Synthesis of a Key Building Block for a Butyrolactone → 1,3-Diol Approach to the Polyol Part of Roflamycoin

Diego Muñoz-Torrero[+] and Reinhard Brückner*

Institut für Organische Chemie der Georg-August-Universität,
Tammannstraße 2, D-37077 Göttingen, Germany

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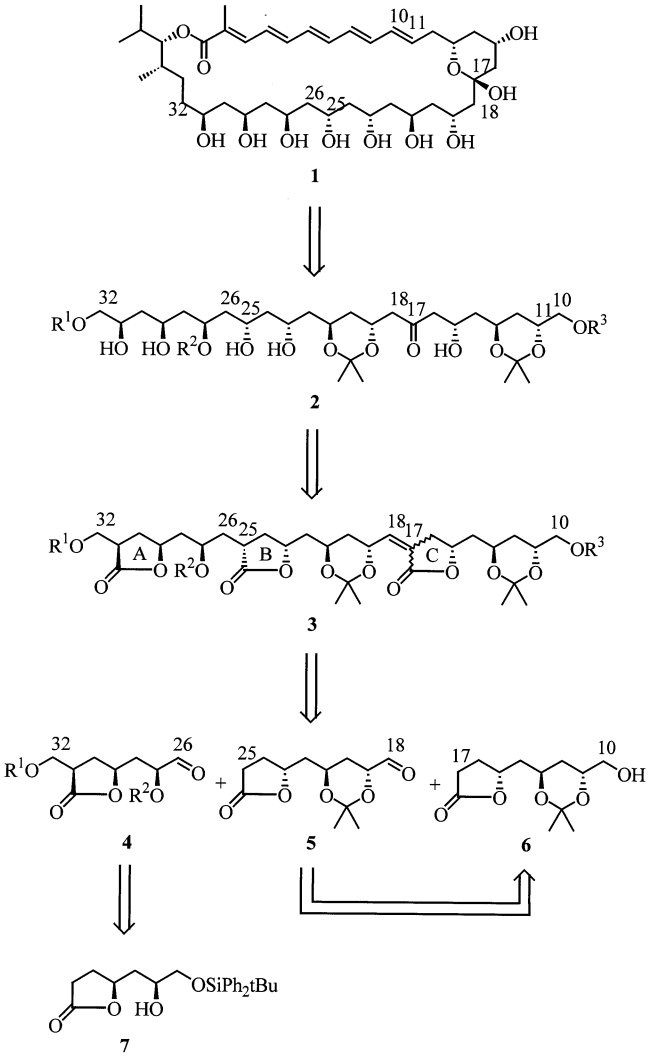
For preparing tris(γ-lactone) **3** the mono(γ-lactone) **6** was synthesized from the dichlorodiol **12** (99.8% *ee*). Bisepoxide **9** – derived from dichlorodiol **12** (99.8% *ee*) – was ring-opened with the Gilman cuprate from 2-lithio-1,5-hexadiene and CuI giving almost exclusively the monoepoxide **21**; in five more steps, γ-lactone **30** with the same stereotriad as the target molecule **6** but a different protecting group was obtained. Monoepoxide **33** – also derived from dichlorodiol **12** – was ring-opened with the same Gilman cuprate affording compound **35**. It was transformed into the correctly protected γ-lactone **6** in seven steps, key reactions being the ozonolysis **35** → **36** and the diastereoselective reduction **36** → *anti*-**37**.

The preceding publication[1] and the present one extend the versatility of our γ-lactone → 1,3-diol approach[2] to stereodefined 1,3,5,7,...-polyols[3] through syntheses of new enantiopure γ-lactone building blocks. The preceding paper[1] presents a γ-lactone precursor for the synthesis of *Tolypothrix* polyethers.[4] The present paper describes an access to the γ-lactone precursor **6** of the polyacetate region of the polyol/polyene antibiotic[5] roflamycoin (**1**).[6] This lactone contains three stereocenters and is obtained from the bis(chlorohydrin) **12** in 11 steps and 13% yield.

Roflamycoin (**1**) has attracted synthetic chemists since more than a decade.[7] Its total synthesis has been accomplished by Rychnovsky's group in 1997.[8] Scheme 1 shows, how *we* plan to derive the polyol section **2** of this molecule by our γ-lactone → 1,3-diol strategy: through the oxidative degradation of the tris(γ-lactone) **3**. The lactone rings A and B of this compound are *cis*-configured *α,γ-dialkyl*-γ-butyrolactones. In our strategy this stereostructure makes each of them a precursor of a *syn*-configured 1,3-diol.[2][3] Ring C of tris(γ-lactone) **3**, however, is an *α-alkylidene-γ-alkyl*-γ-butyrolactone. This is a substitution pattern which we have not yet tested in a γ-lactone → 1,3-diol degradation. We hope that if the *α-alkyl*-γ-butyrolactone rings A and B are degraded at C_α to an *alcohol*, the *α-alkylidene*-γ-butyrolactone ring C renders an *enol* at C_α. The $C^{18}{=}C^{17}{-}OH$ portion of this enol would tautomerize spontaneously to the $C^{18}H_2C^{17}{=}O$ moiety of the polyol segment **2** of roflamycoin.

Continuing the retrosynthetic analysis of Scheme 1, tris(γ-lactone) **3** is traced back to the three mono(γ-lactones) **4**–**6**. Lactone **4** should be accessible from lactone **7** for which syntheses are known.[9][10] The hitherto unknown

Scheme 1. Retrosynthetic analysis of the polyol part of roflamycoin



[+] New address: Laboratorio de Química Farmacéutica, Facultad de Farmacia, Universidad de Barcelona, Av. Diagonal s/n, E-08028 Barcelona, Spain.

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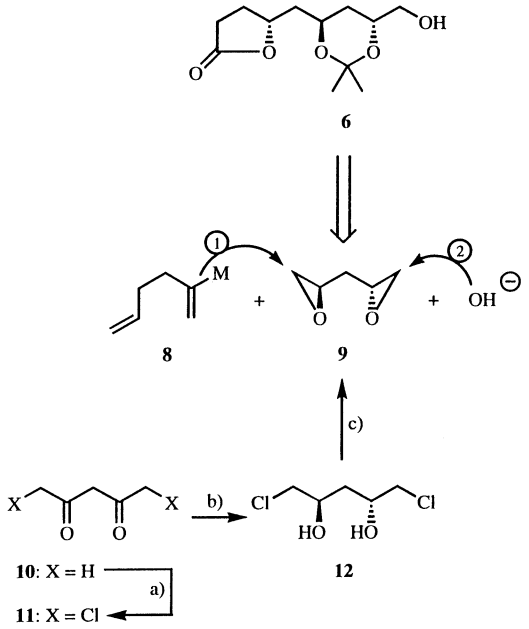
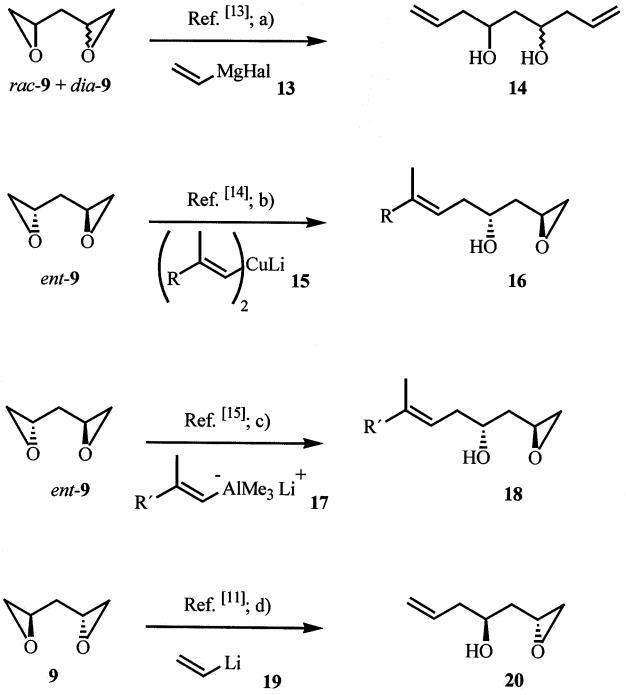
lactone **5** is an oxidation product of the equally unknown lactone **6** whose synthesis, therefore, became our objective.

Scheme 2. a) (i) $AlCl_3$ (1.0 equiv.), nitrobenzene/1,2-dichloroethane, addition of **10** at 0°C; chloroacetyl chloride (2 equiv.), → 60°C, 6 h; cold HCl, 12 h; (ii) satd. aqueous $Cu(OAc)_2$ solution, room temp., 20 min; (iii) H_2SO_4/H_2O, 10:1, *t*BuOMe, room temp., 10 min; 25% overall (ref.[11] 34%). – b) H_2 (70 bar), $[RuCl_2(S)\text{-BINAP})]_2\text{-}NEt_3$[12] (0.46 mol-%), MeOH, 100°C, 1.75 h; 53% / 99.8% *ee* (ref.[11] 64%/>97% *ee*). – c) KOH (6.6 equiv.), Et_2O, room temp., 3 h; 95% (ref.[11] 89%)



Scheme 3. Known ring-opening reactions of bisepoxide **9** by alkenyl metal compounds. a) Vinyl Grignard reagent, CuI; no other details given. – b) *t*BuLi (5.4 equiv.) in pentane, alkenyl iodide (2.6 equiv.) in Et_2O, −120°C → −78°C, 1 h; CuI (1.3 equiv.), −25°C; 2 h; → −65°C; *ent*-**9**, 4 h; 53%. – c) *t*BuLi (3.3 equiv.) in pentane, alkenyl bromide (1.5 equiv.) in Et_2O, −78°C, 30 min; Me_3Al (2.0 equiv.), 30 min; → −30°C, *ent*-**9**, → 0°C, 2 h; 82%. – d) Vinyllithium (> 1.2 equiv.) in Et_2O, **9** in THF, −78°C; $BF_3{\cdot}OEt_2$ (1.3 equiv.), 30 min; > 56%

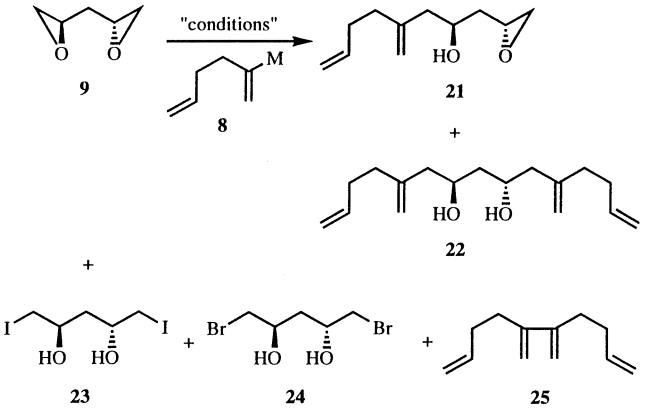


We wanted to reach **6** starting from the known bisepoxide **9**[11] (Scheme 2) which was synthesized from acetyl acetone (**10**) in 13% instead of 19% yield.[11] We planned to ring-open one epoxide ring of bisepoxide **9** with an appropriate metalohexadiene **8** and the other epoxide ring with hydroxide ions. The feasability of ring-opening reactions between compound **9** (or its enantiomer or diastereomer) and metaloalkenes was documented in the literature (Scheme 3).[11][14][15] We were aware, however, of the easiness of an over-reaction between these species at the second epoxide ring of **9**, *ent*-**9** or *syn*-**9**.[11][13] Also, to the best of our knowledge a *secondary* metaloalkene (cf. metaloalkene **8**!) had not been examined with respect to a selective mono-attack upon a bisepoxide. Due to their greater steric hindrance, one would expect that *secondary* metaloalkenes ring-open an epoxide still more sluggishly than the already not too reactive *primary* metaloalkenes (vide infra and the reference cited in footnote[10]).

Table 1 documents how difficult it was, indeed, to realize the desired ring-opening reaction **9** → **21**. A plethora of side-products was initially encountered: the mono(ring-opening) product from the nucleophilic attack of Br^-; diol **22** formed through the twofold attack of metaloalkene **8**; diol **23** formed through the twofold nucleophilic attack of I^-; diol **24** formed through the twofold nucleophilic attack of Br^-, (2*R*,4*S*)-1-bromo-6-methylene-9-decen-2,4-diol formed through one nucleophilic attack each of the metaloalkene **8** and of Br^-; the tetraene **25** formed through the oxidative dimerization of the metaloalkene. We varied the metal part of metaloalkene **8** by preparing this species in several ways. Inter alia, we started from 2-bromo-1,5-hexadiene[16] and (1) *t*BuLi followed by $BF_3{\cdot}Et_2O$ (→ **8**, M = Li or BF_2), (2) Mg (→ **8**, M = MgBr), (3) Mg followed by cat. CuI [→ **8**, M = $(CuMgBr)_{1/2}$] or (4) Mg followed by AgOTf[17] (→ **8**, M = MgOTf). In addition, we prepared metaloalkenes **8** from 2-(tributylstannyl)-1,5-hexadiene[18] by treatment with (1) *n*BuLi followed by $BF_3{\cdot}Et_2O$ (→ **8**, M = Li or BF_2) or (2) *n*BuLi followed by cat. CuI [→ **8**, M = $(CuLi)_{1/2}$]. Only the last experiment yielded the desired product **21** at all: Working with a *catalytic* amount of Gilman cuprate **8** besides excess organolithium compound **8**, one obtained 9% **21**. The final variation of Table 1 (last entry) was to make all of the metaloalkene **8** a Gilman cuprate. The desired ring-opening product **21** became now isolable in 72% yield. The concomitantly formed side-products **25** (11%), **23** (2%), **22** (1%), and **24** (0.2%) were removed by flash chromatography on silica gel.[19]

For the transformation of compound **21** into the γ-lactone **30** (Scheme 4) the epoxide ring[20] was opened by basic hydrolysis. The resulting triol **26** (79% yield), triphosgene, and pyridine reacted to two cyclic carbonates.[21] The major product was the dioxolanone **28** (70% isolated yield), the minor the dioxanone **27** (17% yield). The C=C bonds of

Table 1. Ring-opening reactions of bisepoxide **9** starting from hexadienes **8** (M = Br[16] or $SnBu_3$[18])



Reaction conditions	Yield [%] 21	22	23	24	25
Addition of *t*BuLi (2.2 equiv.) to **8** (M = Br; 1.1 equiv.) in THF/Et_2O/pentane, 4:1:1 (v:v:v) at −78°C, 3 h; addition to **9**, THF, −78°C, immediately thereafter $BF_3{\cdot}Et_2O$ (1.5 equiv.), 25 min	–	–	–	9[a]	–
Addition of **8** (M = Br; 1.1 equiv.) to Mg (1.2 equiv.) in THF at room temp., 2 h; → −30°C, CuI (0.10 equiv.), 5 min; addition of **9**, THF, 15 min, →0°C, 2.5 h				20	24[b]
Addition of **8** (M = Br; 1.5 equiv.) to Mg (1.6 equiv.) in THF at room temp., 2 h; → −30°C, CuI (0.15 equiv.), 5 min; addition of **9**, THF, 15 min, equiv.)		36		31	10[d]
Addition of **8** (M = Br; 1.1 equiv.) to Mg (1.2 equiv.) in THF at room temp., 2 h; → −78°C, AgOTf (1.2 equiv.), 45 min; addition to **9** in THF, −78°C → 0°C; 2.5 h					40[e]
Addition of *n*BuLi (1.2 equiv.) to **8** (M = $SnBu_3$; 1.2 equiv.) in THF at −78°C, 1 h; CuI (6 mol-%), 1 h; addition of **9**, THF, −78°Clt}}nBu_3; 1.1 equiv.) in THF at −78°C, 1 h; addition to **9** in THF, immediately thereafter $BF_3{\cdot}Et_2O$ (1.5 equiv.), 30 min		3			
Addition of *t*BuLi (5.4 equiv.) to **8** (M = Br) (2.6 equiv.) in Et_2O at −78°C, 3 h; addition to CuI (1.3 equiv.) in Et_2O at −25°C, 2 h, → −78°C ; addition of **9** in Et_2O, −78°C, 4 h (method:[14b])	72	1	2	0.2	11

[a] In addition, we isolated 10% (2*R*,4*S*)-1-bromo-6-methylene-9-decen-2,4-diol. – [b] In addition, we isolated 25% (*R*)-3-bromo-1-(*R*-oxiran-2-yl)-2-propanol and 3% (2*R*,4*S*)-1-bromo-6-methylene-9-decen-2,4-diol and recovered 5% **9**. – [c] In addition, we isolated 17% (2*R*,4*S*)-1-bromo-6-methylene-9-decen-2,4-diol. – [d] In addition, we isolated 5% (2*R*,4*S*)-1-bromo-6-methylene-9-decen-2,4-diol. – [e] 30% **9** was recovered. – [f] 12% **9** was recovered.

