Chemistry of Unusual Macrolides. 1. Preparation of the Aglycons of Concanamycin A and Elaiophylin

Kai U. Bindseil and Axel Zeeck*

Institut für Organische Chemie der Universität Göttingen, Tammannstr.2, D-37077 Göttingen, Germany

Received April 6, 1993•

The aglycons of the concanamycins (1, 2) and elaiophylin (11) have been prepared for direct comparison to the vacuolar-type ATPase inhibitor bafilomycin A_1 (10). The deglycosylation was achieved by acid hydrolysis in the absence of MeOH, while acid-catalyzed methanolysis proceeded with unexpected displacement of carbohydrate residues rather than methoxy groups. Structure assignments of the derivatives were made with the help of one- and two-dimensional NMR studies. Especially helpful were the 9-*O*-acetylated concanamycin derivatives because they showed reduced flexibility of the macrolactone ring. As a result of a detailed analysis of the *O*-methyl derivatives of elaiolide (15) the structure of an earlier reported aglycon derivative of elaiophylin has to be revised to 12.

Introduction

The remarkable biological properties of so-called unusual macrolides[1] has stimulated the interest of many organic chemists and pharmaceutical companies. While the avermectins and milbemycins have become commercially important, the practical use of other members of this group is limited because of their almost fatal toxicity. The 18-membered concanamycins A (1) and C (2) and the C_2-symmetric 16-membered elaiophylin[2] (11) belong to similar classes of unusual macrolides[3] and are closely related to the 16-membered bafilomycins.[4] The unique and most striking structural element of the three macrolide families is the stereospecific formation of an intramolecular hemiacetal within a long side chain. The resulting tetrahydropyran ring and the macrolactone are linked by a C_3 spacer and a hydrogen bonding system.[5] The members within the families differ in the substituents, which are attached to the hemiacetal portion (carbohydrates as in 1, 2, and 11, fumaric acid as in viranamycin A,[6] and bafilomycin C_1 or fumaric acid derivatives as in virustomycin[7] and bafilomycin B_1). Bafilomycin A_1 (10) is unique because of its free hydroxy group instead of further substituents in this position. Besides other interesting biological properties 10 represents the first specific potent inhibitor of vacuolar ATPases from *Neurospora*.[8] The concanamycins and some of their deglycosylated derivatives exhibited similar effects[9] with slightly improved specifity on the different kinds of ATPases[10] whereas 11 shows no inhibitory effect on vacuolar ATPases.[10] We were interested in the preparation of the aglycons of the concanamycins (1, 2) and elaiophylin (11) in order to assess their inhibitory effect on various membrane ATPases in direct comparison to bafilomycin A_1 (10) and to utilize them as intermediates in the synthesis of further semisynthetic derivatives. This paper describes the preparation of concanolide A, elaiolide, and some of their *O*-methyl derivatives and presents the complete NMR assignments of these new compounds.

Results and Discussion

Concanamycin. The concanamycins were originally isolated from *Streptomyces diastatochromogenes* as inhibitors of the proliferation of mouse splenic lymphocytes, and their structures were established by chemical degradation,[11] NMR spectroscopy,[12] and X-ray analysis,[13] but an assignment of the carbon resonances of the concanamycins has never been reported. We have isolated the concanamycins from the mycelium extract of a new soil isolate *Strepomyces sp.* (Gö 22/15) in the course of our chemical screening program.[14] For an unambiguous structure determination of our target, the concanamycin A and C aglycon, concanolide A (6), with the help ^{13}C NMR spectra, it was necessary to assign all carbon resonances of concanamycin A (1). Most of the carbon resonances of the macrolactone were not indicated in the spectra at room temperature. This effect is not dependent on the solvent and might be caused by the conformational flexibility of the 18-membered ring.[15] The signal situation improved in the case of 9,3′-di-*O*-acetylconcanamycin A

• Abstract published in *Advance ACS Abstracts,* August 15, 1993.

(1) Omura, S. Macrolide-like Antibiotics. In *Macrolide Antibiotics. Chemistry, Biology and Practice*; Omura, S., Ed.; Academic Press: New York, 1984; pp 510–546.

(2) Gerlitz, M.; Hammann R.; Thiericke, R.; Rohr, J. *J. Org. Chem.* **1992**, 57, 4030.

(3) Bindseil, K. U.; Zeeck, A. *Helv. Chim. Acta* **1993**, *76*, 150.

(4) Werner, G.; Hagenmeier, H.; Drautz, H.; Baumgartner, A.; Zähner, H. *J. Antibiot.* **1984**, *37*, 110.

(5) (a) Ley, S. V.; Neuhaus, D; Williams, D. J. *Tetrahedron Lett.* **1982**, *23*, 1207. (b) Baker, G. H.; Brown, P. J.; Dorgan, R. J. J.; Everett, J. R. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1073. (c) Everett, J. R.; Baker, G. H.; Dorgan, R. J. J. *J. Chem. Soc., Perkin Trans. 2* **1990**, 717.

(6) Hayakawa, Y.; Takaku, K.; Furihata, K.; Nagai, K.; Seto, H. *J. Antibiot.* **1991**, *44*, 1294.

(7) Omura, S.; Imamura, N.; Hinotozawa, K.; Otoguru, K.; Lukacs, G.; Faghih, R.; Tolmann, R.; Arison, B. H.; Smith, J. L. *J Antibiot.* **1983**, *36*, 1783.

(8) Bowman, E. J.; Siebers, A.; Altendorf K. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 7972.

(9) Kataoka, T.; Magae, J.; Kasamo, K.; Yamanishi, H.; Endo, A.; Yamasaki, M.; Nagai, K. *J. Antibiot.* **1992**, *45*, 1618.

(10) Dröse, S.; Bindseil, K. U.; Bowman, E. J.; Siebers, A.; Zeeck, A. Altendorf, K. *Biochemistry* **1993**, *32*, 3902.

(11) Kinashi, H.; Someno, K.; Sakaguchi, K.; Higashijama, T.; Miyazawa, T. *Tetrahedron Lett.* **1981**, *22*, 3857.

(12) Kinashi, H.; Someno, K.; Sakaguchi, K. *J. Antibiot.* **1984**, *37*, 1233.

(13) (a) Westley, J. W.; Liu, C.-M.; Sello, L. H. Evans, R. H.; Troupe, N.; Blount, J. F.; Chiu, A. M.; Todaro, L. J.; Miller, P. A. *J. Antibiot.* **1984**, *37*, 1738. (b) Nakai, H.; Matsutani, S. *Acta Crystallogr.* **1992**, *48C*, 1519.

(14) (a) Zähner, H.; Drautz, H.; Weber, W. Novel Approaches to Metabolite Screening. In *Bioactive Microbial Products Search and Discovery*; Bu' Lock, J. D.; Nisbet, L. J.; Winstanley, D. J., Eds.; Academic Press: London, New York, 1982; pp 51–70. (b) Bindseil, K. U.; Henkel, T.; Zeeck, A.; Bur, D.; Niederer, D.; Sequin U. *Helv. Chim. Acta* **1991**, *74*, 1281.

