

Chemistry and Biology of Mycotoxins and Related Fungal Metabolites

Stefan Bräse,* Arantxa Encinas,[†] Julia Keck,[‡] and Carl F. Nising[§]

Institut für Organische Chemie, Karlsruhe Institute of Technology, Fritz-Haber-Weg 6, D-76131 Karlsruhe, Germany

Received October 1, 2007

Contents

| | |
|---------------------------------------------------------------|------|
| 1. Introduction | 3903 |
| 1.1. Occurrence of Mycotoxins | 3905 |
| 1.2. Toxicology/Mycotoxicoses/Risks | 3905 |
| 1.2.1. Aflatoxins | 3906 |
| 1.2.2. Ochratoxins | 3906 |
| 1.2.3. Trichothecenes | 3906 |
| 1.2.4. Fumonisin | 3906 |
| 1.2.5. Patulin | 3907 |
| 2. Total Synthesis | 3907 |
| 2.1. Aflatoxins | 3935 |
| 2.2. Citrinin | 3938 |
| 2.3. Ergot Alkaloids | 3939 |
| 2.4. Fumonisin | 3939 |
| 2.5. Ochratoxin | 3942 |
| 2.6. Patulin | 3945 |
| 2.7. Trichothecenes | 3946 |
| 2.7.1. Introduction | 3946 |
| 2.7.2. Total Syntheses of the Sesquiterpenoid Core | 3948 |
| 2.7.3. Macrocyclic Trichothecenes | 3949 |
| 2.7.4. Other Small Trichothecenes | 3952 |
| 2.8. Zearalenone and Related Macrolactones | 3952 |
| 2.9. Other mycotoxins | 3956 |
| 2.9.1. <i>Alternaria</i> metabolites | 3956 |
| 2.9.2. Skyrisins | 3958 |
| 2.9.3. Xanthones | 3960 |
| 2.9.4. Cytochalasans | 3961 |
| 2.9.5. Peptidic Mycotoxins | 3963 |
| 3. Biosynthesis | 3964 |
| 3.1. Polyketide-Derived Mycotoxins | 3964 |
| 3.2. Terpenoid Mycotoxins | 3968 |
| 3.3. Mycotoxins Incorporating Amino Acids | 3968 |
| 3.3.1. Mixed Biosynthesis | 3969 |
| 3.3.2. Directed Biosynthesis | 3970 |
| 4. Structure–Activity Relationships | 3970 |
| 5. Mycotoxins and Related Compounds As Potential Therapeutics | 3974 |
| 6. Conclusions/Summary | 3975 |
| 7. Abbreviations | 3975 |
| 8. Acknowledgments | 3975 |
| 9. References | 3975 |

1. Introduction

Nature produces a variety of different species, prokaryotes and eukaryotes. Among them, fungi play a very important, but yet mostly unexplored role. Their widespread occurrence on land and in marine life makes them a challenge and a risk for humans.

During their lifespan, fungi metabolize and produce a broad range from simple to very complex organic compounds. Most of them exhibit certain biological activities. However, a specific characteristic is the production of toxins. Mycotoxins (from “myco” fungus and toxin) are nonvolatile,¹ relatively low-molecular weight,² fungal³ secondary metabolic products that may affect exposed vertebrates such as animals in a variety of ways. In contrast, other metabolites such as penicillins, only (or mainly) affecting prokaryotes or other eukaryotes, are in general not classified as mycotoxins.

Mycotoxins are considered secondary metabolites because they are not necessary for fungal growth and are simply a product of primary metabolic processes. The functions of mycotoxins have not been clearly established, but they are believed to play a role in eliminating other microorganisms competing in the same environment. They are also believed to help parasitic fungi invade host tissues.⁴ The amount of toxins needed to produce adverse health effects varies widely among toxins, as well as within each person’s immune system.

Some mycotoxins are carcinogenic, some are vasoactive, and some cause central nervous system damage. Often, a single mycotoxin can cause more than one type of toxic effect. We will discuss this briefly in section 1.2.

Fungi that produce mycotoxins are referred to as toxigenic fungi. The most frequently studied mycotoxins (see Table 2) are produced by species of *Aspergillus*, *Claviceps*,⁵ *Fusarium*, *Penicillium*,⁶ *Stachybotrys*, and *Myrothecium*.⁷

However, toxins have been detected from many other fungi under certain growth conditions. An important and steadily increasing number of natural products have been isolated from marine⁸ and pathogenic insecticidal fungi.⁹ In most cases, the toxicology has not yet been fully elaborated, and thus, their status remains unclear. We have included the most important fungal metabolites in this review. The type and amount of toxin produced depends on the fungal strain, the growing conditions, and the presence or absence of other organisms.

Fungi may be classified by the humidity, Xerophiles (e.g., *Aspergillus restrictus*, *A. glaucus*, *A. versicolor*) and Hygrophilic (e.g., *Cladosporium*, *Fusarium*, *Mucorales*), or by temperature, Thermophiles (e.g., *Byssoschlamys*, *Aspergillus fumigatus*), Thermotolerants (e.g., *Aspergillus niger*), Mesophilic (e.g., *Penicillium chrysogenum*, *P. expansum*, *P.*

* To whom correspondence should be addressed. Fax +49 721 608 8581. E-mail: braese@kit.edu..

[†] New address of A.E.: Elara Pharmaceuticals, Heidelberg, Germany.

[‡] New address of J.K.: Evonik Degussa, Rheinfelden, Germany.

[§] New address of C.N.: Bayer Cropscience, Monheim, Germany.



Stefan Bräse was born in Kiel, Germany, in 1967. After he studied in Göttingen, Bangor (U.K.), and Marseille, he received his Ph.D. in 1995, after working with Armin de Meijere in Göttingen. After postdoctoral appointments at Uppsala University (Jan E. Bäckvall) and The Scripps Research Institute, La Jolla (K. C. Nicolaou), he began his independent research career at the RWTH Aachen, Germany, in 1997 (associated to Dieter Enders). In 2001, he finished his Habilitation and moved to the University of Bonn as professor for organic chemistry. Since 2003, he is full professor at the University of Karlsruhe, Germany. He is recipient (among other awards) of the OrChem award of the GDCh and the Lilly award. His research interests include methods in drug discovery (including drug delivery), combinatorial chemistry towards the synthesis of biologically active compounds, and total synthesis of natural products and nanotechnology.



Julia Keck, née Gall, was born 1980 in Ludwigshafen/Rhein, Germany, in 1980. She studied chemistry at the University of Karlsruhe, where she received her diploma degree in 2004. During her graduate studies in the research group of Stefan Bräse, she worked on the total synthesis of pharmacologically active natural products. After completing her Ph.D. work in 2007, she joined Evonik Degussa GmbH as R&D scientist (Innovation Management Silanes). Her research interests include asymmetric catalysis, natural product chemistry, and synthesis of organometallic compounds.

cyclopium, *Aspergillus versicolor*, *A. flavus*, *A. nidulans*, *A. fumigatus*), and Cryophiles (e.g., *Cladosporium*, *Alternaria*).

Mycotoxins accumulate on fungal spores, cell fragments, and substrates (nutrient sources). Although the toxic effects of fungal metabolites have been known for centuries (St. Anthony's fire), nowadays the threat of adverse effects from mycotoxins has gained dramatic importance due to the reduced application of antifungal treatment on food.¹⁰

According to the literature, far more than 400 mycotoxins are produced by some 350 species of fungi.¹¹ However, we found a significantly higher number of relevant bioactive/toxic fungal metabolites: around 1000 compounds are presented in this review.



Arantxa Encinas López was born in Madrid, Spain, in 1977. She studied at the Autonomía University of Madrid and received her Ph.D. in 2006 at the Medicinal Chemistry Institute of CSIC in Madrid (Ana Castro). After a postdoctoral appointment at Karlsruhe University (Stefan Bräse), she joined as a postdoctoral fellow in the Chemical Biology core department of EMBL in Heidelberg (Joe Lewis). Since January 2009, she is working as medicinal chemist in Elara pharmaceuticals GmbH on the design and synthesis of pharmacologically active compounds as novel and efficacious medicines for the treatment of cancer. Her research focuses on medicinal chemistry, including the synthesis of natural products and small molecules with biological activity and combinatorial chemistry.



Carl Nising was born in 1979 in Troisdorf, Germany. He studied chemistry at the University of Bonn, where he received his diploma degree in 2003. He then moved to the University of Karlsruhe (TH), where he obtained his Ph.D. under the supervision of Stefan Bräse in 2006. After performing postdoctoral studies at Harvard University with Andrew G. Myers, he joined Bayer CropScience AG in late 2007, where he is currently head of laboratory in fungicide research. His research interests are natural product chemistry, heterocyclic chemistry, and the development of new synthetic methods. His research was supported by fellowships of the Studienstiftung des Deutschen Volkes and the Scheringstiftung. Additionally, he was recipient of the Klaus Grohe Prize and the Wolff&Sohn Award.

In this review, the chemistry such as the total synthesis and semisynthesis of the most important mycotoxins is discussed.¹² Some aspects have been reviewed earlier.^{13–17}

Many secondary metabolites have been isolated from fungi; however, since mycotoxins are always affiliated with biological activity, this is a requirement to be considered in this review. If a member of a structural class is recognized as a mycotoxin, the whole group is mentioned (e.g., anthraquinones). While mycotoxins with particular significance in terms of food safety¹⁸ and human health are discussed in detail, less abundant and rare mycotoxins are only mentioned briefly. Since the biosynthesis of mycotoxins is an important issue, we will outline the current status (section 3). Recent studies (by Hertweck and colleagues) have demonstrated that some mycotoxins (rhizoxin and

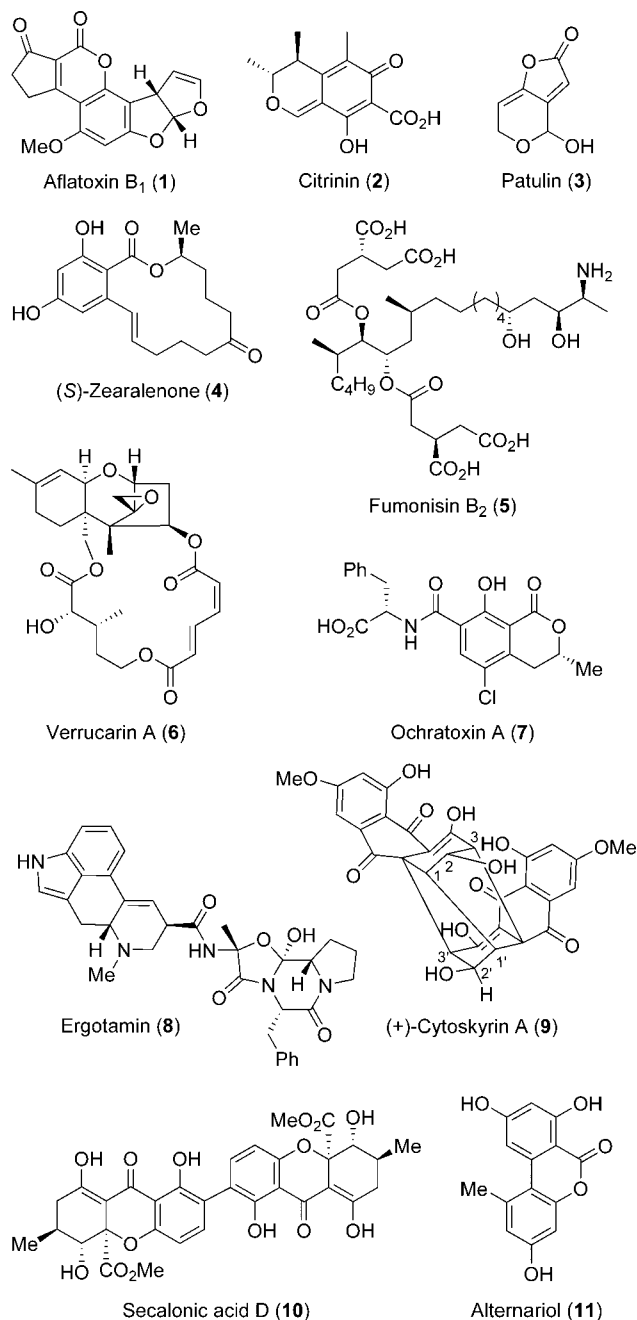


Figure 1. Important mycotoxins.

rhizonin) are not produced by fungi but by endosymbiotic bacteria that live within the fungal cytosol.¹⁹

1.1. Occurrence of Mycotoxins

Mycotoxins occur in many varieties of fungi. Several mycotoxins are unique to one species, but most mycotoxins are produced by more than one species. The most widespread mycotoxin is roquefortine C, which is produced by 25 species.²⁰ The most important mycotoxins are described in Figure 1 and Tables 1 and 2. Some of the compounds were also isolated from higher plants and bacteria; however, these sources are not included in this review. Because of the high number of mycotoxins,²¹ only their names are listed in the tables. A full list of structures published by the end of 1980/ mid 1990s can be found in comprehensive references,^{16,22} in the *Dictionary of Natural Products*, in the useful database *Antibase*, and on several Web sites.^{7,23,24}

To illustrate the variety of mycotoxins produced by fungi, Table 2 shows the mycotoxins produced by *Aspergillus* sp.

As a general overview, Table 3 includes all relevant mycotoxins and some related fungal metabolites (with alternate name, putative stereochemistry/sign of optical rotation, CA number/molecular formula if necessary, and/or common abbreviation in parentheses), together with their fungal source, their biological activity, and (if available) their total synthesis. It is organized by chemical classification of the core structure and then arranged alphabetically. Part of the Chemical Abstracts name was used for classification in the case of complex structures. Because of the large number of references, a selection was made.

1.2. Toxicology/Mycotoxicoses/Risks

The association of mycotoxins with human and animal health is not a recent phenomenon; for example, in the past, *ergotism* was suspected of being a toxicosis resulting from these toxic fungal metabolites. Nowadays, more is known regarding this family of compounds.^{841,842} The mycotoxins can be acutely or chronically toxic, or both, depending on the kind of toxin, the dose, the health, the age and nutritional status of the exposed individual or animal, and the possible synergistic effects between mycotoxins.⁸⁴³ Mycotoxin-producing fungi grow on a wide spectrum of feeds that include cereal grains, ground nuts, beans, and peas. They can invade the food supply at any time during production, processing, transport, or storage.

The exposure to mycotoxins is mostly by ingestion but can also occur by dermal contact or inhalation. The affection produced by these toxins is known as mycotoxicosis, which is named primary mycotoxicosis when it is provoked by consuming contaminated food and feed, or secondary mycotoxicosis when produced by eating meat or milk from animals that ingested forage containing mycotoxins.⁸⁴⁴

Mycotoxins affect specific tissues or organs depending on the particular toxin involved. In general, mycotoxins are specifically associated with a particular feed, are not transmissible from organism to organism (except when special circumstances are considered, like milk production for future human consumption), and are usually not responsive to any kind of direct treatment. Animals are more often affected by mycotoxins through the interference with nutrient absorption and metabolism, by affecting endocrine and neuroendocrine functions, or by suppression of the immune system. However, in humans, the presence of mycotoxins in food can be cumulative, leading to cancers (in liver, kidney, digestive tract, or reproductive system) and to immunodeficiency diseases.⁸⁴⁵ The impact of these fungi in human carcinogenesis has been the subject of intensive study only since the early 1960s, because a mycotoxicosis can provoke tumor formation or even rapid death.

Mycotoxicoses in animals are better understood than in humans, due to the fact that the experimental studies appear more reliable.⁸⁴⁶ Some diseases in humans involving mycotoxins are outlined in Table 4.⁸⁴⁷

Mycotoxins of global importance such as aflatoxins B₁ (1), B₂ (15), G₁ (13), and G₂ (19); deoxynivalenol (231); zearalenone (4); fumonisin B₁ (92); T-2 toxin (224); and ochratoxin A (7), produced by fungi on pre- and postharvest food and feeds, have led to the contamination of the food chain, resulting in severe economic losses and serious health problems in human beings and livestock. There are more than 350 types of mycotoxins that can occur in food.

Table 1. Chemical Classification of Mycotoxins According to Bérđy Modified after Betina¹⁶

| code number | divisions | representative |
|-------------|----------------------------------------------------|---------------------------------------|
| 2 | macrocyclic lactones | |
| 2.3.53 | Brefeldin type | Zearalenone (4) |
| 3 | quinone and similar compounds | |
| 3.1.3.2 | dianthraquinone derivatives | Rugolysin |
| 3 | amino acid, peptide compounds | |
| 4.1.3.2 | diketopiperazine derivatives | |
| 4.1.3.2.1 | Gliotoxin type | Gliotoxin (527) |
| 6 | oxygen-containing heterocycles | |
| 6.1 | furan derivatives | |
| 6.1.2.1 | Aflatoxin type | Aflatoxin B ₁ (1) |
| 6.2 | pyran derivatives | |
| 6.2.3.2 | Citreoviridin type | Citreoviridin |
| 6.3 | benzo[g]pyran derivatives | |
| 6.3.4.1 | dibenzo[g]pyrone derivatives | Secalonic acid D (10) |
| 6.4. | small lactones | |
| 6.4.2.1 | small lactones condensed with hetero- or alicycles | Patulin (3) |
| 6.4.2.5 | isocoumarin derivatives | Ochratoxin A (7) |
| 7 | alicyclic compounds | |
| 7.3 | oligoterpenes | |
| 7.3.3.1 | Trichodermin type | T-2 toxin (224) |
| 8 | aromatic compounds | |
| 8.2.1.1 | Griseofulvin type | Griseofulvin |

Nowadays, concern exists about interactions among mycotoxins that can produce additive and sometimes synergistic effects.⁸⁴⁸

Since these mycotoxins are natural contaminants, they cannot be completely eliminated without damaging food. For this reason, there are food-safety programs⁸⁴⁹ that evaluate the levels of aflatoxins, trichothecenes, ergots, ochratoxins, and, particularly, patulin.

Most mycotoxins have specific effects on a given system in an animal, but many of them affect several systems simultaneously. To understand the different levels of toxicity provoked by mycotoxins, it is crucial to have knowledge of their biological activation. Some details of the main mycotoxins are outlined in the following sections.

1.2.1. Aflatoxins

Aflatoxins grow mainly on grains and legumes. Corn, peanuts, and cotton seed are the materials with the highest risk of contamination, but aflatoxins are also detected in almonds, figs, and a variety of other foods and feeds. Milk, milk products (nonfat powdered milk, cheese, and yogurt), eggs, and meat products are contaminated because of animal consumption of aflatoxin-contaminated feed. Moreover, aflatoxins found in tobacco have been demonstrated to be toxic to animals after inhalation and ingestion.⁸⁵⁰

Exposure to aflatoxins is typically through the ingestion of contaminated foodstuff, while dermal exposure results in slow and insignificant absorption.⁸⁵⁰ Aflatoxins are most commonly known for causing acute or chronic liver disease,⁸⁵¹ but they are also considered immunosuppressive, hepatotoxic, mutagenic, teratogenic, and carcinogenic.⁸⁵²

Currently, the maximum concentration of aflatoxins permitted in food is set by the U.S. Food and Drug Administration (FDA). Food and milk for human consumption is allowed to contain 20 ppb and 0.5 ppb of AF, respectively. High levels up to 300 ppb are allowed in feed for cattle, hogs, and poultry. Currently, there are no standards for workplace or environmental aflatoxin exposures.

1.2.2. Ochratoxins

Ochratoxin A (**7**) is a main contaminant of cereals (corn, barley, wheat) and to some extent beans (coffee, soy, cocoa).

On the basis of studies conducted on animals, it is easily absorbed through the gastrointestinal tract mainly in the duodenum and jejunum.⁸⁵³ There are no studies on skin or inhalational absorption. When absorbed, it has a high binding affinity for plasma protein. In humans, ochratoxin A (**7**) interacts primarily with the kidney but, when present in high doses, it interacts with other organs such liver or spleen, or the immune system.⁸⁵⁴

The toxicity of ochratoxin A (**7**) involves several mechanisms:⁸⁵⁵ (a) inhibition of protein synthesis through competition with the phenylalanine aminoacylation reaction catalyzed by Phe-tRNA synthase, resulting in the prevention of protein as well as DNA and RNA synthesis; (b) disruption of hepatic microsomal calcium homeostasis by impairing the endoplasmic reticulum membrane via lipid peroxidation. Ochratoxin A produces nephrotoxicity, mild liver damage, enteritis, immunosuppression, teratogenesis, and carcinogenesis (kidney tumors).⁸⁵⁶

1.2.3. Trichothecenes

Trichothecenes are present in crops, food, and animal feed contaminated with *Fusarium* species. Their mechanism of toxicity can be due to (a) inhibition of protein synthesis (specifically in eukaryotes),⁸⁵⁷ (b) inhibition of DNA synthesis,⁸⁵⁸ or (c) inhibition of the mitochondrial electron-transport system.⁸⁵⁹

The most important trichothecenes are deoxynivalenol (**230**), T-2 toxin (**224**), and zearalenone (**4**). They are responsible for the alimentary toxic aleukia (ATA) in humans and farm animals. Zearalenone (**4**) is a genotoxin that has estrogenic potency and causes reproductive problems in animals, particularly in swine.

The 12,13-epoxide of the trichothecenes is essential for their toxicity.⁸⁶⁰ As a matter of fact, the de-epoxidation of T-2 (**224**) in mammalian systems results in a loss of toxicity.

1.2.4. Fumonisin

Fumonisin are common contaminants of corn, corn-based foods (such as sorghum and rice), and maize. There is no report on the transfer of fumonisins into milk or their absorption in tissues.

Table 2. Mycotoxins Produced by *Aspergillus* sp.

| fungus | mycotoxin produced |
|------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Aspergillus aculeatus</i> | Secalonic acid D (10) |
| <i>Aspergillus albertensis</i> | Ochratoxin A (7), Ochratoxin B (155) |
| <i>Aspergillus alliaceus</i> | Ochratoxin A (7), Ochratoxin B (155) |
| <i>Aspergillus auricomus</i> | Ochratoxin A (7), Ochratoxin B (155) |
| <i>Aspergillus bombycis</i> | Aflatoxin B ₁ (1), Aflatoxin G (13) |
| <i>Aspergillus brevipes</i> | Viriditoxin |
| <i>Aspergillus caespitosus</i> | Fumitremorgin A |
| <i>Aspergillus candidus</i> | Citrinin (2), Acetylisonicosolaniol |
| <i>Aspergillus carneus</i> | Citrinin (2) |
| <i>Aspergillus clavatus</i> | Patulin (3), Tryptoquivaline A (C), Cytochalasin E (443) |
| <i>Aspergillus flavipes</i> | Citrinin (2) |
| <i>Aspergillus flavus</i> | Aflatoxin B ₁ (1), Aflatoxin B ₂ (15), Aflatoxin M ₁ (12), Cyclopiazonic acid, Aflatrem (indole alkaloid), 3-Nitropropionic acid, Sterigmatocystin (62), Versicolorin A (597), Aspertoxin Xanthomegnin (591) |
| <i>Aspergillus fresenii</i> | Fumitremorgin A, Verruculogen (543), Gliotoxin (527), Fumagillin, Helvolic acid, Sphingofungins, Brevianamide A (545), Phthioic acid, Fumigaclavin C, Aurasperone C |
| <i>Aspergillus fumigatus</i> | Patulin (3) |
| <i>Aspergillus giganteus</i> | Ochratoxin A (7), Viomellein, Xanthomegnin (591) |
| <i>Aspergillus melleus</i> | Aspothalasin |
| <i>Aspergillus microcysticus</i> | Sterigmatocystin (62), Dechloronidulin, Emestrin |
| <i>Aspergillus nidulans</i> (<i>Emericella nidulans</i>) | Malformin, Ochratoxin A (7), Fumonisin B ₂ (5) |
| <i>Aspergillus niger</i> | Aflatoxin B ₁ (1), Aflatoxin B ₂ (15), Aflatoxin G ₁ (13), Aflatoxin G ₂ (19) |
| <i>Aspergillus nomius</i> | Aflatoxin B ₁ (1), Sterigmatocystin (62) |
| <i>Aspergillus ochraceoroseus</i> | Ochratoxin A (7), Ochratoxin B (155), Ochratoxin C (156), Viomellein, Penicillic acid (187) |
| <i>Aspergillus ochraceus</i> | Cyclopiazonic acid, Maltoryzine, 3-Nitropropionic acid |
| <i>Aspergillus oryzae</i> | Ochratoxin A (7) |
| <i>Aspergillus ostianus</i> | Aflatoxin B ₁ (1), Aflatoxin B ₂ (15), Aflatoxin G ₁ (13), Aflatoxin G ₂ (19), Aflatoxin M ₁ (12), Versicolorin A (597) |
| <i>Aspergillus parasiticus</i> | Ochratoxin A (7) |
| <i>Aspergillus petrakii</i> | Cyclopiazonic acid, Aflatoxin B ₁ (1) |
| <i>Aspergillus pseudotamarii</i> | Restrictocin |
| <i>Aspergillus restrictus</i> | Ochratoxin B (155) |
| <i>Aspergillus sclerotiorum</i> | Ochratoxin A (7), Ochratoxin B (155) |
| <i>Aspergillus sulfureus</i> | Territrein A, ²⁵ Citreoviridin, Citrinin (2), Gliotoxin (527), Patulin (3), Terrein, Terreic acid, Terretonin, Itaconic acid, Aspulvinone, Asterriquinone, butyrolactone I, Emodin (573), Geodin, Itaconate, Lovastatin, ²⁶ Questin, Sulochrin, Terrecyclic acid. |
| <i>Aspergillus terreus</i> | Austdiol, Austin, Austocystin A, Sterigmatocystin (62) |
| <i>Aspergillus ustus</i> | Sterigmatocystin (62) |
| <i>Aspergillus varicolor</i> | Sterigmatocystin (62), Cyclopiazonic acid, Versicolorin A (597) |
| <i>Aspergillus versicolor</i> | Viriditoxin |
| <i>Aspergillus viridinitans</i> | Emodin (573), 3-Nitropropionic acid, Ochratoxin A (7), Ochratoxin B (155), |
| <i>Aspergillus wentii</i> | Aflatoxins (1, 12–22) |
| <i>Emericella venezuelensis</i> | Echinulin, Neoechinulin, Gliotoxin (527), Xanthocillin |
| <i>Eurotium chevalieri</i> | Fumitremorgin A, Fumitremorgin C, Verruculogen (543), |
| <i>Neosartorya fischeri</i> | Tryptoquivaline A (C) |

In animals, they provoke cerebral edema and liquefaction necrosis, and even centrilobular necrosis (hypoxic hepatitis) and hepatic fibrosis are observed in severe cases.⁸⁶¹ Liver disease, including tumors of the liver have also been associated with fumonisin intoxication. It has been reported that chronic exposure to fumonisins induces immunotoxicity, although this is still an area of active research.

However, the major reason for interest in fumonisins is their possible role as environmental tumor promoters in causing human cancer (concretely esophageal carcinoma).^{862,863} Their mechanism of toxicity consists of the inhibition of the sphingolipid synthesis, due to their structural similarity with sphingoid bases, resulting in the disruption of sphingomyelin.⁸⁶⁴ The disruption of sphingomyelin and metabolism in cells provokes cell damage, apoptosis, necrosis, and compensatory hyperplasia.⁸⁶⁵ Unfortunately, awareness of its tumor-promotion mechanism

has been limited by the general lack of understanding in this field. In recent years, fumonisin research has become one of the most active areas in fungal secondary metabolism.⁸⁶⁶

1.2.5. Patulin

Patulin is most frequently found in fruits such as apples, pears, and grapes. As a major symptom, it provokes congestion and edema of pulmonary, hepatic, and intestinal blood vessels and tissues. Moreover, sarcomas were observed when large doses of patulin were injected into animals. However, the mechanisms through which patulin causes toxicity are still not well-understood.⁸⁶⁷

2. Total Synthesis

Numerous mycotoxins have been targeted by total synthesis. In this section, we present the most important mycotoxins and their syntheses.

Table 3. Selected Mycotoxins and Other Secondary Metabolites: Isolation, Producing Fungus, Synthesis