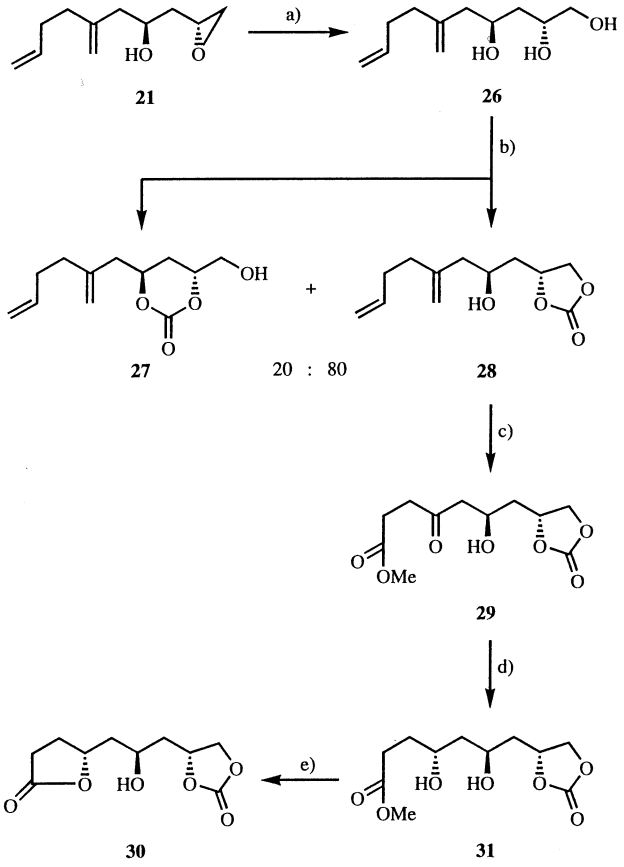
the major carbonate **28** were ozonolyzed under previously used conditions.[22] As desired, the $C_{quat}{=}CH_2$ moiety yielded a C=O function and the CH=CH_2 moiety a C(=O)OMe group. Hence, we obtained the γ-keto ester **29** (62% yield). The following step was an OH-directed *anti* reduction of the β-hydroxyketone substructure of compound **29** with Evans' reagent Me_4N^+ $BH(OAc)_3^-$.[23] It delivered the diol **31** as a crystalline solid (69% yield, 77% based on recovered starting material) and 93:7 mixture of the *anti* and the *syn* diastereomer. An acid-catalyzed lactonization of this mixture in warm toluene ensued. It yielded 78% of the carbonate-protected γ-lactone **30** as a slightly stereopurer 96:4 diastereomeric mixture. **30** possesses the stereostructure of the roflamycoin building block **6** but is equipped with a different protection pattern.

We stopped pursuing the route of Scheme 4 because the preparation of mono-epoxide **21** (Table 1) and its hydrolysis to dienetriol **26** (Scheme 4) remained difficult experiments; also, carbonate **28** arose together with its regioisomer **27**. The newly developed synthesis of Schemes 5 and 6 exhibits both higher reproducibility and efficieny.

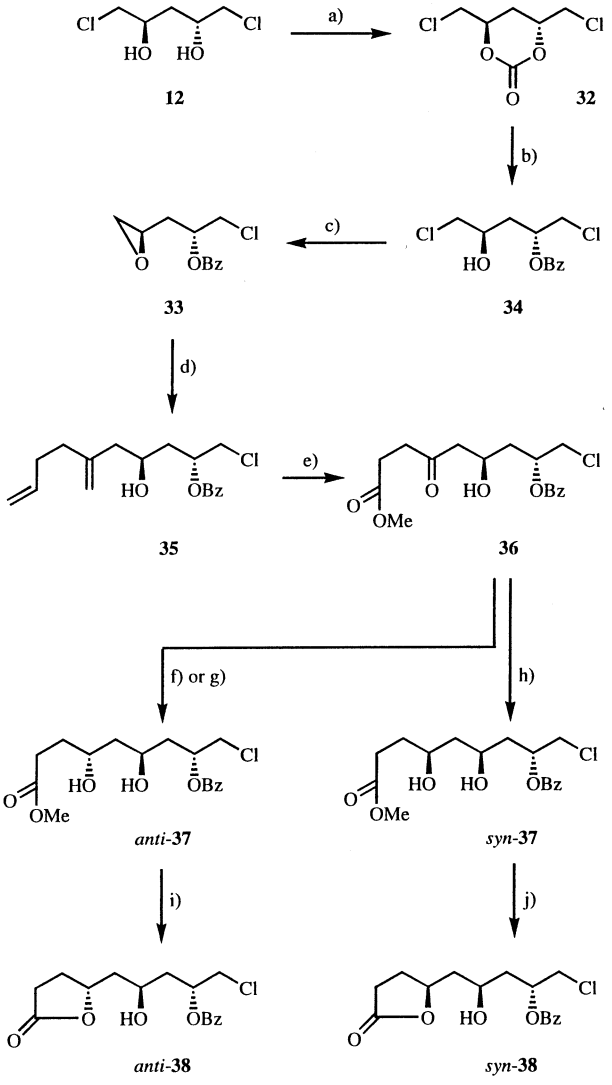
At the beginning, we broke the symmetry of the diol-producing reagent. Circumventing accordingly the *bis*epoxide **9**, we converted the bis(chlorohydrin) intermediate **12** (cf. Scheme 2) into the *mono*-epoxide **33** (Scheme 5). To this end, we first condensed it with triphosgene/pyridine to the dichlorocarbonate **32**. Then, we subjected this 6-membered ring carbonate to Nicolaou's 5-membered ring carbonate → acyclic hydroxybenzoate conversion.[24] We had to use less PhLi (1.2 equiv.) than in the 5-membered ring cases (1.25−10 equiv.) since the risk of a follow-up reaction between our primary product Li^+ $^-O{-}C^{\gamma}HR{-}C^{\beta}HR'{-}C^{\alpha}HR''[{-}O{-}C(=O){-}Ph]$ and excess PhLi was greater − because of the greater distance between the negative charge and the C=O bond − than in Nicolaou et al.'s Li^+ $^-O{-}C^{\beta}HR'{-}C^{\alpha}RR'[{-}O{-}C(=O){-}Ph]$. A selective conversion into the bis-chlorinated hydroxybenzoate **34** took place. The yield of **34** was 88% based on the starting material **32** but 96% taking into account 8% of re-formed − through over-reaction of the primary product **34** with PhLi − and recovered precursor **12**. Gratifyingly, another selective reaction ensued when the dichlorohydroxybenzoate **34** was treated with solid KOH in diethyl ether:[25] an intramolecular Williamson ether synthesis. It led to 85% of the mono-epoxide **33**.

The epoxide **33** was ring-opened smoothly by the Gilman cuprate derived from two equivalents of bromide **8** (M = Br),[16] four equivalents of *t*BuLi, and one equivalent of

Scheme 4. a) KOH, DMSO/H_2O (85:15), 100°C, 2 h; 79%.[20] – b) Triphosgene (1.0 equiv.), CH_2Cl_2, −70°C; addition of pyridine (10.5 equiv.); addition of **26** in CH_2Cl_2, → room temp.; 17% of **27**, 70% of **28**.[21] – c) (i) O_3, MeOH, −78°C; (ii) NEt_3 (2.5 equiv.), Ac_2O (1.2 equiv.), THF, room temp., 30 min; NEt_3 (1.4 equiv.), Ac_2O (0.8 equiv.); 62%.[22] – d) Tetramethylammonium triacetoxyborohydride (10 equiv.), HOAc, acetonitrile, room temp., 30 min, −40°C; addition of **29** in acetonitrile, −40°C, 18 h; 69%.[23] – e) Camphorsulfonic acid (0.3 equiv.), toluene, 40°C, 4 h; 78%



Scheme 5. a) Triphosgene (1.0 equiv.), CH_2Cl_2, −70°C; pyridine (10.5 equiv.); **12**[11] in CH_2Cl_2, → room temp.; 81%.[21] – b) Phenyllithium (1.2 equiv.), THF, −78°C, 30 min; 88% of **34**, 8% of **12**.[24] – c) KOH (3.3 equiv.), Et_2O, 0°C → room temp., 3 h; 85%.[25] – d) *t*BuLi (4.1 equiv.), **8** (M = Br)[16] (2.0 equiv.) in Et_2O, −78°C, 3 h; addition to CuI (1.0 equiv.) in Et_2O at −25°C, 2 h, → −78°C; addition of **33** in Et_2O, −78°C, 4 h; 80%.[26] – e) (i) O_3, MeOH, −78°C; (ii) NEt_3 (2.3 equiv.), Ac_2O (1.1 equiv.), THF, room temp., 30 min; NEt_3 (1.4 equiv.), Ac_2O (0.7 equiv.); 74%.[22] – f) Tetramethylammonium triacetoxyborohydride (10 equiv.), HOAc, acetonitrile, room temp., 30 min, → −40°C; **23** in acetonitrile, −40°C, 18 h; 69% of a 90:10 mixture of *anti*- and *syn*-**37**.[23] – g) $LiClO_4$ (5 equiv.), **36**, THF, 0°C, 10 min; → −78°C, 2,6-lutidine·BH_3 (2.4 equiv.), → room temp., 12 h; 68% of a 82:18 mixture of *anti*- and *syn*-**37**.[27] – h) Triethylborane (1.2 equiv.), MeOH/THF 1:4, room temp., 1 h, → −78°C; addition of **36** in THF, −78°C, 1 h; $NaBH_4$ (1.2 equiv.), −78°C, 12 h; 60%.[28] – i) Camphorsulfonic acid (0.3 equiv.), toluene, 40°C, 4 h; 82% (78% overall yield from **36** when working with crude *anti*-**37**). – j) Same as i); 85%

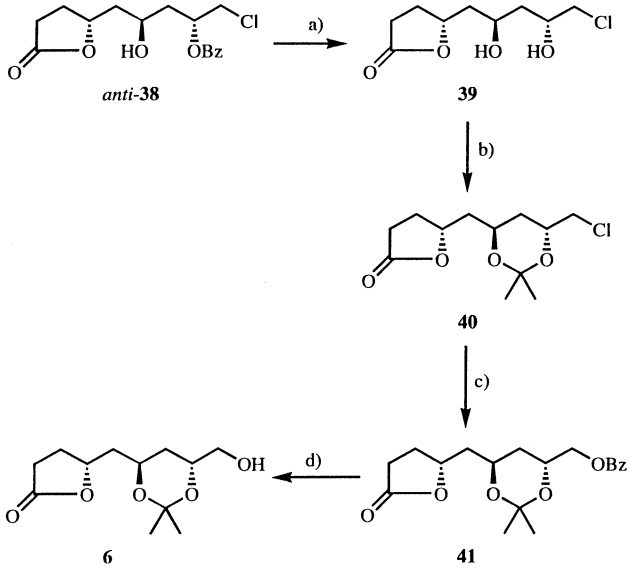


CuI. The chloro and benzoyloxy substituents survived these reaction conditions essentially unchanged so that we isolated 80% of the diene **35**. Exposure of diene **35** to the ozonolysis procedure already used in the oxidative cleavage **28** → **29** furnished the γ-keto ester **36** (74%). This species is also a β-hydroxyketone. As such we made it the substrate of Evans' triacetoxyborohydride reduction.[23] Thereby, we obtained preponderantly the diol *anti*-**37** albeit only as an unseparable 90:10 mixture with its *syn* diastereomer. Again (cf. the related reduction **29** → **31**), this selectivity lies at the lower limit of the literature precedence.[23] A recent protocol for *anti*-selective reductions of β-hydroxyketones with amine-complexed BH_3 in the presence of $LiClO_4$[27] worked still less satisfactorily in the case of substrate **36** because an 82:18 mixture of *anti*- and *syn*-**37** resulted. The stereocomplimentary chelation-controlled reduction of the same substrate **36** succeeded under Narasaka conditions:[28] through successive reactions with $Et_2B(OMe)$ and $NaBH_4$. The diol *syn*-**37** was obtained as a single diastereomer. It served as a reference compound for assigning the minor signals in the ^1H- and ^{13}C-NMR spectra of the previously isolated 90:10 and 82:18 *anti*-**37**/*syn*-**37** mixtures. In the presence of camphorsulfonic acid, each diastereomer of diol

37 lactonized. The 90:10 mixture of *anti*- and *syn*-**37** delivered an identically composed mixture of the lactones *anti*- and *syn*-**38** in 82% yield while the diastereopure sample of diol *syn*-**37** provided diastereopure lactone *syn*-**38**. Here, this last reaction was only carried out for identifying safely the minor resonances in the mentioned 90:10 *anti*/*syn*-**38** mixture. It is evident, however, that being able to access also selectively the γ-lactone *syn*-**38** is another contribution to extending the scope of our butyrolactone → 1,3-diol approach to 1,3,5,7,... -polyols in general.