(15) A detailed report on the general chemistry and spectroscopical properties of the concanamycins will be reported elsewhere: Bindseil, K. U.; Zeeck, A. Manuscript in preparation.

0022-3263/93/1958-5487$04.00/0

Table I. ^{13}C NMR Chemical Shifts (δ, ppm) of Some Acetylated Concanamycin Derivatives[a]

carbon	3 in $CDCl_3$	7 in CD_2Cl_2	9 in $CDCl_3$	mult
1	166.6	166.5	166.5	s
2	141.6	142.0*	141.6*	s
2-OMe	59.1	60.1	59.1	q
3	130.4	131.5	130.4	d
4	132.4	132.4	132.4	s
4-Me	14.1	14.2	14.1	q
5	139.1	140.0	139.1	d
6	34.9	35.3	34.8	d
6-Me	16.8	17.0	16.8	q
7	74.9	74.9	74.8	d
8	43.9	44.4	43.8	d
8-CH_2	21.4	21.8	21.4	t
8-Et	11.9	12.1	11.9	q
9	79.9	80.0	79.8	d
10	33.8	34.1	33.8	d
10-Me	21.0	21.4	21.3	q
11	45.3	45.7	45.3	t
12	142.1	142.5*	142.0*	s
12-Me	16.2	16.3	16.2	q
13	123.7	124.0	123.6	d
14	133.4	133.7	133.4	d
15	127.7	128.1	127.6	d
16	81.5	82.6	81.4	d
16-OMe	55.7	56.5	55.7	q
17	75.7	76.3	75.6	d
18	36.8	38.5**	36.7	d
18-Me	9.4	10.4	9.3	q
19	70.3	69.9	70.1	d
20	41.7	38.6**	41.5	d
20-Me	7.1	7.5	7.0	q
21	99.7	104.2	99.5	s
21-OMe		46.8		q
22	39.3	34.7	39.9	t
23	76.3	79.6	73.4	d
23-OMe		56.0		q
24	41.5	41.5	40.8	d
24-Me	13.4	13.4	13.3	q
25	75.4	77.0	74.9	d
26	131.2	131.2	130.6	d
27	127.5	129.4	128.0	d
28	17.7	17.9	17.7	q
1′	96.2			d
2′	37.2			t
3′	71.1			d
4′	75.4			d
4′-CO	155.9			s
5′	70.0			d
6′	17.5			q
Ac-CO	170.7/170.5	171.0	170.8/170.4	s
Ac-Me	20.6/20.7	21.2	21.1/21.0	q

[a] Assignments based on ^1H, ^{13}C correlation and HMBC (9) experiments. * and ** signals may be interchanged.

(3), which was obtained by acylation of 1 with acetic anhydride/pyridine at room temperature.[16] The ^{13}C NMR data of 3 are summarized in Table I and were established by ^1H COSY and ^1H,^{13}C HETCOR experiments. They represent the first assignment of all carbon resonances of concanamycin A (1).

Concanolide A. The acid-catalyzed deglycosylation of macrolide antibiotics normally proceeds with high yields,[17] but despite many attempts to remove the carbohydrate moiety from the concanamycins or elaiophylin, respectively, the free aglycons have never been reported.[18] Nevertheless, Seebach et al. converted elaiophylin (11) into a deglycosylated compound upon treatment with *p*-toluenesulfonic acid in MeOH.[19]

Initially we applied the methanolysis procedure according to Seebach to concanamycin C (2),[20] with the intention of removing the 21-*O*-methyl group, with subsequent Lewis acid catalysis, because Kinashi et al. had demonstrated the reversibility of the acetalization on intact concanamycins.[12] To our surprise, the ^1H NMR data of our main product revealed the replacement of the sugar residue by a methoxy group (compound 5), indicated by the fact that the 21-OH resonance was found unchanged at δ 5.62, while the signal of 23-H got a diagnostic high-field shift to δ 3.25. The observed shifts are similar to those reported for the natural product L681,110 B_1,[21] which is the corresponding methylated bafilomycin derivative.[5] The detailed analysis of the coupling constants of 5 reveals that the displacement proceeds with retention of configuration. The mechanism of this substitution is quite unclear. We suppose that it is controlled by a neighboring group effect involving the C-21 acetal moiety. The originally expected 21-*O*-methylation was only a side reaction leading to the 21,23-di-*O*-methylconcanolide A (4), which was isolated as a minor component. To our surprise, in TLC with $CHCl_3$–MeOH solvent systems the monomethylated 5 runs faster than the dimethylated derivative 4. Attempts to reproduce the reaction with MeOH and *p*-toluenesulfonic acid of technical grade gave 4 as the main product. The structure assignments were strongly supported by the spectral data and by acylation experiments. Acetylation of 4 or 5 with acetic anhydride/pyridine resulted in the exclusive formation of the 9-*O*-acetyl derivatives 7 or 8, respectively. Even under more vigorous conditions using DMAP as catalyst we never achieved 23-O-acetylation. 7 and 8 can be prepared alternatively by acid methanolysis of 3. However, treatment of 4 with catalytic amounts of $FeCl_3$ resulted in the exclusive formation of 5 within 10 min. The cleavage of the methyl ether in position 23 of 5 requires more vigorous reaction conditions and it was necessary to use a 20-fold exess of $FeCl_3$ to obtain the free concanolide A (6) in a very small yield, while the reaction with catalytic amounts of $AlCl_3$ led to a complete decomposition of 5.

We therefore decided to effect the deglycosylation in the absence of MeOH. The best results were obtained upon careful treatment of concanamycin C (2) with *p*-toluenesulfonic acid in CH_3CN/H_2O (2:1) at 0 °C leading to 6 in 56% yield and different elimination products. In the NMR spectra, most of the macrolide ring resonances were broadened as in 1 or 2. For an unambiguous identification, 6 was converted into 9,23-di-*O*-acetylconcanolide A (9) by reaction with acetic anhydride/pyridine.

Elaiolide. Seebach et al. reported 11,11′-di-*O*-methylelaiopylidene to be the main product of the acid-catalyzed methanolysis of elaiophylin (11). On the basis of the ^1H NMR assignments the strong association with two molecules of MeOH was postulated.[19] Their procedure was modified by Hammann et al. by performing a Lewis acid catalyzed acetalization followed by the deglycosylation

(16) A mixture of 90% of 1 and 10% of the lower homologue concanamycin B was used for acetylation.

(17) Mrozik, H.; Eskola, P.; Arison, B. H.; Albers-Schönberg, G.; Fisher, M. H. *J. Org. Chem.* **1982**, *47*, 489.

