198. 19-*O*-Acetylchaetoglobosin B and 19-*O*-Acetylchaetoglobosin D, Two New Metabolites of *Chaetomium globosum*

by **Alessandro Probst** and **Christoph Tamm**[1])

Institut für Organische Chemie der Universität Basel, St. Johanns-Ring 19, CH-4056 Basel

(26.VI.81)

Summary

Two new metabolites have been isolated from cultures of *Chaetomium globosum*. The structures of 19-*O*-acetylchaetoglobosin B (**4**) and 19-*O*-acetylchaetoglobosin D (**5**) are assigned. The ^{13}C-NMR. spectra of chaetoglobosin A (**1**), 19-*O*-acetylchaetoglobosin A (**2**), chaetoglobosin C (**3**), 19-*O*-acetylchaetoglobosin B (**4**), 19-*O*-acetylchaetoglobosin D (**5**) and of cytochalasin G (**6**), a (3-indolyl)-[11]cytochalasan isolated from *Pseudeurotium zonatum*, have been interpreted.

Chaetoglobosin A (**1**), 19-*O*-acetylchaetoglobosin A (**2**), chaetoglobosin B, C (**3**), D, E, F, G and J [1], members of the growing family of the cytochalasans, have been isolated from cultures of *Chaetomium globosum*. Some of them display interesting biological effects [2]. We report here the structural determination of two additional metabolites isolated from culture filtrates of the same microorganism. On the basis of the spectra and chemical transformations we assigned the structures of 19-*O*-acetylchaetoglobosin B (**4**) and 19-*O*-acetylchaetoglobosin D (**5**).

The culture filtrates of *Chaetomium globosum* (Strain *Lederle* H-124)[2]) were extracted with methyline chloride and the major metabolites, chaetoglobosin A (**1**) and 19-*O*-acetyl-chaetoglobosin A (**2**) separated by crystallization. The remaining extract was purified by column chromatography on silica gel. In the fractions eluted between those containing the rest of metabolites **1** and **2**, chaetoglobosin C (**3**), 19-*O*-acetylchaetoglobosin B (**4**) and D (**5**) were enriched. Crystallization of chaetoglobosin C (**3**) led to a mixture of **4** and **5**, which were separated and obtained pure by chromatography on silica gel (**5** being more polar) using the chromatotron.

The mass spectra of **4**, **5** and **2** are very similar. The peak of the molecular ion appears at *m/z* 570. Fragments at *m/z* 528 ($M^+ - 42$, loss of acetyl), 130 (indolylmethyl group), 103 (fragmentation of the indolylmethyl group), 60 (acetic acid) and 43 (acetyl), indicated for **4** and **5** the same molecular formula ($C_{34}H_{38}N_2O_6$) as for 19-*O*-acetylchaetoglobosin A (**2**). The UV. spectra are also practically super-

[1]) Author to whom correspondence should be addressed.

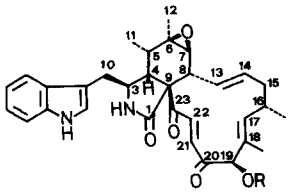
[2]) We thank Dr. *G.A. Ellestad, Lederle* Laboratories, Pearl River, N.Y., U.S.A. for the gift of this strain.

0018-019X/81/7/2056-09$01.00/0

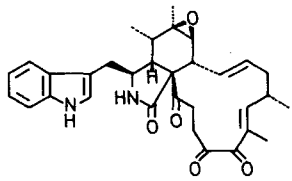
imposable on that of 19-*O*-acetylchaetoglobosin A (**2**). Solutions of 19-*O*-acetylchaetoglobosin B (**4**) and D (**5**) in ethanol show absorption maxima corresponding to the indole chromophore.

The IR. spectra of both **4** and **5** exhibit a broad absorption between 3200 and 3600 cm^{-1}, indicating the presence of a hydroxyl group. Further absorptions are observed at 1730 cm^{-1} and between 1670 and 1710 cm^{-1} (acetyl, lactam and conjugated carbonyl groups), and at 970 cm^{-1} ((*E*)-substituted double bonds). The spectrum of 19-*O*-acetylchaetoglobosin D (**5**) shows additional absorption at 900 cm^{-1}, indicating the presence of a terminal double bond.

