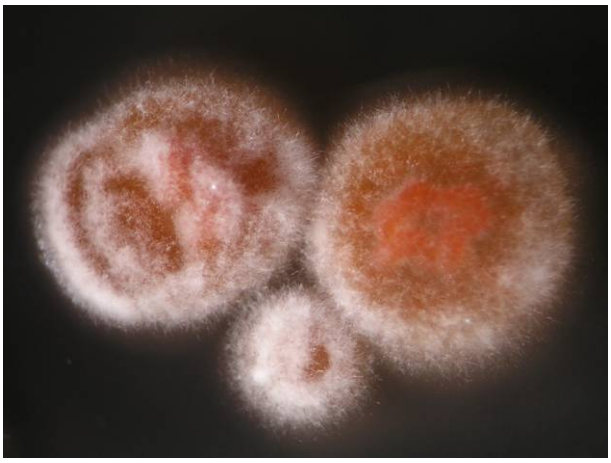


Reference:

Richter, M.; J.M. Willey, R. Süssmuth, G. Jung & H.-P. Fiedler. FEMS Microbiol. Lett. 163: 165-171, 1998

Tetracenomycins B3, D3

Producing organism: *Streptomyces olivaceus* Tü 2353-R

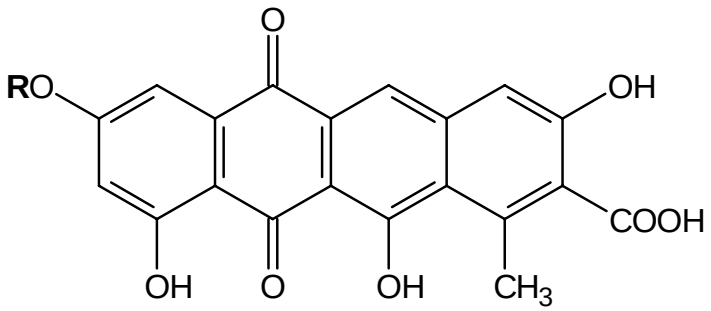


Habitat: terrestrial; Ellora, India

Screening method: HPLC-DAD

Biological activity: antibacterial (tetracenomycin D3)

Structures:



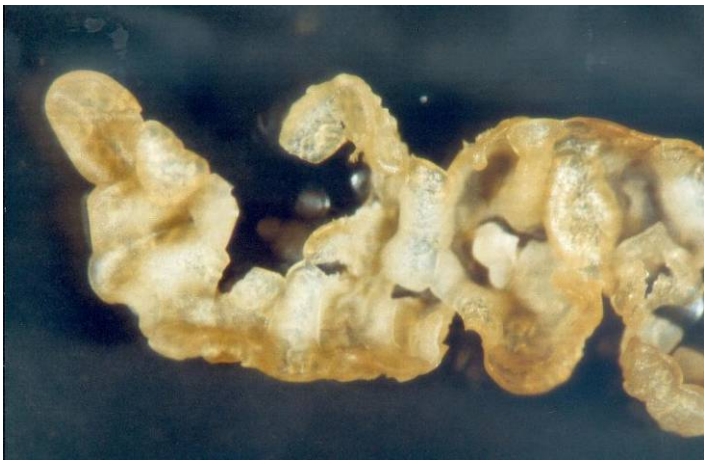
B_3 : R = CH_3
D_3 : R = H

Reference:

Rohr, J.; S. Eick, A. Zeeck, P. Reuschenbach, H. Zähner & H.-P. Fiedler. J. Antibiotics 41: 1066-1073, 1988

Tigloside

Producing organism: *Amycolatopsis* sp. NNO 21702

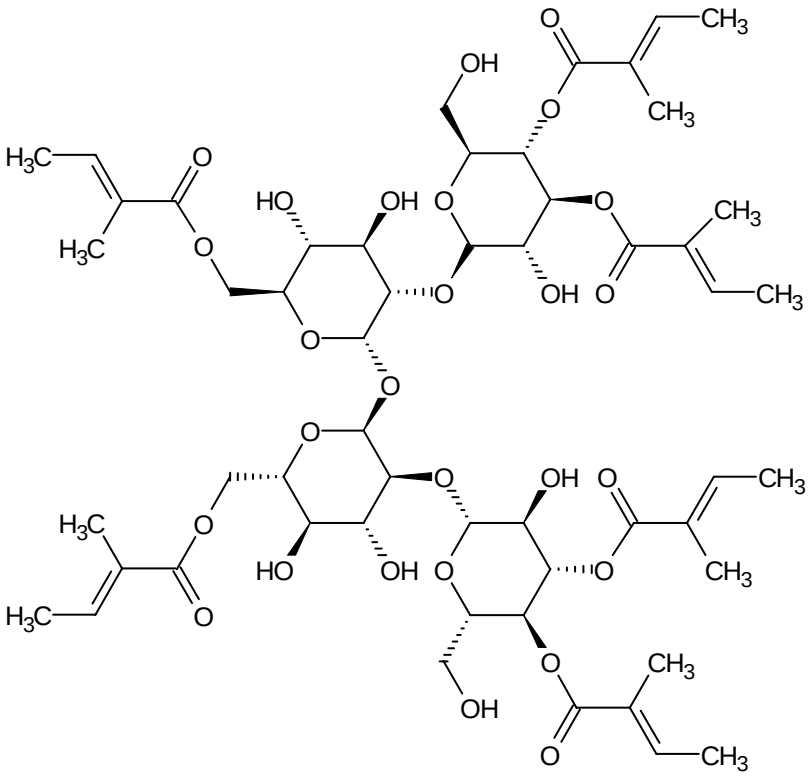


Habitat: terrestrial, Australia

Screening method: HPLC-DAD

Biological activity: none

Structure:



Reference:

Breinholt, J.; A. Kulik, H. Gürtler & H.-P. Fiedler. Acta Chem. Scand. 52: 1239-1242, 1998

Warkmycin

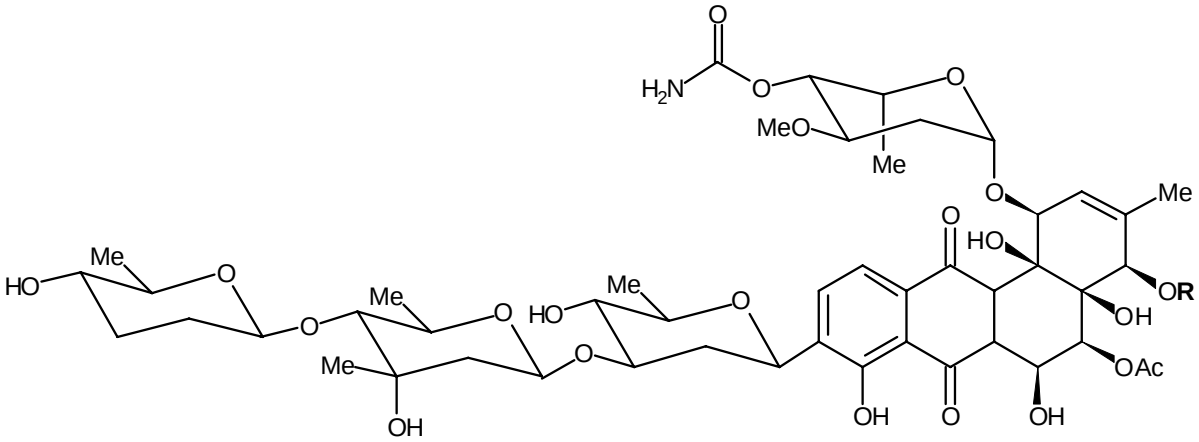
Producing organism: *Streptomyces* sp. Acta 2930

Habitat: terrestrial; alkaline soil from sand dune, Warkworth, Northumberland, UK

Screening method: HPLC-DAD

Biological activity: antibacterial, antitumor

Structures:



Warkmycin: R = COMe

Deacetyl-Warkmycin: R = H

Reference:

Helaly, S.E.; M. Goodfellow, H. Zinecker, J.F. Imhoff, R.D. Süssmuth & H.-P. Fiedler. J. Antibiotics, in press 2013

III. Coworkers Involved in Metabolite Screening

My special thanks are due to my doctoral students who were involved in the sceening for novel secondary metabolites and fermentation studies. Their names are in chronological order:

Willi Kuhn (1993)
Uwe Hartjen (1993)
Uwe Pfefferle (1994)
Sabine Blum (1995)
Christoph Pfefferle (1997)
Monika Richter (1997)
Judith Schimana (1999)
Markus Kempf (1999)
Klaus Gebhardt (2001)
Anke Dieter (2002)
Marcelo Bertasso (2002)
Noèmi Antal (2004)
Julia Riedlinger (2006)
Dirk Schulz (2009)
Nadine Horlacher (2012)
Marcell Wagner (2012)

Besides the doctoral students the following diploma students contributed to the progress in screening of secondary metabolites:

Thomas Fritz, Jan Mirko Gutterer, Nicole Zwicker, Armin Maier, Antje Seidel, Miriam Langbecker, Elisabeth Zürn, Andreas Reicke, Tatiana Binder, Stefanie Baur, Grit Hanschel, Bettina Wieser, Andreas Gierth, Claudia Hohmann, Sonja Gern, Philipp Jetter, Nicole Klüglein, Niko Manderscheid and Rebekka Jacek.

