Stereoselective Synthesis of Alcohols; LII:[1] Synthesis of the C-10 to C-18 Part of the Mycalamides

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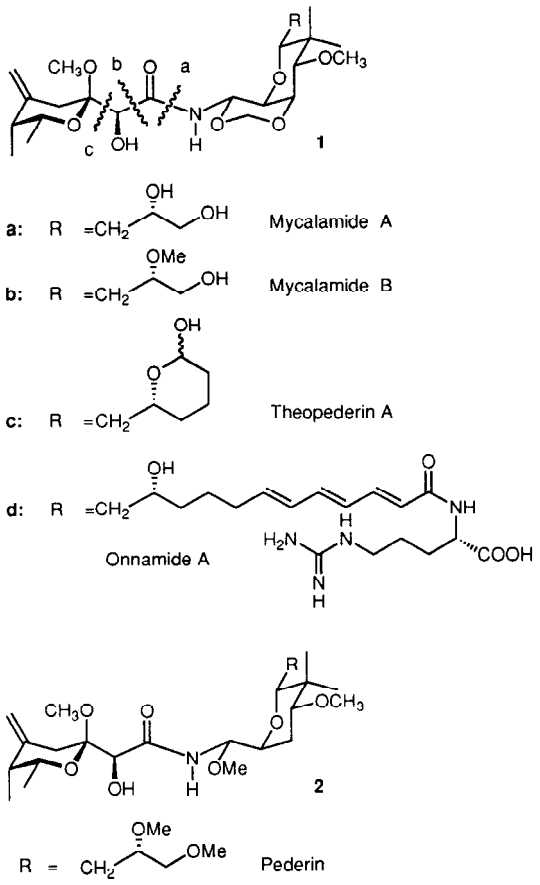
Received 3 October 1997; revised 20 October 1997

Abstract: A synthesis of the right hand fragment, C-10 to C-18, of mycalamide B is described using three stereogenic centers of D-arabinose. This synthesis profits from the peculiar conformational properties of the trioxa-*cis*-decalin ring system, which has a high tendency to populate an *O*-proximal conformation. The described synthesis supersedes earlier attempts to reach the right hand fragment of the mycalamides from the C-10-epi-series.

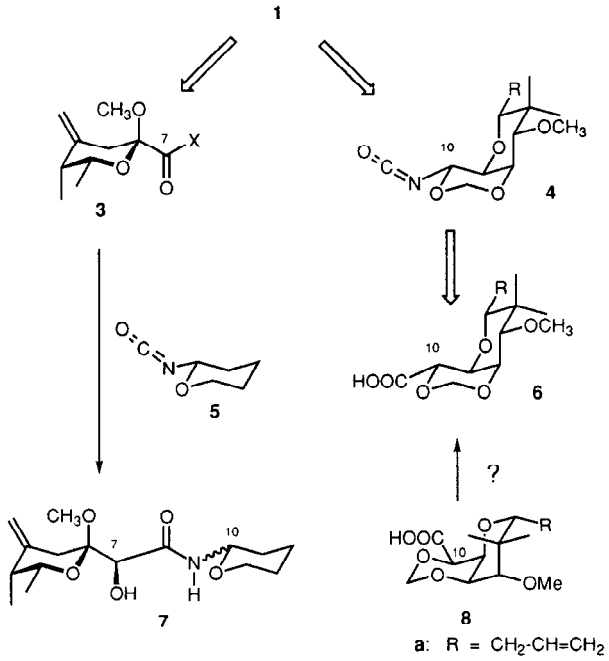
Key words: mycalamides, D-arabinose, trioxa-*cis*-decalin system

The mycalamides **(1a** and **1b)**,[2] together with pederin **(2)**, the theopederins **(1c)**[3] and the onnamides **(1d)**[4] form an interesting class of biologically highly active molecules. These compounds inhibit protein synthesis at a subnanomolecular level.[5] The mycalamides have also a very strong immunosuppressive activity.[6]



Scheme 1

The biological activity of these compounds stimulated widespread synthetic efforts: Pederin was the first of these molecules to be synthesized.[7] The mycalamides and onnamide have since been synthesized in a pioneering study by the Kishi group.[8,9] The previous syntheses used either a disconnection at bond "a" or bond "c".[10] We considered that a disconnection at bond "b" should allow an efficient entry into this class of compounds, i.e. we hoped to reach the mycalamides by connecting the left hand building block **3** with a right hand building block **4**. The feasibility of this approach was successfully demonstrated in a model study[11] with the mockup right hand fragment **5** to give the amide **7**, a sort of truncated mycalamide.

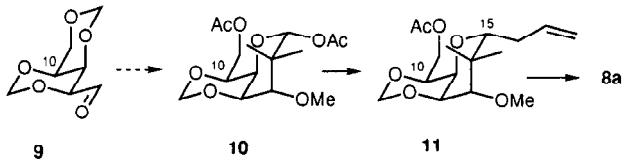


Scheme 2

In order to realize an efficient synthesis of the right hand fragment **4**, we envisioned a Curtius degradation of the carboxylic acid **6**. In fact, Curtius degradation of suitable carboxylic acids is an attractive route to the right hand fragment of pederin **(2)**, the mycalamides and their analogs.[12–14] In this manuscript we describe a synthesis of the carboxylic acid **6**. Our efforts focussed initially[14] on the C-10 (mycalamide numbering) epimeric acid **8**, which we hoped to equilibrate to the required acid **6**.

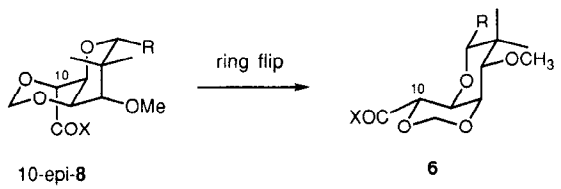
Synthesis of the C-10 Epimeric Carboxylic Acid 8

Our choice to proceed via the C-10 epimeric carboxylic acid **8** was motivated by the ready availability of a starting material **9**[15] that provided already the 1,3-dioxane ring and two stereogenic centers of **6** with the correct absolute configuration.



Scheme 3

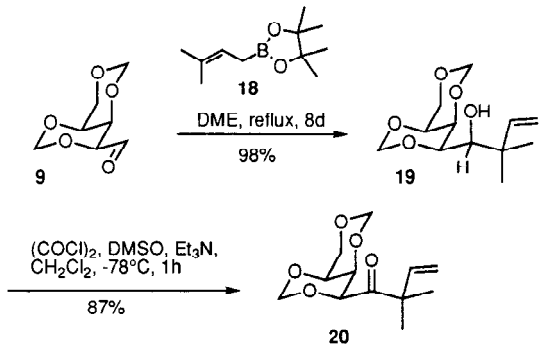
Evolution of the synthesis from **9** should generate the acetate **10**, which was anticipated to exist in the conformation of the trioxa-*cis*-decalin ring system shown.[12,16,17] This would allow axial introduction[18] of the side chain with the correct relative configuration at C-15, cf. **11**. At this point we could leave it open whether the allylic side chain would be modified into that of the mycalamides before reaching **8** or after epimerization to **6**. We hoped that at the stage of 10-epi-**8** the epimerization at C-10 would proceed readily, because ring inversion of the decalin system would bring three alkyl groups from an axial into an equatorial position.



Scheme 4

To put this plan to practice, we investigated the allylboration of the aldehyde **9**, hoping that reagent control of diastereoselectivity would furnish the desired alcohol **14**.

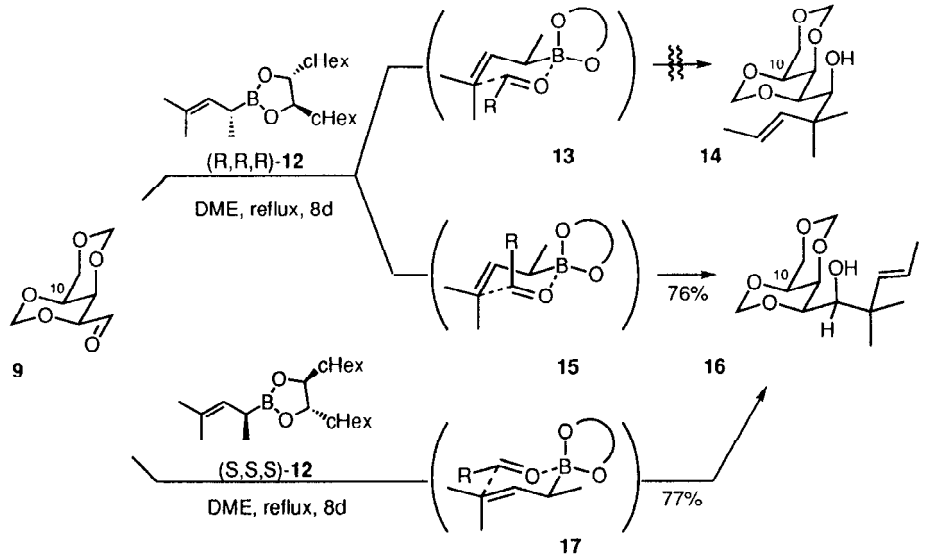
However, reaction of **9** with the (*R*,*R*,*R*)-boronate **12**[19] did not lead to **14**, but furnished rather its epimer **16** as the predominant (>9 : 1) diastereomer in 76% yield. This constitutes one of the rare cases[20] in which substrate control of diastereoselectivity overrides the asymmetric induction from chiral α-substituted allyl boronates. The relative configuration of **16** was secured by a crystal structure analysis of a derivative of **16**.[21] The reaction proceeded therefore unexpectedly via transition state **15** with an axial arrangement of the aldehyde residue, rather than via transition state **13** with the usual equatorial placement of the aldehyde residue. While of no relevance to our synthesis, it may be added, that the (*S*,*S*,*S*)-boronate *ent*-**12** reacted with good diastereoselectivity via the transition state **17**[22] to give also the (undesired) diastereomer **16** in 76% yield. The reaction between the aldehyde **9** and the allyl boronates **12** is therefore stereoconvergent, but it leads to the wrong product **16**. For that matter, reaction of **9** with the achiral boronate **18** furnished the alcohol **19** with the same relative configuration as **16** in high yield with a 9:1 diastereoselectivity.



