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Short Diastereoselective Synthesis of the C1–C13 (AB Spiroacetal) and C17–C28 Fragments (CD Spiroacetal) of Spongistatin 1 and 2 through Double Chain-Elongation Reactions

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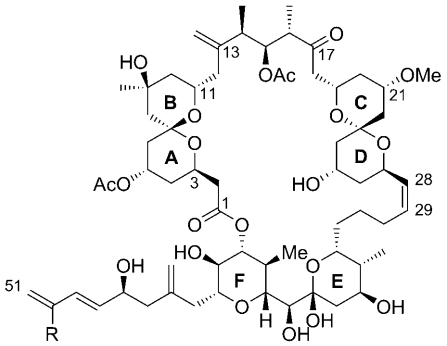
Abstract: A unique and practical synthetic sequence for rapid access to polyketides and to further the spiroacetals derived from them, which utilizes a bidirectional Hosomi–Sakurai allylation approach around key allylsilanes in the synthesis of the AB and CD ring systems of spongistatin 1 and 2, is reported. The synthesis of the AB spiroacetal **9** requires 13 steps, with a longest linear sequence of seven steps in an overall yield of 27%. The synthesis of the CD spiroacetal **13** requires 15 steps, with a longest linear sequence of 11 steps in an overall yield of 30%. Both syntheses start from but-3-enol.

Keywords: double chain elongation · enantioselectivity · Hosomi–Sakurai reaction · spiro compounds · spongistatin

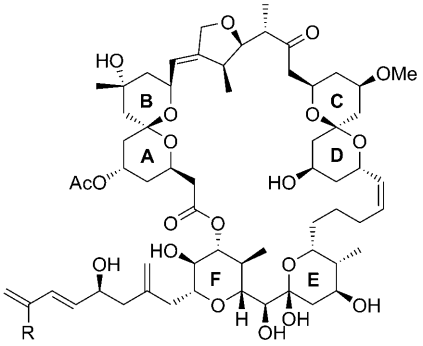
Introduction

Spiroacetals, and in particular their 6,6-congeners, are key structural elements of a variety of natural products of biological interest, for example, marine macrolides, ionophores and polyether antibiotics.[1] The spiroacetal fragments are often very important for the biological activity of the compounds containing them. In particular, spongistatins (altohyrtins, for example, **1**–**5**), which were isolated from marine sponges of the genus *Spongia* by three research groups in 1993,[2] display two highly oxygenated 6,6-spiroacetals in their macrolactone skeleton (Figure 1). These marine macrolides are potent cancer cell growth inhibitors and thus represent promising leads for the development of new anticancer agents.[3,4]

In addition to seminal reports by the groups of Evans,[5] Kishi,[6] Paterson,[7] Smith,[8] Crimmins,[9] Heathcock,[10] and Ley[11] on the total syntheses of spongistatins 1 and 2, much effort has been devoted to the implementation of straightforward and high-yielding pathways towards the ABCD "northern" hemisphere[12] and the EF tetrahydropyran subunits.[13] Our group has presented an early synthesis of the



1: R = Cl, altohyrtin A, spongistatin 1
2: R = Br, altohyrtin B
3: R = H, altohyrtin C, spongistatin 2



4: R = Cl, spongistatin 9
5: R = H, spongistatin 8

Figure 1. Representative members of the spongistatin (altohyrtin) family.

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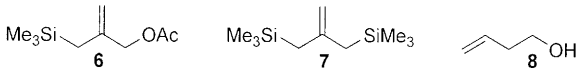
C29–C51 fragments of spongistatin 1[14] and has developed a noniterative approach to the asymmetric synthesis of fifteen-carbon polyketides, including advanced precursors of AB[15] and CD[16] spiroacetals of spongistatin 1–3 starting from 2,2′-methylidenedifuran.[17] Because of their limited supply from nature[18] any clinical evaluation of spongistatins must rely upon synthetic sources. Gram-scale synthesis of **1** and **3** is now a major priority, the group of Heathcock[19] and, more recently, the group of Smith[20] have made substantial progresses toward this objective.[21] We disclose here our efforts to realize quicker and more efficient access to polyketides and to further the 6,6-spiroacetals (1,7-dioxaspiro[5,5]undecanes) derived from them. Based on bidirectional, dissymmetrical double Hosomi–Sakurai allylations[22] of allylsilanes **6**[23] and **7**,[24,25] efficient syntheses of



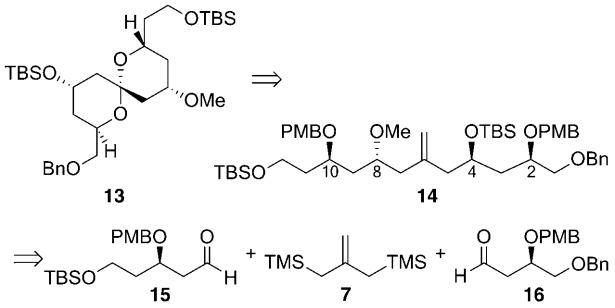
C1–C13 and C17–C28 fragments of **1**–**3** have been realized starting from inexpensive but-3-enol (**8**). C_2-Symmetrical long-chain polyketides have been prepared by Barrett and co-workers by using a bidirectional symmetrical allylboration of aldehydes.[26]

Retrosyntheses

AB spiroacetal: The C1–C14 fragment of spongistatin 1 and 2 contains five stereogenic centers arrayed on a 6,6-spiroacetal framework. The configuration of the anomeric carbon C7 of this system corresponds to the thermodynamically favored diaxial, double anomerically stabilized arrangement.[27] The synthetic strategy adopted to tackle the synthesis of the AB spiroacetal **9** was based upon a bidirectional dissymmetrical allylation strategy around 2-((trimethylsilyl)-methyl)allyl acetate (**6**).

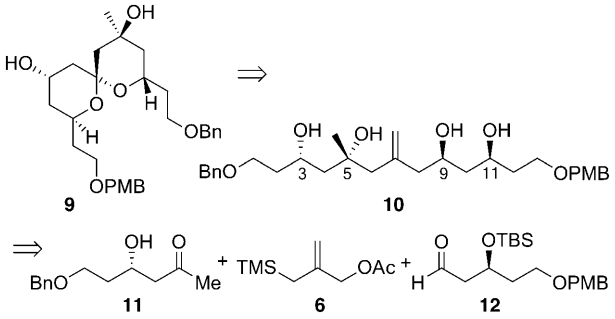
We identified key polyketide precursor **10** as the desired intermediate, which after ozonolysis and under thermodynamically controlled cyclization conditions should provide the required spiroacetal **9**. Accordingly, fragment **10** could be generated through two consecutive allylation reactions by using optimized substrate/Lewis acid conditions (Scheme 1). Central to this approach was the use of **6** that provided an efficient means of masking one of the two bis-allylating functionalities to circumvent concurrent and problematic hydrogen–ene reactions.[28]

CD spiroacetal: As common to most C17–C28 CD spiroacetal syntheses, our retrosynthesis identifies key acyclic precursor **14** as the desired intermediate to the CD spiroacetal **13**, which upon ozonolysis and under kinetically controlled cyclization conditions[29] should provide the required partially anomerically stabilized spiroacetal. Accordingly, fragment **14** could be generated through two consecutive Hosomi–Sakurai reactions by using optimized substrate/Lewis acid conditions to set up the required polyketide precursor **14** rapidly in a double elongation reaction sequence. Pivotal to this approach was the use of a core bis-allyl silane **7**[24] that provided an efficient means to the definition of the required stereogenic centers at C4 and C8 in the carbon-forming steps when amalgamated with known aldehydes **15**[30] and **16**[31] (Scheme 2).