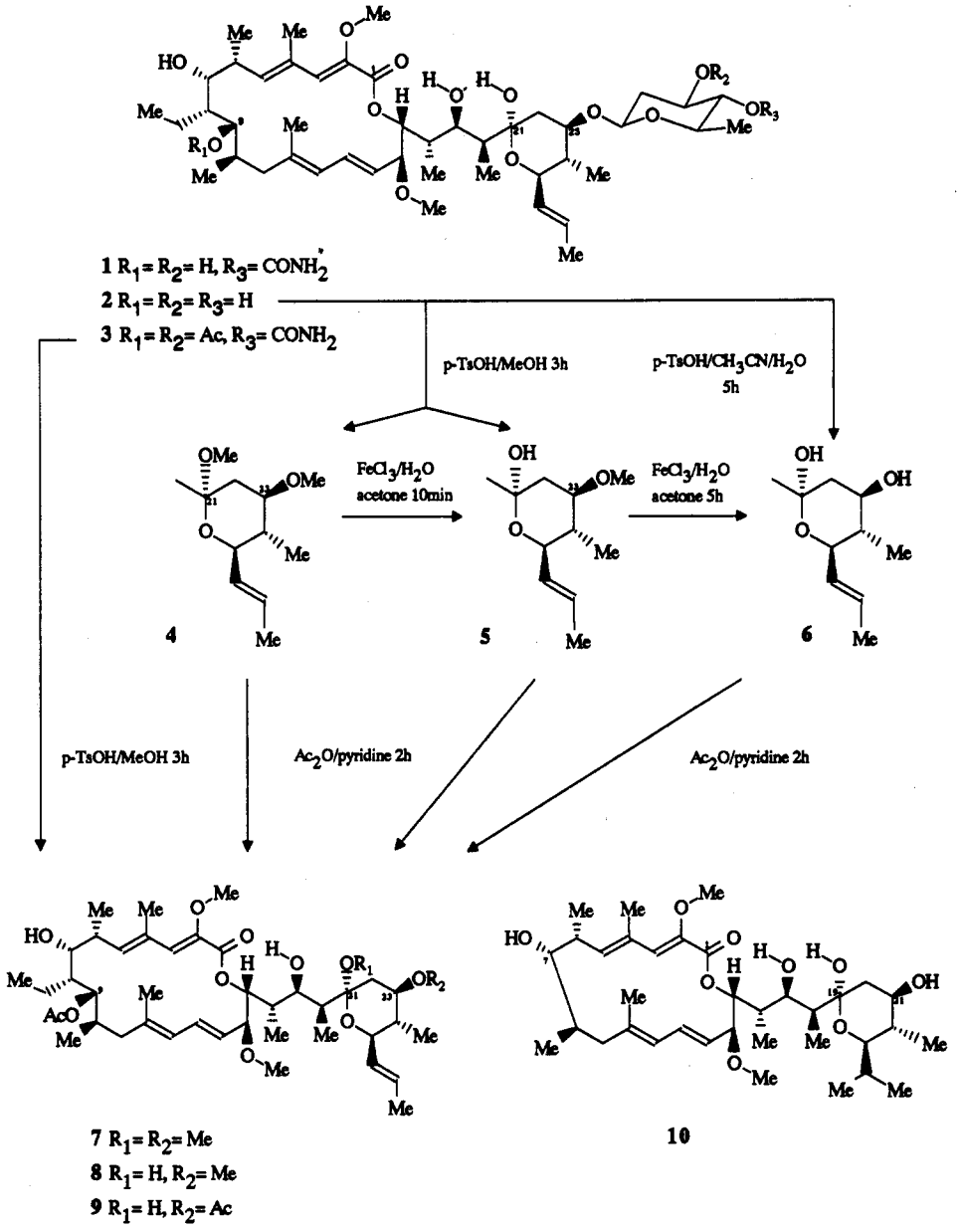
(18) Toshima, K.; Tatsuta, K.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2369 and references cited herein.

(19) Seebach, D.; Chow, H.-F.; Jackson, R. F. W.; Sutter, M. A.; Thaisrivongs, S.; Zimmermann, J. *Liebigs Ann. Chem.* **1986**, 1281.

(20) Concanamycin C (2) was used as starting material because concanmycin A (1) contains up to 30% of its lower homologue concanamycin B and the separation of these compounds on reversed-phase silica gel is a time-consuming process.

(21) Henses, O. D.; Monaghan, R. L.; Huang, L.; Albers-Schönberg, G. *J. Am. Chem. Soc.* **1983**, *105*, 3672.

Scheme I



with *p*-toluenesulfonic acid.[22] Nevertheless both groups failed in the removal of the *O*-methyl groups of the acetal and in further modification of the supposed free 13,13′-hydroxy groups. Because of the inconsistencies with the reactivity of the concanamycins we decided to reinvestigate the methanolysis of 11 according to the original procedure of Seebach et al. Comparison of the ^{1}H NMR spectra (C_6D_6) and the optical rotation values with those reported in literature[19] showed that our main product had the same spectroscopical and physicochemical properties as the 11,11′-di-*O*-methylelaiopylidene described by Seebach et al., but in fact the ^{13}C NMR spectrum and the FAB-MS were indicating a tetra-*O*-methyl derivative of the aglycon, which should be called elaiolide, as shown in structure **12**. By treatment with $FeCl_3$ in acetone/H_2O the acetals of **12** were converted stereoselectively into the semiacetals as shown in **13**. The ^{1}H NMR spectrum of **13** shows the signals of the semiacetal hydroxy groups at δ 5.36, and the ^{13}C NMR spectrum reveals the expected high-field shift for the C-11 resonance and a low-field shift of the 12-methylene group whereas the C-13 signal remains nearly

Table II. ^{1}H NMR Chemical Shifts (δ, ppm) of Concanamycin Derivatives in $CDCl_3$[a]

hydrogen	4	5	6	9
17	5.15 d br 10	5.02 d br 10	5.02 d br 10	5.01 dd 10/5
19	3.43 dd 10/5	4.07 ddd 10/5/2	4.02 d br 10	4.02 d br 10
19-OH	~3.85 obs	4.61 sbr	4.60 s br	4.62 s br
21-OH		5.62 s	5.73 s br	5.74 s br
21-OMe	3.02 s			
22_{eq}	2.46 dd 12/5	2.46 dd 12/5	2.31 dd 12/5	2.36 dd 12/5
23	3.13 ddd 10/10/5	3.25 ddd 10/10/5	3.73 m	4.99 ddd
23-OMe	3.33 s	3.38 s		
25	3.49 dd 10/8	3.98 dd 10/8	3.96 dd 10/8	4.08 dd 10/8

[a] Assignments based on H,H COSY experiments.

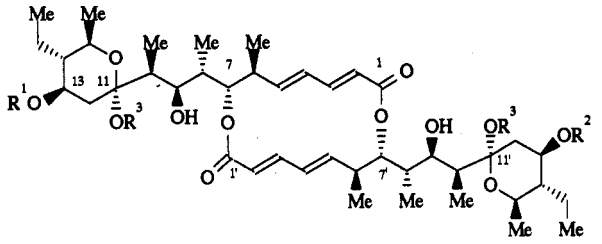
(22) Hammann, P.; Kretschmar, G.; Seibert, G. *J. Antibiot.* **1990**, *43*, 1431.

