Model Studies towards the Synthesis of the Right-Hand Part of Pederin

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Bicyclic acetal derivatives of the type **3** were prepared based either on a dihydroxyaldehyde **5** or an oxiranebutanal **6** (*cf. Scheme 2*). *Lewis* acid catalyzed reaction of the bicyclic acetal with allyltrimethylsilane introduces the side chain (as yet unfunctionalized) and sets the stereogenic centers at the tetrahydro-2*H*-pyran ring of the pederin moiety.

Introduction. – The mycalamides **1** and the pederins **2** are representatives of a class of natural products with high biological activity (*Fig. 1*). They inhibit protein synthesis at subnanomolar concentrations [1], and they display a strong immunosuppressive activity [2]. This stimulated widespread synthetic efforts culminating in several total syntheses (mycalamides [3–9], pederin [10–16]) that had to cope with the intricate density of functional groups in these molecules.

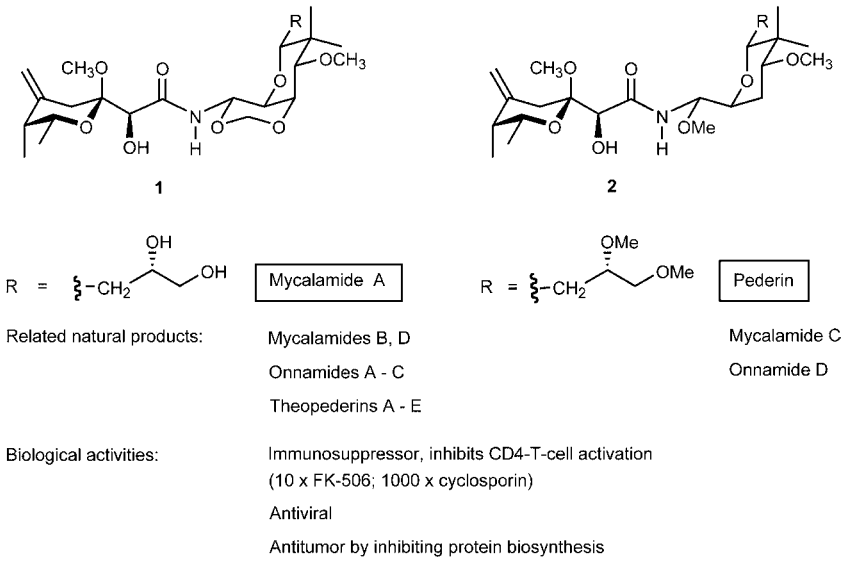
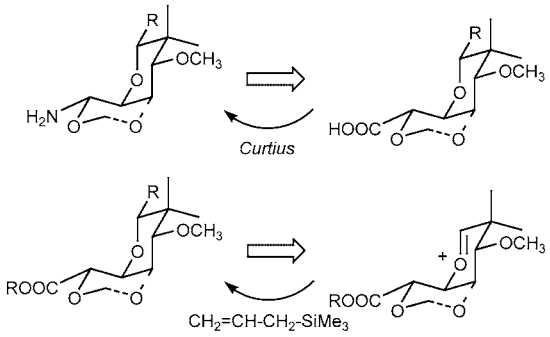


Fig. 1. *Mycalamides and Pederins*

In considering shorter syntheses to these compounds, some aspects of the previous efforts were noteworthy: First, the sensitive aminal function can be generated by a *Curtius* degradation of a carboxylic acid precursor [9][15][17][18] (*Scheme 1*). Second,

the side chain R on the tetrahydro-2*H*-pyran ring in the right fragment of these molecules can be attached *via* reaction of an oxonium ion with a suitable C-nucleophile such as an allylsilane [4][16][18][19] (see *Scheme 1*).

Scheme 1

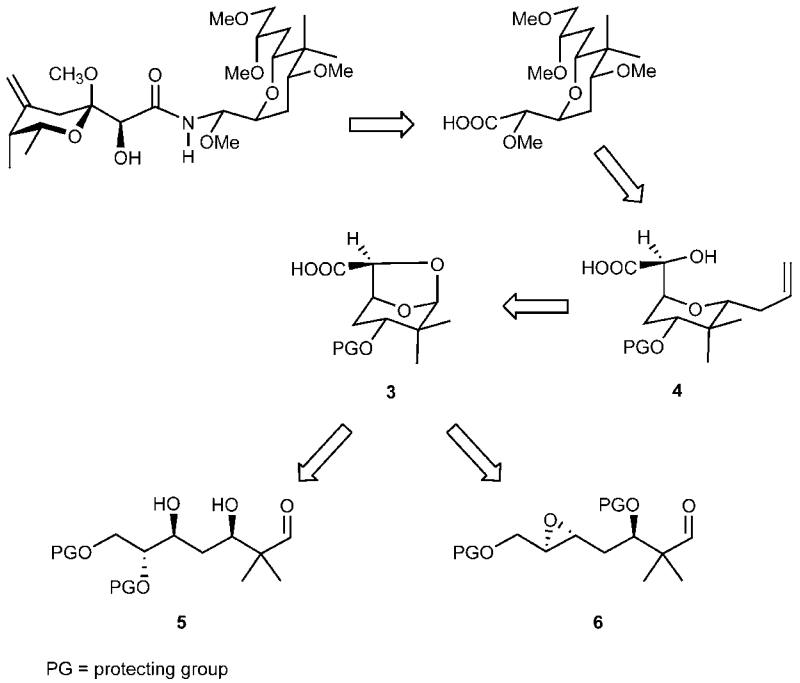


As acetals are precursors of oxonium ions, this suggested to us the following potential synthesis of the right-hand fragment of pederin, in which the bicyclic acetal **3** is a key intermediate [20] (*Scheme 2*). The ring opening of a bicyclic acetal such as **3** with an allylsilane under inversion of configuration to give **4** is known [19] (*cf.* also [20]). Thus, the possible synthesis of a bicylic acetal was evaluated. Two routes appeared attractive at first sight, an acetalization of a 3,5-dihydroxyaldehyde **5**, and an acetalization of a δ,ε-epoxy-aldehyde (=oxiranebutanal) **6**, which proceeds under inversion at the stereogenic centre in δ-position [21]. We report here some model studies along both of these lines.

The Oxiranebutanal Route to Bicyclic Acetals. – To evaluate the feasibility of the route to the bicyclic acetal **3** *via* cyclization of an oxiran-aldehyde, we looked for a rapid access to oxiranebutanal **6**. We started from the racemic diol **7** [22], which was converted to oxirane **8** by treatment with NaH and 1-tosyl-1*H*-imidazole [23] (*Scheme 3*). The crude oxirane **8** was allowed to react with 3-[(tetrahydro-2*H*-pyran-2-yl)oxy]prop-1-ynyllithium to give the alcohol **9** in 78% yield. Protection and deprotection gave the primary alcohol **10**. Its $LiAlH_4$ reduction furnished the allylic alcohol **11**, which was subjected to a *Sharpless* epoxidation [24]. Since we started from racemic **11**, we obtained a 3:2 mixture of diastereoisomers **12**. The configuration of the oxirane stereogenic centers was assigned on the basis of the *Sharpless* mnemonic [24]. MPLC Separation of the diastereoisomers became possible at the stage of **13** after protection of the free alcohol function as a (*tert*-butyl)dimethylsilyl (TBDMS) ether. The diastereoisomers **13** showed characteristic differences in the ^3J(H,H) coupling constants of H–C(3)[1]). To use these for an assignment of the relative configuration, we carried out force-field calculations with the MM3 force field implemented in the MACROMODEL program [25], using a Monte Carlo search of the conformational space. *Boltzmann* averaging over the conformers allowed an estimation of the coupling

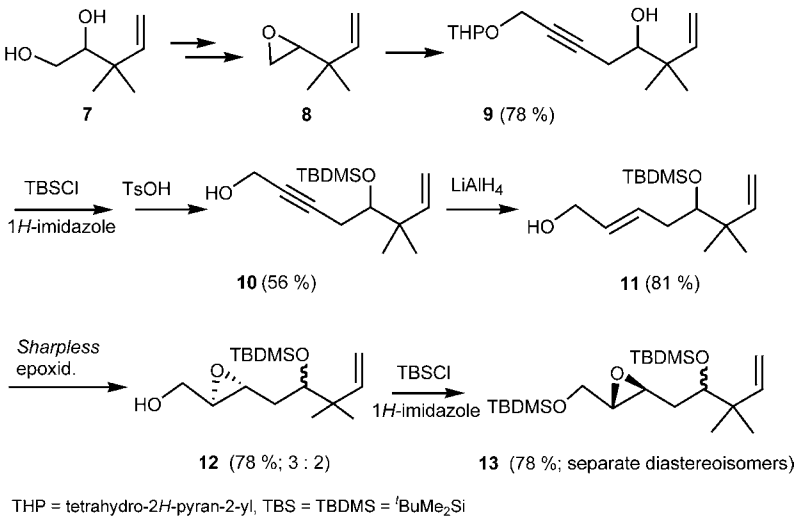
[1]) Arbitrary numbering (see *Fig. 2*); for systematic names, see *Exper. Part.*

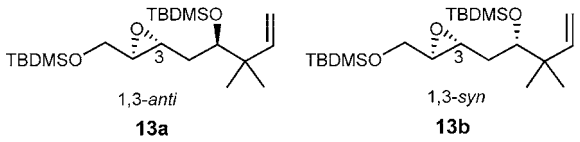
Scheme 2



constants for the two diastereoisomers, as shown in *Fig. 2.* Comparison with the experimental coupling constants led to the above tentative assignment of the relative configuration.

