33. The Synthesis of Boronolide

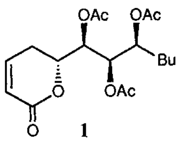
by **Charles W. Jefford*** and **Marie-Claude Moulin**

Department of Organic Chemistry, University of Geneva, CH-1211 Geneva 4

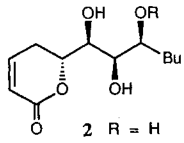
(3.XII.90)

Racemic boronolide (**1**) is prepared in six steps in 4.4% overall yield from acrolein dimer **6** and 1-(trimethylsilyl)hex-1-yne (**8**). The latter, by hydromagnesiation, is condensed with **6** to give the corresponding *threo*-allylic alcohol **13** (*Scheme 2*). Conversion of **13** to the *erythro*-allylic alcohol **5** (*Scheme 3*), bis-hydroxylation, and acetylation afford **1**.

Introduction. – *Tetradenia fruticosa* is a shrub belonging to the Lamiacea family which grows in Madagascar where it is used for medicinal purposes. In 1971, the active principle was extracted from the bark and branches and identified as boronolide [1]. Fourteen years later the relative configuration of boronolide was determined by X-ray analysis, and the (*R*)-configuration was assigned to the C(6) position by application of *Hudson*'s lactone rule to the molecular rotation [2]. Subsequently, in 1987, by means of chemical degradation, the absolute configuration of boronolide was established as (1′*R*,2′*R*,3′*S*,6*R*)-5,6-dihydro-6-[1′,2′,3′-tris(acetoxy)heptyl]-2*H*-pyran-2-one (**1**) [3].



1



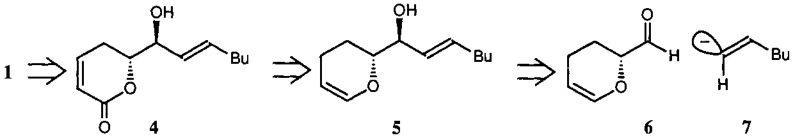
2 R = H

3 R = Ac

Boronolide has also been isolated from the dried leaves of *T. barberae* [3] while deacetylated (**2**) and dideacetylated (**3**) derivatives have been obtained from *T. riparia* [4] (formerly *Iboza*), a central-African species widely used as a tribal medicine. Typically, the Zulu employ extracts of the root as an emetic, while an infusion of the leaf has been reported to be effective against malaria [5].

So far no synthesis of **1** in either its racemic or enatiomerically pure form has been reported. On the basis of precedent [6–8], acrolein dimer **6** would be an ideal starting point for **1** as the disconnective analysis shows (*Scheme 1*). The triacetate **1**, through its corresponding triol, has as a possible precursor the *erythro*-allylic alcohol **4** from which it would have to be derived by stereoselective bis-hydroxylation. The α,β-unsaturated δ-lactone function in **4** could be introduced by appropriate oxidation of the dihydro-2*H*-pyran **5**. Attachment of the side chain should be realizable by addition of the (*Z*)-hex-1-

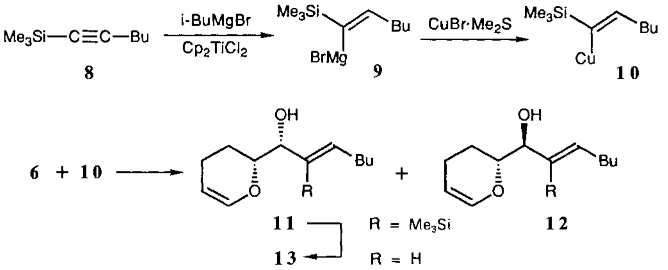
Scheme 1



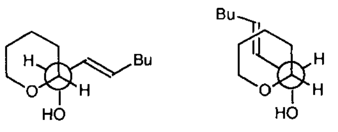
enyl anion (7) to acrolein dimer 6, provided the diastereoselectivity can be controlled to afford the desired *erythro*-alcohol.