Table III. ^{1}H NMR Chemical Shifts (δ, ppm) of Elaiolide (15) and Its Derivatives in $CDCl_3$[a]

hydrogen	12	13	14		15
7/7′	4.92 dd 10/2	4.91 dd 10/2	4.73 d br 10		4.73 d br 10
9/9′	3.48 dd 11/4	4.13 d br 10	4.10–4.15 m		4.11 d br 10
9-OH/ 9′-OH	obs	4.16 s	4.10–4.15 m		4.13 s
11-OH/ 11′-OH		5.36 d 2	5.25 d 2	5.33 d 2	5.23 d 2
11-OMe/ 11-OMe′	3.04 s				
12-H_{eq}/ 12′-H_{eq}	2.46 dd 12/5	2.46 dd 12/5	2.30 dd 12/5	2.39 dd 12/5	2.30 dd 12/5
13/13′	3.32 ddd 10/10/5	3.47 ddd 10/10/5	3.85–4.05 m		3.95 ddd 10/10/5
13-OMe/ 13′-OMe	3.30 s	3.37 s			
15/15′	3.43 dq 11/6	3.88 dq 11/6	3.85–4.05 m		3.85 dq 10/7
1‴/1⁗			5.06 s br		

[a] Assignments based on H,H COSY experiments.

unchanged. Both spectra indicate the presence of two methoxy groups, whose stability during hydrolysis strongly supported their covalent bond at C-13 and C-13′ instead of strongly associated MeOH. The position of the methoxy groups was proved unambiguously by correlation signals in the COLOC spectrum (as depicted in Table IV) and the Delay-COSY[23] of 13. The signals of the 6-membered semiacetal rings are well separated, and the main diagnostic connectivities could readily be obtained from the spectra.



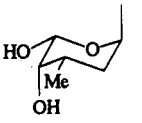
11 $R^1 = R^2 = A$, $R^3 = H$

12 $R^1 = R^2 = R^3 = CH_3$

13 $R^1 = R^2 = CH_3$, $R^3 = H$

14 $R^1 = A$, $R^2 = R^3 = H$

15 $R^1 = R^2 = R^3 = H$

A = 

The isolated methoxy derivatives reveal a close relationship in the chemical reactivity of the concanamycins and elaiophylin. Deglycosylation in the presence of MeOH proceeds obviously with displacement of the carbohydrate moiety with a methoxy group, while the formation of the methyl acetals is only a side reaction. The latter can be cleaved by Lewis acids under moderate conditions whereas the methyl ethers in positions 13 and 13′ are quite stable to weak acids. Their cleavage requires acidic conditions which force elimination reactions. Also, the reported structure of 11,11′-di-*O*-methylelaiopylidene has to be revised to 12. In earlier literature the failure to achieve glycosylation or acylation of the 13-OH group was explained on the basis of steric hindrance,[24] but in fact there is no free secondary alcohol, so that the reactivity of this hydoxy group has to be reinvestigated.

Table IV. ^{13}C NMR Data and ^nJ Couplings (δ, ppm) of Elaiolide (15) and its *O*-Methyl Derivatives

carbon	12 in $CDCl_3$	13 in C_6D_6	^2J and ^3J couplings in the COLOC spec. of 13	15 in $CDCl_3$	mult
1	169.5	170.2	2, 3, 7′	170.6	s
2	121.3	121.3	4	121.0	d
3	145.0	145.1	4, 5	145.1	d
4	131.7	132.2	2	132.0	d
5	144.5	144.3	3,6-Me	144.3	d
6	38.0	40.8	4, 6-Me	40.8	d
6-Me	15.1	14.5	5	14.9	q
7	77.9	78.3	6-Me, 8-Me	77.9	d
8	36.6	36.2	8-Me	35.9	d
8-Me	10.0	9.9	7	9.9	q
9	69.7	71.1	8-Me, 10-Me	70.6	d
10	41.3	42.3	9-OH, 10-Me, 11-OH	41.6	d
10-Me	7.2	7.5	9	7.0	q
11	103.4	99.6	10-Me, 11-OH, 12-H_2	99.1	s
11-OMe	46.6				q
12	34.2	39.7	11-OH	43.5	t
13	75.8	76.3	13-OMe	67.1	d
13-OMe	56.3	56.0			q
14	48.1	49.9	12-Heq, 15-Me	51.0	d
14-Et	19.4	20.0		19.4	t
14-Et	9.5	8.7	14	8.7	q
15	68.4	67.5	15-Me	66.8	d
15-Me	19.2	19.7		19.2	q

The deglycosylation of 11 in the absence of MeOH proved to be more difficult and afforded a mixture of monoglycosyl aglycon 14 and aglycon 15, besides decomposition products. The composition of the reaction mixture varied with time. 14 is formed slowly, and the amounts of 14 decreased due to the formation of an unsymmetrical elimination product with one carbohydrate moiety. After 6 h 14 and the unsymmetrical product were predominant, and after 15 h 15 reached the highest yields and different elimination products were detectable by TLC. The instability of elaiolide (15) under acidic conditions precluded yields of more than 20% and can be explained by the fact that the aglycon has two, hidden, labile β-ketol type structures instead of one in the monoglycosyl aglycon. The signals in the NMR spectra of 14 are complex and essentially superimposable because of its lack of symmetry, but nevertheless they indicate the presence of only one 2,6-deoxyfucose residue and of two free semiacetals with different chemical environments. In contrast to 14, the NMR spectra of 15 showed very sharp signals, and the detailed analysis of chemical shifts and coupling constants, accomplished by ^{1}H COSY experiments, supports the structure assignment and precludes isomerization or inversion of the centers of chirality.

Conclusions

In summary, the acid catalyzed deglycosylation is a convenient method to produce the aglycons of the concanamycins and elaiophylin. While the amounts of concanamycin aglycon derived from fermentation broth are very small,[25] the semisynthetic preparation provides aglycons on a scale that allows further modifications to be carried out. The aglycon of elaiophylin has, to our knowledge, never been reported and might be a key intermediate for the investigation of structure–activity relationships. In further inhibitor studies we are going to

(23) Bax, A.; Freeman, R. *J. Magn. Reson.* **1981**, *44*, 542.
(24) Hammann, P.; Kretschmar, G. *Z. Naturforsch.* **1990**, *45b*, 515.
(25) Woo, J.-T.; Shinohara, C; Sakai, K.; Hasumi, K.; Endo, A. *J. Antibiot.* **1992**, *45*, 1108.

determine the extent to which the carbohydrate moieties of 1, 2, and 11 enhance the biological activities. Concanolide A (6) is directly comparable to bafilomycin A_1 (10) and allows us to study the effect of the macrolactone ring size on vacuolar ATPases.[10] The different methyl acetals will be used to investigate the importance of an intact hydrogen bonding system for the biological activities of the concanamycins and elaiophylin. The NMR spectra of the new compound have been studied in detail and will be used in further studies regarding structure–activty relationships.

Experimental Section

General. NMR chemical shifts are reported in parts per million with TMS (^1H) or solvent signal (^{13}C) as internal standards. ^1H NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants in Hz, integration, interpretation). FAB mass spectra were recorded with 3-nitrobenzyl alcohol as matrix. The concanamycins were isolated from the mycelium of strain Gö 22/15 and purified as described elsewhere;[3] pure elaiophylin was obtained from Dr. J. Rohr. Reagents and solvents were purchased from common commercial suppliers and were used as received or distilled from the appropiate drying agent. Column chromatography was performed with Machery and Nagel silica gel 60 (<0.8 mm), and thin-layer chromatography was performed on Merck silica gel 60 F_{254} precoated plates with the solvent systems indicated. The compounds were visualized by spraying the sheets with anisaldehyde/H_2SO_4 and subsequent heating. The usual workup procedure consists of 3-fold extraction of the reaction mixture with the solvent indicated, washing with water, drying with Na_2SO_4, and removal of the solvent in vacuo.