Scheme 3



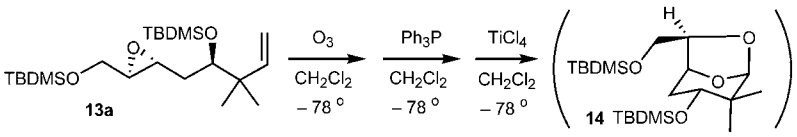


^3J(H,H) of H-C(3)[1]		
Calc.:	1.5; 5.5 Hz	2.7; 8.3 Hz
Exper.:	3.5; 7.4 Hz	2.2; 9.7 Hz

Fig. 2. *Estimation of the coupling constants of the diastereoisomers* **13**

Next we tried to convert the alkenyloxirane **13a** to the bicyclic acetal by ozonolysis followed by treatment with $TiCl_4$. We were, however, unable to isolate the desired acetal **14** (*Scheme 4*).

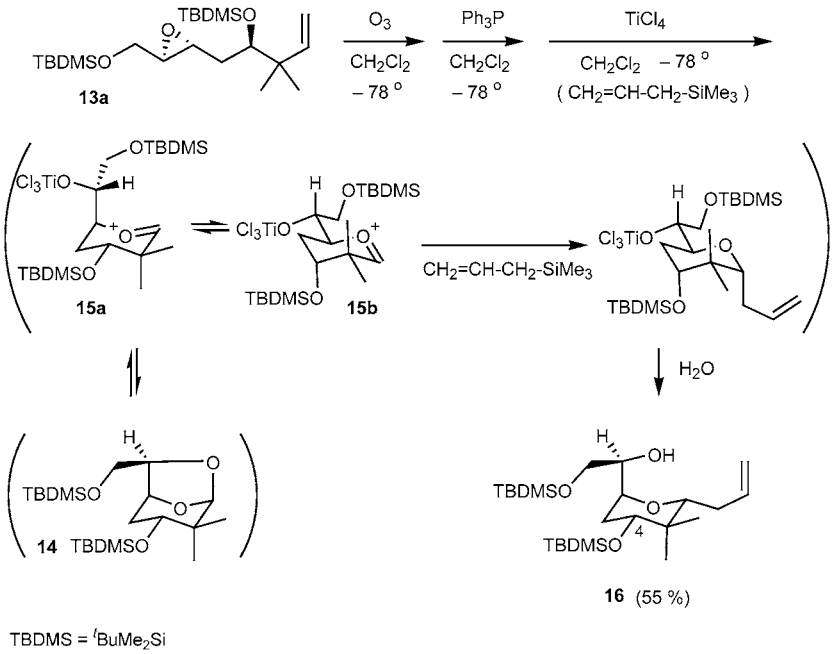
Scheme 4



Rather than trying to optimize this reaction, we turned to an *in situ* allylation reaction, pioneered by *Rychnovsky* and *Dahanukar* [26]. Treatment of the solution of the crude oxirane-aldehyde with allyltrimethylsilane and $TiCl_4$ led indeed to 55% of the desired tetrahydro-2*H*-pyranmethanol **16** (*Scheme 5*). The acetal **14** may be involved in this reaction in a blind-alley equilibrium. The relative configuration of product **16** was assigned by analogy to precedents [19][26]. The ^3J(H,H) coupling constants of H–C(4) of 10.8 and 2.6 Hz show an equatorial disposition of the silyloxy group. The formation of **16** with the shown relative configuration requires a rapid interconversion of the half chairs **15a** and **15b** of the oxonium ion prior to attack at the allyltrimethylsilane.

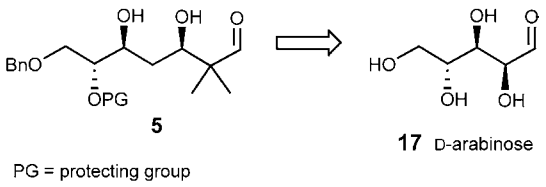
The product **16** obtained in this manner was contaminated with 10% of an impurity. Since the objective was only to demonstrate the feasibility of such an approach, **16** was not purified further. The tetrahydro-2*H*-pyranmethanol **16** is, however, only a few well-precedented steps away from the right-hand fragment of pederin: Asymmetric dihydroxylation of the alkene moiety [3][4][6–8][16][18][27] followed by permethylation of all the free alcohol functions [16][28][29], prior to the sequence of the *Curtius* degradation. For this route to be viable for a synthesis of the right-hand fragment of pederin, the starting material **7** or **8** should be enantiomerically pure. This appears possible either by kinetic resolution of the oxirane **8** [30], or by recourse to an asymmetric dihydroxylation reaction [31]. However, it might be preferable to use an enantiomerically pure starting material from natural sources. This was done in the following synthesis of the bicyclic acetal from a dihydroxy-aldehyde precursor.

Scheme 5



The Dihydroxyaldehyde Route to Bicyclic Acetals. – We felt that a dihydroxyaldehyde **5** could profitably be made from D-arabinose, which contains two of the required three stereogenic centers. This would require a deoxygenation at C(2) of arabinose and a chain extension at C(1), according to *Scheme 6*.

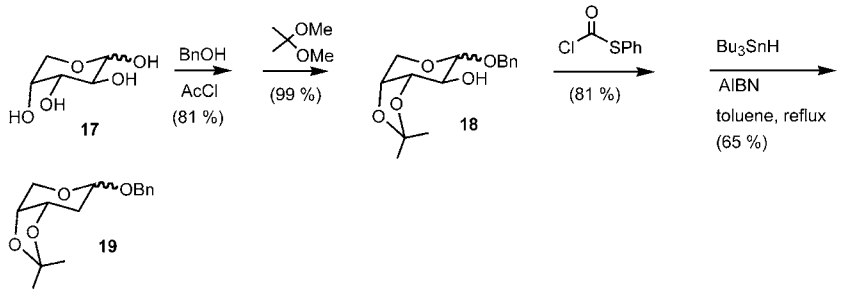
Scheme 6

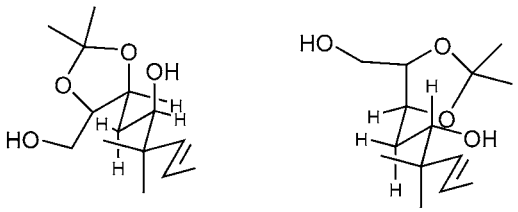


To reach the first goal, D-arabinose (**17**) was converted to benzyl 2-deoxy-3,4-*O*-isopropylidene-D-*erythro*-pentopyranoside (**19**) (*Scheme 7*). Benzyl 3,4-*O*-isopropylidene-D-arabinopyranoside (**18**) was generated as described by *Ballou* [32]. The deoxygenation at the 2-position was effected by the procedure of *Barton* and coworkers [33] to give benzyl 2-deoxy-D-*erythro*-pentopyranoside **19** in 65% yield. Next, the ensuing chain extension was initiated by the hydrogenation of **19** to give the 2-deoxy-3,4-*O*-isopropylidene-D-*erythro*-pentose **20** (*Scheme 8*). Several attempts to react the latter with tributyl(prenyl)stannane and *Lewis* acids ($SnCl_4$, Me_2SnCl_2, $TiCl_4$, or $BF_3 \cdot OEt_2$) failed as well as indium-mediated reactions [34] of prenyl bromide. Therefore, we turned to the reagent-controlled allylboration reaction with the

allylboronate **21** [29]. The lactol **20** was allowed to react with the allylboronate **21** for several days at room temperature under 8–9 kbar of pressure in the presence of pyridin-2-ol as catalyst [35]. This furnished the homoallyl alcohol **22** as a single diastereoisomer in 67% yield. The two possible diastereoisomers **22** and **23** can readily be distinguished based on ^3J(H,H) coupling constants, because each should populate a preferred conformation, based on the ^{t}Bu effect [36] originating from the quaternary centre and the tendency to form an internally H-bonded structure [37] (*Fig. 3*). Thus, in the 1,3-*syn*-diastereoisomer **22**, the indicated protons should give a spin system with two large and two small coupling constants. That of the 1,3-*anti*-diastereoisomer **23** should have one large and three small coupling constants. The isolated diastereoisomer showed coupling constants of 10.3, 1.7, 9.6, and 4.0 Hz establishing it as the 1,3-*syn*-isomer **22.** This is the expected one based on the preference of the reagent to generate the homoallylic alcohol with an (*R*)-configuration [29]. The latter assignment is supported by the (*E*)-geometry (^3J(H,H) = 15.6 Hz) of the newly formed C=C bond.