Results and Discussion. – The logical choice of reagent for the hexenyl carbanion synthon 7 is the silylated hexenylmagnesium bromide 9. Previous work [9–11] has shown that *Grignard* reagents such as 9 by conversion *in situ* to their copper analogues 10 undergo stereoselective addition to aldehydes generating (*E*)-allylic alcohols. Accordingly, 1-(trimethylsilyl)hex-1-yne (8) [12] was treated with i-BuMgBr in the presence of a catalytic amount of Cp_2TiCl_2 (Cp = cyclopentadienyl) resulting in its hydromagnesiation to give exclusively the (*E*)-derivative 9 [13] [14] (*Scheme 2*). When 9 was allowed to react

Scheme 2



with acrolein dimer 6 in THF at −78° together with a slight excess of CuBr and Me_2S, addition of the cuprous intermediate 10 occurred with high diastereoselectivity furnishing the *threo*- and *erythro*-alcohols 11/12 of (*Z*)-configuration in a 15:1 ratio and in a yield of 66%. After chromatography, 11 was treated with Bu_4NF which effected desilylation giving the *threo*-alcohol 13 of (*E*)-configuration in 99% yield [15]. Alcohol 13 was easily distinguishable from its epimer 5 (see below) thanks to their characteristic ^3J(H,H) values in the ^{1}H-NMR spectra [16]. The values of 7.5 and 3.5 Hz are consistent with the arrangement of the pair of methine protons in the preferred staggered conformations adopted by the *threo*- and *erythro*-epimers 13 and 5, respectively (*Fig. 1*).



13 *threo* 5 *erythro*

Fig. 1. *Preferred conformations of epimeric alcohols* 13 *and* 5

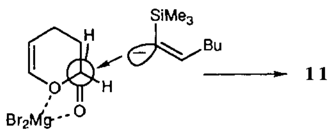
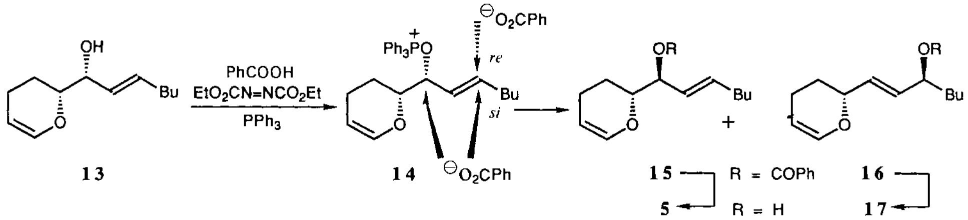


Fig. 2. *Chelation-controlled formation of* 11 *from* 6

Apart from the retention of the geometry of the vinyl entity, the high diastereoselectivity (15:1) in favor of the *threo*-alcohol **11** is noteworthy and is explicable in terms of a transition state resembling the *threo*-product. Chelation by Mg or Cu brings the aldehydic and pyran O-atoms close together, while the vinylcopper reagent **10** attacks the least hindered face of the aldehyde group (*Fig. 2*). Such stereoselectivity is characteristic of acrolein dimer [7] [8] and has also been observed for structurally similar aldehydes such as 2,3-*O*-isopropylideneglyceraldehyde [9] and 2,3-*O*-dibenzylglyceraldehyde [17].

Having secured *threo*-alcohol **13**, it needs to be converted to its *erythro*-epimer **5**. The serviceable method of *Mitsunobu* was selected [18]. Treatment of *threo*-alcohol **13** with PPh_3, diethyl diazoacetate, and benzoic acid led to a 1:1 mixture of the allylic *erythro*-benzoates **15** and **16** in an overall yield of 71% (*Scheme 3*). The *erythro*-configuration of **15** was compatible with its ^1H-NMR spectrum. In any event, the S_N2 reaction of the phosphonium-oxide intermediate **14** with benzoate must occur with inversion. However, in the alternative S_N2' reaction, benzoate could attack **14**, regardless of its preferred conformation, on either the *si* or *re* faces of the vinyl terminus (*Scheme 3*). Experimentally, only a single benzoate, designated as **16**, was obtained. The correctness of this assignment was later confirmed by its conversion after saponification to **1**. The benzoate mixture **15**/**16** was saponified to the corresponding alcohols **5**/**17** in 90% yield.