9,3′-Di-*O*-acetylconcanamycin A (3). General Procedure A. A solution of 1 (180 mg, 0.20 mmol) in 4.0 mL of pyridine was treated with 2.5 mL of acetic anhydride and was stirred for 4 h at room temperature. The reaction mixture was passed into ice–water and extracted with $CHCl_3$. After the usual workup procedure traces of acetic acid were removed in vacuo upon addition of toluene. The crude product was purified by CC ($CHCl_3$–MeOH (9:1)) to give 154 mg (78%) of 3: $C_{50}H_{79}NO_{16}$; TLC R_f 0.62 ($CHCl_3$–MeOH (95:5)) and 0.44 (EtOAc–*n*-hexane (1:2)); $[\alpha]^{20}_D$ = −28 (*c* 0.5, $CHCl_3$); IR (KBr, cm^{-1}) 3430, 2960, 1740, 1720 sh, 1695; 1450, 1360, 1250; UV (MeOH) λ_{max} = 245 (ε 36 000), 283 nm (ε 15 000); ^1H NMR (500 MHz, $CDCl_3$) δ 0.82 (d, *J* = 7, 18-Me), 0.88 (m, 3 H, 8-Et), 0.89 (d, *J* = 6, 3-H, 24-Me), 0.95 (d, *J* = 7, 3 H, 10-Me), 1.04 (d, *J* = 7, 3 H, 6-Me), 1.06 (d, *J* = 7, 3 H, 20-Me), 1.06 (m obs, 2 H, 8-Et), 1.10 (m, 1 H, 22-H_{ax}), 1.25 (m obs, 1 H, 24-H), 1.57–1.65 (m obs, 1 H, 8-H), 1.58 (dd, *J* = 6, 1, 3 H, 28-H_3), 1.69 (m, 2′-H_{ax}), 1.75 (dq, *J* = 7, 2, 1 H, 20-H), 1.88 (s, 3 H, 12-Me), 1.95 (s, 3 H, 4-Me), 2.00 (m obs, 2 H, 11-H_2), 2.05 (s, 3 H, acetyl-Me), 2.10 (s, 3H, acetyl-Me), 2.20 (m obs, 1 H, 2′-H_{ax}), 2.20 (m obs, 1 H, 18-H), 2.32 (dd, *J* = 12, 5, 1 H, 23-H_{eq}), 2.55–2.70 (m, 2 H, 6-H and 10-H), 3.26 (s, 3 H, 16-OMe), 3.40 (dq, *J* = 9, 6, 1 H, 4′-H), 3.57 (s, 3 H, 2-OMe), 3.66 (m, 1 H, 7-H), 3.77 (ddd, *J* = 10, 10, 5, 1 H, 23-H), 3.85 (dd, *J* = 9, 9, 1 H, 16-H), 3.97 (dd, *J* = 11, 8, 1 H, 25-H), 4.04 (ddd, *J* = 11, 4, 1, 1 H, 19-H), 4.58 (t, *J* = 9, 1 H, 3′-H), 4.61 (dd, *J* = 9, 1, 1 H, 1′-H), 4.60–4.68 (br, 2 H, carbamoyl-NH_2), 4.67 (d, *J* = 4, 1 H, 19-OH), 4.84 (d, *J* = 10, 1 H, 9-H), 4.95 (ddd, *J* = 12, 9, 5, 1 H, 3′-H), 5.00 (dd, *J* = 9, 1.5, 1 H, 17-H), 5.21 (ddq, *J* = 15, 6, 1, 1 H, 26-H), 5.23 (dd, *J* = 15, 8.5, 1 H, 15-H), 5.55 (ddq, *J* = 15, 6, 1, 1 H, 27-H), 5.64 (d, *J* = 10, 1 H, 5-H), 5.78 (d, *J* = 10, 1 H, 13-H) 5.80 (s, 1 H, 21-OH), 6.39 (s, 1 H, 3-H), 6.57 (dd, *J* = 15, 10, 1 H, 14-H). ^{13}C NMR see Table I; FAB-MS (positive) 970 (M + Na)$^+$, (negative) 947 (M^-).

21,23-Di-*O*-methylconcanolide A (4). General Procedure B. A solution of 2 (140 mg, 0.17 mmol) in 25.0 mL of MeOH (technical grade) was treated with 20 mg of *p*-toluenesulfonic acid (technical grade). The mixture was poured into 5 mL phosphate buffer (pH = 7). After 3 h the reaction mixture was concentrated in vacuo and extracted with $CHCl_3$. The usual workup followed by CC (EtOAc–*n*-hexane (1:2)) gave 110 mg (89%) of 4 as a white powder: $C_{41}H_{68}O_{10}$; TLC R_f 0.53 ($CHCl_3$–MeOH (95:5)) and 0.50 (EtOAc–*n*-hexane (1:2)); $[\alpha]^{20}_D$ = +9 (*c* 0.3, $CHCl_3$); IR (KBr, cm^{-1}) 3480, 2960, 1690, 1610w; 1440, 1350, 1250, 1100; UV (MeOH) λ_{max} 245 (ε 42 000), 283 nm (ε 18 000); ^1H-NMR (300 MHz, $CDCl_3$) see Table II and δ 2.72 (m, 1 H, H-6), 3.23 (s, 3 H, 16-OMe), 3.64 (s, 3 H, 2-OMe), 3.81 (dd, 1 H, *J* = 9, 9, 16-H), 5.22 (dd, *J* = 15, 9, 1 H, 15-H), 5.40 (ddq, *J* = 15, 8, 1, 1 H, 26-H), 5.67 (ddq, *J* = 15, 6, 1, 1 H, 27-H), 5.79 (d br, *J* = 10, 2 H, 5-H and 13-H), 6.42 (s, 1 H, 3-H), 6.51 (dd, *J* = 15, 10, 1 H, 14-H); FAB-MS (positive) 745 (M + Na)$^+$, (negative) 721 (M^-).

23-*O*-Methylconcanolide A (5) from 2. 5 was prepared from 140 mg of 2 according to general procedure B with MeOH and *p*-toluenesulfonic acid of pro analysi grade. Purification by CC (EtOAc–*n*-hexane (1:2)) afforded 101 mg (86%) of 5 as a white powder: $C_{40}H_{66}O_{10}$; TLC R_f 0.62 ($CHCl_3$–MeOH (95:5)) and 0.44 (EtOAc–*n*-hexane (1:2)); $[\alpha]^{20}_D$ = +16 (*c* 0.3, $CHCl_3$); IR (KBr, cm^{-1}) 3460, 2960, 1690, 1610w, 1440, 1350, 1240, 1100; UV (MeOH) λ_{max} = 245 (ε 40 000), 283 nm (ε 18 000); ^1H NMR see Table II and δ 2.72 (m, 1 H, 6-H), 3.26 (s, 3 H, 16-OCH_3), 3.49 (d br, *J* = 5, 1 H, 7-H), 3.57 (s, 3 H, 2-OCH_3), 3.85 (dd, *J* = 9, 9, 1 H, 16-H), 5.21 (dd, *J* = 15, 9, 1 H 15-H), 5.29 (ddq, *J* = 15, 8, 1, 1 H, 26-H), 5.55 (ddq, *J* = 15, 6, 1, 1 H, 27-H), 5.80 (d br, *J* = 10, 2 H, 13-H and 5-H), 6.39 (s, 1 H, 3-H), 6.54 (dd, *J* = 15, 10, 1 H, 14-H); FAB-MS (negative) 707 (M^-).