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|---------------------|----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|----------------------|
| Aflatoxin | 4- and 22-Hydroxyaflatoxin B1 | <i>d</i> | | MTX |
| Aflatoxin | 5,6-Dimethoxysterigmatocystin | <i>Aspergillus versicolor</i> | | MTX, cyto |
| Aflatoxin | 5-Hydroxydihydrosterigmatocystin | <i>d</i> | 27 | MTX |
| Aflatoxin | 5-Methoxysterigmatocystin (3a,12c-Dihydro-8-hydroxy-6,11-dimethoxy-7H-furo[3',2':4,5]furo[2,3-c]xanthen-7-one) | <i>Aspergillus versicolor</i> | 27 | MTX |
| Aflatoxin | Aflatoxin B ₁ (1) (–) | <i>Aspergillus flavus</i> , ^{c,7} <i>A. nomius</i> ⁷ | <i>rac</i> : 28–31; (–): 32 | MTX |
| Aflatoxin | Aflatoxin B ₂ (15) | <i>Aspergillus flavus</i> , <i>A. nomius</i> ⁷ | <i>rac</i> : 33; (–): 34 | MTX |
| Aflatoxin | Aflatoxin B _{2a} (17) (–) | <i>Aspergillus flavus</i> | <i>rac</i> : 28; (–): 32 | MTX |
| Aflatoxin | Aflatoxin B ₃ (Parasiticol) | <i>Aspergillus flavus</i> , <i>A. parasiticus</i> | | MTX |
| Aflatoxin | Aflatoxin G ₁ (13) | <i>Aspergillus flavus</i> , ^c <i>A. nomius</i> ⁷ | <i>rac</i> : 29 | MTX |
| Aflatoxin | Aflatoxin G ₂ (19) | <i>Aspergillus flavus</i> , ^c <i>A. nomius</i> ⁷ | | MTX |
| Aflatoxin | Aflatoxin G _{2a} (21) | <i>Aspergillus flavus</i> | | MTX |
| Aflatoxin | Aflatoxin GM ₁ (14) | <i>Aspergillus flavus</i> | | MTX |
| Aflatoxin | Aflatoxin GM ₂ (20) | <i>Aspergillus flavus</i> ^c | | MTX |
| Aflatoxin | Aflatoxin GM _{2a} (22) | <i>Aspergillus flavus</i> | | MTX |
| Aflatoxin | Aflatoxin M ₁ (12) | <i>Aspergillus flavus</i> ^c | <i>rac</i> : 29 | MTX |
| Aflatoxin | Aflatoxin M ₂ (16) (Dihydroaflatoxin M ₁) | <i>Aspergillus flavus</i> ^c | | MTX |
| Aflatoxin | Aflatoxin M _{2a} (18) | <i>Aspergillus flavus</i> | | MTX |
| Aflatoxin | Aflatoxin P ₁ | Metabolic products | 35 | MTX ^d |
| Aflatoxin | Aflatoxin R ₀ (Aflatoxicol) (2 Stereoisomers) | Microbial degradation product ^d | | MTX |
| Aflatoxin | Aflatoxin S | <i>Aspergillus flavus</i> | | MTX |
| Aflatoxin | Aspertoxin | <i>Aspergillus flavus</i> | Dihydro, formal synthesis: ³⁶ | MTX |
| Aflatoxin | Demethylsterigmatocystin (598) | <i>Aspergillus nidulans</i> , <i>A. versicolor</i> ³⁷ | | MTX |
| Aflatoxin | Dihydroaflatoxicol | Metabolite | | MTX |
| Aflatoxin | Dihydrodemethylsterigmatocystin (600) (1,2-Dihydro-6,7-hydroxydifuroxanthone) | <i>Aspergillus parasiticus</i> , <i>A. versicolor</i> ^{38,39} | | MTX |
| Aflatoxin | Dihydro- <i>O</i> -methylsterigmatocystin (602) | <i>Aspergillus parasiticus</i> | 40, 41 | MTX |
| Aflatoxin | Dihydrosterigmatocystin (584) (1,2-Dihydro-6-methoxy-7-hydroxydifuroxanthone) | <i>Aspergillus parasiticus</i> , <i>A. versicolor</i> ⁴² | | MTX |
| Aflatoxin | Dothistromin | <i>Cercospora arachidicola</i> ⁴³ | | MTX, cyto, mut |
| Aflatoxin | <i>O</i> -Methylsterigmatocystin (63) (5-Methoxysterigmatocystin) | <i>Aspergillus parasiticus</i> , <i>A. versicolor</i> , <i>Chaetomium virescens</i> ²³ | 40, 41, 44 | MTX |
| Aflatoxin | Sterigmatocystin (62) | <i>Aspergillus versicolor</i> ^{c,7} , <i>A. rugulosus</i> , <i>A. amstelodami</i> , <i>A. chevalieri</i> , <i>A. nidulans</i> , <i>A. ustus</i> , <i>Bipolaris sorokinina</i> , <i>Chaetomium virescens</i> ²³ | | MTX, carc |
| Alkaloid | Fustucine | <i>Acremonium</i> sp. | | MTX |
| Alkaloid | Loline, <i>N</i> -formyllolines, <i>N</i> -acetyllooline, perloline | <i>Acremonium coenophialum</i> | 45 | MTX |
| Alkaloid | Pyroclasin | <i>Penicillium commune</i> | | MTX |
| Alkaloid | Rubrobramide | <i>Cladobotyrum rubrobrunnescens</i> | 46 | w cyto, phytotox |
| Alkynylbenzaldehyde | Frustulosin | <i>Stereum hirsutum</i> | 47 | MTX |
| Alternaria toxin | 5'-Epialtenuene (5'-epi-Altenuene) | <i>Alternaria alternata</i> , ⁴⁸ unidentified freshwater aquatic fungus (<i>Tubeufiaceae</i>) | | MTX |
| Alternaria toxin | Altenuene (391) (ALT) | <i>Alternaria tenuis</i> , <i>A. alternata</i> ^{49–51} | 52 | MTX |
| Alternaria toxin | Altenuic acid I | <i>Alternaria tenuis</i> , <i>A. alternata</i> ^{53–55} | | MTX |
| Alternaria toxin | Altenuic acid II (552) | <i>Alternaria tenuis</i> , <i>A. alternata</i> ^{53,54,56} | | MTX |
| Alternaria toxin | Altenuic acid III | <i>Alternaria tenuis</i> , <i>A. alternata</i> ^{53,54} | | MTX |
| Alternaria toxin | Altenuisol | <i>Alternaria tenuis</i> ^{49,57,58} | | MTX |
| Alternaria toxin | Altenuisin (408) | <i>Alternaria alternata</i> , <i>Penicillium</i> sp. ^{59,60} | 61 | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|-----------------------------------|-----------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------|
| Alternaria toxin | Alternaric acid | <i>Alternaria solani</i> | 62 | Phytotox |
| Alternaria toxin | Alternarin | <i>Alternaria alternata</i> | | MTX |
| Alternaria toxin | Alternariol (11) (AOH) | <i>Alternaria tenuis</i> ^c , <i>Alternaria alternata</i> | 63–65 | MTX |
| Alternaria toxin | Alternariol 9-methyl ether (377) (AME) | <i>Alternaria tenuis</i> , <i>Alternaria alternata</i> ^{51,53} | | MTX |
| Alternaria toxin | Altertenuol | <i>Alternaria tenuis</i> ⁴⁹ | | MTX |
| Alternaria toxin | Altertoxin I (ATX I) (a hydroxyperylenequinone) | <i>Alternaria alternata</i> | | MTX, mut |
| Alternaria toxin | Altertoxin II (ATX II) (a hydroxyperylenequinone) | <i>Alternaria alternata</i> | | MTX, mut |
| Alternaria toxin | Altertoxin III (ATX III) (a hydroxyperylenequinone) | <i>Alternaria alternata</i> | | MTX, mut |
| Alternaria toxin | Dehydroaltenuene A | <i>Tubeufiaceae</i> spp. (unidentified aquatic fungus) ⁶⁶ | | MTX |
| Alternaria toxin | Dehydroaltenuene B | <i>Tubeufiaceae</i> spp. (unidentified aquatic fungus) ⁶⁶ | rac: 67 | MTX |
| Alternaria toxin | Dehydroaltenuin (393) | <i>Alternaria tenuis</i> , <i>Penicillium verruculosum</i> ^{59,68} | rac: 61, 69 | MTX, kin |
| Alternaria toxin | Desmethyldehydroaltenuin | <i>Talaromyces flavus</i> ⁷⁰ | | MTX |
| Alternaria toxin | Dihydroaltenuene A | <i>Tubeufiaceae</i> spp. (unidentified aquatic fungus) ⁶⁶ | | MTX |
| Alternaria toxin | Dihydroaltenuene B | <i>Tubeufiaceae</i> spp. (unidentified aquatic fungus) ⁶⁶ | | MTX |
| Alternaria toxin | Isoaltenuene (392) | <i>Alternaria alternata</i> ^{71–73} | 51, 52 | MTX |
| Alternaria toxin | Neoaltenuene | <i>Alternaria alternata</i> ⁴⁸ | 1074a | MTX |
| Alternaria toxin | Tenuazonic acid ⁷⁴ | <i>Alternaria tenuis</i> ^c , <i>A. alternata</i> , <i>A. nomius</i> , ⁷ <i>Penicillium aurantiogriseum</i> , <i>P. chrysogenum</i> , <i>P. crustosum</i> , <i>P. expansum</i> , <i>P. griseofulvum</i> , <i>P. solitum</i> , <i>P. verrucosum</i> | Analogues: 75 | MTX, cyto |
| Amino acid | Hadacidin (<i>N</i> -formyl- <i>N</i> -hydroxyglycine) | <i>Penicillium frequentans</i> | 76 | MTX, antitumor |
| Amino acid | Mycestericin A–G | <i>Mycelia sterilia</i> | 77, 78 | MTX |
| Amino acid | Myriocin | <i>Isaria sinclairii</i> | 77, 79, 601 | immuno |
| Amino acid | Sulfamisterin (AB 5366) | <i>Pycnidiaella</i> sp. | 77 | MTX |
| Amino acid | Xylariamide A | <i>Xylaria</i> sp. | 80 | brine shrimp assay |
| Amino alkyl citrate antibiotic | Viridifungin A, A2, A4, B, C | <i>Trichoderma viride</i> | 77; A: 81 | micro |
| Anthracenone | Physcion-9-anthrone (Physcioanthrone B) | <i>Aspergillus glaucus</i> , <i>A. chevalieri</i> | | MTX |
| Anthracenone dimer | Physciodianthrone | <i>Aspergillus chevalieri</i> | | MTX |
| Anthraquinoid | 1,8- <i>O</i> -Dimethylaverantin | <i>Penicillium chrysogenum</i> ⁸² | | MTX |
| Anthraquinoid | 1-Acetyl-2,4,5,7-tetrahydroxy- 9,10-anthracenedione | <i>Trichoderma viride</i> | | MTX |
| Anthraquinoid | 2-Hydroxyemodin (Alaternin) | <i>Ventilago leiocarpa</i> | microbiological synthesis: 83 | MTX |
| Anthraquinoid | 8- <i>O</i> -Methylaverufin | <i>Penicillium chrysogenum</i> ⁸² | | MTX |
| Anthraquinoid | Altersolanol A (Stemphylin) | <i>Alternaria solani</i> | 84 | phytotox |
| Anthraquinoid | Altersolanol B (Dactylarin) | <i>Alternaria solani</i> | rac: 85 | MTX, cyto |
| Anthraquinoid | Altersolanol J | <i>Cladosporium</i> sp. ^{d,86} | | MTX |
| Anthraquinoid | Asperthecin ⁸⁷ (1,2,4,5,6-Pentahydroxy-7- hydroxymethylanthraquinone) | <i>Aspergillus quadrilineatus</i> , <i>Emericella venezuelensis</i> ^b | | MTX |
| Anthraquinoid | Averantin (587) (–) | <i>Aspergillus parasiticus</i> , <i>A. versicolor</i> ⁸⁸ | | MTX |
| Anthraquinoid | Averufanin (589) (Avermutin) (+) | <i>Aspergillus versicolor</i> , <i>A. ustus</i> ⁸⁹ | | MTX |
| Anthraquinoid | Averufin (590) ⁹⁰ | <i>Aspergillus parasiticus</i> , <i>A. ustus</i> , <i>A. versicolor</i> , <i>Emericella navahoensis</i> ⁹¹ | 92, 93 | MTX |
| Anthraquinoid | Carviolin (roseo-purpurin) (1,3-Dihydroxy-6- (hydroxymethyl)-8-methoxyanthraquinone) | <i>Penicillium carmine-violaceum</i> , <i>Zopfella longicaudata</i> (Ascomycete) ¹²⁴ | | w immun |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|---------------------------|
| Anthraquinoid | Catenarin (1,4,5,7-Tetrahydroxy-2-methylanthraquinone) | <i>Penicillium islandicum</i> , ^c <i>Pyrenophora graminea</i> , <i>Dreschlera catenaria</i> ⁹⁴ | biotransformation ⁹⁵ | MTX |
| Anthraquinoid | Cercosporin | <i>Cercospora nicotianae</i> , <i>C. beticola</i> ⁹⁶ | | MTX, phyto |
| Anthraquinoid | Chrysazin (danthron, 1,8-dihydroxy-9,10-anthracenedione) | <i>Chaetomium globosum</i> | 97 | MTX |
| Anthraquinoid | Chrysophanol ⁹⁸ (83) | <i>Penicillium islandicum</i> , <i>P. kloeckeri</i> , <i>Trichoderma harzianum</i> ⁷ | 99–102, 117 | MTX, not mut |
| Anthraquinoid | Cynodontin (1,4,5,8-Tetrahydroxy-2-methylanthraquinone) | <i>Helminthosporium cynodontis</i> , ^c <i>pyrenochaeta terrestris</i> , <i>cochliobolus lunatus</i> ¹⁰³ | | MTX |
| Anthraquinoid | Dactylariol (Altersolanol C) | <i>Pleospora</i> sp. ¹⁰⁴ | | MTX, cyto |
| Anthraquinoid | Demethyl solorinic acid | <i>Aspergillus versicolor</i> ¹⁰⁵ | | MTX |
| Anthraquinoid | Deoxyaverufinone | <i>Aspergillus versicolor</i> ¹⁰⁶ | | MTX |
| Anthraquinoid | Dihydrocatenarin | <i>Penicillium islandicum</i> | | MTX |
| Anthraquinoid | Emodic acid | <i>Penicillium albicans</i> | | MTX |
| Anthraquinoid | Emodin (573) | <i>Aspergillus wentii</i> , ^c <i>A. aculeatus</i> ¹⁰⁷ <i>Penicillium islandicum</i> , ^{c,7} <i>Pyrenochaeta terrestris</i> , ¹⁰⁷ <i>Trichoderma viride</i> ⁷ | 101, 108 | MTX, not mut |
| Anthraquinoid | Emodin-2-carboxylic acid | <i>Penicillium islandicum</i> | | MTX |
| Anthraquinoid | Endocrocin (–) | <i>Pyrenochaeta terrestris</i> , ¹⁰⁷ <i>Aspergillus aculeatus</i> , ¹⁰⁷ <i>Penicillium tardum</i> ¹⁰⁹ | 110 | MTX |
| Anthraquinoid | Erythroglaucin | <i>Aspergillus glaucus</i> , ^c <i>A. chevalieri</i> , <i>A. echinulatus</i> , <i>A. niveoglaucus</i> , <i>A. ruber</i> , <i>A. umbrosus</i> , <i>Eurotium</i> sp., <i>Chaetomium globosum</i> ¹⁶⁷ | 111 | Tox, MTX |
| Anthraquinoid | Erythrokyrine | <i>Penicillium islandicum</i> ^{7,112} | 113 | MTX |
| Anthraquinoid | F-742-C | <i>Trichoderma viride</i> ¹¹⁴ | | MTX |
| Anthraquinoid | Hydroxyviocristin | <i>Aspergillus cristatus</i> | 115 | MTX |
| Anthraquinoid | Islandicin | <i>Penicillium islandicin</i> | 116, 117 | MTX |
| Anthraquinoid | Lunatin (1,3,8-trihydroxy-6-methoxyanthraquinone) | <i>Curvularia lunata</i> ^b | | bact |
| Anthraquinoid | Macrosporin | <i>Alternaria porri</i> , <i>A. alternaria</i> , <i>Stemphylium eturmiunum</i> | by degradation from alterporriol A ¹¹⁸ | prob mut |
| Anthraquinoid | Nidurufin (an aflatoxin precursor) | <i>Aspergillus nidulans</i> , <i>Emericella</i> sp. | 92 | MTX, w mut |
| Anthraquinoid | Norsolorinic acid (586) (2- <i>n</i> -Hexanoyl-1,3,6,8-tetrahydroxyanthraquinone) | <i>Aspergillus versicolor</i> , <i>A. parasiticus</i> , <i>Emericella navahoensis</i> ⁹¹ | | MTX, w mut |
| Anthraquinoid | Physcion ¹¹⁹ (Parietin, chrysophanic acid, emodin 3-methyl ether, 6- <i>O</i> -methylemodin, rheochrysidin, Chrysorobin, Parmel yellow, Lichen-chrysophanic acid, Przewalskinone B) | <i>Aspergillus glaucus</i> , ^c <i>A. echinulatus</i> , <i>A. niveoglaucus</i> , <i>A. ruber</i> , <i>A. umbrosus</i> , <i>P. herquei</i> , <i>Eurotium amstelami</i> , ⁷ <i>E. chevalieri</i> , ⁷ <i>E. herbariorum</i> ⁷ <i>Chaetomium globosum</i> ¹⁶⁷ | 100, 102 | MTX |
| Anthraquinoid | Questin (1- <i>O</i> -Methylemodin, Methylemodin) | <i>Zopfiella longicaudata</i> (Ascomycete) | 120 | MTX |
| Anthraquinoid | Rhein | <i>Rheum emodi</i> ¹²¹ | 122 | anticancer ¹²³ |
| Anthraquinoid | Roseopurpurin (Roseo-purpurin, Carviolin) | <i>Penicillium carmine-violaceum</i> , <i>Zopfiella longicaudata</i> (Ascomycete) ¹²⁴ | | MTX, mod immun |
| Anthraquinoid | Rubrocristin | <i>Aspergillus cristatus</i> | | MTX |
| Anthraquinoid | Rubroglaucin (C ₁₆ H ₁₂ O ₅) ²³ | <i>Aspergillus umbrosus</i> , <i>A. ruber</i> , <i>A. neveoglaucus</i> , <i>A. echinulatus</i> , <i>Gliocladium roseum</i> | | MTX |
| Anthraquinoid | Triacetylemodin | <i>Trichoderma polysporum</i> | 125 | HIV |
| Anthraquinoid | Tritisporin | <i>Helminthosporium tritici-vulgaris</i> | | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^d |
|---------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------|
| Anthraquinoid | Versiconal (577) | <i>Aspergillus parasiticus</i> | | MTX |
| Anthraquinoid | Versiconal acetate (574) (S) | <i>Aspergillus flavus</i> , <i>A. parasiticus</i> ²³ | | MTX, prob mut |
| Anthraquinoid | Viocristin | <i>Aspergillus cristatus</i> | 115 | MTX |
| Anthraquinoid | <i>ω</i> -Acetylcarviolin | <i>Aspergillus glaucus</i> , <i>Penicillium frequetans</i> , <i>Zopfiella longicaudata</i> (Ascomycete) | | MTX |
| Anthraquinoid | <i>ω</i> -Hydroxyemodin (citreorosein) | <i>Penicillium islandicum</i> , <i>Zopfiella longicaudata</i> | 126 | w immun |
| Anthraquinoid dimer | 4-Oxyluteoskyrin (–) | <i>Penicillium islandicum</i> | | MTX |
| Anthraquinoid dimer | Alterporriol A (–) (5,6,7,8-Tetrahydro-4,4',5,6,6',7,8-heptahydroxy-2,2'-dimethoxy-7,7'-dimethyl-1,1'-bianthracene-9,9',10,10'-tetrone) | <i>Alternaria porri</i> | 127 | MTX |
| Anthraquinoid dimer | Alterporriol B | <i>Alternaria porri</i> | 128 | MTX |
| Anthraquinoid dimer | Alterporriol C | <i>Alternaria porri</i> | 127 | MTX |
| Anthraquinoid dimer | Alterporriol D | <i>Alternaria porri</i> | | MTX |
| Anthraquinoid dimer | Aurantioskyrin (+) | <i>Penicillium islandicum</i> ¹³⁴ | | MTX |
| Anthraquinoid dimer | Auroskyrin (+) | <i>Penicillium islandicum</i> ¹³⁴ | | MTX |
| Anthraquinoid dimer | Cytoskyrin A (9) | <i>Cytospora</i> sp. ¹²⁹ | (+)-2,2'- <i>epi</i> -Cytoskyrin A (417), ^{130,131} model: 132 | MTX, bact |
| Anthraquinoid dimer | Cytoskyrin B | <i>Cytospora</i> sp. ¹²⁹ | | MTX |
| Anthraquinoid dimer | Deoxyluteoskyrin (–) | <i>Penicillium islandicum</i> | | MTX |
| Anthraquinoid dimer | Deoxyrubroskyrin (–) | <i>Penicillium islandicum</i> | model: 132 | MTX |
| Anthraquinoid dimer | Dianhydrorugulosin (+) | <i>Penicillium islandicum</i> | | MTX |
| Anthraquinoid dimer | Dicatenarin (+) | <i>Penicillium islandicum</i> | | MTX |
| Anthraquinoid dimer | Flavoskyrin (–) | <i>Penicillium islandicum</i> | model: 132 | MTX |
| Anthraquinoid dimer | Iridoskyrin A (+) | <i>Penicillium islandicum</i> | | Not mut |
| Anthraquinoid dimer | Lumluteoskyrin (Photoproduct) | <i>Penicillium</i> sp. | 133 | Mut |
| Anthraquinoid dimer | Luteoskyrin (–) | <i>Penicillium islandicum</i> ^{c,7} | | MTX, carc |
| Anthraquinoid dimer | Oxyskyrin (+) | <i>Penicillium islandicum</i> | | MTX |
| Anthraquinoid dimer | Punicoskyrin (+) | <i>Penicillium islandicum</i> ¹³⁴ | | MTX |
| Anthraquinoid dimer | Rhodoislandin A (+) | <i>Penicillium islandicum</i> ¹³⁴ | | MTX |
| Anthraquinoid dimer | Rhodoislandin B (+) | <i>Penicillium islandicum</i> ¹³⁴ | | MTX |
| Anthraquinoid dimer | Roseoskyrin (+) | <i>Penicillium islandicum</i> ¹³⁴ | | MTX |
| Anthraquinoid dimer | Rubroskyrin (–) | <i>Penicillium islandicum</i> | | Mut |
| Anthraquinoid dimer | Rugulosin (+) | <i>Penicillium rugulosum</i> ^c | (+): 130 | MTX |
| Anthraquinoid dimer | Rugulin (409) | <i>Penicillium islandicum</i> , <i>P. rugulosum</i> ^c | model: 132 | MTX |
| Anthraquinoid dimer | Rugulosin (410) (–) | <i>Penicillium islandicum</i> , ⁷ <i>P. kloeckeri</i> , <i>P. rugulosum</i> , ^{7,23} <i>P. variabile</i> ⁷ | (+): 130 | MTX, mut |
| Anthraquinoid dimer | Skyrin (+) (S) (Rhodophyscin, Endothianin) | <i>Penicillium islandicum</i> , ^c <i>P. rugulosum</i> , <i>P. kloeckeri</i> ²³ | 135; model: 132 | Bact |
| Anthraquinoid dimer | Skyrinol (+) | <i>Penicillium islandicum</i> | | MTX |
| Austocystin ¹³⁶ (Furoxanthenone) | 4,6-Bisdemethylaustocystin A | <i>Aspergillus ustus</i> | | MTX |
| Austocystin ¹³⁶ (Furoxanthenone) | 4-Demethylaustocystin A | <i>Aspergillus ustus</i> ¹³⁷ | | MTX |
| Austocystin ¹³⁶ (Furoxanthenone) | 6-Demethylaustocystin A | <i>Aspergillus ustus</i> ¹³⁷ | | MTX |
| Austocystin ¹³⁶ (Furoxanthenone) | Austocystin A (–) | <i>Aspergillus ustus</i> ⁷ | model: 138 | MTX, mut, cyto |
| Austocystin ¹³⁶ (Furoxanthenone) | Austocystin B | <i>Aspergillus ustus</i> ^{7,89} | | MTX, mut, cyto |
| Austocystin ¹³⁶ (Furoxanthenone) | Austocystin C | <i>Aspergillus ustus</i> ⁷ | | MTX, mut, cyto |
| Austocystin ¹³⁶ (Furoxanthenone) | Austocystin D | <i>Aspergillus ustus</i> ⁷ | | MTX, mut, cyto |
| Austocystin ¹³⁶ (Furoxanthenone) | Austocystin E | <i>Aspergillus ustus</i> ⁷ | | MTX, mut, cyto |
| Austocystin ¹³⁶ (Furoxanthenone) | Austocystin F | <i>Aspergillus ustus</i> ⁷ | | MTX, mut, cyto |
| Austocystin ¹³⁶ (Furoxanthenone) | Austocystin G | <i>Aspergillus ustus</i> ⁷ | | MTX, mut, cyto |
| Austocystin ¹³⁶ (Furoxanthenone) | Austocystin H | <i>Aspergillus ustus</i> ⁷ | | MTX, mut, cyto |
| Austocystin ¹³⁶ (Furoxanthenone) | Austocystin I | <i>Aspergillus ustus</i> ⁷ | | MTX, mut, cyto |
| Azaanthraquinone | Scorpinone | <i>Amorosa littoralis</i> | 139 | MTX |
| Azanaphthoquinone | 8- <i>O</i> -Methylbostrycoidin (Bostrycoidin-9-methyl ether) | <i>Fusarium moniliforme</i> ¹⁴⁰ | 141, 142 | MTX, cyto |
| Azaphilone | Rotiorinols A–C | <i>Chaetomium cupreum</i> CC3303 ¹⁴⁹ | | fung, MTX |
| Azaphilone | Rubrorotiorin (C ₂₃ H ₂₃ ClO ₅) ²³ | <i>Chaetomium cupreum</i> CC3303, ¹⁴⁹ <i>Penicillium hirayamae</i> | 143 | fung, MTX |
| Azaphilone (Benzopyran) | Mitorubrin (+) ¹⁴⁴ | <i>Penicillium rubrum</i> ²¹ | <i>rac</i> : 145; (–): 146 | MTX |
| Azaphilone (Benzopyran) | Mitorubrinic acid (–) | <i>Penicillium funiculosum</i> ²¹ | Semisynthesis: 145; <i>rac</i> : 147 | MTX |
| Azaphilone (Benzopyran) | Mitorubrinic acid B | <i>Penicillium funiculosum</i> ¹⁴⁸ | | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|-----------------------------|-------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------------------------------------------------------------|
| Azaphilone (Benzopyran) | Mitorubrinol (–) ¹⁴⁴ | <i>Penicillium vermiculatum</i> ²¹ | 146 | MTX |
| Azaphilone (Benzopyran) | Mitorubrinol acetate | <i>Hypoylon fragoforme</i> ²¹ | | MTX |
| Azaphilone (Furobenzofuran) | Rotiorin (–) | <i>Chaetomium cupreum</i> CC3303 ¹⁴⁹ | | fung, MTX |
| Benzobutyrolactone | Fumimycin | <i>Aspergillus funisynnematus</i> F746 ¹⁵⁰ | | MTX |
| Benzodiazepine | Cyclophenin (–) ¹⁵¹ | <i>Penicillium cyclopium</i> , <i>P. vulpinum</i> , <i>P. atramentosum</i> , <i>P. crustosum</i> , ⁷ <i>P. echinulatum</i> , <i>P. solitum</i> , ⁷ <i>P. aurantiovirens</i> , <i>P. cyclopium</i> , <i>P. freii</i> , ⁷ <i>P. neochinulatum</i> , <i>P. polonicum</i> , ⁷ <i>P. aurantiocandidum</i> ⁷ <i>P. discolor</i> ⁷ | 152 | MTX |
| Benzodiazepine | Cyclophenol (–) ¹⁵³ | <i>Penicillium cyclopium</i> , <i>P. vulpinum</i> , <i>P. aurantiogriseum</i> , <i>P. aurantiovirens</i> , <i>P. verrucosum</i> , <i>P. crustosum</i> , ⁷ <i>P. echinulatum</i> , <i>P. solitum</i> , ⁷ <i>P. cyclopium</i> , <i>P. freii</i> , ⁷ <i>P. neochinulatum</i> , <i>P. polonicum</i> , ⁷ <i>P. aurantiocandidum</i> , <i>P. discolor</i> ⁷ | ! | MTX |
| Benzodiazepine alkaloid | Asperlicin (–) | <i>Aspergillus alliaceus</i> ¹⁵⁴ | 155; C: 156; E: 156 | MTX |
| Benzodiazepine alkaloid | Benzomalvin A–C | <i>Penicillium</i> sp. | 157; A: 156 | MTX |
| Benzodiazepine alkaloid | Circumdatin A | <i>Aspergillus ochraceus</i> ²¹ | | MTX |
| Benzodiazepine alkaloid | Circumdatin B | <i>Aspergillus ochraceus</i> ²¹ | | MTX |
| Benzodiazepine alkaloid | Circumdatin C | <i>Aspergillus ochraceus</i> ²¹ | 158 | MTX |
| Benzodiazepine alkaloid | Circumdatin D | <i>Aspergillus ochraceus</i> | | MTX |
| Benzodiazepine alkaloid | Circumdatin E | <i>Aspergillus ochraceus</i> | 156 | MTX |
| Benzodiazepine alkaloid | Circumdatin F | <i>Aspergillus ochraceus</i> | 158, 159; rac: 156 | MTX |
| Benzodiazepine alkaloid | Circumdatin G | <i>Aspergillus ochraceus</i> | | MTX |
| Benzodiazepine alkaloid | Circumdatin H | <i>Aspergillus ochraceus</i> | | MTX, mitochondrial NADH oxidase inhibitor |
| Benzodiazepine alkaloid | Sclerotigenin | <i>Penicillium sclerotigenum</i> | 156, 159 | insect |
| Benzodipyrandione | Fuscinarin, fuscin | <i>Oidiodendron griseum</i> | 160 | MTX |
| Benzofuran | Stachybotramide | <i>Stachybotrys chartarum</i> , <i>S. cylindrospora</i> | | MTX |
| Benzofuran | Stachybotrydial | <i>Stachybotrys chartarum</i> ¹⁶¹ | | MTX |
| Benzofuran | Stachybotrylactone (Stachybotrolide) | <i>Stachybotrys chartarum</i> ¹⁶¹ | | MTX |
| Benzofuranone | Leptosin C,F,I,J | <i>Leptoshaeria species</i> | | MTX, cyto |
| Benzofurans | Stachybocin A–D | <i>Stachybotrys chartarum</i> | | MTX |
| Benzoisochromanquinone | Thysanone (+) | <i>Thysanora penicilloides</i> | 162 | 3C-protease inhibitor |
| Benzoaxepine | Koninginin A–E, ¹⁶³ G ¹⁶⁴ | <i>Trichoderma harzianum</i> ⁷ | 165 | MTX |
| Benzopyran | Austdiol ¹⁶⁶ | <i>Aspergillus ustus</i> ⁷ | | MTX, mut, acute tox |
| Benzopyran | Chaetopyranin | <i>Chaetomium globosum</i> ¹⁶⁷ | | Cyto |
| Benzopyran | Citromycetin (Frequentin acid, 8, 9-dihydroxy-2-methyl-4-oxo-4H, 5H-Pyrano[3,2-c]1]benzopyran-10-carboxylic acid) | <i>Penicillium glabrum</i> ^{7,168} | 169 | MTX |
| Benzopyran | Dihydrodeoxy-8-epi-austdiol | <i>Aspergillus ustus</i> | | MTX |
| Benzopyran | Jesterone | <i>Pestalotiopsis jesteri</i> | 170 | fung, dimer: cyto |
| Benzopyran | Lapidosin | <i>Penicillium lapidosum</i> | | no biodata |
| Benzopyrone | Diplodiol (Diplosporin) (557) (5S,6R) | <i>Diplodia macrospora</i> ^{c,171} | | MTX |
| Benzopyrone | Fusarochromanone (FUCH, TDP 1) | <i>Fusarium equiseti</i> ^{7,172} | | MTX, cyto |
| Benzoquinone dimer | Phoenicin (phenicin) | <i>Penicillium phenicum</i> ²¹ | 173 | irreversible inhibition of 3-hydroxy-3-methylglutaryl coenzyme A reductase |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|---------------------------|
| Benzoquinone | 2,5-toluquinone | <i>Penicillium lanosum</i> , <i>P. griseofluvinum</i> , <i>P. urticale</i> | various syntheses (commodity) | MTX |
| Benzoquinone | Bovinine (a 2,5-dihydroxy-1,4-benzoquinone) | <i>Boletus (Suillus) bovinus</i> (higher fungus) ¹⁷⁴ | | MTX |
| Benzoquinone | Spinulosin (Hydroxyfumigatin, 3,6-dihydroxy-4-methoxy-2,5-toluquinone) | <i>Aspergillus fumigatus</i> , <i>Penicillium spinulosum</i> | | MTX |
| Benzoxanthentrione | Bikaverin (Lycopersin; Mycogonin; Passiflorin; Fungal vacuolation factor) | <i>Gibberella fujikuroi</i> , <i>Fusarium oxysporon</i> | 175 | Cyto, prot |
| Bis-naphthopyrone | Asperpyrone A-C | <i>Aspergillus niger</i> , ¹⁷⁶ <i>Aspergillus tubingensis</i> | | Cyto |
| Bis-naphthopyrone | Aurasperone A | <i>Aspergillus niger</i> ¹⁷⁶ | | MTX |
| Bis-naphthopyrone | Aurasperone B | <i>Aspergillus vadensis</i> , <i>A. niger</i> ¹⁷⁷ | | MTX |
| Bis-naphthopyrone | Aurasperone C,D,E,F, iso (E: Fonsecinone D) | <i>Aspergillus niger</i> ¹⁷⁷ | | MTX |
| Butenolide | Spiculisporic acid ¹⁷⁸ (γ -Butenolide) | <i>Penicillium minioluteum</i> , <i>P. craterforme</i> ⁷ | 179 | MTX! |
| Butyrolactam | Fusarin C (87) | <i>Fusarium moniliforme</i> , <i>F. crookwellense</i> , <i>F. avenaceum</i> , ⁷ <i>F. graminearum</i> , ⁷ <i>F. poae</i> , ⁷ <i>F. proliferatum</i> ⁷ | model: 180 | MTX |
| Butyrolactone | Butenolide (4-Acetamido-4-hydroxy-2-butenic acid γ -lactone; 2-Acetamido-2,5-dihydro-5-oxofuran; 4-Acetamido-4-hydroxy-2-butanol- γ -lactone; N-(2,5-Dihydro-5-oxo-2-furanyl)-acetamide) | <i>Fusarium equiseti</i> , <i>F. culmorum</i> , ⁷ <i>F. sporotrichoides</i> , <i>F. trincinctum</i> , <i>F. graminearum</i> , ⁷ <i>F. poae</i> ⁷ | | MTX, cyto |
| Butyrolactone | Penicillic acid (187) | <i>Penicillium verrucosum</i> , ^{c,7} <i>P. atramentosum</i> , <i>P. verrucosum</i> , <i>P. cyclopium</i> , ⁷ <i>P. raistrickii</i> , <i>P. melanoconidium</i> , ⁷ <i>P. neoehinulatum</i> , <i>P. viridicatum</i> , <i>P. pulvorum</i> , <i>P. polonicum</i> , ⁷ <i>P. aurantiocandidum</i> , ⁷ <i>P. brasilanum</i> , ⁷ <i>P. frei</i> , ⁷ <i>Aspergillus ochraceus</i> , ⁷ <i>A. aculeatum</i> , <i>A. aurantiogriseum</i> , ⁷ | 181, 182 | MTX |
| Carbazole alkaloid | Aflavazole (+) | <i>Aspergillus flavus</i> | | MTX, insect |
| Carbazole alkaloid | Tubingesisin A,B | <i>Aspergillus niger</i> (A), <i>A. tubingensis</i> (B) | | MTX, vir (A), cyto (B) |
| Citreoviridin | Citreomontanin | <i>Penicillium pulvillum</i> ¹⁸³ | 184 | MTX |
| Citreoviridin | Citreoviral | <i>Penicillium citro-viride</i> | 185, 186 | MTX |
| Citreoviridin | Citreoviridin A | <i>Aspergillus terreus</i> , ^{c,7} <i>Penicillium citreo-viride</i> ^c | 186–189, 620 (formal) | MTX |
| Citreoviridin | Citreoviridin C ¹⁸⁷ | <i>Aspergillus terreus</i> ⁷ | | MTX |
| Citreoviridin | Citreoviridin D ¹⁸⁷ | <i>Aspergillus terreus</i> ⁷ | | MTX |
| Citrinin type | 3,7-Dimethyl-8-hydroxy-6-methylisochroman | <i>Penicillium steckii</i> | | MTX |
| Citrinin type | Antibiotic Y | <i>Fusarium avenaceum</i> , ^{7,190} <i>F. acuminatum</i> ⁷ | | MTX |
| Citrinin type | Ascochitine (S) (–) (Ascochyta, Acscochitine) | <i>Ascochyta pisi</i> ^{c,191} (<i>Ascochyta pisi</i>) | 192, 193 | MTX, phytotox |
| Citrinin type | Citrinin (2) (–) | <i>Penicillium citrinum</i> , ^{c,7} <i>P. expansum</i> , ⁷ <i>P. hirsutum</i> , <i>P. verrucosum</i> , ⁷ <i>P. radicolica</i> , <i>Aspergillus carneus</i> , <i>A. terreus</i> ⁷ | 194–197; rac: 198; (+): 199; (–): 200 | MTX |
| Citrinin type ²³ | Dihydrocitrinone | <i>Aspergillus carneus</i> | | MTX |
| Coumarin | Dicoumarol (Dicoumarin, dicumarol, dicumarin) | <i>Aspergillus fumigatus</i> | 201 | MTX |
| Coumarin dimer | Aflavarin | <i>Aspergillus flavus</i> | | feed |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|---------------------------------------|------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|-------------------------------------|
| Coumarin dimer | Desertorin A (<i>S</i>) | <i>Emericella</i> sp. | 202 | MTX |
| Coumarin dimer | Desertorin B (<i>R</i>) | <i>Emericella</i> sp. | | MTX |
| Coumarin dimer | Desertorin C (<i>S</i>) | <i>Emericella</i> sp. | | MTX |
| Cyclodepsipeptide | Destruxin A, B, E (E: 549) | <i>Aspergillus ochraceus</i> <i>Metarhizium anisopliae</i> | 203 | MTX, E: Insec, cyto |
| Cyclodepsipeptide | Enniatin A ²⁰⁴ | <i>Fusarium aveanceum</i> , ⁷ <i>F. acuminatum</i> ⁷ | 205 | MTX, cyto, biot, insect, ionophoric |
| Cyclodepsipeptide | Enniatin A1 ²⁰⁴ | <i>Fusarium aveanceum</i> , ⁷ <i>F. acuminatum</i> ⁷ | | MTX, cyto, biot, insect, ionophoric |
| Cyclodepsipeptide | Enniatin A2 ²⁰⁴ | <i>Fusarium langsethiae</i> ^d | | MTX, cyto |
| Cyclodepsipeptide | Enniatin B1 ²⁰⁴ | <i>Fusarium aveanceum</i> , ⁷ <i>F. acuminatum</i> ⁷ | | MTX, cyto, biot, insect, ionophoric |
| Cyclodepsipeptide | Enniatin B ²⁰⁴ | <i>Fusarium aveanceum</i> , ⁷ <i>F. acuminatum</i> ⁷ | | MTX, cyto, biot, insect, ionophoric |
| Cyclodepsipeptide | Enniatin B2 ²⁰⁴ | <i>Fusarium aveanceum</i> , <i>F. acuminatum</i> ⁷ | | MTX, cyto, biot, insect, ionophoric |
| Cyclodepsipeptide | Enniatin B3 ²⁰⁴ | <i>Fusarium aveanceum</i> , ⁷ <i>F. acuminatum</i> ⁷ | | MTX, cyto, biot, insect, ionophoric |
| Cyclodepsipeptide | Enniatin H, I ²⁰⁴ | <i>Fusarium langsethiae</i> ^d | | MTX, cyto |
| Cyclodepsipeptide | Enniatin L, M1, M2, N ²⁰⁴ | Unidentified fungus | | MTX |
| Cyclodepsipeptide | Gliotide | <i>Gliocladium</i> sp. ^b | | Cyto |
| Cyclodepsipeptide | MK1688 | <i>Verticillium hemipterigenum</i> | | MTX |
| Cyclodepsipeptide | Roseocardin | <i>Trichothecium roseum</i> | | Cardiotonic |
| Cyclodepsipeptide | Roseotoxin A | <i>Trichothecium roseum</i> | | MTX, No bio data |
| Cyclodepsipeptide | Roseotoxin B | <i>Trichothecium roseum</i> | | MTX, Tox, insect |
| Cyclodepsipeptide (5 AA) | Pithomycolide | <i>Pithomyces chartarum</i> | 206 | MTX |
| Cyclodepsipeptide (6 AA) | Beauvericin (BEAU) | <i>Beauveria terreus</i> , <i>Fusarium proliferatum</i> ⁷ | 207 | MTX, cyto, biot, insect, ionophoric |
| Cycloheptapeptide | Scytalidamide A,B | <i>Scytalidium</i> sp. ^b | A: 208 | Cyto |
| Cyclohexanecarbaldehyde ²³ | Frequentin | <i>Penicillium brefeldianum</i> , <i>P. frequentans</i> , ²⁰⁹ <i>P. palitans</i> , ²¹⁰ <i>P. verrucosum</i> | | biot, fung |
| Cyclohexanone | Palitanin | <i>Penicillium brefeldianum</i> , <i>P. palitans</i> ²¹⁰ | | MTX |
| Cyclohexenone | Terredionol (4 <i>R</i> ,6 <i>R</i>) | <i>Aspergillus</i> sp. | | MTX |
| Cyclohexenone (Patulin precursor) | Isopoxydon (Epiepoxydon; U–III) (rac and (+)) | <i>Penicillium urticae</i> , ²¹¹ <i>Aplospora montagnei</i> ^b | 212, 213 | MTX, cyto |
| Cyclopentabenzopyran | Presambucoin | <i>Fusarium culmorum</i> | | MTX |
| Cyclopentabenzopyran | Sambucuin | <i>Fusarium sambucinum</i> ²¹⁴ | | MTX |
| Cyclopentanaphthacene | Viridicatumtoxin ²¹⁵ | <i>Penicillium viridicatum</i> ^c , <i>P. brasilanum</i> ⁷ | | MTX, mut |
| Cyclopentenone ²³ | Terrein ²¹⁶ | <i>Aspergillus terreus</i> ⁷ | 217 | MTX |
| Cyclopeptide | Cylindrocyclin A | <i>Cylindrocarpon</i> sp. ²¹⁸ | | cyto |
| Cyclopeptide | Echinocandin B,C (a-30912), D | <i>Aspergillus rugulosus</i> , <i>A. nidulans</i> (C) | 219 | MTX, fung |
| Cyclopeptide | Islanditoxin ²²⁰ (not identical with Cyclochlorotine) | <i>Penicillium islandicum</i> ⁷ | | MTX, carc, hep |
| Cyclopeptide | JM47 (cyclo(Ala-Ala-Aoh-Pro)) | <i>Fusarium</i> sp. ^b | | MTX |
| Cyclopeptide | Okaramines A–R | <i>Penicillium simplicissimum</i> (N–R) | 221; N: 222 | MTX, insect |
| Cyclopeptide | Sporidesmolides I, III, V | <i>Pithomyces chartarum</i> | 223 | MTX |
| Cyclopeptide | Sporidesmolides IV | <i>Pithomyces chartarum</i> , <i>P. maydicus</i> | 224 | MTX |
| Cyclopeptide | Ustiloxin A–F | <i>Ustilagoidea virens</i> | 225 | MTX |
| Cyclopeptide (4 AA) | Aspercolorin | <i>Aspergillus versicolor</i> ²²⁶ | | MTX, tox |
| Cyclopeptide (4 AA) | Tentoxin (548) | <i>Alternaria alternata</i> | 227 | Herb! |
| Cyclopeptide (5 AA) | Argifin | <i>Gliocladium</i> sp. | 228 | MTX |
| Cyclopeptide (5 AA) | Cyclochlorotine ²²⁹ | <i>Penicillium islandicum</i> ⁷ | Dechloro: ²³⁰ | MTX, carc, hep |
| Cyclopeptide (5 AA) | Malformin ²³¹ A1, A2 | <i>Aspergillus niger</i> , ^{c,7} <i>A. tubingensis</i> , <i>Byssoschlamys fulva</i> ⁷ | A: 232 | MTX, cyto |
| Cyclopeptide (5 AA) | Malformin ²³¹ B1, B2, C | <i>Aspergillus niger</i> , ^{c,7} <i>Byssoschlamys fulva</i> ⁷ | C: 233 | MTX, prob cyto |
| Cyclopeptide (modified) | Phomopsin A, ²³⁴ B ²³⁵ | <i>Phomopsis leptostromiformis</i> | model: 236 | MTX |
| Cytochalasan | 18-Deoxy-19,20-epoxycytochalasin Q | <i>Xylaria hypoxylon</i> ²³⁷ | 238 | MTX |
| Cytochalasan | 18-Deoxy-19,20-epoxycytochalasin R | <i>Xylaria hypoxylon</i> ²³⁷ | 238 | MTX |
| Cytochalasan | 19,20-Epoxycytochalasin C | <i>Xylaria hypoxylon</i> ²³⁷ | 238 | MTX |
| Cytochalasan | 19,20-Epoxycytochalasin D | <i>Xylaria hypoxylon</i> ²³⁷ | 238 | MTX |
| Cytochalasan | 19,20-Epoxycytochalasin N | <i>Xylaria hypoxylon</i> ²³⁷ | 238 | MTX |
| Cytochalasan | 19,20-Epoxycytochalasin Q | <i>Xylaria hypoxylon</i> ²³⁷ | 238 | MTX |
| Cytochalasan | 19,20-Epoxycytochalasin Q | <i>Xylaria</i> sp. | 238 | MTX, Antiplasmodial |
| Cytochalasan | 19,20-Epoxycytochalasin R | <i>Xylaria hypoxylon</i> ²³⁷ | 238 | MTX |
| Cytochalasan | 19- <i>O</i> -Acetylchaetoglobosin A-B,D | <i>Chaetomium globosum</i> | | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^d |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|----------------------|
| Cytochalasan | Aspochalasan | <i>Aspergillus microcysticus</i> ^c | | MTX |
| Cytochalasan | Aspochalasin A–L, Z | <i>Aspergillus microcysticus</i> ^{c,239} | 240 | MTX |
| Cytochalasan | Chaetoglobosin A–G, J (B: 7,19-Dihydroxy-10-(indol-3-yl)-5,16,18-trimethyl-[13]cytochalas-6(12),13,17,21-tetraene-20,23-dione) | <i>Chaetomium globosum</i> ^{c,7} <i>Penicillium verrucosum</i> (C), <i>P. discolor</i> ⁷ (A–C), <i>P. expansum</i> ⁷ (C) | C: 241 | MTX, cyto |
| Cytochalasan | Chaetoglobosin K, L | <i>Diplodia macrospora</i> | | MTX |
| Cytochalasan | Chaetoglobosin U | <i>Chaetomium globosum</i> | | MTX |
| Cytochalasan | Cytochalasin A (440) (5,5-Didehydrophomin, NSC 174119) | <i>Phoma exigua</i> ^c <i>Helminthosporium dematiodeum</i> | model: 242 | MTX |
| Cytochalasan | Cytochalasin B (441) (NSC 107658, Phomin) | <i>Phoma exigua</i> ^c <i>Phoma exigua</i> var. <i>Heteromorpha</i> ²⁴³ <i>Curvularia lunata</i> , <i>Helminthosporium dematiodeum</i> | 244–247; model:242 | MTX |
| Cytochalasan | Cytochalasin C | <i>Metarhizium anisopliae</i> ^c | model: 248–252 | MTX |
| Cytochalasan | Cytochalasin D (442) (NSC 209835, Zygospurin A) | <i>Metarhizium anisopliae</i> ^c | 253; 6-epi: 254; model: 251, 255, 256; degradation studies: 257 | MTX |
| Cytochalasan | Cytochalasin E (443) (NSC 175151) | <i>Rosellinia necatrix</i> ^c <i>Aspergillus clavatus</i> ⁷ | | MTX, tox |
| Cytochalasan | Cytochalasin F (Cytochalasin F6) | <i>Helminthosporium dematiodeum</i> ^c <i>Nigrosalbulum</i> sp. ^c <i>Phoma exigua</i> var. <i>heteromorpha</i> ²⁴³ | | MTX |
| Cytochalasan | Cytochalasin G (444) | <i>Phomopsis paspali</i> ^c <i>pseudeurotium zonatum</i> | 258, 259 | MTX |
| Cytochalasan | Cytochalasin H (445) (Kodocytochalasin 1, Paspalin P I) | <i>Phomopsis paspali</i> ^c <i>Phomopsis</i> sp. 68-GO-164 ²⁶⁰ | 261, 262 | MTX |
| Cytochalasan | Cytochalasin I | <i>Daldania vernicosa</i> | | MTX, cyto |
| Cytochalasan | Cytochalasin J (Deacetylcytochalasin H, Kodocytochalasin 2, Paspalin P II) | <i>Phomopsis</i> sp. 68-GO-164 ²⁶⁰ | | MTX |
| Cytochalasan | Cytochalasin K | <i>Chalara microspora</i> ^c | | MTX |
| Cytochalasan | Cytochalasin L (446) | <i>Chalara microspora</i> ^c | | MTX |
| Cytochalasan | Cytochalasin M | <i>Chalara microspora</i> ^c | | MTX |
| Cytochalasan | Cytochalasin N | <i>Phomopsis</i> sp. ²⁶³ <i>Phomopsis</i> sp. 68-GO-164 ²⁶⁰ | | MTX |
| Cytochalasan | Cytochalasin O (447), Cytochalasin Ohyp | <i>Phomopsis</i> sp. ²⁶³ | 253 | MTX |
| Cytochalasan | Cytochalasin P | <i>Phomopsis</i> sp. ²⁶³ | | MTX |
| Cytochalasan | Cytochalasin Q | <i>Hirsutella</i> sp. ²⁶⁴ <i>Halorosellinia oceanica</i> BCC 5149, ²⁶⁵ <i>Xylaria hypoxylon</i> ²³⁷ | | MTX, cyto |
| Cytochalasan | Cytochalasin R | <i>Phomopsis</i> sp. 68-GO-164, ²⁶⁰ <i>Xylaria hypoxylon</i> ²³⁷ | | MTX |
| Cytochalasan | Cytochalasin S | <i>Phomopsis</i> sp. 68-GO-164 ²⁶⁰ | | MTX |
| Cytochalasan | Cytochalasin T | <i>Phoma exigua</i> var. <i>heteromorpha</i> ²⁴³ | | MTX |
| Cytochalasan | Cytochalasin U, V | <i>Phoma exigua</i> var. <i>heteromorpha</i> ²⁶⁶ | | MTX |
| Cytochalasan | Cytochalasin W | <i>Phoma exigua</i> var. <i>heteromorpha</i> ²⁶⁷ | | MTX |
| Cytochalasan | Cytochalasin X, Y, Z | <i>Pseudeurotium zonatum</i> ²⁶⁸ | | MTX |
| Cytochalasan | Cytochalasin Z1, Z2, Z3 | <i>Pyrenophora semeniperda</i> ²⁶⁹ | | MTX |
| Cytochalasan | Cytochalasin Z4, Z5, Z6 | <i>Phoma exigua</i> var. <i>heteromorpha</i> ²⁷⁰ <i>Phoma</i> spp. ^{c,271} | | MTX |
| Cytochalasan | Deoxaphomin (Desoxyphomin; (7S,16R,20R)-7,20-Dihydroxy-5,16-dimethyl-10-phenyl-(13)cytochalas-6(12),13(t),21(t)-triene-1,23-dione) | | | MTX |
| Cytochalasan | Dihydrocytochalasin B (21,22-Dihydrophomin) | <i>Pyrenophora</i> sp. ^d | | MTX |
| Cytochalasan | Engleromycin | <i>Engleromyces goetzei</i> ^c | | MTX |
| Cytochalasan | Epoxycytochalasin H | <i>Phomopsis</i> sp. 68-GO-164 ²⁶⁰ | | MTX |
| Cytochalasan | Epoxycytochalasin J | <i>Phomopsis</i> sp. 68-GO-164 ²⁶⁰ | | MTX |
| Cytochalasan | L-696,474 (446) | <i>Hypoxylon fragiforme</i> | 247 | MTX |
| Cytochalasan | Protophomin | <i>Phoma exigua</i> ^c | | MTX |
| Cytochalasan | Proxiphomin | <i>Phoma exigua</i> ^c | 272, 273 | MTX |
| Cytochalasan | Zygosporin D | <i>Zygosporium masonii</i> | | MTX |
| Cytochalasan | Zygosporin E | <i>Zygosporium masonii</i> | 274, 275 | MTX |
| Cytochalasan | Zygosporin F | <i>Zygosporium masonii</i> | | MTX |
| Cytochalasan | Zygosporin G | <i>Zygosporium masonii</i> | | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|--------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|------------------------------------|
| Depsicyclopeptide (Peptolide) | Lateritin (<i>R,R</i>) | <i>Fusarium moniliforme</i> , <i>F. culmorum</i> , <i>F. avenaceum</i> , <i>F. nivale</i> , <i>Isaria japonica</i> , <i>Gibberella lateritium</i> IFO 7188 ²⁷⁶ | | MTX, cyto, apoptosis inducer |
| Depsidone | Excelsione | Endophytic fungus | 277 | MTX |
| Depsidone | Mollicellin A | <i>Chaetomium mollicellum</i> | 278 | MTX |
| Depsidone | Mollicellin B–G | <i>Chaetomium mollicellum</i> | | MTX |
| Depsidone | Ustin ²³ (Ustin-I, Nornidulin) | <i>Aspergillus nidulans</i> ²⁷⁹ | | MTX, biot |
| Depsipeptide (peptolide) ²⁸⁰ | Sambucinin (Sambucynin) (C ₂₄ H ₄₂ O ₇ N ₂) ^d | <i>Fusarium sambucinum</i> , <i>F. verticillioides</i> , ^d <i>F. equiseti</i> , ^d <i>F. oxsporum</i> , ^d <i>F. culmorum</i> , ^d <i>F. solani</i> , ^d <i>F. avenaceum</i> , ^d <i>F. roseum</i> , ^d <i>F. nivale</i> ^d | | MTX, biot |
| Diarylether | Neoplaether | <i>Neoplaconema napellum</i> IFB-E016 (endophyte metabolite) ²⁸¹ | | Cyto, fung |
| Dibenzofurandione | Usnic acid (+) (<i>R</i>) | <i>Phomopsis</i> sp. (mainly produced by lichen) | | MTX, tox |
| Diisocyanide | Xanthoascin (Toxin-B) | <i>Aspergillus candidus</i> ²⁸² | | MTX |
| Diisocyanide | Xanthocillin X | <i>Penicillium notatum</i> ^c , <i>Aspergillus chevalieri</i> | | MTX |
| Diisocyanide | Xanthocillin X methylether | <i>Aspergillus</i> sp. | 283 | MTX |
| Diketopiperazine | <i>cyclo</i> (Ala-Try) | <i>Aspergillus chevalieri</i> | | MTX |
| Diketopiperazine | <i>cyclo</i> (D-Val-Try) | <i>Aspergillus chevalieri</i> | | MTX |
| Diketopiperazine | Cycloechinulin | <i>Aspergillus ochraceus</i> ²⁸⁴ | | MTX, insect |
| Diketopiperazine | Dechlorogriseofulvin | <i>Memmoniella echinata</i> ²⁸⁵ | | MTX |
| Diketopiperazine | Dipodazine ((<i>Z</i>)-1',3- Didehydro-3-(3''- indolylmethylene)-piperazine- 2,5-dione) | <i>Penicillium verrucosum</i> , ²⁸⁶ <i>P. dipodomys</i> , <i>P. nalgiovense</i> | 287 | MTX, prob insect |
| Diketopiperazine | Echinulin | <i>Chaetomium globosum</i> , <i>Aspergillus chevalieri</i> , <i>Aspergillus amstelodami</i> | | MTX |
| Diketopiperazine | Gypsetin | <i>Nannizzia gypsea</i> | 472 | MTX |
| Diketopiperazine | Spirotryprostatin A, B (A: 542) | <i>Aspergillus fumigatus</i> | A: 288; B: 289 | MTX |
| Diketopiperazine | Tryprostatin A | <i>Aspergillus fumigatus</i> ^{b,290} | 291 | MTX |
| Diketopiperazine | Tryprostatin B | <i>Aspergillus fumigatus</i> ^{21,290} | 292, 293, 472 | MTX |
| Diketopiperazine | Verrucine A-E | <i>Myrothecium verrucaria</i> , ^c <i>Penicillium verrucosum</i> ⁷ | | MTX |
| Diketopiperazine (Indole alkaloid) | Austamide (544) (+) (NSC 159629) | <i>Aspergillus ustus</i> , ^{7,294} <i>Penicillium italicum</i> ⁴⁶⁴ | 295 | MTX, acute tox |
| Diketopiperazine (Indole alkaloid) | Brevianamide F (<i>cyclo</i> (Pro-Trp) (<i>cis</i> -Cyclo(Pro, Trp), <i>L,L</i> -Cyclo (tryptophanylprolyl)) | <i>Penicillium</i> <i>brevicompectum</i> ^{b,473,296} | | MTX |
| Diketopiperazine (Indole alkaloid) | Deoxyisoaustamide (+) | <i>Penicillium italicum</i> ⁴⁶⁴ | 295 | MTX |
| Diketopiperazine (Indole alkaloid) | Hydratoaustamide (+) | <i>Penicillium italicum</i> ⁴⁶⁴ | 295 | MTX |
| Diketopiperazine (Indole alkaloid) | Verruculogen ²⁹⁷ (543) (TR 1 toxin) (–) | <i>Aspergillus caespitosus</i> , <i>A. fumigatus</i> , ⁷ <i>Penicillium verrucosum</i> , <i>P. picaium</i> , <i>P. janthinellum</i> , <i>P. paxillii</i> , <i>P. brasilanum</i> , ⁷ <i>Neosatorya fischeri</i> ⁷ | 298, 299 | MTX |
| Diketopiperazine alkaloid | Fructigenine A (Rugulosuvine B, puberuline) (–) | <i>Fusarium moniliforme</i> , <i>F. culmorum</i> , <i>F. avenaceum</i> , <i>F. roseum</i> , <i>Penicillium fructigenum</i> , <i>P. auratiogriseum</i> , <i>P. rugulosum</i> ³⁰⁰ | | MTX, cyto |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^d |
|----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|-------------------------------|
| Diketopiperazine alkaloid | Fructigenine B ²³ (Verrucofortine) (-) | <i>Penicillium auratiogriseum</i> , <i>P. verrucosum</i> , <i>P. aurantiovirens</i> , <i>P. cyclopium</i> , <i>P. polonicum</i> , <i>P. tricolor</i> ³⁰¹ | | MTX, cyto |
| Diketopiperazine alkaloid Dipeptide | Rugulosuvine A (Puberulin A) Aspergillazine A–E (A: 546) | <i>Penicillium rugulosum</i> ³⁰⁰ <i>Aspergillus unilateralis</i> , ³⁰² <i>Spicaria elegans</i> ^b | | MTX MTX, cyto |
| Dipeptide | Trichodermamide A | <i>Aspergillus unilateralis</i> , ³⁰² <i>Trichoderma virans</i> ^b , <i>Spicaria elegans</i> ^b | | Cyto |
| Dipeptide | Trichodermamide B | <i>Aspergillus unilateralis</i> , ³⁰² <i>Trichoderma virans</i> ^b | 303 | MTX, cyto |
| Diterpene | Fusicoccin | <i>Fusicoccum amygdali</i> (<i>fungus imperfectus</i>) <i>Stachybotrys chartarum</i> ³⁰⁵ | model: 304 | Cyto, phytohormonal MTX |
| Diterpenoid (Atranone) | 6 β -Hydroxydolabella-3E,7E,12E- trien-14-one (1S*,6S*,11S*) | <i>Stachybotrys chartarum</i> ³⁰⁶ | | MTX, w cyto |
| Diterpenoid (Atranone) | Atranone A–G | <i>Myrothecium verrucaria</i> ^d | | MTX |
| Diterpenoid (Atranone) | Atranone H, J | <i>Stachybotrys chartarum</i> | | MTX |
| Diterpenoid (Atranone) | Epoxydolabellane | <i>Gliocladium roseum</i> ¹⁸⁹ | | MTX |
| Epipolythiopiperazine-3,6-dione | 11-Deoxyverticillin A | <i>Arachniotus aureus</i> ^{307,308} | | MTX |
| Epipolythiopiperazine-3,6-dione | Acetylaranotin (A 21101- IV, LL-S 88 α) | <i>Arachniotus aureus</i> ³⁰⁹ | degradation: 310 | MTX |
| Epipolythiopiperazine-3,6-dione | Aranotin (530) (A-21101-III; Ariotin) | <i>Arachniotus aureus</i> ^{311,308} | | MTX |
| Epipolythiopiperazine-3,6-dione | Aspirochlorine (A-30641) | <i>Aspergillus flavus</i> ³¹² | 313; model: 314 | MTX |
| Epipolythiopiperazine-3,6-dione | Aurantimetrin | <i>Emericella striata</i> ³²⁷ | | MTX |
| Epipolythiopiperazine-3,6-dione | Bis(anhydrodethio) itomycin | <i>Gliocadium deliquescens</i> | | MTX |
| Epipolythiopiperazine-3,6-dione | Bis(anhydrodethio) methylthiohydrogliotoxin | <i>Gliocadium deliquescens</i> | | MTX |
| Epipolythiopiperazine-3,6-dione | Bisdethio(methylthio) dehydrogliotoxin | <i>Gliocadium deliquescens</i> | | MTX |
| Epipolythiopiperazine-3,6-dione | Bisdethiobis(methylthio)gliotoxin (Bisdethio(bismethylthio)gliotoxin, FR-49175, Dehydroxybisdethiobis(methylthio) gliotoxin) | <i>Gliocadium deliquens</i> ³¹⁵ | | MTX |
| Epipolythiopiperazine-3,6-dione | Chaetomin (Chetomin) | <i>Chaetomium cochiliodes</i> ^c , <i>C. globosum</i> ^{7,344,316,317} | | MTX |
| Epipolythiopiperazine-3,6-dione | Chetracin A | <i>Chaetomium retardatum</i> ^{c,318} | | MTX |
| Epipolythiopiperazine-3,6-dione | <i>Cis</i> -3,6-Dibenzyl-3,6-bis (methylthio)piperazine- 2,5-dione | <i>Aspergillus terreus</i> | 319 | MTX |
| Epipolythiopiperazine-3,6-dione | Dethiosecoemestin | <i>Emericella striata</i> ³²⁷ | | MTX |
| Epipolythiopiperazine-3,6-dione | Didehydrogliotoxin (Didehydroaspergillin) | <i>Penicillium terlikowskii</i> ^{c,320} <i>Aspergillus ustus</i> | rac: 321 | MTX |
| Epipolythiopiperazine-3,6-dione | Dihydroxychetocin (11a,11'a- Dihydroxychaetocin, Melinacidin IV) | <i>Acrostalagmus chartartum</i> ^{c,322,323} | | MTX |
| Epipolythiopiperazine-3,6-dione | Dithiosilvatin | <i>Aspergillus silvaticus</i> , <i>emericella</i> sp. ³²⁴ | bimethyl: 325 | MTX |
| Epipolythiopiperazine-3,6-dione | Emestrin A (Emestrin, EQ-1) | <i>Aspergillus</i> sp., <i>Emericella striata</i> 80-NE-22 ^{327,326} | | MTX |
| Epipolythiopiperazine-3,6-dione | Emestrin B | <i>Emericella striata</i> ³²⁷ | | MTX |
| Epipolythiopiperazine-3,6-dione | Emethallicin B | <i>Emericella heterothallica</i> ³²⁸ | | MTX |
| Epipolythiopiperazine-3,6-dione | Emethallicin C | <i>Emericella heterothallica</i> ³²⁸ | | MTX |
| Epipolythiopiperazine-3,6-dione | Epicorazine A,B | <i>Epicoccum nigrum</i> ^c , <i>podaxis pistillaris</i> | | MTX |
| Epipolythiopiperazine-3,6-dione | Epicorazine C (antibiotic F 3822) | <i>Stereum hirsutum</i> , ^{329,c} <i>podaxis pistillaris</i> | | micro |
| Epipolythiopiperazine-3,6-dione | Epoxyserohilone | <i>Nigrospora spaerica</i> | | MTX |
| Epipolythiopiperazine-3,6-dione | Exserohilone (535) | <i>Exserohilum holmii</i> | | MTX |
| Epipolythiopiperazine-3,6-dione | Gliocladin A–E | <i>Gliocladium roseum</i> ¹⁸⁹ | (+)-C: 330 | MTX |
| Epipolythiopiperazine-3,6-dione | Gliotoxin (527) (Aspergillin) | <i>Aspergillus fumigatus</i> ^{c,7} <i>A. niger</i> , <i>Trichoderma lignorum</i> ^c , <i>T. virens</i> , ⁷ <i>Gliocladium flavofusum</i> ⁷ | 321 | MTX, cyto |
| Epipolythiopiperazine-3,6-dione | Gliotoxin acetate | <i>Penicillium obscurum</i> | | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|---------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|-------------------|----------------------|
| Epipolythiopiperazine-3,6-dione | Gliotoxin E (Thiogliotoxin) | <i>Aspergillus fumigatus</i> | | MTX |
| Epipolythiopiperazine-3,6-dione | Gliotoxin G (Dithiogliotoxin) | <i>Penicillium terlikowskii</i> , <i>Aspergillus fumigatus</i> , <i>Thermoascus crustaceus</i> | 331; partial: 332 | MTX |
| Epipolythiopiperazine-3,6-dione | Gliovirin ²³ | <i>Aspergillus niger</i> , <i>Trichoderma virens</i> ^{7,333} | | MTX |
| Epipolythiopiperazine-3,6-dione | Hyalodendrin | <i>Hyalodendron</i> sp. | 321, 334, 335 | MTX |
| Epipolythiopiperazine-3,6-dione | Leptosin D,E,F A-K (Chaetocin derivative) | <i>Leptosphaeria</i> sp. OUPS-4 | | MTX, cyto |
| Epipolythiopiperazine-3,6-dione | Melinacidin II | <i>Acrostalagmus chartartum</i> ^{c,322} | | MTX |
| Epipolythiopiperazine-3,6-dione | Melinacidin III | <i>Acrostalagmus chartartum</i> ^{c,322} | | MTX |
| Epipolythiopiperazine-3,6-dione | Methylthiodioxopiperazine | <i>Gliocadium deliquescens</i> | | MTX |
| Epipolythiopiperazine-3,6-dione | MPC 1001 (529) | <i>Cladorrhinum</i> sp. | | MTX, tumor, biot |
| Epipolythiopiperazine-3,6-dione | Pretrichdermamide A | <i>Trichoderma</i> sp. BCC 5926 | | MTX |
| Epipolythiopiperazine-3,6-dione | Rostratins A-D (531–534) | <i>Exserohilum rostratum</i> ³³⁶ | model: 468 | MTX, cyto |
| Epipolythiopiperazine-3,6-dione | Scabrosin ester A-D (536–539) | <i>Xanthoparmelia scabrosa</i> (lichen) ³³⁷ | | Cyto |
| Epipolythiopiperazine-3,6-dione | Silvathione | <i>Emericella striata</i> ³²⁷ | | MTX |
| Epipolythiopiperazine-3,6-dione | Sirodesmin A-C,G | <i>Leptosphaeria maculans</i> , <i>Sirodesmium diversum</i> | model: 338 | MTX |
| Epipolythiopiperazine-3,6-dione | Sporidesmin A (528) | <i>Verticillium</i> sp. ^c , <i>Pithomyces chartarum</i> | 339; model: 340 | MTX |
| Epipolythiopiperazine-3,6-dione | Sporidesmin B,G-J | <i>Pithomyces chartarum</i> | | MTX |
| Epipolythiopiperazine-3,6-dione | Sporidesmin D,F, Diacetylsporidesmin C | <i>Pithomyces chartarum</i> | | MTX, w tox |
| Epipolythiopiperazine-3,6-dione | Sporidesmin E | <i>Pithomyces chartarum</i> ³⁴¹ | | MTX |
| Epipolythiopiperazine-3,6-dione | Verticillin A | <i>Verticillium</i> sp., <i>Gliocladium roseum</i> ¹⁸⁹ | | MTX |
| Epipolythiopiperazine-3,6-dione | Verticillin B, C | <i>Verticillium</i> sp. | | MTX |
| Epipolythiopiperazine-3,6-dione | Violaceic acid | <i>Emericella striata</i> ³²⁷ | | MTX |
| Epipolythiopiperazine-3,6-dione dimer | Chaetocin (Chetocin) | <i>Chaetomium</i> sp. ³⁴² | | MTX |
| Epipolythiopiperazine-3,6-dione dimer | Chaetocin B,C (Chetocin) | <i>Chaetomium minutum</i> ^{c,342–344} | | MTX |
| Epipolythiopiperazine-3,6-dione dimer | Dihydrochaetocin (Dihydrochetocin) | <i>Chaetomium retardatum</i> ^c | | MTX |
| Epoxycyclohexenone/ Farnesylcyclohexenones (terpene) | Yanuthone A–E, 1-hydroxyyanuthone A, 1-hydroxyyanuthone C, and 22-deacetylyanuthone A, 7-deacetoxyyanuthone A | <i>Penicillium notatum</i> ^{345,346} | Yanuthone: 347 | MTX, cyto |
| (Epoxymethano)phenanthro [2,3-b:6,7-b']bisoxirene | Hexacyclinol | <i>Panus rudis</i> strain HKI 0254 ³⁴⁸ | 349 | MTX |
| Epoxyquinone | Enaminomycin A–C, | <i>Penicillium claviforme</i> , <i>P. griseofulvum</i> | | MTX, str cyto, micro |
| Epoxyquinone | Epiepoformin (Desoxyepiepoxydon) | <i>Penicillium claviforme</i> , <i>P. griseofulvum</i> | 350 | MTX, str cyto, micro |
| Epoxyquinone | Epoformin (Desoxyepoxydon) | <i>Penicillium claviforme</i> , <i>P. griseofulvum</i> | 350, 351 | MTX, str cyto, micro |
| Epoxyquinone | Epoxydon | <i>Phoma</i> sp. | 213, 352 | Phytotox |
| Eremofortins | Eremofortin A–E | <i>Penicillium roqueforti</i> | B: 353 | MTX |
| Ergot alkaloid | Agroclavine-I (Agroclavine 1) | <i>Claviceps purpurea</i> | 354 | MTX |
| Ergot alkaloid | Auranthine ³⁵⁵ | <i>Penicillium aurantiogriseum</i> ⁷ | model: 356 | MTX, nephro |
| Ergot alkaloid | Aurantioclavine | <i>Penicillium vitale</i> ³⁵⁷ | 358 | MTX |
| Ergot alkaloid | Chanoclavine-I | <i>Claviceps purpurea</i> , <i>epichloe typhina</i> ³⁵⁹ | 360 | MTX |
| Ergot alkaloid | Chlororugulovasine A, B ³⁷⁵ | <i>Penicillium rubrum</i> , <i>P. islandicum</i> | | MTX |
| Ergot alkaloid | Cladosporic acid | <i>Cladosporium</i> sp. | | MTX |
| Ergot alkaloid | Clavicipic acid (–) (<i>cis</i>) | <i>Claviceps fusiformis</i> | 361 | MTX |
| Ergot alkaloid | Costaclavine | <i>Aspergillus fumigatus</i> , <i>Penicillium chermesinum</i> | 362 | MTX |
| Ergot alkaloid | Dihydroelymoclavine | <i>Claviceps</i> sp. | | MTX |
| Ergot alkaloid | Egrine | <i>Claviceps</i> sp. | | MTX |
| Ergot alkaloid | Elymoclavine | <i>Claviceps</i> sp. | 363 | MTX |
| Ergot alkaloid | Epoxyagroclavine-I | <i>Penicillium fellutanum</i> | | MTX |
| Ergot alkaloid | Ergocornine (Cyclol tripeptide) | <i>Claviceps purpurea</i> | | MTX |
| Ergot alkaloid | Ergocorninine | <i>Claviceps purpurea</i> | | MTX |
| Ergot alkaloid | Ergocristine (Cyclol tripeptide) | <i>Claviceps purpurea</i> | | MTX |
| Ergot alkaloid | Ergocristinine | <i>Claviceps purpurea</i> ^d | | MTX |
| Ergot alkaloid | Ergocrystine | <i>Claviceps purpurea</i> | | MTX |
| Ergot alkaloid | Ergometrine | <i>Claviceps purpurea</i> | | MTX, drug |
| Ergot alkaloid | Ergometrinine | <i>Claviceps purpurea</i> | | MTX |
| Ergot alkaloid | Ergonovine | <i>Claviceps</i> sp. | 371 | MTX, oxytocic |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^d |
|-----------------------------------|-------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------|
| Ergot alkaloid | Ergosecaline | <i>Claviceps purpurea</i> ³⁶⁴ | | MTX |
| Ergot alkaloid | Ergosecalinine | <i>Claviceps purpurea</i> ³⁶⁴ | | MTX |
| Ergot alkaloid | Ergotamine (8) (Cyclol tripeptide) | <i>Claviceps purpurea</i> | 365 | MTX |
| Ergot alkaloid | Ergotaminine | <i>Claviceps purpurea</i> | | MTX |
| Ergot alkaloid | Ergotocine ³⁶⁶ | <i>Claviceps</i> sp. | | MTX |
| Ergot alkaloid | Ergotoxine: mixture of equal proportions of ergocristine, ergocornine and ergocryptine | <i>Claviceps purpurea</i> | | MTX |
| Ergot alkaloid | Festuclavine (8,9-Dihydro-agroclavine) | <i>Aspergillus fumigatus</i> , <i>Claviceps gigantea</i> | | MTX |
| Ergot alkaloid | Fumigaclavine A–C ³⁶⁷ (Fumiclavine A–C) | <i>Aspergillus fumigatus</i> , ⁷ <i>Penicillium palitans</i> ⁷ (A,B), <i>P. roqueforti</i> (B,C) | 368 | MTX, C: anorexia |
| Ergot alkaloid | Isofumigaclavine A,B | <i>Penicillium roqueforti</i> ⁷ | 369 | MTX |
| Ergot alkaloid | Isolysergol | <i>Claviceps purpurea</i> | 363 | MTX |
| Ergot alkaloid | Isosetoclavine | <i>Penicillium chermesinum</i> | 370 | MTX |
| Ergot alkaloid | Lysergic acid (85) | <i>Claviceps paspali</i> | 371–373 | MTX |
| Ergot alkaloid | Pyroclavine | <i>Claviceps purpurea</i> . | | MTX |
| Ergot alkaloid | Rugulovasine A,B ³⁷⁴ | <i>Penicillium expansum</i> , <i>P. rubrum</i> , <i>P. bifforme</i> , <i>P. verruculosum</i> , ²³ <i>P. craterforme</i> , ⁷ <i>P. atramentoseum</i> ⁷ <i>P. commune</i> , ⁷ <i>P. islandicum</i> | 375–377 | MTX |
| Ergot alkaloid | α-Ergocryptine (α-Ergokryptine, 12-Hydroxy-2-(1-methylethyl)-5-α-(2-methylpropyl)ergotaman-3,6,18-trione) (Cyclol tripeptide) | <i>Claviceps purpurea</i> , <i>C. zizaniae</i> | 371 | MTX |
| Ergot alkaloid | α-Ergocryptinine (α-Ergokryptinine) | <i>Claviceps purpurea</i> , <i>C. zizaniae</i> | | MTX |
| Ergot alkaloid | β-Ergocryptine (β-Ergokryptine) | <i>Claviceps purpurea</i> | | MTX |
| Ergot alkaloid | β-Ergocryptinine (β-Ergokryptinine) | <i>Claviceps purpurea</i> | | MTX |
| Ergot alkaloid (diketopiperazine) | Aurantiamine ³⁷⁸ (alkaloid 302) (analog of viridamine) | <i>Penicillium aurantiogriseum</i> , ⁷ <i>P. freii</i> , ⁷ <i>P. neochinulatum</i> | 379 | MTX |
| Ergot alkaloid (diketopiperazine) | Viridamine (540) | <i>Penicillium viridicatum</i> | 380 | MTX |
| Fatty acid | Phthiolic acid | <i>Aspergillus fumigatus</i> | 381 | MTX |
| Fescue alkaloid | Dihydroergosine (DHESN) | <i>Claviceps africana</i> ³⁸² | | MTX |
| Fescue alkaloid | Ergosine (Cyclotripeptide) | <i>Claviceps purpurea</i> , <i>Epichloe typhina</i> | | MTX |
| Fescue alkaloid | Ergosinine | <i>Claviceps purpurea</i> , <i>Epichloe typhina</i> | | MTX |
| Fescue alkaloid | Ergovaline | <i>Claviceps purpurea</i> | | MTX |
| Fescue alkaloid (ergoxine group) | β-Ergonine | <i>Claviceps</i> sp. | 383 | MTX |
| Fescue alkaloid (ergoxine group) | β-Ergoptine | <i>Claviceps</i> sp. | 383 | MTX |
| Fescue Alkaloids | Lysergamide (Lysergic acid amide, ergine) | <i>Claviceps paspali</i> | | MTX |
| Five-membered Lactone | Ascladiol (186) (<i>E</i>), (<i>Z</i>) (<i>E</i> : Patulin precursor) | <i>Aspergillus clavatus</i> ^{c,7,384} | | MTX |
| Five-membered lactone | Avenaciolide (–) | <i>Aspergillus avenaceus</i> ³⁸⁵ | (–): e.g., 386, 387 | MTX, fung |
| Five-membered Lactone | Neopatulin (185) | <i>Penicillium patulum</i> | 388 | MTX, cyto |
| Five-membered Lactone | Patulin (3) (Clavacin, Claviformin, Expansin, Penicidin, Terinin, Mycoin) | <i>Aspergillus clavatus</i> ^{c,7} <i>A. terreus</i> , ⁷ <i>Claviceps paspali</i> ^c , <i>P. claviforme</i> , <i>P. expansum</i> , ⁷ <i>P. griseofulvum</i> , ⁷ <i>P. roquefortii</i> , <i>P. verrucosum</i> , <i>P. carneum</i> , ⁷ <i>P. paneum</i> , ⁷ <i>P. clavigerum</i> , <i>Emericella striata</i> , <i>Byssoschlamys fulva</i> , ⁷ <i>Paecilomyces variotii</i> ⁷ | 388–394 | MTX |
| Five-membered Lactone | Tetronic acid | <i>Aspergillus panamensis</i> ²³ | 395 | MTX |
| Five-membered Lactone | γ-Methyltetronic acid (4-Hydroxy-5-methyl-2(5H)-furanone) | <i>Penicillium charlesii</i> ³⁹⁶ | | MTX |
| Fumonisin | AAL toxin TA ₁ (136) | <i>Alternaria alternata</i> f. sp. <i>lycopersici</i> ³⁹⁷ | 398 | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|--------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|-------------------------|
| Fumonisin | AAL toxin TA ₂ (137) | <i>Alternaria alternata</i> f. sp. <i>lycopersici</i> ³⁹⁷ | | MTX |
| Fumonisin | AAL toxin TB ₁ | <i>Fusarium moniliforme</i> | | MTX |
| Fumonisin | AAL toxin TB ₂ | <i>Fusarium moniliforme</i> | | MTX |
| Fumonisin | AAL toxin TC ₁ | <i>Fusarium moniliforme</i> | | MTX |
| Fumonisin | AAL toxin TC ₂ | <i>Fusarium moniliforme</i> | | MTX |
| Fumonisin | AAL toxin TD ₁ | <i>Fusarium moniliforme</i> | | MTX |
| Fumonisin | AAL toxin TD ₂ | <i>Fusarium moniliforme</i> | | MTX |
| Fumonisin | AAL toxin TE ₁ | <i>Fusarium moniliforme</i> | | MTX |
| Fumonisin | AAL toxin TE ₂ | <i>Fusarium moniliforme</i> | | MTX |
| Fumonisin | Fumonisin A ₁ (88) | <i>Fusarium</i> sp. | | MTX |
| Fumonisin | Fumonisin A ₂ (89) | <i>Fusarium</i> sp. | | MTX |
| Fumonisin | Fumonisin A ₃ (90) | <i>Fusarium</i> sp. | | MTX |
| Fumonisin | Fumonisin A ₄ (91) | <i>Fusarium</i> sp. | | MTX |
| Fumonisin | Fumonisin B ₁ (92) | <i>Fusarium moniliforme</i> , ³⁹⁹ <i>F. proliferatum</i> ⁷ | hexaacetate: 400 | MTX |
| Fumonisin | Fumonisin B ₂ (5) | <i>Fusarium moniliforme</i> , ³⁹⁹ <i>F. proliferatum</i> ⁷ | 401 | MTX |
| Fumonisin | Fumonisin B ₃ (93) | <i>Fusarium proliferatum</i> ⁷ | | MTX |
| Fumonisin | Fumonisin B ₄ (94) | <i>Fusarium proliferatum</i> . ⁷ | | MTX |
| Fumonisin | Fumonisin C ₁ (95) | <i>Fusarium</i> spp. ⁴⁰² <i>F. proliferatum</i> ⁷ | | MTX |
| Fumonisin | Fumonisin C ₂ (96) | <i>Fusarium</i> spp. | | MTX |
| Fumonisin | Fumonisin C ₃ (97) | <i>Fusarium</i> spp. ⁴⁰² <i>F. proliferatum</i> ⁷ | | MTX |
| Fumonisin | Fumonisin C ₄ (98) | <i>Fusarium moniliforme</i> , ⁴⁰² <i>F. proliferatum</i> ⁷ | | MTX |
| Fumonisin | Fumonisin P ₁ (99) | <i>Fusarium</i> spp. ⁴⁰² <i>F. proliferatum</i> ⁷ | | MTX |
| Fumonisin | Fumonisin P ₂ (100) | <i>Fusarium</i> spp. ⁴⁰² <i>F. proliferatum</i> ⁷ | | MTX |
| Fumonisin | Fumonisin P ₃ (101) | <i>Fusarium</i> spp. | | MTX |
| Fumonisin | Fumonisin P ₄ (102) | <i>Fusarium</i> spp. | | MTX |
| Furan | 5-Hydroxymethylfurfural | <i>Monocillium</i> sp. ⁷⁰ | various dozen ("commodity") | MTX, cyto |
| Furan dimer | Terrestric acid ⁴⁰³ | <i>Penicillium terrestre</i> , ⁴⁰⁴ <i>Penicillium expansum</i> , <i>Penicillium hirsutum</i> , ⁷ <i>Penicillium verrucosum</i> , <i>Penicillium carneum</i> , ⁷ <i>Penicillium crustosum</i> , ⁷ <i>Penicillium hordei</i> ⁷ | | MTX |
| Furan terpenoid | 1,4-Ipomeadiol (1-(3-furyl)-1,4-pentanediol) | <i>Fusarium</i> sp. ⁴⁰⁵ | 406 | MTX |
| Furandione | Aspergillus acid A-D ⁴⁰⁷ | <i>Aspergillus flavus</i> ^{6,7} <i>Aspergillus wentii</i> , <i>A. sojae</i> ⁷ | 408 | MTX |
| Furanocoumarin | 4,5',8'-Trimethylpsoralen (4,2',8'-Trimethylpsoralen, NSC 71047, TMP) | <i>Sclerotinia sclerotiorum</i> | 409 | MTX |
| Furanocoumarin | Bergapten | <i>Fusarium oxysporon</i> | 410 | MTX |
| Furanocoumarin | Bergaptol (5-Hydroxypsoralen) | <i>Phytophthora megasperma</i> (Plant toxin) | 411 | MTX |
| Furanocoumarin | Psoralen | <i>Fusarium oxysporon</i> | 412 | MTX |
| Furanocoumarin | various Furanocoumarins | <i>Sclerotinia</i> | | MTX |
| Furanocoumarin | Xanthotoxin | <i>Fusarium sporotrichoides</i> , <i>Sclerotinia sclerotiorum</i> | 413 | MTX |
| Furanocoumarin | (8-Methoxypsoralen, Ammoidin) | | | |
| Furanocyclopentane | Communiol | <i>Podospira communis</i> | A–C: 414; C: 415; E, F: 416 | MTX |
| Furanone | 1893B (+) | <i>Fungal strain 1893</i> | 417 | MTX |
| Furo[3,4-g]-1-benzopyran | Austalide A-L (B: (–)) | <i>Aspergillus ustus</i> ⁸⁹ | B: 418 | MTX |
| Furobenzofuran | Monascin | <i>Monascus purpureus</i> ^{419,420} | | MTX, cyto |
| Furobenzofuran | Monascorubrin | <i>Monascus purpureus</i> | | MTX, cyto |
| Furobenzofuran | Rubropunctatin | <i>Monascus purpureus</i> | | MTX, cyto |
| Furobenzopyran | Xyloketal A–F | <i>Xylaria</i> sp. (#2508) | 421 | calcium channel blocker |
| Furoindenobenzoxepine | Anditomin ²³ | <i>Aspergillus varicolor</i> ⁴²² | | MTX |
| Furopyran | Isopatulin | <i>Penicillium urticae</i> | 423 | |
| Furopyrone | Benesudon (–) (4S,5R,6S) | <i>Mollisia benesuada</i> | 424 | MTX |
| Furopyranphenanthrene | Niveulone | <i>Dasyscyphus niveus</i> (Ascomycete) ⁷²⁷ | | Cyto |
| Furopyrone | Oxysporone ²³ | <i>Fusarium oxysporum</i> ⁴²⁵ | | MTX |
| Furopyrone | Pintulin | <i>Penicillium vulpinum</i> ⁴²⁶ | | tumor |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|------------------------------------|----------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|--------------------------------------|
| Fusariotoxin ²³ | Moniliformin ⁴²⁷ (Semisquaric acid, potassium salt) | <i>Fusarium moniliforme</i> , <i>F. oxysporum</i> , ⁷ <i>F. avenaceum</i> , ⁷ <i>F. acuminatum</i> , ⁷ <i>F. proliferatum</i> ⁷ | 428 | MTX, cyto, cardiotox |
| Gibberelene ²³ | Gibberellic acid | <i>Fusarium avanaceum</i> , <i>F. Lateritium</i> , <i>F. monilifokuroi</i> , <i>giberella tricinta</i> , | 429 | MTX |
| Grisandiene | Bisdechlorogeodin (+) | <i>Penicillium glabrum</i> , <i>P. frequentans</i> ⁴³⁰ | | MTX |
| Grisandiene | Dechlorogeodin (−) | <i>Chrysosporium FO-4712</i> ⁴³¹ | | MTX, herb |
| Grisandiene | Dihydrogeodin | <i>Aspergillus terreus</i> , ^{432,433} <i>Penicillium glabrum</i> | | MTX |
| Grisandiene | Geodin (+) | <i>Aspergillus terreus</i> , ^{432,433} <i>Penicillium glabrum</i> | 434 | MTX, vir |
| Hirsutane | Phellodonic Acid | <i>Phellodon melaleucus</i> | 435 | MTX |
| Imidazopyridindole ²³ | Meleagrins ⁴³⁶ | <i>Penicillium vulpinum</i> , <i>P. melanoconidium</i> , <i>P. chrysogenum</i> ⁷ | | MTX |
| Indole | 20-Hydroxyaflavinine | <i>Aspergillus flavus</i> | | feed |
| Indole | Acremoauxin A | <i>Acremonium roseum</i> ⁴³⁷ | 438 | MTX, plant growth regulator |
| Indole | Aflavine | <i>Aspergillus flavus</i> | | MTX ^e |
| Indole | Cyclopiazonic acid ⁴³⁹ | <i>Aspergillus flavus</i> , ^c <i>A. oryzae</i> , ⁷ <i>A. flavus</i> , ⁷ <i>Penicillium verrucosum</i> , <i>P. commune</i> , ⁷ <i>P. griseofulvum</i> , ⁷ <i>P. solitum</i> , <i>P. camemberti</i> , ⁷ <i>P. palitans</i> ⁷ | rac: 440–445 | MTX |
| Indole | Deoxytryptoquivaline | <i>Aspergillus clavatus</i> ⁴⁴⁶ | | MTX |
| Indole | Desoxynortryptoquivaline | <i>Aspergillus clavatus</i> | | MTX |
| Indole | Dihydroxyaflavinine (20,25-Dihydroxyaflavinine; Dihydroxyallavanine) | <i>Aspergillus flavus</i> ⁴⁴⁷ | | Insec ^e |
| Indole | Epoxyfumitremorgin C | <i>Aspergillus fumigatus</i> | | MTX |
| Indole | Mellamide | <i>Aspergillus melleus</i> | | Insec |
| Indole | Nortryptoquivaline | <i>Aspergillus clavatus</i> | | MTX |
| Indole | Nortryptoquivalone | <i>Aspergillus clavatus</i> | | MTX |
| Indole (Paspalitrems type) | Aflatrem | <i>Aspergillus flavus</i> | | MTX, neuro |
| Indole (Penitremes) | Pennigritrem C ₃₇ H ₄₄ ClNO ₆ | <i>Penicillium nigricans</i> , <i>P. janczewskii</i> ⁴⁴⁸ | | MTX |
| Indole alkaloid | Communesin A ⁴⁴⁹ | <i>Penicillium expansum</i> ⁷ | model: 450 | MTX |
| Indole alkaloid | Communesin B ⁴⁴⁹ | <i>Penicillium expansum</i> ⁷ | 450, 451; model: 452 | MTX, cyto |
| Indole alkaloid | Communesin C ⁴⁴⁹ | <i>Penicillium</i> sp. ^{b,453} <i>P. expansum</i> ^{7,454} | | MTX |
| Indole alkaloid | Communesin D ⁴⁴⁹ | <i>Penicillium</i> sp. | | MTX |
| Indole alkaloid | Communesin E ⁴⁴⁹ | <i>Penicillium</i> sp. | | MTX |
| Indole alkaloid | Communesin F | <i>Penicillium</i> sp. | 455 | MTX |
| Indole alkaloid | Communesin G ⁴⁴⁹ | <i>Penicillium rivulum</i> ⁴⁵⁶ | | MTX |
| Indole alkaloid | Communesin H ⁴⁴⁹ | <i>Penicillium</i> sp. | | MTX |
| Indole alkaloid | Cryptoechinulin A-D, E6, E10, G | <i>Aspergillus amstelodami</i> | | MTX |
| Indole alkaloid | Marcfortine A (−) ⁴⁵⁷ | <i>Penicillium paneum</i> , ⁷ <i>P. roqueforti</i> | | MTX |
| Indole alkaloid | Marcfortine B (−) ⁴⁵⁷ (30-Demethylmarcfortine A) | <i>Penicillium paneum</i> , ⁷ <i>P. roqueforti</i> | rac: 458 | MTX |
| Indole alkaloid | Marcfortine C | <i>Penicillium roqueforti</i> | rac: 459 | MTX |
| Indole alkaloid | Neoxaline | <i>Aspergillus japonicus</i> | model: 460 | MTX |
| Indole alkaloid | Oxaline ⁴⁶¹ | <i>Penicillium atramentoseum</i> , ⁷ <i>P. oxalicum</i> ⁷ | model: 460 | MTX |
| Indole Alkaloid | Stephacidin A | <i>Aspergillus ochraceus</i> | 462 | mitochondrial NADH oxidase inhibitor |
| Indole alkaloid | β-Aflatrem | <i>Aspergillus flavus</i> | 463 | MTX |
| Indole alkaloid (diketopiperazine) | 12,13-Dihydro-12-hydroxy-austamide | <i>Aspergillus ustus</i> | | MTX |
| Indole alkaloid (diketopiperazine) | 12,13-Dihydroaustamide (+) | <i>Aspergillus ustus</i> , <i>Penicillium italicum</i> ⁴⁶⁴ | | MTX |
| Indole alkaloid (diketopiperazine) | Bipolaramide (541) | <i>Bipolaris sorokiana</i> ⁴⁶⁵ | 466, 467; model: 468 | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^d |
|------------------------------------------|----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|---------------------------------------------------------|
| Indole alkaloid (diketopiperazine) | Brevianamide A ⁴⁶⁹ (545) (+) | <i>Aspergillus ustus</i> , <i>Penicillium verrucosum</i> , ⁷ <i>P. viridicatum</i> , <i>P. brevicompactum</i> ^{7,470} | rac: 471, 472 | MTX |
| Indole alkaloid (diketopiperazine) | Brevianamide B | <i>Penicillium verrucosum</i> , ⁷ <i>P. viridicatum</i> , <i>P. brevicompactum</i> ⁴⁷³ | 474 | MTX |
| Indole alkaloid (diketopiperazine) | Brevianamide C, D | <i>Penicillium brevicompactum</i> ⁴⁷³ | | MTX |
| Indole alkaloid (diketopiperazine) | Brevianamide E | <i>Penicillium brevicompactum</i> ⁴⁷⁵ | 476, 472 | MTX |
| Indole alkaloid (diketopiperazine) | Brevianamide M | <i>Penicillium verrucosum</i> | | prob MTX |
| Indole alkaloid (diketopiperazine) | Deoxybrevianamide B | <i>Aspergillus ustus</i> | | MTX |
| Indole alkaloid (diketopiperazine) | Isoroquefortine C | <i>Penicillium roqueforti</i> | 477 | MTX |
| Indole alkaloid (diketopiperazine) | Roquefortine A | <i>Penicillium roqueforti</i> , ^c <i>P. hirsutum</i> | | MTX, muscle relaxant, antidepressant, local anaesthetic |
| Indole alkaloid (diketopiperazine) | Roquefortine B | <i>Penicillium roqueforti</i> , <i>p. expansum</i> , <i>P. verrucosum</i> | | MTX |
| Indole alkaloid (diketopiperazine) | Roquefortine C ⁴⁷⁸ | <i>Penicillium roqueforti</i> , ⁷ <i>P. griseofulvum</i> , ⁷ <i>P. chrysogenum</i> , ⁷ <i>P. claviforme</i> , <i>P. hirsutum</i> , ⁷ <i>P. expansum</i> , ⁷ <i>P. crustosum</i> , ⁷ <i>P. italicum</i> , <i>P. verrucosum</i> , <i>P. carneum</i> , ⁷ <i>P. hordei</i> , ⁷ <i>P. melanoconidium</i> ⁷ <i>P. paneum</i> , ⁷ | 479 | MTX |
| Indole alkaloid (diketopiperazine) | Roquefortine D | <i>Penicillium crustosum</i> | 480 | MTX |
| Indole alkaloid (diketopiperazine) | TR2-Toxin (TR-2, verruculogen TR 2) | <i>Penicillium verrucosum</i> ⁴⁸¹ | 298, 482 | Not mut |
| Indole alkaloid (Paspalin/penitem class) | Secopenitrem B | <i>Aspergillus sulfureus</i> | | MTX, insect |
| Indole alkaloid (Paspalin/penitem class) | Sulpinine A-C | <i>Aspergillus sulfureus</i> | | MTX, insect |
| Indole alkaloid ²³ | Asterriquinone A, B1, B, E | <i>Aspergillus terreus</i> | B: 483; E: 484; Demethy-BI: 485 | Cyto |
| Indole dipeptide | Aurechinulin | <i>Aspergillus amstelodami</i> | 486 | MTX |
| Indole dipeptide | Echinulin | <i>Eurotium (Aspergillus) repens</i> , <i>E. amstelodami</i> , ⁷ <i>E. Chevalieri</i> , ⁷ <i>E. herbariorum</i> ⁷ | 487 | MTX |
| Indole dipeptide | Neoechinulin A, B, C, D, E, E7, E8 | <i>Eurotium chevalieri</i> , <i>Aspergillus amstelodami</i> | 488 | MTX |
| Indole diterpene ²³ | Radarin A–D | <i>Aspergillus sulfureus</i> | | MTX |
| Indole diterpenoid | Nominine | <i>Aspergillus flavus</i> , <i>Penicillium roqueforti</i> | 489, 490 | MTX |
| Indole terpenoid | Aflavinine | <i>Aspergillus flavus</i> , <i>Eupenicillium crustaceum</i> | model: 491 | MTX, antiinsec |
| Indole terpenoid | Emindole DA, DB, SA | <i>Emericella desertorum</i> ^{327,327} | model: 492 | MTX |
| Indole terpenoid | Thiersinine A, B | <i>Penicillium sp. (NRRL 28147)</i> ⁴⁹³ | | insec |
| Indolizidine alkaloid | Slaframine (1S,6S,8aS-1-Acetoxy-6-aminooctahydroindolizidine) | <i>Rhizoctonia leguminicola</i> | 494 | MTX, neuro |
| Indolo diketopiperazine | Paraherquimide | <i>Penicillium sp.</i> | 495 | MTX |
| Isocoumarin | 3-Methyl-6-methoxy-8-hydroxy-3,4-dihydroisocoumarin (S) (-) | <i>Aspergillus caespitosus</i> , <i>Talaromyces thailandiasis</i> ⁴⁹⁶ | | MTX |
| Isocoumarin | 5,6-Dihydroxymellein | <i>Plectophomella sp.</i> , <i>Cryptosporiopsis sp.</i> , | | MTX |
| Isocoumarin | 5-Carboxymellein (R)(3,4-Dihydro-8-hydroxy-3-methyl-1-oxo-1H-2-benzopyran-5-carboxylic acid) | <i>Halorosellinia oceanica</i> 1893 ^b , <i>valsa ceratosperma</i>) ²⁶⁵ | | Cyto |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|----------------------|
| Isocoumarin | 5-Chloro-6-hydroxymellein | <i>Plectophomella</i> sp., <i>Cryptosporiopsis</i> sp., | | MTX |
| Isocoumarin | 5-Chloro-6-methoxymellein | <i>Coniothyrium</i> sp., <i>Periconia macrospinosa</i> ⁴⁹⁷ | | MTX |
| Isocoumarin | 5-Methylmellein (3,4-Dihydro-8-hydroxy-3,5-dimethyl-1 <i>H</i> -2-benzopyran-1-one, 5-Methylchloracin) | <i>Phomopsis</i> sp. | 498 | MTX |
| Isocoumarin | 6,7,8-Trihydroxy-3-methyl-1 <i>H</i> -2-benzopyran-1-one (6,7,8-Trihydroxy-3-methylisocoumarin) | <i>Emericella navahoensis</i> ^{55,91,499} | | MTX |
| Isocoumarin | 6-Hydroxymellein ⁵⁰⁰ | <i>Plectophomella</i> sp., <i>Cryptosporiopsis</i> sp. | 501 | MTX |
| Isocoumarin | 6-Methylcitreoisocoumarin (6-Methoxy-citreoisocoumarin, 3-(2 <i>S</i> -Hydroxy-4-oxopentyl)-8-hydroxy-6-methoxy-isocoumarin, LL-Z 1640–6 ⁶⁵⁰) | <i>Penicillium nalgiovense</i> ⁵⁰² | | MTX |
| Isocoumarin | 8-Carboxy-3,4-dihydro-9-hydroxy-3-methylisocoumarin | <i>Penicillium viridicatum</i> | 503 | MTX |
| Isocoumarin | 8-O-Methylasperentin (Asperentin-8-O methyl ether, Methylcladosporin) | <i>Aspergillus flavus</i> | 504 | MTX |
| Isocoumarin | Asperentin (Cladosporin) | <i>Aspergillus flavus</i> | 504 | MTX |
| Isocoumarin | Dichlorodiaporthin (3-(3,3-dichloro-2-hydroxypropyl)-8-hydroxy-6-methoxy-isochromen-1-one) | <i>Penicillium nalgiovense</i> ⁵⁰² | | MTX |
| Isocoumarin | Monocerin | <i>Helminthosporium monoceras</i> , <i>Exserohilum monoceras</i> | 505 | MTX, phytotox |
| Isocoumarin | Ramulosin | <i>Pestalotia ramulosa</i> ⁵⁰⁶ | 501, 507 | MTX |
| Isocoumarin | Semi-Vioxanthin (605) (Semivioxanthin) | <i>Penicillium citreo-viride</i> | 508 | MTX |
| Isocoumarin | Viriditoxin (SC-28762) | <i>Aspergillus viridinutans</i> , ²³ <i>Paecilomyces variotii</i> ⁷ | | MTX |
| Isocoumarin | Xanthomegnin ⁵⁰⁹ (607) | <i>Penicillium viridicatum</i> ^{c,7} <i>P. aurantiogriseum</i> , <i>P. cyclopium</i> , ⁷ <i>P. freii</i> , ⁷ <i>P. tricolor</i> , <i>P. cyclopium</i> , <i>Aspergillus sulfureus</i> , <i>A. ochraceus</i> ⁷ | 510 | MTX |
| Isocoumarin dimer | Viomellein ⁵¹¹ | <i>Aspergillus ochraceus</i> ^{c,7} <i>A. sulfureus</i> , <i>Penicillium viridicatum</i> ^{c,7} <i>P. cyclopium</i> , <i>P. expansum</i> , <i>P. freii</i> , ⁷ <i>P. tricolor</i> , <i>P. verrucosum</i> , <i>P. viridicatum</i> , <i>P. citro-viride</i> | | MTX |
| Isocoumarin dimer | Vioxanthin (606) | <i>Penicillium freii</i> , ⁷ <i>P. viridicatum</i> , ⁷ <i>Aspergillus ochraceus</i> ⁷ | 512 | MTX |
| Isocoumarin-dibenzopyran | Rubrosulphin (Rubrosulfin) | <i>Aspergillus sulfureus</i> | | MTX |
| Isocoumarin-dibenzopyran | Viopurpurin | <i>Aspergillus sulfureus</i> , <i>Trichophyton</i> spp., <i>Penicillium viridicatum</i> | | MTX |
| Isoechinulin-type Alkaloids | Variocolorins A–L | <i>Aspergillus varicolor</i> ⁵¹³ | | MTX |
| Isoindolone | Dihydrocytochalasin B γ lactone | <i>Phoma</i> spp. | | MTX |
| Isoprenoid | Austin | <i>Aspergillus ustus</i> ^{7,514} | | MTX |
| Isoprenoid | Austinol | <i>Aspergillus ustus</i> ⁵¹⁵ | | MTX |
| Isoprenoid | Dehydroaustin | <i>Aspergillus ustus</i> ⁵¹⁶ | | MTX |
| Janthitrem | Janthitrem A | <i>Penicillium janthinellum</i> ^c | | MTX |
| Janthitrem | Janthitrem B | <i>Penicillium janthinellum</i> ^c | | MTX |
| Janthitrem | Janthitrem C | <i>Penicillium janthinellum</i> ^c | | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|------------------------------------|--------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|-------------------------------------------------------------------------------------------|
| Janthitrems | Janthitrem D | <i>Penicillium janthinellum</i> ^c | | MTX |
| Janthitrems | Janthitrem E | <i>Penicillium janthinellum</i> ^c | | MTX |
| Janthitrems | Janthitrem F (10- <i>O</i> -Acetyljanthitrem E) | <i>Penicillium janthinellum</i> ^c | | MTX |
| Janthitrems | Janthitrem G | <i>Penicillium janthinellum</i> ^c | | MTX |
| Macrolactone | 4-Keto-clonostachydiol, clonostachydiol | <i>Gliocladium</i> sp. ^b , <i>Clonostachys cylindrospora</i> | 517 | Cyto |
| Macrolactone | Brefeldin A (cyanein, decumbin, ascotoxin, synergisidin) | <i>Penicillium simplicissimum</i> , <i>P. verrucosum</i> , <i>P. brefeldianum</i> | 518 | MTX |
| Macrolactone | Brefeldin C (7- Deoxybrefeldin-A) | <i>Penicillium brefeldianum</i> ⁵¹⁹ | | MTX |
| Macrolactone | Microcarpalide | Unidentified endophytic fungus | 520 | cyto |
| Macrolactone | Phomol (+) | <i>Phomopsis</i> sp. ⁵²¹ | | Cyto, fung, bact |
| Macrolactone | Vermiculine (−) ²³ | <i>Talaromyces wortmannii</i> | 522 | MTX |
| Meroterpenoid | Montadial A | <i>Bondarzewia montana</i> (polypore) ⁵²³ | | Cyto |
| Naphthalene | Phomopsidin (+) | <i>Phomopsis</i> sp. | 524 | Antimicrotubuli |
| Naphthalene ²³ | Solanapyrone A–E (Salnopyrone) (−) | <i>Ascochyta rabiei</i> | A: 525; D, E: 526 | MTX |
| Naphthaquinone | Herbarin A, B | <i>Cladosporium herbarum</i> | | MTX |
| Naphthopyrone | Dehydroherbarin | <i>Torula herbarum</i> | 538 | prob cyto |
| Naphthopyrone | Fonsecin B (TMD 256B2) | <i>Aspergillus fonsecaeus</i> , <i>A. niger</i> | | MTX |
| Naphthopyrone | general structure | <i>Aspergillus niger</i> , ⁷ <i>A. carbonarius</i> ⁷ | | MTX |
| Naphthopyrone | Rubrofusarin (609) (5,6-dihydroxy- 8-methoxy-2-methyl-4 <i>H</i> - naphtho[2,3- <i>b</i>]pyran-4-one) | <i>Aspergillus carbonarius</i> , <i>A. niger</i> , <i>A. sp. M39</i> , ^{142,527–529} <i>Fusarium culmorum</i> | 530 | MTX |
| Naphthopyrone | Rubrofusarin B (Hemnigerone, TMD 256A2) | <i>Aspergillus fonsecaeus</i> | | MTX |
| Naphthopyrone dimer | Nigerone (−) (<i>S</i>) | <i>Aspergillus niger</i> ⁵³¹ | (+), (−): 532 | MTX |
| Naphthoquinone | 2-Hydroxyjuglone | <i>Fusarium decemcellulare</i> ⁵³³ | various syntheses, see, e.g.: 534 | MTX |
| Naphthoquinone | 9- <i>O</i> -Methylfusarubin (9- <i>O</i> - Methyl-fusarubin, Fusarubin 9-methyl ether) | <i>Fusarium moniliforme</i> ^{535,536} | | MTX |
| Naphthoquinone | Bostrycoidin (NSC-103645) | <i>Fusarium decemcellulare</i> ¹⁴² _{533,537} | deoxy: 538; semisynthesis: 539 | MTX, prob cyto |
| Naphthoquinone | <i>cis</i> -Dihydrofusarubin | <i>Fusarium</i> sp. ^d | | MTX |
| Naphthoquinone | Fusarubin | <i>Fusarium decemcellulare</i> , ⁵³³ <i>F. javanicum</i> ²¹ | | MTX |
| Naphthoquinone | Javanicin (Yavanicin) | <i>Fusarium culmorum</i> , <i>F. graminearum</i> , <i>F. oxysporum</i> , <i>F. roseum</i> , <i>F. verticillioides</i> , <i>F. avenaceum</i> , <i>F. equiseti</i> , <i>F. nivale</i> , <i>F. decemcellulare</i> , <i>F. solani</i> | 540 | MTX |
| Naphthoquinone | <i>Trans</i> -Dihydrofusarubin | <i>Fusarium solani</i> ²¹ | | MTX |
| Naphthoquinone | various pigments | <i>Fusarium oxysporum</i> , ⁷ <i>F. proliferatum</i> ⁷ | | MTX |
| Naphthoxirene | Phaseolinone (+) | <i>Macrophomina phaseolina</i> , <i>Xylaria</i> sp. | formal: 541 | MTX, mut, phyto tox, leish, RNA polymerase inhibitor, Antiplasmodial Phytotox |
| Naphthoxocin (naphthazarin) | Isomarticin (+) | <i>Fusarium martiella</i> , <i>F. solani</i> | | |
| Naphtho- γ -pyrone dimer | Chaetochromin A–D | <i>Chaetomium</i> sp. ⁵⁴² | | MTX, ter, mut |
| Naphtho- γ -pyrone dimer | Ustilaginoidin A, D, E dihydroisoustilaginoidin A | <i>Dermocybe austroveneta</i> ⁵⁴³ (A) | | MTX |
| Napthalene | Tanzawaic acid A–D | <i>Penicillium citrinum</i> , <i>P. chrysogenum</i> , ⁷ <i>P. steckii</i> | 544 | MTX |
| Napthalene ²³ | Equisetin ⁵⁴⁵ (Equestin ²³) | <i>Fusarium equiseti</i> , ⁷ <i>F. semitectum</i> ⁷ | 546 | MTX |
| Napthoquinone | Nectriafurone | <i>Fusarium culmorum</i> ⁷ | 547 | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|-----------------------------|
| Naphthoquinone dimer | Aurofusarin (608) (5,5'-Dihydroxy-8,8'-dimethoxy-2,2'-dimethyl-[7,7'-bi-4H-naphtho[2,3-b]pyran]-4,4',6,6',9,9'-hexone) | <i>Fusarium culmorum</i> ⁵²⁸ | | MTX |
| Nephrotoxic glycopeptides | various structures ⁵⁴⁸ | <i>Penicillium aurantiogriseum</i> , ⁷ <i>P. polonicum</i> ⁷ | | MTX |
| Nucleoside | Mizoribine | <i>Eupenicillium brefeldianum</i> ²¹ | | MTX, immun |
| Ochratoxin | Ochratoxin A (7) (–) | <i>Penicillium viridicatum</i> ^c , <i>P. crustosum</i> , <i>P. expansum</i> , <i>P. verrucosum</i> , ⁷ <i>P. nordicum</i> , ⁷ <i>Aspergillus fumigatus</i> , <i>A. versicolor</i> , <i>A. ochraceus</i> , ⁷ <i>A. niger</i> , ⁷ <i>A. carbonarius</i> , ⁷ <i>Petromyces alliaceus</i> ⁷ | rac: 503, 549–551; formal: 552 | MTX, nephrotox |
| Ochratoxin | Ochratoxin A methyl ester (158) | <i>Aspergillus ochraceus</i> | | MTX |
| Ochratoxin | Ochratoxin B (155) (OTB, Dechloroochratoxin) | <i>Aspergillus ochraceus</i> | rac: 503 | MTX |
| Ochratoxin | Ochratoxin B ethyl ester (160) | <i>Aspergillus ochraceus</i> | | MTX |
| Ochratoxin | Ochratoxin B methyl ester (159) | <i>Aspergillus ochraceus</i> | | MTX |
| Ochratoxin | Ochratoxin C (156) (Ochratoxin A ethyl ester) | <i>Aspergillus ochraceus</i> | | MTX |
| Ochratoxin | Ochratoxin D (4-Hydroxyochratoxin A) | | 553 | MTX |
| Ochratoxin | Ochratoxin α (157) | <i>Aspergillus ochraceus</i> | R: 552 | MTX |
| Octahydrobenzopyran | Sambutoxin | <i>Fusarium sambucinum</i> | 554 | Tox |
| Oligophenalenone dimer | Bacillisporin A–E | <i>Talaromyces bacillisporus</i> ⁵⁵⁵ | | cyto |
| Oligophenalenone dimer | Duclauxin | <i>Penicillium duclauxi</i> , <i>P. stipitatum</i> , <i>P. emmonsii</i> , <i>Talaromyces bacillisporus</i> , <i>T. macrosprum</i> ⁷ | | MTX, tumor, biot |
| Oxaazabicyclo[3.2.1]octane | Awajanomycin | <i>Acremonium</i> sp. AWA16–1 ^b | 556 | Cyto |
| Oxaazaspiro[4.4]nonene | Synerazol | <i>Aspergillus fumigatus</i> | 557; directed biosynthesis: 558 | cyto ⁵⁵⁸ |
| Oxaazaspiro[4.4]nonene | Pseurotin A (Pseurotin) | <i>Aspergillus fumigatus</i> | 559 | Neuritogenic activity, biot |
| Oxatricyclononene | Massarinolin B | <i>Massarina tunica</i> | 560 | MTX |
| Oxirenoisobenzofuran | Integrasone | sterile mycelium from an unknown fungus | 561 | MTX |
| Paspalitrem type | Paspaline | <i>Claviceps paspali</i> , <i>Aspergillus</i> sp. | 562 | MTX, tem |
| Paspalitrem type | Paspalinine (+) | <i>Penicillium paxilli</i> | | MTX |
| Pentaketide | Flaviolin (2,5,7-trihydroxy-1,4-naphthoquinone) | <i>Claviceps paspali</i> <i>Aspergillus fetidus</i> , <i>phialophora lagerbergii</i> , ²³ <i>Sporothrix schenckii</i> | 563 | MTX |
| Pentenoid acid | Verruculone ⁵⁶⁴ (Verrucolone, Arabenoic acid) | <i>Penicillium italicum</i> , ⁷ <i>P. nordicum</i> , ⁷ <i>P. olsonii</i> , <i>P. verrucosum</i> ^{7,565} | | MTX, herb |
| Peptide | Cyclosporin A | <i>Tolypocladium inflatum</i> | 566 | MTX, biot |
| Peptide | Sillucin | <i>Mucor pusillus</i> | | micro |
| Peptide (4 AA) ²³ | Viridic acid ⁵⁶⁷ | <i>Penicillium viridicatum</i> ⁷ | 568 | MTX |
| Peptide (Amanita toxins) | α-Amanitine | <i>Amanita</i> sp. ⁵⁶⁹ | 570 | MTX |
| Peptide (Peptaibol) | Alamethicin (more than one) | <i>Trichoderma viride</i> ⁷ | 571 | biot |
| Peptide (Peptaibol) | Suzukacillin ⁵⁷² | <i>Trichoderma viride</i> ^{573,7} | | MTX, biot |
| Peptide (Peptaibol) | Trichorzianine A,B (Alamethicins) | <i>Trichoderma harzianum</i> ⁷ | | MTX |
| Peptide (Peptaibol) | Trichotoxin A40, A50 | <i>Trichoderma viride</i> ⁷ | (A50) | MTX, biot |
| Peptide (Peptaibol) | Trichovirin (Trichotoxin B) | <i>Trichoderma viride</i> | Trichovirin I: 574 | biot |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^d |
|------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|------------------------------------------------------|
| Perilene | Calphostin A-C (A: UCN-1028A; C: Cladochrome E) ^{26,575,576} | <i>Cladosporium</i> sp. | 577 | MTX, kin |
| Perilene | Calphostin D ²⁶ (ent-Isophleichrome) | <i>Cladosporium</i> sp. ⁵⁷⁸ | 576, 577, 579 | MTX, kin |
| Phenylene | Funalenone | <i>Aspergillus niger</i> | | HIV, cyto, collagenase inhibitor |
| Phenelanone | Atrovenetinone | <i>Penicillium</i> sp. FKI-1463 | | HIV |
| Phenol | Clavatul | <i>Aspergillus clavatus</i> , <i>Trichoderma pseudokoningii</i> | 580, 581 | MTX |
| Phenol | Flavipin ²³ | <i>Epicoccum nigrum</i> , <i>Aspergillus terreus</i> , <i>Fennelia flavipes</i> , <i>Chaetomium globosum</i> | 582 | MTX |
| Phenol | Fomecin B | <i>Tricholomopsis rutilans</i> (Basidiomycete) ⁵⁸³ | 584 | Cyto |
| Phenol | Parvisporin | <i>Stachybotrys parvispora</i> ⁵⁸⁵ | | Neuritogenic |
| Phenol | Raistrick phenols: 2,4-Dihydroxy-6-(2-oxypropyl)benzoic acid, 2,4-Dihydroxy-6-(1-hydroxy-2-oxypropyl)benzoic acid, and 2,4-Dihydroxy-6-(1,2-dioxopropyl)benzoic acid ⁵⁸⁶ | <i>Penicillium brevicompactum</i> ⁷ | | MTX |
| Phenol | Sorbicillin | <i>Aspergillus clavatus</i> | 581 | MTX |
| Phomactins | Phomactin A | <i>Phoma</i> sp. ⁵⁸⁷ | 588–590 | MTX |
| Phomactins | Phomactin B–G | <i>Phoma</i> sp. | 591 | MTX |
| Phthalide | 3-Butyl-7-hydroxyphthalide (–) | <i>Penicillium vulpinum</i> | 592 | cyto |
| Phthalide | 3-Ethyl-5,7-dihydroxy-3,6-dimethylphthalide | <i>Aspergillus unguis</i> | | MTX |
| Phthalide | Cyclopaldic acid ⁵⁹³ | <i>Penicillium aurantiogriseum</i> , <i>P. commune</i> ⁷ | | MTX |
| Phthalide | Mycophenolic acid ⁵⁹⁴ | <i>Penicillium brevicompactum</i> ^{c,7} <i>P. roqueforti</i> , ⁷ <i>P. verrucosum</i> , <i>P. carneum</i> ⁷ | 595 | MTX, immun |
| <i>p</i> -Methoxyphenylquinolinone | Yaequinolone A–I | <i>Penicillium</i> sp. | | Insec |
| Polyketide | PM-toxin B | <i>Phyllosticta maydis</i> | 596 | MTX, pathotoxin |
| Polyketide (Octahydronaphthalene) | Diplodiatoxin (+) | <i>Diplodia maydis</i> ⁵⁹⁷ | 598 | MTX |
| Polyol | Sphingofungin A–F | <i>Aspergillus</i> sp. ⁵⁹⁹ | 77, 600, 601 | MTX |
| Polyol (Bisepoxide) | Depudecin (–) | <i>Alternaria brassicicola</i> | 602 | antiangiogenic, Histone deacetylase inhibitor, plasm |
| Propionic acid ²³ | 3-Nitropropionic acid (Hiptalonic acid, Hiptagenic acid, Bovinocidin, Oryzacin, Oryzasazine) | <i>Arthrinium</i> sp., <i>Aspergillus oryzae</i> , ⁷ <i>A. flavus</i> , ⁷ <i>Penicillium melinii</i> | commodity | MTX |
| Purine | Uric acid | <i>Penicillium cyclopium</i> ⁶⁰³ | various syntheses | MTX |
| Pyran | Chlamydozporiol (4-Methoxy-5-hydroxyethyl-6-(3-butan-2-ol)-2H-pyran-2-one) | <i>Fusarium</i> spp. ⁶⁰⁴ | | MTX, prob cyto |
| Pyrandione | Grevellin B, C, D | <i>Suillus grevillei</i> | 605, 735 | MTX |
| Pyranobenzopyrandione | Phelligrudin C–G | <i>Phellinus igniarius</i> ⁶⁰⁶ | | Cyto |
| Pyranoisindole | SMTP-1 to -6 | <i>Stachybotrys microspora</i> | | MTX, plasminogen activator |
| Pyranoisindole | Stachybotrin A (+) [144373-26-2] ⁷⁵³ | <i>Stachybotrys</i> sp. ⁶⁰⁷ | | MTX, fung |
| Pyranoisindole | Stachybotrin B (+) | <i>Stachybotr.</i> sp. ⁶⁰⁷ | | MTX |
| Pyranoisindole | Stachybotrin C | <i>Stachybotrys parvispora</i> ⁵⁸⁵ | | Neuritogenic |
| Pyranoisindole | Staplabin | <i>Stachybotrys microspora</i> ⁶⁰⁸ | | MTX |
| Pyranoisindole dimer | SMTP-7 (Orniplapin) | <i>Stachybotrys chartarum</i> , ²¹ <i>S. microspora</i> | | MTX |
| Pyranoisindole dimer | SMTP-8 | <i>Stachybotrys microspora</i> | | MTX, plasminogen activator |
| Pyrone | Asperlin (+) | <i>Aspergillus</i> sp. | 609 | MTX |
| Pyrone | Asteltoxin | <i>Aspergillus stellatus</i> | 610 | MTX |
| Pyrone | Aszonnapyrone A | <i>Aspergillus zonatus</i> ⁶¹¹ | | MTX |
| Pyrone | Citreoviridin X (Citreoviridinol) | <i>Penicillium citro-viride</i> | 612 | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^d |
|---------------------------|-----------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|--------------------------------------|
| Pyrone | Fusapyrone | <i>Fusarium semitectum</i> ^{7,613} | | MTX |
| Pyrone | Gibepyrone A | <i>Fusarium oxysporum</i> ⁷ | 614 | MTX |
| Pyrone | Gibepyrone F | <i>Fusarium oxysporum</i> ⁷ | | MTX |
| Pyrone | Isoasperlin | <i>Macrophomina phaseolina</i> | | Phytotox |
| Pyrone | Kojic acid ⁶¹⁵ | <i>Aspergillus fumigatus</i> , ^c <i>A. oryzae</i> , ⁷ <i>A. parasiticus</i> , <i>A. tamari</i> , <i>A. flavus</i> , ⁷ <i>A. nomius</i> , ⁷ <i>A. sojae</i> , ⁷ <i>Penicillium jensenii</i> , <i>P. lanosum</i> , <i>Petromyces alliaceus</i> ⁷ | biotransformation from glucose | MTX, mut |
| Pyrone | Phomalactone (Phomalactone) (+) | <i>Macrophomina phaseolina</i> , <i>Nigrospora sphaerica</i> | 609, 616; Acetyl p.: 617 | Phytotox |
| Pyrone | Verrucosidin ⁶¹⁸ (Verrucosidin A) (+) ²³ | <i>Penicillium melanoconidium</i> , ⁷ <i>P. aurantiogriseum</i> , <i>P. polonicum</i> , ⁷ <i>P. viridicatum</i> , <i>P. verrucosum</i> | (+): 619–621 | MTX, trem |
| Pyranopyridine | Acuminatopyrone | <i>Fusarium acuminatum</i> , <i>F. chlamydosporum</i> ^{604,622,623} | | MTX |
| Pyranopyrone | Chlamydosporol (–) | <i>Fusarium culmorum</i> , <i>F. chlamydosporum</i> , <i>F. acuminatum</i> , ⁷ <i>avenaceum</i> ^{7,623} | | MTX, cyto |
| Pyrazine | Aspergillic acid (+) | <i>Aspergillus</i> sp. | rac: 624 | MTX |
| Pyrazine | Flavacol | <i>Aspergillus ochraceus</i> | 625 | mitochondrial NADH oxidase inhibitor |
| Pyrazinone | Neoaspergillic acid | <i>Aspergillus stertiorum</i> | 626 | Biot |
| Pyrazinoquinazoline | Fumiquinazoline A–G (A: 547) | <i>Aspergillus fumigatus</i> ^b | 627 | MTX |
| Pyridine (alkaloid) | Flavipucine (3'-Isovaleryl-6-methylpyridine-3-spiro-2'-oxiran-2(1H),-4(3H)-dione), brunnescin | <i>Cladobotryum rubrobrunnescens</i> ⁶²⁸ | 629 | Cyto, biot |
| Pyridine derivative | Fusaric acid | <i>Fusarium oxysporum</i> , ⁷ <i>F. proliferatum</i> ⁷ | 630 | MTX, cyto, hypotensive agent |
| Pyridone | Fischerin | <i>Neosatorya fischeri</i> | | MTX, Tox |
| Pyridopyrazin Alkaloid | 10-Epi-Verruculotoxin (3-Toluyloctahydro-2H-pyrido-[1,2-a]pyrazine) | <i>Penicillium verrucosum</i> ²¹ | 631, 632 | MTX |
| Pyridopyrazin Alkaloid | Verruculotoxin (S,S) (3-Toluyloctahydro-2H-pyrido-[1,2-a]pyrazine) | <i>Penicillium verrucosum</i> ^{21,633} | 631, 632 | MTX |
| Pyrone | Radicinin | <i>Alternaria radicinin</i> | model: 634 | MTX |
| Pyrone | Radicinol, epi-Radicinol | <i>Alternaria Chrysanthemi</i> , <i>A. radicina</i> , <i>Cochliobolus lunata</i> <i>Aspergillus versicolor</i> ⁶³⁵ | | MTX |
| Pyrrolidine ²³ | Versimide (MM4086) (Methyl (methylsuccinimido)acrylate) (R) (+) | <i>Acremonium</i> sp. | 637 | |
| Pyrrolizidine alkaloid | UCS 1025A | <i>Penicillium verrucosum</i> , ⁶³⁸ <i>Aspergillus</i> spp. | | MTX |
| Quinazoline alkaloid | Anacine ⁶³⁹ (1S, 3S) | <i>Penicillium aurantiogriseum</i> , ⁷ <i>P. nordicum</i> , ⁷ <i>P. polonicum</i> , <i>P. verrucosum</i> | 640 | MTX |
| Quinazoline alkaloid | Chrysogenin ⁶⁴¹ (Chrysogine) (S) (–) | <i>Penicillium chrysogenum</i> , ⁷ <i>P. griseoroseum</i> , <i>P. nalgiovense</i> , ⁷ <i>Fusarium culmorum</i> , <i>F. equiseti</i> , ⁷ <i>F. graminearum</i> , ⁷ <i>F. semitectum</i> ⁷ | 642 | MTX |
| Quinolinone alkaloid | 3-Methoxyviridicatin (3-O-Methylviridicatin) | <i>Penicillium polonicum</i> | 643 | MTX |
| Quinolinone alkaloid | Penigequinolone A, B (+) | <i>Penicillium verrucosum</i> ⁶⁴⁴ | | MTX |
| Quinolinone alkaloid | Viridicatin (2,3-Dihydroxy-4-phenylquinoline) | <i>Penicillium cyclopium</i> , <i>P. aurantiogriseum</i> , <i>P. solitum</i> , <i>P. aurantiovirens</i> , <i>P. frei</i> , <i>P. polonicum</i> ²³ | 645 | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|-----------------------|--------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|----------------------|
| Quinolinone alkaloid | Viridicatol (Carbostyryl) | <i>Penicillium cyclopium</i> , <i>P. aurantiovirens</i> , <i>P. p. frei</i> , <i>P. neoehinullatum</i> , <i>P. polonicum</i> ²³ | | MTX |
| Quinone | Cochlioquinone A | <i>Drechslera sacchari</i> | | MTX, kin |
| Quinone | Epi-Cochlioquinone A | <i>Stachybotrys bisbyi</i> | | MTX |
| Quinone | Terreic acid (5,6-Epoxy-2-hydroxytoluquinone, Y-8980, Anti-HeLa-cell substance) | <i>Aspergillus terreus</i> ^{c,646,647} | 647, 648 | MTX |
| Resorcylic lactone | 11-Acetyldehydrocurvularin ⁶⁶¹ | <i>Cercospora scirpola</i> | | MTX |
| Resorcylic lactone | 12-Oxocurvularin | <i>Penicillium citreo-viride</i> | 649 | MTX |
| Resorcylic lactone | 3'-Hydroxyzearalenone (two diastereomers) | <i>Fusarium roseum</i> | | MTX |
| Resorcylic lactone | 5'-Dihydroxyzearalenone-4-methylether | Unidentified fungus ⁶⁵⁰ | | MTX |
| Resorcylic lactone | 5-Formylzearalenone | <i>Gibberella zeae</i> | | MTX |
| Resorcylic lactone | 6',8'-Dihydroxyzearalene | <i>Fusarium roseum</i> ⁶⁵¹ | | MTX |
| Resorcylic lactone | 7'-Dehydrozearalenone (1',7'-Zearaldienone) | <i>Gibberella zeae</i> ^{652,653} | | MTX |
| Resorcylic lactone | 8'-Hydroxyzearalenone (two diastereomers) | <i>Fusarium roseum</i> | | MTX |
| Resorcylic lactone | Aigialomycin A,B,C,D (D: 356) ⁶⁵⁴ | <i>Aigialus parvus</i> | 655–658 | MTX |
| Resorcylic lactone | Curvularin ⁶⁶¹ | <i>Curvularia</i> sp., <i>Alternaria cinerariae</i> | 659 | MTX |
| Resorcylic lactone | Dehydrocurvularin ^{660,661} | <i>Drechslera australiensis</i> | | MTX, phytotoxin |
| Resorcylic lactone | Hypothemycin (355) (+) | <i>Hypomyces trichothecoides</i> | 662 | MTX |
| Resorcylic lactone | LL-Z1640-2 | unidentified fungus ⁶⁵⁰ | | MTX |
| Resorcylic lactone | LL-Z1640-3 | unidentified fungus ⁶⁵⁰ | | MTX |
| Resorcylic lactone | Monocillin I (Dechloromonorden) | <i>Monocillium nordinii</i> | 663, 664 | MTX |
| Resorcylic lactone | Monocillin II (353) | <i>Monocillium nordinii</i> | | MTX |
| Resorcylic lactone | Monocillin III–V (III: 604) | <i>Monocillium nordinii</i> | | MTX |
| Resorcylic lactone | Monorden (352) (Radicicol) | <i>Monosporium bonorden</i> | 665 | MTX |
| Resorcylic lactone | Pochonin A (376) | <i>Pochonia chlamydosporia</i> | 666 | MTX |
| Resorcylic lactone | Pochonin B | <i>Pochonia chlamydosporia</i> | | MTX |
| Resorcylic lactone | Pochonin C (354) | <i>Pochonia chlamydosporia</i> | 667 | MTX |
| Resorcylic lactone | Pochonin D | <i>Pochonia chlamydosporia</i> | 668 | MTX |
| Resorcylic lactone | Pochonin E, F | <i>Pochonia chlamydosporia</i> | | |
| Resorcylic lactone | Queenslandon (357) | <i>Chrysosporium queenslandicum</i> | model: 669 | MTX |
| Resorcylic lactone | Zearanol | <i>Cochliobolus lunata</i> , unidentified fungus ⁶⁵⁰ | | MTX |
| Resorcylic lactone | Zearalanol (Zearanol, Zeranol) see α - or β -Zearalanol (318 , 319) | <i>Fusarium graminearum</i> | | MTX |
| Resorcylic lactone | Zearalanone (315) (Zanone) | <i>Fusarium graminearum</i> , <i>F. crookwellense</i> , <i>F. culmorum</i> , <i>F. equiseti</i> , <i>F. moniliform</i> <i>F. verticillioides</i> | 670 | MTX |
| Resorcylic lactone | Zearalenone (4) (–) (S,E) (F 2 toxin, Toxin F2) | <i>Gibberella zeae</i> ^e <i>Fusarium crookwellense</i> , <i>F. equiseti</i> , ⁷ <i>F. graminearum</i> , ⁷ <i>F. semitectum</i> ⁷ | 671–676 | MTX |
| Resorcylic lactone | α -Zearalanol (318) | <i>Fusarium</i> sp. | 1074b | MTX |
| Resorcylic lactone | α -Zearalanol (316) (S) (–) | <i>Fusarium roseum</i> | | MTX |
| Resorcylic lactone | β -Hydroxycurvularin ⁶⁶¹ | <i>Alternaria tomata</i> | | MTX |
| Resorcylic lactone | β -Zearalanol (319) | <i>Fusarium</i> sp. | | MTX |
| Resorcylic lactone | β -Zearalanol (317) | <i>Fusarium roseum</i> | | MTX |
| Ribotoxin (149 AA) | Restrictocin | <i>Aspergillus fumigatus</i> | | Ribotoxin, cyto |
| Sesquiterpene | PR imine | <i>Penicillium roqueforti</i> | | MTX |
| Sesquiterpene | Spirocyclic drimane sesquiterpenes, e.g., phenylspirodrimanes (spiro-lactones and spiro-lactams) | <i>Aspergillus ustus</i> | 677 | MTX |
| Sesquiterpene lactone | Expansolide | <i>Penicillium expansum</i> | | MTX |
| Sesquiterpene | HM-3, HM-4 | <i>Helicobasidium mompa</i> | 678 | MTX |
| Sesquiterpene | Insulicolide A (–) | <i>Aspergillus versicolor</i> , <i>A. insulicola</i> ^b | | MTX, cyto |
| Sesquiterpene | Insulicolide B (–) | <i>Aspergillus versicolor</i> | | Cyto |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^d |
|-------------------------------------------|----------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|------------------------------------------|
| Sesquiterpene | PR toxin (PR-toxin) | <i>Penicillium roqueforti</i> ^{7c} , <i>P. expansum</i> , <i>P. verrucosum</i> , <i>P. chrysogenum</i> | | MTX |
| Sesquiterpene | Terrecyclic acid A (TCA) | <i>Aspergillus terreus</i> | 679 | CMTX, cytotox, anti cancer Cyto |
| Sesquiterpene (Cyclopropindene) | Isovelleral | <i>Lactarius vellereus</i> (Basidiomycete) | 680 | |
| Sesquiterpene (Quinone) | Lagopodin A | <i>Coprinus cinereus</i> | 681 | MTX |
| Sesquiterpene (trichthecene precursor) | Trichodiene (611) | <i>Fusarium sporotrichoides</i> , <i>Stachybotrys</i> sp., <i>Trichothecium roseum</i> ⁶⁸² | 683 | MTX |
| Six-membered lactone | Aurovertin B (NSC 329699) | <i>Calcarisporium arbuscula</i> ⁶⁸⁴ | 685 | MTX |
| Six-membered lactone | Aurovertin D | <i>Calcarisporium arbuscula</i> ⁶⁸⁶ | | MTX |
| Sphingosine | 2-Amino-14,16-dimethyloctadecan-3-ol (2-AOD-3-ol) | <i>Fusarium avenaceum</i> ⁶⁸⁷ | | Cyto |
| Spirobenzofuran | Griseofulvin ⁶⁸⁸ | <i>Penicillium griseofulvum</i> ⁷ | 689 | MTX, fung |
| Spirofuroisindole | Stachybotral | <i>Stachybotrys elegans</i> ⁶⁹⁰ | | MTX |
| Spirofuroisindole | Stachybotrin (Stachybotrin) | <i>Stachybotrys elegans</i> , <i>S. alternans</i> , <i>S. atra</i> | | MTX |
| Spirofuroisindole | Stachybotrine A (+) [256620-70-4] ⁷⁵³ | <i>Stachybotrys elegans</i> ⁶⁹⁰ | | MTX |
| Statin | Compactin ²⁶ (Mevastatin) | <i>Penicillium cyclopium</i> , <i>P. citrinum</i> , <i>P. solitum</i> ⁷ | 691 | MTX |
| Steroid | Ergosterol ²³ | <i>Gaeumannomyces graminis</i> , <i>Penicillium aurantiogriseum</i> , <i>P. verrucosum</i> | | MTX |
| Steroid | Fumitoxin A-D ^{e,692} | <i>Aspergillus fumigatus</i> ⁷ | | MTX |
| Steroid | Helvolic acid (Fumigacin) | <i>Aspergillus fumigatus</i> ^c | | Bact |
| Steroid | Poaeufusarin | <i>Fusarium sporotrichioides</i> | | MTX |
| Steroid | Sporofusarin | <i>Fusarium sporotrichioides</i> | | MTX |
| Steroidal | Viridin | <i>Trichoderma viride</i> , <i>Gliocladium virens</i> , <i>Penicillium funiculosum</i> <i>Myrothecium roridum</i> | 693 | MTX, bact |
| Steroidal | Wortmannin (+) | <i>Fusarium</i> sp., <i>Talaromyces wortmannii</i> , <i>Penicillium wortmannii</i> , <i>P. funiculosum</i> <i>Trichoderma viride</i> , <i>Gliocladium virens</i> , <i>Myrothecium roridum</i> | Formal total synthesis: 694 | Cyto |
| Steroidal (Cyclopentaphenanthrofurane) | Desmethoxyviridin | <i>Nodulisporium hinnuleum</i> , <i>Trichoderma viride</i> , <i>Gliocladium virens</i> , <i>Penicillium funiculosum</i> <i>Myrothecium roridum</i> | | MTX |
| Steroidal (Cyclopentaphenanthrofurane) | Desmethoxyviridol ⁶⁹⁵ | <i>Nodulisporium hinnuleum</i> | | MTX |
| Sterol | Terretonin ⁶⁹⁶ | <i>Aspergillus terreus</i> unidentified fungus ⁶⁹⁷ | | MTX |
| Structure unknown | Antibiotic C3368-A | <i>Byssoschlamys fulva</i> ⁷ | | MTX |
| Structure unknown | Byssotoxin A (C ₂₅ H ₂₆ N ₂ O ₃) ⁶⁹⁸ | <i>Aspergillus candidus</i> ⁶⁹⁹ | | MTX |
| Structure unknown | Candidulin (C ₁₁ H ₁₅ NO ₃) ²³ | <i>Aspergillus flavus</i> , <i>A. parasiticus</i> | | biot |
| Structure unknown | Flavutoxin (Flavotoxin) | <i>Myrothecium</i> sp. ⁷⁰⁰ | | MTX |
| Structure unknown | Necrocitin | <i>Aspergillus nidulans</i> , <i>A. versicolor</i> ⁷ | | biot, phytotox |
| Structure unknown | Nidulotoxin ⁷⁰¹ | <i>Penicillium islandicum</i> ⁷⁰² | | MTX |
| Structure unknown | Pibasterol | <i>Aspergillus amstelodami</i> , <i>A. repens</i> ⁷⁰³ | | Bact, not mut |
| Structure unknown | Prechinulin | | | MTX |
| Structure unknown | Simatoxin | <i>Penicillium islandicum</i> | | Mut |
| Talaromycins | Talaromycin A | <i>Talaromyces stipitatus</i> | 704-714; model: 715; formal: 716 | MTX |
| Talaromycins | Talaromycin B | <i>Talaromyces stipitatus</i> | 704, 707, 709-711, 713, 714, 717-722; formal: 716 | MTX |
| Talaromycins | Talaromycin C | <i>Talaromyces stipitatus</i> | 709, 710, 723 | MTX |
| Talaromycins | Talaromycin D | <i>Talaromyces stipitatus</i> | | MTX |
| Talaromycins | Talaromycin E | <i>Talaromyces stipitatus</i> | 709, 710, 723 | MTX |
| Terpene | 15-Hydroxyculmorone | <i>Fusarium culmorum</i> | | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|--------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|
| Terpene | Culmorin (–) ⁷²⁴ | <i>Fusarium culmorum</i> , ⁷ <i>F. crookwellense</i> , ⁷ <i>F. graminearum</i> ⁷ | 725 | MTX |
| Terpene | Pleurotin | <i>Pleurottia griseus</i> | 726 | MTX, cyto |
| Terpenoid | Dasyscyphin B | <i>Dasyscyphus niveus</i> (Ascomycete) ⁷²⁷ | | Cyto |
| Terpenoid | Dasyscyphin C | <i>Dasyscyphus niveus</i> ⁷²⁷ | | Cyto |
| Terphenyl | prenylated <i>p</i> -terphenyl metabolite | <i>Aspergillus candidus</i> ⁷²⁸ | | MTX |
| Terphenylin | Candidusin A,B | <i>Aspergillus candidus</i> ^{21,729} | | MTX |
| Terphenylin | Candidusin C (2'-Epoxy-3',4'',6'-trimethoxy-1,1'-4',1''-terphenyl-4,5-diol), 3,3-dihydroxyterphenyllin, 3-hydroxyterphenyllin | <i>Aspergillus candidus</i> ²¹ | | MTX |
| Terphenylin-type | Terphenylin | <i>Aspergillus</i> sp. | | MTX |
| Tetrahydrofuran-benzopyran | Alboatrin | <i>Verticillium alboatrum</i> | 730 | MTX, phytotox |
| Tetrahydrofuran | Botryodiploidin (–) ⁷³¹ (PSX-1, Cytostipin) | <i>Penicillium brasilianum</i> , ⁷ <i>P. brevicompactum</i> , <i>Talaromyces stipidatus</i> | 732 | MTX, mutic |
| Tetrahydrofuran | Varitriol | <i>Emericella venezuelensis</i> ^b | 733 | MTX |
| Tetrahydroquinoline alkaloid/ indole diterpenoid | Aspernomine | <i>Aspergillus nomius</i> | | MTX, insect |
| TetrahydroxyAnthraquinoid | Ziganein | <i>Exserohilum monoceras</i> | | MTX, phytotox |
| Tetrapeptide | Apicidin A, B, C | <i>Fusarium</i> sp. | A: 734 | Cyto |
| Tetronic acid | Aspulvinone A–E (E: Aspergillide B1) | <i>Aspergillus terreus</i> | 735 | MTX |
| Tetronic acid | Byssochlamic acid ²³ | <i>Byssochlamys fulva</i> , <i>B. nivea</i> ^{7,736} | 737 | MTX |
| Tetronic acid | Carlic acid | <i>Penicillium charlesii</i> ⁷³⁸ | 739 | MTX |
| Tetronic acid | Carlosic acid | <i>P. verrucosum</i> , <i>P. charlesii</i> ⁷³⁸ | 739, 740 | MTX |
| Tetronic acid | Carolic acid (+) | <i>P. verrucosum</i> , <i>P. charlesii</i> ⁷³⁸ | 739 | MTX |
| Tetronic acid | Carolinic acid | <i>Penicillium charlesii</i> ⁵ | 741 | MTX |
| Tetronic acid | Italicic acid | <i>Penicillium italicum</i> ⁷ | | MTX |
| Tetronic acid | Multicolanic acid (188) | <i>Penicillium</i> spp. | 742 | MTX |
| Tetronic acid | Multicolic acid ²³ | <i>Penicillium multicolor</i> ⁷⁴⁴ | methyl ester: 743 | MTX |
| Tetronic acid | Multicolosic acid ²³ | <i>Penicillium multicolor</i> ⁷⁴⁴ | | MTX |
| Tetronic acid | Rubratoxin A | <i>Penicillium rubrum</i> , ^c <i>P. craterforme</i> ⁷ | | MTX |
| Tetronic acid | Rubratoxin B ²³ | <i>Penicillium rubrum</i> ^{c,745} <i>P. craterforme</i> ⁷ | | MTX |
| Tetronic acid | Scytalidin | <i>Scytalidium</i> sp. ⁷⁴⁶ | | fung |
| Tetronic acid | Vertinolide | <i>Verticillium intertextum</i> | 747 | no bio data |
| Toluquinone ²³ | Glioresein | <i>Gliocadium roseum</i> ⁷⁴⁸ | | MTX |
| Tremorgen | Desoxypaxillin | <i>Penicillium paxilli</i> | | MTX |
| Tremorgen | α-Paxitriol | <i>Acremonium lolii</i> , <i>Penicillium crustosum</i> | 749 | MTX |
| Tremorgen | β-Paxitriol | <i>Penicillium crustosum</i> | 749 | MTX |
| Tremorgen (Indole) | Fumitremorgin A ⁷⁵² (Fumitremorgen A) ⁷⁵⁰ | <i>Aspergillus fumigatus</i> ^{c,7} <i>Penicillium brasilianum</i> , ⁷ <i>Neosatorya fischeri</i> ⁷ | | MTX |
| Tremorgen (Indole) | Fumitremorgin B ⁷⁵² (Fumitremorgen B, lonosulin) | <i>Aspergillus fumigatus</i> ^{c,7} <i>A. caespitosus</i> , <i>Penicillium brasilianum</i> , ⁷ <i>Neosatorya fischeri</i> ⁷ | 751 | MTX |
| Tremorgen (Indole) | Fumitremorgin C ⁷⁵² (Tryptoquivaline C, Tryptoquivaline A, Tryptoquivaline) [CAS: 55387-45-6] ⁷⁵³ | <i>Aspergillus clavatus</i> , ⁷ <i>A. fumigatus</i> , ^{7,754} <i>Penicillium digitatum</i> , ⁷ | 755, 756; model: 757 | MTX |
| Tremorgen (Indole) | Fumitremorgin D–M (Tryptoquivaline D–M) | <i>Aspergillus fumigatus</i> | G: 758 | MTX |
| Tremorgen (Indole) | Lolitrein B, C | <i>Acremonium</i> sp. | | MTX |
| Tremorgen (Indole) | Lolitrein E | <i>Acremonium</i> sp. | | MTX |
| Tremorgen (Indole) | Lolitriol | <i>Neotyphodium lolii</i> | | neuro |
| Tremorgen (Indole) | Tryptoquivaline N (Deoxynortryptoquivalone, Fumitremorgin N) | <i>Aspergillus clavatus</i> ⁷⁵⁹ | | MTX |
| Tremorgen/ Paspalitrem type | 1'- <i>O</i> -Acetyl paxilline (1'-Acetoxypaxilline) | <i>Emericella striata</i> ⁷⁶⁰ | | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|----------------------|
| Tremorgen/ Paspalitrems type | Paxilline (+) ⁷⁶¹ | <i>Penicillium paxillif</i> | | MTX |
| Tremorgen/ Penitrems | Bromopenitrems E, F ²¹ | <i>Penicillium simplicissimum</i> ⁷⁶² | | MTX |
| Tremorgen/ Penitrems | Penitrems A ^{763,764} | <i>Penicillium crustosum</i> , ⁶⁷ <i>P. expansum</i> , <i>P. janczewskii</i> , <i>P. melanoconidium</i> , ⁷ <i>P. verrucosum</i> , <i>P. carneum</i> , <i>P. clavigenum</i> | | MTX |
| Tremorgen/ Penitrems | Penitrems B ^{763,764} | <i>Penicillium crustosum</i> | | MTX |
| Tremorgen/ Penitrems | Penitrems C ^{763,764} | <i>Penicillium crustosum</i> | | MTX |
| Tremorgen/ Penitrems | Penitrems D ^{763,764} | <i>Penicillium crustosum</i> | 765 | MTX |
| Tremorgen/ Penitrems | Penitrems E ^{763,764} | <i>Penicillium crustosum</i> | | MTX |
| Tremorgen/ Penitrems | Penitrems F ^{763,764} | <i>Penicillium crustosum</i> | | MTX |
| Tremorgen/ Penitrems | Penitremsone A | <i>Penicillium</i> sp. | | MTX |
| Tremorgen/Territrems | Territrems A (TRA) ^{25,766} | <i>Aspergillus terreus</i> , ⁷ <i>Penicillium echinulatum</i> ⁷ | | MTX, neuro, trem |
| Tremorgen/Territrems | Territrems B ²⁵ | <i>Aspergillus terreus</i> , ⁷ <i>Penicillium echinulatum</i> ⁷ | | MTX |
| Tremorgen/Territrems | Territrems B ^{25,766} | <i>Aspergillus terreus</i> , ⁷ <i>Penicillium echinulatum</i> ⁷ | Analogues: 767 | MTX |
| Tremorgen/Territrems | Territrems C ^{25,766} | <i>Aspergillus terreus</i> , ⁷ <i>Penicillium echinulatum</i> ⁷ | | MTX |
| Trichothecene | 12,13-Deoxytrichodermadiene | <i>Mycothecium verrucaria</i> ⁷⁶⁸ | | MTX |
| Trichothecene | 12,13-Epoxytrichothec-9-ene-8-one-3,15-diol | <i>Fusarium culmorum</i> | | MTX |
| Trichothecene | 12,13-Epoxytrichothec-9-ene (205) | <i>Trichothecium roseum</i> | | MTX |
| Trichothecene | 12,13-Epoxytrichothec-9-ene-3,15-diol | <i>Fusarium culmorum</i> | | MTX |
| Trichothecene | 12,13-Epoxytrichothec-9-ene-4 β ,8 α -diol (218) | <i>Trichothecium roseum</i> | | MTX |
| Trichothecene | 15-Acetoxy-scirpenol (Monoacetoxy-scirpenol, 4-Deacetylanguidin) (216) | <i>Fusarium roseum</i> | | MTX |
| Trichothecene | 15-Deacetyl-8-oxocalonecitrin | <i>Fusarium culmorum</i> | | MTX |
| Trichothecene | 15-Deacetylcalonecitrin (617) | <i>Calonectria nivalis</i> ⁷⁶⁹ | partial synthesis: 770 | MTX |
| Trichothecene | 15-Deacetylneosolaniol (222) (NT-2 toxin; 4 β -Acetoxy-12,13-epoxy-trichothec-9-ene-3 α ,8 α ,15-triol) | <i>Fusarium sporotrichioides</i> | | MTX |
| Trichothecene | 15-O-Acetyl-4-deoxynivalenol (15-A-DON) | <i>Fusarium</i> sp. | | MTX |
| Trichothecene | 2'-Dehydroverrucarin A | <i>Mycothecium verrucaria</i> | | MTX |
| Trichothecene | 3'-Hydroxy HT-2 toxin (TC-1; 3-Hydroxy-4 α ,15-diacetoxy-8 α -(isovaleryloxy)-12,13-epoxytrichothec-9-ene; 3'-OH-T-2) | <i>Fusarium heterosporum</i> , <i>F. oxysporum</i> ⁷⁷¹ | | MTX |
| Trichothecene | 3'-Hydroxy T-2 toxin | <i>Fusarium sporotrichiella</i> | partial synthesis: 792 | MTX |
| Trichothecene | 3-Acetyldeoxynivalenol (231) (3-Acetylvomitoxin, 3-A-DON) | <i>Fusarium culmorum</i> , <i>F. roseum</i> | partial synthesis: 772 | MTX |
| Trichothecene | 3-Acetylneosolaniol (620) (3-Ac-NEOS) | <i>Fusarium tumidum</i> | | MTX |
| Trichothecene | 3-Deacetylcalonecitrin | <i>Fusarium culmorum</i> | | MTX |
| Trichothecene | 4-Acetoxy-scirpendiol | <i>Fusarium roseum</i> , <i>Paecilomyces tenuipes</i> | | MTX |
| Trichothecene | 4-Deacetylneosolaniol (TMR-1; 15-Acetyl-T-2 tetraol; 15-Acetyltoxin T 2-tetraol; 15-Acetoxy-3 α ,4 β ,8 α -trihydroxy-12,13-epoxytrichothec-9-ene) | <i>Fusarium sporotrichioides</i> ⁷⁷³ | | Cyto |
| Trichothecene | 4 β ,15-Diacetoxy-12,13-epoxytrichothec-9-ene-3 α ,7 α ,8 α -triol ^d | <i>Fusarium</i> sp. | | MTX |
| Trichothecene | 4 β ,8 α ,15-Triacetoxy-12,13-epoxytrichothec-9-ene-3 α ,7 α -diol ^d | <i>Fusarium</i> sp. ⁷⁷⁴ | | MTX |
| Trichothecene | 7,8-Dihydroxycalonecitrin | <i>Fusarium culmorum</i> ⁷⁷⁵ | formal synthesis: 776 | MTX |
| Trichothecene | 7 α -Hydroxydiacetoxy-scirpenol (4,15-Diacetoxy-12,13-epoxy-9-trichothecene-3,7-diol) | <i>Fusarium lateritium</i> ⁷⁷⁷ | | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-------------------------|----------------------|
| Trichothecene | 7 α -Hydroxytrichodermol | <i>Myrothecium roridum</i> ⁷⁷⁸ | | MTX |
| Trichothecene | 7 β ,8 β -Epoxyroridin E | <i>Cylindrocarpon</i> sp. ⁷⁷⁹ | | MTX |
| Trichothecene | 7 β ,8 β -Epoxyroridin H | <i>Cylindrocarpon</i> sp. ⁷⁷⁹ | | MTX |
| Trichothecene | 7 β ,8 β , 2',3'-Diepoxyroridin H | <i>Cylindrocarpon</i> sp. ⁷⁷⁹ | | MTX |
| Trichothecene | 8-Acetoxy-T-2 tetraol (8-Acetyl-T-2-tetrol, TMR 2) | <i>Fusarium acuminatum</i> ⁷⁸⁰ | | MTX |
| Trichothecene | 8-Hydroxycalonectrin | <i>Fusarium culmorum</i> ⁷⁸¹ | | MTX |
| Trichothecene | 8 α -(3-Hydroxy-3-methylbutyryloxy)-12,13-epoxytrichothec-9-ene-3 α ,4 β ,15-triol (3'-Hydroxy T-2 triol; 3 α ,4 β ,15-Trihydroxy-8 α -(3-hydroxy-3-methylbutyryloxy)-12,13-epoxytrichothec-9-ene) | <i>Fusarium</i> sp. ⁷⁸² | | MTX |
| Trichothecene | Acetyl-T-2 toxin (225) (Ac-T-2 toxin, 3,4,15-Triacetoxy-8-(3-methylbutyryloxy)-12,13-epoxytrichothec-9-ene) | <i>Fusarium poae</i> ⁷⁸³ | | MTX |
| Trichothecene | Apotrichodiol (3 α ,13-Dihydroxyapotrichothecene) | <i>Fusarium</i> sp. ⁷⁸⁴ | | MTX |
| Trichothecene | Baccharin B4 (269) | <i>Baccharis megapotamica</i> | | no MTX, but related |
| Trichothecene | Baccharin B5 (268) | <i>Baccharis megapotamica</i> | 785 | no MTX, but related |
| Trichothecene | Calonectrin (211) | <i>Calonectria nivalis</i> , ⁷⁶⁹ <i>Fusarium culmorum</i> | 786; AB-ring model: 787 | MTX |
| Trichothecene | Crotocin (227) | <i>Cephalosporium crotocinigenum</i> , <i>Acremonium crotocinigenum</i> ^d , <i>Trichothecium roseum</i> | | MTX, nec |
| Trichothecene | Deepoxydiacetoxyscirpenol | <i>Fusarium graminearum</i> ⁷⁸⁸ | | MTX |
| Trichothecene | Deoxynivalenol (230) (Vomitoxin) | <i>Fusarium culmorum</i> , ^c <i>F. graminearum</i> , <i>F. verticillioides</i> ²³ | | MTX |
| Trichothecene | Diacetoxyscirpenol (217) (Anguidin, DAS, 4,15- Diacetoxyscirpenol) | <i>Fusarium equiseti</i> , ^c <i>F. scirpi</i> , <i>F. sporotrichioides</i> | 789 | MTX, cyto |
| Trichothecene | Di-O-acetylverrucarol (210) (4,15-Diacetylverrucarol) | <i>Myrothecium</i> sp. ⁷⁹⁰ | | MTX |
| Trichothecene | epi-Isororidin E | <i>Myrothecium verrucaria</i> | | MTX, cyto |
| Trichothecene | epi-roridin E | <i>Stachybotrys chartarum</i> | | MTX, cyto |
| Trichothecene | Fusarenone | <i>Fusarium crookwellense</i> | | MTX |
| Trichothecene | Fusarenone X (233) | <i>Fusarium nivale</i> ^e | | MTX |
| Trichothecene | Harzianum A | <i>Hypocrea</i> sp. F000527 ⁷⁹¹ | | MTX, cyto |
| Trichothecene | HT-2 toxin (223) | <i>Fusarium culmorum</i> , <i>F. sporotrichioides</i> | partial synthesis: 792 | MTX |
| Trichothecene | Iso T-2 toxin | <i>Fusarium sporotrichioides</i> | | MTX |
| Trichothecene | Isonesolaniol (221) (NT-1 toxin, 4 β ,8 α -Diacetoxy-12,13-epoxytrichothec-9-ene-3 α , 15-diol) | <i>Fusarium sporotrichioides</i> , <i>F. tricinctum</i> | partial synthesis: 793 | MTX |
| Trichothecene | Isororidin A | <i>Myrothecium verrucaria</i> | | MTX |
| Trichothecene | Isororidin E | <i>Stachybotrys chartarum</i> , <i>Cylindrocarpon</i> sp. | | MTX, cyto |
| Trichothecene | Iso-Satratoxin | <i>Stachybotrys</i> sp. | | MTX, prob cyto |
| Trichothecene | Iso-Satratoxin F | <i>Stachybotrys chartarum</i> | | MTX, prob cyto |
| Trichothecene | Iso-Satratoxin G | <i>Stachybotrys chartarum</i> | | MTX, prob cyto |
| Trichothecene | Iso-Satratoxin H | <i>Stachybotrys chartarum</i> | | MTX, cyto |
| Trichothecene | Iso-T-2 toxin | <i>Fusarium sporotrichioides</i> ⁷⁷¹ | | MTX |
| Trichothecene | Isotrichodermol (616) | <i>Fusarium venenatum</i> | | MTX |
| Trichothecene | Miophytocen A,B,C (A: 271) | <i>Myrothecium verrucaria</i> | | MTX |
| Trichothecene | Miotoxin A (270) (4-Hydroxyroridin E) | <i>Baccharis coridifolia</i> | | MTX |
| Trichothecene | Myrotoxin A (266) | <i>Trichoderma roseum</i> , ^c <i>Myrothecium verrucaria</i> | | MTX |
| Trichothecene | Myrotoxin B | <i>Trichoderma roseum</i> ^c | | MTX |
| Trichothecene | Neosolaniol (220) | <i>Myrothecium verrucaria</i> <i>Fusarium culmorum</i> , ^c <i>F. sporotrichioides</i> | partial synthesis: 792 | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^a |
|-----------------|-----------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|----------------------|
| Trichothecene | Neosolaniol monoacetate (8-Acetylneosolaniol ^d) | <i>Fusarium tricinctum</i> | | MTX |
| Trichothecene | Neosporol (296) ⁷⁹⁴ | <i>Fusarium sporotrichoides</i> | 800, 795 | MTX |
| Trichothecene | Nivalenol (232) | <i>Fusarium nivale</i> , ^c <i>F. crookwellense</i> <i>Fusarium nivale</i> | formal synthesis: 772, 796 | MTX |
| Trichothecene | Nivalenol 4,15-diacetate (Saubinin I) (234) | <i>Fusarium nivale</i> | | MTX |
| Trichothecene | Roridin A (263) (1'-Deoxy-1'-hydroethylverrucarin A) | <i>Myrothecium roridum</i> ^f | | MTX |
| Trichothecene | Roridin D (264) | <i>Myrothecium roridum</i> | | MTX |
| Trichothecene | Roridin E (262) (Satratoxin D) | <i>Stachybotrys chartarum</i> , <i>S. atra</i> , ⁷⁹⁷ <i>Myrothecium verrucaria</i> | 785 | MTX, cyto |
| Trichothecene | Roridin H, J, K acetate | <i>Myrothecium verrucaria</i> | | MTX, cyto |
| Trichothecene | Roridin L-2 | <i>Stachybotrys chartarum</i> | | MTX, cyto |
| Trichothecene | Sambucinol (297) (11,12-Epoxy-trichothec-9-en-3,13-diol) | <i>Fusarium graminearum</i> , <i>F. culmorum</i> | | MTX |
| Trichothecene | Satratoxin (Satratoxin A) ^d | <i>Stachybotrys atra</i> | | MTX |
| Trichothecene | Satratoxin B | <i>Stachybotrys atra</i> ^c | | MTX, prob cyto |
| Trichothecene | Satratoxin F | <i>Stachybotrys atra</i> ^{c,797} | | MTX, prob cyto |
| Trichothecene | Satratoxin G | <i>Stachybotrys chartarum</i> , <i>S. atra</i> ⁷⁹⁷ | | MTX, prob cyto |
| Trichothecene | Satratoxin H (265) ⁷⁹⁸ | <i>Stachybotrys atra</i> , ^{c,797} <i>S. chartarum</i> | | MTX, cyto |
| Trichothecene | Scirpentriol (215) (SCIRP) | <i>Fusarium roseum</i> ^c | | cyto |
| Trichothecene | Sporol (295) | <i>Fusarium sporotrichioides</i> | 799, 800 | MTX |
| Trichothecene | Sporotrichiol (226) | <i>Fusarium trichiodes</i> , ^c <i>F. sporotrichioides</i> | partial synthesis: 792 | MTX |
| Trichothecene | Stachybotryotoxins see trichothecenes, roridin E, verrucarol | <i>Stachybotrys</i> sp. | 801 | MTX |
| Trichothecene | T-2 tetraol (219) | <i>Fusarium</i> sp. | 802 | MTX |
| Trichothecene | T-2 tetraol tetraacetate (T-2-4ol-4Ac) | <i>Fusarium</i> sp. | | MTX |
| Trichothecene | T-2 toxin (224) (Insariotoxin, Fusariotoxin T 2) | <i>Fusarium tricinctum</i> ^c , <i>F. sporotrichiella</i> ²³ | partial synthesis: 792 | MTX |
| Trichothecene | T-2 triol | <i>Fusarium sporotrichiella</i> | | MTX |
| Trichothecene | Trichodermadiene (208) | <i>Myrothecium verrucaria</i> ^c | | MTX |
| Trichothecene | Trichodermadienediol A, B (209a , 209b) | <i>Myrothecium roridum</i> | | MTX |
| Trichothecene | Trichodermin (207) (12,13-Epoxy-Trichothec-9-en-4-ol acetate) | <i>Trichoderma viride</i> , ^{c,7} <i>T. polysporum</i> , <i>T. sporulosum</i> , ²³ <i>memmoniella echinata</i> , ²⁸⁵ <i>Stachybotrys cylindrospora</i> , <i>S. chartarum</i> | | MTX, biot |
| Trichothecene | Trichodermol (206) (Roridin C) | <i>Myrothecium roridum</i> , ^c <i>Trichoderma polysporum</i> , <i>T. sporulosum</i> , ²³ <i>Memmoniella echinata</i> , ²⁸⁵ <i>Stachybotrys cylindrospora</i> , <i>S. chartarum</i> | 803 | MTX |
| Trichothecene | Trichothecin (229) ⁸⁰⁴ | <i>Trichothecium roseum</i> ²³ | 805 | MTX, biot |
| Trichothecene | Trichothecolone (228) (12,13-Epoxy-4hydroxy-trichothec-9-en-8-one) | <i>Trichothecium roseum</i> ^d | | Cyto |
| Trichothecene | Trichoverrin A (213a) | <i>Stachybotrys chartarum</i> , <i>Myrothecium verrucaria</i> | | MTX, w cyto |
| Trichothecene | Trichoverrin B (213a) | <i>Stachybotrys chartarum</i> , <i>Myrothecium verrucaria</i> | 806 | MTX, w cyto |
| Trichothecene | Trichoverrin C | <i>Myrothecium verrucaria</i> | | MTX |
| Trichothecene | Trichoverrol A (212a) | <i>Stachybotrys atra</i> , <i>S. chartarum</i> ⁸⁰⁷ | | MTX |
| Trichothecene | Trichoverrol B (212b) | <i>Stachybotrys atra</i> , <i>S. Chartarum</i> ⁸⁰⁷ | 807 | MTX |
| Trichothecene | Verrucarin A (6) | <i>Mycothecium verrucaria</i> | 808, 809 | MTX, cyto |
| Trichothecene | Verrucarin B (261) | <i>Mycothecium verrucaria</i> | | MTX, cyto |
| Trichothecene | Verrucarin J (260) (Satratoxin C) | <i>Stachybotrys atra</i> , ⁷⁹⁷ <i>S. Chartarum</i> | 810 | MTX; Cyto |
| Trichothecene | Verrucarin K | <i>Mycothecium verrucaria</i> ⁸¹¹ | | MTX |

