Total Synthesis of Hemibrevetoxin B and (7aα)-*epi*-Hemibrevetoxin B

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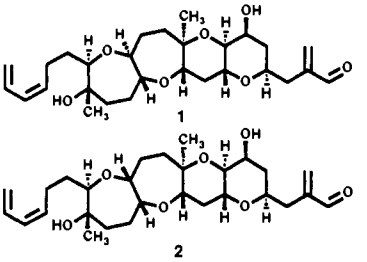
Abstract: The total synthesis of hemibrevetoxin B (**1**) and (7aα)-*epi*-hemibrevetoxin B (**2**) is described. The synthesis of the epimer (**2**) was achieved through a convergent approach involving coupling of the carboxylic acid **17** carrying the bicyclic pyran system with the hydroxy compound **31** containing the monocyclic pyran system, thionation of the resulting diester **32** to the dithionoester **33**, photolytic closure to the oxepane enol ether **34**, and hydroxy ketone cyclization to the dioxepane system **40**. The *Z*-diene system was established using a selenyl-Wittig reaction followed by syn elimination of the selenoxide to the diene. The α-vinyl functionality was installed using the Eschenmoser's salt methodology. The synthesis of hemibrevetoxin B (**1**) was achieved through a linear approach involving sequential formation of the oxepane rings (**65** → **67** → **73**) using the method of thionolactone formation followed by nucleophilic addition and regio/stereoselective hydroboration (**67** → **68**, **75** → **76**). Elaboration of the side chains was carried out in a similar fashion as described for the epimer. The stereochemistry of the ring junctures in **1** and **2** and intermediates leading to them was established by X-ray crystallographic analysis carried out on compounds **45** and **54**. Biological studies with (7aα)-*epi*-hemibrevetoxin B (**2**) revealed no binding for this molecule to the brevetoxin receptors.

Introduction

Among the most prominent toxins associated with the "red tide" phenomenon,[1] periodically occurring in the Gulf of Mexico and the coasts of Florida, are the brevetoxins. These compounds are neurotoxins produced by the dinoflagellate strain *Gymnodinium breve* Davis,[1] and they have been implicated in the massive fish kills, molusk poisonings, and human intoxications periodically observed during outbreaks of the "red tide" catastrophes. The brevetoxins exert their biological effects by activating sodium channels and causing repetitive firing in neurons.[2] They bind to a receptor different to that for other known toxins.[2] However, the precise nature of their binding site is presently unknown and under investigation.

The first members of this class of marine natural products to be structurally elucidated were brevetoxin A[3] and brevetoxin B.[4] Since then, a number of other brevetoxin structures appeared.[5] In 1989, Shimizu et al.[6] isolated a new series of compounds having molecular size approximately half that of the brevetoxins. These compounds were named hemibrevetoxins. The structure of hemibrevetoxin B (**1**) was assigned based on spectroscopic data and comparisons to the other known brevetoxins.[6] Hemibrevetoxin B has a 7,7,6,6-tetracyclic ether skeleton and contains 10 stereocenters, an α-vinyl aldehyde moiety, and a *Z*-diene system.

Scheme I. Structures of Hemibrevetoxin B (**1**) and (7aα)-*epi*-Hemibrevetoxin B (**2**)



From a synthetic viewpoint, these molecules provide many challenges and opportunities due to their unusual polycyclic ether framework and novel functionalities. Several studies directed toward new synthetic methods and toward the total synthesis of members of this class have been reported from these laboratories.[7] Herein we report in detail a total synthesis of hemibrevetoxin B (**1**) and its (7aα)-epimer, (7aα)-*epi*-hemibrevetoxin B (**2**)[8,9] (Scheme I).

The retrosynthetic analysis on which the first strategy towards hemibrevetoxin B (**1**) was based, is shown in Scheme II. According to this analysis, the indicated C–O bond in the target structure was disconnected to unravel, after further manipulation,

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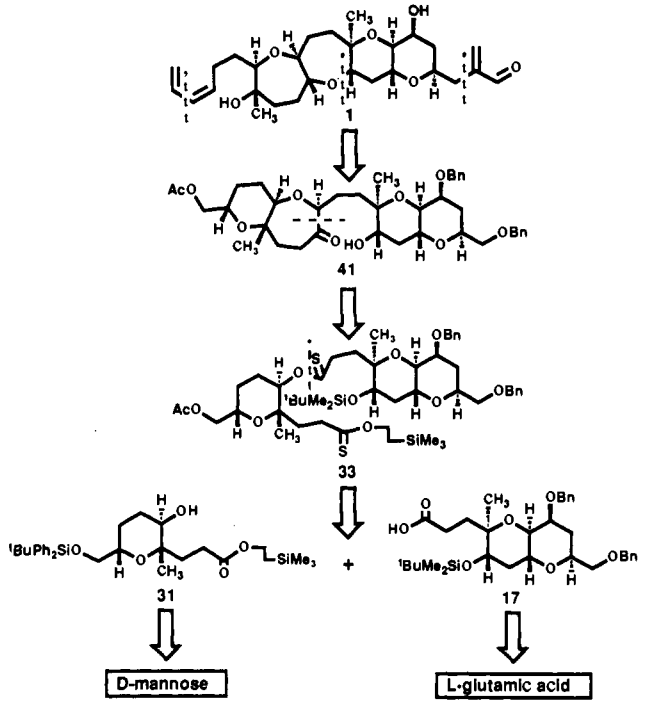
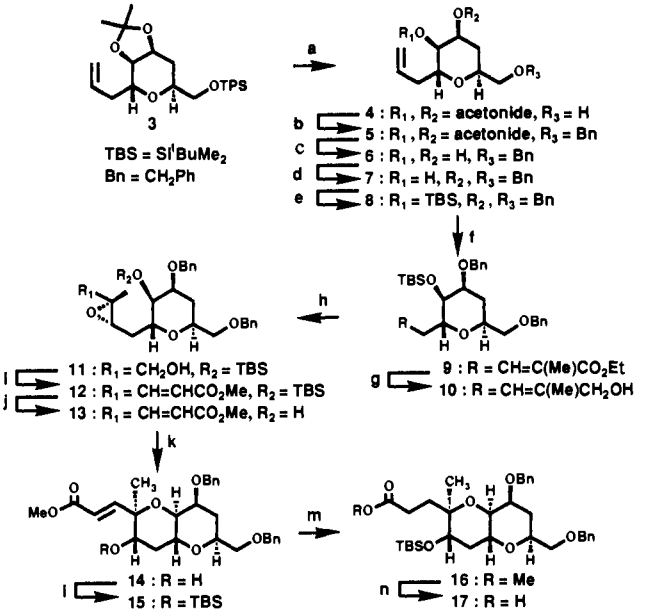
Scheme II. Retrosynthetic Analysis of Hemibrevetoxin B (**1**) (Convergent Approach)



the hydroxy ketone **41** as a potential precursor. Noteworthy was the introduction of the extra tetrahydropyran ring in the structure, which in the end was to be dismantled and converted into the diene system. The purpose for the introduction of this ring was 2-fold: first the projected cyclizations to construct macrocycles and oxepanes were expected to be much more efficient due to entropy reasons, as already demonstrated in several models in this program,[7] and second, it was to serve as a masked equivalent to the hydroxy diene system of the target molecule, thus simplifying protection issues. Further disconnection of the indicated C–C bond dismantled the second oxepane ring, leading to key intermediate dithionoester **33** which was then disconnected to two further simplified fragments **31** and **17**. These tetrahydropyran systems were envisioned to arise via regio- and stereoselective epoxide opening–ring closure procedures[7a] and were further traced back to the readily available starting materials D-mannose and L-glutamic acid. A convergent strategy was thus designed involving coupling of the acid and alcohol intermediates **17** and **31**, followed by projected stepwise construction of the oxepane rings and final elaboration to hemibrevetoxin B (**1**). Even though the initial synthetic design targeted hemibrevetoxin B (**1**), in the event, this approach led to its (7aα)-epimer (**2**) due to the delivery of the "wrong" epimer of an advanced intermediate. The synthesis of **2** is described below.

Synthesis of (7aα)-*epi*-Hemibrevetoxin B (2). The synthesis of the bicyclic tetrahydropyran acid key intermediate **17** started from the known compound **3** (obtained from D-mannose in six steps)[10] as shown in Scheme III. Desilylation of **3** (**4**, 80% yield), followed by benzylation of the resulting primary alcohol, afforded fully protected **5** in 90% yield. This was then further subjected to acetonide removal using trifluoroacetic acid, which gave diol **6** in quantitative yield. Selective monobenzylation of the equatorial hydroxyl was accomplished according to Nashed's procedure.[11] Thus, treatment of diol **6** with dibutyltin oxide in methanol, followed by addition of benzyl bromide and cesium fluoride in DMF and stirring at room temperature for 12 h, gave benzyl ether **7** in 81% yield. Silylation of the remaining free

Scheme III[a]



[a] (a) 1.2 equiv of TBAF, THF, 25 °C, 1 h, 80%; (b) 1.5 equiv of NaH, 0.2 equiv of $^nBu_4NI$, 1.2 equiv of BnBr, THF, 25 °C, 24 h, 90%; (c) 5 equiv of TFA, toluene, 0 °C, 15 min, 98%; (d) (i) 1.1 equiv of Bu_2SnO, MeOH, 60 °C, 1.5 h; (ii) 1.5 equiv of BnBr, 1.2 equiv of CsF, DMF, 16 h, 25 °C, 81%; (e) 1.2 equiv of TBSOTf, 1.5 equiv of 2,6-lutidine, CH_2Cl_2, 0 °C, 0.5 h, 82%; (f) (i) O_3, CH_2Cl_2, −78 °C, 10 min, then Ph_3P, 25 °C, 1 h; (ii) 1.2 equiv of $Ph_3P{=}C(Me)CO_2Me$, benzene, 80 °C, 2 h, 68%; (g) 2.2 equiv of DIBAL, CH_2Cl_2, −78 °C, 1 h, 85%; (h) 0.2 equiv of (+)-DET, 0.15 equiv of $Ti(O^iPr)_4$, 1.5 equiv of ^tBuOOH, CH_2Cl_2, 4-Å MS, −20 °C, 16 h, 97%; (i) (i) 2 equiv of SO_3·py, 4 equiv of Et_3N, CH_2Cl_2–DMSO (4:1), 0 °C, 2 h; (ii) 1.5 equiv of $Ph_3P{=}CHCOOMe$, benzene 25 °C, 12 h, 77%; (j) 1.2 equiv of TBAF, THF, 25 °C, 2 h, 97%; (k) 0.3 equiv of CSA, CH_2Cl_2, 25 °C, 4 h, 76%; (l) 1.2 equiv of TBSOTf, 2.0 equiv of 2,6-lutidine, CH_2Cl_2, 0 °C, 0.5 h, 81%; (m) (i) H_2, 5% Pc/C, EtOAc, 12 h, 90%; (n) 2.0 equiv of LiOH, THF–H_2O (3:1), 50 °C, 12 h, 86%.

alcohol with TBSOTf and 2,6-lutidine in dichloromethane afforded fully protected compound **8** in 82% yield. Ozonolysis of the terminal alkene in **8**, followed by stirring with (carbethoxyethylene)triphenylphosphorane under reflux in benzene for 2 h, gave trans α,β-unsaturated ester **9** as the only product, with no cis compound detected. The ester was then reduced to the alcohol under DIBAL conditions to afford allylic alcohol **10** in 85% yield. This compound was thus set up to undergo the Sharpless asymmetric epoxidation reaction.[12] The transformation of allylic alcohol **10** to epoxide **11** proceeded smoothly under standard conditions at −20 °C, using (+)-diethyl tartrate, and gave one isomer as product in 97% yield. Oxidation of the primary hydroxyl to the aldehyde using SO_3–pyridine and then immediate treatment with the Wittig reagent methyl (triphenylphosphoranylidene)acetate afforded the trans α,β-unsaturated ester **12** in 77% overall yield for the two steps. Compound **12** was desilylated under standard conditions using $^nBu_4NF$ in THF to give hydroxy epoxide **13** in 97% yield. Compound **13** was appropriately designed to further undergo an epoxide opening–ring closure type reaction, to give preferentially the 6-endo over the 5-exo product.[7a] This acid-catalyzed reaction proceeded smoothly using CSA in dichloromethane at room temperature. Thus **13** was converted to the bicyclic tetrahydropyran **14** in 76% yield. Treatment of the resulting secondary hydroxyl with TBSOTf and 2,6-lutidine in dichloromethane afforded **15** in 81% yield, which was then further treated with 5% Pd/C under a hydrogen atmosphere for 12 h to give saturated ester **16** in 90% yield. Finally, the conversion of the methyl ester in **16** to the free carboxylic acid **17** was achieved using lithium hydroxide in THF–H_2O (3:1) at 50 °C (12 h), (86% yield, Scheme III).

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(11) Nashed, M. *Carbohydr. Res.* **1978**, *60*, 200.
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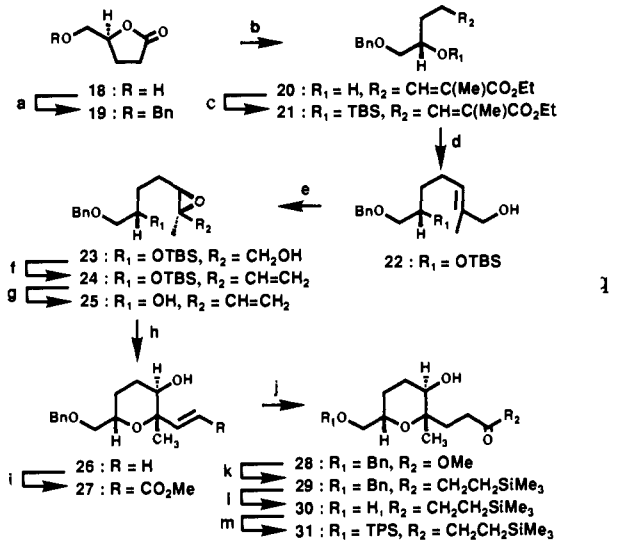
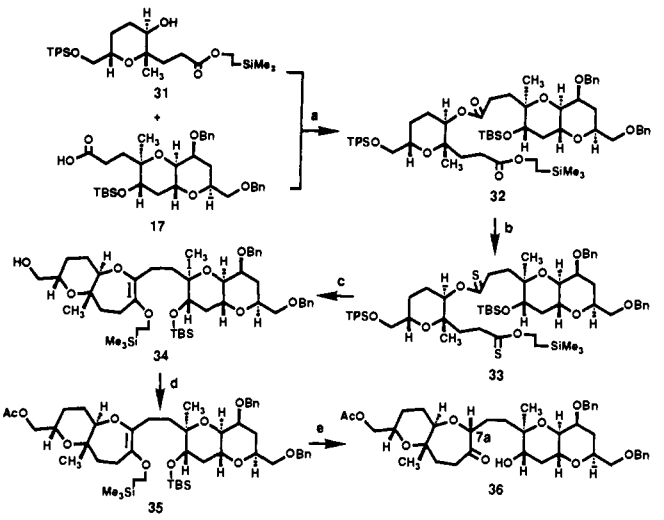
Scheme IV[a]



[a] (a) 1.2 equiv of $Cl_3CC(=NH)OCH_2C_6H_5$, 0.2 equiv of HOTf, CH_2Cl_2–petroleum ether (2:1), 0 °C, 0.5 h, 70%; (b) (i) 1.2 equiv of DIBAL, CH_2Cl_2, −78 °C, 0.5 h; (ii) 1.2 equiv of $Ph_3P{=}C(Me)CO_2Et$, benzene, 80 °C, 0.5 h, 98%; (c) 1.1 equiv of TBSCl, 1.5 equiv of imidazole, DMF, 25 °C, 12 h, 96%; (d) 2.2 equiv of DIBAL, CH_2Cl_2, −78 °C, 0.5 h, 91%; (e) 0.12 equiv of (−)-DET, 0.1 equiv of $Ti(O^iPr)_4$, 1.5 equiv of ^{t}BuOOH, 4-Å MS, CH_2Cl_2, −20 °C, 12 h, 80%; (f) (i) 2 equiv of SO_3·py, 4 equiv of Et_3N, EtOAc, 0 °C, 2 h; (ii) 1.4 equiv of CH_3Ph_3PBr, 1.2 equiv of $NaN(SiMe_3)_2$, THF, 0 °C, 1 h, 72%; (g) 1.3 equiv of TBAF, THF, 25 °C, 2.5 h, 76%; (h) 0.05 equiv of CSA, CH_2Cl_2, 25 °C, 4 h, 78%; (i) (i) O_3, CH_2Cl_2, −78 °C, then 2 equiv of Ph_3P, 25 °C, 3 h; (ii) 1.2 equiv of $Ph_3P{=}CHCOOMe$, benzene, 80 °C, 2 h, 86%; (j) H_2, 5% Pd/C, EtOAc, 1.5 h, 95%; (k) 10 equiv of $Me_3Si(CH_2)_2OH$, 0.2 equiv of NaH, THF, 0 °C, 15 min, 73%; (l) H_2, $Pd(OH)_2$, EtOAc, 1 h, 100%; (m) 1.1 equiv of TPSCl, 2.0 equiv of imidazole, DMF, 0.5 h, 25 °C, 81%.

The synthesis of the monocyclic tetrahydropyran precursor **31** started from commercially available (*R*)-(−)-dihydro-5-(hydroxymethyl)-2(3*H*)-furanone (**18**) (also obtained from L-glutamic acid in two steps)[13] (Scheme IV). Acid-catalyzed benzylation of **18** afforded lactone **19** in 70% yield. Standard benzylation conditions proved unsuccessful and resulted in decomposition of the starting material. Lactone **19** was reduced with DIBAL to the corresponding lactol intermediate which was in equilibrium with the corresponding aldehyde. Direct treatment of this DIBAL product with (carbethoxyethylene)triphenylphosphorane in benzene under reflux for 30 min afforded trans α,β-unsaturated ester **20** in 98% overall yield for the two steps. The resulting free hydroxyl group in **20** was silylated under standard conditions furnishing TBS-protected derivative **21** in 96% yield. The ester functionality in **21** was reduced under DIBAL conditions to furnish allylic alcohol **22** in 91% yield. Once again the Sharpless asymmetric epoxidation reaction was applied using the (−)-diethyl tartrate under standard conditions at −20 °C to afford hydroxy epoxide **23** in 80% yield as the only product. Oxidation of the primary alcohol in **23** to the aldehyde with SO_3–pyridine and direct exposure to the Wittig reaction using methyltriphenylphosphonium bromide and sodium bis(trimethylsilyl)amide in THF at 0 °C, afforded terminal alkene **24** in an overall yield of 72% for the two steps. Desilylation of **24** to alcohol **25** was carried out under standard conditions using ^{n}Bu$_4$NF and proceeded in 76% yield. Once again the epoxide opening–ring closure reaction[7a] to afford the 6-endo over the 5-exo product could be applied. Thus, using CSA catalysis, hydroxy epoxide **25** was converted regio- and stereoselectively to the tetrahydropyran system **26** in 78% yield. The remaining steps to the final precursor **31** were now a matter of side-chain manipulation. Ozonolysis of the terminal olefin followed by Wittig reaction using methyl (triphenylphosphoranylidene)acetate in benzene under reflux furnished trans α,β-unsaturated ester **27** in 86% yield. Hydrogenation of the double bond in **27** using 5% Pd/C as catalyst gave saturated ester **28** in 95% yield. In order for the ester to withstand drastic conditions later in the scheme (Lawesson's reagent, high temperature), the methyl ester of **28** had to be converted to the more stable 2-(trimethylsilyl)ethyl ester **29**. This transformation was accomplished via a transesterification process by addition of catalytic amounts of sodium hydride to 2-(trimethylsilyl)ethanol followed by addition of the methyl ester **28**, giving **29** in 73% yield. Finally, debenzylation of **29** to alcohol **30** (quantitative) and then silylation of the primary alcohol in **30** afforded the monocyclic tetrahydropyran alcohol precursor **31** in 81% yield (Scheme IV).

Scheme V[a]



[a] (a) 0.4 equiv of DMAP, 0.2 equiv of CSA, 1.3 equiv of DCC, CH_2Cl_2, 25 °C, 3 h, 85%; (b) 4 equiv of Lawesson's reagent, 4 equiv of $S{=}C(NMe)_2$, xylenes, 175 °C, 1.5 h, 49%; (c) (i) *hν*, $NaHCO_3$, benzene, 70 °C, 2 h; (ii) 1.5 equiv of TBAF, THF, 25 °C, 12 h, 47% (overall two steps); (d) 1.1 equiv of Ac_2O, 3 equiv of Et_3N, 0.1 equiv of DMAP, CH_2Cl_2, 25 °C, 2 h, 86%; (e) HF–py, CH_2Cl_2, 0 °C, 1 h, 90%.