5 from 4. A mixture of 4 (80 mg. 0.11 mmol) and $FeCl_3$ (3 mg, 0.02 mmol) in 10 mL of acetone and 5.0 mL of water was stirred for 10 min at room temperature and then poured into 5 mL of phosphate buffer (pH = 7). The organic solvent was removed in vacuo and the aqueous residue was extracted with $CHCl_3$. The usual workup, followed by filtration through silica gel (EtOAc–*n*-hexane (1:1) as eluent), gave 71 mg (90%) of 5.

Concanolide A (6). A solution of 2 (118 mg, 0.14 mmol) in 15 mL of CH_3CN and 3.5 mL of water was treated with 97 mg (0.56 mmol) of *p*-toluenesulfonic acid and was stirred for 20 h at room temperature. The solution was cooled to 0 °C, and 30 mL of saturated aqueous $NaHCO_3$ was added. The resulting mixture was extracted with $CHCl_3$. The usual workup, followed by CC (EtOAc–*n*-hexane (2:1)), gave 55 mg (56%) of 6 as a colorless oil: $C_{39}H_{64}O_{10}$; TLC R_f 0.29 ($CHCl_3$–MeOH (95:5)) and 0.17 (EtOAc–*n*-hexane (1:2)); $[\alpha]^{20}_D$ = +11 (*c* 0.3, $CHCl_3$); IR (KBr, cm^{-1}) 3460, 2960, 1690, 1620w, 1450, 1250, 1100; 960; UV (MeOH) λ_{max} = 245 (ε 32 000), 283 nm (ε 17 000); ^1H NMR see Table II and δ 2.72 (m, 1 H, 6-H), 3.26 (s, 3 H, 16-OCH_3), 3.59 (s, 3 H, 2-OCH_3), 3.85 (dd, *J* = 9, 9, 1 H, 16-H), 5.22 (dd, *J* = 15, 9, 1 H 15-H), 5.28 (ddq, *J* = 15, 8, 1, 1 H, 26-H), 5.55 (ddq, *J* = 15, 6, 0.5, 1 H, 27-H), 5.78 (d br, *J* = 10, 2 H, 13-H and 5-H), 6.37 (s, 1 H, 3-H), 6.54 (dd, *J* = 15, 10, 1 H, 14-H); FAB-MS (negative) 693 (M^-).

6 from 5. A mixture of 5 (80 mg, 0.111 mmol) and $FeCl_3$ (160 mg, 0.98 mmol) in 6 mL of acetone and 3 mL of water was stirred for 5 h (TLC control showed a maximum of 6) at room temperature. The mixture was poured into 5 mL of phosphate buffer (pH = 7), and acetone was removed in vacuo. The extraction with $CHCl_3$ followed by usual workup procedure and CC (EtOAc–*n*-hexane (2:1)) gave 16 mg of 5 and 11 mg of 6 (14%).

9-*O*-Acetyl-21,23-di-*O*-methylconcanolide A (7) from 4. From 37 mg (0.05 mmol) of 4 according to general procedure A and purification by CC (EtOAc–*n*-hexane (1:2)) was prepared 35 mg (89%) of 7: $C_{43}H_{70}O_{11}$; TLC R_f 0.56 (EtOAc–*n*-hexane (1:2)); $[\alpha]^{20}_D$ = +5 (*c* 0.5, $CHCl_3$); IR (KBr, cm^{-1}) 3420, 2960, 1740, 1690, 1620 w, 1450, 1370, 1250, 1100; 1010; UV (MeOH) λ_{max} = 245 (ε 42 000), 283 nm (ε 21 000); ^1H NMR (300 MHz, $CDCl_3$) δ 1.72 (dd, *J* = 6, 1, 3 H, 28-H_3), 1.87 (s, 3 H, 12-Me), 1.98 (d, *J* = 0.5, 3 H, 4-Me), 2.05 (s, 3 H, acetyl-Me), 2.46 (dd, *J* = 13, 5, 1 H, 22-H_{eq}), 2.58–2.73 (m, 2 H, 6-H and 10-H), 3.05 (s, 3 H, 21-OMe), 3.15 (ddd, 10, 10, 5, 1 H, 23-H), 3.23 (s, 3 H, 16-OMe), 3.36 (s, 3 H, 23 O-Me), 3.45 (dd, *J* = 10, 5, 1 H, 19-H), 3.51 (dd, *J* = 10, 8, 1 H, 25-H), 3.67 (s, 3 H, 2-OMe), 3.76 (m, 1 H, 7-H), 3.77 (dbr, *J* = 5, 1 H, 19-OH), 3.82 (dd, *J* = 9, 9, 1 H, 16-H), 4.85 (d, *J* = 11, 1 H, 9-H), 5.12 (dd, *J* = 10, 0.5, 1 H, 17-H), 5.26 (dd, *J* = 15, 9, 1 H, 15-H), 5.43 (ddd, 15, 7, 1.5, 1 H, 26-H), 5.66 (dbr, *J* = 10, 1 H, 5-H), 5.69 (ddq, *J* = 15, 6, 1, 1 H, 27-H), 5.79 (dbr, *J* = 10, 1 H, 13-H), 6.47 (s, 1 H, 3-H), 6.55 (dd, *J* = 15, 10, 1 H, 14-H); ^{13}C NMR see Table I; FAB-MS (positive) 787 (M + Na)$^+$, (negative) 763 (M^-).

7 from 3. 7 (17 mg, 66%) was prepared from 32 mg of 3 according to general procedure B.