The terminating steps of our synthesis of the precursor **6** of the polyol part **2** of roflamycoin (**1**) is shown in Scheme 6. A base-catalyzed methanolysis cleaved the benzoate substituent off the substrate *anti*-**38**.[29] Acetonide formation was best performed with the resulting *crude* diol **39** and dimethoxypropane. This delivered the acetal **40** in 66% yield over the two steps from benzoate *anti*-**38**. **40** represented a 95:5 mixture of the shown stereoisomer with the presumed rest of the initial 10% of the minor diastereomer. Fortunately, the percentage of the contaminating minor diastereomer continued to shrink during the subsequent steps due to the partial removal of this isomer during the respective chromatographic purifications. A nucleophilic displacement of chloride through benzoate (**40** → 88% **41**) followed[30] as well as a methanolysis of this benzoate with NaOMe/MeOH.[29] This last step provided the desired lactone **6** in 79% yield *as a pure stereoisomer.*

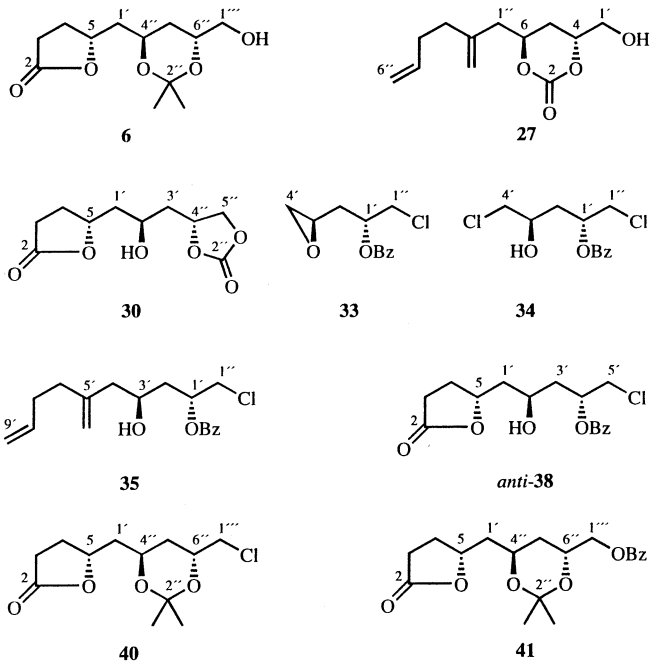
Scheme 6. a) NaOMe (0.4 equiv.), MeOH, room temp., 3 h; 63%.[29] – b) 2,2-Dimethoxypropane (13 equiv.), camphorsulfonic acid (cat.), acetone, room temp., 3 h; 74% (66% overall yield from *anti*-**38** when working with crude **39**). – c) Sodium benzoate (2 equiv.), DMSO, 165°C, 4 h; 88%.[30] – d) Same as a); 79%.[29]



The stereostructure of the acetonide rings of compounds **6**, **40**, and **41** are unmistakably *trans*. This is concluded from the Rychnovsky/Evans criteria for the ^{13}C-NMR resonances of the protecting group of *trans*-4,6-disubstituted acetonides.[31] These resonances fall in all three cases exactly into the typical shift ranges: On the one hand, the $C_{quat}{}^{13}Me_2$ signals appear at δ = 2 × 24.71 (**6**), 24.46/24.62 (**40**), and 24.58/24.64 (**41**); this matches the typical δ-value of 2 × 24.5 ±1.5. On the other hand, the $^{13}C_{quat}Me_2$ resonances are δ = 100.69 (**6**), 100.85 (**40**), and 100.83 (**41**) and as such very similar to the standard value of δ ≈ 100.5.

With lactone **6** in our hands, efforts are underway to incorporate this compound, the corresponding aldehydolactone **5**, and a type-**4** lactone into the trislactone precursor **3** of the roflamycoin fragment **2**.

Scheme 7: Position numbers used in the description of the NMR spectra of select compounds



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Experimental Section

General Comments: Ref.[1]. – Products were purified by flash chromatography[19] on Merck silica gel 60 [eluents given in brackets; eluent changes performed gradually; volume of each collected fraction (ml)/column diameter (cm): 1.3/1.0, 4/1.5, 8/2.0, 14/2.5, 20/3.0, 30/4, 50/5, 80/6, 125/75]. – ^{13}C NMR as APT spectra; peak orientations in accord with assignments.

(5R)-4,5-Dihydro-5-{[(4S,6R)-6-(hydroxymethyl)-2,2-dimethyl-1,3-dioxan-4-yl]methyl}-2(3H)-furanone (**6**)[32]: NaOMe (6.0 mg, 0.11 mmol, 0.4 equiv.) was added to a solution of benzoate **41** (63.0 mg, 0.181 mmol) in dry MeOH (1 ml). The mixture was stirred at room temp. for 3 h, concentrated in vacuo, diluted with brine (1 ml), and extracted with petroleum ether (2 × 5 ml) in order to remove the methyl benzoate formed. The aqueous phase was then extracted with CH_2Cl_2 (3 × 15 ml) and the combined dichloromethane extracts were dried with Na_2SO_4, filtered, and evaporated at reduced pressure to give pure alcohol **6** (34.5 mg, 79%) as a colorless oil. – $[\alpha]_D{}^{24} = -39.7$ (c = 1.83 in CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3480 cm^{-1}, 2985, 2940, 1780, 1770, 1380, 1225, 1170, 1130,

940, 915, 815, 655. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 [s, 2′′-$(CH_3)_2$], 1.53 (ddd, J_{gem} = 12.9, $J_{5''\text{-H}(1),4''}$ = 9.9, $J_{5''\text{-H}(1),6''}$ = 6.8, 5′′-H^1)*,**, 1.69 (ddd, J_{gem} = 12.9, $J_{5''\text{-H}(2),6''}$ = 9.0, $J_{5''\text{-H}(2),4''}$ = 5.9, 5′′-H^2)*,**, 1.76–1.81 (m, 1′-H_2), 1.88 (dddd, J_{gem} = 12.9, $J_{4\text{-H}(1),3\text{-H}(1)}$ = $J_{4\text{-H}(1),3\text{-H}(2)}$ = 9.3, $J_{4\text{-H}(1),5}$ = 8.4, 4-H^1)*,***, 2.04 (br. s, OH), 2.35 (dddd, J_{gem} = 12.9, $J_{4\text{-H}(2),3\text{-H}(1)}$ ≈ $J_{4\text{-H}(2),3\text{-H}(2)}$ ≈ $J_{4\text{-H}(2),5}$ ≈ 6.6, 4-H^2)***, 2.51–2.57 (m, 3-H_2), AB signal (δ_A = 3.53, δ_B = 3.62, J_{AB} = 11.7, in addition split by $J_{A,6''}$ = 6.9, 1′′′-H_2), 3.96 (m_c, presumably interpretable as dddd, $J_{6'',5''\text{-H}(2)}$ = 12.0, $J_{6'',5''\text{-H}(1)}$ ≈ $J_{6'',1'''\text{-H}(1)}$ ≈ 6.8, $J_{6'',1'''\text{-H}(2)}$ = 3.0, 6′′-H)****, superimposes in part 4.03 (m_c, 4′′-H)****, 4.69 (m_c, speculatively interpretable as dddd, $J_{5,4\text{-H}(1)}$ ≈ $J_{5,1'\text{-H}(1)}$ ≈ 8.1, $J_{5,4\text{-H}(2)}$ = 6.6, $J_{5,1'\text{-H}(2)}$ = 4.5, 5-H); * *vicinal* coupling constants interchangeable; ** distinguished from 1′-H/4-H through the existence of cross-peaks both to dddd at δ = 3.96 (6′′-H) and to dddd at δ = 4.03 (4′′-H); *** distinguished from 3-H_2 through the presence of cross-peak with the 5-H resonance (δ = 4.69) in a H,H-correlation spectrum and assuming that only a 4-H but not a 3-H can resonate as much high-field as $\delta_{H\text{-}(1)}$ = 1.88; **** distinguishable by the absence (4′′-H) or presence (6′′-H) of a cross-peak with the AB signal at δ_A = 3.53 and δ_B = 3.62 (1′′′-H_2) in a H,H-correlation spectrum. – ^{13}C NMR (50.3 MHz, $CDCl_3$; contamination at δ = 26.92): δ = 24.71 [2′′-$(CH_3)_2$)], 28.33 (C-4)*, 28.76 (C-3)*, 33.80 (C-5′′)*, 41.91 (C-1′)*, 63.48 (C-4′′)**, 65.24 (C-1′′′), 67.41 (C-6′′)**, 77.57 (C-5)**, 100.69 (C-2′′), 177.04 (C-2); *, ** distinguishable by a C,H-correlation spectrum. This ^{13}C-NMR spectrum is consistent with the absence of any contaminating isomer. – $C_{12}H_{20}O_5$ (244.3): calcd. C 59.00, H 8.25; found C 59.18, H 8.29.

(2R,4S)-1,2-Epoxy-6-methylene-9-decen-4-ol (**21**): To a solution of bromodiene **8** (M = Br; 2.73 g, 16.9 mmol, 2.60 equiv. with respect to **9**) in anhydrous diethyl ether (30 ml) at −78°C under argon was added *t*-butyllithium (21.5 ml of a 1.64 M solution in pentane, 35.3 mmol, 5.42 equiv. with respect to **9**). The mixture was stirred at −78°C for 3 h and then transferred via cannula to a suspension of CuI (1.56 g, 8.45 mmol, 1.30 equiv. with respect to **9**) in anhydrous diethyl ether (6 ml) kept at −25°C under argon. The mixture was stirred at −25°C for 2 h, cooled to −65°C, and to the resulting cuprate solution was added bisepoxide **9** (651 mg, 6.51 mmol). The reaction mixture was stirred at −65°C for 4 h, treated with a mixture of saturated aqueous ammonium chloride and conc. ammonia (130 ml of a 9:1 v/v mixture), warmed to room temp., and extracted with *t*BuOMe (3 × 100 ml). The combined organic extracts were dried with $MgSO_4$ and the solvent was evaporated in vacuo to afford an oily residue (1.3374 g) which was submitted to flash chromatography (silica gel, 4.0 cm, PE/MTB, 95:5 → 70:30). In the first fraction, homocoupling product **25** (152.2 mg, 11%) was isolated. Subsequently, we eluted the overreacted product **22** (fraction 19, 10.6 mg, 1%), monoepoxide **21** (fractions 20–21, 501.3 mg, 42%) as well as a mixture (fractions 22–29) containing again monoepoxide **21** (357.7 mg, 30%, 72% total yield), diiododiol **23** (38.1 mg, 2%), and dibromodiol **24** (3.3 mg, 0.2%). – $[\alpha]_D^{24}$ = +33.3 (*c* = 1.87 in CH_2Cl_2). – IR ($CDCl_3$): $\tilde{\nu}$ = 3550 cm^{-1}, 3080, 2935, 1640, 1435, 1415, 1260, 1060, 1000, 850. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.54 (ddd, J_{gem} = 14.3, $J_{3\text{-H}(1),2}$ = 6.8, $J_{3\text{-H}(1),4}$ = 3.5, 3-H^1)*,**, 1.83 (ddd, J_{gem} = 14.3, $J_{3\text{-H}(2),4}$ = 8.9, $J_{3\text{-H}(2),2}$ = 4.0, 3-H^2)*,**, 2.06–2.19 (m, 5-H^1, 7-H_2, 8-H_2, OH), 2.26 (dd, J_{gem} = 14.3, $J_{5\text{-H}(2),4}$ = 4.4, 5-H^2) 2.56 (dd, J_{gem} = 4.8, $J_{1\text{-H}(1),2}$ = 2.7, 1-H^1)***, 2.82 (t, J_{gem} = $J_{1\text{-H}(2),2}$ = 4.8, 1-H^2)***, 3.15 (m_c, 2-H), 3.95 (m_c, 4-H), 4.86 and 4.90 (2s, 6=CH_2), ca. 4.96 (dm_c, J_{cis} ≈ 10, *E*-10-H), superimposes in part ca. 5.02 (dm_c, J_{trans} ≈ 16, *Z*-10-H), 5.79 (ddt, J_{trans} = 16.8, J_{cis} = 10.2, $J_{9,8}$ = 6.3, 9-H); * assignment corroborated by C,H-correlation spectrum; ** coupling constants assigned on the basis of the intensity of coupling in the H,H-correlation spectrum; *** assignment corroborated by C,H-correlation spectrum. – ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 31.76 (C-8), 34.98 (C-7), 39.29 (C-3)*, 44.67 (C-5), 47.05 (C-1)**, 49.97 (C-2), 66.57 (C-4), 112.83 and 114.83 (6=CH_2, C-10), 137.92 (C-9), 145.36 (C-6); * assignment corroborated by C,H-correlation spectrum; ** coupling constants assigned on the basis of the intensity of coupling in the H,H-correlation spectrum. – $C_{11}H_{18}O_2$ (182.3): calcd. C 72.49, H 9.95; found C 72.29, H 9.99.

(7S,9S)-5,11-Dimethylene-1,14-pentadecadiene-7,9-diol (**22**): $[\alpha]_D^{24}$ = +15.6 (*c* = 1.78 in CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3385 cm^{-1}, 3320, 3075, 2975, 2930, 1645, 1435, 1060, 995, 910, 635. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.62 (dd, *J* = 6.5, *J*′ = 5.3, 8-H_2), 2.12–2.28 (m, 3-H_2, 4-H_2, 6-H_2, 10-H_2, 12-H_2, 13-H_2), 2.63 (br. s, 2 × OH), 4.09 (dddd, $J_{7(9),6(10)\text{-H}(1)}$ = $J_{7(9),6(10)\text{-H}(2)}$ = $J_{7(9),8\text{-H}(1)}$ = $J_{7(9),8\text{-H}(2)}$ = 6.2, 7-H, 9-H), 4.87 and 4.90 (br. s and d, respectively, J_{gem} = 1.5, 5=CH_2, 11=CH_2), 4.97 (dm_c, J_{cis} = 10.2, *E*-1-H, *E*-15-H), 5.03 (ddt, J_{trans} = 17.1, J_{gem} = J_{allyl} = 1.5, *Z*-1-H, *Z*-15-H), 5.81 (ddt, J_{trans} = 17.1, J_{cis} = 10.2, $J_{2(14),3(13)}$ = 6.3, 2-H, 14-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 31.78 (C-3, C-13)*, 35.01 (C-4, C-12)*, 42.31 (C-8)**, 44.51 (C-6, C-10)**, 66.20 (C-7, C-9), 112.57 and 114.76 (5=CH_2, 11=CH_2, C-1, C-15), 137.97 (C-2, C-14), 145.65 (C-5, C-11); * assignment based on a Specinfo increment calculation which predicts $\delta_{C\text{-}3}$ = $\delta_{C\text{-}13}$ = 32.28, $\delta_{C\text{-}4}$ = $\delta_{C\text{-}12}$ = 33.27; ** assigned on the basis of the 1:2 intensities ratio of the signals at δ = 42.31 and δ = 44.51, although not in agreement with the values predicted by Specinfo increment calculation ($\delta_{C\text{-}6}$ = $\delta_{C\text{-}10}$ = 41.16 and $\delta_{C\text{-}8}$ = 45, period51). – $C_{17}H_{28}O_2$ (264.4): calcd. C 77.22, H 10.67; found C 76.93, H 10.43.