Table 3. Continued

| mycotoxin class | name (stereochemistry) (alternative name) | producing fungus (example) | ref for synthesis | comment ^d |
|----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|---------------------------|----------------------|
| Trichothecene | Verrucarol L | <i>Mycrothecium verrucaria</i> | | MTX |
| Trichothecene | Verrucarol M | <i>Myrothecium verrucaria</i> ⁸¹² | | MTX |
| Trichothecene | Verrucarol (214) | <i>Stachybotrys atra</i> ^d | rac: 813–815; (–): 816 | MTX |
| Trichothecene | Vertisporin (267) | <i>Verticimonosporium diffractum</i> ^{c,817} | | MTX |
| Tropolone derivative | Puberulic acid ⁸¹⁸ | <i>Penicillium aurantiogriseum</i> , <i>P. aurantiocandidum</i> ⁷ | 819 | MTX |
| Tropolone derivative | Puberulonic acid | <i>Penicillium aurantio-virens</i> ²¹ | 820, 821 | MTX |
| Versicolorin | 6,8- <i>O</i> -Dimethylversicolorin A | <i>Aspergillus versicolor</i> ^{c,822} | | MTX, gen |
| Versicolorin | 6,8- <i>O</i> -Dimethylversicolorin B | <i>Aspergillus</i> sp. ^d | | MTX, gen |
| Versicolorin | 6-Deoxyversicolorin A | <i>Aspergillus versicolor</i> ^{c,823} | | MTX |
| Versicolorin | 8-Deoxy- <i>O</i> -methylversicolorin A | <i>Aspergillus ustus</i> | | MTX |
| Versicolorin | Aversin (Versicolorin B dimethylether, 2,3,3a,12a-tetrahydro-4-hydroxy-6,8-dimethoxyanthra[2,3- <i>b</i>]furo[3,2- <i>d</i>]furan-5,10-dione) | <i>Aspergillus versicolor</i> , <i>A. ustus</i> ⁸²⁴ | | MTX |
| Versicolorin | Tri- <i>O</i> -methylversicolorin B (<i>O</i> -methylaversin) | <i>Aspergillus versicolor</i> | 825 | MTX |
| Versicolorin | Versicolorin A (597) (2,3-Bisfurano-1,6,8-trihydroxy-anthraquinone) ⁸²⁶ | <i>Aspergillus versicolor</i> ^c , <i>A. parasiticus</i> , <i>A. flavus</i> | | MTX, mut, carc |
| Versicolorin | Versicolorin B (64) (–) (2,3-Bistetrahydrofurano-1,6,8-trihydroxyanthraquinone) | <i>Aspergillus versicolor</i> ^{c,827} | | MTX |
| Versicolorin | Versicolorin C (±) (2,3-Bistetrahydrofurano-1,6,8-trihydroxyanthraquinone) ⁸²⁸ | <i>Aspergillus versicolor</i> ^c , <i>A. parasiticus</i> , <i>A. flavus</i> | 829 | MTX |
| Versicolorin | Versicolorin D | <i>Aspergillus versicolor</i> ^c | | MTX |
| Xanthone | 7-Chloro-2-(3-furyl)-1,3,8-trimethoxyxanthone | <i>Aspergillus ustus</i> ⁸³⁰ | | MTX |
| Xanthone | Ascherxanthone A | <i>Aschersonia</i> sp. BCC 8401 ⁸³¹ | | Cyto |
| Xanthone | Blennolide A–E ⁸⁴⁰ | <i>Blennoria</i> sp. | 832 | MTX |
| Xanthone | Dicerandrol A, B, C | <i>Phomopsis longicolla</i> | | Cyto |
| Xanthone | Diversonol (426) | <i>Penicillium diversum</i> ⁸³³ | 834 | MTX |
| Xanthone | Lichexanthone | <i>Penicillium patulum</i> , <i>P. diversum</i> | 835 | MTX |
| Xanthone | Ravenelin (581) | <i>Helminthosporium ravenelii</i> ⁸³⁶ | | MTX |
| Xanthone | Sterigmatin | <i>Aspergillus versicolor</i> | | MTX |
| Xanthone | Varietoxanthone A, C | <i>Emericella</i> sp. ^d , <i>Aspergillus nidulans</i> ⁸³⁷ | | MTX |
| Xanthone | Varietoxanthone B (Emericellin) | <i>Emericella</i> sp. ^d , <i>Aspergillus nidulans</i> ^{837,838} | | MTX |
| Xanthone | Vinaxanthone | <i>Penicillium vinceum</i> | 839 | MTX |
| Xanthone | α,β-Diversonolic acid ⁸⁴⁰ | <i>Penicillium diversum</i> | 832b | MTX |
| Xanthone dimer | Phomoxanthone B (427) (–) | <i>Phomopsis</i> sp. | | MTX |
| Xanthone dimer | Secalonic acid A (Ergochrome AA) | <i>Pyrenochaeta terrestris</i> , ¹⁰⁷ <i>Aspergillus aculeatus</i> ¹⁰⁷ | | MTX |
| Xanthone dimer | Secalonic acid B (SAB, Ergochrome BB) | <i>Aspergillus aculeatus</i> | | MTX |
| Xanthone dimer | Secalonic acid C (SAC, Ergochrome AB) | <i>Aspergillus aculeatus</i> | | MTX |
| Xanthone dimer | Secalonic acid D (10) (Ergochrome EE, <i>ent</i> -Secalonic acid A, SAD) | <i>Penicillium oxalicum</i> ^{c,7} , <i>Gliocladium</i> sp. ^b | | MTX, cyto |
| Xanthone dimer | Secalonic acid E | <i>Pyrenochaeta terrestris</i> , ¹⁰⁷ <i>Aspergillus aculeatus</i> ¹⁰⁷ | | MTX |
| Xanthone dimer | Secalonic acid F (SAF) | <i>Aspergillus japonicus</i> , <i>Penicillium oxalicum</i> ^{c7} | | MTX |
| Xanthone dimer | Secalonic acid G | <i>Pyrenochaeta terrestris</i> , ¹⁰⁷ <i>Aspergillus aculeatus</i> ¹⁰⁷ | | MTX |

^a **MTX**: important mycotoxin; **MTX**: less abundant/important mycotoxin; **MTX**: mycotoxin status questionable; **bact**: antibacterial; **biot**: antibiotic; **carc**: carcinogenic; **cyto**: cytotoxic; **drug**: used as a drug; **feed**: antifeedant; **fung**: antifungal; **gen**: genotoxic; **hep**: hepatotoxic; **herb**: herbicide; **immun**: immunosuppressive; **insec**: insecticidal; **kin**: kinase inhibitor; **leish**: antileishmanial; **micro**: antimicrobial; **mut**: mutagenic; **nec**: necrotic; **neph**: nephrotoxic; **neuron**: neurotoxic; **plasm**: antiplasmodial; **prot**: antiprozoic; **ter**: teratogen; **trem**: tremorgen; **tumor**: antitumor; **vir**: antiviral; **mod**: moderate; **str**: strong; **w**: weak; **prob**: probably. ^b Marine origin. ^c See ref 8. ^d Uncertain/inconsistent data. ^e No toxic effects, but putative biogenic precursor.

Table 4. Human Diseases Provoked by Mycotoxins⁸⁴⁷

| disease | substrate | principal fungus | toxin |
|---------------------------------------|-------------------------------------------------------------|---------------------------------------------------|-----------------------------|
| Akakabi-byo | wheat, barley, oats, rice | <i>Fusarium</i> spp. | <i>Fusarium</i> metabolites |
| Alimentary toxic aleukia | cereal grains (toxic bread) | <i>Fusarium</i> spp. | |
| Balkan nephropathy | cereal grains | <i>Penicillium</i> | |
| Cardiac beriberi | rice | <i>Aspergillus</i> spp., <i>Penicillium</i> spp. | |
| Celery harvester's disease | celery (pink rot) | <i>Sclerotinia</i> | |
| Dendrochiotoxicosis | fodder (skin contact, inhaled fodder particles) | <i>Dendrochium toxicum</i> | |
| Ergotism | rye, cereal grains | <i>Claviceps purpurea</i> | Ergot alkaloids |
| Esophageal tumors | corn heterocycles | <i>Fusarium moniliforme</i> | |
| Hepatocarcinome (acute aflatoxicosis) | cereal grains, peanuts | <i>Aspergillus flavus</i> , <i>A. parasiticus</i> | |
| Kashin Beck disease (Urov disease) | cereal grains | <i>Fusarium</i> | <i>Fusarium</i> metabolites |
| Kwashiorkor | cereal grains | <i>Aspergillus flavus</i> , <i>A. parasiticus</i> | Aflatoxins |
| Onyalai | millet | <i>Phoma sorghina</i> , <i>Fusarium</i> sp. | <i>Fusarium</i> metabolites |
| Reye's syndrome | cereal grains | <i>Aspergillus</i> | |
| Stachybotryotoxicosis | rye, cereal grains, fodder (skin contact, inhaled rye dust) | <i>Stachybotrys atra</i> | Trichothecenes |
| Kodua poisoning | | <i>Aspergillus</i> sp.; <i>Penicillium</i> sp. | Cyclopiazonic acid |

2.1. Aflatoxins

The most carcinogenic substances known to date, the aflatoxins, also gained much interest among organic chemists⁸⁶⁸ since the elucidation of their structure by Büchi and co-workers in 1963.⁸⁶⁹ Even though numerous syntheses of racemic aflatoxins were reported in the following years,^{28–31,33} it took 40 years for the first enantioselective total synthesis of (–)-aflatoxin B₁ (**1**) and B_{2a} (**17**) to be published by Trost et al.³² Their approach resembles in part (construction of the DE ring system) the first total synthesis of (±)-aflatoxin by Büchi et al.²⁸ (Scheme 1).

For the key intermediate coumarin **25**, there exist various syntheses, of which the Wittig reaction route of the original 1966's publication is presented here. After oxidation to the corresponding aldehyde **26**, the ABC ring system was formed by reduction to the lactone **27**, which was cleaved again under the conditions of the Pechmann condensation with β-oxoadipate **29** upon formation of the D ring. The resulting methoxy acetal **30** with *trans*-oriented substituents exhibited the right stereochemistry for the lactonization to carboxylic acid **31** with *cis*-fused B and C rings. Friedel-Crafts acylation and reduction of the lactone gave aflatoxin B_{2a} (**17**), which, in 1966, had not yet been identified as a naturally occurring mycotoxin. Acetylation and pyrolysis resulted in racemic (±)-aflatoxin B₁ (**1**).

In 2003 Trost et al. presented the first enantioselective total synthesis of aflatoxin B₁ (**1**).^{32,870} Their strategy was based on a palladium-catalyzed dynamic kinetic asymmetric transformation (DYKAT, see Scheme 2) of γ-acyloxybutenolide

Scheme 1. First Total Synthesis of Racemic Aflatoxin B₁ (1**) by Büchi et al.²⁸**

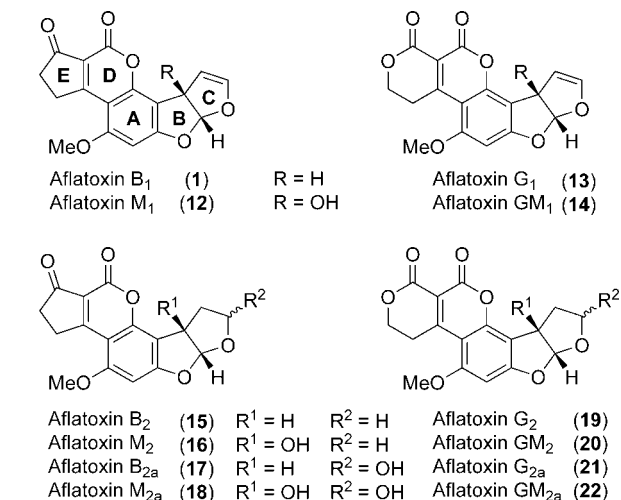
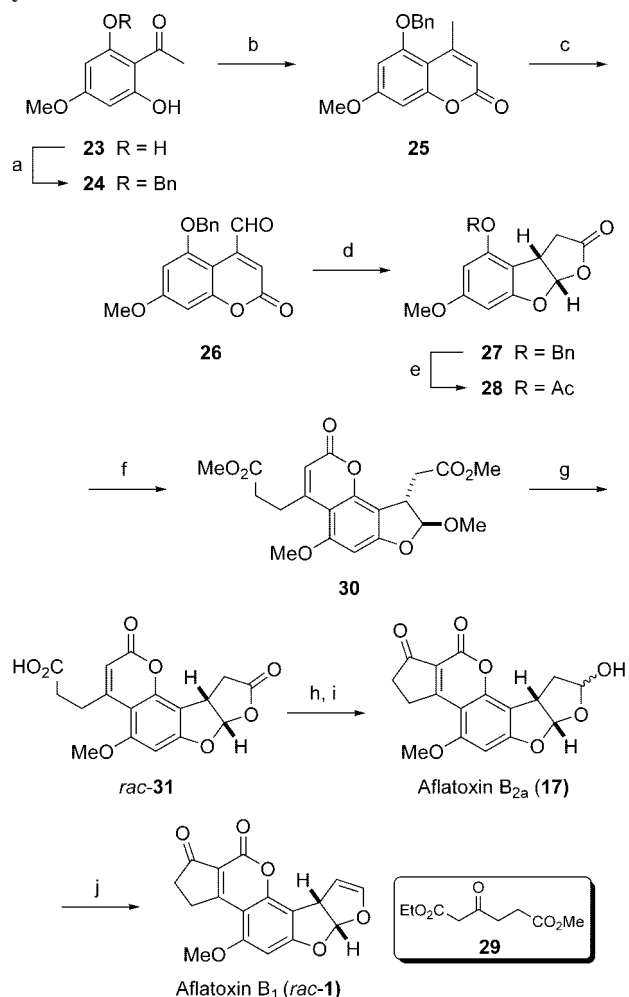
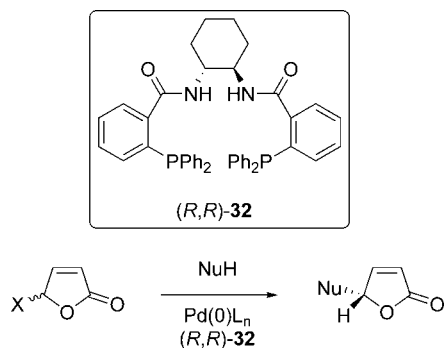
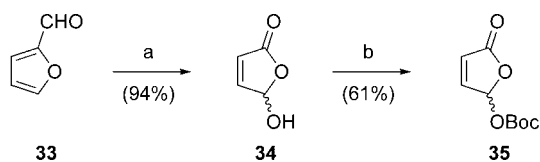


Figure 2. Aflatoxins.

Scheme 2. Dynamic Kinetic Asymmetric Transformation (DYKAT) of γ -Acetoxybutenolides³²

Scheme 3. Preparation of the Key Intermediate for DYKAT by Trost et al.³²


Reagents and conditions: (a) $^1\text{O}_2$, hv, rose bengal, MeOH. (b) Boc₂O, py, THF.

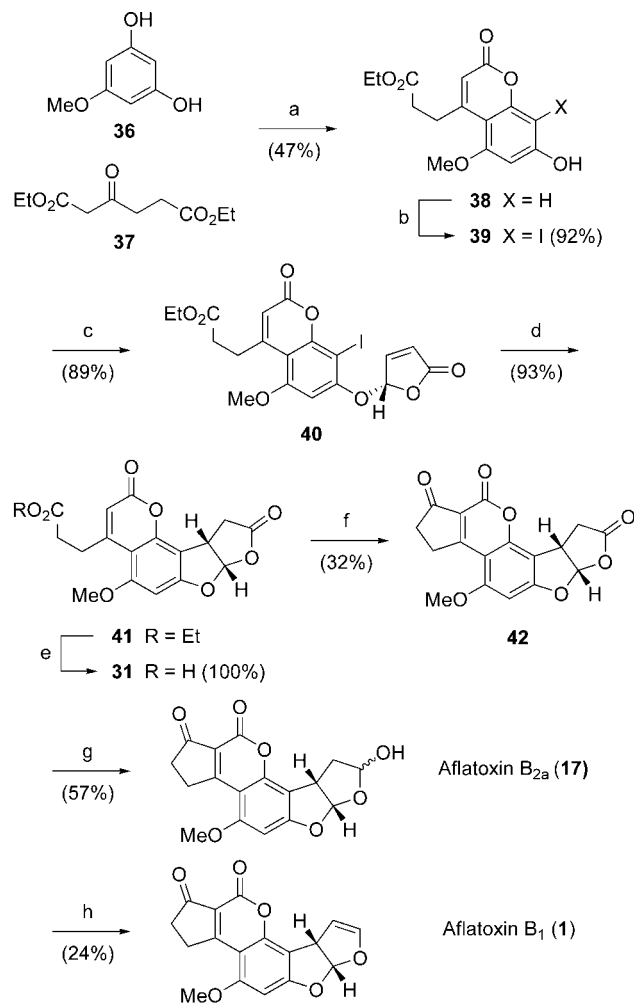
35. This intermediate was prepared from furfural (**33**) in two steps (Scheme 3).

The DYKAT was performed after the assembly of the AD ring system by Pechmann condensation of the phloroglucinol monomethyl ether (**36**) with β -oxoadipate **37** (in analogy to precedent racemic syntheses)^{28,33} and iodination to intermediate **39**. The intramolecular reductive Heck reaction produced tetracyclic coumarin **41** with an enantiomeric excess of >95%. Conversion to aflatoxin B₁ (**1**) followed the Büchi route²⁸ with modified protocols for the Friedel–Crafts acylation to **42** and the reduction producing aflatoxin B_{2a} (**17**). The complete synthesis comprised 9 consecutive steps (Scheme 4).

A very short total synthesis of aflatoxin B₂ (**15**) was published by Corey and co-workers in 2005.³⁴ The 8-step approach comprises an asymmetric [3 + 2]-cycloaddition using chiral oxazaborolidinium catalyst **45** for the enantioselective formation of the ABC ring system (Scheme 5). A similar quinone approach for intermediate **49** had previously been reported by Noland et al.⁸⁷¹

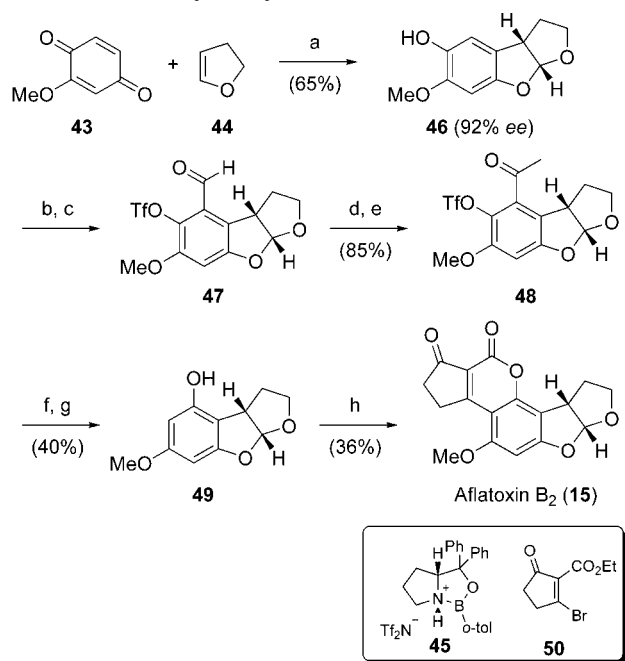
Starting from 2-methoxy-1,4-benzoquinone (**43**) and 2,3-dihydrofuran (**44**), cycloadduct **46** was obtained with 92% ee (GC), nearly enantiomerically pure after recrystallization. The next six steps involved a relocation of the hydroxy group: orthoformylation and triflate ester formation followed by Grignard addition and Dess–Martin oxidation resulted in the corresponding methyl ketone **48**. The acetate group was replaced by the hydroxy group through Baeyer–Villiger oxidation and saponification; the triflate was removed by reduction with Raney nickel. Condensation of intermediate **49** with β -bromo- α,β -enone **50** in the presence of zinc carbonate directly gave rise to aflatoxin B₂ (**15**).

This condensation was already elaborated by Büchi and Weinreb during their total syntheses of aflatoxins M₁ (**12**), B₁ (**1**), and G₁ (**13**) in 1971²⁹ and is outlined in Scheme 6. The advantage was the attachment of the complete ring E, which enables straightforward variation between the five-membered cyclic ketone for aflatoxins of the B- and M-type and the six-membered lactone for aflatoxins of the G-type (see also Figure 2).

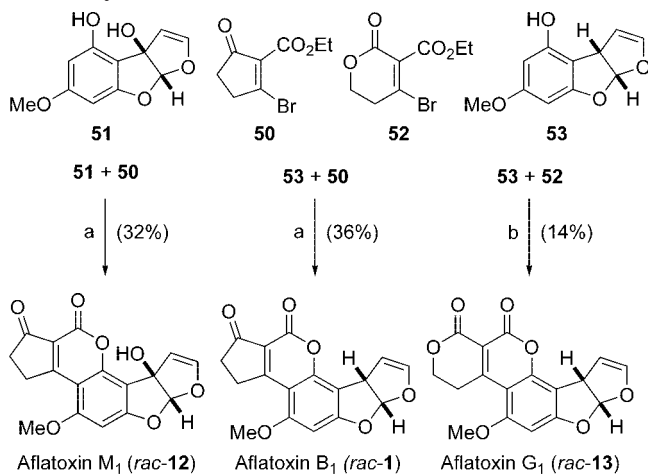
Scheme 4. Enantioselective Total Synthesis of Aflatoxins B_{2a} and B₁ by Trost et al.³²


Reagents and conditions: (a) HCl, EtOH. (b) ICl, CH₂Cl₂, rt. (c) **35**, 2.5% Pd₂dba₃·CHCl₃, 7.5% (R,R)-**32**, 30% Bu₄NCl, 0.1 M CH₂Cl₂, rt. (d) 10% (CH₃CN)₂PdCl₂, NEt₃, HCO₂H, DMF, 50 °C. (e) HOAc, HCl, H₂O. (f) Sc(OTf)₃, LiClO₄. (g) DIBAL-H (2:1 β : α). (h) (1) Ac₂O, AcOH; (2) 240 °C.

The syntheses of the building blocks **50** and **53** were described (in part) in previous publications.^{28b,872} Summarized here is the total synthesis of aflatoxin M₁ (**12**, milk toxin) starting with coumaranone **54** (Scheme 7). After the successive introduction of the protective groups, bromination with phenyltrimethylammonium perbromide and conversion into the benzyl ether **57**, ring C was built up through the Grignard addition of allylmagnesium bromide with subsequent Lemieux–Johnson oxidation to form the epimeric aldehydes **58**, which after step-by-step hydrogenolysis were cyclized to diacetate **60**. Key intermediate vinyl ether **51** was formed by flash pyrolysis and saponification of the acetate. Pechmann condensation with 2-carbethoxycyclopentane-1,3-dione was not possible due to the sensitivity of **51** to acidic catalysts. Thus, the more nucleophilic bromide **50** was prepared from the corresponding enol and oxalyl bromide, and it could be condensed with phenol **51** under mild conditions with either zinc carbonate or magnesium carbonate. In the synthesis of aflatoxin G₁ (**13**), the analogous bromide **52** turned out to be much less reactive, but the addition of anhydrous lithium iodide delivered improved yields, presumably due to in situ formation of the corresponding vinyl iodide.

Scheme 5. Short, Enantioselective Total Synthesis of Aflatoxin B₂ (15) by Corey et al.³⁴


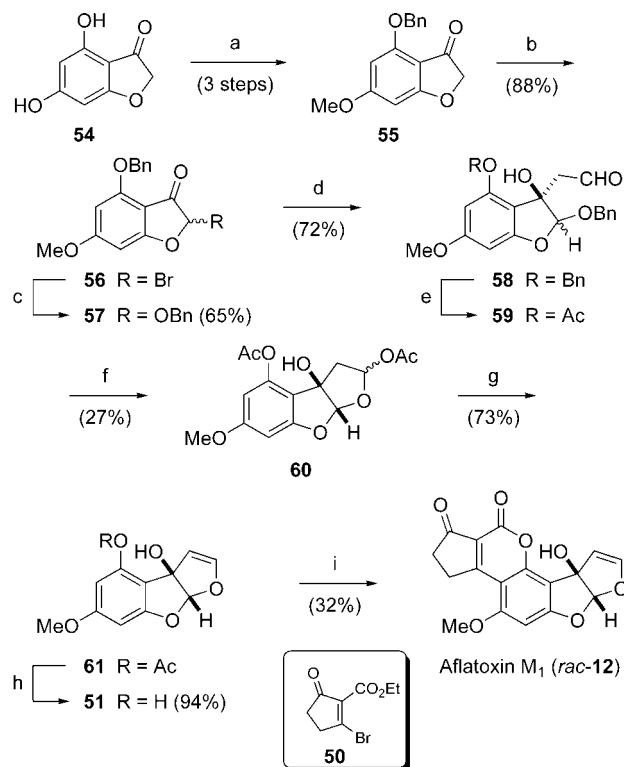
Reagents and conditions: (a) **45**, CH₃CN/CH₂Cl₂ 1:1, -78 °C → rt, 7 h. (b) (CH₂)₆N₄ (HMT), AcOH, 110 °C, 48 h, (ca. 40%). (c) Tf₂O, py, 0 °C, 2 h, (ca. 80%). (d) MeMgBr, THF, -20 °C, 2 h. (e) Dess-Martin, CH₂Cl₂, 23 °C, 3 h. (f) CF₃CO₃H, CH₂Cl₂, 48 h. (g) Raney Ni, MeOH, H₂, 4 h. (h) **50**, ZnCO₃, CH₂Cl₂, 23 °C, 24 h

Scheme 6. Modular Synthesis of Racemic Aflatoxins M₁, B₁, and G₁ by Büchi et al.²⁹


Reagents and conditions: (a) NaHCO₃, ZnCO₃, CH₂Cl₂. (b) ZnCO₃, Lil, CH₂Cl₂.

In summary, most syntheses have this common approach: starting from the phloroglucinol core, the tetrahydro- or dihydrofuro[2,3-*b*]benzofuran ring system (ABC tricycle) is formed and the annulation of the D and E rings is effected through a modified Pechmann condensation.

A large number of important contributions to synthetic mycological chemistry were made by Roberts and co-workers, who entered the aflatoxin field with their work on the *Aspergillus* metabolite sterigmatocystin (**62**),⁸⁷³ a biosynthetic precursor to the aflatoxins. Roberts et al. published several syntheses of toxic metabolites (Figure 3), including the first total synthesis of (±)-aflatoxin B₂ (*rac*-**15**),³³ a synthesis of the coumarinolactone system of aflatoxin G₂ (**19**),⁸⁷⁴ and the first total syntheses of (±)-*O*-methylsterig-

Scheme 7. Total Synthesis of Racemic Aflatoxin M₁ (12) by Büchi et al.²⁹


Reagents and conditions: (a) (1) Me₂SO₄, K₂CO₃, DME, reflux (79%); (2) 2 equiv. AlCl₃, CH₂Cl₂, reflux (64%); (3) BnBr, K₂CO₃, DME/DMF, reflux (74%). (b) Me₃PhNBr₃, THF. (c) BnOH, CaCO₃. (d) AllylMgBr, THF/Et₂O, 0 °C; then OsO₄, NaIO₄, dioxane/H₂O 2:1, NaHCO₃, 7:1 epimeric mixture. (e) H₂, Pd/C, Ac₂O, NaOAc, benzene. (f) (1) H₂, Pd/C, EtOAc; (2) Ac₂O, py, -70 °C → -30 °C. (g) flash pyrolysis 450 °C. (h) NaHCO₃, MeOH/H₂O 1:1. (i) **50**, NaHCO₃, ZnCO₃, CH₂Cl₂.

matocystin (**63**)⁴⁰ and (±)-tri-*O*-methylversicolorin B (**65**, (±)-*O*-methylaversin).⁸²⁵

For the synthesis of (±)-*O*-methylsterigmatocystin (**63**), the key step was presumed to be a modified Ullmann condensation of the known^{28b} lactone **66** and bromo ester **67**, as in preliminary studies on (±)-dihydro-*O*-methylsterigmatocystin. However, under basic conditions, the resulting Büchi lactone (**66**) was too labile, so that an alternative route using the ring-opened compound **68** was developed (Scheme 8).⁴⁰

The Ullmann-type diaryl ether formation of **69** proceeded well, and after several ring-closing reactions, namely lac-

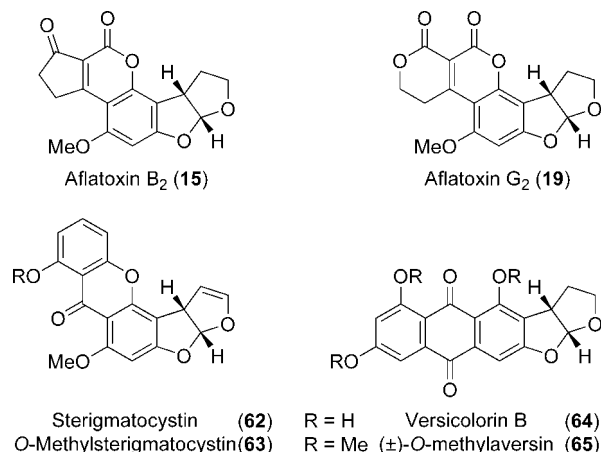
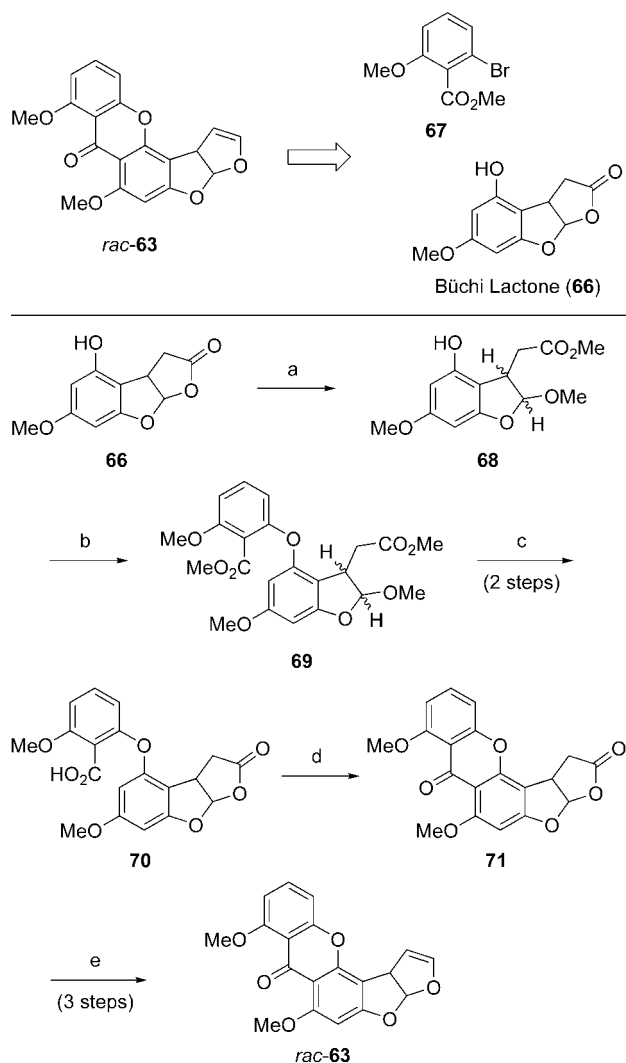


Figure 3. *Aspergillus* metabolites synthesized by Roberts et al.

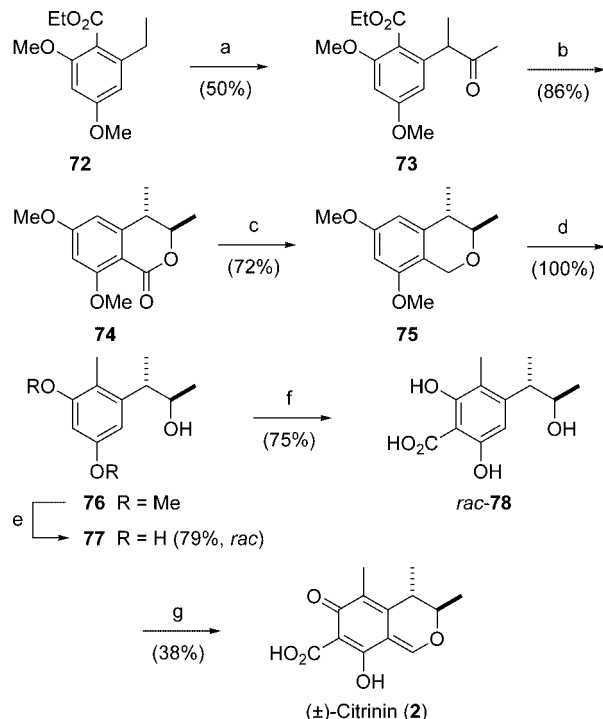
Scheme 8. Total Synthesis of Racemic *O*-Methylsterigmatocystin (63**) by Roberts et al.⁴¹**

tonization and acylation, precursor **71** was obtained. The vinyl ether system of sterigmatocystin (**62**) was introduced following the protocol reported by Büchi et al.²⁸

2.2. Citrinin

The fungal metabolite citrinin (**2**) was first obtained from *Penicillium citrinum*.^{875,876} Citrinin (**2**) displays antibiotic activity against Gram-positive bacteria⁸⁷⁷ and has been described as a promising insecticide.⁸⁷⁸ However, because of its high toxicity, it has not been applied as a drug.

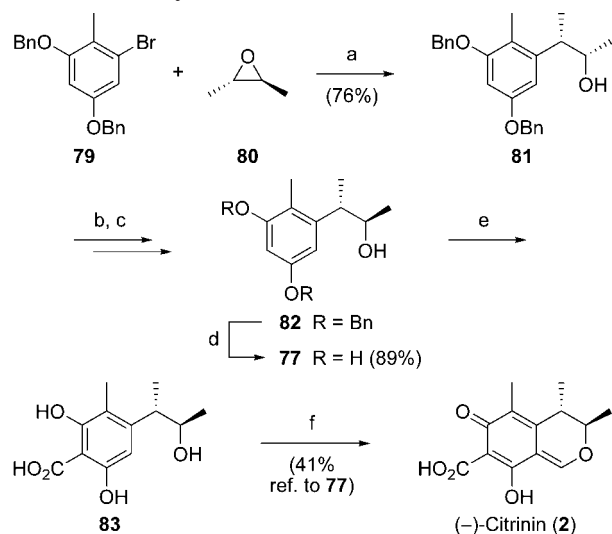
The structure was elucidated in the groups of Whalley and Cram at the end of the 1940s by extensive degradation studies.^{879,880} The absolute configuration of the two methyl groups in natural (–)-citrinin (**2**) was shown to be (3*R*,4*S*) by chemical correlation (Figure 1).⁸⁸¹ Starting from the degradation product **77**, several partial syntheses of optically active and racemic citrinin (**2**) have been described,^{195,197} involving a subsequent carboxylation/formylation strategy. Warren et al. extended this method to other aldehydes and ketones and received a series of analogues for the establishment of structure–activity relationships.⁸⁸²

Scheme 9. First Diastereoselective Total Synthesis of (±)-Citrinin (2**) by Barber and Staunton¹⁹⁸**

A stereoselective synthesis of racemic (±)-citrinin (**2**) using toluate anion chemistry was published by Staunton et al. in 1986¹⁹⁸ and could be expanded to an asymmetric total synthesis of the unnatural enantiomer (+)-citrinin.¹⁹⁹ Acetylation of ethyl 2-ethyl-4,6-dimethoxybenzoate (**72**) furnished ketone **73**, which could be reduced to the *threo*-diastereoisomer of lactone **74**. Successive reduction of the carbonyl group with DIBAL and hydrogenolysis with a palladium–charcoal catalyst installed the methylene group at the aryl part. After ether cleavage using boron tribromide, the diphenol **77** was obtained, which was identical to the racemic degradation product generally referred to as phenol B. The further conversion into (±)-citrinin (**2**) required carboxylation, formylation, and cyclization and was accomplished following previous partial syntheses. Carboxylation with carbon dioxide and potassium hydrogen carbonate^{194–196} yielded the acid **78**, which was then formylated using ethyl orthoformate⁸⁸³ to give an aldehyde that cyclized in situ to the required quinomethide structure **2** (Scheme 9).

Subsequent studies seeking the enantioselective synthesis of citrinin (**2**) involved the generation of the *ortho*-toluate carbanion of **72** with a chiral lithium amide base.¹⁹⁹ It underwent addition to acetaldehyde with asymmetric induction at the nucleophilic center to produce two diastereomeric lactones (dr 3:1), however, with enantioselectivities of only ~70% ee. The mixture could be converted into the desired *threo*-lactone, but unfortunately it resulted in an unnatural enantiomer.

The first enantioselective total synthesis of (–)-citrinin (**2**) was not achieved until Rödel and Gerlach announced their Grignard approach in 1995 (Scheme 10).²⁰⁰ The key step was a reaction of enantiomerically pure oxirane **80** with the corresponding magnesium organyl of **79** in the presence of

Scheme 10. First Enantioselective Total Synthesis of (–)-Citrinin (2) by Rödel and Gerlach²⁰⁰


Reagents and conditions: (a) (1) Mg, THF; (2) (S,S)-**80**, cat. (MgBr₂, COD CuCl). (b) Ph₃P, HCO₂H, toluene; then DEAD (59%). (c) KOH, MeOH/H₂O/THF, reflux (99%). (d) H₂, Pd/C, AcOH/MeOH. (e) KHCO₃, CO₂, glycerol. (f) HC(OEt)₃, HCl.

1,5-cyclooctadienecopper(I) chloride as the catalyst. Stereo-selective ring-opening yielded (2*S*,3*S*)-**81** with the undesired *erythro* configuration. The *cis*-dimethyloxirane would lead directly to the *threo* product; however, as a *meso*-compound, it gave the racemic alcohol. The indirect route thus involved a Mitsunobu reaction that, after hydrolysis, yielded the (2*R*,3*S*)-alcohol **82** (>99% de) with the configuration of natural (–)-citrinin (**2**). The remaining steps toward the mycotoxin required debenzoylation to give **77** (so-called “phenol A”) and the known carboxylation–formylation–ring-closure sequence.

The contributions of Whalley et al. in the field of citrinin and other mycotoxins are rereported in several publications by the Royal Chemical Society with the series title “The Chemistry of Fungi”.^{195,196,880,884}

2.3. Ergot Alkaloids

The ergot alkaloids are isolated from the dried sclerotium of the fungus *Claviceps purpurea* and are classified as indole alkaloids derived from a tetracyclic ergoline ring system (**84**, Figure 4). These include lysergic acid (**85**), lysergic acid amide (precursor for the illegal narcotic, lysergic acid diethylamide (**86**), commonly known as LSD), and ergopeptines such as ergotamine (**8**). These alkaloids have attracted the attention of synthetic chemists for decades, and the total synthesis of relevant peptide derivatives has already been reviewed in several papers.^{377,885} For this reason, we will not focus our attention on these derivatives but encourage an examination of the references cited below.³⁷³

2.4. Fumonisin

Species of the mold fungus *Fusarium* occur in almost every environment, largely due to their ability to live without oxygen; they are the most important pathogens of corn and other grains.⁸⁸⁶ *Fusarium* spp. produce several mycotoxins, among them sesquiterpenols—the trichothecenes (see section 2.7)—or the potent mutagen Fusarin C (**87**, Figure 5), which is surprisingly not involved in the carcinogenicity of the fungus, as Vlegaar et al. reported in 1988.⁸⁸⁷ However, they

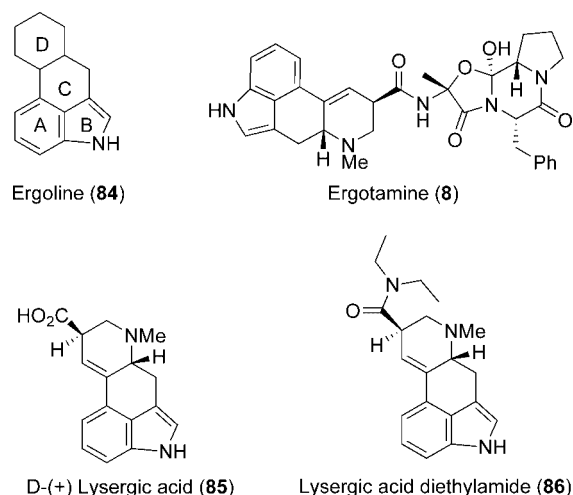


Figure 4. Representative ergot alkaloids.

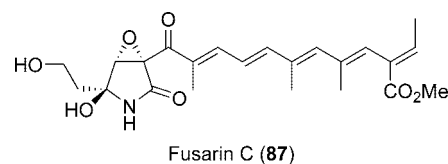


Figure 5. Fusarin C (**87**).

discovered that a novel class of mycotoxins, the fumonisins, are structurally similar to the sphingoid backbone of the sphingolipids.⁸⁸⁸ The consumption of contaminated food has been directly correlated with human esophageal cancer.⁸⁸⁹

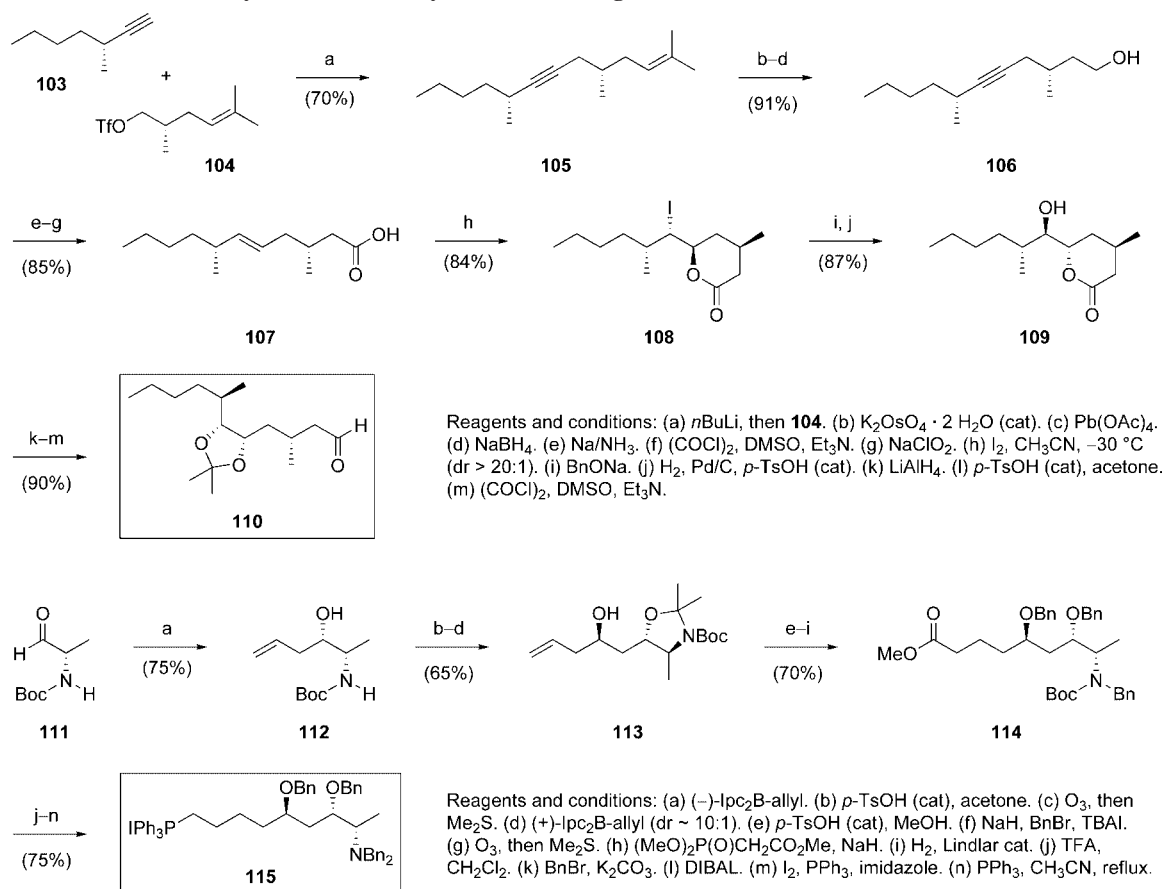
Fumonisin of the B-series (FB_{1–3}) have the most widespread occurrence (Table 5). Their *N*-acetylated congeners (A-series) and the analogues FC_{1–4}, which lack the terminal methyl group, contribute to less than 5% of the total fumonisin abundance. In 1996, Musser et al. reported about a new series, the fumonisins P_{1–3}, bearing a 3-hydroxypyridinium moiety at C-2 instead of at the amine, which occur at levels up to 30% of FB₁.⁸⁹⁰

Since the first characterization of the fumonisins in 1988, many groups, namely, those of Kishi, ApSimon, Hoyer/Shier,

Table 5. Fumonisin

| No. | R ¹ | R ² | R ³ | R ⁴ | trivial name |
|------------|----------------|----------------|-----------------|-------------------|--------------------------|
| 88 | OH | OH | CH ₃ | NHAc | Fumonisin A ₁ |
| 89 | H | OH | CH ₃ | NHAc | Fumonisin A ₂ |
| 90 | OH | H | CH ₃ | NHAc | Fumonisin A ₃ |
| 91 | H | H | CH ₃ | NHAc | Fumonisin A ₄ |
| 92 | OH | OH | CH ₃ | NH ₂ | Fumonisin B ₁ |
| 5 | H | OH | CH ₃ | NH ₂ | Fumonisin B ₂ |
| 93 | OH | H | CH ₃ | NH ₂ | Fumonisin B ₃ |
| 94 | H | H | CH ₃ | NH ₂ | Fumonisin B ₄ |
| 95 | OH | OH | H | NH ₂ | Fumonisin C ₁ |
| 96 | H | OH | H | NH ₂ | Fumonisin C ₂ |
| 97 | OH | H | H | NH ₂ | Fumonisin C ₃ |
| 98 | H | H | H | NH ₂ | Fumonisin C ₄ |
| 99 | OH | OH | CH ₃ | pyOH ^a | Fumonisin P ₁ |
| 100 | H | OH | CH ₃ | pyOH ^a | Fumonisin P ₂ |
| 101 | OH | H | CH ₃ | pyOH ^a | Fumonisin P ₃ |
| 102 | H | H | CH ₃ | pyOH ^a | Fumonisin P ₄ |

^a pyOH = 3-hydroxypyridinium.

Scheme 11. Fumonisin B₂ (5) by Kishi et al.⁴⁰¹ (Synthesis of the Segments)

and Powell, have worked on the elucidation of their structure, especially of their relative and absolute configuration. Finally, in 1994, the stereochemistry of the fumonisin B₁ (**92**)⁸⁹¹ and the fumonisin B₂ (**5**)⁸⁹² backbones was clarified, followed by reports about the absolute configuration of the tricarballylic acid (TCA) moiety that was eventually proved through synthesis by the Kishi group.⁸⁹³

The same group published the first enantioselective total synthesis of fumonisin B₂ (**5**) two years later.⁴⁰¹ Their strategy was to build up the two halves containing clustered stereogenic centers separately and then to connect them by Wittig reaction. Furthermore, the TCA segments **116** (Scheme 12) were synthesized by an asymmetric Michael addition in a similar way to what had been previously reported⁸⁹³ and were attached at a late stage of the synthesis. The construction of the left segment (aldehyde **110**) and the right segment (Wittig ylide precursor **115**) is outlined in Scheme 11.

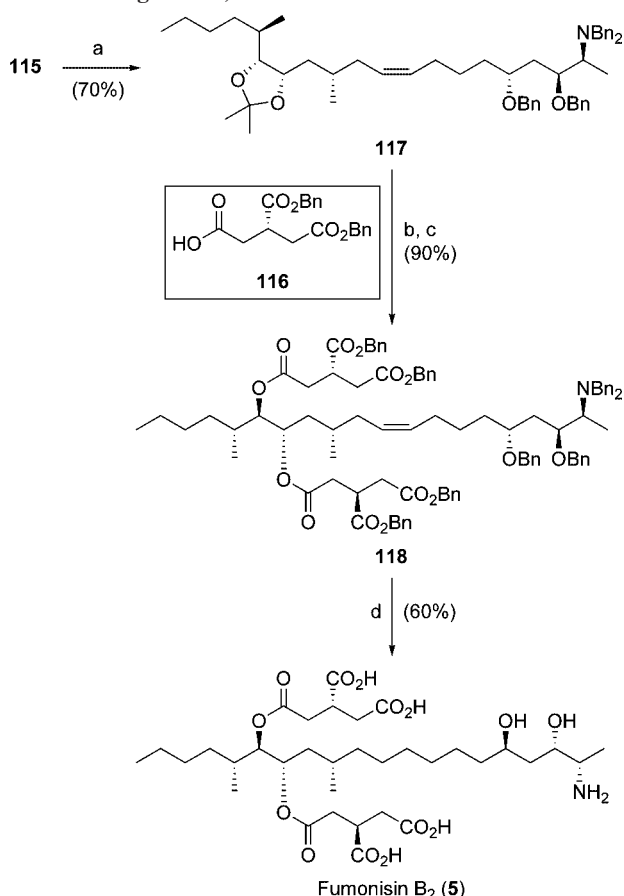
The first step of the synthesis was the coupling of chiral alkyne **103**, prepared by a Swern oxidation/Corey–Fuchs protocol from (*R*)-2-methyl-1-hexanol, and the triflate **104**, synthesized using the pseudoephedrine-based asymmetric alkylation developed by Myers. The resulting alkyne **105** was then cleaved at its double bond, reduced to the alcohol **106**, and converted into acid **107** by reduction to the *trans*-alkene, followed by Swern and Kraus oxidation. The vicinal hydroxyl groups were introduced by iodolactonization, ring-opening of the lactone with benzyl alcoholate to furnish an epoxide, and deprotection of the resulting benzyl ester with concomitant epoxide ring-opening. Via this sequence, the stereogenic centers were modulated into the desired configuration, so that the preparation of the left segment **110** could be completed by protection and adjustment of the oxidation state.

The right part **115** of fumonisin B₂ (**5**) was synthesized by two reiterative Brown allylations of Boc-protected α -amino propanal (**111**). The resulting allyl alcohol **113** was then subjected to various modifications of the protective groups and transformed into the aldehyde by ozonolysis. A chain elongation was achieved by Horner–Wadsworth–Emmons olefination to give ester **114**, which was converted into the phosphonium salt **115**. The three building blocks **110**, **115**, and **116** of the convergent total synthesis were thus at hand for interconnection.

Fumonisin B₂ (**5**) synthesis was completed by the Wittig reaction and acylation with the tricarballylic acid **116**. Hydrogenation of the double bond and hydrogenolysis of all benzyl protecting groups was accomplished in a single step using Pearlman's catalyst (Scheme 12).

One year later, in 1998, Gurjar et al. reported an approach toward the development of the backbone of fumonisin B₁ (**92**).⁴⁰⁰ It comprised the stereoselective synthesis of the hexaacetate derivative **135** starting from natural carbohydrates as chiral substrates (Scheme 13).

The left part arising from D-glucose (**119**) was converted into the 5-ulose derivative **120**. The butyl group was introduced by Wittig olefination and palladium-catalyzed reduction. However, the reaction was not diastereoselective, so that the required isomer had to be isolated by chromatography. Inversion of the configuration at the sugar moiety was effected by an oxidation/reduction sequence to give **121**. After oxidative cleavage of the diol with sodium periodate, the lactone **123** was formed by Horner–Wadsworth–Emmons olefination and treatment with a base. The reduction to **124** was performed in two steps to achieve maximum induction during hydrogenation of the olefin. Chain elongation toward **125** included hydrolysis of the lactol and Wittig olefination,

Scheme 12. Fumonisin B₂ (5) by Kishi et al. (Combination of the Building Blocks)⁴⁰¹

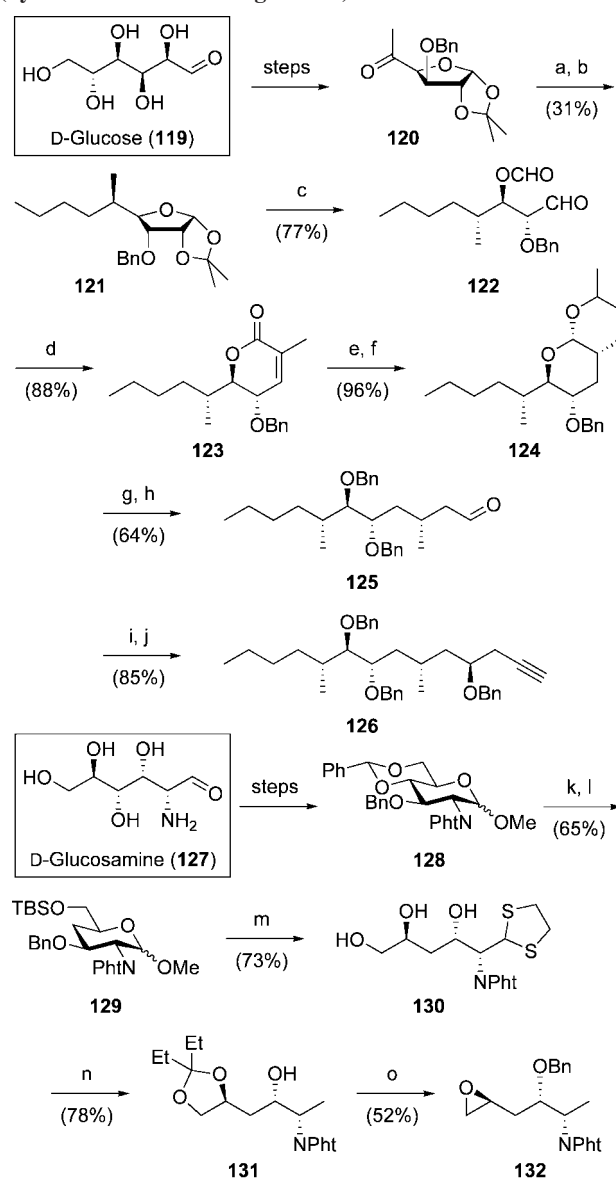
Reagents and conditions: (a) *n*BuLi, then **110**. (b) TFA · H₂O. (c) **116**, EDC, DMAP. (d) H₂ (1 atm), Pd(OH)₂/C, HCl, *t*BuOH, THF.

followed by hydroboration and oxidation. The subsequent addition of propargyl bromide in the presence of zinc dust resulted in a diastereomeric mixture of alcohols, which had to be separated by chromatography. Thus, the sequence comprises two nonstereoselective steps, so that the application of asymmetric reactions would improve the synthesis substantially. Building block **126** was finally obtained after benzylation.

The right segment of fumonisin B₁ (**92**) with its amino group can be traced back to D-glucosamine (**127**), which was thoroughly protected with orthogonal groups according to the literature. The resulting actual starting material **128** was then subjected to a Barton–McCombie deoxygenation at the 4-position, leading to **129**. Ring-opening occurred by conversion into the dithiolane **130** and complete reduction with Raney-nickel, with subsequent acetalization yielding precursor **131**. Transformation into the second building block **132** was realized in four steps including tosylation and epoxidation under basic conditions.

To complete the synthesis (Scheme 14), the two segments **126** and **132** were linked via an epoxide opening with the corresponding lithium acetylide. Removal of the phthalimido protective group and overall acetylation after debenzoylation finally produced hexaacetyl fumonisin B₁-AP (**135**).

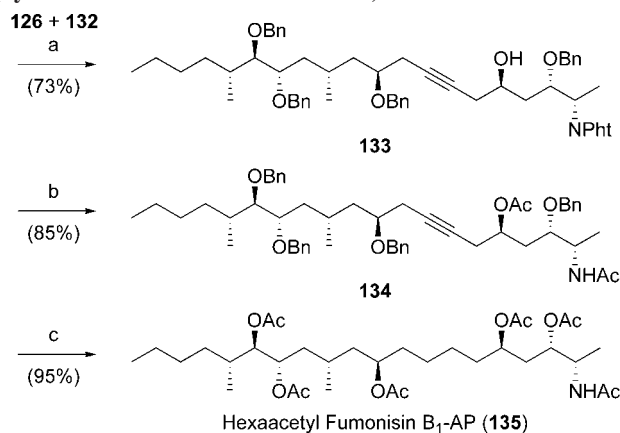
A structurally closely related group of mycotoxins are the AAL-toxins TA₁ (**136**) and TA₂ (**137**) isolated from *Alternaria alternata* f. sp. *lycopersici* (for toxic *Alternaria* metabolites, see also section 2.9.1).³⁹⁷ They were found to be tumor promoters⁸⁹⁴ and—because of their similar structure—an

Scheme 13. Fumonisin B₁ (92) Backbone by Gurjar et al. (Synthesis of the Building Blocks)⁴⁰⁰

Reagents and conditions: (a) (1) C₄H₉PPh₃Br, *n*BuLi, THF; (2) Pd/C, H₂, EtOAc. (b) (1) Ca/liq.NH₃, Et₂O; (2) IBX, DMSO; (3) NaBH₄, MeOH; (4) BnBr, NaH, THF. (c) (1) 70% aq. AcOH, H₂SO₄ (cat); (2) NaIO₄, MeOH/H₂O 4:1. (d) (1) (MeO)₂P(O)CH(CH₃)CO₂Et, NaH, THF; (2) K₂CO₃, MeOH. (e) (1) DIBAL, PhMe; (2) *i*PrOH, CSA. (f) Rh-Al₂O₃, H₂ (1 atm), Et₂O. (g) (1) 70% aq. AcOH, H₂SO₄ (cat); (2) CH₃PPh₃, *n*BuLi, THF; (3) BnBr, NaH, THF. (h) (1) 9-BBN, THF, NaOH, H₂O₂; (2) (COCl)₂, DMSO, Et₃N, CH₂Cl₂. (i) C₃H₃Br, Zn, aq. NH₄Cl, THF. (j) NaH, BnBr, THF. (k) (1) 60% aq. AcOH; (2) TBSCl, Im, CH₂Cl₂. (l) (1) NaH, CS₂, MeI, THF; (2) Bu₃SnH, AIBN (cat), PhMe. (m) (1) MeOH, *p*TsOH; (2) BF₃·Et₂O, HSCH₂CH₂SH, CH₂Cl₂. (n) (1) Raney-Ni, EtOH; (2) Et₂CO, CSA, CH₂Cl₂. (o) (1) NaH, BnBr, THF; (2) MeOH, *p*TsOH; (3) TsCl, Py, CH₂Cl₂; (4) NaH, THF.

inhibitor of sphingolipid biosynthesis.⁸⁹⁵ The AAL-toxins are the first known compounds inducing apoptosis in both mammalian and plant cells.⁸⁹⁶ The relative and absolute stereochemistry of the sphingosine backbone was elucidated by the groups of Kishi and Oikawa.⁸⁹⁷ The latter group also published the first total synthesis of AAL-toxin TA₁ (**136**) in 1999, with a retrosynthetic disconnection between C-9 and C-10 (Figure 6).³⁹⁸

The synthesis of lactone **138** started from methyl 3-hydroxy-2-methylpropionate (**141**), which was converted into oxirane **142** involving vinylation and dihydroxylation reac-

Scheme 14. Fumonisin B₁ (92) Backbone by Gurjar et al. (Synthesis of Hexaacetate Derivative)⁴⁰⁰


Reagents and conditions: (a) *n*BuLi, BF₃·Et₂O, THF. (b) (1) MeNH₂, MeOH; (2) Ac₂O, Et₃N, CH₂Cl₂. (c) (1) Pd(OH)₂, H₂, MeOH; (2) Ac₂O, Et₃N, CH₂Cl₂.

tions for the implementation of the two new stereogenic centers. The epoxide was opened by acetylide addition to produce **143**, which was transformed into lactone **144** under sequential hydrolytic conditions, followed by deprotection of the silyl ether moiety, Swern oxidation, and Wittig olefination. The remaining steps comprised hydrogenation and acidic debenzylation as well as the final α -methylation toward lactone **138** (Scheme 15).

The synthesis of building blocks **139** and **140** had already been published in a preceding paper in 1996.⁸⁹⁸ Protected 5-pentynol and (*R*)-glycidol were reacted, and the resulting homopropargylic alcohol was hydrogenated to the *cis*-olefin **147**, which in turn was subjected to an asymmetric dihydroxylation. The major product was the *anti*-triol **148** that was globally protected with benzyl groups and subsequently transformed into the second building block **139** by a Corey–Fuchs reaction (Scheme 16).

The tricarballic acid segment **140** was obtained from racemic methyl 2-benzylsuccinate (**150**). A kinetic resolution was achieved by employing lipase-catalyzed hydrolysis of the primary ester. The (*S*)-isomer **150a** was then fully hydrolyzed, TMSE-protected (TMSE = trimethylsilylethyl), and converted into the acid **140** through degradation of the phenyl ring.

Finally, the total synthesis was completed with the combination of the three fragments (Scheme 17): acetylide

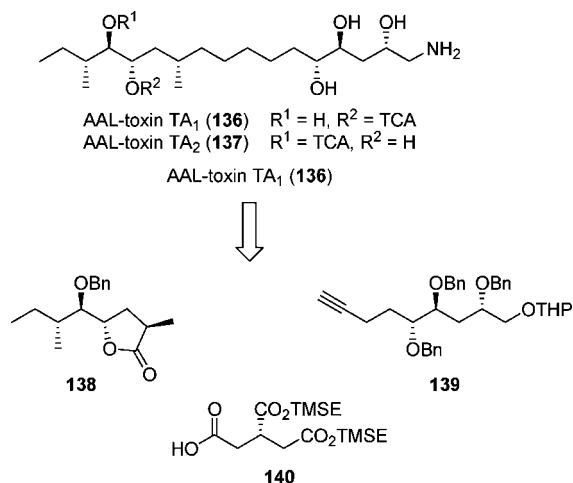
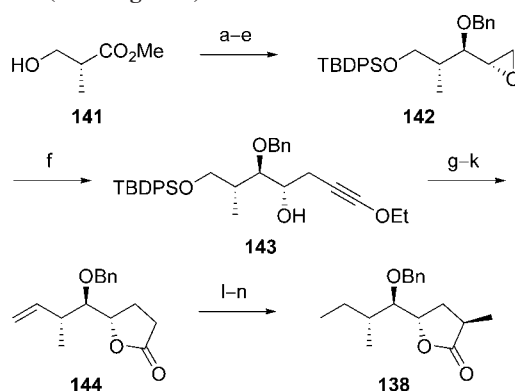


Figure 6. AAL-toxins and retrosynthetic analysis.

Scheme 15. Total Synthesis of AAL-Toxin TA₁ (136) by Oikawa (Left Segment)³⁹⁸


Reagents and conditions: (a) TBDPSCI, Im, DMF, (quant.). (b) DIBAL, Et₂O, -78 °C; then vinylMgBr (dr = 1:1, 77%). (c) NaH, BnBr, TBAI, THF (91%); chromatographic separation. (d) OsO₄, NMO, acetone/H₂O 8:1 (dr = 6:1, 91%). (e) (1) MeC(OMe)₃, cat. PPTS, CH₂Cl₂; (2) AcBr, CH₂Cl₂; (3) K₂CO₃, MeOH (77%). (f) ethyl ethynyl ether, *n*BuLi, BF₃·Et₂O, THF, -78 °C. (g) HgCl₂, EtOH. (h) K₂CO₃, MeOH; then 3 M HCl (59% over 3 steps). (i) TBAF, THF (80%). (j) Swern oxidation. (k) H₃CPPh₃Br, *n*BuLi, THF (19% over 2 steps, 70% recovered aldehyde). (l) H₂, Pd/C, EtOAc. (m) CCl₃C(NH)OBn, TfOH, CH₂Cl₂/cyclohexane 1:1 (57% over 2 steps). (n) LiHMDS, MeI, THF, -78 °C (dr = 8.7:1, 68%).

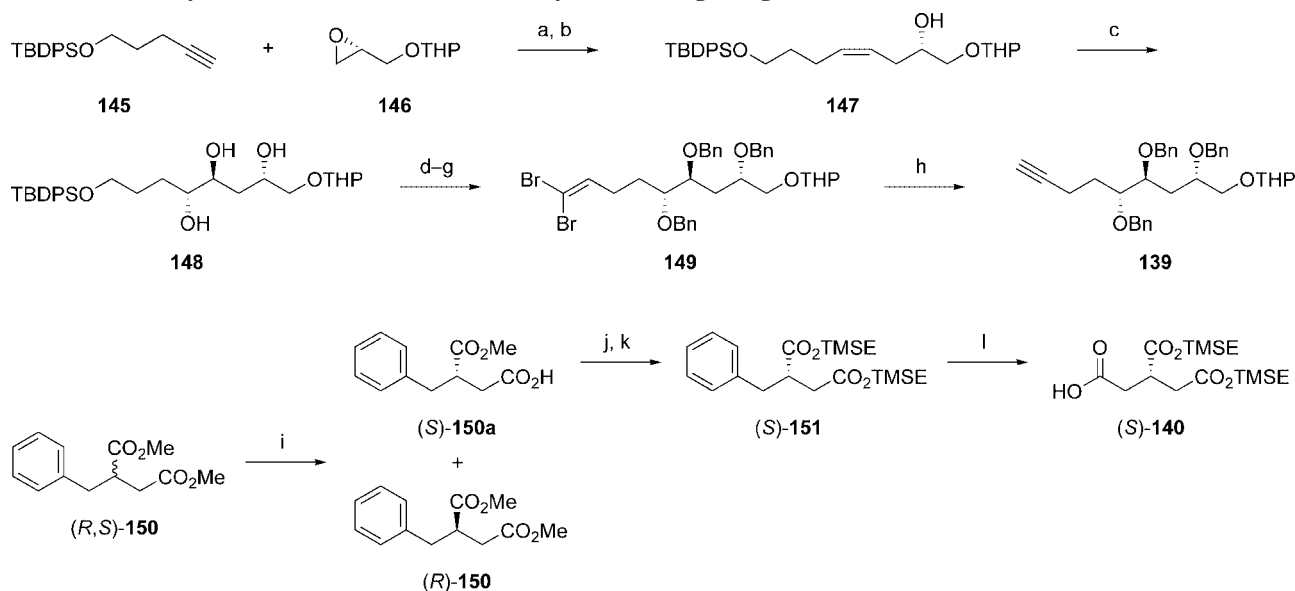
addition to lactone **138** afforded ynone **152** that was deoxygenized under palladium catalysis after Luche reduction and formylation. Transformation of the THP–acetal (THP = tetrahydropyranyl) **153** into the azide **154** was effected under Mitsunobu conditions, and esterification with the tricarballic acid moiety **140** was attained by applying the Yamaguchi method. Deprotection and exhaustive hydrogenation provided the AAL-toxin TA₁ (**136**).

All indicated syntheses were performed in a quite convergent manner. The cumulated arrangement of the stereogenic centers in this class of natural products gave rise to strategies that throughout set the retrosynthetic dissection in the middle of the backbone. The chiral segments were either built up by asymmetric synthesis or derived from natural products such as sugars (chiral pool strategy). The modular approach offered the possibility of producing fumonisin analogues that could be applied in structure–activity relationship (SAR) investigations. Various aspects of biological activity of fumonisins and AAL-toxins that are particularly interesting for the understanding of the importance of this family of mycotoxins have been included in this review.⁸⁹⁹

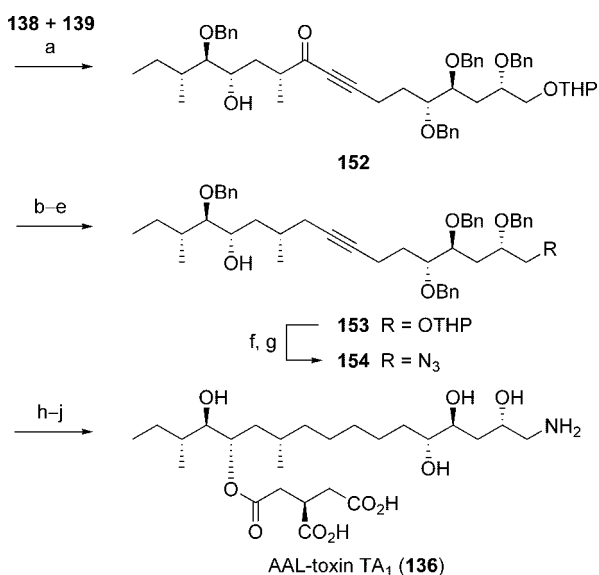
2.5. Ochratoxin

The ochratoxins are the first major group of mycotoxins identified after the discovery of the aflatoxins; among the *Aspergillus* toxins, only ochratoxin is potentially as important as the aflatoxins. Ochratoxin A (OA, **7**) and B (OB, **155**) were characterized in 1965 by Steyn and co-workers.^{900,901}

Biosynthetically, the ochratoxins are pentaketides, consisting of a dihydroisocoumarin coupled with β -phenylalanine. There are OA (**7**) and its dechloro analogue OB (**155**), their corresponding methyl esters (**158a** and **159a**, respectively) and also their ethyl esters (**156** and **159b**), ochratoxin C (OC, **156**), the 4-hydroxy derivatives from OA (**160a** and **160b**), and the dihydroisocoumarin carboxylic acid (ochratoxin α , **157**) (see Figure 7). The dihydroisocoumarins represent an extensive class of naturally occurring compounds that display a wide range of biological activities.

Scheme 16. Total Synthesis of AAL-Toxin TA₁ (136) by Oikawa (Right Segment and TCA)³⁹⁸

Reagents and conditions: (a) *n*BuLi, BF₃·Et₂O, THF, -78 °C (75%). (b) H₂, Pd/BaSO₄, quinoline (93%). (c) cat. OsO₄, DHQD-IND, K₃Fe(CN)₆, K₂CO₃, *t*BuOH/H₂O (dr = 4:1, 85%). (d) NaH, BnBr, TBAI, THF, reflux (81%). (e) TBAF, THF (89%). (f) Oxidation. (g) CBr₄, PPh₃, DIPEA, CH₂Cl₂ (75%). (h) *n*BuLi, BF₃·Et₂O, THF, -78 °C (75%). (i) lipase (PPL), KH₂PO₄-buffer (pH 7.2). (j) 1 M NaOH, MeOH. (k) TMSCH₂CH₂OH, EDC, Et₃N, DMAP, CH₂Cl₂ (79% over 2 steps). (l) RuCl₂, NaIO₄, CCl₄/CH₃CN/H₂O 2:2:3 (59%).

Scheme 17. Total Synthesis of AAL-Toxin TA₁ (136) by Oikawa et al.³⁹⁸

Reagents and conditions: (a) **139**, *n*BuLi, Et₂O, -20 °C; then **138** (72%). (b) NaBH₄, CeCl₃, MeOH (85%). (c) Ac₂O, HCO₂H, Py (97%). (d) Pd(OAc)₂, *n*Bu₃P, THF (84%). (e) LAH, THF. (f) PPTS, EtOH (89% over 2 steps). (g) HN₃, PPh₃, DEAD, toluene (69%). (h) 2,4-(NO₂)₂C₆H₄COCl, **140**, Et₃N, toluene; then **154**, DMAP (71%). (i) TBAF, THF. (j) H₂, Pd/C, *t*BuOH/THF/1 M HCl 3:1:0.04 (76% over 2 steps).

Ochratoxin A (**7**) is the most important and most commonly occurring member of the family of ochratoxins, and is the subject of several publications.^{902,903} It is produced by *Aspergillus ochraceus* and several related *Aspergillus* species, by a single *Penicillium* species (*P. verrucosum*), and by *A. carbonarius* with a small percentage of isolates of the closely related *A. niger*. It was first isolated by Steyn and co-workers.

