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Practical Construction of Taxoid C-Ring Segments with a Consecutive Heterodomino Transformation as the Key Reaction Step

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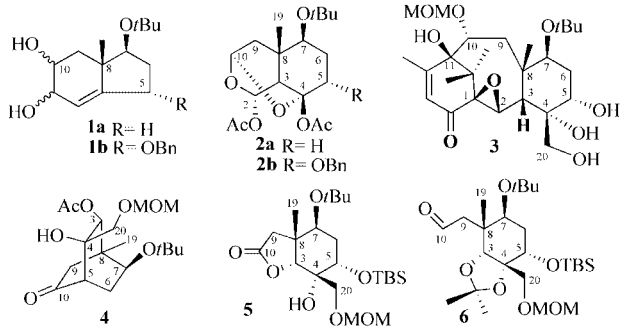
An efficient preparation of fully functional, optically homogeneous, taxoid C-ring C-10 electrophiles **5**, **6** and C-10 nucleophiles **18**, **19** that offer distinct linking possibilities with various A-ring precursors is described. The key feature of the synthetic scheme reported in this paper is the lead tetraacetate mediated consecutive domino reaction that enables the transformation of fused bicyclic diol **1** into bridged bicyclic aldol **7** in a single synthetic operation. Our retrosynthetic analysis calls for an introduction of the missing C-2 carbon in a post-coupling operation where an alkoxymethylenation would provide the electrophilic partner in the C-1–C-2 bonding.

Introduction

Three out of six total syntheses of taxol[1] used a convergent A + C approach; in such an approach, two six-membered ring fragments have to be constructed, coupled and elaborated to form the taxoid diterpene skeleton. Nicolaou,[1a] in his total synthesis of taxol, by proceeding in the A + C direction, constructed the C-ring precursor starting from mucic acid, whereas Danishefsky synthesized a fully functional C-ring starting from (*S*)-(+)-Wieland–Miescher ketone.[1c] Finally, Kuawajima[1f] started the synthesis of his C-ring precursor from 2-bromocyclohexenone, which was converted in eight steps into a cyclohexadiene derivative and used in the segment coupling. Recent papers from these laboratories have described a route to taxoid C-ring systems of type **2** that involved a $Pb(OAc)_4$ mediated domino[2] reaction (oxidative cleavage/cycloaddition/oxymetallation/ring expansion) of (*S*)-(+)-Hajos–Parrish ketone derived unsaturated diols of type **1** (Scheme 1). Our previous work, a convergent A + C approach to the taxoid ABC framework with a Still α-alkoxylithium methodology[3] (top side linking) and an intramolecular aldol reaction (bottom side linking) as key bond constructions, had demonstrated the suitability of the domino chemistry to access ABC-taxoid diterpene skeleton **3** (longest linear sequence: eight steps).[4] Although this method was reliable, we investigated an alternative route, which would produce the desired products more briefly without recourse to post-coupling operations at the C-ring level.



Scheme 1.

Even though a retrosynthetic analysis to construct a pentafunctionalized six-membered ring containing two quaternary centers may seem an easy task, severe length and selectivity problems could be encountered towards its realization. Our desire to improve the overall efficiency of this process and expand its applicability to related ring systems prompted us to examine modifications to this sequence. Despite the anticipated difficulty, on the basis of the proposed mechanism[5] of carrying out a domino reaction with a hindered unsaturated bicyclic diol such as **1b** we first investigated the latter as a model system containing the C-5 α-hydroxy group that is necessary for esterification.[6] To secure the formation of domino product **2b**, diol **1b** was treated with lead tetraacetate in a preheated oil bath at 100 °C (instead of the usual 25 °C) and provided the desired domino product in 21% isolated yield; far too inefficient to be synthetically useful because of the low mass recovery and low purity of the crude reaction product. Notwithstanding the high degree of oxygenation of **2b** thus obtained, its synthetic utility was compromised and so we had

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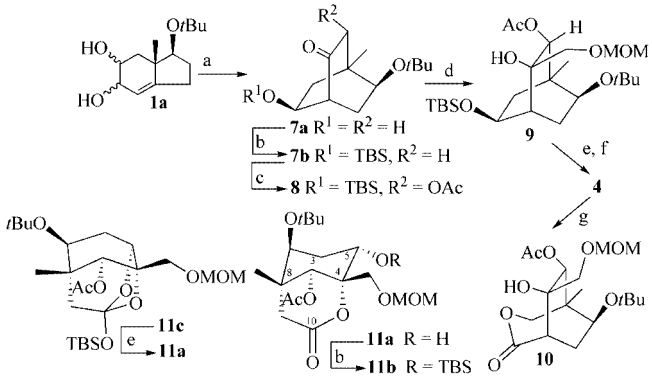
to seek an alternative strategy. The synthetic route chosen for the construction of the taxoid C-ring is based on the recently developed building block approach to bicyclo[2.2.2]aldol **7a** (Scheme 2) which utilizes a more benign version of the $Pb(OAc)_4$ induced heterodomino transformations with the use of only 1 equiv. of lead tetraacetate.[7] This three-reagent consecutive domino reaction initiated by $PhI(OAc)_2$ (oxidative/pericyclic), continued by $Pb(OAc)_4$ (ring expansion), and completed by a mild base consisting of solid K_2CO_3 (ring system interchange) all in one-pot allowed for a large scale preparation of key intermediate **7a**. This bicyclic aldol framework offered chemoselectivity because of the threefold different oxygenation pattern, and stereoselectivity, given that chemical modifications of bridged polycyclic compounds are highly stereoselective. Thus, with the aim of minimizing post-coupling elaboration, we focused on **11a** as an exact embodiment of a taxoid right-half moiety (C-ring), which contains all of the stereogenic centers in the desired absolute configuration and functionality at C-3/C-10 for linking with the A-ring counterpart. Our new goal, therefore, became the generation of a more functionalized C-ring candidate of type **5** or **6**, prior to C-10–C-11 linkage (taxoid numbering used throughout the text). Described below is an efficient route starting from bicyclic diol **1a**, which was converted to heavily substituted cyclohexane derivatives of type **5**, **6**, **18**, or **19** through a consecutive domino reaction followed by oxidation ring opening maneuvers (Schemes 3, 4, 5 and 6).

Results and Discussion

The taxoid C-ring has to contain a functional moiety that could ultimately be used to introduce the C-5 α-OH and the C-20 carbon that would offer further functionality; this would therefore ensure access to oxirane-, oxetane-, or olefin-containing taxoid families. The synthesis started with the experimentally simple reactions employed in effecting the one-pot transformation of fused bicyclic diol **1a** to bridged bicyclic aldol **7a** (Scheme 2) and hence to its TBS-protected derivative **7b** in large scale by using the protocol published in ref.[7] Two straightforward steps were then required for the incorporation of the oxygen functionalities at C-3 and the C-20 hydroxymethyl substituent. The best conversion of **7b** into requisite acyloin **8** was achieved by the anomalous ozonization of the silyl enol ether derivative of **7b** (MeOH, –78 °C) as described in the preceding article. This resulted in a 77.4% combined yield of a 21.7:1 mixture of *endo*-**8** and its corresponding *exo*-**8** adduct, separated by chromatography. On the other hand, direct acetoxylation of **7b** by treatment with $Pb(OAc)_4$ in benzene (90 °C, 2 d) afforded a modest 35% isolated yield of required α-acetoxyacyloin **8** along with unreacted starting material (40%). Subsequent addition of the α-alkoxyorganolithium derived from Bu_3SnCH_2OMOM[8] by transmetalation with *n*BuL*i* (*n*BuLi, Bu_3SnCH_2OMOM, in dry THF, –78 °C, 30 min) gave a mixture of two products: **9** and its deacetylated counterpart in a 75% combined yield and 1:2.7 ratio, together with recovered starting material (10%). All were separated by SiO_2 flash chromatography and isolated pure; the deacetylated product was quantitatively recycled by reacetylation (Ac_2O, pyridine, DMAP). Compound **9** was desilylated with tetrabutylammonium fluoride (TBAF, THF, 0 °C, 91%) to afford the corresponding alcohol which was further oxidized with the Dess–Martin protocol to required ketone **4** in nearly quantitative yield (Dess–Martin periodinane, CH_2Cl_2, pyridine, 25 °C, 96%).

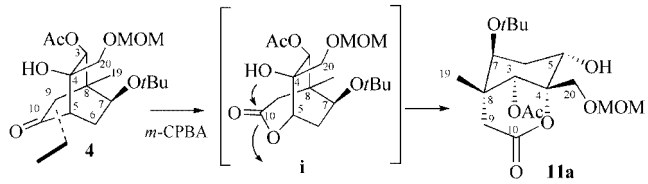


Scheme 2. a) 1.2 equiv. $PhI(OAc)_2$, 24 h, then 1.2 equiv. $Pb(OAc)_4$, PhMe, 15 h; then K_2CO_3–MeOH, H_2O, 25 °C; b) TBSOTf, collidine, CH_2Cl_2, 0 °C, 30 min; c) $Pb(OAc)_4$, PhH, 90 °C, 48 h; d) Bu_3SnCH_2OMOM, *n*BuLi, –78 °C; e) TBAF, THF, 0 °C; f) DMP, pyridine, CH_2Cl_2, 25 °C, 1 h; g) *m*-CPBA, $NaHCO_3$, CH_2Cl_2, 25 °C.