Without the support by my Post-Docs as the responsible persons, the various projects could not be realized. I appreciate in particular the work of Dr. Uwe Theobald, Dr. Johannes Müller, Dr. Judith Schimana and Dr. Christina Bruntner.

Last but not least, the assistance of the technical staff contributed greatly to the success of the research: Dip. Ing. Georg Grewe, Dipl. Ing. Andreas Kulik, Dipl. Ing. Jochen Schinko, Dipl. Biol. Barbara Holz, Mrs. Jutta Wachter, Mrs. Brigitte Maurer, Mr. Mulugeta Nega, Mr. Mete Bayraktar and Mr. Christian Tänzer.

IV. Collaborations and Fundings

National and international collaborations with collegues from various universities and chemical-pharmaceutical companies were essential in the screening of microbial strains and determining the biological activities and structures of the isolated metabolites.

Professor Dr. Michael Goodfellow and Professor Dr. Alan C. Ward from the University of Newcastle, Newcastle upon Tyne, UK, provided us with alkaliphilic, acidophilic and thermophilic actinomycetes strains from terrestrial soils and fresh water sediments collected at various sites in the UK. Halophilic actinomycetes from Egypt and marine actinomycetes isolated from sediments of deep sea trenches and various regions of the North Atlantic completed the spectrum of extreme habitats. Full taxonomic characterization was done in Newcastle in the case of antibiotic producing strains.

Professor Dr. Alan T. Bull from University of Kent, Canterbury, UK, provided us with marine actinomycetes from sediments of the Pacific and Atlantic Ocean including deep sea trenches, with terrestrial actinomycetes from Antarctica and with actinomycetes isolated from the Atacama Desert in Chile.

Professor Dr. Vikineswary from the University of Malaya, Kuala Lumpur, Malaysia, provided us with a huge collection of new isolated actinomycetes strains from pristine tropical habitats in Malaysia.

Dr. Patricia S.M. Sommer from University of Rio Grande do Norte, Natal, Brasil, provided us with actinomycetes strains which were isolated from Brazilian medicinal plants.

Professor Dr. Konrad Dettner from University of Bayreuth, Germany, provided us with endosymbiotic actinomycetes and fungi, which were isolated from the guts of a huge diversity of arthropods, especially insects and millipedes.

Professor Dr. Erko Stackebrandt and Professor Dr. Rainer-Michael Kroppenstedt supported the taxonomic characterization of new actinomycete isolates and in the specialist training of some of my doctoral students in taxonomical techniques.

With Dr. Ingrid Groth from Hans-Knöll-Institut für Naturstoff-Forschung, Jena, we had a fruitful long-term collaboration in taxonomic characterization of new isolated actinomycetes, resulting in various common publications.

Professor Dr. Rüdiger Hampp from the Department of Physiological Ecology of Plants and Professor Dr. Karl Poralla from the Institute of Microbiology of the University of Tübingen provided us with streptomycetes acting as mycorrhiza helper bacteria.

Without chemical characterization of the isolated metabolites the whole research in screening for new biologically active secondary metabolites would be only patchwork. Therefore, my deepest thanks are due to the groups of Professor Dr. Axel Zeeck, Dr. Jürgen Rohr and Dr. Stephanie Grond and their teams from the Organic Chemistry

Department of the University of Göttingen (they moved recently to the Organic Chemistry Department of the University of Tübingen), Professor Dr. Günther Jung and his team from the Organic Chemistry Department of the University of Tübingen, Professor Dr. Gerhard Bringmann and his team from the Organic Chemistry Department of the University of Würzburg, Dr. Thomas Paululat from the Organic Chemistry Department of the University of Siegen, and last but not least my friend Professor Dr. Roderich Süssmuth from the Chemical Institute of the Technical University of Berlin, who started his career in Tübingen and moved in 2004 to Berlin. Roderich and his team of diploma and doctoral students were mainly involved during the last decade in structural elucidation of our isolated secondary metabolites. Without their enthusiasm for natural products our research could not be realized. But not only chemists from the various universities, also chemists from chemical-pharmaceutical companies contributed to the success of my group, as Dr. Jens Breinholt from Novo Nordisk, Denmark, Dr. Olivier Potterat and Dr. Carsten Puder from Boehringer-Ingelheim Pharma, Biberach, Germany.

Due to the limited facilities in determining the biological activities of the isolated new secondary metabolites, the collaboration in biological assays has been an essential part in my work. Professor Dr. Winfried Beil from the Medizinische Hochschule Hannover, Germany, performed antitumor assays to investigate activities against various human tumor cell lines. Professor Dr. Reto Brun from the Swiss Tropical Institute, Basel, took the part in screening for antiparasitic activities against various protozoan pathogens. Professor Dr. Johannes Imhoff from GEOMAR Helmholtz-Zentrum für Ozeanforschung Kiel, participated with testing our compounds in extended antibacterial, antifungal, antitumor and enzymatic assays.

Without financial support no reaserch would be possible. Therefore, my warmest thanks are due to following organisations and companies:

The Deutsche Forschungsgemeinschaft contributed with a basic support for fermentation and HPLC equipment within SFB 323 during the years 1988-1999.

The Bundesministerium für Forschung und Technologie (BMFT) Germany, supported our research in the optimisation of the biotechnological manufacturing of secondary metabolites within the ‘Zentrales Schwerpunktprojekt Bioverfahrenstechnik’ from 1988-98.

Novo Nordisk A/S, Bagsværd, Denmark, supported from 1995-1998 our research in secondary metabolites from the families *Streptosporangiaceae* and *Micomonosporaceae*.

The Bundesministerium für Bildung, Wissenschaft, Forschung und Technologie (BMBF) Germany together with BASF AG, Ludwigshafen, Germany, supported our research in secondary metabolites from endosymbiotic actinomycetes over a 6-year period from 1996-2001.

The European Commission supported our research within the 5th framework, project ACTAPHARM in the screening for new bioactive secondary metabolites from various actinomycetes genera from 2001-2004.

Boehringer Ingelheim Pharma GmbH, Biberach, Germany, supported our research in secondary metabolites from marine actinomycetes from 2002-2004.

The Deutsche Forschungsgemeinschaft contributed from 2002-2010 within 'Graduiertenkolleg Infektionsbiologie' with the support of doctoral theses to our research on the interaction of soil streptomycetes, mycorrhization and plants.

V. List of Publications

Fiedler, E.; H.-P. Fiedler, A. Gerhard, W. Keller-Schierlein, W.A. König & H. Zähner: Synthese und Biosynthese substituierter Tryptanthrine. Arch. Microbiol. 107: 249-256, 1976.

Fiedler, H.-P.: Isolierung von mikrobiellen Stoffwechselprodukten mit Hilfe von Adsorberharzen. Chem. Rundschau 30: 2-3, 1977.

Fiedler, H.-P. & J. Sauerbier: Isolation and quantitative determination of siderochromes. Europ. J. Appl. Microbiol. Biotechnol. 5: 51-57, 1978.

Hartmann, A.; H.-P. Fiedler & V. Braun: Uptake and conversion of the antibiotic albomycin by *Escherichia coli* K112. Europ. J. Biochem. 99: 517-524, 1979.

Hagenmaier, H.; W.A. König, H. Zähner, H.-P. Fiedler, W. Dehler, A. Keckeisen, H. Holst & G. Zoebelein: Neue Nikkomycine, ein Verfahren zu ihrer Herstellung, sowie ihre Verwendung als Schädlingsbekämpfungsmittel (1979). Europ. Patentschrift 0022 964 vom 9.2.1983, Anmeldetag: 4.7.1980, Offenlegungstag: 28.1.1981.

König, W.A.; W. Hass, W. Dehler, H.-P. Fiedler & H. Zähner: Strukturaufklärung und Partialsynthese des Nucleosidantibiotikums Nikkomycin B. Liebigs Ann. Chem. 1980: 622-628, 1980.

Hagenmaier, H.; A. Keckeisen, W. Dehler, H.-P. Fiedler, H. Zähner & W.A. König: Konstitutionsaufklärung der Nikkomycine I, J, N und M. Liebigs Ann. Chem. 1981: 1018-1024, 1981.

Fiedler, H.-P.: Quantitation of nikkomycins in biological fluids by ion-pair reversed-phase high-performance liquid chromatography. J. Chromatogr. 204: 313-318, 1981.