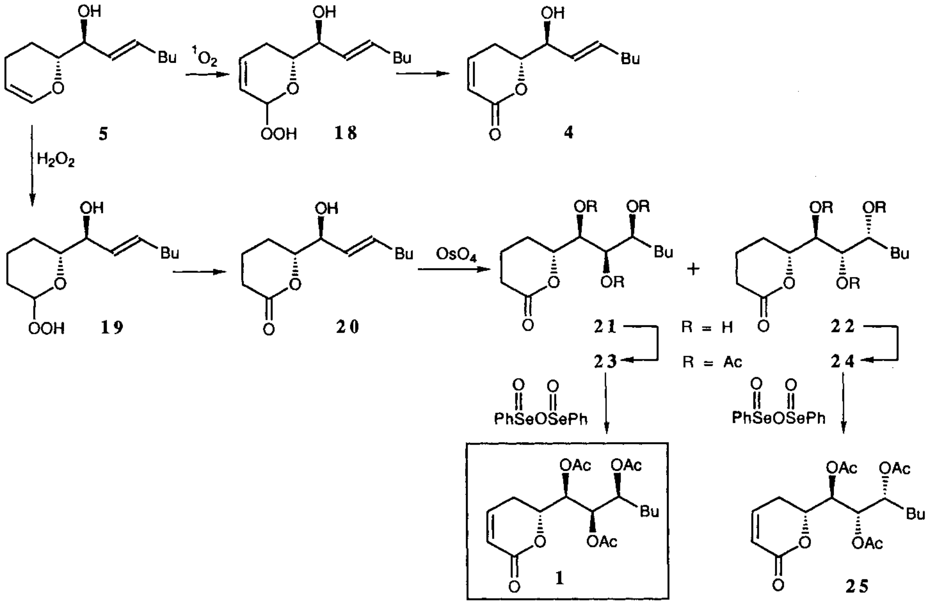
Scheme 3



Trial experiments indicated that the photo-oxygenation of *erythro*-alcohol **5** was straightforward giving hydroperoxide **18** which could be dehydrated to the unsaturated δ-lactone **4** (*Scheme 4*). Unfortunately, **4** was not suitable for hydroxylation with OsO_4 as several decomposition products arose from oxidation of the endocyclic double bond. Consequently, we decided to convert the dihydro-2*H*-pyran ring into the saturated δ-lactone **20**. This step was readily accomplished by the acid-catalyzed addition of H_2O_2 to **5**. Dehydration of the intermediate hydroperoxide **19** gave **20** in 90% yield as a viscous white solid (*Scheme 4*).

At first sight, bis-hydroxylation of **20** in the desired stereoselective sense is unpromising. Whatever predictive model is employed [19–21], the expectation is that an allylic alcohol of the (*E*)-configuration such as **20** would suffer osmylation with modernate stereoselectivity to favor the wrong configuration [22] [23]. However, it is entirely possible that the tetrahydro-2*H*-pyran substituent might exert a countervailing electronic effect and thereby alter the stereoselectivity. Bis-hydroxylation of **20** was accomplished using catalytic quantities of OsO_4 regenerated by *N*-methylmorpholine *N*-oxide [24] [25]. Two triols **21** and **22** having the desired and undesired configurations, respectively, were obtained in a ratio of 1:3 (*Scheme 4*). Treatment of the mixture with Ac_2O in the presence

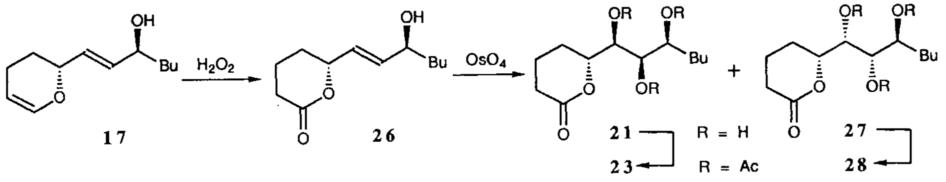
Scheme 4



of pyridine gave the corresponding triacetates **23** and **24** in 20 and 59% yield, respectively. This stereoselective result confirms the influence of the tetrahydro-2*H*-pyran substituent in substantially diminishing the stereoselectivity without actually reversing it. Nonetheless, the triacetate portion of boronolide is introduced with little trouble. Next, the acetates **23** and **24** were easily separated by chromatography so that the endocyclic double bond could be reestablished. Dehydrogenation was brought about using benzeneseleninic anhydride in chlorobenzene at 130° [26]. The triacetate **23** furnished racemic boronolide **1** in 61% yield as a colorless solid. Its ^{13}C- and ^1H-NMR spectra were identical with those of the natural material. For the sake of completeness and for comparative purposes, the isomeric triacetate **24** was similarly oxidized to the isomer **25** of boronolide, easily distinguishable from **1** by its different NMR spectra.

