Ring Contraction of an Ascomycin Derivative to a 19-Membered Macrolactam[1])

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Starting from readily available (22*R*)-26,33-bis-*O*-[(*tert*-butyl)dimethylsilyl]-22,22-*O*-dihydroisoascomycin (**5**), the synthesis of a doubly ring-contracted ascomycin derivative, the 19-membered macrolactam **10**, is described.

Introduction. – Ascomycin (**1**) is a 23-membered macrolactam isolated from the fermentation broth of *Streptomyces hygroscopicus var. ascomyceticus* [2]. Derivatives of ascomycin (**1**) have shown high activities in animal models of skin inflammation [3], and clinical efficacy was confirmed with SDZ ASM 981 (**2**) in patients with atopic dermatitis, allergic contact dermatitis, and psoriasis [4]. In our search for new derivatives with interesting pharmacological profiles, we embarked on the chemical modification of isoascomycins, featuring a 21-membered instead of a 23-membered macrolactam ring [1] (see **3**–**5**). They are readily available from 22,22-*O*-dihydroascomycin[2]) precursors by a base-induced intramolecular acyl shift from 26-*O* to 24-*O* [1a,c]. Surprisingly, no further shift to 22-*O* has been observed thus far. Here, we report the first synthesis of a doubly ring-contracted 19-membered ascomycin macrolactam isomer, derived from (22*R*)-28,29-epoxy-22,22-*O*-dihydroisoascomycin[2]) (**9**).

Results and Discussion. – Epoxide **9** is accessible *via* deprotected (22*R*)-22,22-*O*-dihydroisoascomycin (**8**) followed by a regiospecific epoxidation of the C(28)=C(29) bond (*Scheme 1*). For the deprotection of (22*R*)-26,33-bis-*O*-[(*tert*-butyl)dimethylsilyl]-22,22-*O*-dihydroisoascomycin (**5**) [1c], we first used as routinely aqueous HF in MeCN solution. However, the reaction with aqueous HF solution yielded unexpectedly the pyran derivative **6**. Exhaustive acetylation of **6** with an excess of Ac_2O/4-(dimethylamino)pyridine (DMAP) gave only the 33-*O*-acetyl derivative **7** and confirmed the absence of free OH groups at C(22) and C(26)[3]). As deduced unambiguously from the ^{1}H-NMR data, the newly formed pyran ring in **6** and **7** exists in

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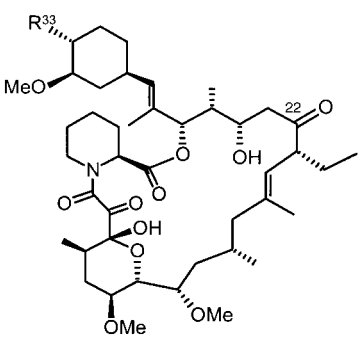
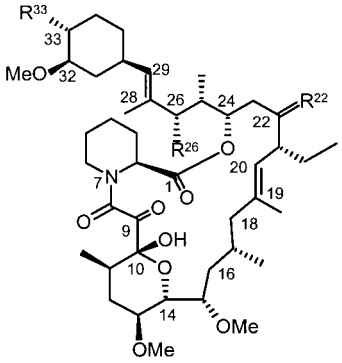
[1]) Synthetic Modifications of Ascomycin, Part IV; for Part III see [1d].

[2]) Arbitrary numbering.

[3]) Systematic numbering.





1 R^{33} = OH **ascomycin**[2]
2 R^{33} = *epi*-Cl **SDZ ASM 981**[2]

3 R^{33} = R^{26} = OH, R^{22} = O **isoascomycin**[2]
4 R^{33} = R^{26} = OH, R^{22} = H, (*S*)-OH
(22*S*)-dihydroisoascomycin[2]
5 R^{26} = R^{33} = ^{t}BuMe$_2$SiO, R^{22} = H, *(R)*-OH
26,33-bis-*O*-[(*tert*-butyl)dimethylsilyl]-dihydroisoascomycin[2]