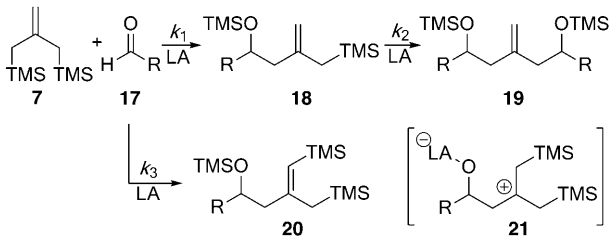


Scheme 2. Retrosynthesis of CD spiroacetal **13**.

Owing to the ß-silyl effect[32] (see the intermediate or limiting structure of the transition state **21**, Scheme 3) the bis-silyl allyl reagent **7** was expected to react significantly faster towards electrophiles, such as aldehyde **17**, than the corresponding monoallylsilane **18** that resulted from the sila-ene reaction ($k_1 > k_2$, Scheme 3). Provided that reaction conditions favor the Hosomi–Sakurai reaction over the hydrogen–ene reaction (**7**+**17**→**20**), which has been observed for the reaction of allylsilane **7** with non-oxygen based electrophiles,[33] this methodology should provide rapid access to



Scheme 1. Retrosynthesis of AB spiroacetal **1**.

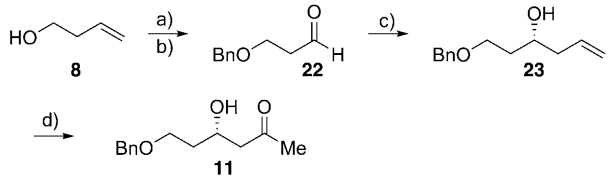


Scheme 3. Hosomi–Sakurai reactions (k_1, k_2) with (2-((trimethylsilyl) methyl)allyl) trimethylsilane (**7**) and the competing hydrogen (ene) reaction (k_3). LA: Lewis acid.

polyketide fragments. In their convergent synthesis of polyol chains, Rychnovsky and co-workers used allylsilane **7** to join two different 4-acetoxy-1,3-dioxanes, demonstrating that well-chosen electrophilic partners can lead to the required chemoselectivities ($k_1 > k_2 \gg k_3$).[25]

Results and Discussion

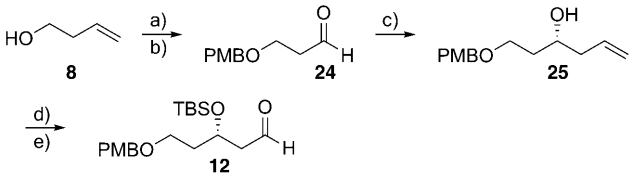
Construction of methyl ketone **11** was initiated with but-3-enol (**8**), which was first protected as the benzyl ether followed by ozonolysis to give aldehyde **22**. A Brown allylation gave a single enantiomer of the homoallylic alcohol **23** with an enantiomeric excess (*ee*) greater than 95%.[7a] Homoallylic alcohol **23** was then transformed to the methyl ketone **11** through a Wacker oxidation by using $PdCl_2$, CuCl, and oxygen[34] to give the desired product in acceptable yields (Scheme 4).



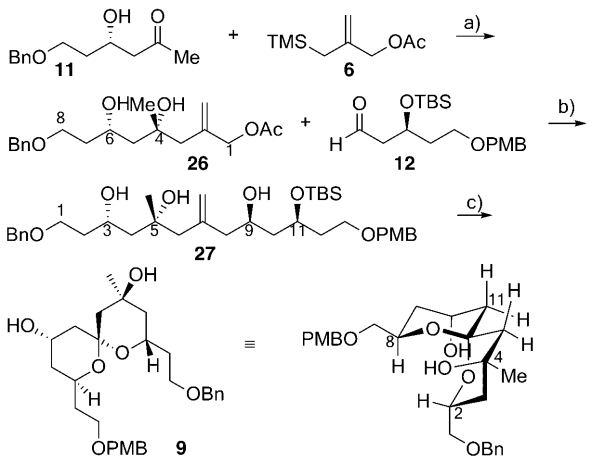
Scheme 4. Synthesis of methyl ketone **11**. Reagents and conditions: a) BnBr, NaH, THF, TBAI, 16 h, RT, (85%); b) O_3, PPh_3, DCM, −78 °C, (94%); c) $(ipc)_2BOMe$, allylmagnesium bromide, Et_2O, 18 h, then NaOH, H_2O_2, 1 h reflux, (98%); d) $PdCl_2$, CuI, O_2, DMF/H_2O, 3 h, RT, (54%). IPC: isopinocampheyl.

Assembly of the complementary 3-hydroxyaldehyde **12** commenced with the *para*-methoxybenzyl (PMB) protection of **8** to give **24**. In a similar manner to the preparation of methyl ketone **11** (Scheme 4), fragment **25** was elaborated with a Brown allylation in greater than 95% *ee*,[35] followed by *tert*-butylsilyl (TBS) protection and ozonolysis to give the desired aldehyde **12** in 58% yield over the five steps (Scheme 5).

2-((Trimethylsilyl)methyl)allyl acetate (**6**)[23] and methyl ketone **11** were smoothly reacted with $SnCl_4$. The highly stereocontrolled course of this transformation had significant implications for ensuring the generation of diastereotopically pure allyl acetate **26** (Scheme 6). $SnCl_4$ was chosen be-



Scheme 5. Synthesis of aldehyde **12**. Reagents and conditions: a) PMBCl, NaH, THF, TBAI, 16 h, RT, (88%); b) O_3, PPh_3, DCM, −78 °C, (87%); c) $(ipc)_2BOMe$, allylmagnesium bromide, Et_2O, 18 h, then NaOH, H_2O_2 1 h reflux, (96%); d) TBSCl, imidazole, DMF, RT, (91%); e) O_3, PPh_3, DCM, −78 °C, (87%).