Allylic alcohol **17** which accompanied the formation of **5** is also of preparative utility. It too was oxidized with H_2O_2 to δ-lactone **26** (*Scheme 5*). Bis-hydroxylation of the latter proceeded with the same selectivity as before, delivering triols **21** and **27** in a ratio of 1:3, which were acetylated to the triacetates **23** and **28** in the same ratio and in 75% yield.

Scheme 5



Proof of the configuration of **23**, and by extrapolation that which was arbitrarily assigned to **17**, was secured by carrying out the α,β-dehydration of the δ-lactone ring. Once again, boronolide (**1**) was obtained in 63% yield.

Conclusion. – The preparation of boronolide (**1**) has been achieved from acrolein dimer **6** in essentially six steps in an overall yield of 4.4%. Although not attempted, resolution of the racemic product is feasible by chromatography over cellulose triacetate [27]. Consequently, the simplicity and cheapness of the aforementioned procedure recommends it for making other structurally similar naturally occurring δ-lactones.

We wish to thank the *Swiss National Science Foundation* for financial support of this work (grant No. 2.812-0.85).

Experimental Part

General. Solvents were purchased from *Fluka AG*, *Aldrich AG*, *Merck AG*, and *Tokyo Kasei*, dried, and purified before use. TLC: silica gel *60* (*F_{254} Merck*) coated plates. Column chromatography: *Merck* silica gel *60* (230–400 mesh ASTM). Gas-phase chromatography: *Hewlett-Packard-HP588A* chromatograph; anal. capillary columns packed with dimethylsilicone (12.5 and 25 m long and 0.5 mm internal diameter); N_2 flow of 50 ml/min. M.p. *Reichert* hot-plate instrument; uncorrected. IR spectra: *Perkin-Elmer-618* spectrometer; $CHCl_3$ solns.; absorptions in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Varian-XL-200* and *Bruker-WH-360* instruments; $CDCl_3$ as solvent; chemical shifts (δ) in ppm with reference to tetramethylsilane (TMS); signal intensities are normalized to 1 H; coupling constants (*J*) in Hz. MS: *Finnigan-4000* and *VG-70-70E* spectrometers. Elemental analyses were performed by Dr. *H.J. Eder*, Service de Microchimie, Institut de Chimie Pharmaceutique, University of Geneva.

(1RS,Z)-1-[(2SR)-3,4-Dihydro-2H-pyran-2-yl]-2-(trimethylsilyl)hept-2-en-1-ol (**11**). Cp_2TiCl_2 (80 mg, 0.3 mmol) was added to a soln. of i-BuMgBr (10 mmol) in Et_2O (13 ml) at 0° under Ar. After stirring the soln. for 30 min at 0°, 1-(trimethylsilyl)hex-1-yne [12] (**8**; 1.617 g, 10.5 mmol) was added dropwise while stirring was continued for 6 h at 25°. Next, the solvent was evaporated at 15 Torr; the residue was dissolved in THF (50 ml) at −70° after which $CuBr \cdot Me_2S$ (2.47 g, 12 mmol) was added followed by stirring for 30 min. Acrolein dimer **6** (678 mg, 6.05 mmol) was then added dropwise; stirring was continued for 30 min at −78°, thereafter the temp. was allowed to reach 20–25° overnight. The resulting mixture containing *threo/erythro*-mixture **11/12** (15:1 according to ^1H-NMR) was filtered and separated by chromatography (hexane/AcOEt 15:1) into **11/12** (1.1 g, 66%) followed by pure **11**, pale yellow oil (997 mg, 61%). IR: 3500vs, 3060*s*, 2960–2850vs, 1650*s*, 1610*m*, 1460*s*, 1240vs, 1070vs, 980*m*, 850vs, 760*m*, 730*m*. ^1H-NMR: 0.18 (*s*, 9 H); 0.9 (*t*, *J* = 7, 3 H); 1.3 (*m*, 10 H); 2.5 (*d*, *J* = 2, 1 H); 3.8 (*ddd*, *J* = 10, 8, 2, 1 H); 4.1 (*d*, *J* = 8, 1 H); 4.7 (*m*, 1 H); 6.25 (*t*, *J* = 8, 1 H); 6.4 (*d*, *J* = 6, 1 H). MS: 55, 73 (100), 75, 83, 84, 113, 127, 169, 185, 211, 235, 268 (M^+). Anal. calc. for $C_{15}H_{28}SiO_2$: C 67.11, H 10.51; found: C 67.00, H 10.62.

