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Thiersindoles A−C: New Indole Diterpenoids from *Penicillium thiersii*

Chen Li,[†] James B. Gloer,*[,†] and Donald T. Wicklow[‡]

Department of Chemistry, University of Iowa, Iowa City, Iowa 52242, and Mycotoxin Research Unit, Agricultural Research Service, National Center for Agricultural Utilization Research, USDA, Peoria, Illinois 61604

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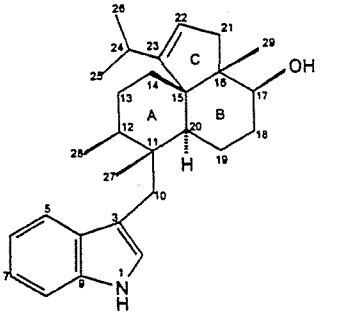
Three new 3-substituted indole diterpenoids (thiersindoles A−C; **1**−**3**) have been isolated from organic extracts of a new *Penicillium* species (*P. thiersii*). Their structures, including absolute stereochemistry, were determined by analysis of NMR data and application of Mosher's method. Thiersindoles A−C are biogenetically related to the aflavinines, although the [6,6,5] tricyclic diterpenoid skeleton in compounds **1** and **2** is unprecedented in any of the known members of this class.

During our investigations of fungicolous and mycoparasitic fungi that colonize sclerotia or stromata of wood decay fungi,[1−2] we have recently encountered a new *Penicillium* species (*P. thiersii*) (MYC-500 = NRRL 28147). Extracts of *P. thiersii* cultures showed potent antiinsectan activity, and initial chemical studies of this species led to the discovery of members of two distinct types of antiinsectan compounds, including thiersinines A and B,[3] which are indole diterpenoids with a new ring system, and decaturin B,[4] a metabolite related to the oxalicines that contains a rare pyridinyl-α-pyrone unit. Continuing studies of this species have provided three additional new indole diterpenoids with structures quite different from those isolated previously from *P. thiersii*. Details of the isolation and structure determination of these metabolites (thiersindoles A−C; **1**−**3**) are presented here.

Sephadex LH-20 column chromatography of the EtOAc extract of solid-substrate fermentation cultures of *P. thiersii* afforded several active fractions. Further separation of these fractions using silica gel column chromatography and reversed-phase HPLC yielded thiersindoles A−C (**1**−**3**).

The molecular formula of thiersindole A (**1**) was established as $C_{28}H_{39}NO$ by analysis of NMR and HRESIMS data. The EI mass spectrum of **1** contained a base peak at *m/z* 130, which is characteristic of a 3-substituted indole moiety. Comparison of the NMR data for **1** with literature values for 3-substituted indole metabolites[5−7] supported assignment of this unit. An AB pattern for an isolated methylene unit (H_2-10), with δ-values suggestive of attachment at the indole 3-position, was evident in the ^{1}H NMR spectrum. Only two other sp^2 carbon signals (δ 119.4, d; 161.2, s) were observed, indicating the presence of a trisubstituted olefin. On the basis of these data and DEPT NMR results, three additional rings and a free OH group must therefore be present to account for the molecular formula. One-bond C−H correlations for compound **1** were assigned using HMQC data, and assembly of the structural units was enabled by analysis of COSY and HMBC data (Table 1).

HMBC correlations of the two isolated methylene protons (H_2-10) with C-2, C-3, and C-4 confirmed the direct attachment of C-10 to C-3. Further correlations of H_2-10 with C-11, C-12, C-20, and C-27, together with correlations of H_3-27 with C-10, 11, 12, and 20, and of H_3-28 with C-11, C-12, and C-13, established the C10−C13/C20/C27/C28



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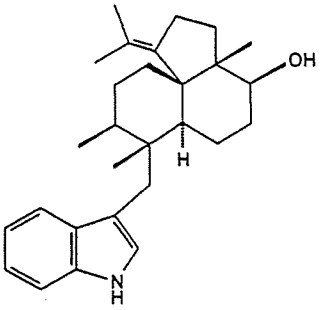