Scheme 6. Synthesis of AB spiroacetal **9**. Reagents and conditions: a) SnCl4, 13 h, −78 °C, (94%); b) $[Pd_2(dba)_3]$, bis(pinacolacto)diborane, DMSO, 16 h, RT, (77%, 4:1); c) O_3, DMS, PPTS, DCM, −78 °C, (77%). PPTS: pyridinium paratoluenesulfonate.

cause Allais and Cossy indicated in the case of unprotected β-hydroxy aldehydes that high levels of 1,3-*syn* induction are observed.[12n] This reaction has not yet been mechanistically investigated but it would appear that it does not occur through a simple Lewis acid coordination/activation of the carbonyl, but instead undergoes a transmetallation with the allylsilane to produce an allyl stannane that is the active allylating reagent. This is reinforced by our observation that the reaction does not occur when a solution of $SnCl_4$ is added dropwise to the ketone and the allylsilane, but requires overnight premixing with the allylsilane. The resulting allyl acetate **26** was transformed and reacted through an in situ allylboration, developed by Miyaura,[36] with aldehyde **12**. The desired 1,3-*syn*-oxygenated system was formed in a 4:1 ratio with the desired polyol **27** arising from both a Felkin control model, which was reinforced by 1,5-*anti* induction.[37]

Successful elaboration of polyketide **9** involved a one-pot ozonolysis/deprotection/cyclization sequence. The cyclization occurred smoothly under conditions previously used on similar fragments to give the desired thermodynamic axial, axial spiroacetal **9** (Scheme 6).[4] The relative configuration of the latter could be verified through NOE correlation 2D ^{1}H NMR. Key NOEs between H_{ax}–C5 and H_{ax}–C11, H_{eq}–C5 and H_{eq}–C11, along with H–C8 and H–C2 confirmed the relative configuration of the AB spiroacetal. These observations were in agreement with the literature (Figure 2).[4]

The synthesis of aldehyde **15** (Scheme 2) commenced with but-3-enol (**8**), which was first TBS protected, then the terminal olefin was exposed to ozone followed by reductive workup, and the resulting aldehyde **28** was asymmetrically allylated in 98% *ee*[7b] by applying conditions developed by Brown.[38] The homoallylic alcohol **29** was protected as the PMB ether **30** and the desired aldehyde **15** was obtained through ozonolysis (five steps, 60% yield), with purifications

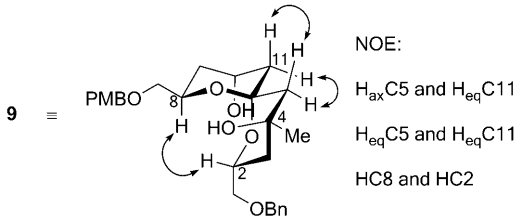
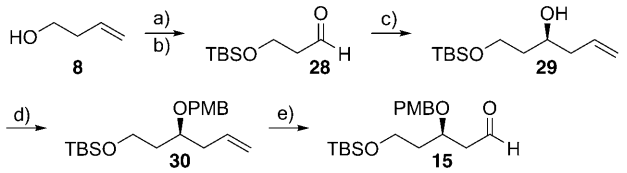


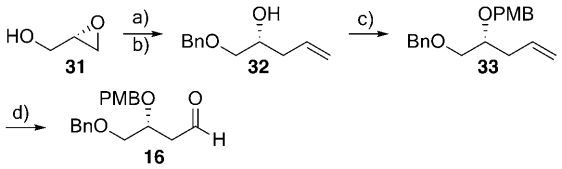
Figure 2. Diagnostic ^{1}H NMR NOEs in AB spiroacetal **9**.

required only for the allyl alcohol **29** and aldehyde **15** (Scheme 7).



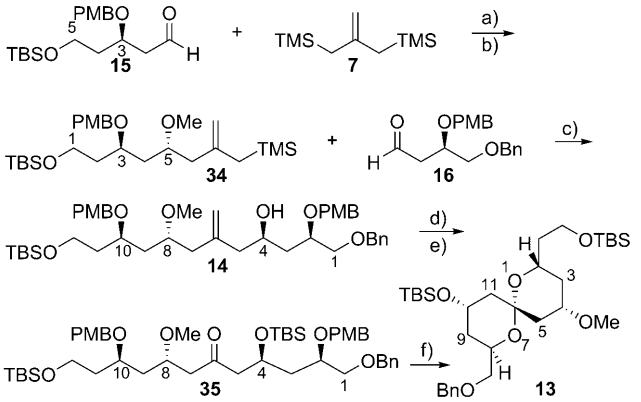
Scheme 7. Synthesis of aldehyde **15**. Reagents and conditions: a) TBSCl, imidazole, CH_2Cl_2, 2 h, RT, (97%); b) O_3, Me_2S, CH_2Cl_2, −78 °C, (89%); c) $(ipc)_2BOMe$, allylmagnesium bromide, Et_2O, 18 h, then NaOH, H_2O_2, 1 h, reflux, (86%); d) NaH, PMBCl, DMF, 16 h, 0 °C, (84%); e) O_3, PPh_3, CH_2Cl_2, −78 °C, (96%).

Aldehyde **16** was readily accessed through a standard procedure developed by Crimmins and co-workers.[31] (*S*)-Glycidol **31** was protected as the benzyl ether prior to the epoxide being regioselectively opened by the vinyl cuprate generated from vinyl magnesium bromide. The chiral alcohol **32** was then sequentially PMB protected and reacted with ozone, which after reductive workup gave the desired aldehyde **16** in 51 % yield over the five steps (Scheme 8).



Scheme 8. Synthesis of aldehyde **16**. Reagents and conditions: a) BnBr, NaH, THF, 18 h, 0 °C, (90%); b) vinylmagnesium bromide, CuI, −20 °C, 20 min (86%); c) PMBCl, NaH, DMF, 0 °C, (84%); d) O_3, Me_2S, MeOH, −78 °C, (79%).

With the key aldehyde fragments **15** and **16** in hand, their union around **7** was investigated (Scheme 9). As expected,[37] when $MgBr_2{\cdot}OEt_2$ was stirred with the chiral aldehyde **15** in CH_2Cl_2 at −78 °C, followed by the dropwise addition of bis-silane **7**, the desired allylation product was formed in high yields as a single observable 1,3-*anti* diastereomer, as predicted from a chelating model with an appropriate Lewis acid. This alcohol was methylated under conditions to provide key allylsilane **34** ready for a consecutive Hosomi–Sakurai reaction with aldehyde **16**. The advantage of this order of the two successive allylations became clear, with heavy



Scheme 9. Synthesis of CD spiroacetal **13**. Reagents and conditions: a) 1 equiv. $MgBr_2{\cdot}OEt_2$, CH_2Cl_2, 1 h, −78 °C, (97%); b) MeI, NaH, THF, 0 °C, (87%); c) 1equiv. $BF_3{\cdot}OEt_2$, CH_2Cl_2, 1 h, −78 °C, (84%); d) TBSCl, imidazole, CH_2Cl_2, 3 d, RT, (91%); e) O_3, Me_2S, CH_2Cl_2, −78 °C, (91%); f) DDQ, CH_2Cl_2, 0 °C, (72%). DDQ: dichlorodicyanobenzoquinone.

substitution at C2 of the allylsilane, after the second reaction in which Felkin-inducing conditions were used to form the 1,3-*syn* relationship by using $BF_3{\cdot}OEt_2$.[37b] With this advanced polyketide **14** in hand the final manipulations were effected. The secondary alcohol was protected under standard conditions as the TBS silyl ether and ozonolysis of the olefin moiety afforded ketone **35** in high yields. The final one-pot deprotection/cyclization sequence was initiated with 5,6-dichloro-2,5-dicyanobenzoquinone and under these mild conditions the dihydroxyketone spontaneously cyclized to the desired "non-anomeric" equatorial, axial-spiroacetal **13** (Scheme 9).

The relative configuration of the formed spiroacetal **13** was confirmed through ^{1}H NMR NOE experiments. Critical correlations between H−C4−H_{eq}−C11, H−C2−H_{eq}−C11, and H−C4 and H−C2 confirmed the proposed relative configuration and structure of **13** (Figure 3).