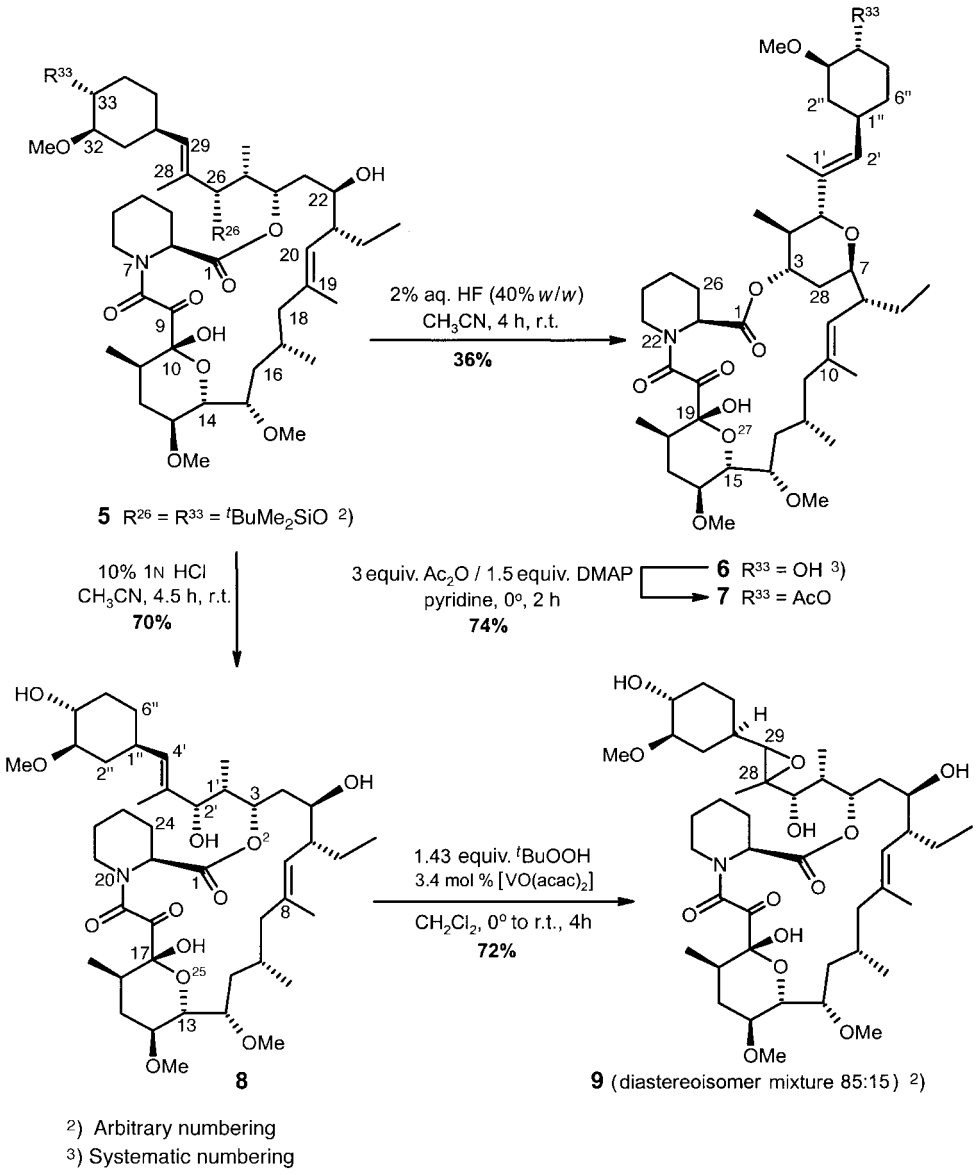
a chair conformation with all substituents in equatorial positions, with exception of the C(22) residue. It is interesting to note that the configuration at C(26) of **6** is reversed as compared to the starting material **5**, thus indicating that ring closure probably occurs *via* an intramolecular nucleophilic attack of OH–C(22) at C(26).