(2R,4R)-1,5-Diiodo-2,4-pentanediol (**23**): IR (KBr): $\tilde{\nu}$ = 3420 cm^{-1}, 3335, 3120, 3005, 2940, 2885, 1400, 1380, 1315, 1265, 1180, 1145, 1085, 1025, 895, 840, 815, 675, 625. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.85 (dd, *J* = 6.2, *J*′ = 5.5, 3-H_2), 2.54 (d, J_{vic} = 5.3, 2 × OH), 3.28 [dd, J_{gem} = 10.2, $J_{1(5)\text{-H}(1),2(4)}$ = 6.8, 1-H^1, 5-H^1], 3.38 [dd, J_{gem} = 10.2, $J_{1(5)\text{-H}(2),2(4)}$ = 4.5, 1-H^2, 5-H^2], 3.93 (m_c, 2-H, 4-H). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.02 (C-1, C-5), 41.58 (C-3), 68.37 (C-2, C-4).

(2R,4R)-1,5-Dibromo-2,4-pentanediol (**24**): IR (KBr): $\tilde{\nu}$ = 3375 cm^{-1}, 2960, 2895, 2875, 1635, 1615, 1395, 1320, 1275, 1245, 1200, 1160, 1090, 1045, 905, 870, 830, 655. – ^{1}H NMR (300 MHz, $CDCl_3$, contaminated): δ = 1.81 (dd, *J* = 6.6, *J*′ = 5.5, 3-H_2), 2.73 (d, J_{vic} = 4.9, 2 × OH), 3.44 (dd, J_{gem} = 10.4, $J_{1(5)\text{-H}(1),2(4)}$ = 7.0, 1-H^1, 5-H^1), 3.55 (dd, J_{gem} = 10.2, $J_{1(5)\text{-H}(2),2(4)}$ = 4.1, 1-H^2, 5-H^2), 4.14 (m_c, 2-H, 4-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 39.17 (C-3), 39.55 (C-1, C-5), 68.22 (C-2, C-4).

5,6-Dimethylene-1,9-decadiene (**25**): IR ($CDCl_3$): $\tilde{\nu}$ = 3080 cm^{-1}, 2935, 1640, 1595, 1465, 1445, 1365, 1200, 1080, 1000. – ^{1}H NMR (300 MHz, $CDCl_3$; contains ca. 19 mol-% = 11 weight-% *t*BuOMe): δ = 2.20 (tdm_c, $J_{3(8),4(7)}$ = $J_{3(8),2(9)}$ = 6.8, 3-H_2, 8-H_2), 2.30–2.37 (m, 4-H_2, 7-H_2), 4.95 and 5.09 (2 br. s, 5=CH_2, 6=CH_2), 4.97 (presumably dm_c, J_{cis} = 10.2, *E*-1-H, *E*-10-H), superimposes in part 5.02 (ddt, J_{trans} = 17.1, J_{gem} = J_{allyl} = 1.7, *Z*-1-H, *Z*-10-H), 5.83 (ddt, J_{trans} = 17.1, J_{cis} = 10.2, $J_{2(9),3(8)}$ = 6.6, 2-H, 9-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 32.83 (C-3, C-8), 33.58 (C-4, C-7), 111.91 and 114.48 (C-1, C-10, 5=CH_2, 6=CH_2), 138.46 (C-2, C-9), 146.80 (C-5, C-6).

(2R,4S)-6-Methylene-9-decene-1,2,4-triol (**26**): To a solution of **21** (95.0 mg, 0.52 mmol) in DMSO/water (85:15 v/v, 9 ml), freshly powdered KOH (157.0 mg, 2.81 mmol) was added. The reaction mixture was heated at 100°C for 2 h, cooled in an ice bath, diluted with water (12 ml), and extracted with MTB (3 × 50 ml). The combined organic extracts were washed with water (3 × 10 ml),

dried with Na_2SO_4, and the solvent was evaporated in vacuo to afford **26** (81.9 mg, 79%) as a colorless oil. − $[\alpha]_D^{24}$ = +12.5 (*c* = 1.21 in CH_2Cl_2). − IR (NaCl): $\tilde{\nu}$ = 3360 cm^{-1}, 3075, 2935, 1640, 1440, 1070, 1015, 910. − ^1H NMR (300 MHz, $CDCl_3$, contains contaminant-peaks as m_c at δ = 2.8, 3.85, and 4.15): δ = 1.52 (ddd, J_{gem} = 14.5, $J_{3\text{-}H(1),2}$ = 8.6, $J_{3\text{-}H(1),4}$ = 3.5, 3-H^1)*, 1.69 (ddd, J_{gem} = 14.4, $J_{3\text{-}H(2),4}$ = 9.0, $J_{3\text{-}H(2),2}$ = 2.9, 3-H^2)**, 2.10−2.26 (m, 5-H_2, 7-H_2, 8-H_2), 2.65 and 3.49 (2d, J_{vic} = 2.1 and 4.2, respectively, 2-OH, 4-OH), 2.89 (br. t, J_{vic} = 5.3, 1-OH), ca. 3.48−3.56 (m, 1-H^1), 3.64 (ddd, J_{gem} = 10.8, $J_{1,OH}$ = 5.3, $J_{1\text{-}H(2),2}$ = 3.6, 1-H^2), 3.98−4.10 (m, 2-H, 4-H), [4.87 (s) and 4.92 (d, J_{gem} = 1.2) (6=CH_2)], ca. 4.98 (dm_c, $J_{cis} \approx$ 10, *E*-10-H), superimposes in part ca. 5.04 (dm_c, $J_{trans} \approx$ 17, *Z*-10-H), 5.81 (ddt, J_{trans} = 17.0, J_{cis} = 10.2, $J_{9,8}$ = 6.5, 9-H); * coupling constants assigned tentatively on the basis of the intensity of cross-peaks with 2-H (more intense) and 4-H (less intense) in the H,H-correlation spectrum; ** coupling constants assigned tentatively on the basis of the intensity of cross-peaks with 2-H (less intense) and 4-H (more intense) in the H,H-correlation spectrum. − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 31.80 (C-8)*, 35.05 (C-7)*, 39.04 (C-3), 44.59 (C-5)*, 66.03 (C-2)**, 66.89 (C-1), 69.36 (C-4)**, 112.73 (6=CH_2)***, 114.86 (C-10)***, 137.96 (C-9), 145.48 (C-6); * distinguishable by a C,H-correlation spectrum from C-3 but not from one another, hence, these assignments are interchangeable; ** interchangeable; *** distinguishable by a C,H-correlation spectrum. − $C_{11}H_{20}O_3$ (200.3): calcd. C 65.97, H 10.07; found C 65.74, H 10.04.

(4R)-4-[(2S)-2-Hydroxy-4-methylene-7-octenyl]-1,3-dioxolan-2-one (**28**): Dry pyridine (1.87 ml, 1.83 g, 23.1 mmol, 10.5 equiv.) and a solution of triol **26** (439.5 mg, 2.20 mmol) in anhydrous CH_2Cl_2 (7 ml) were added at −70°C to a stirred solution of triphosgene (637.1 mg, 2.20 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (7 ml). The reaction mixture was allowed to warm to room temp. and the resulting solution was treated with saturated aqueous NH_4Cl (35 ml) and washed with saturated aqueous $NaHCO_3$ (35 ml), brine (35 ml), and dried with $MgSO_4$. The organic layer was filtered and concentrated in vacuo to give an oily residue (529.0 mg) which was submitted to flash chromatography (silica gel, 3.0 cm, PE/MTB, 50:50 → MTB → MTB/MeOH, 98:2) to afford the five-membered cyclic carbonate **28** (fractions 5−18, 350.0 mg, 70%) as a colorless oil and the six-membered cyclic carbonate **27** (fractions 22−28, 83.0 mg, 17%).

28: $[\alpha]_D^{24}$ = +39.9 (*c* = 3.02 in CH_2Cl_2). − IR (NaCl): $\tilde{\nu}$ = 3485 cm^{-1}, 3075, 2980, 2925, 2855, 1795, 1640, 1440, 1395, 1175, 1065, 910, 775, 715. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.75 (ddd, J_{gem} = 13.8, $J_{1'\text{-}H(1),4}$ = 10.4, $J_{1'\text{-}H(1),2'}$ = 5.6, 1′-H^1)*, 1.96 (dd, J_{vic} = $^4J_{OH,1'\text{-}H(2)}$ = 1.8, OH), 2.01 (dddd, J_{gem} = 13.8, $J_{1'\text{-}H(2),2'}$ = 7.2, $J_{1'\text{-}H(2),4}$ = $^4J_{1'\text{-}H(2),OH}$ = 1.8, 1′-H^2)**, 2.06−2.23 (m, 3′-H^1, 5′-H_2, 6′-H_2), 2.27 (dd, J_{gem} = 14.1, $J_{3'\text{-}H(2),2'}$ = 3.6, 3′-H^2), 3.94 (m_c, 2′-H), 4.17 (dd, J_{gem} = 8.7, $J_{5\text{-}H(1),4}$ = 7.5, 5-H^1), 4.60 (dd, J_{gem} = 8.7, $J_{5\text{-}H(2),4}$ = 8.0, 5-H^2), [4.89 (s) and 4.96 (d, J_{gem} = 1.5) (4′=CH_2)], ca. 4.94 - ca. 4.98 (m, 4-H)***, ca. 4.99 (dm_c, $J_{cis} \approx$ 10, *E*-8′-H), superimposes in part ca. 5.04 (dm_c, $J_{trans} \approx$ 17, *Z*-8′-H), 5.80 (ddt, J_{trans} = 17.0, J_{cis} = 10.2, $J_{7',6'}$ = 6.4, 7′-H); * coupling constants assigned on the basis of the intensity of cross-peaks with 4-H (more intense) and 2′-H (less intense) in the H,H-correlation spectrum; ** coupling constants assigned on the basis of the intensity of cross-peaks with 2′-H (more intense) and 4-H (less intense) in the H,H-correlation spectrum; *** assigned on the basis of the integration of the signal in the ^1H NMR spectrum and the H,H- and H,C-correlation spectra. − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 31.72 (C-6′)*, 34.87 (C-5′)*, 40.98 (C-1′)**, 44.98 (C-3′)**, 65.16 (C-2′), 70.28 (C-5), 75.30 (C-4), 113.51 (4′=CH_2)***, 115.02 (C-8′)***, 137.69 (C-7′), 144.66 (C-4′), 155.00 (C-2); * interchangeable; **, *** distinguishable by a C,H-correlation spectrum. − $C_{12}H_{18}O_4$ (226.3): calcd. C 63.70, H 8.02; found C 63.87, H 7.88.

(4R,6S)-4-(Hydroxymethyl)-6-(2-methylene-5-hexenyl)-1,3-dioxan-2-one (**27**)[32]: It was isolated during the preparation of **28**. − $[\alpha]_D^{24}$ = −64.2 (*c* = 1.89 in CH_2Cl_2). − IR (NaCl): $\tilde{\nu}$ = 3485 cm^{-1}, 3075, 2925, 1745, 1640, 1440, 1385, 1260, 1200, 1125, 1000, 910, 765. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.98 (ddd, J_{gem} = 14.7, $J_{5\text{-}H(1),4}$ = 6.3*, $J_{5\text{-}H(1),6}$ = 5.7*, 5-H^1), 2.10−2.27 (m, 5-H^2, 3′′-H_2, 4′′-H_2, OH), 2.33 (partly resolved ddd, J_{gem} = 14.4, $J_{1''\text{-}H(1),6}$ = 7.7, J_{allyl} = 0.6, 1′′-H^1), 2.59 (br. dd, J_{gem} = 14.4, $J_{1''\text{-}H(2),6}$ = 6.9, 1′′-H^2), AB signal (δ_A = 3.72, δ_B = 3.80, J_{AB} = 10.8, in addition split by $J_{A,4}$ = $J_{B,4}$ = 3.9, 1′-H_2), 4.65 (dddd, $J_{4,5\text{-}H(1)}$ = 7.2**, $J_{4,5\text{-}H(2)}$ = 5.1**, $J_{4,1'\text{-}H(1)}$ = $J_{4,1'\text{-}H(2)}$ = 3.9, 4-H)***, 4.74 (m_c, 6-H)***, [4.87 (br. d, J_{gem} = 0.9) and 4.95 (br. d, J_{gem} = 1.2) (2′′=CH_2)], ca. 4.99 (dm_c, $J_{cis} \approx$ 10, *E*-6′′-H), superimposes in part ca. 5.04 (dm_c, $J_{trans} \approx$ 17, *Z*-6′′-H), 5.81 (ddt, J_{trans} = 17.1, J_{cis} = 10.5, $J_{5'',4''}$ = 6.5, 5′′-H); *, ** exchangeable; *** distinguishable by the ocurrence (4-H) or non-ocurrence (6-H) of a cross-peak with 1′-H_2 in a H,H-correlation spectrum. − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 27.13 (C-5)*, 31.69 (C-4′′)**, 35.20 (C-3′′)**, 41.09 (C-1′′), 72.69 (C-1′), 74.54 (C-4)***, 75.20 (C-6)***, 113.88 (2′′=CH_2)****, 115.09 (C-6′′)****, 137.62 (C-5′′), 142.79 (C-2′′), 148.68 (C-2); * distinguishable from C-3′′ and C-4′′ by a C,H-correlation spectrum; ** interchangeable; ***, **** distinguishable by a C,H-correlation spectrum. − $C_{12}H_{18}O_4$ (226.3): calcd. C 63.70, H 8.02; found C 63.90, H 7.88.