It was expected that Baeyer–Villiger oxidations of bridged bicyclic aldol **4** could afford lactones with reasonable control of bridgehead migration over methylene migration. In light of the intended application of this approach to the construction of taxoid C-ring precursors **5** and **6**, this concern had to be addressed. It thus turned out to be our initial objective to demonstrate that bicyclo[2.2.2]aldol **4** could be transformed into corresponding lactone **11a**; reductive or hydrolytic opening of the latter would in turn allow access to the desired C-ring candidates. To this end, **4** was oxidized with excess *m*-chloroperbenzoic acid in sodium hydrogencarbonate buffered dichloromethane, at room temperature to lactones **10** and **11a**, which result from methylene and bridgehead migration, respectively, in 60% isolated yield and a **10**/**11a** ratio of 1:4, along with recovered starting material (35%). The isomers were separated by chromatography and the major product was identified as lactone **11a**. The course of the Baeyer–Villiger oxidation[9] of **4** was readily determined, as the regiochemistry of the oxygen insertion was unambiguously confirmed by long-range heteronuclear couplings observed in the HMBC spectra. Ratios of the bridgehead to methylene migrated lactones were determined by SiO_2 separation and by comparison of the integrated areas for the methylene protons that are adjacent to the carbonyl group in bridgehead-migrated lactone **11a** (at δ = 2.24 and 2.52 ppm) to the oxygen in methylene-migrated lactone **10** (δ = 3.74 and 4.58 ppm) and the bridgehead proton at δ = 3.18 ppm in **10** which is absent in **11a**. Interestingly, this oxidation, unlike bicyclo[2.2.2]octanone counterpart **7a**,[6] gave a significant

amount of isomeric lactone **10**. At this stage it was decided to investigate procedures to improve both the yields and the **11a/10** ratio. On the basis of precedent, it seemed likely that the nature of the peroxy acid used may influence the results obtained. Among the various oxidants tried, including tBuO$_2$H, NaOH, THF,[10] NaBO$_3$, AcOH,[11] MMPP, DMF,[12] H$_2$O$_2$, AcONa, AcOH,[13] PhSeO$_2$H, H$_2$O$_2$, CH$_2$Cl$_2$, and H$_2$O,[14] none led to either one of the lactones; the only new compound was the C-3 deacetylated starting material when basic conditions were used (tBuO$_2$H–NaOH). The Sc(OTf)$_3$ or Yb(OTf)$_3$ catalyzed[15] Baeyer–Villiger oxidation with *m*-CPBA in CH$_2$Cl$_2$ was also tried but lead only to some tBu-deprotection and poor mass balance. The reactions were run under variable conditions. The temperature, number of equivalents of the oxidizing reagent, reaction times, and the nature of the oxidant used were all varied. Microbial Baeyer–Villiger oxidation[16] was also tried with the use of the fungus *Cunninghamella echinulata*[17] but failed to produce any lactone in a detectable amount. To summarize, while all attempts to increase the yields of lactones **10/11a** were unsuccessful, we were happy with an isolated 60% yield because the unreacted starting material (35%) was easily recovered by chromatography because of its large R_f difference and could therefore be recycled. Also, despite efforts to minimize the formation of undesired lactone **10**, the product distribution remained in the range of 4:1. One of the main points about the bridge migration during Baeyer–Villiger oxidation of bicyclic aldol **4** was that lactone **i** (oxabicyclo[3.2.2]nonan), initially formed as an electronically controlled transition state, is an intermediate in the formation of lactone **11a** (oxabicyclo[3.3.1]-nonan) towards which it evolves by spontaneous translactonization (Scheme 3).

The illustrated stereochemistries at the newly installed stereogenic centers, as well as bond connectivities, within these products follow from extensive NMR spectroscopic studies and were further corroborated by an X-ray crystallographic study on **10** and **11a** (Figure 1).



Scheme 3.

With lactone **11a** available, its conversion to **14** was explored (Scheme 4). TBS protection[18] of the free hydroxy group at C-5 (TBSOTf, collidine, CH$_2$Cl$_2$, 0 °C, 30 min) led to **11b** (Scheme 2), together with orthoester **11c** (95% combined yield, 4.3:1 ratio), which upon fluoride deprotection (TBAF, THF, 0 °C), was converted to **11a** and recycled. Reductive opening of the lactone was first accomplished by treatment with excess LiAlH$_4$, in THF at 0 °C. These conditions caused partial cleavage of the TBS ether to afford desired triol **12** (52%) accompanied by tetraol **13** (30%) and fused bicyclic lactone **5** (11%), which results from partial saponification at C-3 and subsequent intramolecular translactonization. Triol **12** was then converted into target C-ring C-10 electrophile **6** in two straightforward steps. Selective acetonide formation (acetone, *p*-TsOH, 25 °C, 3 h) furnished desired isopropylidene alcohol **14** (84% isolated yield), which in turn was oxidized with the use of the Dess–Martin protocol (DMP, pyridine, CH$_2$Cl$_2$, 25 °C, 30 min) to afford **6** (86%). Tetraol **13** could also be obtained by direct reduction of C-5-unprotected lactone **11a** under the same conditions. Subsequent selective acetonide formation (acetone, *p*-TsOH, 0 °C, 2.5 h) furnished **15** in 80% isolated yield. The latter can be used in the synthesis due to easy differentiation of the C-5/C-10 positions. The synthesis of a

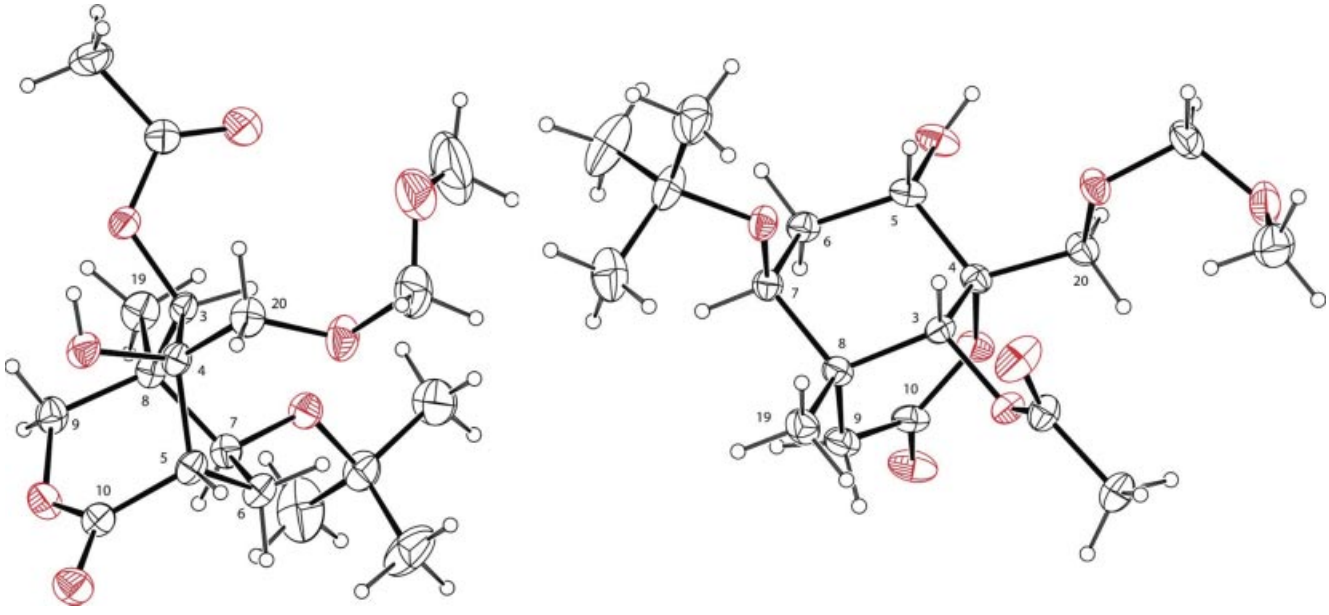
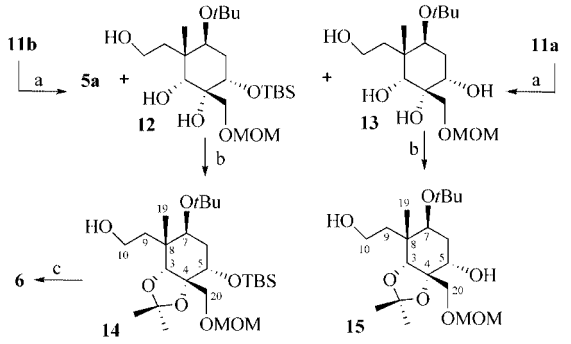


Figure 1. X-ray structures of **10** and **11a**.

fully functional taxoid C-ring precursor, C-10 electrophile **6**, which offers linking possibilities, is portrayed in Scheme 4.

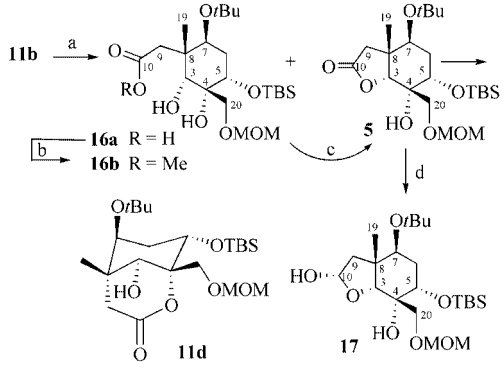


Scheme 4. a) $LiAlH_4$, THF, 0 °C, 2 h; b) acetone, *p*-TsOH, 25 °C, 2.5 h; c) Dess–Martin periodinane, CH_2Cl_2, pyridine, 25 °C, 0.5 h.

As mentioned above, reductive lactone opening was somehow complicated by loss of the *tert*-butyldimethylsilyl group which could reach levels as high as 30% depending upon reaction time and work up conditions. Other reducing agents were screened for transformation of **11b** into target molecule **6**, though without any significant improvement. To obviate these complications, we turned our attention to a hydrolytic lactone opening with K_2CO_3/MeOH-H_2O. Subjecting **11b** to these conditions for 20 h at room temperature gave a 90% combined yield of **16a** and **5** in a 4:1 ratio, respectively. Compound **16a**, which shows a marked tendency to lactonize on standing, was esterified ($TMSCHN_2$, Et_2O, MeOH, 25 °C, 1 h) to afford a 90% yield of **16b**, which again showed the same tendency towards formation of lactone **5**. Nearly quantitative formation of lactone **5** was secured while attempting to form the corresponding isopropylidene derivative (*p*-TsOH, acetone, 25 °C, 12 h).

As portrayed in Scheme 5, during the conversion of bridged bicyclic lactone **11b** to desired cyclohexane **16** upon hydrolytic lactone opening, **11d** is formed initially but rapidly converts to fused bicyclic lactone **5** by an intramolecular transesterification to give a less sterically congested product. This was proven experimentally by isolating and identifying **11d** during conversion. DIBAL reduction of **5** (DIBAL, PhMe, –78° to –40 °C, 2 h) gave a 93% isolated yield of lactol **17** along with trace amounts of its epimer (not isolated pure). Single-crystal X-ray diffraction analysis of crystalline lactol **17** (Figure 2), enabled unequivocal stereochemical assignment and further confirmed the correctness of previous assignments by NMR techniques throughout the synthetic scheme.