The desired deprotection of **5** without concomitant ring closure was achieved by applying aqueous HCl instead of HF solution to give the (22*R*)-22,22-*O*-dihydroisoascomycin derivative **8** in good yield (*Scheme 1*). Compound **8** was easily converted to epoxide **9** by selective epoxidation of the allylic C(28)=C(29) bond with a catalytic amount of [VO(acac)$_2$] (acac = pentane-2,4-dione) and 1.43 equiv. of *tert*-butyl hydroperoxide in CH_2Cl_2 solution [5] (72% yield; diastereoisomer mixture 85 : 15).

Next we achieved further functionalizations of epoxide **9**. Upon treatment with *Lewis* acids, epoxides are known to undergo various rearrangement reactions, *via* ring opening and concomitant alkyl or hydride migrations (for a review, see [6]). Treatment of **9** with $BF_3 \cdot OEt_2$, however, did not result in products from the expected rearrangement reactions. Instead, the 19-membered macrolactam derivative **10** was isolated as the major product, together with several minor, not-yet-identified by-products (*Scheme 2*).

The structure of **10** and of its tri-*O*-acetyl derivative **11** was assigned by NMR analysis with the exception of the absolute configurations at the newly generated stereocenters C(28) and C(29). The formation of **10** can be explained assuming a ring contraction (acyl shift from 24-*O* to 22-*O*) followed by a *Lewis*-acid-catalyzed intramolecular epoxide-ring opening, occurring *via* a nucleophilic attack of the liberated 24-OH group at C(28) of the epoxide. Thus far, no *Lewis*-acid-mediated ring contraction was observed starting from the unmodified (22*S*)-22,22-*O*-dihydroisoascomycin (**4**) or its (22*R*)-isomer derivative **5**. Whether this is due to a rapid equilibrium between the 21- and 19-membered ring size is not yet clear. However, this indicates that the observed **9** → **10** ring contraction might be driven by the subsequent capture of the 24-OH group *via* intramolecular epoxide ring opening and tetrahydrofuran formation.

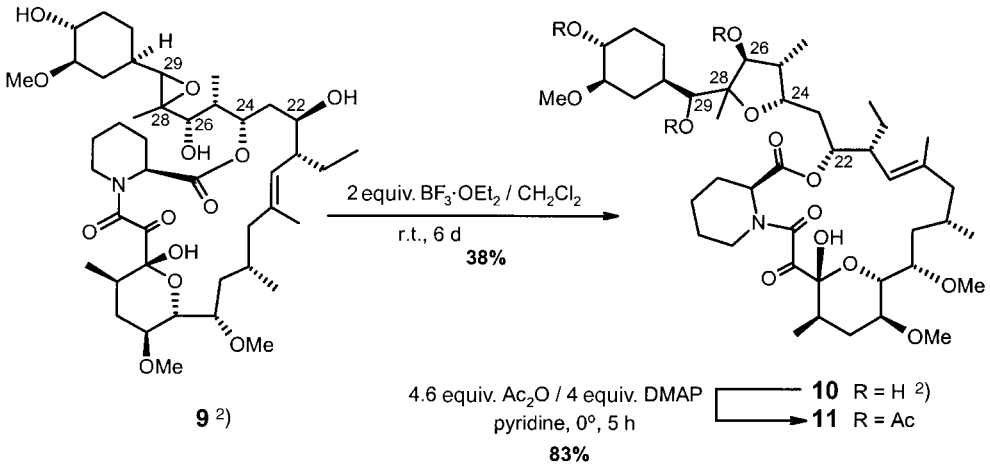
Scheme 1



Conclusion. – In summary, a double ring contraction of an ascomycin derivative to a 19-membered macrolactam has been established for the first time. Investigations addressing the general applicability of this ring contraction to related macrolactams are ongoing.

R. Z. thanks the *Fonds zur Förderung der wissenschaftlichen Forschung in Österreich* for a 'Karl-Landsteiner-Stipendium'.