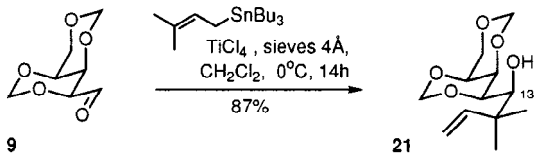
Scheme 6

While **19** could be readily oxidized to the ketone **20** (87%), attempts at stereoselective reduction of **20** to **21** remained unrewarding[21] and were abandoned in favor of a chelation controlled Lewis acid-mediated[23] prenylation of the aldehyde **9**. The latter gave the alcohol **21** with the required configuration at C-13 (mycalamide numbering) with >95% diastereoselectivity in 87% yield.

The further evolution of the synthesis proceeded without significant problems. Methylation of the hydroxy group of **21** furnished the ether **22** (93%). Selective cleavage of



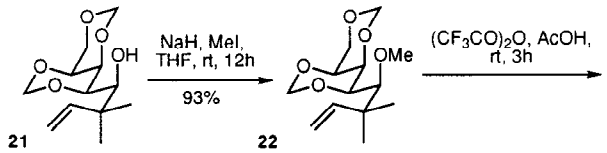
Scheme 5



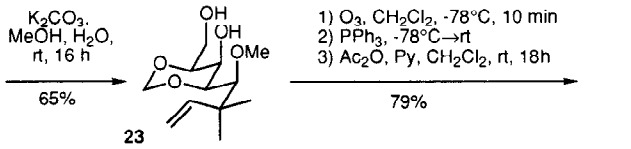
9 21

Scheme 7

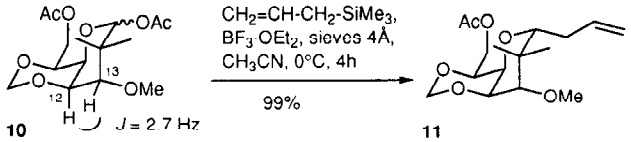
the less substituted dioxane ring could be realized with Ac_2O/H_2SO_4 in acetic acid.[24] Yet, the alternative cleavage with trifluoroacetic anhydride in acetic acid[25] turned out to be more reliable.



21 22



23



10 11

Scheme 8

The resulting acetates were cleaved with K_2CO_3/methanol to give the diol **23** in 65% yield. Ozonolysis of the latter followed by treatment with acetic anhydride gave 79% of the lactol acetates **10** as a 3:1-anomeric mixture. Since the allyl group in **11** was to be introduced from the axial direction,[26] the conformation of the trioxa-decaline ring system in **10** is of concern. A 2.7 Hz (2.4 Hz in the other anomer) coupling between the hydrogens at C-12 and C-13 (mycalamide numbering) in **10** showed that the expected *O*-proximal conformation of the trioxadecalin system prevailed, cf. the conformer equilibrium of the tetraoxadecalin **24**[27] (cf. also References 16, 17, 28).

24

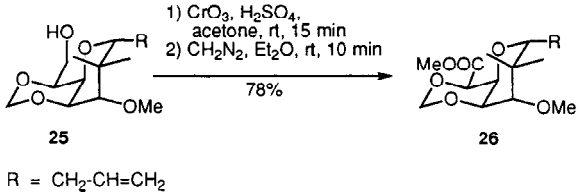
Scheme 9

Allylation of the lactol acetates **10** finally furnished a single diastereomer of the desired compound **11** in 99 % yield.

The Epimerisation of 8 at C-10 to Give 6

With compound **11** we had reached a compound which has already the carbon skeleton of **8**. Refunctionalization of **11** should lead to the aldehyde **28** and the ester **26**, allowing us to address the critical question of whether **8a** can be epimerized to **6a**.

Saponification of the acetate group in **11** led in quantitative yield to the alcohol **25**. Dess–Martin oxidation of the latter furnished 87% of the aldehyde **28**. Jones' oxidation of **25** followed by esterification (CH_2N_2) gave 78% of the ester **26**.

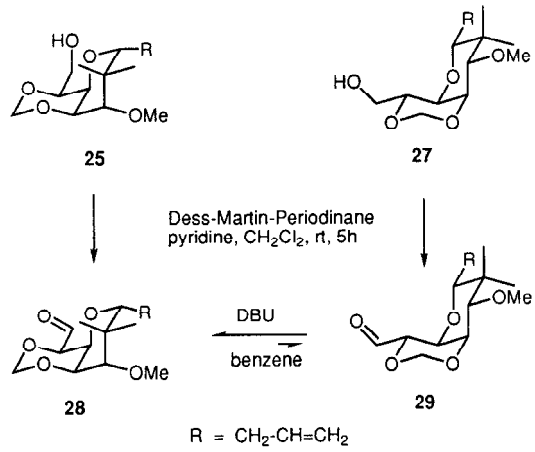


25 26

R = CH_2-CH=CH_2

Scheme 10

Treatment of the ester **26** with 0.05 equivalents of lithium diisopropylamide in THF yielded no sign of the desired methyl ester of **6**. Rather **26** was reisolated in 62 % yield. It appeared that 10-epi-**8**, even if it was generated under these conditions, meets either a high thermodynamic or a kinetic barrier to undergo the ringflip to **6**. We therefore turned to an epimerization of the aldehyde **28**. Neither treatment with piperidine/pivalic acid nor treatment with methanolic K_2CO_3 resulted in detectable amounts of the desired C-10 epimeric aldehyde **29**. Treatment of a benzene solution of **28** with DBU led to additional aldehydic proton NMR signals, but of overall low intensity. Warming of the solution led to increasing formation of uncharacterized products (aldolization?).



25 27 28 29

R = CH_2-CH=CH_2

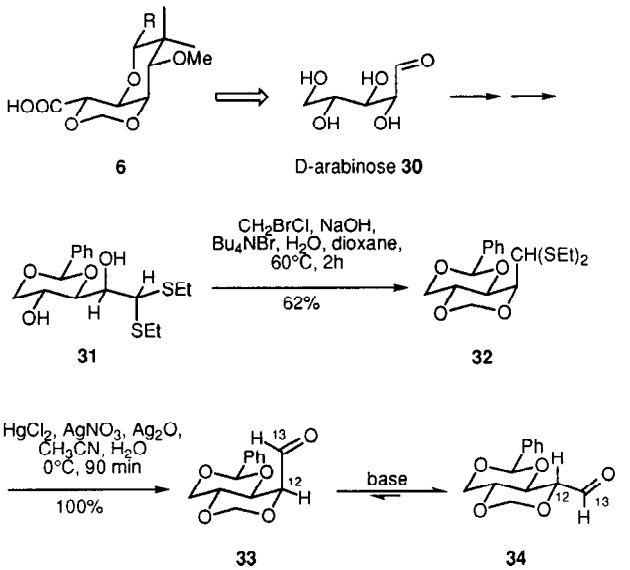
Scheme 11

This suggests that the equilibrium between **28** and **29** may lie, contrarily to our expectation, on the side of **28**. This could be the case, if stabilization of **28** by the gauche arrangement of two O–C–C–O-units[17] exceeds the destabilization caused by two axially oriented alkyl groups. That this analysis is correct, could be shown later, after the alcohol **27** became available by a different route (see below). Dess–Martin oxidation of **27** generated the aldehyde

29. Treatment of the latter in benzene-D_6 with DBU led to the appearance of five new aldehydic signals in the ^1H NMR spectrum. The major one (67% of the RCHO intensity) corresponded to that of **28**, while the signal of **29** had decreased to 10%. The availability of **29** allowed then to ascertain that ca. 10% of **29** had been formed on treatment of **28** with DBU. The failure to isomerize **28** quantitatively to **29**, or for that matter of **26** to the methyl ester of **6** rendered our plan to synthesize **6** via the 10-epi-series obsolete. Probably the situation would not be significantly different with **26** and **28**, bearing a fully elaborated side chain. For this reason we had to devise a new synthesis of **6**, introducing the correct C-10 configuration early on.

The Synthesis of the Carboxylic Acid 6 with a Fully Elaborated Side Chain

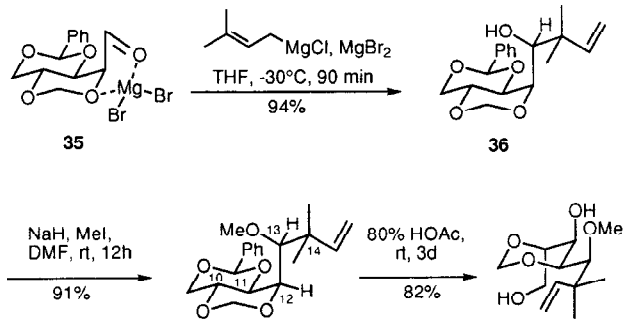
The necessity to devise another synthesis of **6** brought the challenge to find an even shorter approach than the one considered before. The prime requirement was to realize the correct configuration at C-10 much earlier. For such highly oxygenated targets as **6** carbohydrates are obvious starting materials. Inspection of the configuration of the stereogenic centers in **6** suggests D-arabinose (**30**) as a suitable precursor.



Scheme 12

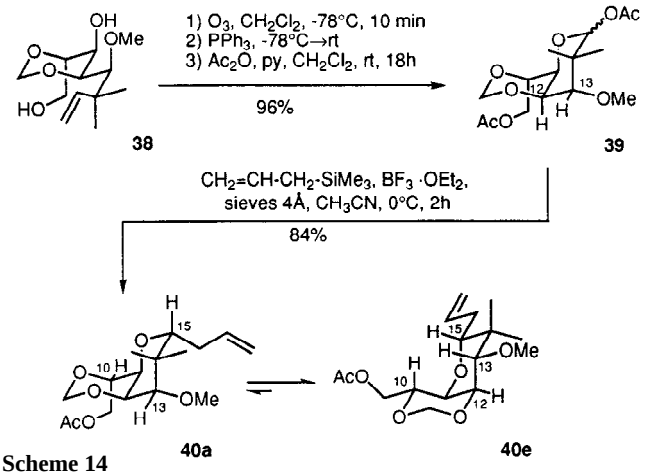
In fact, a two-step conversion of D-arabinose into the benzylidene acetal **31** had already been described.[29] The further task was to convert **31** into the methylene acetal **32**. The presence of the benzylidene acetal in **31** demanded a methylenation under basic conditions, such as the one described by Fleet[30] using CH_2Br_2 and sodium hydroxide under phase-transfer catalysis. When applied to **31**, only low yields (<30%) of **32** could be obtained. We surmised, correctly or not, that a slower second alkylation step should be beneficial and changed the alkylating agent to CH_2ClBr. This resulted in a 62% yield of **32**. Even more challenging was the hydrolysis of the dithioacetal moiety without epimerization of the resulting aldehyde **33**. Standard treatment of the dithioacetal **32** with HgO and $HgCl_2$ led to a 1:1 mixture of **33** and **34**. Structural assignment was possible with reference to the HC-12/HC-13 coupling constants: 6.8 Hz in **33** and 9.5 Hz in **34**. Various other methods were tested [31] to effect the cleavage of the thioacetal moiety maintaining the integrity of **33**. Eventually replacement of the mercuric oxide by silver oxide and addition of silver nitrate resulted in a reagent cocktail that allowed a clean and quantitative conversion of **32** into **33**.