Scheme 7





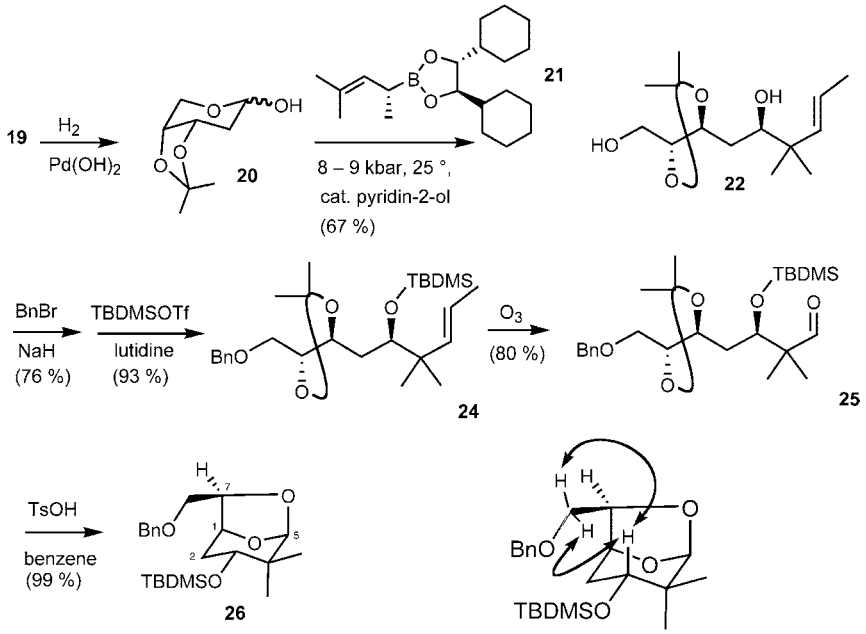
1,3-*syn* 1,3-*anti*

22 **23**

Fig. 3. *Conformation fo the diastereoisomers* **22** *and* **23**

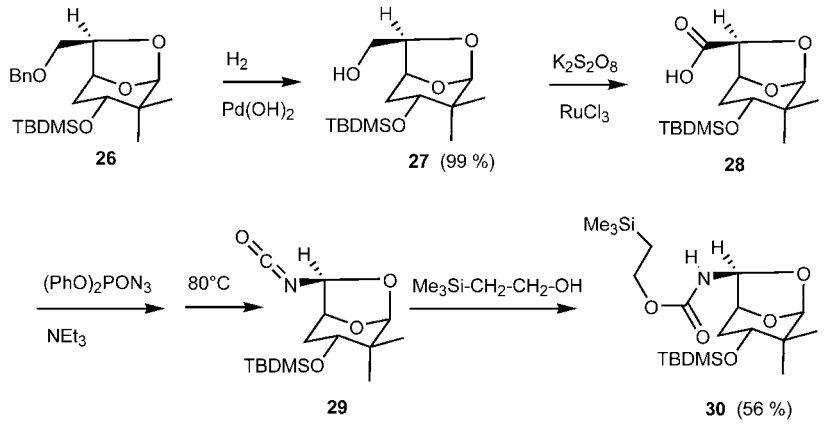
Next, protective groups were installed, a benzyl ether at the primary position and a TBDMS ether at the homoallylic position to give **24**. Ozonolysis furnished the protected tetrahydroxy-aldehyde **25**, which was immediately treated with TsOH in moist benzene to effect transacetalization to the desired bicyclic acetal **26**. The relative configuration of the latter was secured by the strong NOE contacts indicated in *Scheme 8*.

Scheme 8



Further Exploratory Experiments. – With the acetal **26** in hand, we could explore the feasibility of the *Curtius* degradation. While not directly relevant to a synthesis of pederin, we did these studies on the bicyclic structure **26**. To this end, the benzyl ether in **26** was deprotected by hydrogenolysis, and the resulting alcohol **27** was oxidized to a carboxylic acid **28** [38] (*Scheme 9*). The latter was subjected as obtained to a *Curtius* degradation furnishing carbamate **30** in 56% yield.

Scheme 9



It appeared attractive to couple [14][39] carbamate **30** with the left-hand part of pederin to provide a pederin analogon with a bicyclic acetal as a right-hand part. These studies and the further elaboration of the right-hand fragment of pederin were, however, postponed until a reliable coupling method for the two fragments will be at hand. Such reservation was indicated after some initial attempts to couple the isocyanate **29** with the left-hand fragment of pederin following our earlier model studies [40] failed [41].

In summary, these studies indicate that a short and efficient synthesis of a right-hand building block for pederin and its analogues *via* a *Lewis* acid catalyzed ring opening of bicyclic acetals of type **14** or **26** with an allylsilane is feasible. This would require subsequent refunctionalization of the side chain such as asymmetric dihydroxylation, *O*-methylation of alcohols, and a *Curtius* degradation. The studies reported here and precedents from previous studies bode well for such an approach.

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Experimental Part

General. See [42].

1. rac-*3,3-Dimethyl-8-[(tetrahydro-2*H*-pyran-2-yl)oxy]oct-1-en-6-yn-4-ol* (**9**). At 0°, an 80% NaH suspension in white oil (8.00 g, 0.26 mol) was added in small portions to a soln. of *3,3-dimethylpent-4-en-1,2-diol* [22] (**7**; 13.8 g, 106 mmol) in THF (350 ml). The mixture was stirred for 2 h at r.t. and then cooled again to 0°. A soln. of 1-tosyl-1*H*-imidazole (25.0 g, 115 mmol) in THF (100 ml) was added dropwise. The mixture was stirred for 1 h at r.t. and for 30 min under reflux, and then the soln. of oxirane **8** was cooled to −78°.

A soln. of the lithiated acetylide was prepared from 3-[(tetrahydro-2*H*-pyran-2-yl)oxy]prop-1-yne (17.0 g, 125 mmol) in THF (150 ml) and 1.84M BuLi in hexane (68.0 ml, 125 mmol). This soln. was cooled to 0° and added *via* canula to the precooled soln. of oxirane **8**. $BF_3 \cdot Et_2O$ (50 ml, 0.4 mol) was added dropwise resulting in strong frothing. The mixture was stirred for 12 h at −78°. Sat. aq. $NaHCO_3$ soln. (300 ml) was added slowly at −60°. The mixture was allowed to reach r.t. The aq. layer was extracted with ^{t}BuOMe (3 × 100 ml), the combined org. layer washed with brine (150 ml), dried (Na_2SO_4), and evaporated, and the residue filtered with petroleum ether/^{t}BuOMe 3:1 over silica gel. The crude product was heated for 5 h to 50° at $2 \cdot 10^{-2}$ mbar to remove excess 3-[(tetrahydro-2*H*-pyran-2-yl)oxy]prop-1-yne: **9** (diastereoisomer mixture; 20.9 g, 78%). Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.98 (*s*, Me); 0.99 (*s*, Me); 1.46–1.75 (*m*, $CH_2CH_2CH_2$ (thp)); 2.11 (*dd*, ^3J = 3.6, 8.5, C*H*OH); 2.20 ($d_{AB}dt$, $^2J_{AB}$ = −16.7, ^3J = 8.5, ^5J = −2.4, $CH_2C{\equiv}C$); 2.35 (*t*, $CH_2C{\equiv}C$); 3.42–3.48 (*m*, H_{eq}−CHO (thp) and OH); 3.79–3.84 (*m*, H_{ax}−CHO (thp)); 4.12–4.23 (*m*, $C{\equiv}CCH_2$); 4.75 (*q*, OCHO); 4.96 ($d_{AB}d$, $^2J_{AB}$ = −1.3, ^3J = 17.4, H_{cis}−CH=CH); 5.02 ($d_{AB}d$, $^2J_{AB}$ = −1.3, ^3J = 10.9, H_{trans}−CH=CH); 5.84 (*dd*, ^3J = 10.9, ^3J = 17.4, CH_2=C*H*). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.0; 22.4; 23.0; 23.1; 25.3; 30.2; 41.0; 54.6; 54.7; 61.8; 76.3; 78.2; 84.0; 96.9; 113.0; 144.4. Anal. calc. for $C_{15}H_{24}O_3$ (252.35): C 71.39, H 9.59; found: C 71.48, H 9.81.

