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Bioactive Nitronaphthalenes from an Endophytic Fungus, *Coniothyrium* sp., and Their Chemical Synthesis

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Four natural nitro metabolites, 1-hydroxy-5-methoxy-2-nitronaphthalene (**2**), 1,5-dimethoxy-4-nitronaphthalene (**3**), 1-hydroxy-5-methoxy-2,4-dinitronaphthalene (**4**), and 1,5-dimethoxy-4,8-dinitronaphthalene (**5**), known from chemical synthesis but new as natural products, were isolated together with two known compounds, 1-hydroxy-5-methoxynaphthalene (**1**) and ergosterol (**6**) from an endophytic fungus, *Coniothyrium* sp. The structures of **1**–**6** were determined by spectroscopic methods including 1D and 2D NMR experiments and by mass spectrometric measurements. The structures of **1**–**4** were confirmed by chemical synthesis. The nitronaphthols showed considerable antibacterial, antifungal, and antialgal properties.

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Introduction

Although nitro compounds are generally rare as fungal metabolites, a number of natural nitro compounds are known from bacterial sources.[1] Some exhibit remarkable biological activities; the best known is perhaps the antibiotic chloramphenicol, isolated from the bacterium *Streptomyces venezuelae*. There are two major pathways for the biosynthesis of nitro compounds in nature: nitration, or oxygenation of amines.[1] During the past years, our research group has consistently isolated new biologically active secondary metabolites from diverse structural groups from endophytic fungi,[2–5] with 3-nitropropionic acid as the only nitro compound.[6] In connection with this work, we investigated the constituents of the endophytic fungus, *Coniothyrium* sp., internal strain number 7721, isolated from the shrub *Sideritis chamaedryfolia*, from an arid habitat near Alicante, Spain. The culture extract of the fungus was found to have strong antibacterial, antifungal, and antialgal activities. Extensive column and preparative thin-layer chromatography of the ethyl acetate culture extract afforded four natural nitro metabolites 1-hydroxy-5-methoxy-2-nitronaphthalene (**2**), 1,5-dimethoxy-4-nitronaphthalene (**3**), 1-hydroxy-5-methoxy-2,4-dinitronaphthalene (**4**), and 1,5-dimethoxy-4,8-dinitronaphthalene (**5**), known from chemical synthesis, but new as natural products, together with two known metabolites 1-hydroxy-5-methoxynaphthalene (**1**)[7] and ergosterol (**6**).[8] Here we describe the isolation, the structural elucidation and the synthesis, as well as the antibacterial, antifungal and algicidal activities of these new natural metabolites.

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Results and Discussion

The ethyl acetate extract of the endophytic fungus, *Coniothyrium* sp., with antibacterial, antifungal, and antialgal activities, was submitted to repeated column chromatography to afford six compounds **1**–**6** (Figure 1) as described in the Experimental Section.

Compound **2** was obtained as orange crystals (m.p. 152 °C). The empirical formula $C_{11}H_9NO_4$ was deduced from HREIMS and ^{13}C NMR data. Its IR spectra had absorptions for a hydroxy group ($\tilde{\nu}$ = 3400 cm). The ^1H NMR spectrum of **2** showed signals for a methoxy and a deshielded hydroxy group at δ = 4.01 (s, 3 H) and 12.14 (s, 1 H), respectively, and for five aromatic protons. Analysis of the coupling pattern of the aromatic protons confirmed two protons with *ortho* coupling as an AB system [δ = 7.98, 7.77 (d, J = 9.6 Hz, 3-H, 4-H)] and three vicinal protons [δ = 8.07 (dd, J = 0.5, 8.2 Hz, 1 H, 8-H), 7.53 (t, J = 8.2 Hz, 1 H, 7-H), 7.06 (dd, J = 0.5, 8.2 Hz, 1 H, 6-H)]. The ^{13}C NMR spectrum of compound **2** showed resonances for 11 carbon atoms, and the DEPT spectrum indicated the presence of one methoxy group, five methine atoms and five quaternary carbon atoms. These observations suggested that compound **2** has a naphthalene skeleton. By comparison with NMR spectroscopic data of the known compound