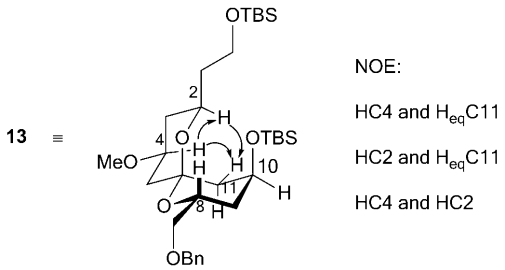


Figure 3. Diagnostic ^{1}H NMR NOEs in CD spiroacetal **13**.

Conclusion

The present route to the C1–C13 AB spiroacetal ring system **9** is concise, convergent and highly stereocontrolled. The key amalgamation was based around a bis-allyl core system **6** that allowed for an efficient and high yielding convergent synthesis. Notably, the synthesis used a minimal number of protecting groups, minimal redox fluctuations, and the qua-

ternary center was set up in the skeletal carbon-forming reaction and was not introduced in subsequent steps, as is often employed in the synthesis of the AB spiroacetals. The synthetic route to **9** was achieved in 13 steps with a longest linear sequence of seven steps (overall yield of longest linear sequence is 27%) from inexpensive but-3-enol (**8**).

A practical, efficient and highly convergent route has been opened to the synthesis of the C17–C28 CD spiroacetal **13** of spongistatins in which the pseudo C_2 symmetry, in the terms of the carbon framework and functionality, has been exploited around a core bis-silane **7** in a novel manner. The synthetic route to **13** required 14 steps with a longest linear sequence of 11 steps (overall yield of longest linear sequence is 30%), also from **8**. The chemistry disclosed here should be applied to the quick generation of long-chain polyketides of other natural products and analogues of biological interest.

Experimental Section

General methods

The general methods are described in the Supporting Information.

Synthesis of C1–C13 AB spiroacetal

Synthesis of (4*R*,6*S*)-8-(benzyloxy)-4,6-dihydroxy-4-methyl-2-methylene-1-octyl acetate (26): $SnCl_4$ (1.45 mL, 3.22 g, 12.37 mmol) was added dropwise to a solution of 2-((trimethylsilyl)methyl)allyl acetate (**6**, 2.63 mL, 2.32 g, 12.37 mmol) in CH_2Cl_2 (30 mL) and the solution was stirred at 25 °C for 12 h. The solution was transferred by a canula to a round-bottom flask containing a solution of (4*S*)-6-(benzyloxy)-4-hydroxyhexan-2-one (**11**, 2.5 g, 11.25 mmol) in CH_2Cl_2 (10 mL) at −78 °C. The mixture was allowed to stir for 1 h. The mixture was quenched with MeOH (2 mL), saturated aqueous NH_4Cl solution (5 mL), and extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/AcOEt, 8:2) to give **26** (3.42 g, 94%) as a colorless oil. $[\alpha]_{589}^{25}=-8.5$ ($c=1.93$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.40$–7.30 (m, 5H: H-C(Bn)), 5.18 (brs, 1H; H_A-C(1′)), 4.98 (brs, 1H; H_B-C(1′)), 4.88 (s, 2H; H_2-C(1)), 4.55 (s, 2H; H_2-C(Bn)), 4.29 (brdtt, 1H, $J=2.5$, 8.5 Hz: H-C(6)), 3.91 (brs, 1H; O*H*), 3.75–3.69 (m, 3H; H_2-C(8) and O*H*), 2.25 (s, 2H; H_2-C(3)), 2.13 (s, 3H; H_3-C(OAc)), 1.80–1.60 (m, 4H; H_2-C(7) and H_2-C(5)), 1.32 ppm (s, 3H; Me-C(4)); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=186.7$ (s, C-(Ac)), 140.8 (s, C(2)), 138.5 (s, C_{arom}), 128.5, 127.8 (2d, C_{arom}), 112.9 (t, CH_2-C(1″)), 73.4 (t, CH_2-(Bn)), 72.7 (s, C-C(4)), 69.1 (d, CH-C(6)), 68.8 (t, CH_2-C(1)), 67.5 (t, CH_2-C(8)), 47.7 (t, CH_2-C(5)), 46.0 (t, CH_2-C(3)), 37.2 (t, CH_2-C(7)), 26.3 (q, CH_3-C(1′)), 21.0 ppm (q, CH_3-(Ac)); IR (film): $\tilde{\nu}=3410$, 3050, 2941, 1735, 1503, 1368, 1244, 1111, 1034, 735, 631 cm^{-1}; HRMS (MALDI): calcd for $C_{19}H_{30}O_5$ 338.9937: [*M*+H]; found: 338.9939.

Synthesis of a 4:1 mixture of (3*S*,5*R*,9*R*,11*S*)-1-(benzyloxy)-11-((*tert*-butyl)dimethylsilyloxy)-13-(4-methoxybenzyloxy)-5-methyl-7-methylenetridecane-3,5,9-triol (27) and (3*S*,5*R*,9*S*,11*S*)-1-(benzyloxy)-11-((*tert*-butyl)-dimethylsilyloxy)-13-(4-methoxybenzyloxy)-5-methyl-7-methylenetridecane-3,5,9-triol (27′): $[Pd_2(dba)_3]$ (0.022 g, 0.024 mmol, 4 mol%), **12** (0.251 g, 0.713 mmol), DMSO (10 mL), and 26 (0.200 g, 0.594 mmol) were sequentially added to a round-bottomed flask and the resulting mixture was mixed for 10 min at 25 °C. Bis(pinacolato)diboran (Miyaura's reagent) (0.151 g, 0.594 mmol) was added portion-wise to this mixture. The resulting greenish solution was stirred at 25 °C for 16 h. It was quenched with H_2O (5 mL) and stirred for 30 min. Et_2O (20 mL) was added and the organic phase was washed with brine (5×10 mL). The organic layer was dried (Na_2SO_4), filtered, and evaporated under vacuum. The residue was purified by flash chromatography (petroleum ether/Et_2O, 1:1) to give 0.290 g (77%) as a colorless oil, which was a 4:1 mixture favoring the desired diastereoisomer **27**. $[\alpha]_{589}^{25}=-14.1$ ($c=0.50$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) of **27** (major): $\delta=7.38$–7.30 (m, 5H; H-C(Bn)), 7.29 (d, 2H, $J=8.2$; H-C(PMB)), 6.89 (d, 2H, $J=8.2$ Hz; H-C(PMB)), 4.99 (brs, 1H; H_A-C(1′)), 4.89 (brs, 1H; H_B-C(1′)), 4.55 (m, 2H; H_2-C(PMB)), 4.44 (m, 2H; H_2-C(Bn)), 4.29 (m, 1H; H-C(11)), 4.19 (m, 1H; H-C(3)), 4.09 (m, 1H; H-C(9)), 3.94 (brs, 1H; O*H*), 3.80 (brs, 1H; O*H*), 3.82 (s, 3H; MeO(PMB)), 3.75–3.69 (m, 3H; H_2-C(1), O*H*), 3.51 (m, 2H; H_2-C(C13)), 2.40–2.20 (m, 4H; H_2-C(6) and H_2-C(8)), 1.93–1.76 (m, 4H; H_2-C(2) and H_2-C(12)), 1.72–1.51 (m, 4H; H_2-C(4) and H_2-C(10)), 1.32 (s, 3H; Me-C(5)), 0.90 (s, 9H; H-C(TBS)), 0.12 ppm (2×s, 6H; H-C(TBS)); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=146.3$ (s, C_{arom}), 143.7 (s, C(7)), 138.5 (s, C_{arom}), 130.3 (s, C_{arom}), 129.4, 129.3, 128.5, 127.7 (4d, C_{arom}), 117.6 (t, C-(1″)), 113.8 (d, C_{arom}), 74.1 (s, C(5)), 73.1 (t, CH_2-(Bn)), 72.7 (t, CH_2-(PMB)), 69.6 (d, CH-C(11)), 69.2 (d, CH-C(9)), 69.0 (d, CH-C(3)), 67.7 (t, CH_2-C(1)), 66.4 (t, CH_2-C(13)), 55.3 (q, CH_3-(PMB)), 48.9 (t, CH_2-C(6)), 48.8 (t, CH_2-C(8)), 45.4 (t, CH_2-C(4)), 42.7 (t, CH_2-C(10)), 37.5 (t, CH_2-C(2)), 37.5 (t, CH_2-C(12)), 30.8 (s, C-(TBS)), 30.3 (q, CH_3-C(1′)), 25.9 (q, CH_3-(TBS)), −4.4 ppm (q, CH_3-(TBS)); IR (film): $\tilde{\nu}=3402$, 3050, 2927, 2855, 1708, 1512, 1371, 1246, 1088, 1034, 834, 731 cm^{-1}; HRMS (MALDI): calcd for $C_{36}H_{59}O_7Si$: 631.3952 [*M*+H]; found: 631.3943.