2. rac-*4-{[(*tert*-Butyl)dimethylsilyl]oxy}-3,3-dimethyl-8-[(tetrahydro-2*H*-pyran-2-yl)oxy]oct-1-en-6-yne.* (*tert*-Butyl)chlorodimethylsilane (50% in hexane; 10.0 g, 33.2 mmol) and 1*H*-imidazole (3.20 g, 47.0 mmol) were added to a soln. of **9** (7.89 g, 31.3 mmol) in DMF (30 ml). After stirring for 10 h at 45°, MeOH (5 ml) was added, and stirring was continued for 15 min. H_2O (40 ml) was added, and the mixture was extracted with petroleum ether (3 × 100 ml). The combined org. layers were washed with brine (100 ml) and evaporated. FC (petroleum ether/^{t}BuOMe 10:1 → 1:1) furnished the product (diastereoisomer mixture; 6.71 g, 59%), besides recovered **9** (2.52 g, 32%). ^{1}H-NMR (300 MHz; $CDCl_3$): 0.06 (*s*, MeSi); 0.11 (*s*, MeSi); 0.88 (*s*, ^{t}BuSi); 0.97 (*s*, Me); 0.98 (*s*, Me); 1.45–1.73 (*m*, $CH_2CH_2CH_2$ (thp)); 2.11 ($d_{AB}dt$, $^2J_{AB}$ = −17.2, ^3J = 6.5, ^5J = 2.1, $CH_2C{\equiv}C$); 2.41 ($d_{AB}dt$, $^2J_{AB}$ = −17.2, ^3J = 4.0, ^5J = 2.3, $CH_2C{\equiv}C$); 3.46–3.54 (*m*, H_{eq}−CHO (thp), overlapped by *dd*, ^3J = 4.0, 6.5, CHOSi); 3.77–3.85 (*m*, H_{ax}−CHO (thp)); 4.12–4.23 (*m*, $C{\equiv}CCH_2$); 4.75 (*m*, OCHO); 4.96 ($d_{AB}d$, $^2J_{AB}$ = −1.9, ^3J = 18.0, H_{cis}−CH=CH); 4.97 ($d_{AB}d$, $^2J_{AB}$ = −1.9, ^3J = 10.6, H_{trans}−CH=CH); 5.84 (*dd*, ^3J = 10.6, ^3J = 18.0, CH_2=C*H*). ^{13}C-NMR (75 MHz, $CDCl_3$): −4.5; −3.8; 18.2; 19.1; 22.3; 24.2; 24.3; 25.4; 26.0; 30.3; 42.5; 54.6; 54.7; 61.8; 77.5; 78.6; 85.6; 85.7; 96.6; 96.7; 112.1; 145.3. Anal. calc. for $C_{21}H_{38}O_3Si$ (366.62): C 68.80, H 10.66; found: C 68.68, H 10.48.

3. rac-*5-{[(*tert*-Butyl)dimethylsilyl]oxy}-6,6-dimethyloct-7-en-2-yn-1-ol* (**10**). TsOH (*ca.* 10 mg) was added to a soln. of *rac*-4-{[(*tert*-butyl)dimethylsilyl]oxy}-3,3-dimethyl-8-[(tetrahydro-2*H*-pyran-2-yl)oxy]oct-1-en-6-yne (3.60 g, 9.82 mmol) in EtOH (150 ml). After stirring for 1 d at r.t., the mixture was poured into a vigorously stirred emulsion of H_2O (100 ml) and ^{t}BuOMe (100 ml). K_2CO_3 (1 g) was added, the aq. layer extracted with ^{t}BuOMe (5 × 100 ml), the combined org. layer washed with brine (50 ml), dried (Na_2SO_4), and evaporated, and the residue filtered with petroleum ether/^{t}BuOMe 3:1 over silica gel: **10** (2.61 g, 94%). Colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.08 (*s*, 1 MeSi); 0.14 (*s*, 1 MeSi); 0.90 (*s*, ^{t}BuSi); 0.98 (*s*, 1 Me); 0.99 (*s*, 1 Me); 2.18 ($d_{AB}ddd$, $^2J_{AB} = -14.3$, $^3J = 4.4$, $^5J = 1.8$, 1.8, 1 H, $CH_2C{\equiv}C$); 2.46 ($d_{AB}ddd$, $^2J_{AB} = -14.3$, $^3J = 6.5$, $^5J = 2.2$, 2.4, 1 H, $CH_2C{\equiv}C$); 3.53 (*dd*, $^3J = 4.3$, 6.5, CHOSi); 4.239 ($d_{AB}dd$, $^2J_{AB} = -2.2$, $^5J = 2.2$, 1.8, 1 H, $C{\equiv}CCH_2OH$); 4.244 ($d_{AB}dd$, $^2J_{AB} = -2.2$, $^5J = 2.4$, 1.8, 1 H, $C{\equiv}CCH_2OH$); 4.97 ($d_{AB}d$, $^2J_{AB} = -1.5$, $^3J = 18.2$, H_{cis}–CH=CH); 4.98 ($d_{AB}d$, $^2J_{AB} = -1.5$, $^3J = 10.3$, H_{trans}–CH=CH); 5.86 (*dd*, $^3J = 10.3$, 18.2, CH_2=C*H*); OH signal missing. ^{13}C-NMR (75 MHz, $CDCl_3$): −4.4; −3.7; 18.3; 22.3; 24.2; 24.4; 25.4; 26.0; 42.6; 78.6; 79.8; 85.8; 112.2; 145.3. Anal. calc. for $C_{16}H_{30}O_2Si$ (282.48): C 68.03, H 10.70; found: C 67.81, H 10.87.

4. rac-*5-{[(*tert*-Butyl)dimethylsilyl]oxy}-6,6-dimethylocta-2,7-dien-1-ol* (**11**). At 0°, **10** (900 mg, 3.20 mmol) was added to a suspension of $LiAlH_4$ (450 mg, 12.8 mmol) in THF (70 ml). The mixture was heated to reflux for 12 h. After cooling to 0°, AcOEt (1.5 ml), H_2O (0.5 ml), 15% aq. NaOH soln. (0.5 ml), and H_2O (0.5 ml) were added sequentially. The mixture was filtered through Na_2SO_4, which was subsequently washed with ^{t}BuOMe (5 × 20 ml). The combined filtrates were evaporated. FC (petroleum ether/^{t}BuOMe 10:1 → 1:1) of the residue furnished **11** (737 mg, 81%). Colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.02 (*s*, MeSi); 0.03 (*s*, MeSi); 0.91 (*s*, ^{t}BuSi); 0.99 (*s*, 2 Me); 1.65 (br. *s*, OH); 2.00–2.14 (*m*, 1 H, CH_2C=C); 2.29–2.33 (*m*, 1 H, CH_2C=C); 3.41 (*dd*, $^3J = 4.0$, 6.7, CHOSi); 4.09 (br. *s*, C=CCH_2OH); 4.96 ($d_{AB}d$, $^2J_{AB} = -1.5$, $^3J = 17.1$, H_{cis}–CH=CH); 4.97 ($d_{AB}d$, $^2J_{AB} = -1.5$, $^3J = 11.3$, H_{trans}–CH=CH); 5.57–5.62 (*m*, C*H*=CH); 5.68–5.73 (*m*, CH=C*H*); 5.86 (*dd*, $^3J = 11.3$, 17.1, CH_2=C*H*). ^{13}C-NMR (126 MHz, $CDCl_3$): −4.1; −3.3; 18.3; 22.8; 24.6; 26.0; 36.9; 42.5; 63.8; 79.3; 111.6; 130.2; 131.7; 146.1. Anal. calc. for $C_{16}H_{32}O_2Si$ (284.51): C 67.55, H 11.35; found: C 67.46, H 11.61.

5. *(2*R*,3*R*)-3-{(2*R/S*)-2-{[(*tert*-Butyl)dimethylsilyl]oxy}-3,3-dimethylpent-4-enyl}oxirane-2-methanol* (**12**). A soln. of (−)-diisopropyl tartrate (115 mg, 0.50 mol) and of titanium tetraisopropoxide (112 mg, 0.40 mmol) in CH_2Cl_2 (20 ml) was stirred at −30° for 30 min over 3-Å molecular sieves. A soln. of **11** (586 mg, 2.06 mmol) in CH_2Cl_2 (2 ml) was added, and stirring was continued at −30° for 10 min. A soln. of 7M ^{t}BuOOH in CH_2Cl_2 (1.5 ml) was added, and the mixture was stored in a freezer at −25° for 3 d. Aq. 10% tartaric acid (10 ml) was added dropwise, and the mixture was allowed to reach r.t. and filtered over 'Kieselgur'. The filtrate was concentrated onto silica gel (3 g). FC (petroleum ether/^{t}BuOMe 1:1) furnished **12** (3:2 diastereoisomer mixture by NMR; 480 mg, 78%). Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.03 (*s*, MeSi); 0.04 (*s*, MeSi); 0.86 (*s*, ^{t}BuSi); 0.92 (*s*, Me); 0.93 (*s*, Me); 1.31–1.55 (*m*, SiOC–CH_2); 1.63 (br. *s*, OH); 2.81–2.89 (*m*, C*H*OCH); 3.05 (*m*, CHOC*H*); 3.49–3.56 (*m*, CH_2OH); 3.65 (*m*, CHOSi); 4.86–4.95 (*m*, CH_2=CH); 5.84 (*dd*, $^3J = 10.2$, 18.0, CH_2=C*H*). ^{13}C-NMR (50 MHz, $CDCl_3$): major (2*R*,2′*S*,3R)-diastereoisomer: −4.0; 18.2; 21.6; 22.8; 26.0; 35.8; 42.0; 53.7; 60.0; 76.6; 111.8; 145.4; 1 C obscured; minor (2*R*,2′*R*,3*R*)-diastereoisomer: −4.3; −4.0; 18.2; 22.3; 24.6; 25.7; 36.7; 42.0; 54.2; 59.3; 112.0; 145.4; 2 C obscured. Anal. calc. for $C_{16}H_{32}O_3Si$ (300.21): C 63.95, H 10.73; found (diastereoisomer mixture): C 63.94, H 10.94.