Scheme 2



Experimental Part

General. All reactions were performed in flame-dried reaction vessels under a slight pressure of dry Ar. Solvents were dried by standard methods. All other commercially available reagents were applied without further purification. All reactions were monitored by TLC on glass-backed silica-gel plates with fluorescent stain (UV detection at λ_{max} 254 nm); visualization of the reaction components by spraying with a soln. of molybdatophosphoric acid (20% in EtOH/H_2O 3:1). Column chromatography (CC): silica gel (0.040–0.063 mm), from *E. MERCK*. ^{1}H- and ^{13}C-NMR Spectra: *Bruker-WM-250* and *Bruker-AMX-500*; the solvent $CDCl_3$ was used as internal standard ($\delta_{(H)}$ 7.27, $\delta_{(C)}$ 77.0); due to complicated overlapping *m*, only relevant ^{1}H-NMR data are reported. Mass spectra: fast-atom-bombardment (FAB) spectra; *VG-70-SE* instrument (*VG* anal.) operating at 8 kV accelerating voltage.

(*3*S,*4*R,5R,*7*R,*8*R,*9*E,*12*S,*14*S,*15*R,*16*S,*18*R,*19*R,*26a*S)*-8-Ethyl-4,5,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-19-hydroxy-5-{(*E*)-[1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl}-14,16-dimethoxy-4,10,12,18-tetramethyl-15,19-epoxy-3,7-methano-3*H,*7*H*-pyrido[2,1-c][1,20,4]dioxaazacyclotricosine-1,20,21(23*H*)-trione*[3]) (**6**). A soln. of (22*R*)-26,33-*O*-bis[(*tert*-butyl)dimethylsilyl]-22,22-*O*-dihydroisoascomycin (**5**) (399 mg, 0.39 mmol) in MeCN (10 ml) was treated with 40% aq. HF soln. (100 µl) for 4 h at r.t. The volatile components were evaporated, and the oily residue was purified by CC (hexane/AcOEt 1:1): **6** (110 mg, 36%). Colorless foam. Mixture of two conformers (3:1), major conformer: ^{1}H-NMR ($CDCl_3$)[2]): 5.54 (*d*, *J* = 1.5, OH); 5.19 (*d*, *J* = 9, H–C(29)); 4.86 (*dt*, *J* = 4, 11, H–C(24)); 4.63 (br. *s*, H–C(2)); 4.38 (br. *d*, *J* = 11.5, H_{eq}–C(6)); 3.40, 3.35, 3.31 (3*s*, 3 MeO); 1.66 (*s*, Me–C(19)); 1.26 (*s*, Me–C(28)); 1.04 (*d*, *J* = 6.5, Me–C(17)); 0.94 (*d*, *J* = 7, Me–C(11)); 0.82 (*d*, *J* = 6.5, Me–C(25)); 0.73 (*t*, *J* = 7, H–C(37)). ^{13}C-NMR ($CDCl_3$)[2]): 194.7 (C(9)); 170.2 (C(1)); 167.3 (C(8)); 136.6 (C(19)); 134.1 (C(29)); 132.4 (C(28)); 126.9 (C(20)); 98.1 (C(10)); 84.2 (C(32)); 81.3 (C(26)); 76.7 (C(22)); 75.5 (C(15)); 75.3 (C(14)); 75.2 (C(24)); 74.5 (C(13)); 73.5 (C(33)); 58.5, 56.7, 56.6, 55.4 (C(2), 3 MeO); 48.1 (C(18)); 39.4 (C(6)); 39.2 (C(21)); 38.0 (C(25)); 35.1 (C(16)); 35.0 (C(30)); 34.6 (C(31)); 33.9 (C(11)); 33.0 (C(23)); 30.5 (C(35)); 27.4 (C(17)); 26.7 (C(3)); 24.5 (C(5)); 24.1 (C(36)); 21.2 (C(4)); 20.7 (*Me*–C(17)); 16.2 (*Me*–C(11)); 15.9 (*Me*–C(19)); 13.6 (*Me*–C(25)); 11.5, 11.4 (C(37), *Me*–C(28)).