The right- (**17**) and left- (**31**) hand precursors to the hemibrevetoxin B ring skeleton were then ready to be coupled and elaborated further towards the target molecule. Scheme V depicts the chemistry leading to key intermediate **36**. Coupling of acid **17** with alcohol **31** was accomplished with DCC, DMAP, and CSA in dichloromethane, furnishing diester **32** in 85% yield. Conversion of this diester to dithionoester **33** proved to be more challenging than expected. After several attempts with different reaction conditions varying time, temperature, number of equivalents of reagents, different reagents (Davy's reagent,[14] Belleau's reagent,[15] P_2S_5[16]), and different bases, it was found that best yields were obtained using Lawesson's reagent[17] and 1,1,3,3-tetramethylthiourea in xylenes at 175 °C for 1.5 h leading to dithionoester **33** in 49% yield. Photolytic closure[7e] of the dithionoester **33** was carried out by irradiation using a Hanovia quartz lamp at 450 nm for 2 h at 70 °C. Addition of solid sodium bicarbonate to the solution of starting material in degassed benzene proved to be essential for the prevention of product enol ether decomposition. Formation and then disappearance of the dithietane intermediate via diradical coupling and disulfur extrusion

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(14) (a) Davy, H. *J. Chem. Soc., Chem. Commun.* **1982**, 457. (b) Davy, H.; Metzner, P. *J. Chem. Res. Synop.* **1985**, 272.

(15) Lajoie, G.; LePine, F.; Maziak, L.; Belleau, B. *Tetrahedron Lett.* **1983**, *24*, 3815.

(16) Reid, E. E. *Organic Chemistry of Bivalent Sulfur*; Chem. Pub.: New York, 1960; Vol. 3, Chapter 2.

(17) For a review on thionation reactions of Lawesson's reagent, see: Cava, M. P.; Levinson, M. *Tetrahedron* **1985**, *41*, 5061.

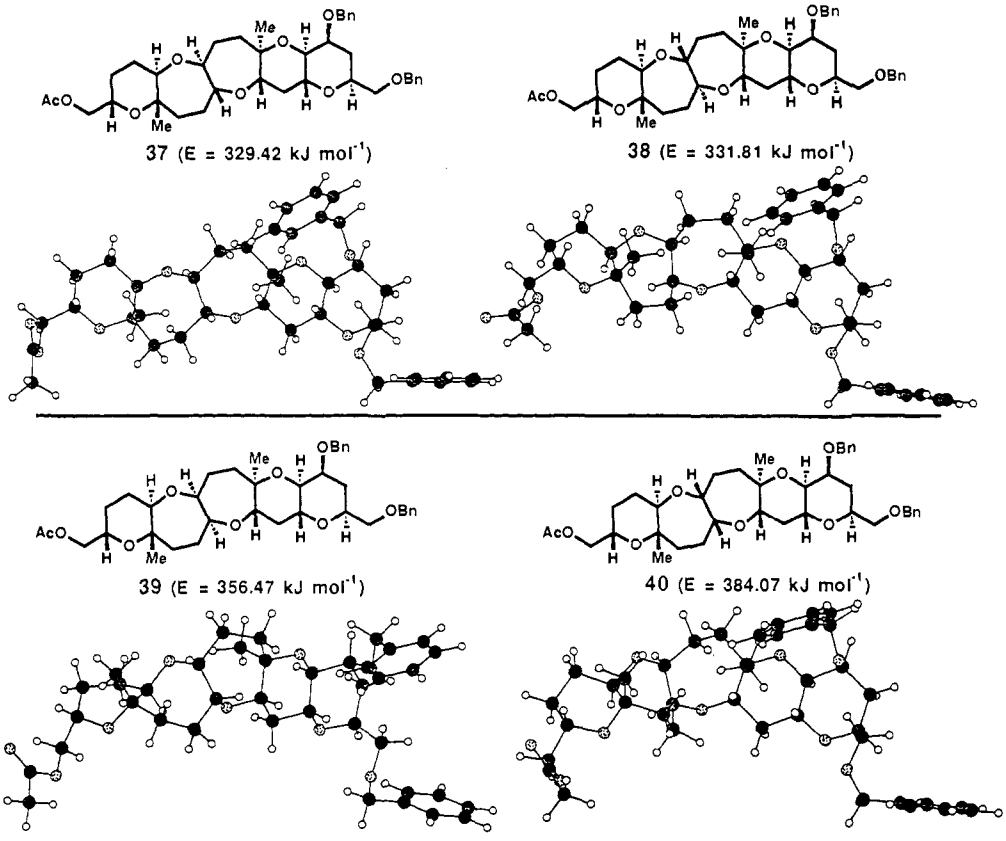


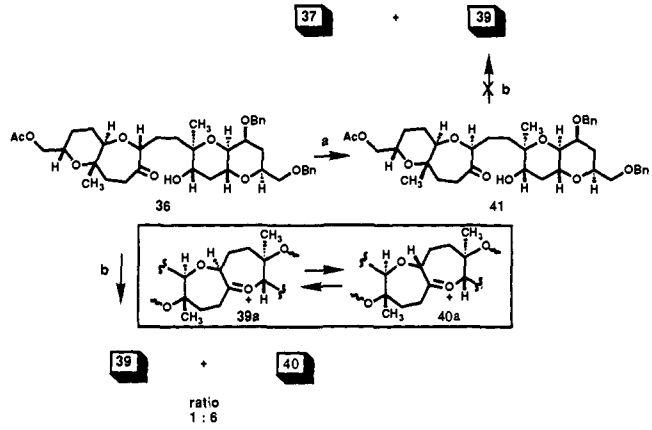
Figure 1. Energy-minimized (MM2 Macromodel) structures of dioxepane ring junction isomers (**37–40**).

could be observed by thin-layer chromatography. The resulting enol ether compound was directly subjected to selective desilylation using $^{n}Bu_4NF$, to afford stable enol ether **34** in an overall yield of 47%. The primary alcohol of **34** was then protected as its acetate **35** under standard conditions in 86% yield. This particular protecting-group exchange was found essential for the success of subsequent steps. Removal of both silyl protecting groups from **35** using HF/pyridine resulted in hydroxy ketone **36** in 90% yield. Here it is noteworthy that acidic conditions in the desilylation (HF/pyridine) resulted in the (7aα)-epimer of the hydroxy ketone, whereas basic conditions ($^{n}Bu_4NF$) used in previous model systems[7g] had always resulted in the formation of the (7aβ)-hydroxy ketones.

In an attempt to predict the outcome of the key cyclization, energy minimizations were carried out using the MM2 Macromodel program. Among the four possible ring junction isomers the two trans isomers (**37** and **38**) were found to have minimum energy of stabilization, out of which the natural product framework was the lowest at 329.4 kJ mol^{-1}. The two α and β cis isomers **39** and **40** were at 356.47 and 384.07 kJ mol^{-1}, respectively (Figure 1). On the basis of these results with 30–50 kJ mol^{-1} difference in cis and trans isomers and lower energy for the required trans isomer, cyclization was anticipated to yield the trans isomer **37**.

Isomerization of the (7aα)-hydroxy ketone **36** to the (7aβ)-hydroxy ketone **41** (Scheme VI) was effected by treatment with DBU in toluene under reflux (90% yield). However, when these hydroxy ketones (**36**, **41**) were subjected to cyclization conditions[7g] using Ph_2MeSiH–TMSOTf, only **36** reacted to afford dioxepane systems **39** and **40** in 81% total yield (ca. 1:6 ratio **39**:**40**) contrary to the predictions made by the MM2 calculations. The stereochemistry of compounds **39** and **40** as well as that of **36** and **41** was determined by 2D COSY and NOESY NMR experiments and later confirmed by X-ray crystallographic analysis (vide infra). The failure of **41** to respond favorably to various cyclization conditions excluded initial epimerization of **36** as a step in the formation of **40**. Whereas no reasonable explanation could be

Scheme VI[a]

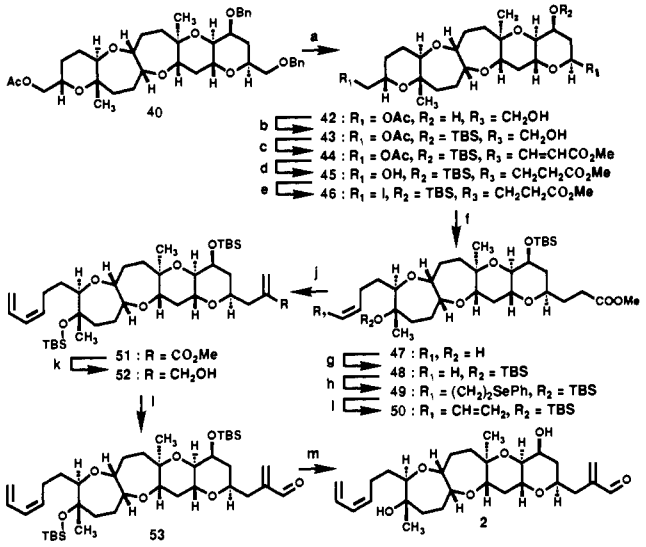


[a] (a) 10 equiv of DBU, toluene, 110 °C, 2 h, 90%; (b) 3 equiv of Ph_2MeSiH, 3 equiv of TMSOTf, CH_3NO_2, 0 °C, 15 min, 81% (6:1 ratio).

offered for this observation as well as for the failure of forming a trans dioxepane system in these experiments, a speculative mechanistic explanation for the formation of **40** from **36** involving the intermediate oxonium species **40a** is shown in Scheme VI.

In order to work out reaction conditions leading to the final molecule, and also to examine the biological activity for different isomers of hemibrevetoxin B (**1**), we continued with compound **40** (major isomer) and targeted (7aα)-*epi*-hemibrevetoxin B (**2**) for total synthesis. As seen in Scheme VII, compound **40** was debenzylated by hydrogenolysis to afford diol **42** in quantitative yield. This diol (**42**) was then submitted to bis(silylation) and selectively desilylated at the primary position by exposure to CSA in MeOH–CH_2Cl_2, furnishing monosilylated product **43** in 87% yield. The primary alcohol in **43** was oxidized to the corresponding aldehyde using Swern conditions and then immediately treated with methyl(triphenylphosphoranylidene)acetate in benzene to

Scheme VII[a]



[a] (a) H_2, $Pd(OH)_2$, EtOH, 2 h, 100%; (b) (i) 2.4 equiv of TBSOTf, 4 equiv of 2,6-lutidine, −20 °C, 1 h; (ii) 1.0 equiv of CSA, MeOH–CH_2Cl_2 (1:1), 0 °C, 5 min, 87%; (c) (i) Swern oxidation; (ii) 2 equiv of Ph_3P=CHCOOMe, benzene, 25 °C, 2 h, 71%; (d) (i) H_2, $Pd(OH)_2$, MeOH, 2 h; (ii) 2 equiv of K_2CO_3, MeOH, 50 °C, 0.5 h, 87%; (e) 2 equiv of I_2, 2 equiv of Ph_3P, 4 equiv of imidazole, benzene, 80 °C, 0.5 h, 87%; (f) 10 equiv of Zn, 5 equiv of NH_4Cl, 5 equiv of H_2O, EtOH, 78 °C, 0.5 h, 95%; (g) 1.2 equiv of TBSOTf, 2 equiv of 2,6-lutidine, CH_2Cl_2, 25 °C, 1 h, 91%; (h) (i) O_3, CH_2Cl_2, −78 °C, then 2 equiv of Ph_3P, 25 °C, 3 h; (ii) 10 equiv of $PhSe(CH_2)_3Ph_3P^+Br^-$, 5 equiv of ^{n}BuLi, 10 equiv of HMPA, THF, −78 °C, 1 h, 82%; (i) H_2O_2, 10 equiv of $NaHCO_3$, THF, 25 °C, 4 h, 88%; (j) (i) 15 equiv of $NaN(SiMe_3)_2$, THF, −78 °C, 45 min, then 15 equiv of $Me_2(CH_2)N^+I^-$, 0 °C, 15 min; (ii) 20 equiv of MeI, MeOH, 25 °C, 0.5 h; (iii) 10 equiv of DBU, benzene, 25 °C, 1 h, 51% overall; (k) 5 equiv of DIBAL, CH_2Cl_2, −78 °C, 0.5 h, 87%; (l) Swern oxidation, 85%; (m) HF–py, CH_2Cl_2, 0 °C, 15 min, 70%.

furnish the trans Wittig product **44** in 71% yield overall. Hydrogenation of the double bond using $Pd(OH)_2$/C in methanol followed by treatment with potassium carbonate gave saturated alcohol **45** in 87% yield. The terminal tetrahydropyran ring could now be dismantled to unravel the requisite functionality. This goal was accomplished through a two-step process: first by conversion of the alcohol **45** to the iodide **46** and then by treatment with zinc metal to induce ring opening and formation of hydroxyalkene **47** in 95% yield. The tertiary alcohol of **47** was converted to its TBS silyl ether furnishing **48** in 91% yield. In order to assure the cis nature of the terminal diene system, in the subsequent step, a nonstabilized Wittig reagent was used for the olefination process. Thus, ozonolysis of **48** to the corresponding aldehyde followed by treatment with the ylide derived from $PhSe(CH_2)_3Ph_3P^+I^-$ and ^{n}BuLi resulted in compound **49** in 82% yield. The cis nature of the double bond was confirmed by the characteristic coupling constant of J = 10 Hz in the ^{1}H NMR spectrum of **49**. Oxidation of selenide **49** to the corresponding selenoxide using hydrogen peroxide buffered with sodium bicarbonate, and subsequent elimination, gave diene **50** in 88% yield. The left-hand side of the molecule was thus set, leaving the formation of the α-vinyl aldehyde system on the right-hand side as the only remaining task. This was accomplished through a three-step process: first, ester **50** was treated with sodium bis(trimethylsilyl)amide and Eschenmoser's salt;[18] second, the resulting amine was treated with iodomethane in methanol; and third, the resulting amine salt was treated with DBU in benzene to afford **51** in 51% yield overall for the three steps. The next few steps leading to the final molecule involved standard chemistry and proceeded smoothly. Thus, the ester **51** was reduced to the corresponding alcohol using DIBAL to afford allylic alcohol **52** in 87% yield. Oxidation of alcohol **52** to aldehyde **53** was achieved using Swern conditions (85% yield). Finally, removal of the two silyl ether protecting groups using HF/pyridine afforded (7aα)-*epi*-hemibrevetoxin B (**2**) in 70% yield (Scheme VII). As expected, the spectral data of **2** were similar but not identical to those of the naturally occurring hemibrevetoxin B (**1**).[6]

(18) Schreiber, J.; Maag, H.; Hashimoto, N.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 330.

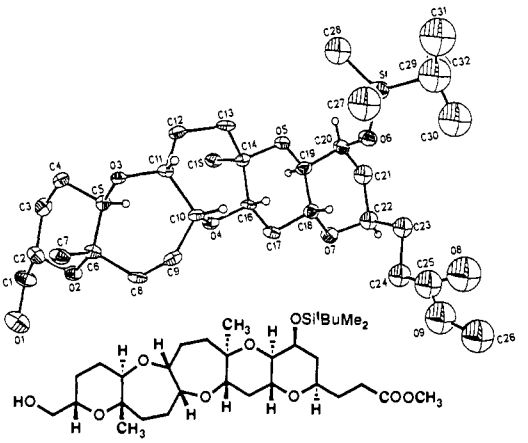


Figure 2. ORTEP drawing of **45**.

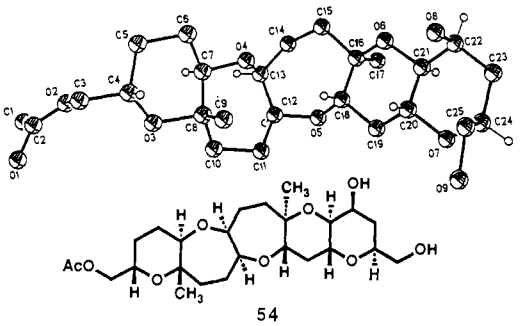


Figure 3. ORTEP drawing of **54**.

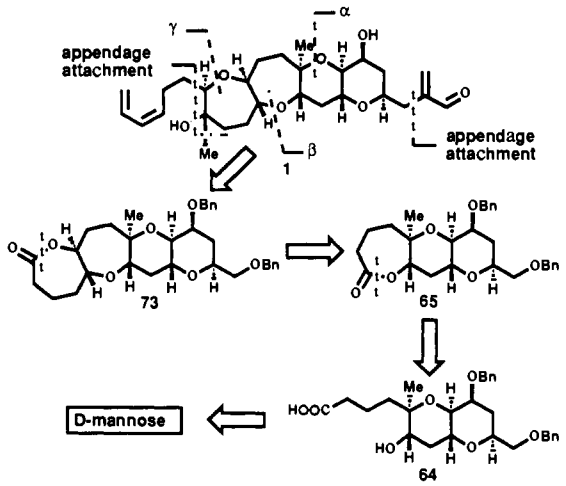
As mentioned earlier, the stereochemistry of the oxepane–oxepane ring juncture in the two isomers **39** and **40** and in all compounds derived from them was strongly suggested from ^{1}H NMR data. X-ray crystallographic analysis carried out on intermediates **45** and **54** confirmed these stereochemical assignments (Figures 2 and 3, respectively). Compound **54** was prepared from **39** by hydrogenolysis of the two benzyl groups (H_2, $Pd(OH)_2$/C, 94% yield).

The next task was to design a successful synthesis of hemibrevetoxin B (**1**) by adjusting the original strategy according to the gained knowledge. This was achieved as described below.

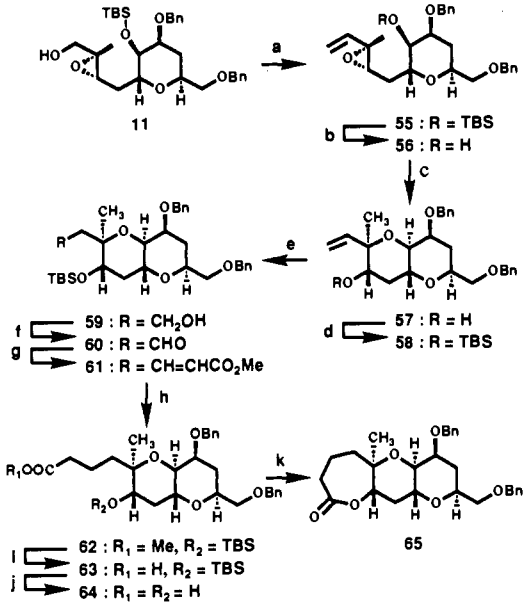
Second Retrosynthetic Analysis of Hemibrevetoxin B, A Linear Approach. After the abortive attempt to construct hemibrevetoxin B (**1**) via a convergent sequence, we focused our efforts on a linear strategy in which each ring was sequentially constructed. Scheme VIII depicts the retrosynthetic disconnections and key intermediates defined for this strategy. Thus, sequential dismantling of the target molecule along the sequence γ, β, α led to D-mannose as the starting material. This one ring at a time, sequential approach may, in fact, be Nature's way of forming the brevetoxins.

Synthesis of Hemibrevetoxin B (1). The execution of the synthesis of hemibrevetoxin B (**1**) according to this new plan was carried out as outlined in Schemes IX–XI. Thus, starting with previously prepared hydroxy epoxide **11** (vide supra), oxidation to the aldehyde with SO_3–pyridine, followed by treatment with ylide derived from methyltriphenylphosphonium bromide and sodium bis(trimethylsilyl)amide in THF at 0 °C, afforded alkene **55** in 87% yield (Scheme IX). Removal of the silyl protecting group from **55** with ^{n}Bu$_4$NF gave alcohol **56**, which underwent

Scheme VIII. Retrosynthetic Analysis of Hemibrevetoxin B (**1**) (Linear Approach)



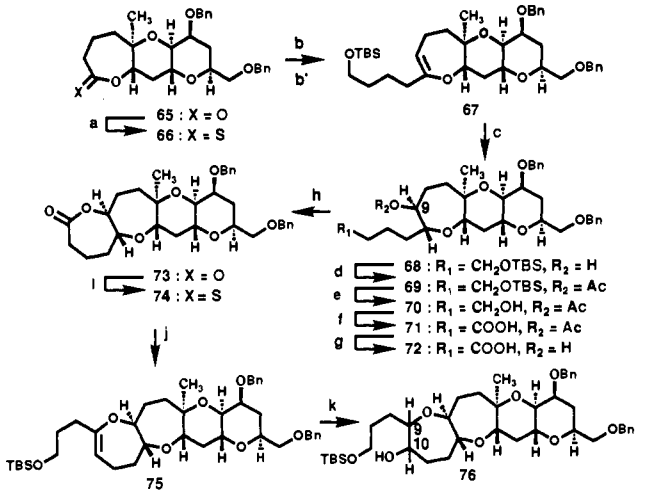
Scheme IX[a]



[a] (a) (i) 2 equiv of SO_3·py, 4 equiv of Et_3N, CH_2Cl_2–DMSO (4:1), 0 °C, 2 h; (ii) 1.5 equiv of $Ph_3P^+CH_3Br^-$, 1.3 equiv of $NaN(SiMe_3)_2$, THF, 0 °C, 1 h, 87%; (b) 1.2 equiv of TBAF, THF, 25 °C, 2 h, 97%; (c) (i) 0.3 equiv of CSA, CH_2Cl_2, 0 °C, 5 h, 90%; (d) 1.2 equiv of TBSOTf, 1.5 equiv of 2,6-lutidine, CH_2Cl_2, 0 °C, 10 min, 85%; (e) 1.2 equiv of BH_3–THF, THF, 0 °C, 1 h, NaOH–H_2O_2, 90%; (f) Swern oxidation, 98%; (g) 1.2 equiv of $Ph_3P{=}CHCO_2Me$, benzene, 25 °C, 3 h, 89%; (h) H_2, 5% Pd/C, EtOAc, 15 h, 96%; (i) 1.5 equiv of LiOH–H_2O, THF–H_2O (1:1), 50 °C, 1 h, 92%; (j) 1.2 equiv of TBAF, THF, 25 °C, 18 h, 95%; (k) 1.1 equiv of 2,4,6-trichlorobenzoyl chloride, 1.5 equiv of Et_3N, THF, 0 °C, 6 equiv of DMAP, benzene, 80 °C, 3 h, 97%.

an epoxide opening–ring closure reaction[7a] as described earlier in the convergent approach. Thus, treatment of alcohol **56** with CSA in CH_2Cl_2 at 0 °C gave regio- and stereoselectively bicyclic product **57** in 90% yield. The secondary hydroxyl group in **57** was then protected as its TBS ether by standard chemistry, furnishing compound **58** (85%). Construction of the third ring required hydroxy acid **64**, which was derived from **58** by elaboration of its alkene side chain as follows. Hydroboration of the double bond using BH_3·THF gave alcohol **59** in 90% yield. This product was then oxidized to aldehyde **60** under Swern conditions and then treated with the Wittig reagent methyl (triphenylphosphoranylidene)acetate to furnish trans α,β-unsaturated ester **61** in 89% yield. Hydrogenation of the double bond in **61** using 5% Pd/C gave saturated ester **62** in 96% yield.