Fiedler, H.-P.: Preparative scale HPLC of ferricrocin, a microbial product. J. Chromatogr. 209: 103-106, 1981.

Fiedler, H.-P.; W. Wörner, H. Zähner, H.P. Kaiser, A. Müller & W. Keller-Schierlein: Isolation and characterization of niphithricins A, B, and elaiophylin, antibiotics produced by *Streptomyces violaceoniger*. J. Antibiot. 34: 1107-1118, 1981.

Fiedler, H.-P.; R. Kurth & W. Dehler: Nikkomycin quantitation in fermentation process by high-performance liquid chromatography. Biotechnol. Lett. 3: 303-308, 1981.

Fiedler, H.-P.; R. Kurth, J. Langhärig, J. Delzer & H. Zähner: Nikkomycins, microbial inhibitors of the chitin synthase. J. Chem. Technol. Biotechnol. 32: 271-280, 1982.

Delzer, J.; H.-P. Fiedler, H. Müller, H. Zähner, R. Rathmann, K. Ernst & W.A. König: New nikkomycins by mutasynthesis and directed fermentation. J. Antibiot. 37: 80-82, 1984.

Fiedler, H.-P.: Screening for new microbial products by HPLC using a photodiode array detector. J. Chromatogr. 316: 487-494, 1984.

Fiedler, H.-P. & H.P. Reuschenbach: Precolumnm switching in HPLC quantitation of small amounts of microbial metabolites as an alternative method to off-line extraction. Chromatographia 19: 246-250, 1985.

Fiedler, H.-P.; F. Walz, A. Döhle & H. Zähner: Albomycin: studies on fermentation, isolation and quantitative determination. Appl. Microbiol. Biotechnol. 21: 341-347, 1985.

Fiedler, H.-P.; A. Plaga & R. Schuster: Automated on-column derivatization of the antibiotics phosphinothricin and phosphinothricyl-alanyl-alanine with o-phthalaldehyde and microbore column high-performance liquid chromatography for quantitative determination in biological cultures. J. Chromatogr. 353: 201-206, 1986.

Fiedler, H.-P.; J. Rohr & A. Zeeck: Elloramycins B, C, D, E and F: minor congeners of the elloramycin producer *Streptomyces olivaceus*. J. Antibiot. 39: 856-859, 1986.

Fiedler, H.-P.: Identification of new elloramycins, anthracycline-like antibiotics, in biological cultures by high-performance liquid chromatography and diode array detection. J. Chromatogr. 361: 432-436, 1986.

Fiedler, H.-P. & A. Plaga: Separation of amino acids and antibiotics by narrow-bore and normal-bore high-performance liquid chromatography with pre-column derivatization. J. Chromatogr. 386: 229-241, 1987.

Fiedler, H.-P.: Substanzidentifizierung in biologischen Proben mit HPLC und Diodenarray-Detektion. *In* 3. Waldbronner Themen, Vol. 1. *Ed.* J. Leyrer, Hewlett-Packard Part No. 0787-0250, Waldbronn, 1987.

Fiedler, H.-P.; T. Hörner & A. Wörn: Separation of polypeptide antibiotics by reversed-phase high-performance liquid chromatography. Chromatographia 24: 433-438, 1987.

Rohr, J.; S. Eick, A. Zeeck, P. Reuschenbach, H. Zähner & H.-P. Fiedler: Tetracenomycins B_3 and D_3, key intermediates of the elloramycin and tetracenomycin C biosynthesis. J. Antibiot. 41: 1066-1073, 1988.

Zähner, H.; H. Drautz, H.-P. Fiedler, R. Grote, W. Keller-Schierlein, W.A. König & A. Zeeck: Ways to new metabolites from actinomycetes. *In* Biology of Actinomycetes '88. *Eds*. Y. Okami *et al*., pp. 171-177, Japan Scientific Soc. Press, Tokyo, 1988.

Werner, R.-G.; H. Zähner, G. Jung, T. Hörner, R. Kellner & H.-P. Fiedler: Antibiotic polypeptide, process for preparing it an the use of therof. US Patentschrift Nr. 219698, Anmeldetag: 18.07.1988.

Fiedler, H.-P.; T. Hörner & H. Decker: Purification of the hydrophilic antibiotics epidermin, gallidermin and nikkomycin Z by preparative reversed-phase HPLC. Chromatographia 26: 215-220, 1988.

Fiedler, H.-P.: Nikkomycins and polyoxins. *In* Natural Products Isolation. *Eds.* G.H. Wagman & R. Cooper, pp. 153-189, Journal of Chromatography Library, Vol. 43, Elsevier, Amsterdam, 1989.

Decker, H.; C. Bormann, H.-P. Fiedler, H. Zähner, H. Heisch & W.A. König: Isolation of new nikkomycins from *Streptomyces tendae*. J. Antibiot. 42: 230-235, 1989.

Heitsch, H.; W.A. König, H. Decker, C. Bormann, H.-P. Fiedler & H. Zähner: Structure of the new nikkomycins pseudo-Z and pseudo-J. J. Antibiot. 42: 711-717, 1989.

Bormann, C.; S. Mattern, H. Schrempf, H.-P. Fiedler & H. Zähner: Isolation of *Streptomyces tendae* mutants with an altered nikkomycin spectrum. J. Antibiot. 42: 913-918, 1989.

Fiedler, H.-P.: Off-line HPLC-Inprozesskontrollen. BTF Biotech Forum 6: 173-177, 1989.

Fiedler, H.-P.; J. Stümpfel, A. Plaga, J. Meiwes & I. Rindfleisch: HPLC-Anwendungen in der Fermentationsanalytik. *In* 5. Waldbronner Themen. *Ed.* D. Lipinski, Hewlett-Packard Part No.0689-0420GE, Bad Homburg, 1989.

Fiedler, H.-P. & J. Meiwes: HPLC-Analytik der Ferrioxamin-Produktion. PeakInfo 2/89: 1-3, 1989.

Plaga, A.; J. Stümpfel & H.-P. Fiedler: Determination of carbohydrates in fermentation processes by high-performance liquid chromatography. Appl. Microbiol. Biotechnol. 32: 45-49, 1989.

Decker, H.; F. Walz, C. Bormann, H. Zähner, H.-P. Fiedler, H. Heitsch & W.A. König: Nikkomycins W_Z and W_X, new chitin synthetase inhibitors from *Streptomyces tendae*. J. Antibiot. 43: 43-48, 1990.

Bormann, C.; K. Aberle, H.-P. Fiedler & H. Schrempf: Genetic complementation of *Streptomyces tendae* deficient in nikkomycin production. Appl. Microbiol. Biotechnol. 32: 424-430, 1990.

Hörner, T.; V. Ungermann, H. Zähner, H.-P. Fiedler, R. Utz, R. Kellner & G. Jung: Comparative studies on the fermentation of lantibiotics, produced by staphylococci. Appl. Microbiol. Biotechnol. 32: 511-517, 1990.

Meiwes, J.; H.-P. Fiedler, H. Zähner, S. Konetschny-Rapp & G. Jung: Production of desferrioxamin E and new analogues by directed fermentation and feeding fermentation. Appl. Microbiol. Biotechnol. 32: 505-510, 1990.

Meiwes, J.; H.-P. Fiedler, H. Haag, H. Zähner, S. Konetschny-Rapp & G. Jung: Isolation and characterization of staphyloferrin A, a compound with siderophore activity from *Staphylococcus hyicus* DSM 20459. FEMS Microbiol. Lett. 67: 201-206, 1990.

Fiedler, H.-P.; J. Meiwes, I. Werner, S. Konetschny-Rapp & G. Jung: Identification of new ferrioxamines by HPLC and diode array detection. J. Chromatogr. 513: 255-262, 1990.

Huber, L. & H.-P. Fiedler: HPLC with computerized diode array detection in pharmaceutical research. *In* HPLC in the Pharmaceutical Industry. *Eds.* G.W. Fong & S.K. Lam, pp. 123-146, Marcel Dekker, New York, 1991.

Fiedler, H.-P. & J. Wachter: High-performance liquid chromatographic analysis of bleomycins. J. Chromatogr. 536: 343-347, 1991.

Ungermann, V.; T. Hörner, R. Utz, H.-P. Fiedler & H. Zähner: Comparative studies on the fermentation of lantibiotics, produced by staphylococci. *In* Biochemical Engineering – Stuttgart. *Eds.* M. Reuss *et al*., pp. 301-305, Gustav Fischer, Stuttgart, 1991.

Decker, H.; U. Pfefferle, C. Bormann, H. Zähner, H.-P. Fiedler, K.-H. van Pée, M. Rieck & W.A. König: Enzymatic bromation of nikkomycin Z. J. Antibiot. 44: 626-634, 1991.