In order to attain a prenylation of **33** with the correct stereochemistry we used a chelation controlled ($MgBr_2$) addition of prenylmagnesium chloride. This gave 94% of a single homoallylic alcohol which we expected to be **36**. Formation of a five-membered magnesium chelate, cf. **35**, should set the stage for a selective generation of **36**. Confirmation of this structural assignment was realized after methylation of **36** to give 91% of **37**. The quarternary nature of C-14 requires it to orient antiperiplanar to the C-11/C-12 bond. Then, the fact that the HC-12/HC-13 coupling constant was small (1.77 Hz) and that the methoxy group showed an NOE contact to HC-10, but not to HC-12 established the relative configuration at C-13 of **37**.



Scheme 13

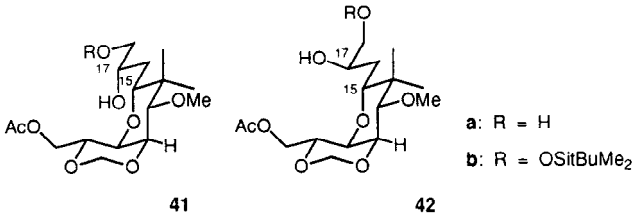
From the stage of **37** onwards we could rely on the experience gained in the C-10-epi series discussed before. Cleavage of the benzylidene acetal in **37** was effected in 80% acetic acid to give the diol **38** (82%). Ozonolysis, reductive workup with triphenylphosphane, and subsequent acetylation furnished 96% of the anomeric acetates **39**.



Scheme 14

The acetates **39** exist in the ring conformation shown, maximizing the attractive gauche effects between the oxygen atoms at C-10, C-11, and C-12, as **39** shows a small coupling constant of 1.96 (2.22) Hz between HC-12 and HC-13. This conformation is the one required to introduce the C-15 side chain from the axial side on reaction with allyltrimethylsilane/$BF_3{\cdot}OEt_2$. This reaction furnished 84% of a single allylation product **40**. Inspection of the HC-12/HC-13 coupling constant (10.3 Hz) showed that introduction of the allyl residue to give **40a** was followed by ring- inversion of the trioxadecalin ring system to give **40e**. The relative configuration at C-15 was secured by a NOE contact between HC-15 and HC-10. The gauche effect between the oxygen atoms in the trioxadecalin ring can therefore compensate in this system for axial placement of two (cf. **39**), but not of three alkyl substituents (cf. **40**). Treatment of **40** with methanolic K_2CO_3 furnished the alcohol **27** referred to above.

We took the allyl compound **40** as the starting point for the elaboration of the C-15 side chain. This followed closely the precedent set by the Kishi group[8,9] utilizing the Sharpless asymmetric dihydroxylation reaction. Best, but not yet satisfactory, results were obtained with dihydroquinine-9-phenanthryl ether as auxiliary. This led to 92% of a 2:1 mixture of the unseparable diastereomers **41a** and **42a**. Separation of the diastereomers became possible after protecting the primary hydroxy group with *tert*-butylchlorodimethylsilane. The diastereomers differ significantly in the chemical shift of the carbons C-17 and C-15: **41b**: C-17 δ = 71.6, C-15, 79.0; **42b**: C-17, 67.9, C-15, 74.1. These differences identify **41** as a 1,3-*syn* diol derivative.[32] Moreover, the chemical shifts of **41** at C-17 and C-15 correspond closely to those of Mycalamide A.

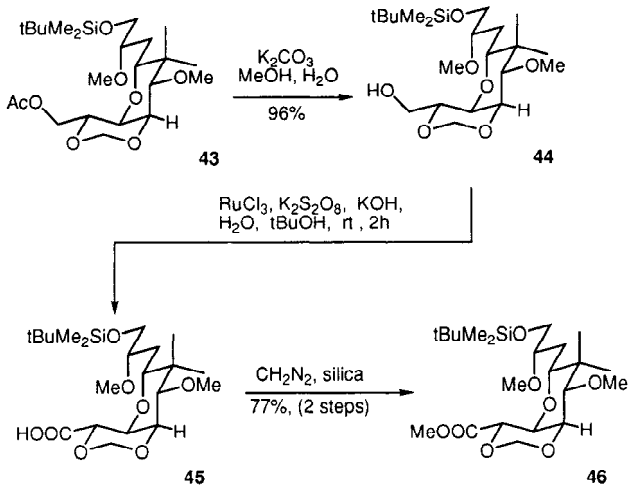


Scheme 15

Finally, the secondary hydroxyl group was methylated with diazomethane in the presence of silica gel.[33] For reaching high conversions, e.g. 82% for **43**, the silica gel needed special pretreatment.[34]

At this stage the oxidation level at C-10 had to be modified to reach the desired mycalamide building block **45** representing **6**. Removal of the acetoxy group by methanolic K_2CO_3 furnished 96% of the alcohol **44**, which was oxidized with potassium peroxidisulfate in the presence of $RuCl_3$ to give 80% of the crude, unstable acid **45**, which was immediatly converted to the methyl ester **46** by treatment with diazomethane.

This synthesis of **45** marks the hitherto shortest approach[8,9,10] to the right-hand fragment of the mycalamides. It took advantage of D-arabinose as the source of three stereogenic centers with correct configuration. Our approach depended critically on the conformational flexibility and the conformational preferences of the trioxa-decaline ring system, being switchable from the *O*-proximal to the *O*-distal conformation depending on the number and arrangement of substituents present. In this context it should be mentioned that the methyl ester **46** derived from **45** populates a mixture of the two ring conformations of the trioxa-*cis*-decalin ring system, as evident from the "averaged" vicinal coupling constants. Ring inversion occurs at such a rate that line broadening is seen for certain ^{13}C NMR signals as in Mycalamide A.[2] In consequence, if the ^{13}C NMR spectra are recorded at –50°C a doubled set of signals is observed in a nearly 1:1 ratio.



Scheme 16

All temperatures quoted are not corrected. ^1H NMR, ^{13}C NMR: Bruker AC-300 and AMX-500. Boiling range of petroleum ether: 40–60 °C. pH 7 buffer: 56.2 g $NaH_2PO_4 \times 2H_2O$ + 213.2 g $Na_2HPO_4 \times 2\ H_2O$ in 1.0 L of water. Flash chromatography: Silica gel Si 60 E. Merck AG, Darmstadt, 40–63 µm.

(1*S*,5*R*,6*R*)-5-[(1*R*,3*E*)-1-Hydroxy-2,2-dimethylpent-3-enyl]-2,4,7,9-tetraoxabicyclo[4.4.0]decane (16):

2,4:3,5-Dimethylene-L-xylose (**9**;[15] 0.348 g, 2.0 mmol) and (4*R*,5*R*)-4,5-dicyclohexyl-2-[(1*R*)-1,3-dimethylbut-2-enyl]-1,3,2-dioxaborolane (**12**;[19] 0.700 g, 2.2 mmol) were heated in 1,2-dimethoxyethane (10 mL) for 8 d at reflux. Triethanolamine (0.328 g, 2.2 mmol) was added and the mixture was stirred for 3 h at r.t. Semisaturated aq NH_4Cl solution (10 mL) was added, the phases were separated and the aqueous phase was extracted with Et_2O (4 × 20 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. The ^{13}C NMR spectrum of the crude product revealed the presence of ca. 5% of another diastereomer. Flash chromatography with petroleum ether/EtOAc (1:1) furnished 0.393 g (76%) of **16** as a colorless liquid; $[\alpha]_D^{26}$ –32.0 (*c* = 2.01, $CHCl_3$).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (s, 3 H), 1.07 (s, 3H), 1.68 (d, *J* = 4.9 Hz, 3 H), 2.27 (d, *J* = 4.2 Hz, 1 H), 3.47–3.54 (m, 2 H), 3.58 (dd, *J* = 7.6, 4.2 Hz, 1 H), 3.80 (dd, *J* = 12.6, 1.9 Hz, 1 H), 3.84 (s, 1 H), 4.08 –4.16 (m, 1 H), 4.71 (d, *J* = 6.3 Hz, 1 H), 4.74 (d, *J* = 6.3 Hz, 1 H), 5.16 (d, *J* = 6.2 Hz, 1 H), 5.18 (d, *J* = 6.2 Hz, 1 H), 5.38–5.56 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.2, 22.5, 25.6, 40.1, 69.7, 70.8 (2C), 75.1, 78.6, 92.6, 93.2, 123.7, 137.4.
$C_{13}H_{22}O_5$ (258.3): calcd. C, 60.45; H, 8.58; found C, 60.35; H, 8.43.

Using (S,S,S)-**12**: Compound **9** (0.522 g, 3.0 mmol) and (4*S*,5*S*)-4,5-dicyclohexyl-2-[(1*S*)-1,3-dimethylbut-2-enyl-]-1,3,2-dioxaborolane [(*S*,*S*,*S*)-**12**; 0.955 g, 3.0 mmol] were allowed to react as described above to furnish 0.590 g (77%) of **16**. The crude product showed no evidence of the presence of any other diastereomer.

(1*S*,5*R*,6*R*)-5-[(1*R*)-1-Hydroxy-2,2-dimethylbut-3-enyl]-2,4,7,9-tetraoxabicyclo[4.4.0]decane (19):
Compound **9**[15] (5.60 g, 32 mmol) and 2-(3-methylbut-2-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7.84 g, 50 mmol) and triethanolamine (5.97 g) were allowed to react as described for **16**. ^{13}C NMR analysis of the crude product (7.66 g, 98%) revealed the presence of **19** and its epimer in a 9:1 ratio. Flash chromatography as described for **16** furnished a mixture of **19** and its epimer; $[\alpha]_D^{25}$ –33.0 (c = 2.88, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (s, 3 H), 1.09 (s, 3 H), 2.38 (d, *J* = 4.4 Hz, 1 H), 3.50–3.54 (m, 2 H), 3.62 (dd, *J* = 7.6, 4.4 Hz, 1 H), 3.79 (dd, *J* = 12.6, 1.9 Hz, 1 H), 3.83 (s, 1 H), 4.13 (d, *J* = 12.6 Hz, 1 H), 4.70 (d, *J* = 6.3 Hz, 1 H), 4.74 (d, *J* = 6.3 Hz, 1 H), 5.03 (dd, *J* = 17.4, 1.4 Hz, 1 H), 5.04 (dd, *J* = 11.1, 1.4 Hz, 1 H), 5.15 (d, *J* = 6.3 Hz, 1 H), 5.16 (d, *J* = 6.3 Hz, 1 H), 5.93 (dd, *J* = 17.4, 11.1 Hz, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.2, 24.8, 40.8, 69.6, 70.7 (2C), 75.1, 78.5, 92.6, 93.1, 112.8, 144.7.
$C_{12}H_{20}O_5$ (244.3): calcd. C, 59.00, H; 8.25; found C; 58.91; H; 8.18.