6. *(2*R*,3*R*)-2-{(2*R/S*)-2-{[(*tert*-Butyl)dimethylsilyl]oxy}-3,3-dimethylpent-4-enyl}-3-{[[(*tert*-butyl)dimethylsilyl]oxy}methyl}oxirane* (**13**). (*tert*-Butyl)chlorodimethylsilane (50% in hexane; 763 mg, 2.60 mmol) and 1*H*-imidazole (255 mg, 5.2 mmol) were added to a soln. of the alcohols **12** (380 mg, 1.30 mmol) in DMF (2 ml). After stirring for 12 h, MeOH (1 ml) was added, and stirring was continued for 15 min. A pH 7 buffer soln. (10 ml) and ^{t}BuOMe (15 ml) were added, and the aq. layer was extracted with ^{t}BuOMe (3 × 10 ml). The combined org. layer was washed with H_2O (10 ml) and brine (2 × 25 ml), dried (Na_2SO_4), and evaporated, and the residue was subjected to FC (petroleum ether/^{t}BuOMe/AcOEt 50:1:1): **13** (diastereoisomer mixture; 423 mg, 78%). The diastereoisomers were separated by MPLC (petroleum ether/AcOEt 99:1).

*(2*R*,2′*R*,3*R*)-Isomer* **13a**: Less polar. $[\alpha]_D^{21} = +12.9$ (*c* = 0.31, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$): 0.07 (*s*, 1 MeSi); 0.08 (*s*, 1 MeSi); 0.10 (*s*, 1 MeSi); 0.12 (*s*, 1 MeSi); 0.91 (*s*, 1 ^{t}BuSi); 0.93 (*s*, 1 ^{t}BuSi); 0.98 (*s*, 1 Me); 0.99 (*s*, 1 Me); 1.56 ($d_{AB}dd$, $^2J_{AB} = -14.45$, $^3J = 3.29$, 7.27, 1 H, CH_2CHOSi); 1.70 ($d_{AB}dd$, $^2J_{AB} = -14.53$, $^3J = 4.27$, 7.43, 1 H, CH_2CHOSi); 2.83 (*m*, C*H*OCH); 2.99 (*m*, CHOC*H*); 3.61 (*dd*, $^3J = 3.47$, 7.36, CHOSi); 3.65 ($d_{AB}d$, $^2J_{AB} = -11.88$, $^3J = 4.71$, 1 H, CH_2OSi); 3.80 ($d_{AB}d$, $^2J_{AB} = -11.76$, $^3J = 3.27$, 1 H, CH_2OSi); 4.96–4.99 (*m*, CH_2=CH); 5.87 (*dd*, $^3J = 10.45$, 17.87, CH_2=C*H*). ^{13}C-NMR (126 MHz, $CDCl_3$): −5.3; −3.9; −3.8; 18.3; 22.7; 24.5; 25.9; 26.1; 36.2; 42.1; 53.9; 60.1; 63.4; 76.8; 111.8; 145.7. Anal. calc. for $C_{22}H_{46}O_3Si_2$ (414.78): C 63.71, H 11.17; found: C 63.97, H 10.93.

*(2*R*,2′*S*,3*R*)-Isomer* **13b**: More polar. ^{1}H-NMR (300 MHz, $CDCl_3$): −0.01 (*s*, 1 MeSi); 0.03 (*s*, 1 MeSi); 0.04 (*s*, 1 MeSi); 0.08 (*s*, 1 MeSi); 0.88 (*s*, 1 ^{t}BuSi); 0.90 (*s*, 1 ^{t}BuSi); 0.91 (*s*, 1 Me); 0.93 (*s*, 1 Me); 1.39–1.73

(*m*, CH_2CHOSi); 2.74 (*m*, C*H*OCH); 2.92 (*m*, CHOC*H*); 3.53 (*dd*, ^3J = 2.2, 9.7, CHOSi); 3.57 ($d_{AB}d$, $^2J_{AB}$ = −11.8, ^3J = 4.6, 1 H, CH_2OSi); 3.73 ($d_{AB}d$, $^2J_{AB}$ = −11.8, 1 H, CH_2OSi); 4.95 (*d*, ^3J = 12.0, H_{trans}−CH=CH); 4.95 (*d*, ^3J = 16.3, H_{cis}−CH=CH); 5.85 (*dd*, ^3J = 12.0, 16.3, CH_2=C*H*). ^{13}C-NMR (75 MHz, $CDCl_3$): −5.2; −4.8; −4.1; −4.0; 18.1; 18.2; 21.7; 22.6; 24.4; 25.8; 26.0; 36.0; 41.9; 53.8; 63.3; 76.7; 111.6; 145.6.

7. *(*α*R,2S,4R,6R)-4-{[(*tert*-Butyl)dimethylsilyl]oxy}-α-{{[(*tert*-butyl)dimethylsilyl]oxy}methyl}tetrahydro-5,5-dimethyl-6-(prop-2-enyl)-2*H*-pyran-2-methanol* (**16**). A stream of O_3 in O_2 was introduced at −78° very slowly into a soln. of **13a** (19.9 mg, 48.1 μmol) in CH_2Cl_2/MeOH 1:3 (5 ml) until TLC indicated consumption of the starting material. PPh_3 (13.3 mg, 48.1 μmol) was added, and the mixture was stirred for 12 h at r.t. Petroleum ether/^{t}BuOMe 1:1 (15 ml) was added, and the precipitated PPh_3=O was filtered over 'Kieselgur'. The filtrate was dried ($MgSO_4$) and evaporated. The crude aldehyde was taken up under N_2 in CH_2Cl_2 (5 ml) and evaporated again. This step was repeated three times. The aldehyde was taken up once more in CH_2Cl_2 (5 ml) and dried with 3-Å molecular sieves (0.5 g). Allyltrimethylsilane (50 ml, 0.3 mmol) was added, and the mixture was cooled to −78°. A soln. of 2M $TiCl_4$ in CH_2Cl_2 (2 drops) was added, and the mixture was stirred for 1 d at −78°. Upon slowly warming to −50°, TLC indicated the formation of a new product. A pH 7 buffer soln. (1 ml) was added at −50°, and the mixture was allowed to reach r.t. The aq. layer was extracted with ^{t}BuOMe (3 × 5 ml), the combined org. layer washed with brine (2 × 1 ml), dried (Na_2SO_4), and evaporated, and the residue subjected to FC (petroleum ether/^{t}BuOMe 20:1 → 10:1): **16** (12.4 mg, 55%) containing 10% of an impurity. Colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.08 (*s*, 2 MeSi); 0.09 (*s*, 2 MeSi); 0.90 (*s*, 2 ^{t}BuSi); 0.94 (*s*, 1 Me); 0.98 (*s*, 1 Me); 1.51 (br. *s*, OH); 1.65–1.74 (*m*, CH_2CH=CH_2); 1.95–2.02 (*m*, 1 H, CH_2CHOSi); 2.18–2.22 (*m*, 1 H, CH_2CHOSi); 3.25 (*dd*, ^3J = 2.6, 10.8, CHOSi); 3.52–3.56 (*m*, 1 H, CH_2OTBS); 3.61 (*dd*, ^3J = 4.0, 8.1, C*H*OH); 3.76 (*m*, 1 H of CH_2OTBS, 2 CHO); 5.05 (*dd*, ^3J = 12.1, 15.7, CH=CH_2); 5.78–5.86 (*m*, C*H*=CH_2). ^{13}C-NMR (75 MHz, $CDCl_3$): −5.4; −5.0; −4.3; 18.0; 18.3; 24.9; 25.8; 25.9; 30.5; 33.6; 38.4; 64.4; 70.0; 70.7; 73.0; 80.0; 128.8; 132.5; quat. C-atom not detected.

8. *Benzyl* D-*Arabinoside*. Acetyl chloride (5.0 ml, 70 mmol) was added to a soln. of D-(−)-arabinose (25.0 g, 167 mmol) in benzyl alcohol (125 ml), and the mixture was held at 50° for 1 d. After cooling, the mixture was filtered, and the solid was taken up in ^{t}BuOMe (30 ml). The mixture was suspended in toluene (400 ml), ^{t}BuOMe (100 ml), $CHCl_3$ (100 ml), and pyridine (10 ml), heated to 90°, and filtered while hot. The product was dried *in vacuo:* 27.0 g (67%) of solid material. On standing, the mother liquor deposited further 5.4 g. Total yield: 32.4 g (81%). M.p. 169–171° ([32]: 169–171°). $[\alpha]_D^{19}$ = −217.6 (*c* = 0.71, MeOH). ^{1}H-NMR (300 MHz, (D_6)DMSO): 3.45 (*dd*, ^3J = 2.7, 11.8, H−C(2)); 3.55–3.75 (*m*, H−C(3), H−C(4), 2 H−C(5)); 4.52 (d_{AB}, ^2J = −12.3, H_B of PhCH_2); 4.59–4.79 (*m*, H_A of PhCH_2, H−C(1), 3 OH); 7.19–7.35 (*m*, Ph). ^{13}C-NMR (75 MHz, (D_6)DMSO): 63.5; 68.4; 68.6; 68.8; 69.3; 99.1; 127.5; 127.6; 128.3; 138.4. Anal. calc. for $C_{12}H_{16}O_5$ (240.26): C 59.98, H 6.71; found: C 59.68, H 6.52.

