202. Synthesis of New Unnatural Macrocyclic Trichothecenes: 4-Epiverrucarin A

47th Communication on Verrucarins and Roridins[1])

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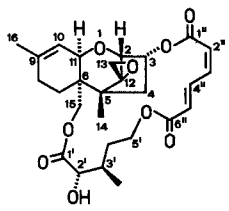
The 4-epiverrucarin A (**24**), a new unnatural macrocyclic trichothecene, was synthesized starting from 4-epiverrucarol (**20**). The latter was obtained by metal-hydride reduction of the 4-oxo derivative **19**. Subsequent conversion of **20** into the monoester **30** and then the diester **32** followed by macrolactonization of the latter yielded 4-epiverrucarin A (**24**). Attempts to invert the configuration of the naturally occuring 3α-OH group of a trichothecene were unsuccessful. The cytostatic (P-815) and immunosuppressive (MLR) activity of several natural and unnatural trichothecenes was determined *in vitro*.

Introduction. – In the preceeding communication [1], first results of our programme directed to the synthesis of new unnatural macrocyclic trichothecenes were described, namely the synthesis of 3-isoverrucarin ((1″-*O*)(4→3)*abeo*-verrucarin A; **1**) and the two novel macrocyclic by-products verrucinol and verrucene (**2**). In continuation of these efforts, the next goal was the preparation of 3- and 4-hydroxytrichothecenes possessing unnatural configurations and to use them for the synthesis of additional macrocyclic analogues of verrucarin A (**3**). Such compounds will give more detailed information on the relationship between chemical structure and biological activity.

Results. – Initially, the epimerization of the 3α-OH group of anguidine (**4**) or of the calonectrin (**5**) derivative **6** was attempted using the *Mitsunobu*'s procedure (Ph_3P, diethyl azodicarboxylate, AcOH [2]). No reaction of the secondary 3α-OH group was observed, neither at room temperature nor upon heating. Recently, the lack of reactivity of the OH groups at C(3) or C(4) of the trichothecene skeleton during *Mitsunobu*'s procedure was also observed by *Wani et al.* [3]. These OH groups are probably not attached by Ph_3P because of steric hindrance. When anguidine (**4**) was submitted to a modified *Mitsunobu* procedure [4], it was also inert at room temperature. However, upon heating, two products were isolated which were identified as the triacetate **7** and the carbonate **8**. Both compounds were formed with retention of configuration. This unexpected behaviour suggests a nucleophilic attack of the OH group on activated acetate or diethyl azodicarboxylate. The configuration of the OH group at C(3) was assigned by ^{1}H-NMR on the basis of the value of 5 Hz for J(H–C(2),H–C(3)) which is due to the dihedral angle of 25–30° between these protons. The inverse configuration would lead to a dihedral angle of *ca.* 90–100°, hence to a J of *ca.* 0–2 Hz. Moreover, the 3α-configuration of **7** and **8** was

[1]) 46th Commun.: [1].



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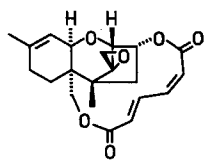

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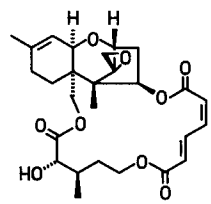

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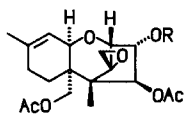
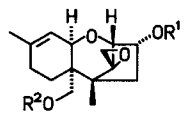
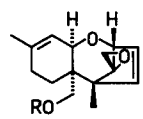


4 R = H
7 R = Ac
8 R = COOEt



5 R^1, R^2 = Ac
6 R^1 = H, $R^2 = COCH_2CH_2COCH_3$
9 $R^1 = SO_2CH_3$, $R^2 = COCH_2CH_2COCH_3$
10 $R^1 = SO_2C_6H_4CH_3$, $R^2 = COCH_2CH_2COCH_3$
11 $R^1 = SO_2CF_3$, $R^2 = COCH_2CH_2COCH_3$
14 $R^1 = SO_2C_6H_4CH_3$, R^2 = H



12 R = $COCH_2CH_2COCH_3$
13 R = H

confirmed by acetylation (Ac_2O, pyridine) of anguidine (**4**) which yielded a product identical with **7**.

Next, we attempted substitution at C(3) by activating the 3α-OH group as the mesylate **9**, tosylate **10**, or triflate **11**. Standard procedures yielded the sulfonates without any difficulties. Several methods to introduce O-nucleophiles at C(3) by the S_N2 mechanism were applied but did not yield the desired products (see *Table 1*) [5–9]. The mesylate **9** and tosylate **10**, in most cases, did not react, while the triflate **11** often yielded the elimination product **12** or **13**, or products in which epoxide opening had occurred or which still contained the sulfonate group. Compound **14** was obtained in quantitative

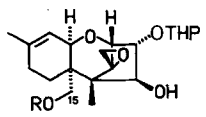
Table 1. *Experiments for the Inversion of the 3α-OH Group of Trichothecenes*

Starting material	Method	Product	Lit.
9	CsAc (4 equiv.), DMF (90%), 17 h	–	[5]
	CsAc (3 equiv.), [18]crown-6 (0.75 equiv.), benzene, 80°, 19 h	–	[6]
10	CsAc (3 equiv.), [18]crown-6 (0.75 equiv.), benzene, 80°, 16 h	–	[5]
	$Cs(CH_3CH_2COO)$ (2.2 equiv.), 1,3-dimethyl-2-imidazolidinone, 150°, 6 h	–	[10]
	Et_4NAc (2–4 equiv.), acetone, 56°	[a])	[7]
	NaOH (6 equiv.), H_2O, MeOH, 23°, 20 h	**14** (98%)	
11	Et_4NAc (2 equiv.), acetone, 20°, 6 d	**12** (18%)+[a])	[7]
	Et_4NAc (2 equiv.), DMF, 85°, 17 h	[a])	[7]
	LiAc (4 equiv.), DMF, 80°, 24 h	**12** (19%)	[7]
	Bu_4NNO_3 (1.5 equiv.), toluene, 80°, 16 h	**12** (13%)	[8]
	KO_2, DMSO, 20°, 16 h	**13** (97%)	[9]
4	diethyl azodicarboxylate, Ph_3P, $ZnAc_2$, toluene, 95%, 23 h	**7** (41%)+ **8** (11%)	[4]

[a]) The products which were formed (< 10%) were not determined. According to ^{1}H-NMR, epoxide opening occurred, or the sulfonate groups were still present.

yield after hydrolysis of **10** by NaOH. The method to epimerize the 4α-OH group of a 12,13-deoxytrichothecene derivative which was used in a verrucarin synthesis [10] also failed in our hands. The product, in which the 12,13-epoxy group was lacking according to ^{1}H-NMR, decomposed on storage and, therefore, its constitution could not be determined. We did not attempt an epimerization of a 12,13-deoxygenated derivative.