(1*S*,5*S*,6*R*)-5-(2,2-Dimethyl-1-oxobut-3-enyl)-2,4,7,9-tetraoxabicyclo[4.4.0]decane (20):
A solution of DMSO (3.13 g, 40.0 mmol) in CH_2Cl_2 (5 mL) was added to a solution of oxalyl chloride (1.72 mL, 20.0 mmol) in CH_2Cl_2 (60 mL) at –78 °C. After stirring for 15 min at –78 °C, a solution of **19** (3.66 g, 15.0 mmol) in CH_2Cl_2 (5 mL) was added dropwise. After stirring for 1 h, Et_3N (11.1 mL, 80.0 mmol) was added dropwise and stirring was continued for another hour at –78 °C. After reaching r.t. H_2O (30 mL) was added, the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$) and concentrated. Flash chromatography of the residue with petroleum ether/EtOAc (1:1) furnished 3.17 g (87%) of **20** as a slightly yellowish solid; mp 116–118 °C; $[\alpha]^{24}_D$ –99.5 (c = 1.16, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (s, 3 H), 1.34 (s, 3 H), 3.55 (d, *J* = 1.2 Hz, 1 H), 3.81 (dd, *J* = 12.7, 1.9 Hz, 1 H), 4.07 (s, 1 H), 4.14 (dt, *J* = 12.7, 1.2 Hz, 1 H), 4.28 (d, *J* = 1.9 Hz, 1 H), 4.67 (d, *J* = 6.4 Hz, 1 H), 4.72 (d, *J* = 6.4 Hz, 1 H), 5.05 – 5.11 (m, 3 H), 5.28 (d, *J* = 6.4 Hz, 1 H), 6.15 (dd, *J* = 17.3, 10.9 Hz, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6, 23.8, 50.5, 69.4, 70.7, 70.9, 82.5, 92.6, 93.2, 114.2, 141.7, 207.1.
$C_{12}H_{18}O_5$ (242.3): calcd C, 59.49; H, 7.49; found C, 59.60; H, 7.45.

(1*S*,5*R*,6*R*)-5-[(1*S*)-1-Hydroxy-2,2-dimethylbut-3-enyl]-2,4,7,9-tetraoxabicyclo[4.4.0]decane (21):
A solution of **9**[15] (1.74 g, 10.0 mmol) in CH_2Cl_2 (100 mL) was dried for 30 min over molecular sieves (4 Å). To this solution was added at 0 °C a solution of $TiCl_4$ (1.20 mL, 11.0 mmol) in CH_2Cl_2 (10 mL), which had been predried over molecular sieves (4 Å). After stirring for 30 min at 0 °C, a solution of tributyl(3-methylbut-2-enyl)stannane (3.80 g, 10.6 mmol) in CH_2Cl_2 (10 mL, predried over molecular sieves, 4 Å) was added dropwise. After stirring for 14 h at 0 °C the mixture was quenched by addition of satd aq $NaHCO_3$ solution (50 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$) and concentrated. ^{13}C NMR spectrum of the crude product showed the presence of only a single diastereomer. Flash chromatography with petroleum ether/EtOAc (1:1) furnished 2.13 g (87%) of **21** as a slightly yellowish oil; $[\alpha]_D^{26}$ –23.8 (c = 0.71, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (s, 3 H), 1.04 (s, 3 H), 2.88 (d, *J* = 1.3 Hz, 1 H), 3.47 (s, 1 H), 3.56–3.58 (m, 3 H), 3.74 (dd, *J* = 12.6, 1.8 Hz, 1 H), 4.09 (d, *J* = 12.6 Hz, 1 H), 4.64 (d, *J* = 6.3 Hz, 1 H), 4.76 (d, *J* = 6.3 Hz, 1 H), 4.96 (dd, *J* = 10.8, 1.3 Hz, 1 H), overlayed with 4.99 (dd, *J* = 17.5, 1.2 Hz, 1 H), 5.11 (d, *J* = 6.2 Hz, 1 H), 5.20 (d, *J* = 6.3 Hz, 1 H), 5.85 (dd, *J* = 17.6, 10.8 Hz, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.3, 25.5, 41.0, 69.3, 70.4, 73.0, 75.9, 76.6, 92.8, 93.0, 111.8, 145.6.
$C_{12}H_{20}O_5$ (244.3): calcd C, 59.00; H, 8.25; found C, 59.05; H, 8.23.

(1*S*,5*R*,6*R*)-5-[(1*S*)-1-Methoxy-2,2-dimethylbut-3-enyl]-2,4,7,9-tetraoxabicyclo[4.4.0]decane (22):
To a suspension of NaH (80% in white oil, 0.18 g, 6.0 mmol) in THF (10 mL) was added over 5 min a solution of the alcohol **21** (0.660 g, 2.70 mmol) in THF (5 mL). After stirring for 2 h, MeI (0.850 g, 6.0 mmol) was added. After stirring for 12 h, a satd aq NH_4Cl solution (10 mL) was added dropwise. After addition of Et_2O (10 mL), the phases were separated and the aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. Flash chromatography of the residue with petroleum ether/EtOAc (2:1) furnished 0.653 g (93%) of **22** as a colorless solid; mp 98–100 °C; $[\alpha]_D^{26}$ –42.6 (c = 1.00, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03 (s, 3 H), 1.05 (s, 3 H), 3.26 (d, *J* = 7.8 Hz, 1 H), 3.42 (br s, 1 H), 3.50 (s, 3 H), 3.50–3.56 (m, 2 H), 3.72 (dd, *J* = 12.6, 1.9 Hz, 1 H), 4.11 (d, *J* = 12.6 Hz, 1 H), 4.58 (d, *J* = 6.2 Hz, 1 H), 4.76 (d, *J* = 6.4 Hz, 1 H), 4.91 (dd, *J* = 10.7, 1.3 Hz, 1 H), 4.96 (dd, *J* = 17.6, 1.3 Hz, 1 H), 5.12 (d, *J* = 6.2 Hz, 1 H), 5.26 (d, *J* = 6.4 Hz, 1 H), 5.94 (dd, *J* = 17.6, 10.7 Hz, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 26.7, 41.6, 62.1, 69.6, 70.3, 71.1, 80.2, 84.1, 93.0, 93.4, 110.6, 146.1.
$C_{13}H_{22}O_5$ (258.3): calcd C, 60.45; H, 8.58; found C, 60.28; H, 8.45.

(4S,5R,6S)-5-Hydroxy-6-hydroxymethyl-4-[(1S)-1-methoxy-2,2-dimethylbut-3-enyl]-1,3-dioxane (23):
Compound **22** (2.96 g, 11.5 mmol) was added to a mixture of trifluoroacetic anhydride (11 mL, 78 mmol) and AcOH (2.0 mL, 35 mmol). After stirring for 3 h at r.t., satd aq $NaHCO_3$ solution (25 mL) and Et_2O (60 mL) were added, the phases were separated and the aqueous phase was extracted with Et_2O (5 × 50 mL). The combined organic phases were concentrated and the residue was taken up in MeOH (60 mL) and H_2O (30 mL). Solid K_2CO_3 (7.92 g, 57.4 mmol) was added and the mixture was stirred for 16 h at r.t. The mixture was concentrated in vacuo and the residue was dissolved in H_2O (25 mL) and the solution was extracted with Et_2O (5 × 30 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. Flash chromatography of the residue with Et_2O furnished 1.83 g (65%) of the diol **23** as a viscous yellowish oil; $[\alpha]_D^{22}$ –22.1 (c = 1.52, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (s, 3 H), 1.03 (s, 3 H), 2.92 (br s, 1 H), 3.07 (d, *J* = 5.2 Hz, 1 H), 3.18 (br d, *J* = 9.5 Hz, 1 H), 3.47 (s, 3 H), overlaid with 3.41–3.80 (m, 5 H), 4.71 (d, *J* = 6.2 Hz, 1 H), 4.96 (d, *J* = 11.8 Hz, 1 H), overlaid with 4.96 (d, *J* = 16.4 Hz, 1 H), 5.13 (d, *J* = 6.2 Hz, 1 H), 5.88 (dd, *J* = 17.8, 10.5 Hz, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0, 25.6, 42.0, 61.8, 62.5, 67.2, 79.6, 80.1, 86.7, 93.8, 112.0, 145.4.
$C_{12}H_{22}O_5$ (246.3): calcd C, 58.52; H, 9.00; found C, 58.25; H, 8.75.

(1*R*,5*S*,6*R*,10*S*)-8-Acetoxy-5-acetoxymethyl-9,9-dimethyl-10-methoxy-2,4,7-trioxabicyclo[4.4.0]decane (10):
A stream of ozone in oxygen was introduced at –78 °C into a solution of the diol **23** (1.30 g, 5.3 mmol) in MeOH (60 mL) and CH_2Cl_2 (60 mL). After the blue color had persisted, excess of ozone was purged with a stream of argon. Ph_3P (2.22 g, 8.45 mmol) was added and the mixture was allowed to reach r.t. The solvents were removed in vacuo and the residue was taken up in CH_2Cl_2 (60 mL) and pyridine

(30 mL). Ac_2O (5.0 mL, 53 mmol) was added and, after stirring for 36 h, the mixture was poured onto ice water (80 mL). The phases were separated and the aqueous phase was extracted with Et_2O (4 × 60 mL). The combined organic phases were washed with 1 N HCl (60 mL) and brine (20 mL), dried ($MgSO_4$) and concentrated. Flash chromatography of the residue with petroleum ether/Et_2O (1:1) furnished 1.38 g (79%) of **10** as a 3:1 anomer mixture.

$C_{15}H_{24}O_8$ (332.4): calcd C, 54.21; H, 7.28; found C, 54.09; H, 7.14.