Fiedler, H.-P.; H. Drautz, T. Schüz, J. Wachter & U. Hartjen: Anwendungen von HPLC, Diodenarraydetektion und Spektrenbibliothek beim Screening nach neuen Naturstoffen. *In* 7. Waldbronner Themen. *Ed*. L. Winzer, pp. 173-185, Hewlett-Packard Part.-Nr. 0791-0705GE, Bad Homburg, 1991.

Decker, H.; H. Zähner, H. Heitsch, W.A. König & H.-P. Fiedler: Structure-activity relationships of the nikkomycins. J. Gen. Microbiol. 137: 1805-1813, 1991.

Ungermann, V.; K. Goeke, H.-P. Fiedler & H. Zähner: Optimization of fermentation and purification of gallidermin and epidermin. *In* Nisin and Novel Lantibiotics. *Eds.* G. Jung & H.P. Sahl, pp. 410-421, Escom, Leiden, 1991.

Schüz, T.C.; H.-P. Fiedler, H. Zähner, M. Rieck & W.A. König: Nikkomycins S_z, S_x, S_{oz} and S_{ox}, new intermedates associated to the nikkomycin biosynthesis of *Streptomyces tendae*. J. Antibiot. 45: 199-206, 1992.

Fiedler, H.-P. & A. Kohn: HPLC screening of new bacterial drugs using UV absorbance spectral libraries. Hewlett-Packard Application Note, Publication No. 12-5091-4331E, 1992.

Thiermann, F.; G. Bongs, K.-H. van Pée, D. Braun, H.-J. Cullmann, H.-P. Fiedler & H. Zähner: In vitro- and in vivo-halogenation of natural products by bacterial peroxidases. *In* DECHEMA Biotechnology Conferences, Vol. 5. *Eds.* G. Kreysa & A.J. Driesel, pp. 17-20, VCH Verlagsgesellschaft, Weinheim, 1992.

Braun, D.; H.-J. Cullmann, H.-P. Fiedler, H. Zähner, F. Thiermann & K.-H. van Pée: Enzymatic halogenation of microbial metabolites with a non-heme bromoperoxidase from *Streptomyces aureofaciens* TÜ 24. *In* DECHEMA Biotechnology Conferences, Vol. 5. *Eds.* G. Kreysa & A.J. Driesel, pp. 225-230, VCH Verlagsgesellschaft, Weinheim, 1992.

Fiedler, H.-P.; A. Kulik, J. Sauerbier & T.C. Schüz: Preparative liquid chromatographic methods for separation of nucleoside-peptide antibiotics of highest purity. *In* DECHEMA Biotechnology Conferences, Vol. 5. *Eds.* G. Kreysa & A.J. Driesel, pp. 635-641, VCH Verlagsgesellschaft, Weinheim, 1992.

Tschierske, M.; K. Goeke, H.-P. Fiedler & H. Zähner: Desferrioxamine E: optimization of the production process and new hydroxamate-type siderophores obtained by precursor directed biosynthesis. *In* DECHEMA Biotechnology Conferences, Vol. 5. *Eds.* G. Kreysa & A.J. Driesel, pp. 761-764, VCH Verlags-gesellschaft, Weinheim, 1992.

Hoff, H.; H. Drautz, H.-P. Fiedler, J.E. Schultz, W. Keller-Schierlein, S. Philips, M. Ritzau & A. Zeeck: Metabolic products of microorganisms. 261. Obscurolides, a novel class of phosphodiesterase inhibitors from *Streptomyces*. I. Production, isolation, structural elucidation and biological activitiy of obscurolides A_1 to A_4. J. Antibiot. 45: 1096-1107, 1992.

Fiedler, H.-P.; T. Schüz & H. Decker: An overview of nikkomycins: history, biochemistry, and applications. *In* Cutaneous Antifungal Agents: Compounds in

Clinical Practice and Development. *Eds.* J.W. Rippon & R.A. Fromtling, pp. 325-352, Marcel Dekker, New York, 1993.

Fiedler, H.-P. & A. Kohn: High performance liquid chromatographic screening of new bacterial drugs using UV absorbance spectral libraries. Europ. Microbiol. 2 (1): 39-44, 1993.

Seiffert, A.; K. Goeke, H.-P. Fiedler & H. Zähner: Production of the siderophore enterobactin: use of four different fermentation systems and identification of the compound by HPLC. Biotechnol. Bioeng. 41: 237-244, 1993.

Fiedler, H.-P.: Biosynthetic capacities of actinomycetes. 1. Screening for secondary metabolites by HPLC and UV-visible absorbance spectral libraries. Nat. Prod. Lett. 2: 119-128, 1993.

Schüz, T.C.; H.-P. Fiedler & H. Zähner: Optimized nikkomycin production by fed-batch and continuous fermentation. Appl. Microbiol. Biotechnol. 39: 433-437, 1993.

Sanglier, J.J.; E.M.H. Wellington, V. Behal, H.-P. Fiedler, R. Ellouz Ghorbel, C. Finance, M. Hacene, A. Kamoun, D. Kelly, D.K. Mercer, S. Prinzis & C. Trigo: Novel bioactive compounds from actinomycetes. Res. Microbiol. 144: 661-663, 1993.

Haag, H.; H.-P. Fiedler, J. Meiwes, H. Drechsel, G. Jung & H. Zähner: Isolation and biological characterization of staphyloferrin B, a compound with siderophore activity from staphylococci. FEMS Microbiol. Lett. 115: 125-130, 1994.

Fiedler, H.-P.; A. Kulik, T.C. Schüz, C. Volkmann & A. Zeeck: Biosynthetic capacities of actinomycetes. 2. Juglomycin Z, a new naphthoquinone antibiotic from *Streptomyces tendae*. J. Antibiot. 47: 1116-1122, 1994.

Zähner, H. & H.-P. Fiedler: The need for new antibiotics: possible ways forward. *In* Fifty Years of Antimicrobials. *Eds.* G.K. Darby *et al*., pp. 67-84, Cambridge University Press, Cambridge, 1995.

Volkmann, C.; U. Hartjen, A. Zeeck & H.-P. Fiedler: Biosynthetic capacities of actinomycetes. 3. Naphthgeranine F, a minor congener of the naphthgeranine group produced by *Streptomyces violaceus*. J. Antibiot. 48: 522-524, 1995.

Blum, S.; H.-P. Fiedler, I. Groth, C. Kempter, .H. Stephan, G.Nicholson, J.W. Metzger & G. Jung: Biosynthetic capacities of actinomycetes. 4. Echinoserine, a new member of the quinoxaline group, produced by *Streptomyces tendae*. J. Antibiot. 48: 619-625, 1995.

Kuhn, W. & H.-P. Fiedler: Sekundärmetabolismus bei Mikroorganismen. Beiträge zur Forschung. Attempto Verlag, Tübingen, 1995.

Fiedler, H.-P.: The Nikkomycin Story. *In* Sekundärmetabolismus bei Mikro-organismen. *Eds.* W. Kuhn & H.-P. Fiedler, pp. 79-89, Attempto Verlag, Tübingen, 1995.

Pfefferle, U.; K. Ochi & H.-P. Fiedler: The stringent response and the induction of nikkomycin production in *Streptomyces tendae*. Actinomycetol. 9: 118-123, 1995.

Blum, S.; I. Groth, J. Rohr & H.-P. Fiedler: Biosynthetic capacities of actinomycetes. 5. Dioxolides, novel secondary metabolites from *Streptomyces tendae*. J. Basic Microbiol. 36: 19-25, 1996.

Burkhardt, K.; H.-P. Fiedler, S. Grabley, R. Thiericke & A. Zeeck: New cineromycins and musacins obtained by metabolite pattern analysis of *Streptomyces griseoviridis* (FH-S 1832). I. Taxonomy, fermentation, isolation and biological activity. J. Antibiot. 49: 432-437, 1996.

Fiedler, H.-P.; M. Nega, C. Pfefferle, I. Groth, C. Kempter, H. Stephan & J.W. Metzger: Kanchanamycins, new polyol macrolide antibiotics produced by *Streptomyces olivaceus* Tü 4018. I. Taxonomy, fermentation, isolation and biological activities. J. Antibiot. 49: 758-764, 1996.

Stephan, H.; C. Kempter, J.W. Metzger, G. Jung, O. Potterat, C. Pfefferle & H.-P. Fiedler: Kanchanamycins, new polyol macrolide antibiotics produced by *Streptomyces olivaceus* Tü 4018. II. Structure elucidation. J. Antibiot. 49: 765-769, 1996.

Pfefferle, C.; C. Kempter, J.W. Metzger & H.-P. Fiedler: (*E*)-4-oxonon-2-enoic acid, an antibiotically active fatty acid produced by *Streptomyces olivaceus* Tü 4018. J. Antibiot. 49: 826-828, 1996.

Breckel, A.; H.-P. Fiedler, H. Zähner & M. Harder: Production of gallidermin by *Staphylococcus gallinarum* Tü 3928. *In* Biochemical Engineering 3. *Ed.* R.D. Schmid, pp. 62-66, Kurz, Stuttgart, 1996.