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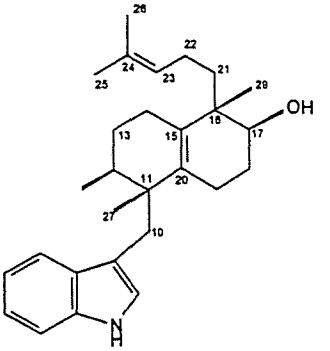

3

structural subunit. This unit was extended to incorporate C14 and C17−C19 on the basis of COSY and HMBC results. The singlet for H_3-29 revealed key correlations with C-15, C-16, C-17, and C-21. These data, together with correlations of H_2-18 with C-16, and of H_2-14 and H-20 with C-15 and C-16, enabled closure of the A and B rings of **1** with the substitution pattern shown. The downfield chemi-

* To whom correspondence should be addressed. Tel: 319-335-1361. Fax: 319-335-1270. E-mail: james-gloer@uiowa.edu.
† University of Iowa.
‡ USDA.

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Table 1. NMR Data for Thiersindoles A and B (**1** and **2**) in $CDCl_3$

	thiersindole A			thiersindole B		
position	^1H δ_H (mult, J_H)	^{13}C δ_C	HMBC (H→C)	^1H δ_H (mult, J_H)	^{13}C δ_C	HMBC (H→C)
1 NH	8.05 (br s)		3, 4	8.01 (br s)		3, 4
2	6.94 (d, 2.4)	121.7	3, 4, 9, 10	6.94 (d, 2.4)	121.5	3, 4, 9, 10
3		113.1			113.2	
4		129.4			129.5	
5	7.59 (br d, 7.8)	119.2	7, 9	7.59 (br d, 7.8)	119.2	7, 9
6	7.05 (ddd, 7.8, 7.2, 1)	119.3	4, 8	7.06 (ddd, 7.8, 7.2, 1)	119.3	4, 8
7	7.13 (ddd, 8.4, 7.2, 1)	121.7	5, 9	7.13 (ddd, 8.4, 7.2, 1)	123.6	5, 9
8	7.32 (br d, 8.4)	110.9	4, 6	7.29 (br d, 8.4)	110.7	4, 6
9		136.0			135.8	
10	2.74 (d, 15)	33.5	2, 3, 4, 11, 12, 20, 27	2.75 (d, 15)	33.8	2, 3, 4, 11, 12, 20
	2.94 (d, 15)		2, 3, 4, 11, 12, 20, 27	2.96 (d, 15)		2, 3, 4, 11, 12, 20, 27
11		41.7			42.9	
12	1.54 (m)	35.7	11, 13, 14, 20, 27, 28	1.85 (m)	35.7	
13 eq	1.13 (m)	28.3	14	1.26 (m)	28.7	14, 15, 28
13 ax	1.41 (dt, 3, 13)		11, 12, 14	1.44 (m)		11, 14, 15, 28
14 ax	0.78 (dt, 4, 14)	30.7	12, 13, 15, 16, 23	1.08 (m)	35.0	23
14 eq	1.50 (ddd, 14, 3, 3)		12, 13, 15, 16, 20	1.70 (m)		15, 23
15		55.2			52.7	
16		50.5			50.2	
17	3.41 (dd, 12, 4)	74.6	16, 18, 19, 21, 29	3.35 (dd, 11, 4)	72.5	18, 21, 29
18 eq	1.59 (m)	29.0	16, 17	1.58 (m)	29.4	17, 19, 20
18 ax	1.62 (ddd, 13, 12, 4)		16, 17	1.64 (m)		17, 19, 20
19 ax	1.38 (m)	24.4	11, 17, 20	1.39 (m)	23.2	11, 17
19 eq	2.19 (ddd, 15, 3, 3)		11, 15, 17, 20	2.12 (m)		
20	1.78 (br d, 7)	34.0	10, 11, 15, 16, 18, 19, 23, 27	2.30 (br d, 6)	36.1	10, 11, 15, 16, 18, 19, 23, 27
21	1.97 (br d, 16)	40.9	15, 16, 17, 22, 23, 29	1.36 (m)	32.2	16, 17, 22
	2.13 (dd, 16, 3)		15, 16, 17, 22, 23	1.70 (m)		16, 17
22	5.02 (br s)	119.4	15, 16, 21, 23, 24	1.96 (br dd, 15, 8)	29.7	16, 23
				2.20 (m)		23
23		161.2			145.1	
24	1.25 (m)	26.6	22, 23, 25		121.0	
25	0.55 (d, 6.6)	23.4	23, 24, 26	0.41 (br s)	18.8	23, 24, 26
26	0.36 (d, 6.6)	24.3	23, 24, 25	1.25 (br s)	24.6	23, 24, 25
27	1.05 (s)	19.2	10, 11, 12, 20	1.07 (s)	19.5	10, 11, 12, 20
28	1.04 (d, 6)	17.4	11, 12, 13	1.09 (d, 6)	17.3	11, 12, 13
29	1.13 (s)	14.9	15, 16, 17, 21	1.07 (s)	15.3	15, 16, 17, 21