α-anomer:

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (s, 3 H), 1.21 (s, 3 H), 2.05 (s, 3 H), 2.06 (s, 3 H), 2.92 (dd, *J* = 2.4, 0.6 Hz, 1 H), 3.39 (s, 3 H), 3.66–3.68 (m, 1 H), 3.71 (dd, *J* = 4.9, 4.3 Hz, 1 H), 3.85–3.90 (m, 1 H), 4.22 (d, *J* = 5.7 Hz, 2 H), 4.71 (d, *J* = 6.3 Hz, 1 H), 5.14 (d, *J* = 6.3 Hz, 1 H), 5.78 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8, 21.0, 21.3, 25.4, 36.1, 59.6, 61.1, 63.8, 72.2, 75.8, 82.6, 93.0, 97.0, 169.7, 170.8.

ß-anomer:

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (s, 3 H), 1.16 (s, 3 H), 2.06 (s, 3 H), 2.07 (s, 3 H), 3.00 (d, *J* = 2.7 Hz, 1 H), 3.38 (s, 3 H), 3.61 (dd, *J* = 2.7, 1.5 Hz, 1 H), 3.76–3.78 (m, 1 H), 3.87 (ddd, *J* = 7.5, 4.6, 2.0 Hz, 1 H), 4.20 (dd, *J* = 11.9, 7.5 Hz, 1 H), 4.30 (dd, *J* = 11.9, 4.6 Hz, 1 H), 4.67 (d, *J* = 6.3 Hz, 1 H), 5.12 (d, *J* = 6.3 Hz, 1 H), 5.59 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.2, 20.8, 20.9, 21.2, 37.6, 59.3, 63.6, 68.1, 72.5, 75.6, 85.1, 92.8, 96.1, 169.5, 170.8.

(1*R*,5*S*,6*R*,8*R*,10*S*)-5-Acetoxymethyl-10-methoxy-9,9-dimethyl-8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (11):

Allyltrimethylsilane (91 mg, 0.8 mmol) followed by BF_3•OEt_2 (31 mg, 0.22 mmol) were added at 0 °C to a solution of **10** (66 mg, 0.2 mmol) in MeCN (5 mL). After stirring for 4 h at 0 °C, satd aq $NaHCO_3$ solution (5 mL) and Et_2O (10 mL) were added. The phases were separated and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with brine (5 mL), dried ($MgSO_4$) and concentrated. Flash chromatography of the residue with petroleum ether/EtOAc (3:1) furnished 62 mg (99%) of **11** as a colorless oil; $[\alpha]_D^{25}$ –26.1 (c = 1.85, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (s, 3 H), 1.22 (s, 3 H), 2.05 (s, 3 H), 2.10 - 2.20 (m, 1 H), 2.79 (ddd, *J* = 15.6, 12.1, 8.2 Hz, 1 H), 2.87 (dd, *J* = 2.4, 1.0 Hz, 1 H), 3.37 (s, 3 H), 3.55 (dd, *J* = 12.1, 3.8 Hz, 1 H), 3.59–3.63 (m, 2 H), 3.84 (ddd, *J* = 7.6, 4.0, 1.7 Hz, 1 H), 4.20 (dd, *J* = 12.1, 7.6 Hz, 1 H), 4.28 (dd, *J* = 12.1, 4.0 Hz, 1 H), 4.69 (d, *J* = 6.3 Hz, 1 H), 4.96–5.07 (m, 2 H), 5.14 (d, *J* = 6.3 Hz, 1 H), 5.68–5.82 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9, 22.6, 27.7, 32.3, 36.1, 59.3, 59.9, 64.4, 73.0, 76.6, 80.7, 84.3, 93.0, 115.7, 136.5, 170.9.

$C_{16}H_{26}O_6$ (314.4): calcd C, 61.13; H, 8.34; found C, 61.08; H, 8.34.

(1*R*,5*S*,6*R*,8*R*,10*S*)-5-Hydroxymethyl-10-methoxy-9,9-dimethyl-8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (25):

Solid K_2CO_3 (3.55 g, 25.7 mmol) was added to a solution of **11** (1.28 g, 4.08 mmol) in MeOH (60 mL) and H_2O (30 mL). After stirring for 16 h the solvents were removed in vacuo and the residue was partitioned between H_2O (20 mL) and Et_2O (50 mL). The phases were separated and the aqueous phase was extracted with Et_2O (4 × 50 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. Flash chromatography of the residue with Et_2O furnished 1.11 g (100%) of **25** as a slightly yellowish oil; $[\alpha]_D^{20}$ –30.7 (c = 1.286, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (s, 3 H), 1.21 (s, 3 H), 2.10–2.19 (m, 1 H), 2.42–2.46 (m, 1 H), 2.76–2.88 (m, 2 H), 3.36 (s, 3 H), 3.56–3.81 (m, 6 H), 4.69 (d, *J*= 6.1 Hz, 1 H), 4.99–5.09 (m, 2 H), 5.12 (d, *J* = 6.1 Hz, 1 H), 5.70–5.83 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.5, 27.6, 32.3, 36.1, 59.3, 60.4, 62.2, 73.0, 78.0, 80.4, 84.1, 93.0, 115.9, 137.3.

$C_{14}H_{24}O_5$ (272.3): calcd C, 61.74; H, 8.88; found C, 61.52; H, 9.15.

(1*R*,5*R*,6*S*,8*R*,10*S*)-5-Formyl-10-methoxy-9,9-dimethyl-8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (28):

Pyridine (1.6 mL, 20 mmol) and Dess-Martin-periodinane[35] (1.2 g, 2.8 mmol) were added to a solution of the alcohol **25** (550 mg, 2.0 mmol) in CH_2Cl_2 (30 mL). After stirring for 5 h the mixture was poured into a mixture of H_2O (50 mL), satd aq $NaHCO_3$ solution (50 mL), $Na_2S_2O_3$ (2.20 g, 14 mmol) and *tert*-butyl methyl ether (100 mL). After stirring for 90 min the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 100 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$) and concentrated. Flash chromatography with *tert*-butyl methyl ether furnished 469 mg (87%) of the aldehyde **28** as a slightly yellowish oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (s, 3 H), 1.21 (s, 3 H), 2.08–2.17 (m, 1 H), 2.80 (ddd, *J* = 15.5, 12.1, 7.7 Hz, 1 H), 2.89 (d, *J* = 2.0 Hz, 1 H), 3.38 (s, 3 H), 3.51 (dd, *J* = 12.1, 3.7 Hz, 1 H), 3.69 (dd, *J* = 1.9, 1.9 Hz, 1 H), 4.07–4.12 (m, 2 H), 4.72 (d, *J* = 6.3 Hz, 1 H), 4.95–5.04 (m, 2 H), 5.22 (d, *J* = 6.3 Hz, 1 H), 5.60–5.74 (m, 1 H), 9.54 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.6, 27.6, 32.2, 36.0, 59.4, 60.9, 72.6, 81.3, 82.0, 84.1, 92.3, 115.8, 136.2, 198.4.

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 10 µL) was added to a solution of the aldehyde **28** (55 mg, 0.2 mmol) in benzene-d_6 (1 mL). After 12 h at r.t., the ^{13}C NMR spectroscopy showed essentially the signals for the starting material **28**. At δ = 9.43, 9.75, and 10.07 further signals of low intensity were recorded. The signal at δ = 9.75 (C_6D_6) corresponds to that of **29**.

(1*R*,5*R*,6*S*,8*R*,10*S*)-10-Methoxy-5-methoxycarbonyl-9,9-dimethyl-8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (26):

A solution of CrO_3 (6.68 g, 66.8 mmol) in H_2O (20 mL) and H_2SO_4 (5.6 mL) was added dropwise to a solution of the alcohol **25** (136 mg, 0.5 mmol) in acetone (10 mL) until the orange color persisted. After stirring further for 15 min, i-PrOH (2 mL) was added, followed by satd aq $NaHCO_3$ solution (10 mL). The pH of the solution was brought to 14 by the addition of solid KOH. The mixture was extracted with Et_2O (2 × 20 mL) and the aqueous phase was acidified with 1 N HCl to pH 1. The aqueous phase was extracted with Et_2O (5 × 50 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. The residue was taken up in Et_2O (10 mL). An ethereal solution of diazomethane (ca. 0.5 M) was added dropwise until the yellow color persisted. After stirring for 10 min, AcOH was added dropwise to decompose the excess of diazomethane. Satd aq $NaHCO_3$ solution (10 mL) was added, the phases were separated and the aqueous phase was extracted with Et_2O (3 × 50 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. Flash chromatography of the residue with petroleum ether/*tert*-butyl methyl ether (1:3) furnished 117 mg (78%) of **26** as a slightly yellowish oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (s, 3 H), 1.21 (s, 3 H), 2.08 – 2.16 (m, 1 H), 2.71–2.83 (m, 1 H), 2.89 (d, *J* = 2.5 Hz, 1 H), 3.38 (s, 3 H), 3.54 (dd, *J* = 11.9, 3.5 Hz, 1 H), 3.71 (br s, 1 H), 3.75 (s, 3 H), 4.00 (s, 1 H), 4.31 (d, *J* = 2.0 Hz, 1 H), 4.71 (d, *J* = 6.3 Hz, 1 H), 4.92–5.03 (m, 2 H), 5.22 (d, *J* = 6.3 Hz, 1 H), 5.64–5.78 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.7, 27.7, 32.0, 36.1, 52.1, 59.3, 61.1, 72.7, 77.4, 81.5, 84.3, 92.4, 115.3, 136.2, 168.4.

(*R*)-3,5-*O*-Benzylidene-2,4-*O*-methylene-D-arabinose Diethylthioacetal (32):

To a mixture of dioxane (500 mL) and 50% aq NaOH (500 mL) was added at 60 °C under stirring a solution of Bu_4NBr (0.50 g ,1.6 mmol) in bromochloromethane (100 mL, 1.49 mol). The diethylthioacetal **31**[29] (5.00 g, 14.5 mmol) in dioxane (250 mL) was added over 1 h with vigorous stirring. Stirring was continued for 30 min at 60 °C. After reaching r.t., the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 300 mL). The combined organic phases were washed with brine (30 mL), dried (Na_2SO_4)

and concentrated. Flash chromatography of the residue with petroleum ether/*tert*-butyl methyl ether (7:1) furnished 3.21 g (62%) of **32** as a colorless solid; mp 83 °C; $[\alpha]_D^{20}$ +97.4 (c = 1.252, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.4 Hz, 3 H), 1.27 (t, *J* = 7.4 Hz, 3 H), 2.60–2.85 (m, 4 H), 3.74–3.81 (m, 1 H), 4.12–4.24 (m, 2 H), 4.33 (dd, *J* = 10.3, 4.5 Hz, 1 H), 4.40 (d, *J* = 7.5 Hz, 1 H), 4.47 (dd, *J* = 7.5, 5.4 Hz, 1 H), 4.85 (d, *J* = 6.4 Hz, 1 H), 5.27 (d, *J* = 6.4 Hz, 1 H), 5.63 (s, 1 H), 7.33–7.38 (m, 3 H), 7.48–7.52 (m, 2 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 14.2, 24.7, 24.9, 50.2, 67.0, 69.1, 75.3, 77.0, 89.8, 102.2, 126.2 (2C), 128.2 (2C), 129.0, 137.2.
$C_{17}H_{24}O_4S_2$ (356.5): calcd C, 57.27; H, 6.79; found C, 57.41; H, 6.70.