Our attention was then directed towards the epimerization of the 4β-OH group. It is reported that trichothecen-3-ones are attacked by $NaBH_4$ exclusively from the *'exo'*-side leading to the 3α-hydroxy derivatives [11]. Thus, the 15-OH group of the diol **15**[2]) was selectively acetylated (Ac_2O, pyridine) to the 15-monoacetate **16** (yield 58%) and the latter oxidized to the ketone **17** (88%) using *Swern*'s procedure [12]. Unfortunately, when **17** or the deprotected 3α-hydroxy ketone **18** were submitted to the reduction procedure using either $NaBH_4$ or lithium tri(*tert*-butoxy)aluminium hydride, a rapid decomposition of the starting material was observed. On the other hand, the 4-keto compound **19** was readily reduced by metal hydrides.



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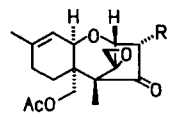
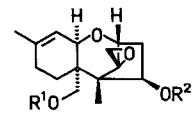
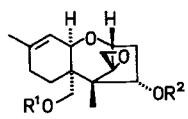
16 R = Ac



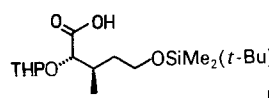
17 R = OTHP
18 R = OH
19 R = H



21 R^1, R^2 = H
22 R^1 = Ac, R^2 = H



20 R^1, R^2 = H
23 R^1 = Ac, R^2 = H
28 R^1 = H, R^2 = Ac
29 R^1, R^2 = Ac



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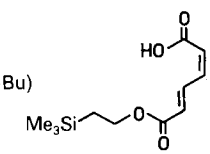

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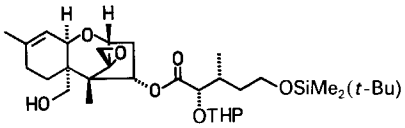
THP = Tetrahydro-2*H*-pyranyl

The preparation of 4-epiverrucarol (**20**) started with the protection of the 15-OH group of verrucarol (**21**). Acetylation (Ac_2O, pyridine, CH_2Cl_2) gave the monoacetate **22** in 63% yield. The subsequent oxidation of the 4-OH group afforded **19** in almost quantitative yield. Reduction of **19** using $NaBH_4$ yielded a mixture of 31% of the monoacetate **23** and of 40% of 4-epiverrucarol (**20**), while lithium tri(*tert*-butoxy)aluminium hydride yielded 79% of **23** as the only product which was hydrolyzed to **20**.

Having obtained 4-epiverrucarol (**20**), we decided to synthesize 4-epiverrucarin A (**24**) by the same route as that used in the synthesis of verrucarin A [13]. We planned to begin with the selective esterification of the 15-OH group with the verrucarinic-acid derivative **25** and accordingly to attach the muconic halfester **26** to the remaining 4-OH group. However, when 4-epiverrucarol (**20**) and **25** were submitted to the condensation procedure according to *Neises* and *Steglich* (dicyclohexylcarbodiimide (DCC), 4-(dimeth-

[2]) For the preparation of **15**, see [1].



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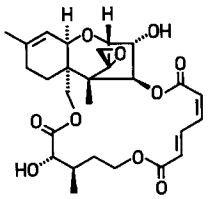

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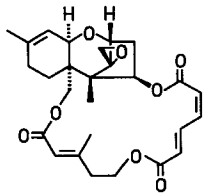

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ylamino)pyridine ((Me$_2$N)Py), Et$_3$N) [14], the reverse reactivity of the OH groups at C(4) and C(15) as compared to verrucarol (**21**) was observed. According to the ^{1}H-NMR, the 4α-monoacylated product **27** was formed as main product. It was not possible to cleanly separate the products by column chromatography. Therefore, the selectivity of the acylation was determined using AcOH and **20**. After careful column chromatography, 71% of the 4α-monoacetate **28**, 9.6% of the 15-monoacetate **23**, and 8.4% of the diacetate **29** were obtained. Similar differences of the reactivity of the OH groups were observed during other acetylation procedures. Using Ac$_2$O or AcCl in pyridine and CH_2Cl_2, the 4-OH group of **20** was slightly favoured. The 15-OH group of verrucarol (**21**) was predominately acetylated using Ac$_2$O in pyridine, while AcCl in pyridine favoured the 4β-OH group [15]. This procedure using Et$_3$N instead of pyridine was also selective for the 15-OH group of 4-epiverrucarol (**20**). The results of the acetylation procedures are summarized in *Table 2.*

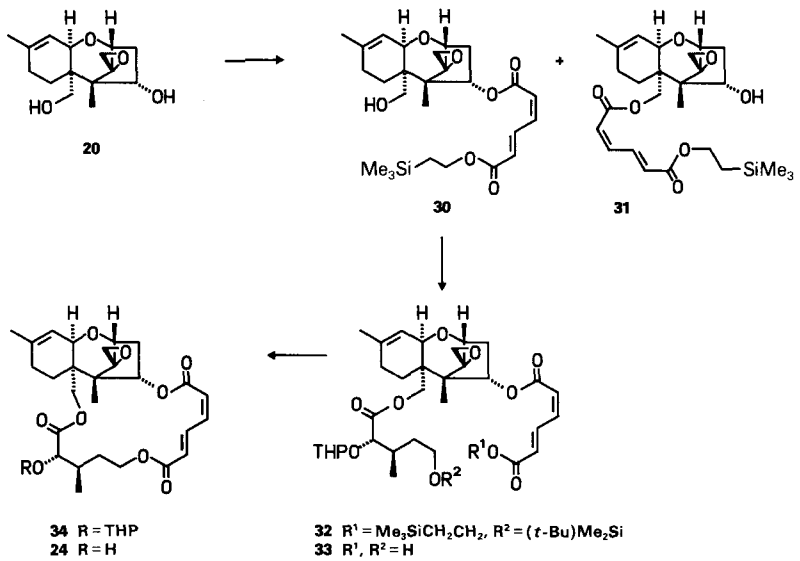
Table 2. *Acetylation of 4-Epiverrucarol* (**20**)

Method	Ratio [%] **23**/**28**[a])
Ac$_2$O (2 equiv.), pyridine (6 equiv.), CH_2Cl_2, 20°	31:45
AcCl (1 equiv.), pyridine (3 equiv.), CH_2Cl_2, 0°	33:54
AcCl (1 equiv.), Et$_3$N (3 equiv.), CH_2Cl_2, 0°	60:25
AcCl (1 equiv.), (i-Pr)$_2$EtN (3 equiv.), CH_2Cl_2, 0°	60:34

[a]) The ratio of the products was determined in ^{1}H-NMR. No diacetylated product was found.