cal shifts of H/C-17 (δ_H 3.35; δ_C 72.5) signaled placement of the OH group at this position. COSY correlations between H_2-21 and H-22 (δ_H 5.02) and HMBC correlations of H_2-21 with olefinic carbons C-22 and C-23 indicated connection of C-21 to the trisubstituted olefin unit as shown. H_2-21 also showed correlations with C-15, C-16, and C-17, requiring attachment of C-21 to C-16. An isopropyl group comprising C-24, -25, and -26 was easily recognized, and its direct connection to C-23 was established on the basis of HMBC correlations. HMBC correlations of H_2-14 and H-20 with C-23 enabled the connection of C-15 to C-23, thus completing the gross structure of thiersindole A as shown in **1**.

The relative stereochemistry of **1** was determined on the basis of NOESY and ^1H NMR data. The unusual upfield shifts of the methyl signals for H_3-25 (δ 0.55) and H_3-26 (δ 0.36) suggested that they were located in the shielding region of the aromatic ring. This conclusion was supported by the fact that all of the isopropyl group proton signals (H-24, H_3-25, and H_3-26) showed strong NOESY correlations with indole protons H-1, H-2, and H-5. These data required the five-membered C ring and the indole moiety to be oriented on the same face of the A–B ring system, thereby setting the relative stereochemistry of C-11, C-15, and C-16 as shown. H-20 also showed NOESY correlations with H-12, both C-10 protons, and all of the isopropyl group proton signals, placing C-10, H-20, and H-12 on the same face of the A ring. This requires both H-12 and H-20 to adopt axial orientations and the two cis-fused six-membered rings to adopt chair conformations (Figure 1). The 12 Hz trans-diaxial value for $J_{H17-H18ax}$ and a NOESY correlation between H-17 and H-21b enabled completion

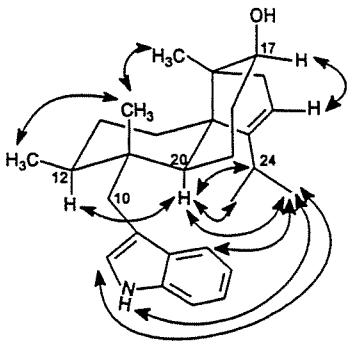
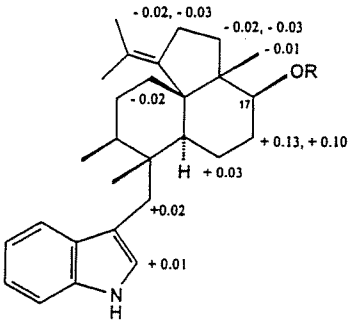


Figure 1. Perspective view of thiersindole A (**1**) including key NOESY correlations (↔).

of the assignment of the relative stereochemistry of thiersindole A as depicted in **1**.