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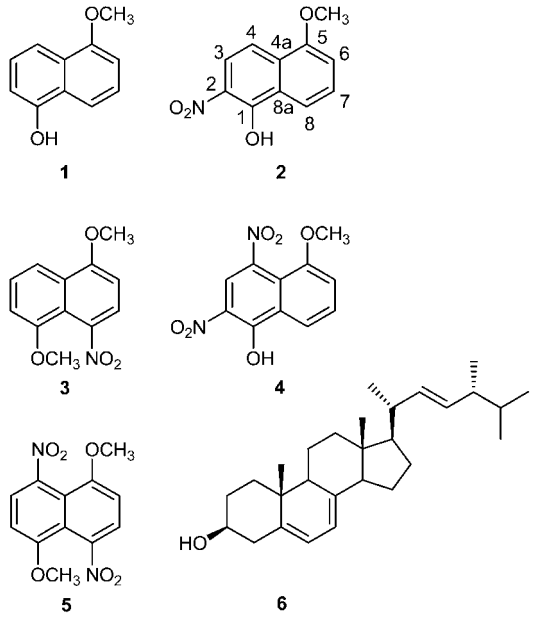


Figure 1. Compounds isolated from *Coniothyrium sp.*

1, the hydroxy and methoxy groups must be located at C-1 and C-5, respectively. According to the molecular formula $C_{11}H_9NO_4$, the structure of compound **2** should contain a nitro group which could be located at C-2, based on the chemical shift of the hydroxy group (δ = 12.14 ppm). Investigation of the HMBC spectrum showed correlation peaks in accordance with this suggestion. Cross peaks were observed between the proton resonating at δ = 7.98 (3-H) and the carbon resonances at δ = 126.1 (C-4a) and 155.3 (C-1), and from the proton resonance at δ = 12.14 (1-OH) to C-2 (δ = 126.5 ppm) and C-8a (δ = 126.1 ppm). Furthermore, in the HMBC spectrum the proton resonating at δ = 8.07 (8-H) showed ^2J and ^3J cross peaks with resonances at δ = 126.1 (C-8a) and δ = 129.2 (C-4a). Therefore, compound **2** was assigned as 1-hydroxy-5-methoxy-2-nitronaphthalene. This compound, synthesized in 1987, was isolated for the first time from a natural source.[9]

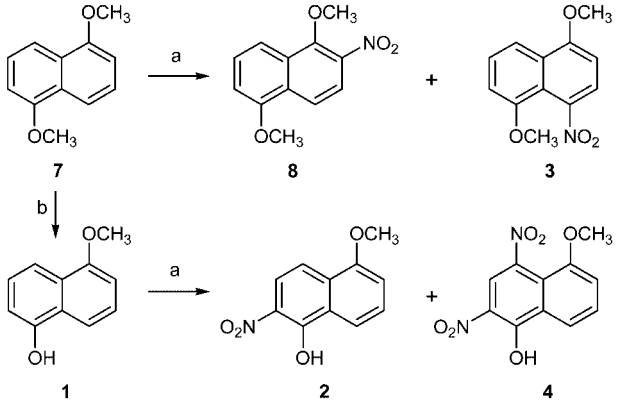
Compound **3** was obtained as yellow crystals (m.p. 164.5 °C). The empirical formula $C_{12}H_{11}NO_4$ was deduced from HREIMS and ^{13}C NMR data. ^1H NMR spectroscopic data of **3** indicated that it was structurally related to compound **2**. Comparison of their ^1H NMR spectra showed that signals assignable to a hydroxy group (δ = 12.14 ppm) of **2** were missing. However, the $^1H/^{13}C$ NMR spectrum of **3** showed resonances for two methoxy groups ($\delta_{H/C}$ = 4.03/56.0, 3.92/56.1), which were located at C-1 and C-5. As a result of the HMBC experiment, the nitro group was found to be located at C-4. Therefore, the nitro compound **3** was assigned as 1,5-dimethoxy-4-nitronaphthalene, first synthesized in 1947.[10]

Compound **4**, which was obtained as orange crystals (m.p. 173.5–175 °C), has an empirical formula of $C_{11}H_8N_2O_6$, as deduced from HREIMS and ^{13}C NMR data. The observed molecular ion in the EIMS differed by 46 mass units from compound **2**, corresponding to an additional nitro group. The ^1H NMR spectrum displayed the resonance of a chelated proton suggesting the location of one nitro group at C-2. The absence of any resonances with *ortho* coupling suggested that the second nitro group resides at C-3 or C-4. This was confirmed by the observation of three vicinal proton resonances of the B ring at δ = 8.21 (dd, J = 0.9, 8.2 Hz, 1 H, 8-H), 7.70 (t, J = 8.2 Hz, 1 H, 7-H), 7.25 (dd, J = 0.9, 8.2 Hz, 1 H, 6-H). Finally, the nitro group was located at C-4 according to an HMBC experiment. Strong ^3J correlation was observed from the proton signal at δ = 8.15 (3-H) to C-1 (δ = 156.0 ppm). From the above evidence, the structure of compound **4**, which was synthesized in 1947,[10] was established as 1-hydroxy-5-methoxy-2,4-dinitronaphthalene.