To complete the synthesis of 4-epiverrucarin A (**24**), the muconic halfester **26** was selectively attached (DCC, (Me$_2$N)Py, Et$_3$N) to the 4α-OH group *(Scheme)*. The muconates **30** and **31** were obtained with a yield of 61 and 29%, respectively, without isomerization of the (*Z*)-double bond (*cf.* [13]). However, the condensation of the primary OH group in **30** with the acid **25** turned out to be more difficult: 2.5 equiv. of **25** were necessary in order to achieve a quantitative conversion using the same acylation procedure (DCC, (Me$_2$N)Py, Et$_3$N). Moreover, the desired ester **32** could not be completely separated from by-products. The limited amounts of starting materials prevented us from investigating other acylation procedures. After the removal of the silyl protecting groups by Bu$_4$NF, the seco-acid **33** was submitted to the mixed-anhydride lactonization procedure using pivalic acid, Et$_3$N, and (Me$_2$N)Py [17]. The subsequent removal of the tetrahydro-2*H*-pyranyl (Thp) group of the cyclized product **34** with pyridinium *p*-toluenesulfonate in EtOH afforded 4-epiverrucarin A (**24**) in 29% yield (from **30**).

Scheme



Biological Activity. – Biological evaluation of several new trichothecenes, especially of macrocyclic derivatives, was carried out using the P-815 mastocytoma cell line [18] (cytostatic activity) and the murine mixed lymphocyte reaction [19] (MLR; immunosuppressive activity) by determining the inhibitory concentration (IC_{50}) for cell growth. The

Table 3. *Biological Activity*

	IC_{50} [μg/ml]	
	P-815	MLR
Verrucarol (**21**)	> 1	0.183
15-*O*-Acetylverrucarol (**22**)	0.03	0.42
4-*O*-Acetylverrucarol	> 10	> 1
4,15-Di-*O*-acetylverrucarol	0.26	0.147
4-Epiverrucarol (**20**)	> 1	> 1
15-*O*-Acetyl-4-epiverrucarol (**23**)	> 1	> 1
4-*O*-Acetyl-4-epiverrucarol (**28**)	> 1	> 1
4,15-*O*-Diacetyl-4-epiverrucarol (**29**)	> 1	> 1
Anguidine (**4**)	0.0016	< 0.008
Triacetoxyscirpenol (**7**)	0.0081	< 0.008
Calonectrin (**5**)	> 1	0.074
Verrucarin A (**3**)	< 0.0008	< 0.0008
3α-Hydroxyverrucarin A (**35**)	< 0.0008	< 0.008
Verrucarin J (**36**)	0.0003	< 0.0008
2″,3″,4″,5″-Tetrahydroverrucarin J	0.0018	0.014
Verrucarin K (12,13-deoxyverrucarin A)	< 0.008	0.019
4-Epiverrucarin A (**24**)	0.0076	0.017
3-Isoverrucarin A ((1″-*O*)(4→3)*abeo*-Verrucarin A; **1**)	> 1	0.099
Verrucene (**2**)	> 1	0.159

results are summarized in *Table 3*[3]). A comparison of the acetyl derivatives of verrucarol (**21**) and 4-epiverrucarol (**20**) demonstrates the necessity of the β-configuration at the 4-position of simple trichothecene esters. On the other hand, a change of the configuration at C(4) of the macrocyclic verrucarin A (**3**) decreases the activity but does not effect a complete loss of activity (see **24**). The change of the attachment of the macrolidic bridge from C(4β) to C(3α) leads to a complete loss of the activity as demonstrated by 3-Isoverrucarin A ((1″-*O*)(4→3)*abeo*-verrucarin A; **1**) and verrucene (**2**) [1]. In contrast to the simple trichothecene esters, an additional OH group in 3α-position does not change the *in vitro* activity of verrucarin A (**3**), as demonstrated by the comparison of 4β,15-di-*O*-acetylverrucarol with anguidine (**4**) and 3α-hydroxyverrucarin A (**35**) with verrucarin A (**3**), respectively. The loss of the (*Z*,*E*)-diene system also results in a decreased activity as shown by 2″,3″,4″,5″-tetrahydroverrucarin J in comparison with verrucarin J (**36**). All tested compounds also show immunosuppressive activity which points to a general cytotoxicity and not to a selective cytostatic or immunosuppressive activity. The presence of the 12,13-epoxy group has been shown to be essential for the biological activity of simple trichothecene esters [20] [21]. Verrucarin K (= 12,13-deoxyverrucarin A), the first natural trichothecene lacking the 12,13-epoxy group, has been isolated some years ago [22]. Interestingly, a high cytotoxic activity was found for this compound. This result suggests that the macrolidic part possesses a cytotoxic activity independent of the epoxybearing trichothecene moiety. The cytotoxic activities of macrocyclic trichothecene model compounds which do not possess the trichothecene moiety support this hypothesis [23]. However, with the data available at present, it is too early to draw final conclusions for the structural requirements for the biological activity of trichothecene mycotoxins.

The financial support of these investigations by the *Swiss National Science Foundation* is gratefully acknowledged.

Experimental Part

General. H_2O-sensitive reactions were carried out under Ar or N_2. CH_2Cl_2 and toluene were dried by filtering through an Al_2O_3 column and stored over molecular sieves (4 Å). THF and DMSO were dried by distilling over $LiAlH_4$ or CaH_2, respectively. All org. extracts were dried (Na_2SO_4) and evaporated under reduced pressure bellow 50°. TLC: silica gel *60 F_{254} (Merck)*; detection with 10% H_2SO_4 in MeOH or $KMnO_4$ soln. Prep. TLC: silica gel *60 F_{254} (Merck)*; 20 × 20-cm plates, thickness of layer: 0.25 or 0.55 mm. CC (column chromatography): silica gel *60* (60–200 μm or 35–70 μm; *Merck*); Al_2O_3 (Typ *507C* neutral, *Fluka*). M.p.: *Kofler* block; corrected. $[\alpha]_D^t$: *Perkin-Elmer-141* polarimeter. IR: *Perkin-Elmer-177* grating spectrometer. NMR: *Varian-EM-360* spectrometer (^{1}H, 60 MHz), *Bruker-WH-90* spectrometer with *Fourier* transform (^{1}H, 90 MHz; ^{13}C, 22.63 MHz), *Varian-VXR-400* spectrometer with *Fourier* transform (^{1}H, 400 MHz; ^{13}C, 101 MHz); 300-MHz ^{1}H-NMR were recorded by *Ciba-Geigy*, Basel; $CDCl_3$ was used as solvent, and the chemical shifts are reported in ppm downfield from internal TMS. MS: *VG-70-250* spectrometer (Cl by NH_3). DCC = dicylohexylcarbodiimide.

Mitsunobu *Procedure. Method A:* To a soln. of 30 mg (0.082 mmol) of anguidine (**4**) and 19.4 mg (0.074 mmol) of Ph_3P in 5 ml of benzene, 0.0116 ml (0.074 mmol) of diethyl azodicarboxylate and 0.0045 ml (0.079 mmol) of AcOH in 2 ml of benzene were added within 5 min under stirring. The mixture was stirred for 22 h and then heated to reflux for an additional 7 h. No product formation could be detected (TLC) during this procedure: **2** was recovered (*ca.* 90%) by CC.