9. *Benzyl 3,4-*O-*Isopropylidene-*D-*arabinoside* (**18**). Dimethoxypropane (12.0 g, 116 mmol) and TsOH (5 mg) were added to a soln. of benzyl D-arabinoside (13.9 g, 57.8 mmol) in acetone (200 ml). After stirring for 40 h, 25% aq. ammonia (0.3 ml) was added, and the soln. was evaporated. The residue was taken up in CH_2Cl_2 (150 ml), the soln. washed with sat. aq. $NaHCO_3$ soln. (100 ml), dried (Na_2SO_4), and evaporated, and the residue dried at $2 \cdot 10^{-2}$ mbar: 16.2 g of a sirup, which slowly solidified on standing. $[\alpha]_D^{19}$ = −171.2 (*c* = 1.07, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 1.27 (*s*, 3 H, Me_2CO_2); 1.45 (*s*, 3 H, Me_2CO_2); 2.79 (br. *s*, OH); 3.67–3.75 (*m*, H−C(2)); 3.86 (d_{AB}, $^2J_{AB}$ = −13.3, 1 H−C(5)); 3.91 ($d_{AB}d$, $^2J_{AB}$ = −13.3, ^3J = 1.9, 1 H−C(5)); 4.11 (*m*, H−C(3), H−C(4)); 4.47 (d_{AB}, $^2J_{AB}$ = −16.1, 1 H, PhCH_2); 4.65 (d_{AB}, $^2J_{AB}$ = −16.4, 1 H, PhCH_2); 4.85 (*d*, ^3J = 3.6, H−C(1)); 7.19–7.30 (*m*, Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): 25.8; 27.7; 59.6; 69.6; 69.9; 72.8; 75.8; 97.0; 110.0; 127.8; 128.3; 137.2. Anal. calc. for $C_{15}H_{20}O_5$ (280.32): C 64.27, H 7.19; found: C 64.24, H 7.28.

10. *Benzyl 3,4-*O-*Isopropylidene-2-*O-*[(phenylthio)carbonyl]-*D-*arabinoside. S*-Phenyl carbonochloridothioate (8.0 ml, 58 mmol) was added slowly to a soln. of **18** (16.2 g, 57.8 mmol) in pyridine (36 ml) and MeCN (120 ml). The dark red mixture was stirred for 1 h at r.t. *N*-Hydroxysuccinimide (35 mg) was added, and stirring was continued for 5 h. ^{t}BuOMe (100 ml) and H_2O (50 ml) were added. The aq. layer was extracted with ^{t}BuOMe (3 × 100 ml), the combined org. layer washed with brine (100 ml), dried (Na_2SO_4), and evaporated, and the residue subjected to FC (petroleum ether/^{t}BuOMe 10:1): product (19.4 g, 81%). Light yellow oil. $[\alpha]_D^{18}$ = −182.7 (*c* = 1.06, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 1.41 (*s*, 3 H, Me_2CO_2); 1.60 (*s*, 3 H, Me_2CO_2); 4.09 (br. *s*, 2 H−C(5)); 4.34 (*dt*, ^3J = 5.5, H−C(4)); 4.58 (*dd*, ^3J = 2.6, 5.5, H−C(3)); 4.60 (d_{AB}, $^2J_{AB}$ = −12.4, 1 H, $PhCH_2$); 4.79 (d_{AB}, $^2J_{AB}$ = −12.4, 1 H, PhCH_2); 5.27 (*d*, ^3J = 3.5, H−C(1)); 5.46 (*dd*, ^3J = 3.5, 8.1, H−C(2)); 7.08–7.41 (*m*, 2 Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): 26.4; 28.0; 59.0; 69.6; 72.6; 73.7; 81.2; 94.2; 109.6; 121.8; 126.6; 127.6; 128.0; 128.5; 129.4; 137.0; 153.4; 194.8. Anal. calc. for $C_{22}H_{24}O_6S$ (416.49): C 63.45, H 5.81; found: C 63.34, H 5.81.

11. *Benzyl 2-Deoxy-3,4*-O-*isopropylidene*-D-erythro-*pentopyranoside* (**19**). Tributylstannane (8.50 ml, 32.2 mmol) was added to a soln. of the thiocarbonate described in *Exper. 10* (11.2 g, 26.9 mmol) in toluene (350 ml). The soln. was heated to 80°, and a soln. of azobis[isobutyronitrile] (400 mg) in toluene (40 ml) was added at a rate of 4 ml/min *via* a syringe pump. After 10 h stirring (TLC monitoring), further azobis[isobutyronitrile] (100 mg) in toluene (20 ml) was added at a rate of 10 ml/min. Then, the mixture was evaporated and the residue subjected to FC (petroleum ether/^{t}BuOMe 1:0 → 10:1): crude **19** (5.42 g, 76%) and starting material (2.02 g, 18%). Bulb-to-bulb distillation of **19** at $1 \cdot 10^{-2}$ mbar (bath of 100°) gave a colorless solid. To remove traces of S-contaminants, the product was dissolved in EtOH (15 ml) and stirred with *Raney*-Ni (*ca.* 500 mg). The mixture was filtered over 'Kieselgur', the filtrate evaporated, the residue taken up in ^{t}BuOMe (50 ml), and the soln. dried ($MgSO_4$) and evaporated: pure **19** (4.31 g, 65%). M.p. 43–44°. $[\alpha]_D^{20} = -117.8$ ($c = 4.75$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 1.33 (*s*, 3 H, Me_2CO_2); 1.49 (*s*, 3 H, Me_2CO_2); 1.85 ($d_{AB}dd$, $^2J = -14.7$, $^3J = 4.6$, 6.1, 1 H–C(2)); 2.16 ($d_{AB}t$, $^2J = -14.7$, $^3J = 4.9$, 1 H–C(2)); 3.75 ($d_{AB}d$, $^2J = -12.9$, $^3J = 2.4$, 1 H–C(5)); 3.89 ($d_{AB}d$, $^2J = -12.9$, $^3J = 2.9$, 1 H–C(5)); 4.13 (*dt*, $^3J = 2.7$, $^3J = 6.6$, 1 H–C(4)); 4.42–4.47 (*m*, H–C(3)); 4.49 (d_{AB}, $^2J_{AB} = -11.9$, 1 H, PhCH_2); 4.76 (d_{AB}, $^2J_{AB} = -11.9$, 1 H, PhCH_2); 4.96 (*dd*, $^3J = 4.5$, 6.0, H–C(1)); 7.24–7.33 (*m*, Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): 25.4; 27.2; 31.5; 61.3; 69.2; 69.9; 72.0; 95.7; 108.5; 127.6; 127.7; 128.4; 137.9. Anal. calc. for $C_{15}H_{20}O_4$ (246.32): C 68.16, H 7.63; found: C 68.00, H 7.54.

12. *2-Deoxy-3,4*-O-*isopropyliden*-D-erythro-*pentopyranose* (**20**). $Pd(OH)_2$ (*Pearlman* catalyst, *ca.* 10 mg) was added to a soln. of **19** (407 mg, 1.77 mmol) in THF (30 ml). The soln. was stirred for 12 h under H_2. The mixture was filtered over 'Kieselgur', and the filtrate was evaporated: **20** (anomeric mixture; 308 mg, 100%). Colorless oil. $[\alpha]_D^{19} = -22.4$ ($c = 1.36$, $CHCl_3$; [43]: −18.5 ($c = 4.2$, $CHCl_3$)). ^{1}H-NMR (300 MHz, $CDCl_3$): α-D-anomer: 1.25 (*s*, 3 H, Me_2CO_2); 1.40 (*s*, 3 H, Me_2CO_2); 1.68 ($d_{AB}dd$, $^2J_{AB} = -14.7$, $^3J = 4.2$, 7.5, 2 H–C(2)); 2.05–2.18 (*m*, H–C(3), H–C(4)); 2.48 (*q*, $J = 6.8$, 2 H–C(5)); 4.53 (br. *s*, OH); 5.12 (*dd*, $^3J = 4.5$, 7.1, H–C(1)); β-D-anomer (selected signals): 1.23 (*s*, 3 H, Me_2CO_2); 1.44 (*s*, 3 H, Me_2CO_2); 1.86–2.01 (*m*, 2 H–C(5)); 4.89 (*t*, $J =$ 4.7, H–C(1)). ^{13}C-NMR (75 MHz, $CDCl_3$): α-D-anomer: 25.2; 27.1; 32.1; 61.8; 70.6; 71.4; 90.7; 108.6; β-D-anomer: 25.5; 27.8; 33.2; 60.8; 70.4; 71.8; 91.5; 109.2. Anal. calc. for $C_8H_{14}O_4$ (174.20): C 55.16, H 8.10; found: C 55.07, H 8.38.