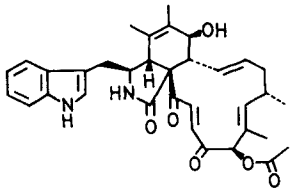
Most useful for the structural determination of the new metabolites were ^1H- and ^{13}C-NMR. spectroscopy combined with spin-spin decoupling. In *Table 1* the assignments of the H-atoms of 19-*O*-acetylchaetoglobosins A (**2**), B (**4**) and D (**5**) are listed. The spectrum of **5** differs from that of **2** essentially in the chemical shifts and coupling constants of the H-atoms at C(3), C(5), C(7), C(8) and C(12). The singlet for $H_3C(12)$, appearing at 1.28 ppm in **2**, is not observed in **5** whereas three new broad singlets at 5.41, 5.19 and 1.88 ppm, the latter exchangeable with D_2O, indicate the presence of an exocyclic double bond at C(12) and of a hydroxyl group. The downfield shift of 1.5 ppm for H–C(7) indicates the presence of the new hydroxyl group at this position. The downfield shift of 1.0 ppm for H–C(5), due to the allylic double bond, smaller shifts for H–C(3) and H–C(8), due to the conformational change of the isoindolone unit (**5** shows a coupling constant $^3J_{7,8}$ of 10 Hz, indicating a *trans*-diaxial disposition of the H-atoms, while **2** shows



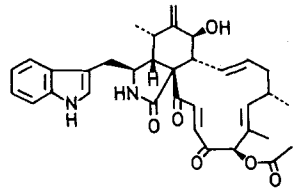
R = H: Chaetoglobosin A (**1**)
R = Ac: 19-*O*-Acetylchaetoglobosin A (**2**)



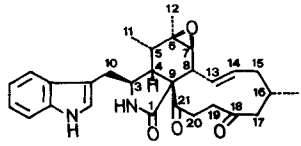
Chaetoglobosin C (**3**)



19-*O*-Acetylchaetoglobosin B (**4**)



19-*O*-Acetylchaetoglobosin D (**5**)



Cytochalasin G(**6**)

a $^3J_{7,8}$ of 5 Hz), and the fact that the resonances of the H-atoms of the macrocyclic unit are approximately identical in both spectra, suggests for **5** the proposed structure.

In an analogous manner the structure of 19-*O*-acetylchaetoglobosin B (**4**) can be deduced. The shifts to lower field of $H_3C(11)$ and $H_3C(12)$, which appear as broad singlets, the signal at 1.88 ppm (exchangeable with D_2O), and the shifts of the H-atoms at C(3), C(4) and C(7), suggest structure **4** for the new metabolite.

Table 1. *400 MHz ^{1}H-NMR.*[a]) *data ($CDCl_3$) of the 19-O-acetylchaetoglobosins A* (**2**), *B* (**4**) *and D* (**5**)

H-atom	19-*O*-acetylchaetoglobosin		
	A (**2**)	B (**4**)	D (**5**)
H–N(2)	6.05, br.*s*	5.84, br.*s*	5.88, br.*s*
H–C(3)	3.80, *m*	3.55, *m*	3.48, *m*
H–C(4)	2.93, *d*×*d*	3.24, br.*s*	2.96, ψt
	J = 3 and 5	J < 1	J = 5 and 5
H–C(5)	1.84, *m*	–	2.84, *m*
H–C(7)	2.80, *d*	3.92, br.*d*	3.95, br.*d*
	J = 5	J = 10	J = 10
H–C(8)	2.14, *d*×*d*	2.09, ψt	2.33, ψt
	J = 10 and 5	J = 10 and 10	J = 10 and 10
2 H–C(10)	2.91, *d*×*d*	2.86, *d*×*d*	3.04, *d*×*d*
	^2J = 15, ^3J = 4	^2J = 14, ^3J = 6	^2J = 14, ^3J = 3.5
	2.67, *d*×*d*	2.71, *d*×*d*	2.62, *d*×*d*
	^2J = 15, ^3J = 7.5	^2J = 14, ^3J = 8	^2J = 14, ^3J = 9
3 H–C(11)	1.22, *d*	1.63, br.*s*	1.31, *d*
	J = 7		J = 7
3 H–C(12)	1.28, *s*	1.72, br.*s*	5.41, br.*s*
(2 H–C(12))			5.19, br.*s*
H–C(13)	6.08, *d*×*d*	6.18, *d*×*d*	5.92, *d*×*d*
	J = 15 and 10	J = 16 and 10	J = 15 and 10
H–C(14)	5.18, *m*	5.28, *m*	5.31, *m*
2 H–C(15)	2.2–2.3, *m*	2.3–2.4, *m*	2.3–2.4, *m*
	1,9–2.0, *m*	2.0–2.1, *m*	2.0–2.1, *m*
H–C(16)	2.4–2.6, *m*	2.4–2.6, *m*	2.4–2.6, *m*
H–C(17)	5.66, *d*×*d*	5.64, *d*×*d*	5.70, *d*×*d*
	^3J = 9, ^4J = 1	^3J = 10, ^4J = 1	^3J = 9.5, ^4J = 1
H–C(19)	5.90, *s*	5.87, *s*	5.98, *s*
H–C(21)	7.55, *d*	7.54, *d*	7.88, *d*
	J = 17	J = 17	J = 17
H–C(22)	6.61, *d*	6.73, *d*	6.55, *d*
	J = 17	J = 17	J = 17
H_3C–C(16)	0.99, *d*	1.02, *d*	0.99, *d*
	J = 6.5	J = 6.5	J = 7
H_3C–C(18)	1.45, *d*	1.51, *d*	1.48, *d*
	^4J = 1	^4J = 1	^4J = 1
3 H–*O*(19)–acetyl	2.17, *s*	2.17, *s*	2.16, *s*
H–N(1′)	8.31, br.*s*	8.20, br.*s*	8.30, br.*s*
5 H-indolyl	7.0–7.5	7.0–7.5	7.0–7.5
H–O(7)	–	1.88, br.*s*	1.88, br.*s*