Schrenk, D.; D. Riebniger, M. Till, S. Vetter & H.-P. Fiedler: Tryptanthrins: a novel class of agonists of the aryl hydrocarbon receptor. Biochem. Pharmacol. 54: 165-171, 1997.

Zwicker, N.; U. Theobald, H. Zähner & H.-P. Fiedler: Optimization of fermentation conditions for the production of ethylene-diamine-disuccinic acid by *Amycolatopsis orientalis*. J. Industr. Microbiol. Biotechnol. 19: 280-285, 1997.

Kempf, M.; U. Theobald & H.-P. Fiedler: Influence of dissolved O_2 on the fermentative production of gallidermin by *Staphylococcus gallinarum*. Biotechnol. Lett. 19: 1063-1065, 1997.

Pfefferle, C.; J. Breinholt, H. Gürtler & H.-P. Fiedler: 1-Hydroxy-4-methoxy-2-naphthoic acid, a herbicidal compound produced by *Streptosporangium cinnabarinum* ATCC 31213. J. Antibiot. 50: 1067-1068, 1997.

Breinholt, J.; A. Kulik, H. Gürtler & H.-P. Fiedler: Tigloside: a new tigloylated tetrasaccharide from *Amycolatopsis* sp.. Acta Chem. Scand. 52: 1239-1242, 1998.

Kulik, A. & H.-P. Fiedler: Some aspects of the purification of anthraquinone antibiotics by preparative reversed-phase chromatography. J. Chromatogr. A 812: 117-121, 1998.

Richter, M.; J.M. Willey, R. Süssmuth, G. Jung & H.-P. Fiedler: Streptofactin, a novel biosurfactant with aerial mycelium inducing acitivity from *Streptomyces tendae* Tü 901/8c. FEMS Microbiol. Lett. 163: 165-171, 1998.

Höltzel, A.; C. Kempter, J.W. Metzger, G. Jung, I. Groth, T. Fritz & H.-P. Fiedler: Spirofungin, a new antifungal antibiotic from *Streptomyces violaceusniger* Tü 4113. J. Antibiot. 51: 699-707, 1998.

Paululat, T.; A. Zeeck, J.M. Gutterer & H.-P. Fiedler: Biosynthesis of polyketomycin produced by *Streptomyces diastatochromogenes* Tü 6028. J. Antibiot. 52: 96-101, 1999.

Kempf, M.; U. Theobald & H.-P. Fiedler: Economic improvement of the fermentative production of gallidermin by *Staphylococcus gallinarum*. Biotechnol. Lett. 21: 663-667, 1999.

Maier, A.; J. Müller, P. Schneider, H.-P. Fiedler, I. Groth, F.S.K. Tayman, F. Teltschik, C. Günther & G. Bringmann: (2*E*,4*Z*)-Decadienoic acid and (2*E*,4*Z*,7*Z*)-decatrienoic acid, two herbicidal metabolites from *Streptomyces viridochromogenes* Tü 6105. Pestic. Science 55: 733-739, 1999.

Stegmann, E.; U. Theobald, N. Zwicker, K. Wilken, H.-P. Fiedler & W. Wohlleben: *S,S*-EDDS (Ethylendiamindisuccinat): Ein mikrobiologisch hergestellter Komplexbildner – eine Alternative zu EDTA? GIT Labor-Fachzeitschr. 43: 1044-1046, 1999.

Kempf, M.; U. Theobald & H.-P. Fiedler: Correlation between the consumption of amino acids and the production of the antibiotic gallidermin by *Staphylococcus gallinarum*. Biotechnol. Lett. 21: 959-963, 1999.

Kempf, M.; U. Theobald & H.-P. Fiedler: Production of the antibiotic gallidermin by *Staphylococcus gallinarum* – development of a scale-up procedure. Biotechnol. Lett. 22: 123-128, 2000.

Pfefferle, C.; J. Breinholt, C.E. Olsen, R.M. Kroppenstedt, E.M.H. Wellington, H. Gürtler & H.-P. Fiedler: Kyanomycin, a complex of unusual anthracycline-phospholipid hybrids from *Nonomuria* species. J. Nat. Prod. 63: 295-298, 2000.

Pfefferle, C.; U. Theobald, G. Gürtler & H.-P. Fiedler: Improved secondary metabolite production in the genus *Streptosporangium* by fermentation. J. Biotechnol. 80: 135-142, 2000.

Ferguson, A.D.; V. Braun, H.-P. Fiedler, J.W. Coulton, K. Diederichs & W. Welte: Crystal structure of the antibiotic albomycin in complex with the outer membrane transporter FhuA. Protein Science 9: 956-963, 2000.

Schimana, J.; H.-P. Fiedler, I. Groth, R. Süssmuth, W. Beil, M. Walker & A. Zeeck: Simocyclinones, novel cytostatic angucyclinone antibiotics produced by *Streptomyces antibioticus* Tü 6040. I. Taxonomy, fermentation, isolation and biological activities. J. Antibiot. 53: 779-787, 2000.

Kempf, M.; U. Theobald & H.-P. Fiedler: The antibiotic gallidermin – evolution of a production process. *In* Novel Frontiers in the Production of Compounds for Biomedical Use, Vol. 1A. *Eds.* A. van Broekhoven *et al*., pp. 35-55, Kluwer Academic Press, Dordrecht, 2001.

Fiedler, H.-P.; P. Krastel, J. Müller, K. Gebhardt & A. Zeeck: Enterobactin: the characteristic catecholate siderophore of *Enterobacteriaceae* is produced by *Streptomyces* species. FEMS Microbiol. Lett. 196: 147-151, 2001

Theobald, U.; J. Schimana & H.-P. Fiedler: Microbial growth and production kinetics of *Streptomyces antibioticus* Tü 6040. Antonie van Leeuwenhoek 78: 307-313, 2000.

Gebhardt, K.; R. Pukall & H.-P. Fiedler: Streptocidins A-D, novel cyclic decapeptide antibiotics produced by *Streptomyces* sp. Tü 6071. I. Taxonomy, fermentation, isolation and biological properties. J. Antibiot. 54: 428-433, 2001.

Höltzel, A.; R.D. Süssmuth, R.W. Jack, G.J. Nicholson, K. Gebhardt, H.-P. Fiedler & G. Jung: Streptocidins A-D, novel cyclic decapeptide antibiotics produced by *Streptomyces* sp. Tü 6071. II. Structure elucidation. J. Antibiot. 54: 434-440, 2001.

Bertasso, M.; M. Holzenkämpfer, A. Zeeck, F. Dall'Antonia & H.-P. Fiedler: Bagremycin A and B, novel antibiotics from *Streptomyces* sp. Tü 4128. J. Antibiot. 54: 730-736, 2001

Tünnemann, R.; M. Mehlmann, R. Süssmuth, B. Bühler, S. Pelzer, W. Wohlleben, H.-P. Fiedler, K.-H. Wiesmüller, G. Gauglitz & G. Jung: Optical biosensors. Monitoring studies of glycopeptide antibiotic fermentation using white light interference. Anal. Chem. 73: 4313-4318, 2001.

Schimana, J.; M. Walker, A. Zeeck & H.-P. Fiedler: Simocyclinones: diversity of metabolites is dependent on fermentation conditions. J. Ind. Microbiol. Biotechnol. 27: 144-148, 2001.

Fiedler, H.-P. & H. Zähner: Screening for new secondary metabolites from micro-organisms. *In* Microbial Fundamentals of Biotechnology. *Eds*., V. Braun & F. Götz, pp.16-51, Wiley-VCH, Weinheim, 2001.

Holzenkämpfer, M.; M. Walker, A. Zeeck, J. Schimana & H.-P. Fiedler: Simocyclinones, novel cytostatic angucyclinone antibiotics produced by *Streptomyces antibioticus* Tü 6040. II. Structure elucidation and biosynthesis. J. Antibiot. 55: 301-307, 2002.

Trefzer, A.; S. Pelzer, J. Schimana, S. Stockert, C. Bihlmaier, H.-P. Fiedler, K. Welzel, A. Vente & A. Bechthold: Biosynthetic gene cluster of simocyclinone, a natural multihybrid antibiotic. Antimicrob. Agents Chemother. 46: 1174-1182, 2002.

Schimana, J.; K. Gebhardt, J. Müller, A. Höltzel, D.G. Schmid, R. Süssmuth, R. Pukall & H.-P. Fiedler: Arylomycins A and B, new biaryl-bridged lipopeptide antibiotics produced by *Streptomyces* sp. Tü 6075. I. Taxonomy, fermentation, isolation and biological activities. J. Antibiot. 55: 565-570, 2002

Höltzel, A.; D.G. Schmid, G.J. Nicholson, S. Stevanovic, J. Schimana, K. Gebhardt, H.-P. Fiedler & G. Jung: Arylomycins A and B, new biaryl-bridged lipopeptide antibiotics produced by *Streptomyces* sp. Tü 6075. II. Structure elucidation. J. Antibiot. 55: 571-577, 2002.