Scheme X[a]



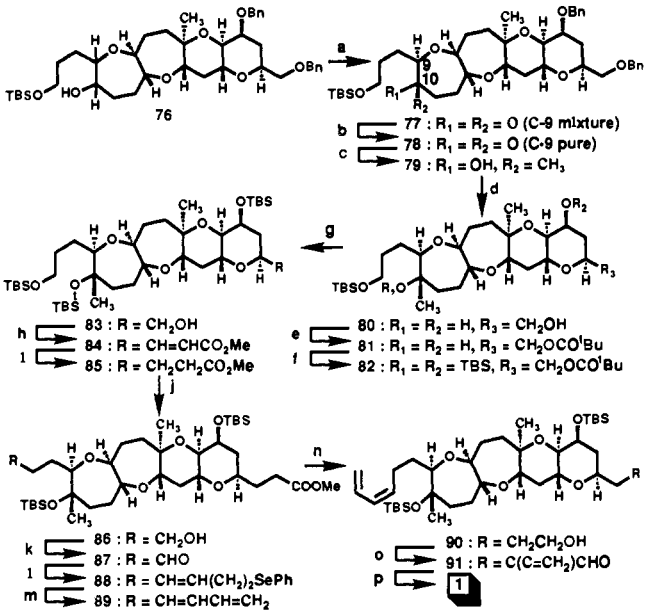
[a] (a) 2 equiv of Lawesson's reagent, toluene, 110 °C, 3 h, 82%; (b) 3 equiv of $TBSO(CH_2)_4(2\text{-Th})(CN)CuLi_2$, ether, −78 °C to 10 °C, 4 equiv of $I(CH_2)_4I$, 5 equiv of pempidine, 1 h, 85%; (b′) (i) **65**, 1.2 equiv of $LiN(TMS)_2$, 1.5 equiv of $PhNTf_2$, 10 equiv of HMPA, THF, −78 °C to 0 °C, 3 h; (ii) 3 equiv of $TBSO(CH_2)_4(2\text{-Th})(CN)CuLi_2$, ether, −78 °C to −30 °C, 0.5 h (75% from two steps); (c) 1.2 equiv of BH_3–THF, THF, NaOH–H_2O_2, 0 °C, 1 h, 89%; (d) 1.1 equiv of Ac_2O, 1.1 equiv of Et_3N, 0.2 equiv of DMAP, CH_2Cl_2, 1 h, 25 °C, 95%; (e) 0.2 equiv of CSA, MeOH–CH_2Cl_2 (1:1), 0 °C, 1 h, 90%; (f) 3 equiv of PDC, DMF, 16 h, 25 °C, 89%; (g) 1.1 equiv of K_2CO_3, MeOH, 3 h, 25 °C, 82%; (h) 1.1 equiv of 2,4,6-trichlorobenzoyl chloride, 1.5 equiv of Et_3N, THF, 0 °C, 6 equiv of DMAP, benzene, 80 °C, 80%; (i) 1.2 equiv of Lawesson's reagent, toluene, 110 °C, 5 h, 75%; (j) 3 equiv of $TBSO(CH_2)_3(2\text{-Th})(CN)CuLi_2$, ether, −78 °C to 0 °C, 4 equiv of $I(CH_2)_4I$, 5 equiv of pempidine, 2 h, 85%; (k) 1.2 equiv of BH_3–THF, THF, 0 °C, 1 h, NaOH–H_2O_2, 89%.

Hydrolysis of ester **62** with LiOH·H_2O in a THF–H_2O medium at 50 °C gave acid **63** in 92% yield. The silyl ether protecting group was then removed using $^nBu_4NF$ in THF, and the resulting hydroxy acid **64** was subjected to the Yamaguchi lactonization conditions[19] (2,4,6-trichlorobenzoyl chloride, Et_3N, THF, 0 °C, then DMAP, benzene, 80 °C) to furnish tricyclic lactone **65** in 97% yield.

Further elaboration of lactone **65** was carried out using previously developed technology involving thionolactone formation, followed by an organometallic reagent addition and sulfur elimination sequence,[7f,20] as shown in Scheme X. Thus, treatment of lactone **65** with Lawesson's reagent in toluene under reflux for 3 h gave thionolactone **66** in 82% yield. Reaction of **66** with the organocopper reagent $(TBSO(CH_2)_4(2\text{-Th})(CN)CuLi_2)$[21] in ether at −78 °C followed by addition of 1,4-diiodobutane and pempidine, gave enol ether intermediate **67** in 70% overall yield. The alternative procedure via the enol triflate of **65** involving side-chain addition developed by Murai[22] also proved to be successful. Thus, treatment of lactone **65** with lithium bis(trimethylsilyl)amide, *N*-phenyltrifluoromethanesulfonimide, and HMPA, in THF at −78 °C, followed by cuprate addition as above also gave enol ether **67** in an 75% overall yield. Regio- and stereoselective hydroboration of **67** using BH_3·THF at 0 °C, as previously developed,[20] led to **68** together with its diastereomer in 89% total yield (the two epimers were separated chromatographically **68**:**68**α, ca. 4:1 ratio). The side chain of **68** was then further elaborated, using standard chemistry, toward the tetracyclic lactone **73**. Thus, protection of the secondary hydroxyl

(19) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989.
(20) Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Kim, B. H.; Ogilvie, W. W.; Yiannikouros, G.; Prasad, C. V. C.; Hark, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 6263.
(21) For an excellent review on organocopper reagents, see: Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135.
(22) Tsushima, K.; Araki, K.; Murai, A. *Chem. Lett.* **1989**, 1313.

Scheme XI[a]



[a] (a) Swern oxidation, 90%; (b) 0.3 equiv of DBU, toluene, 110 °C, 2 h, 92%; (c) 1.1 equiv of MeMgI, ether, −78 °C to −10 °C, 4 h, 94%; (d) H_2, $Pd(OH)_2$, EtOAc, 40 psi, 4 h, 89%; (e) 1.2 equiv of ^tBuCOCl, 1.4 equiv of DMAP, CH_2Cl_2, 1 h, 90%; (f) 2.2 equiv of TBSOTf, 3 equiv of 2,6-lutidine, CH_2Cl_2, 3 h, 25 °C, 82%; (g) 2.2 equiv of DIBAL, CH_2Cl_2, −78 °C, 0.5 h, 95%; (h) (i) Swern oxidation; (ii) 1.1 equiv of $Ph_3P{=}CHCO_2Me$, benzene, 3 h, 80% overall; (i) H_2, 5% Pd/C, EtOAc, 16 h, 95%; (j) 0.2 equiv of CSA, MeOH–CH_2Cl_2 (1:1), 0 °C, 3 h, 86%; (k) Swern oxidation, 90%; (l) 1.5 equiv of $PhSe(CH_2)_3Ph_3P^+I^-$, 1.1 equiv of ^nBuLi, THF, −78 °C to 25 °C, 15 min, 72%; (m) H_2O_2, $NaHCO_3$, THF, 16 h, 25 °C, 78%; (n) 2.2 equiv of DIBAL, CH_2Cl_2, −78 °C, 3 h, 95%; (o) Swern oxidation, 1.5 equiv of $Me_2(CH_2)N^+I^-$, −78 °C to 25 °C, 24 h, 90%; (p) SiF_4, CH_3CN–CH_2Cl_2 (1:1),0 °C, 2 h, 82%.

group in **68** as its acetate **69** and removal of the silyl protecting group using CSA in MeOH–CH_2Cl_2, gave alcohol **70** in 90% yield. Oxidation of the primary alcohol to carboxylic acid **71** was accomplished using PDC in DMF in 85% yield. The acetate protecting group was then removed to give hydroxy acid **72**, which was submitted to the Yamaguchi lactonization conditions as described earlier, to furnish tetracyclic lactone **73** in 80% yield. Enol ether intermediate **75** was synthesized from **73** by two alternative routes as described above for **67**. The route via thionation gave thionolactone **74** in 75% yield and then enol ether compound **75** in 85% yield. The route via enol triflate formation gave the same product **75** in 75% overall yield. Repeat of the side chain attachment then followed. Thus, hydroboration of the enol ether **75** using BH_3·THF at 0 °C gave alcohol **76** in 94% yield.

The final sequence of the synthesis is shown in Scheme XI. Thus, oxidation under Swern conditions afforded a mixture of C-9 epimeric ketones **77**. Equilibration to a single compound **78**, which apparently is the thermodynamically most stable isomer, was achieved with DBU in refluxing toluene (92% yield). The tetracyclic skeleton of hemibrevetoxin B (**1**) was thus constructed and what remained was side-chain manipulation. The second quaternary center was constructed by MeMgI addition to ketone **78** at −78 °C in 94% yield, which led to a 3:2 epimeric (at C-10) mixture of alcohols, from which the major isomer **79** was isolated by chromatography. Removal of the benzyl ether protecting groups from **79** by hydrogenolysis afforded triol **80** in 89% yield. The primary hydroxyl group was protected as its pivalate **81**, and the resulting diol was converted to the disilylated compound **82** in 82% yield by standard chemistry. Removal of the pivalate protecting group with DIBAL led to **83** (95%), which was followed by Swern oxidation of the primary alcohol and addition of methyl (triphenylphosphoranylidene)acetate in benzene, furnishing the trans α,β-unsaturated ester **84** in 80% yield. Hydrogenation of the double bond using 5% Pd/C as catalyst gave saturated compound **85**, which was then treated with CSA in MeOH–CH_2Cl_2 to remove the primary TBS group, affording alcohol **86** in 86% yield. Swern oxidation to aldehyde **87** (90%), followed by treatment with the ylide derived from $PhSe(CH_2)_3Ph_3P^+Br^-$ and ^nBuLi, gave selenide **88** (cis double bond) in 72% yield. Oxidation and subsequent syn elimination using H_2O_2 and $NaHCO_3$ in THF afforded diene **89** (cis) in 78% yield. The left side of the molecule was thus constructed, and what remained was formation of the α-vinyl aldehyde moiety on the right-hand side. To this end, the ester functionality was reduced using DIBAL, leading to alcohol **90**, which was oxidized to the corresponding aldehyde under Swern conditions and treated with Eschenmoser's salt,[23] followed by workup to give **91** in 90% yield. Finally, removal of the silyl ether protecting groups under neutral conditions using SiF_4 in CH_3CN–CH_2Cl_2[24] afforded hemibrevetoxin B (**1**) in 70% yield. Synthetic hemibrevetoxin B (**1**) exhibited the expected spectral data which were identical to those reported for the naturally derived material.[6,25]

Biological Studies. In biological investigations carried out by Dr. D. G. Baden, University of Miami, on (7aα)-*epi*-hemibrevetoxin B (**2**) and intermediates **42** and **54**, neither were recognized by brevetoxin PbTx-3 antibodies nor did they displace tritiated brevetoxin PbTx-3 from its receptors. These preliminary results indicate that the altered shape of the hemibrevetoxin B skeleton induced by the change of one stereocenter (7a) is sufficient to remove its binding affinity toward its receptor and point to the importance of precise molecular architecture for biological action in these compounds.

Conclusion. The described total synthesis of (7aα)-*epi*-hemibrevetoxin B (**2**) and hemibrevetoxin B (**1**) demonstrate the power of some recently developed synthetic technology for the construction of cyclic ethers. Specifically, the methods involving hydroxy epoxide[7a] and hydroxy ketone cyclizations[7g] were successfully applied. Furthermore, the chemistry of thionolactones and thionoethers involving photolytically-induced ring closures[7e] and nucleophilic additions[20] were also employed with success. The importance of choosing a linear versus a convergent approach for the total synthesis of hemibrevetoxin B (**1**) was demonstrated. The linear nature of the sequence did, however, make the synthesis considerably longer than otherwise expected. The importance of the all-trans stereochemistry of the ring fusions for receptor binding was also demonstrated.

With the technology for construction of cyclic ethers and its application to the synthesis of these hemibrevetoxins (**1** and **2**) now well established, the road toward the total synthesis of brevetoxins of higher complexity is open.

Experimental Section

General Methods. NMR spectra were recorded on a Bruker AM-250, AM-300, or AMX-500 MHz instrument. IR spectra were recorded on a Perkin-Elmer 1600 Series FT-IR or Nicolet 205 FT-IR infrared spectrophotometer. High-resolution mass spectra (HRMS) were recorded on a V G 7070 HS mass spectrometer under chemical ionization (CI) conditions or on a V G ZAB-VSE double-focusing instrument equipped with a cesium ion gun under FAB conditions. Melting points were acquired on a Thomas-Hoover Unimelt apparatus or Mettler FP62 melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter. Elemental analyses were performed by the Galbraith Laboratories, Knoxville, TN.

All reactions were monitored by thin layer chromatography carried out on 0.25-nm E. Merck silica gel plates (60F-254) using UV light and 7% ethanolic phosphomolybdic acid or *p*-anisaldehyde solution (2.5% *p*-anisaldehyde, 90% EtOH, 3.5% concentrated H_2SO_4, 3.0% H_2O, 1.0% AcOH) and heat as developing agent. Preparative thin layer chroma-

(23) Takano, S.; Inomata, K.; Samizu, K.; Tomita, S.; Yanase, M.; Suzuki, M.; Iwabuchi, Y.; Sugihara, T.; Ogasawara, K. *Chem. Lett.* **1989**, 1283.
(24) Corey, E. J.; Yi, K. Y. *Tetrahedron Lett.* **1992**, *33*, 2289.
(25) We thank Professor Y. Shimizu for providing us with spectral data of the natural product.

tography was performed on 0.5 or 0.25 mm × 20 cm × 20 cm E. Merck silica gel plates (60F-254). E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography.

All reactions were carried out under argon atmosphere with dry, freshly distilled solvents under anhydrous conditions unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated.

Experimental procedures for compounds **4–11** and **19–31** are given in the supplementary material.

Methyl (*E*)-4,5:7,11-Dianhydro-9,12-*O*-dibenzyl-4-*C*-methyl-8-*O*-(*tert*-butyldimethylsilyl)-2,3,6,10-tetradeoxy-D-*threo*-L-*altro*-dodec-2-enonate (12). To a solution of epoxy alcohol **11** (18.80 g, 34.63 mmol) in DMSO–CH_2Cl_2 (1:5, 346 mL) at 0 °C was added triethylamine (19.31 mL, 138.5 mmol) and SO_3–pyridine (11.02 g, 69.26 mmol), and the resulting solution was stirred at 0 °C for 2 h. The reaction mixture was diluted with EtOAc (1 L) and washed with H_2O (500 mL), saturated NH_4Cl (500 mL), and brine (200 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. The crude aldehyde was dissolved in benzene (346 mL) and cooled to 0 °C. To this solution was added $Ph_3P{=}CHCOOCH_3$ (17.37 g, 51.94 mmol), and the resulting solution was stirred at room temperature for 12 h. The solvent was removed under vacuum. Flash column chromatography (silica, 30% ether in petroleum ether) gave 16 g (77%) of **12**. **12**: colorless oil; R_f = 0.27 (silica, 30% ether in petroleum ether); $[\alpha]^{25}_D$ +19.76° (*c* 0.55, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2950, 2920, 2850, 1725, 1490, 1320, 1255, 1125, 1090, 1070, 840, 775 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.36 (m, 10 H, Ar), 6.76 (d, *J* = 15.7 Hz, 1 H, vinyl), 6.02 (d, *J* = 15.8 Hz, 1 H, vinyl), 4.47–4.60 (m, 4 H, CH_2Ar), 3.97–4.02 (m, 2 H, HCO), 3.81 (dd, *J* = 10.0, 7.0 Hz, 1 H, HCO), 3.72 (s, 3 H, OCH_3), 3.68–3.71 (m, 1 H, HCO), 3.61–3.62 (m, 1 H, HCO), 3.55 (dd, *J* = 10.0, 5.2 Hz, 1 H, HCO), 3.06 (t, *J* = 5.9 Hz, 1 H, HCO), 2.03 (m, 1 H, CH_2), 1.79–1.87 (m, 3 H, CH_2), 1.41 (s, 3 H, CH_3), 0.90 (s, 9 H, ^{t}BuSi), 0.06 (s, 3 H, CH_3Si), 0.05 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.00 (OC=O), 149.94 (vinyl), 138.47 (Ar), 138.35 (Ar), 128.31 (Ar), 127.66 (Ar), 127.52 (Ar), 121.15 (vinyl), 74.41 (CO), 73.27 (CO), 72.35 (CO), 71.66 (CO), 71.04 (CO), 70.29 (CO), 63.17 (CO), 51.65 (CO), 30.18, 29.15, 25.81, 18.07, 15.32, –4.12, –4.83; HRMS calcd for $C_{34}H_{48}O_7Si$ (M + Cs) 729.2224, found 729.2224. Anal. Calcd: C, 68.42; H, 8.11. Found: C, 68.36; H, 7.84.

Methyl (*E*)-4,5:7,11-Dianhydro-9,12-*O*-dibenzyl-4-*C*-methyl-2,3,6,10-tetradeoxy-D-*threo*-L-*altro*-dodec-2-enonate (13). To a solution of **12** (16 g, 26.81 mmol) in THF (134 mL) at 0 °C was added ^{n}Bu$_4$NF (32.17 mL of a 1 M solution in THF, 32.17 mmol), and the resulting solution was allowed to warm and stir at room temperature for 2 h. The solvent was removed under vacuum. Flash column chromatography (silica, 80% ether in petroleum ether) gave 12.6 g (97%) of hydroxy epoxide **13**. **13**: colorless oil; R_f = 0.24 (silica, 80% ether in petroleum ether); $[\alpha]^{25}_D$ +67.50° (*c* 0.40, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3540, 2910, 2855, 1720, 1455, 1440, 1320, 1290, 1175, 1075, 990 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.38 (m, 10 H, Ar), 6.77 (d, *J* = 15.7 Hz, 1 H, vinyl), 6.02 (d, *J* = 15.7 Hz, 1 H, vinyl), 4.65 (d, *J* = 11.6 Hz, 1 H, CH_2Ar), 4.54 (d, *J* = 3.2 Hz, 2 H, CH_2Ar), 4.49 (d, *J* = 11.5 Hz, 1 H, CH_2Ar), 3.96–3.99 (m, 2 H, HCO), 3.73–3.81 (series of multiplets, 5 H, HCO, OCH_3), 3.59–3.60 (m, 1 H, HCO), 3.53 (dd, *J* = 10.0, 5.4 Hz, 1 H, HCO), 3.05 (t, *J* = 5.8 Hz, 1 H, HCO), 2.46 (d, *J* = 6.4 Hz, 1 H, OH), 1.86–2.01 (m, 4 H, CH_2), 1.42 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.50 (OC=O), 149.81 (vinyl), 138.17 (Ar), 137.53 (Ar), 128.59 (Ar), 128.37 (Ar), 128.03 (Ar), 127.76 (Ar), 127.68 (Ar), 127.64 (Ar), 121.20 (vinyl), 73.30 (CO), 71.92 (CO), 71.20 (CO), 70.68 (CO), 69.51 (CO), 62.90 (CO), 57.89 (CO), 51.68 (CO), 30.03, 28.33, 15.36; HRMS calcd for $C_{28}H_{34}O_7$ (M + Cs) 615.1359, found 615.1371.