[a]) We thank Dr. *H.P. Kellerhals*, Mr. *R. Hoerdt* and Mr. *J. Sonderegger*, *Spectrospin* AG., Fällanden/ZH, for the measurement of these spectra.

Further support for the proposed structures was provided by the ^{13}C-NMR. spectra. The ^{13}C-NMR. spectra of chaetoglobosin A (**1**), 19-*O*-acetylchaetoglobosin A

Table 2. *^{13}C-NMR. data of the chaetoglobosins A* (**1**), *C*(**3**), *the 19-O-acetylchaetoglobosins A* (**2**), *B* (**4**), *D* (**5**) *and cytochalasin G* (**6**)

C-Atom	Chaetoglobosin		19-*O*-Acetylchaetoglobosin			Cytochalasin G (**6**)[c]
	A (**1**)[a]	C (**3**)[b]	A (**2**)[a]	B (**4**)[c]	D (**5**)[c]	
C(1)	173.2	173.9	173.6	172.4	171.9	173.3
C(3)	52.8	52.3	52.8	57.8	52.0	51.8
C(4)	46.8	48.4	47.3	46.9	44.8	47.4
C(5)	36.3	36.2	36.4	125.2	31.3	36.3
C(6)	58.0	56.6	58.0	133.7	151.0	57.0
C(7)	62.4	60.5	62.3	67.7	70.1	60.8
C(8)	48.8	48.4	48.3	50.1	47.9	49.1
C(9)	63.4	62.4	63.4	60.8	61.3	64.1
C(10)	33.7	32.0	34.0	31.7	31.8	32.5
C(11)	13.2	12.3	13.3	14.4	13.4	12.1
C(12)	19.7	19.1[e]	19.7	16.9	111.4	19.0
C(13)	128.3	127.2	128.3	127.2	128.3	128.5
C(14)	133.1	133.1	133.4	133.7[f]	133.1[f]	132.8
C(15)	41.7	–[d]	41.3	–[d]	–[d]	42.2
C(16)	32.0	32.6	32.2	32.0	32.3	27.4
C(17)	139.9	155.6	142.5	141.7	141.9	46.2
C(18)	132.3	131.1	127.6	127.2	127.4	206.6[j]
C(19)	81.7	196.1	83.4	83.1	82.8	35.7[k]
C(20)	201.4	205.3	194.8	194.0	194.2	36.8[k]
C(21)	131.6	32.0	133.4	134.1[f]	133.3[f]	207.5[j]
C(22)	136.1	37.1	134.8	135.2	136.0	-
C(23)	197.1	208.1	196.9	199.8	198.9	-
C(16)CH_3	20.9	19.4[e]	20.7	20.3	20.3	22.4
C(18)CH_3	10.5	10.0	11.5	11.1	11.1	-
Acetyl–CH_3	-	-	20.7	20.6	20.6	-
Acetyl–CO	-	-	170.1	169.2	169.3	-
C(2′)[g]	121.7	120.9	122.3	121.0	120.8	120.7
C(3′)	109.4	108.2	110.1	109.9	109.4	108.4
C(3a′)	127.4	127.7	127.3	126.1	126.4	127.7
C(4′)[h]	118.4	118.4	118.3	118.1	118.0	118.5
C(5′)[g]	124.0	125.1	123.7	123.5	124.0	125.0
C(6′)[h]	119.3	118.7	119.9.	118.4	118.4	118.5
C(7′)	111.7	111.4	111.7	111.4	111.4	111.0
C(7a′)	136.6	135.9	136.5	136.2	136.2	136.1

[a] In $CDCl_3$.
[b] In $(CH_3)_2SO$ (with D_2O as external deuterium lock).
[c] In $(CD_3)_2SO$.
[d] The signal is covered by the solvent signal.
[e] Assignments of C(12) and C(16)CH_3 may be interchanged.
[f] Assignments of C(14) and C(21) may be interchanged.
[g] Assignments of C(2′) and C(5′) may be interchanged.
[h] Assignments of C(4′) and C(6′) may be interchanged.
[j] Assignments of C(18) and C(21) may be interchanged.
[k] Assignments of C(19) and C(20) may be interchanged.