Galm, U.; J. Schimana, H.-P. Fiedler, J. Schmidt, S.-M. Li & L. Heide: Cloning and analysis of the simocyclinone biosynthetic gene cluster of *Streptomyces antibioticus* Tü 6040. Arch. Microbiol. 178: 102-114, 2002.

Gebhardt, K.; J. Schimana, P. Krastel, K. Dettner, J. Rheinheimer, A. Zeeck & H.-P. Fiedler: Endophenazines A-D, new phenazine antibiotics from the arthropod associated endosymbiont *Streptomyces anulatus*. I. Taxonomy, fermentation, isolation and biological properties. J. Antibiot. 55: 794-800, 2002.

Krastel, P.; A. Zeeck, K. Gebhardt, H.-P. Fiedler & J. Rheinheimer: Endophenazines A-D, new phenazine antibiotics from the arthropod associated endosymbiont *Streptomyces anulatus*. II. Structure elucidation. J. Antibiot. 55: 801-806, 2002.

Muschko, K.; G. Kienzlen, H.-P. Fiedler, W. Wohlleben & D. Schwartz: Tricarboxylic acid cycle aconitase activity during the life cycle of *Streptomyces viridochromogenes* Tü494. Arch. Microbiol. 178: 499-505, 2002.

Gebhardt, K.; J. Schimana, J. Müller, H.-P. Fiedler, H.G. Kallenborn, M. Holzenkämpfer, P. Krastel, A. Zeeck, J. Vater, A. Höltzel, J. Rheinheimer & K. Dettner: Screening for biologically active metabolites with endosymbiotic bacilli isolated from arthropods. FEMS Microbiol. Lett. 217: 199-205, 2002.

Bertasso, M.; M. Holzenkämpfer, A. Zeeck, E. Stackebrandt, W. Beil & H.-P. Fiedler: Ripromycin and other polycyclic macrolactams from *Streptomyces* sp. Tü 6239: taxonomy, fermentation, isolation and biological properties. J. Antibiot. 56: 364-371, 2003.

Dieter, A.; A. Hamm, H.-P. Fiedler, M. Goodfellow, W.E.G. Müller, R. Brun, W. Beil & G. Bringmann: Pyrocoll, an antibiotic, antiparasitic and antitumor compound produced by a novel alkaliphilic *Streptomyces* strain. J. Antibiot. 56: 639-646, 2003.

Fiedler, H.-P.; R.D. Süssmuth, H. Zähner & A.T. Bull: Polyzyklische Makrolactone. P 43 326 DE, October 1, 2003

Höltzel, A.; A. Dieter, D.G. Schmid, R. Brown, M. Goodfellow, W. Beil, G. Jung & H.-P. Fiedler: Lactonamycin Z, an antibiotic and antitumor compound produced by *Streptomyces sanglieri* strain AK 623. J. Antibiot. 56: 1058-1061, 2003.

Fiedler, H.-P.: Screening for bioactivity. *In* Microbial Diversity and Bioprospecting. *Ed*., A.T. Bull, pp. 324-335, ASM Press, Washington, 2004.

Riedlinger, J.; A. Reicke, H. Zähner, B. Krismer, A.T. Bull, L.A. Maldonado, A.C. Ward, M. Goodfellow, B. Bister, D. Bischoff, R. Süssmuth & H.-P. Fiedler: Abyssomicins, inhibitors of the *para*-aminobenzoic acid pathway produced by the marine *Verrucosispora* strain AB-18-032. J. Antibiot. 57: 271-279, 2004

Bister, B.; D. Bischoff, M. Ströbele, J. Riedlinger, A. Reicke, F. Wolter, A.T. Bull, H. Zähner, H.-P. Fiedler & R.D.Süssmuth: Abyssomicin C – a polycyclic antibiotic from a marine *Verrucosispora* strain as an inhibitor of the *p*-aminobenzoic acid/tetrahydrofolate biosynthesis pathway. Angew. Chem. Int. Ed. 43: 2574-2576, 2004.

Maier, A.; J. Riedlinger, H.-P. Fiedler & R. Hampp: Actinomycetales bacteria from a spruce stand: characterization and effects on growth of root symbiotic, and plant parasitic soil fungi in dual culture. Mycol. Progr. 3: 129-136, 2004.

Fiedler, H.-P. & M. Goodfellow: Alkaliphilic streptomycetes as a source of novel secondary metabolites. Microbiol. Australia 25 (2): 27-29, 2004.

Gebhardt, K.; J. Schimana, A. Höltzel, K. Dettner, S. Draeger, W. Beil, J. Rheinheimer & H.-P. Fiedler: Aspochalamins A-D and aspochalasin Z produced by the endosymbiotic fungus *Aspergillus niveus* LU 9575. I. Taxonomy, fermentation, isolation and biological activities. J. Antibiot. 57: 707-714, 2004.

Höltzel, A.; D.G. Schmid, G.J. Nicholson, P. Krastel, A. Zeeck, K. Gebhardt, H.-P. Fiedler & G. Jung: Aspochalamins A-D and aspochalasin Z produced by the endosymbiotic fungus *Aspergillus niveus* LU 9575. II. Structure elucidation. J. Antibiot. 57: 715-720, 2004.

Bertasso, M.; M. Holzenkämpfer, A. Zeeck, W. Beil & H.-P. Fiedler: Bagremycins are new para-coumaric acid derived antibiotics produced by *Streptomyces* sp. Tü 4128. *In* Biotechnological Advances and Applications in Bioconversion of Renewable Raw Materials. *Eds.*, R. Jonas *et al*., pp.86-91, Döringdruck, Braunschweig, 2004.

Antal, N.; H.-P. Fiedler, E. Stackebrandt, W. Beil, K. Ströch & A. Zeeck: Retymicin, galtamycin B, saquayamycin Z and ribofuranosyllumichrome, novel secondary metabolites from *Micromonospora* sp. Tü 6368. I. Taxonomy, fermentation, isolation and biological properties. J. Antibiot. 58: 95-102, 2005.

Ströch, K.; A. Zeeck, N. Antal & H.-P. Fiedler: Retymicin, galtamycin B, saquayamycin Z and ribofuranosyllumichrome, novel secondary metabolites from *Micromonospora* sp. Tü 6368. II. Structure elucidation. J. Antibiot. 58: 103-110, 2005.

Fiedler, H.-P.; C. Bruntner, A.T. Bull, A.C. Ward, M. Goodfellow, O. Potterat, C. Puder & G. Mihm: Marine actinomycetes as a source of novel secondary metabolites. Antonie van Leeuwenhoek 87: 37-42, 2005.

Flatman, R.H.; A.J. Howells, L. Heide, H.-P. Fiedler & A. Maxwell: Simocyclinone D8: an inhibitor of DNA gyrase with a novel mode of action. Antimicrob. Agents Chemother. 49: 1093-1100, 2005.

Bruntner,C.; T. Binder, W. Pathom-aree, M. Goodfellow, A.T. Bull, O. Potterat, C. Puder, S. Hörer, A. Schmid, W. Bolek, K. Wagner, G. Mihm & H.-P. Fiedler: Frigocyclinone, a novel angucyclinone antibiotic produced by a *Streptomyces* strain from Antarctica. J. Antibiot. 58: 346-349, 2005.

Bringmann, G.; G. Lang, K. Maksimenka, A. Hamm, T.A.M. Gulder, A. Dieter, A.T. Bull, J.E.M. Stach, N. Kocher, W.E.G. Müller & H.-P. Fiedler: Gephyromycin, the first bridged angucyclinone, from *Streptomyces griseus* strain NTK 14. Phytochemistry 66: 1365-1372, 2005.

Riedlinger, J.; S.D. Schrey, M.T. Tarkka, R. Hampp, M. Kapur & H.-P. Fiedler: Auxofuran, a novel metabolite that stimulates the growth of fly agaric, is produced by the mycorrhiza helper bacterium *Streptomyces* AcH 505. Appl. Environ. Microbiol. 72: 3550-3557, 2006.

Radzom, M.; A. Zeeck, N. Antal & H.-P. Fiedler: Fogacin, a novel cyclic octaketide produced by *Streptomyces* strain Tü 6319. J. Antibiot. 59: 315-317, 2006.

Baur, S.; J. Niehaus, A.D. Karagouni, E.A. Katsifas, K. Chalkou, C. Meintanis, A. Jones, M. Goodfellow, A.C. Ward, W. Beil, K. Schneider, R.D. Süssmuth & H.-P. Fiedler: Fluostatins C~E novel members of the fluostatin family produced by *Streptomyces* strain Acta 1383. J. Antibiot. 59: 293-297, 2006.