Methyl (6R)-6-Hydroxy-4-oxo-7-[(4R)-2-oxo-1,3-dioxolan-4-yl]heptanoate (**29**): The carbonate **28** (350.0 mg, 1.55 mmol) was ozonolyzed in methanol (13 ml) at −78°C until persistance of blue color (20 min). Oxygen was bubbled through this solution for 1 h. The resulting colorless solution was treated with camphorsulfonic acid (70.0 mg, 0.32 mmol, 0.21 equiv.). After removal of the cold bath, the reaction mixture was stirred for 1.5 h and treated with $NaHCO_3$ (90.0 mg, 1.07 mmol) for 15 min. The resulting suspension was filtered and the filtrate evaporated at reduced pressure. The residue was dissolved in MTB (4 × 25 ml) and evaporated in vacuo to remove traces of methanol. The resulting oily residue was taken up in anhydrous THF (20 ml) and the resulting solution treated dropwise with dry triethylamine (0.53 ml, 385 mg, 3.8 mmol, 2.5 equiv.) and acetic anhydride (0.18 ml, 190 mg, 1.9 mmol, 1.2 equiv.). After stirring at room temp. for 30 min, the solution was treated again with dry triethylamine (0.30 ml, 217 mg, 2.2 mmol, 1.4 equiv.) and acetic anhydride (0.11 ml, 120 mg, 1.2 mmol, 0.8 equiv.) and stirred for an additional 30-min period. The reaction mixture was treated with saturated aqueous $NaHCO_3$ (5 ml) and extracted with CH_2Cl_2 (4 × 20 ml). The combined organic extracts were dried with $NaSO_4$, filtered and concentrated in vacuo to give a yellow oily residue (423.5 mg) which was submitted to flash chromatography (silica gel, 45 g, 3.0 cm, PE/MTB 30:70 → MTB → MTB/MeOH, 97:3) to afford the keto ester **29** (250.2 mg, 62%) as a colorless oil. − $[\alpha]_D^{24}$ = −5.1 (*c* = 0.91 in CH_2Cl_2). − IR (NaCl): $\tilde{\nu}$ = 3485 cm^{-1}, 2955, 1800, 1730, 1715, 1440, 1365, 1175, 1065, 775, 730. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.84 (ddd, J_{gem} = 14.1, $J_{7\text{-}H(1),6}$ = 10.2*, $J_{7\text{-}H(1),4'}$ = 6.0*, 7-H^1), 1.95 (dddd, J_{gem} = 14.1, $J_{7\text{-}H(2),4'}$ = 7.2**, $J_{7\text{-}H(2),6}$ = 3.0**, $J_{7\text{-}H(2),OH}$ = 1.5, 7-H^2), 2.58−2.78 (m, 2-H_2, 3-H_2, 5-H_2), 3.44 (dd, J_{vic} = 3.8, $J_{OH,7\text{-}H(2)}$ = 1.5, OH), 3.69 (s, CH_3), 4.18 (dd, J_{gem} = 9.0, $J_{5'\text{-}H(1),4'}$ = 7.8, 5′-H^1), 4.30 (m_c, 6-H), 4.61 (dd, J_{gem} = 9.0, $J_{5'\text{-}H(2),4'}$ = 8.1, 5′-H^2), 4.95 (dddd, $J_{4',5'\text{-}H(1)}$*** = $J_{4',5'\text{-}H(2)}$*** = $J_{4',7\text{-}H(2)}$*** = 7.5, $J_{4',7\text{-}H(1)}$*** = 6.0, 4′-H); *, **, *** exchangeable. − ^{13}C NMR [50.3 MHz, $CDCl_3$, peaks of contaminant(s) at δ = 26.44, 26.90, 37.80, 49.00, 53.38, 64.33, 103.67]: δ = 27.54 (C-2), 37.57 (C-3), 40.29 (C-7), 49.34 (C-5), 51.95 (CH_3), 64.50 (C-6),

70.20 (C-5′), 74.96 (C-4′), 154.86 (C-2′), 173.23 (C-1), 209.25 (C-4). − $C_{11}H_{16}O_7$ (260.2): calcd. C 50.77, H 6.20; found C 50.61, H 6.35.

(5R)-4,5-Dihydro-5-{(2S)-2-hydroxy-3-[(4R)-2-oxo-1,3-dioxolan-4-yl]propyl}-2(3H)-furanone (**30**)[32]: To a solution of hydroxy ester **31** (100.0 mg, 0.38 mmol) in toluene (3 ml) was added camphorsulfonic acid (22.0 mg, 0.10 mmol) and the mixture was heated at 40°C for 4 h. The resulting solution was allowed to reach room temp., treated with $NaHCO_3$ (40.0 mg, 0.48 mmol) for 15 min, and filtered. The filtrate was evaporated at reduced pressure to give a white solid (112.3 mg) which was submitted to flash chromatography (silica gel, 9 g, 1.5 cm, MTB → MTB/MeOH, 95:5) to afford lactone **30** (68.0 mg, 78%) as a colorless oil which solidified on standing (m.p. 65−66°C). − $[\alpha]_D^{24} = -13.9$ (c = 3.14 in CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3430 cm^{-1}, 3130, 2995, 2955, 2910, 1795, 1735, 1435, 1400, 1375, 1280, 1180, 1130, 1065, 1035, 985, 960, 920, 775. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68−1.82 (m, 1′-H^1, 3′-H^1)*, 1.83−2.07 (m, from high- to low-field in this order**: 1′-H^2*, 3′-H^2*, 4-H^1), 2.40 (dddd, J_{gem} = 13.5, $J_{4\text{-H}(2),3\text{-H}(1)} \approx J_{4\text{-H}(2),3\text{-H}(2)} \approx J_{4\text{-H}(2),5} \approx$ 6.8, 4-H^2)***, 2.53−2.62 (m, 3-H$_2$), 4.00 (br. s, OH), 4.14 (dd, J_{gem} = 8.6, $J_{5''\text{-H}(1),4''}$ = 7.4, 5″-H^1), 4.26 (very br. dd, $J_{vic,a} \approx J_{vic,b} \approx$ 9.9, 2′-H), 4.59 (dd, $J_{gem} \approx J_{5''\text{-H}(2),4''} \approx$ 8.1, 5″-H^2), 4.88 (m$_c$, 5-H)****, 5.01 (m$_c$, presumably interpretable as dddd, $J_a \approx$ 10.2, $J_{4'',5''\text{-H}(1)} \approx J_{4'',5''\text{-H}(2)} \approx$ 7.4, $J_b \approx$ 3.0, 4″-H)****; * assignment in accordance with cross-peaks with the corresponding geminal proton in the H,H-correlation spectrum; ** as deduced from the recognition of *gem*-relationships with respect to - the independently assigned - 1′-H^1, 3′-H^1 and 4-H^2 in the C,H-correlation spectrum; *** distinguished from 3-H$_2$ through the presence of cross-peaks with 5-H resonance (δ = 4.88) in a H,H-correlation spectrum and assuming that only a 4-H but not a 3-H can resonate as much high-field as δ = 1.83−2.07; **** distinguished by the presence (4″-H) or absence (5-H) of cross-peaks with the 5″-H resonances at δ = 4.14 and δ = 4.59 in a H,H-correlation spectrum. − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 27.80 (C-4)*, 28.62 (C-3)*, 41.63 (C-3′)*, 43.26 (C-1′)*, 63.50 (C-2′)**, 69.77 (C-5″), 74.65 (C-4″)**, 77.97 (C-5)**, 155.42 (C-2″), 178.33 (C-2); *, ** distinguishable by a C,H-correlation spectrum. − $C_{10}H_{14}O_6$ (230.2): calcd. C 52.17, H 6.13; found C 52.07, H 6.10.

Methyl (4R,6S)-4,6-Dihydroxy-7-[(4R)-2-oxo-1,3-dioxolan-4-yl]heptanoate (**31**): To a solution of tetramethylammonium triacetoxyborohydride (2.860 g, 10.87 mmol) in anhydrous acetonitrile (5 ml) was added anhydrous acetic acid (5.3 ml) and the mixture was stirred at room temp. for 30 min. The mixture was cooled to −40°C and a solution of keto ester **29** (285.0 mg, 1.096 mmol) in anhydrous acetonitrile (2 ml) was added via cannula. The reaction mixture was stirred at −40°C for 18 h, treated with saturated aqueous K_2CO_3 (14 ml), allowed to warm to room temp., and extracted with CH_2Cl_2 (4 × 50 ml). The combined organic extracts were dried with Na_2SO_4, filtered and concentrated in vacuo. The resulting residue was taken up in methanol (3 × 20 ml) and evaporated at reduced pressure in order to remove possible volatile boron species. A yellow oil (304.6 mg) remained which was submitted to flash chromatography (silica gel, 25 g, 2.0 cm, PE/MTB, 30:70 → MTB → MTB/MeOH, 95:5). From the early fractions, starting material **29** (32.3 mg, 11%) was recovered while the late fractions provided hydroxy ester **31** (197.7 mg, 69%, 77% based on reacted **29**) as a white solid (m.p. 74−75°C). − $[\alpha]_D^{24} = +14.8$ (c = 0.61 in CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3225 cm^{-1}, 3015, 2935, 1795, 1715, 1445, 1400, 1260, 1240, 1210, 1175, 1130, 1065, 910, 845, 775. − ^{1}H NMR (300 MHz, $CDCl_3$; contaminated by m at δ = ca. 2.6 − ca. 2.7): δ = 1.67 (dd, $J_{5,4} = J_{5,6}$ = 5.9, 5-H$_2$)*, 1.71−1.92 (m, 7-H^1, 3-H$_2$), superimposes partly 1.95 (ddd, J_{gem} = 14.2, $J_{7\text{-H}(2),4'}$ = 7.7, $J_{7\text{-H}(2),6}$ = 3.2, 7-H^2)**, extreme AB signal [δ_A = 2.49, δ_B = 2.53, J_{AB} = 16.5, in addition split by $J_{A,3\text{-H}(1)} = J_{A,3\text{-H}(2)} = J_{B,3\text{-H}(1)} = J_{B,3\text{-H}(2)}$ = 6.9, 2-H$_2$], 3.24 (br. d, J_{vic} = 4.2, 4-OH)***, 3.46 (br. d, J_{vic} = 5.1, 6-OH)***, 3.70 (s, CH_3), 3.99 (m$_c$, 4-H)****, 4.18 (dd, J_{gem} = 8.7, $J_{5'\text{-H}(1),4'}$ = 7.5, 5′-H^1), superimposes ca. 4.16−4.22 (m, 6-H)****, 4.61 (dd, J_{gem} = 8.7, $J_{5'\text{-H}(2),4'}$ = 7.8, 5′-H^2), 4.99 (dddd, $J_{4',5'\text{-H}(1)} = J_{4',5'\text{-H}(2)} = J_{4',7\text{-H}(2)}$ = 7.5, $J_{4',7\text{-H}(1)}$ = 5.7, 4′-H); * distinguished from 3-H and 7-H by the absence of cross-peaks with the AB signal at δ_A = 2.49, δ_B = 2.53 (2-H$_2$) and with the dddd at δ = 4.99 (4′-H); ** distinguished from 3-H and 5-H through the cross-peak with the dddd at δ = 4.99 (4′-H); *** assignment corroborated by H,H-correlation spectrum; **** distinguished by the absence (4-H) or presence (6-H) of a cross-peak with the 7-H resonances in a H,H-correlation spectrum. − ^{13}C NMR [75.5 MHz, $CDCl_3$; contains peaks of contaminant(s) in a 1:13 ratio at δ = 37.56, 40.29, 52.01, 64.55, 70.37, 75.01]: δ = 30.73 (C-2)*, 31.95 (C-3)*, 41.20 (C-7)**, 42.88 (C-5)**, 51.95 (CH_3), 65.44 (C-6)***, 68.80 (C-4)***, 70.25 (C-5′), 75.26 (C-4′), 155.24 (C-2′), 175.07 (C-1); *, **, *** distinguishable by a C,H-correlation spectrum. − $C_{11}H_{18}O_7$ (262.3): calcd. C 50.38, H 6.92; found C 50.08, H 7.22.

(4R,6R)-4,6-Bis(chloromethyl)-1,3-dioxan-2-one (**32**): To a stirred solution of triphosgene (3.40 g, 11.8 mmol) in anhydrous CH_2Cl_2 (40 ml) dry pyridine (9.8 ml, 120 mmol) and a solution of dichlorodiol **12** (1.98 g, 11.4 mmol) in anhydrous CH_2Cl_2 (50 ml) were added at −70°C. The reaction mixture was allowed to warm to room temp. and then treated with saturated aqueous NH_4Cl (200 ml), washed with saturated aqueous $NaHCO_3$ (200 ml), and brine (200 ml), and dried with $MgSO_4$. The organic layer was filtered and concentrated in vacuo to give pure carbonate **32** (1.84 g, 81%) as a white solid (m.p. 61−62°C). − $[\alpha]_D^{24} = -40.6$ (c = 1.72 in CH_2Cl_2). − IR ($CDCl_3$): $\tilde{\nu}$ = 2965 cm^{-1}, 1765, 1440, 1375, 1255, 1185, 1125. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 (dd, $J_{5,4} = J_{5,6}$ = 6.1, 5-H$_2$), AB signal [δ_A = 3.72, δ_B = 3.78, J_{AB} = 11.7, in addition split by $J_{A,4(6)}$ = 6.8, $J_{B,4(6)}$ = 4.5, 1′-H$_2$, 1″-H$_2$], 4.81 (m$_c$, 4-H, 6-H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 25.60 (C-5), 44.00 (C-1′, C-1″), 74.64 (C-4, C-6), 147.22 (C-2). − $C_6H_8Cl_2O_3$ (199.0): calcd. C 36.21, H 4.05; found C 36.39, H 4.07.

[(1R,3R)-1-(Chloromethyl)-3,4-epoxybutyl] Benzoate (**33**)[32]: To a 0°C solution of **34** (1.14 g, 4.12 mmol) in diethyl ether (40 ml), freshly powdered KOH (0.77 g, 13.8 mmol, 3.3 equiv.) was added. The reaction mixture was stirred at room temp. for 3 h and filtered through a plug of $MgSO_4$. The solvent was removed in vacuo to give a yellow oily residue (0.97 g) which was submitted to flash chromatography (silica gel, 50 g, 3.0 cm, PE/MTB, 95:5 → 70:30) to afford epoxide **33** (0.84 g, 85%) as a colorless oil. − $[\alpha]_D^{24} = +40.2$ (c = 2.25 in CH_2Cl_2). − IR (NaCl): $\tilde{\nu}$ = 3060 cm^{-1}, 2995, 2925, 1720, 1600, 1585, 1450, 1435, 1350, 1315, 1270, 1175, 1110, 1070, 1025, 850, 710. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.89 (ddd, J_{gem} = 14.7, $J_{2'\text{-H}(1),3'}$ = 7.1, $J_{2'\text{-H}(1),1'}$ = 5.1, 2′-H^1)*, 2.20 (ddd, J_{gem} = 14.7, $J_{2'\text{-H}(2),1'}$ = 8.1, $J_{2'\text{-H}(2),3'}$ = 4.5, 2′-H^2)**, 2.54 (dd, J_{gem} = 5.1, $J_{4'\text{-H}(1),3'}$ = 2.4, 4′-H^1), 2.78 (dd, $J_{gem} \approx J_{4'\text{-H}(2),3'} \approx$ 5.1, 4′-H^2), 3.06 (m$_c$, perhaps interpretable as dddd, $J_{3',2'\text{-H}(1)}$ = 7.1, $J_{3',2'\text{-H}(2)} \approx J_{3',4'\text{-H}(2)} \approx$ 4.5, $J_{3',4'\text{-H}(1)}$ = 2.4, 3′-H), AB signal (δ_A = 3.77, δ_B = 3.88, J_{AB} = 12.0, in addition split by $J_{A,1'}$ = 5.0, $J_{B,1'}$ = 4.5, 1″-H$_2$), 5.50 (dddd, $J_{1',2'\text{-H}(2)}$ = 7.8, $J_{1',1''\text{-H}(1)} \approx J_{1',1''\text{-H}(2)} \approx J_{1',2'\text{-H}(1)} \approx$ 4.8, 1′-H), 7.46 (br. dd, $J_{3(5),2(6)} \approx J_{3(5),4} \approx$ 7.2, 3-H, 5-H), 7.59 (ddm$_c$, $J_{4,3} = J_{4,5}$ = 7.2, 4-H), 8.07 (dm$_c$, $J_{2(6),3(5)}$ = 7.2, 2-H, 6-H); * coupling constants assigned on the basis of the intensity of cross-peaks with 1′-H (less intense) and 3′-H (more intense) in the H,H-correlation spectrum; ** coupling constants assigned on the basis of the intensity

of cross-peaks with 1′-H (more intense) and 3′-H (less intense) in the H,H-correlation spectrum. – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 35.22 (C-2′), 45.63 (C-1′′)*, 46.92 (C-4′)*, 48.67 (C-3′), 71.24 (C-1′), 128.42 (C-3, C-5), 129.52 (C-1), 129.64 (C-2, C-6), 133.29 (C-4), 165.62 (C=O); * assignment corroborated by a H,C-correlation spectrum. – $C_{12}H_{13}ClO_3$ (240.7): calcd. C 59.88, H 5.44; found C 60.07, H 5.43.