(**2**) and cytochalasin G (**6**), a (3-indolyl)-[11]cytochalasan from *Pseudeurotium zonatum* (Strain CMI 171.019) [3], were measured especially with a view to biogenetic incorporation experiments with ^{13}C-labelled precursors. Comparison of these spectra and that of chaetoglobosin C (**3**) with those of the new metabolites confirms the proposed structures. The chemical shifts of the C-atoms of **1**–**6** are compared in *Table 2*. In the spectra of chaetoglobosin A (**1**) and 19-*O*-acetylchaetoglobosin A (**2**) the signals of the aromatic C-atoms were identified by comparison with the data from 3-methylindole [4a]. The remaining singlet in the olefinic region is assigned to C(18). The additional *O*-acetyl group of **2** shifts, as compared to **1**, the signals of C(17)–C(23) [5a], while the chemical shifts of C(13) and C(14), which appear with nearly identical frequencies as in cytochalasins B and D [6], remain unchanged. This fact allowed the complete assignment of the olefinic and carbonyl C-atoms in both spectra. The observation that the 3-indolyl-group shifts C(10) about 9.5 ppm to higher field as with the phenyl group [5b] of cytochalasins B and D [6] allowed the distinction of the two triplets of C(10) and C(15). The atoms C(4), C(7), C(8), C(11) and C(12) were identified by comparison with the data of cytochalasin G (**6**). The unambiguous distinction of C(6) and C(9), and of C(5) and C(16) was achieved by the incorporation of doubly labelled sodium-[1,2-$^{13}C_2$]-acetate [7]. Finally, comparison of the spectra of **1** and **2** allowed the assignment of the methyl groups at C(18) and of the *O*-acetyl group.

The chemical shifts of the isoindolone unit of cytochalasin G (**6**) and of **1** and **2** are nearly identical. Single frequency decoupling experiments with **6** allowed the unambiguous assignment of the resonance frequencies of C(3), C(4), C(7), C(10), C(12), C(13) and C(14) in the three spectra. From comparison with the spectra of **1** and **2**, C(5), C(6), C(9) and C(15) followed; C(17) was identified by comparison of model compounds [4b], while C(19)/C(20) and C(18)/C(21) could not by differentiated.

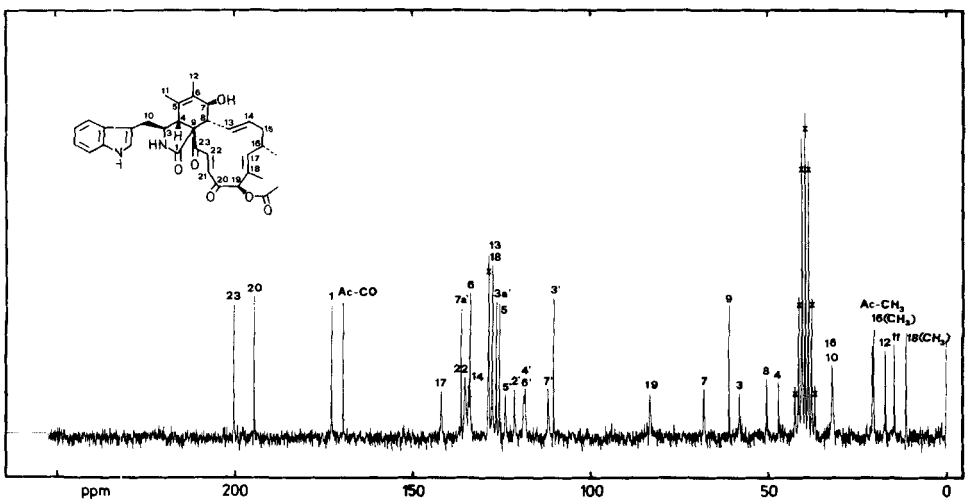


Fig. 1. *^{13}C-NMR. spectrum of 19-O-acetylchaetoglobosin B* (**4**) *in* $(CD_3)_2SO$ (22.63 MHz)