Ochratoxin A (**7**) is the most toxic of the ochratoxins, exhibiting teratogenic, nephrotoxic, immunosuppressive and carcinogenic properties.⁹⁰⁴⁻⁹⁰⁶ Two years after having isolated

Ochratoxin A (**7**) and B (**155**) from some strains of *Aspergillus ochraceus*,^{900,901} Steyn and co-workers reported the first total synthesis of racemic ochratoxin α (**157**), the carboxylic acid component of the biologically active ochratoxin A (**7**) (Scheme 18).⁹⁰⁷

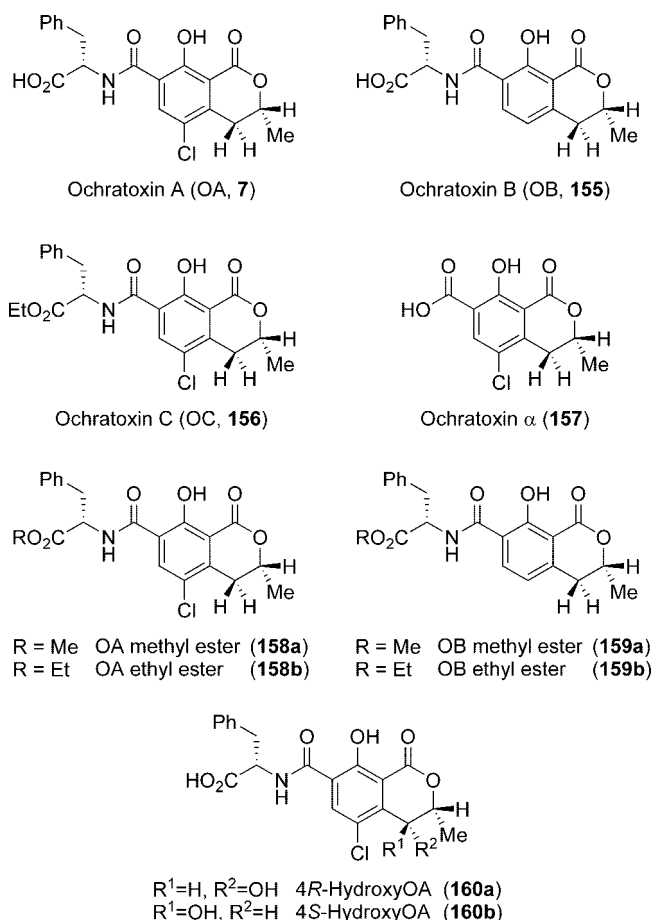
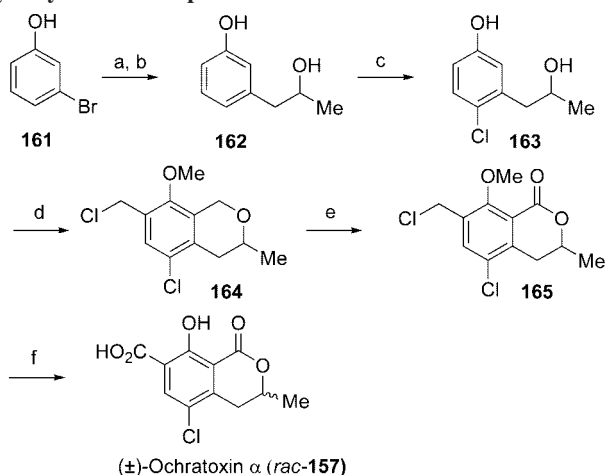
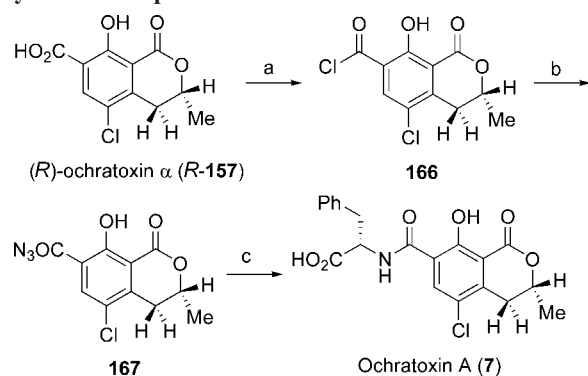


Figure 7. Structures of ochratoxins.

Scheme 18. First and Improved Synthesis of Ochratoxin α by Steyn and Holzzapfel⁹⁰⁷


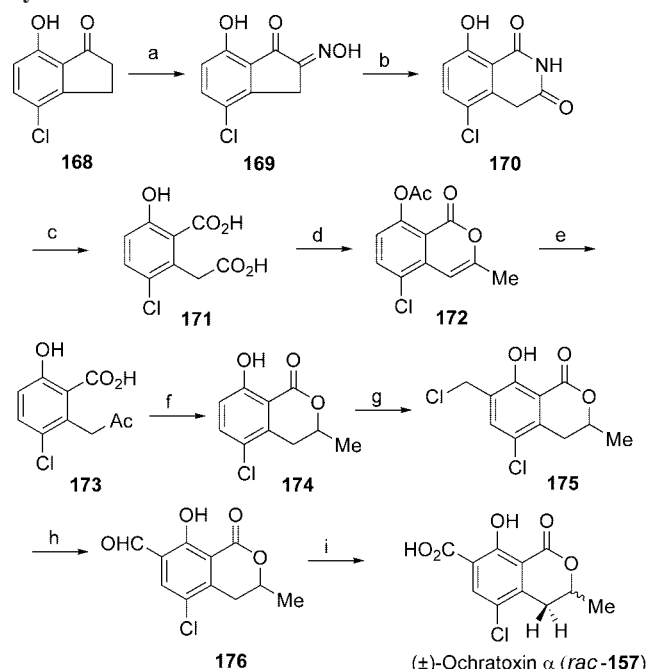
Reagents and conditions: (a) DHP, HCl, 60 °C. (b) (1) EtMgBr, THF, 1 h, 0 °C; (2) propylene oxide, 16 h; (3) MeOH-1N HCl, 12 h, rt. (c) Cl₂ (g), nitromethane, 0 °C, 15 min. (d) ZnCl₂, chloromethylether, reflux, 45 min. (e) AcOH, CrO₃, 0 - 5 °C, 30 min. (f) (1) (CH₂)₆N₄; (2) aqueous AcOH; (3) Ag₂O; (4) ZnCl₂.

Scheme 19. First Total Synthesis of Ochratoxin A (7) by Steyn and Holzzapfel⁹⁰⁷


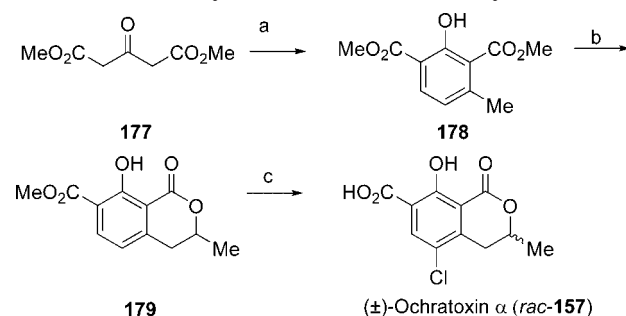
Reagents and conditions: (a) SOCl₂, reflux, 2 h; (b) NaN₃, 0 °C, DMF, 30 min.; (c) L-phenylalanine, H₂O, Et₃N, 5 °C, 55 h.

For the synthesis of ochratoxin A (7), the authors employed the enantiomerically pure (*R*)-ochratoxin α (*R*-157) obtained through hydrolysis of the natural product as starting material, instead of the derivative *rac*-157 obtained through chemical synthesis (Scheme 19).

Three years later, Roberts and Woollven⁵⁵¹ reported an alternative synthesis of racemic ochratoxin α in eight steps with an overall yield of 62% (Scheme 20). In this case, the authors employed 4-chloro-7-hydroxyindanone (168) as starting material, with the advantage being that this compound possesses the phenolic hydroxyl group and the chlorine function in suitable positions. The synthetic pathway toward racemic ochratoxin α consisted of the initial formation of the isocoumarin skeleton 172 employing modifications to known procedures that employed the transformation of 168 to the corresponding oximino-compound 169, homophthalimide 170 and homophthalic acid 171.⁹⁰⁸ The isocoumarin framework 172 was then converted in the dihydroisocoumarin 174 (via the benzoic acid 173). Ultimately, the introduction of the required substituent at the C7-position was achieved through successive applications of the *Rieche* reaction⁹⁰⁹ to obtain the methylene chlorinated derivative 175, Sommelet reaction⁹¹⁰ to the corresponding

Scheme 20. Alternative Synthesis of Racemic Ochratoxin α by Roberts and Woollven⁵⁵¹


Reagents and conditions: (a) C₆H₁₁ONO-HCl. (b) *p*-MeC₆H₄SO₂Cl. (c) (1) NaOH; (2) HCl. (d) Ac₂O-AcONa. (e) (1) NaOH; (2) HCl. (f) (1) NaBH₄; (2) HCl. (g) ClCH₂PMe-TiCl₄. (h) (1) (CH₂)₆N₄; (2) aq. AcOH. (i) Ag₂O.

Scheme 21. Short Synthesis of Ochratoxin α by Kraus⁵⁵⁰


Reagents and conditions: (a) CH₃COCHCONa (50%). (b) LDA, CH₂CHO, THF (69%). (c) (1) SO₂Cl₂, CH₂Cl₂; (2) LiOH H₂O, MeOH (58%).

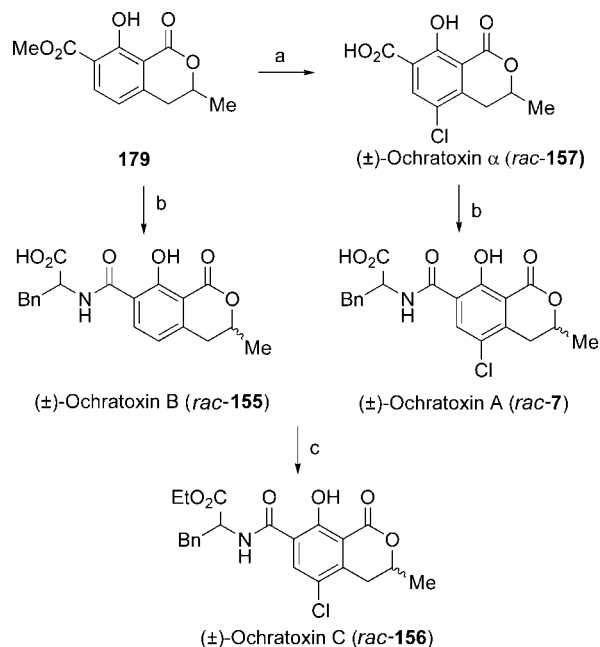
aldehyde 176, and mild oxidation to the desired racemic ochratoxin α (*rac*-157).

Finally, by condensation of the synthesized racemic ochratoxin α (*rac*-157) with the *tert*-butyl ester of L(-)phenylalanine (employing EEDQ⁹¹¹(2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline)) and subsequent removal of the protecting *tert*-butyl group, Roberts and Woollven obtained a diastereoisomeric mixture of ochratoxin A (7), which was resolved by repeated preparative thin-layer chromatography (TLC), leading to Ochratoxin A (7) in 90% isomeric purity.

With the aim of attaining a simple, direct, and inexpensive synthesis of ochratoxins, Kraus developed a more efficient synthetic route toward racemic ochratoxin α (*rac*-157) in 1981 (see Scheme 21).⁵⁵⁰ With this methodology, he claimed (i) to improve the low overall yield, (ii) to shorten the lengthy route, and (iii) to avoid the use of several highly expensive chemicals that had been used in previous syntheses.^{907,551}

One year later, Kraus extended the application of his methodology to the syntheses of ochratoxin B (155) and C (156). This work was reported in a patent that includes the

Scheme 22. Simple, Direct, and Inexpensive Synthesis of Ochratoxin A (*rac*-7), B (*rac*-155), and C (*rac*-156) by Kraus⁹¹²



Reagents and conditions: (a) (1) SO_2Cl_2 , CH_2Cl_2 ; (2) LiOH H_2O , MeOH . (b) L-(–)-phenylalanine t-butyl ester, EEDQ, THF, rt, 15 h. (c) EtOH .

synthetic route that allows, for the first time, small and industrial-scale syntheses of ochratoxins A, B, and C in pure form, with good yields and minimal synthetic steps (see Scheme 22).⁹¹²

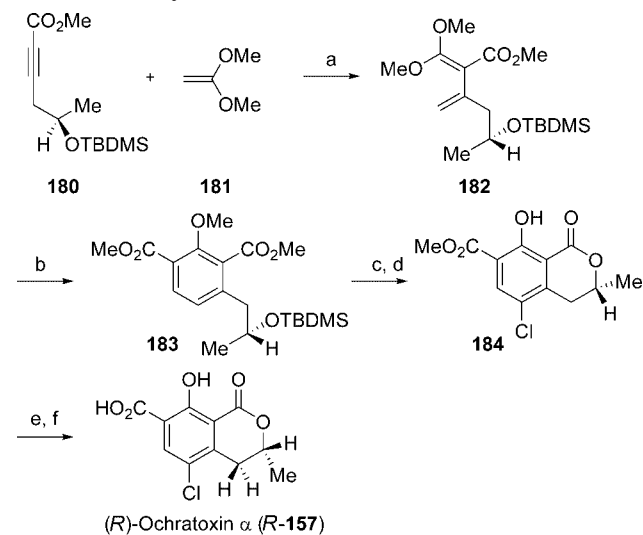
More recently, Donner and Gill reported the first total synthesis of enantiomerically pure (*R*)-ochratoxin α (*R*-157) in nine steps and with 10% overall yield.⁵⁵² Starting from commercially available (*R*)-propylene oxide, they applied the same strategy that they had previously developed for the stereospecific synthesis of melleins,⁹¹³ consisting of an initial cycloaddition reaction between an enantiomerically pure (*R*)-acetylenic ester **180** (derived from (*R*)-propylene oxide in three steps⁹¹³) and ketene dimethyl acetal **181** to obtain the diene **182**, which after Diels–Alder cycloaddition with methyl propiolate, lactonization, and appropriate functionalization yielded the desired enantiomerically pure (*R*)-ochratoxin α (*R*-157) (Scheme 23).

Taking into account that the previous synthesis of the isocoumarin nucleus **157** yielded only racemic or, at best, enantiomerically enriched material, the synthetic route developed by Donner and Gill—to the enantiomerically pure intermediate (*R*)-ochratoxin α (*R*-157), which can be converted to (*R*)-ochratoxin A (**7**) by employing the methodology developed by Steyn and co-workers (see Scheme 19)—can be considered the first formal total synthesis of enantiomerically pure ochratoxin A (**7**) and still represents the only synthesis of (*R*)-ochratoxin α published to date.⁹¹⁴

2.6. Patulin

The ylidenebutenolide mycotoxin patulin (**3**) is produced by several *Penicillium* and *Aspergillus* species and is known as a common contaminant in food (e.g., apple juice). The molecule possesses antibiotic (notably antibacterial) properties⁹¹⁵ and is also a general plant toxin.⁹¹⁶ Patulin (**3**) also shows mutagenic⁹¹⁷ and carcinogenic activity, because of its ability to inhibit DNA, RNA, and protein synthesis.⁹¹⁸ Since

Scheme 23. Total Synthesis of Enantiomerically Pure Ochratoxin α by Donner and Gill⁵⁵²



Reagents and conditions: (a) sealed tube, 165 °C, 23 h. (b) methyl propiolate, sealed tube, 145 °C, 22 h, (69%, 2 steps). (c) *p*-TsOH, CH_2Cl_2 , rt, 72 h (82%). (d) BCl_3 , CH_2Cl_2 , 0 °C, 10 min (92%). (e) SO_2Cl_2 , CH_2Cl_2 , rt, 48 h. (f) MeOH , $\text{LiOH}\cdot\text{H}_2\text{O}$, reflux, 5 h (68%, 2 steps).

its isolation in the 1930s, patulin (**3**) (isolated from *Penicillium patulum*⁹¹⁹) has been known under several names, such as clavacin,⁹²⁰ clavatin,⁹²¹ claviformin (isolated from *P. claviforme*⁹²²), expansin,⁹²³ mycoin, penicidin,⁹²⁴ and tercinin.⁹²⁵ Despite its apparently simple structure, patulin (**3**) has incited large interest within the field of natural product chemistry. Upon closer inspection, it reveals pronounced reactivity and sensitive functionality in the small bicyclic ring system, i.e., a cyclic hemiacetal, an enol ester, an allylic acetal, and a conjugate dienolate. Patulin (**3**) belongs to the family of ylidenebutenolides and is related to other fungal tetrone acid metabolites like penicillic acid (**187**) (see Figure 8).

The first study on the structure of patulin (**3**) entitled “Investigations Relating to the Synthesis of Patulin” resulted in the postulation of an incorrect structure.⁹²⁶ One year later, in 1949, the correct structure⁹²⁷ was published and confirmed by a partial synthesis, followed by the first total synthesis^{389,928} of patulin (**3**) by Woodward and Singh, but only in very low yields.

A more practicable total synthesis was published concurrently by Gill/Pattenden^{388,392} and Riguera³⁹¹ in the late 1980s. Starting from L-arabinose (**189**) as an enantiopure precursor, the acetal of patulin **194** was synthesized stereoselectively; despite this result, rapid racemization occurred after its

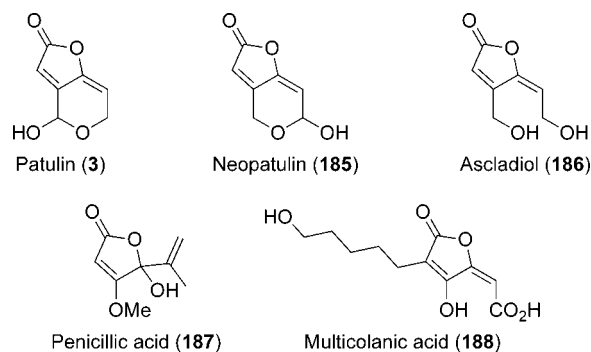
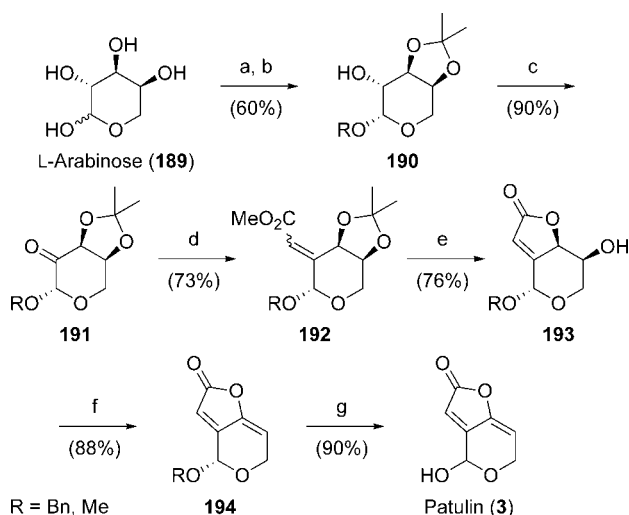
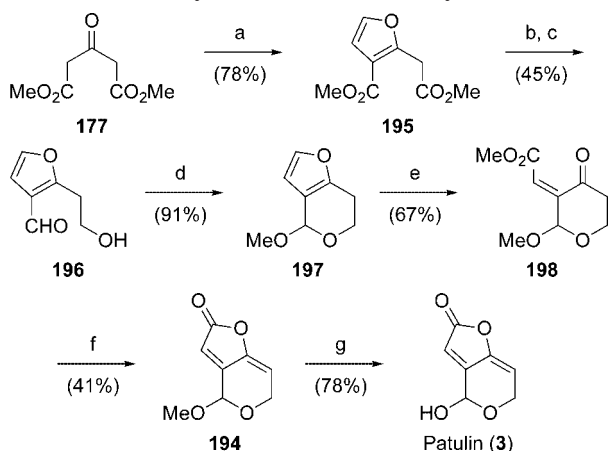
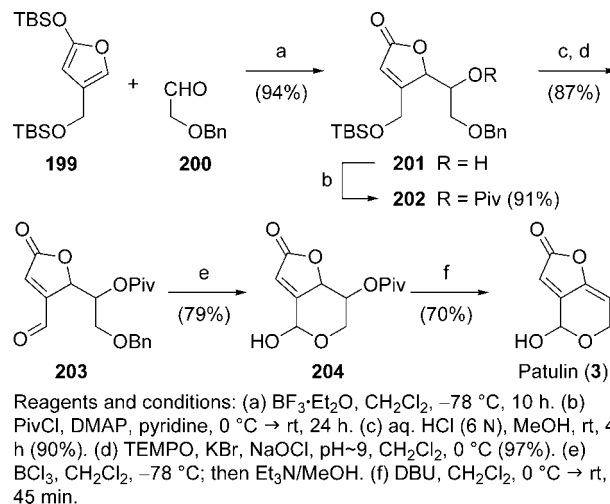


Figure 8. Patulin (**3**) and related fungal metabolites.

Scheme 24. Total Synthesis of Patulin (3) by Pattenden et al.^{388,391,392}**Scheme 25. Total Synthesis of Patulin (3) by Tada et al.**³⁹³

conversion into the hemiacetal, similarly to natural patulin (3), which also is a racemate. The first steps comprised the transformation of L-arabinose (189) into the isopropylidene derivative 190 with methyl or benzyl protected β -acetal. After oxidation and olefination, the α,β -unsaturated ester 192 was converted into the bicyclic lactone 193. *Anti*-elimination and acetal cleavage completed the synthesis, and patulin (3) was obtained in good yield after seven steps (Scheme 24, yields from ref 388).

In 1994, Tada et al. synthesized patulin (3) via oxidation of furan derivatives and subsequent enol-lactonization (Scheme 25).³⁹³ The furan ring was formed by condensation of acetonedicarboxylic acid methyl ester (177) with chloroacetaldehyde in pyridine. Reduction of the ester moieties and reoxidation at the benzylic position gave aldehyde 196, which was condensed to the methyl acetal 197 upon treatment with *p*-toluenesulfonate in refluxing methanol/benzene with a Dean–Stark water trap. The key oxidation with *m*-CPBA (meta-Chloroperoxybenzoic acid), followed by methylation,

Scheme 26. Short Total Synthesis of Patulin (3) by Boukouvalas³⁹⁴

yielded keto-ester 198, which was again subjected to condensation conditions. With calcium hydroxide as a catalyst, efficient cyclization to the lactone 194 took place. Demethylation performed with TFA gave the natural product patulin (3) in 7% overall yield after eight steps.

The shortest synthesis in this context is the one published by Boukouvalas et al. in 1995 (Scheme 26).³⁹⁴ After the 4-step synthesis of neopatulin (185)⁹²⁹—the penultimate biogenetic precursor of 3—they reported the synthesis of patulin (3) starting from the same building block, silyloxyfuran 199. An aldol reaction with benzyloxyacetaldehyde (200) under Lewis acid catalysis provided alcohol 201 as a mixture of diastereoisomers. The transformation into the pivaloyl ester 202 enabled the protection of the hydroxyl group as well as its activation in the later β -elimination. Desilylation and TEMPO oxidation yielded aldehyde 203, which was immediately converted into the hemiacetal 204 through treatment with boron trichloride. Previously mentioned β -elimination was accomplished under basic conditions (DBU) and furnished patulin (3) with a 41% overall yield. This synthesis comprises only six steps with readily available, achiral starting materials (Scheme 26).

These approaches show how patulin (3) is available synthetically; however, most interest concerned its biosynthesis, as patulin (3) was repeatedly used as a model compound for the detailed examination of polyketide synthesis⁹³⁰ in nature.^{931,932}

2.7. Trichothecenes

2.7.1. Introduction

The trichothecenes are produced by various *Fungi imperfecti*, mainly of the genus *Fusarium*, but also by other genera such as *Myrothecium*, *Trichothecium*, *Trichoderma*, *Cylindrocarpum*, *Cephalosporium*, *Verticimonosporium*, or *Stachybotrys*. The family comprises a large number of substances, of which most are toxic, but only some members constitute the group of main natural contaminants of grains: deoxynivalenol (DON, 230), nivalenol (NIV, 232), T-2 toxin (T-2, 224), HT-2 toxin (HT-2, 223), and diacetoxyscirpenol (DAS, 217). The historically reported health problems of humans intoxicated by infested food have been mainly caused by these representatives.¹²

The first known member of the trichothecene family was trichothecin (229),⁸⁰⁴ characterized in 1948; however, the



Figure 9. Structure and numbering system of “trichothecane” and 12,13-epoxytrichothec-9-enes.

individual members were not included into this class of compounds until 1967, when the sesquiterpenoid skeleton structure was given the name “trichothecane” by Tamm et al. (Figure 9).⁹³³ Most naturally occurring trichothecenes are tetracyclic, as they contain an epoxide in the 12,13-position—which appears to be critical for bioactivity, including antiproliferative activity,⁹³⁴ ability to induce apoptosis,⁹³⁵ antimalarial activity,⁹³⁶ and antiviral effects⁹³⁷—and they comprise a double bond at C-9,10. Thus, they can be classified as 12,13-epoxytrichothec-9-enes.

Yet, the trichothecenes can be divided into two subgroups: nonmacrocylic (alcoholic derivatives and simple esters) and macrocylic (more complex di- and triesters including a macrocylic ring between C-4 and C-15). Over the decades, several classification systems have been stated by researchers engaged in this field, which exist in parallel and are listed below.

In his work,⁹³⁸ Ueno defined four types according to their chemical properties and resulting fungi: type A represented by T-2 toxin (**224**) and diacetoxyscirpenol (anguidine, **217**); type B with a carbonyl function at C-8 represented by nivalenol (**232**) and deoxynivalenol (vomitoxin, **230**); type C characterized by a second epoxy function at C-7,8 (e.g., crotoxin **227**) or C-9,10; and finally type D consisting of macrocylic trichothecenes with a macrocylic ring between C-4 and C-15 (e.g., verrucarins, roridins, satratoxins, and baccharinoids).

Another classification by Tamm and Tori⁹³⁹ deals with the position of oxygen substituents at the trichothecane skeleton: (i) trichothecenes without an oxygen function at the C-8 position (Table 6); (ii) trichothecenes with an oxygen function other than a ketone at the C-8 position (Table 7); (iii) trichothecenes with a ketone at the C-8 position (Table 8); and (iv) macrocylic trichothecenes (see Figures 11–13).

With the discovery of trichoverroids, Jarvis established a novel nomenclature⁹⁴⁰ that differentiates between the macrocylic representatives and those that follow biogenetic pathways. The relationship between the four types—trichothecenoid (**I**) or anguinoid (**I'**), trichoverroid (**II**), roridoid (**III**), and verrucaroid (**IV**)—is depicted in Figure 10.

The trichoverroids are biosynthetic precursors of the roridins and verrucarins. Their characterization and isolation

Table 6. Most Common Trichothecenes without an Oxygen Function at the C-8 Position

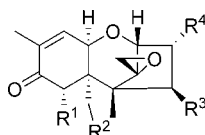
| no. | R^1 | R^2 | R^3 | trivial name |
|---------------|-------|-------|-------|---------------------------------------------------------|
| 205 | H | H | H | 12,13-Epoxytrichothec-9-ene |
| 206 | H | OH | H | Trichodermol (Roridin C) |
| 207 | H | OAc | H | Trichodermin |
| 208 | H | X | H | Trichodermediene |
| 209a,b | H | Y | H | Trichodermedienediol A (<i>S,S</i>), B (<i>S,R</i>) |
| 210 | OAc | OAc | H | Di- <i>O</i> -acetylverrucarol |
| 211 | OAc | H | OAc | Calonectrin |
| 212a,b | OH | Y | H | Trichoverrol A (<i>S,S</i>), B (<i>S,R</i>) |
| 213a,b | Z | Y | H | Trichoverrin A (<i>S,S</i>), B (<i>S,R</i>) |
| 214 | OH | OH | H | <i>Verrucarol</i> ^a |
| 215 | OH | OH | OH | Scirpentriol |
| 216 | OAc | OH | OH | 15-Acetoxyscirpenol |
| 217 | OAc | OAc | OH | Diacetoxyscirpenol (Anguidine) |

^a Non-naturally occurring trichothecenes in italics.

Table 7. Most Common Trichothecenes with an Oxygen Function Other than Ketone at the C-8 Position

| no. | R^1 | R^2 | R^3 | R^4 | trivial name |
|------------|------------------------|-------|----------------|-------|---------------------------------------------------------|
| 218 | OH | H | OH | H | 12,13-Epoxytrichothec-9-ene-4 β ,8 α -diol |
| 219 | OH | OH | OH | OH | T-2 tetraol |
| 220 | OH | OAc | OAc | OH | Neosolaniol |
| 221 | OAc | OH | OAc | OH | NT-1 toxin (Isoneosolaniol) |
| 222 | OH | OH | OAc | OH | NT-2 toxin (15-Deacetylneosolaniol) |
| 223 | iV ^a | OAc | OH | OH | HT-2 toxin |
| 224 | iV ^a | OAc | OAc | OH | T-2 toxin |
| 225 | iV ^a | OAc | OAc | OAc | Acetyl-T-2 toxin |
| 226 | iV ^a | OH | H | OH | Sporotrichiol |
| 227 | 7 β -O-8 β | H | B ^b | H | Crotoxin |

^a iV = isovalerate (3-methylbutyrate). ^b B = but-2-enoate.

Table 8. Most Common Trichothecenes with a Ketone at the C-8 Position

| no. | R^1 | R^2 | R^3 | R^4 | trivial name |
|------------|-------|-------|----------------|-------|------------------------------------|
| 228 | H | H | OH | H | <i>Trichothecolone^b</i> |
| 229 | H | H | B ^a | H | Trichothecin |
| 230 | OH | OH | H | OH | Deoxynivalenol (Vomitoxin) |
| 231 | OH | OH | H | OAc | 3-Acetyldeoxynivalenol |
| 232 | OH | OH | OH | OH | Nivalenol |
| 233 | OH | OH | OAc | OH | Fusarenone X |
| 234 | OH | OAc | OAc | OH | Nivalenol diacetate |

^a B = but-2-enoate. ^b Non-naturally occurring trichothecenes in italics.

from *Myrothecium verrucaria* was described by Jarvis in 1982.⁹⁴¹ They are nonmacrocyclic but already contain the ester side chains necessary. The trichoverrins A (**213a**) and B (**213b**) undergo ring-closure to yield roridin E (**262**), which is further developed into the other roridins. They were obtained as sets of diastereomers, epimeric at C-7' (the stereogenic center that corresponds to C-13' in the roridins), similarly to the trichoverrols A (**212a**) and B (**212b**), as well as the trichodermadienediols A (**209a**) and B (**209b**) (see Table 6). In all three cases, the addendum "A" indicates the *threo*-configuration (*S,S*) and "B" stands for the *erythro*-configuration (*S,R*). Note that the C-6' centers in the trichoverrins and trichoverrols are (*S*) and those in the ring-closed macrocyclic trichothecenes are (*R*).

2.7.2. Total Syntheses of the Sesquiterpenoid Core

Formal saponification of the trichoverrins yields verrucarol (**214**), the sesquiterpenoid moiety of the majority of the trichoverroids and the macrocyclic trichothecene derivatives.

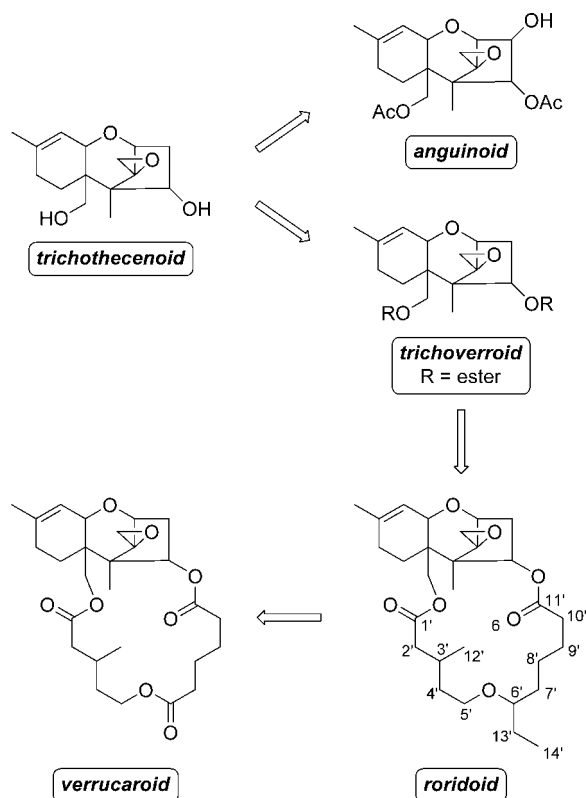


Figure 10. Jarvis's nomenclature of trichothecenes.

For this reason, verrucarol (**214**) was the focus of much synthetic interest, even though it is not a naturally occurring trichothecene itself. The first total synthesis of racemic

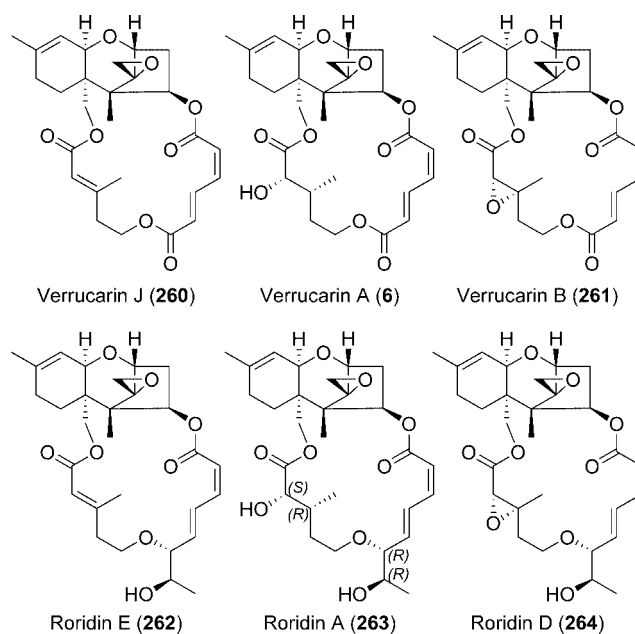


Figure 11. Examples of the verrucarins and roridins.

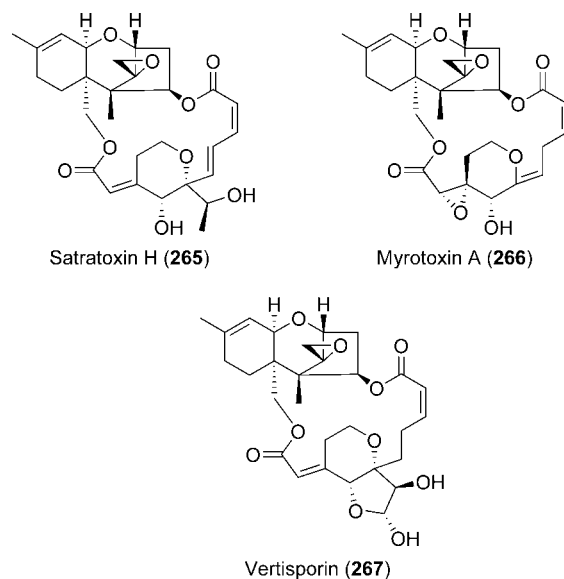


Figure 12. Macrocyclic trichothecenes with an additional tetrahydropyran moiety.

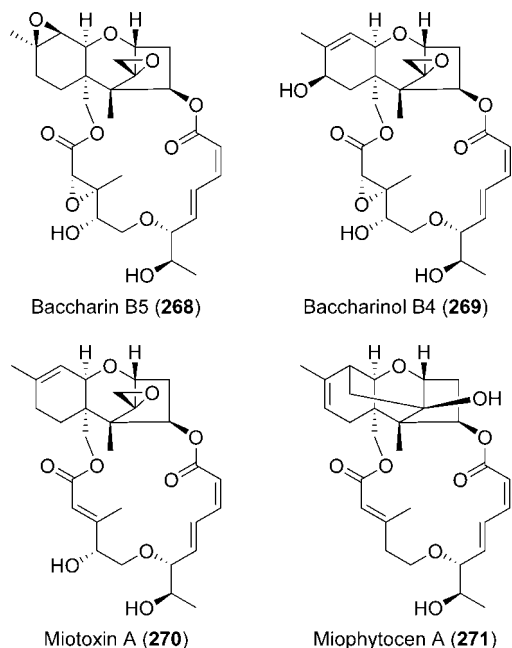


Figure 13. Macrocyclic trichothecenes isolated from *Baccharis* spp.

verrucarol (*rac*-**214**) was accomplished by Schlessinger et al. in 1982⁸¹³ and gave 3.4% yield over 17 steps (Scheme 27).

The synthesis starts with the formation of the ring system **235** according to Hajos and Parrish.⁹⁴² Through various oxidative methods, Wittig reaction, and esterification, the complex bicyclic **239** was formed, which underwent a Diels–Alder cycloaddition with **240** to build up the spiro compound **241**. Saponification of the lactone and methyl addition to the keto group, followed by reduction of the carboxylic acid, resulted in precursor **242** (undetermined configuration at C⁹) that was transformed into the desired trichothecene skeleton **243** by allylic addition. The *endo* double bond was protected by hydrobromination for the selective epoxidation of the *exo* double bond. Regeneration of the first was accomplished by treatment with sodium ethylamide to give racemic verrucarol (*rac*-**214**).

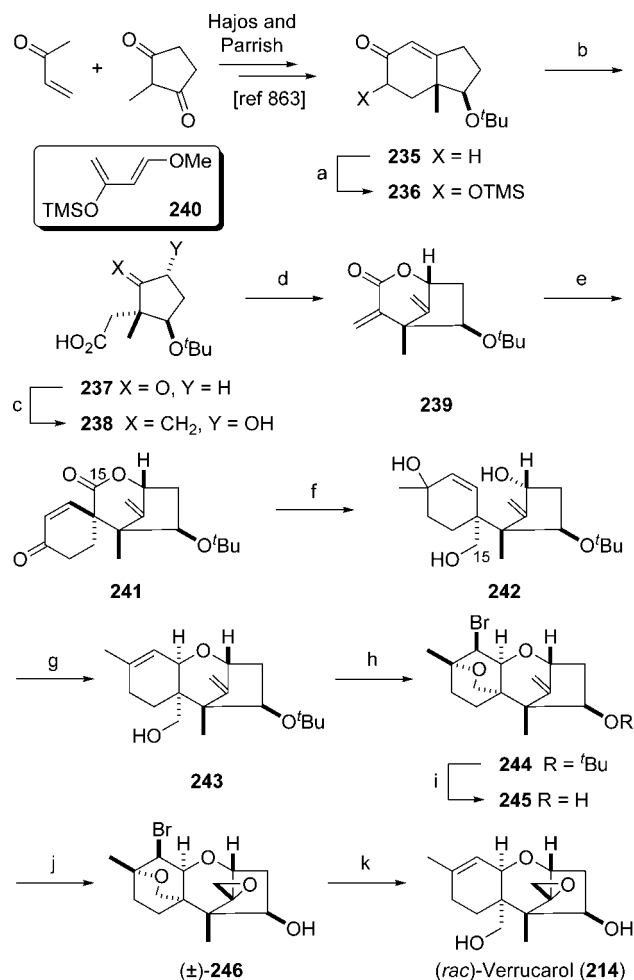
Studies toward a total synthesis were also presented by Roush in 1980,⁹⁴³ and another synthesis of (±)-verrucarol (*rac*-**214**) was published by Trost in 1982.⁸¹⁵ The first enantioselective total synthesis of (–)-verrucarol (**214**) was finally accomplished by Tadano et al. in 1998,⁸¹⁶ starting from the lactone **248** derived of D-glucose (Scheme 28).

The enantiopure starting material **248** was thus derived from the chiral pool and was subjected to an aldol reaction with protected aldehyde **249**. Exchange of the protective groups and Jones oxidation yielded lactone **252**, which was converted into tricycle **253** by a Dieckmann-like condensation. The following rearrangement of the carbon skeleton into **256** with subsequent Wittig reaction gave rise to the core structure **257** of the trichothecenes. The intramolecular hydrobromination strategy for the protection of the *endo* double bond and the selective epoxidation was already described in the Schlessinger synthesis.⁸¹³ Thus, (–)-verrucarol (**214**) could be obtained in 22 steps from **248**.

2.7.3. Macrocyclic Trichothecenes

The synthesis of macrocyclic trichothecenes was reviewed in 1989 by Tamm and Jeker.⁹⁴⁴ Examples of the most

Scheme 27. Total Synthesis of Verrucarol by Schlessinger et al.⁸¹³



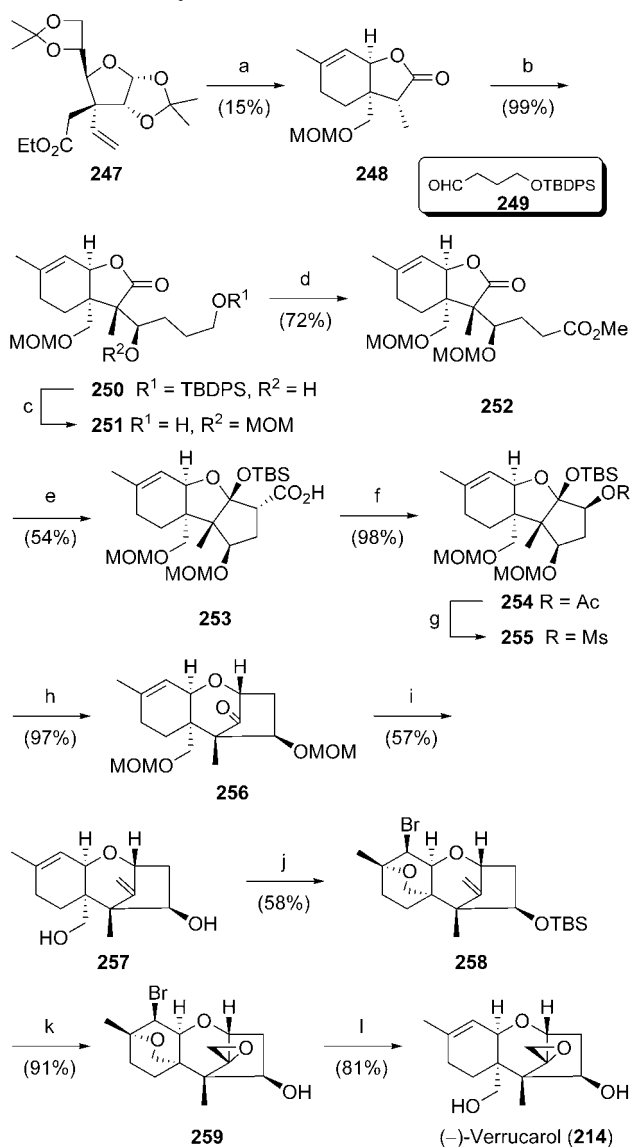
Reagents and conditions: (a) (1) LDA, THF, then TMSCl; (2) *m*CPBA. (b) (1) O₃; (2) NaIO₄, CrO₃ (53% from **235**). (c) (1) Ph₃P=CH₂; (2) SeO₂, *t*BuOOH (dr = 5:1). (d) (1) TsOH (55% from **237**); (2) LDA, then CH₂O (62%). (e) (1) **240**, 140 °C; (2) Amberlite IR-120 (76% from **239**). (f) (1) MeLi, THF (93%); (2) LiAlH₄. (g) TsOH (73%). (h) NBS, acetone. (i) TiCl₄ (85% from **243**). (j) *m*CPBA (70%). (k) Na, EtNH₂, THF (62%).

interesting macrocyclic trichothecenes are summarized in Figures 11–13. Although some trichothecenes like miophytocen A were isolated from shrubs, it is believed that they are primarily/generally produced by fungi.

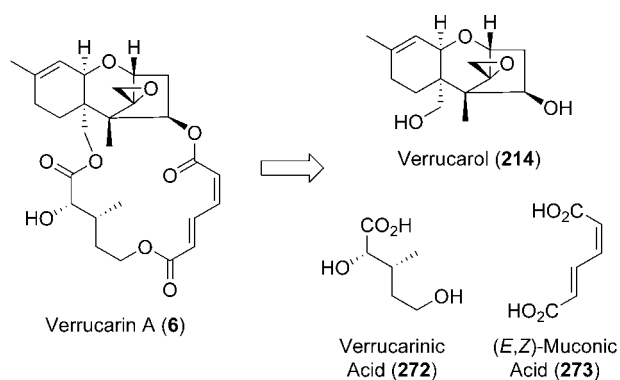
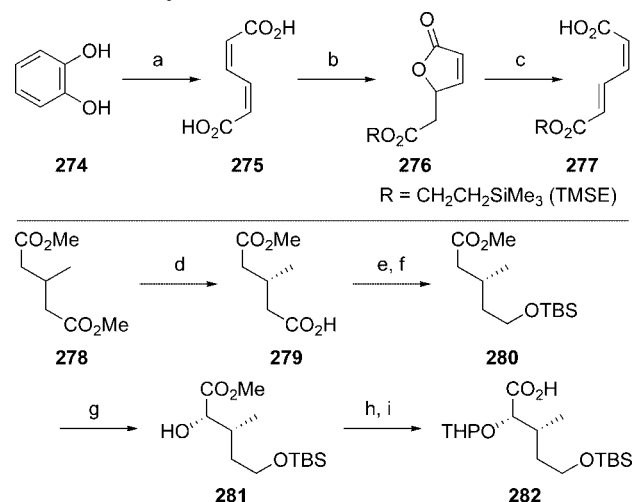
One of the most important and best described macrocyclic trichothecenes is verrucarol (**214**). Landmarks in research on macrocyclic trichothecenes are linked with Christoph Tamm, so his synthesis of this crucial representative is described (Scheme 29–31).⁸⁰⁹

The molecule was retrosynthetically disconnected through cleavage of the ester bonds. Thus, the starting substances for the total synthesis were verrucarol (**214**), a derivative of verrucarinic acid (**272**), and a half-ester (*E,Z*)-muconic acid (**273**). The synthesis of the key intermediates is shown in Scheme 30.

Oxidative cleavage of catechol (**274**) with a peracid resulted in the symmetric diacid (*Z,Z*)-**275** that was—after monoprotection through treatment with DCC (dicyclohexylcarbodiimide) and DMAP (4-(dimethylamino)pyridine)—converted into the lactone **276**. Saponification of the latter with the *a* *Eschenmoser* base (3,3,6,9,9-pentamethyl-2,10-diazabicyclo[4.4.0]-1-decene) and con-

Scheme 28. Enantioselective Total Synthesis of (–)-Verrucarol by Tadano et al.⁸¹⁶


Reagents and conditions: (a) 19 steps. (b) LDA, THF/toluene, $-78\text{ }^{\circ}\text{C}$; then **249** (dr = 1:1). (c) (1) TBAF (81%); (2) PivCl (87%); (3) MOMCl (83%); (4) NaOMe. (d) (1) Jones ox.; (2) CH_2N_2 . (e) (1) KHMDS, THF, $-78\text{ }^{\circ}\text{C}$ (dr = 5:3, 82%); (2) TBSOTf (dr = 5:3, 81%); (3) KOH (single diastereomer, 81%). (f) (1) WSC, DMAP, *t*-BuSH, O_2 ; (2) Ac_2O , Py (dr = 2:3). (g) (1) DIBAL; (2) MsCl (99%). (h) TBAF. (i) (1) $\text{Ph}_3\text{P}=\text{CH}_2$ (73%); (2) TMSBr, $-30\text{ }^{\circ}\text{C}$ (78%). (j) (1) TBSOTf; (2) NBS. (k) (1) TBAF; (2) *m*CPBA. (l) Zn–Ag, EtOH.

Scheme 29. Retrosynthetic Analysis of Verrucarol A by Tamm et al.⁸⁰⁹

Scheme 30. Synthesis of the Key Intermediates of Verrucarol A by Tamm et al.⁸⁰⁹


Reagents and conditions: (a) peracid oxidation. (b) $\text{Me}_3\text{Si}(\text{CH}_2)_2\text{OH}$, DCC, DMAP, $\text{CH}_2\text{Cl}_2/\text{DMF}$ (80%). (c) *Eschenmoser's* base (75%). (d) pig liver esterase (95%). (e) $\text{BH}_3\cdot\text{SMe}_2$, THF. (f) TBSCl, NEt_3 , DMAP, CH_2Cl_2 . (g) (1) LDA, THF; (2) $\text{MoO}_5\cdot\text{Py}\cdot\text{HMPA}$, $-78\text{ }^{\circ}\text{C}$, 2 h (40%). (h) DHP, PPTS. (i) KOH, MeOH.

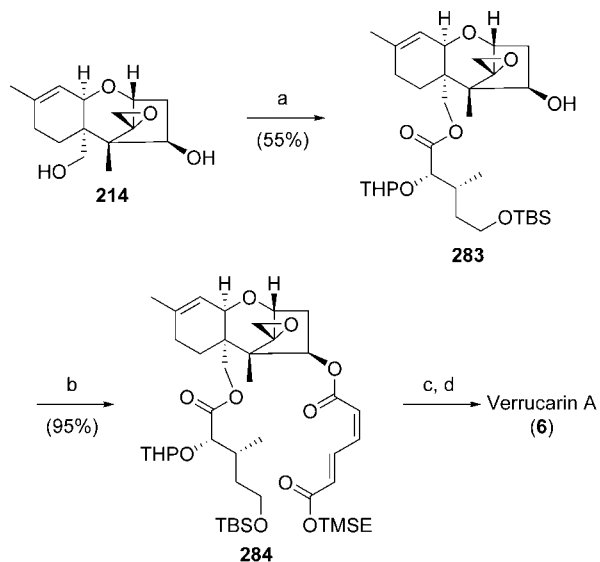
comitant elimination gave (*E,Z*)-half-ester **277**. The protected verrucaric acid **282** was received in enantiomerically pure form from the achiral compound 3-methylglutaric acid dimethylester (**278**). For this purpose, the diester **278** was selectively cleaved with pig liver esterase (PLE), reduced with borane dimethylsulfide complex, and silylated. A selective α -hydroxylation with molybdenum oxide finally resulted in the verrucaric acid derivative **281**, which was converted into the desired product **282** by protective group manipulation.

For the total synthesis, verrucarol (**214**) was successively esterified with **282** and **277** using the method developed by Steglich.⁹⁴⁵ The primary and secondary hydroxyl functions were differentiated by their reactivity without any protecting groups. After deprotection of positions C-5' and C-6', a Yamaguchi macrolactonization and the cleavage of the THP–acetal with PPTS were conducted, yielding the mycotoxin verrucarol (**6**, Scheme 31).

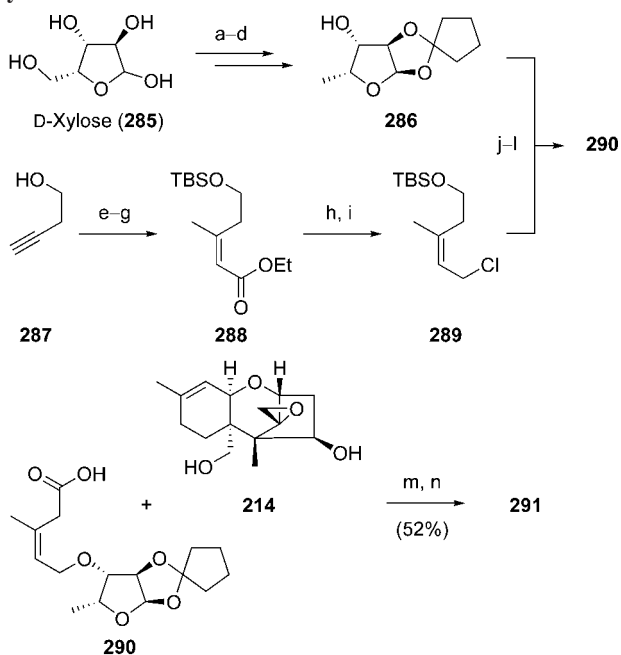
It should be noted that, one year earlier, Still et al. had published the very first total synthesis of verrucarol (**6**). They started from naturally occurring anguidine (**217**) for the preparation of verrucarol (**214**), as well as propargyl alcohol and furfural as precursors of verrucaric acid (**272**) and (*E,Z*)-muconic acid (**273**), respectively.⁸⁰⁸ In 1984, the same research group also reported the first total synthesis of a roridin, namely, roridin E (**262**), as well as of baccharin B5 (**268**).⁷⁸⁵

In contrast to the synthesis of verrucarins (macrocyclic triesters), the macrocycle of roridines cannot be obtained by biomimetic lactonization. The macrocycle synthesis was achieved by intramolecular Horner–Wadsworth–Emmons reaction. The source of the C-6' and C-13' stereogenic centers was D-xylose (**285**), which was easily converted into **286** in four steps. The achiral C-1'–C-5' segment was prepared from butynol (**287**) by ethoxycarbonylation of the lithium acetylide, conjugate methylation, and reduction. Coupling of the fragments **294** and **289** followed after conversion into the chloride; Jones oxidation finally yielded **290** (Scheme 32).

The sesquiterpenoid moiety verrucarol (**214**) was derived from anguidine (**217**)⁹⁴⁶ or obtained by fermentation of *M.*

Scheme 31. Total Synthesis of Verrucaric Acid (214) by Tamm et al.⁸⁰⁹

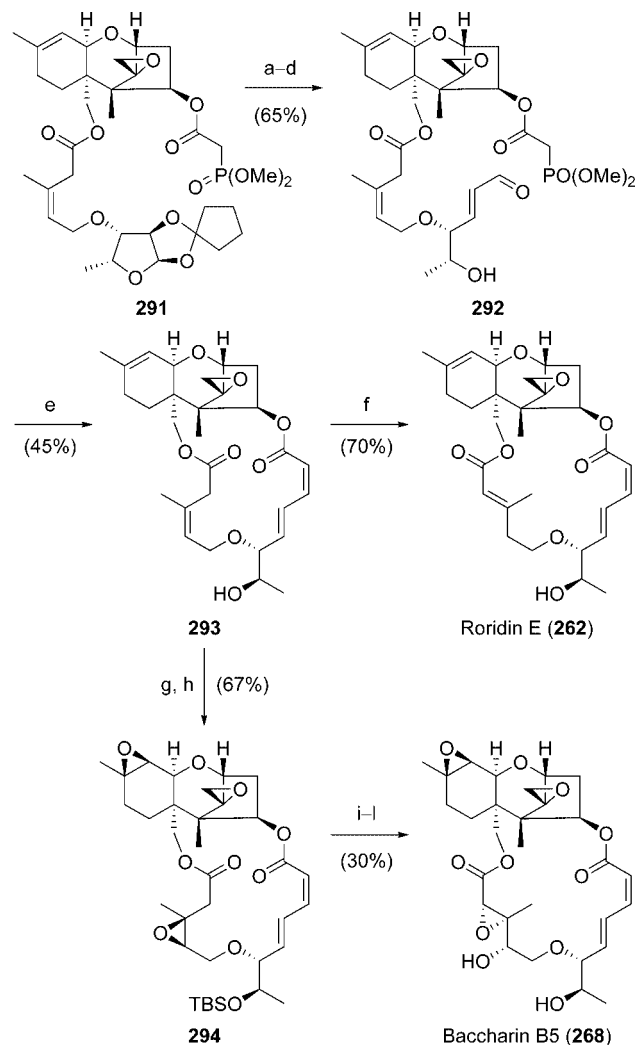
Reagents and conditions: (a) DCC, **282**, DMAP or PPy. (b) DCC, **277**, DMAP or PPy. (c) TBAF, THF. (d) (1) TCBACl, NEt₃, THF; (2) DMAP, toluene, reflux (50%).

Scheme 32. Synthesis of the Components of Roridin E (262) by Still et al.⁷⁸⁵

Reagents and conditions: (a) cyclopentanone, CuSO₄, cat. H₂SO₄. (b) 0.2% HCl. (c) TsCl, py. (d) LAH (65% over 4 steps). (e) TBSCl. (f) (1) BuLi; (2) ClCO₂Et. (g) Me₂CuLi. (h) LAH (45% over 4 steps). (i) NCS, Me₂S. (j) (1) **294**, NaH; (2) cat. TBAI, HMPA. (k) TBAF. (l) CrO₃, H₂SO₄ (75% over 4 steps). (m) DCC, 0.1 mol% 4-PPy (95% yield at 55% conversion). (n) HO₂CCH₂PO(OMe)₂, DCC, 4-PPy (quant.).

verrucaria (ATCC 24751, Strain UV-2). Esterification of its C-15 hydroxy group with **290** yielded an advanced intermediate that was subsequently converted into phosphono ester **291**, the precursor for the ring-closing olefination (see Scheme 33).

The concluding steps for the synthesis of roridin E (**262**) comprised, among others, the conversion into aldehyde **292** by deprotection, diol cleavage, deformylation, and chain elongation through a Wittig reaction. Macrocyclization to

Scheme 33. Total Synthesis of Roridin E (262) and Baccharin B5 (268) by Still et al.⁷⁸⁵

Reagents and conditions: (a) TsOH. (b) NaIO₄. (c) Et₃N, MeOH. (d) Ph₃PCHCHO (65% over 4 steps, *E/Z* = 4:1). (e) K₂CO₃, 18-crown-6 (45%). (f) KO^tBu (70%). (g) TBSOTf, lutidine (95%). (h) *m*CPBA (70%). (i) KO^tBu (90%). (j) ^tBuOOH, VO(acac)₂ (90%). (k) HCO₂H, DEAD, PPh₃ (40% conversion/90% yield). (l) TBAF (99%).

the common precursor **293** of roridin E (**262**) and baccharin B5 (**268**) was achieved by Horner–Wadsworth–Emmons reaction. Isomerization of the (*Z*)-3',4'-double bond into a (*E*)-2',3'-double bond was effected by treatment with a base and yielded roridin E (**262**) after 16 linear steps (Scheme 33).

In the same article, the total synthesis of baccharin B5 (**268**) was reported. The use of achiral C-1'–C-5' precursor **293** and the establishment of stereogenic centers on that segment by substrate-induced stereocontrol are the interesting features of this work. After silyl protection of **293**, the compound was treated with *m*CPBA and yielded the triepoxide **294** as a single product. Stereoselectivity was >15:1 for both the nuclear and the macrocyclic epoxide. Thus, four new stereogenic centers were established, apparently controlled by the conformation of the macrocycle. Elimination of the C-3'–C-4' epoxide yielded the corresponding allylic alcohol with (*E*)-2',3'-double bond. Moreover, allylic epoxidation produced the epimer of baccharin B5 (**268**), which was converted into the natural product by Mitsunobu reaction (inversion of C-4').

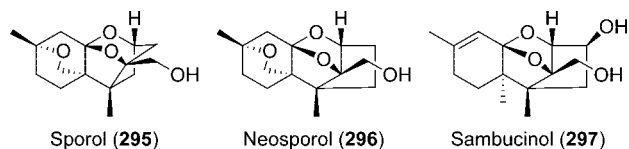
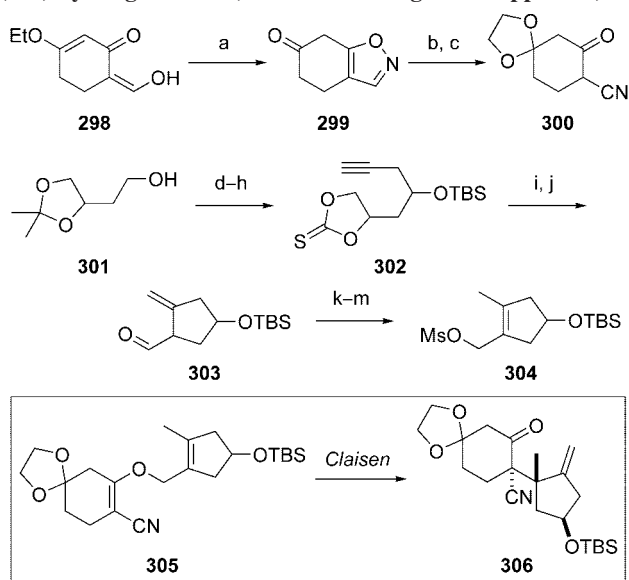


Figure 14. Structures of trichothecenes with a modified skeleton.

Scheme 34. Total Synthesis of Sporol (295) and Neosporol (296) by Ziegler et al. (Claisen Rearrangement Approach)⁸⁰⁰



Reagents and conditions: (a) $\text{NH}_2\text{OH}\cdot\text{HCl}$, aq. EtOH, reflux (76%). (b) $\text{HO}(\text{CH}_2)_2\text{OH}$, TsOH, benzene (98%). (c) $t\text{BuOK}$, HMPA. (d) Swern. (e) propargyl bromide, Zn/Hg, THF (79% over 2 steps). (f) TsOH, MeOH. (g) $(\text{Im})_2\text{C}=\text{S}$, CH_2Cl_2 (51%). (h) TBSOTf, Et_3N , CH_2Cl_2 , 0 °C (41% over 3 steps). (i) Bu_3SnH , AIBN, toluene, reflux (60%). (j) Dess-Martin. (k) DMAP, CH_2Cl_2 (84% over 2 steps). (l) NaBH_4 , MeOH. (m) Ms_2O , Et_3N , DMAP.

2.7.4. Other Small Trichothecenes

Besides the trichothecenes already described, there exists a group of other small representatives of that mycotoxin class with a modified skeleton (non-classical trichothecane structure) as shown in Figure 14

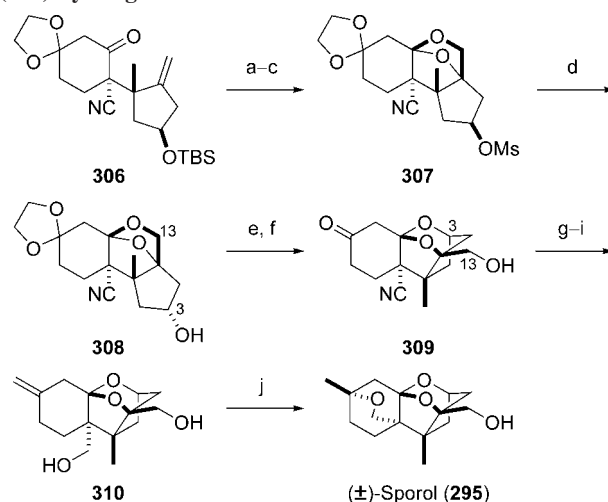
Sporol (**295**) was isolated in 1986.⁷⁷³ The initially proposed structure was synthesized in stages by Ziegler et al. in 1987⁹⁴⁷ and proved to be neosporol (**296**). A structure revision in 1988⁷⁹⁴ including the synthesis of neosporol (**296**)⁷⁹⁵ and the new structure of sporol (**295**) which was confirmed through synthesis in 1992.⁷⁹⁹ A full paper with both syntheses (shown in Schemes 34–36) was published in 1993 also by Ziegler et al.⁸⁰⁰ The crucial step to build up the tertiary stereogenic centers is a Claisen rearrangement.⁸⁰⁰

2.8. Zearalenone and Related Macrolactones

Zearalenone (**4**) and related metabolites belong to the class of benzannulated macrolactones (Figure 15).⁹⁴⁸

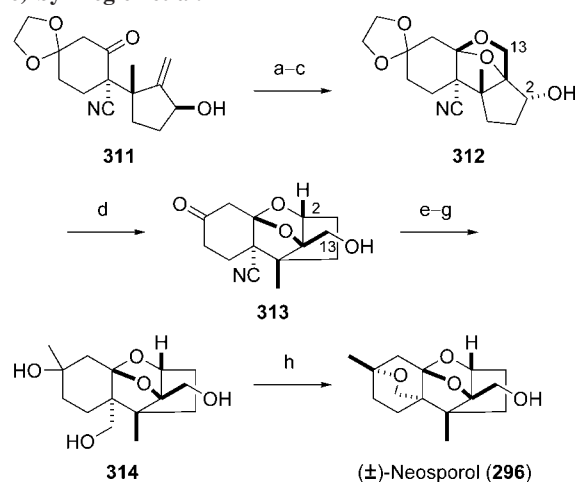
The nonaketide zearalenone (**4**) was first isolated from *Gibberella zeae* (perfect stage of *Fusarium graminearum*) in 1962.⁹⁴⁹ It mostly occurs socialized with other *Fusarium* mycotoxins, albeit it is not categorized as toxic itself; even a sample of 20 g/(kg of weight) does not lead to death in rats.⁹⁵⁰ Its activity in vivo resembles that of hormones; it presumably regulates the formation of the fruiting body of the fungus. This correlates with the anabolic activity of zearalenone (**4**) and its use in feed as an animal-growth

Scheme 35. Completion of the Total Synthesis of Sporol (295) by Ziegler et al.⁸⁰⁰



Reagents and conditions: (a) $\text{HF}/\text{CH}_3\text{CN}$, Na_2CO_3 , CH_2Cl_2 (94%). (b) urea- H_2O_2 , TFAA, Na_2CO_3 , CH_2Cl_2 (45%). (c) Ms_2O , DMAP, Et_3N , CH_2Cl_2 . (d) K_2O , DMSO, 18-crown-6. (e) CSA, CH_2Cl_2 . (f) HCl (32% over 4 steps). (g) $\text{Ph}_3\text{PCH}_3\text{Br}$, $t\text{BuOK}$, THF, reflux (82%). (h) DIBAL; then aq. H_2SO_4 . (i) DIBAL (37% over 2 steps). (j) CSA, CH_2Cl_2 , reflux (45%).

Scheme 36. Completion of the Total Synthesis of Neosporol (296) by Ziegler et al.⁸⁰⁰



Reagents and conditions: (a) $\text{F}_3\text{CCO}_3\text{H}$, Na_2CO_3 , CH_2Cl_2 , 0 °C. (b) Swern (39% over 2 steps). (c) $\text{LiAl}(\text{tBuO})_3\text{H}$, THF (dr = 12:1). (d) 3 N HCl/dioxane, reflux (75%). (e) MeCeCl_2 , THF (48%). (f) LiAlH_4 , then aq. HOAc. (g) LiAlH_4 (80% over 2 steps). (h) $\text{BF}_3\cdot\text{Et}_2\text{O}$, CH_2Cl_2 .

promoter. Otherwise, zearalenone (**4**) possesses antibacterial and carcinogenic properties.⁹⁵¹ However, the best-known trait of zearalenone (**4**) and its derivatives is its estrogenic activity, which was described in 1971 by Mirocha in connection with the discovery of the mycotoxin. α -Zearalenol (**316**) is 3–4 times more active as zearalenone (**4**) or the β -isomer **317**.⁹⁵³ The degree of action can be explained by the topologic resemblance to estradiol and the resulting binding to the human estrogenic receptor $\text{ER}\beta$. Thus, it can cause damage to tissues with high expression rates of this receptor. Given its properties, reports have been produced on mamma carcinomas, fetal skeleton anomalies, and uterotrophic and embryopathic activity.⁹⁵⁴

For zearalenone-like mycotoxins, there exist numerous total syntheses, with the major challenges being the establishment of the stereogenic centers and the formation of the 14-membered macrolactone. Enantioselective approaches

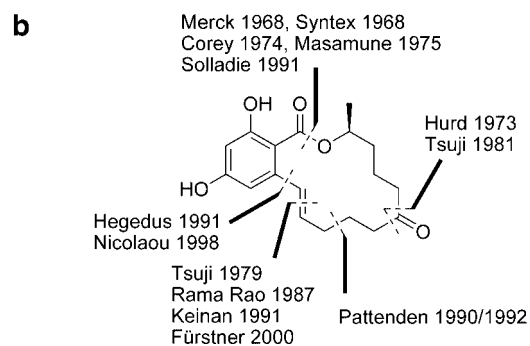
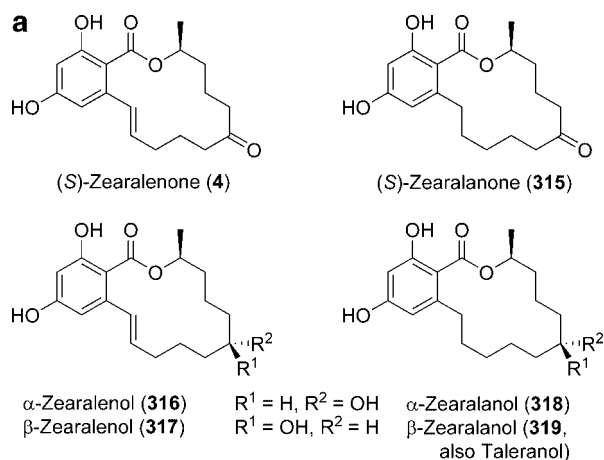


Figure 15. (a) Zearalenone family and (b) overview.

comprise classical resolution methods,⁶⁷³ chiral pool strategies,⁹⁵⁵ and asymmetric methods.⁹⁵⁶ The different approaches for the cyclization step are shown in Figure 15b.

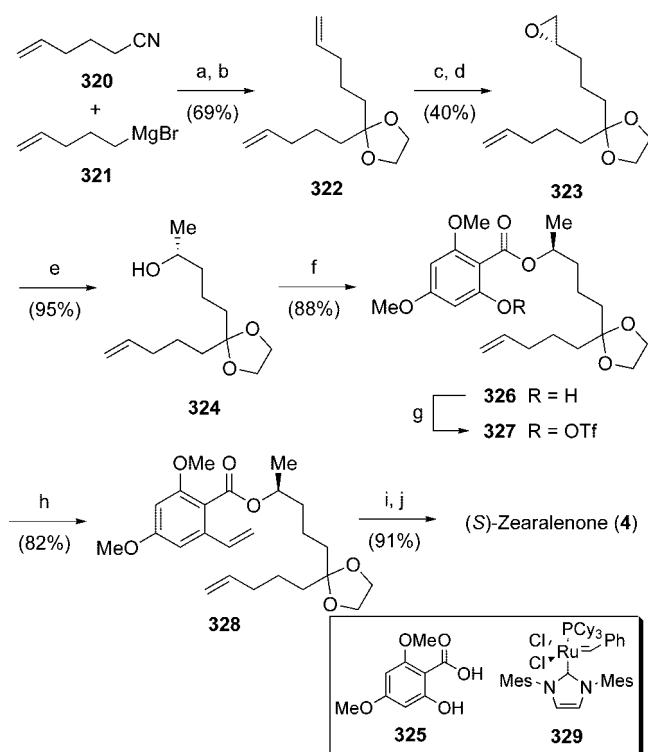
Early total syntheses from the 1960s and 1970s led to racemic material and mostly dealt with macrolactonization methods, such as the very first synthesis of zearalenone (*rac*-**4**) by the Merck group,⁶⁷² as well as the one by Syntex.⁹⁵⁷ Important improvements were facilitated in the mid-1970s with the development of new techniques; for example, with their synthesis of zearalenone, Corey and Nicolaou presented their new mild macrolactonization method using thioesters⁹⁵⁸ as well as the application of the Masamune reaction with thiophilic metal salts.⁹⁵⁹ Other racemic approaches were those of Tsuji⁶⁷¹ or Hurd⁶⁵⁵ with the quite atypical retrosynthetic disconnection at the ketone; the ring closure was accomplished by alkylation of a cyanohydrin or a Dieckmann condensation, respectively.

The first enantioselective synthesis of (*S*)-zearalenone (**4**) used an unusual 14-*endo-trig*-macrocyclization. In the last step of their synthesis, Pattenden et al. reacted a cinnamyl radical intramolecularly with an α,β -unsaturated electrophile to yield 55% of the desired macrocycle.^{676,675}

The first enantioselective synthesis of (*S*)-zearalenone (**4**) using a macrolactonization was reported in 1991 by Solladie et al.,⁹⁶⁰ who generated the chiral precursor via an asymmetric sulfoxide.

Olefinations reactions are involved in a number of total syntheses of enantiopure (*S*)-zearalenone (**4**) as shown through the approaches of Tsuji,⁹⁶¹ Rama Rao,⁹⁶² Keinan,⁹⁵¹ and Fürstner.⁶⁷³ The latter is the most recent total synthesis using a ring-closure metathesis (RCM) with a Grubbs II ruthenium catalyst **329** as the crucial step in the formation of the macrocycle. The enantiomerically pure starting material, epoxide **323**, was obtained by Jacobsen resolution⁹⁶³ (Scheme 37).

Scheme 37. Total Synthesis of (*S*)-(-)-Zearalenone (**4**) by Fürstner et al.⁶⁷³

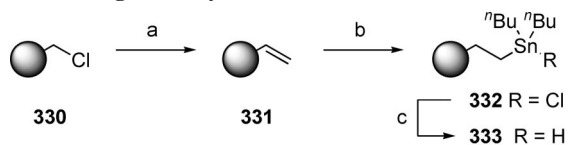


Reagents and conditions: (a) Et₂O, reflux, 3 h (70%). (b) ethylene glycol, PPTS cat., toluene, reflux, 4 h (98%). (c) *m*CPBA, CH₂Cl₂, 16 h (41%). (d) Jacobsen resolution (99%, 41% ee). (e) LiEt₃H, THF, 1 h. (f) **325**, PPh₃, DEAD, Et₂O, rt, 3 h. (g) Tf₂O, py, CH₂Cl₂, 3 h (89%). (h) ethylene (40 bar), LiCl, Et₃N, PdCl₂(PPh₃)₂ (5 mol%), DMF, 90 °C. (i) **4** (5 mol%), toluene, 80 °C, 4 h (91%). (j) (1) aq. acetone, TsOH, 40 °C, 26 h (97%); (2) BCl₃, BBr₃, CH₂Cl₂, 0 °C, 10 min (55%).

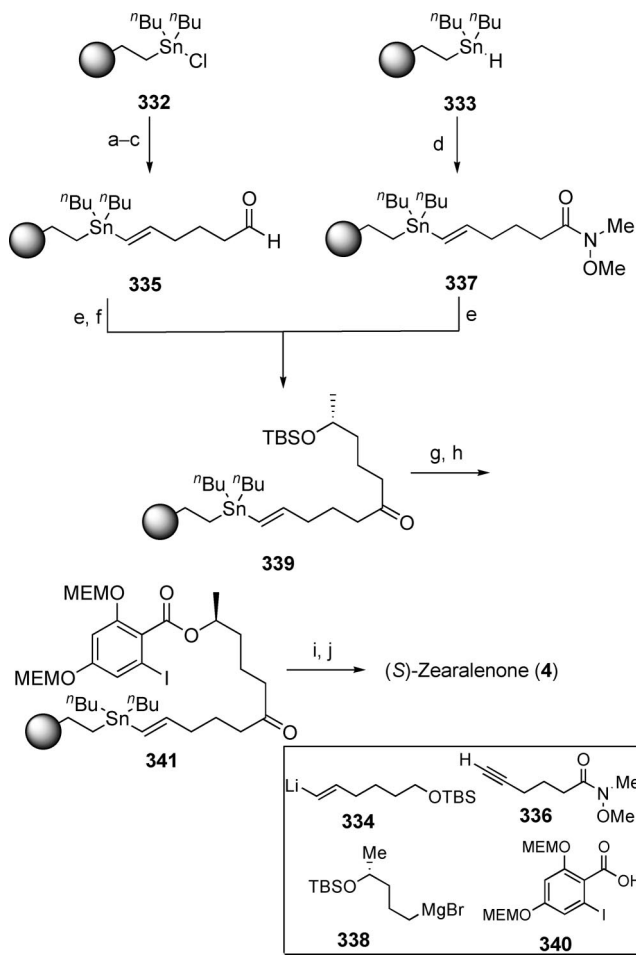
The enantioselectivity was only moderate in that step, but the symmetric starting material **322** was readily available. The chiral epoxide **323** was opened regioselectively with lithium triethylborohydride, so that the secondary alcohol **324** was on hand for esterification with **325** under Mitsunobu conditions. A subsequent Heck reaction gave the styrene derivative **328**, which was cyclized via metathesis. Removal of the protective groups yielded (*S*)-zearalenone (**4**) in 15% yield after 10 steps (Scheme 37).

An alternative retrosynthetic disconnection at the macrocycle can be placed next to the aromatic moiety (see Figure 15) corresponding to a vinyl aryl cross-coupling. This strategy was chosen by Hegedus et al., who conducted a Stille type coupling between an aryl iodide and a vinyl tin reagent in their total synthesis in 1991.⁶⁵² An extension to this approach was presented seven years later by the Nicolaou group (Scheme 39). They used the Stille reaction under cleavage from the polymer resin and concomitant cyclization to the product (Scheme 38).⁹⁵⁵ Starting from tin reagent **332** or **333** on solid supports (for preparation, see Scheme 38), the aliphatic part of the mycotoxin was built up and finally esterified under Mitsunobu conditions with the aromatic moiety **340**. The palladium-catalyzed cross-coupling provided the cyclized product in the liquid phase, so that only the conclusive removal of the protecting groups was not accomplished on the resin.

The related lactones α -Zearalenol (**316**) and β -Zearalenol (**317**) contain two stereogenic centers at the aliphatic macrocycle. However, they lie so far apart that direct substrate control is out of the question even in the presence

Scheme 38. Polymer-Bound Tin Reagent for Stille Coupling under Cleavage and Cyclization


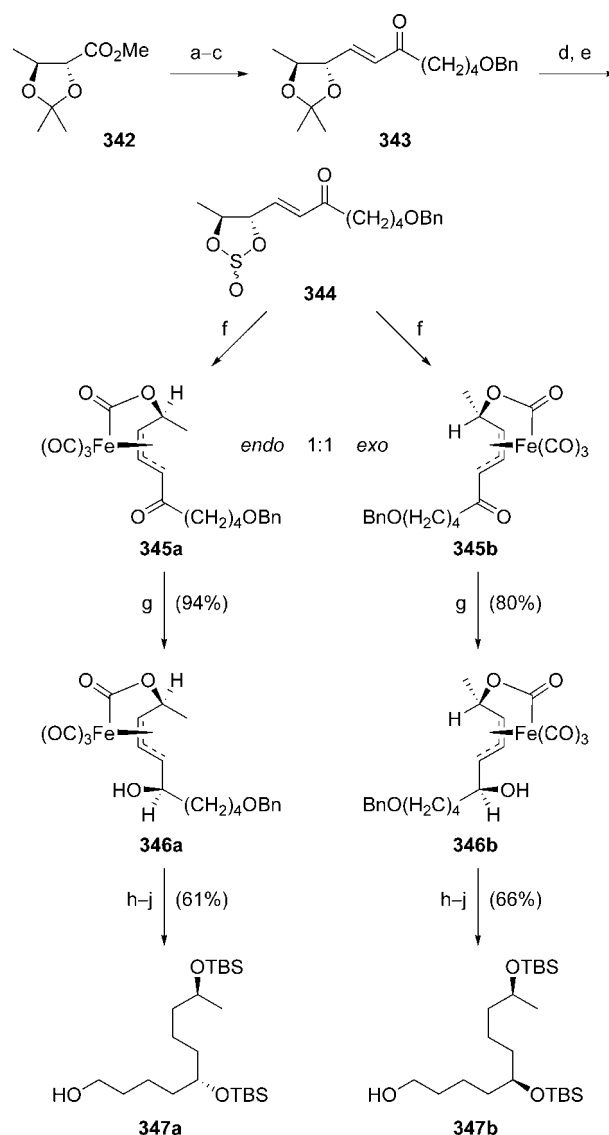
Reagents and conditions: (a) (1) K_2CO_3 , DMSO, 145 °C, 15 h; (2) $Ph_3P=CH_2$, THF, rt, 8 h. (b) nBu_2SnCl_2 , nBu_2SnH_2 , AIBN, $h\nu$, toluene, 0 °C, 4 h (90% over 2 steps). (c) $LiBH_4$, THF, rt, 4 h.

Scheme 39. Total Synthesis of (*S*)-(-)-Zearalenone (4) by Nicolaou et al.⁹⁵⁵


Reagents and conditions: (a) **334**, THF, -78 °C \rightarrow rt, 4 h (87%). (b) TBAF, THF, rt, 5 h (94%). (c) NCS, Me_2S , 0 °C, 15 min; then addition of resin, 0 °C, 1 h; then Et_3N , 0 °C \rightarrow rt, 30 min. (d) **336**, AIBN, toluene, 100 °C, 4 h (90%). (e) **338**, THF, 0 °C \rightarrow rt, 4 h (92% c+e). (f) see c) (97%). (g) TBAF, THF, rt, 13 h. (h) **340**, PPh_3 , DIAD, 0 °C \rightarrow rt, 6 h (76% g+h). (i) $Pd(PPh_3)_4$, toluene, 100 °C, 48 h (54%). (j) 5% HCl/THF (1:2), rt, 5 d (80%).

of one stereogenic center. Regardless, the total synthesis by Ley et al. provides access to both diastereomers.⁹⁵⁶ Formation of the chiral π -allyl tricarbonyl iron complex **345a** or **345b** fixed the conformation of the aliphatic chain, so that the stereoinformation was located closer to the position of the newly built stereogenic center. Thus, the reduction with tripropyl aluminum was conducted asymmetrically, and after decomplexation with sodium triacetoxyborohydride, the epimeric precursors of the macrocycle, **347a** or **347b**, respectively, could be prepared separately (Scheme 40).

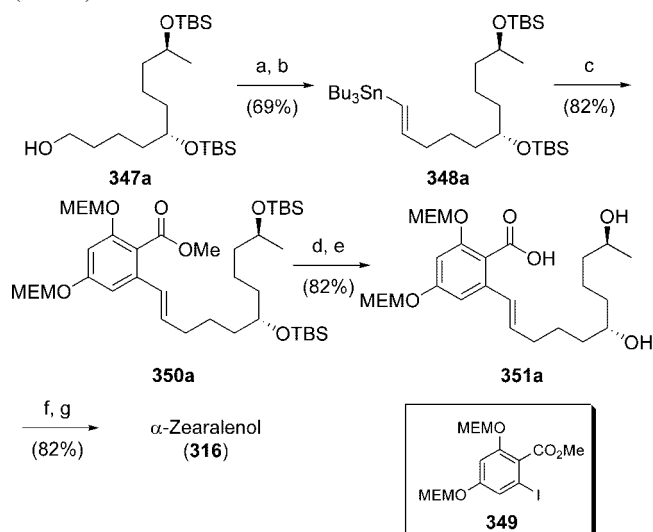
After transformation into the corresponding tin organyl **348a**, and subsequent Stille coupling with **349**, the open-chain precursor **350a** was generated. Removal of the protect-

Scheme 40. Total Synthesis of Zearalenol by Ley et al. (Part 1)⁹⁵⁶


Reagents and conditions: (a) $LiAlH_4$, Et_2O , 0 °C, 2 h. (b) $(COCl)_2$, DMSO, Et_3N , CH_2Cl_2 , -78 °C, 3 h. (c) $(EtO)_2P(O)CH_2CO(CH_2)_4OBn$, NaH, THF, -78 °C, 1 h (83% over 3 steps). (d) $AcOH/H_2O$ (1:1), 40 °C, 24 h (92%). (e) $SOCl_2$, Et_3N , Et_2O , 0 °C, 30 min (89%). (f) $Fe_2(CO)_9$, benzene, sonication, 30 °C, 3 h (70%, dr = 1:1). (g) Al^iPr_3 , CH_2Cl_2 , 0 °C. (h) $NaBH(OAc)_3$, THF, 3 d. (i) TBSCl, imidazole, DMF, 0 °C, 30 min, then rt, 24 h. (j) Pd/C (10%), H_2 , $EtOAc$, 30 min.

ing groups yielded the dihydroxy acid, which was subjected to a Mukaiyama macrolactonization,⁹⁶⁴ and after cleavage of the MEM-groups (β -methoxyethoxymethyl ether), α -Zearalenol (**316**) and β -Zearalenol (**317**) were obtained (Scheme 41).

Further members of this mycotoxin subclass are shown in Figure 16. They also contain a 12- or 14-membered macrocycle but differ in the substitution patterns. Radicicol (**352**), the monocillins, and the pochonins exhibit an α,β -unsaturated ketone for example. Hypothemycin (**355**) is a more exotic relative that has recently been demonstrated as a potent and irreversible inhibitor of selected kinases bearing a cysteine residue in the ATP-binding pocket.⁹⁶⁵ Its structure was falsely assigned at first, and the revised structure was not published until 1993.⁹⁶⁶ A convergent stereospecific synthesis followed in 2002 by Sellès and

Scheme 41. Total Synthesis of Zearalenol by Ley et al.⁹⁵⁶ (Part 2)

Reagents and conditions: (a) $(\text{COCl})_2$, DMSO, Et_3N , CH_2Cl_2 , $-78\text{ }^\circ\text{C}$, 3 h (86%). (b) Bu_3SnCH_2 , CrCl_2 , DMF, $0\text{ }^\circ\text{C}$ (67%). (c) **349**, $\text{Pd}_2(\text{dba})_3$, $\text{P}(\text{fur})_3$, toluene, $100\text{ }^\circ\text{C}$, 4 h (82%). (d) HF-py, pyridine, THF, 12 h (95%). (e) 10 M aq. KOH, $\text{HO}(\text{CH}_2)_2\text{OH}$, $120\text{ }^\circ\text{C}$, 4 h (87%). (f) syringe pump addition of **351a**, Et_3N , MeCN over 10 h to 1-methyl-2-chloropyridinium iodide, MeCN, reflux (64%). (g) 1.5 M aq. HCl, THF, $40\text{ }^\circ\text{C}$ (93%).

Lett.⁹⁶⁷ Queenslandon (**357**), an antifungal agent produced by *Chrysosporium queenslandicum* (class of *Ascomycetes*),⁹⁶⁸ and the Aigialomycins⁶⁵⁴ resemble more closely the zearalene family. Several approaches exist in order to achieve total synthesis, e.g., a concise strategy to the core structure (macrolide) of Queenslandon (**357**) by Maier et al. from the year 2006.⁶⁶⁹ The Aigialomycins, especially Aigialomycin D (**356**), were elaborated by Danishefsky,⁶⁵⁵ Winssinger,⁶⁵⁶ and Pan.⁶⁵⁷ More recently, *cis*-enone resorcylic acid lactones related to hypothemycin have attracted the attention of synthetic chemists for their potent kinase inhibitory activity.⁹⁶⁹

The resorcylic acid lactone radicicol (**352**), first synthesized by Lett et al.,⁹⁷⁰ came into focus after a NCI (National Cancer Institute) screening, as it proved to be a very potent inhibitor

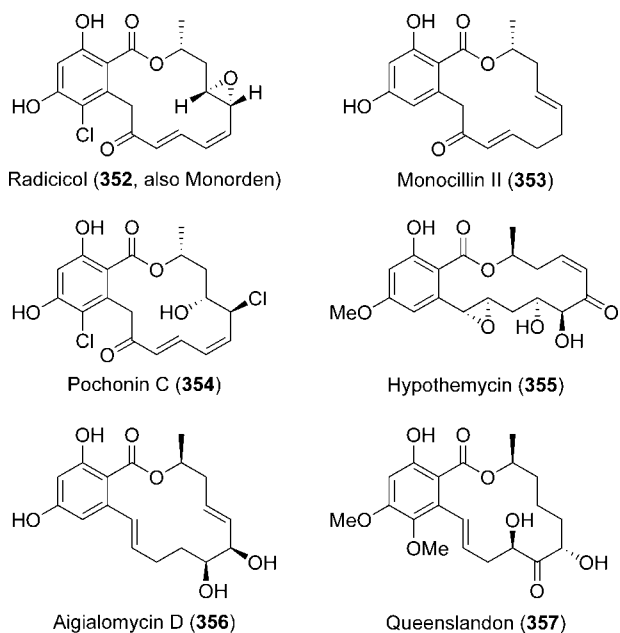
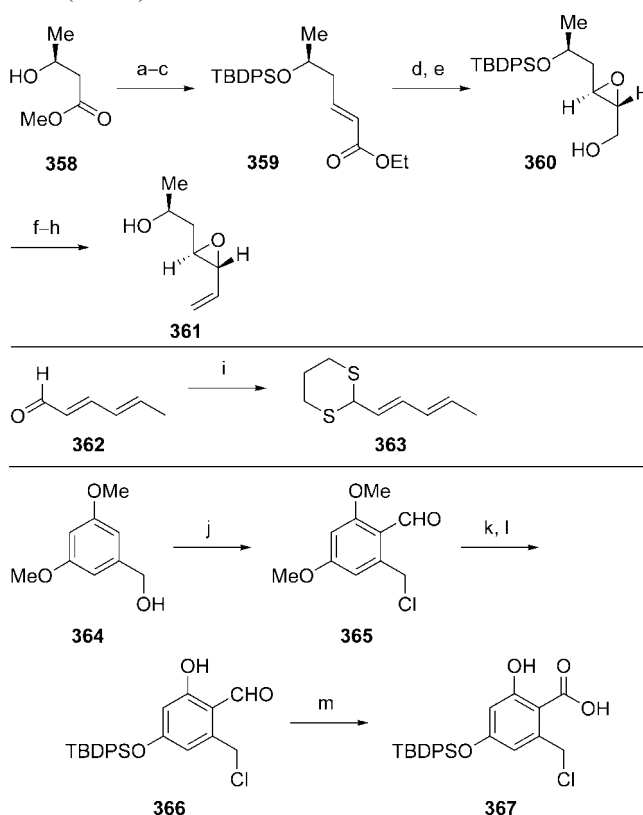


Figure 16. Related mycotoxins.