Finally, a two-step umpolung sequence applied to taxoid C-ring C-10 electrophile **6** then afforded α-alkoxyorganostannanes **18** and **19** to be used as the C-10 nucleophile precursors in our A + C approach (Scheme 6). Treatment of **6** with lithium tributylstannylate (in dry THF, –78 °C, 20 min) followed by protection of the resulting alcohol with chloromethyl methyl ether in the presence of Hünig's base (iPr_2NEt) gave a mixture of two products, **18** and **19** (75%



Scheme 5. a) K_2CO_3/MeOH/H_2O, 25 °C; b) $TMSCHN_2$, Et_2O, MeOH, 25 °C, 1 h; c) *p*-TsOH, acetone, 25 °C, 12 h; d) DIBAL, PhMe, –78° to –40 °C, 2 h.

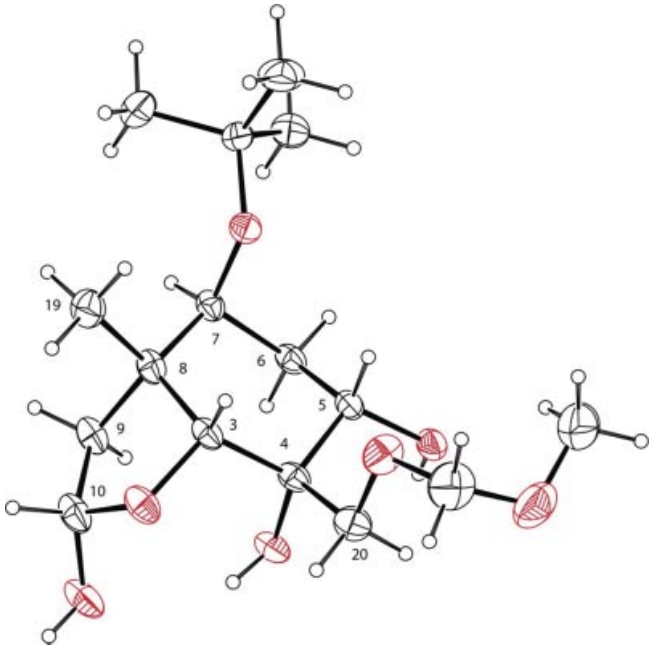
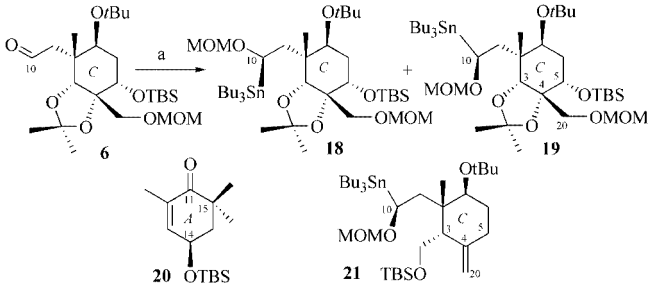


Figure 2. X-ray structure of **17**.

in 1:1 ratio), which were separated by chromatography and isolated pure. The two α-alkoxyorganostannanes thus obtained will herein be arbitrarily referred to as higher-R_f **18** and lower-R_f **19**.



Scheme 6. a) Bu_3SnH, LDA, THF, –78 °C; then MOMCl, iPr_2Net, CH_2Cl_2, 25 °C.

This completes the synthesis of second generation taxoid C-ring precursors. This process is considerably improved over the previously published routes. The observation that Still coupling is a useful reaction for the union of subunits **20** and **21** (first generation taxoid A- and C-rings, respectively) justifies the use of this reaction sequence in convergent strategies. By preparing compounds **5**, **6**, **18**, and **19** an additional functionalization step (the C-5 α-hydroxy function) was inserted prior to the beginning of the linear synthesis, while the C-20 hydroxymethyl group at the quaternary C-4 center was already installed.

Conclusions

From a practical standpoint, unraveling the bicyclo[2.2.2]octane moiety in a single step from bicyclic diol **1a**, rapidly introducing the C-3 then C-20 substituents and subjecting it to Baeyer–Villiger conditions offered the opportunity to prepare the second generation C-ring precursors. The most critical issues of our synthesis were the *m*-CPBA mediated Baeyer–Villiger oxidation and subsequent reductive lactone ring opening. Although the yields of these conversions were far from excellent, practical access to the required substrates became available. Overall, the approach represents an interesting application of LTA-mediated domino methodology, which provides fully functional, optically pure C-ring precursors minimizing post-coupling elaboration and nicely complements the C-ring syntheses published to date.

Experimental Section

General experimental details were previously described.[7] The term "usual work up" refers to washing the organic layer with brine, drying with anhydrous $MgSO_4$, and evaporating the solvent in vacuo with a rotary evaporator at aspirator pressure. Experimental evidence favoring the structures came from a comprehensive range of ^{1}H- and ^{13}C NMR spectroscopic data (1D and 2D experiments) and corroborated by spatial proximity (n.O.e) studies. X-ray analysis of **10**, **11a**, and **17** supports the suggested structures. CCDC-618901 (**10**), -618902 (**11a**), and -618903 (**17**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Elaboration of the C-4 Quaternary Center – Preparation of 9: To a magnetically stirred solution of Bu_3SnCH_2OMOM (6.46 g, 17.6 mmol) in anhydrous THF (15 mL) cooled to –78 °C under an argon atmosphere, *n*BuLi (1.6 M in hexane, 10.8 mL, 17.2 mmol) was added, and the mixture was stirred at this temperature for 10 min before **8** (2.93 g, 7.37 mmol) was added. After stirring 30 min at –78 °C, the reaction mixture was diluted with ethyl acetate and quenched with a saturated solution of NH_4Cl. Following usual work up, SiO_2 column chromatography (heptane/EtOAc, 15:1 to EtOAc) afforded 699 mg (20%) of **9**, 1.75 g (55%) of C-3-saponified diol **9**, along with recovered starting material **8** (295 mg, 10%).

7-*tert*-Butoxy-5-(*tert*-butyldimethylsilanyloxy)-3-hydroxy-3-methoxymethoxymethyl-1-methylbicyclo[2.2.2]oct-2-yla Acetate (9): $[\alpha]_D^{20}$ = +47 (*c* 1.0, $CHCl_3$). M.p. 137–139 °C (CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3451, 2973, 2953, 2934, 2858, 1731, 1247, 1046 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 3 H), 0.10 (s, 3 H), 0.87 (s, 3 H), 0.90 (s, 9 H), 1.13 (s, 9 H), 1.53 (ddd, *J* = 1.7, 9.5, 14.7 Hz, 1 H), 1.62 (ddd, *J* = 2.5, 8.8, 15.0 Hz, 1 H), 1.74 (ddd, 1 H, *J* = 2.3, 3.9, 15.0 Hz, 1 H), 1.82 (dd, *J* = 2.3, 14.7 Hz, 1 H), 2.07 (s, 3 H), 2.15 (q, *J* = 3.5 Hz, 1 H), 3.22 (dd, *J* = 2.2, 8.8 Hz, 1 H), 3.39 (s, 3 H), 3.60 (d, *J* = 10.9 Hz, 1 H), 4.00 (ddd, *J* = 2.3, 3.7, 9.5 Hz, 1 H), 4.09 (dd, *J* = 2.7, 10.9 Hz, 1 H), 4.54 (d, *J* = 1.5 Hz, 1 H), 4.69 (s, 2 H), 4.95 (d, *J* = 2.5 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.1, –4.9, 17.7, 20.9, 21.3, 25.7, 28.6, 33.0, 36.5, 37.0, 37.3, 55.4, 71.0, 71.1, 73.2, 73.3, 73.5, 97.2, 170.9 ppm. ESIMS (MeOH): *m*/z (%) = 497.2 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{24}H_{46}O_7NaSi$ 497.2911, found 497.2916. $C_{24}H_{46}O_7Si$ (474.30): calcd. C 60.72, H 9.77; found C 60.89, H 10.56.

7-*tert*-Butoxy-5-(*tert*-butyldimethylsilanyloxy)-3-methoxymethoxymethyl-1-methylbicyclo[2.2.2]octane-2,3-diol: $[\alpha]_D^{20}$ = +52 (*c* 1.6, $CHCl_3$). M.p. 42–43 °C (CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3394, 2956, 2930, 2860, 1043, 839 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (2s, 6 H), 0.90 (s, 9 H), 0.93 (s, 3 H), 1.11 (s, 9 H), 1.48 (ddd, *J* = 1.7, 9.7, 14.5 Hz, 1 H), 1.56 (dt, *J* = 3.3, 14.9 Hz, 1 H), 1.74 (ddd, *J* = 3.2, 9.3, 14.9 Hz, 1 H), 1.79 (dd, *J* = 4.4, 14.5 Hz, 1 H), 2.10 (q, *J* = 3.2 Hz, 1 H), 3.23 (dd, *J* = 3.4, 9.3 Hz, 1 H), 3.39 (s, 3 H), 3.41 (d, *J* = 1.7 Hz, 1 H), 3.46 (s, 1 H), 3.50 (d, *J* = 10.8 Hz, 1 H), 3.70 (dd, *J* = 1.7, 10.8 Hz, 1 H), 3.95 (ddd, *J* = 3.0, 4.4, 9.7 Hz, 1 H), 4.67 (d, *J* = 6.5 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.2, –4.8, 17.8, 20.4, 25.7, 28.6, 33.6, 36.0, 37.2, 38.4, 55.3, 68.4, 70.6, 71.7, 72.4, 73.1, 74.2, 96.9 ppm. ESIMS (MeOH): *m*/*z* (%) = 455.2 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{22}H_{44}O_6SiNa$ 455.2805; found 455.2812. $C_{22}H_{44}O_6Si$ (432.29): calcd. C 61.07, H 10.25; found C 61.08, H 10.24.

Preparation of the Baeyer–Villiger Precursor – Bicyclic Ketone 4: To a magnetically stirred solution of **9** (1.64 g, 3.46 mmol) in dry THF (35 mL) at –75 °C was added tetrabutylammonium fluoride (1 M in tetrahydrofuran, 10.4 mmol). The reaction mixture was stirred and warmed from –75 °C to –45 °C for 1 h 30 min (TLC monitoring). Ethyl acetate was then added, and following extraction the crude mixture was worked up as usual and purified by silica gel column chromatography (heptane/EtOAc, 3:1 to EtOAc) to give the diol-acetate (1.14 g, 91%).