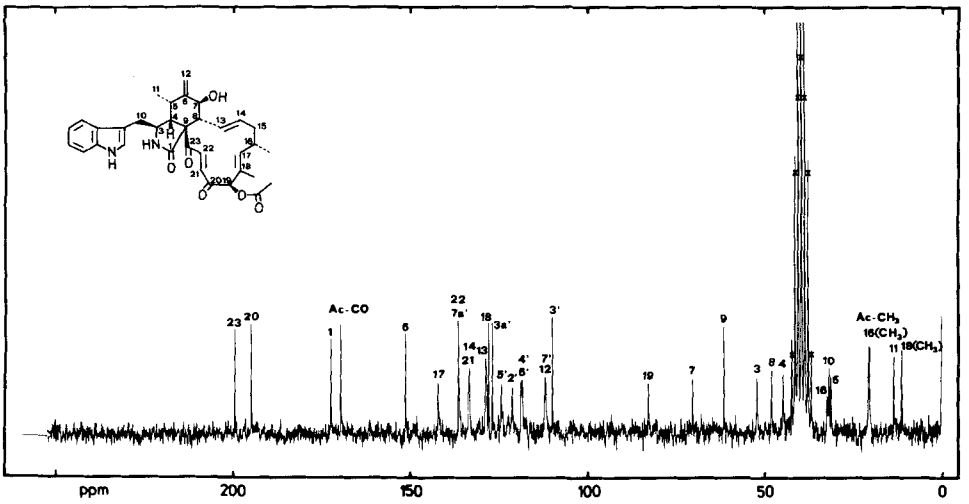


Fig. 2. *^{13}C-NMR. spectrum of 19-O-acetylchaetoglobosin D* (**5**) *in $(CD_3)_2SO$* (22.63 MHz)

The measurement of the ^{13}C-NMR. spectrum of chaetoglobosin C (**3**) was difficult because of its poor solubility and because three signals were covered by the signal of (D_6)-dimethyl sulfoxide. The second problem could be circumvented by using undeuteriated dimethyl sulfoxide (with D_2O as external deuterium lock). Comparison of this spectrum with that of **1** allowed the assignment of the resonance frequencies of all C-atoms except those of C (21) and C (22). The identification of these two C-atoms and confirmation of the other assignments was achieved by the transformation of samples of metabolite **1**, after incorporation of [1-^{13}C]- and [2-^{13}C]-acetate [7] into correspondingly enriched samples of **3**.

The spectra of **4** and **5** differ from that of **2** only in the chemical shifts and multiplicity of some of the signals of the substituted isoindolone unit. In 19-*O*-acetyl-chaetoglobosin D (**5**) (see *Fig. 2*) the signals of C (7), C (12) and C (6) appear at 70.1,

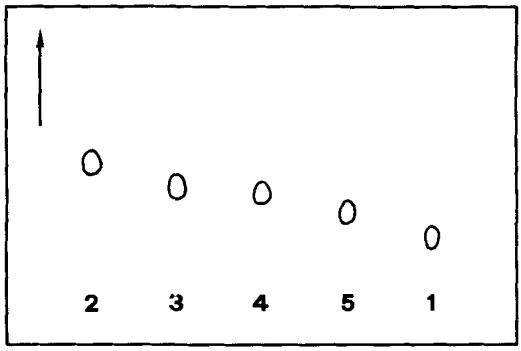


Figure 3

114.4 and 151.0 ppm respectively, and C(5) is shifted to higher field by *ca.* 5 ppm, owing to the allylic double bond. The assignments of the remaining C-atoms are based on comparison with the spectra of **1** and of 7, 19-di-*O*-acetylchaetoglobosin D.

In a similar manner all signals of the spectrum of 19-*O*-acetylchaetoglobosin B (**4**) (see *Fig. 1*) were assigned. They confirmed the proposed structure. The signals of C(5) and C(6) appear in the olefinic region and could be distinguished by comparison with the spectrum of 7, 19-di-*O*-acetylchaetoglobosin B. The differences of the chemical shifts of C(3), C(11) and C(12) in **1** and **4** can be explained by the loss of the γ-effect [8] between C(3) and C(11), due to the conformational change of the isoindolone unit, and the appearance of a new γ-effect between C(11) and C(12), due to the endocyclic double bond.

Finally the absolute configuration of **4** and **5** was deduced from the absolute configuration of 19-*O*-acetylchaetoglobosin A (**2**). Treatment of a solution of **2** in chloroform with hydrochloric acid afforded 19-*O*-acetylchaetoglobosin B (**4**) and D (**5**) in good yield, whereas attempts to deacetylate compounds **4** and **5** led to very complex mixtures.

The support of these investigations by the *Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung* is gratefully acknowledged.

Experimental Part

General Methods. See [9]. Chromatography using the chromatotron was carried out on silica gel 60 GF_{254} from *E. Merck AG*, Darmstadt. The 360-MHz-^{1}H-NMR. spectrum was measured by *Spectrospin* AG., Fällanden.