Method B: To a soln. of 50 mg (0.137 mmol) of **4** in 2 ml of CH_2Cl_2/toluene 1:3, 72 mg (0.275 mmol) of Ph_3P and 19 mg (0.104 mmol) of dried (100°/0.05 Torr, 15 h) $Zn(OAc)_2$ were added. After 5 min, 0.0408 ml (0.260 mmol)

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[3]) The biological tests were carried out by *P. Hiestand, Sandoz AG*, Basel. We are very grateful for his help.

of diethyl azodicarboxylate were added within 3 min to the stirred soln. Stirring was continued for 15 h at r.t. During this period, no product formation could be detected (TLC). The mixture was then heated at 90–100°. After 23 h, the $Zn(OAc)_2$ was filtered off and the filtrate evaporated. CC (CH_2Cl_2/acetone 98:2) afforded 23 mg (41%) of **7** and 7 mg (11%) of **8**.

12,13-Epoxytrichothec-9-ene-3α,4β,15-triyl Triacetate (**7**). Crystallization from CH_2Cl_2, Et_2O, and petroleum ether. M.p. 123.3–124.3°. ^{1}H-NMR (300 MHz): 0.78 (*s*, CH_3(14)); 1.74 (*s*, CH_3(16)); 2.08 (*s*, Ac); 2.13 (*s*, Ac); 2.16 (*s*, Ac); 2.79, 3.09 (*AB*, J = 4, CH_2(13)); 3.88 (*d*, J = 5, H–C(2)); 4.00 (br. *d*, J = 5.5, H–C(11)); 4.11, 4.28 (*AB*, J = 12, CH_2(15)); 5.21 (*dd*, J = 3.5, 5, H–C(3)); 5.49 (br. *d*, J = 5.5, H–C(10)); 5.75 (*d*, J = 3.5, H–C(4)). CI-MS: 426 (100, $[M + NH_4]^+$), 409 ($[M + H]^+$), 349.

4β,15-Diacetoxy-12,13-epoxytrichothec-9-en-3α-yl Ethyl Carbonate (**8**). ^{1}H-NMR (300 MHz): 0.74 (*s*, CH_3(14)); 1.33 (*t*, J = 7, CH_3CH_2O); 1.71 (*s*, CH_3(16)); 2.05 (*s*, Ac); 2.10 (*s*, Ac); 2.78, 3.07 (*AB*, J = 4, CH_2(13)); 3.89 (*d*, J = 5, H–C(2)); 4.01 (br. *d*, J = 5, H–C(11)); 4.04, 4.54 (*AB*, J = 12, CH_2(15)); 4.53 (*q*, J = 7, CH_3CH_2O); 5.08 (*dd*, J = 3.5, 5, H–C(3)); 5.50 (br. *d*, J = 5.5, H–C(10)); 5.80 (*d*, J = 3.5, H–C(4)). ^{13}C-NMR (101 MHz): 6.5; 14.2; 20.8; 21.1; 21.3; 23.2; 27.9; 44.0; 47.2; 48.9; 63.5; 64.1; 64.6; 67.9; 77.5; 79.1; 81.2; 118.3; 140.6; 154.2 (OCOO); 170.4; 170.6. CI-MS: 456 (100, $[M + NH_4]^+$), 440, 439 ($[M + H]^+$), 379, 349, 229.

12,13-Epoxy-3α-[(methanesulfonyl)oxy]trichothec-9-en-15-yl 4-Oxopentanoate (**9**). To a soln. of 50 mg (0.137 mmol) of **6** in 0.5 ml of pyridine at 0°, 0.0213 ml (0.276 mmol) of MsCl were added. Then, the icebath was removed and the soln. stirred at r.t. for an additional 22 h. It was diluted with Et_2O and washed with 1N HCl and H_2O. After evaporation CC (CH_2Cl_2/acetone 9:1) afforded 58 mg (96%) of **9**. ^{1}H-NMR (90 MHz): 0.87 (*s*, CH_3(14)); 1.78 (*s*, CH_3(16)); 2.17 (*s*, CH_3CO); 2.80, 3.05 (*AB*, J = 4, CH_2(13)); 3.05 (*s*, CH_3SO_3); 3.65 (*d*, J = 5, H–C(2)); 3.85, 4.05 (*AB*, J = 12, CH_2(15)); 4.03 (*d*, J = 5, H–C(11)); 5.00 (*m*, H–C(3)); 5.42 (br. *d*, J = 5, H–C(10)). CI-MS: 460 (100, $[M + NH_4]^+$), 444, 364, 344, 327, 231.

12,13-Epoxy-3α-[(toluenesulfonyl)oxy]trichothec-9-en-15-yl 4-Oxopentanoate (**10**). As for **9**, 50 mg (0.137 mmol) of **6** were treated with 52 mg (0.274 mmol) of TsCl, and 0.5 ml of pyridine. CC (Et_2O, petroleum ether 8:2) yielded 69 mg (97%) of **10** as a colourless oil. ^{1}H-NMR (90 MHz): 0.78 (*s*, CH_3(14)); 1.75 (*s*, CH_3(16)); 2.15 (*s*, CH_3CO); 2.48 (*s*, $CH_3C_6H_4$); 2.78, 2.98 (*AB*, J = 4, CH_2(13)); 3.38 (*d*, J = 5, H–C(2)); 3.81, 4.01 (*AB*, J = 12, CH_2(15)); 3.93 (H–C(11)); 4.88 (*m*, H–C(3)); 5.40 (br. *d*, J = 5, H–C(10)); 7.36 (*d*, J = 8, 2 arom. H); 7.83 (*d*, J = 8, 2 arom. H). CI-MS: 536 (100, $[M + NH_4]^+$), 518 ($[M + H]^+$), 438, 428, 231.

12,13-Epoxy-3α-[(trifluoromethylsulfonyl)oxy]trichothec-9-en-15-yl 4-Oxopentanoate (**11**). A soln. of 83 mg (0.22 mmol) of **6** and 0.037 ml (0.456 mmol) of pyridine in 1.5 ml of CH_2Cl_2 was cooled to 0°. After 5 min, a soln. of 0.057 ml (0.347 mmol) of trifluoromethanesulfonic anhydride in 1.5 ml of CH_2Cl_2 was added within 9 min to the stirred soln. After 1 h, the icebath was removed and Et_2O added. It was washed with H_2O. The Et_2O was evaporated and the residue filtered over SiO_2 (Et_2O) to yield 111 mg (98%) of **11**. ^{1}H-NMR (90 MHz): 0.90 (*s*, CH_3(14)); 1.77 (*s*, CH_3(16)); 2.03 (*s*, CH_3CO); 2.93, 3.12 (*AB*, J = 4, CH_2(13)); 3.82 (*d*, J = 5, H–C(2)); 3.95, 4.12 (*AB*, J = 12, CH_2(15)); 4.05 H–C(11)); 5.40 (*m*, H–C(3)); 5.53 (br. *d*, J = 5, H–C(10)). CI-MS: 514 (100, $[M + NH_4]^+$), 364, 134.