7-*tert*-Butoxy-3,5-dihydroxy-3-methoxymethoxymethyl-1-methylbicyclo[2.2.2]oct-2-yl Acetate: $[\alpha]_D^{20}$ = +75 (*c* 1.1, $CHCl_3$). M.p. 99–100 °C (CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3396, 2973, 2934, 1732, 1455, 1368, 1247, 1046 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (s, 3 H), 1.13 (s, 9 H), 1.57 (td, *J* = 3.3, 14.9 Hz, 1 H), 1.65 (ddd, *J* = 1.8, 9.8, 14.7 Hz, 1 H), 1.74 (ddd, *J* = 3.0, 9.2, 14.9 Hz, 1 H), 1.84 (dd, *J* = 3.9, 14.7 Hz, 1 H), 2.11 (s, 4 H), 2.13 (m, 1 H), 3.26 (dd, *J* = 3.0, 9.2 Hz, 1 H), 3.39 (s, 3 H), 3.66 (d, *J* = 10.9 Hz, 1 H), 3.87 (td, *J* = 3.6, 9.8 Hz, 1 H), 3.94 (br. s, 1 H), 3.96 (d, *J* = 10.9 Hz, 1 H), 4.63 (d, *J* = 6.5 Hz, 1 H), 4.67 (d, *J* = 6.5 Hz, 1 H), 4.74 (d, *J* = 1.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6, 20.9, 28.7 (3 C), 33.8, 37.3, 37.5, 38.1, 55.6, 70.0, 70.8, 72.2, 73.5, 74.3, 74.5, 97.4, 170.9 ppm. ESIMS (MeOH): *m*/*z* (%) = 383.2 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{18}H_{32}O_7Na$ 383.2046; found 383.2061. $C_{18}H_{32}O_7$ (360,21): calcd. C 59.98, H 8.95; found C 60.07, H 8.95.

7-*tert*-Butoxy-3-hydroxy-3-methoxymethoxymethyl-1-methyl-5-oxobicyclo[2.2.2]oct-2-yl Acetate (4): A dry flask was charged with starting diols (1.13 g, 3.14 mmol) in dichloromethane (28 mL), pyridine (2.5 mL, 28.3 mmol), and Dess–Martin periodinane (3.62 g, 8.54 mmol). The mixture was stirred at room temperature for 1 h, (TLC monitoring). The reaction was then diluted with dichloromethane, quenched with a saturated aqueous solution of sodium hydrogencarbonate, and worked up as usual to afford, after purifi-

cation on silica gel column chromatography (heptane/EtOAc 2:1 to EtOAc), 1.08 g (96%) of **4**.$[\alpha]_D^{20}$ = +71 (*c* 1.2, MeOH). M.p. 92–93 °C (CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3446, 2972, 1735, 1373, 1232, 1055 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.92 (s, 3 H), 1.12 (s, 9 H), 1.73 (td, *J* = 3.0, 15.2 Hz, 1 H), 1.81 (dd, *J* = 1.7, 19.2 Hz, 1 H), 2.02 (ddd, *J* = 3.0, 9.4, 15.2 Hz, 1 H), 2.06 (s, 3 H), 2.54 (d, *J* = 19.1 Hz, 1 H), 2.54 (t, *J* = 3.1 Hz, 1 H), 3.04 (s, 1 H), 3.33 (s, 3 H), 3.45 (dd, *J* = 3.0, 9.3 Hz, 1 H), 3.74 (d, *J* = 11.0 Hz, 1 H), 3.91 (d, *J* = 11.0 Hz, 1 H), 4.57 (d, *J* = 6.5 Hz, 1 H), 4.61 (d, *J* = 6.5 Hz, 1 H), 4.93 (d, *J* = 1.9 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.7, 20.7, 28.5 (3 C), 31.6, 41.1, 42.4, 51.4, 55.5, 70.4, 71.0, 72.4, 73.4, 73.8, 97.2, 170.7, 211.5 ppm. ESIMS (MeOH): *m*/*z* (%) = 381.1 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{18}H_{30}O_7Na$ 381.1889; found 381.1854. $C_{18}H_{30}O_7$ (358.20): calcd. C 60.32, H 8.44; found C 60.27, H 8.52.

Baeyer–Villiger Oxidation of 4: Sodium hydrogencarbonate (642 mg, 7.64 mmol) and *m*-chloroperbenzoic acid (3.30 g, 19.10 mmol) were added to **4** (1.14 g, 3.18 mmol) in dichloromethane (20 mL) at 0 °C. The mixture was stirred at room temperature for approximately 17 h (TLC monitoring). The crude reaction mixture was diluted with dichloromethane and filtered through a plug of Celite. The excess peracid was decomposed by washing with aqueous 5% sodium sulfite. Finally, the organic phase was washed with saturated $NaHCO_3$ and worked up as usual to afford, after purification by flash chromatography (CH_2Cl_2/Me_2C=O, 95:5), 398 mg (35%) of starting material, 142 mg (12%) of **10**, and 571 mg (48%) of **11a**. For large scale experiments the lactone separation is better carried out after the TBS-protection step.

9-*tert*-Butoxy-7-hydroxy-7-methoxymethoxymethyl-5-methyl-2-oxo-3-oxabicyclo[3.2.2]non-6-yl Acetate (10): $[\alpha]_D^{20}$ = +109 (*c* 0.3, $CHCl_3$). M.p. 113–114 °C (CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3446, 2972, 1735, 1373, 1232, 1055 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.83 (s, 3 H), 1.18 (s, 9 H), 1.72 (ddd, *J* = 4.4, 6.0, 15.3 Hz, 1 H), 2.15 (s, 3 H), 2.42 (ddd, *J* = 3.0, 8.8, 15.3 Hz, 1 H), 3.18 (dd, *J* = 3.1, 4.3 Hz, 1 H), 3.34 (s, 1 H), 3.39 (s, 3 H), 3.57 (d, *J* = 10.5 Hz, 1 H), 3.62 (d, *J* = 10.5 Hz, 1 H), 3.74 (dd, *J* = 1.5, 12.2 Hz, 1 H), 3.84 (dd, *J* = 6.0, 8.8 Hz, 1 H), 4.58 (d, *J* = 12.2 Hz, 1 H), 4.61 (d, *J* = 6.5 Hz, 1 H), 4.64 (d, *J* = 6.5 Hz, 1 H), 5.11 (d, *J* = 1.5 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8, 20.9, 28.7 (3 C), 32.3, 42.5, 48.8, 55.8, 68.6, 71.1, 71.9, 72.0, 73.7, 74.1, 97.4, 170.2, 172.9 ppm. ESIMS (MeOH): *m*/*z* (%) = 397.1 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{18}H_{30}O_8Na$ 397.1838; found 397.1830. $C_{18}H_{30}O_8$ (374.19): calcd. C 57.74, H 8.08; found C 57.77, H 8.07.

6-*tert*-Butoxy-8-hydroxy-1-methoxymethoxymethyl-5-methyl-3-oxo-2-oxabicyclo[3.3.1]non-9-yl Acetate 11a: $[\alpha]_D^{20}$ = +44 (*c* 1.6, $CHCl_3$). M.p. 143–145 °C (CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3454, 2973, 1737, 1372, 1228, 1036 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.95 (s, 3 H), 1.20 (s, 9 H), 1.46 (ddd, *J* = 2.6, 11.9, 14.5 Hz, 1 H), 2.12 (s, 3 H), 2.16 (ddd, *J* = 2.8, 5.2, 14.5 Hz, 1 H), 2.28 (d, *J* = 19.0 Hz, 1 H), 2.54 (d, *J* = 19.0 Hz, 1 H), 3.35 (s, 3 H), 3.36 (d, *J* = 8.6 Hz, 1 H), 3.44 (t, *J* = 2.7 Hz, 1 H), 3.60 (d, *J* = 9.8 Hz, 1 H), 3.82 (d, *J* = 9.8 Hz, 1 H), 4.23 (ddd, *J* = 5.2, 8.6, 11.5 Hz, 1 H), 4.58 (d, *J* = 6.5 Hz, 1 H), 4.64 (d, *J* = 6.5 Hz, 1 H), 5.38 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6, 22.5, 28.7 (3 C), 34.0, 38.2, 39.8, 55.6, 65.4, 67.0, 67.6, 72.9, 74.7, 85.3, 97.1, 169.4, 169.7 ppm. ESIMS (MeOH): *m*/*z* (%) = 397.1 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{18}H_{30}O_8Na$ 397.1838; found 397.1804. $C_{18}H_{30}O_8$ (374.19): calcd. C 57.74, H 8.08; found C 57.59, H, 8.01.

Baeyer–Villiger Oxidation of **4** with *t*BuO_2H as the oxidant yielded only deacetylated **4**. A mixture of aldol **4** (51.3 mg, 0.14 mmol), *tert*-butyl hydroperoxide (70% aq., 55 µL, 0.43 mmol), and NaOH (10% aq., 68 µL, 0.17 mmol) in THF (1.4 mL) cooled to 0 °C was stirred for 30 min, and the mixture was then warmed to room temperature and stirred for ca. 6 h (TLC monitoring). The crude reaction mixture was taken up in ether (20 mL), the excess peracid was decomposed by washing with aqueous 5% sodium sulfite, and the organic phase was worked up as usual to give, after purification by silica gel column chromatography (heptane/AcOEt, 2:1 to AcOEt), only deacetylated starting material (C-3-OH)-**4** [41.6 mg (81%)].

8-*tert*-Butoxy-5,6-dihydroxy-6-methoxymethoxymethyl-4-methylbicyclo[2.2.2]octan-2-one: $[\alpha]_D^{20}$ = +72 (*c* 0.9, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3442, 2973, 2933, 1726, 1366, 1075, 1038 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.04 (s, 3 H), 1.15 (s, 9 H), 1.65 (ddd, *J* = 2.7, 3.8, 15.1 Hz, 1 H), 1.75 (dd, *J* = 2.1, 19.1 Hz, 1 H), 2.07 (ddd, *J* = 3.6, 9.4, 15.1 Hz, 1 H), 2.52 (d, *J* = 19.1 Hz, 1 H), 2.53 (dd, *J* = 2.7, 3.4 Hz, 1 H), 3.1 (d, *J* = 6.4 Hz, 1 H), 3.41 (s, 3 H), 3.45 (dd, *J* = 3.8, 9.4 Hz, 1 H), 3.63 (d, *J* = 11.0 Hz, 1 H), 3.77 (dd, *J* = 1.9, 6.0 Hz, 1 H), 3.88 (d, *J* = 11.0 Hz, 1 H), 3.99 (s, 1 H), 4.66 (d, *J* = 6.6 Hz, 1 H), 4.69 (d, *J* = 6.6 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5, 28.6 (3 C), 32.0, 42.2 (2 C), 51.4, 55.8, 68.2, 70.7, 72.0, 73.0, 73.7, 97.5, 212.1 ppm. ESIMS (MeOH): *m*/*z* (%) = 339.1 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{16}H_{28}O_6Na$ 339.1784; found 339.1788. $C_{16}H_{28}O_6$ (319.19) ·0.7H_2O: calcd. C 58.41, H 9.01; found C 58.43, H 8.75.