*(3*S,*4*R,5*R*,*7*R,*8*R,*9*E,*12*S,*14*S,*15*R,*16*S,*18*R,*19*R,*26a*S)*-5-{(*E*)-[(1*R*,*3*R,*4*R)*-4-(Acetyloxy)-3-methoxycyclohexyl]-1-methylethenyl}-8-ethyl-4,5,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-19-hydroxy-14,16-dimethoxy-4,10,12,18-tetramethyl-15,19-expoxy-3,7-methano-3*H*,*7*H*-pyrido[2,1-c][1,20,4]dioxaazacyclotricosine-1,20,21(23*H*)-trione*[3]) (**7**). To a soln. of **6** (110 mg, 0.143 mmol) in dry pyridine (1 ml) at 0°, DMAP (25 mg, 0.205 mmol) and Ac_2O (41.5 µl, 0.43 mmol) were added, and the soln. was stirred at 0° for 2 h. The mixture was diluted with Et_2O (10 ml), washed with 0.1N HCl soln. (3 × 6 ml) and brine (1 × 5 ml), dried ($MgSO_4$) and evaporated. The oily residue was submitted to CC (silica gel, hexane/AcOEt, 3:1): **7** (86 mg, 74%). Mixture of two conformers (3:1), major conformer: ^{1}H-NMR ($CDCl_3$)[2]): 5.55 (*d*, *J* = 1, OH); 5.21 (*qd*, *J* = 1.5, 9, H–C(29)); 4.87 (*dt*, *J* = 4, 11, H–C(24)); 4.39 (br. *d*, *J* = 12, H_{eq}–C(6)); 3.62 (*dd*, *J* = 5, 10.5, H–C(22)); 3.54

(*d*, *J* = 10, H–C(26)); 3.38, 3.34, 3.32 (3 *s*, 3 MeO); 2.92 (*dt*, *J* = 3, 13, H_{ax}–C(6)); 2.08 (*s*, AcO–C(33)); 1.69 (*s*, Me–C(19)); 1.67 (*s*, Me–C(28)); 1.05 (*d*, *J* = 6.5, Me–C(11)); 0.91 (*d*, *J* = 7, Me–C(17)); 0.82 (*t*, *J* = 7, H–C(37)); 0.75 (*d*, *J* = 6.5, Me–C(25)). ^{13}C-NMR ($CDCl_3$)^2): 194.5 (C(9)); 170.5, 170.1 (C(1), *C*OMe); 167.3 (C(8)); 136.6 (C(19)); 133.7 (C(29)); 132.7 (C(28)); 126.9 (C(20)); 98.1 (C(10)); 81.3 (C(26)); 80.7 (C(32)); 76.7 (C(22)); 75.8 (C(33)); 75.5 (C(15)); 75.3, 75.2 (C(14), C(24)); 74.5 (C(13)); 58.4, 57.3 (*Me*O–C(13), *Me*O–C(32)); 56.6 (C(2)); 55.3 (*Me*O–C(15)); 48.1 (C(18)); 39.4 (C(6)); 39.2 (C(21)); 38.0 (C(25)); 36.2 (C(31)); 35.1 (C(16)); 34.8 (C(30)); 33.9 (C(11)); 33.1 (C(23)); 29.8 (C(35)); 27.4 (C(17)); 26.7 (C(3)); 24.5 (C(5)); 24.2 (C(36)); 21.3, 21.2, 20.8 (C(4), *Me*CO, *Me*–C(17)); 16.2 (*Me*–C(11)); 15.9 (*Me*–C(19)); 13.6 (*Me*–C(25)); 11.5, 11.4 (C(37), *Me*–C(28)).