Thiersindole B (**2**) possesses the same molecular formula as **1** ($C_{28}H_{39}NO$), as revealed by ^{13}C NMR, DEPT, and HRESIMS data. The NMR data indicated very close similarities between the two compounds. The major differences in the ^1H NMR spectra (Table 1) were the absence of the olefinic proton signal and the replacement of the two doublet methyl signals by broad vinylic methyl singlets. Like the isopropyl methyl doublets in **1**, these were also unusually upfield (δ 0.41 and 1.25), again suggesting their presence in an anisotropic shielding environment. In addition, the isopropyl methine and the olefinic proton evident in **1** were absent in **2** and were replaced by an additional methylene unit. ^{13}C NMR signals for a tetrasubstituted olefin were observed, with one carbon (C-23) shifted significantly upfield (from 161.2 to 145.1) relative



2a R = (R)-MTPA

2b R = (S)-MTPA

Figure 2. Observed chemical shift differences ($\Delta\delta = \delta_R - \delta_S$, ppm, 600 MHz) for selected protons of the *R*- and *S*-MTPA esters of thiersindole B (**2**).

to its position in the spectrum of **1**. All of these observations strongly suggested that **2** is a double-bond regioisomer of **1**. Analysis of COSY, HMQC, HMBC, and NOESY data led to the assignment of the structure and relative stereochemistry of thiersindole B as shown in **2**.

NMR and MS data for a third related metabolite (**3**), which is also an isomer of thiersindoles A (**1**) and B (**2**), suggested close structural similarities with **1** and **2**. However, the ^{13}C NMR data indicated the existence of two olefin units in this case, requiring one less ring than in **1** and **2**. Analysis of COSY, HMQC, and HMBC data led to the assignment of the structure of **3**. The presence of a 4-methyl-3-pentenyl group was deduced from COSY and HMBC data. This side chain has been observed in other known fungal indole diterpenoids, including nominine,[6] emeniveol,[8] and emindoles DA and SA.[9] H_3-29 showed HMBC correlations with C-15, -16, and -17, as well as C-21 of the side chain, thereby locating this unit at C-16. The position of the second (tetrasubstituted) double bond was identified by analysis of the HMBC data. H_2-10 and H_3-27 showed correlations with one of the olefinic carbons (C-20; δ_C 135.0), while H_2-21 and H_3-29 showed correlations with the other (C-15; δ_C 134.8), locating the tetrasubstituted double bond and permitting establishment of the gross structure of thiersindole C as shown in **3**. Its relative stereochemistry was independently assigned on the basis of a NOESY experiment and was found to be analogous to that of thiersindoles A (**1**) and B (**2**).

The absolute chemistry of the most abundant metabolite, thiersindole B (**2**), was assigned by application of the modified Mosher NMR method.[10] Treatment of **2** with (*S*)-MTPACl or (*R*)-MTPACl in the presence of DMAP afforded the (*R*)-MTPA ester (**2a**) or the (*S*)-MTPA ester (**2b**), respectively. Formation of the esters was confirmed by a significant downfield shift of the signal for H-17 and the appearance of the expected new aromatic and methoxy signals in the ^1H NMR spectra. Upon comparison of the ^1H NMR chemical shifts for **2a** and **2b** ($\Delta\delta$ values shown in Figure 2), the shifts of the adjacent methylene protons showed the greatest differences, although several other signals did show small variations. All of the $\Delta\delta$ values noted were consistent with assignment of the *S* absolute configuration at C-17, leading to the proposal of the overall absolute stereochemistry as shown. The other two thiersindoles are assumed to possess analogous absolute stereochemistry.

Although some other compounds isolated from this extract showed potent antiinsectan activity,[3,4] none of the thiersindoles showed significant activity in dietary assays[11] against the fall armyworm *Spodoptera frugiperda* at levels up to 1000 ppm or in disk assays against *Candida albicans* ATCC 90029 and *Staphylococcus aureus* ATCC 29213 at 200 μg/disk.

The thiersindoles are structurally related to the aflavinines[5,12] and bear a close biogenetic relationship to these and other indole diterpenoids.[6,9] However, the [6,6,5] tricyclic ring system found in thiersindoles A (**1**) and B (**2**) is not present in any of the known members of this class. In fact, to our knowledge, the *Pseudopterogorgia* metabolites elisabethin A[13] and elisabethin D[14] are the only two natural products that contain this specific tricyclic ring system, and their substitution patterns are significantly different from those of thiersindoles A and B.