Methyl (*E*)-4,8:7,11-Dianhydro-9,12-*O*-dibenzyl-5-hydroxy-4-*C*-methyl-2,3,6,10-tetradeoxy-D-*threo*-L-*allo*-dodec-2-enonate (14). To a solution of alcohol **13** (12.60 g, 26.11 mmol) in dichloromethane (261 mL) at 0 °C was added CSA (1.82 g, 7.84 mmol), and the resulting solution was stirred at room temperature for 4 h. The excess CSA was quenched with Et_3N (4 mL) and the solvent removed under vacuum. Flash column chromatography (silica, 100% ether) gave 9.63 g (76%) of bicyclic compound **14**. **14**: colorless oil; R_f = 0.42 (silica, 100% ether); $[\alpha]^{25}_D$ +26.02° (*c* 0.98, $CHCl_3$); IR (neat) ν_{max} 3580, 2950, 2900, 1720, 1455, 1440, 1310, 1095, 1075, 1040 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.35 (m, 10 H, Ar), 7.15 (d, *J* = 15.1 Hz, 1 H, vinyl), 6.12 (d, *J* = 15.1 Hz, 1 H, vinyl), 4.75 (d, *J* = 12.3 Hz, 1 H, CH_2Ar), 4.58 (d, *J* = 12.3 Hz, 1 H, CH_2Ar), 4.54 (s, 2 H, CH_2Ar), 4.04–4.12 (m, 2 H, HCO), 3.85 (m, 1 H, HCO), 3.72–3.77 (m, 4 H, HCO, OCH_3), 3.58 (dd, *J* = 11.7, 4.4 Hz, 1 H, HCO), 3.51 (dd, *J* = 9.7, 4.4 Hz, 1 H, HCO), 3.38 (dd, *J* = 9.8, 2.3 Hz, 1 H, HCO), 2.16–2.20 (m, 1 H, CH_2), 1.89–2.00 (m, 2 H, CH_2), 1.63–1.70 (m, 1 H, CH_2), 1.33 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.38 (OC=O), 151.71 (vinyl), 138.95 (Ar), 138.32 (Ar), 128.37 (Ar), 128.31 (Ar), 128.24 (Ar), 127.81 (Ar), 127.75 (Ar), 127.60 (Ar), 127.12 (Ar), 118.95 (vinyl), 73.38 (CO), 72.89 (CO), 72.63 (CO), 71.57 (CO), 70.74 (CO), 69.87 (CO), 63.46 (CO), 51.66 (CO), 34.38, 31.09, 14.61, 14.57; HRMS calcd for $C_{28}H_{34}O_7$ (M + Cs) 615.1359, found 615.1359.

Methyl (*E*)-4,8:7,11-Dianhydro-9,12-*O*-dibenzyl-4-*C*-methyl-5-*O*-(*tert*-butyldimethylsilyl)-2,3,6,10-tetradeoxy-D-*threo*-L-*allo*-dodec-2-enonate (15). To a solution of alcohol **14** (9.63 g, 19.95 mmol) in dichloromethane (80 mL) at –20 °C was added 2,6-lutidine (4.65 mL, 39.9 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (5.50 mL, 23.94 mmol), and the reaction mixture was allowed to warm to 0 °C. The reaction was then diluted with ether (500 mL) and washed with H_2O (200 mL) and brine (200 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 40% ether in petroleum ether) gave 9.64 g (81%) of **15**. **15**: colorless oil; R_f = 0.27 (silica, 40% ether in petroleum ether); $[\alpha]^{25}_D$ +24.93° (*c* 0.88, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2940, 2920, 2855, 1725, 1455, 1310, 1275, 1115, 1050, 840 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.36 (m, 10 H, Ar), 7.10 (d, *J* = 15.7 Hz, 1 H, vinyl), 6.08 (d, *J* = 15.7 Hz, 1 H, vinyl), 4.76 (d, *J* = 12.4 Hz, 1 H, CH_2Ar), 4.59 (d, *J* = 12.4 Hz, 1 H, CH_2Ar), 4.56 (s, 2 H, CH_2Ar), 4.03–4.10 (m, 2 H, HCO), 3.85 (m, 1 H, HCO), 3.74 (s, 3 H, OCH_3), 3.71–3.74 (m, 1 H, HCO), 3.51–3.57 (m, 2 H, HCO), 3.38 (dd, *J* = 9.9, 2.5 Hz, 1 H, HCO), 2.06–2.10 (m, 1 H, CH_2), 1.99 (dd, *J* = 14.6, 3.1 Hz, 1 H, CH_2), 1.89–1.93 (m, 1 H, CH_2), 1.60–1.70 (m, 1 H, CH_2), 1.29 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.06 (s, 3 H, CH_3Si), 0.05 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.26 (OC=O), 152.29 (vinyl), 138.93 (Ar), 138.35 (Ar), 128.29 (Ar), 128.23 (Ar), 127.73 (Ar), 127.55 (Ar), 127.29 (Ar), 127.12 (Ar), 118.24 (vinyl), 77.83 (CO), 73.26 (CO), 72.96 (CO), 72.56 (CO), 71.63 (CO), 69.99 (CO), 63.29 (CO), 51.49 (CO), 35.02, 31.02, 25.62, 17.78, 14.79, –4.26, –5.10; HRMS calcd for $C_{34}H_{48}O_7Si$ (M + Cs) 729.2224, found 729.2201.

Methyl 4,8:7,11-Dianhydro-9,12-*O*-dibenzyl-4-*C*-methyl-5-*O*-(*tert*-butyldimethylsilyl)-2,3,6,10-tetradeoxy-D-*threo*-L-*allo*-dodeconate (16). To a solution of α,β-unsaturated ester **15** (9.64 g, 16.15 mmol) in EtOAc (161 mL) was added 5% Pd/C (0.96 g, 10% by weight of the alkene), and the resulting mixture was placed under a hydrogen atmosphere and stirred for 12 h. The catalyst was then filtered, and the solvent was removed under vacuum. Flash column chromatography (silica, 20% ether in petroleum ether) gave 8.70 g (90%) of ester **16**. **16**: colorless oil; R_f = 0.31 (20% ether in petroleum ether); $[\alpha]^{25}_D$ +25.13° (*c* 1.36, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2925, 2910, 2855, 1735, 1470, 1255, 1115, 1080, 840 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.34 (m, 10 H, Ar), 4.69 (d, *J* = 12.6 Hz, 1 H, CH_2Ar), 4.53–4.56 (m, 3 H, CH_2Ar), 4.03–4.08 (m, 2 H, HCO), 3.75–3.77 (m, 1 H, HCO), 3.68–3.71 (m, 1 H, HCO), 3.66 (s, 3 H, CH_3), 3.49–3.53 (m, 2 H, HCO), 3.26 (dd, *J* = 9.9, 2.6 Hz, 1 H, HCO), 2.43 (t, *J* = 8.4 Hz, 2 H, CH_2), 1.77–2.07 (series of multiplets, 5 H, CH_2), 1.45–1.65 (m, 1 H, CH_2), 1.28 (s, 3 H, CH_3), 0.87 (s, 9 H, ^{t}BuSi), 0.08 (s, 3 H, CH_3Si), 0.07 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.55 (OC=O), 139.20 (Ar), 138.44 (Ar), 128.35 (Ar), 128.30 (Ar), 128.26 (Ar), 128.17 (Ar), 127.77 (Ar), 127.54 (Ar), 127.16 (Ar), 127.01 (Ar), 126.96 (Ar), 72.97 (CO), 72.89 (CO), 72.35 (CO), 71.66 (CO), 71.47 (CO), 70.06 (CO), 63.58 (CO), 51.52 (CO), 35.13, 34.89, 31.02, 27.99, 25.66, 17.79, 15.03, –3.90, –4.95; HRMS calcd for $C_{34}H_{50}O_7Si$ (M + Cs) 731.2380, found 731.2380.

4,8:7,11-Dianhydro-9,12-*O*-dibenzyl-4-*C*-methyl-5-*O*-(*tert*-butyldimethylsilyl)-2,3,6,10-tetradeoxy-D-*threo*-L-*allo*-dodecanoic Acid (17). To a solution of ester **16** (8.70 g, 14.53 mmol) in THF–H_2O (3:1, 29 mL) was added LiOH (1.22 g, 29.06 mmol), and the resulting mixture was heated to 50 °C for 12 h. The reaction mixture was then brought to pH 6 by addition of 3 N HCl, diluted with EtOAc (500 mL), and washed with brine (200 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 50% ether in petroleum ether, then 100% ether) gave 7.31 g (86%) of acid **17**. **17**: colorless oil; R_f = 0.36 (silica, 50% ether in petroleum ether); $[\alpha]^{25}_D$ +27.99° (*c* 1.11, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3150, 3010, 2925, 2860, 1720, 1460, 1370, 1255, 1110, 1085, 845, 780 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24–7.36 (m, 10 H, Ar), 4.64 (d, *J* = 12.2 Hz, 1 H, CH_2Ar), 4.55 (s, 2 H, CH_2Ar), 4.52 (d, *J* = 12.2 Hz, 1 H, CH_2Ar), 4.01–4.08 (m, 2 H, HCO), 3.77 (m, 1 H, HCO), 3.65–3.69 (m, 1 H, HCO), 3.48–3.54 (m, 2 H, HCO), 3.28 (dd, *J* = 9.9, 2.6 Hz, 1 H, HCO), 2.47 (t, *J* = 7.8 Hz, 2 H, CH_2), 1.80–2.08 (series of multiplets, 5 H, CH_2), 1.58–1.65 (m, 1 H, CH_2), 1.15 (s, 3 H, CH_3), 0.86 (s, 9 H, ^{t}BuSi), 0.08 (s, 3 H, CH_3Si), 0.07 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ

178.95 (OC=O), 138.82 (Ar), 138.36 (Ar), 128.31 (Ar), 128.22 (Ar), 127.79 (Ar), 127.57 (Ar), 127.29 (Ar), 76.74 (CO), 72.99 (CO), 72.81 (CO), 72.26 (CO), 71.44 (CO), 69.94 (CO), 63.44 (CO), 35.07, 34.43, 30.58, 28.30, 25.65, 17.77, 15.15, -3.91, -4.96; HRMS calcd for $C_{33}H_{48}O_7Si$ (M + Cs) 717.2224, found 717.2245. Anal. Calcd C, 67.77; H, 8.27. Found: C, 67.76; H, 8.31.

Diester 32. To a solution of acid **17** (5.39 g, 9.22 mmol) and alcohol **31** (5.13 g, 9.22 mmol) in dichloromethane (92 mL) at 0 °C was added DMAP (0.45 g, 3.69 mmol), CSA (0.43 g, 1.84 mmol), and DCC (2.47 g, 11.99 mmol), and the resulting solution was stirred at room temperature for 3 h. The resulting urea was filtered off, and the solvent was removed under vacuum. Flash column chromatography (silica, 20% ether in petroleum ether) gave 8.82 g (85%) of diester **32**. **32**: colorless oil; R_f = 0.22 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +11.45° (*c* 1.21, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2940, 2930, 2845, 1730, 1475, 1435, 1255, 1170, 1110, 1090, 840 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.12–7.57 (m, 20 H, Ar), 4.58 (d, *J* = 12.6 Hz, 1 H, CH_2Ar), 4.54 (dd, *J* = 11.5, 4.8 Hz, 1 H, CH_2Ar), 4.43–4.47 (m, 3 H, CH_2Ar, HCO), 3.92–4.00 (m, 4 H, HCO), 3.66 (m, 1 H, HCO), 3.58 (m, 1 H, HCO), 3.51–3.54 (m, 2 H, HCO), 3.38–3.43 (m, 3 H, HCO), 3.15 (dd, *J* = 9.9, 2.6 Hz, 1 H, HCO), 2.24–2.32 (m, 4 H, CH_2), 1.22–1.96 (series of multiplets, 12 H, CH_2), 1.06 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.94 (s, 9 H, ^{t}BuSi), 0.82 (m, 2 H, CH_2Si), 0.76 (s, 9 H, ^{t}BuSi), 0.09 (s, 3 H, CH_3Si), 0.08 (s, 3 H, CH_3Si), 0.01 (s, 9 H, Me_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.04 (OC=O), 173.13 (OC=O), 139.14 (Ar), 138.44 (Ar), 135.58 (Ar), 133.62 (Ar), 129.57 (Ar), 128.31 (Ar), 128.19 (Ar), 127.77 (Ar), 127.59 (Ar), 127.19 (Ar), 126.94 (Ar), 74.06 (CO), 73.15 (CO), 73.09 (CO), 73.00 (CO), 72.26 (CO), 71.57 (CO), 71.49 (CO), 70.39 (CO), 70.09 (CO), 67.03 (CO), 63.60 (CO), 35.11, 34.95, 34.89, 30.94, 27.85, 27.52, 26.77, 25.72, 25.67, 24.43, 19.23, 17.79, 17.26, 16.31, 15.12, -1.53, -3.92, -4.92; HRMS calcd for $C_{64}H_{94}O_{11}Si_3$ (M + Cs) 1255.5158, found 1255.5199. Anal. Calcd C, 68.41; H, 8.43. Found: C, 68.23; H, 8.40.

Dithionoester 33. To a solution of diester **32** (8.82 g, 7.85 mmol) in xylenes (78 mL) was added Lawesson's reagent (12.70 g, 31.40 mmol) and 1,1,3,3-tetramethylthiourea (4.15 g, 31.40 mmol), and the resulting mixture was heated to 175 °C for 1.5 h in sealed tubes. The reaction mixture was alllowed to cool to room temperature and directly purified by flash column chromatography (silica, petroleum ether, then 2% ethyl acetate in benzene) to give 4.49 g (49%) of dithionoester **33**. **33**: colorless oil; R_f = 0.57 (silica, 30% ether in petroleum ether); $[\alpha]^{25}_D$ +23.13° (*c* 0.32, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2940, 2910, 2880, 1475, 1370, 1280, 1260, 1120, 850, 695 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.24–7.69 (m, 20 H, Ar), 5.38 (dd, *J* = 11.4, 4.9 Hz, 1 H, HCO), 4.74 (d, *J* = 12.6 Hz, 1 H, CH_2Ar), 4.54–4.60 (m, 3 H, CH_2Ar), 4.49 (m, 1 H, HCO), 4.04–4.09 (m, 2 H, HCO), 3.78 (m, 1 H, HCO), 3.63–3.71 (m, 3 H, HCO), 3.51–3.55 (m, 3 H, HCO), 3.27 (dd, *J* = 9.8, 2.5 Hz, 1 H, HCO), 3.14 (m, 1 H, HCO), 2.76–2.85 (m, 4 H, CH_2), 1.79–2.06 (series of multiplets, 9 H, CH_2), 1.59–1.63 (m, 2 H, CH_2), 1.42 (m, 1 H, CH_2), 1.25 (s, 3 H, CH_3), 1.14 (s, 3 H, CH_3), 1.09 (m, 2 H, CH_2Si), 1.05 (s, 9 H, ^{t}BuSi), 0.88 (s, 9 H, ^{t}BuSi), 0.08 (s, 3 H, CH_3Si), 0.07 (s, 3 H, CH_3Si), 0.04 (s, 9 H, Me_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 224.27 (OC=S), 223.46 (OC=S), 139.19 (Ar), 138.46 (Ar), 135.60 (Ar), 133.60 (Ar), 129.59 (Ar), 128.33 (Ar), 128.24 (Ar), 127.79 (Ar), 127.63 (Ar), 127.56 (Ar), 127.17 (Ar), 127.01 (Ar), 80.16 (CO), 74.39 (CO), 73.21 (CO), 73.01 (CO), 72.68 (CO), 72.36 (CO), 71.51 (CO), 70.58 (CO), 70.11 (CO), 67.03 (CO), 63.62 (CO), 41.69, 40.56, 38.51, 35.14, 31.03, 27.39, 26.80, 25.73, 22.94, 19.25, 17.83, 17.02, 16.69, 15.31, -1.45, -1.79, -3.88, -4.76; HRMS calcd for $C_{64}H_{94}O_9S_2Si_3$ (M + Cs) 1287.4701, found 1287.4733.

Hydroxy Enol Ether 34. To a solution of dithionoester **33** (4.49 g, 3.88 mmol) in degassed benzene (776 mL) was added solid $NaHCO_3$ (5.0 g), and the resulting mixture was placed in a photolysis reaction vessel. The reaction was irradiated (Hanovia lamp, 450 W using a Pyrex filter) for 2 h at 70 °C. The $NaHCO_3$ was then filtered and the solvent removed under vacuum. The crude enol ether was then dissolved in THF (38.80 mL), nBu_4NF (5.82 mL of a 1 M solution in THF, 5.82 mmol) was added, and the reaction mixture was stirred at room temperature for 12 h. The reaction was then diluted with ether (100 mL) and washed with H_2O (50 mL) and brine (30 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 60% ether in petroleum ether) gave 1.55 g (47% overall) of enol ether **34**. **34**: colorless oil; R_f = 0.35 (silica, 60% ether in petroleum ether); $[\alpha]^{25}_D$ +41.36° (*c* 0.16, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3605, 2950, 2940, 1720, 1460, 1380, 1280, 1255, 1110, 1040, 830 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.23–7.34 (m, 10 H, Ar), 4.70 (d, *J* = 12.5 Hz, 1 H, CH_2Ar), 4.49–4.54 (m, 3 H, CH_2Ar), 4.02–4.04 (m, 2 H, HCO), 3.64–3.76 (m, 3 H, HCO), 3.25–3.55 (series of multiplets, 8 H, HCO), 2.63 (t, *J* = 8.2 Hz, 1 H, CH_2), 1.56–2.03 (series of multiplets, 15 H, CH_2), 1.23 (m, 1 H, CH_2), 1.13 (s, 3 H, CH_3), 1.09 (s, 3 H, CH_3), 0.96 (m, 1 H, CH_2), 0.85 (s, 9 H, ^{t}BuSi), 0.06 (s, 6 H, Me_2Si), 0.01 (s, 9 H, Me_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.00 (vinyl), 142.48 (vinyl), 139.48 (Ar), 138.53 (Ar), 128.29 (Ar), 128.14 (Ar), 127.76 (Ar), 127.51 (Ar), 127.21 (Ar), 127.08 (Ar), 84.52 (CO), 77.59 (CO), 73.42 (CO), 72.94 (CO), 72.86 (CO), 72.63 (CO), 71.52 (CO), 70.19 (CO), 69.46 (CO), 67.23 (CO), 65.98 (CO), 63.69 (CO), 39.28, 37.64, 35.33, 31.68, 27.37, 25.72, 24.96, 23.37, 18.52, 17.82, 14.78, 14.33, -1.48, -3.87, -4.73; HRMS calcd for $C_{48}H_{76}O_9Si_2$ (M + Cs) 985.4082, found 985.4044.

Enol Ether Acetate 35. To a solution of alcohol **34** (1.55 g, 1.82 mmol) in dichloromethane (18.20 mL) was added triethylamine (0.76 mL, 5.46 mmol), DMAP (0.022 g, 0.18 mmol), and acetic anhydride (0.189 mL, 2 mmol), and the resulting solution was stirred at room temperature for 2 h. The reaction mixture was then diluted with ether (100 mL) and washed with saturated $NaHCO_3$ (30 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 30% ether in petroleum ether) gave 1.4 g (86%) of acetate **35**. **35**: colorless oil; R_f = 0.20 (silica, 30% ether in petroleum ether); $[\alpha]^{25}_D$ +59.13° (*c* 0.58, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2940, 2860, 2845, 1740, 1450, 1375, 1250, 1160, 1110, 1045, 855, 840, 780 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.28–7.42 (m, 10 H, Ar), 4.91 (d, *J* = 12.4 Hz, 1 H, CH_2Ar), 4.61 (s, 2 H, CH_2Ar), 4.58 (d, *J* = 12.4 Hz, 1 H, CH_2Ar), 3.99–4.14 (m, 4 H, HCO), 3.84–3.88 (m, 2 H, HCO), 3.72–3.77 (m, 1 H, HCO), 3.54–3.65 (m, 4 H, HCO), 3.33 (dd, *J* = 9.9, 2.4 Hz, 1 H, HCO), 3.15 (dd, *J* = 11.6, 4.5 Hz, 1 H, HCO), 2.50–2.56 (m, 2 H, CH_2), 2.17–2.21 (m, 2 H, CH_2), 2.12 (s, 3 H, OCH_3), 2.10 (m, 1 H, HCO), 1.90–1.96 (m, 3 H, CH_2), 1.54–1.84 (series of multiplets, 8 H, CH_2), 1.37 (m, 1 H, CH_2), 1.28 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 0.93 (m, 1 H, CH_2), 0.92 (s, 9 H, ^{t}BuSi), 0.14 (s, 3 H, CH_3Si), 0.12 (s, 3 H, CH_3Si), 0.01 (s, 9 H, Me_3Si); ^{13}C NMR (500 MHz, $CDCl_3$) δ 171.00 (OC=O), 150.93 (vinyl), 142.52 (vinyl), 139.46 (Ar), 138.51 (Ar), 128.28 (Ar), 128.18 (Ar), 128.13 (Ar), 128.09 (Ar), 127.74 (Ar), 127.70 (Ar), 127.49 (Ar), 127.19 (Ar), 127.08 (Ar), 84.24 (CO), 77.57 (CO), 77.32 (CO), 73.41 (CO), 72.93 (CO), 72.83 (CO), 72.61 (CO), 71.50 (CO), 70.16 (CO), 67.18 (CO), 63.28 (CO), 37.63, 35.31, 31.66, 28.17, 25.76, 25.72, 25.67, 24.93, 23.33, 20.94, 18.50, 17.81, 14.78, 14.09, -1.46, -3.87, -4.75; HRMS calcd for $C_{50}H_{78}O_{10}Si_2$ (M + Cs) 1027.4188, found 1027.4188.