*(3*S*,5*R*,6*R*,7*E*,10*S*,12*S*,13*R*,14*S*,16*R*,17*R*,24a*S*)-6-Ethyl-4,5,6,9,10,11,12,13,14,15,16,17,22,23,24,24a-hexadecahydro-5,17-dihydroxy-3-{(1*S*,2*S*,3*E*)-2-hydroxy-4-[(1*R*,3*R*,4*R*)-4-hydroxy-3-methoxycyclohexyl]-1,3-dimethylbut-3-enyl}-12,14-dimethoxy-8,10,16-trimethyl-13,17-epoxy-3*H*-pyrido[2,1-c][1,4]oxaazacycloheneicosine-1,18,19(21*H*)-trione*^{3}) (**8**). A soln. of **5** (3.20 g, 3.13 mmol) in MeCN (50 ml) was treated with 1N HCl (6 ml) at r.t. for 4.5 h. The mixture was neutralized with sat. aq. $NaHCO_3$ soln. and extracted with Et_2O (3 × 30 ml). The extract was dried ($MgSO_4$) and evaporated. CC (CH_2Cl_2/MeOH 95 : 5) of the residue yielded **8** (1.73 g, 70%). Colorless foam. ^{1}H-NMR ($CDCl_3$)^2): 5.12 (*d*, *J* = 9, H–C(29)); 5.01 (*d*, *J* = 5, H–C(2)); 4.97 (*dt*, *J* = 2.5, 7, H–C(24)); 4.76 (*d*, *J* = 10.5, H–C(20)); 4.43 (br.*d*, *J* = 11, H_{eq}–C(6)); 4.01 (*s*, OH); 3.81 (*d*, *J* = 7.5, H–C(26)); 3.63 (*d*, *J* = 10, H–C(14)); 3.39, 3.37, 3.29 (3 *s*, 3 MeO); 3.01 (*ddd*, *J* = 4.5, 9, 11, H–C(32)); 2.84 (*dt*, *J* = 3, 13.5, H_{ax}–C(6)); 2.80 (br.*s*, OH); 1.63 (*s*, Me–C(28)); 1.55 (*s*, Me–C(19)); 1.02 (*d*, *J* = 6.5, Me–C(11)); 0.97 (*d*, *J* = 7, Me–C(25)); 0.90 (*d*, *J* = 6.5, Me–C(17)); 0.80 (*t*, *J* = 7.5, H–C(37)). ^{13}C-NMR ($CDCl_3$)^2): 197.0 (C(9)); 169.7 (C(1)); 166.0 (C(8)); 137.1 (C(19)); 134.9 (C(28)); 132.4 (C(29)); 126.9 (C(20)); 96.0 (C(10)); 84.3 (C(32)); 79.7 (C(26)); 74.9, 74.8 (C(15), C(22)); 73.7 (C(13), C(33)); 72.9 (C(14)); 72.3 (C(24)); 57.4, 57.0, 56.6, 56.5 (3 MeO, C(2)); 50.3 (C(21)); 48.1 (C(18)); 39.5 (C(6)); 37.6 (C(25)); 35.7 (C(23)); 35.0, 34.9 (C(30), C(31)); 34.6 (C(11)); 32.8 (C(16)); 32.1 (C(12)); 31.5 (C(34)); 30.6 (C(35)); 27.5 (C(3)); 26.4 (C(17)); 24.6, 24.5 (C(5), C(36)); 22.1 (C(4)); 20.4 (*Me*–C(17)); 16.3 (*Me*–C(11)); 15.7 (*Me*–C(19)); 11.9, 11.7 (*Me*–C(28), C(37)); 9.0 (*Me*–C(25)). FAB-MS: 776 ([*M* – H_2O]$^+$), 758 ([*M* – 2 H_2O]$^+$), 560, 266, 254, 241, 220.