Experimental Section

General Experimental Procedures. General experimental procedures have been described elsewhere.[3,15] ^1H NMR data were obtained at 600 MHz (Bruker AMX-600), and ^{13}C NMR data were obtained at 90 MHz (Bruker WM-360). COSY, HMQC, HMBC, and NOESY data were recorded at 600 MHz (^1H-dimension; Bruker AMX-600). NMR data were recorded in $CDCl_3$, and the chemical shifts were referenced to the residual solvent signals (δ_H 7.24/δ_C 77.0).

Organism. Details of the isolation of *Penicillium thiersii* (MYC-500 = NRRL 28147) and methods employed for its cultivation have been described previously.[3]

Extraction and Isolation. The EtOAc extract (3.6 g) from rice solid-substrate fermentation cultures of *P. thiersii* (eight 500 mL Erlenmeyer flasks, each containing 50 g of rice) was partitioned between CH_3CN and hexane. The CH_3CN-soluble portion (2.3 g) was subjected to Sephadex LH-20 column chromatography using a hexane–CH_2Cl_2–acetone solvent gradient, and the fraction (231 mg) that eluted with 1:4 hexane–CH_2Cl_2 was further fractionated on a silica gel column. A subfraction that eluted with 3:2 hexane–EtOAc (67 mg) was further separated by reversed-phase HPLC (Alltech HS Hyperprep 100 BDS, C_{18} column, 5 μm particles, 1.0 × 25 cm; flow rate 2.0 mL/min; 85% CH_3OH in H_2O) to yield thiersindole A (**1**, 8.5 mg, t_R 29.3 min) and thiersindole B (**2**, 15.2 mg, t_R 31.9 min). A second fraction that eluted from the Sepahadex column with 1:4 hexane–CH_2Cl_2 (99 mg) was also further fractionated on a silica gel column. A subfraction (12 mg) that eluted with 3:2 hexane–EtOAc was subjected to reversed-phase HPLC (same conditions as listed for **1** except for elution with 60% to 100% CH_3CN in H_2O over 40 min) to afford thiersindole C (**3**, 2.2 mg, t_R 44.8 min).

Thiersindole A (1): white solid; mp 89–92 °C; $[\alpha]_D$ +26° (*c* 0.1, CH_2Cl_2); UV (MeOH) λ_{max} (log ε) 227 (4.26), 254 (3.43), 292 (3.48); IR (CH_2Cl_2) ν_{max} 3411, 3355, 3046, 2970, 2923, 2856, 1621, 1461 cm^{-1}; ^1H NMR, ^{13}C NMR, and HMBC data, see Table 1; NOESY data (H ↔ H#) H-1 ↔ H-2, H-8, H_3-25, H_3-26; H-2 ↔ H-1, H_2-10, H_2-19, H-20, H_3-25, H_3-26; H-5 ↔ H-6, H_2-10, H_2-19, H-20, H_3-25, H_3-26, H_3-28; H-6 ↔ H-5, H-7, H_3-25; H-7 ↔ H-6, H-8, H_3-25; H-8 ↔ H-1, H-7, H_3-25, H_3-26; H_2-10 ↔ H-2, H-5, H_2-19, H-20; H-12 ↔ H-14ax, H-20; H-13ax ↔ H-13eq, H-14eq; H-13eq ↔ H-13ax, H-14eq; H-14ax ↔ H-12, H-20; H-14eq ↔ H_2-13; H-17 ↔ H-18eq, H-19ax, H_2-21, H-22, H_3-25; H-18ax ↔ H_3-29; H-18eq ↔ H-17; H-19ax ↔ H-2, H-5, H_2-10, H-17; H-19eq ↔ H-2, H-5, H_2-10; H-20 ↔ H-2, H-5, H_2-10, H-12, H-14ax, H-24; H_2-21 ↔ H-17, H-22, H_3-29; H-22 ↔ H-17, H_2-21, H_3-25, H_3-26; H-24 ↔ H-20, H_3-25, H_3-26; H_3-25 ↔ H-1, H-2, H-5, H-6, H-7, H-8, H-17, H-22, H-24; H_3-26 ↔ H-1, H-2, H-5, H-8, H-22, H-24; H_3-27 ↔ H-5, H_3-28, H_3-29; H_3-28 ↔ H_3-27; H_3-29 ↔ H-18ax, H_2-21, H_3-27; EIMS (70 eV) *m/z* 405 (M^+; rel int 3), 275 (5), 257 (18), 215 (5), 187 (7), 161 (8), 145 (7), 130 (100); HRESIMS, obsd *m/z* 406.3109, calcd for $C_{28}H_{39}NO$ + H, 406.3110.