Hydroxy Ketone 36. To a solution of enol ether **35** (1.35 g, 1.50 mmol) in dichloromethane (15 mL) at 0 °C was added HF–pyridine (1.5 mL of a 48% solution), and the resulting solution was allowed to stir for 1 h. The reaction mixture was then diluted with EtOAc (50 mL) and washed with saturated $NaHCO_3$ (2 × 20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 100% ether) gave 924 mg (90%) of hydroxy ketone **36**. **36**: colorless oil; R_f = 0.18 (silica, 100% ether); $[\alpha]^{25}_D$ +40.91° (*c* 0.11, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3625, 3050, 2940, 2850, 1730, 1450, 1375, 1350, 1240, 1100, 1040 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.24–7.37 (m, 10 H, Ar), 4.72 (d, *J* = 12.2 Hz, 1 H, CH_2Ar), 4.48–4.51 (m, 3 H, CH_2Ar), 3.97–4.08 (series of multiplets, 3 H, HCO), 3.92 (dd, *J* = 11.5, 2.9 Hz, 1 H, HCO), 3.85 (dd, *J* = 11.5, 6.1 Hz, 1 H, HCO), 3.80 (m, 1 H, HCO), 3.69–3.79 (m, 2 H, HCO), 3.61 (m, 1 H, HCO), 3.47 (dd, *J* = 9.8, 4.5 Hz, 1 H, HCO), 3.29 (dd, *J* = 9.8, 2.4 Hz, 1 H, HCO), 2.97 (dd, *J* = 11.5, 4.9 Hz, 1 H, HCO), 2.84 (m, 1 H, CHC=O), 2.34 (m, 1 H, CHC=O), 2.04–2.18 (m, 2 H, CH_2), 2.03 (s, 3 H, OCH_3), 1.54–1.97 (series of multiplets, 10 H, CH_2), 1.41 (m, 1 H, CH_2), 1.32 (s, 3 H, CH_3), 1.21 (s, 3 H, CH_3), 1.12 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.85 (C=O), 170.95 (OC=O), 139.08 (Ar), 138.38 (Ar), 128.26 (Ar), 128.23 (Ar), 127.79 (Ar), 127.74 (Ar), 127.51 (Ar), 127.21 (Ar), 126.91 (Ar), 126.86 (Ar), 85.20, 76.74, 76.46, 76.16, 73.34, 72.99, 72.92, 72.39, 71.49, 70.92, 69.93, 67.33, 66.91, 63.80, 39.57, 37.71, 36.41, 34.77, 31.02, 27.63, 26.88, 21.48, 20.88, 15.22, 14.80; HRMS calcd for $C_{39}H_{52}O_{10}$ (M + Cs) 813.2615, found 813.2654.

Hydroxy Ketone 41. To a solution of hydroxy ketone **36** (20 mg, 0.029 mmol) in toluene (2 mL) was added DBU (0.043 mL, 0.29 mmol), and the resulting solution was heated to reflux for 2 h. The solvent was removed under vacuum. Flash column chromatography (silica, 100% ether) gave 18 mg (90%) of hydroxy ketone **41**. **41**: colorless oil; R_f = 0.33 (silica, 100% ether); $[\alpha]^{25}_D$ +4.07° (*c* 0.39, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3590, 2940, 2880, 1750, 1730, 1490, 1410, 1280, 1135, 1050 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25–7.36 (m, 10 H, Ar), 4.73 (d, *J* = 12.5 Hz, 1 H, CH_2Ar), 4.51–4.56 (m, 3 H, CH_2Ar), 4.00–4.08 (series of multiplets, 3 H, HCO), 3.94 (dd, *J* = 11.5, 6.1 Hz, 1 H, HCO),

3.67–3.81 (series of multiplets, 4 H, HCO), 3.55 (dd, J = 11.7, 4.5 Hz, 1 H, HCO), 3.50 (dd, J = 8.9, 3.5 Hz, 1 H, HCO), 3.26 (dd, J = 9.8, 2.5 Hz, 1 H, HCO), 2.97 (dd, J = 11.5, 4.7 Hz, 1 H, HCO), 2.69 (m, 1 H, CHC=O), 2.22 (m, 1 H, CHC=O), 2.11–2.19 (m, 1 H, CH_2), 2.07 (s, 3 H, OCH_3), 1.55–2.03 (series of multiplets, 13 H, CH_2), 1.30 (s, 3 H, CH_3), 1.15 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 216.91 (C=O), 171.01 (OC=O), 139.24 (Ar), 138.43 (Ar), 128.31 (Ar), 128.21 (Ar), 127.80 (Ar), 127.56 (Ar), 127.16 (Ar), 126.88 (Ar), 87.49 (CO), 82.49 (CO), 76.03 (CO), 73.34 (CO), 73.02 (CO), 72.67 (CO), 72.44 (CO), 71.52 (CO), 70.81 (CO), 69.92 (CO), 67.44 (CO), 66.99 (CO), 63.85, 38.82, 36.56, 35.50, 34.61, 31.12, 27.85, 26.42, 25.99, 20.94, 15.06, 14.87; HRMS calcd for $C_{39}H_{52}O_{10}$ (M + Cs) 813.2615, found 813.2649.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*b*]pyrano[2,3-*f*]oxepin, 11-[(Acetyloxy)methyl]-4-(benzyloxy)-2-[(benzyloxy)methyl]hexadecahydro-5a,12a-dimethyl-, [2α,4α,4aβ,5aβ,7aα,8aβ,11α,12aβ,14aα,15aα,16aα]- (39) and Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*b*]pyrano[2,3-*f*]oxepin, 11-[(Acetyloxy)methyl]-4-(benzyloxy)-2-[(benzyloxy)methyl]hexadecahydro-5a,12a-dimethyl-, [2α,4α,4aβ,5aβ,7aβ,8aβ,11α,12aβ,14aβ,15aα,16aα]- (40). To a solution of hydroxy ketone **41** (800 mg, 1.17 mmol) in CH_3NO_2 (117 mL) at 0 °C was added Ph_2MeSiH (0.70 mL, 3.61 mmol) and then TMSOTf (0.68 mL, 3.51 mmol), and the resulting solution was stirred for 15 min. The reaction mixture was then diluted with ether (300 mL) and washed with saturated $NaHCO_3$ (2 × 100 mL) and brine (100 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 80% ether in petroleum ether) gave 542 mg of cyclized product **39** and 90 mg of cyclized product **40** (81% overall, ratio 6:1). **39**: colorless oil; R_f = 0.20 (silica, 50% ether in petroleum ether); $[\alpha]^{25}_D$ +3.57° (c 1.40, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2960, 2825, 1725, 1450, 1375, 1255, 1120, 1090, 1060, 1050 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.24–7.36 (m, 10 H, Ar), 4.74 (d, J = 12.4 Hz, 1 H, CH_2Ar), 4.53–4.55 (m, 3 H, CH_2Ar), 3.96–4.11 (series of multiplets, 3 H, HCO), 3.88–3.91 (m, 1 H, HCO), 3.81–3.84 (m, 2 H, HCO), 3.67–3.75 (m, 2 H, HCO), 3.50 (dd, J = 9.7, 4.4 Hz, 1 H, HCO), 3.46 (dd, J = 9.9, 2.3 Hz, 1 H, HCO), 3.38 (dd, J = 11.6, 4.6 Hz, 1 H, HCO), 2.93 (dd, J = 12.3, 3.6 Hz, 1 H, HCO), 2.07 (s, 3 H, OCH_3), 1.93–2.03 (m, 5 H, CH_2), 1.65–1.73 (m, 6 H, CH_2), 1.43–1.58 (m, 4 H, CH_2), 1.32 (m, 1 H, CH_2), 1.27 (s, 3 H, CH_3), 1.19 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.05 (OC=O), 139.35 (Ar), 138.49 (Ar), 128.29 (Ar), 128.26 (Ar), 128.13 (Ar), 127.85 (Ar), 127.51 (Ar), 127.08 (Ar), 126.93 (Ar), 86.89 (CO), 85.46 (CO), 80.85 (CO), 77.64 (CO), 73.43 (CO), 73.39 (CO), 73.34 (CO), 72.99 (CO), 72.51 (CO), 71.55 (CO), 69.83 (CO), 67.24 (CO), 64.71, 36.92, 35.61, 32.93, 31.33, 29.67, 27.94, 27.59, 27.19, 25.90, 20.98, 15.29, 14.51; HRMS calcd for $C_{39}H_{52}O_9$ (M + Cs) 797.2666, found 797.2661. **39**: colorless oi; R_f = 0.42 (silica, 80% ether in petroleum ether); $[\alpha]^{25}_D$ +28.48° (c 2.24, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2920, 2850, 1725, 1460, 1375, 1245, 1090, 1050 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26–7.36 (m, 10 H, Ar), 4.83 (d, J = 12.4 Hz, 1 H, CH_2Ar), 4.55–4.57 (m, 3 H, CH_2Ar), 4.03–4.10 (m, 3 H, HCO), 3.96–4.00 (m, 1 H, HCO), 3.89–3.94 (m, 2 H, HCO), 3.78–3.86 (m, 2 H, HCO), 3.72–3.77 (m, 1 H, HCO), 3.53 (dd, J = 9.7, 4.5 Hz, 1 H, HCO), 3.48 (dd, J = 12.1, 4.7 Hz, 1 H, HCO), 3.32 (dd, J = 9.8, 2.5 Hz, 1 H, HCO), 2.93 (dd, J = 11.0, 4.2 Hz, 1 H, HCO), 2.08 (s, 3 H, OCH_3), 1.90–2.07 (m, 6 H, CH_2), 1.64–1.78 (m, 6 H, CH_2), 1.43–1.57 (m, 3 H, CH_2), 1.32 (s, 3 H, CH_3), 1.25 (s, 1 H, CH_2), 1.21 (s, 3 H, CH_3); ^{13}C NMR (500 MHz, $CDCl_3$) δ 171.06 (OC=O), 139.49 (Ar), 138.55 (Ar), 128.29 (Ar), 128.13 (Ar), 127.58 (Ar), 127.50 (Ar), 127.11 (Ar), 88.71 (CO), 85.15 (CO), 80.94 (CO), 77.39 (CO), 76.89 (CO), 73.12 (CO), 73.07 (CO), 72.80 (CO), 72.67 (CO), 72.57 (CO), 71.42 (CO), 70.29 (CO), 67.27, 67.16, 64.17, 37.21, 35.31, 34.56, 31.37, 28.37, 27.23, 26.05, 25.93, 20.98, 15.18, 14.91; HRMS calcd for $C_{39}H_{52}O_9$ (M + Cs) 797.2666, found, 797.2650.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*b*]pyrano[2,3-*f*]oxepin, 11-[(Acetyloxy)methyl]-4-hydroxy-2-(hydroxymethyl)hexadecahydro-5a,-12a-dimethyl-,[2α,4α,4aβ,5aβ,7aα,8aβ,11α,12aβ,14aα,15aα,16aα]- (42). To a solution of **39** (595 mg, 0.895 mmol) in ethanol (8.9 mL) was added $Pd(OH)_2$ (60 mg, 10% by weight of starting material). The reaction mixture was placed under a hydrogen atmosphere and stirred for 2 h. The catalyst was then filtered and the solvent removed under vacuum. Flash column chromatography (silica, 100% ethyl acetate) gave 434 mg (100%) of diol **42**. **42**: colorless oil; R_f = 0.14 (silica, 100% ethyl acetate); $[\alpha]^{25}_D$ +5.75° (c 0.43, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3520, 3380, 2940, 1725, 1460, 1430, 1380, 1245, 1220, 1090, 1080, 1040, 990 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.88–4.13 (series of multiplets, 6 H, HCO), 3.77–3.82 (m, 2 H, HCO), 3.71–3.75 (m, 1 H, HCO), 3.56 (dd, J = 11.9, 3.7 Hz, 1 H, HCO), 3.35–3.41 (m, 3 H, HCO), 2.97 (dd, J = 12.2, 3.6 Hz, 1 H, HCO), 2.80 (bs, 1 H, OH), 2.68 (bs, 1 H, OH), 1.84–2.12 (series of multiplets, 10 H, OCH_3, CH_2), 1.64–1.74 (m, 6 H, CH_2), 1.35–1.59 (m, 3 H, CH_2), 1.31 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.10 (OC=O), 86.89 (CO), 85.71 (CO), 80.73 (CO), 78.37 (CO), 73.51 (CO), 72.69 (CO), 72.04 (CO), 67.28 (CO), 65.33 (CO), 64.10 (CO), 63.39 (CO), 36.80, 35.65, 32.88, 31.49, 27.99, 27.61, 27.20, 25.96, 21.01, 15.35, 15.08; HRMS calcd for $C_{25}H_{40}O_9$ (M + Cs) 617.1727, found 617.1727.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*b*]pyrano[2,3-*f*]oxepin, 11-[(Acetyloxy)methyl]-2-(hydroxymethyl)-4-[(*tert*-butyldimethylsilyl)oxy]-hexadecahydro-5a,12a-dimethyl-, [2α,4α,4aβ,5aβ,7aα,8aβ,11α,12aβ,-14aα,15aα,16aα]- (43). To a solution of diol **42** (418 mg, 0.862 mmol) in dichloromethane (4.3 mL) at –20 °C were added 2.6-lutidine (0.40 mL, 3.45 mmol) and TBSOTf (0.48 mL, 2.07 mmol), and the resulting solution was allowed to warm to room temperature. The reaction mixture was diluted with ether (20 mL) and washed with H_2O (5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. The crude compound was dissolved in MeOH–CH_2Cl_2 (1:1, 8.6 mL, 0.1 M) and cooled to 0 °C, and CSA (200 mg, 0.862 mmol) was added. The reaction mixture was stirred for 5 min, then diluted with EtOAc (20 mL), and washed with saturated $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 80% ether in petroleum ether) gave 450 mg (87%) of alcohol **43**. **43**: colorless oil; R_f = 0.36 (silica, 80% ether in petroleum ether); $[\alpha]^{25}_D$ +8.49° (c 1.11, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3590, 2940, 2920, 2850, 1730, 1470, 1390, 1250, 1110, 1080, 1030, 840 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.25 (dd, J = 11.9, 9.2 Hz, 1 H, HCO), 3.88–4.05 (series of multiplets, 5 H, HCO), 3.78–3.83 (m, 2 H, HCO), 3.72–3.74 (m, 1 H, HCO), 3.37–3.43 (m, 2 H, HCO), 3.32 (dd, J = 9.8, 2.3 Hz, 1 H, HCO), 2.92 (dd, J = 12.3, 3.6 Hz, 1 H, HCO), 2.39 (bs, 1 H, OH), 1.91–2.11 (series of multiplets, 8 H, OCH_3, CH_2), 1.63–1.71 (m, 7 H, CH_2), 1.44–1.56 (m, 3 H, CH_2), 1.30 (m, 1 H, CH_2), 1.28 (s, 3 H, CH_3), 1.19 (s, 3 H, CH_3), 0.88 (s, 9 H, ^{t}BuSi), 0.05 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.07 (OC=O), 86.99 (CO), 85.51 (CO), 80.84 (CO), 77.62 (CO), 73.41 (CO), 73.38 (CO), 73.38 (CO), 72.37 (CO), 67.27 (CO), 66.71 (CO), 63.91 (CO), 63.53 (CO), 36.82 (CO), 35.61, 34.18, 32.90, 27.97, 27.61, 27.18, 25.93, 25.83, 20.99, 18.24, 15.32, 14.83, –4.15, –5.16; HRMS calcd for $C_{31}H_{54}O_9Si$ (M + Cs) 731.2591, found 731.2604.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*b*]pyrano[2,3-*f*]oxepin-2-prop-2-enoate, 11-[(Acetyloxy)methyl]-4-[(*tert*-butyldimethylsilyl)oxy]-hexadecahydro-5a,12a-dimethyl-[2*R*-[2α,4α,4aβ,5aβ,7aα,8aβ,11α,12aβ,-14aα,15aα,16aα]]-, Methyl Ester (44). To a solution of oxalyl chloride (0.98 mL, 1.13 mmol) in dichloromethane (7.51 mL) at –78 °C was added DMSO (0.11 mL, 1.50 mmol), and the resulting solution was stirred for 20 min. To this solution was added a solution of alcohol **43** (450 mg, 0.751 mmol), and this solution was stirred at –78 °C for 1 h. Next was added triethylamine (0.42 mL, 3.00 mmol). The reaction mixture was stirred at –78 °C for 30 min and then allowed to warm to room temperature. The reaction was diluted with ether (50 mL) and washed with saturated NH_4Cl (10 mL), H_2O (2 × 10 mL), and brine (10 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum to give the crude aldehyde. This aldehyde, without further purification, was dissolved in benzene (7.5 mL), and to this was added methyl (triphenylphosphoranylidene)acetate (502 mg, 1.50 mmol), and the resulting solution was stirred for 2 h. The solvent was removed under vacuum. Flash column chromatography (silica, 50% ether in petroleum ether) gave 350 mg (71%) of α,β-unsaturated ester **44**. **44**: colorless oil; R_f = 0.34 (silica, 50% ether in petroleum ether); $[\alpha]^{25}_D$ +1.56° (c 1.60, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2955, 2925, 2830, 1725, 1475, 1440, 1380, 1280, 1250, 1110, 1100, 1080, 1050, 1000, 840 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.16 (dd, J = 15.9, 4.2 Hz, 1 H, vinyl), 5.91 (dd, J = 15.9, 2.1 Hz, 1 H, vinyl), 4.50 (m, 1 H, HCO), 4.08 (m, 1 H, HCO), 4.03 (dd, J = 11.4, 4.4 Hz, 1 H, HCO), 3.98 (dd, J = 11.4, 6.5 Hz, 1 H, HCO), 3.70–3.93 (m, 7 H, OCH_3, CH_2), 3.39 (dd, J = 11.6, 4.6 Hz, 1 H, HCO), 3.34 (dd, J = 9.8, 2.1 Hz, 1 H, HCO), 2.90 (dd, J = 12.3, 3.6 Hz, 1 H, HCO), 2.15 (m, 1 H, CH_2), 2.07 (s, 3 H, OCH_3), 1.92–2.05 (m, 4 H, CH_2), 1.86 (dd, J = 14.2, 3.6 Hz, 1 H, CH_2), 1.64–1.72 (m, 6 H, CH_2), 1.42–1.56 (m, 3 H, CH_2), 1.32 (m, 1 H, CH_2), 1.27 (s, 3 H, CH_3), 1.19 (s, 3 H, CH_3), 0.84 (s, 9 H, ^{t}BuSi), 0.03 (s, 3 H, CH_3Si), 0.02 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.12 (OC=O), 166.87 (OC=O), 149.94 (vinyl), 119.04 (vinyl), 86.98 (CO), 85.53 (CO), 80.91 (CO), 77.67 (CO), 73.46 (CO), 72.31 (CO), 70.81 (CO), 67.35 (CO), 67.31 (CO), 67.05 (CO), 64.64 (CO), 51.48 (CO), 37.88, 36.82, 35.67, 32.67, 28.04, 27.68, 27.21, 25.99, 25.74, 21.06, 18.18, 15.37, 14.84, –4.26, –4.93; HRMS calcd for $C_{34}H_{56}O_{10}Si$ (M + Cs) 785.2697, found 785.2680.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*b*]pyrano[2,3-*f*]oxepin-2-propanoate, 11-(Hydroxymethyl)-4-[(*tert*-butyldimethylsilyl)oxy]hexadecahydro-5a,12a-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aα,8aβ,11α,12aβ,14aα,15aα,16aα]]-, Methyl Ester (45). To a solution of **44** (350 mg, 0.536 mmol) in methanol (5.36 mL) was added $Pd(OH)_2$ (35 mg, 10% by weight of starting material), and the resulting mixture was placed under hydrogen atmosphere and stirred for 2 h. The catalyst was filtered, and K_2CO_3 (148 mg, 1.07 mmol) was added. The reaction mixture was heated to 50 °C for 30 min and then diluted with EtOAc (50 mL) and washed with H_2O (20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 80% ether in petroleum ether) gave 286 mg (87%) of alcohol **45**. **45**: white solid; mp 166.6 °C; R_f = 0.36 (silica, 80% ether in petroleum ether); $[\alpha]^{25}_D$ +7.45° (*c* 1.10, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3595, 2955, 2920, 2825, 1730, 1440, 1360, 1245, 1110, 1090, 1050, 830, 725 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.05 (m, 1 H, HCO), 3.92 (m, 1 H, HCO), 3.80–3.90 (m, 2 H, HCO), 3.61–3.72 (series of multiplets, 5 H, OCH_3, HCO), 3.56 (dd, *J* = 11.1, 2.9 Hz, 1 H, HCO), 3.46 (dd, *J* = 11.1, 6.9 Hz, 1 H, HCO), 3.37 (dd, *J* = 11.3, 4.9 Hz, 1 H, HCO), 3.28 (dd, *J* = 9.8, 2.3 Hz, 1 H, HCO), 2.92 (dd, *J* = 12.7, 3.6 Hz, 1 H, HCO), 2.65–2.70 (m, 1 H, CH_2), 2.32–2.39 (m, 2 H, CH_2), 2.18 (bs, 1 H, OH), 1.88–2.03 (m, 5 H, CH_2), 1.35–1.74 (series of multiplets, 12 H, CH_2), 1.26 (s, 3 H, CH_3), 1.19 (s, 3 H, CH_3), 0.88 (s, 9 H, ^{t}BuSi), 0.04 (s, 3 H, CH_3Si), 0.03 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.13 (OC═O), 87.14 (CO), 85.45 (CO), 80.88 (CO), 77.43 (CO), 73.63 (CO), 72.61 (CO), 71.92 (CO), 69.51 (CO), 67.41 (CO), 65.93 (CO), 63.07 (CO), 51.48 (CO), 36.81, 36.34, 35.71, 32.87, 31.57, 28.31, 27.59, 27.17, 27.06, 25.89, 25.78, 18.19, 15.47, 14.82, –4.23, –5.15; HRMS calcd for $C_{32}H_{56}O_9Si$ (M + Cs) 745.2748, found 745.2759.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*b*]pyrano[2,3-*f*]oxepin-2-propanoate, 11-(Iodomethyl)-4-[(*tert*-butyldimethylsilyl)oxy]hexadecahydro-5a,12a-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aα,8aβ,11α,12aβ,14aα,15aα,16aα]]-, Methyl Ester (46). To a solution of alcohol **45** (286 mg, 0.467 mmol) in benzene (4.7 mL) were added triphenylphosphine (245 mg, 0.934 mmol), imidazole (127 mg, 1.868 mmol), and iodine (237 mg, 0.934 mmol), and the reaction mixture was heated under reflux for 30 min. The reaction was then diluted with ether (50 mL) and washed with saturated sodium thiosulfate (20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 20% ether in petroleum ether) gave 292 mg (87%) of iodide **46**. **46**: colorless oil; R_f = 0.15 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +19.01° (*c* 0.95, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3025, 2950, 2920, 2855, 1730, 1450, 1410, 1260, 1140, 1110, 1080, 1045, 920, 845 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.05 (m, 1 H, HCO), 3.89 (m, 1 H, HCO), 3.82 (m, 2 H, HCO), 3.58–3.69 (series of multiplets, 5 H, OCH_3, HCO), 3.39 (dd, *J* = 11.8, 5.0 Hz, 1 H, HCO), 3.28 (dd, *J* = 9.8, 2.4 Hz, 1 H, HCO), 3.07–3.15 (m, 2 H, CHI), 2.92 (dd, *J* = 12.3, 3.6 Hz, 1 H, HCO), 2.68 (m, 1 H, CH_2), 2.34–2.39 (m, 2 H, CH_2), 1.91–2.03 (m, 6 H, CH_2), 1.44–1.72 (series of multiplets, 10 H, CH_2), 1.28 (m, 1 H, CH_2), 1.26 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3), 0.88 (s, 9 H, ^{t}BuSi), 0.04 (s, 3 H, CH_3Si), 0.03 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.19 (OC═O), 87.14 (CO), 85.43 (CO), 80.93 (CO), 77.49 (CO), 73.41 (CO), 72.68 (CO), 71.99 (CO), 69.51 (CO), 67.46 (CO), 63.11 (CO), 51.54, 36.87, 36.41, 35.53, 32.90, 31.64, 31.12, 28.37, 27.85, 27.19, 25.99, 25.85, 18.25, 15.48, 14.85, 9.63, –4.17, –5.08; HRMS calcd for $C_{32}H_{55}IO_8Si$ (M + Cs) 855.1765, found 855.1766.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanoate, 10-Hydroxy-4-[(*tert*-butyldimethylsilyl)oxy]-9-(1-butenyl)hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aα,9α,10β,12aα,13aα,14aα]]-, Methyl Ester (47). To a solution of iodide **46** (292 mg, 0.404 mmol) in ethanol (4.0 mL) were added zinc (264 mg, 4.04 mmol), NH_4Cl (108 mg, 2.02 mmol), and H_2O (0.036 mL, 2.02 mmol), and the resulting mixture was heated under reflux for 30 min. The zinc was then filtered, and the reaction mixture was diluted with EtOAc (30 mL) and washed with saturated sodium thiosulfate (10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 70% ether in petroleum ether) gave 230 mg (95%) of alcohol **47**. **47**: colorless oil; R_f = 0.50 (silica, 70% ether in petroleum ether); $[\alpha]^{25}_D$ +34.78° (*c* 0.78, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3560, 2930, 2910, 2820, 1730, 1450, 1370, 1255, 1080, 1050, 1000, 845 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.80–5.89 (m, 1 H, vinyl), 5.03–5.12 (m, 2 H, vinyl), 4.74 (bs, 1 H, OH), 4.03–4.12 (m, 2 H, HCO), 3.91–3.98 (m, 1 H, HCO), 3.84–3.89 (m, 1 H, HCO), 3.76 (d, *J* = 10.7 Hz, 1 H, HCO), 3.69 (s, 3 H, OCH_3), 3.67 (m, 1 H, HCO), 3.23 (dd, *J* = 9.7, 2.4 Hz, 1 H, HCO), 3.04 (dd, *J* = 11.9, 4.2 Hz, 1 H, HCO), 2.68–2.73 (m, 1 H, CH_2), 2.38–2.42 (m, 2 H, CH_2), 2.25–2.28 (m, 1 H, CH_2), 2.08–2.15 (m, 3 H, CH_2), 1.96–2.05 (m, 2 H, CH_2), 1.45–1.88 (series of multiplets, 11 H, CH_2), 1.24 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.05 (s, 3 H, CH_3Si), 0.04 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.07 (OC═O), 137.26 (vinyl), 115.90 (vinyl), 83.14 (CO), 81.88 (CO), 81.22 (CO), 79.22 (CO), 76.38 (CO), 72.13 (CO), 72.06 (CO), 67.09 (CO), 62.88 (CO), 52.05, 39.66, 36.11, 35.66, 32.91, 31.93, 18.24, 15.60, –4.22, –5.06; HRMS calcd for $C_{32}H_{56}O_8Si$ (M + Cs) 729.2799, found 729.2761.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanoate, 4,10-Bis[(*tert*-butyldimethylsilyl)oxy]-9-(1-butenyl)hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aα,9α,10β,12aα,13aα,14aα]]-, Methyl Ester (48). Experimental procedure was followed as described for compound **15**. **48**: colorless oil; R_f = 0.32 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +1.91° (*c* = 0.87, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2950, 2930, 2825, 1740, 1470, 1360, 1250, 1175, 1090, 1060, 1005, 840, 770 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.79–5.84 (m, 1 H, vinyl), 4.94–5.05 (m, 2 H, vinyl), 4.02–4.07 (m, 2 H, HCO), 3.77–3.84 (m, 2 H, HCO), 3.62–3.68 (m, 4 H, OCH_3, HCO), 3.28 (m, 1 H, HCO), 3.20 (dd, *J* = 9.7, 2.4 Hz, 1 H, HCO), 3.00 (dd, *J* = 12.1, 4.1 Hz, 1 H, HCO), 2.66–2.68 (m, 1 H, CH_2), 2.25–2.37 (m, 3 H, CH_2), 1.42–2.01 (series of multiplets, 15 H, CH_2), 1.28 (m, 1 H, CH_2), 1.22 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 0.87 (s, 9 H, ^{t}BuSi), 0.83 (s, 9 H, ^{t}BuSi), 0.06 (s, 6 H, Me_2Si), 0.04 (s, 3 H, CH_3Si), 0.03 (s, 3 H, CH_3Si); ^{13}C NMR (500 MHz, $CDCl_3$) δ 174.16 (OC═O), 138.93 (vinyl), 114.52 (vinyl), 83.08 (CO), 82.04 (CO), 80.51 (CO), 78.12 (CO), 77.41 (CO), 72.46 (CO), 71.92 (CO), 67.36 (CO), 62.74 (CO), 51.51 (CO), 39.03, 37.29, 36.32, 33.00, 31.62, 31.21, 29.98, 29.71, 28.37, 26.55, 25.87, 25.83, 25.70, 22.55, 18.24, 18.13, 15.39, –1.93, –2.08, –4.20, –5.09; HRMS calcd for $C_{38}H_{70}O_8Si_2$ (M + Cs) 843.3664, found 843.3679.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanoate, 4,10-Bis(*tert*-butyldimethylsiloxy)-9-[6-(phenylselenyl)-3-hexenyl]hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aα,9α,10β,12aα,13aα,14aα]]-, Methyl Ester (49). To a solution of alkene **46** (250 mg, 0.352 mmol) in dichloromethane (7 mL) at –78 °C was bubbled ozone until a blue color persisted. Excess ozone was removed by bubbling oxygen through the solution until it became colorless. To this solution at –78 °C was added triphenylphosphine (185 mg, 0.704 mmol), and the solution was warmed to room temperature and stirred for 3 h. The solvent was removed under vacuum, and the crude aldehyde was passed quickly through silica using 20% ether in petroleum ether. The aldehyde was dissolved in THF (3.5 mL) and added at –78 °C to an already prepared mixture containing $PhSe(CH_2)_3PPh_3Br$ (1.9 g, 3.52 mmol), ^{n}BuLi (0.704 mL of a 1.6 M solution in hexanes, 1.76 mmol), and HMPA (0.612 mL, 3.52 mmol) in THF (3.52 mL). The reaction mixture was allowed to warm to room temperature and then was diluted with EtOAc (50 mL) and washed with H_2O (20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 20% ether in petroleum ether) gave 258 mg (82%) of selenide **49**. **49**: colorless oil; R_f = 0.30 (silica, 10% ether in petroleum ether); $[\alpha]^{25}_D$ +13.07° (*c* 0.75, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2940, 2930, 2850, 1730, 1460, 1430, 1255, 1120, 1090, 1060, 955, 845 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.49–7.51 (m, 2 H, Ar), 7.23–7.27 (m, 3 H, Ar), 5.38 (m, 2 H, vinyl), 4.04–4.06 (m, 2 H, HCO), 3.79–3.84 (m, 2 H, HCO), 3.64–3.68 (m, 4 H, OCH_3, HCO), 3.31 (d, *J* = 9.0 Hz, 1 H, HCO), 3.22 (dd, *J* = 9.7, 2.4 Hz, 1 H, HCO), 3.01 (dd, *J* = 12.1, 3.9 Hz, 1 H, HCO), 2.92 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.68 (m, 1 H, CH_2), 2.18–2.47 (series of multiplets, 5 H, CH_2), 1.84–2.02 (m, 6 H, CH_2), 1.43–1.75 (series of multiplets, 10 H, CH_2), 1.22 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.83 (s, 9 H, ^{t}BuSi), 0.06 (s, 3 H, CH_3Si), 0.05 (s, 6 H, Me_2Si), 0.04 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.15 (OC═O), 132.54, 131.48, 130.29, 128.97, 128.31, 128.23, 126.71, 82.97 (CO), 81.86 (CO), 80.43 (CO), 78.19 (CO), 76.74 (CO), 72.42 (CO), 71.89 (CO), 67.32 (CO), 62.69 (CO), 51.49, 39.08, 37.23, 36.29, 32.98, 31.59, 30.63, 28.34, 27.62, 27.328, 26.50, 25.80, 24.89, 22.55, 18.08, –1.97, –2.11, –4.21, –5.11; HRMS calcd for $C_{46}H_{78}O_8SeSi_2$ (M + Cs) 1027.3465, found 1027.3459.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanoate, 4,10-Bis[(*tert*-butyldimethylsilyl)oxy]-9-(3,5-hexadienyl)hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aα,9α(*Z*),10β,12aα,13aα,14aα]]-, Methyl Ester (50). To a solution of selenide **49** (250 mg, 0.280 mmol) in THF (2.8 mL) were added $NaHCO_3$ (235 mg, 2.80 mmol) and H_2O_2 (1.0 mL of a 30% solution), and the reaction mixture was stirred at room temperature for 4 h. The reaction mixture was then diluted with ether (50 mL) and washed with H_2O (20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 20% ether in petroleum ether) gave 181