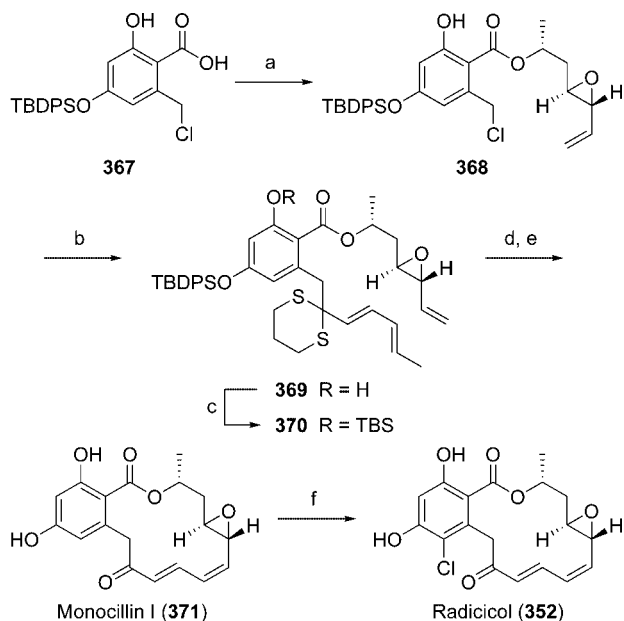
Scheme 42. Total Synthesis of Radicicol by Danishefsky et al.⁶⁶³ (Part 1)

Reagents and conditions: (a) TBDPSCI, imidazole (>95%). (b) DIBAL, $-78\text{ }^\circ\text{C}$ (92%). (c) LiCl, DIPEA, $(\text{EtO})_2\text{P}(\text{O})\text{CH}_2\text{CO}_2\text{Et}$ (95%). (d) DIBAL, $-20\text{ }^\circ\text{C}$ (96%). (e) (+)-DET, $\text{Ti}(\text{O}^i\text{Pr})_4$, $^t\text{BuOOH}$ (90%, >95% ee). (f) $\text{SO}_3\cdot\text{py}$, Et_3N , DMSO (90%). (g) $\text{Ph}_3\text{PCH}_2\text{Br}$, NaHMDS, $0\text{ }^\circ\text{C}$ (82%). (h) TBAF (89%). (i) $\text{HS}(\text{CH}_2)_3\text{SH}$, MgClO_4 , H_2SO_4 (64%). (j) POCl_3 , DMF, $75\text{ }^\circ\text{C}$ (93%). (k) BBr_3 (85%). (l) TBDPSCI (95%). (m) NaClO_4 (95%).

of the ATP-dependent chaperone Hsp90. The latter takes part in the folding of various oncogenic enzymes in cells that are exposed to external stress.^{971–973} Radicicol docks in the ATP-binding pocket with an IC_{50} of 19 nM.⁹⁷⁴ Thus, it is the most potent competitive antagonist of ATP in Hsp90. However, radicicol cannot be employed therapeutically, because it shows no activity in vivo. Efforts have been made to find synthetic alternatives that can be metabolized less rapidly. A prominent example is Cycloproparadicicol, synthesized by Danishefsky et al. with the epoxide oxygen replaced by a methylene group.^{975–977}

The first synthesis of radicicol dimethylether⁹⁷⁸ was published by Danishefsky et al. in 2000. The natural product was not obtained, as the conditions for the ether cleavage resulted in epoxide opening and decomposition. After modification of the strategy, the total syntheses of radicicol (**352**) and monocillin I (**371**) were reported in 2001.⁶⁶³ The highly convergent syntheses were accomplished by the coupling of three key intermediates **361**, **363**, and **367** and final RCM. Alcohol **361** was obtained from (*S*)-3-hydroxybutyric acid (**358**). DIBAL-H-reduction to the aldehyde with subsequent Wadsworth–Horner–Emmons homologation under Roush–Masamune conditions yielded ester **359**. A second reduction to the *trans*-allylic alcohol and Sharpless-epoxidation gave epoxide **360** that was transformed into vinylepoxide **361**, containing all required stereogenic centers, through Parikh–Doering oxidation and Wittig reaction.

The second component, dienyldithiane **363**, was generated from 2,4-hexadienal (**362**) through treatment with pro-

Scheme 43. Total Synthesis of Radicicol by Danishefsky et al.⁶⁶³ (Part 2)


Reagents and conditions: (a) **361**, P(fur)₃, DIAD, benzene, 24 h (75%). (b) **363**, *n*BuLi, -78 °C (50%). (c) TBSCl (88%). (d) Grubbs II catalyst **329**, 42 °C (60%). (e) (1) *m*CPBA; (2) Ac₂O, Et₃N, H₂O, 60 °C; (3) NaHCO₃, MeOH (60%). (f) SO₂Cl₂ (58%).

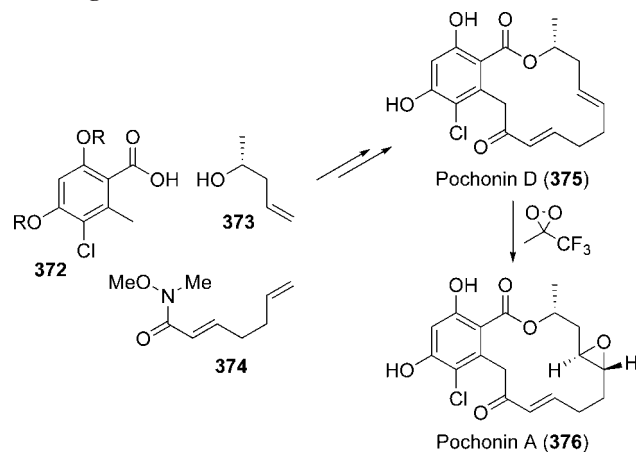
panedithiol. The resorcylic acid derivative **367** was obtained from 3,5-dimethoxybenzylic alcohol (**364**) by Vilsmeier–Haack formylation with concomitant formation of the chloride, manipulation of the protective groups, and Krauss oxidation (Scheme 42).

Esterification of **367** with **361** under Mitsunobu conditions and reaction with the acylanion equivalent of **363** gave the open-chain precursor **369**. The following metathesis with a second-generation Grubbs catalyst resulted in the natural product monocillin I (**371**) that was transformed into radicicol (**352**) by chlorination of the aromatic core (Scheme 43).

A closely related class of mycotoxins has gained attention since its discovery in 2003. The pochonins A–F were isolated from the fermentation broth of *Pochonia chlamydosporia* var. *catenulata* and characterized.⁹⁷⁹ The absolute configuration of pochonin C (**354**) was elucidated by total synthesis in 2004 by Winssinger et al., confirming the assumption that pochonin C is formed by epoxide opening from radicicol (**352**).⁶⁶⁷

Tests concerning the biological properties of the pochonins exhibited activity against *Herpes Simplex* virus as well as antiparasitic activity (*Eimeria tenella*). In contrast to the structurally related zearalenone (**4**), none of the pochonins has an effect on the human estrogenic receptor ER β . Potential antitumor activity was examined after the total syntheses of pochonin D (**375**) and pochonin A (**376**) by the Winssinger group. Following the total synthesis of pochonin C (**354**) and one further solid-phase-assisted synthesis,⁶⁶⁵ the group presented a short route to the simplest representative of the class, pochonin D (**375**), in a study of potential Hsp90 inhibitors.⁶⁶⁸ On the basis of this approach, the synthesis of pochonin A (**376**) followed with just one additional epoxidation step (Scheme 44).⁶⁶⁶

Essentially, the synthesis comprised an esterification of the *ortho*-methylresorcylic acid derivative **372** with the chiral secondary alcohol **373**, an addition to the Weinreb amide **374**, and a metathesis reaction for the macrocyclization. The

Scheme 44. Synthesis of Pochonin D and A According to Winssinger et al.^{666,668}


epoxidation was accomplished with modest selectivity through treatment with methyl(trifluoromethyl)dioxirane.

2.9. Other mycotoxins

Although many mycotoxins are presented in the literature, only a few have yet been synthesized.

2.9.1. Alternaria metabolites

Among the various secondary metabolites produced by *Alternaria* fungi, the resorcylic lactones alternariol (**11**) and alternariol 9-methyl ether (**377**) represent the main toxic metabolites (Figure 17).⁹⁸⁰

Although their toxicity is low compared to other prominent mycotoxins, as, for example, the aflatoxins,⁹⁸¹ their relevance in the context of rotting fruits and crop has led to considerable interest within the synthetic community. Recently, Podlech and co-workers developed an interesting synthetic access to alternariol (**11**), which is based on a Suzuki coupling as the key step.^{65,982} A summary of their synthesis is given in Scheme 45: Suzuki coupling of aldehyde precursor **378** and boronic acid **379** formed biaryl **380**, which, upon oxidation and demethylation, generated a separable mixture of alternariol (**11**) and alternariol 9-methyl ether (**377**). The complete synthesis comprises seven steps and produces **11** and **377** in good overall yield.

In the past decades, various groups have also developed total syntheses of alternariol and structural analogues.^{64,983–985} In this context, a special emphasis has been placed on biomimetic syntheses of **11** and **377**. Harris et al. reported on the cyclization of hemiketals **383** and **384**, which are formed from the triketo ester precursors **381** and **382** upon the cleavage of the benzyl protecting group (Scheme 46).⁹⁸³ The cyclization of these hemiketals under weak basic conditions led to the direct formation of alternariol 9-methyl ether (**377**) and alternariol (**11**), respectively. From a mechanistic viewpoint, this reaction was thought to proceed

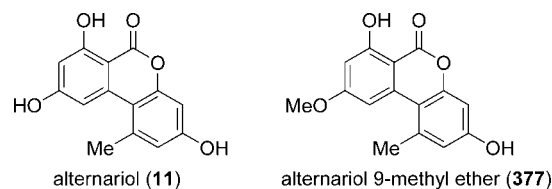
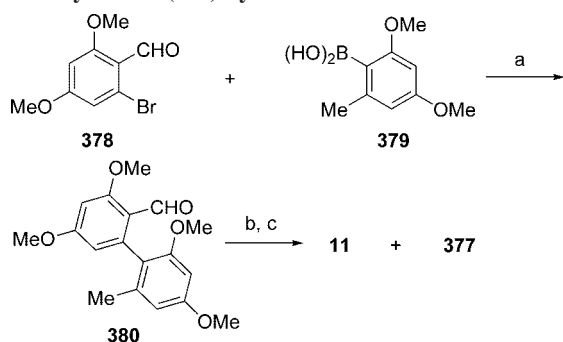
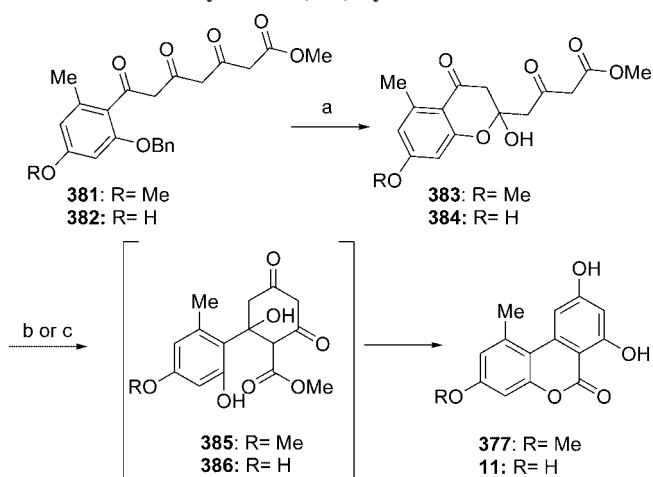


Figure 17. Molecular structures of alternariol (**11**) and alternariol 9-methyl ether (**377**).

Scheme 45. Synthesis of Alternariol (11) and Alternariol 9-Methyl Ether (377) by Podlech et al.⁶⁵

Reagents and conditions: (a) K_2CO_3 , 10 mol% $Pd(PPh_3)_4$, DMF, 100 °C, 4 h (78%). (b) NaH_2PO_4 , $NaClO_2$, 2-methyl-2-butene, $tBuOH/H_2O$ (5:1), rt, 2 h (85%). (c) BBr_3 , CH_2Cl_2 , 0 °C, 24 h (73% of 11) and (20% of 377).

Scheme 46. Biomimetic Synthesis of Alternariol (11) and Alternariol 9-Methyl Ether (377) by Harris et al.⁹⁸³

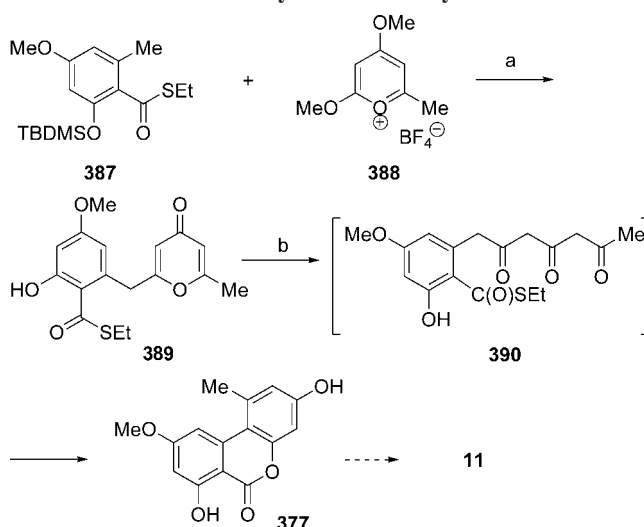
Reagents and conditions: (a) H_2 , Pd/C, EtOH, rt, (86%, R=Me), (70%, R=H). (b) NaOAc, MeOH, rt, 23 h (64%, R=Me). (c) NaOAc, HOAc, MeOH, rt, 9 d, (52%, R=H).

through the hemiketal opening of **383** and **384**, followed by aldol condensation to yield the common intermediates **385** and **386**, which subsequently undergo lactone formation and aromatization to give **11** and **377**. The success of this synthetic strategy gave strong support for the proposed mechanism of biosynthesis, which is also likely to proceed through aldol condensations and lactone formation of a C-14-polyketide chain.¹⁵

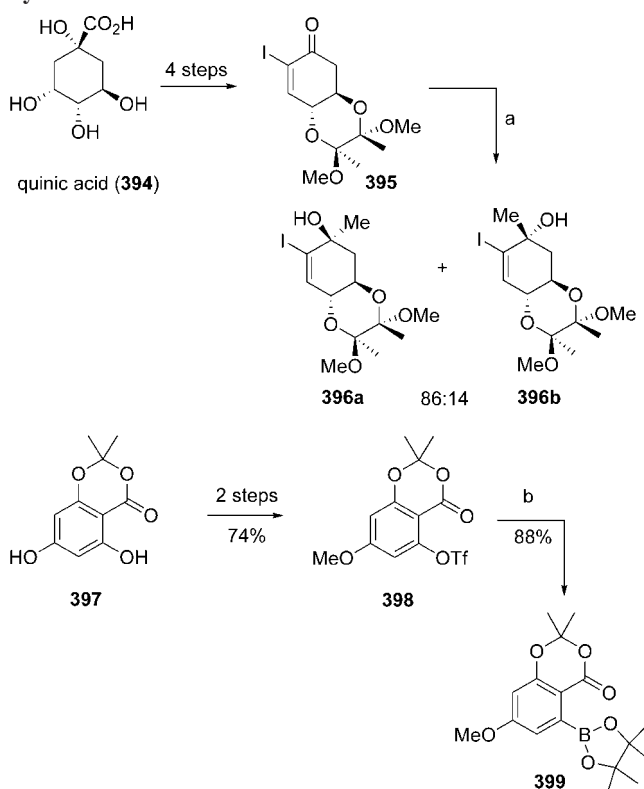
Another biomimetic approach to **11** and **377** was reported by Staunton and co-workers.⁹⁸⁴ They employed a nucleophilic addition to the β -carbon of pyrylium salts as the key step. To this end, the addition of lithiated orsellinate thioester **387** to the tetrafluoroborate pyrylium salt **388** yielded pyrone **389**, after the cleavage of the silyl protecting group (Scheme 47). This pyrone served as a precursor for the tricarbonyl compound **390**, which is believed to be a biosynthetic intermediate in the formation of **11** and **377**. Treatment of pyrone **389** with alcoholic sodium hydroxide solution led to the exclusive formation of alternariol 9-methyl ether **377**, which was then transformed into alternariol **11**.⁹⁸⁵

By altering the reaction conditions for the formation of **377**, the proposed cyclization intermediate **390** could also be isolated; thus, further studies toward its potential in vivo behavior were performed.

Altenuene (**391**), isoaltenuene (**392**), and dehydroaltenuin (**393**) represent minor secondary metabolites of *Alternaria*

Scheme 47. Biomimetic Synthesis of 11 by Staunton et al.⁹⁸⁴

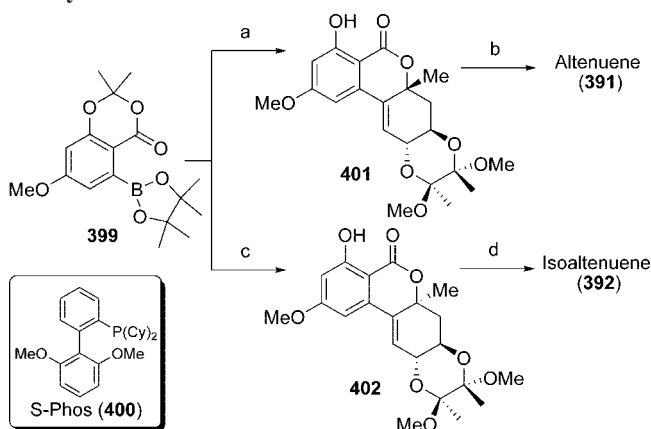
Reagents and conditions: (a) LDA, THF, -78 °C, acidic workup, (20%). (b) NaOH, MeOH/ H_2O (1:4), acidic workup, (80%).

Scheme 48. Preparation of Key Intermediates 396 and 399 by Podlech et al.⁵²

Reagents and conditions: (a) 2 equiv. MeMgBr, THF, -40 °C \rightarrow rt, (68%). (b) 3 equiv. pinacol borane, 3 equiv. Et_3N , 5 mol% $Pd(PPh_3)_4$, dioxane, 80 °C, 2 h, (88%).

fungi and a variety of other species (Figure 18).^{70,71,986} While altenuene displayed interesting cytotoxic activity in screenings for biological activity, dehydroaltenuin was reported to be a strong mammalian DNA-polymerase α inhibitor.^{987,988}

Very recently, Podlech et al. published a short total synthesis of altenuene (**391**) and isoaltenuene (**392**) starting from quinic acid (**394**) and comprising 10 synthetic steps.⁵² The synthesis of the key intermediates is outlined in Scheme 48: according to the literature, 2-iodocyclohexenone **395** was prepared starting from quinic acid (**394**). Reaction of **395** with methyl magnesium bromide gave a mixture of diaster-

Scheme 49. Completion of the Total Synthesis of 391 and 392 by Podlech et al.⁵²


Reagents and conditions: (a) **396b**, 2 mol% Pd(OAc)₂, 4 mol% **400**, 3 equiv. Cs₂CO₃, dioxane/H₂O 5:1, 80 °C, 2 h. (70%). (b) TFA/H₂O 9:1, 10 min., RT, (55%). (c) **396a**, 2 mol% Pd(OAc)₂, 4 mol% **400**, 3 equiv. Cs₂CO₃, dioxane/H₂O 5:1, 80 °C, 2 h. (72%). (d) TFA/H₂O 9:1, 10 min., RT, (62%).

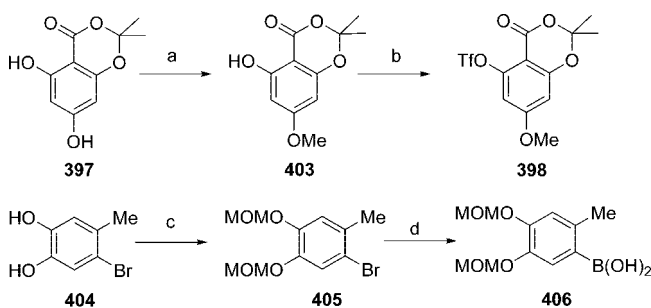
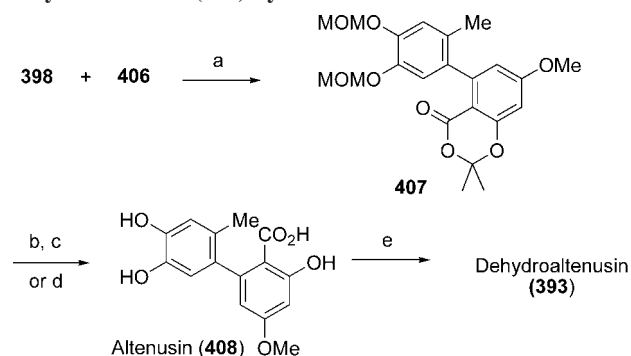
omers **396a** and **396b** that could be separated by chromatography and employed in the synthesis of **391** and **392**, respectively. Boronic ester **399**, on the other hand, was prepared in three steps starting from commercially available acetal **397** (Scheme 48).

Subsequent Suzuki coupling of **396a,b** and boronic ester **399** was most effectively accomplished using the S-Phos ligand (**400**) developed by Buchwald and co-workers,⁹⁸⁹ together with palladium acetate as the catalyst precursor (Scheme 49). Interestingly, application of these reaction conditions resulted not only in Suzuki coupling but also in the direct formation of lactones **401** and **402** through cleavage of the acetal group in precursor **399**. Consequently, lactones **401** and **402** could be isolated in good yields and gave altenuene (**391**) and isoaltenuene (**392**), respectively, upon acidic cleavage of the diol protecting group (Scheme 49).

When comparing the absolute configuration of synthesized altenuene (**391**) with a microbiologically prepared sample (commercially available through Sigma-Aldrich), Podlech and co-workers discovered that the enantiomeric excess of natural altenuene is only 2%. Although further experiments regarding this finding have not thus far been performed, it seems likely that the low enantiomeric excess is related to the biosynthesis of altenuene and its related metabolites.

Dehydroaltenuenin (**393**) has been isolated from *Alternaria tenuis* and a variety of other fungi. Because of its promising biological activity,⁹⁸⁸ which has been mentioned above, it is an interesting target for total synthesis. In 2003, Takahashi and co-workers reported the first total synthesis of **393** (Scheme 51).^{61,69} By employing a Suzuki coupling as the key step,⁹⁸² **393** was reduced to triflate **397** (compare to Scheme 47) and aryl boronic acid **406** as the key precursors, which were readily available in only a few synthetic steps (Scheme 50).

Palladium-catalyzed cross-coupling of **398** and **406** gave rise to biaryl **407** in good yield, which was subsequently transformed into altenuenin (**408**) by sequential cleavage of the protecting groups (Scheme 51). Essentially the same results could be achieved by simply treating biaryl **407** with boron trichloride, thus cleaving both the methoxymethyl (MOM) and acetonide groups. The final oxidation of altenuenin (**408**)—yielding dehydroaltenuenin (**393**)—was performed using iron trichloride, producing an 82% yield.

Scheme 50. Synthesis of Key Intermediates 398 and 406 by Takahashi et al.^{61,69}

Scheme 51. Completion of the Total Synthesis of Dehydroaltenuenin (393) by Takahashi et al.^{61,69}


Reagents and conditions: (a) 5 mol% Pd(PPh₃)₄, 1.50 equiv. K₃PO₄, 1.00 equiv. KBr, dioxane, 100 °C, (93%). (b) 2N KOH, EtOH, 60 °C. (c) 10% HCl-MeOH, CH₂Cl₂, rt, (64% over two steps). (d) 10.0 equiv. BCl₃, CH₂Cl₂, 0 °C → rt, (60%). (e) FeCl₃, aq. EtOH, rt, (82%).

In summary, the total synthesis of racemic **393** comprised seven steps with an overall yield of 18%. Further studies regarding an asymmetric synthesis of **393** or structural analogues might be difficult given that it racemizes quickly via a five-membered dehydroaltenuenin II (see Scheme 69).

2.9.2. Skyriins

The skyriins represent an interesting class of bisanthraquinone natural products that have recently attracted considerable interest. Some of the most prominent members (see Figure 19) of this class of mycotoxins are cytoskyrin A (**9**),¹²⁹ rugulin (**409**),⁹⁹⁰ and rugulosin (**410**, Figure 19).^{134,991}

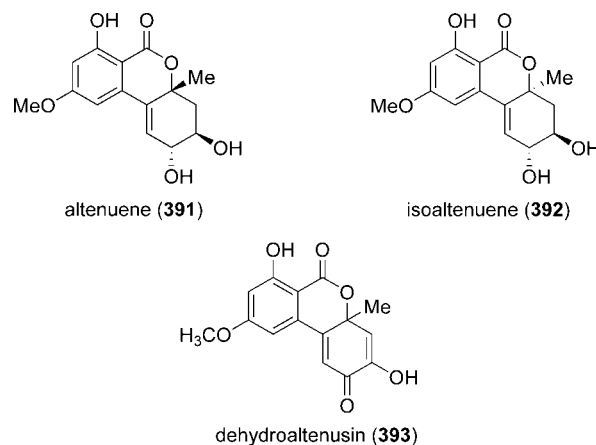


Figure 18. Molecular structures of altenuene (**391**), isoaltenuene (**392**), and dehydroaltenuenin (**393**).

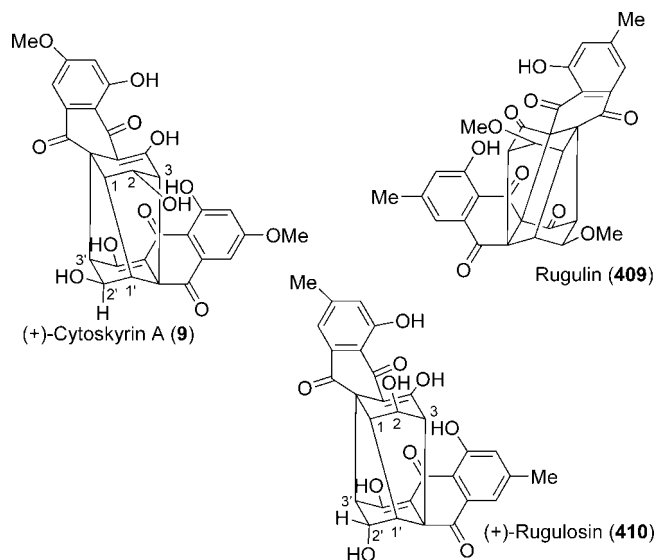


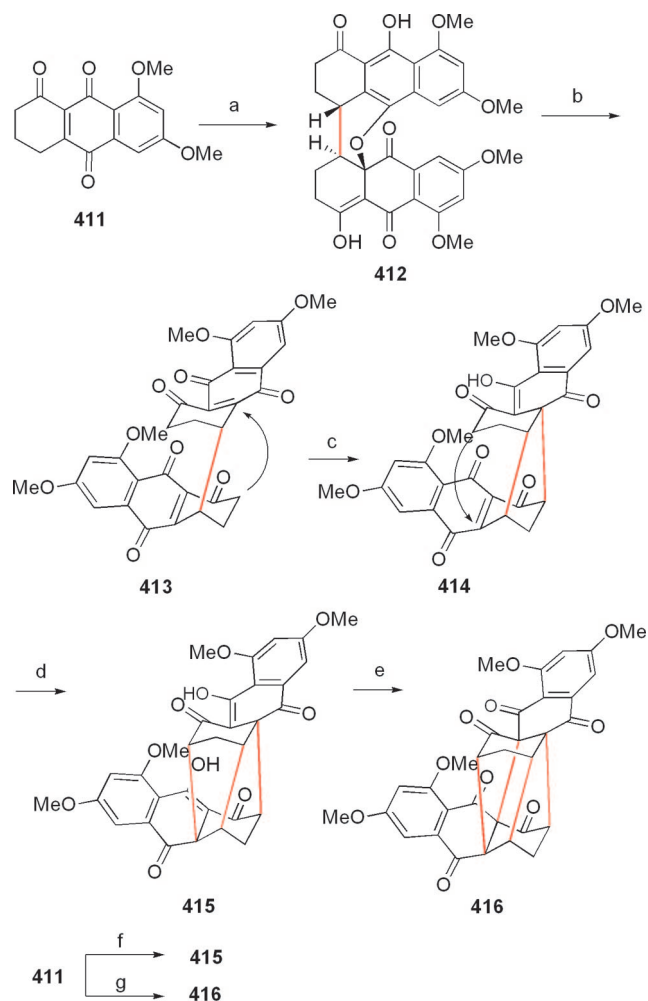
Figure 19. Prominent bisanthraquinone natural products.

Isolated from an endophytic fungus (*Cytospora* sp.), cytoskyrin A (**9**)¹²⁹ displays particularly promising biological activity such as strong cytotoxicity (12.5 ng mL^{-1}) in the biochemical induction assay (BIA). Because of these facts and their challenging cage-like structures, the skyrins represent interesting targets for total synthesis.

Recently, Nicolaou and co-workers developed an elegant synthetic access to cytoskyrin A (**9**)¹²⁹ and rugulosin (**410**),⁹⁹¹ which was based on a cascade reaction (“cytoskyrin cascade”).¹³² In preliminary model studies, it was established that readily available quinone **411** could be converted into **412** in a single step involving enolization and dimerization (Scheme 52). The dimer **412** could in turn be oxidized to yield bisanthraquinone **413** in good yield. With this intermediate in hand, further studies toward cage-like model systems were performed. In this context, exposure of **413** to mild basic conditions resulted in C–C-bond formation through enolization, furnishing the dimeric intermediate **414**. However, an even more complex structure **415** could be obtained through prolonged exposure of **413** to basic conditions.

Although the step-by-step formation of the cytoskyrin-type structure **415** and its transformation into the rugulin-type structure **416** (through oxidation) were themselves impressive, the Nicolaou group found an even more pleasing solution to this synthetic challenge. Since all synthetic steps mentioned previously only required weak bases (NEt_3) or oxidants (MnO_2), it was reasoned that **415** and **416** should also be accessible in a one-pot cascade sequence. Consequently, **411** could be converted with excellent yields into the nonacyclic cytoskyrin system **415** in one synthetic operation involving five steps (enolization–dimerization–oxidation–double intramolecular Michael reaction). Under very similar conditions, **411** was transformed into the rugulin-type model system **416** in a one-pot-procedure. These elegant transformations, which were elucidated by careful reactivity analysis of the given systems, highlight the power of cascade reactions in targeting complex molecular structures.⁹⁹² With these transformations in hand, the stage was now set for the total synthesis of skyrin natural products (**9**, **409**, **410**). Indeed, Nicolaou and co-workers reported the total synthesis of rugulosin (**410**, Figure 20) and 2,2'-*epi*-cytoskyrin A (**417**) shortly after the discovery of the cytoskyrin cascade.¹³⁰

Scheme 52. Synthesis of Model Compounds by Nicolaou et al.¹³²



Reagents and conditions: (a) CSA, CH_2Cl_2 , 25°C , 1 h (94%). (b) MnO_2 , CH_2Cl_2 , 25°C , 1 h (83%). (c) Et_3N , CH_2Cl_2 , 25°C , 1 h (65%). (d) Et_3N , CH_2Cl_2 , 45°C , 16 h (95%). (e) MnO_2 , CH_2Cl_2 , 25°C , 20 h (95%). (f) CSA, CH_2Cl_2 , 25°C , 1 h; then MnO_2 , 25°C , 88 h (75%). (g) CSA, CH_2Cl_2 , 25°C , 1 h; then MnO_2 , Et_3N , 45°C , 36 h (66%).

When comparing the model systems (**412**–**416**, Scheme 52) with the targeted natural products **410** and **417**, it becomes apparent that two hydroxyl functions (at C2 and C2') had to be attached to the molecular structure of the model systems. However, the introduction of hydroxyl-substituted precursors into the cytoskyrin cascade was considered a challenge due to possible elimination reactions prior to the first dimerization step in the cascade.⁹⁹³ Moreover, issues regarding the stereochemical outcome of the early dimerization reaction of the cytoskyrin cascade had to

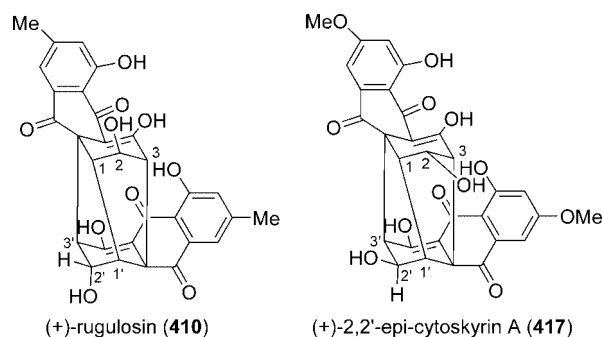


Figure 20. Rugulosin (**410**) and 2,2'-*epi*-cytoskyrin A (**417**).

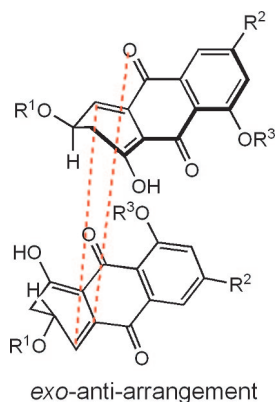


Figure 21. Suggested spatial arrangement for the dimerization of **418**.

be addressed, since a chiral starting material was employed, leading to the formation of three new stereogenic centers. In this context, several spatial arrangements for the dimerization were considered and it was argued that an arrangement as in Figure 21 (*exoanti*) should be favored due to steric preferences.

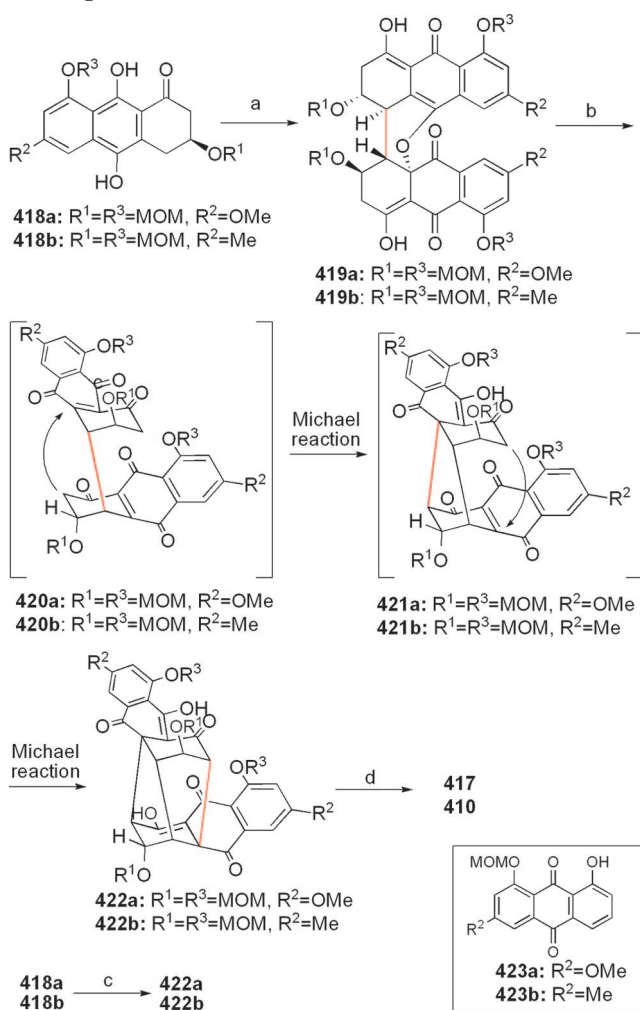
Indeed, exposure of readily available anthradihydroquinones **418a** and **418b** to the previously developed oxidative conditions¹³² led to the formation of the dimeric compounds **419a** and **419b** as single diastereomers and in good yield (Scheme 53).

This reaction presumably proceeds via oxidation of the anthradihydroquinone moiety followed by enolization and dimerization. After careful optimization of the workup procedures and the reaction conditions, compounds **419a** and **419b** could then be transformed into the highly complex precursors **422a** and **422b** through another cascade process involving an oxidation and two Michael reactions. Most importantly, further optimization of the reaction conditions allowed for the direct transformation of tricyclic compounds **418a** and **418b** into precursors **422a** and **422b** through a fascinating seven-step cascade. An interesting feature of these cascade processes is their high selectivity. The only side-products that could be isolated were monomers **423a** and **423b** resulting from the aforementioned elimination/aromatization process. Starting from precursors **422a** and **422b**, the last step that remained was the removal of the acetal protective groups, which could easily be achieved by exposure to acidic conditions, yielding (+)-2,2'-*epi*-cytoskyrin **417** and (+)-rugulosin **410** in excellent yield. In summary, these impressive total syntheses of bioactive mycotoxins should serve as inspiring examples for the power of cascade sequences to attain highly complex molecular targets.

2.9.3. Xanthenes

The xanthone structure is a very interesting framework that exhibits a large variety of pharmacological activities.⁹⁹⁴ The biological activity of these compounds is due to their tricyclic scaffold but varies depending on the nature and position of the substituents. While DMXAA (**424**, Figure 22) is undergoing clinical trials as an antitumor agent, mangiferin (**425**) possesses antioxidant, anti-inflammatory, immunomodulatory, and antiviral effects. Because the range of natural xanthenes is relatively limited due to their biosynthetic pathways, there has been a growing interest in the development of synthetic xanthenes with different substitution pattern.^{995,996}

Scheme 53. Synthesis of (+)-2,2'-*epi*-Cytoskyrin A (**417**) and (+)-Rugulosin (**410**)^{130,131}



Reagents and conditions: (a) MnO₂, CH₂Cl₂, 25 °C, 1 h (64% **419a**), (32% **419b**). (b) MnO₂, Et₃N, CH₂Cl₂, 45 °C, 12 h (71% **422a**), (81% **422b**). (c) MnO₂, CH₂Cl₂, 25 °C, 10 min; then MnO₂, Et₃N, 45 °C, 12 h (60% **422a**), (50% **422b**). (d) conc. HCl, MeOH, THF, 60 °C, 12 h (93% **417**), (98% **410**).

Because of their importance for medicinal chemistry, recent developments in isolation and characterization of naturally occurring xanthenes, the classic and new synthetic routes to obtain them, together with new insights into their biological activities, have recently been reviewed.⁹⁹⁷ For this reason, we will focus our interest herein on the synthesis of tetrahydroxanthenones, which represent the core of many natural products (see examples **10**, **426–428** in Figure 22) but have so far received limited attention, with only a few stereoselective syntheses of these natural products having been reported.^{998,999}

Because the structure of diversinol (**426**) is very similar to that of the secalonic acid monomers (compare structures of **10** and **426**, Figure 22),⁸⁴⁰ the total synthesis of diversinol (**426**) was expected to be a step toward the total synthesis of the secalonic acids. In 2006, Bräse et al. published the first total synthesis of diversinol (**426**) in racemic form (Scheme 54).⁸³⁴ The synthetic sequence was based on access to the tetrahydroxanthenone framework that had previously been developed by the same group in 2004¹⁰⁰⁰ and consisted of the domino oxa-Michael-aldol condensation between a substituted salicylic aldehyde (**429**) and 4-hydroxycyclohexenone (**430**). The tetrahydroxanthenone derivative **431**

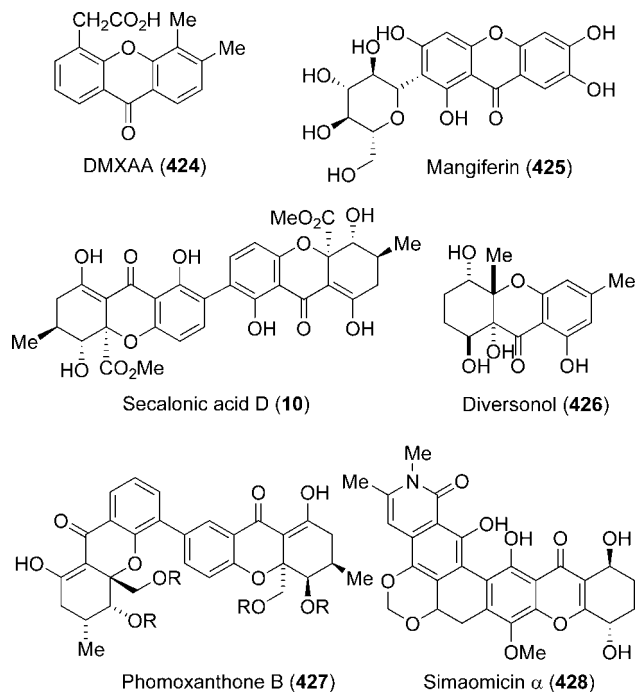
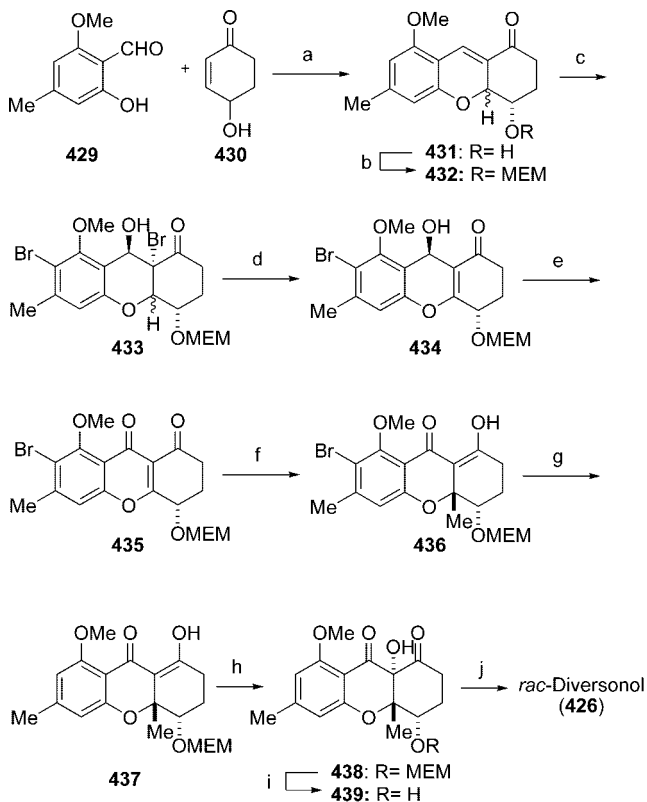


Figure 22. Bioactive natural and synthetic xanthenes.

Scheme 54. First Total Synthesis of Racemic Diversonol (426) by Bräse et al.⁸³⁴



Reagents and conditions: (a) imidazole, dioxane/H₂O, sonication, 9 d (61%). (b) MEMCl, *i*PrNEt, CH₂Cl₂, rt, 3 h (75%). (c) tetrabutylammonium tribromide, THF/H₂O, rt, 5 h (52%). (d) DABCO, dioxane, rt, 16 h (53%). (e) TPAP, NMO, CH₂Cl₂/CH₃CN, sonication (40%). (f) MeLi, CuCN, Et₂O, -78 °C, 5 h (52%). (g) *t*BuLi, THF, -78 °C, NaHCO₃, 4 h (93%). (h) magnesium monoperoxophthalate, EtOH, rt, 5 h (57%). (i) BBr₃, CH₂Cl₂, rt, 7 h (40%). (j) NaBH₄, MeOH, -78 °C, 20 min (66%).

obtained after this reaction was further functionalized. Starting with the protection of the free hydroxyl functionality as a MEM ether, the resulting derivative **432** was then

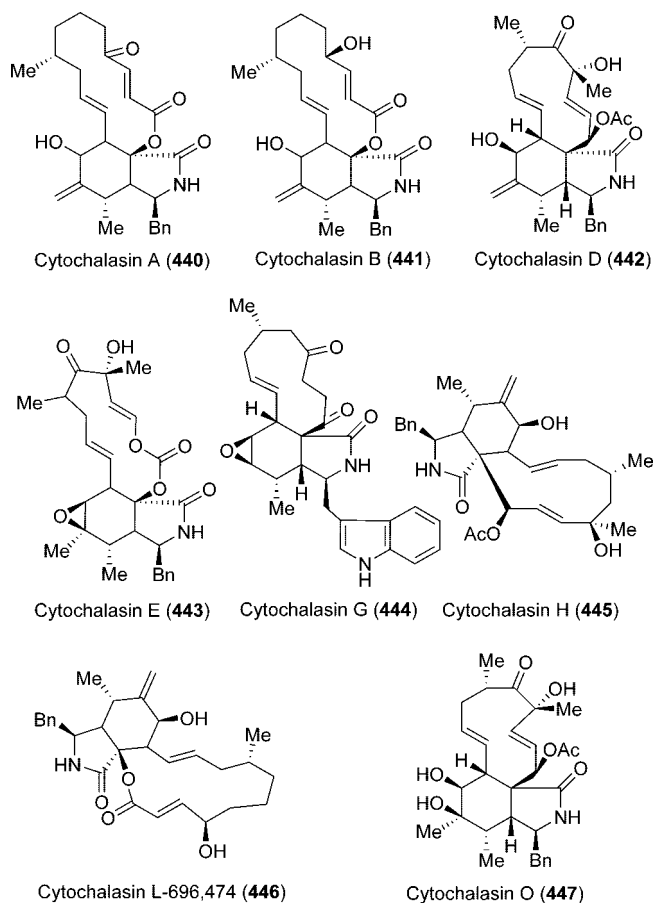


Figure 23. Structure of some Cytochalasins with different macrocyclic fused rings.

stereoselectively converted in the bromohydrin **433**, which after elimination of hydrogen bromide yielded the conjugated system **434**. Oxidation under Ley conditions to the corresponding diketone **435** and subsequent cuprate addition allowed the incorporation of the methyl substituent in position 4a. The concluding stages comprised dehalogenation, diastereoselective hydroxylation on C9a, and final MEM deprotection.

2.9.4. Cytochalasins

The cytochalasins are metabolic products of microorganisms, and in some cases of molds, of considerable importance because of their potent biological activity. As a matter of fact, their name is derived from Greek (*cytos*, cell; *chalsis*, relaxation) owing to this unique biological property.

The isolation of the first two substances of this class and the determination of their structures were achieved at about the same time—independently of each other—by Tamm¹⁰⁰¹ and by Aldridge et al.¹⁰⁰² in the research laboratories of ICI Ltd. in England. To date, more than 80 cytochalasins have been isolated from a range of fungi such as *Phomopsis*,^{260,263} *Chalara*,¹⁰⁰³ *Hyposylon*,¹⁰⁰⁴ *Xylaria*,^{237,1005} *Daldinia*,^{1006–1008} *Pseudeurotium*,²⁶⁸ and *Phoma exigua*.²⁷⁰

Cytochalasins are structurally characterized by the presence of a hydrogenated and highly substituted bicyclic isoindolone unit fused to a macrocyclic ring. The macrocyclic appendage varies widely within the cytochalasins. It can either be a lactone, a carbonate, or more frequently a carbocycle as exemplified by cytochalasin B, E, and D, respectively (see Figure 23), and seems to play an important role in the determination of biological activity.

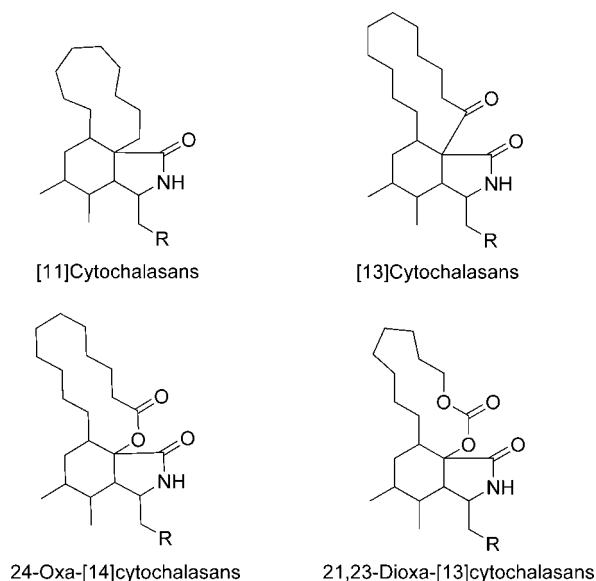


Figure 24. Nomenclature of the Cytochalasan scaffold.

The systematic nomenclature applied to cytochalasans consists of taking the hydrogenated isoindole as core structure (including the macrocycle and carbon substituents on the isoindole except for the benzyl ring) and naming it “cytochalasan”. The size of the macrocycle is indicated by the corresponding number in brackets (see Figure 24).

The total synthesis of cytochalasans has been of considerable interest for several years; both inter- and intramolecular Diels–Alder reactions have been used to assemble the isoindolone components stereoselectively. The stereogenic centers around the macrocyclic ring can be introduced either before or after the Diels–Alder reaction. In this sense, the general synthetic routes toward the formation of cytochalasans can be divided into two strategies:

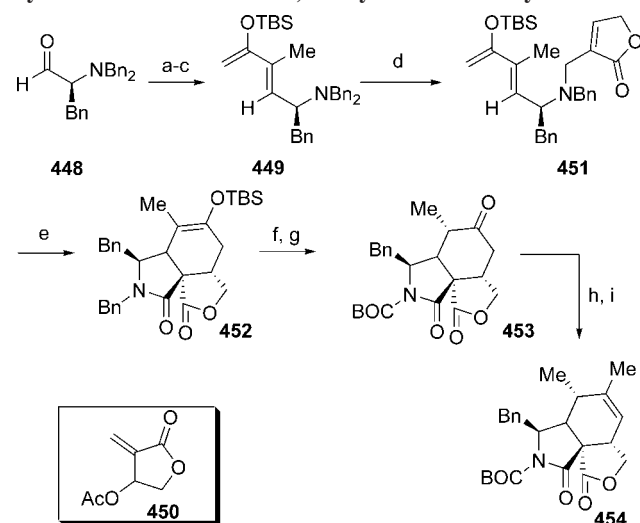
- (1) Simultaneous formation of the six-membered isoindolone ring and the large macrocycle in a late-stage Diels–Alder cyclization.^{253,258,273,1009–1011}
- (2) Initial formation of the isoindolone core (through the use of an intramolecular Diels–Alder reaction) and subsequent appendix of the macrocycle.^{274,240}

Although the Diels–Alder strategy was most often used to generate the eleven-membered ring of the [11]cytochalasans, other reaction types have been performed with this purpose, such as ring-expansion,^{275,1012,1013} ring-fragmentation,²⁴⁹ Pd-assisted macrocyclizations,¹⁰¹⁴ or Reformatsky reactions.¹⁰¹⁵ Moreover, most of the cytochalasans are commercially available¹⁰¹⁶ for biological studies, which explains why there are only a few total syntheses known in the field.

Cytochalasin B was the first cytochalasin isolated (together with cytochalasin A (**440**), *dehydropomin*) and was originally named *phomin*.¹⁰⁰¹ Cytochalasin A and B are both [14] cytochalasans and are produced by *Helminthosporium dematioideum*.

The first total synthesis of cytochalasin B was reported by Stork and co-workers²⁴⁵ in 1978 and consisted of the simultaneous formation of the isoindolone core and the macrocyclic fused ring in a late-stage intramolecular Diels–Alder condensation. Most recently, Myers and Haidle²⁴⁷ have developed an enantioselective and convergent synthetic route in which the isoindolone core is synthesized first by a Diels–Alder reaction, with the macrocyclic appendage (previously functionalized with the right stereo-

Scheme 55. Synthesis of a Key Tricyclic Precursor (454) to Cytochalasins B and L-696,474 by Haidle and Myers²⁴⁷



Reagents and conditions: (a) Diethyl 3-oxo-2-butylphosphonate, Ba(OH)₂, THF–H₂O, 23 °C. (b) 2,3-Dichloro-5,6-dicyanobenzoquinone, CH₂Cl₂–pH 7 buffer, 23 °C. (c) *tert*-Butyldimethylsilyl trifluoromethanesulfonate, 2,6-lutidine, CH₂Cl₂, –78 – 23 °C. (d) **450**, MeOH, 23 °C. (e) *m*-Xylene, 150 °C. (f) H₂, 10% Pd/C, BOC₂O, Et₃N, 23 °C. (g) TBAF, AcOH, THF, 0 °C. (h) (1) KHDMS, THF, –78 °C; (2) 2-[*N,N*-bis(trifluoromethylsulfonyl)amino]-5-chloropyridine. (i) (CH₃)₂CuLi, THF, –78 °C → 0 °C.

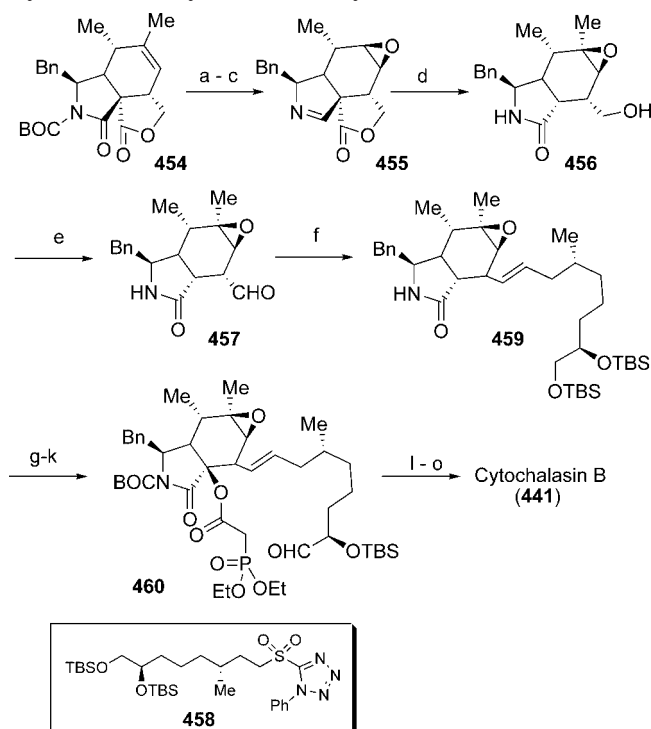
chemistry) introduced at a late(r) stage in the synthetic sequence. It is also possible to synthesize cytochalasin L-696,474 (**446**) employing this strategy by using common precursors **454** (Scheme 55) and a late-stage macrocyclization reaction (namely, through an intramolecular Horner–Wadsworth–Emmons olefination ring closure (Schemes 56 and 57)).^{1017–1019}

Cytochalasin H (445). This cytochalasin is an isomer of Cytochalasin D (**442**), differing from the latter given the lack of carbonyl function at C(17) and the opposite configuration at C-18. The synthesis of the eleven-membered ring precursor **473** of cytochalasin H (**445**) (Scheme 57) was reported by Thomas and Whitehead¹⁰¹⁰ in 1986. Afterward, the same group reported the first total synthesis of cytochalasin H (**445**) by using an intramolecular Diels–Alder reaction in a highly stereoselective way.²⁶² The stereogenic centers at C-16 and C-18 were introduced prior to cyclization using conventional acyclic stereochemical control (Scheme 58).

Three years later, the same authors reported an alternative approach in which the conformational preferences of the rings control the stereochemistry. They employed a shorter route for the synthesis of the intermediate **477** (Scheme 59).¹⁰²⁰

Cytochalasin D (442), a carbocyclic cytochalasin, is an isomer of cytochalasin H (**445**), differing from the latter given a carbonyl function at C-17 and the opposite configuration at C-18. It was isolated from the microorganism *Metarrhizum anisopliae*, and its first total synthesis was published by Vedejs and Reid in 1984.¹⁰²¹ These authors had previously reported the advantages of using *N*-acylpyrrolinones for Diels–Alder reactions in the cytochalasin area.¹⁰²²

Some years later, Merifield and Thomas, who had previously achieved the total synthesis of cytochalasin H (**445**), developed another synthetic route for the total synthesis of cytochalasin D (**442**). The strategy consisted of employing the same approach used for cytochalasin H (**445**)—an intramolecular Diels–Alder reaction to form the reduced

Scheme 56. Enantioselective and Modular Total Synthesis of Cytochalasin B by Haidle and Myers²⁴⁷


Reagents and conditions: (a) Dimethyldioxirane, acetone, 23 °C. (b) TFA, CH₂Cl₂, 0 °C. (c) [Bis(trifluoroacetoxy)iodo]benzene, 4 Å MS, CH₂Cl₂, 23 °C. (d) Ethylenediamine, tert-amylalcohol, 23 °C. (e) Dess-Martin periodinane, NaHCO₃, CH₂Cl₂, 23 °C. (f) (1) **458**, KHMDS, THF, -78 °C, (2) **457**, -100 °C → -40 °C. (g) Lithium bis(trimethylsilyl)amide, THF, -78 °C; BOC₂O, -78 → -40 °C. (h) KHMDS, THF, -78 °C; trans-2-(phenylsulfonyl)-3-phenyloxazirine, -100 → -78 °C. (i) Diethylphosphonoacetic acid, 1,3-dicyclohexylcarbodiimide, CH₂Cl₂, 23 °C. (j) HF-Pyridine, THF, 20 °C. (k) Dess-Martin periodinane, NaHCO₃, CH₂Cl₂, 23 °C. (l) NaOCH₂CF₃, CF₃CH₂OH, DME, 23 °C. (m) Mg(OCH₃)₂, MeOH, 23 °C. (n) TBAF, THF, 23 °C. (o) MgSO₄, benzene, 70 °C.

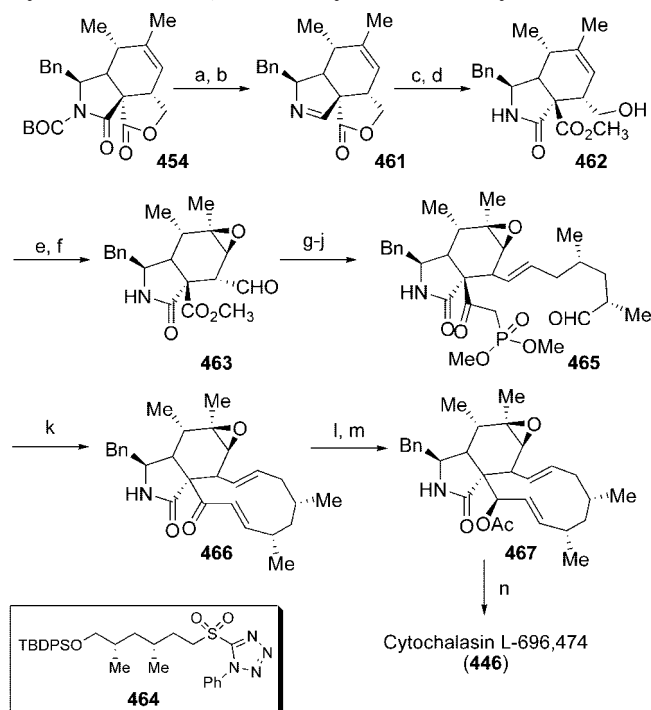
isoindolone ring and the macrocycle simultaneously (Scheme 60).¹⁰¹¹ Through this method, only the stereogenic centers at C-16 and C-3 were present before the cyclization. The remaining parts of the molecule were introduced either during the Diels–Alder reaction itself or later in the synthesis using the conformational preference of the macrocyclic ring to control the stereochemistry.

Cytochalasin G (444). Unlike the aforementioned cytochalasins A, B, H, and L, which are derived biosynthetically from phenylalanine (as indicated by the presence of the phenyl substituent at C-10), cytochalasin G incorporates tryptophan during its biosynthesis; this is the reason why it possesses an indolylmethyl substituent at C-3.

The first total synthesis of this molecule was described by Thomas and co-workers in 1986.^{258,259} Their approach consisted of performing the acylation of a (5*R*)-*N*-benzoyl-5-indolylmethylpyrrolidinone (**507**, previously synthesized following Scheme 62) by using a long-chain imidazolide **487** followed by oxidation and Diels–Alder cyclization (Scheme 61).

The synthesis of the two key intermediates **487** and **486** was performed in an asymmetrical way by the authors and is described in detail in the corresponding papers.

Cytochalasin O. The total synthesis of this¹¹ cytochalasin was performed by Merifield and Thomas during the course of their work in the total synthesis of cytochalasin D (**442**).²⁵³

Scheme 57. Enantioselective and Modular Total Synthesis of Cytochalasin L-696,474 (446) by Haidle and Myers²⁴⁷


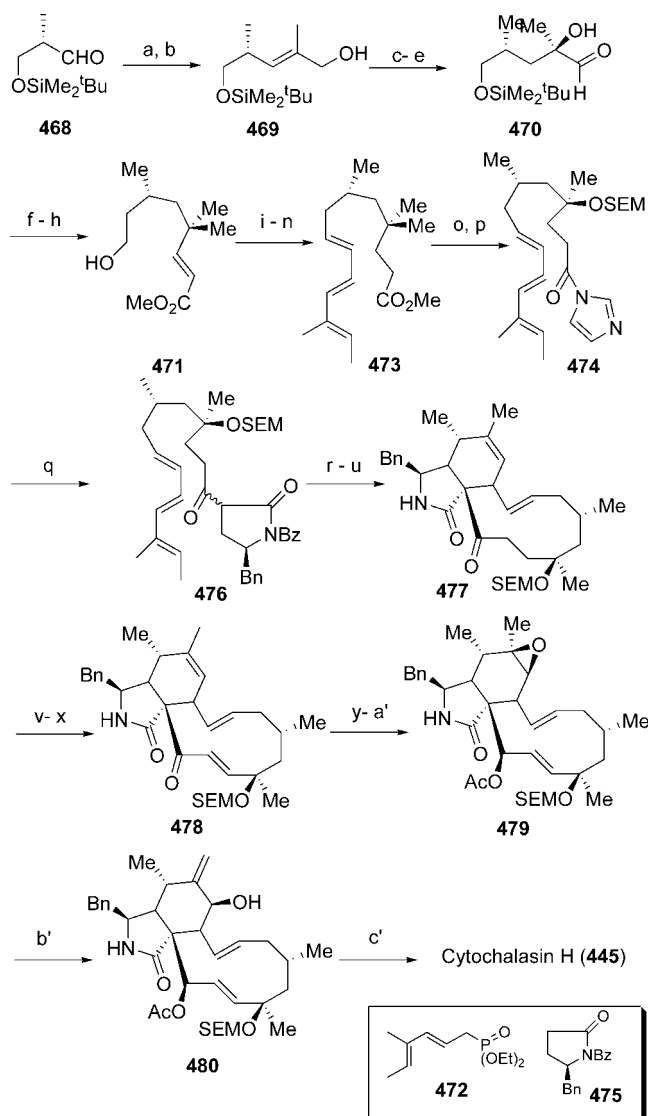
Reagents and conditions: (a) TFA, CH₂Cl₂, 0 °C. (b) [Bis(trifluoroacetoxy)iodo]benzene, 2,6-lutidine, 4 Å MS, CH₂Cl₂, 23 °C. (c) 1,3-diaminopropane, CF₃CH₂OH, Et₂O, 23 °C; Et₂O-pH 7 buffer. (d) KOH, I₂, MeOH, 23 °C. (e) Dimethyldioxirane, acetone, 23 °C. (f) Dess-Martin periodinane, NaHCO₃, CH₂Cl₂, 23 °C. (g) (1) **463**, KHMDS, THF, -78 °C; (2) **464**, -100 °C → 40 °C. (h) (CH₃O)₂POCH₂Li, THF, -78 °C → 23 °C. (i) TBAF, AcOH, THF, 23 °C. (j) Dess-Martin periodinane, NaHCO₃, CH₂Cl₂, 23 °C. (k) NaOCH₂CF₃, CF₃CH₂OH, DME, 80 °C. (l) CeCl₃·7H₂O, NaBH₄, THF-MeOH, -40 °C. (m) Ac₂O, Py, 23 °C. (n) MgSO₄, benzene, 70 °C.

They realized that, when carrying out the oxidation of the Diels–Alder adduct **448** (Scheme 60) in the presence of excess osmium tetroxide, they obtained the tetraol **515** (Scheme 63) as a major product, together with **499** (the intermediate for the synthesis of cytochalasin D (**442**)) and **516**.

Synthesis of Intermediates. Because of the complexity of this family of molecules, some research groups have decided to prepare structurally simplified analogues of the cytochalasins. In 1975, Weinreb and Auerbach described the first stereospecific synthesis of the isoindolone nucleus by internal Diels–Alder addition of a diene ester and butenolide.¹⁰²³ Through this method, the regiochemistry of the cycloaddition was controlled, but the stereochemistry of the C-3 benzyl center was not. Another example is the asymmetric synthesis of perhydroisoindolone intermediates designed by Krafft et al.¹⁰²⁴ The key reaction of this synthetic pathway consisted of a Diels–Alder reaction/addition between trienes and optically active pyrrolidenones that had been previously synthesized (Scheme 64).

2.9.5. Peptidic Mycotoxins

Many mycotoxins contain a cyclopeptide core structure; in particular, a dipeptide moiety (hence, diketopiperazines) can be found in important mycotoxins. Besides the incorporation of tryptophanes yielding indole alkaloids, fungi produce a large number of epipolythiodiketopiperazines such as gliotoxin (**527**), which are depicted in Figure 25. In

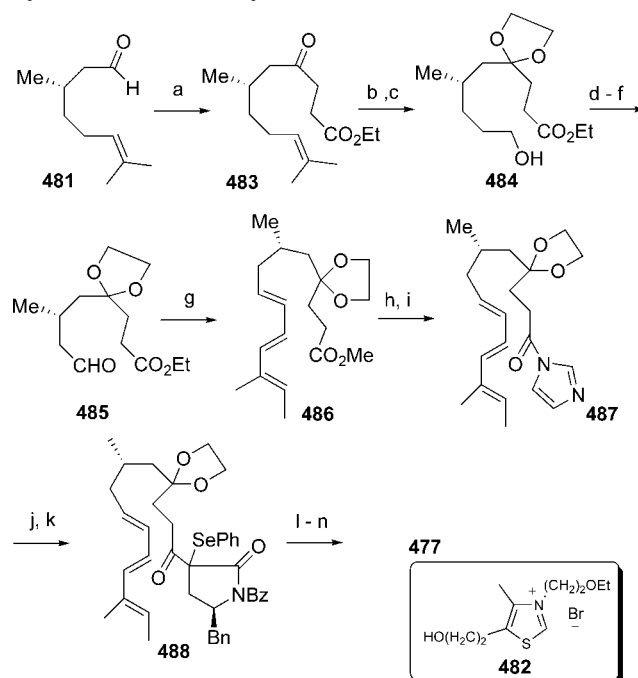
Scheme 58. Total Synthesis of Cytochalasin H (445) by Thomas and Whitehead²⁶²

Reagents and conditions: (a) $\text{Ph}_3\text{PC}(\text{Me})\text{CO}_2\text{Me}$, benzene, reflux. (b) LiAlH_4 . (c) MCPBA. (d) LiAlH_4 . (e) *N*-chlorosuccinimide, Me_2S , Et_3N , CH_2Cl_2 , -20°C . (f) $\text{Ph}_3\text{PCHCO}_2\text{Me}$. (g) $\text{ClCH}_2\text{OCH}_2\text{CH}_2\text{SiMe}_3$, Et_2NPr^t . (h) Dowex 50W-X8. (i) H_2 , Pd-C, MeOH. (j) Me_2SO , oxalyl chloride. (k) $\text{Ph}_3\text{P}=\text{CH}_2$. (l) 9-BBN, H_2O_2 , OH^- . (m) Me_2SO , oxalyl chloride. (n) phosphonate (**472**)-Li. (o) NaOH, H_2O -MeOH then tartaric acid. (p) carbonyl-1,1-di-imidazole. (q) **474**, $\text{LiN}(\text{SiMe}_3)_2$ (r) $\text{LiN}(\text{SiMe}_3)_2$, PhSeCl. (s) MCPBA, H_2O_2 , -40°C (15 min), 0°C . (t) toluene, 80 – 100°C . (u) KOH, MeOH. (v) LDA, Me_3SiCl . (w) Bu^n_4NF , PhSeCl. (x) H_2O_2 , Py. (y) NaBH_4 . (z) excess of Ac_2O , Py, DMAP. (a') MCPBA. (b') Ac_2O , Py, DMAP. (c') aqueous HF in MeCN.

addition, many cyclic and noncyclic peptides can be found as toxic metabolites of fungi, exemplified in Figure 26.

3. Biosynthesis

Fungal products such as mycotoxins, antibiotics, alkaloids, and so forth are often referred to as secondary metabolites—a term introduced into microbial biochemistry by Bu'Lock. In this paragraph, the biosyntheses of mycotoxins are discussed since this has an impact on the formation of the different classes of mycotoxins. However, it is not intended to provide a full review of this field. For comprehensive overviews, we refer to recent topical reviews^{875,1025,1026} and book chapters.¹⁰²⁷

Scheme 59. Alternative Synthesis of the Intermediate 477 of Cytochalasin H (445) by Thomas and Whitehead²⁶²

Reagents and conditions: (a) ethyl acrylate, **482**, Et_3N , Dioxane, 80°C . (b) ethylene glycol, toluene *p*-sulfonic acid, benzene, reflux. (c) (1) O_3 , $\text{CH}_2\text{Cl}_2/\text{MeOH}$, -70°C ; (2) NaBH_4 . (d) PBu_3 , *o*-nitrophenylselenocyanate, THF. (e) $\text{H}_2\text{O}_2/\text{NaOH}$, THF, 0°C . (f) (1) O_3 , MeOH; (2) O_2 , Me_2S . (g) (1) **472**, *n*-BuLi, THF, -60°C , -30°C ; (2) -72°C . (h) (1) NaOH, EtOH, rt; (2) tartaric acid. (i) CDI, THF, rt. (j) **475**, $\text{LiN}(\text{SiMe}_3)_2$, THF, -72°C . (k) $\text{LiN}(\text{SiMe}_3)_2$, PhSeCl. (l) MCPBA, H_2O_2 , CHCl_3 , -50°C (m) toluene, 80°C (n) NaOH, MeOH, rt.

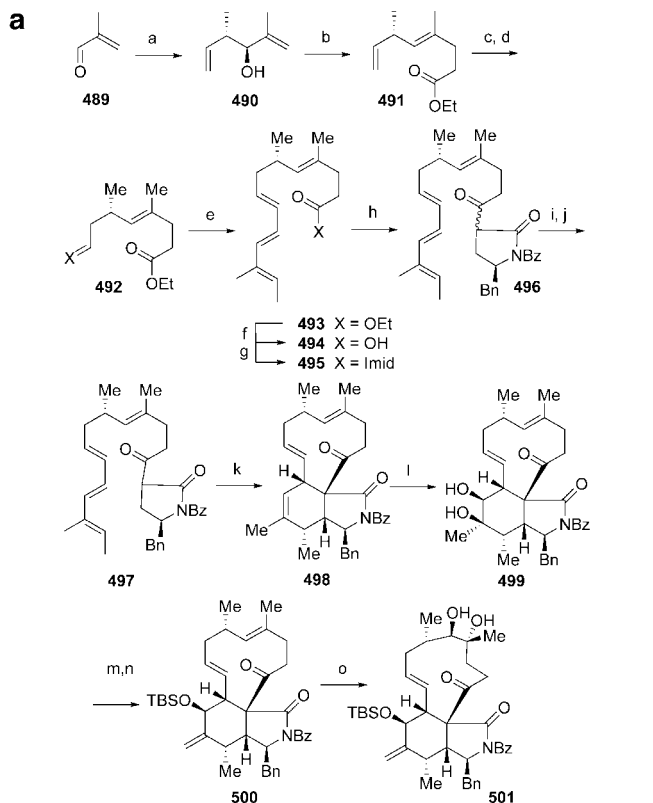
Several physiological factors play regulatory roles in both the primary and secondary metabolism of microorganisms. During the last few years, many efforts have been undertaken not only to elucidate the biochemical origin of mycotoxins but also to use this knowledge either to influence the biosynthesis (to produce more, less,^{1028,1029} and/or different mycotoxins by incorporation of new building blocks⁵⁵⁸) or to monitor mycotoxins on a molecular level.

The publication of the genomes of *A. fumigatus*, a human pathogen, *A. oryzae*, used in food production, and *A. nidulans*, a genetic model organism, represents an important milestone in the *Aspergillus* research community, expanding knowledge of their physiology and mechanisms of gene regulation. Three additional genome projects are being funded by the NIAID with the goals of better elucidating the *A. fumigatus* genome and improving the genome annotation: *N. fischeri* (*A. fischerianus*), *A. clavatus*, and *A. terreus*. Since a growing number of filamentous fungi have been sequenced, one can assume that this genetic information will have a great impact on the analysis of mycotoxin formation in the coming decade (see Table 9).

3.1. Polyketide-Derived Mycotoxins

Most of the fungal metabolites (such as Patulin (**3**) and related compounds, the anthraquinoids, etc.) are polyketides.⁹³⁰ The mechanisms of biosynthesis are known in great detail for many mycotoxins^{1031,1032} (see, e.g., the cytochalasins (**440**–**447**)¹⁰³³) and have been reviewed several times. Fungal polyketide biosynthesis typically involves multiple enzymatic steps, and the encoding genes are often found in gene clusters. It has been demonstrated that this

Scheme 60. (a) Total Synthesis of Cytochalasin D (442) by Merifield and Thomas;¹⁰¹¹ (b) Total Synthesis of Cytochalasin D (442) by Merifield and Thomas (Part 2)¹⁰¹¹

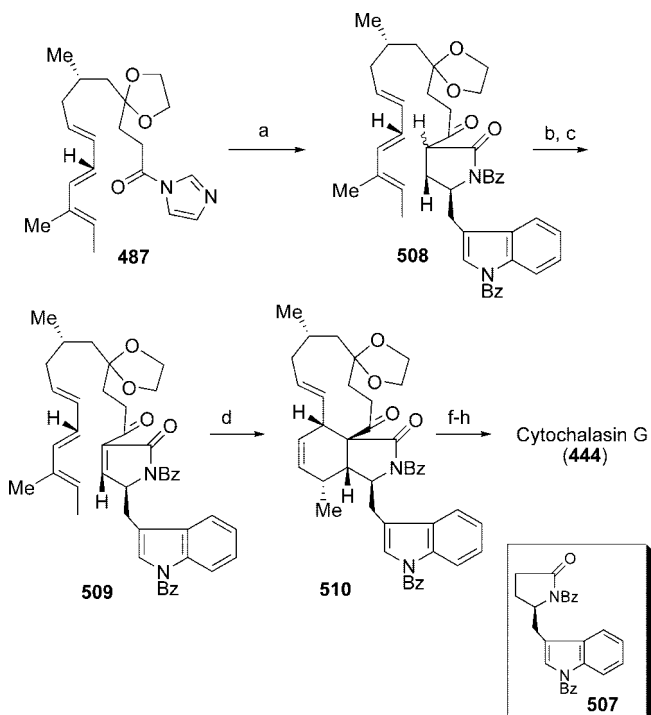


b

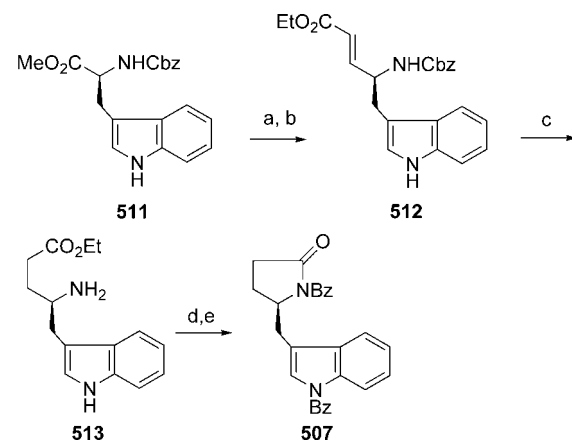
Reagents and conditions: (p) 2,2-dimethoxypropane, CHCl_3 , toluene-*p*-sulphonic acid. (q) LDA, PhSeCl. (r) KOH, MeOH. (s) H_2O_2 , H_2O . (t) NaBH_4 , CeCl_3 . (u) Ac_2O , Et_3N , 4-dimethylaminopyridine. (v) Bu_4NF . (w) SEMCl, $i\text{Pr}_2\text{CN}$. (x) H_3O^+ . (y) $(\text{COCl})_2$, DMSO. (z) HF, MeCN, H_2O .

biosynthesis is strongly dependent on the growth environment.¹⁰³⁴ The enzymatic machinery for the formation of the

Scheme 61. Total Synthesis of Cytochalasin G (444) by Thomas et al.²⁵⁸

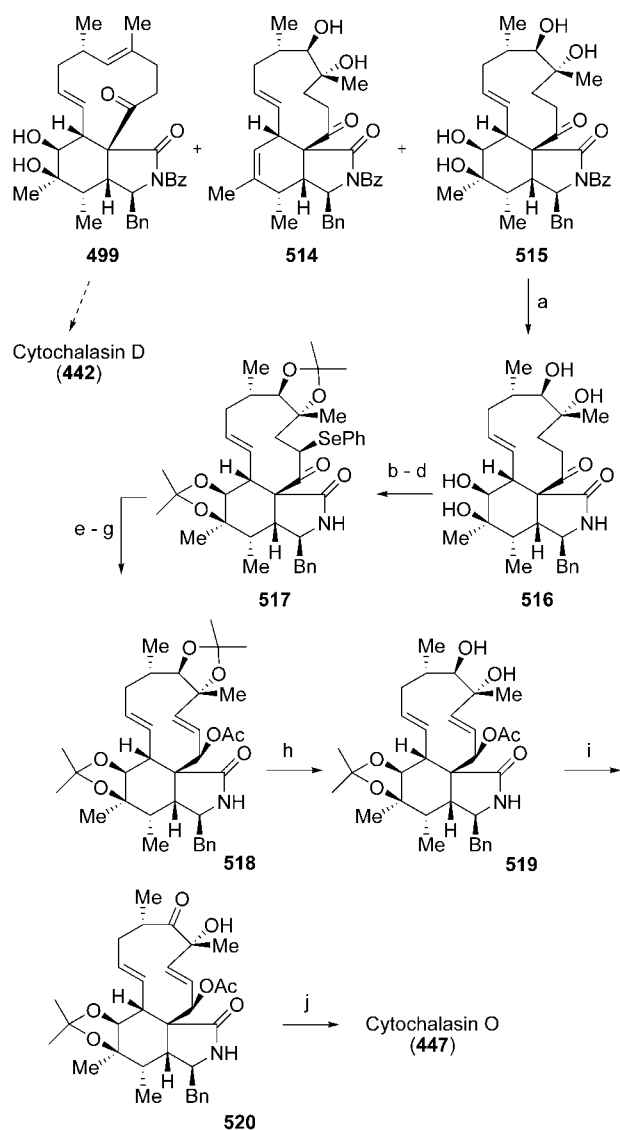


Scheme 62. Asymmetric Synthesis of the Pyrrolidinone Intermediate 507

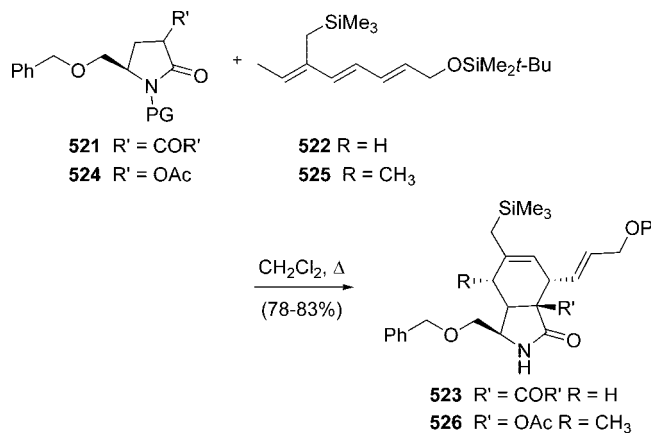


polyketides consists of different modules characteristic of each fungus (e.g., keto synthases, acyl transferases,¹⁰³⁵ carboxylases, cyclases, dehydrases, aromatases, reductases, thioesterases, (Claisen) cyclases, laccases, etc.) It is interesting to note that, while bacteria do have similar enzymes, the folding of the growing polyketide chain delivers different structures.¹⁹

Depending on the chain length, different classes of mycotoxins are formed: tetraketides (e.g., patulin (**3**)), pentaketides (e.g., citrinin (**2**), ochratoxin A (**7**)) (Scheme 66–68), hexaketides (e.g., Diaporthin), heptaketides (e.g., *Alternaria* toxins^{1036,1037}), octaketides (e.g., aflatoxins (**1**)), xanthones like secalonic acids (such as **10**); nonaketides (e.g., resorcylic lactones such as zearalenone (**4**)¹⁰³⁸), and decaketides (e.g., vioxanthin (**606**)).

Scheme 63. Total Synthesis of Cytochalasin O by Merifield and Thomas²⁵³


Reagents and conditions: (a) NaOH aq., MeOH. (b) 2,2-dimethoxypropane, b) *p*-toluene sulfonic acid. (c) LDA, benzeneselenenylchloride. (d) NaOH aq., MeOH. (e) aq. H₂O₂, Py. (f) NaBH₄, CeCl₃. (g) acetic anhydride, Et₃N, DMAP. (h) toluene-*p*-sulfonic acid, MeOH. (i) oxalyl chloride, Me₂SO, Et₃N. (j) aq. HCl, MeOH, reflux.

Scheme 64. Asymmetric Synthesis of Perhydroisoidolones by Krafft et al.¹⁰²⁴


Patulin (**3**) is formed via the oxidative cleavage of the tetraketide 6-methylsalicylic acid (**550**, Scheme 65). This

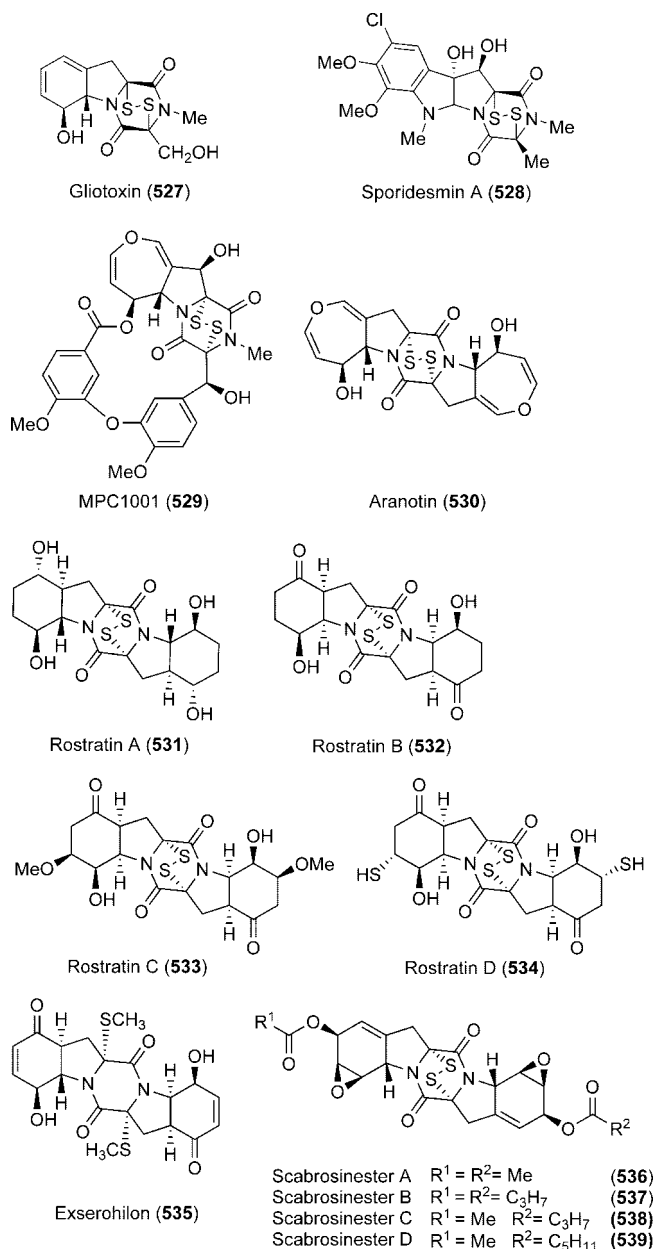


Figure 25. Some peptidic polyepithiodiketopiperazines.

transformation comprises monooxygenase-mediated epoxidation of gentisaldehyde (**554**) to the epoxyquinone phyllostine and rearrangement of the latter to neopatulin (**185**), the ylidenebutenolide isomer of patulin (**3**). Enzymatic reduction of neopatulin (**185**) to (*E*)-ascladiol (**186**) and oxidative ring-closure then yields patulin (**3**).

The ochratoxins A and B (**7**, **155**) are derived from the pentaketide intermediate ochratoxin β (**563**).^{1040,1041} The already-chlorinated ochratoxin α (**157**) was biotransformed into ochratoxin A (**7**), indicating that chlorination is primarily a penultimate biosynthetic step in the biosynthesis of ochratoxin A (**7**). Experiments illustrated that some ochratoxin B (**155**) may arise through dechlorination of ochratoxin A (**7**).