TBS-protection of C-5-OH: To a stirred solution of **11a** (163 mg, 0.44 mmol) and collidine (0.17 mL, 1.31 mmol) in dry dichloromethane (4.0 mL) at 0 °C under an argon atmosphere, was added TBSOTf (0.20 mL, 0.87 mmol). The mixture was stirred at room temperature for 30 min (TLC monitoring), diluted with heptane, washed with diluted $NaHCO_3$ and worked up as usual. After purification by silica gel column chromatography (heptane/AcOEt, 5:1 to AcOEt), 163 mg (77%) of **11b**, and 39 mg (18%) of secondary product **11c** were obtained.

6-*tert*-Butoxy-8-(*tert*-butyldimethylsilanyloxy)-1-methoxymethoxymethyl-5-methyl-3-oxo-2-oxabicyclo[3.3.1]non-9-yl Acetate (11b): $[\alpha]_D^{20}$ = +6 (*c* 0.8, $CHCl_3$). M.p. 89–90 °C (CH_2Cl_2). IR (film): $\tilde{\nu}$ = 2930, 2857, 1741, 1228, 1116, 1038, 837 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 3 H), 0.07 (s, 3 H), 0.88 (s, 9 H), 0.94 (s, 3 H), 1.21 (s, 9 H), 1.55 (ddd, *J* = 2.6, 11.7, 14.3 Hz, 1 H), 1.99 (ddd, *J* = 3.0, 5.0, 14.3 Hz, 1 H), 2.12 (s, 3 H), 2.24 (d, *J* = 19.0 Hz, 1 H), 2.52 (d, *J* = 19.0 Hz, 1 H), 3.33 (s, 3 H), 3.40 (t, *J* = 2.7 Hz, 1 H), 3.59 (d, *J* = 9.1 Hz, 1 H), 3.72 (d, *J* = 9.1 Hz, 1 H), 4.26 (dd, *J* = 5.0, 11.7 Hz, 1 H), 4.54 (d, *J* = 6.6 Hz, 1 H), 4.59 (d, *J* = 6.6 Hz, 1 H), 5.39 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.8, –4.1, 18.0, 20.7, 22.7, 25.8 (3 C), 28.7 (3 C), 34.6, 38.4, 39.8, 55.9, 64.6, 66.9, 67.7, 73.2, 74.5, 85.6, 97.3, 169.5, 169.8 ppm. ESIMS (MeOH): *m*/*z* (%) = 511.2 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{24}H_{44}O_8NaSi$ 511.2703; found 511.2669. $C_{24}H_{44}O_8Si$ (488.28): calcd. C 58.99, H 9.08; found C 59.16, H, 9.03.

5-*tert*-Butoxy-1-(*tert*-butyldimethylsilanyloxy)-8-methoxymethoxymethyl-6-methyl-2,9-dioxatricyclo[4.1.1.$1^{1,6}$]dec-7-yl Acetate (11c): $[\alpha]_D^{20}$ = +61 (*c* 0.5, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2929, 2857, 1746, 1367, 1232, 1039, 840 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.18 (s, 6 H), 0.84 (s, 3 H), 0.91 (s, 9 H), 1.15 (s, 9 H), 1.54 (ddd, *J* = 0.9, 7.5, 14.7 Hz, 1 H), 1.69 (d, *J* = 13.6 Hz, 1 H), 2.00 (d, *J* = 13.6 Hz, 1 H), 2.14 (s, 3 H), 2.51 (ddd, *J* = 4.2, 8.1, 14.7 Hz, 1 H), 3.35 (s, 3 H), 3.47 (d, *J* = 10.0 Hz, 1 H), 3.57 (d, *J* = 10.0 Hz, 1 H), 3.71 (t, *J* = 7.8 Hz, 1 H), 4.19 (dd, *J* = 0.9, 4.2 Hz, 1 H), 4.58 (d, *J* = 6.5 Hz, 1 H), 4.63 (d, *J* = 6.5 Hz, 1 H), 5.15 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –3.4, –3.3, 17.8, 20.7, 20.9, 25.8 (3 C), 28.7 (3 C), 35.5, 39.6, 46.8, 55.4, 67.6, 68.3, 73.3, 73.6, 74.6, 80.6, 97.0, 117.1, 170.7 ppm. ESIMS (MeOH): *m*/*z* (%) = 511.2 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{24}H_{44}O_8NaSi$

511.2703; found 511.2697. $C_{24}H_{44}O_8Si$ (488.28): calcd. C 58.99, H 9.08; found C 58.82, H 9.03.

Reductive Opening of Lactone 11b with Lithium Aluminum Hydride and Selective Acetonide Formation: To a magnetically stirred suspension of $LiAlH_4$ (24 mg, 0.64 mmol) in THF (2 mL) at 0 °C was added a solution of **11b** (156 mg, 0.32 mmol) in THF (2.5 mL). The mixture was stirred at this temperature for 1 h (TLC monitoring), diluted with diethyl ether, worked up as usual to give, after purification on silica gel column chromatography (heptane/AcOEt, 5:1 to AcOEt) 15.7 mg (11%) of **5**, 75 mg (52%) of **12**, along with its TBS-deprotected counterpart **13** (32 mg, 30%).

4-*tert*-Butoxy-6-(*tert*-butyldimethylsilanyloxy)-3-(2-hydroxyethyl)-1-methoxymethoxymethyl-3-methyl-cyclohexane-1,2-diol (12): $[\alpha]_D^{20}$ = +13 (*c* 1.3, $CHCl_3$). M.p. 50 °C (CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3418, 2956, 2929, 2887, 2857, 1471, 1362, 1252, 1045, 836 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 6 H), 0.91 (s, 9 H), 1.10 (s, 3 H), 1.20 (s, 9 H), 1.26 (td, *J* = 3.2, 15.0 Hz, 1 H), 1.60 (br. s, 1 H), 1.75 (ddd, *J* = 4.0, 4.9, 13.3 Hz, 1 H), 1.91 (ddd, *J* = 2.0, 11.5, 13.3 Hz, 1 H), 2.45 (td, *J* = 7.6, 15.0, Hz, 1 H), 2.70 (br. s, 1 H), 3.30 (dd, *J* = 2.3, 4.0 Hz, 1 H), 3.35 (d, *J* = 9.2 Hz, 1 H), 3.39 (s, 3 H), 3.65 (s, 1 H), 3.76 (m, 3 H), 3.77 (d, *J* = 9.2 Hz, 1 H), 4.20 (d, *J* = 5.2, 11.4 Hz, 1 H), 4.63 (d, *J* = 6.2 Hz, 1 H), 4.67 (d, *J* = 6.2 Hz, 1 H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = –4.9, –4.1, 18.0, 21.6, 25.8 (3 C), 28.8 (3 C), 33.4, 39.2, 42.1, 55.5, 58.9, 67.2, 68.1, 70.8, 73.5, 74.1, 77.2, 97.0 ppm. ESIMS (MeOH): *m*/*z* (%) = 473.2 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{22}H_{46}O_7NaSi$ 473.2911; found 473.2937. $C_{22}H_{46}O_7Si$ (450.30)·0.25H_2O: calcd. C 57.28, H 10.16; found C 57.55, H 9.79.

5-*tert*-Butoxy-4-(2-hydroxyethyl)-2-methoxymethoxymethyl-4-methylcyclohexane-1,2,3-triol (13): $[\alpha]_D^{20}$ = +20 (*c* 1.0, MeOH). M.p. 50 °C (CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.03 (s, 3 H), 1.13 (s, 9 H), 1.60 (td, *J* = 5.6, 14.6 Hz, 1 H), 1.76 (td, *J* = 4.3, 13.1 Hz, 1 H), 2.01 (ddd, *J* = 2.0, 12.0, 13.2 Hz, 1 H), 2.28 (ddd, *J* = 6.8, 8.2, 14.6 Hz, 1 H), 3.36 (s, 3 H), 3.54 (dd, *J* = 2.0, 4.3 Hz, 1 H), 3.54 (s, 1 H), 3.54 (d, *J* = 8.9 Hz, 1 H), 3.58 (d, *J* = 8.9 Hz, 1 H), 3.63 (m, 1 H), 3.71 (m, 1 H), 4.09 (dd, *J* = 4.7, 12.0 Hz, 1 H), 4.62 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.2, 29.1 (3 C), 33.7, 37.9, 43.5, 55.5, 59.6, 66.6, 69.8, 72.7, 74.4, 74.5, 77.4, 97.9 ppm. ESIMS (MeOH): *m*/*z* (%) = 359.2 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{16}H_{32}O_7Na$ 359.2046; found 359.2044.

2-[5-*tert*-Butoxy-7-(*tert*-butyldimethylsilanyloxy)-7a-methoxymethoxymethyl-2,2,4-trimethyl-hexahydrobenzo[1,3]dioxol-4-yl]ethanol (14): To a stirred solution of **12** (190 mg, 0.42 mmol) in acetone (2 mL), dry Na_2SO_4 (1.0 g) and *p*-TsOH (20 mg) were added at 0 °C. The mixture was stirred at room temperature for 1 h 15 min (TLC monitoring) and then filtered through alumina. Purification by silica gel column chromatography (heptane/AcOEt, 7:1 to 3:1) afforded 173 mg (84%) of isopropylidene alcohol **14** and 8.3 mg (7%) of overprotection in the form of mixed acetal. Compound **14**: $[\alpha]_D^{20}$ = +25 (*c* 0.6, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3471, 2955, 2930, 2857, 1255, 1081, 1041, 835 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 3 H), 0.09 (s, 3 H), 0.92 (s, 9 H), 0.95 (s, 3 H), 1.19 (s, 9 H), 1.38 (s, 3 H), 1.50 (s, 3 H), 1.71 (ddd, *J* = 3.9, 8.6, 14.1 Hz, 1 H), 1.86 (m, 2 H), 1.95 (ddd, *J* = 5.0, 6.0, 14.1 Hz, 1 H), 2.60 (br. s, 1 H), 3.37 (s, 3 H), 3.48 (d, *J* = 10.5 Hz, 1 H), 3.58 (d, *J* = 10.5 Hz, 1 H), 3.77 (m, 2 H), 3.89 (dd, *J* = 3.9, 6.0 Hz, 1 H), 3.90 (dd, *J* = 5.0, 8.6 Hz, 1 H), 4.13 (s, 1 H), 4.64 (d, *J* = 6.5 Hz, 1 H), 4.67 (d, *J* = 6.5, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.6, –4.2, 17.0, 18.7, 26.2, 26.5 (3 C), 26.9, 29.1 (3 C), 36.6, 39.0, 41.3, 55.5, 59.1, 68.5, 68.7, 70.1, 73.5, 81.3, 82.1, 96.8, 107.4 ppm. ESIMS (MeOH): *m*/*z* (%) = 513.3 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{25}H_{50}O_7NaSi$ 513.3224; found 513.3208. $C_{25}H_{50}O_7Si$ (490.33)·0.2C_7H_{16}: calcd. C 62.08, H 10.50; found C 62.24, H 10.28.