mg (88%) of diene **50**. **50**: colorless oil; R_f = 0.16 (silica, 10% ether in petroleum ether); $[\alpha]^{25}_D$ +15.15° (*c* 0.51, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2960, 2945, 2810, 1730, 1460, 1430, 1255, 1125, 1100, 1055, 840, 800 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.60–6.68 (m, 1 H, vinyl), 6.01 (t, *J* = 10.8 Hz, 1 H, vinyl), 5.45 (m, 1 H, vinyl), 5.08–5.20 (m, 2 H, vinyl), 4.06 (m, 2 H, HCO), 3.82 (m, 2 H, HCO), 3.63–3.69 (m, 4 H, OCH_3, HCO), 3.34 (d, *J* = 9.2 Hz, 1 H, HCO), 3.22 (dd, *J* = 9.7, 2.3 Hz, 1 H, HCO), 3.00 (dd, *J* = 12.7, 4.0 Hz, 1 H, HCO), 2.68 (m, 1 H, CH_2), 2.32–2.41 (m, 3 H, CH_2), 2.17–2.21 (m, 1 H, CH_2), 1.43–2.02 (m, 14 H, CH_2), 1.32 (m, 1 H, CH_2), 1.22 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 0.88 (s, 9 H, ^{t}BuSi), 0.84 (s, 9 H, ^{t}BuSi), 0.07 (s, 3 H, CH_3Si), 0.06 (s, 3 H, CH_3Si), 0.05 (s, 3 H, CH_3Si), 0.04 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.23 (OC=O), 132.75 (vinyl), 132.39 (vinyl), 129.56 (vinyl), 117.00 (vinyl), 83.15 (CO), 82.20 (CO), 80.57 (CO), 78.19 (CO), 72.50 (CO), 71.96 (CO), 67.41 (CO), 62.79 (CO), 51.56 (CO), 39.04, 37.23, 36.37, 31.67, 30.67, 26.61, 25.91, 25.87, 25.26, 22.54, 15.29, –1.89, –2.03, –4.15, –5.04; HRMS calcd for $C_{40}H_{72}O_8Si_2$ (M + Cs) 869.3820, found 869.3838.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanoate, 4,-10-Bis[(*tert*-butyldimethylsilyl)oxy]-9-(3,5-hexadienyl)hexadecahydro-5a,10-dimethyl-α-methylene-, [2*R*-[2α,4α,4aβ,5aβ,7aα,9α(*Z*),10β,12aα,-13aα,14aα]]-, Methyl Ester (51). To a solution of $NaN(SiMe_3)_2$ (0.814 mL of a 1 M solution in THF, 0.814 mmol) at –78 °C was added a solution of ester **50** (40 mg, 0.054 mmol) in THF (0.54 mL), and the resulting solution was stirred at –78 °C for 45 min. To this solution was then added Eschenmoser's salt (0.151 g, 0.814 mmol), and the resulting mixture was stirred at 0 °C for 15 min. The reaction mixture was then diluted with EtOAc (20 mL) and washed with saturated NH_4Cl (10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$), concentrated under vacuum, and filtered through silica. The resulting amine was then dissolved in methanol (0.54 mL, 0.1 M), and to this solution was added methyl iodide (0.068 mL, 1.086 mmol). The reaction mixture was stirred at room temperature for 30 min, and then the solvent was removed under vacuum. The crude amine salt was then dissolved in benzene (0.54 mL, 0.1 M), DBU (0.081 mL, 0.54 mmol) was added, and the resulting solution was stirred for 1 h. The solvent was removed under vacuum. Flash column chromatography (silica, 20% ether in petroleum ether) gave 20.7 mg (51%) of unsaturated ester **51**. **51**: colorless oil; R_f = 0.26 (silica, 10% ether in petroleum ether); $[\alpha]^{25}_D$ +20.00° (*c* 0.10, $CHCl_3$); IR (neat) ν_{max} 2929, 2856, 1723, 1463, 1438, 1251, 1140, 1089, 1052, 1006, 834, 774 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.87 (dt, *J* = 10.25, 16.88 Hz, 1 H, vinyl), 6.41 (d, *J* = 1.5 Hz, 1 H, vinyl), 6.20 (t, *J* = 10.8 Hz, 1 H, vinyl), 5.67–5.71 (m, 2 H, vinyl), 5.23 (dd, *J* = 16.9, 1.1 Hz, 1 H, vinyl), 5.13 (d, *J* = 10.2 Hz, 1 H, vinyl), 4.27 (m, 1 H, HCO), 3.99–4.09 (m, 2 H, HCO), 3.74 (dd, *J* = 15.1, 10.8 Hz, 1 H, HCO), 3.58–3.63 (m, 2 H, HCO), 3.47 (s, 3 H, OCH_3), 3.30 (dd, *J* = 9.8, 2.4 Hz, 1 H, HCO), 3.08 (dd, *J* = 12.2, 4.0 Hz, 1 H, HCO), 2.60 (dd, *J* = 14.9, 3.5 Hz, 1 H, CH_2), 2.49 (m, 1 H, CH_2), 1.40–2.28 (series of multiplets, 15 H, CH_2), 1.33 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 1.16 (s, 9 H, ^{t}BuSi), 1.07 (s, 9 H, ^{t}BuSi), 0.22 (s, 6 H, Me_2Si), 0.21 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.41 (OC=O), 139.65 (vinyl), 133.02 (vinyl), 132.79 (vinyl), 130.24 (vinyl), 125.76 (vinyl), 117.17 (vinyl), 84.09 (CO), 83.95 (CO), 80.41 (CO), 78.49 (CO), 77.92 (CO), 77.56 (CO), 72.95 (CO), 71.27 (CO), 68.01 (CO), 63.29 (CO), 51.37, 39.01, 37.98, 36.63, 36.17, 34.99, 31.16, 30.22, 28.79, 26.63, 22.51, 15.18, –1.66, –1.78, –3.88, –4.80; HRMS calcd for $C_{41}H_{72}O_8Si_2$ (M + Cs) 881.3820, found 881.3835.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanol, 4,10-Bis[(*tert*-butyldimethylsilyl)oxy]-9-(3,5-hexadienyl)hexadecahydro-5a,-10-dimethyl-α-methylene-, [2*R*-[2α,4α,4aβ,5aβ,7aα,9α(*Z*),10β,12aα,-13aα,14aα]]- (52). To a solution of ester **51** (10 mg, 0.013 mmol) in dichloromethane (2 mL) at –78 °C was added DIBAL (0.065 mL of a 1 M solution in dichloromethane, 0.065 mmol), and the resulting solution was stirred for 30 min. The reaction mixture was diluted with EtOAc (10 mL) and washed with saturated Na/K tartrate (2 × 5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 50% ether in petroleum ether) gave 8.4 mg (87%) of alcohol **52**. **52**: colorless oil; R_f = 0.38 (silica, 30% ether in petroleum ether); $[\alpha]^{25}_D$ +18.00° (*c* 0.10, $CHCl_3$); IR (neat) ν_{max} 3436, 2929, 2840, 1646, 1463, 1372, 1087, 1050, 835, 774, 666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.74 (dt, *J* = 17.1, 11.1 Hz, 1 H, vinyl), 5.97 (t, *J* = 10.9 Hz, 1 H, vinyl), 5.40 (m, 1 H, vinyl), 5.14 (dd, *J* = 16.9, 1.9 Hz, 1 H, vinyl), 5.05 (m, 2 H, vinyl), 4.90 (s, 1 H, vinyl), 3.96–4.03 (m, 4 H, HCO), 3.71–3.81 (m, 2 H, HCO), 3.28 (d, *J* = 9.0 Hz, 1 H, HCO), 3.19 (dd, *J* = 9.7, 2.4 Hz, 1 H, HCO), 3.10 (dd, *J* = 15.1, 10.7 Hz, 1 H, HCO), 2.95 (dd, *J* = 12.0, 4.0 Hz, 1 H, HCO), 2.29–2.33 (m, 2 H, CH_2), 2.12–2.23 (m, 2 H, CH_2), 1.40–2.00 (series of multiplets, 14 H, CH_2), 1.18 (s, 3 H, CH_3), 1.08 (s, 3 H, CH_3), 0.85 (s, 9 H, ^{t}BuSi), 0.80 (s, 9 H, ^{t}BuSi), 0.02 (s, 6 H, Me_2Si), 0.01 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.45 (vinyl), 132.72 (vinyl), 132.35 (vinyl), 129.52 (vinyl), 116.95 (vinyl), 113.43 (vinyl), 83.24 (CO), 82.40 (CO), 80.49 (CO), 78.19 (CO), 77.27 (CO), 72.30 (CO), 67.34 (CO), 66.32 (CO), 63.07 (CO), 38.84, 38.40, 37.24, 36.56, 32.81, 29.71, 26.59, 25.90, 22.70, 22.40, 15.17, –1.92, –2.06, –4.21, –4.96; HRMS calcd for $C_{40}H_{72}O_7Si_2$ (M + Cs) 852.3871, found 853.3899.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanal, 4,10-Bis[(*tert*-butyldimethylsilyl)oxy]-9-(3,5-hexadienyl)hexadecahydro-5a,-10-dimethyl-α-methylene-, [2*R*-[2α,4α,4aβ,5aβ,7aα,9α(*Z*),10β,12aα,-13aα,14aα]]- (53). Experimental procedure for Swern oxidation was followed as described for compound **44**. **53**: colorless oil; R_f = 0.27 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +6.00° (*c* 0.10, $CHCl_3$); IR (neat) ν_{max} 2927, 2856, 1695, 1462, 1371, 1251, 1088, 939, 835, 775, 662 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.35 (s, 1 H, HC=O), 6.64 (dt, *J* = 16.2, 10.3 Hz, 1 H, vinyl), 6.34 (s, 1 H, vinyl), 6.08 (s, 1 H, vinyl), 6.01 (t, *J* = 10.6 Hz, 1 H, vinyl), 5.45 (m, 1 H, vinyl), 5.18 (dd, *J* = 16.9, 1.7 Hz, 1 H, vinyl), 5.10 (d, *J* = 10.2 Hz, 1 H, vinyl), 4.05 (m, 2 H, HCO), 3.93 (m, 1 H, HCO), 3.78–3.86 (m, 1 H, HCO), 3.27–3.49 (m, 2 H, HCO), 3.23 (dd, *J* = 9.7, 2.2 Hz, 1 H, HCO), 3.02 (dd, *J* = 12.0, 3.9 Hz, 1 H, HCO), 1.46–2.37 (series of multiplets, 18 H, CH_2), 1.22 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 0.90 (s, 9 H, ^{t}BuSi), 0.84 (s, 9 H, ^{t}BuSi), 0.07 (s, 6 H, Me_2Si), 0.06 (s, 3 H, CH_3Si), 0.05 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.62 (HC=O), 148.16 (vinyl), 135.84 (vinyl), 132.70 (vinyl), 132.33 (vinyl), 129.51 (vinyl), 116.95 (vinyl), 83.11 (CO), 82.24 (CO), 80.51 (CO), 78.99 (CO), 78.81 (CO), 72.39 (CO), 71.03 (CO), 67.40 (CO), 62.74 (CO), 60.42 (CO), 38.93, 37.25, 36.58, 32.87, 29.70, 26.56, 25.89, 25.21, 15.19, 14.20, –0.45, –1.94, –2.08, –4.20, –4.95, –4.99; HRMS calcd for $C_{40}H_{70}O_7Si_2$ (M + Cs) 851.3714, found 851.3714.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanal, 9-(3,5-Hexadienyl)hexadecahydro-4,10-dihydroxy-5a,10-dimethyl-α-methylene-, [2*R*-[2α,4α,4aβ,5aβ,7aα,9α(*Z*),10β,12aα,13aα,14aα]]- (*epi*-Hemibrevetoxin B, 2). Experimental procedure was followed as described for compound **36**. **2**: colorless oil; R_f = 0.35 (silica, 100% ether); $[\alpha]^{25}_D$ +24.00° (*c* 0.05, $CHCl_3$); IR (neat) ν_{max} 3473, 2927, 1688, 1442, 1372, 1217, 1083, 1044, 914, 674 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.48 (s, 1 H, HC=O), 6.58 (dt, *J* = 16.8, 10.3 Hz, 1 H, vinyl), 6.31 (s, 1 H, vinyl), 6.05 (s, 1 H, vinyl), 6.00 (t, *J* = 10.9 Hz, 1 H, vinyl), 5.40 (m, 1 H, vinyl), 5.16 (d, *J* = 16.9 Hz, 1 H, vinyl), 5.07 (d, *J* = 10.1 Hz, 1 H, vinyl), 4.00 (m, 2 H, HCO), 3.90 (m, 1 H, HCO), 3.83 (m, 1 H, HCO), 3.69 (m, 1 H, HCO), 3.58 (bs, 1 H, OH), 3.38 (d, *J* = 10.8 Hz, 1 H, OH), 3.22 (dd, *J* = 9.8, 2.7 Hz, 1 H, HCO), 3.16 (dd, *J* = 14.4, 10.4 Hz, 1 H, HCO), 3.05 (dd, *J* = 11.9, 4.3 Hz, 1 H, HCO), 2.40 (dd, *J* = 14.5, 4.7 Hz, 1 H, CH_2), 1.60–2.33 (series of multiplets, 17 H, CH_2), 1.49 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3); HRMS calcd for $C_{28}H_{42}O_7$ (M + Cs) 623.1985, found 623.1960.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*b*]pyrano[2,3-*f*]oxepin, 11-[(Acetyloxy)methyl]-4-hydroxy-2-(hydroxymethyl)hexadecahydro-5a,-12a-dimethyl-, [2α,4α,4aβ,5aβ,7aβ,8aβ,11α,12aβ,14aβ,15aα,16aα]- (54). Experimental procedure was followed as described for compound **42**. **54**: white solid; mp 178.3 °C; R_f = 0.20 (silica, 100% ethyl acetate); $[\alpha]^{25}_D$ +34.30° (*c* = 0.77, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3595, 3450, 2975, 2960, 1730, 1425, 1355, 1235, 1080, 1040, 1030, 810 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.15 (dd, *J* = 12.0, 8.4 Hz, 1 H, HCO), 4.01–4.04 (m, 2 H, HCO), 3.87–3.99 (series of multiplets, 4 H, HCO), 3.83 (t, *J* = 6.2 Hz, HCO), 3.73–3.79 (m, 1 H, HCO), 3.57 (m, 1 H, HCO), 3.44 (dd, *J* = 12.0, 4.7 Hz, 1 H, HCO), 3.25 (dd, *J* = 9.8, 2.7 Hz, 1 H, HCO), 2.80 (bs, 1 H, OH), 2.68 (bs, 1 H, OH), 2.05–2.09 (m, 4 H, CH_2, OCH_3), 1.93–2.00 (m, 3 H, CH_2), 1.84–1.91 (m, 2 H, CH_2), 1.63–1.76 (m, 6 H, CH_2), 1.45–1.57 (m, 3 H, CH_2), 1.35 (m, 1 H, CH_2), 1.29 (s, 3 H, CH_3), 1.23 (s, 3 H, CH_3); ^{13}C NMR (500 MHz, $CDCl_3$) δ 171.01 (OC=O), 88.94 (CO), 85.05 (CO), 80.94 (CO), 78.01 (CO), 77.26 (CO), 72.64 (CO), 72.55 (CO), 71.42 (CO), 67.19 (CO), 67.11 (CO), 65.06 (CO), 63.76 (CO), 37.03, 34.99, 34.35, 31.30, 28.35, 27.05, 25.98, 25.86, 20.94, 15.59, 14.90; HRMS calcd for $C_{25}H_{40}O_9$ (M + H) 485.2751, found 485.2755.