The mycotoxin alternariol and its congeners were formed starting from a heptaketide pathway (Scheme 69).^{1042,1043}

The biosyntheses of octaketide-derived mycotoxins are still the subject of a number of investigations since the crucial classes of aflatoxins, xanthenes, and many anthraquinones are octaketides (Scheme 71). Pioneering works by Franck

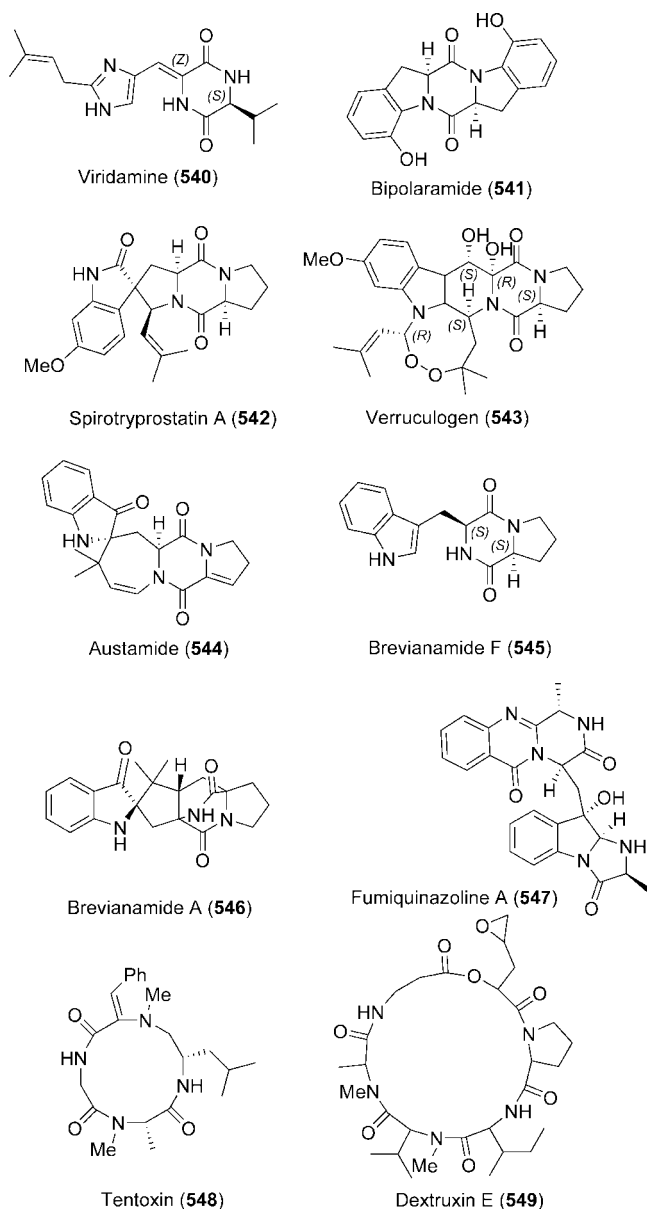
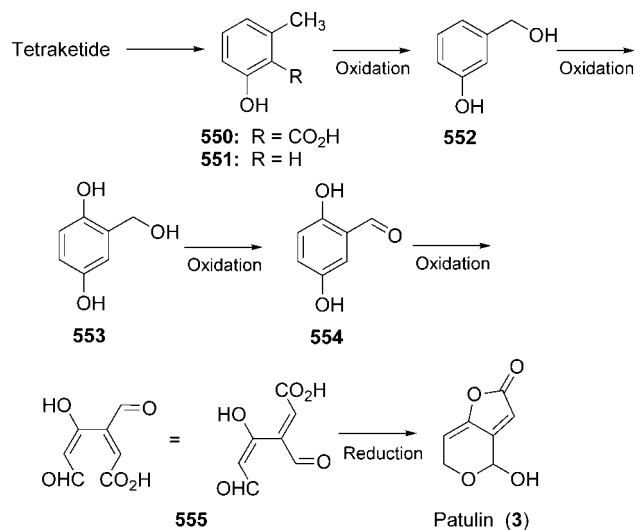


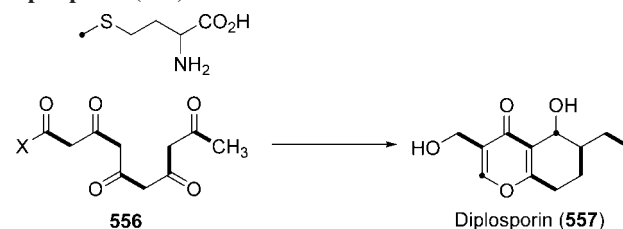
Figure 26. Peptidic mycotoxins.

et al. for the synthesis of xanthenes and recently detailed investigations of Townsend in the field of aflatoxin biosynthesis¹⁰⁴⁴ have unified mycotoxins' biosynthetic origin into a greater picture (see above). The concurrent incorporation of labeled anthraquinones into secalonic acid D (10) by *Penicillium oxalicum* was studied by Franck et al.¹⁰⁴⁵ Emodin (573) and islandicin (577) were partially incorporated into

Scheme 65. Example of a Tetraketide Biosynthesis: Patulin^{1031,1039}



Scheme 66. Example of a Pentaketide Biosynthesis: Diplosporin (557)¹⁰³¹



secalonic acid D (10) by way of chrysophanol (83); however, islandicin (577) is presumed to be a shunt pathway. Ergochromes are thus secoanthraquinones.⁸⁴⁰

The key transformation is a Bayer–Villiger-type ring-opening to a carboxylic acid 578, which in turn reacts either in a 1,2-addition to form tajixanthone-type xanthenes or by a conjugate 1,4-addition to generate the ergochromes.¹⁰⁴⁶

Depending on the folding pattern, nonaketides produce resorcylic lactones like zearalenones or the recently isolated pochonins.¹⁰³¹

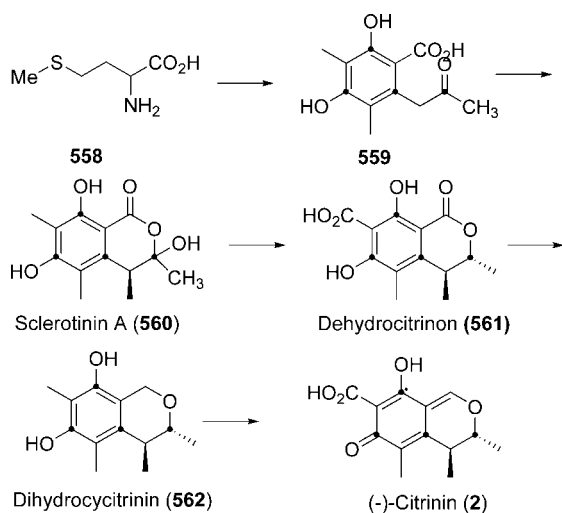
The biosynthesis of aflatoxin proceeds via numerous transformations, which are mostly well-studied.^{1031,1048}

Many mycotoxins consist of homodimers of phenolic compounds. Examples include vioxanthin and the secalonic acids. Recent studies have shed light on the biosynthesis of oxidative biaryl coupling promoted by various enzymes.¹⁰⁴⁹

The biosynthetic pathway for aurofusarin (608) in *Fusarium graminearum* reveals a close link between the naphthoquinones and naphthopyrones.¹⁰³²

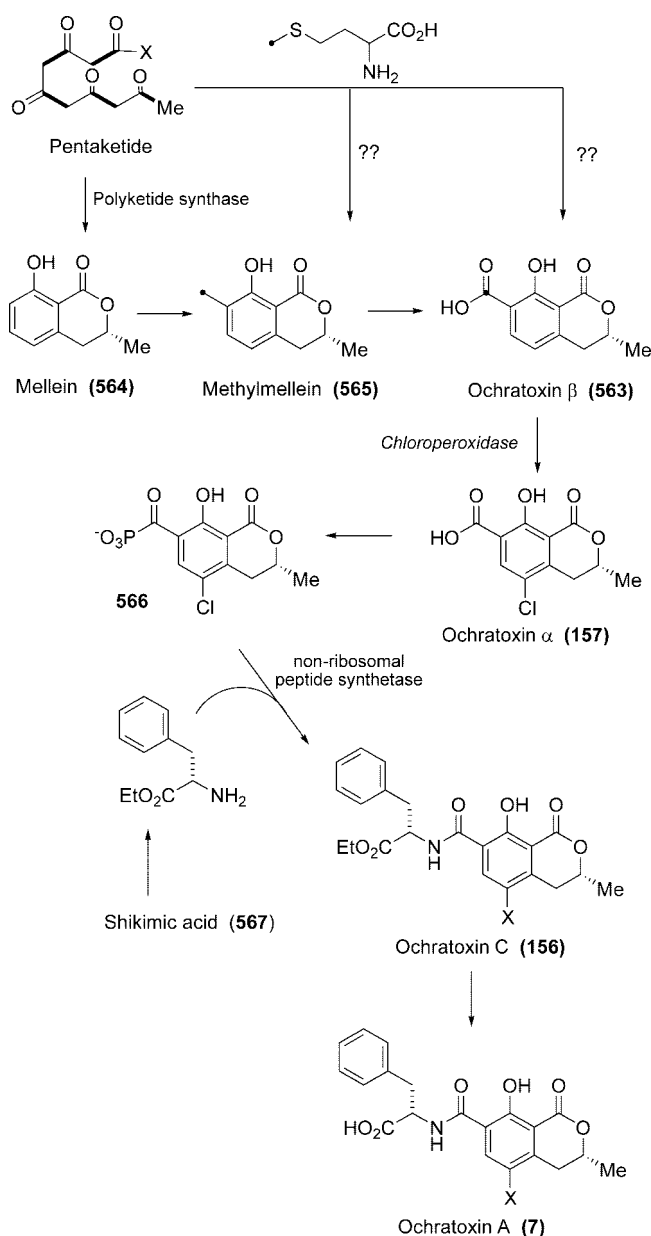
Table 9. Overview over Mycotoxin Biosynthesis with Examples

| Polyketide Acetate–Malonate | Terpene Mevalonate | Citrate-Based Pyruvate–Acetate | Amino Acid |
|--------------------------------|--------------------------|-----------------------------------|----------------------------------|
| Aflatoxins | Fumagallin | Byssochlamic acid | Aspergillitic acid |
| Alternariol (11) | Roridin | Erythrokyrin | Cyclopenein |
| Citrinin (2) | Trichothecene | Glauconic acid | Cyclophenol ¹⁵³ |
| Citroviridin | Diacetoxyscripenol (217) | Rubratoxin | Cyclopiazonic acid |
| Emodin ¹⁰³⁰ (573) | Fusicoccin | | Ergot alkaloids |
| Luteoskyrin | | | Clavin alkaloids |
| Maltoryzin | | | Fumitremogen |
| Ochratoxins | | | Gliotoxin (527) |
| Patulin (3) | | | Islandoxin |
| Penicillinic acid | | | Paspalin |
| Sterigmatocystin (62) | | | Tryptoquivaline |
| Zearalenone (4) | | | Penitrem Sporidesmin (e.g., 528) |

Scheme 67. Example of a Pentaketide Biosynthesis: Citrinin (2)¹⁰³¹

Fungal polyketide biosynthesis typically involves multiple enzymatic steps, and the encoding genes are often found in gene clusters. A gene cluster containing PKS12—the polyketide synthase gene⁹³⁰ responsible for the synthesis of the pigment aurofusarin (**608**)—was analyzed through gene replacement using an *Agrobacterium tumefaciens*-mediated transformation to detect the biosynthetic pathway of aurofusarin (**608**). Replacement of *aurR1* with *hygB* shows that it encodes a positive-acting transcription factor that is required for the full expression of PKS12, *aurJ*, *aurF*, *gip1*, and FG02329.1, which belong to the gene cluster. *AurR1* and PKS12 deletion mutants are unable to produce aurofusarin (**608**) and rubrofusarin (**609**, Figure 27). Bio- and chemoinformatics combined with chemical analysis of replacement mutants (DaurJ, DaurF, Dgip1, DaurO, and DPKS12) indicate a five-step enzyme-catalyzed pathway for the biosynthesis of aurofusarin (**608**), with rubrofusarin (**609**) as an intermediate. This links the biosynthesis of naphthopyrones and naphthoquinones together. Replacement of the putative transcription factor *aurR2* results in an increased level of rubrofusarin relative to aurofusarin (**608**). *Gip1*, a putative laccase, is proposed to be responsible for the dimerization of two oxidized rubrofusarin molecules, resulting in the formation of aurofusarin (Figure 27).

Fumonisin (**5**, **88–102**) are polyketide-derived mycotoxins produced by the maize pathogen *Fusarium verticillioides*. Previous analyses identified naturally occurring variants of the fungus that are deficient in fumonisin C-10 hydroxylation or that do not produce any fumonisins. It has been demonstrated that gene deletion and genetic complementation localized the C-10 hydroxylation deficiency to a cytochrome P450 monooxygenase gene in the fumonisin biosynthetic gene (FUM) cluster.¹⁰⁵⁰ Sequence analysis indicated that the hydroxylation deficiency resulted from a single nucleotide insertion that caused a frame shift in the coding region of the gene. Genetic complementation localized the fumonisin-nonproduction phenotype to the polyketide synthase gene in the FUM cluster, and sequence analysis indicated that the nonproduction phenotype resulted from a nucleotide substitution, which introduced a premature stop codon in the coding region. These results provide the first direct evidence that altered fumonisin production phenotypes of naturally occurring *F. verticillioides* variants can result from single-point mutations in the FUM cluster.

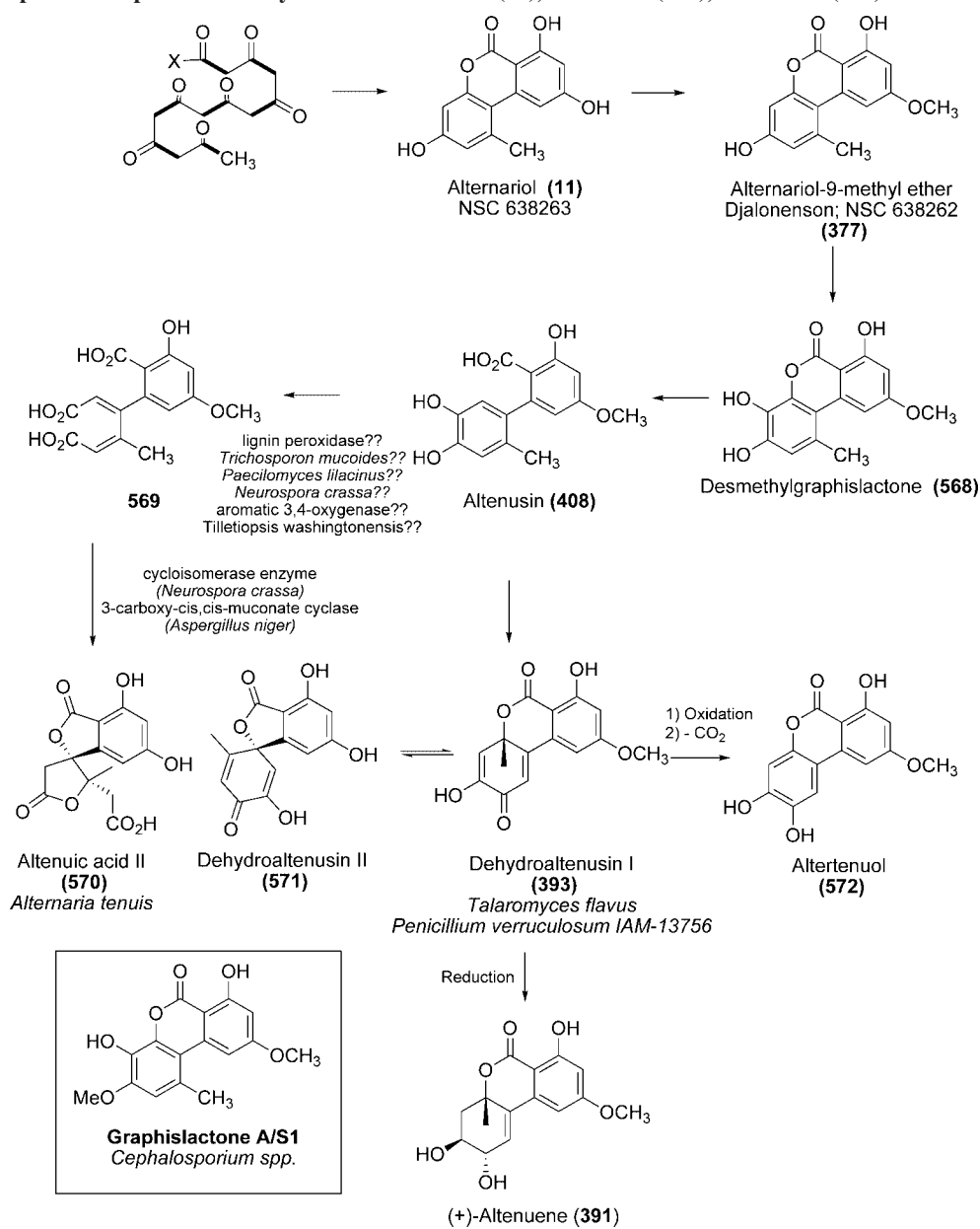
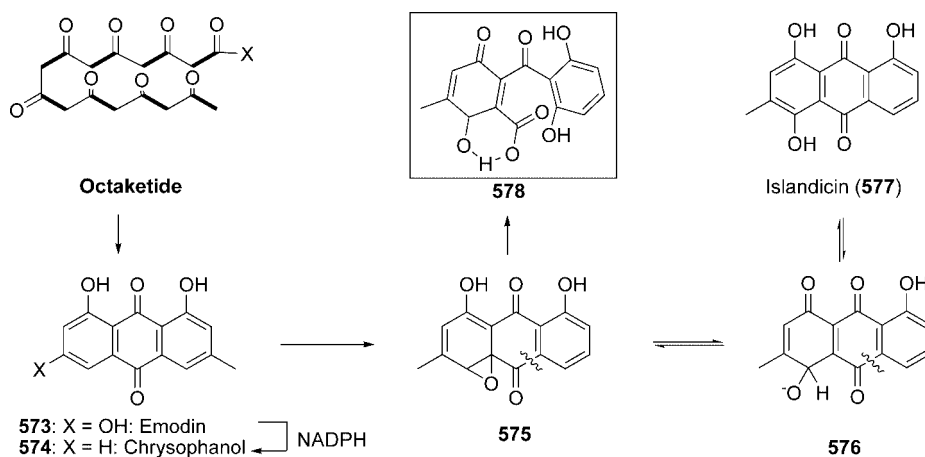
Scheme 68. Example of a Pentaketide Biosynthesis: Ochratoxins¹⁰³¹

3.2. Terpenoid Mycotoxins

The trichothecenes (**205–234**)¹⁰³⁵ are prototypical terpenoid mycotoxins. Their biosynthesis has been elucidated in great detail^{1051,1052} and been recently reviewed.¹⁰⁵³ The biosyntheses of the verrucarins (**6**, **260–261**) and roridins (**262–264**)¹⁰⁵⁴ have also been investigated.

3.3. Mycotoxins Incorporating Amino Acids

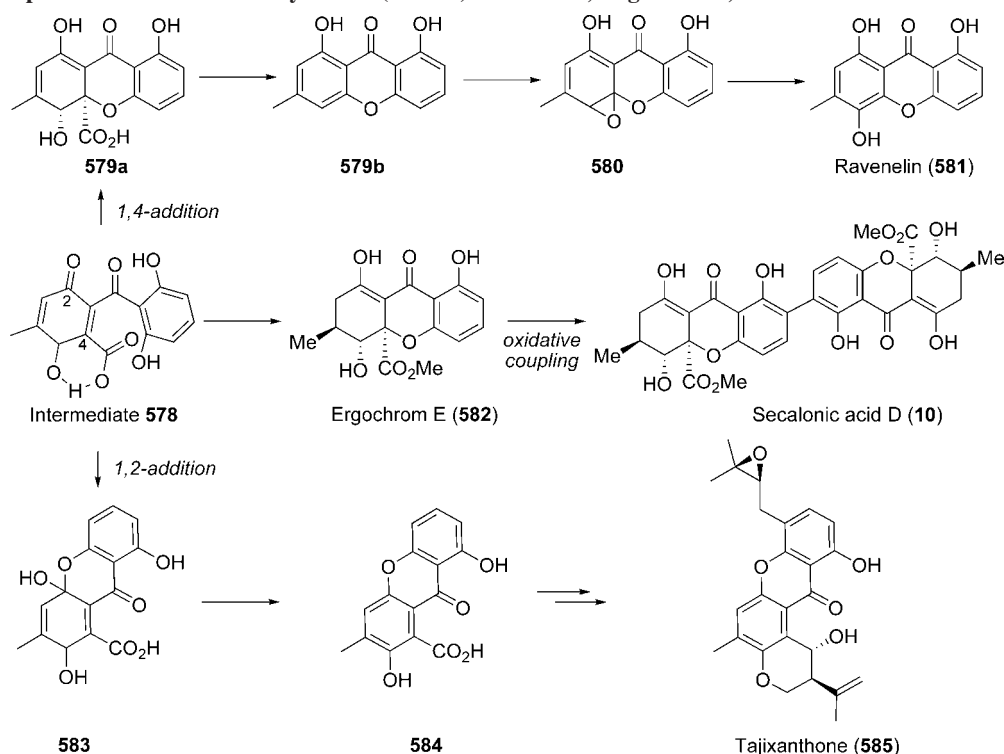
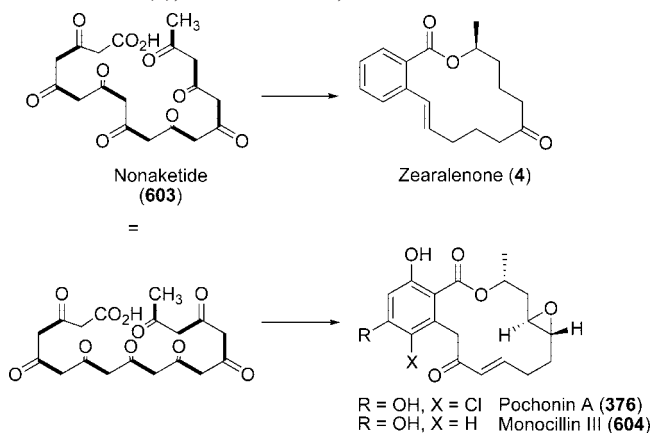
Fungi use amino acids in relatively high amounts/concentrations. Quite often, mycotoxins incorporating amino acids are partially derived from polyketides or terpenoids. A number of cyclopeptides (e.g., enniatin¹⁰⁵⁵) derived from fungi are cytotoxic and, therefore, are per se mycotoxins. Cyclic dipeptides such as epipolythiodioxopiperazines are common structures, whose biosyntheses have been recently reviewed.^{1056,1057}

Scheme 69. Example of a Heptaketide Biosynthesis: Alternariol (11), Altenusin (408), Altenuene (391)^{1042,1043}Scheme 70. Example of an Octaketide Biosynthesis (Part I): Emodin (573) and Islandicin (577)¹⁰⁴⁶

3.3.1. Mixed Biosynthesis

In some cases, a mixed origin has been established for mycotoxins. For example, the mycotoxins austin and terre-

tonin in *Aspergillus ustus* and *A. terreus*, respectively, are mixed polyketides—terpenoids shown by incorporation of 3,5-dimethylorsellinate.¹⁰⁵⁸

Scheme 71. Example of an Octaketide Biosynthesis (Part II): Ravenelin, Ergochroms, and Secalonic Acids^{1046,1047}Scheme 72. Example of a Nonaketide Biosynthesis: Zearalenone (4), Pochonins 376, and Monocillins 604¹⁰³¹

3.3.2. Directed Biosynthesis

The biosynthesis of novel mycotoxins can be influenced either by genetic modification or by feeding of biosynthetic precursors. For example, *Aspergillus fumigatus* TP-F0196 produces pseurotin A, synerazol, and gliotoxin (**527**). Phenylalanine is a common biosynthetic precursor of these antibiotics. Feeding fluorophenylalanine to the culture induced the production of novel fluorinated analogues.⁵⁵⁸ These fluorinated antibiotics were obtained from the culture broth through solvent extraction and purified via chromatography, and their antimicrobial and antitumor activities were investigated. Among the novel fluorinated analogues, 19- and 20-fluorosynerazols exhibited potent antiangiogenic activity in the chorioallantoic membrane assay. In addition, 19-fluorosynerazol displayed more potent cytotoxic activity against several cancer cell lines than synerazol.

4. Structure–Activity Relationships

The structure–activity relationship among the best-known mycotoxins was reviewed by Betina almost 20 years ago.¹⁰⁵⁹ In that work, the following features were described as common structural characteristics important for bioactivity present in most mycotoxins (Figure 28):

(1) The oxirane ring. Appears in cytochalasins and trichothecenes. Some trichothecenes even have two epoxy rings in their structure.

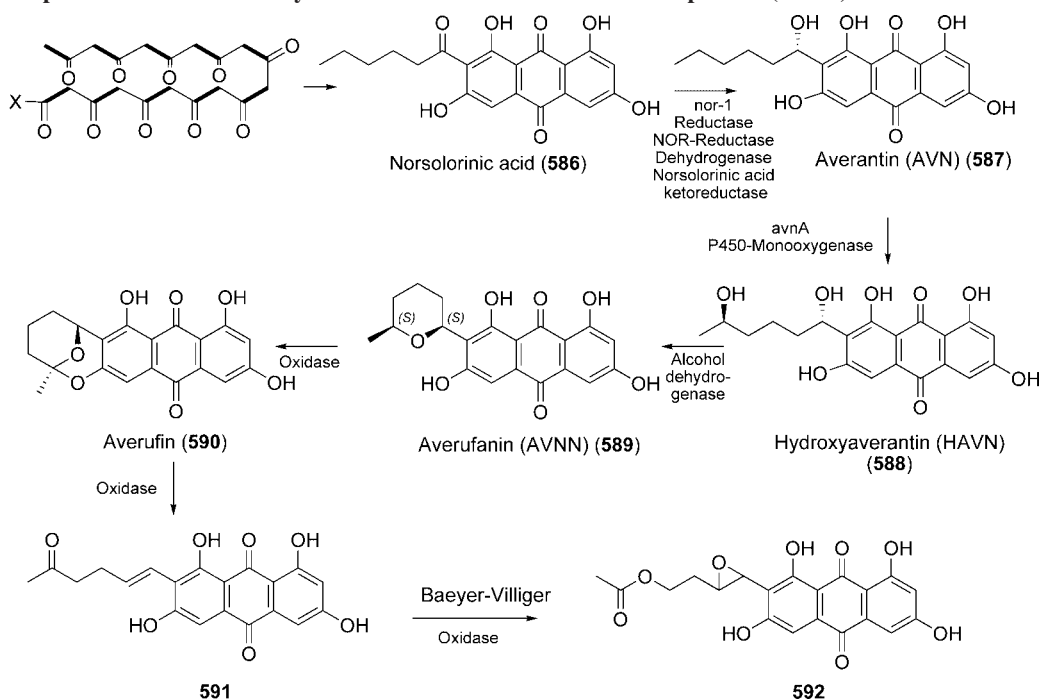
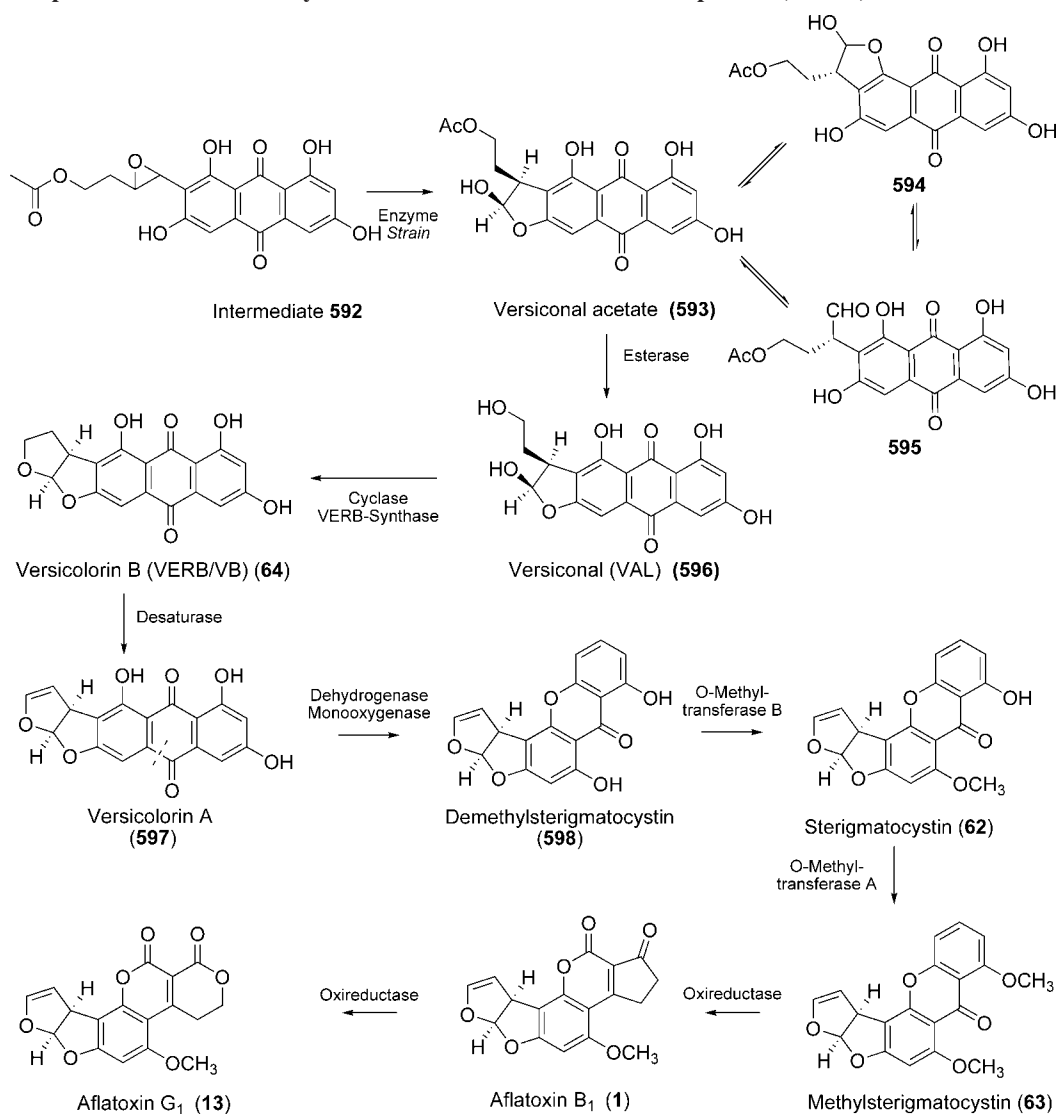
(2) Quinoid moieties (benzoquinone, naphthoquinone, and anthraquinone). An example is the benzoquinone moiety of terreic acid—a diabetogenic mycotoxin.

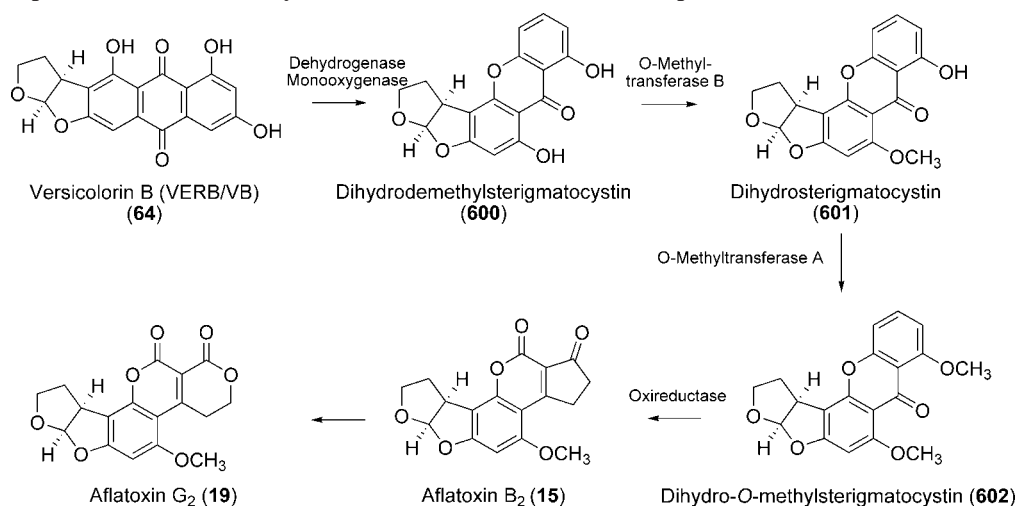
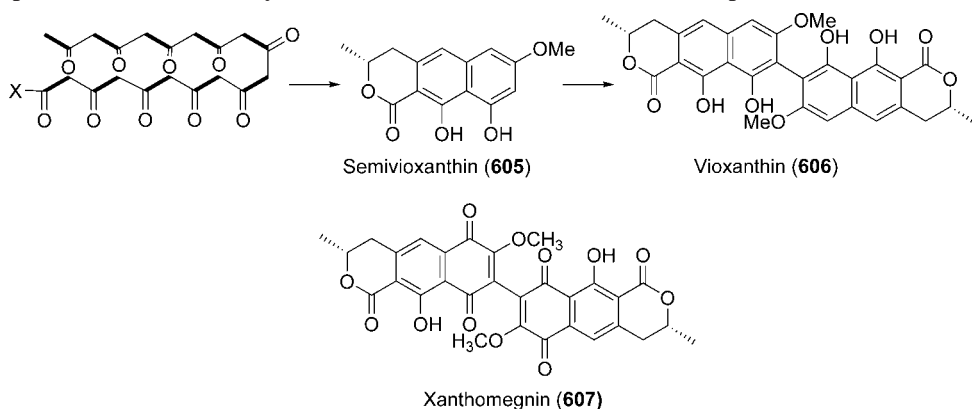
(3) Five-membered or six-membered lactones, either saturated or unsaturated. Small lactones are known to be highly toxic, acting as potential alkylating agents. As an example, Patulin (**3**) can react as an alkylating agent with DNA molecules. That is the reason why this family of molecules has mutagenic, carcinogenic, or teratogenic activity.

(4) Macrocyclic structures. Macrocyclic lactones (present in zearalenones like **4**, cytochalasins, and some trichothecenes) act as mycoestrogens, whereas other macrocyclic compounds (such as cytochalasins or zygosporins like **440**) are cytotoxic compounds with particular effect on mammalian, protozoal, fungal, plant, and bacterial cells.

(5) Isocoumarins (with ochratoxins as the best example). The dihydroisocoumarin moiety in combination with *L*-β-phenylalanine (in ochratoxin A (**7**)) leads to inhibition of protein synthesis at the stage of amino acid activation, whereas in combination with benzoquinone (as in viomellein mycotoxins) it produces the uncoupling of oxidative phosphorylation.

After a detailed description of the common structural features present in mycotoxins crucial for the biological activities, some structure–activity relationship conclusions were drawn regarding the main mycotoxin families:

Scheme 73. Example of a Decaketide Biosynthesis: Aflatoxins and Related Compounds (Part I)¹⁰³¹Scheme 74. Example of a Decaketide Biosynthesis: Aflatoxins and Related Compounds (Part II)¹⁰³¹

Scheme 75. Example of a Decaketide Biosynthesis: Aflatoxins and Related Compounds (Part IV)¹⁰³¹Scheme 76. Example of a Decaketide Biosynthesis: Vioixanthin (606) and Related Compounds¹⁰³¹

Aflatoxins. The structural characteristics of primary importance in the biological activity of aflatoxins are as follows (Figure 29):

- The dihydrofuran moiety;
- The double bond in C2–C3; and
- The substituents linked to the coumarin skeleton.

Aflatoxin B₁, containing a cyclopentanone ring system, is much more potent than aflatoxin G₁ (13) with its unsaturated δ -lactone. When the coumarin ring is replaced by xanthon in sterigmatocystin (62), the main features of bioactivity of the aflatoxins are retained. In versicolorin A (597), the coumarin is replaced by an anthraquinoid moiety, changing the mode of action to an uncoupling of oxidative phosphorylation. The order of toxicity of the four major aflatoxins is B₁ > G₁ > B₂ > G₂.

Ochratoxins. By comparing the toxicity of ochratoxin A (7), B, C, and α and their structural differences, it could be said that the presence of the chlorine atom and the L- β -phenylalanine moiety are responsible for its toxicity and the inhibition of protein synthesis. Ochratoxin A (7) is the most

toxic of the ochratoxins, and its structure comprises ochratoxin α linked to L- β -phenylalanine.

Trichothecenes. The most important features for this class are as follows:

- The double bond at C9–C10.
- The presence of the 12,13-epoxide. Verrucarins K, the first natural trichothecene lacking the 12,13-epoxy group, has not shown general toxicity; however, it presents high cytotoxic activity, suggesting that the macrocyclic part itself possesses cytotoxic activity.
- The presence of hydroxyl or other substituents at appropriate positions of the trichothecene nucleus. Baccharins that have a different O-substituent in the A ring have higher antileukemic activity than roridins and verrucarins.
- The structure and position of the side chain.
- The presence of a second oxirane ring at C9–C10 on the trichothecene nucleus.
- The presence of a macrocycle, because it is important for their antileukemic activity.

Depending on the structure of the trichothecene, its biological activity can range from antibiotic, phytotoxic, cytotoxic, cancerostatic, antileukemic, immunosuppressive, antiviral, to insecticidal. As an example, the simple opening of the 12,13-epoxide ring results in nontoxic compounds (Verrucarins A is highly toxic but Verrucarins K is not). The presence of a C4 hydroxyl group in nivalenol (232) in comparison to the absence in Deoxynivalenol (230) makes it 10 times more toxic. Since that publication, a systematic

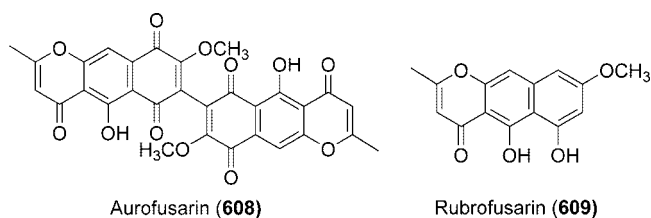
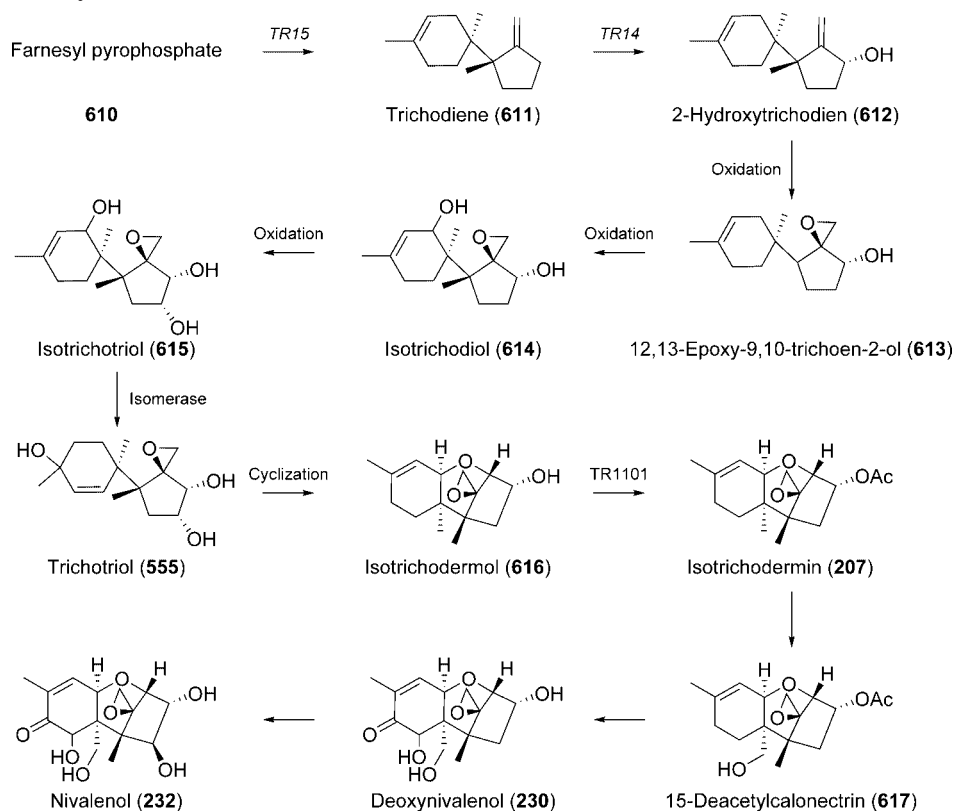
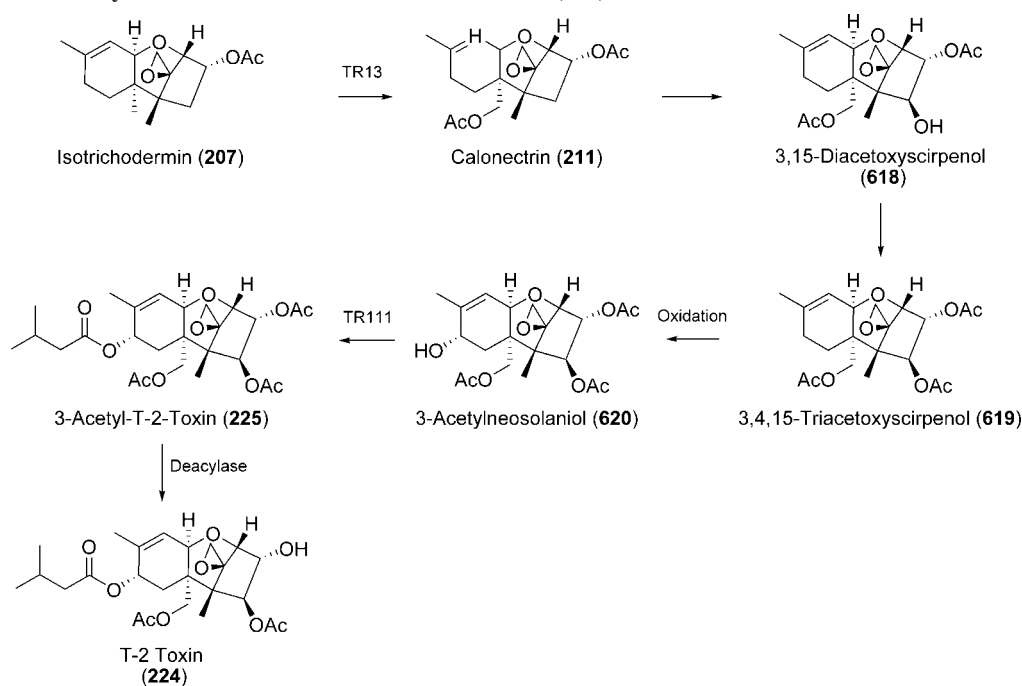


Figure 27. Aurofusarin (608) and rubrofusarin (609).

Scheme 77. Putative Biosynthesis of the Trichothecenes: Nivalenol (232)¹⁰⁵³**Scheme 78. Putative Biosynthesis of the Trichothecenes: T-2 Toxin (224)**¹⁰⁵³

evaluation of structure—activity relationships (SARs) has not been conducted in the mycotoxin area.

Only a few studies have evaluated fumonisin analogues for their cytotoxicity, plant toxicity, and sphingolipid alterations. The results regarding the effects of fumonisin on the elevation of free sphingoid bases¹⁰⁶⁰ suggest that hydrolysis to remove the tricarballylic side chains reduces the biological activity and acetylation of the amino group eliminates the activity. The most potent inhibitors of ceramide synthase were the *Alternaria alternata* toxin, toxins TA_{1,2} (136/137),

which have a number of structural differences from that of FB1 (92), most notably a shorter hydrocarbon chain backbone than fumonisin, positioning of the amino group C1 instead of C2, and the absence of one of the TCA groups.

The reduced ability of hydrolyzed fumonisins to block ceramide synthase, and the different potencies of the other analogues relative to each other, could be related to varying degrees of membrane permeability and thereby differences in accessibility of the toxins to ceramide synthase sites within the liver cells.

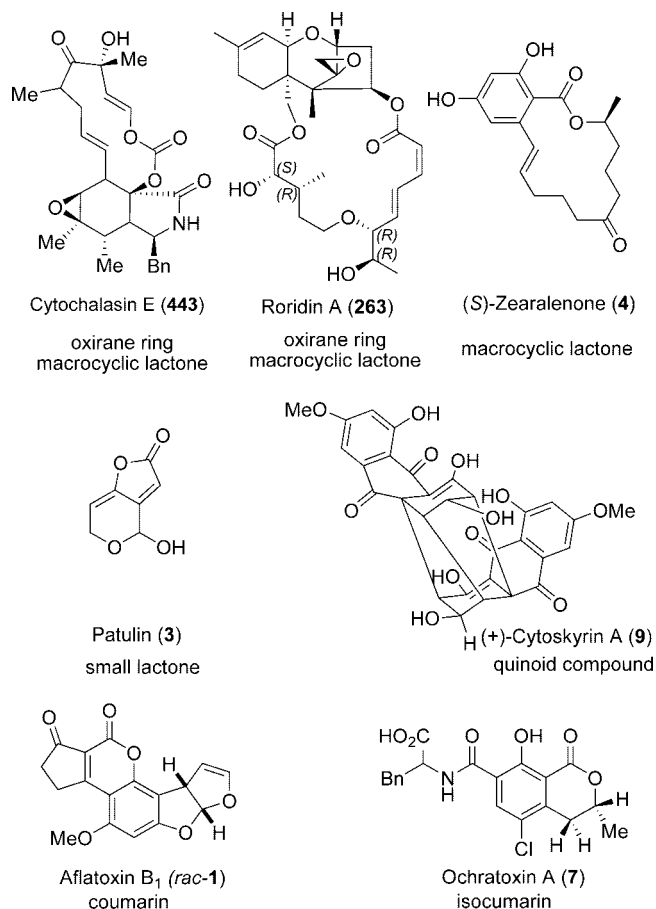


Figure 28. Common features in mycotoxins.

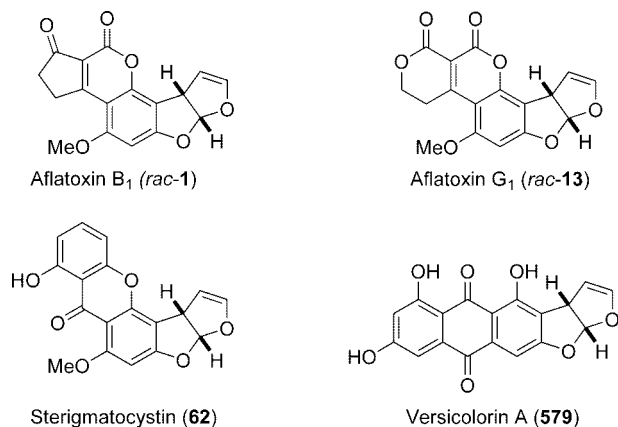


Figure 29. Structure of different aflatoxins.

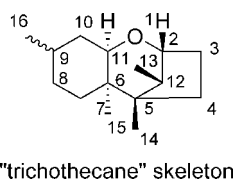


Figure 30. Main structure of the trichothecene skeleton.

In 2001, a SAR study on zearalenones was undertaken to better understand their estrogenicity on a human estrogen receptor.¹⁰⁶¹ The estrogenicity of zearalenone and 16 structural analogues was compared. Overall, about one-half of the analogues examined in that study exhibited higher estrogenicity than zearalenone (the most abundant toxin of the class produced by *Fusarium* species). The analogues examined provided information about the roles played by

several parts of the zearalenone molecule in estrogenic activity with the human estrogen receptor of MCF7. The 6' functional group has the largest effect on estrogenicity. The strongest estrogenicity was observed with α -zearalenol (320) (α -OH at the 60 position). The order of estrogenicity for 60 substituents is α -OH \gg NH₂ \geq O $<$ β -OH \approx β -OAc. Current activity with trichothecenes has focused on immune responses and cell-signaling pathways.

5. Mycotoxins and Related Compounds As Potential Therapeutics

There is increasing interest in plant extracts as potential therapeutic agents.¹⁰⁶² In general, as we have explained in section 1.2, mycotoxins are toxic metabolites. In contrast, some of the compounds provide interesting pharmaceutical use.

The ergot alkaloids exhibit complex and variable pharmacological impacts because of their action as agonist or antagonist at the adrenergic, dopaminergic, and serotonergic receptors. The earliest authenticated reports of the effects of ergot were located in Chinese writings in \sim 1100 BC, when the substance was used in obstetrics. Nowadays, there are several commercialized derivatives, most of which are not naturally occurring, that are indicated by the Food and Drug Administration (FDA) for the treatment of different diseases. These applications were thoroughly reviewed by Schiff in 2006. As an example, the ergonovine, a lysergic acid amide alkaloid, behaves as an agonist of tryptaminergic receptors in smooth muscles. For this reason, it is employed for uterine stimulation in the routine management of postpartum uterine atony and hemorrhage. It is also utilized as a diagnosis test for Prinymetal's angina. Ergotamine derivatives, such as ergotamine (8) or dihydroergotamine, are peptide alkaloids used in abortions or prevention of vascular headaches, such as migraines, migraine variants, cluster headaches, and histaminic cephalaea. Bromocriptine, also a peptide alkaloid, is a semisynthetic derivative commercialized for the treatment of Parkinsonism juxtaposed with L-dopa therapy in patients who are experiencing a deteriorating response or fluctuating reactions to the drug. Another indication of bromocriptine is the therapy of hyperprolactinemia (state of persistent elevation of serum prolactin levels that may result in infertility and amenorrhea in females and galactorrhea in both males and females). Although the hallucinogen ergot alkaloid Lysergic acid diethyl amide (LSD) is no longer clinically employed, it was used unsuccessfully in psychiatry (just after the discovery of its pharmacological effects) for the treatment of acute obsessive illnesses such as alcoholic schizophrenia.

The trichothecenes have been associated with various biological properties, such as the following:

(a) Antiviral, especially as inhibitors of the replication of Herpes Simplex Virus type 2¹⁰⁶³ and type 1.¹⁰⁶⁴ Some derivatives have also shown inhibition capacity against arnavirus Junin (JUNV), the ethiological agent of the Argentine hemorrhagic fever.⁹³⁷

(b) Antibiotic.

(c) Antimalarial.^{936,1065}

(d) Antileukemic.¹⁰⁶⁶

(e) Immunotoxic.¹⁰⁶⁷

In 2004, the Oshima group described the development of synthetic spirocyclic trichothecenes with activity in neurotrophic factor biosynthesis.¹⁰⁶⁸ Recently, Zaichenko reviewed the experimental data in the biological activity of macrocyclic trichothecenes from the last 30 years. The

authors have shown the multifaceted biological effects of, in particular, their antibiotic, phytotoxic, insecticidal, cytotoxicity, and antitumor activities.¹⁰⁶⁹

Zearalenone is classified as a nonsteroidal estrogen or mycoestrogen. It has been used to treat postmenopausal symptoms in women, and its reduced form, zearalenol, has shown increased estrogenic activity and has been commercialized as an anabolic agent to promote growth in sheep and cattle. Moreover, zearalenone and zearalenol (**320**) are patented as oral contraceptives.

Citrinin displays antibiotic activity against Gram-positive bacteria⁸⁷⁷ and was even described as the “antibiotic of the future” in 1952.¹⁰⁷⁰ More recently citrinin has been tested against *Leshmania*, showing very promising activity in the inhibition of growth.¹⁰⁷¹

Patulin is known as bacterial mycotoxin. It inhibits potassium uptake and activates the p38 kinase. In the 1990s, *Fusarium* sp. was shown to inhibit HIV-1 integrase.¹⁰⁷² Some mycotoxins derivatives are described as antimetabolic agents.¹⁰⁷³

6. Conclusions/Summary

Mycotoxins are a major threat to human life.⁸⁴⁶ While a number of diseases associated with the toxicological impact of mycotoxins have been eradicated, globally increasing population density, together with a stricter usage of fungicides, has caused increasing awareness of the different classes of mycotoxins. Refinements of chromatographical techniques and methods of chemical and biological characterization have led to the discovery of new toxins excreted from lower and higher fungi.

The structure–activity relationship has been established for some classes of mycotoxins; however, most mycotoxins remain unexplored. The comprehensive understanding of biochemical pathways—both production and metabolism of fungal metabolites—should be a goal in mycology.

It is expected that microarray techniques will be extremely helpful in this regard; the first “mycochips” are already on the market. However, simple and reliable methods for the detection of mycotoxins are still needed.

7. Abbreviations

| | |
|-----|---------------------------------|
| AA | amino acid |
| Aoh | (s)-2-amino-7-oxoheptanoic acid |
| TCA | tricarballic acid |

8. Acknowledgments

We would like to thank those in Karlsruhe’s Mycotoxin group—namely, J. Podlech, W. Holzapfel, R. Geisen, M. Metzler, and R. Fischer—for their help and advice. In addition, we are grateful to our colleagues K. Krohn (Paderborn), P. Steyn (Stellenbosch), H. Laatsch (Göttingen), K. F. Nielsen (Copenhagen), W. Steglich (Munich), C. Hertweck (Jena), and E. Vaupel (Munich), who provided unpublished data and gave valuable advice. Our research has been funded by the DFG, the Fonds der Chemischen Industrie (fellowship to J.K.), and the Scheringstiftung (fellowship to C.F.N.).

9. References

- (1) While some mycotoxins have a distinct smell, we would like to emphasize their distinction from pheromones.
- (2) In some cases, toxic fungal polypeptides are also called mycotoxins.
- (3) In most cases, filamentous fungi are sources of mycotoxins.
- (4) Thomma, B. P. H. J. *Mol. Plant Path.* **2003**, *4*, 225.
- (5) Panaccione, D. G. *FEMS Microbiology Lett.* **2005**, *251*, 9.
- (6) For a very detailed review: Frisvad, J. C.; Smedsgaard, J.; Larsen, T. O.; Samson, R. A. *Stud. Mycol.* **2004**, *49*, 201.
- (7) Some useful databases: (a) <http://www.cbs.knaw.nl/databases/index.htm>; (b) <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>; (c) <http://www.eagleih.com/mycotoxins.html>. (d) Laatsch, H. *AntiBase 2009*, A Data Base for Rapid Dereplication and Structure Determination of Microbial Natural Products; Wiley-VCH: Weinheim, Germany, see <http://www.user.gwdg.de/nucoc/laatsch/AnitBase.htm>.
- (8) Review: Biabani, M. A. F.; Laatsch, H. *J. Prakt. Chemie/Chem.-Ztg.* **1998**, *340*, 589.
- (9) Isaka, M.; Kittakoop, P.; Kirtikara, K.; Hywel-Jones, N.; Thebthanonth, Y. *Acc. Chem. Res.* **2005**, *38*, 813.
- (10) Weidenbörner, M. *Encyclopedia of Food Mycotoxins*; Springer: Berlin, 2001.
- (11) Kuhn, D. M.; Ghannoum, M. A. *Clin. Microbiol. Rev.* **2003**, *16*, 144, and references therein.
- (12) Ueno, Y., Ed. *Trichothecenes—Chemical, Biological and Toxicological Aspects. Developments in Food Science*; Elsevier: Amsterdam, 1983; Vol. 4.
- (13) Vaillancourt, V.; Pratt, N. E.; Perron, F.; Albizati, K. F. *Total Synth. Nat. Prod.* ApSimon, J., Eds.; Wiley: New York, 1992; p 533.
- (14) Nishimura, S.; Kohmoto, K. *Ann. Rev. Phytopath.* **1983**, *21*, 87.
- (15) Dewick, P. M. *Medicinal Natural Products—A Biosynthetic Approach*, 2nd ed.; John Wiley: New York, 2001.
- (16) Betina, V. *Mycotoxins (Bioactive Molecules)*; Elsevier Science Publishers: Amsterdam, 1989; Vol. 9.
- (17) Goldblatt, L. A., Ed. *Aflatoxin: Scientific Background, Control, and Implications (Food Science and Technology)*; Academic Press: London, 1969; Vol. 7.
- (18) (a) An An, Z., Ed. *Handbook of industrial mycology*; CRC Press: Boca Raton, FL, 2004. (b) Arora, K., Ed. *Handbook of fungal biotechnology (Mycology, 20)*; Marcel Dekker: New York, 2004.
- (19) (a) Partida-Martinez, L. P.; Flores de Looß, C.; Ishida, K.; Ishida, M.; Roth, M.; Buder, K.; Hertweck, C. *App. Environ. Microbiol.* **2007**, *73*, 793. (b) Partida-Martinez, L. P.; Hertweck, C. *Nature (London)* **2005**, *437*, 884. (c) Scherlach, K.; Partida-Martinez, L. P.; Dahse, H. M.; Hertweck, C. *J. Am. Chem. Soc.* **2006**, *128*, 11529.
- (20) Lugauskas, A. *Bot. Lith.* **2005**, Suppl. 7:3.
- (21) For a list of the 474 mycotoxins and fungal metabolites, see: Nielsen, K. F.; Smedsgaard, J. *J. Chromatogr. A* **2003**, *1002*, 111.
- (22) Steyn, P. S. *Toxicol. Lett.* **1995**, *82/83*, 843.
- (23) For example: (a) www.cabi-bioscience.org/metabolitestrains.asp; (b) http://www.bioasso.org/EHP/eseect_d/SEP/L.html.
- (24) A useful database: <http://www.cbs.knaw.nl/databases/index.htm>.
- (25) Ling, K. H.; Yang, C.-K.; Peng, F.-T. *Appl. Environ. Microbiol.* **1979**, *37*, 355.
- (26) Although this compound affects vertebrates, this is not a *sensu stricto* mycotoxin.
- (27) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 186.
- (28) (a) Büchi, G.; Foulkes, D. M.; Kurono, M.; Mitchell, G. F. *J. Am. Chem. Soc.* **1966**, *88*, 4534. (b) Büchi, G.; Foulkes, D. M.; Kurono, M.; Mitchell, G. F.; Schneider, R. S. *J. Am. Chem. Soc.* **1967**, *89*, 6745.
- (29) (a) Büchi, G.; Weinreb, S. M. *J. Am. Chem. Soc.* **1969**, *91*, 5408. (b) Büchi, G.; Weinreb, S. M. *J. Am. Chem. Soc.* **1971**, *93*, 746.
- (30) Total syntheses: (a) Castellino, A. J.; Rapoport, H. *J. Org. Chem.* **1986**, *51*, 1006. (b) Horne, S.; Weeratunga, G.; Rodrigo, R. *J. Chem. Soc., Chem. Commun.* **1990**, 39.
- (31) Formal syntheses: (a) Weeratunga, G.; Horne, S.; Rodrigo, R. *J. Chem. Soc., Chem. Commun.* **1988**, 721. (b) Sloan, C. P.; Cuevas, J. C.; Quesnelle, C.; Snieckus, V. *Tetrahedron Lett.* **1988**, *29*, 4685. (c) Hoffmann, H. M. R.; Schmidt, B.; Wolff, S. *Tetrahedron* **1989**, *45*, 6113. (d) Koreeda, M.; Dixon, L. A.; Hsi, J. D. *Synlett* **1993**, 555. (e) Pirrung, M. C.; Lee, Y. R. *Tetrahedron Lett.* **1996**, *37*, 2391. (f) Kraus, G. A.; Wang, X. *Tetrahedron Lett.* **1999**, *40*, 8513. (g) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 3543. (h) Eastham, S. A.; Ingham, S. P.; Hallett, M. R.; Herbert, J.; Quayle, P.; Raftery, J. *Tetrahedron Lett.* **2006**, *47*, 2299.
- (32) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2003**, *125*, 3090.
- (33) Roberts, J. C.; Sheppard, A. H.; Knight, J. A.; Roffey, P. *J. Chem. Soc. (C)* **1968**, 22.
- (34) Zhou, G.; Corey, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 11958.
- (35) Büchi, G.; Spitzner, D.; Paglialonga, S.; Wogan, G. N. *Life Sci.* **1973**, *13*, 1143.
- (36) Huchinson, R. D.; Holzapfel, C. W. *Tetrahedron* **1971**, *27*, 425.
- (37) Hamasaki, T.; Nakagomi, T.; Hatsuda, Y.; Fukuyama, K.; Katsube, Y. *Tetrahedron Lett.* **1977**, 2765.
- (38) Cole, R. J.; Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 91.

- (39) Hatsuda, Y.; Hamasaki, T.; Ishida, M.; Matsui, K.; Hara, S. *Agric. Biol. Chem.* **1972**, *36*, 521.
- (40) (a) Rance, M. J.; Roberts, J. C. *Tetrahedron Lett.* **1969**, *10*, 277. (b) Rance, M. J.; Roberts, J. C. *Tetrahedron Lett.* **1970**, *11*, 2799.
- (41) (a) Rance, M. J.; Roberts, J. C. *J. Chem. Soc. (C)* **1971**, 1247. (b) Horne, S.; Rodrigo, R. *J. Org. Chem.* **1990**, *55*, 4520.
- (42) (a) Cole, R. J., Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 73. (b) Sax, N. I. *Dangerous Properties of Industrial Materials*, 6th ed.; Van Nostrand-Reinhold: New York, 1984; p 995.
- (43) Stoessl, A.; Stothers, J. B. *Can. J. Chem.* **1985**, *63*, 1258.
- (44) Casillas, L. K.; Townsend, C. A. *J. Org. Chem.* **1999**, *64*, 4050.
- (45) (a) Blakemore, P. R.; Schulze, V. K.; White, J. D. *Chem. Commun.* **2000**, 1263. (b) Blakemore, P. R.; Kim, S.-K.; Schulze, V. K.; White, J. D.; Yokochi, A. F. T. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1831. (c) Prager, R. H.; Were, S. T. *Aust. J. Chem.* **1983**, *36*, 1441. (d) Kasum, B.; Prager, R. H. *Aust. J. Chem.* **1983**, *36*, 1455. (e) Ridley, A. B.; Taylor, W. C. *Aust. J. Chem.* **1987**, *40*, 631.
- (46) Wagner, C.; Anke, H.; Sterner, O. *J. Nat. Prod.* **1998**, *61*, 501.
- (47) Goddard, M.-L.; Tabacchi, R. *Tetrahedron Lett.* **2006**, *47*, 909.
- (48) Bradburn, N.; Coker, R. D.; Blunden, G.; Turner, C. H.; Crabb, T. A. *Phytochem.* **1994**, *35*, 665.
- (49) Pero, R. W.; Owens, R. G.; Dale, S. W.; Harvan, D. J. *Biochim. Biophys. Acta* **1971**, *230*, 170.
- (50) Stinson, E. E. *J. Food Protect.* **1985**, *48*, 80.
- (51) Griffin, G. F.; Chu, F. S. *Appl. Environ. Microbiol.* **1983**, *46*, 1420.
- (52) Altemöller, M.; Podlech, J.; Fenske, D. *Eur. J. Org. Chem.* **2006**, 1678.
- (53) Thomas, R. *Biochem. J.* **1961**, *80*, 234.
- (54) Rosett, T.; Sankhala, R. H.; Stickings, C. E.; Taylor, M. E. U.; Thomas, R. *Biochem. J.* **1957**, *67*, 390.
- (55) Furutani, Y.; Shimada, M.; Hamada, M.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1975**, *28*, 558.
- (56) Williams, D. J.; Thomas, R. *Tetrahedron Lett.* **1973**, 639.
- (57) Chu, F. S. *J. Am. Oil Chem. Soc.* **1981**, *58*, 1006A.
- (58) Pero, R. W.; Harvan, D.; Blois, M. C. *Tetrahedron Lett.* **1973**, 945.
- (59) Nakanishi, S.; Toki, S.; Saitoh, Y.; Tsukuda, E.; Kawahara, K.; Ando, K.; Matsuda, Y. *Biosci. Biotechnol. Biochem.* **1995**, *59*, 1333.
- (60) Uchida, R.; Tomoda, H.; Dong, Y.; Omura, S. *J. Antibiot.* **1999**, *52*, 572.
- (61) Takahashi, S.; Kamisuki, S.; Mizushima, Y.; Sakaguchi, K.; Sugawara, F.; Nakata, T. *Tetrahedron Lett.* **2003**, *44*, 1875.
- (62) (a) Trost, B. M.; Probst, G. D.; Schoop, A. *J. Am. Chem. Soc.* **1998**, *120*, 9228. (b) Tabuchi, H.; Hamamoto, T.; Miki, S.; Tejima, T.; Ichihara, A. *J. Org. Chem.* **1994**, *59*, 4749.
- (63) Hay, J. V.; Harris, T. M. *J. Chem. Soc., Chem. Commun.* **1972**, 953.
- (64) Kanakam, C. C.; Mani, N. S.; Subba Rao, G. S. R. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2233.
- (65) Koch, K.; Podlech, J.; Pfeiffer, E.; Metzler, M. *J. Org. Chem.* **2005**, *70*, 3275.
- (66) Xiao, P.; Gloer, J. B.; Campbell, J.; Shearer, C. A. *J. Nat. Prod.* **2006**, *69*, 612.
- (67) Soorukram, D.; Qu, T.; Barrett, A. G. M. *Org. Lett.* **2008**, *10*, 3833.
- (68) (a) Cole, R. J., Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 634. (b) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; pp 132–133.
- (69) Kamisuki, S.; Takahashi, S.; Mizushima, Y.; Hanashima, S.; Kuramochi, K.; Kobayashi, S.; Sakaguchi, K.; Nakata, T.; Sugawara, F. *Tetrahedron* **2004**, *60*, 5695.
- (70) Ayer, W. A.; Racok, J. S. *Can. J. Chem.* **1990**, *68*, 2085.
- (71) Visconti, A.; Bottalico, A.; Solfrizzo, M.; Palmisano, F. *Mycotoxicol. Res.* **1989**, *5*, 69.
- (72) Palmisano, F.; Sibilia, A.; Visconti, A. *Chromatographia* **1990**, *29*, 333.
- (73) Nawaz, S.; Scudamore, K. A.; Rainbird, S. C. *Food Addit. Contam.* **1997**, *14*, 249.
- (74) (a) Stickings, C. E. *Biochem. J.* **1959**, *72*, 332. (b) Stickings, C. E.; Townsend, R. J. *Biochem. J.* **1961**, *78*, 412.
- (75) Yuki, H.; Tsujimoto, T.; Sawada, T.; Takiura, K.; Yamaguchi, T. *Yakugaku Zasshi* **1976**, *96*, 536.
- (76) Jahngen, E. G. E., Jr.; Rossomando, E. F. *Synth. Commun.* **1982**, *12*, 601.
- (77) Review: Byun, H.-S.; Lu, X.; Bittmann, R. *Synthesis* **2006**, 2447.
- (78) For example: (a) Shibata, K.; Shingu, K.; Vassilev, V. P.; Nishide, K.; Fujita, T.; Node, M.; Kajimoto, T.; Wong, C.-H. *Tetrahedron Lett.* **1996**, *37*, 2791. (b) Iwabuchi, Y.; Furukawa, M.; Esumi, T.; Hatelyama, S. *Chem. Commun.* **2001**, 2030. (c) Byun, H.-S.; Lu, X.; Bittman, R. *Synthesis* **2006**, 2447.
- (79) (a) Gonda, J.; Martinkova, M.; Raschmanova, J.; Balentova, E. *Tetrahedron: Asymmetry* **2006**, *17*, 1875. (b) Lee, K.-Y.; Oh, C.-Y.; Kim, Y.-H.; Joo, J.-E.; Ham, W.-H. *Tetrahedron Lett.* **2002**, *43*, 9361. (c) Oishi, T.; Ando, K.; Chida, N. *Chem. Commun.* **2001**, 1932. (d) Hatakeyama, S.; Yoshida, M.; Esumi, T.; Iwabuchi, Y.; Irie, H.; Kawamoto, T.; Yamada, H.; Nishizawa, M. *Tetrahedron Lett.* **1997**, *38*, 7887. (e) Banfi, L.; Beretta, M. G.; Colombo, L.; Gennari, C.; Scolastico, C. *J. Chem. Soc., Chem. Commun.* **1982**, 488. (f) Byun, H.-S.; Lu, X.; Bittman, R. *Synthesis* **2006**, 2447.
- (80) (a) Davis, R. A. *J. Nat. Prod.* **2005**, *68*, 769. (b) Davis, R. A.; Kotiw, M. *Tetrahedron Lett.* **2005**, *46*, 5199.
- (81) (a) Morokuma, K.; Takahashi, K.; Ishihara, J.; Hatakeyama, S. *Chem. Commun.* **2005**, 2265. (b) Pollex, A.; Millet, A.; Müller, J.; Hiersemann, M.; Abraham, L. *J. Org. Chem.* **2005**, *70*, 5579.
- (82) Maskey, R. P.; Grun-Wollny, I.; Laatsch, H. *J. Antibiot.* **2003**, *56*, 459.
- (83) Morooka, N.; Nakano, S.; Itoi, N.; Ueno, Y. *Agric. Biol. Chem.* **1990**, *54*, 1247.
- (84) Krohn, K.; Markus, H.; Kraemer, H. P.; Frank, W. *Liebigs Ann.* **1988**, 1033.
- (85) Kelly, T. R.; Montury, M. *Tetrahedron Lett.* **1978**, 4309.
- (86) Hoeller, U.; Gloer, J. B.; Wicklow, D. T. *J. Nat. Prod.* **2002**, *65*, 876.
- (87) Birkinshaw, J. H.; Gourlay, R. *Biochem. J.* **1961**, *81*, 618.
- (88) (a) Thomson, R. H. *Naturally Occurring Quinones II*; Springer: Heidelberg, Germany, 1988; p 483. (b) Townsend, C. A. *Tetrahedron Lett.* **1986**, *27*, 887. (c) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 187, 188, and 191.
- (89) (a) Thomson, R. H. *Naturally Occurring Quinones II*; Springer: Heidelberg, Germany, 1988; p 487. (b) Horak, R. M.; Steyn, P. S.; Vleggaar, R.; Rabie, C. J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 345.
- (90) (a) Cole, R. J., Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 107. (b) Townsend, C. A.; Christensen, S. B. *J. Am. Chem. Soc.* **1985**, *107*, 270.
- (91) Yamazaki, M.; Satoh, Y.; Maebayashi, Y.; Horie, Y. *Chem. Pharm. Bull.* **1988**, *36*, 670.
- (92) O'Malley, G. J.; Murphy, R. A., Jr.; Cava, M. P. *J. Org. Chem.* **1985**, *50*, 5533.
- (93) (a) Townsend, C. A.; Christensen, S. B.; Davis, S. G. *J. Chem. Soc., Perkin Trans. 1* **1988**, 839. (b) Koreeda, M.; Hulin, B.; Yoshihara, M.; Townsend, C. A.; Christensen, S. B. *J. Org. Chem.* **1985**, *50*, 5426. (c) Castonguay, A.; Brassard, P. *Can. J. Chem.* **1977**, *55*, 1324.
- (94) (a) Raistrick, H.; Robinson, R.; Todd, A. R. *Biochem. J.* **1934**, *28*, 559. (b) Arai, K.; Aoki, Y.; Yamamoto, Y. *Chem. Pharm. Bull.* **1989**, *37*, 621.
- (95) (a) Braun, M. *Liebigs Ann.* **1981**, 2247. (b) Chandrasenan, K.; Neelakantan, S.; Seshadri, T. R. *Proc. Indiana Acad. Sci.* **1960**, *51A*, 296. (c) Anslow, W. K.; Raistrick, H. *Biochem. J.* **1941**, *35*, 1006.
- (96) (a) Schlösser, E. *Phytopath. Z.* **1962**, *44*, 295. (b) Kuyuma, S.; Tamura, T. *J. Am. Chem. Soc.* **1957**, *79*, 5727. (c) Yamazaki, S.; Ogawa, T. *Agric. Biol. Chem.* **1972**, *36*, 1707. (d) Yamazaki, S.; Okubo, A.; Akiyama, Y.; Fuwa, K. *Agric. Biol. Chem.* **1975**, *39*, 287. (e) Lynch, F. J.; Geoghegan, M. *J. Trans. Brit. Mycol. Soc.* **1977**, *69*, 496. (f) Ragunathan, V.; Govindarajulu, T. *Curr. Trends Life Sci.* **1979**, *6*, 49. (g) Matsueda, S.; Takagaki, K.; Shimoyama, M.; Shiota, A. *J. Pharmacol. Soc. Jpn.* **1980**, *100*, 900.
- (97) (a) Mueller, K.; Mayer, K. K.; Wiegrebe, W. *Arch. Pharm.* **1986**, *319*, 1009. (b) Naylor, C. A., Jr.; Gardner, J. H. *J. Am. Chem. Soc.* **1931**, *53*, 4109.
- (98) Howard, B. H.; Raistrick, H. *Biochem. J.* **1950**, *46*, 49.
- (99) (a) Kuhnert, N.; Molod, H. Y. *Tetrahedron Lett.* **2005**, *46*, 7571. (b) Kraus, G. A.; Cho, H.; Crowley, S.; Roth, B.; Sugimoto, H.; Prugh, S. *J. Org. Chem.* **1983**, *48*, 3439. (c) Jung, M. E.; Lowe, J. A. *J. Chem. Soc., Chem. Commun.* **1978**, 95.
- (100) Krohn, K. *Tetrahedron Lett.* **1980**, *21*, 3557.
- (101) Ahmed, S. A.; Bardshiri, E.; Simpson, T. J. *J. Chem. Soc., Chem. Commun.* **1987**, 883.
- (102) Ayyangar, N. R.; Bapat, D. S.; Joshi, B. S. *J. Sci. Ind. Res.* **1961**, *20B*, 493.
- (103) Pringle, R. B. *Biochim. Biophys. Acta* **1958**, *28*, 198.
- (104) Assante, G.; Nasini, G. *Phytochemistry* **1987**, *26*, 703.
- (105) (a) Nielsen, K. F. Ph. D. thesis, Mould growth on building material, Statens Byggeforskningsinstitut, Denmark, 2002. (b) Cole, R. J., Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981.
- (106) (a) Berger, Y.; Jadot, J.; Ramaut, J. *Bull. Soc. Chim. Belg.* **1976**, *85*, 161. (b) Thomson, R. H. *Naturally Occurring Quinones III*; Springer: Heidelberg, Germany, 1988; p 495.
- (107) Kurobane, I.; Vining, L. C.; McInnes, A. G. *J. Antibiot.* **1979**, *32*, 1256.
- (108) (a) Teich, L.; Daub, K. S.; Kruegel, V.; Nissler, L.; Gebhardt, R.; Eger, K. *Bioorg. Med. Chem.* **2004**, *12*, 5961. (b) Khan, A. T.;

- Blessing, B.; Schmidt, R. R. *Synthesis* **1994**, 255. (c) Banville, J.; Grandmaison, J. L.; Lang, G.; Brassard, P. *Can. J. Chem.* **1974**, 52, 80. (d) Hirose, Y.; Kuroiwa, M.; Yamashita, H.; Tanaka, T.; Megumi, T. *Chem. Pharm. Bull.* **1973**, 21, 2790. (e) Wells, J. M.; Cole, R. J.; Kirksey, J. W. *Appl. Microbiol.* **1975**, 30, 26.
- (109) Tatsuno, T.; Kobayashi, N.; Okubo, K.; Tsunoda, H. *Chem. Pharm. Bull.* **1975**, 23, 351.
- (110) (a) Waser, M.; Lackner, B.; Zuschrader, J.; Müller, N.; Falk, H. *Tetrahedron Lett.* **2005**, 46, 2377. (b) Franck, B.; Ohnsorge, U.; Flasch, H. *Tetrahedron Lett.* **1970**, 3773. (c) Steglich, W.; Reininger, W. *Chem. Commun.* **1970**, 178.
- (111) Braun, M. *Tetrahedron Lett.* **1979**, 2885.
- (112) Shoji, J.; Shibata, S.; Sankawa, U.; Taguchi, H.; Shibamura, Y. *Chem. Pharm. Bull.* **1965**, 13, 1240.
- (113) Dixon, D. J.; Ley, S. V.; Gracza, T.; Szolcsanyi, P. *J. Chem. Soc., Perkin Trans. 1* **1999**, 839.
- (114) Betina, V.; Sedmera, P.; Vokoun, J.; Podojil, M. *Experientia* **1986**, 42, 196.
- (115) Laatsch, H.; Anke, H. *Liebigs Ann.* **1982**, 2189.
- (116) Smith, C. W.; Ambler, S. J.; Steggles, D. J. *Tetrahedron Lett.* **1993**, 34, 7447.
- (117) Nicoletti, T. M.; Raston, C. L.; Sargent, M. V. *J. Chem. Soc., Chem. Commun.* **1988**, 1491.
- (118) Suemitsu, R.; Yamamoto, T.; Miyai, T.; Ueshima, T. *Phytochemistry* **1987**, 26, 3221.
- (119) King, N. M. *J. Am. Pharm. Assoc.* **1957**, 46, 271.
- (120) Banville, J.; Brassard, J. *Chem. Soc., Perkin Trans. 1* **1976**, 1852.
- (121) Agarwal, S. K.; Singh, S. S.; Verma, S.; Kumar, S. *J. Ethnopharmacol.* **2000**, 72, 43.
- (122) Tisserand, S.; Baati, R.; Nicolas, M.; Mioskowski, C. *J. Org. Chem.* **2004**, 69, 8982.
- (123) Huang, Q.; Lu, G.; Shen, H. M.; Chung, M. C.; Ong, C. N. *Med. Res. Rev.* **2007**, 27, 609.
- (124) Fujimoto, H.; Nakamura, E.; Okuyama, E.; Ishibashi, M. *Chem. Pharm. Bull.* **2004**, 52, 1005.
- (125) Song, G.; Wu, J.; He, X. *Huaxue Xuebao* **1985**, 43, 145. [CAN: 102:220356].
- (126) Rajagopalan, T. R.; Seshadri, T. R. *Proc. Indiana Acad. Sci.* **1956**, 44A, 418.
- (127) Suemitsu, R.; Horiuchi, K.; Ohnishi, K.; Kubota, M. *J. Chromatogr.* **1990**, 503, 282.
- (128) Suemitsu, R.; Horiuchi, K.; Ohnishi, K.; Yanagawase, S. *J. Chromatogr. Suppl.* **1988**, 454, 406.
- (129) Brady, S. F.; Singh, M. P.; Janso, J. E.; Clardy, J. *Org. Lett.* **2000**, 2, 4047.
- (130) Nicolaou, K. C.; Lim, Y. H.; Papageorgiou, C. D.; Piper, J. L. *Angew. Chem., Int. Ed.* **2005**, 44, 7917.
- (131) Nicolaou, K. C.; Lim, Y. H.; Piper, J. L.; Papageorgiou, C. D. *J. Am. Chem. Soc.* **2007**, 129, 4001.
- (132) Nicolaou, K. C.; Papageorgiou, C. D.; Piper, J. L.; Chadha, R. K. *Angew. Chem., Int. Ed.* **2005**, 44, 5846.
- (133) Stark, A. A.; Townsend, J. M.; Wogan, G. N.; Demain, A. L.; Manmade, A.; Ghosh, A. C. *J. Env. Path. Toxicol.* **1978**, 2, 313.
- (134) Oghihara, Y.; Kobayashi, N.; Shibata, S. *Tetrahedron Lett.* **1968**, 1881.
- (135) Franck, B.; Chahin, R.; Eckert, H. G.; Langenberg, R.; Radtke, V. *Angew. Chem.* **1975**, 87, 846.
- (136) Steyn, P. S.; Vleggaar, R. *J. Chem. Soc., Perkin Trans. 1* **1974**, 2250.
- (137) Horak, R. M.; Steyn, P. S.; Vleggaar, R.; Rabie, C. J. *S. Afr. J. Chem.* **1982**, 35, 60.
- (138) Gorst-Allman, C. P.; Nolte, M. J.; Steyn, P. S. *S. Afr. J. Chem.* **1978**, 31, 143.
- (139) Choshi, T.; Kumemura, T.; Nobuhiro, J.; Hibino, S. *Tetrahedron Lett.* **2008**, 49, 3725.
- (140) (a) Thomson, R. H. *Naturally Occurring Quinones II*; Springer: Heidelberg, Germany, 1988; p 642. (b) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 124. (c) Baker, R. A.; Tatum, J. H.; Nemeč, S., Jr. *Mycopathologia* **1990**, 111, 9.
- (141) Cameron, D. W.; Deutscher, K. R.; Feutrill, G. I. *Aust. J. Chem.* **1982**, 35, 1439.
- (142) Cameron, D. W.; Deutscher, K. R.; Feutrill, G. I. *Tetrahedron Lett.* **1980**, 21, 5089.
- (143) Gray, R. W.; Whalley, W. B. *J. Chem. Soc.* **1971**, 3575.
- (144) Büchi, G.; White, J. D.; Wogan, G. N. *J. Am. Chem. Soc.* **1965**, 87, 3484.
- (145) Chong, R.; Gray, R. W.; King, R. R.; Whalley, W. B. *J. Chem. Soc., Perkin Trans. 1* **1971**, 21, 3571.
- (146) Zhu, J.; Porco, J. A., Jr. *Org. Lett.* **2006**, 8, 5169.
- (147) Marsini, M. A.; Gowin, K. M.; Pettus, T. R. *Org. Lett.* **2006**, 8, 3481.
- (148) Natsume, M.; Takahashi, Y.; Marmo, S. *Agric. Biol. Chem.* **1985**, 49, 2517.
- (149) Kanokmedhakul, S.; Kanokmedhakul, K.; Nasomjai, P.; Louang-souphanh, S.; Soyong, K.; Isobe, M.; Kongsaree, P.; Prabpai, S.; Suksamrarn, A. *J. Nat. Prod.* **2006**, 69, 891.
- (150) Kwon, Y.-J.; Sohn, M.-J.; Zheng, C.-J.; Kim, W.-G. *Org. Lett.* **2007**, 9, 2449.
- (151) Bracken, A.; Pocker, A.; Raistrick, H. *Biochem. J.* **1954**, 57, 587.
- (152) (a) Rhee, R. P.; White, J. D. *J. Org. Chem.* **1977**, 42, 3650. (b) Martin, P. K.; Rapoport, H.; Smith, H. W.; Wong, J. L. *J. Org. Chem.* **1969**, 34, 1359. (c) Smith, H.; Wegfahrt, P.; Rapoport, H. *J. Am. Chem. Soc.* **1968**, 90, 1668.
- (153) Birkenshaw, J. H.; Luckner, M.; Mohammed, Y. S.; Mothes, K.; Stickings, C. E. *Biochem. J.* **1963**, 89, 196.
- (154) (a) Goetz, M. A.; Lopez, M.; Monaghan, R. L.; Chang, R. S. L.; Lotti, V. J.; Chen, T. B. *J. Antibiot.* **1985**, 38, 1633. (b) Liesch, J. M.; Hensens, O. D.; Springer, J. P.; Chang, R. S. L.; Lotti, V. J. *J. Antibiot.* **1985**, 38, 1638. (c) Sun, H. H.; Byard, S. J.; Cooper, R. *J. Antibiot.* **1994**, 47, 599.
- (155) (a) He, F.; Foxman, B. M.; Snider, B. B. *J. Am. Chem. Soc.* **1998**, 120, 6417. (b) Al-Said, N. H.; Al-Qaisi, L. S. *Tetrahedron Lett.* **2006**, 47, 693.
- (156) Liu, J.-F.; Kaselj, M.; Isome, Y.; Chapnick, J.; Zhang, B.; Bi, G.; Johannes, D.; Yu, L.; Badino, C. M. *J. Org. Chem.* **2005**, 70, 10488.
- (157) Sugimori, T.; Okawa, T.; Eguchi, S.; Yashima, E.; Kehehi, A.; Okamoto, Y. *Tetrahedron* **1998**, 54, 7997.
- (158) Witt, A.; Bergman, J. *J. Org. Chem.* **2001**, 66, 2784.
- (159) Snider, B. B.; Busuyek, M. N. *Tetrahedron* **2001**, 57, 3301.
- (160) Du, C.; Li, L.-Q.; Da, S.-J.; Li, Y.; Xie, Z.-X. *Chin. J. Chem.* **2008**, 26, 693.
- (161) Sakai, K.; Watanabe, K.; Masuda, K.; Tsuji, M.; Hasumi, K.; Endo, A. *J. Antibiot.* **1995**, 48, 447.
- (162) Sperry, J.; Brimble, M. *Synlett* **2008**, 1910. and cited references.
- (163) Parker, S. R.; Cutler, H. G.; Schreiner, P. R. *Biosci. Biotechnol. Biochem.* **1995**, 59, 1126.
- (164) Cutler, H. G.; Cutler, S. J.; Ross, S. A.; Sayed, K. E.; Dugan, F. M.; Bartlett, M. G.; Hill, A. A.; Hill, R. A.; Parker, S. R. *J. Nat. Prod.* **1999**, 62, 137.
- (165) (a) Liu, G.; Wang, Z. *Synthesis* **2001**, 119. (b) Liu, G.; Wang, Z. *Chem. Commun.* **1999**, 1129. (c) Xu, X.-X.; Zhu, Y.-H. *Tetrahedron Lett.* **1995**, 36, 9173. (d) Mori, K.; Abe, K. *Liebigs Ann.* **1995**, 943.
- (166) Vleggaar, R.; Steyn, P. S.; Nagel, D. W. *J. Chem. Soc., Perkin Trans. 1* **1974**, 45.
- (167) Wang, S.; Li, X. M.; Teuscher, F.; Li, D. L.; Diesel, A.; Ebel, R.; Proksch, P.; Wang, B. G. *J. Nat. Prod.* **2006**, 6916.
- (168) Grove, J. F.; Brian, P. W. *Nature (London)* **1951**, 167, 995.
- (169) Yamauchi, M.; Katayama, S.; Watanabe, T. *J. Chem. Soc., Perkin Trans. 1* **1987**, 395.
- (170) (a) Hu, Y.; Li, C.; Kulkarni, B. A.; Strobel, G.; Lobkovsky, E.; Torczynski, R. M.; Porco, J. A., Jr. *Org. Lett.* **2001**, 3, 1649. (b) Mehta, G.; Pan, S. C. *Org. Lett.* **2004**, 6, 811.
- (171) (a) Gorst-Allmann, C. P.; Vleggaar, R. S. *Afr. J. Chem.* **1987**, 40, 116. (b) Cutler, H. G.; Crumley, F. G.; Cox, R. H.; Cole, R. J.; Dorner, J. W.; Latterell, F. M.; Rossi, A. E. *J. Agric. Food Chem.* **1980**, 28, 135. (c) Chalmers, A. A.; Gorst-Allman, C. P.; Kriek, N. P. J.; Marasas, W. F. O.; Steyn, P. S.; Vleggaar, R. S. *Afr. J. Chem.* **1978**, 31, 111. (d) Boutibonnes, P. *IRCS Med. Sci.* **1980**, 8, 850. [CA,90,83595; 94,41957].
- (172) Xie, W.; Mirocha, C. J.; Wen, Y. *J. Nat. Prod.* **1995**, 58, 124.
- (173) Musso, H.; Beecken, H. *Chem. Ber.* **1959**, 92, 1416.
- (174) Beaumont, P. C.; Edwards, R. L. *J. Chem. Soc. C* **1969**, 2398.
- (175) (a) Barton, D. H.; Cottier, L.; Freund, K.; Luini, F.; Magnus, P. D.; Salazar, I. *J. Chem. Soc., Perkin Trans. 1* **1976**, 499. (b) Bekaert, A.; Andrieux, J.; Plat, M. *Tetrahedron Lett.* **1992**, 33, 2805. (c) Hauser, F. M.; Hewawasam, P.; Baghdanov, V. M. *J. Org. Chem.* **1988**, 53, 223. (d) Kjaer, D.; Kjaer, A.; Risbjerg, E. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2815. (e) Katagiri, N.; Nakano, J.; Kato, T. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2710.
- (176) Akiyama, K.; Teraguchi, S.; Hamasaki, Y.; Mori, M.; Tatsumi, K.; Ohnishi, K.; Hayashi, H. *J. Nat. Prod.* **2003**, 66, 136.
- (177) Priestap, H. A. *Tetrahedron* **1984**, 40, 3617.
- (178) (a) Frisvad, J. C.; Filtenborg, O.; Samson, R. A.; Stolk, A. C. *Antonie Van Leeuwenhoek* **1990**, 57, 179. Synthesis: (b) Brown, S. P.; Goodwin, N. C.; MacMillan, D. W. *J. Am. Chem. Soc.* **2003**, 125, 1192.
- (179) Brown, S. P.; Goodwin, N. C.; MacMillan, D. W. *J. Am. Chem. Soc.* **2003**, 125, 119.
- (180) (a) Williams, R. M.; Esslinger, C. S. *Tetrahedron Lett.* **1991**, 32, 3635. (b) Snider, B. B.; Neuber, B. J. *J. Org. Chem.* **2004**, 69, 8952.
- (181) Raphael, R. A. *Nature (London)* **1947**, 160, 261.
- (182) Yeh, C.-L.; Colwell, W. T.; DeGraw, J. I. *Tetrahedron Lett.* **1978**, 3987.
- (183) Steyn, P. S.; Vleggaar, R. *Chem. Commun.* **1985**, 1531.