Synthesis of (2*S*,4*S*,6*R*,8*S*,10*S*)-2-(2-(benzyloxy)ethyl)-8-(2-(4-methoxybenzyloxy)ethyl)-4-methyl-1,7-dioxaspiro[5.5]undecane-4,10-diol (AB spiroacetal 9): O_3 was bubbled through a solution of a 4:1 mixture of **27**:**27′** (0.040 g, 0.077 mmol) in CH_2Cl_2 (5 mL) at −78 °C until the solution was saturated (10 min), which was indicated by the solution turning blue. The ozone generator was then turned off and O_2 was bubbled through the mixture for 10 min. The reaction was flushed with Ar and Me_2S (0.2 mL) was added dropwise at −78 °C. After stirring for 1 h at this temperature the mixture was warmed to 25 °C and stirred for 1 h. The solvent was removed under reduced pressure and the resulting oil suspension was dissolved in CH_2Cl_2 (5 mL) and pyridinium *p*-toluenesulfonate (2 mg, cat.) was added and the reaction was stirred for 16 h. The reaction mixture was quenched with H_2O (5 mL) and extracted with EtOAc (3× 10 mL). The combined organic phases were dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The crude residue was purified by column chromatography (petroleum ether/Et_2O, 8:2) to give **9** (0.030 g, 77%) as a colorless oil. $[\alpha]_{589}^{25}=-30.3$ ($c=0.88$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.38$–7.25 (m, 5H; H-C(Bn)), 7.24 (d, 2H, $J=8.2$; H-C(PMB)), 6.86 (d, 2H, $J=8.2$; H-C(PMB)), 4.48 and 4.41 (2×d, 2H; $J=12.2$ Hz; H_2-C(PMB)), 4.36 (s, 2H; H_2-C(Bn)), 4.26–4.19 (m, 1H; H-C(10)), 4.19–4.12 (m, 1H; H-C(8)), 4.12–4.03 (m, 3H; H-C(2) and H-OC(10) and H-OC(4)), 3.78 (s, 3H; MeO(PMB)), 3.56 (brt, 2H; $J=6.9$ Hz, H-C(2′)), 3.55 (brt, 2H; $J=6.5$ Hz; H-C(2″)), 2.03–1.75 (m, 8H; H_{ax}-C(3), H_A-C(1′), $_A$-C(1″), H_{eq}-C(5), H_{ax}-C(9)), H_{eq}-C(3), H_{eq}-C(11), and H_{ax}-C(5)), 1.74–1.66 (m, 2H; H_B-C(1′) and H_B-C(1″)), 1.56–1.50 (m, 1H; H_{eq}-C(9)), 1.49–1.45 (m, 1H; H_{ax}-C(11)), 1.31 ppm (s, 3H; Me(C4)); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=158.3$ (s, C_{arom}), 138.3 (s, C_{arom}), 136.5 (quat, C_{arom}), 129.3, 128.3, 127.9, 127.6, 127.7 (5×d, C_{arom}), 113.7 (s, C_{arom}), 96.5 (s, spiroacetal-C(6)), 73.1 (t, CH_2-(Bn)), 72.7 (t, CH_2-(PMB)), 67.5 (s, C(4)), 68.1 (t, CH_2-C(2′)), 67.4 (t, CH_2-C(2″)), 66.1 (d, CH-C(10)), 64.9 (d, CH-C(2)), 62.1 (d, CH-C(8)), 55.2 (q, CH_3-(PMB)), 39.7 (t, CH_2-C(3)), 38.0 (t, CH_2-C(9)), 36.0 (t, CH_2-C(5)), 35.5 (t, CH_2-C(11)), 31.9 (t, CH_2-C(2″)), 29.7 (t, CH_2-C(1″)), 22.9 ppm (q, CH_3-C(1‴)); IR (film): $\tilde{\nu}=$ 3402, 3050, 2927, 2855, 1624, 1589, 1571, 1246, 1088, 1034, 834, 731 cm^{-1}; HRMS (MALDI): calcd for $C_{29}H_{41}O_7$: 501.2574 [*M*+H]; found: 501.2583.

Synthesis of C17–C28 CD spiroacetal

Synthesis of (4*R*,6*R*)-8-((*tert*-butyl)dimethylsilyloxy)-6-(4-methoxybenzyloxy)-2-((trimethylsilyl)methyl)oct-1-en-4-ol: Solid $MgBr_2{\cdot}OEt_2$ (0.36 g, 1.41 mmol) was added portion-wise to a stirred mixture of (*R*)-5-(*tert*-butyldimethylsilyloxy)-3-(4-methoxybenzyloxy)pentanal (**15**) (0.50 g, 1.41 mmol) and **7**[24b] (0.284 g, 1.41 mmol) at −78 °C in CH_2Cl_2 (100 mL). The reaction was stirred at −78 °C for 1 h before being quenched with a saturated aqueous solution of NH_4Cl (50 mL) and allowed to warm to 25 °C. The reaction was diluted with Et_2O (100 mL) and the aqueous phase was extracted with Et_2O (50 mL). The combined organic phases were washed with brine (100 mL), dried ($MgSO_4$), and evaporated. The crude residue was purified by column chromatography (petroleum ether/Et_2O, 8:2) to give the product (2.10 g, 97%) of as a colorless oil. $[\alpha]_{589}^{25}=$