[(1R,3R)-4-Chloro-1-(chloromethyl)-3-hydroxybutyl] Benzoate (**34**)[32]: To a solution of carbonate **32** (1.00 g, 5.02 mmol) in anhydrous THF (120 ml), phenyllithium (3.4 ml of a 1.8 M solution in cyclohexane/diethyl ether, 70:30, 6.12 mmol) was added at −78°C. The reaction mixture was stirred at −78°C for 30 min, treated with saturated aqueous NH_4Cl (130 ml), and diluted with MTB (250 ml). The organic layer was separated, washed with brine (200 ml), dried with Na_2SO_4, filtered, and concentrated in vacuo to give an orange oily residue (1.64 g) which was submitted to flash chromatography (silica gel, 100 g, 4.0 cm, PE/MTB, 90:10 → MTB) to afford pure **34** (1.22 g, 88%) as a colorless oil and in later fractions dichlorodiol **12** (68.0 mg, 8%). – $[\alpha]_D^{24}$ = +40.2 (*c* = 5.73 in CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3500 cm^{-1}, 3060, 2960, 2925, 1720, 1600, 1585, 1450, 1430, 1350, 1315, 1275, 1175, 1110, 1070, 1025, 850, 710. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90 (ddd, J_{gem} = 14.4, $J_{2'\text{-H}(1),3'}$ = 10.4, $J_{2'\text{-H}(1),1'}$ = 3.0, 2′-H^1)*, 2.09 (ddd, J_{gem} = 14.4, $J_{2'\text{-H}(2),1'}$ = 9.9, $J_{2'\text{-H}(2),3'}$ = 2.4, 2′-H^2)**, 3.15 (d, J_{vic} = 4.5, OH), AB signal (δ_A = 3.53, δ_B = 3.60, J_{AB} = 11.3, in addition split by $J_{A,3'}$ = 6.5, $J_{B,3'}$ = 4.4, 4′-H_2), AB signal (δ_A = 3.76, δ_B = 3.86, J_{AB} = 12.0, in addition split by $J_{A,1'}$ = 5.1, $J_{B,1'}$ = 4.2, 1′′-H_2), B-part overlaps in part 3.91 (m_c, speculatively interpretable as dddd, $J_{3',2'\text{-H}(1)}$ = 10.5, $J_{3',4'\text{-H}(1)}$ = 6.3, $J_{3',4'\text{-H}(2)}$ = 4.2, $J_{3',2'\text{-H}(2)}$ = 2.7, 3′-H), 5.55 (dddd, $J_{1',2'\text{-H}(2)}$ = 9.9, $J_{1',1''\text{-H}(1)}$ = 5.1, $J_{1',1''\text{-H}(2)}$ = 4.2, $J_{1',2'\text{-H}(1)}$ = 3.0, 1′-H), 7.45 (ddm_c, $J_{3(5),2(6)} \approx J_{3(5),4} \approx$ 7.5, 3-H, 5-H), 7.59 (dddd, $J_{4,3} = J_{4,5}$ = 7.4, $^4J_{4,2} = {}^4J_{4,6}$ = 1.7, 4-H), 8.06 (dm_c, $J_{2(6),3(5)}$ = 8.1, 2-H, 6-H); * coupling constants assigned on the basis of the intensity of cross-peaks with 1′-H (less intense) and 3′-H (more intense) in the H,H-correlation spectrum; ** coupling constants assigned on the basis of the intensity of cross-peaks with 1′-H (more intense) and 3′-H (less intense) in the H,H-correlation spectrum. – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 36.95 (C-2′), 46.43 (C-1′′)*, 49.50 (C-4′)*, 67.48 (C-3′), 70.64 (C-1′), 128.44 (C-3, C-5), 129.22 (C-1), 129.76 (C-2, C-6), 133.46 (C-4), 166.48 (C=O); * distinguishable by a C,H-correlation spectrum. – $C_{12}H_{14}Cl_2O_3$ (277.1): calcd. C 52.01, H 5.09; found C 52.29, H 5.09.

[(1R,3S)-1-(Chloromethyl)-3-hydroxy-5-methylene-8-nonenyl] Benzoate (**35**)[32]: *t*-Butyllithium (1.18 M in pentanes, 5.8 ml, 6.84 mmol, 4.1 equiv. with respect to epoxide **33**) was added at −78°C under nitrogen to a solution of bromodiene **8** (536.0 mg, 3.32 mmol, 2.0 equiv. with respect to **33**) in anhydrous diethyl ether (8 ml). The mixture was stirred at −78°C for 3 h and then transferred via cannula to a suspension of cuprous iodide (310.0 mg, 1.66 mmol, 1.0 equiv. with respect to **33**) in anhydrous diethyl ether (2 ml) kept at −25°C. The mixture was stirred at −25°C for 2 h, cooled to −78°C, and to the resulting cuprate solution was added epoxide **33** (400.0 mg, 1.66 mmol) in anhydrous diethyl ether (2 ml). The reaction mixture was stirred at −78°C for 4 h, treated with saturated aqueous NH_4Cl/conc. NH_3 (35 ml of a 9:1 v/v mixture), warmed to room temp., and extracted with *t*BuOMe (3 × 50 ml). The combined organic extracts were dried with $MgSO_4$. The solvent was evaporated in vacuo to afford an oily residue (638.7 mg) which was submitted to flash chromatography (silica gel, 70 g, 3.5 cm, PE/MTB, 95:5 → 75:25) to afford pure **35** (426.2 mg, 80%) as a colorless oil. – $[\alpha]_D^{24}$ = +33.6 (*c* = 2.64 in CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3500 cm^{-1}, 3425, 3075, 2930, 1720, 1640, 1600, 1450, 1315, 1275, 1175, 1115, 1070, 1025, 910. – ^{1}H NMR (300 MHz, $CDCl_3$; contains ca. 15 mol-% = 5 weight-% *t*BuOMe): δ = 1.78 (ddd, J_{gem} = 14.1, $J_{2'\text{-H}(1),3'}$ = 10.2, $J_{2'\text{-H}(1),1'}$ = 3.6, 2′-H^1)*, 2.02 (ddd, J_{gem} = 14.1, $J_{2'\text{-H}(2),1'}$ = 9.9, $J_{2'\text{-H}(2),3'}$ = 2.4, 2′-H^2)**, overlaps partly 2.05–2.24 (m, 4′-H_2, 6′-H_2, 7′-H_2), 2.53 (d, J_{vic} = 3.3, OH), AB signal (δ_A = 3.76, δ_B = 3.87, J_{AB} = 11.7, in addition split by $J_{A,1'}$ = 5.1, $J_{B,1'}$ = 4.2, 1′′-H_2), superimposes ca. 3.76–3.89 (m_c, 3′-H), [4.85 (s) and 4.89 (poorly resolved d, J_{gem} = 1.5) (5′=CH_2)], 4.94 (dm_c, $J_{cis} \approx$ 10, *E*-9′-H), superimposes in part ca. 4.99 (dm_c, $J_{trans} \approx$ 17, *Z*-9′-H), 5.56 (dddd, $J_{1',2'\text{-H}(2)}$ = 9.9, $J_{1',1''\text{-H}(1)}$ = 5.1, $J_{1',2'\text{-H}(1)} \approx J_{1',1''\text{-H}(2)} \approx$ 3.6, 1′-H), 5.77 (ddt, J_{trans} = 16.9, J_{cis} = 10.2, $J_{8',7'}$ = 6.3, 8′-H), 7.47 (br. dd, $J_{3(5),2(6)} \approx J_{3(5),4} \approx$ 7.5, 3-H, 5-H), 7.60 (dddd, $J_{4,3} = J_{4,5}$ = 7.2, $^4J_{4,2} = {}^4J_{4,6}$ = 1.5, 4-H), 8.08 (incompletely resolved dm_c, $J_{2(6),3(5)}$ = 7.8, 2-H, 6-H); * coupling constants assigned on the basis of the intensity of cross-peaks with 1′-H (less intense) and 3′-H (more intense) in the H,H-correlation spectrum; ** coupling constants assigned on the basis of the intensity of cross-peaks with 1′-H (more intense) and 3′-H (less intense) in the H,H-correlation spectrum. – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 31.81 and 35.18 (C-6′, C-7′)*, 39.66 (C-2′)*, 44.50 (C-4′)**, 46.71 (C-1′′)**, 65.19 (C-3′), 71.27 (C-1′), 112.78 and 114.81 (5′=CH_2, C-9′), 128.44 (C-3, C-5)***, 129.54 (C-1), 129.80 (C-2, C-6)***, 133.35 (C-4)***, 137.94 (C-8′)***, 145.27 (C-5′), 166.55 (C=O); *, **, *** assignment corroborated by H,C-correlation spectrum. – $C_{18}H_{23}ClO_3$ (322.8): calcd. C 66.97, H 7.18; found C 67.01, H 7.21.

Methyl (6R,8R)-8-(Benzoyloxy)-9-chloro-6-hydroxy-4-oxononanoate (**36**): The diene **35** (637.5 mg, 1.98 mmol) was ozonolyzed in MeOH (13 ml) at −78°C until persistance of blue color (35 min). Oxygen was bubbled through this solution for 1 h. The resulting colorless solution was treated with camphorsulfonic acid (81 mg, 0.37 mmol, 0.19 equiv.). After removal of the cold bath, the reaction mixture was stirred for 1.5 h and treated with $NaHCO_3$ (104 mg, 1.07 mmol) for 15 min. The resulting suspension was filtered and the filtrate evaporated at reduced pressure. The residue was dissolved in MTB (4 × 20 ml) and evaporated in vacuo to remove traces of methanol. The resulting oily residue was taken up in anhydrous THF (20 ml) and the resulting solution treated dropwise with dry NEt_3 (0.62 ml, 450 mg, 4.5 mmol, 2.3 equiv.) and Ac_2O (0.21 ml, 220 mg, 2.2 mmol, 1.1 equiv.). After stirring at room temperature for 30 min, the solution was treated again with dry NEt_3 (0.37 ml, 270 mg, 2.7 mmol, 1.4 equiv.) and Ac_2O (0.13 ml, 140 mg, 1.4 mmol, 0.7 equiv.) and stirred for an additional 30-min period. The reaction mixture was treated with saturated aqueous $NaHCO_3$ (5 ml) and extracted with CH_2Cl_2 (4 × 25 ml). The combined organic extracts were dried over $NaSO_4$, filtered and concentrated in vacuo to give a yellow oily residue (805.1 mg) which was submitted to flash chromatography (silica gel, 80 g, 3.5 cm, PE/MTB 60:40): $\tilde{\nu}$ = 3510 cm^{-1}, 2955, 1715, 1600, 1585, 1450, 1435, 1410, 1360, 1315, 1275, 1200, 1175, 1110, 1070, 1025, 715. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = AB signal (δ_A = 1.84, δ_B = 1.96, J_{AB} = 14.4, in addition split by $J_{A,6}$ = 10.4*, $J_{A,8}$ = 3.6*, $J_{B,8}$ = 9.2**, $J_{B,6}$ = 2.9**, 7-H_2), 2.53–2.81 (m, 2-H_2, 3-H_2, 5-H_2), 3.42 (d, J_{vic} = 3.3, OH), 3.66 (s, CH_3), AB signal (δ_A = 3.75, δ_B = 3.88, J_{AB} = 11.7, in addition split by $J_{A,8}$ = 4.8, $J_{B,8}$ = 4.1, 9-H_2), 4.18 (m_c, 6-H), 5.54 (m_c, perhaps interpretable as dddd, $J_{8,7\text{-H}(2)}$ = 9.0, $J_{8,9\text{-H}(1)}$ = 5.0, $J_{8,7\text{-H}(1)} \approx J_{8,9\text{-H}(2)} \approx$ 3.9, 8-H), 7.46 (dd with two small extra-peaks, $J_{3'(5'),2'(6')} \approx J_{3'(5'),4'} \approx$ 7.5, 3′-H, 5′-H), 7.59 (dddd, $J_{4',3'} = J_{4',5'}$ = 7.4, $^4J_{4',2'} = {}^4J_{4',6'}$ = 1.6, 4′-H), 8.07 (dm_c, $J_{2'(6'),3'(5')} \approx$ 8.5, 2′-H, 6′-H); * coupling constants assigned on the basis of the intensity of cross-peaks with 6-H (more intense) and 8-H (less intense) in the H,H-correlation spectrum; ** coupling constants assigned on the basis of the intensity of cross-peaks with

6-H (less intense) and 8-H (more intense) in the H,H-correlation spectrum. − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 27.45 (C-2)*, 37.80 (C-3)*,**, 38.94 (C-7)**, 46.55 (C-9)**, 49.39 (C-5)**, 51.83 (CH_3), 63.91 (C-6), 70.65 (C-8), 128.46 (C-3′, C-5′)***, 129.56 (C-1′), 129.85 (C-2′, C-6′)***, 133.39 (C-4′)***, 166.50 (1′-C=O)****, 173.26 (C-1)****, 208.84 (C-4); * distinguished by comparison with δ calculated from tabulated values ($\delta_{calc.}$ = 29.9 for C-2, $\delta_{calc.}$ = 38.2 for C-3); **, *** distinguishable by a C,H-correlation spectrum; **** distinguished by comparison with **33**, **34**, and **35** whose sole carbonyl group is a benzoyloxy group which resonates at δ = 165.62, 166.48, and 166.55, respectively. − $C_{17}H_{21}ClO_6$ (356.8): calcd. C 57.23, H 5.93; found C 57.46, H 6.09.

Methyl (4R,6S,8R)-8-(Benzoyloxy)-9-chloro-4,6-dihydroxynonanoate [*anti*-**37**; *90:10 (by Method A) and 82:18 (by Method B) Mixture with syn*-**37**] − *Method A:* To a solution of Me_4N^+ $HB(OAc)_3^-$ (4.296 g, 16.3 mmol) in anhydrous acetonitrile (7.5 ml) was added anhydrous HOAc (7.2 ml) and the mixture was stirred at room temp. for 30 min. The mixture was cooled to −40°C and a solution of keto ester **36** (577.5 mg, 1.62 mmol) in anhydrous acetonitrile (2.5 ml) was added via cannula. The reaction mixture was stirred at −40°C for 18 h, treated with saturated aqueous K_2CO_3 (20 ml), allowed to warm to room temp., and extracted with CH_2Cl_2 (4 × 75 ml). The combined organic extracts were dried with Na_2SO_4, filtered and concentrated in vacuo. The resulting residue was taken up in methanol (3 × 25 ml) and evaporated at reduced pressure to give a yellow oil* (543.3 mg) which was submitted to flash chromatography (silica gel, 45 g, 3 cm, PE/MTB, 70:30 → 20:80) to afford hydroxy ester *anti*-**37** (402.9 mg, 69%) as a colorless oil. − $[\alpha]_D^{24}$ = +12.9 (*c* = 2.15 in CH_2Cl_2). - * Note: This crude product can be used for the next step without further purification.