(1RS,E)-1-[(2RS)-3,4-Dihydro-2H-pyran-2-yl]hept-2-en-1-ol (**13**). To a soln. of **11** (536 g, 2 mmol) in THF (2 ml) under N_2 at 0°, *t*-BuOK (224 mg, 2 mmol) and Bu_4NF (2 mmol/2 ml THF) was added. After allowing to stand for 10 min, the soln. was treated with aq. NH_4Cl soln. (2 ml). The soln. was extracted with CH_2Cl_2, the extracts dried ($MgSO_4$), filtered, and evaporated. The residue was purified by chromatography (hexane/AcOEt 10:1) to give **13** as a pale yellow oil (387 mg, 99%). IR: 3580*s*, 2900vs, 1650*s*, 1450*m*, 1390*m*, 1220vs, 1070*s*, 970*s*. ^1H-NMR: 0.84 (*t*, *J* = 7, 3 H); 1.3–2.1 (*m*, 10 H); 2.48 (*s*, 1 H); 3.64 (*ddd*, *J* = 10, 7.5, 2.5, 1 H); 4.0 (*t*, *J* = 7.5, 1 H); 4.7 (*m*, 1 H); 5.44 (*ddt*, *J* = 15.5, 7.5, 1.5, 1 H); 5.78 (*dt*, *J* = 15.5, 6.5, 1 H); 6.38 (*m*, 1 H). MS: 55, 57, 73 (100), 75, 83, 95, 105, 113, 119, 127, 133, 147, 169. Anal. calc. for $C_{12}H_{20}O_2$: C 73.43, H 10.27; found: C 73.23, H 10.39.

(1RS,E)-1-[(2SR)-3,4-Dihydro-2H-pyran-2-yl]hept-2-enyl Benzoate (**15**) *and (1RS)-1-{(E)-2-[(2SR)-3,4-Dihydro-2H-pyran-2-yl]ethenyl}pentyl Benzoate* (**16**). Benzoic acid (135 mg, 1.1 mmol) and diethyl azodicarboxylate (173 μl, 192 mg, 1.1 mmol) were added to **13** (196 mg, 1.0 mmol) in Et_2O (4 ml) under N_2 [18]. To the resulting mixture, PPh_3 (290 mg, 1.1 mmol) in Et_2O (4 ml) was added dropwise and then stirred at 20° overnight. The suspension was filtered, the filtrate evaporated, and the residue purified by chromatography (hexane/AcOEt 20:1): **15/16** (215 mg, 71%), 1:1 ratio.

15: IR: 3060–2850vs, 1720vs,1650*s*, 1450*m*, 1270vs, 1220vs, 1120*s*, 1070*s*. ^1H-NMR: 0.86 (*t*, *J* = 7, 3 H); 1.3 (*m*, 4 H); 1.7–2.2 (*m*, 6 H); 4.02 (*ddd*, *J* = 11, 4, 2, 1 H); 4.7 (*m*, 1 H); 5.62 (*m*, 2 H); 5.9 (*dtd*, *J* = 14.5, 7, 1.5, 1 H); 6.4 (*m*, 1 H); 7.44 (*m*, 2 H); 7.56 (*m*, 1 H); 8.08 (*m*, 2 H).

16: IR: same as that of **15**. ^{1}H-NMR: 0.86 (*t*, *J* = 7, 3 H); 1.2–1.4 (*m*, 4 H); 1.6–2.1 (*m*, 6 H); 4.36 (*m*, 1 H); 4.7 (*m*, 1 H); 5.52 (*dt*, *J* = 7, 6, 1 H); 5.82 (*m*, 2 H); 6.4 (*m*, 1 H); 7.44 (*m*, 2 H); 7.56 (*m*, 1 H); 8.08 (*m*, 2 H).

*(1*RS,E*)-1-[(2*SR*)-3,4-Dihydro-2*H*-pyran-2-yl]hept-2-en-1-ol* (**5**) *and (3*RS,E*)-1-[(2*SR*)-3,4-Dihydro-2*H*-pyran-2-yl]hept-1-en-3-ol* (**17**). A mixture of **15**/**16** (38.4 mg, 0.13 mmol) in EtOH (2 ml), KOH (22 mg, 0.55 mmol), and H_2O (25 µl, 1.4 mmol) was boiled under reflux for 50 min. The soln. was extracted with CH_2Cl_2, the extracts dried ($MgSO_4$), filtered, and evaporated. Chromatography (CH_2Cl_2) gave **5** and **17** each as a colorless oil (11.5 and 11.2 mg, resp.; 90% yield).