Compound **5** was obtained as yellow crystals (m.p. 274.0 °C) and was assigned the molecular formula $C_{12}H_{10}N_2O_6$ on the basis of HREIMS data. Its structure was elucidated by detailed analysis of the 1D and 2D NMR spectra. The ^1H NMR spectrum revealed three sets of spin systems [δ = 8.00 (d, J = 8.5 Hz), 7.30 (d, J = 8.5 Hz), 3.94 (s)], and the ^{13}C NMR spectrum exhibited only five resonances [δ = 57.5 (OCH_3), 107.9 (d), 116.9 (s), 124.5 (d), 140.7 (s)], suggesting a naphthalene skeleton. The structure of compound **5** is thus symmetrical. Comparison of the NMR spectroscopic data of compounds **3** and **5** was important to locate the two methoxy groups at C-1 and C-5. Analysis of its EIMS data suggested two nitro groups, located at C-4 and C-8. Thus, compound **5** was assigned as 1,5-dimethoxy-4,8-dinitronaphthalene. This compound was synthesized in 1947.[10] The co-occurrence of ergosterol (**6**), a typical and common metabolite of fungi, confirms that the unusual nitronaphthalenes isolated from the culture broth are in fact of fungal origin.

Chemical Synthesis

To prove the structure of the nitro compounds and to obtain further compounds for biological testing, 1,5-dimethoxynaphthalene (**7**) and 1-hydroxy-5-methoxynaphthalene (**1**) were subjected to mild nitration conditions by using acetyl nitrate as the nitrating agent (Scheme 1).[9,10]



Scheme 1. (a) $AcONO_2$, HOAc, 0 °C at 1.5 h; (b) BCl_3, CH_2Cl_2, 0 °C at 12 h.

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In both reactions, two major products were isolated. The conversion of 1,5-dimethoxynaphthalene (**7**) afforded the two isomeric mononitro compounds: 1,5-dimethoxy-4-nitronaphthalene (**3**) and 1,5-dimethoxy-2-nitronaphthalene (**8**); **3** was identical with the natural product. The more reactive phenol **1** gave the mononitro compound 1-hydroxy-5-methoxy-2-nitronaphthalene (**2**) and the dinitro compound 1-hydroxy-5-methoxy-2,4-dinitronaphthalene (**4**), both identical with the natural products.

Bioactivity

The results of the biological activity of the pure compounds **1**–**5**, as well as of several antibacterial and antifungal substances as controls, are summarized in Table 1. The fungal metabolites **1**–**4** exhibited moderate to excellent inhibitory activity against the test organisms used in these studies. Metabolites **1** and **4** were active against all the test organisms; **1** had good antifungal and antibacterial activities. Particularly of note are the excellent antifungal activities of compounds **1**–**4**, comparable to that of the fungicide Nystatin. Compound **5** was not active against any of these test organisms.

Table 1. Biological activity of the pure compounds **1**–**5**.[a]

Compound	Bacteria		Alga	Fungus
	Bm	Ec	Cf	Mb
Acetone	0	0	0	0
Penicillin	18	14	0	0
Tetracycline	18	18	10gi	0
Nystatin	0	0	0	20
Actidione	0	0	35	50
1	7	8	10	15
2	0	0	8	13
3	7	0	0	7
4	8	9	15	12
5	0	0	0	0

[a] Compounds **1**–**5** (50 µL at a concentration of 1 µg/µL) were tested in an agar diffusion assay for inhibitions of *Bacillus megaterium* (Bm), *Escherichia coli* (Ec), *Chlorella fusca* (Cf) and *Microbotryum violaceum* (Mb). The radius of zone of inhibition was measured in mm. 0 = inactive. gi = growth inhibition, i.e. there was some growth within the zone of inhibition.