Method B: $LiClO_4$ (3 M in AcOEt, 0.93 ml, 2.8 mmol, 5 equiv.) was added dropwise at 0°C to a solution of keto ester **36** (200.0 mg, 0.56 mmol) in THF (10 ml). The mixture was stirred at 0°C for 10 min, cooled to −78°C, and treated with 2,6-lutidine·BH_3 (162.2 mg, 1.34 mmol, 2.4 equiv.). The reaction mixture was allowed to reach room temp., stirred overnight, treated with 1 N HCl (10 ml), and extracted with CH_2Cl_2 (3 × 25 ml). The combined organic extracts were dried with Na_2SO_4, filtered, and evaporated at reduced pressure to give a yellow oil (351.4 mg) which was submitted to flash chromatography (silica gel, 30 g, 2.5 cm, PE/MTB 70:30 → 20:80) to afford hydroxy ester *anti*-**37** (fractions 12−22, 137.0 mg, 68%) as a colorless oil. Note: When the reaction was carried out under the conditions described in ref.[27] [$LiClO_4$ (3 M in AcOEt, 2.5 equiv.) to **36** in THF at 0°C, 10 min; cooling to −78°C; 2,6-lutidine·BH_3 (1.2 equiv.), from −78°C to 0°C over 2 h, 1 h at 0°C], the starting keto ester was recovered (81%) and no hydroxy ester was isolated. − IR (NaCl): $\tilde{\nu}$ = 3435 cm^{-1}, 2950, 1720, 1715, 1600, 1585, 1450, 1435, 1360, 1315, 1275, 1175, 1115, 1070, 1025, 915, 835, 715. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.62 (m_c, 5-H_2)*,**, 1.71−1.82 (m, 3-H_2)*, 1.88 (m_c, 7-H_2)**, 2.46 (m_c, 2-H_2), 2.96 (almost unresolved d, J_{vic} = 3.4, 4-OH)***, 3.58 (m_c, 6-OH)***, 3.66 (s, CH_3), AB signal (δ_A = 3.75, δ_B = 3.82, J_{AB} = 11.8, in addition split by $J_{A,8}$ = 5.6, $J_{B,8}$ = 4.0, 9-H_2), 3.95 (m_c, 4-H, 6-H), 5.51 (m_c, perhaps interpretable as dddd, $J_{8,7\text{-H}(2)}$ = 9.3, $J_{8,9\text{-H}(1)}$ = 5.7, $J_{8,7\text{-H}(1)} \approx J_{8,9\text{-H}(2)} \approx$ 3.9, 8-H)****, 7.47 (dd with small extra-peaks indicating transition to higher order spectrum or the presence of *syn*-**37**, $J_{3'(5'),2'(6')} \approx J_{3'(5'),4'} \approx$ 7.7, 3′-H, 5′-H), 7.60 (dddd, $J_{4',3'} = J_{4',5'}$ = 7.4, $^4J_{4',2'} = {}^4J_{4',6'}$ = 1.6, 4′-H), 8.05−8.09 (m, 2′-H, 6′-H); * distinguishable by the absence (5-H_2) or presence (3-H_2) of a cross-peak with m_c at δ = 2.46 (2-H_2) in a H,H-correlation spectrum; ** distinguishable by the absence (5-H_2) or presence (7-H_2) of a cross-peak with 8-H resonance (δ = 5.51) in a H,H-correlation spectrum; *** assignment interchangeable; **** coupling constants tentatively assigned by analogy with **36**. − ^{13}C NMR (50.3 MHz, $CDCl_3$; impurity at δ = 130.00): δ = 30.60 (C-2)*, 32.21 (C-3)*, 40.23 (C-7)*, 42.82 (C-5)*, 46.67 (C-9)*, 51.71 (CH_3), 64.64 and 68.21 (C-4, C-6)**, 71.26 (C-8)**, 128.48 (C-3′, C-5′)***, 129.20 (C-1′), 129.91 (C-2′, C-6′)***, 133.56 (C-4′)***, 167.15 (1′-C=O)****, 174.59 (C-1)****; *, *** distinguishable by a C,H-correlation spectrum; ** (groupwise) distinguishable by a C,H-correlation spectrum; **** distinguished by comparison with **33**, **34**, and **35** whose sole carbonyl group is a benzoyloxy group which resonates at δ = 165.62, 166.48, and 166.55, respectively. − $C_{17}H_{23}ClO_6$ (358.8): calcd. C 56.91, H 6.46; found C 56.93, H 6.39.

Methyl (4S,6S,8R)-8-(Benzoyloxy)-9-chloro-4,6-dihydroxynonanoate (*syn*-**37**): Triethylborane (1.0 M in THF, 0.58 ml, 0.58 mmol, 1.2 equiv.) was added dropwise to a mixture of dry MeOH (1 ml) and anhydrous THF (4 ml). The resulting solution was stirred at room temp. for 1 h and cooled to −78°C. A solution of keto ester **36** (170.0 mg, 0.48 mmol) in anhydrous THF (1 ml) was added via cannula and the mixture was stirred at −78°C for an additional 1 h and treated portionwise with $NaBH_4$ (21.8 mg, 0.58 mmol, 1.2 equiv.). The reaction mixture was stirred overnight at −78°C, treated with AcOEt (2.5 ml) and allowed to warm to room temp. The resulting solution was treated with saturated aqueous NH_4Cl (2.5 ml), extracted with *t*BuOMe (3 × 20 ml), dried with Na_2SO_4, filtered and concentrated in vacuo. The resulting residue was taken up in MeOH (5 × 2 ml) and evaporated at reduced pressure to give a yellow oil (166.9 mg) which was submitted to flash chromatography (silica gel, 15 g, 1.5 cm, PE/MTB, 70:30 → 30:70) to afford hydroxy ester *syn*-**37** (102.9 mg, 60%) as a colorless oil. − IR (NaCl): $\tilde{\nu}$ = 3480 cm^{-1}, 2950, 1720, 1715, 1600, 1585, 1435, 1360, 1315, 1275, 1175, 1115, 1070, 1025, 855, 715. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.52−1.65 (m, 5-H_2)*, ca. 1.65 - ca. 1.78 (m, 3-H_2)**, superimposes in part 1.80 (ddd, J_{gem} = 14.0, $J_{7\text{-H}(1),6}$ = 10.2, $J_{7\text{-H}(1),8}$ = 3.3, 7-H^1)***,****, 1.92 (ddd, J_{gem} = 14.0, $J_{7\text{-H}(2),8}$ = 10.4, $J_{7\text{-H}(2),6}$ = 2.6, 7-H^2)***,****, 2.45 (t, $J_{2,3}$ = 7.2, 2-H_2), 3.66 (s, CH_3), AB signal (δ_A = 3.75, δ_B = 3.82, J_{AB} = 11.9, in addition split by $J_{A,8}$ = 5.9, $J_{B,8}$ = 3.8, 9-H_2), B-part partly superimposed by 3.81−3.91 (m, 4-H, 6-H, 4-OH)*****, 4.07 (br. s, 6-OH)*****, 5.49 (m_c, presumably interpretable as dddd, $J_{8,7\text{-H}(2)}$ = 10.2, $J_{8,9\text{-H(A)}}$ = 5.9, $J_{8,7\text{-H}(1)} \approx J_{8,9\text{-H(B)}} \approx$ 3.6, 8-H), 7.47 (dd with two small extra-peaks indicating transition to higher-order spectrum, $J_{3'(5'),2'(6')} \approx J_{3'(5'),4'} \approx$ 7.5, 3′-H, 5′-H), 7.62 (dddd, $J_{4',3'} = J_{4',5'}$ = 7.5, $^4J_{4',2'} = {}^4J_{4',6'}$ = 1.5, 4′-H), 8.06−8.10 (m, 2′-H, 6′-H); * distinguished from 2-H, 3-H, and 7-H through the cross-peaks with the common m for 4-H/6-H (δ = 3.81−3.91) and the absence of cross-peaks with the t at δ = 2.45 (2-H_2) and with the m_c at δ = 5.49 (8-H); ** distinguished from 2-H, 5-H, and 7-H through the cross-peak with the t at δ = 2.45 (2-H_2); *** distinguished from 3-H and 5-H through the cross-peak with the m_c at δ = 5.49 (8-H); **** *vicinal* coupling constants interchangeable; ***** OH-absoptions interchangeable. − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 29.92 (C-2)*, 32.45 (C-3)*, 40.72 (C-7)*, 42.74 (C-5)*, 46.55 (C-9)*, 51.59 (CH_3), 68.22 and 71.22 (C-4, C-6)**, 70.89 (C-8)**, 128.46 (C-3′, C-5′)***, 129.14 (C-1′), 129.87 (C-2′, C-6′)***, 133.54 (C-4′)***, 167.08 (1′-C=O)****, 174.40 (C-1)****; *, **, *** distinguishable by a C,H-correlation spectrum; **** distinguished by comparison with **33**, **34**, and **35** whose sole carbonyl group is a benzoyloxy group which resonates at δ = 165.62, 166.48, and 166.55, respectively.

(5R)-5-[(2S,4R)-4-(Benzoyloxy)-5-chloro-2-hydroxypentyl]-4,5-dihydro-2(3H)-furanone (*anti*-**38**; *Possibly 90:10 Mixture with*

syn-**38**$^{+}$)[32]: Camphorsulfonic acid (112.0 mg, 0.52 mmol, 0.3 equiv.) was added to a solution of hydroxy ester *anti*-**37** (700.0 mg, 1.95 mmol) in toluene (14 ml) and the mixture was heated at 40°C for 4 h. The solution was cooled to room temp., treated with $NaHCO_3$ (215.0 mg, 2.56 mmol) for 15 min, and filtered. The filtrate was evaporated at reduced pressure to give a yellow oil (843.8 mg) which was submitted to flash chromatography (silica gel, 80 g, 4 cm, PE/MTB, 50:50 → MTB) to afford lactone *anti*-**38** (523.7 mg, 82%)* as a colorless oil. − $[\alpha]_D^{24} = -33.6$ (c = 1.85 in CH_2Cl_2). − * Note: Starting from crude hydroxy ester *anti*-**37**, lactone *anti*-**38** was obtained in 78% overall yield for the two steps from keto ester **36**. − IR (NaCl): $\tilde{\nu}$ = 3465 cm^{-1}, 2950, 1770, 1720, 1715, 1700, 1600, 1585, 1455, 1435, 1360, 1315, 1275, 1180, 1155, 1115, 1050, 1025, 915, 830, 805, 715. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70−1.92 (m, 4-H^{1*}, 1′-H_2, 3′-H^1), superimposes in part 1.93 (ddd, J_{gem} = 14.4, $J_{3'\text{-H}(2),4'}$ = 11.4, $J_{3'\text{-H}(2),2'}$ = 2.7, 3′-H^2)**, 2.35 (m_c, 4-H^2)*,***, 2.47−2.54 (m, 3-H_2), 3.49 (br. d, J_{vic} = 3.8, OH), extreme AB signal (δ_A = 3.75, δ_B = 3.79, J_{AB} = 11.9, in addition split by $J_{A,4'}$ = 5.9, $J_{B,4'}$ = 4.4, 5′-H_2), superimposes in part ca. 3.82−3.92 (m, 2′-H), 4.78 (m_c, presumably interpretable as dddd, $J_a \approx J_b \approx$ 8.7, J_c = 6.3, J_d = 4.2, 5-H), 5.52 (m_c, presumably interpretable as dddd, $J_{4',3'\text{-H}(2)}$ = 10.5,**** $J_{4',5'\text{-H}(1)}$ = 6.0, $J_{4',5'\text{-H}(2)}$ = 4.5, $J_{4',3'\text{-H}(1)}$ = 2.6,**** 4′-H), 7.47 (ddm, $J_{3''(5'')2''(6'')} \approx J_{3''(5'')4''} \approx$ 7.5, 3′′-H, 5′′-H), 7.61 (dddd, $J_{4'',3''} = J_{4'',5''}$ = 7.5, $^4J_{4'',2''} = {}^4J_{4'',6''}$ = 1.5, 4′′-H), 8.05−8.09 (m, 2′′-H, 6′′-H); * assignment based on cross-peaks in a C,H-correlation spectrum; ** coupling constants assigned on the basis of the intensity of cross-peaks with 2′-H (vanishing intensity) and 4′-H (very intense) in the H,H-correlation spectrum; *** distinguished from 3-H_2 through the presence of cross-peaks (of low intensity, however) with 5-H resonance (δ = 4.78) in a H,H-correlation spectrum; **** coupling constants distinguished tentatively by the different intensities of cross-peaks with 3′-H^1 (less intense) and 3′-H^2 (more intense) in a H,H-correlation spectrum. − ^{13}C NMR (75.5 MHz, $CDCl_3$; $^{+}$reveals two C-5 peaks at δ_{anti} = 77.78 and δ_{syn} = 78.40 in a 90:10 intensity ratio): δ = 28.39 (C-4)*, 28.80 (C-3)*, 40.79 and 43.03 (C-1′, C-3′)*, 46.51 (C-5′)*, 63.87 (C-2′)**, 71.02 (C-4′)**, 77.78 (C-5)**, 128.59 (C-3′′, C-5′′)***, 129.02 (C-1′′), 130.08 (C-2′′, C-6′′)***, 133.79 (C-4′′)***, 167.53 (1′′-C=O)****, 177.20 (C-2)****; *, **, *** distinguishable by a C,H-correlation spectrum; **** distinguished by comparison with **33**, **34**, and **35** whose sole carbonyl group is a benzoyloxy group which resonates at δ = 165.62, 166.48, and 166.55, respectively. − $C_{16}H_{19}ClO_5$ (326.8): calcd. C 58.81, H 5.86; found C 58.53, H 6.02.