3,4:6,10-Dianhydro-8,11-*O*-dibenzyl-3-*C*-methyl-7-*O*-(*tert*-butyldimethylsilyl)-1,2,5,9-tetradeoxy-D-*threo*-L-*altro*-undec-1-enitol (55). To a solution of epoxy alcohol **11** (55.2 g, 0.102 mol) in DMSO–CH_2Cl_2 (1:5, 1 L) at 0 °C was added triethylamine (56.8 mL, 0.408 mol) and SO_3·py (32.4 g, 0.204 mol), and the resulting solution was stirred at 0 °C for 2 h. The reaction mixture was diluted with EtOAc (2 L) and washed with H_2O (500 mL) and saturated NH_4Cl (500 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum.

To a vigorously stirred suspension of methyltriphenylphosphonium bromide (55.0 g, 153 mmol) in dry THF (300 mL) at 0 °C was added sodium bis(trimethylsilyl)amide (132 mL, 1 M in THF, 132 mmol) dropwise over 10-min period. After stirring for 1 h, the orange ylide was treated dropwise with a solution of the crude aldehyde in THF and the resulting mixture was stirred at 0 °C for 30 min. The reaction mixture was diluted with ether (500 mL) and then washed with H_2O (2 × 200 mL) and brine (200 mL). Drying ($MgSO_4$) and concentration followed by flash column chromatography (silica, 10% ether in petroleum ether) gave the allylic epoxide **55** (47.6 g, 87%) as colorless oil. **55**: R_f = 0.37 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +17.6° (*c* 8.4, $CHCl_3$); IR (neat) ν_{max} 2927, 2884, 2855, 1453, 1359, 1252, 1096, 835, 775, 735, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.24–7.35 (m, 10 H, Ar), 5.67 (dd, *J* = 17.6, 10.7 Hz, 1 H, CH=CH_2), 5.34 (dd, *J* = 17.6, 0.9 Hz, 1 H, CH=CH_2), 5.18 (dd, *J* = 10.7, 0.9 Hz, 1 H, CH=CH_2), 4.62 (br s, 2 H, CH_2Ar), 4.58 (d, *J* = 11.7 Hz, 1 H, CH_2Ar), 4.54 (d, *J* = 11.7 Hz, 1 H, CH_2Ar), 4.06 (ddd, *J* = 9.8, 5.0, 4.9 Hz, 1 H, HCO), 4.01 (ddd, *J* = 9.9, 5.9, 5.2 Hz, 1 H, HCO), 3.83 (dd, *J* = 10.3, 6.8 Hz, 1 H, HCO), 3.72 (ddd, *J* = 5.9, 3.5, 3.4 Hz, 1 H, HCO), 3.68 (dd, *J* = 5.4, 2.0 Hz, 1 H, HCO), 3.58 (dd, *J* = 10.0, 5.4 Hz, 1 H, HCO), 3.05 (dd, *J* = 6.0, 5.9 Hz, 1 H, HCO), 2.04 (ddd, *J* = 13.9, 10.9, 7.3 Hz, 1 H, CH_2), 1.81–1.95 (m, 3 H, CH_2), 1.41 (s, 3 H, CH_3), 0.94 (s, 9 H, ^{t}Bu), 0.11 (s, $SiCH_3$), 0.10 (s, 3 H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.2 (CH=CH_2), 139.00 (Ar), 138.9 (Ar), 128.8 (Ar), 128.7 (Ar), 128.7 (Ar), 128.1 (Ar), 128.0 (Ar), 128.0 (Ar), 127.9 (Ar), 127.9 (Ar), 116.4 (CH=CH_2), 74.8 (CO), 73.7 (CO), 73.6 (CO), 72.4 (CO), 71.9 (CO), 71.3 (CO), 70.6 (CO), 62.9 (CO), 59.3 (CO), 30.6, 29.6, 26.3, 18.6, 15.5 (CH_3), –3.7 ($SiCH_3$), –4.3 ($SiCH_3$); HRMS calcd for $C_{32}H_{46}O_5Si$ (M + Cs) 671.2169, found 671.2169.

3,4:6,10-Dianhydro-8,11-*O*-dibenzyl-3-*C*-methyl-1,2,5,9-tetradeoxy-D-*threo*-L-*altro*-undec-1-enitol (56). Experimental procedure was followed as described for compound **13**. **56**: colorless oil; R_f = 0.30 (silica, 80% ether in petroleum ether); $[\alpha]^{25}_D$ +24.8° (*c* 4.5, $CHCl_3$); IR (neat) ν_{max} 3446, 2930, 2868, 1495, 1453, 1362, 1099, 1074, 921, 736, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.23–7.35 (m, 10 H, Ar), 5.65 (dd, *J* = 17.1, 10.7 Hz, 1 H, CH=CH_2), 5.34 (d, *J* = 17.1 Hz, 1 H, CH=CH_2), 5.18 (d, *J* = 10.7 Hz, 1 H, CH=CH_2), 4.64 (d, *J* = 11.7 Hz, 1 H, CH_2Ar), 4.59 (d, *J* = 13.7 Hz, 1 H, CH_2Ar), 4.57 (d, *J* = 13.7 Hz, 1 H, CH_2Ar), 4.51 (d, *J* = 11.7 Hz, 1 H, CH_2Ar), 4.03 (ddd, *J* = 9.9, 5.0, 4.9 Hz, 1 H, HCO), 3.98 (ddd, *J* = 10.9, 5.5, 4.9 Hz, 1 H, HCO), 3.81 (ddd, *J* = 7.4, 4.0, 3.9 Hz, 1 H, HCO), 3.77 (dd, *J* = 10.4, 6.4 Hz, 1 H, HCO), 3.65 (dd, *J* = 10.9, 4.9 Hz, 1 H, HCO), 3.36 (dd, *J* = 10.0, 4.9 Hz, 1 H, HCO), 3.02 (dd, *J* = 7.4, 5.9 Hz, 1 H, HCO), 2.52 (br d, *J* = 5.4 Hz, 1 H, OH), 1.91–2.00 (m, 2 H, CH_2), 1.81–1.90 (m, 2 H, CH_2), 1.39 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.57 (CH=CH_2), 138.26 (Ar), 137.66 (Ar), 128.57 (Ar), 128.35 (Ar), 128.32 (Ar), 127.98 (Ar), 127.74 (Ar), 127.68 (Ar), 127.60 (Ar), 116.09 (CH=CH_2), 73.53 (CO), 73.33 (CO), 72.62 (CO), 71.57 (CO), 70.59 (CO), 69.39 (CO), 69.09 (CO), 62.16 (CO), 58.90 (CO), 29.86, 28.50, 15.12 (CH_3); HRMS calcd for $C_{26}H_{32}O_5$ (M + Cs) 557.1301, found 557.1321.

3,7:6,10-Dianhydro-8,11-*O*-dibenzyl-3-*C*-methyl-1,2,5,9-tetradeoxy-D-*threo*-L-*allo*-undec-1-enitol (57). Experimental procedure was followed as described for compound **14**. **55**: colorless oil; R_f = 0.30 (silica, 80% ether in petroleum ether); $[\alpha]^{25}_D$ +18.3° (*c* 4.6, $CHCl_3$); IR (neat) ν_{max} 3446, 2933, 2871, 1640, 1495, 1453, 1365, 1100, 919, 736, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.23–7.38 (m, 10 H, Ar), 6.00 (dd, *J* = 17.6, 10.7 Hz, 1 H, CH=CH_2), 5.34 (dd, *J* = 17.6, 1.4 Hz, 1 H, CH=CH_2), 5.18 (dd, *J* = 10.7, 1.5 Hz, 1 H, CH=CH_2), 4.82 (d, *J* = 12.2 Hz, 1 H, CH_2Ar), 4.57 (d, *J* = 18.2 Hz, 1 H, CH_2Ar), 4.54 (d, *J* = 12.2 Hz, 1 H, CH_2Ar), 4.45 (d, *J* = 18.2 Hz, 1 H, CH_2Ar), 4.10–4.15 (m, 1 H, HCO), 4.09 (dd, *J* = 9.9, 8.9 Hz, 1 H, HCO), 3.87 (dd, *J* = 4.9, 2.9 Hz, 1 H, HCO), 3.80 (ddd, *J* = 10.9, 5.5, 5.0 Hz, 1 H, HCO), 3.55 (br d, *J* = 4.4 Hz, 1 H, HCO), 3.52 (dd, *J* = 3.5, 3.4 Hz, 1 H, HCO), 3.43 (dd, *J* = 9.8, 2.4 Hz, 1 H, HCO), 2.20 (ddd, *J* = 9.9, 5.0, 4.4 Hz, 1 H, CH_2), 1.92–2.10 (m, 3 H, CH_2), 1.39 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.0 (CH=CH_2), 139.3 (Ar), 138.4 (Ar), 128.3 (Ar), 128.2 (Ar), 127.8 (Ar), 127.6 (Ar), 127.2 (Ar), 127.0 (Ar), 114.1 (CH=CH_2), 78.0 (CO), 73.5 (CO), 73.3 (CO), 73.0 (CO), 72.8 (CO), 71.6 (CO), 71.3 (CO), 70.0 (CO), 63.9 (CO), 33.9, 31.4, 13.8 (CH_3); HRMS calcd for $C_{26}H_{32}O_5$ (M + Cs) 557.1301, found 557.1308. Anal. Calcd: C, 73.54; H, 7.60. Found: C, 73.52; H, 7.66.

3,7:6,10-Dianhydro-8,11-*O*-dibenzyl-3-*C*-methyl-4-*O*-(*tert*-butyldimethylsilyl)-1,2,5,9-tetradeoxy-D-*threo*-L-*allo*-undec-1-enitol (58). Experimental procedure was followed as described for compound **15**. **58**: R_f = 0.40 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +20.7° (*c* 4.4, $CHCl_3$); IR (neat) ν_{max} 2928, 2855, 1453, 1361, 1251, 1105, 920, 836, 776, 733, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25–7.38 (m, 10 H, Ar), 6.00 (dd, *J* = 17.3, 11.2 Hz, 1 H, CH=CH_2), 5.32 (dd, *J* = 17.3, 2.9 Hz, 1 H, CH=CH_2), 5.08 (dd, *J* = 11.2, 2.9 Hz, 1 H, CH=CH_2), 4.85 (d, *J* = 12.2 Hz, 1 H, CH_2Ar), 4.61 (d, *J* = 20.0 Hz, 1 H, CH_2Ar), 4.59 (d, *J* = 12.2 Hz, 1 H, CH_2Ar), 4.55 (d, *J* = 20.0 Hz, 1 H, CH_2Ar), 4.03–4.16 (m, 1 H, HCO), 4.08 (dd, *J* = 9.9, 8.0 Hz, 1 H, HCO), 3.87 (br d, *J* = 2.4 Hz, 1 H, HCO), 3.77 (dd, *J* = 10.4, 4.9 Hz, 1 H, HCO), 3.51–3.58 (m, 2 H, 2 H, HCO), 3.41 (dd, *J* = 7.8, 1.1 Hz, 1 H, HCO), 2.09 (ddd, *J* = 10.9, 8.4, 8.3 Hz, 1 H, CH_2), 1.99 (dd, *J* = 14.7, 3.4 Hz, 1 H, CH_2), 1.94 (ddd, *J* = 17.4, 7.9, 2.0 Hz, 1 H, CH_2), 1.68 (dd, *J* = 11.7, 2.3 Hz, 1 H, CH_2), 1.27 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.08 (s, 3 H, $SiCH_3$), 0.05 (s, 3 H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.28 (CH=CH_2), 139.29 (Ar), 138.46 (Ar), 128.27 (Ar), 128.14 (Ar), 127.71 (Ar), 127.50 (Ar), 127.13 (Ar), 127.00 (Ar), 112.45 (CH=CH_2), 78.00 (CO), 73.27 (CO), 72.95 (CO), 72.90 (CO), 72.70 (CO), 72.49 (CO), 71.50 (CO), 70.15 (CO), 63.61 (CO), 35.37, 31.35, 25.68, 17.82, 14.82 (CH_3), –4.12 ($SiCH_3$), –4.87 ($SiCH_3$); HRMS calcd for $C_{32}H_{46}SiO_5$ (M + Cs) 671.2165, found 671.2173.

3,7:6,10-Dianhydro-8,11-*O*-dibenzyl-3-*C*-methyl-4-*O*-(*tert*-butyldimethylsilyl)-1,2,5,9-tetradeoxy-D-*threo*-L-*allo*-undecitol (59). A solution of vinyl ether **58** (40.5 g, 75 mmol) in THF (500 mL) was treated with BH_3·THF solution (75 mL, 75 mmol) at 0 °C for 1 h. To this was added an aqueous 3 N NaOH solution (110 mL, 330 mmol), followed immediately by an aqueous 30% H_2O_2 (37 mL, 333 mmol). The ice bath was removed, and stirring was continued for 1 h prior to diluting with ether (1 L), washing with H_2O (2 × 500 mL) and brine (500 mL), and drying ($MgSO_4$). Silica gel chromatography (30% ether in petroleum ether) afforded alcohol **59** (37.5 g, 90%) as colorless oil. **59**: R_f = 0.52 (40% ether in petroleum ether); $[\alpha]^{25}_D$ +21.4° (*c* 3.6, $CHCl_3$); IR (neat) ν_{max} 3487, 2927, 2855, 2359, 1471, 1453, 1359, 1251, 1107, 836, 775, 734, 697, 667 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25–7.40 (m, 10 H, Ar), 4.56 (d, *J* = 12.1 Hz, 1 H, CH_2Ar), 4.55 (d, *J* = 10.9 Hz, 1 H, CH_2Ar), 4.53 (d, *J* = 10.9 Hz, 1 H, CH_2Ar), 4.51 (d, *J* = 12.2 Hz, 1 H, CH_2Ar), 4.05–4.11 (m, 1 H, HCO), 4.00 (t, *J* = 9.8 Hz, 1 H, HCO), 3.84–3.91 (m, 1 H, HCO), 3.74–3.82 (m, 3 H, HCO), 3.71 (ddd, *J* = 12.4, 4.5, 4.4 Hz, 1 H, HCO), 3.52 (dd, *J* = 9.8, 5.4 Hz, 1 H, HCO), 3.32 (dd, *J* = 10.0, 2.9 Hz, 1 H, HCO), 2.03–2.12 (m, 2 H, CH_2), 1.86–1.93 (m, 1 H, CH_2), 1.84 (dd, *J* = 8.8, 2.0 Hz, 1 H, CH_2), 1.81 (dd, *J* = 8.8, 2.4 Hz, 1 H, CH_2), 1.64 (dd, *J* = 12.5, 11.7 Hz, 1 H, CH_2), 1.25 (s, 3 H, CH_3), 0.87 (s, 9 H, ^{t}BuSi), 0.10 (s, 3 H, $SiCH_3$), 0.06 (s, 3 H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.25 (Ar), 137.99 (Ar), 128.30 (Ar), 128.26 (Ar), 127.82 (Ar), 127.76 (Ar), 127.58 (Ar), 80.31 (CO), 73.00 (CO), 72.52 (CO), 72.32 (CO), 71.88 (CO), 71.30 (CO), 70.28 (CO), 69.75 (CO), 63.36 (CO), 59.10 (CO), 40.22, 34.95, 29.34, 25.65, 17.72, 16.04, –3.90 ($SiCH_3$), –4.97 ($SiCH_3$); HRMS calcd for $C_{32}H_{48}O_6Si$ (M + Cs) 689.2275, found 689.2253.