Conclusion

Four nitronaphthalenes (**2**–**5**) were isolated as natural products of fungal origin, and their structures were confirmed by chemical synthesis. To the best of our knowledge, this is the first time that nitronaphthalenes are isolated from natural sources. Moreover, naturally occurring dinitro compounds such as **4** and **5** are very rare in natural environment. Up to date they have only been isolated as mononuclear phenol derivatives such as 3,4-dinitroguajacol or derivatives of (4-hydroxy-3,5-dinitrophenyl)acetic acid or -propionic acid.[13,14] Moreover, all nitro compounds showed considerable antibacterial, antifungal, and antialgal activity.

Experimental Section

General Experimental Procedures: Melting points were determined with a Gallenkamp apparatus and are not corrected. Mass spectra were recorded with a Finnigan MAT 8430 instrument (70 eV). ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Avance 500 spectrometer (^{1}H: 500 MHz; ^{13}C: 125 MHz). Chemical shifts were measured against TMS or $CDCl_3$ as internal standards. The multiplicities in the ^{13}C NMR spectra were deduced from the DEPT spectra; signals appearing as triplets in the spectra are designated as "t", even if they couple with two different protons. Silica gel 60 (230–400 mesh, Merck) was used for column chromatography and silica gel on aluminium foil (Merck) was used for TLC.

Tests for Biological Activity: The tested compounds were dissolved in acetone at a concentration of 1 µg/µL; 50 µL of the solution were pipetted onto a sterile filter disc which was placed onto an appropriate agar growth medium for the respective test organism and subsequently sprayed with a suspension of the test organism.[11] Commencing at the center edge of the filter disc, the radius of the zone of inhibition was measured in mm.

Isolation Procedure: Fungal strain 7721 was cultivated at 21 °C for 21 d on biomalt solid agar medium. The cultures (with agar media) were extracted four times with ethyl acetate to obtain the crude extracts (4.6 g) which were subjected to column chromatography on silica gel by using petroleum ether/EtOAc in order of increasing polarity, then pure EtOAc and finally gradients of EtOAc with up to 20% methanol. The fractions obtained were monitored by TLC, and similar fractions were combined. Further resulting fractions led to the isolation of five pure compounds: **6** (47 mg; petroleum ether/EtOAc, 20:1), **2** (23 mg; petroleum ether/EtOAc, 20:1), **3** (17 mg; petroleum ether/EtOAc, 10:1), **1** (15 mg; petroleum ether/EtOAc, 20:3), **4** (10 mg; petroleum ether/EtOAc, 20:7), **5** (18 mg; petroleum ether/EtOAc, 5:2).

1-Hydroxy-5-methoxy-2-nitronaphthalene (2): Orange crystals. M.p. 152 °C (ref.[9] 152 °C). IR (KBr, film): $\tilde{\nu}_{max}$ = 3290, 2919, 2263, 1268, 743 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 12.14 (s, 1 H, 1-OH), 8.07 (dd, J = 0.5, 8.2 Hz, 1 H, 8-H), 7.98 (d, J = 9.6 Hz, 1 H, 3-H), 7.77 (d, J = 9.6 Hz, 1 H, 4-H), 7.53 (t, J = 8.2 Hz, 1 H, 7-H), 7.06 (dd, J = 0.5, 8.2 Hz, 1 H, 6-H), 4.01 (s, 3 H, OCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.8 (q, OCH_3), 109.5 (d, C-6), 114.5 (d, C-4), 116.7 (s, C-8), 118.3 (s, C-3), 129.2 (s, C-4a), 127.4 (d, C-7), 129.2 (d, C-2), 126.1 (d, C-8a), 155.1 (s, C-5), 155.3 (s, C-1) ppm. MS (EI, 70 eV): *m*/*z* (%) = 219 (100) [M]$^+$, 182 (11), 188 (21), 155 (33), 114 (45), 101 (18), 30 (10). HREIMS (EI, 70 eV; $C_{11}H_9NO_4$): calcd. 219.0532, found 219.0533.