(*R*)-3,5-*O*-Benzylidene-2,4-*O*-methylene-D-arabinose (33):
Ag_2O (7.00 g, 30.2 mmol) and $AgNO_3$ (3.84 g, 22.6 mmol) were added at 0 °C to a solution of 2.69 g (7.5 mmol) of **32** in MeCN (240 mL) and H_2O (80 mL). After stirring for 15 min at 0 °C, a solution of $HgCl_2$ (6.14 g, 22.6 mmol) in MeCN (30 mL) and H_2O (10 mL) was added dropwise over 50 min at 0 °C. Stirring was continued for 25 min. Then a pH 7 buffer solution (200 mL) was added. The mixture was filtered over a pad of Kieselgur, which was subsequently washed with *tert*-butyl methyl ether (700 mL). The phases of the combined filtrate were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 300 mL). The combined organic phases were washed with brine (50 mL), dried (Na_2SO_4) and concentrated, leaving 1.89 g (100%) of **33** as a colorless solid; mp 126 °C; $[\alpha]_D^{20}$ +263.4 (c = 1.240, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.66 (ddd, *J* = 9.8, 9.8, 4.8 Hz, 1 H), 3.80 (dd, *J* = 10.2, 10.2 Hz, 1 H), 4.24–4.32 (m, 2 H), 4.76 (d, *J* = 6.8 Hz, 1 H), 4.94 (d, *J* = 6.3 Hz, 1 H), 5.21 (d, *J* = 6.3 Hz, 1 H), 5.64 (s, 1 H), 7.36–7.48 (m, 5 H), 9.93 (s, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 68.6, 70.3, 75.3, 77.1, 91.3, 102.7, 126.1 (2C), 128.4 (2C), 129.4, 136.6, 199.6.
$C_{13}H_{14}O_5$ (250.2): calcd C, 62.39; H, 5.64; found C, 62.33; H, 5.57.

(1*R*,5*R*,6*R*,8*R*)-5-[(1*S*)-1-Hydroxy-2,2-dimethylbut-3-enyl]-8-phenyl-2,4,7,9-tetraoxabicyclo[4.4.0]decane (36):
A 0.99 M solution of 3-methylbut-2-enylmagnesium chloride in THF (15.0 mL, 14.9 mmol) containing 0.2 M of $MgBr_2$ was added at –30 °C over 40 min to a solution of **33** (1.89 g, 7.55 mmol) in THF (125 mL). After stirring for 90 min, a 1:1 mixture of satd aq NH_4Cl and $NaHCO_3$ solutions (200 mL) was added. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (4 × 100 mL). The combined organic phases were washed with brine (20 mL), dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with petroleum ether/*tert*-butyl methyl ether (4:1, containing 1% of Et_3N) furnished 2.27 g (94%) of **36** as a colorless oil; $[\alpha]^{20}_D$ +61.5 (*c* = 1.157, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (s, 3 H), 1.12 (s, 3 H), 2.04 (d, *J* = 5.6 Hz, 1 H), 3.71 (dd, *J* = 10.2, 10.2 Hz, 1 H), 3.79 (dd, *J* = 5.5, 1.6 Hz, 1 H), 4.04 (dd, *J* = 9.8, 6.9 Hz, 1 H), 4.28 (dd, *J* = 6.7, 1.6 Hz, 1 H), overlayed with 4.31 (dd, *J* = 10.3, 5.0 Hz, 1 H), 4.50 (ddd, *J* = 9.9, 9.9, 5.0 Hz, 1 H), 4.78 (d, *J* = 5.5 Hz, 1 H), 5.09 (dd, *J* = 16.2, 1.2 Hz, 1 H), overlayed with 5.10 (dd, *J* = 12.0, 1.5 Hz, 1 H), 5.49 (d, *J* = 5.5 Hz, 1 H), 5.62 (s, 1 H), 5.91 (dd, *J* = 17.9, 10.4 Hz, 1 H), 7.34–7.39 (m, 3 H), 7.45–7.49 (m, 2 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.0, 23.5, 42.0, 67.3, 69.8, 70.8, 76.4, 76.5, 91.3, 102.2, 113.4, 126.2 (2C), 128.2 (2C), 129.0, 137.4, 145.5.
$C_{18}H_{24}O_5$ (320.4): calcd. C, 67.48; H, 7.84; found C, 67.24; H 7.99.

(1*R*,5*R*,6*R*,8*R*)-5-[(1*S*)-1-Methoxy-2,2-dimethylbut-3-enyl]-8-phenyl-2,4,7,9-tetraoxabicyclo[4.4.0]decane (37):
NaH (80% in white oil, 0.40 g, 13.4 mmol) was added to a solution of **36** (1.43 g, 4.5 mmol) in DMF (75 mL) at 0 °C. After stirring for 10 min, MeI (0.56 mL, 9.0 mmol) was added dropwise. The mixture was stirred for 2 h at 0 °C, allowed to reach r.t. and poured into a mixture of satd aq solutions of NH_4Cl (100 mL) and $NaHCO_3$ (50 mL). *tert*-Butyl methyl ether (150 mL) was added, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (4 × 100mL). The combined organic phases were washed with brine (25 mL), dried (Na_2SO_4) and concentrated. Flash chromatography with petroleum ether/*tert*-butyl methyl ether (7:1 containing 1% Et_3N) furnished 1.36 g (91%) of **37** as a colorless oil; $[\alpha]_D^{20}$ +70.0 (*c* = 1.385, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (s, 3 H), 1.18 (s, 3 H), 3.30 (d, *J* = 1.8 Hz, 1 H), 3.60 (s, 3 H), 3.72 (dd, *J* = 9.9, 9.9 Hz, 1 H), 4.03 (dd, *J* = 9.6, 6.9 Hz, 1 H), 4.27 (dd, *J* = 6.8, 1.8 Hz, 1 H), 4.31–4.45 (m, 2 H), 4.74 (d, *J* = 5.5 Hz, 1 H), 5.00 (dd, *J* = 10.7, 1.4 Hz, 1 H), 5.06 (dd, *J* = 17.6, 1.4 Hz, 1 H), 5.49 (d, *J* = 5.5 Hz, 1 H), 5.63 (s, 1 H), 6.00 (dd, *J* = 17.6, 10.8 Hz, 1 H), 7.36–7.41 (m, 3 H), 7.46– 7.51 (m, 2 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6, 25.1, 49.6, 61.6, 67.7, 70.3, 72.3, 77.0, 88.6, 91.2, 103.0, 111.9, 126.5 (2C), 128.5 (2C), 129.3, 137.8, 146.3.
$C_{19}H_{26}O_5$ (334.4): calcd. C, 68.24; H, 7.84; found C, 68.05; H, 7.89.

(4*S*,5*R*,6*R*)-5-Hydroxy-6-hydroxymethyl-4-[(1*S*)-1-methoxy-2,2-dimethylbut-3-enyl]-1,3-dioxane (38):
Compound **37** (1.36 g, 4.1 mmol) was dissolved in 80% aq AcOH (25 mL) and kept for 3 d at r.t. The mixture was poured under stirring into satd aq $NaHCO_3$ solution (300 mL). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (5 × 100 mL). The combined organic phases were washed with brine (25 mL), dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with *tert*-butyl methyl ether furnished 0.82 g (82%) of the diol **38** as a colorless solid; mp 91 °C; $[\alpha]_D^{20}$ +17.6 (*c* = 1.430, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (s, 3 H), 1.07 (s, 3 H), 2.81 (br dd, *J* = 5.2, 5.2 Hz, 1 H), 3.21 (d, *J* = 4.3 Hz, 1 H), 3.54 (s, 3 H), 3.61–3.70 (m, 3 H), 3.83–3.99 (m, 3 H), 4.84 (d, *J* = 5.9 Hz, 1 H), 4.96 (dd, *J* = 10.9, 1.2 Hz, 1 H), overlayed with 4.98 (dd, *J* = 17.6, 1.3 Hz, 1 H), 5.08 (d, *J* = 5.9 Hz, 1 H), 5.92 (dd, *J* = 17.5, 10.8 Hz, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.9, 25.3, 42.2, 60.4, 61.5, 66.0, 75.3, 78.0, 86.9, 89.2, 111.8, 145.8. $C_{12}H_{22}O_5$ (246.3): calcd. C, 58.52; H, 9.00; found C, 58.40; H, 8.73.