5: IR: 3600*s*, 3000–2860v*s*, 1650*s*, 1450*m*, 1220v*s*, 1070*s*, 970*m*. ^{1}H-NMR: 0.86 (*t*, *J* = 7, 3 H); 1.2–1.4 (*m*, 4 H); 1.6–2.2 (*m*, 6 H); 3.8 (*ddd*, *J* = 11, 3.5, 3.5, 1 H); 4.2 (*m*, 1 H); 4.7 (*m*, 1 H); 5.52 (*ddt*, *J* = 15.5, 7, 1.5, 1 H); 5.8 (*dtd*, *J* = 15.5, 7, 1, 1 H); 6.4 (*m*, 1 H).

17: IR: identical to that of **5**. ^{1}H-NMR: 0.86 (*t*, *J* = 7, 3 H); 1.2–1.4 (*m*, 4 H); 1.4–1.7 (*m*, 4 H); 1.8–2.2 (*m*, 3 H); 4.12 (*dt*, *J* = 6, 6, 1 H); 4.32 (*m*, 1 H); 4.68 (*m*, 1 H); 5.76 (*m*, 2 H); 6.4 (*m*, 1 H).

*(6*RS*)-5,6-Dihydro-6-[(1*SR,E*)-1-hydroxyhept-2-enyl]-2*H*-pyran-2-one* (**4**). A soln. of **5** (392 mg, 2 mmol) and tetraphenylporphin (13 mg) in toluene (6 ml) was irradiated while dry O_2 was passed for 30 min [6]. After addition of Et_3N (0.24 ml) and Ac_2O (0.24 ml), the soln. was stirred overnight and then extracted with Et_2O. The extracts were washed (H_2O aq. sat. NaCl soln.), dried ($NaSO_4$), and evaporated. Chromatography over *Florisil* (hexane/AcOEt 5:2) gave **4** (270 mg, 64% yield). Colorless oil. IR: 3600*s*, 3000–2950v*s*, 1750v*s*, 1380*s*, 1250v*s*, 1150*m*, 975*m*. ^{1}H-NMR: 0.86 (*t*, *J* = 7, 3 H); 1.34 (*m*, 4 H); 2.06 (*m*, 2 H); 2.32 (*dddd*, *J* = 18, 6, 3.5, 1, 1 H); 2.44 (*s*, 1 H); 2.60 (*ddt*, *J* = 18, 12, 2, 1 H); 4.40 (*dq*, *J* = 18, 8, 4, 2 H); 5.46 (*ddt*, *J* = 15, 7, 1.5, 1 H); 5.84 (*dtd*, *J* = 15, 7, 1.5, 1 H); 6.02 (*ddd*, *J* = 9, 3.5, 1, 1 H); 6.94 (*ddd*, *J* = 9, 6, 3, 1 H).

Product **4** was submitted to osmylation according to the procedure described below and gave several unidentified oxidation products.

*(6*RS*)-Tetrahydro-6-[(1*SR,E*)-1-hydroxyhept-2-enyl]-2*H*-pyran-2-one* (**20**). A soln. of **5** (645 mg, 3.29 mmol) in THF (10 ml) and 30% aq. H_2O_2 soln. (1.5 ml, 49 mmol) and conc. H_2SO_4 (2–3 drops) was stirred at 20° for 36 h. The resulting soln. was poured into a sat. $(NH_4)_2SO_4$ soln. and extracted with CH_2Cl_2. The combined org. layers were washed with sat. $NaHCO_3$ and sat. NaCl soln., dried (Na_2SO_4), and filtered. The filtrate, after treatment with Et_3N (400 µl, 2.9 mmol) and Ac_2O (400 µl, 4.2 mmol), was stirred overnight at 20°. The soln. was extracted with CH_2Cl_2 and the combined extract washed with 5% aq. HCl, sat. $NaHCO_3$, and sat. NaCl soln., dried (Na_2SO_4), and filtered. Evaporation and chromatography (hexane/AcOEt 5:1) gave **20** (625 mg, 90%). White viscous solid. IR: 3700–3400v*s*, 2960–2860v*s*, 1760v*s*, 1240*s*, 1050*s*, 970*m*, 910*m*. ^{1}H-NMR: 0.84 (*t*, *J* = 7, 3 H); 1.2–1.4 (*m*, 4 H); 1.6–2.1 (*m*, 6 H); 2.3–2.5 (*m*, 2 H); 2.5–2.64 (*m*, 1 H); 4.3 (*m*, 2 H); 5.44 (*ddt*, *J* = 15.5, 7, 1.5, 1 H); 5.8 (*dtd*, *J* = 15.5, 7, 1, 1 H). MS: 55, 57 (100), 71, 81, 95, 99, 105, 113, 151, 156, 194, 212 (M^+). Anal. calc. for $C_{12}H_{20}O_3$: C 67.89, H 9.50; found: C 67.62, H 9.37.