Thiersindole B (2): white solid; mp 95–98 °C; $[\alpha]_D$ +21° (*c* 0.1, CH_2Cl_2); UV (MeOH) λ_{max} (log ϵ) 224 (4.28), 284 (3.49), 292 (3.45); IR (CH_2Cl_2) ν_{max} 3447, 3377, 3047, 2918, 2863, 1461 cm^{-1}; ^1H NMR, ^{13}C NMR, and HMBC data, see Table 1; EIMS (70 eV) *m/z* 405 (M^+; rel int 11), 275 (4), 257 (19), 215 (4), 187 (12), 161 (13), 145 (15), 130 (100); HRESIMS, obsd *m/z* 428.2908, calcd for $C_{28}H_{39}NO$ + Na, 428.2929.

Thiersindole C (3): colorless oil; $[\alpha]_D$ −42° (*c* 0.1, CH_2Cl_2); UV (MeOH) λ_{max} (log ϵ) 220 (4.26), 288 (3.49), 292 (3.48); IR (CH_2Cl_2) ν_{max} 3408, 2964, 2930, 1457 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.88 (1H, br s, H-1), 7.59 (1H, br d, 7.8, H-5), 7.31 (1H, br d, 8.4, H-8), 7.14 (1H, ddd, 1.2, 7.2, 8.4, H-7), 7.08 (1H, ddd, 1.2, 7.2, 7.8, H-6), 7.02 (1H, br s, H-2), 5.07 (1H, tm, 6, H-23), 3.81 (1H, dd, 3, 11, H-17), 2.89 (1H, d, 15, H-10a), 2.82 (1H, d, 15, H-10b), 2.36 (1H, br d, 16, H-14a), 2.24 (1H, m, H-14b), 2.02 (1H, br d, 11, H-19a), 1.98 (1H, m, H-22a), 1.72 (2H, m, H-22b, H-19b), 1.70 (1H, m, H-12), 1.68 (1H, m, H-18a), 1.66 (3H, br s, H_3-26), 1.58 (1H, ddd, 5, 12, 14, H-21a), 1.53 (3H, br s, H_3-25), 1.47 (1H, dq, 13, 3, H-13a), 1.38 (1H, dt, 6, 13, H-13b), 1.35 (1H, m, H-21b), 1.01 (3H, s, H_3-27), 0.96 (3H, s, H_3-29), 0.84 (3H, d, 7, H_3-28); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5 (C-9), 135.0 (C-20), 134.8 (C-15), 131.2 (C-24), 129.0 (C-4), 124.8 (C-23), 121.7 (C-7), 121.4 (C-2), 119.0 (C-6), 118.7 (C-5), 113.2 (C-3), 110.8 (C-8), 71.0 (C-17), 43.2 (C-16), 42.2 (C-11), 35.6 (C-21), 33.3 (C-12), 31.2 (C-10), 27.6 (C-18), 27.3 (C-13), 25.7 (C-25), 25.0 (C-19), 24.9 (C-14), 23.1 (C-22), 21.7 (C-27), 20.5 (C-29), 17.8 (C-26), 16.8 (C-28); selected key HMBC data ($CDCl_3$) H_2-10 → C-2, 3, 4, 11, 12, 20, 27; H_2-21 → C-15, 16, 17, 22, 23; H-23 → C-25, 26; H_3-25 → C-23, 24, 26; H_3-26 → C-23, 24, 25; H_3-27 → C-10, 11, 12, 20; H_3-28 → C-11, 12, 13; H_3-29 → C-15, 16, 17, 21; EIMS (70 eV) *m/z* 405 (M^+; rel int 1), 275 (38), 257 (24), 215 (3), 189 (10), 187 (6), 175 (17), 161 (7), 147 (10), 145 (8), 130 (100); HRESIMS, obsd *m/z* 428.2854, calcd for $C_{28}H_{39}NO$ + Na, 428.2829.