(5S)-5-[(2S,4R)-4-(Benzoyloxy)-5-chloro-2-hydroxypentyl]-4,5-dihydro-2(3H)-furanone (*syn*-**38**): Camphorsulfonic acid (14.0 mg, 0.07 mmol, 0.3 equiv.) was added to a solution of hydroxy ester *syn*-**37** (85.0 mg, 0.237 mmol) in toluene (2 ml) and the mixture was heated at 40°C for 4 h. The solution was cooled to room temp., treated with $NaHCO_3$ (27.0 mg, 0.32 mmol) for 15 min, and filtered. The filtrate was evaporated at reduced pressure to give a colorless oil (85.3 mg) which was submitted to flash chromatography (silica gel, 12 g, 1.5 cm, PE/MTB 50:50 → MTB) to afford lactone *syn*-**38** (66.4 mg, 85%) as a colorless oil. − $[\alpha]_D^{24} = +39.0$ (c = 1.51 in CH_2Cl_2). − IR (NaCl): $\tilde{\nu}$ = 3480 cm^{-1}, 2970, 1770, 1715, 1450, 1420, 1360, 1315, 1275, 1180, 1115, 1070, 1025, 915, 850, 825, 805, 715. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.78 (ddd, J_{gem} = 14.4, $J_{1'\text{-H}(1),5}$ = 5.1, $J_{1'\text{-H}(1),2'}$ = 4.2, 1′-H^1)*,**, 1.83−2.06 (m, 4-H^1, 1′-H^2, 3′-H_2), 2.35 (dddd, J_{gem} = 12.7, $J_{4\text{-H}(2),3\text{-H}(1)} = J_{4\text{-H}(2),3\text{-H}(2)} = J_{4\text{-H}(2),5}$ = 6.3, 4-H^2)***, 2.48−2.54 (m, 3-H_2), 2.75−3.35 (very br. s, OH), AB signal (δ_A = 3.76, δ_B = 3.83, J_{AB} = 11.9, in addition split by $J_{A,4'}$ = 5.9, $J_{B,4'}$ = 4.1, 5′-H_2), superimposes in part ca. 3.83−3.89 (m, 2′-H), 4.71 (dddd, $J_{5,4\text{-H}(1)} = J_{5,1'\text{-H}(2)}$ = 7.9, $J_{5,4\text{-H}(2)} = J_{5,1'\text{-H}(1)}$ = 6.2, 5-H), 5.52 (m_c, possibly interpretable as dddd, $J_{4',3'\text{-H}(1)}$ = 9.8, $J_{4',5'\text{-H}(1)}$ = 6.0, $J_{4',3'\text{-H}(2)} = J_{4',5'\text{-H}(2)}$ = 3.7, 4′-H), 7.47 (ddm$_c$, $J_{3''(5'')2''(6'')} \approx J_{3''(5'')4''} \approx$ 7.5, 3′′-H, 5′′-H), 7.61 (dddd, $J_{4'',3''} = J_{4'',5''}$ = 7.4, $^4J_{4'',2''} = {}^4J_{4'',6''}$ = 1.6, 4′′-H), 8.06−8.10 (m, 2′′-H, 6′′-H); * distinguished from 4-H, and 3′-H through the cross-peaks with both the m at δ = 3.83−3.89 (2′-H) and the dddd at δ = 4.71 (5-H); ** *vicinal* coupling constants interchangeable; *** distinguished from 3-H_2 through the presence of cross-peaks with 5-H resonance (δ = 4.71) in a H,H-correlation spectrum and corroborated by C,H-correlation spectrum. − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 28.20 (C-4)*, 28.54 (C-3)*, 40.08 (C-3′)*, 42.32 (C-1′)*, 46.60 (C-5′)*, 64.45 (C-2′)**, 71.08 (C-4′)**, 78.40 (C-5)**, 128.49 (C-3′′, C-5′′)***, 129.13 (C-1′′), 129.88 (C-2′′, C-6′′)***, 133.59 (C-4′′)***, 167.08 (1′′-C=O)****, 176.81 (C-2)****; *, **, *** distinguishable by a C,H-correlation spectrum; **** distinguished by comparison with **33**, **34**, and **35** whose sole carbonyl group is a benzoyloxy group which resonates at δ = 165.62, 166.48, and 166.55, respectively. − $C_{16}H_{19}ClO_5$ (326.8): calcd. C 58.81, H 5.86; found C 58.57, H 6.11.

(5R)-5-[(2R,4R)-5-Chloro-2,4-dihydroxypentyl]-4,5-dihydro-2(3H)-furanone (**39**): NaOMe (6.0 mg, 0.11 mmol, 0.4 equiv.) was added to a solution of benzoate *anti*-**38** (92.0 mg, 0.282 mmol) in dry MeOH (1 ml). The reaction mixture was stirred at room temp. for 3 h, concentrated in vacuo, diluted with brine (1 ml), and extracted with CH_2Cl_2 (3 × 10 ml). The combined organic extracts were dried with Na_2SO_4, filtered, and evaporated at reduced pressure to give a colorless oil* (65.3 mg) which was submitted to flash chromatography (silica gel, 6 g, 1 cm, PE/MTB, 30:70 → MTB → MTB/MeOH, 98:2) to afford lactone **39** (39.3 mg, 63%) as a colorless oil. − $[\alpha]_D^{24} = -44.7$ (c = 1.15 in CH_2Cl_2). − * Note: This crude product can be used for the next step without further purification. − IR (NaCl): $\tilde{\nu}$ = 3390 cm^{-1}, 2950, 2920, 1770, 1745, 1730, 1715, 1435, 1415, 1360, 1290, 1190, 1070, 920, 840, 740, 655. − ^{1}H NMR (300 MHz, $CDCl_3$; contains impurity signals which might be caused by some *syn*-isomer): δ = 1.60−1.75 (m, 3′-H_2)*, 1.76−1.85 (m, 1′-H_2)*, superimposes in part 1.91 (m_c, presumably interpretable as dddd, J_{gem} = 12.4, $J_a = J_b$ = 9.0, J_c = 8.3, 4-H^1)**, 2.40 (m_c, 4-H^2)**, 2.53−2.60 (m, 3-H_2), 3.18−3.30 (m, 2′-OH, 4′-OH), AB signal (δ_A = 3.55, δ_B = 3.63, J_{AB} = 11.0, in addition split by $J_{A,4'}$ = 6.8, $J_{B,4'}$ = 4.4, 5′-H_2), ca. 4.14 (m, 4′-H)***, superimposes in part ca. 4.22 (m_c, 2′-H)***, 4.82 (m_c, perhaps interpretable as dddd, $J_{5,4\text{-H}(1)} \approx J_a \approx$ 8.3, J_b = 6.6, J_c = 4.5, 5-H); * distinguishable by the absence (3′-H_2) or presence (1′-H_2) of a cross-peak with 5-H resonance (δ = 4.82) in a H,H-correlation spectrum; ** distinguished from 3-H_2 through the presence of cross-peaks (of low intensity, however) with 5-H resonance (δ = 4.82) in a H,H-correlation spectrum and assuming that only a 4-H but not a 3-H can resonate as much high-field as $\delta_{H\text{-}(1)}$ = 1.91; *** distinguishable by a H,H-correlation spectrum through the presence and absence, respectively, of a cross-peak with the AB signal of 5′-H_2. − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 28.20 (C-4)*, 28.82 (C-3)*, 40.82 (C-3′)*, 43.28 (C-1′)*, 49.96 (C-5′)*, 64.83 (C-2′)**, 68.47 (C-4′)**, 78.09 (C-5)**, 177.83 (C-2); *, ** distinguishable by a C,H-correlation spectrum. − $C_9H_{15}ClO_4$ (222.7): calcd. C 48.55, H 6.79; found C 48.77, H 7.01.

(5R)-5-{[(4S,6R)-6-(Chloromethyl)-2,2-dimethyl-1,3-dioxan-4-yl]methyl}-4,5-dihydro-2(3H)-furanone (**40**)[32][33]: To a solution of lactone **39** (58.0 mg, 0.260 mmol) and 2,2-dimethoxypropane (2.40 ml, 2.04 g, 19.5 mmol) in dry acetone (2 ml) was added a catalytic amount of camphorsulfonic acid and the reaction mixture was stirred at room temp. for 3 h. The resulting solution was treated with aqueous saturated $NaHCO_3$ (9 ml) and extracted with CH_2Cl_2 (3 × 15 ml). The combined organic extracts were dried with

Na_2SO_4, filtered, and evaporated at reduced pressure to give a yellow oil (61.3 mg) which was submitted to flash chromatography (silica gel, 6 g, 1 cm, PE/MTB, 70:30 → 30:70) to afford acetonide **40** (50.2 mg, 74%)* as a colorless oil. − $[\alpha]_D^{24} = -27.5$ ($c = 0.7$ in CH_2Cl_2). − * Note: Starting from crude lactone **39**, acetonide **40** was obtained in 66% overall yield from benzoate *anti*-**38** (after flash chromatography). − IR (NaCl): $\tilde{\nu} = 2985$ cm^{-1}, 2940, 1780, 1770, 1380, 1225, 1175, 1130, 1035, 985, 940, 915, 735. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 and 1.39 [2s, 2′′-$(CH_3)_2$], 1.67 (ddd, $J_{gem} = 12.9$, $J_{5''\text{-H(1)},4''} = 9.8$, $J_{5''\text{-H(1)},6''} = 6.5$, 5′′-H^1)*.**, superimposes in part ca. 1.72−1.83 (m, 1′-H_2, 5′′-H^2), superimposes in part 1.88 (dddd, $J_{gem} = 12.9$, $J_{4\text{-H(1)},3\text{-H(1)}} = J_{4\text{-H(1)},3\text{-H(2)}} = 9.6$, $J_{4\text{-H(1)},5} = 8.4$, 4-H^1)***, 2.36 ($m_c$, 4-H^2)***, 2.51−2.58 (m, 3-H_2), extreme AB signal ($\delta_A = 3.50$, $\delta_B = 3.53$, $J_{AB} = 11.3$, in addition split by $J_{A,6''} = 5.6$, $J_{B,6''} = 6.2$, 1′′′-H_2), 3.98−4.13 (m, 4′′-H, 6′′-H), 4.68 (m_c, 5-H); * assignment based on the existence of a cross-peak with the common m for 4′′-H/6′′-H and the absence of a cross-peak with 5-H in the H,H-correlation spectrum; ** *vicinal* coupling constants interchangeable; *** distinguished from 3-H_2 through the presence of cross-peaks (of low intensity, however) with 5-H resonance (δ = 4.68) in a H,H-correlation spectrum and assuming that only a 4-H but not a 3-H can resonate as much high-field as $\delta_{H\text{-}(1)} = 1.88$. − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.46 and 24.62 [2′′-$(CH_3)_2$)], 28.25 (C-4)*, 28.70 (C-3)*, 35.90 and 41.76 (C-1′, C-5′′)*, 46.67 (C-1′′′)*, 63.30 and 66.85 (C-4′′, C-6′′)**, 77.40 (C-5)**, 100.85 (C-2′′), 176.91 (C-2); *, ** (groupwise) distinguishable by a C,H-correlation spectrum. − $C_{12}H_{19}ClO_4$ (262.7): calcd. C 54.86, H 7.29; found C 54.84, H 7.32.

(5R)-5-{[(4S,6R)-6-(Benzoyloxymethyl)-2,2-dimethyl-1,3-dioxan-4-yl]methyl}-4,5-dihydro-2(3H)-furanone (**41**)[32]: A mixture of acetonide **40** (320.0 mg, 1.22 mmol) and sodium benzoate (360.0 mg, 2.49 mmol, 2.0 equiv.) in anhydrous DMSO (3 ml) was heated at 165°C for 4 h. The resulting solution was allowed to cool to room temp., diluted with 10% aqueous Na_2CO_3 (10 ml), and extracted with *t*BuOMe (3 × 100 ml). The combined organic extracts were washed with water (3 × 10 ml), dried with Na_2SO_4, filtered, and concentrated in vacuo to give a yellow oil (394.2 mg) which was submitted to flash chromatography (silica gel, 40 g, 3 cm, PE/MTB, 70:30 → 40:60) to afford benzoate **41** (375.2 mg, 88%) as a colorless oil. − $[\alpha]_D^{24} = -28.3$ ($c = 2.39$ in CH_2Cl_2). − IR (NaCl): $\tilde{\nu} = 2985$ cm^{-1}, 2940, 1775, 1720, 1600, 1450, 1380, 1315, 1275, 1225, 1170, 1115, 1040, 1025, 915, 715. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39 and 1.41 [2s, 2′′-$(CH_3)_2$], 1.65 (ddd, $J_{gem} = 12.8$, $J_{5''\text{-H(1)},4''} = 9.6$, $J_{5''\text{-H(1)},6''} = 5.9$, 5′′-H^1)*.**, 1.76−1.85 (m, 1′-H_2, 5′′-H^2), superimposes in part 1.89 (dddd, $J_{gem} = 12.6$, $J_{4\text{-H(1)},3\text{-H(1)}} = J_{4\text{-H(1)},3\text{-H(2)}} = 9.0$, $J_{4\text{-H(1)},5} = 8.3$, 4-H^1)***, 2.36 (dddd, $J_{gem} = 13.0$, $J_{4\text{-H(2)},3\text{-H(1)}} \approx J_{4\text{-H(2)},3\text{-H(2)}} \approx J_{4\text{-H(2)},5} \approx 6.6$, 4-H^2)***, 2.51−2.58 (m, 3-H_2), 4.08−4.40 (m, 4′′-H, 6′′-H, 1′′′-H_2), 4.71 (m_c, 5-H), 7.45 (ddm$_c$, $J_{3''''(5'''')},_{2''''(6'''')} \approx J_{3''''(5'''')},_{4''''} \approx 7.5$, 3′′′′-H, 5′′′′-H), 7.58 (dddd, $J_{4'''',3''''} = J_{4'''',5''''} = 7.4$, $^4J_{4'''',2''''} = {}^4J_{4'''',6''''} = 1.6$, 4′′′′-H), 8.03−8.07 (m, 2′′′′-H, 6′′′′-H); * distinguished from 1′-H/4-H through the existence of a cross-peaks with the common m for 4′′-H/6′′-H at δ = 4.40 and the absence of cross-peak with the m_c at δ = 4.71 (5-H); ** *vicinal* coupling constants interchangeable; *** distinguished from 3-H_2 through the presence of cross-peaks with 5-H resonance (δ = 4.71) in a H,H-correlation spectrum and assuming that only a 4-H but not a 3-H can resonate as much high-field as $\delta_{H\text{-}(1)} = 1.89$. − ^{13}C NMR (75.5 MHz, $CDCl_3$; with small contaminant peaks): δ = 24.58 and 24.64 [2′′-$(CH_3)_2$)], 28.37 (C-4)*, 28.81 (C-3)*, 34.55 (C-5′′)*, 41.99 (C-1′)*, 63.39 and 65.03 (C-4′′, C-6′′)**, 66.54 (C-1′′′), 77.52 (C-5)**, 100.83 (C-2′′), 128.37 (C-3′′′′, C-5′′′′)***, 129.64 (C-2′′′′, C-6′′′′)***, 129.98 (C-1′′′′), 133.04 (C-4′′′′)***, 166.43 (1′′′′-C=O)****, 177.02 (C-2)****; *, **, *** distinguishable by a C,H-correlation spectrum; **** distinguished by comparison with **33**, **34**, and **35** whose sole carbonyl group is a benzoyloxy group which resonates at δ = 165.62, 166.48, and 166.55, respectively. − $C_{19}H_{24}O_6$ (348.4): calcd. C 65.50, H 6.94; found C 65.33, H 7.14.

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[97421]