12,13-Epoxytrichotheca-3,9-dien-15-yl 4-Oxopentanoate (**12**). ^{1}H-NMR (300 MHz): 0.98 (*s*, CH_3(14)); 1.73 (*s*, CH_3(16)); 2.21 (*s*, CH_3CO); 2.58 (*m*, CH_2CO); 2.77 (*m*, CH_2COO); 2.98, 3.23 (*AB*, J = 4, CH_2(13)); 3.83, 3.93 (*AB*, J = 12, CH_2(15)); 3.87 (H–C(11)); 4.08 (*d*, J = 3, H–C(2)); 5.42 (*d*, J = 5, H–C(10)); 6.13 (*dd*, J = 3, 5, H–C(3)); 6.42 (*d*, J = 5, H–C(4)). CI-MS: 364 ($[M + NH_4]^+$), 347 ($[M + H]^+$), 249 (100).

12,13-Epoxytrichotheca-3,9-dien-15-ol (**13**). ^{1}H-NMR (300 MHz): 1.03 (*s*, CH_3(14)); 1.72 (*s*, CH_3(16)); 2.97, 3.23 (*AB*, J = 4, CH_2(13)); 3.43, 3.55 (*AB*, J = 12, CH_2(15)); 3.85 (br. *d*, J = 5, H–C(11)); 4.05 (*d*, J = 3, H–C(2)); 5.42 (br. *d*, J = 5, H–C(10)); 6.08 (*dd*, J = 6, 3, H–C(3)); 6.47 (*d*, J = 6, H–C(4)). CI-MS: 266 ($[M + NH_4]^+$), 249 ($[M + H]^+$), 231, 201.

12,13-Epoxy-15-hydroxytrichothec-9-en-3α-yl p-*Toluenesulfonate* (**14**). ^{1}H-NMR (90 MHz, CCl_4): 0.88 (*s*, CH_3(14)); 1.75 (*s*, CH_3(16)); 2.52 (*s*, $CH_3C_6H_4$); 2.77, 2.97 (*AB*, J = 4, CH_2(13)); 3.21–3.93 (H–C(2), H–C(11), CH_2(15)); 4.82 (*m*, H–C(3)); 5.33 (br. *d*, J = 6, H–C(10)); 7.30 (*d*, J = 7.5, 2 arom. H); 7.78 (*d*, J = 7.5, 2 arom. H).

*12,13-Epoxy-4β-hydroxy-3α-[(tetrahydro-2*H*-pyranyl)oxy]trichothec-9-en-15-yl Acetate* (**16**). To a soln. of 2.0 g (5.46 mmol) of **15** in 40 ml of CH_2Cl_2, 2.64 ml (32.8 mmol) of pyridine and 1.03 ml (10.9 mmol) of Ac_2O were added and stirred for 15 h. The solvent was evaporated, the residue dissolved in Et_2O and washed with cold 1N HCl, sat. $NaHCO_3$ soln., and H_2O. Then, the Et_2O was evaporated and the residue purified by CC (Et_2O) to yield 1.296 g (58%) of **16** as a foam. IR ($CHCl_3$): 3580 (OH), 2950, 1735 (ester), 1240. ^{1}H-NMR (90 MHz): 0.82, 0.84 (*s*, CH_3(14)); 1.71 (*s*, CH_3(16)); 2.05 (*s*, Ac); 2.76, 3.03 (*AB*, J = 4, CH_2(13)); 4.71, 4.97 (br., acetal); 5.50 (br. *d*, J = 5, H–C(10)).

12,13-Epoxy-4-oxo-3α-[(tetrahydro-2H-pyranyl)oxy]trichothec-9-en-15-yl Acetate (**17**). To a soln. of 0.0354 ml (0.499 mmol) of DMSO in 1 ml of CH_2Cl_2 at −70°, a soln. of 0.0654 ml (0.469 mmol) of $(CF_3CO)_2O$ in 1 ml of CH_2Cl_2 was added within 5 min under stirring. After 10 min, 63.8 mg (0.156 mmol) of **16** in 1 ml of CH_2Cl_2 were added within 10 min. Stirring at −70° was continued for an additional 30 min. Then, 0.0691 ml (0.499 mmol) of Et_3N were added, and 5 min later, the ice-bath was removed. During 50 min, the soln. was allowed to warm up to r.t. The mixture was diluted with CH_2Cl_2 and washed with H_2O (two times). After removal of the solvent, the residue was purified by CC (CH_2Cl_2/acetone 95:5) to afford 56 mg (88%) of **17**. M.p. 170–189° (diastereoisomers). CI-MS: 424 ($[M + NH_4]^+$), 340, 85 (100).

12,13-Epoxy-3α-hydroxy-4-oxotrichothec-9-en-15-yl Acetate (**18**). To a soln. of 250 mg (0.615 mmol) of **17** in 25 ml of MeOH, 16 mg (0.062 mmol) of pyridinium *p*-toluenesulfonate were added and stirred for 15 h at 50°. The solvent was evaporated, the residue dissolved in CH_2Cl_2 and washed with H_2O. After removal of the CH_2Cl_2, the crude product was purified by CC (CH_2Cl_2/acetone 8:2) to yield 188 mg (95%) of **18**. M.p. 163–168° (crystallized from CH_2Cl_2/Et_2O). ^{1}H-NMR (90 MHz): 0.94 (*s*, CH_3(14)); 1.72 (br. *s*, CH_3(16)); 2.06 (*s*, Ac); 2.88 (*d*, *J* = 3.5, OH, exchangeable with D_2O); 2.95, 3.24 (*AB*, *J* = 4, CH_2(13)); 3.78 (br. *d*, *J* = 5, H–C(11)); 3.84, 4.02 (*AB*, *J* = 12, CH_2(15)); 4.07 (*d*, *J* = 5, H–C(2)); 4.30 (*dd*, *J* = 3.5, 5, H–C(3); after exchange with D_2O, *d*, *J* = 5); 5.44 (br. *d*, *J* = 5, H–C(10)). CI-MS: 340 (100, $[M + NH_4]^+$), 323 ($[M + H]^+$), 305, 263, 245. Anal. calc. for $C_{17}H_{22}O_6$ (322.35): calc. C 63.34, H 6.88; found: C 62.78, H 7.06.