{6-*tert*-Butoxy-3a-methoxymethoxymethyl-7-[2-(1-methoxy-1-methylethoxy)-ethyl]-2,2,7-trimethyl-hexahydrobenzo[1,3]dioxol-4-yloxy}*tert*-butyldimethylsilane: $[\alpha]_D^{20}$ = +19 (*c* 1.0, $CHCl_3$).IR (film): $\tilde{\nu}$ = 2955, 2933, 2886, 2858, 1464, 1377, 1364, 1256, 1041, 837, 775 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 3 H), 0.07 (s, 3 H), 0.91 (s, 9 H), 0.92 (s, 3 H), 1.18 (s, 9 H), 1.33 (s, 6 H), 1.35 (s, 3 H), 1.46 (s, 3 H), 1.67 (ddd, *J* = 4.0, 7.8, 14.0 Hz, 1 H), 1.73–1.88 (m, 2 H), 1.94 (ddd, *J* = 5.2, 6.9, 14.0 Hz, 1 H), 3.19 (s, 3 H), 3.36 (s, 3 H), 3.46 (d, *J* = 10.5 Hz, 1 H), 3.47 (m, 1 H), 3.56 (d, *J* = 10.5 Hz, 1 H), 3.57 (m, 1 H), 3.83 (dd, *J* = 5.3, 7.8 Hz, 1 H), 3.90 (dd, *J* = 3.9, 6.9 Hz, 1 H), 4.00 (s, 1 H), 4.63 (d, *J* = 6.5 Hz, 1 H), 4.65 (d, *J* = 6.5 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.5, –4.1, 17.3, 18.6, 24.4, 24.6, 26.1, 26.4 (3 C), 27.0, 29.1 (3 C), 36.8, 38.4, 38.6, 48.4, 55.5, 57.0, 68.5, 69.3, 70.3, 73.3, 81.1, 81.7, 96.9, 99.9, 107.2 ppm. ESIMS (MeOH): *m*/*z* (%) = 585.3 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{29}H_{58}O_8NaSi$ 585.3799; found 585.3814. $C_{29}H_{58}O_8Si$ (562.39)·0.3H_2O: calcd. C 63.00, H 10.68; found C 63.15, H 10.38.

Oxidation of 14 with Dess–Martin's Periodinane: To a solution of the above isopropylidene alcohol **14** (70 mg, 0.14 mmol) in dry dichloromethane (2 mL) and pyridine (0.12 mL, 1.4 mmol) was added periodinane (182 mg, 0.42 mmol). Stirring was continued at room temperature for 30 min. The reaction was then diluted with dichloromethane, quenched with a saturated aqueous solution of sodium hydrogencarbonate, washed with 5% aqueous $Na_2S_2O_3$ and then brine, and worked up as usual to give, after silica gel column chromatography (heptane/EtOAc, 10:1 to 4:1), 60 mg (86%) of **6** as an oil.

[5-*tert*-Butoxy-7-(*tert*-butyldimethylsilanyloxy)-7a-methoxymethoxymethyl-2,2,4-trimethylhexahydrobenzo[1,3]dioxol-4-yl]acetaldehyde (6): $[\alpha]_D^{20}$ = +38 (*c* 1.4, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2934, 2885, 2857, 1720, 1463, 1377, 1257, 1077, 1040, 836 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 3 H), 0.09 (s, 3 H), 0.92 (s, 9 H), 1.07 (s, 3 H), 1.19 (s, 9 H), 1.34 (s, 3 H), 1.48 (s, 3 H), 1.71 (ddd, *J* = 3.9, 9.1, 14.1 Hz, 1 H), 1.95 (ddd, *J* = 5.1, 5.7, 14.1 Hz, 1 H), 2.49 (dd, *J* = 3.7, 15.4 Hz, 1 H), 2.62 (dd, *J* = 1.5, 15.4 Hz, 1 H), 3.36 (s, 3 H), 3.49 (d, *J* = 10.4 Hz, 1 H), 3.56 (d, *J* = 10.4 Hz, 1 H), 3.91 (dd, *J* = 3.9, 5.7 Hz, 1 H), 4.01 (dd, *J* = 4.9, 9.1 Hz, 1 H), 4.21 (s, 1 H), 4.63 (d, *J* = 6.7 Hz, 1 H), 4.66 (d, *J* = 6.7 Hz, 1 H), 9.88 (dd, *J* = 1.5, 3.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.6, –4.2, 17.6, 18.6, 26.3, 26.5 (3 C), 27.0, 29.1 (3 C), 36.5, 40.0, 52.1, 55.6, 67.6, 68.9, 70.3, 73.8, 81.0, 82.1, 96.9, 107.8, 203.5 ppm. ESIMS (MeOH): *m*/*z* (%) = 511.3 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{25}H_{48}O_7NaSi$ 511.3067; found 511.3065. $C_{25}H_{48}O_7Si$ (488.32)·0.35CH_2Cl_2: calcd. C 58.73, H 9.47; found C 58.52, H 9.45.

Selective Acetonide Formation from Tetraol 13: Proceeding as above, **13** (37 mg, 0.11 mmol) in acetone (1 mL), molecular sieves, dry Na_2SO_4 (500 mg), and *p*-TsOH (catalytic) at 0 °C to room temperature for 3 h afforded, after chromatography (heptane/EtOAc, 3:1 to EtOAc), single acetonide **15** (33 mg, 80%).

{6-*tert*-Butoxy-3a-methoxymethoxymethyl-7-[2-(1-methoxy-1-methylethoxy)ethyl]-2,2,7-trimethylhexahydrobenzo[1,3]dioxol-4-yloxy}*tert*-butyldimethylsilane (15): $[\alpha]_D^{20}$ = +22 (*c* 0.4, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3447, 2975, 2939, 2886, 1380, 1043 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.97 (s, 3 H), 1.21 (s, 9 H), 1.44 (s, 3 H), 1.53 (s, 3 H), 1.75 (ddd, *J* = 4.0, 9.1, 14.4 Hz, 1 H), 1.88 (t, *J* = 6.2 Hz, 2 H), 2.06 (ddd, *J* = 4.8, 5.7, 14.4 Hz, 1 H), 2.29 (br. s, 1 H), 2.50 (br. s, 1 H), 3.38 (s, 3 H), 3.50 (d, *J* = 11.0 Hz, 1 H), 3.63 (d, *J* = 11.0 Hz, 1 H), 3.75 (dd, *J* = 3.5, 6.2 Hz, 1 H), 3.79 (m, 2

H), 3.92 (dd, *J* = 4.7, 8.9 Hz, 1 H), 4.23 (s, 1 H), 4.66 (d, *J* = 6.5 Hz, 1 H), 4.68 (d, *J* = 6.5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.8, 25.5, 26.5, 29.1 (3 C), 34.6, 38.9, 41.1, 55.5, 59.2, 67.8, 68.1, 70.1, 73.8, 81.1, 81.8, 96.8, 107.6 ppm. ESIMS (MeOH): *m*/*z* (%) = 399.2 (100) $[M + Na]^+$. HRESIMS: calcd. for $C_{19}H_{36}O_7Na$ 399.2359; found 399.2354. $C_{19}H_{36}O_7$ (376.25)·0.25H_2O: calcd. C 59.90, H 9.66; found C 59.81, H 9.55.

Cleavage of Lactone 11b by Basic Methanolysis – Preparation of Key C-Ring Precursors: K_2CO_3 (378 mg, 2.73 mmol) in MeOH/H_2O (9 mL, 8:1) was added onto **11b** (445 mg, 0.91 mmol) at 0 °C under an argon atmosphere. The solution was stirred overnight at room temperature. Methanol was removed under reduced pressure. Water and HCl (1 N) were added to neutralize the mixture, and it was then extracted with AcOEt. The organic phase was washed with brine, dried with magnesium sulfate, and concentrated under reduced pressure. Purification by flash chromatography (heptane/AcOEt, 6:1 to AcOEt/MeOH, 9:1) afforded 303 mg (72%) of expected product **16a**, 72 mg (18%) of fused-γ-lactone **5**, 16 mg (4%) of recovered starting material **11b** and its de-acetylated derivative **11d** (15 mg, 4%).

6-*tert*-Butoxy-8-(*tert*-butyldimethylsilanyloxy)-9-hydroxy-1-methoxymethoxymethyl-5-methyl-cyclohexyl-2-oxabicyclo[3.3.1]nonan-3-one (11d): $[\alpha]_D^{20}$ = +19 (*c* 0.7, $CHCl_3$). M.p. 70–71 °C (CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3448, 2956, 2929, 2856, 1734, 1718, 1465, 1253, 1115, 1064, 836 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 (s, 3 H), 0.06 (s, 3 H), 0.87 (s, 9 H), 1.08 (s, 3 H), 1.18 (s, 9 H), 1.55 (ddd, *J* = 2.5, 11.6, 14.4 Hz, 1 H), 1.88 (ddd, *J* = 3.0, 4.9, 14.5 Hz, 1 H), 2.12 (d, *J* = 18.9 Hz, 1 H), 2.64 (d, *J* = 18.9 Hz, 1 H), 3.37 (t, *J* = 2.8 Hz, 1 H), 3.40 (s, 3 H), 3.82 (br. s, 1 H), 3.90 (s, 1 H), 3.92 (d, *J* = 10.4 Hz, 1 H), 3.99 (d, *J* = 10.4 Hz, 1 H), 4.03 (dd, *J* = 4.9, 11.6 Hz, 1 H), 4.66 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.9, –4.2, 17.9, 21.9, 25.7 (3 C), 28.6 (3 C), 34.4, 37.7, 39.8, 55.8, 67.5, 67.9, 69.2, 73.2, 74.1, 85.2, 97.3, 171.1 ppm. ESIMS (MeOH): *m*/*z* (%) = 469.2 (100) $[M + Na]^+$. HRESIMS (MeOH): calcd. for $C_{22}H_{42}O_7NaSi$ 469.2598; found 469.2591. $C_{22}H_{42}O_7Si$ (446.27)·0.5C_7H_{16}: calcd. C 61.66, H 10.15; found C 61.73, H 9.83.