1,5-Dimethoxy-4-nitronaphthalene (3): Yellow crystals. M.p. 164.5 °C (ref.[10] 167 °C). IR (KBr, film): $\tilde{\nu}_{max}$ = 2924, 2365, 1268, 756 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.91 (dd, J = 0.8, 8.5 Hz, 1 H, 5-H), 7.50 (d, J = 8.3 Hz, 1 H, 2-H), 7.49 (t, J = 8.5 Hz, 1 H, 6-H), 7.02 (d, J = 7.7 Hz, 1 H, 7-H), 6.74 (d, J = 8.3 Hz, 1 H, 3-H), 4.03 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 56.0 (s, OCH_3), 56.1 (q, OCH_3), 102.3 (d, C-2), 108.4 (d, C-6), 114.7 (s, C-5), 117.3 (s, C-4a), 121.6 (d, C-2), 127.1 (d, C-6), 127.3 (s, C-8a), 141.1 (s, C-1), 153.8 (d, C-8), 157.1 (s, C-4) ppm. MS (EI, 70 eV): *m*/*z* (%) = 233 (100) [M]$^+$, 187 (5), 172 (12), 156 (8), 144 (8), 127 (27), 115 (12), 101 (6), 30 (8). HREIMS (EI, 70 eV; $C_{12}H_{11}NO_4$): calcd. 233.0688, found 233.0689.

1-Hydroxy-5-methoxy-2,4-dinitronaphthalene (4): Orange crystals. M.p. 173.5–175.0 °C (ref.[10] 173 °C). IR (KBr, film): $\tilde{\nu}_{max}$ = 3299, 2927, 2260, 1268, 743 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 12.00 (s, 1 H, 1-OH), 8.21 (dd, J = 0.9, 8.2 Hz, 1 H, 8-H), 8.15 (s, 1 H,

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3-H), 7.70 (t, J = 8.2 Hz, 1 H, C-7), 7.25 (dd, J = 0.9, 8.2 Hz, 1 H, 6-H), 3.95 (s, 3 H, OCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 56.4 (q, OCH_3), 113.2 (d, C-6), 114.6 (d, C-3), 117.5 (d, C-8), 119.4 (s, C-8a), 126.2 (s, C-2), 127.3 (s, C-4a), 129.5 (d, C-7), 141.0 (s, C-4), 154.2 (s, C-5), 156.0 (s, C-1) ppm. MS (EI, 70 eV): m/z (%) = 264 (100) $[M]^+$, 247 (8), 204 (16), 187 (33), 171 (30), 145 (14), 113 (48), 101 (17), 88 (16), 74 (20), 30 (13). HREIMS (EI, 70 eV; $C_{11}H_8N_2O_6$): calcd. 264.0382, found 264.0387.

1,5-Dimethoxy-4,8-dinitronaphthalene (5): Yellow crystals. M.p. 274.0 °C (ref.[10] 275 °C). IR (KBr, film): $\tilde{\nu}_{max}$ = 3290, 2929, 2270, 1270, 749 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.00 (d, J = 8.5 Hz, 2 H, 3-H), 7.30 (d, J = 8.5 Hz, 2 H, 2-H), 3.94 (s, 6 H, $2\times OCH_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 57.5 (s, $2\times OCH_3$), 107.9 (d, C-2,6), 116.9 (s, C-4a,8a), 124.5 (d, C-3,7), 140.7 (s, C-4,8) ppm. MS (EI, 70 eV): m/z (%) = 278 (100) $[M]^+$, 247 (23), 215 (15), 285 (42), 171 (30), 155 (53), 126 (54), 115 (30), 100 (14), 63 (13), 30 (9). HREIMS (EI, 70 eV; $C_{12}H_{10}N_2O_6$): calcd. 278.0539, found 278.0537.

Synthesis. General Procedure: A solution of acetyl nitrate was prepared by reaction of 70% H_2NO_3 (0.45 g) with of acetic anhydride (3.5 mL). A solution of 1,5-dimethoxynaphthalene (**1**) (100 mg, 0.53 mmol) in acetic acid (2 mL) was treated at 0 °C with a solution of the acetyl nitrate (2 mmol). The reaction was monitored by TLC. After 1.5 h, saturated aqueous sodium hydrogencarbonate (50 mL) was added to the reaction mixture. The aqueous layer was extracted with ethyl acetate (4×50 mL). The ethyl acetate extract was dried with sodium sulfate and concentrated. The residue was purified by column chromatography with petroleum ether/EtOAc (4–25%) to afford **3** (38 mg, 61% yield) and **8** (45 mg, 36% yield) as white crystals. Compound **8** started to decompose at ca. 220 °C, and the determination of its exact melting point was not possible. The compound was also unstable in solution. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.95 (d, J = 8.4 Hz, 1 H, 8-H), 7.34 (t, J = 8.4 Hz, 1 H, 7-H), 7.10 (d, J = 7.8 Hz, 1 H, 3-H), 6.83 (d, J = 7.8 Hz, 1 H, 4-H), 6.70 (d, J = 8.4 Hz, 1 H, 6-H), 4.02 (s, 3 H, 5-OCH_3), 3.03 (s, 3 H, 1-OCH_3) ppm. MS (EI, 70 eV): m/z (%) = 233 (100) $[M]^+$, 186 (8), 172 (12), 155 (6), 145 (12), 126 (27), 112 (21), 101 (5), 30 (14).