12,13-Epoxy-4β-hydroxytrichothec-9-en-15-yl Acetate (**22**). As for **16**, with 100 mg (0.376 mmol) of verrucarol (**21**), 0.182 ml (2.253 mmol) of pyridine, 0.071 ml (0.751 mmol) of Ac_2O, and 2.8 ml of CH_2Cl_2. CC (Et_2O) yielded 73 mg (63%) of **22**. M.p. 149–150° (crystallized from CH_2Cl_2/Et_2O). IR (KBr): 3450, 1720, 1675, 1385, 1255, 1070. ^{1}H-NMR (90 MHz): 0.87 (*s*, CH_3(14)); 1.71 (*s*, CH_3(16)); 2.06 (*s*, Ac); 2.80, 3.11 (*AB*, *J* = 4, CH_2(13)); 3.60 (*d*, *J* = 5.5, H–C(2)); 3.82 (br. *d*, *J* = 5, H–C(11)); 3.92, 4.13 (*AB*, *J* = 12, CH_2(15)); 4.48 (*m*, H–C(4)); 5.41 (br. *d*, *J* = 5, H–C(10)).

12,13-Epoxy-4-oxotrichothec-9-en-15-yl Acetate (**19**). As for **17**, with 0.837 ml (11.81 mmol) of DMSO, 1.55 ml (11.07 mmol) of $(CF_3CO)_2O$, 1.138 g (3.69 mmol) of **22**, 1.64 ml (11.81 mmol) of Et_3N, and 45 ml of CH_2Cl_2. CC (Et_2O) yielded 1.077 g (95%) of **19**. ^{1}H-NMR (90 MHz): 0.93 (*s*, CH_3(14)); 1.73 (br. *s*, CH_3(16)); 2.03 (*s*, Ac); 2.63 (*m*, CH_2(3)); 2.95, 3.23 (*AB*, *J* = 4, CH_2(13)); 3.83 (*d*, *J* = 5, H–C(11)); 3.87, 4.02 (*AB*, *J* = 12, CH_2(15)); 4.11 (*m*, H–C(2)); 5.47 (br. *d*, *J* = 5, H–C(10)).

Reduction of **19** *by* $NaBH_4$. To 36 mg (0.118 mmol) of **19** in 1.5 ml of EtOH, 4.9 mg (0.129 mmol) of $NaBH_4$ were added and stirred for 2 h. To achieve a complete conversion, further 4.9 mg of $NaBH_4$ were added. After 6 h, *ca.* 0.3 ml of 1N HCl were slowly added (pH 2–3), and the pH was adjusted to 6–7 with sat. $NaHCO_3$ soln. The aq. soln. was extracted with CH_2Cl_2 (3 times). After evaporation of the solvent, CC (CH_2Cl_2/acetone 9:5 to 1:1) afforded 13 mg (31%) of **23** and 14.5 mg (40%) of **20**.

Reduction of **19** *by* $LiAlH(t\text{-}OBu)_3$. To a soln. of 115 mg (0.375 mmol) of **19** in 5 ml of THF, 187 mg (0.735 mmol) of $LiAlH(t\text{-}OBu)_3$ were added and stirred for 17 h. An additional 187 mg of $LiAlH(t\text{-}OBu)_3$ were added to complete the reduction. After 6 h, *ca.* 4.5 ml of 1N HCl were carefully added dropwise to the stirred soln. The pH was adjusted to 3–4 with sat. $NaHCO_3$ soln. After 30 min, the mixture was extracted with CH_2Cl_2 (3 times). Removal of the solvent and subsequent CC (CH_2Cl_2/acetone 9:1) of the residue afforded 91 mg (79%) of **23**.

12,13-Epoxy-4α-hydroxytrichothec-9-en-15-yl Acetate (**23**). M.p. 213–215° (subl.). $[\alpha]_D^{21} = -22.9$ (*c* = 0.450, $CHCl_3$). ^{1}H-NMR (90 MHz): 0.92 (*s*, CH_3(14)); 1.72 (br. *s*, CH_3(16)); 2.05 (*s*, Ac); 2.47 (*d*, *J* = 5, OH, exchangeable with D_2O); 2.54 (*m*, CH_2(3)); 2.78, 3.05 (*AB*, *J* = 4, CH_2(13)); 3.66 (*d*, *J* = 5.5, H–C(2)); 3.79, 5.24 (*AB*, *J* = 12, CH_2(15)); 4.20 (br. *d*, *J* = 5, H–C(11)); 4.31 (*ddd*, *J* = 5, 5, 11, H–C(4)); 5.46 (br. *d*, *J* = 5, H–C(10)). CI-MS: 326 ($[M + NH_4]^+$), 309 ($[M + H]^+$), 291, 249 (100). Anal. calc. for $C_{17}H_{24}O_5$ (308.37): C 66.21, H 7.84; found: C 66.23, H 8.10.

12,13-Epoxytrichothec-9-ene-4α,15-diol (= *4-Epiverrucarol;* **20**). To a soln. of 411 mg (1.33 mmol) of **23** in 15 ml of MeOH, 8 ml (8.00 mmol) of 1N NaOH were added and stirred for 40 min. The pH was adjusted to 7–8 by addition of 1N HCl. The aq. soln. was extracted with CH_2Cl_2, the org. layer washed with H_2O, and the solvent evaporated. Crystallization from CH_2Cl_2/hexane yielded 335 mg (94%) of **20**. M.p. 169–172°. $[\alpha]_D^{21} = +38.8$ (*c* = 0.250, $CHCl_3$). IR (KBr): 3305, 3210, 2960, 1675. ^{1}H-NMR (400 MHz): 0.89 (*s*, CH_3(14)); 1.73 (*s*, CH_3(16)); 2.03 (*m*, CH_2(7), CH_2(8)); 2.49 (*m*, H–C(3)); 2.81, 3.10 (*AB*, *J* = 4, CH_2(13)); 3.57, 3.62 (*AB*, *J* = 12, CH_2(15)); 3.60 (OH, exchangeable with D_2O); 3.68 (*d*, *J* = 5.5, H–C(2)); 4.15 (*dd*, *J* = 6, 11, H–C(4)); 4.53 (br. *d*, *J* = 5.5, H–C(11)); 4.85 (br., OH; exchangeable with D_2O); 5.58 (br. *d*, *J* = 5.5, H–C(10)). CI-MS: 248 ($[M + NH_4]^+$), 267 ($[M + H]^+$), 249 (100). Anal. calc. for $C_{15}H_{22}O_4$ (266.33): C 67.65, H 8.33; found: C 67.43, H 8.42.