Bringmann, G.; T.F. Noll, T.A.M. Gulder, M. Grüne, M. Dreyer, C. Wilde, F. Pankewitz, M. Hilker, G.D. Payne, A.L. Jones, M. Goodfellow & H.-P. Fiedler: Different polyketide folding modes converge to an identical molecular architecture. Nature Chem. Biol. 2: 429-433, 2006.

Graf, E.; K. Schneider, G. Nicholson, M. Ströbele, A.L. Jones, M. Goodfellow, W. Beil, R.D. Süssmuth & H.-P. Fiedler: Elloxazinones A and B, new aminophenoxazinones from *Streptomyces griseus* Acta 2871. J. Antibiot. 60: 277-284, 2007.

Schneider, K.; I. Rose, S. Vikineswary, A.L. Jones, M. Goodfellow, G. Nicholson, W. Beil, R. Süssmuth & H.-P. Fiedler: Nocardichelins A and B, siderophores from *Nocardia* strain Acta 3026. J. Nat. Prod. 70: 932-935, 2007.

Keller, S.; G. Nicholson, C. Drahl, E. Sorensen, H.-P. Fiedler & R.D. Süssmuth: Abyssomicins G and H and atrop-abyssomicin C from the marine *Verrucosispora* strain AB-18-032. J. Antibiot. 60: 391-394, 2007.

Textor, A.; I. Papastavrou, J. Siewert, J. Magull, A. Kulik, H.-P. Fiedler, P. von Zezschwitz & S. Grond: Spridionic acid, a novel metabolite from *Streptomyces* sp., part 1: structure elucidation and Diels-Alder-type biosynthesis. Chem. Eur. J. 13: 7416-7423, 2007.

Zhang, X.; L.B. Alemany, H.-P. Fiedler, M. Goodfellow & R.P. Parry: Biosynthetic investigations of lactonamycin and lactonamycin Z: cloning of the biosynthetic gene clusters and discovery of an unusual starter unit. Antimicrob. Agents Chemother. 52: 574-585, 2008.

Fiedler, H.-P.; C. Bruntner, J. Riedlinger, A.T. Bull, G. Knutsen, A.L. Jones, M. Goodfellow, W. Beil, K. Schneider, S. Keller & R.D. Süssmuth: Proximicins A~C, novel aminofuran antibiotics from marine *Verrucosispora* strains. J. Antibiot. 61: 158-163, 2008.

Schneider, K.; S. Keller, F.E. Wolter, L. Röglin, W. Beil, O. Seitz, G. Nicholson, C. Bruntner, J. Riedlinger, H.-P. Fiedler & R.D. Süssmuth: Proximicins A, B and C – antitumor furan analogues of netropsin from the marine actinomycete *Verrucosispora* induce upregulation of p53 and the cyclin kinase inhibitor p21. Angew. Chem. Int. Ed. 47: 3258-3261, 2008.

Huang, X.; J. He, X. Niu, K.-D. Menzel, H.-M. Dahse, S. Grabley, H.-P. Fiedler, I. Sattler & C. Hertweck: Benzopyrenomycin, a cytotoxic bacterial polyketide metabolite with an unprecedented benzo[a]pyrene-type carbacyclic ring system. Angew. Chem. Int. Ed. 47: 3995-3998, 2008.

Schneider, K.; E. Graf, E. Irran, G. Nicholson, F.M. Stainsby, M. Goodfellow, S.A. Borden, S. Keller, R.D. Süssmuth & H.-P. Fiedler: Bendigoles A~C, new steroids from *Gordonia australis* Acta 2299. J. Antibiot. 61: 356-364, 2008.

Paululat, T.; E.A. Katsifas, A.D. Karagouni & H.-P. Fiedler: Grecoketides A and B, new naphthoquinones from *Streptomyces* sp. Acta 1362. Eur. J. Org. Chem. 2008: 5283-5288, 2008.

Fiedler, H.-P.; A. Dieter, T.A.M. Gulder, I. Kajahn, A. Hamm, M. R. Brown, A.L. Jones, Goodfellow, W.E.G. Müller & G. Bringmann: Genoketides A1 and A2, new octaketides and biosynthetic intermediates of chrysophanol produced by *Streptomyces* sp. AK 671. J. Antibiot. 61: 464-473, 2008.

Sommer, P.S.M.; R.C. Almeida, W. Beil, R.D. Süßmuth & H.-P. Fiedler: Nataxazole, a new benzoxazole derivative with antitumor activity produced by *Streptomyces* sp. Tü 6176. J. Antibiot. 61: 683-686, 2008.

Hohmann, C.; K. Schneider, C. Bruntner, R. Brown, A.L. Jones, M. Goodfellow, M. Krämer, J.F. Imhoff, G. Nicholson, H.-P. Fiedler & R.D. Süssmuth,: Albidopyrone, a new α-pyrone containing metabolite from marine-derived *Streptomyces* sp. NTK 227. J. Antibiot. 62: 75-79, 2009.

Hohmann, C.; K. Schneider, C. Bruntner, E. Irran, G. Nicholson, A.T. Bull, A.L. Jones, R. Brown, J.E.M. Stach, M. Goodfellow, W. Beil, J.F. Imhoff, R.D. Süssmuth & H.-P. Fiedler: Caboxamycin, a new antibiotic of the benzoxazole family from deep-sea strain *Streptomyces* sp. NTK 937. J. Antibiot. 62: 99-104, 2009.

Oppegard, L.M.; B.L. Hamann, K.R. Streck, K.C. Ellis, H.-P. Fiedler, A.B. Khodursky & H. Hiasa: *In vivo* and *in vitro* patterns of the activity of simocyclinone D8, an angucyclinone antibiotic from *Streptomyces antibioticus*. Antimicrob. Agents Chemother. 53: 2110-2119, 2009.

Saleh, O.; B. Gust, B. Boll, H.-P. Fiedler & L. Heide: Aromatic prenylation in the phenazine biosynthesis: dihydrophenazine-1-carboxylate dimethylallyltransferase from *Streptomyces anulatus*. J. Biol. Chem. 284: 14439-14447, 2009.

Schulz, D.; J. Nachtigall, J. Riedlinger, K. Schneider, K. Poralla, J.F. Imhoff, W. Beil, G. Nicholson, H.-P. Fiedler & R.D. Süssmuth: Piceamycin and its *N*-acetylcysteine adduct is produced by *Streptomyces* sp. GB 4-2. J. Antibiot. 62: 513-518, 2009.

Helaly, S.; K. Schneider, J. Nachtigall, S. Vikineswary, G.Y.A. Tan, H. Zinecker, J.F. Imhoff, R.D. Süssmuth & H.-P. Fiedler: Gombapyrones, new α-pyrone metabolites produced by *Streptomyces griseoruber* Acta 3662. J. Antibiot. 62: 445-452, 2009.

Laiple, K.J.; T. Härtner, H.-P. Fiedler, W. Wohlleben & T. Weber: The kirromycin gene cluster of *Streptomyces collinus* Tü 365 codes for an aspartate-α-decarboxylase, KirD, which is involved in the biosynthesis of the precursor β-alanine. J. Antibiot. 62: 465-468, 2009.

Le, T.B.K.; H.-P. Fiedler, C.D. den Hengst, S.K. Ahn, A. Maxwell & M.J. Buttner: Coupling of the biosynthesis and export of the DNA gyrase inhibitor simocyclinone in *Streptomyces antibioticus*. Molec. Microbiol. 72: 1462-1474, 2009.

Schneider, K.; J. Nachtigall, A. Hänchen, G. Nicholson, M. Goodfellow, R.D. Süssmuth & H.-P. Fiedler: Lipocarbazoles, new secondary metabolites from *Tsukamurella pseudospumae* Acta 1857 with antioxidative activity. J. Nat. Prod. 72: 1768-1772, 2009.

Bringmann, G.; T.A.M. Gulder, A. Hamm, M. Goodfellow & H.-P. Fiedler: Multiple convergence in polyketide biosynthesis: a third folding mode to the anthraquinone chrysophanol. Chem Commun. 2009: 6810-6812, 2009.

Bringmann, G.; A. Irmer, D. Feineis, T.A.M. Gulder & H.-P. Fiedler: Convergence in the biosynthesis of polyketide natural products from plants, fungi and bacteria. Phytochemistry 70: 1776-1786, 2009.

Edwards, M.J.; R.H. Flatman, L.A. Mitchenall, C.E.M. Stevenson, T.B.K. Le, T.A. Clarke, A.R. McKay, H.-P. Fiedler, M.J. Buttner, D.M. Lawson & A. Maxwell: A crystal structure of the bifunctional antibiotic, simocyclinone D8, bound to DNA gyrase. Science 326: 1415-1417, 2009.

Paululat, T.; A. Kulik, H. Hausmann, A.D. Karagouni, H. Zinecker, J.F. Imhoff & H.-P. Fiedler: Grecocyclines: new angucyclines from *Streptomyces* sp. Acta 1362. Eur. J. Org. Chem. 2010: 2344-2350, 2010.