*(1'*RS*,2'*RS*,3'*SR*,6*RS*)- and (1'*RS*,2'*SR*,3'*RS*,6*RS*)-Tetrahydro-6-[1',2',3'-tris(acetoxy)heptyl]-2*H*-pyran-2-ones* (**23** and **24**). *N*-Methylmorpholine *N*-oxide (2.34M in *t*-BuOH; 1 ml, 2.34 mmol), H_2O (1.22 ml, 68 mmol), and acetone (0.45 ml, 6.1 mmol) were mixed with **20** (470 mg, 2.22 mmol). Then, OsO_4 (2.5% in *t*-BuOH; 71 µl, 5.77 mmol) was added [24] [25]. The mixture was stirred for 8 h, treated with aq. $NaHSO_3$ soln. (0.3 m, 2 ml) and filtered over *Florisil*. The pH was adjusted to 7, acetone evaporated, and *t*-BuOH removed *in vacuo*. To the resulting residue of **21**/**22**, pyridine (30 ml, 372 mmol) was directly added. After cooling to 0°, Ac_2O (6 ml, 63 mmol) was added dropwise. The resulting soln. was stirred for 3 days at 0° and then treated with cold 5% aq. HCl soln. until the pH reached 7. The soln. was then extracted with CH_2Cl_2, the extracts washed with aq. sat. NaCl soln., dried ($MgSO_4$), filtered, and evaporated, and the residue purified by chromatography (hexane/AcOEt 3:2): **23** (143 mg, 20%) and **24** (418 mg, 59%) as a colorless oil and solid (m.p. 79–81°), resp.

23: IR: 3020–2860*s*, 1740v*s*, 1370*m*, 1220v*s*, 1100v*s*. ^{1}H-NMR: 0.88 (*t*, *J* = 7, 3 H); 1.2–2.0 (*m*, 10 H); 2.09 (*s*, 3 H); 2.12 (*s*, 3 H); 2.14 (*s*, 3 H); 2.4–2.7 (*m*, 2 H); 4.44 (*ddd*, *J* = 11, 6, 3, 1 H); 5.04 (*dt*, *J* = 7, 6, 1 H); 5.24 (*dd*, *J* = 6, 5, 1 H); 5.38 (*dd*, *J* = 6, 5, 1 H). MS: 55, 71, 99, 111, 124, 142 (100), 171, 184, 273, 313, 373 ($[M + 1]^+$). Anal. calc. for $C_{18}H_{28}O_8$: C 58.05, H 7.58; found: C 57.77, H 7.80.

24: IR: identical to that of **23**. ^{1}H-NMR: 0.84 (*t*, *J* = 7, 3 H); 1.2–2.0 (*m*, 10 H); 2.03 (2*s*, 6 H); 2.12 (*s*, 3 H); 2.3–2.6 (*m*, 2 H); 4.5 (*dt*, *J* = 16, 3.7, 1 H); 5.16 (*ddd*, *J* = 8, 5.5, 2, 1 H); 5.3 (*m*, 2 H). MS: 55, 71, 84, 99, 112, 124, 142 (100), 159, 171, 184, 201, 231, 273, 313, 373 ($[M + 1]^+$). Anal. calc. for $C_{18}H_{28}O_8$: C 58.05, H 7.58; found: C 58.08, H 7.55.