9-*O*-Acetyl-23-*O*-methylconcanolide A (8). Acetylation of 48 mg of **5** (0.068 mmol) via the general procedure A and purification by CC (EtOAc–*n*-hexane (1:2)) gave 40 mg of **8** (78%): $C_{42}H_{68}O_{11}$; TLC R_f 0.53 (EtOAc–*n*-hexane (1:2)); $[\alpha]^{20}_D$ = +11 (*c* 0.3 , CH_2Cl_2); IR and UV as **7**; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.58 (dd, *J* = 6, 1, 3 H, 28-H_3), 1.87 (s, 3 H, 12-Me), 1.98 (d, *J* = 0.5, 3 H, 4-Me), 2.12 (s, 3 H, acetyl-Me), 2.46 (dd, *J* = 13, 5, 1 H, 22-H_{eq}), 2.58–2.73 (m, 2 H, 6-H and 10-H), 3.22 (ddd, 10, 10, 5, 1 H, 23-H), 3.23 (s, 3 H, 16-OMe), 3.36 (s, 3 H, 23 O-Me), 3.57 (s, 3 H, 2-OMe), 3.76 (m, 1 H, 7-H), 3.82 (dd, *J* = 9, 9, 1 H, 16-H),3.98 (dd, *J* = 10, 8, 1 H, 25-H), 4.04 (d br, *J* = 10, 1 H, 19-H), 4.64 (dbr, *J* = 5, 1 H, 19-OH), 4.85 (d, *J* = 11, 1 H, 9-H), 5.02 (dd, *J* = 10, 0.5, 1 H, 17-H), 5.26 (dd, *J* = 15, 9, 1 H, 15-H), 5.30 (ddd, 15, 7, 1.5, 1 H, 26-H), 5.54 (ddq, *J* = 15, 6, 1, 1 H, 27-H), 5.62 (dbr, *J* = 10, 1 H, 5-H), 5.76 (s, 1 H, 21-OH), 5.79 (dbr, *J* = 10, 1 H, 13-H), 6.38 (s, 1 H, 3-H), 6.55 (dd, *J* = 15, 10, 1 H, 14-H); FAB-MS (negative) 749 (M^-).

9,23-Di-*O*-acetylconcanolide A (9). The diacetate was prepared from 10 mg (0.014 mmol) of **6** according to general procedure A. Purification by CC (EtOAc–*n*-hexane (1:2)) gave 8.5 mg (76%) of **9**: $C_{43}H_{68}O_{12}$; TLC R_f 0.54 (EtOAc–*n*-hexane (1:2)); $[\alpha]^{20}_D$ = +7 (*c* 0.4, CH_2Cl_2); IR (KBr, cm^{-1}) 3420, 2960, 1740, 1690, 1620 w, 1450, 1370, 1250, 1100; 960; UV (MeOH) λ_{max} = 245 (ε 35 000), 283 nm (ε 16 000); ^{1}H NMR (500 MHz, $CDCl_3$) see Table II and δ 0.80 (d, *J* = 6.5, 3 H, 18-Me), 0.81 (d, *J* = 7, 3 H, 24-Me), 0.86 (m, 3 H, 8-CH_2CH_3), 0.90 (d, *J* = 7, 3 H, 10-Me), 1.02 (d, *J* = 7, 3 H, 20-Me), 1.04 (d, *J* = 7, 3 H, 6-Me), 1.21 (dd, *J* = 12, 10, 1 H, 22-H_{ax}), 1.40 (ddq, *J* = 10, 10, 7, 1 H, 24-H), 1.60 (dd, *J* = 6, 1.5, 3 H, 28-H_3), 1.61 (m, 1 H, 8-H), 1.74 (dq, *J* = 7, 2, 1 H, 20-H), 1.86 (s, 3 H, 12-Me), 1.96 (s, 3 H, 4-Me), 2.05 (m, 2 H, 11-H_2), 2.10 (s, 3 H, acetyl-CH_3), 2.10 (s, 3 H, acetyl-CH_3), 2.19 (ddq, *J* = 8, 7, 1.5, 1 H, 18-H), 2.61–2.71 (m, 2 H, 6-H and 10-H), 3.22 (s, 3 H, 16-OMe), 3.57 (s, 3 H, 2-OMe), 3.66 (d br, *J* = 10, 1 H, 7-H), 3.84 (dd, *J* = 9, 9, 1 H, 16-H), 4.85 (d, *J* = 11, 1 H, 9-H), 5.23 (dd, *J* = 15, 10, 1 H, 15-H), 5.30 (ddq, *J* = 15, 8, 1.5, 1 H, 26-H), 5.58 (ddq, *J* = 15, 6, 0.5, 1 H, 27-H), 5.64 (d, *J* = 10, 1 H, 5-H), 5.79 (d, *J* = 10, 1 H, 13-H), 6.39 (s, 1 H, 3-H), 6.57 (dd, *J* = 15, 10, 1 H, 14-H); ^{13}C NMR see Table I; FAB-MS (positive) 799 (M + Na)$^+$, (negative) 776 (M^-).

11,13,11′,13′-Tetra-*O*-methylelaiolide (12). **11** (80 mg) was transformed to **12** according to general procedure B. Purification by CC (EtOAc–*n*-hexane (2:3)) gave 37 mg (58%) of **12**: $C_{46}H_{76}O_{12}$; TLC R_f 0.46 ($CHCl_3$–MeOH (95:5)) and 0.29 (EtOAc–*n*-hexane (1:2)); $[\alpha]^{20}_D$ = +85 (*c* 0.4, $CHCl_3$); IR (KBr, cm^{-1}) 3450, 2980, 1690, 1620 w, 1460, 1380, 1300, 1220; UV (MeOH) λ_{max} = 253 (ε 56 000); ^{1}H NMR (300 MHz, $CDCl_3$) see Table III, other signals similar to **13**, (300 MHz, C_6D_6) δ 0.60 (d, *J* = 7, 3 H, 6-Me), 0.84 (d, *J* = 7, 3 H, 8-Me), 0.95 (t, *J* = 7, 3 H, 14-CH_2CH_3), 1.25 (d, *J* = 6, 3 H, 15-Me), 1.35 (d, *J* = 7, 3 H, 10-Me), 1.4–1.5 (m, obs., 1 H, 14-H), 1.45–1.60 and 1.66–1.70 (m, 2 H, 14-CH_2), 1.74 (dd, *J* = 11, 10, 1 H, 12-H_{ax}), 1.93 (m, 1 H, 8-H), 2.18–2.30 (m, 2 H, H-6 and H-10), 2.87 (dd, *J* = 11, 4, 1 H, 12-Heq), 3.08 (s, 3 H, 11-OMe), 3.15 (s, 3 H, 13-OMe), 3.60 (m, 2 H, 13-H and 15-H), 3.92 (dd, *J* = 10, 4, 1 H, 9-H), 4.13 (d, *J* = 4, 1 H, 19-OH), 5.05 (dd, *J* = 10, 1.5, 1 H, 7-H), 5.13 (dd, *J* = 15, 10, 1 H, 5-H), 5.39 (d, *J* = 16, 1 H, 2-H), 5.72 (dd, *J* = 15, 11, 1 H, 4-H), 7.03 (dd, *J* =16, 11, 1 H, 3-H); ^{13}C NMR see Table IV; FAB-MS (negative) 821 (M^-).