Condensation of **20** *with 5-[((tert-Butyl)dimethylsilyl)oxy]-3-methyl-2-[(tetrahydro-2H-pyranyl)oxy]-pentanoic Acid* (**25**). A soln. of 97 mg (0.365 mmol) of **20**, 139 mg (0.401 mmol) of **25**, and 10 mg (0.082 mmol) of (Me_2N)Py in 3 ml of CH_2Cl_2 was cooled to 0°. After 10 min, 98 mg (0.475 mmol) of DCC were added. The soln. was

stirred for 1 h, then the ice-bath was removed. After an additional stirring at r.t. for 18 h, the precipitated urea was filtered off. The CH_2Cl_2 was evaporated and the residue purified by flash chromatography (SiO_2, 0.035–0.070 mm; CH_2Cl_2/acetone 95:5) 99 mg (46%) of *12,13-epoxy-15-hydroxytrichothec-9-en-4α-yl 5-[(*(tert-*butyl)dimethylsilyl)oxy]-3-methyl-2-[(tetrahydro-2*H*-pyranyl)oxy]pentanoate* (**27**) as a mixture of THP diastereoisomers (ratio 2:1). ^{1}H-NMR (400 MHz): 0.06 (*s*, $(CH_3)_2Si$); 0.90 (*s*, (*t*-Bu)Si); 0.95 (*s*, $CH_3(14)$); 0.99, 1.02 (*d*, $J = 7$, $CH_3(3')$); 1.73 (br. *s*, $CH_3(16)$); 2.67, 2.75 (2*m*, $CH_2(3)$); 2.84, 3.11 (*AB*, $J = 4$, $CH_2(13)$); 5.07, 5.18 (2*dd*, $J = 6$, 10.5, H–C(4)); 5.50 (*m*, H–C(10)). CI-MS: 595 ($[M + H]^+$), 511, 481, 263, 249, 217, 85 (100).

Condensation of **20** *with AcOH*. As for **27** (see above), with 90 mg (0.338 mmol) of **20**, 213 µl (0.372 mmol) of AcOH, 9 mg (0.074 mmol) of (Me_2N)Py, 91 mg (0.439 mmol) of DCC, and 3 ml of CH_2Cl_2. CC (SiO_2, 0.030–0.075 mm; Et_2O/hexane/MeOH 49:49:2) yielded 74 mg (71%) of **28**, 10 mg (9.6%) of **23**, and 7.5 mg (8.4%) of **29**.

12,13-Epoxy-15-hydroxytrichothec-9-en-4α-yl Acetate (**28**). M.p. 172–174° (from CH_2Cl_2/Et_2O/MeOH). $[\alpha]_D^{20} = +37.7$ ($c = 0.310$, $CHCl_3$). ^{1}H-NMR (400 MHz): 0.99 (*s*, $CH_3(14)$); 1.75 (br. *s*, $CH_3(16)$); 1.83 (*dd*, $J = 5$, 16, H–C(3)); 2.16 (*s*, Ac); 2.68 (*ddd*, $J = 5$, 11, 16, H–C(3)); 2.85, 3.11 (*AB*, $J = 4$, $CH_2(13)$); 3.56, 4.18 (br. *AB*, $J = 12$, $CH_2(15)$); 3.71 (*d*, $J = 5.5$, H–C(2)); 4.09 (br. *d*, $J = 5$, H–C(11)); 5.13 (*dd*, $J = 5$, 11, H–C(4)); 5.49 (br. *d*, $J = 5$, H–C(10)). CI-MS: 326 ($[M + NH_4]^+$), 309 ($[M + H]^+$), 249, 169 (100).

12,13-Epoxytrichothec-9-ene-4α,15-diyl Diacetate (**29**). M.p. 157–159° (from CH_2Cl_2/hexane). $[\alpha]_D^{20} = +6.7$ ($c = 0.360$, $CHCl_3$). ^{1}H-NMR (400 MHz): 0.92 (*s*, $CH_3(14)$); 1.73 (*s*, $CH_3(16)$); 2.04 (*s*, Ac); 2.17 (*s*, Ac); 2.67 (*ddd*, $J = 5$, 11, 16, H–C(3)); 2.84, 3.10 (*AB*, $J = 4$, $CH_2(13)$); 3.72 (*d*, $J = 5$, H–C(2)); 3.79, 4.99 (*AB*, $J = 12$, $CH_2(15)$); 4.07 (br. *d*, $J = 5.5$, H–C(11)); 5.17 (*dd*, $J = 5$, 11, H–C(4)); 5.45 (br. *d*, $J = 5.5$, H–C(10)). CI-MS: 368 ($[M + NH_4]^+$), 351 ($[M + H]^+$), 291, 169 (100). Anal. calc. for $C_{19}H_{26}O_6$ (350.41): C 65.13, H 7.48; found: C 64.87, H 7.73.

*12,13-Epoxy-15-hydroxytrichothec-9-en-4α-yl 2-(Trimethylsilyl)ethyl (2′*Z*,4′*E*)-Hexa-2,4-diendioate* (**30**). As above, with 83 mg (0.312 mmol) of **20**, 83 mg (0.343 mmol) of **26**, 3.8 mg (0.031 mmol) of (Me_2N)Py, 77 mg (0.374 mmol) of DCC, and 2.5 ml of CH_2Cl_2. CC (SiO_2, 0.030–0.075 µm; CH_2Cl_2/acetone 95:5) yielded 94 mg (61%) of **30** and 44 mg (29%) of **31**. **30**: M.p. 110–112° (from Et_2O/hexane). $[\alpha]_D^{20} = +25.7$, $[\alpha]_{436}^{20} = +43.3$ ($c = 0.505$, $CHCl_3$). IR (KBr): 3500 (OH), 2950, 2900, 1725, 1715 (ester), 1600. ^{1}H-NMR (400 MHz): 0.05 (*s*, $(CH_3)_3Si$); 1.05 (*m*, CH_2Si); 1.07 (*s*, $CH_3(14)$); 1.73 (br. *s*, $CH_3(16)$); 1.89 (*dd*, $J = 5$, 15.5, H–C(3)); 1.98 (br. *s*, OH, exchangeable with D_2O); 2.77 (*ddd*, $J = 5.5$, 11, 15.5, H–C(3)); 2.87, 3.12 (*AB*, $J = 4$, $CH_2(13)$); 3.52 (*dd*, $J = 5$, 12, H–C(15); after D_2O exchangeable, *d*, $J = 12$); 3.73 (*d*, $J = 5.5$, H–C(2)); 4.03 (*d*, $J = 5.5$, H–C(11)); 4.25 (*dd*, $J = 5$, 12, H–C(15); after D_2O exchange, *d*, $J = 12$); 4.28 (*m*, OCH_2CH_2Si); 5.18 (*dd*, $J = 5$, 11, H–C(4)); 5.45 (br. *d*, $J = 5.5$, H–C(10)); 6.02 (*d*, $J = 11.5$, H–C(2)); 6.14 (*d*, $J = 15.5$, H–C(5′)); 6.70 (*dd*, $J = 11.5$, 11.5, H–C(3′)); 8.31 (*dd*, $J = 11.5$, 15.5, H–C(4′)). CI-MS: 508 ($[M + NH_4]^+$), 491 ($[M + H]^+$), 463, 249, 90 (100).