(1*R*,5*R*,6*R*,10*S*)-8-Acetoxy-5-acetoxymethyl-10-methoxy-9,9-dimethyl-2,4,7-trioxabicyclo[4.4.0]decane (39):
A stream of ozone in oxygen was introduced at –78 °C into a solution of **38** (842 mg, 3.4 mmol) in CH_2Cl_2 (50 mL) and MeOH (50 mL). After the blue color had persisted, excess of ozone was purged by a stream of argon. Ph_3P (3.14 g, 12.0 mmol) was added and the mixture was allowed to reach r.t. After removing the solvents in vacuo, the residue was taken up in CH_2Cl_2 (75 mL). To this solution were added pyridine (20.0 mL, 250 mmol), Ac_2O (3.2 mL, 34 mmol) and 4-dimethylaminopyridine (21 mg, 0.17 mmol). After stirring for 38 h, the mixture was poured onto a mixture of pH 7 buffer (200 mL) and ice (200 g). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (5 × 100 mL). The combined organic phases were washed with brine (25 mL), dried (Na_2SO_4) and concentrated. Pyridine was removed from the residue by coevaporating with toluene (2 × 200 mL). Flash chromatography of the residue with petroleum ether/*tert*-butyl methyl ether (1:2) furnished 1.09 g (96%) of the acetates **39** as a viscous oil. ^{13}C NMR indicated the presence of two anomers in a 2:1 ratio, of which one anomer populated a second backbone conformation to about 5 %. The NMR data of the major components are the following:
^{1}H NMR (300 MHz, $CDCl_3$): major anomer: δ = 0.96 (s, 3 H), 1.09 (s, 3 H), 2.07 (s, 3 H), 2.09 (s, 3 H), 3.36 (s, 1 H), 3.46 (s, 3 H), 3.86–3.99 (m, 2 H), 4.14–4.43 (m, 3 H), 4.90–4.97 (m, 2 H), 5.76 (s, 1 H).
The following signals of the minor anomer could be recorded:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (s, 3 H), 1.12 (s, 3 H), 2.08 (s, 3 H), 3.33 (s, 1 H), 3.47 (s, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): (two major anomers): δ = 17.3, 19.8, 19.9, 20.6, 20.7, 20.9, 23.8, 26.8, 38.4, 38.9, 60.2, 60.4, 62.0, 63.9,

68.8, 70.6, 70.8, 72.2, 74.0, 80.3, 80.4, 87.6, 95.1, 96.6, 169.2, 169.5, 170.3, 170.6.
$C_{15}H_{24}O_8$ (332.4): calcd. C, 54.21; H, 7.28; found C, 58.43; H, 7.29.

(1*R*,5*R*,6*R*,8*R*,10*S*)-5-Acetoxymethyl-10-methoxy-9,9-dimethyl-8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (40):
Molecular sieves 4 Å were added to a solution of the anomers of **39** (1.09 g, 3.28 mmol) in MeCN (45 mL). The mixture was stirred for 30 min at 0 °C and allyltrimethylsilane (3.1 mL, 20 mmol) was added. After stirring for 15 min, BF_3•OEt_2 (0.45 mL, 4.9 mmol) was added dropwise. The mixture was stirred for 2 h at 0 °C and poured into a well agitated mixture of *tert*-butyl methyl ether (300 mL) and satd aq $NaHCO_3$ solution (150 mL). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 150 mL). The combined organic phases were washed with brine (25 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with petroleum ether/*tert*-butyl methyl ether (3:2) furnished 0.870 g (84%) of **40** as a colorless oil; $[\alpha]^{20}_D$ +117 (*c* = 1.180, $CHCl_3$).
^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.85 (s, 3 H), 0.98 (s, 3 H), 2.00–2.08 (m, 1 H), overlayed with 2.08 (s, 3 H), 2.16 (dd, *J* = 14.4, 6.8 Hz, 1 H), 3.25 (dd, *J* = 10.2, 1.9 Hz, 1 H), 3.40 (d, *J* = 10.4 Hz, 1 H), 3.53 (s, 3 H), 3.97 (dd, *J* = 10.7, 6.9 Hz, 1 H), 4.03 (dd, *J* = 12.1, 6.8 Hz, 1 H), 4.15 (2 dd, *J* = 10.3, 6.9 Hz, 2 H), 4.45 (dd, *J* = 12.1, 1.8 Hz, 1 H), 4.84 (d, *J* = 6.6 Hz, 1 H), 4.97 (d, *J* = 6.6 Hz, 1 H), 5.01–5.05 (m, 2 H), 5.75–5.85 (m, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.3, 20.8, 23.1, 33.4, 41.6, 61.7, 63.7, 67.3, 71.2, 73.5, 78.6, 79.2, 86.9, 116.6, 135.8, 170.7.
$C_{16}H_{26}O_6$ (314.4): calcd C, 61.13; H, 8.34; found C, 60.91; H, 8.58.

(1*R*,5*R*,6*R*,8*R*,10*S*)-5-Hydroxymethyl-10-methoxy-9,9-dimethyl-8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (27):
Solid K_2CO_3 (1.01 g, 7.3 mmol) was added to a solution of **40** (535 mg, 1.2 mmol) in MeOH (20 mL) and H_2O (10 mL). After stirring for 30 min the solution was concentrated and the residue was partitioned between H_2O (10 mL) and *tert*-butyl methyl ether (25 mL). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 25 mL). The combined organic phases were washed with brine (5 mL), dried ($MgSO_4$) and concentrated. Flash chromatography of the residue with *tert*-butyl methyl ether furnished 357 mg (99%) of the alcohol **27** as a slightly yellowish oil; $[\alpha]_D^{20}$ +97.4 (*c* = 0.975, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (s, 3 H), 0.96 (s, 3 H), 1.93–2.04 (m, 1 H), 2.10–2.16 (m, 1 H), 2.36 (br s, 1 H), 3.22 (dd, *J* = 10.1, 2.2 Hz, 1 H), 3.51–3.52 (m, 1 H), overlayed with 3.52 (s, 3 H), 3.59–3.65 (m, 1 H), 3.76–3.82 (m, 1 H), 3.95–3.98 (m, 2 H), 4.11 (dd, *J* = 10.4, 6.3 Hz, 1 H), 4.82 (d, *J* = 6.5 Hz, 1 H), 4.96–5.05 (m, 3 H), 5.67–5.91 (m, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1, 23.0, 33.4, 41.5, 61.6, 63.0, 68.0, 73.0, 73.4, 78.4, 79.2, 86.8, 116.8, 135.7.
$C_{14}H_{24}O_5$ (272.3): calcd C, 71.74; H, 8.88; found C, 61.71; H, 9.15.

(1*R*,5*S*,6*S*,8*R*,10*S*)-5-Formyl-10-methoxy-9,9-dimethyl-8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (29):
Compound **27** (274 mg, 1.0 mmol) was oxidized with Dess-Martin-periodinane as described for the preparation of **28** to give 182 mg of crude **29**.
^{1}H NMR (300 MHz, C_6D_6): δ = 0.84 (s, 3 H), 1.01 (s, 3 H), 2.00–2.11 (m, 1 H), 2.34–2.44 (m, 1 H), 2.90 (d, *J* = 7.5 Hz, 1 H), 3.21 (s, 3 H), 3.27 (dd, *J* = 10.7, 2.6 Hz, 1 H), 3.37–3.40 (m, 1 H), 3.87–3.95 (m, 1 H), 4.08 (dd, *J* = 7.6, 5.1 Hz, 1 H), 4.58 (d, *J* = 6.6 Hz, 1 H), 4.64 (d, *J* = 6.6 Hz, 1 H), 5.07–5.14 (m, 2 H), 5.93–6.06 (m, 1 H), 9.43 (d, *J* = 1.1 Hz, 1 H).
^{13}C NMR (75 MHz, C_6D_6): δ = 24.6, 33.4 (2C), 39.0, 60.4, 64.0, 72.8, 78.1, 79.7, 80.9, 87.8, 116.0, 136.7, 197.8.
Treatment of a benzene-d_6 solution of **29** (57 mg) with DBU (5 mg) led to changes in the ^{1}H NMR spectrum. Six signals for aldehydic protons were recorded in a ratio of 16:2:4:67:1:10. The signal of **29** had decreased to a value of 10%, whereas the most intensive signal (67%) corresponded to that of **28**.
When the alcohol **27** was oxidized by the Swern procedure the crude product consisted in a mixture of the aldehyde **29** and **28** in a 1:3 ratio.

(1*R*,5*R*,6*R*,8*R*,10*S*)-5-Acetoxymethyl-8-(2,3-dihydroxypropyl)-10-methoxy-9,9-dimethyl-2,4,7-trioxabicyclo[4.4.0]decane (41a and 42a):
A solution of **40** (0.304 g, 0.97 mmol) in H_2O (4 mL) and *tert*-butyl alcohol (4 mL) was added to a mixture of K_2OsO_4•$2H_2O$ (5 mg, 0.01 mmol), dihydroquinine-9-phenanthryl ether (24 mg, 0.05 mmol), $K_3Fe(CN)_6$ (0.981g, 2.98 mmol) and K_2CO_3 (0.450 g, 3.26 mmol) in *tert*-butyl alcohol (6 mL) and H_2O (6 mL) at 0 °C. After stirring for 3 h at 0 °C Na_2SO_3 (1.103 g, 5.8 mmol) were added. The phases were separated and the aqueous phase was extracted with EtOAc (5 × 20 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4) and concentrated. Flash chromatography with EtOAc furnished 0.31 g (92%) of a 2:1 mixture of the diols **41a** and **42a**.
^{1}H NMR (300 MHz, $CDCl_3$), major diastereomer: δ = 0.80 (s, 3 H), 0.89 (s, 3 H), 1.15–1.58 (m, 3 H), 2.04 (s, 3 H), 3.39–3.53 (m, 7 H), 3.78–3.94 (m, 3 H), 4.00–4.17 (m, 3 H), 4.50 (d, *J* = 11.0 Hz, 1 H), 4.79 (d, *J* = 6.6 Hz, 1 H), 4.93 (d, *J* = 6.6 Hz, 1 H). The following signals of the minor diastereomer could be recorded: δ = 0.77 (s, 3 H), 2.05 (s, 3 H), 4.64 (d, *J* = 11.8 Hz, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$), mixture of diastereomers: δ = 13.0, 13.1, 20.7, 20.8, 22.7, 22.9, 32.1, 32.2, 41.2, 41.6, 61.6, 63.8, 66.4, 66.5, 67.0, 67.2, 67.4, 68.0, 71.1, 71.4, 73.0, 73.3, 74.1, 78.3, 78.7, 79.1, 86.6, 86.7, 171.1, 171.7.
$C_{16}H_{28}O_8$ (348.4): calcd C, 55.16; H, 8.10; found C, 55.14; H, 7.98.