13, 13′-Di-*O*-methylelaiolide (13). **12** (22 mg, 0.027 mmol) was dissolved in a solution consisting of 1.0 mL of water, 9.0 mL of acetone, and 1 mg (6 × 10^{-3} mmol) of $FeCl_3$. The mixture was stirred for 10 min at room temperature and poured into 10 mL of phosphate buffer (pH = 7), and the organic solvent was removed in vacuo. The usual workup procedure followed by CC (EtOAc–*n*-hexane (1:2)) yielded 14 mg (66%) of **13**: $C_{44}H_{72}O_{12}$; TLC R_f 0.77 ($CHCl_3$–MeOH (95:5)) and 0.34 (EtOAc–*n*-hexane (1:2)); $[\alpha]^{20}_D$ = +26 (*c* 0.5, $CHCl_3$); IR (KBr, cm^{-1}) 3450, 2980, 1690, 1640, 1620 w, 1460, 1380, 1300, 1220; UV (MeOH) λ_{max} = 253 (ε 50 000); ^{1}H NMR (300 MHz, $CDCl_3$) see Table III and δ 0.83 (d, *J* = 7, 3 H, 8-Me), 0.87 (t, *J* = 7, 3 H, 14-CH_2CH_3), 1.03 (d, *J* = 7, 3 H, 6-Me or 10-Me) 1.05 (d, *J* = 7, 3 H, 6-Me or 10-Me), 1.10 (d, *J* = 6, 3 H, 15-Me), 1.21 (ddd, *J* = 11, 11, 2, 1 H, 12-H_{ax}), ~1.4 (m, 1 H, 14-H), 1.5–1.7 (m, 2 H, 14-CH_2), 1.98 (t br, 1 H, 8-H), 2.55 (m, 1 H, 6-H), 5.64 (dd, *J* = 15, 9, 1 H, 5-H), 5.70 (d, *J* = 16, 1 H, 2-H), 6.14 (dd, *J* = 15, 12, 1 H, 4-H), 6.98 (dd, *J* = 16, 12, 1 H, 3-H); (500 MHz, C_6D_6) δ 0.62 (d, *J* = 7, 3 H, 6-Me), 0.73 (d, *J* = 7, 3 H, 8-Me), 0.95 (t, *J* = 7, 3 H, 14-CH_2CH_3), 1.18 (d, *J* = 6, 3 H, 15-Me), 1.22 (d, *J* = 7, 3 H, 10-Me), 1.29 (ddd, *J* = 11, 11, 2, 1 H, 12-Hax), 1.43 (m, 1 H, 14-H), 1.47–1.56 and 1.75–1.84 (m, 2 H, 14-CH_2), 1.90 (q br, *J* = 7, 1 H, 10-H), 1.95 (m, 1 H, 8-H), 2.22 (ddq, *J* = 10, 10, 7, 1 H, H-6), 2.74 (dd, *J* = 11, 4, 1 H, 12-Heq), 3.23 (s, 3 H, 13-OMe), 3.80 (ddd, *J* = 11, 11, 4, 1 H, 13-H), 4.17 (dq, *J* = 11, 6, 1 H, 15-H), 4.58 (ddd, *J* = 10, 4, 2, 1 H, 9-H), 4.77 (dd, *J* = 4, 0.5, 1 H, 19-OH), 4.81 (dd, *J* = 10, 1.5, 1 H, 7-H), 5.12 (dd, *J* = 15, 10, 1 H, 5-H), 5.42 (d, *J* = 16, 1 H, 2-H), 5.66 (d, *J* = 2, 1 H, 11-OH), 5.75 (dd, *J* = 15, 11, 1 H, 4-H), 7.03 (dd, *J* =16, 11, 1 H, 3-H); ^{13}C NMR see Table IV; FAB-MS (negative) 793 (M^-).

Monoglycosylelaiolide (14) and Elaiolide (15). A solution of 80 mg (0.086 mmol) of **11** in 10.0 mL of CH_3CN and 5.0 mL of water was cooled to 0 °C. To this mixture a solution of 5 mg of *p*-toluenesulfonic acid in 2.5 mL of CH_3CN and 1.2 mL of water was added. The mixture was allowed to warm up to room temperature and was stirred for 15 h. Analysis by TLC showed after 6 h ~30% of unchanged **11**, 25% of **14**, and 25% of an unsymmetrical elimination product and after 15 h about 25% of **14**, 15% of **15** and different spots of elimination products. The reaction was stopped by adding 20 mL of saturated $NaHCO_3$ and extracting with EtOAc. The usual workup followed by CC (EtOAc–*n*-hexane (4:1)) gave 8 mg (14%) of **15** as a colorless oil: $C_{42}H_{68}O_{12}$; TLC R_f 0.28 ($CHCl_3$–MeOH (9:1)) and 0.32 (EtOAc–*n*-hexane (4:1)); $[\alpha]^{20}_D$ = +28 (*c* 0.3, $CHCl_3$); IR (KBr, cm^{-1}) 3440, 2980, 1700, 1640, 1460, 1380, 1220, 1000; UV (MeOH) λ_{max} = 253 (ε 53 000); ^{1}H NMR (500 MHz, $CDCl_3$) see Table III and δ 0.80 (d, *J* = 7, 3 H, 8-Me), 0.89 (t, *J* = 7, 3 H, 14-CH_2CH_3), 1.00 (d, *J* = 7, 3 H, 10-Me) 1.04 (d, *J* = 7, 3 H, 6-Me), 1.10 (d, *J* = 6, 3 H, 15-Me), 1.17 (ddd, *J* = 11, 11, 2, 1 H, 12-H_{ax}), ~1.4 (m, 1 H, 14-H), 1.5–1.7 (m, 2 H, 14-CH_2), 1.74 (q br, *J* = 7, 1 H, 10-H), 1.96 (t br, 1 H, 8-H), 2.54 (m, 1 H, 6-H), 5.64 (dd, *J* = 15, 9, 1 H, 5-H), 5.70 (d, *J* = 16, 1 H, 2-H), 6.13 (dd, *J* = 15, 12, 1 H, 4-H), 6.97 (dd, *J* = 16, 12, 1 H, 3-H); ^{13}C NMR see Table IV. The second fraction contained an unsymmetrical elimination product, and the third fraction gave 15 mg (22%) of **14** as a white amorphous powder: $C_{48}H_{78}O_{15}$; TLC R_f 0.19 ($CHCl_3$–MeOH (9:1)) and 0.10 (EtOAc–*n*-hexane (4:1)); $[\alpha]^{20}_D$ = −7 (*c* 0.4, $CHCl_3$); IR (KBr, cm^{-1}) 3440, 2980, 1700, 1640, 1460, 1220, 1000; UV (MeOH) λ_{max} = 253 (ε 51 000); ^{1}H NMR (300 MHz, $CDCl_3$) see Table III; ^{13}C NMR (50.3 MHz, $CDCl_3$) characteristic signals δ 33.6 (t, C-2″), 93.2 (d, C-1″), 99.0 and 99.1 (s, C-11 and C-11′), 120.9 (d, C-2 and C-2′), 132.0 (d, C-4 and C-4′), 144.3 (d, C-5 and C-5′), 145.0 (d, C-3 and C-3′) 170.0 (C-1 and C-1′); FAB-MS (positive) 917 (M + Na)$^+$.

Acknowledgment. We are grateful to Priv.-Doz. Dr. Jürgen Rohr for providing us with elaiophylin. We would like to thank Jutta Gerber-Nolte for skilful technical assistance and Reinhard Machinek and Carola Zolke for providing the NMR measurements.

Supplementary Material Available: ^{1}H NMR spectra of all compounds (exept natural products) recorded in $CDCl_3$ and of **12** and **13** recorded in C_6D_6 (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.