*12,13-Epoxy-4α-hydroxytrichothec-9-en-15-yl 2-(Trimethylsilyl)ethyl (2′*Z*,4′*E*)-Hexa-2,4-diendioate* (**31**). ^{1}H-NMR (400 MHz): 0.05 (*s*, $(CH_3)_3Si$); 0.91 (*s*, $CH_3(14)$); 0.99 (*m*, CH_2Si); 1.72 (*s*, $CH_3(16)$); 1.96 (*dd*, $J = 5$, 15, H–C(3)); 2.53 (*ddd*, $J = 5$, 10.5, 15, H–C(3)); 2.67 (br. *d*, $J = 4.5$, OH); 2.79, 3.05 (*AB*, $J = 4$, $CH_2(13)$); 3.67 (*d*, $J = 5.5$, H–C(2)); 3.93, 5.36 (*AB*, $J = 12$, $CH_2(15)$); 4.23 (br. *d*, $J = 5.5$, H–C(11)); 4.27 (*m*, H–C(4), OCH_2CH_2Si); 5.45 (br. *d*, $J = 5.5$, H–C(10)); 5.94 (*d*, $J = 11.5$, H–C(2′)); 6.10 (*d*, $J = 15.5$, H–C(5′)); 6.64 (*dd*, $J = 11.5$, H–C(3′)); 8.31 (*dd*, $J = 11.5$, 15.5, H–C(4′)).

15-{*[5′-[(*tert*-Butyl)dimethylsilyl)oxy]-3′-methyl-2′-[(tetrahydro-2*H*-pyranyl)oxy]pentyl]oxy*}*-12,13-epoxytrichothec-9-en-4α-yl 2-(Trimethylsilyl)ethyl (2″*E*,4″*Z*)-Hexa-2,4-diendioate* (**32**). As above, with 131 mg (0.267 mmol) of **30**, 184 mg (0.534 mmol) of **25**, 122 mg (0.587 mmol) of DCC, 6.5 mg (0.053 mmol) of (Me_2N)Py, and 4 ml of CH_2Cl_2. The mixture was stirred for 21 h. Then, 46 mg (0.136 mmol) of **25** were added and stirred for an additional 20 h. After filtration of the precipitated urea, the solvent was evaporated and the residue purified by CC (petroleum ether/Et_2O 1:1) yielding 253 mg of a mixture which consisted predominantly of **32**. ^{1}H-NMR (400 MHz; diastereoisomers): 0.04, 0.06, 0.08 $(CH_3)_3Si$, $(CH_3)_2Si$; 0.89, 0.90 (2*s*, $CH_3(14)$, (*t*-BuSi); 2.75 (*m*, H–C(3)); 2.84 or 2.86 and 3.13 (*AB*, $J = 4$, $CH_2(13)$); 3.93 and 4.82, 4.01 and 4.94 (2*AB*, $J = 12$, $CH_2(15)$); 4.57, 4.65 (br., 1 H, acetal); 5.21 (*m*, H–C(4)); 5.46 (br. *d*, H–C(10)); 6.03 (*d*, $J = 11.5$, H–C(2″)); 6.13, 6.14 (2*d*, $J = 15.5$, H–C(5″)); 6.71, 6.72 (2*dd*, $J = 11.5$, 11.5, H–C(3″)); 8.43 (*dd*, $J = 11.5$, 15.5, H–C(4″)). CI-MS: 837 (3.9, $[M + NH_4]^+$), 820 (0.4, $[M + H]^+$), 708, 493, 249, 217, 85 (100).

4-Epiverrucarin A (**24**). To a soln. of 83 mg of **32** (exact amount not determined, see above) in 2 ml of THF, 158 mg (0.505 mmol) of Bu_4NF were added and stirred for 2 h. The soln. was diluted with Et_2O (35 ml) and washed with H_2O (5 ml). The Et_2O was evaporated and the residue dried for 2 h (20°/0.02–0.04 Torr, P_2O_5): 55 mg of **33** which were immediately redissolved in 46 ml of CH_2Cl_2. Then, 64 µl (0.455 mmol) of Et_3N, and after 10 min, 44 µl (0.364 mmol) of pivaloyl chloride were added. The soln. was stirred for 10 min, and 11 mg (0.091 mmol) of (Me_2N)Py were added. Stirring was continued for 2 h (discolouration to yellow). The solvent was removed and the product purified by CC (Et_2O/petroleum ether 7:3), yielding 24 mg of an oil which was dissolved in 2 ml of EtOH. Then, 8.9 mg

(0.036 mmol) of pyridinium *p*-toluenesulfonate were added, and the soln. was heated at 50° for 20 h. The solvent was evaporated and the residue purified by prep. TLC (Et_2O): 13 mg (29% from **30**) of **24** as an oil. ^{1}H-NMR (400 MHz): 1.09 (*d*, *J* = 7, CH_3(6′)); 1.20 (*s*, CH_3(14)); 1.66 (*m*, H–C(8)); 1.71 (*s*, CH_3(16)); 1.81 (*m*, H–C(7)); 1.88 (*m*, 2 H–C(4′)); 1.96 (*m*, H–C(3)); 1.96 (*m*, H–C(3′)); 2.33 (*m*, H–C(7)); 2.40 (*m*, H–C(8)); 2.69 (br. *d*, *J* = 5.5, OH); 2.89 (*ddd*, *J* = 5, 10.5, 16, H–C(3)); 2.90, 3.15 (*AB*, *J* = 4, CH_2(13)); 3.76 (*d*, *J* = 5.5, H–C(2)); 3.86 (*m*, H–C(2′)); 3.89 (*m*, H–C(5′)); 4.05 (br. *d*, *J* = 5.5, H–C(11)); 4.23, 4.66 (*AB*, *J* = 12.5, CH_2(15)); 4.81 (*m*, H–C(5′)); 5.05 (*dd*, *J* = 10.5, 5, H–C(4)); 5.43 (br. *d*, *J* = 5.5, H–C(10)); 6.07 (*d*, *J* = 15.5, H–C(5″)); 6.09 (*d*, *J* = 11, H–C(2″)); 6.63 (*dd*, *J* = 11, H–C(3″)); 7.60 (*dd*, *J* = 11, 15.5, H–C(4″)). ^{13}C-NMR (101 MHz): 12.2 (C(14)); 17.1 (C(6′)); 21.9 (C(7)); 23.2 (C(16)); 28.1 (C(4′)); 32.3 (C(8)); 34.8 (C(3)); 35.0 (C(3′)); 44.0 (C(6)); 47.5 (C(5)); 49.1 (C(13)); 62.3 (C(5′)); 64.9 (C(12)); 66.0 (C(15)); 66.7 (C(11)); 74.5 (C(2′)); 77.4 (C(2)); 83.3 (C(4)); 118.2 (C(10)); 126.1 (C(2″)); 128.1 (C(5″)); 136.4 (C(3″)); 137.9 (C(4″)); 141.4 (C(9)); 165.4, 165.7 (C(1″), C(6″)); 175.3 (C(1′)). CI-MS: 520 ($[M + NH_4]^+$), 503 ($[M + H]^+$), 485, 249 (100).

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