Medium and isolation of chaetoglobosins. The microorganism was grown in shake cultures in a medium containing 20 g molasses, 10 g glucose and 5 g bactopeptone per litre of demineralized water; pH adjusted to 7.5 with NaOH before sterilization. The sterilized medium was inoculated with a spore suspension of *Chaetomium globosum* (strain *Lederle* H-124) under sterile conditions. The 500 ml Erlenmeyer flasks, each containing 250 ml of medium were shaken at 28° for 11 days. To the culture broth the same volume of ethanol was then added, the mixture kept overnight at 4° and the mycelium separated by filtration. The ethanol was then evaporated *i.V.* (40–50°) and the aqueous layer extracted 4 times with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and evaporated *i.V.* (40°). The brown residue was dissolved in benzene and kept 3 days at RT. The crystallized mixture of chaetoglobosin A (**1**) and 19-*O*-acetylchaetoglobosin A (**2**) was separated by filtration and chromatographed on silica gel (100:1) using increasing amounts of methanol in CH_2Cl_2. The benzene solution was evaporated *i.V.* (40°) and the residue chromatographed on silica gel (100:1) in the same manner. The isolated yields, referred to a 1-litre scale, are for 19-*O*-acetylchaetoglobosin A (**2**) 200–700 mg, for chaetoglobosin A (**1**) 150–600 mg, for chaetoglobosin C (**3**) 70–80 mg, for 19-*O*-acetylchaetoglobosin D (**5**) 10 mg, and for 19-*O*-acetylchaetoglobosin B (**4**) 6 mg. In *Figure 3* a TLC. in CH_2Cl_2/methanol 95:5 of all five chaetoglobosins is reported, showing increasing polarity from left to right.

Chaetoglobosin A (**1**) was crystallized from acetone/diisopropyl ether, yellow prisms, m.p. 151–153°; $[\alpha]_D^{20} = -372° \pm 2°$ ($c = 0.5$, $CHCl_3$). – UV. (ethanol): 196 (4.63), 220 (4.62), 271 (3.82), 280 (3.82), 290 (372). – IR. (KBr): 3600–3200, 1665, 1610, 1450, 1420, 1380, 1290, 1240, 1040, 965. – ^{1}H-NMR. (400 MHz, $CDCl_3$): 0.99 (*d*, $J = 6.5$, 3 H); 1.25 (*d*, $J = 7.5$, 3 H); 1.30 (*s*, 3 H); 1.32 (*d*, $^4J = 1$, 3 H); 1.85 (*m*, 1 H); 2.0–2.1 (*m*, 1 H); 2.13 (*d*×*d*, $J = 5$ and 10, 1 H); 2.2–2.3 (*m*, 1 H); 2.4–2.6 (*m*, 1 H); 2.64 (*d*×*d*, $^2J = 15$, $^3J = 8$, 1 H); 2.79 (*d*, $J = 5$, 1 H); 2.96 (*d*×*d*, $^2J = 15$, $^3J = 4$, 1 H); 3.03 (*d*×*d*, $J = 3$ and 5, 1 H); 3.81 (*m*, 1 H); 3.87 (*d*, $J = 4$, 1 H; exchangeable with D_2O); 5.03 (*d*, $J = 4$, 1 H); 5.22 (*m*, 1 H); 5.59 (*d*×*d* $^3J = 9$, $^4J = 1$, 1 H); 5.94 (*s*, 1 H; exchangeable with D_2O); 6.06 (*d*×*d*, $J = 15$ and 10, 1 H); 6.48 (*d*, $J = 17$, 1 H); 6.9–7.5 (*m*, 5 H); 7.73 (*d*, $J = 17$, 1 H); 8.25 (br. *s*, 1 H; exchangeable with D_2O). – ^{13}C-NMR. ($CDCl_3$): *cf. Table 2.* – MS.: 528 (M^+), 398, 130.

19-O-Acetylchaetoglobosin A (**2**) was crystallized from benzene, yellow powder, m.p. 223–225°; $[\alpha]_D^{20} = -304° \pm 2°$ ($c = 0.5$, $CHCl_3$). – UV. (ethanol): 196 (4.65), 220 (4.64), 271 (3.83), 280 (3.83), 289 (3.74). – IR. (KBr): 3380, 1675, 1620, 1450, 1425, 1365, 1240, 1220, 1180, 1030, 970, 960. – ^{1}H-NMR. (400 MHz, $CDCl_3$): *cf. Table 1.* – ^{13}C-NMR. ($CDCl_3$): *cf. Table 2.* – MS.: 570 (M^+), 527, 440, 130.

Chaetoglobosin C (**3**) was crystallized from acetone, colourless crystals, m.p. 259–261°. – UV. (ethanol): 220 (4.68), 248 (3.98), 281 (3.82), 290 (3.74). – IR. (KBr): 3460, 3320, 1700, 1645, 1620, 1100, 1050, 985. – ^{13}C-NMR. ($(CH_3)_2SO$): *cf. Table 2.* – MS.: 528 (M^+), 398, 130.

19-*O*-Acetylchaetoglobosin B (**4**) and D (**5**) were separated by silica gel chromatography using the chromatotron, with increasing amounts of acetone in CH_2Cl_2.