(1*R*,5*R*,6*R*,8*R*,10*S*)-5-Acetoxymethyl-8-(3-*tert*-butyldimethylsiloxy-2-hydroxypropyl)-10-methoxy-9,9-dimethyl-2,4,7-trioxabicyclo[4.4.0]decane (41b/42b):
Imidazole (0.11 g, 1.73 mmol) and later *tert*-butylchlorodimethylsilane (0.26g, 1.73 mmol) were added to a solution of the diols **41a**/**42a** (0.547 g, 1.57 mmol) in DMF (50 mL) at 0 °C. The mixture was allowed to reach r.t. with stirring over 19 h and was poured into H_2O (25 mL). The mixture was extracted with *tert*-butyl methyl ether (4 × 25 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4) and concentrated. Flash chromatography with petroleum ether/*tert*-butyl methyl ether (1:1, containing 1% of EtN_3) furnished 0.306 g (42%) of **41b**, 0.130 g (18%) of **42b**, and 0.141 g (19%) of a mixed fraction, which could be combined for separation with the next batch processed.
41b: $[\alpha]_D^{20}$ +72.64 (*c* = 3.013, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.86 (s, 12 H), 0.93 (s, 3 H), 1.40 (ddd, *J* = 14.6, 10.0, 7.9 Hz, 1 H), 1.77 (ddd, *J* = 14.6, 3.9, 2.0 Hz, 1 H), 2.07 (s, 3 H), 2.97 (br s, 1 H), 3.36–3.47 (m, 3 H), 3.49–3.58 (m, 4 H), 3.70 (m, 1 H), 3.98 (dd, *J* = 10.5, 6.8 Hz, 1 H), 4.07–4.23 (m, 3 H), 4.49 (dd, *J* = 11.7, 1.4 Hz, 1 H), 4.83 (d, *J* = 6.6 Hz, 1 H), 4.98 (d, *J* = 6.6 Hz, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.4 (2C), 13.3, 18.2, 20.8, 23.1, 25.8 (3C), 32.4, 41.7, 61.6, 63.8, 66.5, 67.5, 71.2, 71.6, 73.2, 78.6, 79.0, 86.9, 170.7.
$C_{22}H_{42}O_8Si$ (462.7): calcd C, 57.11; H, 9.15; found C, 56.91; H, 8.98.
42b: $[\alpha]_D^{20}$ +90.8 (*c* = 0.595, $CHCl_3$).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.04 (s, 6 H), 0.83 (s, 3 H), 0.87 (s, 9 H), 0.95 (s, 3 H), 1.27–1.45 (m, 2 H), 2.09 (s, 3 H), 2.86 (d, *J* = 4.4 Hz, 1 H), 3.37–3.48 (m, 2 H), 3.53–3.61 (m, 5 H), 3.76–3.80 (m, 1 H), 3.95 (dd, *J* = 10.9, 7.0 Hz, 1 H), 4.04 (dd, *J* = 12.1, 6.7 Hz, 1 H), 4.12–4.23 (m, 2 H), 4.61 (dd, *J* = 12.1, 1.5 Hz, 1 H), 4.85 (d, *J* = 6.6 Hz, 1 H), 5.00 (d, *J* = 6.6 Hz, 1 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = -5.3 (2C), 13.2, 18.3, 20.9, 22.9, 25.9 (3C), 32.1, 41.4, 61.8, 64.0, 67.3, 67.7, 67.9, 71.5, 73.7, 74.1, 79.4, 86.9, 171.1.
$C_{22}H_{42}O_8Si$ (462.7): calcd C, 57.11; H, 9.15; found C, 57.37; H 8.98.

(1*R*,5*R*,6*R*,8*R*,10*S*)-5-Acetoxymethyl-8-[(2*S*)-3-*tert*-butyldimethylsiloxy-2-methoxypropyl]-10-methoxy-9,9-dimethyl-2,4,7-trioxabicyclo[4.4.0]decane (43):

Silica gel 60 was activated by heating at 160 °C at 0.01 Torr for 3 d. To a suspension of the activated silica gel (0.84 g) in Et_2O (50 mL) was added **41 b** (0.11 g, 0.24 mmol). The mixture was cooled to 0 °C and a ca. 1 M solution of CH_2N_2 in Et_2O (40 mL) was added. After stirring for 6 h at 0 °C an additional amount of the CH_2N_2 solution (40 mL) was added. After stirring overnight again silica gel (0.84 g) and CH_2N_2 solution (40 mL) were added. After stirring for 1 d this procedure was repeated once more. H_2O (1 mL) was added and the mixture was stirred for 30 min to decompose excess of CH_2N_2. The mixture was filtered and the silica gel was washed with *tert*-butyl methyl ether. The filtrates were concentrated and the residue was purified by flash chromatography with petroleum ether/*tert*-butyl methyl ether (3:2, containing 1 % of Et_3N). This resulted in 94 mg (82%) of **43** and 19 mg of recovered starting material **41b**.

43: $[\alpha]_D^{20}$ +73.94 (*c* = 2.705, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 (s, 6 H), 0.86 (s, 3 H), 0.88 (s, 9 H), 0.96 (s, 3 H), 1.50 (ddd, *J* = 14.3, 9.9, 4.3 Hz, 1 H), 1.77 (ddd, *J* = 14.3, 8.0, 1.7 Hz, 1 H), 2.09 (s, 3 H), 3.24–3.41 (m, 6 H), 3.54 (s, 3 H), 3.60–3.67 (m, 2 H), 3.95–4.03 (m, 1 H), 4.09–4.18 (m, 3 H), 4.41–4.48 (m, 1 H), 4.85 (d, *J* = 6.6 Hz, 1 H), 5.00 (d, *J* = 6.6 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.4 (2C), 13.3, 18.3, 20.8, 23.3, 25.9 (3C), 30.6, 41.6, 57.1, 61.7, 63.8, 63.9, 67.1, 71.2, 73.3, 76.1, 79.4, 79.7, 86.9, 170.7.

$C_{23}H_{44}O_8Si$ (476.7): calcd C, 57.95; H, 9.30; found C, 57.86; H, 9.14.

(1*R*,5*R*,6*R*,8*R*,10*S*)-8-[(2*S*)-3-*tert*-Butyldimethylsiloxy-2-methoxypropyl]-5-hydroxymethyl-10-methoxy-9,9-dimethyl-2,4,7-trioxabicyclo[4.4.0]decane (44):

The acetate **43** (0.146 g, 0.31 mmol) was saponified as described for the preparation of **25**. Flash chromatography with petroleum ether/*tert*-butyl methyl ether (1:3, containing 1% of Et_3N) furnished 128 mg (96%) of the alcohol **44** as a slightly yellowish oil; $[\alpha]_D^{20}$ +63.7 (*c* = 2.120, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.84 (s, 3 H), 0.86 (s, 9 H), 0.94 (s, 3 H), 1.47 (ddd, *J* = 14.4, 9.7, 4.8 Hz, 1 H), 1.73 (ddd, *J* = 14.4, 7.5, 1.7 Hz, 1 H), 2.58 (br s, 1 H), 3.22–3.34 (m, 5 H), 3.39 (d, *J* = 10.3 Hz, 1 H), 3.53 (s, 3 H), 3.52–3.69 (m, 3 H), 3.81–3.86 (m, 1 H), 3.97–3.98 (m, 2 H), 4.08– 4.14 (m, 1 H), 4.83 (d, *J* = 6.5 Hz, 1 H), 5.00 (d, *J* = 6.5 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.4 (2C), 13.1, 18.2, 23.2, 25.9 (3C), 30.6, 41.7, 57.0, 61.6, 63.3, 64.1, 68.0, 73.3, 73.4, 76.0, 79.3, 80.0, 86.8.

$C_{21}H_{42}O_7Si$ (434.7): calcd C, 58.03; H, 9.74; found C, 58.11; H, 9.88.

(1*R*,5*S*,6*S*,8*R*,10*S*)-8-[(2*S*)-3-*tert*-Butyldimethylsiloxy-2-methoxypropyl]-10-methoxy-5-methoxycarbonyl-9,9-dimethyl-2,4,7-trioxabicyclo[4.4.0]decane (46):

A solution of $RuCl_3 \cdot H_2O$ (7 mg, 0.03 mmol) in H_2O (2 mL) was added to a solution of $K_2S_2O_8$ (0.28 g, 1.1 mmol) in 0.117 M aq KOH solution (40 mL). After stirring for 15 min, a solution of **44** (78 mg, 0.18 mmol) in *tert*-butanol (12.5 mL) was added. The resulting dark green suspension was stirred for 3 h leading to a clear orange colored solution. Satd Na_2SO_3 solution (3 mL) was added, followed by satd aq NaH_2PO_4 (20 mL). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (2 × 50 mL). Satd NaH_2PO_4 solution (20 mL) was added and the aqueous phase was extracted again with *tert*-butyl methyl ether (2 × 50 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. Residual *tert*-butyl alcohol was removed by coevaporating with hexane (2 × 20 mL) in vacuo from the mixture. The crude product (84 mg) was taken up in Et_2O and an ethereal solution of CH_2N_2 (ca. 1 M, 10 mL) was added. After stirring for 30 min satd aq NH_4Cl solution (1 mL) was added to decompose the excess of CH_2N_2. After the yellow color had disappeared, pH 7 buffer (5 mL) was added, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether 4 × 10 mL). The combined organic phases were washed with brine (4 mL), dried (Na_2SO_4) and concentrated. Flash chromatography of the residue with petroleum ether/*tert*-butyl methyl ether (2:1, containing 1% of Et_3N) furnished 64 mg (77%) of **46** as a colorless oil; $[\alpha]^{20}_D$ +69.9 (*c* = 1.102, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$, 323 K): δ = 0.05 (s, 6 H), 0.88 (s, 3 H), 0.89 (s, 3 H), 1.72 (ddd, *J* = 14.5, 8.0, 2.6 Hz, 1 H), 1.82 (ddd, *J* = 14.6, 10.7, 4.0 Hz, 1 H), 3.14 (d, *J* = 6.9 Hz, 1 H), 3.26 (ddd, *J* = 8.3, 4.2, 4.2 Hz, 1 H), 3.33 (s, 3 H), 3.45–3.48 (m, 4 H), 3.64–3.69 (m, 2 H), 3.78 (s, 3 H), 3.96 (dd, *J* = 6.8, 4.7 Hz, 1 H), 4.19 (dd, *J* = 6.3, 4.7 Hz, 1 H), 4.48 (d, *J* = 6.4 Hz, 1 H), 5.00, 4.94 (AB-system, J_{AB} = 6.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$, 323K): δ = –5.4 (2 C), 17.3, 18.3, 25.2, 25.9 (3 C), 29.8, 39.3, 52.2, 57.1, 60.5, 63.9, 65.4, 72.4, 74.1, 77.8, 79.7, 81.7, 88.2, 169.5.

^{13}C NMR (125 MHz, $CDCl_3$, 223 K): δ = –5.5 (2 × 2 C), 12.9, 18.2 (2 × 1 C), 22.7, 22.9, 25.7 (2 × 3 C), 27.3, 27.6, 29.5, 35.5, 41.5, 52.8, 52.9, 57.0, 57.4, 59.4, 60.5, 61.8 (2 × 1 C), 61.9, 68.3, 70.0, 72.0, 73.1, 75.4, 75.6, 78.1, 78.3, 79.5, 79.8, 82.8, 86.2, 90.0, 169.2, 169.7.

We would like to thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support of this study.

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