10.2 ($c=0.17$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.27$ (d, 2H, $J=$ 8.7 Hz; H-C(PMB)), 6.87 (d, 2H, $J=8.7$ Hz; H-C(PMB)), 4.67 (brs, 1H; H_A-C(1)), 4.67 (brs, 1H; H_B-C(1)), 4.52 (s, 2H; H_2-C(PMB)), 4.00 (m, 1H; H-C(6)), 3.90 (dt, 1H, $J=6.8$, 10.0 Hz; H-C(4)), 3.80 (s, 3H; MeO-(PMB)), 3.73 (m, 2H; H_2-C(8)), 2.10 (dddd, 2H, $J=4.7$, 5.5, 14.0 Hz; H_2C(3)), 1.87 (ddd, 1H, $J=6.3$, 13.0 Hz; H_A-C(7)), 1.74 (ddd, 1H, $J=6.3$, 13.3 Hz; H_B-C(7)), 1.66 (m, 2H; H_2-C(5)), 1.54 (s, 2H; H_2C(1′)), 0.90 (s, 9H; H-C(TBS)), 0.06 (s, 6H; H-C(TBS)), 0.03 ppm (s, 9H; H-C(TMS)); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=144.5$ (s, C(2)), 157.9, 136.8 (2×s, C_{arom}), 129.5, 113.8 (2×d, C_{arom}), 110.0 (t, C(1)), 74.9 (d, C(6)), 71.4 (t, CH_2-(PMB)), 64.8 (d, C(4)), 59.7 (t, C(8)), 55.3 (q, CH_3-(PMB)), 46.7 (t, C(3)), 40.6 (t, C(5)), 37.3 (t, C(7)), 26.7 (t, C(1′)), 25.9 (q, CH_3-(TBS)), 18.2 (s, C-(TBS)), −1.4 (q, CH_3-(TMS)), −5.0 ppm (q, CH_3-(TBS)); IR (film): $\tilde{\nu}=3452$, 3050, 2952, 1556, 1346, 1098, 857, 697, 660, 611, 567 cm^{-1}; HRMS (MALDI): calcd for $C_{26}H_{49}O_4Si_2$: 481.3091 [M+H]; found: 481.3091.

Synthesis of *tert*-butyl ((3*R*,5*R*)-5-methoxy-3-(4-methoxybenzyloxy)-7((trimethylsilyl)methyl)oct-7-enyloxy)dimethylsilane (34): NaH (0.110 g, 2.75 mmol) was added portionwise to a solution of (4*R*,6*R*)-8-((*tert*-butyl)dimethylsilyloxy)-6-(4-methoxybenzyloxy)-2-((trimethylsilyl)methyl)-oct-1-en-4-ol (0.66 g, 1.37 mmol) and MeI (1.95 g, 13.73 mmol) in THF (10 mL) at 0 °C. After stirring at 0 °C for 1 h the mixture was stirred at 25 °C for 16 h. The reaction mixture was quenched with dropwise addition of a saturated aqueous solution of NH_4Cl (15 mL) and extracted with ether (50 mL). The organic layers were washed with brine (20 mL), dried ($MgSO_4$), filtered, and concentrated. The crude residue was purified by flash chromatography (petroleum ether/Et_2O, 95:5) to give **34** (0.590 g, 87 %) as a colorless oil. $[\alpha]_{589}^{25}=9.3$ ($c=0.23$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.28$ (d, 2H, $J=8.1$ Hz; H-C(PMB)), 6.88 (d, 2H; $J=8.1$ Hz, H-C(PMB)), 4.64 (brs, 1H; H_A-C(8)), 4.59 (brs, 1H; H_B-C(8)), 4.50 (2×d, 2H; $J=11.1$ Hz; H_2-C(PMB)), 3.80 (s, 3H; MeO-(PMB)), 3.72 (m, 1H; H-C(5)), 3.72 (m, 2H; H_2-C(1)), 3.51 (m, 1H; H-C(3)), 3.27 (s, 3H; MeO-C(5)), 2.31 (dd, 1H, $J=6.4$, 14.0 Hz; H_A-C(6)), 1.97 (dd, 1H, $J=7.0$, 14.0 Hz; H_B-C(6)), 1.74 (m, 2H; H_2-C(2)), 1.76 (m, 1H; H_A-C(4)), 1.53 (m, 1H; H_B-C(4)), 1.55 (s, 2H; H_2-C(1′)), 0.91 (s, 9H; H-C(TBS)), 0.06 (s, 6H; H-C(TBS)), 0.03 ppm (s, 9H; H-C(TMS)); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=144.6$ (s, C-(7)), 156.9, 132.2 (2×s, C_{arom}), 129.5, 113.8 (2×d, C_{arom}), 109.3 (t, C(8)), 88.2 (d, C(5)), 73.9 (d, C(3)), 71.3 (t, CH_2-(PMB)), 64.8 (t, C(1)), 59.6 (q, OMe), 55.2 (q, CH_3-(PMB)), 46.7 (t, C(6)), 40.6 (t, C(4)), 35.7 (t, C(2)), 26.7 (t, CH_2-C(1′)), 25.8 (q, CH_3-(TBS)), 18.2 (s, C-(TBS)), −1.4 (q, CH_3-(TMS)), −5.3 ppm (q, CH_3-(TBS)); IR (film): $\tilde{\nu}=3050$, 2927, 2855,1729, 1513, 1463, 1361, 1247, 1093, 835, 633 cm^{-1}; HRMS (MALDI): calcd for $C_{27}H_{51}O_4Si_2$: 95.3247 [M+H]; found: 495.3258.

Synthesis of (2*R*,4*R*,8*R*,10*R*)-1-(benzyloxy)-12-((*tert*-butyl)dimethylsilyloxy)-8-methoxy-2,10-bis(4-methoxybenzyloxy)-6-methylenedodecan-4-ol (14):

Method A: $BF_3{\cdot}OEt_2$ (0.267 g, 0.380 mL, 0.808 mmol) was added dropwise to a stirred solution of **16**[31,47] (0.305 g, 0.970 mmol) and allyl silane **34** (0.400 g, 0.808 mmol) at −78 °C in CH_2Cl_2 (50 mL). The mixture was stirred at −78 °C for 1 h before being quenched with a saturated aqueous solution of NH_4Cl (20 mL) and allowed to warm to 25 °C. The mixture was diluted with Et_2O (100 mL) and the aqueous phase was extracted with Et_2O (50 mL). The combined organic phases were washed with brine (50 mL), dried ($MgSO_4$), and evaporated. The crude residue was purified by column chromatography (petroleum ether/Et_2O, 8:2) to give **14** (0.502 g, 84 %) as a colorless oil. $[\alpha]_{589}^{25}=14.2$ ($c=0.23$, $CHCl_3$).