- (184) (a) Patel, P.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1941. (b) Venkataraman, H.; Cha, J. K. *Tetrahedron Lett.* **1987**, 28, 2455. (c) Patel, P.; Pattenden, G. *Tetrahedron Lett.* **1985**, 26, 4789.
- (185) (a) Murata, Y.; Kamino, T.; Aoki, T.; Hosokawa, S.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2004**, 43, 3175. (b) Peng, Z.-H.; Woerpel, K. A. *Org. Lett.* **2002**, 4, 2945. (c) Mulzer, J.; Bilow, J.; Wille, G. *J. Prakt. Chem.* **2000**, 342, 773. (d) Hanaki, N.; Link, J. T.; MacMillan, D. W. C.; Overman, L. E.; Trankle, W. G.; Wurster, J. A. *Org. Lett.* **2000**, 2, 223. (e) Ebenezer, W.; Pattenden, G. *Tetrahedron Lett.* **1992**, 33, 4053. (f) Bowden, M. C.; Patel, P.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1947. (g) Trost, B. M.; Lynch, J. K.; Angle, S. R. *Tetrahedron Lett.* **1987**, 28, 375.
- (186) Whang, K.; Venkataraman, H.; Kim, Y. G.; Cha, J. K. *J. Org. Chem.* **1991**, 56, 7174.
- (187) Franck, B.; Gehrken, H. P. *Angew. Chem., Int. Ed.* **1980**, 19, 461.
- (188) Williams, D. R.; White, F. H. *J. Org. Chem.* **1987**, 52, 5067.
- (189) Dong, J.-Y.; He, H.-P.; Shen, Y.-M.; Zhang, K.-Q. *J. Nat. Prod.* **2005**, 68, 1510.
- (190) Goliński, P.; Wnuk, S.; Chełkowski, J.; Visconti, A.; Schollenberger, M. *Appl. Environ. Microbiol.* **1986**, 51, 743.
- (191) (a) Betini, S. *Ann. Sper. Agrar.* **1957**, 11, 545. (b) Seibert, S. F.; Eguereva, E.; Krick, A.; Kehraus, S.; Voloshina, E.; Raabe, G.; Fleischhauer, J.; Leistner, E.; Wiese, M.; Prinz, H.; Alexandrov, K.; Janning, P.; Waldmann, H.; König, G. M. *Org. Biomol. Chem.* **2006**, 4, 2233.
- (192) (a) Galbraith, M. N.; Whalley, W. B. *J. Chem. Soc. C* **1971**, 3557. (b) Colombo, L.; Gennari, C.; Scolastico, C.; Aragozzini, F.; Merendi, C. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2549.
- (193) Galbraith, M. N.; Whalley, W. B. *Chem. Commun.* **1966**, 620.
- (194) Cartwright, N. J.; Robertson, A.; Whalley, W. B. *Nature (London)* **1949**, 163, 94.
- (195) Cartwright, N. J.; Robertson, A.; Whalley, W. B. *J. Chem. Soc.* **1949**, 1563.
- (196) Johnson, D. H.; Robertson, A.; Whalley, W. B. *J. Chem. Soc.* **1949**, 2971.
- (197) Warren, H. H.; Dougherty, G.; Wallis, E. S. *J. Am. Chem. Soc.* **1949**, 71, 3422.
- (198) Barber, J. A.; Staunton, J.; Wilkinson, M. R. *J. Chem. Soc., Perkin Trans. 1* **1986**, 2101.
- (199) Regan, A. C.; Staunton, J. *J. Chem. Soc., Chem. Commun.* **1987**, 520.
- (200) Rödel, T.; Gerlach, H. *Liebigs Ann.* **1995**, 885.
- (201) Ziegler, E.; Nolken, E.; Fuchs, E. *Monatsh. Chem.* **1960**, 91, 1124.
- (202) (a) Hüttel, W.; Nieger, M.; Müller, M. *Synthesis* **2003**, 1803. (b) Baker, R. W.; Kyasnoor, R. V.; Sargent, M. V.; Skelton, B. W.; White, A. H. *Aust. J. Chem.* **2000**, 53, 487. (c) Kyasnoor, R. V.; Sargent, M. V. *A. Chem. Commun.* **1998**, 2713. (d) Rizzacasa, M. A.; Sargent, M. V. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2425.
- (203) (a) Ward, D. E.; Gai, Y.; Lazny, R.; Pedras, M. S. *J. Org. Chem.* **2001**, 66, 7832. (b) Ast, T.; Barron, E.; Kinne, L.; Schmidt, M.; Germeroth, L.; Simmons, K.; Wenschuh, H. *J. Pept. Res.* **2001**, 58, 1. (c) Ward, D. E.; Lazny, R.; Pedras, M. S. *Tetrahedron Lett.* **1997**, 38, 339.
- (204) (a) Ivanova, L.; Skjerve, E.; Eriksen, G. S.; Uhlig, S. *Toxicon* **2006**, 47, 868. (b) Jestoi, M.; Rokka, M.; Yli-Mattila, T.; Parikka, P.; Rizzo, A.; Peltonen, K. *Food Addit. Contam.* **2004**, 21, 794. (c) Thrane, U.; Adler, A.; Clasen, P. E.; Galvano, F.; Langseth, W.; Lew, H.; Logrieco, A.; Nielsen, K. F.; Ritiieni, A. *Int. J. Food Microbiol.* **2004**, 95, 257. (d) Logrieco, A.; Rizzo, A.; Ferracane, R.; Ritiieni, A. *Appl. Environ. Microbiol.* **2002**, 68, 82. (e) Tomoda, H.; Nishida, H.; Huang, X. H.; Masuma, R.; Kim, Y. K.; Omura, S. *J. Antibiot. (Tokyo)* **1992**, 45, 1207. (f) Audhya, T. K.; Russell, D. W. *J. Gen. Microbiol.* **1975**, 86, 327. (g) Audhya, T. K.; Russell, D. W. *Can. J. Microbiol.* **1973**, 19, 1051.
- (205) (a) Shemyakin, M. M.; Ovchinnikov, Y. A.; Kiryushkin, A. A.; Ivanov, V. T. *Izv. Akad. Nauk. SSSR Ser. Khim.* **1965**, 1623. (b) Ovchinnikov, Y. A.; Ivanov, V. T.; Mikhaleva, I. I.; Shemyakin, M. M. *Izv. Akad. Nauk. SSSR Ser. Khim.* **1964**, 1912. (c) Quitt, P.; Studer, R. O.; Vogler, K. *Helv. Chim. Acta* **1964**, 47, 166. (d) Shemyakin, B. M. M.; Ovchinnikov, Y. A.; Kiryushkin, A. A.; Ivanov, V. T. *Tetrahedron Lett.* **1963**, 885.
- (206) Moussa, M. M.; Le Quesne, P. W. *Tetrahedron Lett.* **1996**, 37, 6479.
- (207) (a) Ovchinnikov, Y. A.; Ivanov, V. T.; Mikhaleva, I. I. *Tetrahedron Lett.* **1971**, 159. (b) Hiroshi, T.; Takayuki, D. *Acc. Chem. Res.* **2008**, 41, 32.
- (208) Gu, W.; Silverman, R. B. *J. Org. Chem.* **2003**, 68, 8774.
- (209) Curtis, P. J.; Hemming, H. G.; Smith, W. K. *Nature (London)* **1951**, 167, 557.
- (210) Birkinshaw, J. H.; Raistrick, H. *Biochem. J.* **1936**, 30, 801.
- (211) Sekiguchi, J.; Gaucher, G. M. *Biochem. J.* **1979**, 182, 445.
- (212) Chou, D. T.-W.; Ganem, B. *J. Am. Chem. Soc.* **1980**, 102, 7987.
- (213) Mehta, G.; Islam, K. *Tetrahedron Lett.* **2004**, 45, 7683.
- (214) Lauren, D. R.; Ashley, A.; Blackwell, B. A.; Greenhalgh, R.; Miller, J. D.; Neish, G. A. *J. Agric. Food. Chem.* **1987**, 35, 884.
- (215) Hutchison, R. D.; Steyn, P. S.; Van Rensburg, S. J. *Toxicol. Appl. Pharmacol.* **1973**, 24, 507.
- (216) Raistrick, H.; Smith, G. *Biochem. J.* **1935**, 29, 606.
- (217) (a) Lee, S.; Kim, W.-G.; Kim, E.; Ryoo, I.-J.; Lee, H. K.; Kim, J. N.; Jung, S.-H.; Yoo, I.-D. *Bioorg. Med. Chem. Lett.* **2005**, 15, 471. (b) Kolb, H. C.; Hoffmann, H. M. R. *Tetrahedron: Asymmetry* **1990**, 1, 237. (c) Altenbach, H. J.; Holzapfel, W. *Angew. Chem.* **1990**, 102, 64. (d) Klunder, A. J. H.; Bos, W.; Zwanenburg, B. *Tetrahedron Lett.* **1981**, 22, 4557. (e) Auerbach, J.; Weinreb, S. M. *J. Chem. Soc., Chem. Commun.* **1974**, 298.
- (218) Weber, D.; Erosa, G.; Sterner, O.; Anke, T. *J. Antibiot.* **2006**, 495.
- (219) Renslo, A. R. *Anti-Infect. Agents Med. Chem.* **2007**, 6, 201.
- (220) Hara, M. *Tokyo Igaku* **1964**, 72, 136.
- (221) (a) Hewitt, P. R.; Cleator, E.; Ley, S. V. *Org. Biomol. Chem.* **2004**, 2, 2415. (b) Roe, J. M.; Webster, R. A. B.; Ganesan, A. *Org. Lett.* **2003**, 5, 2825.
- (222) Baran, P. S.; Guerrero, C. A.; Corey, E. J. *J. Am. Chem. Soc.* **2003**, 125, 5628.
- (223) Ovchinnikov, Y. A.; Kiryushkin, A. A.; Shemyakin, M. M. *Tetrahedron Lett.* **1965**, 1111.
- (224) Kiryushkin, A. A.; Ovchinnikov, Y. A.; Shemyakin, M. M. *Tetrahedron Lett.* **1965**, 14.
- (225) (a) Li, P.; Evans, C. D.; Forbeck, E. M.; Park, H.; Bai, R.; Hamel, E.; Joulle, M. M. *Bioorg. Med. Chem. Lett.* **2006**, 16, 4804. (b) Li, P.; Evans, C. D.; Wu, Y.; Cao, B.; Hamel, E.; Joulle, M. M. *J. Am. Chem. Soc.* **2008**, 130, 2351, and cited references.
- (226) Aucamp, P. J.; Holzapfel, C. W. J. S. *Afr. Chem. Inst.* **1969**, 22, 355.
- (227) (a) Rich, D. H.; Bhatnagar, P.; Mathiaparanam, P.; Grant, J. A.; Tam, J. P. *J. Org. Chem.* **1978**, 43, 296. (b) Jacquier, R.; Verducci, J. *Tetrahedron Lett.* **1984**, 25, 2775. (c) Loiseau, N.; Cavellier, F.; Noel, J.-P.; Gomis, J.-M. *J. Pept. Sci.* **2002**, 8, 335. (d) Jimenez, J. C.; Chavarria, B.; Lopez-Macia, A.; Royo, M.; Giralt, E.; Albericio, F. *Org. Lett.* **2003**, 5, 2115.
- (228) Dixon, M. J.; Andersen, O. A.; Van Aalten, D. M. F.; Eggleston, I. M. *Bioorg. Med. Chem. Lett.* **2005**, 15, 4717.
- (229) Ghosh, A. C.; Manmade, A.; Townsend, J. M.; Bousquet, A.; Howes, J. F.; Demain, A. L. *Appl. Environ. Microbiol.* **1978**, 35, 1074.
- (230) Lee, S.; Noda, K.; Aoyagi, H.; Kato, T.; Izumiya, N. *Int. J. Pept. Protein Res.* **1986**, 44.
- (231) Takahashi, N.; Curtis, R. W. *Plant Physiol.* **1961**, 36, 30.
- (232) Bodanszky, M.; Stahl, G. L. *Proc. Natl. Acad. Sci. U.S.A.* **1974**, 71, 2791.
- (233) Kojima, Y.; Sunazuka, T.; Nagai, K.; Julfakyan, K.; Fukuda, T.; Tomoda, H.; Omura, S. *J. Antibiot.* **2008**, 61, 297.
- (234) Chandrasekhar, S.; Chandrasekhar, G. *Tetrahedron: Asymmetry* **2005**, 16, 2209.
- (235) Grimley, J. S.; Sawayama, A. M.; Tanaka, H.; Stohlmeyer, M. M.; Woiwode, T. F.; Wandless, T. J. *Angew. Chem., Int. Ed.* **2007**, 46, 8157.
- (236) Chandrasekhar, S.; Chandrasekhar, G. *Tetrahedron Asymmetry* **2005**, 16, 2209.
- (237) Espada, A.; Rivera-Sagredo, A.; De La Fuente, J. M.; Hueso-Rodriguez, J. A.; Elson, S. W. *Tetrahedron* **1997**, 53, 6485.
- (238) Wang, S.-y.; Mao, W.-w.; She, Z.-g.; Li, C.-r.; Yang, D.-q.; Lin, Y.-c.; Fu, L.-w. *Bioorg. Med. Chem. Lett.* **2007**, 17, 2785.
- (239) (a) Gebhardt, K.; Schimana, J.; Hoeltzel, A.; Dettner, K.; Draeger, S.; Beil, W.; Rheinheimer, J.; Fiedler, H.-P. *J. Antibiot.* **2004**, 57, 707. (b) Holtzel, A.; Schmid, D. G.; Nicholson, G. J.; Krastel, P.; Zeeck, A.; Gebhardt, K.; Fiedler, H.-P.; Jung, G. *J. Antibiot.* **2004**, 57, 715. (c) Rochfort, S.; Ford, J.; Ovenden, S.; Wan, S. S.; George, S.; Wildman, H.; Tait, R. M.; Meurer-Grimes, B.; Cox, S.; Coates, J.; Rhodes, D. *J. Antibiot.* **2005**, 58, 279. (d) Keller-Schierlein, W.; Kupfer, E. *Helv. Chim. Acta* **1979**, 62, 1501. (e) Neupert-Laves, K.; Dobler, M. *Helv. Chim. Acta* **1982**, 65, 1426.
- (240) Trost, B. M.; Ohmori, M.; Boyd, S. A.; Okawara, H.; Brickner, S. J. *J. Am. Chem. Soc.* **1989**, 111, 8281.
- (241) Springer, J. P.; Clardy, J.; Wells, J. M.; Cole, R. J.; Kirksey, J. W.; Mafarlane, R. D.; Torgerson, D. F. *Tetrahedron Lett.* **1976**, 17, 1355.
- (242) Kim, M. Y.; Starrett, J. E., Jr.; Weinreb, S. M. *J. Org. Chem.* **1981**, 46, 5383.
- (243) Capasso, R.; Evidente, A.; Vurro, M. *Phytochemistry* **1991**, 30, 3945.
- (244) Review: Stork, G.; Nakahara, Y.; Nakahara, Y.; Greenlee, W. J. *Int. Congr. Ser.* **1979**, 457 (Stereoel. Synth. Nat. Prod.), 204.
- (245) Stork, G.; Nakahara, Y.; Nakahara, Y.; Greenlee, W. J. *J. Am. Chem. Soc.* **1978**, 100, 7775.
- (246) Stork, G.; Nakahara, Y.; Nakahara, Y.; Greenlee, W. J. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **1978**, 21st, 293.
- (247) Haidle, A.; Myers, A. G. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, 101, 12048.

- (248) Clark, D. A. Ph. D. Thesis, Purdue University, Lafayette, IN, 1979 (CA 1979:540661).
- (249) Clark, D. A.; Fuchs, P. L. *J. Am. Chem. Soc.* **1979**, *101*, 3567.
- (250) Scarpetti, D. Ph. D. Thesis, Purdue University, Lafayette, IN, 1992.
- (251) Anderson, M. B. Ph. D. Thesis, Purdue University, Lafayette, IN, 1989.
- (252) Ranasinghe, M. G. Ph. D. Thesis, Purdue University, Lafayette, IN, 1988.
- (253) Merifield, E.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3269.
- (254) Duncan, S. M. Ph. D. Thesis, University of Wisconsin, Madison, WI, 1996 (CAN 124:342933).
- (255) Arnost, M. J. Ph. D. Thesis, University of Wisconsin, Madison, WI, 1979 (CAN 93:168158).
- (256) Spear, K. L. Ph. D. Thesis, University of Wisconsin, Madison, WI, 1979 (CAN 93:95076).
- (257) Chappuis, G.; Tamm, C. *Helv. Chim. Acta* **1982**, *65*, 521.
- (258) Dyke, H.; Sauter, R.; Steel, P.; Thomas, E. J. *J. Chem. Commun.* **1986**, 1447.
- (259) Dyke, H.; Steel, P.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 525.
- (260) Izawa, Y.; Hirose, T.; Shimizu, T.; Koyama, K.; Natori, S. *Tetrahedron* **1989**, *45*, 2323.
- (261) Thomas, E. J.; Whitehead, J. W. F. *J. Chem. Commun.* **1986**, 727.
- (262) Thomas, E. J.; Whitehead, W. F. *J. Chem. Soc., Perkin Trans. 1* **1989**, 507.
- (263) Tomioka, T.; Izawa, Y.; Koyama, K.; Natori, S. *Chem. Pharm. Bull.* **1987**, *35*, 902.
- (264) Lang, G.; Blunt, J. W.; Cummings, N. J.; Cole, A. L. J.; Munro, M. H. G. *J. Nat. Prod.* **2005**, *68*, 1303.
- (265) Chinworrungsee, M.; Kittakoop, P.; Isaka, M.; Rungrid, A.; Tanticharoen, M.; Thebtaranonth, Y. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1965.
- (266) Evidente, A.; Lanzetta, R.; Capasso, R.; Vurro, M.; Botalico, A. *Tetrahedron* **1992**, *48*, 6317.
- (267) Evidente, A.; Capasso, R.; Vurro, M.; Botalico, A. *Nat. Toxins* **1996**, *4*, 53.
- (268) Feng, Y. J.; Blunt, J. W.; Cole, A. L. J.; Munro, M. H. G. *J. Nat. Prod.* **2002**, *65*, 1274.
- (269) Evidente, A.; Andolfi, A.; Vurro, M.; Zonno, M. C.; Motta, A. *Phytochemistry* **2002**, *60*, 45.
- (270) Evidente, A.; Andolfi, A.; Vurro, M.; Zonno, M. C.; Motta, A. *J. Nat. Prod.* **2003**, *66*, 1540.
- (271) Cole, R. J.; Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 334.
- (272) Tapolczay, D. J.; Thomas, E. J.; Whitehead, J. W. F. *Chem. Commun.* **1985**, 143.
- (273) Thomas, E. J.; Whitehead, J. W. F. *J. Chem. Soc., Perkin Trans. 1* **1989**, 499.
- (274) Vedejs, E.; Rodgers, J. D.; Wittenberger, S. J. *J. Am. Chem. Soc.* **1988**, *110*, 4822.
- (275) Vedejs, E.; Wittenberger, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 4357.
- (276) Hasumi, K.; Shinohara, C.; Iwanaga, T.; Endo, A. *J. Antibiot.* **1993**, *46*, 1782.
- (277) Lang, G.; Cole, A. L. J.; Blunt, J. W.; Robinson, W. T.; Munro, M. H. G. *J. Nat. Prod.* **2007**, *70*, 310.
- (278) Büchi, G.; Williard, P. G. *Heterocycles* **1978**, *11*, 437.
- (279) (a) Kurung, J. M. *Science* **1945**, *102*, 11. (b) Dean, F. M.; Roberts, J. C.; Robertson, A. *J. Chem. Soc.* **1954**, 1432. (c) Dean, F. M.; Erni, A. D. T.; Robertson, A. *J. Chem. Soc.* **1956**, 3545. (d) Dean, F. M.; Robertson, A.; Roberts, J. C.; Raper, K. B. *Nature (London)* **1953**, *172*, 344. (e) Campbell, D. H.; Johnson, F. H. *J. Am. Chem. Soc.* **1946**, *68*, 725. (f) Hogeboom, G. H.; Craig, L. C. *J. Biol. Chem.* **1946**, *162*, 363.
- (280) Schroeder, E.; Luebke, K. *Experientia* **1963**, *19*, 57.
- (281) Wang, F. W.; Ye, Y. H.; Chen, J. R.; Wang, X. T.; Zhu, H. L.; Song, Y. C.; Tan, R. X. *FEMS Microbiol. Lett.* **2006**, *261*, 218.
- (282) Takahashi, C.; Sekita, S.; Yoshihara, K.; Natori, S. *Chem. Pharm. Bull.* **1976**, *24*, 2317.
- (283) Tatsuta, K.; Yamaguchi, T. *Tetrahedron Lett.* **2005**, *46*, 5017.
- (284) De Guzman, F. S.; Gloer, J. B. *J. Nat. Prod.* **1992**, *55*, 931.
- (285) Jarvis, B. B.; Zhou, Y.; Jiang, J.; Wang, S.; Sorenson, W. G.; Hintikka, E. L.; Nikulin, M.; Parikka, P.; Etsel, R. A.; Dearborn, D. G. *J. Nat. Prod.* **1996**, *59*, 553.
- (286) Sorensen, D.; Larsen, T. O.; Christophersen, C.; Nielsen, P. N.; Anthoni, U. *Phytochem.* **1999**, *51*, 181.
- (287) Johnson, A. L.; Janosik, T.; Bergman, J. *Arkivoc* **2002**, 57.
- (288) (a) Edmondson, S. D.; Danishefsky, S. J.; Sepp-Lorenzino, L.; Rosen, N. *J. Am. Chem. Soc.* **1999**, *121*, 2147. (b) Edmondson, S. D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 1138. (c) Onishi, T.; Sebahar, P. R.; Williams, R. M. *Org. Lett.* **2003**, *5*, 3135. (d) Onishi, T.; Sebahar, P. R.; Williams, R. M. *Tetrahedron* **2004**, *60*, 9503. (e) Miyake, F. Y.; Yakushijin, K.; Horne, D. A. *Org. Lett.* **2004**, *6*, 4249.
- (289) (a) Sebahar, P. R.; Williams, R. M. *J. Am. Chem. Soc.* **2000**, *122*, 5666. (b) Wang, H.; Ganesan, A. *J. Org. Chem.* **2000**, *65*, 4685. (c) Von Nussbaum, F.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2175. (d) Overman, L. E.; Rosen, M. D. *Angew. Chem., Int. Ed.* **2000**, *39*, 4596. (e) Bagul, T. D.; Lakshmaiah, G.; Kawabata, T.; Fujii, K. *Org. Lett.* **2002**, *4*, 249. (f) Sebahar, P. R.; Osada, H.; Usui, T.; Williams, R. M. *Tetrahedron* **2002**, *58*, 6311. (g) Meyers, C.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 694. (h) Miyake, F. Y.; Yakushijin, K.; Horne, D. A. *Angew. Chem., Int. Ed.* **2004**, *43*, 5357. (i) Marti, C.; Carreira, E. M. *J. Am. Chem. Soc.* **2005**, *127*, 11505. (j) Trost, B. M.; Stiles, D. T. *Org. Lett.* **2007**, *9*, 2763.
- (290) (a) Cui, C.-B.; Kakeya, H.; Okada, G.; Onose, R.; Ubukata, M.; Takahashi, I.; Isono, K.; Osada, H. *J. Antibiot.* **1995**, *48*, 1382. (b) Cui, C.-B.; Kakeya, H.; Okada, G.; Onose, R.; Osada, H. *J. Antibiot.* **1996**, *49*, 527. (c) Cui, C.-B.; Kakeya, H.; Osada, H. *J. Antibiot.* **1996**, *49*, 534.
- (291) (a) Zhao, S.; Gan, T.; Yu, P.; Cook, J. M. *Tetrahedron Lett.* **1998**, *39*, 7009. (b) Gan, T.; Liu, R.; Yu, P.; Zhao, S.; Cook, J. M. *J. Org. Chem.* **1997**, *62*, 9298.
- (292) (a) Cardoso, A. S. P.; Marques, M. M. B.; Srinivasan, N.; Prabhakar, S.; Lobo, A. M.; Rzepa, H. S. *Org. Biomol. Chem.* **2006**, *4*, 3966. (b) Caballero, E.; Avendano, C.; Menendez, J. C. *J. Org. Chem.* **2003**, *68*, 6944. (c) Wang, B.; Chen, L.; Kim, K. *Tetrahedron Lett.* **2001**, *42*, 1463. (d) Wang, H.; Usui, T.; Osada, H.; Ganesan, A. *J. Med. Chem.* **2000**, *43*, 1577. (e) Depew, K. M.; Danishefsky, S. J.; Rosen, N.; Sepp-Lorenzino, L. *J. Am. Chem. Soc.* **1996**, *118*, 12463.
- (293) Cardoso, A. S.; Lobo, A. M.; Prabhakar, S. *Tetrahedron Lett.* **2000**, *41*, 3611.
- (294) Steyn, P. S. *Tetrahedron Lett.* **1971**, 3331.
- (295) Baran, P. S.; Corey, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 7904.
- (296) (a) Kozlovskii, A. G.; Solov'eva, T. F.; Bukhtiyarov, Y. E.; Shurukhin, Y. V.; Sakharovskii, V. G.; Adanin, V. M.; Nefedova, M. Y.; Pertsova, R. N.; Tokarev, V. G.; Golovleva, L. A. *Mikrobiologiya* **1990**, *59*, 601. (b) Kobayashi, M.; Aoki, S.; Gato, K.; Matsunami, K.; Kurosu, M.; Kitagawa, I. *Chem. Pharm. Bull.* **1994**, *42*, 2449.
- (297) Cole, R. J.; Kirksey, J. W.; Moore, J. H.; Blankenship, B. R.; Diener, U. L.; Davis, N. D. *Appl. Microbiol.* **1972**, *24*, 248.
- (298) Hermkens, P. H. H.; Plate, R.; Ottenheim, H. C. J. *Tetrahedron Lett.* **1988**, *29*, 1323.
- (299) Hino, T.; Nakagawa, M. *Heterocycles* **1997**, *46*, 673.
- (300) Kozlovsky, A. G.; Adanin, V. M.; Dahse, H. M.; Grafe, U. *Appl. Biochem. Microbiol.* **2001**, *37*, 253.
- (301) (a) Hodge, R. P.; Harris, C. M.; Harris, T. M. *J. Nat. Prod.* **1988**, *51*, 66. (b) Arai, K.; Kimura, K.; Mushiroda, T.; Yamamoto, Y. *Chem. Pharm. Bull.* **1989**, *37*, 2937.
- (302) Capon, R. J.; Ratnayake, R.; Stewart, M.; Lacey, E.; Tennant, S.; Gill, J. H. *Org. Biomol. Chem.* **2005**, *3*, 123.
- (303) Lu, C.-D.; Zakarian, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 6829.
- (304) Michalak, K.; Michalak, M.; Wicha, J. *Molecules* **2005**, *10*, 1084.
- (305) Hinkley, S. F.; Mazzola, E. P.; Fettingter, J. C.; Lam, Y.-F.; Jarvis, B. B. *Phytochem.* **2000**, *55*, 663.
- (306) Hinkley, S. F.; More, J. A.; Squillari, J.; Tak, H.; Oleszewski, R.; Mazzola, E. P.; Jarvis, B. B. *Magn. Reson. Chem.* **2003**, 337.
- (307) Cole, R. J.; Cox, R. H., Eds.; *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 608.
- (308) (a) Nagarajan, R.; Huckstep, L. L.; Lively, D. H.; DeLong, D. C.; Marsh, M. M.; Neuss, N. *J. Am. Chem. Soc.* **1968**, *90*, 2980. (b) Nagarajan, R.; Neuss, N.; Marsh, M. M. *J. Am. Chem. Soc.* **1968**, *90*, 6518. (c) Cosulich, D. B.; Nelson, N. R.; Van den Hende, J. H. *J. Am. Chem. Soc.* **1968**, *90*, 6519. (d) Neuss, N.; Nagarajan, R.; Molloy, B. B.; Huckstep, L. L. *Tetrahedron Lett.* **1968**, 4467. (e) Nagarajan, R.; Ocolowitz, J. L.; Neuss, N.; Nash, S. M. *Chem. Commun.* **1969**, 359. (f) Murdock, K. C. *J. Med. Chem.* **1974**, *17*, 827.
- (309) Cole, R. J.; Cox, R. H., Eds.; *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 610.
- (310) Murdock, K. C.; Angier, R. B. *Chem. Commun.* **1970**, 55.
- (311) Cole, R. J.; Cox, R. H., Eds.; *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 607.
- (312) (a) Sakata, K. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **1987**, *29*, 684. (b) Sakata, K.; Maruyama, M.; Uzawa, J.; Sakurai, A.; Lu, H. S. M.; Clardy, J. *Tetrahedron Lett.* **1987**, *28*, 5607. (c) Berg, D. H.; Massing, R. P.; Hoehn, M. M.; Boeck, L. D.; Hamill, R. L. *J. Antibiot.* **1976**, *29*, 394. (d) Monti, F.; Ripamonti, F.; Hawser, S. P.; Islam, K. *J. Antibiot.* **1999**, *52*, 311.
- (313) (a) Miknis, G. F.; Williams, R. M. *J. Am. Chem. Soc.* **1993**, *115*, 536. (b) Williams, R. M.; Miknis, G. F. *Tetrahedron Lett.* **1990**, *31*, 4297.

- (314) Wu, Z.; Williams, L. J.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 3866.
- (315) (a) Kirby, G. W.; Robins, D. J.; Sefton, M. A.; Talekar, R. R. *J. Chem. Soc., Perkin Trans. I* **1980**, 119. (b) Vargaftig, B. B.; Lefort, J.; Chignard, M.; Benveniste, J. *Eur. J. Pharmacol.* **1980**, *65*, 185. (c) Numata, A.; Takahashi, C.; Miyamoto, T.; Matsushita, T.; Kawai, K.; Usami, Y.; Matsumura, E.; Inoue, M.; Ohishi, H.; Shingu, T. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **1991**, *33*, 723. (d) Li, X.; Kim, S.-K.; Nam, K. W.; Kang, J. S.; Choi, H. D.; Son, B. W. *J. Antibiot.* **2006**, *59*, 248.
- (316) Cole, R. J., Cox, R. H., Eds.; *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 601.
- (317) (a) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 538. (b) Waksman, S. A.; Bugie, E. J. *Bact.* **1944**, *48*, 527. (c) Geiger, W. B.; Conn, J. E.; Waksman, S. A. *J. Bact.* **1944**, *48*, 531. (d) Tveit, M. *Nature (London)* **1953**, *172*, 39. (e) Brewer, D.; Duncan, J. M.; Jerram, W. A.; Leach, C. K.; Safe, S.; Taylor, A.; Vining, L. C.; Archibald, R. McG.; Stevenson, R. G. *Can. J. Microbiol.* **1979**, *13*, 15170.
- (318) (a) Saito, T.; Koyama, K.; Natori, S.; Iitaka, Y. *Tetrahedron Lett.* **1985**, *26*, 4731. (b) Saito, T.; Suzuki, Y.; Koyama, K.; Natori, S.; Iitaka, Y.; Kinoshita, T. *Chem. Pharm. Bull.* **1988**, *36*, 1942.
- (319) Kirby, G. W.; Robins, D. J.; Stark, W. M. *Chem. Commun.* **1983**, 812.
- (320) Cole, R. J., Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 576.
- (321) Fukuyama, T.; Nakatsuka, S.; Kishi, Y. *Tetrahedron* **1981**, *37*, 2045.
- (322) Argoudelis, A. D.; Mizsak, S. A. *J. Antibiot.* **1977**, *30*, 468.
- (323) Hauser, D.; Loosli, H. R.; Niklaus, P. *Helv. Chim. Acta* **1972**, *55*, 2182.
- (324) Kawahara, N.; Nozawa, K.; Nakajima, S.; Kawai, K. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2099.
- (325) Yonezawa, Y.; Shimizu, K.; Uchiyama, M.; Kagawa, N.; Shin, C. *Heterocycles* **1997**, *45*, 1151.
- (326) Nazawa, K.; Seya, H.; Nakajima, S.; Kawai, K.; Norizuki, K.; Udagawa, S.; Yamazaki, M. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **1986**, *28th*, 41.
- (327) Kawai, K.; Nozawa, K. *Bioactive Mol.* **1989**, *10*, 205.
- (328) Kawahara, N.; Nozawa, K.; Nakajima, S.; Kawai, K.; Yamazaki, M. *J. Chem. Soc., Chem. Commun.* **1989**, 951.
- (329) Kleinwachter, P.; Dahse, H. M.; Luhmann, U.; Schlegel, B.; Dornberger, K. *J. Antibiot.* **2001**, *54*, 521.
- (330) Overman, L. E.; Shin, Y. *Org. Lett.* **2007**, *9*, 339.
- (331) Kishi, Y.; Fukuyama, T.; Nakasuka, S. *J. Am. Chem. Soc.* **1973**, *95*, 6492.
- (332) Kirby, G. W.; Rao, G. V.; Robins, D. J.; Stark, W. M. *Tetrahedron Lett.* **1986**, *27*, 5539.
- (333) Stipanovic, R. D.; Howell, C. R. *J. Antibiot.* **1982**, *35*, 1326.
- (334) Fukuyama, T.; Nakatsuka, S.; Kishi, Y. *Tetrahedron Lett.* **1976**, 3393.
- (335) Williams, R. M.; Rastetter, W. H. *J. Org. Chem.* **1980**, *45*, 2625.
- (336) Tan, R. X.; Jensen, P. R.; Williams, P. G.; Fenical, W. *J. Nat. Prod.* **2004**, *67*, 1374.
- (337) Ernst-Russell, M. A.; Chai, C. L. L.; Hurne, A. M.; Waring, P.; Hockless, D. C. R.; Elix, J. A. *Aust. J. Chem.* **1999**, *52*, 279.
- (338) Basak, A.; Woolley, G. T.; Wattlely, R. *Indian J. Chem.* **1985**, *24B*, 356.
- (339) Kishi, Y.; Nakatsuka, S.; Fukuyama, T.; Havel, M. *J. Am. Chem. Soc.* **1973**, *95*, 6493.
- (340) Hino, T.; Sato, T. *Chem. Pharm. Bull.* **1974**, *22*, 2866.
- (341) Brewer, D.; Rahman, R.; Safe, S.; Taylor, A. *Chem. Commun.* **1968**, 1571.
- (342) Hauser, D.; Weber, H. P.; Sigg, H. P. *Helv. Chim. Acta* **1970**, *53*, 1061.
- (343) (a) Cole, R. J., Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 599. (b) Udagawa, S.; Muroi, T.; Kurata, H.; Sekita, S.; Yoshihira, K.; Natori, S.; Umeda, M. *Can. J. Microbiol.* **1979**, *25*, 170.
- (344) Sekita, S.; Yoshihira, K.; Natori, S.; Udagawa, S.; Muroi, T.; Sugiyama, Y.; Kurata, H.; Umeda, M. *Can. J. Microbiol.* **1981**, *27*, 766.
- (345) Li, X.; Choi, H. D.; Kang, J. S.; Lee, C. O.; Son, B. W. *J. Nat. Prod.* **2003**, *66*, 1499.
- (346) Maskey, R. P.; Grun-Wollny, I.; Laatsch, H. *J. Nat. Prod.* **2005**, *68*, 865.
- (347) Mehta, G.; Pan, S. C. *Tetrahedron Lett.* **2005**, *46*, 5219.
- (348) Schlegel, B.; Hartl, A.; Dahse, H.-M.; Gollmick, F. A.; Grafe, U.; Dorfeld, H.; Kappes, B. *J. Antibiot.* **2002**, *55*, 814.
- (349) (a) Mehta, G.; Roy, S. *Tetrahedron Lett.* **2008**, *49*, 1458. (b) Rychnovsky, S. D. *Org. Lett.* **2006**, *8*, 2895. (c) Porco, J. A., Jr.; Su, S.; Lei, X.; Bardan, S.; Rychnovsky, S. D. *Angew. Chem., Int. Ed.* **2006**, *45*, 5790.
- (350) Barros, M. T.; Maycock, C. D.; Ventura, M. R. *Tetrahedron* **1999**, *55*, 3233.
- (351) Ichihara, A.; Moriyasu, K.; Sakamura, S. *Agric. Biol. Chem.* **1978**, *42*, 2421.
- (352) Mehta, G.; Pujar, S. R.; Ramesh, S. S.; Islam, K. *Tetrahedron Lett.* **2005**, *46*, 3373. (b) Ichihara, A.; Kimura, R.; Oda, K.; Moriyasu, K.; Sakamura, S. *Agric. Biol. Chem.* **1982**, *46*, 1879.
- (353) Yamakawa, K.; Mashiko, T.; Satoh, T. *Chem. Lett.* **1981**, 929.
- (354) Kiguchi, T.; Hashimoto, C.; Ninomiya, I. *Heterocycles* **1985**, *23*, 2891.
- (355) MacGeorge, K. M.; Mantle, P. G. *Mycopathologia* **1990**, *112*, 139.
- (356) Witt, A.; Gustavsson, A.; Bergman, J. *J. Heterocycl. Chem.* **2003**, *40*, 29.
- (357) Reshetilova, T. A.; Solovyeva, T. F.; Baskunov, B. P.; Kozlovsky, A. G. *Food Addit. Contam.* **1995**, *12*, 461.
- (358) (a) Hegedus, L. S.; Toro, J. L.; Miles, W. H.; Harrington, P. J. *J. Org. Chem.* **1987**, *52*, 3319. (b) Yamada, F.; Makita, Y.; Suzuki, T.; Somei, M. *Chem. Pharm. Bull.* **1985**, *33*, 2162.
- (359) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; pp 403 and 534.
- (360) (a) Yokoyama, Y.; Kondo, K.; Mitsushashi, M.; Murakami, Y. *Tetrahedron Lett.* **1996**, *37*, 9309. (b) Kardos, N.; Genet, J.-P. *Tetrahedron: Asymmetry* **1994**, *5*, 1525. (c) Ninomiya, I.; Habe, N.; Kiguchi, T.; Naito, T. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3275. (d) Somei, M.; Mukaiyama, H.; Nomura, Y.; Nakagawa, K. *Heterocycles* **1990**, *31*, 1919.
- (361) Ku, J.-M.; Jeong, B.-S.; Jew, S.-S.; Park, H.-g. *J. Org. Chem.* **2007**, *72*, 8115.
- (362) (a) Padwa, A.; Heidebaugh, T. M.; Kuethe, J. T. *J. Org. Chem.* **2000**, *65*, 2368. (b) Osanai, K.; Yokoyama, Y.; Kondo, K.; Murakami, Y. *Chem. Pharm. Bull.* **1999**, *47*, 1587.
- (363) Ninomiya, I.; Hashimoto, C.; Kiguchi, T. *Heterocycles* **1984**, *22*, 1035.
- (364) Abe, M.; Yamano, T.; Yamatodani, S.; Kozu, Y.; Kusumoto, M.; Komatsu, H.; Yamada, S. *Bull. Agric. Chem. Soc. Jpn.* **1959**, *23*, 246.
- (365) Hofmann, A.; Frey, A. J.; Ott, H. *Experientia* **1961**, *17*, 206.
- (366) Kharasch, M. S.; Legault, R. R. *J. Am. Chem. Soc.* **1935**, *57*, 1140.
- (367) Cole, R. J.; Kirksey, J. W.; Dorner, J. W.; Wilson, D. M.; Johnson, J., Jr.; Bedell, D.; Springer, J. P.; Chexal, K. K.; Clardy, J.; Cox, R. H. *Ann. Nutr. Aliment.* **1977**, *31*, 685.
- (368) Ninomiya, I.; Kiguchi, T.; Hashimoto, C.; Naito, T. *Chem. Pharm. Bull.* **1991**, *39*, 23.
- (369) Ninomiya, I.; Hashimoto, C.; Kiguchi, T.; Naito, T. *J. Chem. Soc., Perkin Trans. 1* **1985**, 941.
- (370) Moldvai, I.; Temesvari-Major, E.; Gacs-Baitz, E.; Incze, M.; Dornyei, G.; Szantay, C. *Heterocycles* **2006**, *67*, 291.
- (371) Kornfeld, E. C.; Fornefeld, E. J.; Kline, G. B.; Mann, M. J.; Jones, R. G.; Woodward, R. B. *J. Am. Chem. Soc.* **1954**, *76*, 5256.
- (372) Moldvai, I.; Temesvari-Major, E.; Incze, M.; Szentirmay, E.; Gacs-Baitz, E.; Szantay, C. *J. Org. Chem.* **2004**, *69*, 5993.
- (373) For a recent review: Moldvai, I.; Temesvari-Major, E.; Incze, M.; Dornyei, G.; Szentirmay, E.; Szantay, C. *Helv. Chim. Acta* **2005**, *1344*.
- (374) Dorner, J. W.; Cole, R. J.; Hill, R.; Wicklow, D.; Cox, R. H. *Appl. Environ. Microbiol.* **1980**, *40*, 685.
- (375) Cole, J. J.; Kirksey, J. W.; Clardy, J.; Eickman, N.; Weinreb, S. M.; Singh, P.; Kim, D. *Tetrahedron Lett.* **1976**, *53*, 3849.
- (376) Rebek, J., Jr.; Shue, Y. K. *J. Am. Chem. Soc.* **1980**, *102*, 5426.
- (377) Martin, S. F.; Liras, S. *J. Am. Chem. Soc.* **1993**, *115*, 10450.
- (378) (a) Vinokurova, N. G.; Baskunov, B. P.; Zelenkova, N. F.; Arinbasarov, M. U. *Mikrobiologiya* **2004**, *73*, 491 Syntheses. (b) Hayashi, Y.; Orikasa, S.; Tanaka, K.; Kanoh, K.; Kiso, Y. *J. Org. Chem.* **2000**, *65*, 8402. (c) Couladouros, E. A.; Magos, A. D. *Mol. Diversity* **2005**, *9*, 99. (d) Couladouros, E. A.; Magos, A. D. *Mol. Diversity* **2005**, *9*, 111.
- (379) (a) Couladouros, E. A.; Magos, A. D. *Mol. Diversity* **2005**, *9*, 99. (b) Hayashi, Y.; Orikasa, S.; Tanaka, K.; Kanoh, K.; Kiso, Y. *J. Org. Chem.* **2000**, *65*, 8402.
- (380) Bond, R. F.; Bredenkamp, M. W.; Holzapfel, C. W. *Synth. Commun.* **1989**, *19*, 2551.
- (381) Anderson, R. J. *J. Biol. Chem.* **1929**, *83*, 169.
- (382) Mantle, P. G.; Waight, E. S. *Nature (London)* **1968**, *218*, 581.
- (383) Stutz, P.; Stadler, P. A.; Hofmann, A. *Helv. Chim. Acta* **1970**, *56*, 1278.
- (384) Suzuki, T.; Takeda, M.; Tanabe, H. *Chem. Pharm. Bull.* **1971**, *19*, 1786.
- (385) (a) Brookes, D.; Tidd, B. K.; Turner, W. B. *J. Chem. Soc.* **1963**, 5385. (b) Parker, W. L.; Johnson, F. J. *Am. Chem. Soc.* **1969**, *91*, 7208. (c) Herrmann, J. L.; Berger, M. H.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1973**, *95*, 7923. (d) Anderson, R. C.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1975**, *97*, 3870. (e) Parker, W. L.; Johnson, F.

- J. Org. Chem.* **1973**, *38*, 2489. (f) Brookes, D.; Sternhell, S.; Tidd, B. K.; Turner, W. B. *Aust. J. Chem.* **1965**, *18*, 373.
- (386) Anderson, R. C.; Fraser-Reid, B. *J. Org. Chem.* **1985**, *50*, 4781.
- (387) Brackmüller, S.; Brückner, R. *Eur. J. Org. Chem.* **2006**, 2110.
- (388) Bennett, M.; Gill, G. B.; Pattenden, G.; Shuker, A. J.; Stapleton, A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 929.
- (389) Woodward, R. B.; Singh, G. *J. Am. Chem. Soc.* **1950**, *72*, 1428.
- (390) Beeson, M. S. Ph.D. Thesis, Emory University, Atlanta, GA, 1988.
- (391) Seijas, J. A.; Vázquez Tato, M. P.; Estévez, R.; Castedo, L.; Riguera, R. *Heterocycles* **1989**, *29*, 181.
- (392) Gill, G. B.; Pattenden, G.; Stapleton, A. *Tetrahedron Lett.* **1988**, *29*, 2875.
- (393) Tada, M.; Ohtsu, K.; Chiba, K. *Chem. Pharm. Bull.* **1994**, *42*, 2167.
- (394) Boukouvalas, J.; Maltais, F. *Tetrahedron Lett.* **1995**, *36*, 7175.
- (395) (a) Zografos, A. L.; Georgiadis, D. *Synthesis* **2006**, 3157. (b) Schroer, J. G. Abstracts of Papers, 234th ACS National Meeting, Boston, MA, August 19–23, 2007, IEC-001.
- (396) Brandaenge, S.; Flodman, L.; Norberg, A. *J. Org. Chem.* **1984**, *49*, 927.
- (397) (a) Bottini, A. T.; Gilchrist, D. G. *Tetrahedron Lett.* **1981**, *22*, 2719. (b) Bottini, A. T.; Bowen, J. R.; Gilchrist, D. G. *Tetrahedron Lett.* **1981**, *22*, 2723.
- (398) Oikawa, H.; Yamawaki, D.; Kagawa, T.; Ichihara, A. *Tetrahedron Lett.* **1999**, *40*, 6621.
- (399) Gelderblom, W. C.; Jaskiewicz, K.; Marasas, W. F.; Thiel, P. G.; Horak, R. M.; Vlegaar, R.; Kriek, N. P. *Appl. Environ. Microbiol.* **1988**, *54*, 1806.
- (400) Gurjar, M. K.; Rajendran, V.; Rao, B. V. *Tetrahedron Lett.* **1998**, *39*, 3803.
- (401) Shi, Y.; Peng, L. F.; Kishi, Y. *J. Org. Chem.* **1997**, *62*, 5666.
- (402) Abbas, H. K.; Shier, W. T.; Seo, J. A.; Lee, Y. W.; Musser, S. M. *Toxicol.* **1998**, *36*, 2033.
- (403) Birkinshaw, J. H.; Raistrick, H. *Biochem. J.* **1936**, *30*, 2194.
- (404) Birkinshaw, J. H.; Samant, M. S. *Biochem. J.* **1960**, *74*, 369.
- (405) Cole, R. J.; Cox, R. H. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York 1981; p 937.
- (406) Dimitriadis, E.; Massy-Westropp, R. A. *Aust. J. Chem.* **1984**, *37*, 619.
- (407) Raistrick, H.; Clark, A. B. *Biochem. J.* **1919**, *13*, 329.
- (408) Easwar, S.; Argade, N. P. *Synthesis* **2006**, 831.
- (409) Prashant, A.; Krupadanam, G. L. D.; Srimannarayana, G. *Bull. Chim. Soc. Jap.* **1992**, *65*, 1191.
- (410) Danheiser, R. L.; Trova, M. P. *Synlett* **1995**, 573.
- (411) Roux, D.; Makki, S.; Bevalot, F.; Humbert, P. *Synlett* **2007**, 129.
- (412) (a) Zhang, B.-L.; Wang, F.-D.; Yue, J.-M. *Synlett* **2006**, 567. (b) Zubia, E.; Luis, F. R.; Massanet, G. M.; Collado, I. G. *Tetrahedron* **1992**, *48*, 4239.
- (413) Mal, D.; Bandhyopadhyay, M.; Datta, K.; Murty, K. V. S. N. *Tetrahedron* **1998**, *54*, 7525.
- (414) Murga, J.; Falomir, E.; Carda, M.; Marco, J. A. *Tetrahedron Lett.* **2005**, *46*, 8199.
- (415) Enomoto, M.; Kuwahara, S. *Biosci., Biotechnol., Biochem.* **2008**, *72*, 1921.
- (416) Enomoto, M.; Kuwahara, S. *J. Org. Chem.* **2006**, *71*, 6287.
- (417) Yasui, H.; Hirai, K.; Yamamoto, S.; Takao, K.; Tadano, K. *Heterocycles* **2006**, *67*, 123.
- (418) Paquette, L. A.; Wang, T.-Z.; Sivik, M. R. *J. Am. Chem. Soc.* **1994**, *116*, 2665.
- (419) Chen, F. C.; Manchand, P. S.; Whalley, W. B. *J. Chem. Soc., Perkin Trans. 1* **1971**, 3577.
- (420) Kittakoop, P.; Yongsmith, B.; Bavovada, R.; Tanasupawat, S.; Lartpornmatulee, N.; Thebtaranonth, Y.; Jongrungruangchok, S. *Phytochemistry* **2004**, *65*, 2569.
- (421) (a) Pettigrew, J. D.; Wilson, P. D. *Org. Lett.* **2006**, *8*, 1427. (b) Pettigrew, J. D.; Freeman, R. P.; Wilson, P. D. *Can. J. Chem.* **2004**, *82*, 1640. (c) Krohn, K.; Riaz, M.; Flörke, U. *Eur. J. Org. Chem.* **2004**, 1261. (d) Pettigrew, J. D.; Bexrud, J. A.; Freeman, R. P.; Wilson, P. D. *Heterocycles* **2004**, *62*, 445. (e) Wu, X. Y.; Liu, X. H.; Lin, Y. C.; Luo, J. H.; She, Z. G.; Li, H.; Chan, W. L.; Antus, S.; Kurtan, T.; Elsässer, B.; Krohn, K. *Eur. J. Org. Chem.* **2005**, 4061.
- (422) Simpson, T. J.; Walkinshaw, M. D. *Chem. Commun.* **1981**, 914.
- (423) Puetzer, B.; Nield, C. H.; Barry, R. H. *J. Am. Chem. Soc.* **1945**, *67*, 929.
- (424) (a) Clive, D. L. J.; Minaruzzaman; Yang, H. *Org. Lett.* **2007**, *9*, 5315. (b) Clive, D. L. J.; Minaruzzaman; Yang, H. *J. Org. Chem.* **2008**, *73*, 6743.
- (425) Adesogan, E. K.; Alo, B. I. *Phytochemistry* **1979**, *18*, 1886.
- (426) Mikami, A.; Okazaki, T.; Sakai, N.; Ichihara, T.; Hanada, K.; Mizoue, K. *J. Antibiot.* **1996**, *49*, 985.
- (427) Cole, R. J.; Kirksey, J. W.; Cutler, H. G.; Doupnik, B. L.; Peckham, J. C. *Science* **1973**, *179*, 1324.
- (428) Springer, J. P.; Clardy, J.; Cole, R. J.; Kirksey, J. W.; Hill, R. K.; Carlson, M. R.; Isidor, J. L. *J. Am. Chem. Soc.* **1974**, *96*, 2267.
- (429) (a) Corey, E. J.; Guzman-Perez, A.; Loh, T.-P. *J. Am. Chem. Soc.* **1994**, *116*, 3611. (b) Nagaoka, H.; Shimano, M.; Yamada, Y. *Tetrahedron Lett.* **1989**, *30*, 971. (c) Danheiser, R. L. *Strategies Tactics Org. Synth.* **1984**, *21*. (d) Hook, J. M.; Mander, L. N.; Urech, R. *J. Org. Chem.* **1984**, *49*, 3250. (e) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S.; Keck, G. E.; Gopalan, B.; Larsen, S. D.; Siret, P.; Gras, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 8034.
- (430) Mahmoodian, A.; Stickings, C. E. *Biochem. J.* **1964**, 369.
- (431) Tanaka, Y.; Matsuzaki, K.; Zhong, C. L.; Yoshida, H.; Kawakubo, T.; Masuma, R.; Tanaka, H.; Omura, S. *J. Antibiot.* **1996**, *49*, 1056.
- (432) Hargreaves, J.; Park, J. O.; Ghisalberti, E. L.; Sivasithamparam, K.; Skelton, B. W.; White, A. H. *J. Nat. Prod.* **2002**, *65*, 7.
- (433) Raistrick, H.; Smith, G. *Biochem. J.* **1936**, *30*, 1315.
- (434) Katoh, T.; Ohmori, O.; Iwasaki, K.; Inoue, M. *Tetrahedron* **2002**, *58*, 1289.
- (435) Reekie, T. A.; Austin, K. A. B.; Banwell, M. G.; Willis, A. C. *Aust. J. Chem.* **2008**, *61*, 94.
- (436) Reshetilova, T. A.; Solovyeva, T. F.; Baskunov, B. P.; Kozlovsky, A. G. *Food Addit. Contam.* **1995**, *12*, 461.
- (437) Sassa, T.; Yoshida, N.-i.; Haruki, E. *Agric. Biol. Chem.* **1989**, *53*, 3105.
- (438) (a) Yoshida, N.; Sassa, T. *Agric. Biol. Chem.* **1990**, *54*, 2681. (b) Richter, J. M.; Whitefield, B. W.; Maimone, T. J.; Lin, D. W.; Castroviejo, M. P.; Baran, P. S. *J. Am. Chem. Soc.* **2007**, *129*, 12857.
- (439) Holzapfel, C. W. *Tetrahedron* **1968**, *24*, 2101.
- (440) Kozikowski, A. P.; Greco, M. N.; Springer, J. P. *J. Am. Chem. Soc.* **1984**, *106*, 6873.
- (441) Muratake, H.; Natsume, M. *Heterocycles* **1985**, *23*, 1111.
- (442) Greco, M. N. Ph.D. Thesis, University of Pittsburgh, Pittsburgh, PA, 1984 (CAN 104:168658).
- (443) Kozikowski, A. P.; Konoike, T.; Ritter, A. *Carbohydr. Res.* **1987**, *171*, 109.
- (444) Kozikowski, A. P.; Konoike, T.; Ritter, A. *Chem. Ind.* **1988**, 33, 339.
- (445) Haskins, C. M.; Knight, D. W. *Chem. Commun.* **2005**, 3162.
- (446) Cole, R. J.; Cox, R. H., Eds.; *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 426.
- (447) (a) Gloer, J. B.; TePaske, M. R.; Sima, J. S.; Wicklow, D. T.; Dowd, P. F. *J. Org. Chem.* **1988**, *53*, 5457. (b) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; pp 298 and 300.
- (448) Penn, J.; Matle, P. G.; Bilton, J. N.; Sheppard, R. N. *J. Chem. Soc., Perkin Trans. 1* **1992**, 23.
- (449) Jadulco, R.; Edrada, R. A.; Ebel, R.; Berg, A.; Schaumann, K.; Wray, V.; Steube, K.; Proksch, P. *J. Nat. Prod.* **2004**, *67*, 78.
- (450) Yang, J.; Song, H.; Xiao, X.; Wang, J.; Qin, Y. *Org. Lett.* **2006**, *8*, 2187.
- (451) Crawley, S. L.; Funk, R. L. *Org. Lett.* **2003**, *5*, 3169.
- (452) Seo, J. H.; Artman, G. D., III; Weinreb, S. M. *J. Org. Chem.* **2006**, *71*, 891.
- (453) Jadulco, R.; Edrada, R. A.; Ebel, R.; Berg, A.; Schaumann, K.; Wray, V.; Steube, K.; Proksch, P. *J. Nat. Prod.* **2004**, *67*, 78.
- (454) Hayashi, H.; Matsumoto, H.; Akiyama, K. *Biosci. Biotechnol. Biochem.* **2004**, *68*, 753.
- (455) Yang, J.; Wu, H.; Shen, L.; Qin, Y. *J. Am. Chem. Soc.* **2007**, *129*, 13794.
- (456) Dalsgaard, P. W.; Blunt, J. W.; Munro, M. H.; Frisvad, J. C.; Christophersen, C. *J. Nat. Prod.* **2005**, *68*, 258.
- (457) Blanchflower, S. E.; Banks, R. M.; Everett, J. R.; Reading, C. *J. Antibiot. (Tokyo)* **1993**, *46*, 1355.
- (458) Trost, B. M.; Cramer, N.; Bernsmann, H. *J. Am. Chem. Soc.* **2007**, *129*, 3086.
- (459) Greshock, T. J.; Grubbs, A. W.; Williams, R. M. *Tetrahedron* **2007**, *63*, 6124.
- (460) Sunazuka, T.; Shirahata, T.; Tsuchiya, S.; Hirose, T.; Mori, R.; Harigaya, Y.; Kuwajima, I.; Omura, S. *Org. Lett.* **2005**, *7*, 941.
- (461) Larsen, T. O.; Gareis, M.; Frisvad, J. C. *J. Agric. Food Chem.* **2002**, *50*, 6148.
- (462) (a) Artman, G. D., III; Grubbs, A. W.; Williams, R. M. *J. Am. Chem. Soc.* **2007**, *129*, 6336. (b) Greshock, T. J.; Grubbs, A. W.; Tsukamoto, S.; Williams, R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 2262. (c) Baran, P. S.; Guerrero, C. A.; Ambhaikar, N. B.; Hafenstein, B. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 606. (d) Greshock, T. J.; Williams, R. M. *Org. Lett.* **2007**, *9*, 4255.
- (463) TePaske, M. R.; Gloer, J. B.; Wicklow, D. T.; Dowd, P. F. *J. Nat. Prod.* **1992**, *55*, 1080.
- (464) Steyn, P. S. *Tetrahedron* **1973**, *29*, 107.
- (465) Maes, C. M. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2489.
- (466) Somei, M.; Kawasaki, T. *Chem. Pharm. Bull.* **1989**, *37*, 3426.
- (467) Somei, M.; Kawasaki, T. *Heterocycles* **1996**, *42*, 281.
- (468) (a) Friedrich, A.; Jainta, M.; Nieger, M.; Bräse, S. *Synlett* **2007**, 2127. (b) Jainta, M.; Nieger, M.; Bräse, S. *J. Mol. Struct.* **2009**, *921*, 85.

- (469) (*Penicillium viridicatum*): (a) Wilson, B. J.; Yang, D. T.; Harris, T. M. *Appl. Microbiol.* **1973**, *26*, 633(*Penicillium ochraceum*): (b) Robbers, J. E.; Straus, J. W. *Lloydia* **1975**, *38*, 355.
- (470) Williams, R. M.; Kwast, E.; Coffman, H.; Glinka, T. *J. Am. Chem. Soc.* **1989**, *111*, 3064.
- (471) (a) Adams, L. A.; Valente, M. W. N.; Williams, R. M. *Tetrahedron* **2006**, *62*, 5195. (b) Williams, R. M.; Sanz-Cervera, J. F.; Sancenon, F.; Marco, J. A.; Halligan, K. *J. Am. Chem. Soc.* **1998**, *120*, 1090. (c) Williams, R. M.; Glinka, T.; Kwast, E. *J. Am. Chem. Soc.* **1988**, *110*, 5927.
- (472) Schkeryantz, J. M.; Woo, J. C. G.; Silipaivanh, P.; Depew, K. P.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1999**, *121*, 11964.
- (473) Birch, A. J.; Russell, R. A. *Tetrahedron* **1972**, *28*, 2999.
- (474) Adams, L. A.; Valente, M. W. N.; Williams, R. M. *Tetrahedron* **2006**, *62*, 5195.
- (475) Ritchie, R.; Saxton, J. E. *J. Chem. Soc., Chem. Commun.* **1975**, 611.
- (476) Kametani, T.; Kanaya, N.; Ihara, M. *J. Am. Chem. Soc.* **1980**, *102*, 3974.
- (477) Schiavi, B. M.; Richard, D. J.; Joullié, M. M. *J. Org. Chem.* **2002**, *67*, 620.
- (478) (*Penicillium roqueforti*): (a) Polonsky, J.; Merrien, M. A.; Scott, P. M. *Ann. Nutr. Aliment.* **1977**, *31*, 963(*Penicillium commune*): (b) Wagener, R. E.; Davis, N. D.; Diener, U. L. *Appl. Environ. Microbiol.* **1980**, *39*, 882(*Penicillium crustosum*): (c) Kyriakidis, N.; Waight, E. S.; Day, J. B.; Mantle, P. G. *Appl. Environ. Microbiol.* **1981**, *42*, 61.
- (479) (a) Richard, D. J.; Schiavi, B.; Joullié, M. M. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 11971. (b) Shangguan, N.; Hehre, W. J.; Ohlinger, W. S.; Beavers, M. P.; Joullié, M. M. *J. Am. Chem. Soc.* **2008**, *130*, 6281.
- (480) Chen, W.-C.; Joullié, M. M. *Tetrahedron Lett.* **1998**, *39*, 8401.
- (481) Cole, R. J.; Kirksey, J. W.; Cox, R. H.; Clardy, J. *J. Agric. Food Chem.* **1975**, *23*, 1015.
- (482) Hermkens, P. H. H.; Plate, R.; Kruse, C. G.; Scheeren, H. W.; Ottenheim, H. C. J. *J. Org. Chem. Lett.* **1992**, *57*, 3881.
- (483) (a) Tatsuta, K.; Mukai, H.; Mitsumoto, K. *J. Antibiot.* **2001**, *54*, 105. (b) Liu, K.; Wood, H. B.; Jones, A. B. *Tetrahedron Lett.* **1999**, *40*, 5119.
- (484) Harris, G. D., Jr.; Nguyen, A.; App, H.; Hirth, P.; McMahon, G.; Tang, C. *Org. Lett.* **1999**, *1*, 431.
- (485) Perring, M. C.; Li, Z.; Park, K.; Zhu, J. *J. Org. Chem.* **2002**, *67*, 7919.
- (486) Inoue, S.; Takamatsu, N.; Hashizume, K.; Kishi, Y. *Yakugaku Zasshi* **1977**, *97*, 582.
- (487) Inoue, S.; Takamatsu, N.; Kishi, Y. *Yakugaku Zasshi* **1977**, *97*, 564.
- (488) Inoue, S.; Takamatsu, N.; Kishi, Y. *Yakugaku Zasshi* **1977**, *97*, 558.
- (489) Muratake, H.; Natsume, M. *Angew. Chem., Int. Ed. Engl.* **2004**, *43*, 4646.
- (490) Peese, K. M.; Gin, D. Y. *J. Am. Chem. Soc.* **2006**, *128*, 8734.
- (491) Danishefsky, S.; Chackalamanni, S.; Harrison, P.; Silvestri, P. *J. Am. Chem. Soc.* **1985**, *107*, 2474.
- (492) Clark, J. S.; Myatt, J.; Wilson, C.; Roberts, L.; Walshe, N. *Chem. Commun.* **2003**, 1546.
- (493) Li, C.; Gloer, J. B.; Wicklow, D. T.; Dowd, P. F. *Org. Lett.* **2002**, *4*, 3095.
- (494) (a) Gobao, R. A.; Bremmer, M. L.; Weinreb, S. M. *J. Am. Chem. Soc.* **1982**, *104*, 7065. (b) Cossy, J.; Willis, C.; Bellosa, V.; Saint-Jalmes, L. *Synthesis* **2002**, 951. (c) Pourashraf, M.; Delair, P.; Rasmussen, M. O.; Greene, A. E. *J. Org. Chem.* **2000**, *65*, 6966. (d) Comins, D. L.; Fulp, A. B. *Org. Lett.* **1999**, *1*, 1941. (e) Sibi, M. P.; Christensen, J. W. *J. Org. Chem.* **1999**, *64*, 6434. (f) Carretero, J. C.; Arrayas, R. G. *Synlett* **1999**, 49.
- (495) Williams, R. M.; Cao, J.; Tsujishima, H.; Cox, R. J. *J. Am. Chem. Soc.* **2003**, *125*, 12172.
- (496) Dethoup, T.; Manoch, L.; Kijjoa, A.; Pinto, M.; Gales, L.; Damas, A. M.; Silva, A. M. S.; Eaton, G.; Herz, W. *J. Nat. Prod.* **2007**, *70*, 1200.
- (497) Giles, D.; Turner, W. B. *J. Chem. Soc. C* **1969**, *16*, 2187.
- (498) (a) Bhide, B. H.; Kalaria, A. J.; Patel, S. K. *Ind. J. Chem.* **1999**, *38B*, 971. (b) Chatterjea, J. N.; Banerjee, B. K.; Bhakta, C.; Mukerji, J. *J. Indian Chem. Soc.* **1972**, *49*, 791.
- (499) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 84.
- (500) (a) Nukina, M. *Tennen Yuki Kagobustsu Toronkai Koen Yoshishu* **1987**, *29*, 705. (b) Venkatasubbaiah, P.; Chilton, W. S. *J. Nat. Prod.* **1991**, *54*, 1293. (c) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 87.
- (501) Islam, M. S.; Ishigami, K.; Watanabe, H. *Tetrahedron* **2006**, *63*, 1074.
- (502) Larsen, T. O.; Breinholt, J. *J. Nat. Prod.* **1999**, *62*, 1182.
- (503) Sibi, M. P.; Chattopadhyay, S.; Dankwardt, J. W.; Snieckus, V. *J. Am. Chem. Soc.* **1985**, *107*, 6312.
- (504) Grove, J. F. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2400.
- (505) Cassidy, J. H.; Farthing, C. N.; Marsden, S. P.; Pedersen, A.; Slater, M.; Stemp, G. *Org. Biomol. Chem.* **2006**, *4*, 4118.
- (506) Stodola, F. H.; Cabot, C.; Benjamin, C. R. *Biochem. J.* **1964**, *93*, 92. (b) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; pp 87 and 507.
- (507) (a) Schultz, A.; Li, Y.-J. *Tetrahedron Lett.* **1997**, *38*, 2071. (b) Enders, D.; Kaiser, A. *Synthesis* **1996**, 209. (c) Asaoka, M.; Sonoda, S.; Fujii, N.; Takei, H. *Tetrahedron* **1990**, *46*, 1541. (d) Takano, S.; Shimazaki, Y.; Ogasawara, K. *Heterocycles* **1989**, *29*, 2101. (e) Vogt, K.; Schmidt, R. R. *Tetrahedron* **1988**, *44*, 3271. (f) Pietrusiewicz, K. M.; Salamonczyk, I. *J. Org. Chem.* **1988**, *53*, 2837. (g) Mori, K.; Gupta, A. K. *Tetrahedron* **1985**, *41*, 5295. (h) Cordova, R.; Snider, B. B. *Tetrahedron Lett.* **1984**, *25*, 2945.
- (508) Drochner, D.; Müller, M. *Eur. J. Org. Chem.* **2001**, 211.
- (509) (*Trichophyton megnini*): (a) Blank, F.; Day, W. C.; Just, G. *J. Invest. Dermatol.* **1963**, *40*, 133(*Aspergillus sulfureus* and *Aspergillus melleus*): (b) Durley, R. C.; MacMillan, J.; Simpson, T. J.; Glen, A. T.; Turner, W. B. *J. Chem. Soc., Perkin Trans. 1* **1975**, 163.
- (510) Zeeck, A.; Russ, P.; Laatsch, H.; Loeffler, W.; Wehrle, H.; Zaehner, H.; Holst, H. *Chem. Ber.* **1979**, *112*, 957.
- (511) *Aspergillus ochraceus*, *Penicillium cyclopium*, and *Penicillium viridicatum*: Stack, M. E.; Mislivec, P. B. *Appl. Environ. Microbiol.* **1978**, *36*, 552.
- (512) Bode, S. E.; Drochner, D.; Müller, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 5916.
- (513) Wang, W.-L.; Lu, Z.-Y.; Tao, H.-W.; Zhu, T.-J.; Fang, Y.-C.; Gu, Q.-Q.; Zhu, W.-M. *J. Nat. Prod.* **2007**, *70*, 1558.
- (514) (a) Chexal, K. K.; Springer, J. P.; Clardy, J.; Cole, R. J.; Kirksey, J. W.; Dörner, J. W.; Cutler, H. G.; Strawter, B. J. *J. Am. Chem. Soc.* **1976**, *98*, 6748. (b) Cole, R. J.; Cox, R. H., Eds.; *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 802.
- (515) Scott, F. E.; Simpson, T. J.; Trimble, L. A.; Vederas, J. C. *Chem. Commun.* **1986**, 214.
- (516) (a) Hayashi, H.; Mukaiyama, M.; Murao, S.; Arai, M.; Lee, A. Y.; Clardy, J. *Biosci., Biotechnol., Biochem.* **1994**, *58*, 334. (b) Simpson, T. J.; Stenzel, D. J.; Bartlett, A. J.; O'Brien, E.; Holker, J. S. E. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2687.
- (517) (a) Rao, A. V. R.; Murthy, V. S.; Sharma, G. V. M. *Tetrahedron Lett.* **1995**, *36*, 143. (b) Rao, A. V. R.; Murthy, V. S.; Sharma, G. V. M. *Tetrahedron Lett.* **1995**, *36*, 139.
- (518) (a) Wu, Y.; Shen, X.; Yang, Y. Q.; Hu, Q.; Huang, J. H. *J. Org. Chem.* **2004**, *69*, 3857. (b) Seo, S.-Y.; Jung, J.-K.; Paek, S.-M.; Lee, Y.-S.; Kim, S.-H.; Suh, Y.-G. *Tetrahedron Lett.* **2006**, *47*, 6527. (c) Archambaud, S.; Aphecetche-Julienne, K.; Guingant, A. *Synlett* **2005**, 139. (d) Wang, Y.; Romo, D. *Org. Lett.* **2002**, *4*, 3231. (e) Kim, D.; Lee, J.; Shim, P. J.; Lim, J. I.; Jo, H.; Kim, S. *J. Org. Chem.* **2002**, *67*, 764.
- (519) (a) Sunagawa, M.; Ohta, T.; Nozoe, S. *Heterocycles* **1979**, *13*, 267. (b) Trost, B. M.; Lynch, J.; Renault, P.; Steinman, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 284.
- (520) (a) Fürstner, A.; Naganom, T.; Müller, C.; Seidel, G.; Müller, O. *Chem.—Eur. J.* **2007**, *13*, 1452. (b) Garcia-Fortanet, J.; Murga, J.; Falomir, E.; Carda, M.; Marco, J. A. *J. Org. Chem.* **2005**, *70*, 9822. (c) Kumar, P.; Naidu, S. V. *J. Org. Chem.* **2005**, *70*, 4207. (d) Davoli, P.; Spaggiari, A.; Castagnetti, L.; Prati, F. *Org. Biomol. Chem.* **2004**, *2*, 38. (e) Murga, J.; Falomir, E.; Garcia-Fortanet, J.; Carda, M.; Marco, J. A. *Org. Lett.* **2002**, *4*, 3447.
- (521) Weber, D.; Sterner, O.; Anke, T.; Gorzalcanzy, S.; Martino, V. *J. Antibiot.* **2004**, *57*, 559.
- (522) (a) Noda, A.; Aoyagi, S.; Machinaga, N.; Kibayashi, C. *Tetrahedron Lett.* **1994**, *35*, 8237. (b) Wakamatsu, T.; Yamada, S.; Ban, Y. *Heterocycles* **1986**, *24*, 309. (c) Seuring, B.; Seebach, D. *Liebigs Ann.* **1978**, 2044. (d) Burri, K. F.; Cardone, R. A.; Chen, W. Y.; Rosen, P. *J. Am. Chem. Soc.* **1978**, *100*, 7069. (e) Seebach, D.; Seuring, B.; Kalinowski, H. O.; Lubosch, W.; Renger, B. *Angew. Chem.* **1977**, *89*, 270. (f) Fukuyama, Y.; Kirkemo, C. L.; White, J. D. *J. Am. Chem. Soc.* **1977**, *99*, 646. (g) Corey, E. J.; Nicolaou, K. C.; Toru, T. *J. Am. Chem. Soc.* **1975**, *97*, 2287.
- (523) (a) Sontag, B.; Arnold, N.; Steglich, W.; Anke, T. *J. Nat. Prod.* **1999**, *62*, 1425. (b) Byun, H.-S.; Lu, X.; Bittman, R. *Synthesis* **2006**, 2447.
- (524) Suzuki, T.; Usui, K.; Miyake, Y.; Namikoshi, M.; Nakada, M. *Org. Lett.* **2004**, *6*, 553.
- (525) Oikawa, H.; Kobayashi, T.; Katayama, K.; Suzuki, Y.; Ichihara, A. *J. Org. Chem.* **1998**, *63*, 8748.
- (526) Hagiwara, H.; Kobayashi, K.; Miya, S.; Hoshi, T.; Suzuki, T.; Ando, M.; Okamoto, T.; Kobayashi, M.; Yamamoto, I.; Ohtsubo, S.; Kato, M.; Uda, H. *J. Org. Chem.* **2002**, *67*, 5969.
- (527) Ikeda, S.; Sugita, M.; Yoshimura, A.; Sumizawa, T.; Douzono, H.; Nagata, Y.; Akiyama, S. *Int. J. Cancer* **1990**, *45*, 508.
- (528) Baker, P. M. *J. Chem. Soc.* **1966**, 2234.

- (529) Deshpande, V. H.; Khan, R. A.; Ayyangar, N. R. *Ind. J. Chem.* **1996**, *35B*, 965.
- (530) Shibata, S.; Morishita, E.; Arima, Y. *Chem. Pharm. Bull.* **1967**, *15*, 1757.
- (531) Ehrlich, K. C.; DeLuca, A. J., II; Ciegler, A. *Appl. Environ. Microbiol.* **1984**, *48*, 1.
- (532) (a) Kozlowski, M. C.; Dugan, E. C.; DiVirgilio, E. S.; Maksimenka, K.; Bringmann, G. *Adv. Synth. Catal.* **2007**, *349*, 583. (b) DiVirgilio, E. S.; Dugan, E. C.; Mulrooney, C. A.; Kozlowski, M. C. *Org. Lett.* **2007**, *9*, 385.
- (533) Medentsev, A. G.; Arinbasarova, A. I. u.; Akimenko, V. K. *Prikl. Biokhim. Mikrobiol.* **2005**, *41*, 573.
- (534) MacLeod, J. W.; Thomson, R. H. *J. Org. Chem.* **1960**, *25*, 36.
- (535) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 124.
- (536) (a) Baker, R. A.; Tatum, J. H.; Nemece, S., Jr. *Mycopathologia* **1990**, *111*, 9. (b) Gopalakrishnan, S.; Beale, M. H.; Ward, J. L.; Strange, R. N. *Phytochemistry* **2005**, *66*, 1536. (c) Thomson, R. H. *Naturally Occurring Quinones II*; Springer: Heidelberg, Germany, 1988; p 273.
- (537) (a) Medentsev, A. G.; Baskunov, B. P.; Akimenko, V. K. *Biokhimiya* **1988**, *53*, 413. (b) Cajori, F. A.; Otani, T. T.; Hamilton, M. A. *J. Biol. Chem.* **1954**, *208*, 107. (c) Arsenaault, G. P. *Tetrahedron Lett.* **1965**, 4033.
- (538) Kesteleyn, B.; De Kimpe, N. *J. Org. Chem.* **2000**, *65*, 640.
- (539) Parisot, D.; Devys, M.; Barbier, M. J. *Antibiot.* **1989**, *42*, 1189.
- (540) (a) Bergeron, D.; Caron, B.; Brassard, P. *J. Org. Chem.* **1993**, *58*, 509. (b) Widmer, E.; Meyer, J. W.; Walser, A.; Hardegger, E. *Helv. Chim. Acta* **1965**, *48*, 538.
- (541) Kitahara, T.; Kiyota, H.; Kurata, H.; Mori, K. *Tetrahedron* **1991**, *47*, 1649.
- (542) (a) Koyama, K.; Natori, S. *Chem. Pharm. Bull.* **1988**, *36*, 146. (b) Sekita, S.; Yoshihira, K.; Natori, S. *Chem. Pharm. Bull.* **1980**, *28*, 2428.
- (543) Koyama, K.; Aida, S.; Natori, S. *Chem. Pharm. Bull.* **1990**, *38*, 2259.
- (544) Arimoto, H.; Nishimura, K.; Kuramoto, M.; Uemura, D. *Tetrahedron Lett.* **1998**, *39*, 9513.
- (545) Vesonder, R. F.; Tjarks, L. W.; Rohwedder, W. K.; Burmeister, H. R.; Laugal, J. A. *J. Antibiot. (Tokyo)* **1979**, *32*, 759.
- (546) (a) Burke, L. T.; Dixon, D. J.; Ley, S. V.; Rodriguez, F. *Org. Biomol. Chem.* **2005**, *3*, 274. (b) Yuki, K.; Shindo, M.; Shishido, K. *Tetrahedron Lett.* **2001**, *42*, 2517. (c) Burke, L. T.; Dixon, D. J.; Ley, S. V.; Rodriguez, F. *Org. Lett.* **2000**, *2*, 3611. (d) Yuki, K.; Satoyoshi, N.; Shindo, M.; Shishido, K. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu* **1999**, *41*, 295. (e) Turos, E.; Audia, J. E.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 8231.
- (547) Devys, M.; Barbier, M.; Parisot, D. *Heterocycles* **1990**, *31*, 1485.
- (548) Yeulet, S. E.; Mantle, P. G.; Rudge, M. S.; Greig, J. B. *Mycopathologia* **1988**, *102*, 21.
- (549) Kraus, G. A. U.S. Patent Appl. 81-245382 19810319, 1982; *Chem. Abstr.* **1982**, *98*, 4438.
- (550) Kraus, G. A. *J. Org. Chem.* **1981**, *46*, 201.
- (551) Roberts, J. C.; Woollven, P. *J. Chem. Soc. C* **1970**, 278.
- (552) Donner, C. D.; Gill, M. *Aust. J. Chem.* **2002**, *55*, 213.
- (553) Detoxification product: Hutchison, R. D.; Steyn, P. S.; Thompson, D. L. *Tetrahedron Lett.* **1971**, 4033.
- (554) Williams, D. R.; Turske, R. A. *Org. Lett.* **2000**, *2*, 3217.
- (555) Dethoup, T.; Manoch, L.; Kijjao, A.; Nascimento, M. S.; Puaparoj, P.; Silva, A. M.; Eaton, G.; Herz, W. *Planta Med.* **2006**, *72*, 957.
- (556) Jang, J. H.; Kanoh, K.; Adachi, K.; Shizuri, Y. *J. Nat. Prod.* **2006**, *69*, 1358.
- (557) Hayashi, Y.; Shoji, M.; Mukaiyama, T.; Gotoh, H.; Yamaguchi, S.; Nakata, M.; Kakeya, H.; Osada, H. *J. Org. Chem.* **2005**, *70*, 5643.
- (558) Igarashi, Y.; Yabuta, Y.; Sekine, A.; Fujii, K.; Harada, K.-I.; Oikawa, T.; Sato, M.; Furumai, T.; Oki, T. *J. Antibiot.* **2004**, *57*, 748.
- (559) (a) Hayashi, Y.; Shoji, M.; Yamaguchi, S.; Mukaiyama, T.; Yamaguchi, J.; Kakeya, H.; Osada, H. *Org. Lett.* **2003**, *5*, 2287. (b) Aoki, S.-y.; Oi, T.; Shimizu, K.; Shiraki, R.; Takao, K.-i.; Tadano, K.-i. *Heterocycles* **2004**, *62*, 161.
- (560) Rodriguez Lopez, M.; Bermejo, F. A. *Tetrahedron* **2006**, *62*, 8095.
- (561) Mehta, G.; Roy, S. *Chem. Commun.* **2005**, 3210.
- (562) (a) Smith, A. B., III; Mewshaw, R. *J. Am. Chem. Soc.* **1985**, *107*, 1769. (b) Smith, A. B., III; Leenay, T. L. *Tetrahedron Lett.* **1988**, *29*, 2791.
- (563) Smith, A. B., III; Kingery-Wood, J.; Leenay, T. L.; Nolen, E. G.; Sunazuka, T. *J. Am. Chem. Soc.* **1992**, *114*, 1438.
- (564) Andersen, B.; Frisvad, J. C. *J. Agric. Food Chem.* **2004**, *52*, 7507.
- (565) Isaac, B. G.; Ayer, S. W.; Stonard, R. J. *J. Antibiot.* **1991**, *44*, 793.
- (566) Wenger, R. M. *Helv. Chim. Acta* **1984**, *67*, 502.
- (567) Larsen, T. O.; Gareis, M.; Frisvad, J. C. *J. Agric. Food Chem.* **2002**, *50*, 6148.
- (568) Holzapfel, C. W.; Koekemoer, J. M.; Van Dyk, M. S. *S. Afr. J. Chem.* **1986**, *39*, 75.
- (569) Shoham, G.; Lipscomb, W. N.; Wieland, T. *J. Am. Chem. Soc.* **1989**, *111*, 4791.
- (570) Wieland, T. *Int. J. Pept. Protein Res.* **1983**, *22*, 257.
- (571) (a) Schmitt, H.; Jung, G. *Lieb. Ann. Chem.* **1985**, 321. (b) Gisin, B. F.; Davis, D. G.; Borowska, Z. K.; Hall, J. E.; Kobayashi, S. *J. Am. Chem. Soc.* **1981**, *103*, 6373.
- (572) Structure: Katz, E.; Aydin, M.; Licht, N.; König, W. A.; Ooka, T.; Jung, G. *Liebigs Ann. Chem.* **1985**, 1041.
- (573) (a) Structure: Krause, C.; Kirschbaum, J.; Jung, G.; Brückner, H. *J. Pept. Sci.* **2006**, *12*, 321. (b) Inclusion of peptaibols/peptaibols in the group of mycotoxins has been questioned: Degenkolb, T.; Dören, H. V.; Nielsen, K. F.; Samuels, G. J.; Brückner, H. *Chemistry Biodiv.* **2008**, *8*, 671. (c) See also: Toniolo, C.; Brückner, H. *Peptaibiotics*; Wiley: *Fungal Peptides Containing α -Dialkyl α -Amino Acids*; Verlag Helvetica Chimica Acta: Zürich, 2009.
- (574) Brückner, H.; Koza, A. *Pept.* **1992**, Proc. Eur. Pept. Symp., 22nd, **1993**, Meeting Date **1992**, 385.
- (575) (a) Coleman, R. S.; Grant, E. B. *J. Am. Chem. Soc.* **1995**, *117*, 10889. (b) Coleman, R. S.; Grant, E. B. *J. Am. Chem. Soc.* **1994**, *116*, 8795.
- (576) Broka, C. A. *Tetrahedron Lett.* **1991**, *32*, 859.
- (577) Merlic, C. A.; Aldrich, C. C.; Albaneze-Walker, J.; Saghatelian, A.; Mammen, J. *J. Org. Chem.* **2001**, *66*, 1297.
- (578) Kobayashi, E.; Ando, K.; Nakano, H.; Iida, T.; Ohno, H.; Morimoto, M.; Tamaoki, T. *J. Antibiot.* **1989**, *42*, 1470.
- (579) (a) Merlic, C. A.; Aldrich, C. C.; Albaneze-Walker, J.; Saghatelian, A. *J. Am. Chem. Soc.* **2000**, *122*, 3224. (b) Hauser, F. M.; Sengupta, D.; Corlett, S. A. *J. Org. Chem.* **1994**, *59*, 1967.
- (580) For example: Hassall, C. H.; Todd, A. R. *J. Chem. Soc.* **1947**, 611.
- (581) For example: Cram, D. J. *J. Am. Chem. Soc.* **1948**, *70*, 4240.
- (582) Al-Mousawi, S. M.; McOmie, J. F. W. *Chem. Ind. (London, U. K.)* **1981**, 472.
- (583) Liberra, K.; Jansen, R.; Wegner, U.; Lindequist, U. *Pharmazie* **1995**, *50*, 370.
- (584) (a) Hayashi, K.; Tokura, K.; Okabe, K.; Yamamoto, K.; Tawara, K. *Chem. Pharm. Bull.* **1982**, *30*, 2860. (b) Hayashi, K.; Tokura, K.; Okabe, K. *Chem. Pharm. Bull.* **1980**, *28*, 1971. (c) Al-Mousawi, S. M.; Green, R. J. S.; McOmie, J. F. W. *Bull. Soc. Chim. Belg.* **1979**, *88*, 883.
- (585) Nozawa, Y.; Ito, M.; Sugawara, K.; Hanada, K.; Mizoe, K. *J. Antibiot.* **1997**, 641.
- (586) Andersen, B. *Antonie van Leeuwenhoek* **1991**, *60*, 115.
- (587) Sugano, M.; Sato, A.; Iijima, Y.; Oshima, T.; Furuya, K.; Kuwano, H.; Hata, T.; Hanzawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 5463.
- (588) Goldring, W. P. D. *Acc. Chem. Res.* **2006**, *39*, 354.
- (589) Studies: Cole, K. P. *Chem. Commun.* **2005**, 5784.
- (590) Mohr, P. J.; Halcomb, R. L. *J. Am. Chem. Soc.* **2003**, *125*, 1712.
- (591) Huang, J.; Wu, C.; Wulff, W. D. *J. Am. Chem. Soc.* **2007**, *129*, 13366.
- (592) Ohzeki, T.; Mori, K. *Biosci., Biotechnol., Biochem.* **2003**, *67*, 2240.
- (593) (*Aspergillus duricaulis*): Brillinger, G. U.; Heberle, W.; Weber, B.; Achenbach, H. *Arch. Microbiol.* **1978**, *116*, 245.
- (594) Clutterbuck, P. W.; Raistrick, H. *Biochem. J.* **1933**, *27*, 654.
- (595) (a) Covarrubias-Zuniga, A.; Gonzalez-Lucas, A.; Dominguez, M. M. *Tetrahedron* **2003**, *59*, 1989. (b) de la Cruz, R. A.; Talamas, F. X.; Vazquez, A.; Muchowski, J. M. *Can. J. Chem.* **1997**, *75*, 641. (c) Danheiser, R. L.; Gee, S. K.; Perez, J. J. *J. Am. Chem. Soc.* **1986**, *108*, 806. (d) Canonica, L.; Rindone, B.; Santaniello, E.; Scolastico, C. *Tetrahedron* **1972**, *28*, 4395.
- (596) Hosaka, M.; Hayakawa, H.; Miyashita, M. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4227. (b) Suzuki, Y.; Danko, J.; Kono, Y.; Daly, J. M.; Takeuchi, S. *Agric. Biol. Chem.* **1985**, *49*, 149.
- (597) Cole, R. J.; Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 916.
- (598) Ichihara, A.; Kawagishi, H.; Tokugawa, N.; Sakamura, S. *Tetrahedron Lett.* **1986**, *27*, 1347.
- (599) VanMiddlesworth, F.; Giacobbe, R. A.; Lopez, M.; Garrity, G.; Bland, J. A.; Bartizal, K.; Fromtling, R. A.; Polishook, J.; Zwerink, M.; Edison, A. M.; Rozdilsky, W.; Wilson, K. E.; Monaghan, R. L. *J. Antibiot.* **1992**, *45*, 861.
- (600) (a) Li, M.; Wu, A. *Synlett* **2006**, 2985. (b) Lee, K.-Y.; Oh, C.-Y.; Ham, W.-H. *Org. Lett.* **2002**, *4*, 4403. (c) Trost, B. M.; Lee, C. *J. Am. Chem. Soc.* **2001**, *123*, 12191. (d) Wang, B.; Yu, X.-m.; Lin, G.-q. *Synlett* **2001**, 904. (e) Nakamura, T.; Shiozaki, M. *Tetrahedron Lett.* **2001**, *42*, 2701. (f) Liu, D.-G.; Wang, B.; Lin, G.-Q. *J. Org. Chem.* **2000**, *65*, 9114. (g) Kobayashi, S.; Furuta, T. *Tetrahedron* **1998**, *54*, 10275. (h) Mori, K.; Otaka, K. *Tetrahedron Lett.* **1994**, *35*, 9207.
- (601) Oishi, T.; Ando, K.; Inomiya, K.; Sato, H.; Iida, M.; Chida, N. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 1927.