19-O-Acetylchaetoglobosin B (**4**) gave yellow needles, m.p. 154–157°, from benzene; $[\alpha]_D^{20} = -148° \pm 1°$ ($c = 0.5$, $CHCl_3$). – UV. (ethanol): 221 (4.64), 272 (3.83), 279 (3.83), 289 (3.74). – IR. (KBr): 3600–3200, 1730, 1710, 1620, 1455, 1430, 1375, 1290, 1250, 1230, 1035, 970. – ^{1}H-NMR. (400 MHz, $CDCl_3$): *cf. Table 1.* – ^{13}C-NMR. ($(CD_3)_2SO$): *cf. Table 2.* – MS.: 570 (M^+), 528, 185, 173, 130, 103, 60, 43.

19-O-Acetylchaetoglobosin D (**5**) gave yellow prisms, m.p. 239–241°, from $CHCl_3$; $[\alpha]_D^{20} = -176° \pm 1°$ ($c = 0.5$, $CHCl_3$). – UV. (ethanol): 221 (4.64), 272 (3.83), 279 (3.83), 289 (3.74). – IR. (KBr): 3600–3200, 1730, 1700–1680, 1610, 1450, 1425, 1370, 1250, 1230, 1030, 970, 900. – ^{1}H-NMR. (400 MHz, $CDCl_3$): *cf. Table 1.* – ^{13}C-NMR. ($(CD_3)_2SO$): *cf. Table 2.* – MS.: 570 (M^+), 528, 185, 173, 130, 103, 60, 43.

Medium and isolation of cytochalasin G (**6**). The microorganism was grown in standing cultures in a medium containing 50 g cerelose, 2 g $NaNO_3$, 1 g KH_2PO_4, 0.5 g $MgSO_4 \cdot 7\,H_2O$, 0.5 g KCl, 1 g yeast extract and 1 ml minor elements solution per litre of demineralized water; pH (non adjusted) 5,3–5.7. The sterilized medium was inoculated with a spore suspension of *Pseudeurotium zonatum* (CMI 171.019) under sterile conditions. The flasks each containing 1 l of medium were incubated for 25 days at 27°. Both the mycelium and the medium were then extracted twice with ethyl acetate. The organic layer was dried (Na_2SO_4) and evaporated *i.V.* (40°). The dark-brown extract was chromatographed on silica gel (100:1) using increasing amounts of methanol in CH_2Cl_2. In the fractions containing 1.25% methanol **6** was isolated pure by crystallization from acetone/hexane; yield 7 mg per 1 litre of culture.

Cytochalasin G (**6**), colourless crystals, m.p. 254–256°; $[\alpha]_D^{20} = -100° \pm 1°$ ($c = 0.3$, methanol). – UV. (methanol): 198 (3.95), 219 (4.24), 274 (3.75), 281 (3.77), 290 (3.72). – IR. (KBr): 3360, 1710, 1675, 1610, 1450, 1420, 1380, 1355, 1290, 1230, 1100, 1080, 1050, 970. – ^{1}H-NMR. (360 MHz, $(CD_3)_2SO$): 0.88 (*d*, $J = 8$, 3 H); 0.91 (*d*, $J = 8$, 3 H); 1.15 (*s*, 3 H); 1.56 (*m*, 2 H); 1.79 (*d* × *d*, $J = 6$ and 10, 1 H); 1.79 (*m*, 1 H); 2.59 (*d*, $J = 6$, 2 H); 2.69 (*d*, $J = 6$, 1 H); 2.69 (*m*, 2 H); 3.13 (*m*, 1 H); 3.72 (*m*, 1 H); 4.78 (*m*, 1 H); 6.07 (*d* × *d*, $J = 10$ and 15, 1 H); 7.0–7.5 (*m*, 5 H); 8.32 (*s*, 1 H; exchangeable with D_2O); 10.89 (*s*, 1 H; exchangeable with D_2O). – ^{13}C-NMR. ($(CD_3)_2SO$): *cf. Table 2.* – MS.: 474 (M^+), 344, 130, 103, 77.