Method B: 3,5-Bis(trifluoromethyl)phenylboronic acid (11 mg, 0.004 mmol) was added to a solution of mono(2,6-diisopropoxybenzoyl) tartrate (16 mg, 0.044 mmol) in dry propionitrile (1 mL) at 25 °C and the mixture was stirred for 30 min. The mixture cooled to −78 °C. Aldehyde **16** (0.070 g, 0.222 mmol) and allyltrimethylsilane **34** (0.110 g, 0.222 mmol) were added to this solution. After being stirred for 12 h, the reaction mixture was poured into brine (5 mL) and extracted with Et_2O (5 mL, 3 times), dried ($MgSO_4$), and concentrated. The crude residue was purified by column chromatography (petroleum ether/Et_2O, 9:1) to give **14** (0.121 g, 74 %) as a colorless oil. $[\alpha]_{589}^{25}=16.1$ ($c=0.30$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.38$–7.30 (m, 5H; H-C(Bn)), 7.29 (2×d, 4H, $J=$ 7.3 Hz; 2×H-C(PMB)), 6.89 (d, 2H, $J=7.3$ Hz; H-C(PMB)), 6.88 (d, 2H, $J=7.3$ Hz; H-C(PMB)), 4.93, (brs, 1H;H_A-C(1′)), 4.91 (brs, 1H; H_B-C(1′)), 4.63 (2d, 2H, $J=11.3$ Hz; H_2-C(PMB)), 4.47 (2d, 2H, $J=11.9$ Hz; H_2-C(PMB)), 4.58 (s, 2H; H_2-C(Bn)), 4.01 (m, 1H; H-C(2)), 3.94 (m, 1H; H-C(4)), 3.81 (2×s, 6H; MeO(PMB) and MeO(PMB)), 3.75 (m, 1H; H-C(8)), 3.75 (m, 2H; H_2-C(1)), 3.60 (m, 1H; H-C(10)), 3.59 (m, 2H; H_2-C(12)), 3.26 (s, 3H; MeO-C(8)), 2.43–2.27 (m, 1H; H_A-C(5)), 2.26–2.08 (m, 3H; H_B-C(5) and H_2-C(11)), 1.90–1.50 (m, 6H; H_2-C(9) and H_2-C(7) and H_2-C(3), 0.92 (s, 9H, H-C(TBS)), 0.08 ppm (s, 6H, H-C-(TBS)); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=159.6$, 159.5, 144.0 (3×s, C_{arom}), 138.7 (s, C(6)), 129.8, 129.6 (2×s, C_{arom}), 129.9, 128.8, 127.9, 114.3, 114.2, 114.2, 114.1 (7×d, C_{arom}), 115.2 (t, C(1′), 77.4 (d, C(8)), 75.6 (d, C(2)), 73.4 (t, CH_2-(PMB)), 73.4 (d, C(10)), 73.2 (t, CH_2-(PMB)), 72.4 (t, CH_2-(Bn)), 71.4 (t, C(1)), 66.3 (d, C(4)), 60.0 (t, C(12)), 56.9 (q, OMe), 55.8, 55.7 (2q, CH_3-(PMB)), 45.5 (t, C(5)), 40.6 (t, C(7)), 39.5 (t, C(11)), 39.5 (t, C(3)), 38.2 (t, C(9)), 26.4 (q, CH_3-(TBS)), 18.7 (s, C-(TBS)), −4.9 ppm (q, CH_3-(TBS)); IR (film): $\tilde{\nu}=3458$, 3050, 2928, 2855,1612, 1513, 1463, 1248,1092, 1036, 835, 631 cm^{-1}; HRMS (MALDI): calcd for $C_{43}H_{65}O_8S$: 737.4370 [M+H]; found: 737.4371.

Synthesis of (2*R*,4*R*,8*R*,10*R*)-1-(benzyloxy)-4,12-bis((*tert*-butyl)dimethylsilyloxy)-8-methoxy-2,10-bis(4-methoxybenzyloxy)-6-methylenedodecane: Imidazole (0.028 g, 0.407 mmol) was added to a solution of *tert*-butyl-dimethylchlorosilane (0.061 g, 0.407 mmol) in CH_2Cl_2 (5 mL) at 25 °C. Alcohol **14** (0.200 g, 0.271 mmol) was added dropwise to this mixture. Upon completion of the addition, the mixture was stirred for 2 h. The mixture was diluted with Et_2O (20 mL) and washed with H_2O (3×10 mL). The combined organic phase was washed with brine (10 mL), dried ($MgSO_4$), and evaporated. The crude was purified by column chromatography (petroleum ether/Et_2O, 9:1) to give the product (0.210 g, 91 %) as a colorless oil. $[\alpha]_{589}^{25}=10.3$ ($c=0.34$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.35$–7.30 (m, 5H; H-C(Bn)), 7.26 (2×d, 4H; $J=8.4$ Hz, 2×H-C(PMB)), 6.86 (2×d, 4H, $J=8.4$ Hz; 2×H-C(PMB)), 4.82 (brs, 2H; H_A-C(1′) and H_B-C(1′)), 4.55 (s, 2H; H_2-C(Bn)), 4.49 (2×d, 2H, $J=12.0$ Hz; H_2-C(PMB)), 4.44 (2×d, 2H, $J=11.0$ Hz; H_2-C(PMB)), 4.07 (m, 1H; H-C(2)), 3.80 (m, 1H; H-C(4)), 3.80 (s, 3H; MeO(PMB)), 3.79 (s, 3H; MeO(PMB)), 3.75 (m, 1H; H-C(8)), 3.75 (m, 2H; H_2-C(1)), 3.62 (m, 1H; H-C(10)), 3.59 (m, 2H; H_2-C(12)), 3.22 (s, 3H; MeO(C8)), 2.40–2.25 (m, 2H; H_2-C(7)), 2.20–1.93 (m, 2H; H_2-C(11)), 1.84–1.62 (m, 4H; H_2-C(9) and H_2-C(5)), 1.54–1.41 (m, 2H; H_2-C(3)), 0.92 (s, 9H; H-C(TBS)), 0.88 (s, 9H; H-C-(TBS)), 0.08 (s, 6H; H-C(TBS)), 0.05 ppm (s, 6H; H-C(TBS)); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta=159.0$, 158.9, (2×s, C_{arom}), 138.4 (s, C(6)), 129.4, 129.3, 129.2 (3×s, C_{arom}), 128.9, 128.3, 128.1, 127.6, 127.5, 113.7, 113.6 (7× d, C_{arom}) 115.2 (t, C(1′)), 76.4 (d, C(8)), 76.2 (d, C(2)), 75.2 (d, C(10)), 73.5 (t, CH_2-(PMB)), 73.2 (t, CH_2-(PMB)), 72.8 (t, CH_2-(Bn)), 72.7 (t, C(1)), 68.0 (d, C(4)), 59.7 (t, C(12)), 56.4 (q, OMe), 55.2, 55.2 (2q, CH_3-(PMB)), 45.1 (t, C(5)), 40.7 (t, C(7)), 40.6 (t, C(11)), 39.8 (t, C(3)), 37.9 (t, C(9)), 26.0 (q, CH_3-(TBS)), 25.6 (q, CH_3-(TBS)), 18.3 (s, C-(TBS)), 18.0 (s, C-(TBS)), −4.5 (q, CH_3-(TBS)), −5.3 ppm (q, CH_3-(TBS)); IR (film): $\tilde{\nu}=3050$, 2951, 2927, 2855, 1613, 1514, 1463, 1248, 1092, 1039, 834, 774, 632, 541 cm^{-1}; HRMS (MALDI): calcd for $C_{49}H_{79}O_8Si$: 851.5835 [M+H]; found: 851.5842.