[6-*tert*-Butoxy-4-(*tert*-butyldimethylsilanyloxy)-2,3-dihydroxy-3-methoxymethoxymethyl-1-methyl-cyclohexyl]acetic Acid (16a): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.10 (s, 6 H), 0.90 (s, 9 H), 1.18 (s, 9 H), 1.19 (s, 3 H), 1.26 (br. s, 2 H), 1.74 (ddd, *J* = 3.4, 5.5, 13.5 Hz, 1 H), 1.84 (ddd, *J* = 1.7, 11.0, 13.5 Hz, 1 H), 2.49 (d, *J* = 14.7 Hz, 1 H), 3.26 (d, *J* = 14.7 Hz, 1 H), 3.38 (s, 3 H), 3.48 (d, *J* = 9.6 Hz, 1 H), 3.67 (dd, *J* = 1.7, 3.4 Hz, 1 H), 3.71 (d, *J* = 9.4 Hz, 1 H), 3.78 (s, 1 H), 4.13 (dd, *J* = 5.5, 11.0 Hz, 1 H), 4.63 (d, *J* = 6.7 Hz, 1 H), 4.64 (d, *J* = 6.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.0, –4.1, 17.9, 21.4, 25.7 (3 C), 28.6, (3 C) 32.8, 40.3, 41.3, 55.6, 67.2, 70.8, 72.2, 73.6 (3 C), 73.9, 75.5, 97.1, 176.6 ppm. ESIMS (MeOH): *m*/*z* (%) = 487.3 (100) $[M + Na]^+$.

4-*tert*-Butoxy-6-(*tert*-butyldimethylsilanyloxy)-7-hydroxy-7-methoxymethoxymethyl-3a-methylhexahydrobenzofuran-2-one (5): $[\alpha]_D^{20}$ = +20 (*c* 0.4, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3489, 2954, 2929, 2856, 1784, 1039, 1020, 837 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.10 (s, 3 H), 0.12 (s, 3 H), 0.90 (s, 9 H), 1.15 (s, 3 H), 1.18 (s, 9 H), 1.75 (ddd, *J* = 5.2, 7.5, 14.1 Hz, 1 H), 1.81 (ddd, *J* = 3.1, 6.4, 14.1 Hz, 1 H), 2.09 (d, *J* = 16.6 Hz, 1 H), 2.79 (d, *J* = 16.6 Hz, 1 H), 2.81 (s, 1 H), 3.28 (d, *J* = 9.4 Hz, 1 H), 3.36 (s, 3 H), 3.54 (d, *J* = 9.4 Hz, 1 H), 3.90 (dd, *J* = 3.1, 7.5 Hz, 1 H), 4.18 (dd, *J* = 5.2, 6.4 Hz, 1 H), 4.20 (s, 1 H), 4.60 (d, *J* = 6.3 Hz, 1 H), 4.62 (d, *J* = 6.3 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.0, –4.2, 17.9, 23.3, 25.8 (3 C), 28.6 (3 C), 34.7, 42.0, 43.3, 55.7, 65.6, 67.2, 69.0, 73.5, 73.9, 83.5, 96.8, 177.2 ppm. ESIMS (MeOH): *m*/*z* (%) = 469.2 (100) $[M + Na]^+$. HRESIMS: calcd. for $C_{22}H_{42}O_7NaSi$ 469.2598; found 469.2583. $C_{22}H_{42}O_7Si$ (446.27)·0.2C_7H_{16}: calcd. C 60.22, H 9.76; found C 60.23, H 9.41.

Esterification of 16a: To a magnetically stirred solution of **16a** (303 mg, 0.65 mmol) in diethyl ether (6 mL) and methanol (1 mL) was added $TMSCHN_2$ (1.6 mL, 3.27 mmol) at 0 °C. The mixture was stirred for 15 min at 0 °C, concentrated under reduced pressure, and purified by silica gel column chromatography (heptane/AcOEt, 6:1 to 3:1) to afford 279 mg (90%) of expected product **16b** together with γ-lactone **5** (16 mg, 5%).

Methyl [6-*tert*-Butoxy-4-(*tert*-butyldimethylsilanyloxy)-2,3-dihydroxy-3-methoxymethoxymethyl-1-methylcyclohexyl]acetate (16b): $[\alpha]_D^{20}$ = +28 (*c* 1.2, $CHCl_3$). M.p. 61 °C (CH_2Cl_2). IR (film): $\tilde{\nu}$ = 3490, 2954, 2930, 2857, 1734, 1464, 1253, 1148, 1061, 1041, 836, 777 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.11 (s, 6 H), 0.90 (s, 9 H), 1.14 (s, 3 H), 1.19 (s, 9 H), 1.76 (td, *J* = 4.6, 13.5 Hz, 1 H), 1.89 (ddd, *J* = 1.9, 11.5, 13.5 Hz, 1 H), 2.45 (s, 1 H), 2.73 (d, *J* = 14.9 Hz, 1 H), 2.87 (d, *J* = 14.9 Hz, 1 H), 2.99 (br. s, 1 H), 3.38 (s, 3 H), 3.39 (d, *J* = 9.4 Hz, 1 H), 3.66 (s, 3 H), 3.70 (d, *J* = 9.4 Hz, 1 H), 3.70 (s, 1 H), 3.89 (dd, *J* = 1.9, 3.9 Hz, 1 H), 4.21 (dd, *J* = 5.1, 11.5 Hz, 1 H), 4.63 (d, *J* = 6.4 Hz, 1 H), 4.64 (d, *J* = 6.4 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.0, –4.1, 18.0, 21.8, 25.8 (3 C), 28.7 (3 C), 33.0, 38.1, 41.8, 51.3, 55.5, 67.0, 69.0, 70.9, 72.5, 73.6, 75.8, 97.0, 174.1 ppm. ESIMS (MeOH): *m*/*z* (%) = 501.2 (100) $[M + Na]^+$. HRESIMS: calcd. for $C_{23}H_{46}O_8SiNa$ 501.2860; found 501.2856. $C_{23}H_{46}O_8Si$ (478.29): calcd. C 57.71, H 9.69; found C 57.77, H 9.66.

DIBAL Reduction of 5: Diisobutylaluminium hydride (30% in toluene, 0.22 mL, 0.26 mmol) was added slowly to **5** (40 mg, 0.09 mmol) in toluene (1 mL) at –78 °C under an argon atmosphere. The reaction was stirred for 2 h while warming from –78 °C to –40 °C. The mixture was then quenched by the addition of saturated NH_4Cl (a few drops), extracted with ether, and washed with brine. The organic layer was concentrated under reduced pressure and SiO_2 flash chromatography of the residue (heptane/EtOAc, 5:1 to 3:1) gave 37.2 mg (93%) of lactol **17** as the major isomer; the minor lactol could not be characterized as it was isolated in an impure form.

4-*tert*-Butoxy-6-(*tert*-butyldimethylsilanyloxy)-7-methyl-7-methoxymethoxymethyl-3a-methyloctahydrobenzofuran-2,7-diol (17): IR (film): $\tilde{\nu}$ = 3445, 2956, 2930, 2888, 2858, 1472, 1253, 1044, 836 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 3 H), 0.12 (s, 3 H), 0.90 (s, 9 H), 1.07 (s, 3 H), 1.18 (s, 9 H), 1.63 (dd, *J* = 5.1, 12.9 Hz, 1 H), 1.70 (ddd, *J* = 5.0, 6.1, 13.7 Hz, 1 H), 1.87 (ddd, *J* = 2.7, 8.5, 13.7 Hz, 1 H), 1.87 (dd, *J* = 6.2, 12.9 Hz, 1 H), 3.16 (s, 1 H), 3.29 (d, *J* = 9.1 Hz, 1 H), 3.36 (s, 3 H), 3.59 (d, *J* = 9.1 Hz, 1 H), 3.75 (dd, *J* = 2.7, 6.2 Hz, 1 H), 3.39 (s, 1 H), 4.22 (dd, *J* = 4.8, 8.4 Hz, 1 H), 4.58 (d, *J* = 11.5 Hz, 1 H), 4.60 (d, *J* = 6.2 Hz, 1 H), 4.62 (d, *J* = 6.2 Hz, 1 H), 5.48 (ddd, *J* = 5.1, 5.9, 11.5 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.0, –4.2, 18.0, 24.5, 25.8 (3 C), 28.7 (3 C), 34.3, 46.8, 47.7, 55.6, 66.3, 67.4, 69.5, 73.5, 73.6, 82.2, 96.9, 100.1 ppm. ESIMS (MeOH): *m*/*z* (%) = 471.2 (100) $[M + Na]^+$. HRESIMS: calcd. for $C_{22}H_{44}O_7NaSi$ 471.2754; found 471.2753. $C_{22}H_{44}O_7Si$ (448.29)·0.15C_7H_{16}: calcd. C 59.71, H 10.09; found C 59.76, H 10.09.

Preparation of α-Alkoxyorganostannanes – C-10 Nucleophile Precursors: To a magnetically stirred solution of diisopropylamine (0.19 mL, 1.19 mmol) in dry THF (0.7 mL) under an argon atmosphere at 0 °C, *n*BuLi (1.6 M hexane solution, 0.81 mL, 1.35 mmol) was added dropwise. The solution was stirred for 10 min, nBu$_3$SnH (0.36 mL, 1.35 mmol) was added, and stirring was continued for 15 min at 0 °C. The reaction mixture was chilled to –78 °C before a solution of **6** (53 mg, 0.11 mmol) in dry THF (1.8 mL) was added

dropwise. The mixture was stirred at –78 °C for 30 min and then quenched with saturated NH_4Cl, diluted with Et_2O, and extracted. The combined organic layers were washed with brine, dried with magnesium sulfate, and concentrated under reduced pressure. iPr$_2$NEt (0.29 mL, 1.66 mmol) was added, followed by MOMCl (0.08 mL, 1.11 mmol) 10 min later, at 0 °C on the crude residue thus obtained in dichloromethane (1 mL). The solution was stirred overnight at room temperature, quenched with H_2O (at 0 °C), and extracted with CH_2Cl_2. The organic phase was washed with water and saturated $NaHCO_3$ and worked up as usual to afford, after purification by flash chromatography (heptane/AcOEt, 1:0 to 5:1), a 75% combined yield of the desired α-alkoxyorgano stannanes, faster eluting isomer **18** (34 mg) and slower eluting isomer **19** (32 mg), in a 1:1 ratio.