*(1'*RS*,2'*RS*,3'*SR*,6*RS*)-5,6-Dihydro-6-[1',2',3'-tris(acetoxy)heptyl]-2*H*-pyran-2-one* (**1**). A soln. of **23** (41 mg, 0.11 mmol) and benzeneseleninic anhydride (40 mg, 0.11 mmol) in dry chlorobenzene (3 ml) was heated at 130° for 70 h [26]. After cooling, the solvent was evaporated and the residue purified by chromatography (hexane/AcOEt 3:2): **1** (25 mg, 61%). Colorless solid. M.p. 79–81° ([1]: 90°). IR: 3020–2860*s*, 1750v*s*, 1370*s*, 1220v*s*, 1050v*s*. ^{1}H-NMR: 0.84 (*t*, *J* = 7, 3 H); 1.2–1.3 (*m*, 4 H); 1.5–1.6 (*m*, 2 H); 2.03 (*s*, 3 H); 2.06 (*s*, 3 H); 2.1 (*s*, 3 H); 2.2–2.6 (*m*,

2 H); 4.54 (*ddd*, *J* = 12, 6, 4, 1 H); 5.04 (*dt*, *J* = 6, 6, 1 H); 5.34 (*m*, 2 H); 6.04 (*ddd*, *J* = 10, 2.5, 1, 1 H); 6.88 (*ddd*, *J* = 10, 6, 2.5, 1 H). ^{13}C-NMR: 13.78 (*q*); 20.54 (*q*); 20.64 (*q*); 22.30 (*t*); 25.07 (*t*); 26.98 (*t*); 30.21 (*t*); 70.54 (*d*); 70.61 (*d*); 71.58 (*d*); 75.09 (*d*); 121.40 (*d*); 144.02 (*d*); 162.36 (*s*); 169.60 (*s*); 169.81 (*s*); 170.36 (*s*). MS: 55, 68, 82, 97, 110, 122, 140 (100), 159, 171, 182, 201, 242, 273, 313, 371 ($[M + 1]^+$). Anal. calc. for $C_{18}H_{26}O_8$: C 58.37, H 7.08; found: C 58.21, H 7.05.

*(1′*RS*,2′*SR*,3′*RS*,6*RS*)-5,6-Dihydro-6-[1′,2′,3′-tris(acetoxy)heptyl]-2*H*-pyran-2-one* (**25**). The previous experiment was repeated with **24** to give **25** in the same yield. ^{1}H-NMR: 0.86 (*t*, *J* = 7, 3 H); 1.2–1.6 (*m*, 6 H); 2.06 (2*s*, 6 H); 2.14 (*s*, 3 H); 2.5 (*m*, 2 H); 4.56 (*dt*, *J* = 11, 5, 1 H); 5.16 (*m*, 1 H); 5.3 (*dd*, *J* = 8, 3, 1 H); 5.42 (*dd*, *J* = 8, 5, 1 H); 6.02 (*ddd*, *J* = 10, 2.2, 1.3, 1 H); 6.9 (*ddd*, *J* = 10, 5.5, 3, 1 H). ^{13}C-NMR: 13.82 (*q*); 20.70 (*q*); 20.94 (*q*); 22.38 (*t*); 24.45 (*t*); 27.09 (*t*); 30.39 (*t*); 30.86 (*q*); 69.36 (*d*); 70.27 (*d*); 70.84 (*d*); 121.06 (*d*); 144.56 (*d*); 162.72 (*s*); 169.09 (*s*); 170.26 (*s*); 170.60 (*s*). IR, MS: identical to those of **1**. Anal. calc. for $C_{18}H_{26}O_8$: C 58.37, H 7.08; found: C 58.18, H 7.12.

*(1′*RS*,2′*RS*,3′*SR*,6*RS*)- and (1′*SR*,2′*SR*,3′*SR*,6*RS*)-Tetrahydro-6-[1′,2′,3′-tris(acetoxy)heptyl]-2*H*-pyran-2-ones* (**23** and **28**). Treatment of **17** (387 mg, 1.98 mmol) successively with H_2O_2, OsO_4, and Ac_2O according to the previous procedures gave (*via* the saturated lactone **26**, and the alcohols **21** and **27**, which were not isolated) **23** (62.7 mg, 16%) (identical to that obtained previously) and **28** (198 mg, 51.3%) as a colorless oil. **28**: ^{1}H-NMR: 0.85 (*t*, *J* = 7, 3 H); 1.2–2.0 (*m*, 10 H); 2.03 (*s*, 3 H); 2.12 (*s*, 3 H); 2.14 (*s*, 3 H); 2.4–2.7 (*m*, 2 H); 4.40 (*ddd*, *J* = 10, 5, 3, 1 H); 5.03 (*ddd*, *J* = 8, 7, 4, 1 H); 5.30 (*ddd*, *J* = 7, 5, 3, 2 H). IR, MS: identical to those of **23**. Anal. calc. for $C_{18}H_{28}O_8$: C 58.05, H 7.58; found: C 57.88, H 7.63.

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