- (602) Shimada, J.; Kwon, H. J.; Sawamura, M.; Schreiber, S. L. *Chem. Biol.* **1995**, *2*, 517.
- (603) Helbig, F.; Steighardt, J.; Roos, W. *Appl. Environ. Microbiol.* **2002**, *68*, 1524.
- (604) Solfrizzo, M.; Visconti, A.; Savard, M. E.; Blackwell, B. A.; Neson, P. E. *Mycopathologia* **1994**, *127*, 95.
- (605) Lorisich, H. J.; Kopanski, L.; Herrmann, R.; Schmidt, H.; Steglich, W. *Liebig Ann. Chem.* **1986**, 177.
- (606) Mo, S.; Wang, S.; Zhou, G.; Yang, Y.; Li, Y.; Chen, X.; Shi, J. *J. Nat. Prod.* **2004**, *67*, 823.
- (607) Xu, X.; De Guzman, F. S.; Gloer, J. B. *J. Org. Chem.* **1992**, *57*, 6700.
- (608) Shinohara, C.; Hasumi, K.; Hatsumi, W.; Endo, A. *J. Antibiot.* **1996**, *49*, 961.
- (609) (a) Schlessinger, R. H.; Gillman, K. W. *Tetrahedron Lett.* **1999**, *40*, 1257. (b) Akaike, H.; Horie, H.; Kato, K.; Akita, H. *Tetrahedron: Asymmetry* **2008**, *19*, 1100.
- (610) Tadano, K.; Yamada, H.; Idogaki, Y.; Ogawa, S.; Suami, T. *Tetrahedron Lett.* **1990**, *46*, 2353.
- (611) (a) Kimura, Y.; Hamasaki, T.; Isogai, A.; Nakajima, H. *Agric. Biol. Chem.* **1982**, *46*, 1963. (b) Katsube, Y.; Kimura, Y.; Hamasaki, T.; Nakajima, H.; Isogai, A. *Agric. Biol. Chem.* **1985**, *49*, 551.
- (612) Nishiyama, S.; Toshima, H.; Yamamura, S. *Chem. Lett.* **1986**, 1973.
- (613) Evidente, A.; Conti, L.; Altomare, C.; Bottalico, A.; Condon, G.; Segre, A. L.; Logrieco, A. *Nat. Toxins* **1994**, *2*, 4.
- (614) Biagetti, M.; Bellina, F.; Carpita, A.; Viel, S.; Mannina, L.; Rossi, R. *Eur. J. Org. Chem.* **2002**, 1063.
- (615) Friedemann, T. E. *Science* **1934**, *80*, 34.
- (616) For example: Yang, Z.-C.; Jiang, X.-B.; Wang, Z.-M.; Zhou, W.-S. *J. Chem. Soc., Perkin Trans. 1* **1997**, 317.
- (617) Valverde, S.; Herradon, B.; Rabanal, R. M.; Martin-Lomas, M. *Can. J. Chem.* **1987**, *65*, 339.
- (618) Steyn, P. S.; Vlegaar, R. *Fortschr. Chem. Org. Naturst.* **1985**, *48*, 1. [Review: Tremorgenic mycotoxins].
- (619) Whang, K.; Cooke, R. J.; Okay, G.; Cha, J. K. *J. Am. Chem. Soc.* **1990**, *112*, 8985.
- (620) Hatakeyama, S.; Sakurai, K.; Numata, H.; Ochi, N.; Takano, S. *J. Am. Chem. Soc.* **1988**, *110*, 5201.
- (621) Cha, J. K.; Cooke, R. J. *Tetrahedron Lett.* **1987**, *28*, 5473.
- (622) Visconti, A.; Solfrizzo, M.; Fruchier, A.; ApSimon, J. W. *J. Nat. Prod.* **1994**, *57*, 695.
- (623) Grove, J. F.; Hitchcock, P. B. *J. Chem. Soc., Perkin Trans. 1* **1991**, 997.
- (624) Ohta, A.; Fujii, S. *Chem. Pharm. Bull.* **1969**, *17*, 851.
- (625) (a) Okada, Y.; Taguchi, H.; Yokoi, T. *Chem. Pharm. Bull.* **1996**, *44*, 2259. (b) Dunn, G.; Newbold, G. T.; Spring, F. S. *J. Chem. Soc.* **1949**, 2586. (c) Sato, N. *Sci. Synth.* **2004**, *16*, 751.
- (626) Ota, A. *Chem. Pharm. Bull.* **1968**, *16*, 1160.
- (627) (a) Liu, J.-F.; Ye, P.; Zhang, B.; Bi, G.; Sargent, K.; Yu, L.; Yohannes, D.; Baldino, C. M. *J. Org. Chem.* **2005**, *70*, 6339. (b) Snider, B. B.; Zeng, H. *J. Org. Chem.* **2003**, *68*, 545. (c) Snider, B. B.; Zeng, H. *Org. Lett.* **2002**, *4*, 1087. (d) Hernandez, F.; Lumetzberger, A.; Avendano, C.; Sollhuber, M. *Synlett* **2001**, 1387. (e) Wang, H.; Ganesan, A. *J. Comb. Chem.* **2000**, *2*, 186. (f) Wang, H.; Ganesan, A. *J. Org. Chem.* **1998**, *63*, 2432.
- (628) Wagner, C.; Anke, H.; Besl, H.; Sterner, O. *Z. Naturforsch., C* **1995**, *50*, 358.
- (629) (a) Findlay, J. A. *Heterocycles* **1979**, *12*, 389. (b) Girotra, N. N.; Zelawski, Z. S.; Wendler, N. L. *Chem. Commun.* **1976**, 566.
- (630) Vogt, H.; Mayer, H. *Arzneimittelforsch.* **1968**, *18*, 207. (b) Renslo, A. R.; Danheiser, R. L. *J. Org. Chem.* **1998**, *63*, 7840.
- (631) MacMillan, J. G.; Springer, J. P.; Clardy, J.; Cole, R. J.; Kirksey, J. W. *J. Am. Chem. Soc.* **1976**, *98*, 246.
- (632) Williams, R. M.; Brunner, E. J.; Sabol, M. R. *Synthesis* **1988**, 963.
- (633) Cole, R. J.; Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 838.
- (634) (a) Eh, M.; Schomburg, D.; Schicht, K.; Kalesse, M. *Tetrahedron* **1995**, *51*, 8983. (b) Kato, K.; Hirata, Y.; Yamamura, S. *J. Chem. Soc., C* **1969**, 1997.
- (635) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; pp 367 and 368.
- (636) (a) Kay, I. T.; Atkins, P. R. *Chem. Commun.* **1971**, 430. (b) Brown, A. G.; Smale, T. C. *J. Chem. Soc., Perkin Trans. 1* **1972**, 65.
- (637) (a) Lambert, T. H.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2006**, *128*, 426. (b) Hoye, T. R.; Dvornikovs, V. *J. Am. Chem. Soc.* **2006**, *128*, 2550. (c) de Figueiredo, R. M.; Fröhlich, R.; Christmann, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 2883.
- (638) Larsen, T. O.; Frydenvang, K.; Frisvad, J. C.; Christophersen, C. *J. Nat. Prod.* **1998**, *61*, 1154.
- (639) Vinokurova, N. G.; Baskunov, B. P.; Zelenkova, N. F.; Arinbasarov, M. U. *Mikrobiologiya* **2004**, *73*, 491.
- (640) Wang, H.; Sim, M. M. *J. Nat. Prod.* **2001**, *64*, 1497.
- (641) (*Penicillium chrysogenum*): MacDonald, K. D.; Hutchinson, J. M.; Gillett, W. A. *J. Gen. Microbiol.* **1963**, *33*, 375.
- (642) (a) Bergman, J.; Brynolf, A. *Tetrahedron* **1990**, *46*, 1295. (b) Maiti, D. K.; Ghoshdastidar, P. P.; Bhattacharya, P. K. *J. Chem. Res., Synopses* **1996**, 306.
- (643) Ribeiro, N.; Tabaka, H.; Peluso, J.; Fetzer, L.; Nebigil, C.; Dumont, S.; Muller, C. D.; Desaubry, L. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5523.
- (644) Larsen, T. O.; Svendsen, A.; Smedsgaard, J. *Appl. Environ. Microbiol.* **2001**, *67*, 3630.
- (645) Eistert, B.; Selzer, H. Z. *Naturforsch.* **1962**, *17B*, 202.
- (646) (a) Takahashi, S.; Nitta, K.; Okami, Y.; Umezawa, H. *J. Antibiot.* **1961**, *14*, 107. (b) Sheehan, J. C.; Lawson, W. B.; Gaul, R. J. *J. Am. Chem. Soc.* **1958**, *80*, 5536. (c) Read, G.; Westlake, D. W. S.; Vining, L. C. *Can. J. Biochem.* **1969**, *47*, 1071. (d) Kiriya, N.; Higuchi, Y.; Yamamoto, Y. *Chem. Pharm. Bull.* **1977**, *25*, 1265. (e) Read, G. *J. Chem. Soc.* **1965**, 6587. (f) Yamamoto, H.; Moriyama, K.; Jinnouchi, H.; Yagishita, K. *Jpn. J. Antibiot.* **1980**, *33*, 320. (g) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; pp 65 and 66.
- (647) Rashid, A.; Read, G. *J. Chem. Soc., C* **1967**, 1323.
- (648) (a) Enhsen, A.; Karabelas, K.; Heerding, J. M.; Moore, H. W. *J. Org. Chem.* **1990**, *55*, 1177. (b) Sheehan, J. C.; Lo, Y. S. *J. Med. Chem.* **1974**, *17*, 371.
- (649) Lai, S.; Gao, X.; Shizuri, Y.; Yamamura, S. *Chin. Chem. Lett.* **1994**, *5*, 481.
- (650) Ellestad, G. A.; Lovell, F. M.; Perkinson, N. A.; Hargreaves, R. T.; McGahren, W. J. *J. Org. Chem.* **1978**, *43*, 2339.
- (651) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 176.
- (652) Kalivretenos, A.; Stille, J. K.; Hegedus, L. S. *J. Org. Chem.* **1991**, *56*, 2883.
- (653) Munoz, L.; Castro, J. L.; Cardelle, M.; Castedo, L.; Riguera, R. *Phytochemistry* **1988**, *28*, 83.
- (654) Isaka, M.; Suyarnsestakorn, C.; Tanticharoen, M.; Kongsaree, P.; Thebtaranonth, Y. *J. Org. Chem.* **2002**, *67*, 1561.
- (655) Geng, X.; Danishefsky, S. J. *Org. Lett.* **2004**, *6*, 413.
- (656) Barluenga, S.; Dakas, P.-Y.; Ferandin, Y.; Meijer, L.; Winssinger, N. *Angew. Chem., Int. Ed.* **2006**, *45*, 3951. *Angew. Chem.* **2006**, *118*, 4055.
- (657) Lu, J.; Ma, J.; Xie, X.; Chen, B.; She, X.; Pan, X. *Tetrahedron: Asymmetry* **2006**, *17*, 1066.
- (658) Vu, N. G.; Chai, C. L.; Lim, K. P.; Chia, S. C.; Chen, A. *Tetrahedron* **2007**, *63*, 7053.
- (659) Bracher, F.; Schulte, B. *Liebigs Ann./Recueil* **1997**, 1979.
- (660) Robeson, D. J.; Strobel, G. A.; Strange, R. N. *J. Nat. Prod.* **1985**, *48*, 139.
- (661) According to Betina, V. *Mycotoxins (Bioactive Molecules)*; Elsevier Science Publishers: Amsterdam, 1989; Vol. 9; this is not a *sensu stricto* mycotoxin.
- (662) Selles, P.; Lett, R. *Tetrahedron Lett.* **2002**, *43*, 4621.
- (663) Garbaccio, R. M.; Stachel, S. J.; Baeschlin, D. K.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2001**, *123*, 10903.
- (664) Tichkowsky, I.; Lett, R. *Tetrahedron Lett.* **2002**, *43*, 3997.
- (665) Barluenga, S.; Moulin, E.; Lopez, P.; Winssinger, N. *Chem.—Eur. J.* **2005**, *11*, 4935.
- (666) Moulin, E.; Barluenga, S.; Winssinger, N. *Org. Lett.* **2005**, *7*, 5637.
- (667) Barluenga, S.; Lopez, P.; Moulin, E.; Winssinger, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 3467.
- (668) Moulin, E.; Zoete, V.; Barluenga, S.; Karplus, M.; Winssinger, N. *J. Am. Chem. Soc.* **2005**, *127*, 6999.
- (669) Khartulyari, A. S.; Kapur, M.; Maier, M. E. *Org. Lett.* **2006**, *8*, 5833.
- (670) (a) Bracher, F.; Krauss, J. *Monatsh. Chem.* **2001**, *132*, 805. (b) Hurd, T. N.; Shah, D. H. *J. Med. Chem.* **1973**, *16*, 543.
- (671) (a) Girotra, N. N.; Wendler, L. L. *Chem. Ind.* **1967**, 1493. (b) Taub, D.; Girotra, N. N.; Hoffsommer, R. D., Jr.; Kuo, C.-H.; Slates, H. L.; Weber, S.; Wendler, N. L. *Chem. Commun.* **1967**, 225.
- (672) Taub, D.; Girotra, N. N.; Hoffsommer, R. D.; Kuo, C. H.; Slates, H. L.; Weber, S.; Wendler, N. L. *Tetrahedron* **1968**, *24*, 2443.
- (673) Fürstner, A.; Thiel, O. R.; Kindler, N.; Bartkowska, B. *J. Org. Chem.* **2000**, *65*, 7990.
- (674) Takahashi, T.; Ikeda, H.; Tsuji, J. *Tetrahedron Lett.* **1981**, *22*, 1363.
- (675) Hitchcock, S. A.; Pattenden, G. *Tetrahedron Lett.* **1990**, *31*, 3641.
- (676) (a) Hitchcock, S. A.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1323. (b) Navarro, I.; Basset, J.-F.; Hebbe, S.; Major, S. M.; Werner, T.; Howsham, C.; Brackow, J.; Barrett, A. G. M. *J. Am. Chem. Soc.* **2008**, *130*, 10293.
- (677) Malheiros, A.; Filho, V. C.; Schmitt, C. B.; Santos, A. R. S.; Scheidt, C.; Calixto, J. B.; Delle Monache, F.; Yunes, R. A. *Phytochemistry* **2001**, *57*, 103.
- (678) Srikrishna, A.; Ravikumar, P. C. *Tetrahedron* **2006**, *62*, 9393.

- (679) (a) Wender, P. A.; Wolanin, D. J. *J. Org. Chem.* **1985**, *50*, 4418. (b) Kon, K.; Ito, K.; Isoe, S. *Tetrahedron Lett.* **1984**, *25*, 3739. (c) Turbyville, T. J.; Wijeratne, E. M.; Whitesell, L.; Gunatilaka, A. A. *Mol. Cancer Ther.* **2005**, *4*, 1569.
- (680) (a) Bell, R. P. L.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **2001**, *66*, 2350. (b) Jonassohn, M.; Hjertberg, R.; Anke, H.; Dekermendjian, K.; Azallasi, A.; Thines, E.; Witt, R.; Sterner, O. *Bioorg. Med. Chem.* **1997**, *5*, 1363. (c) Bergman, R.; Hansson, T.; Sterner, O.; Wickberg, B. *J. Chem. Soc., Chem. Commun.* **1990**, 865. (d) Thompson, S. K.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 3004. (e) Magnusson, G.; Thoren, S.; Wickberg, B. *Tetrahedron Lett.* **1972**, 1105.
- (681) (a) Srikrishna, A.; Vasantha Lakshmi, B.; Ravikumar, P. C. *Tetrahedron Lett.* **2006**, *47*, 1277. (b) Srikrishna, A.; Babu, R. R.; Ravikumar, P. C. *Synlett* **2007**, 655.
- (682) Hesketh, A. R.; Gledhill, L.; Marsh, D. C.; Bycroft, B. W.; Dewick, P. M.; Gilbert, J. J. *J. Chem. Soc., Chem. Commun.* **1990**, 1184.
- (683) Kitano, Y.; Fududa, J.; Chiba, K.; Tada, M. *J. Chem. Soc., Perkin Trans. 1* **1996**, *8*, 829.
- (684) (a) Nishiyama, S.; Toshima, H.; Kanai, H.; Yamamura, S. *Tetrahedron Lett.* **1986**, 3643. (b) Baldwin, C. L.; Weaver, L. C.; Brooker, R. M.; Jacobsen, T. N.; Osborne, C. E., Jr.; Nash, H. A. *Lloydia* **1964**, *27*, 88. (c) Lardy, H. A.; Connelly, J. L.; Johnson, D. *Biochem.* **1964**, *3*, 1961. (d) Blair, E. L.; Sherratt, H. S. A.; Wood, D. D. *Biochem. J.* **1967**, *104*, 54. (e) Osselton, M. D.; Baum, H.; Beechey, R. B. *Biochem. Soc. Trans. 1* **1974**, *2*, 200. (f) Mulheirn, L. J.; Beechey, R. B.; Leworthy, D. P.; Osselton, M. D. *Chem. Commun.* **1974**, 874.
- (685) Nishiyama, S.; Toshima, H.; Kanai, H.; Yamamura, S. *Tetrahedron* **1988**, *44*, 6315.
- (686) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; pp 173, 174, and 199.
- (687) Uhlig, S.; Petersen, D.; Flaoyen, A.; Wilkins, A. *Toxicon* **2005**, *46*, 513.
- (688) Oxford, A. E.; Raistrick, H.; Simonart, P. *Biochem. J.* **1939**, *33*, 240.
- (689) (a) Day, A. C.; Nabney, J.; Scott, A. I. *Proc. Chem. Soc.* **1960**, 284. (b) Brossi, A.; Baumann, M.; Gerecke, M.; Kyburz, E. *Helv. Chim. Acta* **1960**, *43*, 1444. (c) Kuo, C. H.; Hoffsommer, R. D.; Slates, H. L.; Taub, D.; Wendler, N. L. *Chem. Ind.* **1961**, 1627. (d) Stork, G.; Tomasz, M. *J. Am. Chem. Soc.* **1962**, *84*, 310. (e) Brossi, A.; Brumann, M.; Burkhardt, F. *Helv. Chim. Acta* **1962**, *45*, 1292. (f) Danishefsky, S.; Walker, F. J. *J. Am. Chem. Soc.* **1979**, *101*, 7018. (g) Pirrung, M. C.; Brown, W. L.; Rege, S.; Laughton, P. *J. Am. Chem. Soc.* **1991**, *113*, 8561.
- (690) Kamalov, L. S.; Aripova, S. F.; Isaev, M. I. *Chem. Nat. Compd.* **1999**, *35*, 82.
- (691) (a) Hagiwara, H.; Nakano, T.; Kon-no, M.; Uda, H. *J. Chem. Soc., Perkin Trans. 1* **1995**, 777. (b) Clive, D. L. J.; Murthy, K. S. K.; Wee, A. G. H.; Prasad, J. S.; Da Silva, G. V. J.; Majewski, M.; Anderson, P. C. *Stud. Nat. Prod. Chem.* **1992**, *11*, 335. (c) Burke, S. D.; Deaton, D. N. *Tetrahedron Lett.* **1991**, *32*, 4651. (d) Clive, D. L. J.; Murthy, K. S. K.; Wee, A. G. H.; Prasad, J. S.; Da Silva, G. V. J.; Majewski, M.; Anderson, P. C.; Evans, C. F.; Haugen, R. D.; Heerze, L. D.; Barrie, J. R. *J. Am. Chem. Soc.* **1990**, *112*, 3018. (e) Danishefsky, S. J.; Simoneau, B. *J. Am. Chem. Soc.* **1989**, *111*, 2599. (f) Clive, D. L. J.; Murthy, K. S. K.; Wee, A. G. H.; Prasad, J. S.; Da Silva, G. V. J.; Majewski, M.; Anderson, P. C.; Haugen, R. D.; Heerze, L. D. *J. Am. Chem. Soc.* **1988**, *110*, 6914. (g) Grieco, P. A.; Lis, R.; Zelle, R. E.; Finn, J. *J. Am. Chem. Soc.* **1986**, *108*, 5908. (h) Keck, G. E.; Kachensky, D. F. *J. Org. Chem.* **1986**, *51*, 2487. (i) Rosen, T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1985**, *107*, 3731. (j) Girotra, N. N.; Wendler, N. L. *Tetrahedron Lett.* **1982**, *23*, 5501. (k) Hsu, C. T.; Wang, N. Y.; Latimer, L. H.; Sih, C. J. *J. Am. Chem. Soc.* **1983**, *105*, 593. (l) Hiram, M.; Uei, M. *J. Am. Chem. Soc.* **1982**, *104*, 4251. (m) Wang, N. Y.; Hsu, C. T.; Sih, C. J. *J. Am. Chem. Soc.* **1981**, *103*, 6538.
- (692) Debeaupuis, J. P.; Lafont, P. *Appl. Environ. Microbiol.* **1978**, *36*, 8.
- (693) Anderson, E. A.; Alexanian, E. J.; Sorensen, E. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 1998.
- (694) (a) Sato, S.; Nakada, M.; Shibasaki, M. *Tetrahedron Lett.* **1996**, *37*, 6141. (b) Mizutani, T.; Honzawa, S.; Tosaki, S.-Y.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 4680.
- (695) Cole, R. J.; Kirksey, J. W.; Springer, J. P.; Clardy, J.; Cutler, H. G.; Garren, K. H. *Phytochemistry* **1975**, *14*, 1429.
- (696) Springer, J. P.; Dorner, J. W.; Cole, R. J.; Cox, R. H. *J. Org. Chem.* **1979**, *44*, 4852.
- (697) Su, J.; Zhen, Y. C.; Qi, C. Q.; Hu, J. L. *Cancer Chemother. Pharmacol.* **1995**, *36*, 149.
- (698) Kramer, R. K.; Davis, N. D.; Diener, U. L. *Appl. Environ. Microbiol.* **1976**, *31*, 249.
- (699) Stansly, P. G.; Ananenko, N. H. *Arch. Biochem.* **1949**, *23*, 256.
- (700) Pawar, V. H.; Deshmukh, P. V.; Thirumalachar, M. J. *Hindustan Antibiot. Bull.* **1965**, *8*, 59.
- (701) Lafont, P.; Lafont, J.; Frayssinet, C. *Experientia* **1970**, *26*, 61.
- (702) Ghosh, A. C.; Manmade, A.; Kobbe, B.; Townsend, J. M.; Demain, A. L. *Microbiol.* **1978**, *35*, 563.
- (703) Freire, C. O.; Zozakiewicz, Z.; Russell, R.; Paterson, M. *Mycopathologia* **1999**, *145*, 95.
- (704) Smith, A. B.; Thompson, A. S. *J. Org. Chem.* **1984**, *49*, 1469.
- (705) Schreiber, S. L.; Sommer, T. J.; Satake, K. *Tetrahedron Lett.* **1985**, *26*, 17.
- (706) Midland, M. M.; Gabriel, J. *J. Org. Chem.* **1985**, *50*, 1143.
- (707) Iwata, C.; Fujita, M.; Moritani, Y.; Hattori, K.; Imanishi, T. *Tetrahedron Lett.* **1987**, *28*, 3135.
- (708) Crimmins, M. T.; O'Mahony, R. *J. Org. Chem.* **1989**, *54*, 1157.
- (709) Baker, R.; Boyes, A. L.; Swain, C. J. *Tetrahedron Lett.* **1989**, *30*, 985.
- (710) Baker, R.; Boyes, A. L.; Swain, C. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1415.
- (711) Izquierdo Cubero, I.; Lopez-Espinosa, M. T. *Carbohydr. Res.* **1990**, *205*, 293.
- (712) Redlich, H.; Lenfers, J. B.; Thormaehlen, S. *Synthesis* **1992**, 1112.
- (713) Iwata, C.; Maezaki, N.; Hattori, K.; Fujita, M.; Moritani, Y.; Takemoto, Y.; Tanaka, T.; Imanishi, T. *Chem. Pharmacol. Bull.* **1993**, *41*, 946.
- (714) Mori, K.; Ikunaka, M. *Tetrahedron* **1987**, *43*, 45.
- (715) Guanti, G.; Banfi, L.; Narisano, E.; Zannetti, M. T. *J. Org. Chem.* **1993**, *58*, 1508.
- (716) Whitby, R.; Kocienski, P. *Chem. Commun.* **1987**, 906.
- (717) Kozikowski, A. P.; Scripko, J. G. *J. Am. Chem. Soc.* **1984**, *106*, 353.
- (718) Schreiber, S. L.; Sommer, T. J. *Tetrahedron Lett.* **1983**, *24*, 4781.
- (719) Kocienski, P.; Yeates, C. *Chem. Commun.* **1984**, 151.
- (720) Kay, I. T.; Bartholomew, D. *Tetrahedron Lett.* **1984**, *25*, 2035.
- (721) Kocienski, P.; Yeates, C. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1879.
- (722) Tietze, L. F.; Schneider, C. *J. Org. Chem.* **1991**, *56*, 2476.
- (723) Izquierdo, I.; Plaza, M. T.; Rodriguez, M.; Tamayo, J. A. *Eur. J. Org. Chem.* **2002**, 309.
- (724) Pedersen, P. B.; Miller, J. D. *Nat. Toxins* **1999**, *7*, 305.
- (725) Takasu, K.; Mizutani, S.; Noguchi, M.; Makita, K.; Ihara, M. *J. Org. Chem.* **2000**, *65*, 4112.
- (726) Hart, D. J.; Huang, H. C. *J. Am. Chem. Soc.* **1988**, *110*, 1634.
- (727) Mierau, V.; Rojas de la Parra, V.; Sterner, O.; Anke, T. *J. Antibiot.* **2006**, *59*, 53. (b) Rojas de la Parra, V.; Mierau, V.; Anke, T.; Sterner, O. *Tetrahedron* **2006**, *62*, 1828.
- (728) Stead, P.; Affleck, K.; Sidebottom, P. J.; Taylor, N. L.; Drake, C. S.; Todd, M.; Jowett, A.; Webb, G. *J. Antibiot.* **1999**, *52*, 89.
- (729) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 500.
- (730) Biswas, B.; Sarkar, D.; Venkateswaran, R. V. *Tetrahedron* **2008**, *64*, 6809.
- (731) Frisvad, J. C.; Filtenborg, O.; Samson, R. A.; Stolk, A. C. *Antonie Van Leeuwenhoek* **1990**, *57*, 179.
- (732) (a) McCurry, P. M., Jr.; Abe, K. *J. Am. Chem. Soc.* **1973**, *95*, 5824. (b) Kurth, M. J.; Yu, C. M. *J. Org. Chem.* **1985**, *50*, 1840. (c) Rehnberg, N.; Frejd, T.; Magnusson, G. *Tetrahedron Lett.* **1987**, *28*, 3589. (d) Daub, G. W.; Edwards, J. P.; Okada, C. R.; Allen, J. W.; Maxey, C. T.; Wells, M. S.; Goldstein, A. S.; Dibley, M. J.; Wang, C. J.; Ostercamp, D. P.; Chung, S.; Cunningham, P. S.; Berliner, M. A. *J. Org. Chem.* **1997**, *62*, 1976. (e) Andrey, O.; Vidonne, A.; Alexakis, A. *Tetrahedron Lett.* **2003**, *44*, 7901. (f) Nougier, R.; Gastaldi, S.; Stien, D.; Bertrand, M.; Villar, F.; Andrey, O.; Renaud, P. *Tetrahedron: Asymmetry* **2003**, *14*, 3005.
- (733) Clemens, R. T.; Jennings, M. P. *Chem. Commun.* **2006**, 2720.
- (734) Berst, F.; Ladlow, M.; Holmes, A. B. *Chem. Commun.* **2002**, 508.
- (735) Gill, M.; Kiefel, M. J.; Lally, D. A.; Ten, A. *Aust. J. Chem.* **1990**, *43*, 1497.
- (736) Raistrick, H.; Smith, G. *Biochem. J.* **1933**, *27*, 1814. (b) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 380.
- (737) (a) White, J. D.; Kim, J.; Drapela, N. E. *J. Am. Chem. Soc.* **2000**, *122*, 8665. (b) White, J. D.; Dillon, M. P.; Butlin, R. J. *J. Am. Chem. Soc.* **1992**, *114*, 9673. (c) Stork, G.; Tabak, J. M.; Blount, J. F. *J. Am. Chem. Soc.* **1972**, *94*, 4735.
- (738) Clutterbuck, P. W.; Haworth, W. N.; Raistrick, H.; Smith, G.; Stacey, M. *Biochem. J.* **1934**, *28*, 94.
- (739) Booth, P. M.; Fox, C. M.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1987**, 121.
- (740) Schobert, R.; Jagusch, C. *Synthesis* **2005**, 2421.
- (741) (a) Ley, S. V.; Trudell, M. L.; Wadsworth, D. J. *Tetrahedron* **1991**, *47*, 8285. (b) Haynes, L. J.; Plimmer, J. R.; Stanners, A. H. *J. Chem. Soc.* **1956**, 4661.

- (742) (a) Fell, S. C. M.; Heaps, J.; Holker, J. S. E. *Chem. Soc., Chem. Commun.* **1979**, 81. (b) Ramage, R.; McCleery, P. P. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1555.
- (743) Begley, M. J.; Gedge, D. R.; Pattenden, G. *Chem. Commun.* **1978**, 60.
- (744) Birkinshaw, J. H.; Kalyanpur, M. A.; Stickings, C. E. *Biochem. J.* **1963**, *86*, 237.
- (745) Moss, M. O.; Robinson, F. V.; Wood, A. B. *Chem. Ind.* **1968**, *18*, 587.
- (746) Strunz, G. M.; Kakushima, M.; Stillwell, M. A. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2280.
- (747) (a) Tauchi, T.; Sakuma, H.; Ohno, T.; Mase, N.; Yoda, H.; Takabe, K. *Tetrahedron: Asymmetry* **2006**, *17*, 2195. (b) Matsuo, K.; Sakaguchi, Y. *Chem. Pharm. Bull.* **1997**, *45*, 1620. (c) Datta, A.; Datta, D.; Schmidt, R. R. *Tetrahedron Lett.* **1992**, *33*, 8035. (d) Desmaele, D. *Tetrahedron* **1992**, *48*, 2925.
- (748) (a) Bryant, R. W., Jr.; Light, R. J. *Biochemistry* **1974**, *13*, 1516. (b) Grove, J. F. *J. Chem. Soc., C* **1966**, 985.
- (749) Miles, C. O.; Wilkins, A. L.; Gallagher, R. T.; Hawkes, A. D.; Munday, S. C.; Towers, N. R. *J. Agric. Food Chem.* **1992**, *40*, 234.
- (750) Eickman, N.; Clardy, J.; Cole, R. J.; Kirksey, J. W. *Tetrahedron Lett.* **1975**, 1051.
- (751) (a) Kodato, S.; Nakagawa, M.; Hongu, M.; Kawate, T.; Hino, T. *Tetrahedron* **1988**, *44*, 359. (b) Nakatsuka, S.; Teranishi, K.; Goto, T. *Tetrahedron Lett.* **1986**, *27*, 6361.
- (752) (*Aspergillus caespitosus*): Schroeder, H. W.; Cole, R. J.; Hein, H., Jr.; Kirksey, J. W. *Appl. Microbiol.* **1975**, *29*, 857.
- (753) There are various inconsistencies in the literature on this compound.
- (754) Yamazaki, M.; Fujimoto, H.; Okuyama, E. *Chem. Pharm. Bull.* **1977**, *25*, 2554.
- (755) Nakagawa, M.; Ito, M.; Hasegawa, Y.; Akashi, S.; Hino, T. *Tetrahedron Lett.* **1984**, *25*, 3865.
- (756) (a) Hermkens, P. H. H.; Plate, R.; Ottenheijm, H. C. J. *Tetrahedron* **1988**, *44*, 1991. (b) Hino, T.; Kawate, T.; Nakagawa, M. *Tetrahedron* **1989**, *45*, 1941.
- (757) Harrison, D. M.; Sharma, R. B. *Tetrahedron* **1993**, *49*, 3165.
- (758) Nakagawa, M.; Taniguchi, M.; Sodeoka, M.; Ito, M.; Yamaguchi, K.; Hino, T. *J. Am. Chem. Soc.* **1983**, *105*, 3709.
- (759) Cole, R. J.; Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; pp 430 and 452.
- (760) Nozawa, K.; Horie, Y.; Udagawa, S.; Kawai, K.; Yamazaki, M. *Chem. Pharm. Bull.* **1989**, *37*, 1387.
- (761) Springer, J. P.; Clardy, J.; Wells, J. M.; Cole, R. J.; Kirksey, J. W. *Tetrahedron Lett.* **1975**, *30*, 2531.
- (762) Hayashi, H.; Asabu, Y.; Muraio, S.; Nakayama, M.; Arai, M. *Chem. Exp.* **1993**, *8*, 233.
- (763) De Jesus, A. E.; Steyn, P. S.; Van Heerden, F. R.; Vleggaar, R.; Wessels, P. L.; Hull, W. E. *J. Chem. Soc., Chem. Commun.* **1981**, 289.
- (764) Scuteri, M.; Sala de Miguel, M. A.; Blanco Viera, J.; Planes de Banchero, E. *Mycopathologia* **1992**, *120*, 177.
- (765) Sugiyama, H. *Farumashia* **2001**, *37*, 742.
- (766) Ling, K. H.; Yang, C. K.; Peng, F. T. *Appl. Environ. Microbiol.* **1979**, *37*, 355.
- (767) Zhao, Y.; Ku, Y.-L.; Hao, X.; Lee, S.-S. *Tetrahedron* **2000**, *56*, 8901.
- (768) Jarvis, B. B.; Eppley, R. M.; Mazolla, E. P. In *Trichothecenes—Chemical, Biological, and Toxicological Aspects*; Ueno, Y., Ed.; Elsevier: Amsterdam, 1983; p 20.
- (769) Gardner, D.; Glen, A. T.; Turner, W. B. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2576.
- (770) Cameron, S.; Colvin, E. W. *J. Chem. Soc., Perkin Trans. 1* **1989**, 887.
- (771) Visconti, A.; Treeful, L. M.; Mirocha, C. J. *Biomed. Mass Spectrom.* **1985**, 689.
- (772) Grove, J. F.; McAlees, A. J.; Taylor, A. *J. Org. Chem.* **1988**, *53*, 3860.
- (773) Corley, D. G.; Rottinghaus, G. E.; Tempesta, M. S. *Tetrahedron Lett.* **1986**, *27*, 427.
- (774) Grove, J. F. *J. Chem. Soc., Chem. Commun.* **1969**, 1266.
- (775) Greenhalgh, R.; Blackwell, B. A.; Pare, J. R. J.; Miller, J. D.; Levandier, D.; Meier, R. M.; Taylor, A.; Apsimon, J. W. *Bioact. Mol.* **1986**, *1*, 137.
- (776) Durst, T.; Krantis, A. PCT Int. Appl. (2006), WO 2006006082 A2 20060119 (CAN 144:331575).
- (777) (a) Cole, R. J.; Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 190. (b) Ishii, K. *Phytochemistry* **1975**, *14*, 2469.
- (778) Cutler, H. G.; Cole, P. D.; Arrendale, R. F.; Bassfield, R. L.; Cox, R. H.; Roberts, R. G.; Hanlin, R. T. *Agric. Biol. Chem.* **1986**, *50*, 2667.
- (779) (a) Cole, R. J.; Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 244. (b) Matsu-
- moto, M.; Minati, H.; Uotani, N.; Matsumoto, K.; Kondo, E. *J. Antibiot.* **1977**, *30*, 681. (c) Fabre, J. M.; Torreilles, E.; Gibert, J. P.; Chanaa, M.; Giral, L. *Tetrahedron Lett.* **1977**, 4033. (d) Matsumoto, M. *J. Sci. Hiroshima Univ.* **1979**, *43*, 107. (e) Jarvis, B. B.; Midiwo, J. O.; Tuthill, D.; Bean, G. A. *Science* **1981**, *214*, 460.
- (780) Oltz, E. M.; Nakanishi, K.; Yagen, B.; Corley, D. G.; Rottinghaus, G. E.; Tempesta, M. S. *Tetrahedron* **1986**, *42*, 2615.
- (781) Greenhalgh, R.; Levandier, D.; Adams, W.; Miller, J. D.; Blackwell, B. A.; McAlees, A. J.; Taylor, A. *J. Agric. Food Chem.* **1986**, *34*, 98.
- (782) Cutler, H. G. *Proc. Plant Growth Reg. Soc. Am.* **1984**, *11*, 1. (b) Cole, R. J.; Dorner, J. W.; Cox, R. H.; Cunfer, B. M.; Cutler, H. G.; Stuart, B. P. *J. Nat. Prod.* **1981**, *44*, 324. (c) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 520. (d) Pace, J. G. *Fundam. Appl. Toxicol.* **1986**, *7*, 424.
- (783) (a) Cole, R. J.; Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 194. (b) Kotsonis, F. N.; Ellison, R. A.; Smalley, E. B. *Appl. Microbiol.* **1975**, *30*, 493.
- (784) (a) Sanson, D. R.; Corley, D. G.; Barnes, C. L.; Searles, S.; Schlemper, E. O.; Tempesta, M. S.; Rottinghaus, G. E. *J. Org. Chem.* **1989**, *54*, 4313. (b) Greenhalgh, R.; Fielder, D. A.; Morrison, L. A.; Charland, J. P.; Blackwell, B. A.; Savard, M. E.; ApSimon, J. W. *J. Agric. Food Chem.* **1989**, *37*, 699.
- (785) Still, W. C.; Gennari, C.; Noguez, J. A.; Pearson, D. A. *J. Am. Chem. Soc.* **1984**, *106*, 260.
- (786) Kraus, G. A.; Roth, B.; Frazier, K.; Shimagaki, M. *J. Am. Chem. Soc.* **1982**, *104*, 1114.
- (787) Tomioka, K.; Sugimori, M.; Koga, K. *Chem. Pharm. Bull.* **1987**, *35*, 906.
- (788) Chatterjee, K.; Pawlovsky, R. J.; Mirocha, C. J.; Zhu, T.-X. *Appl. Environ. Microbiol.* **1986**, *52*, 311.
- (789) Brooks, D. W.; Grothaus, P. G.; Mazdiyasi, H. *J. Am. Chem. Soc.* **1983**, *105*, 4472.
- (790) Cole, R. J.; Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 189.
- (791) Corley, D. G.; Miller-Wideman, M.; Durley, R. C. *J. Nat. Prod.* **1994**, *57*, 422.
- (792) Wani, M. C.; Rector, D. H.; Cook, C. E. *J. Org. Chem.* **1987**, *52*, 3468.
- (793) Anderson, D. W.; Black, R. M.; Lee, C. G.; Pottage, C.; Rickard, R. L.; Sandford, M. S.; Webber, T. D.; Williams, N. E. *J. Med. Chem.* **1989**, *32*, 555.
- (794) Ziegler, F. E.; Nangia, A.; Tempesta, M. S. *Tetrahedron Lett.* **1988**, *29*, 1665.
- (795) Ziegler, F. E.; Nangia, A.; Schulte, G. *Tetrahedron Lett.* **1988**, *29*, 1669.
- (796) (a) Grove, J. F. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1731. (b) Ehrlich, K. C. *Mycopathologia* **1989**, *107*, 111.
- (797) Eppley, R. M.; Bailey, W. J. *Science* **1973**, *181*, 758.
- (798) Eppley, R. M.; Mazzola, E. P.; Highet, R. J.; Bailey, W. J. *J. Org. Chem.* **1977**, *42*, 240.
- (799) Ziegler, F. E.; Metcalf, C. A.; Schulte, G. *Tetrahedron Lett.* **1992**, *33*, 3117.
- (800) Ziegler, F. E.; Metcalf, C. A.; Nangia, A.; Schulte, G. *J. Am. Chem. Soc.* **1993**, *115*, 2581.
- (801) Belitskii, G. A.; Khovanova, E. M.; Budunova, I. V.; Sharupich, E. G. *Bull. Eksp. Biol. Med.* **1983**, *96*, 83.
- (802) (a) Dong, J.; Peng, S.; Li, G. *Junshi Yixue Kexueyuan Yuankan* **1998**, *22*, 104. (b) Colvin, E. W.; Egan, M. J.; Kerr, F. W. *Chem. Commun.* **1990**, 1200.
- (803) (a) Still, W. C.; Tsai, M.-Y. *J. Am. Chem. Soc.* **1980**, *102*, 3654. (b) O'Brien, M. K.; Pearson, A. J.; Pinkerton, A. A.; Schmidt, W.; Willman, K. *J. Am. Chem. Soc.* **1989**, *111*, 1499.
- (804) Freeman, G. G.; Morrison, R. I. *Nature (London)* **1948**, *162*, 30.
- (805) Gilbert, J. C.; Selliah, R. D. *Tetrahedron* **1994**, *50*, 1651.
- (806) Esmond, R.; Fraser-Reid, B.; Jarvis, B. B. *J. Org. Chem.* **1982**, *47*, 3358.
- (807) Roush, W. R.; Spada, A. P. *Tetrahedron Lett.* **1983**, *24*, 3693.
- (808) Still, W. C.; Ohmizu, H. *J. Org. Chem.* **1981**, *46*, 5242.
- (809) Mohr, P.; Tori, M.; Grossen, P.; Herold, P.; Tamm, C. *Helv. Chim. Acta* **1982**, *65*, 1412.
- (810) Roush, W. R.; Blizzard, T. A. *J. Org. Chem.* **1983**, *48*, 758.
- (811) Breitenstein, W.; Tamm, C. *Helv. Chim. Acta* **1977**, *60*, 1522.
- (812) Shindo, K. *J. Antibiot.* **2001**, *54*, 980.
- (813) Schlessinger, R. H.; Nugent, R. A. *J. Am. Chem. Soc.* **1982**, *104*, 1116.
- (814) Trost, B. M.; McDougal, P. G.; Haller, K. J. *J. Am. Chem. Soc.* **1984**, *106*, 383.
- (815) Trost, B. M.; McDougal, P. G. *J. Am. Chem. Soc.* **1982**, *104*, 6110.
- (816) Ishihara, J.; Nonaka, R.; Terasawa, Y.; Shiraki, R.; Yabu, K.; Kataoka, H.; Ochiai, Y.; Tadano, K. *J. Org. Chem.* **1998**, *63*, 2679.

- (817) (a) Cole, R. J., Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 241. (b) Minato, H.; Katayama, T.; Tori, K. *Tetrahedron Lett.* **1975**, 2579.
- (818) Birkinshaw, J. H.; Raistrick, H. *Biochem. J.* **1932**, 26, 441.
- (819) (a) Banwell, M. G.; Collis, M. P.; Mackay, M. F.; Richards, S. L. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1913. (b) Johns, R. B.; Johnson, A. W.; Murray, J. *J. Chem. Soc.* **1954**, 198.
- (820) Bentley, R.; Thiessen, C. P. *Nature (London)* **1959**, 184, 552.
- (821) Nozoe, T.; Doi, K.; Hashimoto, T. *Bull. Chim. Soc. Jap.* **1960**, 33, 1071.
- (822) Thomson, R. H. *Naturally Occurring Quinones II*; Springer: Heidelberg, Germany, 1988; p 491. (b) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; p 184.
- (823) Elsworthy, G. C.; Holker, J. S. E.; McKeown, J. M.; Robinson, J. B.; Mulheim, L. J. *J. Chem. Soc., Chem. Commun.* **1970**, 1069.
- (824) Brumley, W. C.; Nesheim, S.; Trucksess, M. W.; Trucksess, E. W.; Drefuss, P. A.; Roach, J. A. G.; Andrzejewski, D.; Eppley, R. I. M.; Pohland, A. E.; Thorpe, C. W.; Sphon, J. A. *Anal. Chem.* **1981**, 53, 2003.
- (825) Holmwood, G. M.; Roberts, J. C. *J. Chem. Soc., C* **1971**, 3899.
- (826) (a) Cole, R. J., Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 95. (b) Chen, P. N.; Kingston, D. G.; Vercelotti, J. R. *J. Org. Chem.* **1977**, 42, 3599.
- (827) Cole, R. J., Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 99.
- (828) (a) Cole, R. J., Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 102. (b) Steyn, P. S.; Vleggaar, R.; Wessels, P. L.; Cole, R. J.; Scott, D. B. *J. Chem. Soc., Perkin Trans. 1* **1979**, 451.
- (829) Graybill, T. L.; Casillas, E. G.; Pal, K.; Townsend, C. A. *J. Am. Chem. Soc.* **1999**, 121, 7729.
- (830) Steyn, P. S.; Vleggaar, R. *J. Chem. Soc., Perkin Trans. 1* **1974**, 2250.
- (831) Isaka, M.; Palasarn, S.; Kocharin, K.; Saenboonrueng, J. *J. Nat. Prod.* **2005**, 68, 945.
- (832) (a) Gérard, E. M. C.; Bräse, S. *Chem.—Eur. J.* **2008**, 14, 8086. (b) Nicolaou, K. C.; Li, A. *Angew. Chem., Int. Ed.* **2008**, 47, 6579; *Angew. Chem.* **2008**, 120, 6681.
- (833) Turner, W. B. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1621.
- (834) (a) Nising, C. F.; Ohnemüller, U. K.; Bräse, S. *Angew. Chem., Int. Ed.* **2006**, 45, 307. (b) See ref 832. 4-Desoxy-diversonol: (c) Tietze, L. F.; Spiegl, D. A.; Stecker, F.; Major, J.; Raith, C.; Große, C. *Chem.—Eur. J.* **2008**, 14, 8956. 4-Desoxy-diversonol: (d) Volz, N.; Bröhmer, M. C.; Bräse, S. *Synlett* **2009**, 550.
- (835) Grover, P. K.; Shah, G. D.; Shah, R. C. *J. Sci. Ind. Res.* **1956**, 15B, 629.
- (836) Raistrick, H.; Robinson, R.; White, D. E. *Biochem. J.* **1936**, 30, 1303.
- (837) Turner, W. B.; Aldridge, D. C. *Fungal Metabolites II*; Academic Press: New York, 1983; pp 157 and 159.
- (838) Kawahara, N.; Nozawa, K.; Nakajima, S.; Kawai, K. *J. Chem. Soc., Perkin Trans. 1* **1988**, 907.
- (839) Tatsuta, K.; Kasai, S.; Amano, Y.; Yamaguchi, T.; Seki, M.; Hosokawa, S. *Chem. Lett.* **2007**, 36, 10.
- (840) Structure revision for diversonolic esters: Zhang, W.; Krohn, K.; Zia-Ullah; Flörke, U.; Pescitelli, G.; Di Bari, L.; Antus, S.; Kurtán, T.; Rheinheimer, J.; Draeger, S.; Schulz, B. *Chem.—Eur. J.* **2008**, 14, 4913.
- (841) Richard, J. L. *Int. J. Food Microbiol.* **2007**, 119, 3.
- (842) Boermans, H. J.; Leung, M. C. K. *Int. J. Food Microbiol.* **2007**, 119, 95.
- (843) Bennet, J. W.; Klich, M. *Clin. Microbiol. Rev.* **2003**, 497.
- (844) Carrillo, L. *Microbiología Agrícola*; 2003; Universidad Nacional de Salta, Argentina. Chapter 6 (ISBN 987-9381-16-5).
- (845) Fokunang, C. N.; Tembe-Fokunang, E. A.; Tomkins, P.; Barkwan, S. *Outlook Agric.* **2006**, 35, 247.
- (846) *Mycotoxins: Risks in Plant, Animal, and Human Systems*; Council for Agricultural Science and Technology: Ames: Iowa, 2003; No. 139.
- (847) Bryden, W. L. *Asia Pac. J. Clin. Nutr.* **2007**, 16, 95.
- (848) Mattsson, J. L. *Toxicol. Appl. Pharmacol.* **2007**, 223, 125.
- (849) Sugiyama, K.; Konishi, Y. *Gekkan Fudo Kemikaru* **2007**, 23, 73.
- (850) Eaton, D. L.; Groopman, J. D. *The Toxicology of Aflatoxins*; Academic Press: New York, 1994; p 383.
- (851) Chao, T. C.; Maxwell, S. M.; Wong, S. Y. *J. Pathol.* **1991**, 164, 225.
- (852) Patten, R. C. *Am. J. Trop. Med. Hyg.* **1981**, 30, 422.
- (853) Galtier, P. *Vet. Sci. Commun.* **1978**, 1, 349.
- (854) Stormer, F. C.; Lea, T. *Toxicology* **1995**, 95, 45.
- (855) Marquardt, R. R.; Frohlich, A. A. *J. Anim. Sci.* **1992**, 70, 3968.
- (856) Smith, J. E.; Moss, M. O. *Mycotoxins. Formation and significance*; Wiley: Chichester, U.K., 1985.
- (857) Rotter, B. A.; Prelusky, D. B.; Pestka, J. J. *Toxicol. Environ. Health* **1996**, 48, 1.
- (858) Ueno, Y. *Ann. Nutr. Aliment.* **1977**, 31, 885.
- (859) Khachatourians, G. G. *Can. J. Physiol. Pharmacol.* **1989**, 68, 1004.
- (860) Shima, J.; Takase, S.; Takahashi, Y.; Iwai, Y.; Fujimoto, H.; Yamazaki, M.; Ochi, K. *Appl. Environ. Microbiol.* **1997**, 63, 3825.
- (861) Kellerman, T. S.; Maras, W. F.; Thiel, P. G.; Gelderblom, W. C.; Cawood, M. E. *J. Vet. Res.* **1990**, 57, 269.
- (862) Chu, F. S.; Li, G. Y. *Appl. Environ. Microbiol.* **1994**, 60, 847.
- (863) (a) Shier, W. T.; Tiefel, P. A.; Abbas, H. K. *ACS Symp. Ser.* **2000**, 745, 54. (b) Bennett, J. W.; Klich, M. *Clin. Microbiol. Rev.* **2003**, 16, 497. (c) Trucksess, M. W. *J. AOAC Int.* **2005**, 88, 314. (d) Du, L.; Yu, F.; Zhu, X.; Zaleta-Rivera, K.; Bojja, R. S.; Ding, Y.; Yi, H.; Wang, Q. *ACS Symp. Ser.* **2007**, 955, 81. (e) Bondy, G. S.; Pestka, J. J. *J. Toxicol. Environ. Health B: Crit. Rev.* **2000**, 3, 109. (f) Abou-Karam, M.; Abbas, H. K.; Shier, W. T. *J. Toxicol., Toxin Rev.* **2004**, 23, 123. (g) Kumagai, S. *Mycotoxins* **2008**, 58, 15. (h) Konishi, Y.; Sugiyama, K.-i. *Shokuhin Eiseigaku Zasshi* **2008**, 49, 1. (i) Yu, K.; Yuan, X.; Huang, B. *Siliao Yanjiu* **2006**, 35. (j) Rychlik, M.; Asam, S. *Anal. Bioanal. Chem.* **2008**, 390, 617. (k) Guedon, D.; Brum, M.; Taoubi, K.; Bizet, D.; Bizot, S.; Bourny, E.; Compagnon, P. A.; Kergosien, H.; Quintelas, L. G.; Respaud, J.; Saperas, O.; Seigneuret, J. M.; Urizzi, P. *STP Pharma Pratiques* **2007**, 17, 209. (l) Boermans, H. J.; Leung, M. C. K. *Int. J. Food Microbiol.* **2007**, 119, 95. (m) Richard, J. L. *Int. J. Food Microbiol.* **2007**, 119, 3.
- (864) Wang, J. S.; Groopman, J. D. *Mutat. Res.* **1999**, 424, 167.
- (865) Haschek, W. M.; Voss, K. A.; Beasley, V. R. Selected mycotoxins affecting animal and human health. In *Handbook of Toxicologic Pathology*, 2nd ed.; Haschek, W. M., Roussex, C. G., Wallig, M. A., Eds.; Academic Press: New York, 2002; pp 645–698.
- (866) Du, L.; Yu, F.; Zhu, X.; Zaleta-Rivera, K.; Bojja, R. S.; Ding, Y.; Yi, H.; Wang, Q. *ACS Symp. Ser.* **2007**, 955, 81.
- (867) Iwahashi, Y.; Hosoda, H.; Park, J.-H.; Lee, J.-H.; Suzuki, Y.; Kitagawa, E.; Satomi, M. M.; Jwa, N.-S.; Gu, M.-B.; Iwahashi, H. *J. Agric. Food Chem.* **2006**, 54, 1936.
- (868) Schuda, P. F. *Top. Curr. Chem.* **1980**, 91, 75. and cited references.
- (869) (a) Asao, T.; Büchi, G.; Abdel-Kader, M. M.; Chang, S. B.; Wick, E. L.; Wogan, G. N. *J. Am. Chem. Soc.* **1963**, 85, 1706. **1965**, 87, 882 Absolute configurations: (b) Brechbühler, S.; Büchi, G.; Milne, G. J. *Org. Chem.* **1967**, 32, 2641. X-ray: (c) Cheung, K. K.; Sim, G. A. *Nature (London)* **1964**, 201, 1185.
- (870) Enantioselective formal syntheses: (a) Marino, J. P. *Pure Appl. Chem.* **1993**, 65, 667. (b) Civitello, E. R.; Rapoport, H. *J. Org. Chem.* **1994**, 59, 3775. (c) Bando, T.; Shishido, K. *Synlett* **1997**, 665.
- (871) Noland, W. E.; Kedrowsky, B. L. *Org. Lett.* **2000**, 2, 2109.
- (872) Büchi, G.; Roberts, E. C. *J. Org. Chem.* **1968**, 33, 460.
- (873) (a) Davies, J. E.; Kirkaldy, D.; Roberts, J. C. *J. Chem. Soc.* **1960**, 2169. (b) Bullock, E.; Roberts, J. C.; Underwood, J. G. *J. Chem. Soc.* **1962**, 4179. (c) Knight, J. A.; Roberts, J. C.; Roffey, P. *J. Chem. Soc., C* **1966**, 1308.
- (874) Bycroft, B. W.; Hatton, J. R.; Roberts, J. C. *J. Chem. Soc., C* **1970**, 281.
- (875) Hetherington, A. C.; Raistrick, H. *Proc. R. Soc., Ser. B* **1931**, 220, 269.
- (876) For new structures, see: Clark, B. R.; Capon, R. J.; Lacey, E.; Tennant, S.; Gill, J. H. *Org. Biomol. Chem.* **2006**, 4, 1520.
- (877) (a) Pollock, A. V. *Nature (London)* **1947**, 160, 331. (b) Oxford, A. E. *Chem. Ind.* **1942**, 48.
- (878) Dobias, J.; Betina, V.; Nemeš, P. *Biologia* **1980**, 35, 431.
- (879) (a) Brown, J. P.; Cartwright, N. J.; Robertson, A.; Whalley, W. B. *Nature (London)* **1948**, 162, 72. Relative configuration: (b) Cram, D. J. *J. Am. Chem. Soc.* **1950**, 72, 1001. X-ray: (c) Rodig, O. R.; Shiro, M.; Fernando, Q. *J. Chem. Soc., Chem. Commun.* **1971**, 1553.
- (880) Brown, J. P.; Cartwright, N. J.; Robertson, A.; Whalley, W. B. *J. Chem. Soc.* **1949**, 867.
- (881) (a) Mehta, P. P.; Whalley, W. B. *J. Chem. Soc.* **1963**, 3777. (b) Hill, R. K.; Gardella, L. A. *J. Org. Chem.* **1964**, 29, 766.
- (882) (a) Warren, H. H.; Dougherty, G.; Wallis, E. S. *J. Am. Chem. Soc.* **1957**, 79, 3812. (b) Warren, H. H.; Finkelstein, M.; Scola, D. A. *J. Am. Chem. Soc.* **1962**, 84, 1926.
- (883) Gore, T. S.; Talavdekar, R. V.; Venkataraman, K. *Curr. Sci.* **1950**, 19, 20.
- (884) Brown, J. P.; Cartwright, N. J.; Robertson, A.; Whalley, W. B. *J. Chem. Soc.* **1949**, 859.
- (885) (a) Yamada, F.; Makita, Y.; Somei, M. *Heterocycles* **2007**, 72, 599. (b) Moldvai, I.; Temesvari-Major, E.; Incze, M.; Doerner, G.; Szentirmay, E.; Szantay, C. *Helv. Chim. Acta* **2005**, 88, 1344. (c) Yokoyama, Y.; Hikawa, H.; Mitsuhashi, M.; Uyama, A.; Hiroki, Y.; Murakami, Y. *Eur. J. Org. Chem.* **2004**, 1244. (d) Liras, S.;

- Lynch, C. L.; Fryer, A. M.; Vu, B. T.; Martin, S. F. *J. Am. Chem. Soc.* **2001**, *123*, 5918. (e) Carr, M. A.; Creviston, P. E.; Hutchison, D. R.; Kennedy, J. H.; Khau, V. V.; Kress, T. J.; Leanna, M. L.; Marshall, J. D.; Martinelli, M. J.; Peterson, B. C.; Varie, D. L.; Wepsiec, J. P. *J. Org. Chem.* **1997**, *62*, 8640. (f) Martin, S. F. *Pure Appl. Chem.* **1997**, *69*, 571. (g) Saa, C.; Crotts, D. D.; Hsu, G.; Vollhardt, K. P. C. *Synlett* **1994**, 487. (h) Nakagawa, K.; Somei, M. *Heterocycles* **1991**, *32*, 873. (i) Ninomiya, I.; Hashimoto, C.; Kiguchi, T.; Naito, T.; Barton, D. H. R.; Lusinchi, X.; Milliet, P. *J. Chem. Soc., Perkin Trans. 1* **1990**, *3*, 703.
- (886) (a) Booth, C. *The Genus Fusarium*; Commonwealth Mycological Institute: Kew, U.K., 1971. (b) Marasas, W. F. O.; Nelson, P. E.; Toussoun, T. A. *Toxicogenic Fusarium species. Identity and Mycotoxicology*; Pennsylvania State University Press: Pittsburgh, PA, 1984.
- (887) Bezuidenhout, S. C.; Gelderblom, W. C. A.; Gorst-Allman, C. P.; Horak, R. M.; Marasas, W. F. O.; Spitteller, G.; Vlegaar, R. *J. Chem. Soc., Chem. Commun.* **1988**, 743.
- (888) (a) ApSimon, J. W. *Environ. Health Perspect.* **2001**, *109*, 245. (b) ApSimon, J. W.; Blackwell, B. A.; Edwards, O. E.; Fruchier, A.; Miller, J. D.; Savard, M.; Young, J. C. *Pure Appl. Chem.* **1994**, *66*, 2315.
- (889) Sydenham, E. W.; Gelderblom, W. C. A.; Thiel, P. G.; Marasas, W. F. O. *J. Agric. Food Chem.* **1990**, *38*, 285.
- (890) Musser, S. M.; Gay, M. L.; Mazzola, E. P. *J. Nat. Prod.* **1996**, *59*, 970.
- (891) Relative and absolute stereochemistry of the fumonisin B1 backbone: (a) Hoye, T. R.; Jiménez, J. I.; Shier, W. T. *J. Am. Chem. Soc.* **1994**, *116*, 9409. For work on the right half of the fumonisin B1 backbone, see: (b) ApSimon, J. W.; Blackwell, B. A.; Edwards, O. E.; Fruchier, A. *Tetrahedron Lett.* **1994**, *35*, 7703. (c) Poch, G. K.; Powell, R. G.; Plattner, R. D.; Weisleder, D. *Tetrahedron Lett.* **1994**, *35*, 7707. For work on the left half of the fumonisin B1 backbone, see: (d) Blackwell, B. A.; Edwards, O. E.; ApSimon, J. W.; Fruchier, A. *Tetrahedron Lett.* **1995**, *36*, 1973.
- (892) Harmange, J.-C.; Boyle, C. D.; Kishi, Y. *Tetrahedron Lett.* **1994**, *35*, 6819.
- (893) (a) Boyle, C. D.; Kishi, Y. *Tetrahedron Lett.* **1995**, *36*, 4579. Confusion of the previously suggested configuration by: (b) Shier, W. T.; Abbas, H. K.; Badria, F. A. *Tetrahedron Lett.* **1995**, *36*, 1571.
- (894) (a) Mirocha, C. J.; Gilchrist, D. G.; Shier, W. T.; Abbas, H. K.; Wen, Y.; Vesonder, R. F. *Mycopathologia* **1992**, *117*, 47. (b) Gilchrist, D. G.; Ward, B.; Moussatos, V.; Mirocha, C. J. *Mycopathologia* **1992**, *117*, 57.
- (895) Merrill, A. H., Jr.; Wang, E.; Gilchrist, D. G.; Riley, R. T. *Adv. Lipid Res.* **1993**, *26*, 215.
- (896) Gilchrist, D. G. *Cell Death Differ.* **1997**, *4*, 689.
- (897) (a) Boyle, C. D.; Harmange, J.-C.; Kishi, Y. *J. Am. Chem. Soc.* **1994**, *116*, 4995. (b) Oikawa, H.; Matsuda, I.; Kagawa, T.; Ichihara, A.; Kohmoto, K. *Tetrahedron* **1994**, *50*, 13347. (c) Oikawa, H.; Matsuda, I.; Ichihara, A.; Kohmoto, K. *Tetrahedron Lett.* **1994**, *35*, 1223.
- (898) Oikawa, H.; Kagawa, T.; Kobayashi, T.; Ichihara, A. *Tetrahedron Lett.* **1996**, *37*, 6169.
- (899) For 18 reviews regarding various aspects of biological activity of fumonisins and AAL-toxins, see: *Mycopathologia* **1992**, *117*, 1.
- (900) Van der Merwe, K. J.; Steyn, P. S.; Fourie, L.; Scott, D. B.; Theron, J. *J. Nature (London)* **1965**, *205*, 1112.
- (901) Van der Merwe, K. J.; Steyn, P. S.; Fourie, L. *J. Chem. Soc.* **1965**, 7083.
- (902) Benford, D.; Boyle, C.; Dekant, W.; Dekant, W.; Fuchs, R.; Gaylor, D. W.; Hard, G.; McGregor, D. B.; Pitt, J. I.; Plestina, R.; Shepahard, G.; Solfrizzo, M.; Verger, P. J. P.; Walker, R. *FAO Food Nutr. Pap.* **2001**, *74*, 281.
- (903) Pohland, A. E.; Nesheim, S.; Friedman, L. *Pure Appl. Chem.* **1992**, *64*, 1029.
- (904) Smith, J. E.; Moss, M. O. *Mycotoxins. Formation and significance*; Wiley: Chichester, U.K., 1985.
- (905) Beardall, J. M.; Miller, J. D.; Trenholm H. L., Eds. *Mycotoxins in grains. Compounds other than aflatoxin*; Eagan Press: St. Paul, MN, 1994; p 487.
- (906) Kuiper-Goodman, T.; Scott, P. M. *Biomed. Environ. Sci.* **1989**, *2*, 179.
- (907) (a) Steyn, P. S.; Holzapfel, C. W. *Tetrahedron* **1967**, *23*, 4449. (b) Roberts, J. C.; Woolven, P. *J. Chem. Soc., C* **1970**, 278.
- (908) (a) Matsui, M.; Mori, K.; Arasaki, S. *Agric. Biol. Chem.* **1964**, *28*, 896. (b) Matsui, M.; Mori, K.; Ozawa, Y. *Agric. Biol. Chem.* **1966**, *30*, 193.
- (909) (a) Rieche, A.; Gross, E.; Höft, E. *Chem. Ber.* **1960**, *93*, 88. (b) Rieche, A.; Höft, E. *Angew. Chem., Int. Ed.* **1967**, *6*, 335.
- (910) Angyal, S. J.; Morris, P. M.; Tetaz, J. R.; Wilson, J. G. *J. Chem. Soc.* **1950**, 2141. (b) Angyal, S. *Org. React.* **1954**, *8*, 197.
- (911) Belleau, B.; Malek, G. *J. Am. Chem. Soc.* **1968**, *90*, 1651.
- (912) Kraus, G. A. U. S. Patent 4,346,039, 1982; *Chem. Abstr.* **1982**, *94*, 47077m.
- (913) Dimitriadis, C.; Gill, M.; Harte, M. F. *Tetrahedron: Asymmetry* **1997**, *8*, 2153.
- (914) Donner, C. D.; Gill, M.; Tewerik, L. M. *Molecules* **2004**, *9*, 498.
- (915) Pattenden, G. *Fortsch. Chem. Org. Naturst.* **1978**, *35*, 133.
- (916) Ellis, J. R.; McCalla, T. M. *Appl. Microbiol.* **1973**, *25*, 562.
- (917) Lee, K.-S.; Röschenhaler, R. *J. Appl. Environ. Microbiol.* **1986**, *52*, 1046.
- (918) (a) Hatey, F.; Moule, Y. *Ann. Nutr. Aliment.* **1977**, *31*, 867. (b) Hatey, F.; Moule, Y. *Toxicology* **1979**, *13*, 223. (c) Morton, J. G.; Jeffery, F. H.; Miller, J. K. *FEMS. Microbiol. Lett.* **1981**, *10*, 179.
- (919) Anslow, W. K.; Raistrick, H.; Smith, G. *J. Soc. Chem. Ind.* **1943**, *62*, 236.
- (920) Katzman, P. A.; Hays, E. E.; Cain, C. K.; van Wyk, J. J.; Reithel, F. J.; Thayer, S. A.; Doisy, E. A. *J. Biol. Chem.* **1944**, *154*, 475.
- (921) Bergel, F.; Morrison, A. L.; Moss, A. R.; Klein, R.; Rinderknecht, H.; Ward, J. L. *Nature (London)* **1943**, *152*, 750.
- (922) Chain, E.; Florey, H. W.; Jennings, M. A.; Callow, D. *Brit. J. Exp. Path.* **1942**, *23*, 202.
- (923) Oosterhuis, H. K. *Antibiotica uit Schimmels*; University of Amsterdam: Amsterdam, 1956; p 116.
- (924) Atkinson, N. *Aust. J. Exp. Biol. Med. Sci.* **1942**, *20*, 287.
- (925) Cole, R. J.; Cox, R. H. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981.
- (926) Földi, Z.; Fodor, G.; Demjén, I. *J. Chem. Soc.* **1948**, 1295.
- (927) (a) Woodward, R. B.; Singh, G. *J. Am. Chem. Soc.* **1949**, *71*, 758. (b) Dauben, H. J.; Weisenborn, F. L. *J. Am. Chem. Soc.* **1949**, *71*, 3853.
- (928) Woodward, R. B.; Singh, G. *Nature (London)* **1950**, *165*, 928.
- (929) Boukouvalas, J.; Maltais, F. *Tetrahedron Lett.* **1994**, *35*, 5769.
- (930) Weissman, K. J. *Science* **2008**, *320*, 186.
- (931) Ciegler, A.; Detroy, R. W.; Lillehoj, F. B. In *Microbial Toxins*; Ciegler, A., Ed.; Academic: New York, 1971; Vol. 6, p 409.
- (932) Dean, F. M. *Naturally Occurring Oxygen Ring Compounds*; Butterworths: London, 1963.
- (933) Godtfredsen, W. O.; Grove, J. F.; Tamm, C. *Helv. Chim. Acta* **1967**, *50*, 1666.
- (934) Johannisson, A.; Björkhaug, B.; Hansson, W.; Gadhasson, I.-L.; Thuvander, A. *Cell Biol. Toxicol.* **1999**, *15*, 203.
- (935) Zhou, H. R.; Harkema, J. R.; Hotchkiss, J. A.; Yan, D.; Roth, R. A.; Pestka, J. J. *Toxicol. Sci.* **2000**, *53*, 253.
- (936) Isaka, M.; Punya, J.; Lertwerawat, Y.; Tanticharoen, M.; Thebtaranonth, Y. *J. Nat. Prod.* **1999**, *62*, 329.
- (937) Garcia, C. C.; Rosso, M. L.; Bertoni, M. D.; Maier, M. S.; Damonte, E. B. *Planta Med.* **2002**, *68*, 209.
- (938) Ueno, Y. *CRC Crit. Revs. Toxicol.* **1985**, *14*, 99.
- (939) Tamm, C.; Tori, M. In *Mycotoxins—Production, Isolation, Separation and Purification*; Betina, V., Ed.; Elsevier: Amsterdam, 1984; p 131.
- (940) (a) Jarvis, B. B.; Wang, S. *J. Nat. Prod.* **1999**, *62*, 1284. (b) Jarvis, B. B.; Wang, S.; Ammon, H. L. *J. Nat. Prod.* **1996**, *59*, 254.
- (941) Jarvis, B. B.; Stahly, G. P.; Pavanassivam, G.; Midiwo, J. O.; DeSilva, T.; Holmlund, C. E.; Mazzola, E. P.; Geoghegan, R. F., Jr. *J. Org. Chem.* **1982**, *47*, 1117.
- (942) Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1974**, *39*, 1615.
- (943) (a) Roush, W. R.; D'Ambra, T. E. *J. Org. Chem.* **1980**, *45*, 3927. (b) Roush, W. R.; D'Ambra, T. E. *J. Am. Chem. Soc.* **1983**, *105*, 1058.
- (944) Tamm, C.; Jeker, N. *Tetrahedron* **1989**, *45*, 2385.
- (945) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed.* **1978**, *17*, 522.
- (946) Tulshian, D. B.; Fraser-Reid, B. *Tetrahedron Lett.* **1980**, *21*, 4549.
- (947) Ziegler, F. E.; Nangia, A.; Schulte, G. *J. Am. Chem. Soc.* **1987**, *109*, 3987.
- (948) For a recent review about chemistry and biology of resorcylic acid lactones: Winssinger, N.; Barluenga, S. *Chem. Commun.* **2007**, 22.
- (949) (a) Stob, M.; Baldwin, R. S.; Tuite, J.; Andrews, F. N.; Gillette, K. G. *Nature (London)* **1962**, *196*, 1318. (b) Mirocha, C. J.; Christensen, C. M.; Nelson, G. H. *Appl. Microbiol.* **1967**, *15*, 497. (c) Urry, W. H.; Wehrmeister, H. L.; Hodge, E. B.; Hidy, P. H. *Tetrahedron Lett.* **1966**, *7*, 3109.
- (950) Marasas, W. F. O.; van Rensburg, S. J.; Mirocha, C. *J. Agric. Food Chem.* **1979**, *27*, 1108.
- (951) Keinan, E.; Sinha, S. C.; Sinha-Bagchi, A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3333.
- (952) Mirocha, C. J.; Christensen, C. M.; Nelson, G. H. In *Microbial Toxins, Vol. VII; Algal and Fungal Toxins*; Kadis, S., Ciegler, A., Ajl, S. S., Eds.; Academic Press: New York, 1971; p 107.
- (953) Hagler, W. M.; Mirocha, C. J.; Pathre, S. V.; Behrens, J. C. *Appl. Environ. Microbiol.* **1979**, *37*, 849.
- (954) Betina, V. *Mycotoxins (Bioactive Molecules, Vol. 9)*; Elsevier Science Publishers: Amsterdam, 1989; p 217.

- (955) Nicolaou, K. C.; Winsinger, N.; Pastor, J.; Murphy, F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2534; *Angew. Chem.* **1998**, *110*, 2677.
- (956) (a) Ley, S.; Burckhardt, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3028. (b) Burckhardt, S.; Ley, S. *J. Chem. Soc., Perkin Trans. 1* **2002**, 874.
- (957) Vlattas, I.; Harrison, I. T.; Tökes, L.; Fried, J. H.; Cross, A. D. *J. Org. Chem.* **1968**, *33*, 4176.
- (958) Corey, E. J.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1974**, *96*, 5614.
- (959) Masamune, S.; Kamata, S.; Schilling, W. *J. Am. Chem. Soc.* **1975**, *97*, 3515.
- (960) Solladie, G.; Maestro, M. C.; Rubio, A.; Pedregal, C.; Carreno, M. C.; Ruano, J. L. G. *J. Org. Chem.* **1991**, *56*, 2317.
- (961) (a) Takahashi, T.; Kasuga, K.; Takahashi, M.; Tsuji, J. *J. Am. Chem. Soc.* **1979**, *101*, 5072. (b) Takahashi, T.; Toshiharu, N.; Tsuji, J. *Chem. Lett.* **1980**, 369.
- (962) Rama Rao, A. V.; Deshmukh, M. N.; Sharma, G. V. M. *Tetrahedron* **1987**, *43*, 779.
- (963) (a) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936. (b) Furrow, M. E.; Schaus, S. E.; Jacobsen, E. N. *J. Org. Chem.* **1998**, *63*, 6776.
- (964) Mukaiyama, T.; Usui, M.; Saigo, K. *Chem. Lett.* **1976**, 49.
- (965) Schirmer, A.; Kennedy, J.; Murlis, S.; Reid, R.; Santi, D. V. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 4234.
- (966) Agatsuma, T.; Takahashi, A.; Kabuto, C.; Nozoe, S. *Chem. Pharm. Bull.* **1993**, *41*, 373.
- (967) (a) Sellès, P.; Lett, R. *Tetrahedron Lett.* **2002**, 4621. (b) Sellès, P.; Lett, R. *Tetrahedron Lett.* **2002**, 4627.
- (968) Hoshino, Y.; Ivanova, V. B.; Yazawa, K.; Ando, A.; Mikami, Y.; Zaki, S. M.; Karam, A.-Z. A.; Youssef, Y. A.; Gräfe, U. *J. Antibiot.* **2002**, *55*, 516.
- (969) (a) Dakas, P. Y.; Barluenga, S.; Totzke, F.; Zirrgiebel, U.; Winsinger, N. *Angew. Chem., Int. Ed. Engl.* **2007**, *46*, 6899. (b) Hofmann, T.; Altmarm, K.-H. *Synlett* **2008**, 1500.
- (970) Lampilas, M.; Lett, R. *Tetrahedron Lett.* **1992**, *33*, 777.
- (971) Isaacs, J. S.; Xu, W.; Neckers, L. W. *Cancer Cell* **2003**, *3*, 213.
- (972) Mosser, D. D.; Morimoto, R. I. *Oncogene* **2004**, *23*, 2907.
- (973) Prodromou, C.; Pearl, L. H. *Curr. Cancer Drug Targets* **2003**, *3*, 301.
- (974) Roe, S. M.; Prodromou, C.; O'Brien, R.; Ladbury, J. E.; Piper, P. W.; Pearl, L. H. *J. Med. Chem.* **1999**, *42*, 260.
- (975) Yamamoto, K.; Garbaccio, R. M.; Stachel, S. J.; Solit, D. B.; Chiosis, G.; Rosen, N.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 1280.
- (976) Yang, Z.-Q.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2003**, *125*, 9602.
- (977) Yang, Z.-Q.; Geng, X.; Solit, D.; Pratilas, C. A.; Rosen, N.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2004**, *126*, 7881.
- (978) Garbaccio, R. M.; Danishefsky, S. J. *Org. Lett.* **2000**, *2*, 3127.
- (979) Hellwig, V.; Mayer-Bartschmid, A.; Müller, H.; Greif, G.; Kleymann, G.; Zitzmann, W.; Tichy, H.-V.; Stadler, M. *J. Nat. Prod.* **2003**, *66*, 829.
- (980) Cole, R. J.; Cox, R. H., Eds. *Handbook of Toxic Fungal Metabolites*; Academic Press: New York, 1981; p 614.
- (981) (a) Pero, R. W.; Posner, H.; Blois, M.; Harvan, D.; Spalding, J. W. *Environ. Health Perspect.* **1973**, *87*. (b) Davis, V. M.; Stack, M. E. *Appl. Environ. Microbiol.* **1994**, *60*, 3901.
- (982) (a) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; p 49. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
- (983) Harris, T. M.; Hay, J. V. *J. Am. Chem. Soc.* **1977**, *99*, 1631.
- (984) (a) Abell, C.; Bush, B. D.; Staunton, J. *J. Chem. Soc., Perkin Trans. 1* **1986**, *15*. (b) Leeper, F. J.; Staunton, J. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1053.
- (985) Sóti, F.; Incze, M.; Kajtár-Peredy, M.; Baitz-Gács, E.; Imre, L.; Farkas, L. *Chem. Ber.* **1977**, *110*, 979.
- (986) (a) McPhail, A. T.; Miller, R. W.; Harvan, D.; Pero, R. W. *J. Chem. Soc., Chem. Commun.* **1973**, 682. (b) Coombe, R. G.; Jacobs, J. J.; Watson, T. R. *Aust. J. Chem.* **1970**, *23*, 2343.
- (987) Murakami-Nakai, C.; Maeda, N.; Yonezawa, Y.; Kuriyama, I.; Kamisuki, S.; Takahashi, S.; Sugawara, F.; Yoshida, H.; Sakaguchi, K.; Mizushima, Y. *Biochim. Biophys. Acta* **2004**, *1674*, 193.
- (988) Mizushima, Y.; Kamisuki, S.; Mizuno, T.; Takemura, M.; Asahara, H.; Linn, S.; Yamaguchi, T.; Matsukage, A.; Hanaoka, F.; Yoshida, S.; Saneyoshi, M.; Sugawara, F.; Sakaguchi, K. *J. Biol. Chem.* **2000**, *275*, 33957.
- (989) (a) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685. (b) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 1871.
- (990) Sedmera, P.; Podojil, M.; Vokoun, J.; Betina, V.; Nemeč, P. *Folia Microbiol.* **1978**, *23*, 64.
- (991) (a) Yang, D.-M.; Sankawa, U.; Ebizuka, Y.; Shibata, S. *Tetrahedron* **1976**, *32*, 333. (b) Takeda, N.; Seo, S.; Ogihara, Y.; Sankawa, U.; Iitaka, I.; Kitawaga, I.; Shibata, S. *Tetrahedron* **1973**, *29*, 3703.
- (992) For reviews on cascade reactions, see: (a) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115. (b) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134; *Angew. Chem.* **2006**, *118*, 7292.
- (993) Snider, B. B.; Gao, X. *J. Org. Chem.* **2005**, *70*, 6863.
- (994) Pinto, M. M. M.; Sousa, M. E.; Nascimento, M. S. *J. Curr. Med. Chem.* **2005**, *12*, 2517.
- (995) Roberts, J. C. *Chem. Rev.* **1961**, *61*, 591.
- (996) Sousa, M. E.; Pinto, M. M. *Curr. Med. Chem.* **2005**, *12*, 2447.
- (997) Entire issue of *Curr. Med. Chem.* **2005**, *12*.
- (998) (a) Nicolaou, K. C.; Yu, H.; Wartmann, M. *Angew. Chem.* **2005**, *117*, 766. (b) Tisdale, E. J.; Slobodov, I.; Theodorakis, E. A. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12030.
- (999) The synthesis of a hemisecalonic acid was reported by: Franck, B.; Stöckigt, J.; Zeidler, U.; Franckowiak, G. *Chem. Ber.* **1973**, *196*, 1198.
- (1000) (a) Lesch, B.; Bräse, S. *Angew. Chem.* **2004**, *116*, 118. (b) Lesch, B.; Bräse, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 115. Benzopyran synthesis: (c) Lesch, B.; Toräng, J.; Vanderheiden, S.; Bräse, S. *Adv. Synth. Cat.* **2005**, *4*, 555. For an independent study, see: (d) Lee, K. Y.; Kim, J. M. *Bull. Korean Chem. Soc.* **2003**, *24*, 17.
- (1001) Rothweiler, W.; Tamm, C. *Experientia* **1966**, *22*, 750.
- (1002) Aldridge, D. C.; Armstrong, J. J.; Speake, R. N.; Turner, W. B. *Chem. Commun.* **1967**, 26.
- (1003) Fex, T. *Tetrahedron Lett.* **1981**, *22*, 2703.
- (1004) Edwards, R. L.; Maitland, D. J.; Whalley, A. J. S. *J. Chem. Soc., Perkin Trans. 1* **1989**, *1*, 57.
- (1005) Dagne, E.; Gunatillaka, A. A. L.; Asmellash, S.; Abate, D.; Kingston, D. G. I.; Hoffmann, G. A.; Johnson, R. K. *Tetrahedron* **1994**, *50*, 5615.
- (1006) Buchanan, M. S.; Hashimoto, T.; Asakawa, Y. *Phytochemistry* **1995**, *40*, 135.
- (1007) Buchanan, M. S.; Hashimoto, T.; Asakawa, Y. *Phytochemistry* **1996**, *41*, 821.
- (1008) Buchanan, M. S.; Hashimoto, T.; Asakawa, Y. *Phytochemistry* **1996**, *42*, 173.
- (1009) Stork, G.; Whitehead, J. W. F. *J. Am. Chem. Soc.* **1983**, *105*, 5510.
- (1010) Thomas, E. J.; Whitehead, W. F. *J. Chem. Soc., Chem. Commun.* **1986**, 724.
- (1011) Merifield, E.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1990**, 464.
- (1012) Vedejs, E.; Arnost, M. J.; Eustache, J. M.; Krafft, G. A. *J. Org. Chem.* **1982**, *47*, 4384.
- (1013) Vedejs, E.; Reid, J. G.; Rodgers, J. D.; Wittenberg, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 4351.
- (1014) Trost, B. M.; Brickner, S. J. *J. Am. Chem. Soc.* **1983**, *105*, 568.
- (1015) Vedejs, E.; Ahmad, S. *Tetrahedron* **1988**, *29*, 2291.
- (1016) Technical Bulletin AL-126, Aldrich.
- (1017) Wadsworth, W. S. *Org. React.* **1977**, *25*, 73.
- (1018) Kelly, S. E. *Comprehensive Organic Synthesis 1*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; p 729.
- (1019) Nicolaou, K. C.; Härter, M. W.; Gunzner, J. L.; Nadin, A. *Liebigs Ann./Recueil.* **1997**, 1283.
- (1020) Thomas, E. J.; Whitehead, W. F. *J. Chem. Soc., Perkin Trans. 1* **1989**, 519.
- (1021) Vedejs, E.; Reid, J. G. *J. Am. Chem. Soc.* **1984**, *106*, 4617.
- (1022) Vedejs, E.; Gadwood, R. C. *J. Org. Chem.* **1978**, *43*, 376.
- (1023) Auerbach, J.; Weinreb, S. M. *J. Org. Chem.* **1975**, *40*, 3311.
- (1024) Krafft, G. A.; García, E. A.; Guram, A.; O'Shaughnessy, B.; Xu, X. *Tetrahedron Lett.* **1986**, *27*, 2691.
- (1025) Sweeney, M. J.; Dobson, A. D. W. *FEMS Microbiology Lett.* **1999**, *175*, 149.
- (1026) Molecular biology of fusarium mycotoxins: Desjardins, A. E.; Proctor, R. H. *Int. J. Food Microbiol.* **2007**, *119*, 47.
- (1027) Steyn, P. S., Ed. *The Biosynthesis of Mycotoxins, A Study in Secondary Metabolism*; Academic Press: New York, 1980.
- (1028) Review: Fumonsins: Kimura, M.; Takahashi-Ando, N.; Nishiuchi, T.; Ohsato, S.; Tokai, T.; Ochiai, N.; Fujimura, M.; Kudo, T.; Hamamoto, H.; Yamaguchi, I. *Pestic. Biochem. Physiol.* **2006**, *86*, 117.
- (1029) Kim, J. H.; Yu, J.; Molyneux, R. J.; Mahoney, N.; Palumbo, J. D.; Chan, K. L.; Bhatnagar, D.; Cleveland, T. E.; Nierman, W. C.; May, G. S.; Campbell, B. C. *Abstracts of Papers, 232nd ACS National Meeting, San Francisco, CA, Sept. 10-14, 2006*; AGFD-224.
- (1030) Ljungberg, S. *Pharm. Acta Helv.* **1950**, *25*, 351.
- (1031) Review: Steyn, P. S. *Pure Appl. Chem.* **1980**, *52*, 189.
- (1032) Aurofusarin/rubrofusarin: Frandsen, R. J. N.; Nielsen, N. J.; Maolanon, N.; Soerensen, J. C.; Olsson, S.; Nielsen, J.; Giese, H. *Mol. Microbiol.* **2006**, *61*, 1069.
- (1033) (a) Lebet, C. R.; Tamm, C. *Helv. Chim. Acta* **1974**, *57*, 1785. (b) Graf, W.; Robert, J. L.; Vederas, J. C.; Tamm, C.; Solomon, P. H.; Miura, I.; Nakanishi, K. *Helv. Chim. Acta* **1974**, *57*, 1801. (c) Schuermann, J.; Hertweck, C. *J. Am. Chem. Soc.* **2007**, *129*, 9564.

- (1034) Miller, M. J.; Linz, J. E. *Food Science and Technology; Food Biotechnology*, 2nd ed.; Taylor Francis: Boca Raton, FL, 2006; Vol. 148, p 1505.
- (1035) For example: Peplow, A. W.; Meek, I. B.; Wiles, M. C.; Phillips, T. D.; Beremand, M. N. *Appl. Environ. Microbiol.* **2003**, *69*, 5935.
- (1036) Haegglblom, P.; Hiltunen, M. *Mycotoxin Res.* **1991**, *7*, 8.
- (1037) Abell, C.; Garson, M. J.; Leeper, F. J.; Staunton, J. *Chem. Commun.* **1982**, 1011.
- (1038) Gaffoor, I.; Trail, F. *Appl. Environ. Microbiol.* **2006**, *72*, 1793.
- (1039) Scott, A. I.; Yalpani, M. *Chem. Commun.* **1967**, 945.
- (1040) Harris, J. P.; Mantle, P. G. *Phytochemistry* **2001**, *58*, 709.
- (1041) O'Callaghan, J.; Dobson, A. D. *Adv. Appl. Microbiol.* **2006**, *58*, 227.
- (1042) Thomas, R. *Biochem. J.* **1961**, *80*, 234.
- (1043) Kostecki, M.; Grabarkiewicz-Szczesna, J.; Chelkowski, J. *Mycotoxin Res.* **1991**, *7*, 3.
- (1044) For the biosynthesis of dothistromin, an analogue of versicolorin B (64): Bradshaw, R. E.; Zhang, S. *Mycopathologia* **2006**, *162*, 201.
- (1045) Franck, B.; Bringmann, G.; Flohr, G. *Angew. Chem.* **1980**, *92*, 483.
- (1046) Henry, K. M.; Townsend, C. A. *J. Am. Chem. Soc.* **2005**, *127*, 3724.
- (1047) Birch, A. J.; Baldas, J.; Hlubucek, J. R.; Simpson, T. J.; Westerman, P. W. *J. Chem. Soc., Perkin Trans. 1* **1976**, 898.
- (1048) (a) Payne, G. A.; Brown, M. P. *Ann. Rev. Phytopathol.* **1998**, *36*, 329. (b) Yabe, K.; Nakajima, H. *Appl. Microbiol. Biotechnol.* **2004**, *64*, 745.
- (1049) For the biosynthesis of biaryls: Hüttel, W.; Müller, M. *ChemBioChem* **2007**, *8*, 521. and cited references.
- (1050) Proctor, R. H.; Plattner, R. D.; Desjardins, A. E.; Busman, M.; Butchko, R. A. E. *J. Agric. Food Chem.* **2006**, *54*, 2424.
- (1051) Schütte, H. *Prog. Botany* **2000**, *61*, 269.
- (1052) Oxidation steps: Tokai, T.; Koshino, H.; Takahashi-Ando, N.; Sato, M.; Fujimura, M.; Kimura, M. *Biochem. Biophys. Res. Commun.* **2007**, *353*, 412.
- (1053) Grove, J. F. *Fortschr. Chem. Org. Naturst.* **2007**, *88*, 63.
- (1054) Achini, R.; Mueller, B.; Tamm, C. *Helv. Chim. Acta* **1974**, *57*, 1442.
- (1055) Hornbogen, T.; Glinski, M.; Zocher, R. *Eur. J. Plant Pathol.* **2002**, *108*, 713.
- (1056) Gardiner, D. M.; Waring, P.; Howlett, B. *J. Microbiology* **2005**, *151*, 1021.
- (1057) Mantle, P. G. *Soc. Appl. Bact. Symp. Ser.* **1989**, *18* (Filamentous Fungi Foods Feeds), 83S.
- (1058) McIntyre, C. R.; Simpson, T. J.; Stenzel, D. J.; Bartlett, A. J.; O'Brien, E.; Holker, J. S. E. *Chem. Commun.* **1982**, 781.
- (1059) Betina, V. *Chem. Biol. Interactions* **1989**, *71*, 105. and cited references.
- (1060) Norred, W. P.; Plattner, R. D.; Meredith, F. I.; Riley, R. T. *Toxicol. Appl. Pharmacol.* **1997**, *147*, 63.
- (1061) Shier, W. T.; Shier, A. C.; Xie, W.; Mirocha, C. J. *Toxicon* **2001**, *39*, 1435.
- (1062) Gibbons, S. *Expert Opin. Ther. Pat.* **2003**, *13*, 489.
- (1063) Ozakaki, K.; Yoshizaka, T.; Kimura, S. *Agric. Biol. Chem.* **1988**, *52*, 795.
- (1064) Tani, N.; Dohi, Y.; Onji, Y.; Yonemasu, K. *Microbiol. Immunol.* **1995**, *39*, 635.
- (1065) Zhang, H. J.; Tamez, P. A.; Aydogmus, Z.; Tan, G. T.; Saikawa, Y.; Hashimoto, K.; Nakata, M.; Hung, N. V.; Xuan, L. T.; Cuong, N. M.; Soejarto, D. D.; Pezzuto, J. M.; Fong, H. H. *Planta Med.* **2002**, *68*, 1088.
- (1066) Kupchan, S. M.; Streelman, D. R.; Jarvis, B. B.; Dailey, R. G., Jr.; Sneden, A. T. *J. Org. Chem.* **1977**, *42*, 4221.
- (1067) Hughes, B. J.; Hsieh, G. C.; Jarvis, B. B.; Sharma, R. P. *Arch. Environ. Contam. Toxicol.* **1989**, *3*, 88.
- (1068) Kikuchi, H.; Miyagawa, Y.; Sahashi, Y.; Inatomi, S.; Haganuma, A.; Nakahata, N.; Oshima, Y. *J. Org. Chem.* **2004**, *69*, 652.
- (1069) Zaichenko, A. M.; Rubezhniak, I. G.; Andrienko, E. V.; Kobzistaia, O. P.; Tsyganenko, E. S. *Mikrobiol. Z.* **2003**, *65*, 141.
- (1070) Bastin, R. *Rev. Ferment. Ind. Aliment.* **1952**, *7*, 11.
- (1071) do Rosario, A. M.; Rodrigues-Filho, E.; Moitinho, M. L. R.; Santos, L. S. *J. Braz. Chem. Soc.* **2005**, *16*, 280.
- (1072) Cotellet, R. *Rec. Pat. Anti-Infect. Drug Disc.* **2006**, *1*, 1.
- (1073) Papathanassiou, A. E. U. S. Patent 6528489, Mycotoxin derivatives as antimetabolic agents, 2003.
- (1074) Note addin in proof: (a) Total synthesis of neoaltenuene: Altemöller, M.; Podlech, J. *Eur. J. Org. Chem.* **2009**, 2275. (b) ∞ -Zearalanol: Fürstner, A.; Seidel, G.; Kindler, N. *Appl. Microbiol. Biotechnol.* **1999**, *55*, 821.

CR050001F