13. *(*αR,*4*S,*5*R*)-*α-*[(2*E*)-1,1-Dimethylbut-2-enyl]-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-ethanol* (**22**). A soln. of **20** (411 mg, 2.36 mmol), (4*R*,5*R*)-2-[(1*R*)-1,3-dimethylbut-2-enyl)-4,5-dicyclohexyl-1,3,2-dioxaborolane [29] (**21**; 977 mg, 3.07 mmol), and pyridin-2-ol (22 mg, 0.23 mmol) in CH_2Cl_2 (1 ml) was pressurized for 7 d to 8–9 kbar. GC analysis indicated a 75% conversion. The mixture was subjected to FC (silica gel, petroleum ether/^{t}BuOMe 1:0 → 0:1). Excess reagent **21** (302 mg) eluted with the nonpolar solvent. The product was eluted with the polar fractions which were taken up in CH_2Cl_2 (5 ml), after evaporation. Triethanolamine (=2,2′,2″-nitrilotris[ethanol]; 0.5 g) was added, and the mixture was stirred for 2 h. Silica gel was added, and the mixture was evaporated. FC (petroleum ether/^{t}BuOMe 2:1) furnished **22** (single diastereoisomer; 408 mg, 67%). Colorless oil. $[\alpha]_D^{19} = +39.5$ ($c = 0.98$, $CHCl_3$). ^{1}H-NMR (500 MHz, C_6D_6): 1.16 (*s*, 1 Me); 1.17 (*s*, 1 Me); 1.21 (*s*, 3 H, Me_2CO_2); 1.31 (*s*, 3 H, Me_2CO_2); 1.54 ($d_{AB}ddd$, $^2J_{AB} = -14.20$, $^3J = 9.85$, 10.27, $^4J = -0.16$, 1 H, $CH_2(\beta)$); 1.66 (*dd*, $^3J = 6.32$, $^4J = -1.59$, *Me*CH=CH); 1.71 ($d_{AB}ddd$, $^2J_{AB} = -14.20$, $^3J =$ 1.61, 3.96, $^4J = -0.13$, 1 H, $CH_2(\beta)$); 3.17 (br. *s*, 1 OH); 3.39 (br. *s*, 1 OH); 3.43 (*ddd*, $^3J = 1.61$, 10.27, $^4J = -0.23$, H–C(α)); 3.61–3.65 (*m*, CH_2OH); 4.20 (*m*, H–C(5)); 4.36 (*dddd*, $^3J = 3.96$, $^3J = 6.08$, 9.85, $^4J = -0.23$, H–C(4)); 5.44 ($d_{AB}q$, $^3J = 6.32$, $^3J_{AB} = 15.57$, MeC*H*=CH); 5.62 ($d_{AB}q$, $^3J_{AB} = 15.57$, $^4J = -1.59$, MeCH=C*H*). ^{13}C-NMR (50 MHz, $CDCl_3$): 18.2; 22.7; 24.0; 25.5; 28.1; 30.3; 40.3; 61.6; 77.3; 78.0; 78.4; 108.6; 123.1; 137.7. Anal. calc. for $C_{14}H_{26}O_4$ (258.36): C 65.09, H 10.14; found: C 65.33, H 10.33.

14. *(*αR,*4*S,*5*R*)-5-[(Benzyloxy)methyl]-*α-*[(2*E*)-1,1-dimethylbut-2-enyl]-2,2-dimethyl-1,3-dioxolan-4-ethanol*. Benzyl bromide (385 µl, 3.22 mmol) and 80% NaH in white oil (92 mg, 3.06 mmol) were added to a soln. of **22** (832 mg, 3.22 mmol) in DMF/THF 1:1 (10 ml). After stirring for 10 h, pH 7 buffer soln. (2 ml) and ^{t}BuOMe (5 ml) were added. The aq. layer was extracted with ^{t}BuOMe (3 × 25 ml) and the combined org. layer washed with H_2O (2 × 10 ml) and brine (2 × 5 ml), dried (Na_2SO_4), and evaporated. FC (petroleum ether/^{t}BuOMe 5:1 → 1:2) furnished the benzyl ether (853 mg, 76%) and **22** (70 mg, 8%). $[\alpha]_D^{19} = +3.71$ ($c = 1.12$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.97 (*s*, 2 Me); 1.33 (*s*, 3 H, Me_2CO_2); 1.39 (*s*, 3 H, Me_2CO_2); 1.65 (*d*, $^3J =$ 4.7, *Me*CH=CH); 1.73 ($d_{AB}dd$, $^2J_{AB} = -14.4$, $^3J = 1.4$, 3.2, 1 H, $CH_2(\beta)$); 1.78 ($d_{AB}dd$, $^2J_{AB} = -14.4$, $^3J = 1.5$, 2.9, 1 H, $CH_2(\beta)$); 3.21 (*d*, $^3J = 1.6$, OH); 3.44–3.53 (*m*, H–C(α), BnOCH_2); 4.25–4.37 (*m*, H–C(4), H–C(5)); 4.49 (d_{AB}, $^2J_{AB} = -12.0$, 1 H, PhCH_2); 4.55 (d_{AB}, $^2J_{AB} = -12.0$, 1 H, PhCH_2); 5.33–5.47 (*m*, MeC*H*=CH); 7.28–7.38 (*m*, Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.2; 22.5; 24.0; 25.5; 28.0; 30.7; 40.3; 68.9; 73.5; 76.4; 78.1; 78.6; 108.6; 122.7; 127.7; 128.4; 137.8; 138.1. Anal. calc. for $C_{21}H_{32}O_4$ (348.48): C 72.38, H 9.26; found: C 72.47, H 9.46.

15. *[(4*R,*5*S*)-4-[(Benzyloxy)methyl]-5-[(2*R,*4*E*)-2-[[(*tert*-butyl)dimethylsilyl]oxy]-3,3-dimethylhex-4-enyl]-2,2-dimethyl-1,3-dioxolane* (**24**). At 0°, 2,6-lutidine (=2,6-dimethylpyridine; 105 µl, 0.86 mmol) and (*tert*-

butyl)dimethylsilyl trifluoromethanesulfonate (160 µl, 0.60 mmol) were added to a soln. of the alcohol prepared in *Exper. 14* (150 mg, 0.43 mmol) in CH_2Cl_2 (3 ml). After stirring for 2 h, MeOH (1 ml) was added. Stirring was continued for 15 min, and silica gel (*ca.* 1 g) was added. The mixture was evaporated and the residue subjected to FC (petroleum ether/^{t}BuOMe 30:1): **24** (184 mg, 93%). Colorless oil. $[\alpha]_D^{19} = +4.48$ ($c = 1.19$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.03 (*s*, 1 MeSi); 0.05 (*s*, 1 MeSi); 0.89 (*s*, ^{t}BuSi); 0.90 (*s*, 1 Me); 0.91 (*s*, 1 Me); 1.30 (*s*, 3 H, Me_2CO_2); 1.40 (*s*, 3 H, Me_2CO_2); 1.51–1.61 (*m*, 1 H, CH_2CHOSi); 1.58 (*d*, $^3J = 5.6$, *Me*CH=CH); 1.79–1.89 (*m*, 1 H, CH_2CHOSi); 3.33–3.46 (*m*, CH_2CHOSi, BnOCH_2); 4.14–4.28 (*m*, H–C(4), H–C(5)); 4.52 (d_{AB}, $^2J_{AB} = -12.1$, 1 H, PhCH_2); 4.54 (d_{AB}, $^2J_{AB} = -12.1$, 1 H, PhCH_2); 5.25–5.40 (*m*, MeC*H*=C*H*); 7.26–7.33 (*m*, Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): −4.1; −3.7; 18.3; 18.4; 22.1; 25.2; 25.5; 26.1; 28.1; 33.6; 41.6; 69.3; 73.4; 75.2; 76.1; 76.6; 107.5; 121.8; 127.7; 127.7; 128.3; 138.0; 138.9. Anal. calc. for $C_{27}H_{46}O_4Si$ (462.74): C 70.08, H 10.02; found: C 69.84, H 9.75.

16. *(β*R*,4*S*,5*R*)-5-[(Benzyloxy)methyl]-β-[[(*tert*-butyl)dimethylsilyl]oxy]-α,α,2,2-tetramethyl-1,3-dioxolane-4-butanal* (**25**). At −78°, a stream of O_3 in O_2 was introduced very gently into a soln. of **24** (198 mg, 0.43 mmol) in CH_2Cl_2/MeOH 1:3 (10 ml) until TLC indicated consumption of the starting material (less than 1 min!). PPh_3 (161 mg, 0.62 mmol) was added and the mixture was allowed to reach r.t. over 12 h. The mixture was evaporated and the residue subjected to FC (petroleum ether/^{t}BuOMe 10:1): **25** (154 mg, 80%). Colorless oil. $[\alpha]_D^{21} = -9.3$ ($c = 0.57$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.15 (*s*, 1 MeSi); 0.16 (*s*, 1 MeSi); 0.80 (*s*, 1 Me); 1.01 (*s*, 1 Me, ^{t}BuSi); 1.15 (*s*, 1 Me); 1.37 (*s*, 1 Me); 1.47–1.60 (*m*, $CH_2(\delta)$); 3.45 (*m*, BnOCH_2); 3.72 (*dd*, $^3J = 2.6$, $^3J = 11.9$, H–C(β)); 3.86–3.94 (*m*, H–C(3), H–C(4)); 4.32 (d_{AB}, $^2J_{AB} = -12.1$, 1 H, PhCH_2); 4.36 (d_{AB}, $^2J_{AB} = -12.1$, 1 H, PhCH_2); 7.06–7.28 (*m*, Ph); 9.52 (*s*, CHO). ^{13}C-NMR (75 MHz, $CDCl_3$): −4.3; −4.2; 16.8; 18.5; 18.6; 19.5; 25.8; 26.1; 30.0; 48.9; 70.0; 71.9; 73.1; 73.5; 74.8; 98.7; 127.7; 127.8; 128.5; 138.9; 205.4. Anal. calc. for $C_{25}H_{42}O_5Si$ (450.69): C 66.63, H 9.39; found: C 66.41, H 9.27.