*(3*S*,5*R*,6*R*,7*E*,10*S*,12*S*,13*R*,14*S*,16*R*,17*R*,24a*S*)-6-Ethyl-4,5,6,9,10,11,12,13,14,15,16,17,22,23,24,24a-hexadecahydro-5,17-dihydroxy-3-{(1*S*,2*S*)-2-hydroxy-2-{3-[(1*R*,3*R*,4*R*)-4-hydroxy-3-methoxycyclohexyl]-2-methyloxiran-2-yl}-1-methylethyl}-12,14-dimethoxy-8,10,16-trimethyl-13,17-epoxy-3*H*-pyrido[2,1-c][1,4]oxaazacycloheneicosine-1,18,19(21*H*)-trione*^{3}) (**9**). To a soln. of **8** (370 mg, 0.466 mmol) in CH_2Cl_2 (20 ml) *t*-BuOOH (0.23 ml, 0.699 mmol; 3M soln. in toluene) and [VO(acac)$_2$] (9 mg, 0.024 mmol) were added at 0°. After 0.5 h at 0°, the mixture was warmed to r.t. and stirred for 4 h. The resulting soln. was diluted with toluene (10 ml) and evaporated. The crude product (338 mg) was purified by CC (AcOEt/toluene 3 : 1): **9** (270 mg, 72%). Colorless foam. Mixture of two diastereoisomers (85 : 15), major diastereoisomer: ^{1}H-NMR ($CDCl_3$)^2): 5.17 – 5.06 (*m*, H–C(24)); 4.84 (*d*, *J* = 9.5, H–C(20)); 4.41 (br.*d*, *J* = 11, H_{eq}–C(6)); 4.19 (*s*, OH); 3.82 (br.*s*, H–C(26)); 3.41, 3.37, 3.29 (3 *s*, 3 MeO); 2.84 (*d*, *J* = 8.5, H–C(29)); 1.57 (*s*, Me–C(19)); 1.24 (*s*, Me–C(28)); 0.98, 0.94 (2 *d*, *J* = 6.5 each, Me–C(11), Me–C(17)); 0.87 (*d*, *J* = 7, Me–C(25)); 0.81 (*t*, *J* = 7, H–C(37)). FAB-MS: 816 ([*M* + Li]$^+$), 686, 333, 313, 266, 221.

*(3*R*,4*R*,5*E*,8*S*,10*S*,11*R*,12*S*,14*R*,15*R*,22a*S*)-4-Ethyl-4,7,8,9,10,11,12,13,14,15,20,21,22,22a-tetradecahydro-15-hydroxy-10,12-dimethoxy-6,8,14-trimethyl-3-{[(2*S*,3*R*,4*S*)-tetrahydro-4-hydroxy-5-{hydroxy[(1*R*,3*R*,4*R*)-4-hydroxy-3-methoxycyclohexyl]methyl}-3-methylfuran-2-yl}methyl}-11,15-epoxy-3*H*-pyrido[2,1-c][1,4]oxaazacyclononadecine-1,16,17(19*H*)-trione*^{3}) (**10**). A soln. of (22*R*)-28,29-epoxy-22,22-*O*-dihydroisoascomycin (**9**; 115 mg, 0.142 mmol) in CH_2Cl_2 (5 ml) was treated with $BF_3 \cdot Et_2O$ (10 drops) for 6 d at r.t. Workup with sat. aq. $NaHCO_3$ soln., extraction with CH_2Cl_2, drying ($MgSO_4$), and evaporation afforded the crude product (63 mg) which was submitted to CC (AcOEt/toluene 3 : 1): **10** (44 mg, 38%). Colorless foam. ^{1}H-NMR ($CDCl_3$)^2): 5.16 (*dd*, *J* = 5, 10, H–C(22)); 4.44 (br.*d*, *J* = 13.5, H_{eq}–C(6)); 4.27 (*d*, *J* = 7.5, H–C(26)); 4.13 (*s*, OH); 3.74 (*dd*, *J* = 2, 9.5, H–C(14)); 3.42, 3.38, 3.29 (3 *s*, 3 MeO); 2.99 (*ddd*, *J* = 4.5, 9, 11.5, H–C(32)); 2.75, 2.48 (2 br.*s*, 2 OH); 1.40 (*s*, Me–C(19)); 1.05 (*s*, Me–C(28)); 0.98, 0.93, 0.91 (3 *d*, *J* = 7 each, Me–C(11), Me–C(17), Me–C(25)); 0.86 (*t*, *J* = 7, H–C(37)). ^{13}C-NMR ($CDCl_3$)^2): 196.5 (C(9)); 169.2 (C(1)); 165.4 (C(8)); 137.1 (C(19)); 123.9 (C(20)); 96.8 (C(10)); 88.2 (C(28)); 84.6 (C(32)); 79.9 (C(26)); 77.6 (C(29)); 75.5 (C(24)); 75.2 (C(15)); 73.6 (C(13)); 73.3 (C(22), C(33)); 72.3 (C(14)); 56.6, 56.3, 56.2 (3 MeO); 56.1 (C(2)); 50.0 (C(18)); 43.9 (C(21)); 42.2 (C(23)); 39.1 (C(6)); 37.9 (C(25)); 34.7 (C(30)); 33.1, 32.4, 31.9, 31.4, 31.1, 29.6 (C(11), C(12), C(16), C(31), C(34)); 28.5 (C(3)); 25.5 (C(17)); 24.8, 24.7, 24.6 (C(5), C(35), C(36)); 21.4 (C(4)); 20.5 (*Me*–C(17)); 16.8 (*Me*–C(28)); 16.0 (*Me*–C(11)); 15.3 (*Me*–C(19)); 11.8 (C(37)); 10.0 (*Me*–C(25)). FAB-MS: 833 ([*M* + Na]$^+$), 792 ([*M* – H_2O]$^+$), 632, 447, 307, 266.