{6-*tert*-Butoxy-3a-methoxymethoxymethyl-7-[2-methoxymethoxy-2-(tributylstannanyl)ethyl]-2,2,7-trimethylhexahydrobenzo[1,3]dioxol-4-yloxy}*tert*-butyldimethylsilane (18/19): Faster Eluting Isomer **18**: $[\alpha]_D^{20}$ = –13 (*c* 1.0, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2956, 2928, 2856, 1463, 1377, 1252, 1146, 1042, 836 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08 (s, 6 H), 0.86–0.94 (m, 9 H), 0.93 (s, 9 H), 0.95 (s, 3 H), 1.18 (s, 9 H), 1.25–1.40 (m, 6 H), 1.35 (s, 3 H), 1.48 (s, 3 H), 1.48–1.56 (m, 6 H), 1.60–1.69 (m, 6 H), 1.72 (ddd, *J* = 4.5, 5.8, 14.0 Hz, 1 H), 1.75 (dd, *J* = 3.1, 14.6 Hz, 1 H), 2.03 (ddd, *J* = 6.4, 8.5, 14.0 Hz, 1 H), 2.31 (dd, *J* = 12.0, 14.6 Hz, 1 H), 3.34 (s, 3 H), 3.37 (s, 3 H), 3.52 (d, *J* = 10.2 Hz, 1 H), 3.59 (d, *J* = 10.2 Hz, 1 H), 3.73 (t, *J* = 5.8 Hz, 1 H), 4.05 (dd, *J* = 4.5, 8.9 Hz, 1 H), 4.31 (dd, *J* = 3.1, 11.3 Hz, 1 H), 4.39 (s, 1 H), 4.49 (d, *J* = 6.7 Hz, 1 H), 4.58 (d, *J* = 6.7 Hz, 1 H), 4.62 (d, *J* = 6.5 Hz, 1 H), 4.64 (d, *J* = 6.5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.3, –4.1, 9.7, 13.6 (3 C), 16.3, 17.5 (2 C), 18.5, 26.2, 26.4 (3 C), 26.9 (2 C), 27.0, 27.6, 27.9 (2 C), 29.2 (3 C), 29.3, 37.2, 40.8 (2 C), 55.4, 55.9, 67.6, 69.6, 69.7, 70.4, 73.3, 81.2, 82.5, 96.0, 96.9, 106.9 ppm. ESIMS (MeOH): *m*/*z* (%) = 847.4 (100) $[M + Na]^+$. HRESIMS: calcd. for $C_{39}H_{80}O_8NaSiSn$ 847.4542; found 847.4497. $C_{39}H_{80}O_8SiSn$ (824.46)·0.9C_7H_{16}: calcd. C 59.45, H 10.40; found C 59.44, H 10.09. Slower Eluting Isomer **19**: $[\alpha]_D^{20}$ = +16 (*c* 0.3, $CHCl_3$).IR (film): $\tilde{\nu}$ = 2956, 2927, 2856, 1463, 1377, 1257, 1147, 1041, 834 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08 (s, 3 H), 0.09 (s, 3 H), 0.86–0.95 (m, 15 H), 0.93 (s, 9 H), 1.08 (s, 3 H), 1.21 (s, 9 H), 1.25–1.36 (m, 6 H), 1.37 (s, 3 H), 1.46 (s, 3 H), 1.47–1.56 (m, 6 H), 1.71 (ddd, *J* = 3.7, 8.7, 14.1 Hz, 1 H), 1.88 (d, *J* = 14.3 Hz, 1 H), 1.91 (ddd, *J* = 5.0, 5.9, 14.1 Hz, 1 H), 2.26 (dd, *J* = 11.3, 14.3 Hz, 1 H), 3.37 (s, 3 H), 3.38 (s, 3 H), 3.49 (d, *J* = 10.5 Hz, 1 H), 3.60 (d, *J* = 10.5 Hz, 1 H), 3.81 (dd, *J* = 5.0, 8.8 Hz, 1 H), 3.91 (dd, *J* = 3.7, 5.9 Hz, 1 H), 4.20 (s, 1 H), 4.44 (d, *J* = 11.0 Hz, 1 H), 4.54 (d, *J* = 6.5 Hz, 1 H), 4.56 (d, *J* = 6.5 Hz, 1 H), 4.66 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.5, –4.1, 9.5 (3 C), 13.7 (3 C), 17.4, 18.7, 26.2, 26.6 (3 C), 27.0, 27.6 (3 C), 29.2 (3 C), 29.4, 29.7 (2 C), 36.7, 40.7, 43.6, 55.4, 56.2, 69.0, 69.4, 70.5, 71.3, 73.3, 81.1, 81.2, 96.9, 97.0, 107.1 ppm. ESIMS (MeOH): *m*/*z* (%) = 847.4 (100) $[M + Na]^+$. HRESIMS: calcd. for $C_{39}H_{80}O_8NaSiSn$ 847.4542; found 847.4564. $C_{39}H_{80}O_8SiSn$ (824.46)·1.1C_7H_{16}: calcd. C 59.97, H 10.52; found C 60.16, H 10.04.

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[1] a) K. C. Nicolaou, H. Ueno, J.-J. Liu, P. G. Nantermet, Z. Yang, J. Renaud, K. Paulvannan, R. Chadha, *J. Am. Chem. Soc.* **1995**, *117*, 653–659 and preceding papers; b) R. A. Holton, H.-B. Kim, C. Somoza, F. Liang, R. J. Biediger, P. D. Boatman, M. Shindo, C. C. Smith, S. Kim, H. Nadizadeh, Y. Suzuki, C. Tao, P. Vu, S. Tang, P. Zhang, K. K. Murthi, L. N. Gentile, J. H. Liu, *J. Am. Chem. Soc.* **1994**, *116*, 1599–1600 and preceding papers; c) S. J. Danishefsky, J. J. Masters, W. B. Young, J. T. Link, L. B. Snyder, T. V. Magee, D. K. Jung, R. C. A. Isaacs, W. G. Bornmann, C. A. Alaimo, C. A. Cobrun, M. J. Di Grandi, *J. Am. Chem. Soc.* **1996**, *118*, 2843–2859 and preceding papers; d) P. A. Wender, N. F. Badham, S. P. Conway, P. E. Floreansic, T. E. Glass, J. B. Houze, N. E. Krauss, D. Lee, D. J. Marquess, P. L. McGrane, W. Meng, M. G. Natchus, A. J. Shuker, J. C. Sutton, R. E. Taylor, *J. Am. Chem. Soc.* **1997**, *119*, 2757–2758 and preceding papers; e) T. Mukaiyama, I. Shiina, H. Iwadare, M. Saitoh, T. Nishimura, N. Ohkawa, H. Sakoh, K. Nishimura, Y. Tani, M. Hasegawa, K. Yamada, K. Saitoh, *Chem. Eur. J.* **1999**, *5*, 121–161 and preceding papers; f) H. Kusama, R. Hara, S. Kawahara, T. Nishimori, H. Kashima, N. Nakamura, K. Morihara, I. Kuwajima, *J. Am. Chem. Soc.* **2000**, *122*, 3811–3820 and preceding papers. Review articles: A. N. Boa, P. R. Jenkins, N. J. Lawrence, *Contemp. Org. Synth.* **1994**, *1*, 47–75; K. C. Nicolaou, W. M. Dai, R. K. Guy, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 15–44; O. N. Zefirova, E. V. Nurieva, A. N. Ryzhov, N. V. Zyk, N. S. Zefirov, *Russ. J. Org. Chem.* **2005**, *41*, 315–351.

[2] According to Tietze's classification, a sequence of reactions with different mechanisms are called "heterodomino" reactions while in a consecutive reaction, another reagent is added after the first transformation without isolation of the first formed product: L. F. Tietze, U. Beifuss, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 131–163; L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115–136; L. F. Tietze, A. Modi, *Med. Res. Rev.* **2000**, *20*, 304–322.

[3] W. C. Still, *J. Am. Chem. Soc.* **1978**, *100*, 1481–1486.

[4] J. I. Martín Hernando, M. Rico Ferreira, J. I. Candela Lena, N. Birlirakis, S. Arseniyadis, *Tetrahedron: Asymmetry* **2000**, *11*, 951–973.

[5] C. Unaleroglu, V. Aviyente, S. Arseniyadis, *J. Org. Chem.* **2002**, *67*, 2447–2452.

[6] Usually, taxoids of the C-4(20)-olefin containing group are esterified at C-5: G. Appendino, *Nat. Prod. Rep.* **1995**, *12*, 349–360.

[7] L. Finet, J. I. Candela, T. Kaoudi, N. Birlirakis, S. Arseniyadis, *Chem. Eur. J.* **2003**, *9*, 3813–3820.

[8] R. L. Danheiser, K. R. Romines, H. Koyama, S. F. Gee, C. R. Johnson, J. R. Medich, *Org. Synth.* **1992**, *71*, 133–139.

[9] The factors which determine the regioselectivity in Baeyer–Villiger oxidations, electronic, steric, and stereoelectronic, have been reviewed: G. R. Krow, *Org. React.* **1993**, *43*, 251–798.

[10] P. A. Grieco, T. Oguri, C. L. J. Wang, E. Williams, *J. Org. Chem.* **1977**, *42*, 4113.

[11] A. McKillop, J. A. Tarbin, *Tetrahedron* **1987**, *43*, 1753.

[12] P. Brougham, M. S. Cooper, D. A. Cummerson, H. Heaney, N. Thompson, *Synthesis* **1987**, 1015.

[13] Z. Grudzinski, S. M. Roberts, C. Howard, R. F. Newton, *J. Chem. Soc., Perkin Trans. 1* **1978**, 1182.

[14] P. A. Grieco, Y. Yokoyama, S. Gilman, Y. Ohfune, *J. Chem. Soc., Chem. Commun.* **1977**, 870.

[15] H. Kotsuki, K. Arimura, T. Araki, T. Shinohara, *Synlett* **1999**, 462–464.

[16] M. D. Mihovilovic, B. Muller, P. Stanetty, *Eur. J. Org. Chem.* **2002**, 3711–3730.

[17] J. Lebreton, V. Alphand, R. Furstoss, *Tetrahedron* **1997**, *53*, 145–160.

[18] Our initial plans to introduce at this stage the TMS group at C-5 were abandoned because this function proved too labile to survive the conditions of the ensuing reactions.

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