Abdel-Mageed, W.M.; B.F. Milne, M. Wagner, M. Schumacher, P. Sandor, W. Pathom-aree, M. Goodfellow, A.T. Bull, K. Horikoshi, R. Ebel, M. Diedrich, H.-P. Fiedler & M. Jaspars: Dermacozines, a new phenazine family from deep-sea dermacocci isolated from a Mariana Trench sediment. Org. Biomol. Chem. 8: 2352-2362, 2010.

Nachtigall, J.; D. Schulz, W. Beil, R.D. Süssmuth & H.-P. Fiedler: Aranciamycin anhydride, a new anthracycline-type antibiotic isolated from *Streptomyces* sp. Tü 6384. J. Antibiot. 63: 397-399, 2010.

Nachtigall, J.; K. Schneider, G. Nicholson, M. Goodfellow, H. Zinecker, J.F. Imhoff, R.D.Süssmuth & H.-P. Fiedler: Two new aurachins from *Rhodococcus* sp. Acta 2257. J. Antibiot. 63: 567-569, 2010.

Goodfellow, M. & H.-P. Fiedler: A guide to successful bioprospecting: informed by actinobacterial systematics. Antonie van Leeuwenhoek 98: 119-142, 2010.

Gebhardt, K.; S.W. Meyer, J. Schinko, G. Bringmann, A. Zeeck & H.-P. Fiedler: Phenalinolactones A-D, terpenoglycoside antibiotics from *Streptomyces* sp. Tü 6071. J. Antibiot. 64: 229-232, 2011.

Brötz, E.; A. Kulik, S. Vikineswary, C.-T. Lim, G.Y.A. Tan, H. Zinecker, J.F. Imhoff, T. Paululat & H.-P. Fiedler: Phenelfamycins G and H, new elfamycin-type antibiotics produced by *Streptomyces albospinus* Acta 3619. J. Antibiot. 64: 257-266, 2011.

Helaly, S.E.; A. Pesic, H.-P. Fiedler & R.D. Süssmuth: Elaiomycins B and C: alkylhydrazide antibiotics from *Streptomyces* sp. BK 190. Org. Lett. 13: 1052-1054, 2011.

Le, T.B.K.; C.E.M. Stevenson, H.-P. Fiedler, A. Maxwell, D.M. Lawson & M.J. Buttner: Structures of the TetR-like simocyclinone efflux pump repressor, SimR, and the mechanism of ligand-mediated derepression. J. Molec. Biol. 408: 40-56, 2011.

Pohle, S.; C. Appelt, M. Roux, H.-P. Fiedler & R.D. Süssmuth: The biosynthetic gene cluster of the non-ribosomally synthesized cyclodepsipeptide skyllamycin – deciphering new ways of unusual hydroxylation reactions. J. Am. Chem. Soc. 133: 6194-6205, 2011.

Gottardi, E.M.; J.M. Krawczyk, H. von Suchodoletz, S. Schadt, A. Mühlenweg, G.C. Uguru, S. Pelzer, H.-P. Fiedler, M.J. Bibb, J.E.M. Stach & R.D. Süssmuth: Abyssomicin biosynthesis: formation of an unusual polyketide, antibiotic-feeding studies and genetic analysis. ChemBioChem 12: 1401-1410, 2011.

Nachtigall, J.; K. Schneider, C. Bruntner, A.T. Bull, M. Goodfellow, H. Zinecker, J.F. Imhoff, G. Nicholson, E. Irran, R.D. Süssmuth & H.-P. Fiedler: Benzoxacystol, a benzoxazine-type enzyme inhibitor from the deep-sea strain *Streptomyces* sp. NTK 935. J. Antibiot. 64: 453-457, 2011.

Kim, B.-Y.; S. Willbold, A. Kulik, S.E. Helaly, H. Zinecker, J. Wiese, J.F. Imhoff, M. Goodfellow, R.D. Süssmuth & H.-P. Fiedler: Elaiomycins B and C, novel alkylhydrazides produced by *Streptomyces* sp. BK 190. J. Antibiot. 64: 595-597, 2011.

Nachtigall, J.; A. Kulik, S. Helaly, A.T. Bull, M. Goodfellow, J.A. Asenjo, A. Maier, J. Wiese, J.F. Imhoff, R.D. Süssmuth & H.-P. Fiedler: Atacamycins A-C, 22-membered antitumor macrolactones produced by *Streptomyces* sp. C38. J. Antibiot. 64: 775-780, 2011.

Kim, B.-Y.; T.D. Zucci, H.-P. Fiedler & M. Goodfellow: *Streptomyces cocklensis* sp. nov., a dioxamycin-producing actinomycete. Int. J. Syst. Evol. Microbiol. 62: 279-283, 2012.

Saleh, O.; K. Flinspach, L. Westrich, A. Kulik, B. Gust, H.-P. Fiedler & L. Heide: Mutational analysis of a phenazine biosynthetic gene cluster in *Streptomyces anulatus* 9663. Beilstein J. Org. Chem. 8: 501-513, 2012.

Saleh, O.; T. Bonitz, K. Flinspach, A. Kulik, N. Burkard, A. Mühlenweg, A. Vente, S. Polnick, M. Lämmerhofer, B. Gust, H.-P. Fiedler & L. Heide: Activation of a silent phenazine biosynthetic gene cluster reveals a novel natural product and a new resistance mechanism against phenazines. Med. Chem. Commun. 3, 1009-1019, 2012.

Helaly, S.E.; A. Kulik, H. Zinecker, K. Ramachandaran, G.Y.A. Tan, J.F. Imhoff, R.D. Süssmuth, H.-P. Fiedler and V. Sabaratnam: Langkolide, a 32-membered macrolactone antibiotic produced by *Streptomyces* sp. Acta 3062. J. Nat. Prod. 75: 1018-1024, 2012.

Kim, B.-Y.; T.D. Zucchi, H.-P. Fiedler & M. Goodfellow: *Streptomyces staurosporinus* sp. nov., a staurosporine-producing actinomycetel. Int. J. Syst. Evol. Microbiol. 62: 966-970, 2012.

Schulz, D.; J. Nachtigall, U. Geisen, H. Kalthoff, J.F. Imhoff, H.-P. Fiedler & R.D. Süssmuth: Silvalactam, a 24-membered macrolactam antibiotic produced by *Streptomyces* sp. Tü 6392. J. Antibiot. 65: 369-372, 2012.

Schrey, D.S.; E. Erkenbrack, E. Früh, S. Fengler, K. Hommel, N. Horlacher, D. Schulz, M. Ecke, A. Kulik, H.-P. Fiedler, R. Hampp & T.M. Tarkka: Production of fungal and bacterial growth modulating secondary metabolites is widespread among mycorrhiza-associated streptomycetes. BMC Microbiol. 12: 164, 2012.

Goodfellow, M.; J.E.M. Stach, R. Brown, A.N.V. Bonda, A.L. Jones, J. Mexson, H.-P. Fiedler, T.D. Zucchi & A.T. Bull: *Verrucosispora maris* sp. nov., a novel deep-sea actinomycete isolated from a marine sediment which produces abyssomicins. Antonie van Leeuwenhoeck 101: 185-193, 2012.

Manderscheid, N.; S.E. Helaly, A. Kulik, J. Wiese, J.F. Imhoff, H.-P. Fiedler & R.D. Süssmuth: Elaiomycins K and L, new azoxy antibiotics from *Streptomyces* sp. Tü 6399. J. Antibiot. 66: 85-88, 2013.

Horlacher, N.; J. Nachtigall, D. Schulz, R.D. Süssmuth, R. Hampp, H.-P. Fiedler & S.D. Schrey: Biotransformation of the fungal phytotoxin fomannoxin by soil streptomycetes. J. Chem. Ecol. DOI: 10.1007/s10886-013-0290-3, 2013.

Kalyon, B.; G.-Y.A. Tan, J.M. Pinto, C.-Y. Foo, J. Wiese, J.F. Imhoff, R.D. Süssmuth, V. Sabaratnam & H.-P. Fiedler: Langkocyclines, novel angucycline antibiotics from *Streptomyces* sp. Acta 3024. J. Antibiot. DOI:10.1038/ja.2013.53, 2013.

Helaly, S.E.; M. Goodfellow, H. Zinnecker, J.F. Imhoff, R.D. Süssmuth & H.-P. Fiedler: Warkmycin, a novel angucycline antibiotic produced by *Streptomyces* sp. Acta 2930. J. Antibiot., in press 2013.

Jetter, P.; C. Steinert, M. Knauer, G. Zhang, T. Bruhn, J. Wiese, J.F. Imhoff, H.-P. Fiedler & G. Bringmann: New bhimamycins from *Streptomyces* sp. AK 671. J. Antibiot., in press 2013.