Acetylation of **4** *and* **5**. A solution of 81 mg (0.14 mmol of **5** or 57 mg (0.1 mmol) of **4** in 2 ml of absolute pyridine and 2 ml (*ca.* 20 mmol) of acetic anhydride was stirred at RT. for 16 h. The solution was then evaporated i.HV. and the residue purified by crystallization from CH_2Cl_2/hexane. Acetylation of **4** yielded 55 mg (0.09 mmol) of 7,19-di-*O*-acetylchaetoglobosin B, m.p. 152–154°. – IR. (KBr): 3400, 1735, 1690, 1450, 1425, 1230, 1030, 970. – ^{13}C-NMR. ($(CD_3)_2SO$): 11.1, 14.2, 16.9, 20.4 (3 C), 31.5, 32.0, 46.6, 46.9, 57.8, 60.0, 70.8, 83.0, 109.8, 111.5, 118.0, 118.4, 121.0, 123.6, 125.3, 126.0, 127.1, 128.4, 128.7, 134.5, 134.8, 135.0, 136.2, 141.7, 169.3, 169.7, 171.8, 194.0, 199.3. – Acetylation of **5** yielded 80 mg (0.13 mmol) of 7,19-di-*O*-acetylchaetoglobosin D, m.p. 141–143°. – IR. (KBr): 3400, 1740, 1690, 1450, 1425, 1370, 1230, 1030, 970, 900. – ^{13}C-NMR. ($(CD_3)_2SO$): 11.1, 13.0, 20.3, 20.5, 20.7 (2 C), 31.5, 31.8, 32.3, 44.3, 44.6, 52.0, 60.7, 71.3, 82.7, 109.3, 111.4, 114.2, 118.0, 118.4, 120.8, 123.9, 125.9, 127.4, 134.3, 135.3, 136.2, 141.5, 146.4, 169.3, 169.5, 171.5, 194.3, 198.1.

Chaetoglobosin C (**3**) *from* **1**. To a solution of 75 mg (0.14 mmol) **1** in 3 ml methanol, 0.5 ml of triethylamine was added, and the mixture stirred at RT. for 16 h. The colourless precipitate was then filtered and washed with CH_2Cl_2. Crystallization from acetone yielded 57 mg (0.11 mmol) of pure **3**, identical with an authentic sample (m.p., Rf in different solvents, IR. and ^{13}C-NMR.).

19-O-Acetylchaetoglobosin B (**4**) *and D* (**5**) *from* **2**. HCl-gas was passed through a solution of 334 mg (0.59 mmol) **2** in 5 ml $CHCl_3$ during 2 min, and the mixture then stirred at RT. The reaction was followed by TLC. (CH_2Cl_2/methanol 95:5). After 5 h all starting material had disappeared. After neutralization with solid Na_2CO_3 and filtration, the solution was evaporated *i.V.* (40°). The residue was purified by silica gel chromatography using the chromatotron (CH_2Cl_2/acetone), yielding 164 mg (0.29 mmol) of pure **4** and 141 mg (0.25 mmol) of pure **5**, identical with authentic samples (m.p., Rf in different solvents, IR., ^{1}H- and ^{13}C-NMR.).

REFERENCES

[1] *S. Sekita, K. Yoshihira, S. Natori & H. Kuwano,* Tetrahedron Lett. *1973,* 2109; *I.V. Silverton, T. Akiyama, C. Kabuto, S. Sekita, K. Yoshihira & S. Natori,* Tetrahedron Lett. *1976,* 1349; *J.P. Springer, J. Clardy, J.M. Wells, R.J. Cole, J.W. Kirksey, R.D. Macfarlane & D.F. Torgerson,* Tetrahedron Lett. *1976,* 1355; *S. Sekita, K. Yoshihira, S. Natori & H. Kuwano,* Tetrahedron Lett. *1976,* 1351; *S. Sekita, K. Yoshihira, S. Natori & H. Kuwano,* Tetrahedron Lett. *1977,* 2771; *S. Natori* in 'Mycotoxins in Human and Animal Health', J.V. Rodricks, C.W. Hesseltine & M.A. Mehlmann (Ed.), Pathotox Publishers Inc., Park Forest South, Illinois 1977, p.565.

[2] S.W. Tanenbaum (Ed.), 'Cytochalasins – Biochemical and Cell Biological Aspects', Elsevier/North Holland Biochemical Press, Amsterdam, New York, Oxford 1978.

[3] *A.F. Cameron, A.A. Freer, B. Hesp & C.J. Strawson,* J. Chem. Soc., Perkin II *1974,* 1741.

[4] a) *L.F. Johnson & W.C. Jankowski,* 'Carbon-13 NMR. Spectra', Wiley & Sons Inc., New York, London, Sidney, Toronto 1972, Nr.341; b) *ibid.* Nr.180 & Nr.397.

[5] *E. Breitmaier & W. Voelter,* '^{13}C-NMR.-Spectroscopy', Verlag Chemie, Weinheim 1974, a) p.142, b) p.260.

[6] *W. Graf, J.L. Robert, J.C. Vederas, Ch. Tamm, P.H. Solomon, I. Miura & K. Nakanishi,* Helv. Chim. Acta *57,* 1801 (1974).

[7] *A. Probst & Ch. Tamm,* Helv. Chim. Acta *64,* 2065 (1981).

[8] *F.W. Wehrli & T. Wirthlin,* 'Interpretation of Carbon-13-NMR. Spectra', Heyden & Sons Ltd., London, Philadelphia, Rheine 1978, p.27.

[9] *T. Schmidlin & Ch. Tamm,* Helv. Chim. Acta *63,* 121 (1980).