17. *{[(1*S*,3*R*,5*S*,7*R*)-7-[(Benzyloxy)methyl]-4,4-dimethyl-6,8-dioxabicyclo[3.2.1]oct-3-yl}oxy}(*tert*-butyl)-dimethylsilane* (**26**). TsOH·H_2O (15 mg) and H_2O (0.1 ml) were added to a soln. of **25** (286 mg, 0.64 mmol) in benzene (50 ml). The mixture was placed in a distillation apparatus and heated until liquid distilled over at 79° (*ca.* 45 min). The residue was cooled to r.t., K_2CO_3 (0.5 g), silica gel (*ca.* 1 g), and Et_3N (2 drops) were added, and the mixture was evaporated. FC (petroleum ether/^{t}BuOMe 5:1) furnished **26** (250 mg, 100%). Colorless oil. $[\alpha]_D^{23} = -68.9$ ($c = 0.78$, $CHCl_3$). ^{1}H-NMR (500 MHz, C_6D_6): −0.01 (*s*, 1 MeSi); 0.02 (*s* 1 MeSi); 0.99 (*s*, ^{t}BuSi); 1.05 (*s*, 1 Me); 1.06 (*s*, 1 Me); 1.59 ($d_{AB}dd$, $^2J = -13.9$, $^3J = 1.50$, 6.46, 1 H–C(2)); 1.77 ($d_{AB}dd$, $^2J = -14.1$, $^3J = 11.5$, 4.63, 1 H–C(2)); 3.46 (*dd*, $^2J = -9.99$, $^3J = 7.02$, 1 H, BnOCH_2); 3.70 (*dd*, $^2J = -9.11$, $^3J = 6.11$, 1 H, BnOCH_2); 3.89 (*dd*, $^3J = 6.34$, 10.57, H–C(3)); 4.21 (*dt*, $^3J = 1.72$, $^3J = 4.31$, H–C(1)); 4.29 (*td*, $^3J = 6.68$, 4.0, H–C(7)); 4.37 (d_{AB}, $^2J_{AB} = -12.36$, 1 H, PhCH_2); 4.43 (d_{AB}, $^2J_{AB} = -12.36$, 1 H, PhCH_2); 5.14 (*s*, H–C(5)); 7.20–7.29 (*m*, Ph). ^{13}C-NMR (75 MHz, C_6D_6): −4.8; −4.0; 18.2; 18.3; 23.3; 26.0; 32.8; 41.4; 67.8; 71.4; 73.5; 74.7; 77.7; 108.9; 127.9; 128.7; 128.8; 138.5. Anal. calc. for $C_{22}H_{36}O_4Si$ (392.61): C 67.30, H 9.24; found: C 67.11, H 9.40.

18. *(1*S*,3*R*,5*S*,7*R*)-3-[(*tert*-Butyl)dimethylsilyl]oxy}-4,4-dimethyl-6,8-dioxabicyclo[3.2.1]octane-7-methanol* (**27**). $Pd(OH)_2$ (*Pearlman* catalyst; *ca.* 10 mg) was added to a soln. of **26** (207 mg, 0.53 mmol) in THF (20 ml). The soln. was stirred for 12 h under H_2. The mixture was filtered over 'Kieselgur', the filtrate evaporated, and the residue subjected to FC (petroleum ether/^{t}BuOMe 1:1): **27** (158 mg, 99%). Colorless solid. M.p. 64–67°. $[\alpha]_D^{28} = -76.9$ ($c = 0.54$, $CHCl_3$). ^{1}H-NMR (300 MHz, C_6D_6): 0.04 (*s*, 1 MeSi); 0.14 (*s*, 1 MeSi); 0.97 (*s*, ^{t}BuSi); 1.03 (*s*, 1 Me); 1.04 (*s*, 1 Me); 1.41 (br. *s*, OH); 1.54 ($d_{AB}dd$, $^2J = -13.9$, $^3J = 1.3$, 6.6, 1 H–C(2)); 1.70 ($d_{AB}dd$, $^2J = -14.0$, $^3J = 4.0$, 10.0, 1 H–C(2)); 3.46 ($d_{AB}d$, $^2J = -11.3$, $^3J = 5.9$, 1 H, CH_2OH); 3.72 ($d_{AB}d$, $^2J = -11.3$, $^3J = 6.9$, 1 H, CH_2OH); 3.91 (*dd*, $^3J = 6.5$, 10.5, H–C(3)); 3.95 (*m*, H–C(7)); 4.07 (*dt*, $^3J = 1.7$, 4.1, H–C(1)); 5.10 (*s*, H–C(5)). ^{13}C-NMR (75 MHz, C_6D_6): −4.8; −3.9; 18.2; 18.4; 23.4; 26.0; 32.9; 41.4; 60.9; 71.5; 74.4; 79.7; 109.0. Anal. calc. for $C_{15}H_{30}O_4Si$ (302.49): C 59.56, H 10.00; found: C 59.38, H 10.15.

19. *{(1*S*,3*R*,5*S*,7*S*)-3-[[(*tert*-Butyl)dimethylsilyl]oxy}-4,4-dimethyl-6,8-dioxabicyclo[3.2.1]oct-7-yl}carbamic Acid 2-(Trimethylsilyl)ethyl Ester* (**30**). $RuCl_3 \cdot 3\,H_2O$ (15 mg, 0.06 mmol) was added to a soln. of dipotassium peroxodisulfate (728 mg, 2.70 mmol) in 0.117M aq. KOH (100 ml, 11.7 mmol). After stirring for 30 min, a soln. of **27** (180 mg, 0.60 mmol) in ^{t}BuOH (30 ml) was added. After stirring for 2 h, sat. aq. $Na_2S_2O_3$ soln. (8 ml) was added followed by solid NaH_2PO_4 until the pH reached 5–6. The aq. layer was extracted with ^{t}BuOMe (2 × 100 ml). The pH value was again adjusted by addition of NaH_2PO_4 soln., and the mixture was once more extracted with ^{t}BuOMe (2 × 100 ml). The combined org. layer was washed with brine (2 × 20 ml), dried (Na_2SO_4) and evaporated. Remaining ^{t}BuOH was removed by addition of hexane (10 ml) and distillation of the solvent. This was repeated twice. The residue, the crude carboxylic acid **28**, was dried at $2 \cdot 10^{-2}$ mbar.

To a suspension of crude **28** in petroleum ether (20 ml), Et_3N (108 µl, 715 µmol) and diphenylphosphoryl azide (154 µl, 715 µmol) were added at 0°. The mixture was allowed to reach r.t. over 12 h. After filtration over

'Kieselgur' and evaporation, the residue was taken up in benzene (20 ml) and heated to reflux for 1 h. The solvent was evaporated. To an aliquot of the resulting crude isocyanate **29** (76 mg, 0.244 mmol) in THF (20 ml), 2-(trimethylsilyl)ethanol (72 µl, 0.5 mmol) was added, and the soln. was heated for 10 h under reflux. The soln. was evaporated and the residue subjected to FC (petroleum ether/^{t}BuOMe 7:1): **30** (59 mg, 56%). Colorless oil. $[\alpha]_D^{21} = -62.3$ ($c = 0.41$, $CHCl_3$). ^{1}H-NMR (400 MHz, (D_6)acetone; double set of signals due to amide rotamers): 0.06–0.12 (*m*, 3 H, MeSi); 0.86 (*s*, 3 H, Me); 0.89 (*s*, 3 H, Me); 0.92 (*s*, 18 H, ^{t}BuSi); 0.94 (*s*, 3 H, Me); 0.95 (*s*, 3 H, Me); 0.99–1.04 (*m*, 4 H, Me_3SiCH_2); 1.65–1.82 (*m*, 2 H, CH_2); 2.00 (*m*, 2 H, CH_2); 3.82 (*dd*, $J = 6.1$, 10.4, 1 H, CHO); 4.08 (*dd*, $J = 6.4$, 10.6, 1 H, CHO); 4.16–4.20 (*m*, 4 H, CHO); 4.27 (*m*, 1 H, CHO); 4.36 (*m*, 1 H, CHO); 4.89 (*s*, 1 H, OCHO); 5.01 (*s*, 1 H, OCHO); 5.38 (*dd*, $^3J = 4.0$, 7.5, 1 H, NCHO); 5.43 (br. *d*, $^3J = 9.5$, 1 H, NCHO); 6.48 (br. *s*, 1 H, NH); 6.68 (br. *s*, 1 H, NH). ^{13}C-NMR (126 MHz, (D_8)toluene; 348 K; double set of signals due to amide rotamers): −5.4; −5.2; −4.6; −4.5; −2.0; 18.0; 18.1; 18.2; 18.3; 23.3; 23.4; 26.1; 32.1; 34.5; 41.4; 41.5; 63.3; 63.7; 70.9; 71.8; 73.6; 78.7; 82.2; 82.9; 108.9; 109.4; 155.5; even in (D_6)DMSO, a double set of signals was observed up to 373 K. Anal. calc. for $C_{20}H_{41}NO_5Si_2$ (431.72): C 55.64, H 9.57, N 3.24; found: C 55.64, H 9.30, N 3.42.

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