1-Hydroxy-5-methoxynaphthalene (1): A solution of 1,5-dimethoxynaphthalene (100 mg, 0.53 mmol) in dichloromethane (20 mL) was treated at –30 °C under argon with boron trichloride (0.53 mmol). The reaction was monitored by TLC; after stirring for 1 h, the reaction mixture was warmed progressively to 0 °C and stirred for another 12 h. The reaction mixture was then quenched by addition of water and the organic layer extracted with dichloromethane (4×100 mL). The dichloromethane extract was dried with sodium sulfate and concentrated at reduced pressure. The residue was purified by column chromatography with petroleum ether/EtOAc (4:1) to afford 75.5 mg of **1** (0.43 mmol, 82% yield) as white crystals, m.p. 139.5 °C. For ^1H and ^{13}C NMR data, see ref.[12]

1-Hydroxy-5-methoxy-2-nitronaphthalene (2) and 1-Hydroxy-5-methoxy-2,4-dinitronaphthalene (4): Nitration of 1-hydroxy-5-methoxynaphthalene (**1**) (100 mg, 0.57 mmol) according to the procedure described above gave two major compounds, **4** (25 mg, 33% yield) and **2** (47.1 mg, 37% yield). Their NMR spectroscopic data were identical with those reported for the natural products (see isolation procedure).

Supporting Information (see footnote on the first page of this article): ^1H NMR spectra of compounds **2**–**5** and **8** and ^{13}C NMR spectra of compounds **2**–**5**.

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[1] R. Winkler, C. Hertweck, *ChemBioChem* **2007**, *8*, 973–977.
[2] J. Dai, K. Krohn, B. Elsässer, U. Flörke, S. Draeger, B. Schulz, G. Pescitelli, P. Salvadori, S. Antus, T. Kurtán, *Eur. J. Org. Chem.* **2007**, 4845–4854.
[3] K. Krohn, U. Farooq, U. Flörke, B. Schulz, S. Draeger, G. Pescitelli, P. Salvadori, S. Antus, T. Kurtán, *Eur. J. Org. Chem.* **2007**, 3206–3211.
[4] K. Krohn, I. Kock, B. Elsässer, U. Flörke, B. Schulz, S. Draeger, G. Pescitelli, S. Antus, T. Kurtán, *Eur. J. Org. Chem.* **2007**, 1123–1129.
[5] J. Dai, K. Krohn, U. Flörke, S. Draeger, B. Schulz, A. Kiss-Szikszai, S. Antus, T. Kurtán, T. van Ree, *Eur. J. Org. Chem.* **2006**, 3498–3506.
[6] B. Elsässer, K. Krohn, U. Flörke, N. Root, H.-J. Aust, S. Draeger, B. Schulz, S. Antus, T. Kurtán, *Eur. J. Org. Chem.* **2005**, 4563–4570.
[7] C.-C. Wu, C.-F. Peng, I.-L. Tsai, M. H. Abd El-Razek, H.-S. Huang, I.-S. Chen, *Phytochemistry* **2007**, *68*, 1338–1343.
[8] G. Goulston, E. I. Mercer, L. J. Goad, *Phytochemistry* **1975**, *14*, 457–462.
[9] M. Lemaire, A. Guy, J. Roussel, J.-P. Guette, *Tetrahedron* **1987**, *43*, 835–844.
[10] R. H. Thomson, E. Race, F. M. Rowe, *J. Chem. Soc.* **1947**, 350–355.
[11] U. Höller, A. D. Wright, G. F. Matthée, G. M. König, S. Draeger, H.-J. Aust, B. Schulz, *Mycol. Res.* **2000**, *104*, 1354–1365.
[12] S. Ghosh, S. Ramakrishnan, *Macromolecules* **2005**, *38*, 676–686.
[13] K. Ohta, M. Takagi, *Phytochemistry* **1977**, *16*, 1085–1086.
[14] W. Al-Zereini, I. Schuhmann, H. Laatsch, E. Helmke, H. Anke, *J. Antibiot.* **2007**, 301–308.

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