***(R)*- and *(S)*-MTPA Esters of Thiersindole B (2).** A solution of **2** (1.5 mg, 4 μmoL) in CH_2Cl_2 (300 μL) was treated with (*S*)-2-methoxy-2-trifluoromethylphenylacetyl chloride [(*S*)-MTPACl, 10 μL, 50 μmoL] and DMAP (one crystal). The mixture was stirred at 25 °C for 50 h. Aqueous saturated $NaHCO_3$ (1 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 1.5 mL). The combined organic extracts were concentrated, filtered, and evaporated to give a white solid, which was then subjected to HPLC (Alltech Platinum CN column, 5 μm particles, 1.0 × 25 cm; flow rate 2.0 mL/min; 5% EtOH in hexane) to afford (*R*)-MTPA ester **2a** (1.5 mg, t_R 16.8 min; 66% yield). Analogous treatment of **2** (1.3 mg) using (*R*)-MTPACl afforded (*S*)-MTPA ester **2b** (1.5 mg, t_R 16.8 min; 75% yield).

***(R)*-MTPA ester 2a:** colorless solid; ^1H NMR (600 MHz, $CDCl_3$) δ 7.99 (1H, br s, H-1), 7.57 (1H, br d, 7.8, H-5), 7.53 (2H, m, Ar-H), 7.38 (3H, m, Ar-H), 7.30 (1H, br d, 8.4, H-8), 7.14 (1H, ddd, 1.2, 7.2, 8.4, H-7), 7.06 (1H, ddd, 1.2, 7.2, 7.8, H-6), 6.94 (1H, br s, H-2), 4.91 (1H, dd, 13, 4, H-17), 3.55 (3H, s, O-Me), 2.94 (1H, d, 15, H-10a), 2.77 (1H, d, 15, H-10b), 2.35 (1H, br d, 6, H-20), 2.30 (1H, m, H-22a), 2.18 (1H, br d, 12, H-19a), 1.97 (1H, m, H-22b), 1.84 (2H, m, H-12, H-18b), 1.75 (1H, m, H-18a), 1.68 (1H, br d, 11, H-21a), 1.38 (1H, m, H-19b), 1.32 (1H, m, H-21b), 1.26 (3H, s, H_3-26), 1.12 (1H, m, H-14b), 1.08 (6H, br s, H_3-27, 28), 1.04 (3H, s, H_3-29), 0.41 (3H, s, H_3-25).

***(S)*-MTPA ester 2b:** colorless solid; ^1H NMR (600 MHz, $CDCl_3$) δ 7.98 (1H, br s, H-1), 7.57 (1H, br d, 7.8, H-5), 7.53 (2H, m, Ar−H), 7.38 (3H, m, Ar−H), 7.30 (1H, br d, 8.4, H-8), 7.14 (1H, ddd, 1.2, 7.2, 8.4, H-7), 7.06 (1H, ddd, 1.2, 7.2, 7.8, H-6), 6.94 (1H, br s, H-2), 4.89 (1H, dd, 13, 4, H-17), 3.52 (3H, s, O-Me), 2.92 (1H, d, 15, H-10a), 2.75 (1H, d, 15, H-10b), 2.33 (2H, m, H-20, 22a), 2.14 (1H, br d, 12, H-19a), 1.99 (1H, m, H-22b), 1.84 (1H, m, H-12), 1.71 (2H, m, H-18b, H-21a), 1.64 (1H, m, H-18a), 1.39 (1H, m, H-19b), 1.34 (1H, m, H-21b), 1.26 (3H, s, H_3-26), 1.14 (1H, m, H-14b), 1.08 (6H, br s, H_3-27, 28), 1.05 (3H, s, H_3-29), 0.41 (3H, s, H_3-25).

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Supporting Information Available: ^1H and ^{13}C NMR spectra for thiersindoles A–C (**1–3**). This material is available free of charge via the Internet at http://pubs.acs.org.

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