Synthesis of (2*R*,4*R*,8*R*,10*R*)-1-(benzyloxy)-4,12-bis((*tert*-butyl)dimethylsilyloxy)-8-methoxy-2,10-bis(4-methoxybenzyloxy)-6-methylenedodecan-6-one (35): O_3 was bubbled through a solution of the olefin obtained above (0.210 g, 0.285 mmol) in CH_2Cl_2 (6 mL) at −78 °C until the solution was saturated (5 min), which was indicated by the solution turning blue. The ozone generator was then turned off and O_2 was bubbled through the solution for 10 min. The reaction was flushed with Ar and Me_2S (0.50 mL) was added dropwise at −78 °C. After stirring for 1 h at this temperature the reaction was warmed to 25 °C and stirred for 1 h. The solvent was removed under reduced pressure. The crude was purified by column chromatography (petroleum ether/Et_2O, 9:1) to give **35** (0.192 g, 91 %) as s colorless oil. $[\alpha]_{589}^{25}=8.4$ ($c=0.2$, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.38$–7.33 (m, 5H; H-C(Bn)), 7.29 (d, 2H, $J=$ 7.7 Hz; H-C(PMB)), 7.27 (d, 2H, $J=7.7$ Hz; H-C(PMB)), 6.88 (d, 2H, $J=7.7$ Hz; H-C(PMB)), 6.86 (d, 2H, $J=7.7$ Hz; H-C(PMB)), 4.55 (s, 2H; H_2-C(Bn)), 4.67–4.35 (m, 4H, 2×H_2-C(PMB)), 3.86 (m, 1H; C(2)), 3.80 (2×s, 6H; 2×MeO(PMB)), 3.72 (m, 1H; H-C(8)), 3.71 (m, 1H; H-C(4)), 3.71 (m, 2H, H_2-C(1)), 3.70 (m, 2H; H_2-C(12)), 3.55 (m, 1H; H-C(10)),

3.25 (s, 3H; MeO(C8)), 2.71–2.53 (m, 3H; H_2-C(7) and H_A-C(5)), 2.51–2.41 (m, 1H; H_B-C(5)), 1.90–1.77 (m, 2H; H_2-C(11)), 1.77–1.68 (m, 2H; H_2-C(9), 1.68–1.57 (m, 2H; H_2-C(3)), 0.91 (s, 9H; H-C(TBS)), 0.87 (s, 9H; H-C(TBS)), 0.07 (s, 6H; H-C(TBS)), 0.03 ppm (s, 6H; H-C(TBS)); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 207.6$ (s, C(6)), 159.1, 159.0, 138.3, 131.7, 131.0 (5×s, C_{arom}), 129.7, 129.3, 129.2, 128.4, 127.6, 113.8, 113.6 (7×d, C_{arom}), 75.2 (d, C(8)), 75.1 (d, C(10)), 73.3 (t, CH_2-(PMB)), 73.0 (d, C(2)), 72.8 (t, CH_2-(PMB)), 71.2 (t, C(1)), 70.7 (t, CH_2-(Bn)), 66.3 (d, C(4)), 59.6 (t, C(12)), 57.1 (q, OMe), 55.2 (q, CH_3-(PMB)), 55.2 (q, CH_3-(PMB)), 52.3 (t, C(5)), 49.1 (t, C(7)), 40.6 (t, C(11)), 40.5 (t, C(3)), 37.7 (t, C(9)), 25.9 (q, CH_3-(TBS)), 25.8 (q, CH_3-(TBS)), 18.3 (s, C-(TBS)), 18.0 (s, C-(TBS)), −4.6 (q, CH_3-(TBS)), −5.3 ppm (q, CH_3-(TBS)); IR (film): $\tilde{\nu} = 3050$, 2928, 1698, 1601, 1512, 1249, 1093, 834, 776, 632, 539 cm^{-1}; HRMS (MALDI): calcd for $C_{48}H_{77}O_9Si_2$: 853.5128 [*M*+H]; found: 853.5125.

Synthesis of (2-((2*R*,4*S*,6*R*,8*R*,10*S*)-8-(benzyloxymethyl)-4-methoxy-10-((*tert*-butyl)dimethylsilyloxy)-2–2-(*tert*-butyl)dimethylsilyoxy)ethyl)-1,7-dioxaspiro[5.5]undecane (CD spiroacetal 13): 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (0.015 g, 0.064 mmol) was added to a solution of ketone **35** (0.050 g, 0.059 mmol) in 1:1 CH_2Cl_2/H_2O (5 mL) at 0 °C. The solution was stirred for 1 h at 0 °C before it was allowed to warm to 25 °C and stirred for another 1 h. TLC indicated the consumption of the starting material and the mono-deprotection; the reaction mixture was stirred for 16 h. The solvent was removed under reduced pressure. The crude residue was purified by column chromatography (petroleum ether/Et_2O, 7:3) to give **13** (0.025 g, 72 %) as a colorless oil. $[\alpha]_{589}^{25} = -15.1$ ($c = 0.34$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.38$–7.35 (m, 5H; H-C(Bn)), 4.59 (s, 2H; H_2-C(Bn)), 4.20 (m, 1H; H-C(8)), 3.89 (m, 1H; H-C(10)), 3.79 (m, 1H; H_A-C(2′)), 3.71 (m, 1H; H_B-C(2′)), 3.59–3.51 (m, 2H; H-C(2) and H_A-C(1″)), 3.50–3.44 (m, 2H; H-C(4) and H_B-C(1″)), 3.36 (s, 3H; MeO), 2.29 (dd, 1H, $J = 3.9$, 13.4 Hz; H_{eq}-C(11)), 2.16 (dd, 1H, $J = 3.4$, 12.0 Hz; H_{eq}-C(5)), 2.06 (dd, 1H, $J = 3.4$, 11.5 Hz; H_{ax}-C(5)), 1.93 (m, 1H; H_{eq}-C(9)) 1.90 (m, 1H; H_A-C(1′)), 1.74–1.69 (m, 2H; H_B-C(1′) and H_{ax}-C(9)), 1.40 (m, 1H; H_{eq}-C(3)), 1.39–1.25 (m, 2H; H_{ax}-C(11) and H_{ax}-(3)), 0.90 (2×s, 9H; H-C(TBS)), 0.89 (2×s, 9H; H-C(TBS)), 0.07 (2×s, 6H; H-C(TBS)), 0.06 ppm (2×s, 6H; H-C(TBS)); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.4$ (s, C_{arom}), 128.3, 127.7, 127.4 (3×d, C_{arom}), 99.7 (s, spiroC-C(6)), 74.1 (d, C(4)), 73.4 (t, CH_2-(Bn)), 72.9 (t, C(1″)), 68.9 (d, C(10)), 68.2 (t, C(2′)), 64.6 (d, C(2)), 60.3 (d, C(8)), 55.5 (t, OMe), 42.1 (t, C(5)), 39.5 (t, C(11)), 39.2 (t, C(3)), 38.1 (t, C(1′)), 37.4 (t, C(9)), 26.0 (q, CH_3-(TBS)), 25.9 (q, CH_3-(TBS)), 18.4 (s, C-(TBS)), 18.0 (s, C-(TBS)), −4.5 (q, CH_3-(TBS)), −5.2 ppm (q, CH_3-(TBS)); IR (film): $\tilde{\nu} = 3050$, 2927, 2825, 1603, 1589, 1513, 1462, 1360, 1247, 1093, 835, 633 cm^{-1}; HRMS (MALDI): calcd for $C_{32}H_{59}O_6Si_2$: 595.3792 [*M*+H]; found: 595.3790.

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