*(3*R*,4*R*,5*E*,8*S*,10*S*,11*R*,12*S*,14*R*,15*R*,22a*S*)-3-{[(2*S*,3*R*,4*S*)-4-(Acetyloxy)-5-{(acetyloxy)[(1*R*,3*R*,4*R*)-4-(acetyloxy)-3-methoxycyclohexyl]methyl}-tetrahydro-3-methylfuran-2-yl}methyl]-4-ethyl-4,7,8,9,10,11,12,13,14,15,20,21,22,22a-tetradecahydro-15-hydroxy-10,12-dimethoxy-6,8,14-trimethyl-11,15-epoxy-3*H*-pyrido[2,1-c][1,4]-oxaazacyclononadecine-1,16,17(19*H*)-trione*[3]) (**11**). According to the acetylation of **6**, a mixture of **10** (44 mg, 0.054 mmol), Ac_2O (24 µl, 0.25 mmol) and DMAP (26.5 mg, 0.217 mmol) in pyridine (0.5 ml) was stirred for 5 h at 0° and then worked up. Purification by CC (cyclohexane/acetone 5:1) afforded **11** (42 mg, 83%). ^{1}H-NMR ($CDCl_3$)[2]): 5.17 (*dd*, *J* = 4.5, 10, H–C(22)); 5.09 (*d*, *J* = 5.5, H–C(20)); 4.97 (br. *d*, *J* = 6, H–C(2)); 4.86 (*d*, *J* = 10.5, H_{eq}–C(6)); 4.58 (*d*, *J* = 6, H–C(26)); 4.15 (*s*, OH); 3.75 (*dd*, *J* = 2, 9.5, H–C(14)); 3.40, 3.36, 3.27 (3*s*, 3 MeO); 2.08, 2.05, 2.04 (3*s*, 3 AcO); 1.38 (*s*, Me–C(19)); 1.10 (*s*, Me–C(28)); 1.00, 0.89, 0.82 (3*d*, *J* = 6.5 each, Me–C(11), Me–C(17), Me–C(25)). ^{13}C-NMR ($CDCl_3$)[2]): 196.5 (C(9)); 170.7, 170.6, 169.7 (3 AcO); 168.9 (C(1)); 165.4 (C(8)); 137.4 (C(19)); 123.7 (C(20)); 96.6 (C(10)); 86.5 (C(28)); 80.7 (C(32)); 79.2, 79.0 (C(26), C(29)); 77.5, 75.7, 75.0, 74.0, 73.2 (C(13), C(15), C(22), C(24), C(33)); 72.2 (C(14)); 57.3, 56.6, 56.3, 56.0 (C(2), 3 MeO); 49.9 (C(18)); 42.0, 41.5 (C(21), C(23)); 39.1 (C(6)); 36.0, 34.8, 34.7, 32.5, 32.3, 29.3, 28.7 (C(11), C(12), C(16), C(25), C(30), C(31), C(34)); 26.1, 25.5, 24.7, 24.6 (C(3), C(5), C(17), C(35), C(36)); 21.4 (C(4)); 20.8, 20.5 (*Me*–C(17), 3 AcO); 16.1, 16.0 (*Me*–C(11), *Me*–C(28)); 15.3 (*Me*–C(19)); 11.9 (C(37)); 9.3 (*Me*–C(25)). FAB-MS: 942 ($[M + Li]^+$), 918, 898, 882, 313.

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