3,7:6,10-Dianhydro-8,11-*O*-dibenzyl-3-*C*-methyl-4-*O*-(*tert*-butyldimethylsilyl)-1,2,5,9-tetradeoxy-D-*threo*-L-*allo*-undecose (60). Experimental procedure for Swern oxidation was followed as described for compound **44**. **60**: R_f = 0.55 (silica, 40% ether in petroleum ether); IR (neat) ν_{max} 2927, 2854, 1721, 1495, 1453, 1360, 1252, 1107, 837, 777, 731, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.87 (t, *J* = 2.9 Hz, 1 H, HCO), 7.22–7.40 (m, 10 H, Ar), 4.64 (d, *J* = 12.7 Hz, 1 H, CH_2Ar), 4.57 (br s, 2 H, CH_2Ar), 4.57 (d, *J* = 12.7 Hz, 1 H, CH_2Ar), 4.02–4.11 (m, 1 H, HCO), 4.06 (dd, *J* = 11.0, 8.3 Hz, 1 H, HCO), 3.79 (ddd, *J* = 10.9, 9.9, 2.5 Hz, 1 H, HCO), 3.73 (ddd, *J* = 5.5, 5.4, 4.4 Hz, 1 H, HCO), 3.63 (dd, *J* = 12.4, 6.5, 4.4 Hz, 1 H, HCO), 3.52 (dd, *J* = 8.9, 4.4 Hz, 1 H, HCO), 3.34 (dd, *J* = 10.9, 2.4 Hz, 1 H, HCO), 2.56 (dd, *J* = 15.4, 3.4 Hz, 1 H, CH_2), 2.46 (dd, *J* = 15.4, 2.9, 1 H, CH_2), 2.08 (ddd, *J* = 15.4, 7.9, 4.4 Hz, 1 H, CH_2), 1.97 (dd, *J* = 14.7, 3.4 Hz, 1 H, CH_2), 1.89 (ddd, *J* = 6.8, 2.9, 1.7 Hz, 1 H, CH_2), 1.63 (dd, *J* = 23.4, 11.7 Hz, 1 H, CH_2), 1.29 (s, 3 H, CH_3), 0.87 (s, 9 H, ^{t}Bu), 0.09 (s, 3 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.55 (HCO), 139.00 (Ar), 138.40 (Ar), 128.33 (Ar), 128.31 (Ar), 127.83 (Ar), 127.59 (Ar), 127.28 (Ar), 126.98 (Ar), 77.40 (CO), 73.36 (CO), 73.02 (CO), 72.73 (CO), 72.49 (CO), 72.17 (CO), 71.54 (CO), 69.97 (CO), 63.34 (CO), 52.98, 34.92, 31.02, 25.70, 25.58, 17.78, 15.76, –3.89 ($SiCH_3$), –4.94 ($SiCH_3$); HRMS calcd for $C_{32}H_{46}O_6Si$ (M + Cs) 687.2118, found 687.2132.

Methyl (*E*)-5,9:8,12-Dianhydro-10,13-*O*-dibenzyl-5-*C*-methyl-6-*O*-(*tert*-butyldimethylsilyl)-2,3,4,7,11-pentadeoxy-D-*threo*-L-*allo*-tridec-2-enonate (61). Experimental procedure for methyl (triphenylphosphoranylidene)acetate condensation was followed as described for compound **44**. **61**: R_f = 0.60 (silica, 40% ether in petroleum ether); $[\alpha]^{25}_D$ +24.73° (*c* 1.50, $CHCl_3$); IR (neat) ν_{max} 2950, 2856, 1724, 1655, 1252, 1107, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.23–7.39 (m, 10

H, Ar), 7.03 (dt, J = 15.6, 6.8 Hz, 1 H, C*H*=CH), 5.62 (d, J = 15.6 Hz, 1 H, C*H*=CH), 4.73 (d, J = 12.2 Hz, 1 H, CH_2Ar), 4.58 (s, 2 H, CH_2Ar), 4.57 (d, J = 12.2 Hz, 1 H, CH_2Ar), 4.05–4.12 (m, 2 H, HCO), 3.80 (dd, J = 4.1, 2.1 Hz, 1 H, HCO), 3.73 (s, 3 H, CH_3), 3.67–3.74 (m, 2 H, HCO), 3.56–3.59 (m, 1 H, HCO), 3.30 (dd, J = 9.8, 2.4 Hz, 1 H, HCO), 2.26–2.36 (m, 2 H, CH_2), 2.08 (dt, J = 11.7, 4.9 Hz, 1 H, CH_2), 1.98 (dd, J = 14.7, 3.4 Hz, 1 H, CH_2), 1.91 (ddd, J = 9.3, 6.4, 2.4 Hz, 1 H, CH_2), 1.73–1.80 (m, 1 H, CH_2), 1.58–1.69 (m, 1 H, CH_2), 1.17 (s, 1 H, CH_3), 0.89 (s, 9 H, ^{t}Bu), 0.10 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.55 (C=O), 162.00 (CH=CH), 139.01, 138.41, 128.33, 128.32, 128.24, 127.83, 127.80, 127.60, 127.57, 127.98, 127.28, 77.73, 73.34, 73.02, 72.74, 72.49, 72.18, 71.55, 69.98, 63.34, 52.99, 34.93, 34.93, 31.02, 25.66, 17.79, 15.76, –3.89, –4.94.

Methyl 5,9:8,12-Dianhydro-10,13-*O*-dibenzyl-5-*C*-methyl-6-*O*-(*tert*-butyldimethylsilyl)-2,3,4,7,11-pentadeoxy-D-*threo*-L-*allo*-trideconate (62). Catalytic hydrogenation procedure was followed as described for compound **16**. **62**: R_f = 0.60 (silica, 40% ether in petroleum ether); $[\alpha]^{25}_D$ +17.4° (c 2.7, $CHCl_3$); IR (neat) ν_{max} 2929, 2855, 1738, 1453, 1360, 1251, 1107, 836, 775, 734, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24–7.38 (m, 10 H, Ar), 4.74 (d, J = 12.7 Hz, 1 H, CH_2Ar), 4.56 (d, J = 12.7 Hz, 1 H, CH_2Ar), 4.54 (d, J = 9.9 Hz, 1 H, CH_2Ar), 4.52 (d, J = 9.9 Hz, 1 H, CH_2Ar), 4.02–4.11 (m, 2 H, HCO), 3.76–3.80 (m, 1 H, HCO), 3.66–3.72 (m, 1 H, HCO), 3.64 (s, 3 H, CH_3), 3.51–3.57 (m, 2 H, HCO), 3.27 (dd, J = 9.8, 2.4 Hz, 1 H, HCO), 2.32 (dd, J = 9.8, 3.4 Hz, 1 H, CH_2), 2.30 (dd, J = 9.8, 2.9 Hz, 1 H, CH_2), 2.04 (dt, J = 11.7, 4.4 Hz, 1 H, CH_2), 1.96 (dd, J = 14.4, 3.4 Hz, 1 H, CH_2), 1.89 (ddd, J = 14.4, 6.8, 2.9 Hz, 1 H, CH_2), 1.71–1.80 (m, 2 H, CH_2), 1.61–1.67 (m, 1 H, CH_2), 1.62 (dd, J = 23.4, 11.7 Hz, 1 H, CH_2), 1.41–1.49 (m, 1 H, CH_2), 1.13 (s, 3 H, CH_3), 0.85 (s, 9 H, ^{t}Bu), 0.08 (s, 3 H, $SiCH_3$), 0.06 (s, 3 H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0 (CO), 139.3 (Ar), 138.5 (Ar), 128.3 (Ar), 128.1 (Ar), 127.8 (Ar), 127.5 (Ar), 127.1 (Ar), 127.0 (Ar), 77.6 (CO), 73.1 (CO), 73.0 (CO), 72.4 (CO), 71.7 (CO), 71.5 (CO), 70.2 (CO), 63.7 (CO), 51.4, 39.4, 35.2, 34.7, 34.2, 31.1, 24.6, 18.6, 17.8, 15.2, –3.9 ($SiCH_3$), –5.0 ($SiCH_3$); HRMS calcd for $C_{35}H_{52}O_7Si$ (M + Cs) 745.2537, found 745.2553. Anal. Calcd C, 68.56; H, 8.56. Found: C, 68.53; H, 8.62.

5,9:8,12-Dianhydro-10,13-*O*-dibenzyl-5-*C*-methyl-6-*O*-(*tert*-butyldimethylsilyl)-2,3,4,7,11-pentadeoxy-D-*threo*-L-*allo*-trideconic Acid (63). Ester hydrolysis procedure was followed as described for compound **17**. **63**: R_f = 0.49 (silica, 40% ether in petroleum ether); $[\alpha]^{25}_D$ +13.4° (c 4.5, $CHCl_3$); IR (neat) ν_{max} 2951, 2856, 1708, 1495, 1360, 1251, 1107, 837, 775, 735, 697, 667 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.38 (m, 10 H, Ar), 4.73 (d, J = 12.7 Hz, 1 H, CH_2Ar), 4.58 (d, J = 12.7 Hz, 1 H, CH_2Ar), 4.57 (d, J = 11.4 Hz, 1 H, CH_2Ar), 4.55 (d, J = 11.4 Hz, 1 H, CH_2Ar), 4.08–4.12 (m, 1 H, HCO), 4.06 (dd, J = 17.6, 8.3 Hz, 1 H, HCO), 3.79 (br d, J = 5.4 Hz, 1 H, HCO), 3.77 (ddd, J = 14.6, 9.8, 6.8 Hz, 1 H, HCO), 3.56 (dd, J = 11.2, 4.4 Hz, 1 H, HCO), 3.52 (dd, J = 9.3, 3.9 Hz, 1 H, HCO), 3.29 (dd, J = 10.0, 2.5 Hz, 1 H, HCO), 2.30–2.40 (m, 2 H, CH_2), 2.02–2.08 (m, 1 H, CH_2), 1.99 (dd, J = 14.7, 2.9 Hz, 1 H, CH_2), 1.90 (ddd, J = 14.7, 8.4, 2.9 Hz, 1 H, CH_2), 1.74–1.82 (m, 2 H, CH_2), 1.65–1.70 (m, 1 H, CH_2), 1.63 (dd, J = 23.4, 11.7 Hz, 1 H, CH_2), 1.48–1.55 (m, 1 H, CH_2), 1.15 (s, 3 H, CH_3), 0.87 (s, 9 H, ^{t}Bu), 0.09 (s, 3 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.30 (CO), 139.16 (*C*H_2Ar), 128.30 (*C*H_2Ar), 128.30 (Ar), 128.15 (Ar), 127.77 (Ar), 127.53 (Ar), 127.14 (Ar), 127.04 (Ar), 77.73 (CO), 73.09 (CO), 72.98 (CO), 72.94 (CO), 72.34 (CO), 71.46 (CO), 70.11 (CO), 63.67 (CO), 39.07, 35.13, 34.50, 30.93, 25.66, 18.35, 17.79, 15.31, –3.86 ($SiCH_3$), –4.98 ($SiCH_3$); HRMS calcd for $C_{34}H_{50}O_7Si$ (M + Cs) 731.2830, found 731.2833.

5,9:8,12-Dianhydro-10,13-*O*-dibenzyl-5-*C*-methyl-2,3,4,7,11-pentadeoxy-D-*threo*-L-*allo*-trideconic Acid (64). Desilylation procedure was followed as described for compound **13**. **64**: R_f = 0.39 (silica, ethyl acetate); $[\alpha]^{25}_D$ +15.0° (c 0.4, $CHCl_3$); IR (neat) ν_{max} 3412, 2928, 1718, 1569, 1166, 1103, 1026, 837, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23–7.38 (m, 10 H, Ar), 4.71 (d, J = 12.7 Hz, 1 H, CH_2Ar), 4.55 (d, J = 12.7 Hz, 1 H, CH_2Ar), 4.56 (d, J = 19.5 Hz, 1 H, CH_2Ar), 4.52 (d, J = 19.5 Hz, 1 H, CH_2Ar), 4.06–4.12 (m, 1 H, HCO), 4.06 (dd, J = 18.7, 8.3 Hz, 1 H, HCO), 3.79 (dd, J = 5.9, 2.9 Hz, 1 H, HCO), 3.71 (ddd, J = 11.2, 10, 4.4 Hz, 1 H, HCO), 3.60 (dd, J = 11.7, 4.4 Hz, 1 H, HCO), 3.51 (dd, J = 9.3, 3.9 Hz, 1 H, HCO), 3.29 (dd, J = 9.8, 2.5 Hz, 1 H, HCO), 2.33–2.40 (m, 2 H, CH_2), 2.12–2.16 (m, 1 H, CH_2), 1.96 (dd, J = 14.7, 2.9 Hz, 1 H, CH_2), 1.89 (dd, J = 6.4, 2.5 Hz, 1 H, CH_2), 1.55–1.85 (m, 5 H, CH_2), 1.19 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.72 (CO), 139.14 (Ar), 138.40 (Ar), 128.31 (Ar), 128.18 (Ar), 127.83 (Ar), 127.57 (Ar), 127.19 (Ar), 127.05 (Ar), 73.29 (CO), 73.04 (CO), 72.93 (CO), 72.42 (CO), 71.53 (CO), 70.78 (CO), 70.73 (CO), 69.45 (CO), 63.82 (CO), 38.88, 34.56, 34.03, 30.95, 18.23, 15.05 (CH_3); HRMS calcd for $C_{28}H_{36}O_7$ (M + Cs) 617.1515, found 617.1515.

Tricyclic Lactone 65. 2,4,6-Trichlorobenzoyl chloride (0.56 mL, 3.60 mmol) was added to a mixture of the hydroxy acid **64** (1.75 g, 3.60 mmol) and triethylamine (0.76 mL, 5.4 mmol) in THF (3.6 mL) and stirred for 2 h at room temperature. After removal of triethylamine hydrochloride by filtration, the filtrate was diluted with toluene (1.4 L) and added to a refluxing solution of 4-(dimethylamino)pyridine (2.65 g, 21.6 mmol) in toluene (350 mL) over a period of 2 h. The reaction was continued at reflux temperature for another 1 h, cooled, diluted with ether, and washed with saturated oxalic acid solution (2 × 100 mL) followed by water (3 × 200 mL) and saturated sodium bicarbonate solution (3 × 100 mL). The organic layer was dried and concentrated under vacuum. Flash column chromatography (silica, 80% ether in petroleum ether) furnished pure lactone **63** (1.62 g, 97%) as colorless oil: R_f = 0.37 (silica, 80% ether in petroleum ether); $[\alpha]^{25}_D$ –26.32° (c 2.37, $CHCl_3$); IR (neat) ν_{max} 2939, 2869, 1738, 1453, 1354, 1279, 1093, 1039, 911, 735, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.35 (m, 10 H, Ar), 4.73 (d, J = 12.4 Hz, 1 H, Ar), 4.54–4.57 (m, 3 H, Ar), 4.24 (dd, J = 11.7, 5.2 Hz, 1 H, HCO), 4.04–4.12 (m, 2 H, HCO), 3.81 (m, 1 H, HCO), 3.72–3.78 (m, 1 H, HCO), 3.52 (dd, J = 10.0, 4.6 Hz, 1 H, HCO), 3.33 (dd, J = 9.8, 2.7 Hz, 1 H, HCO), 2.66 (dd, J = 14.3, 6.5 Hz, 1 H, CHC=O), 2.57–2.59 (m, 1 H, CHC=O), 2.24–2.28 (m, 1 H, CH_2), 1.89–2.00 (m, 4 H, CH_2), 1.81 (d, J = 12.0 Hz, 1 H, CH_2), 1.64–1.71 (m, 2 H, CH_2), 1.22 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1 (C=O), 139.1 (CH_2Ar), 138.3 (CH_2Ar), 128.3 (Ar), 128.1 (Ar), 127.7 (Ar), 127.5 (Ar), 127.2 (Ar), 126.9 (Ar), 77.6 (CO), 75.4 (CO), 73.0 (CO), 72.7 (CO), 72.5 (CO), 72.6 (CO), 71.5 (CO), 69.9 (CO), 63.2 (CO), 42.9, 34.0, 32.4, 30.9, 19.6, 14.6; HRMS calcd for $C_{28}H_{34}O_6$ (M + Cs) 599.1410, found 599.1422. Anal. Calcd: C, 72.06; H, 7.34. Found: C, 72.10; H, 7.32.

Tricyclic Thionolactone 66. A mixture of lactone **65** (7 g, 15 mmol) and Lawesson's reagent (12 g, 30 mmol) in toluene (200 mL) was stirred at reflux for 3 h. The reaction was cooled, concentrated under reduced pressure, and subjected to flash chromatography (silica, 30% ether in petroleum ether) to give **66** (6 g, 82%) as an oil: R_f = 0.20 (30% ether in petroleum ether); $[\alpha]^{25}_D$ –71.78° (c 0.36, $CHCl_3$); IR (thin film) ν_{max} 2935, 2865, 1452, 1338, 1282, 1221, 1187, 1115, 1087, 1002, 737, 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.40 (m, 10 H, Ar), 4.72 (d, J = 12.4 Hz, 1 H, CH_2Ar), 4.56 (d, J = 12.4 Hz, 1 H, CH_2Ar), 4.55 (s, 2 H, CH_2Ar), 4.52 (dd, J = 11.7, 5.2 Hz, 1 H, HCO), 4.10–4.14 (m, 1 H, HCO), 4.05 (dd, J = 10.0, 8.6 Hz, 1 H, HCO), 3.81 (dd, J = 5.7, 2.8 Hz, 1 H, HCO), 3.73–3.78 (m, 1 H, HCO), 3.53 (dd, J = 10.0, 4.8 Hz, 1 H, HCO), 3.48 (dd, J = 14.3, 7.3 Hz, 1 H, HCO), 3.35 (dd, J = 9.8, 2.8 Hz, 1 H, CH_2), HCO), 2.82 (br t, J = 12.2 Hz, 1 H, CH_2C=S), 2.35 (dt, J = 12.2, 4.9 Hz, 1 H, CH_2C=S), 1.90–2.00 (m, 5 H, CH_2), 1.62–1.75 (m, 2 H, CH_2), 1.23 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 224.90 (C=S), 139.1 (Ar), 138.4 (Ar), 128.3 (Ar), 128.2 (Ar), 127.8 (Ar), 127.5 (Ar), 127.2 (Ar), 126.9 (Ar), 82.4 (CO), 75.0 (CO), 73.1 (CO), 72.8 (CO), 72.5 (CO), 71.6 (CO), 69.9 (CO), 63.2 (CO), 45.6, 42.7, 32.5, 30.9, 21.6, 15.1; HRMS calcd for $C_{28}H_{34}O_5S$ (M + Cs) 615.1181, found 615.1181.

Cuprate Addition to 66 and Hydroboration Product 68. To a solution of 1-[(*tert*-butyldimethylsilyl)oxy]-4-iodobutane (9.4 g, 30 mmol) in ether (300 mL) at –78 °C was added 1.7 M ^{t}BuLi (35.3 mL, 60 mmol), and the mixture was stirred for 30 min before addition of 0.25 M (2-thienyl)-cyanocopper lithium (7.5 mL, 30 mmol). The reaction mixture was further stirred for 30 min at –40 °C and cooled back to –78 °C. A solution of thionolactone **66** (4.87 g, 10.1 mmol) in ether was added followed by diiodobutane (5.31 mL, 40 mmol) and pempidine (9.04 mL, 50 mmol). The temperature was raised to –10 °C over a period of 1 h. The reaction was quenched, diluted with ether (1 L), washed with water (3 × 200 mL), and dried ($MgSO_4$). Solvent was removed, and the crude product was directly used for the next reaction.

To stirred solution of crude enol ether **67** in THF at 0 °C was added 1 M BH_3·THF (12 mL, 12 mmol) dropwise. The stirring was continued for 30 min. The borane was oxidized via slow addition of 3 N NaOH (10.6 mL, 16 mmol) and hydrogen peroxide (8.2 mL, 30% solution in H_2O). After 30 min the reaction mixture was diluted with ether (750 mL), washed with water (3 × 100 mL), dried ($MgSO_4$), and concentrated. The residue was purified by silica gel flash column chromatography (40 → 60% ether in petroleum ether) to afford **68** (4 g, 60%) and **68**-α-isomer (1 g, 15%). **68**: colorless oil; R_f = 0.29 (silica, 40% ether in petroleum ether); $[\alpha]^{25}_D$ –0.81° (c 1.24, $CHCl_3$); IR (neat) ν_{max} 3456, 2927, 2857, 1462, 1371, 1360, 1255, 1089, 835, 776, 735, 697 cm^{-1}; ^{1}H NMR (500

MHz, $CDCl_3$) δ 7.24–7.36 (m, 10 H, Ar), 4.78 (d, J = 12.4 Hz, 1 H, CH_2Ar), 4.52–4.57 (m, 3 H, CH_2Ar), 4.03–4.08 (m, 2 H, HCO), 3.80 (m, 1 H, HCO), 3.68–3.73 (m, 1 H, HCO), 3.61 (t, J = 5.9 Hz, 2 H, HCO), 3.52 (m, 2 H, HCO), 3.25–3.32 (m, 2 H, HCO), 3.22 (dd, J = 9.9, 2.3 Hz, 1 H, HCO), 1.76–2.04 (series of multiplets, 5 H, CH_2), 1.37–1.60 (m, 9 H, CH_2), 1.21 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.05 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.5 (CH_2Ar), 138.5 (CH_2Ar), 128.3 (Ar), 128.1 (Ar), 127.8 (Ar), 127.6 (Ar), 127.1 (Ar), 127.0 (Ar), 82.6 (CO), 73.1 (CO), 72.9 (CO), 72.8 (CO), 72.4 (CO), 71.6 (CO), 71.4 (CO), 70.1 (CO), 64.3 (CO), 63.1 (CO), 40.3, 33.9, 32.8, 32.2, 31.9, 31.0, 26.0, 22.2, 18.4, 15.6, –5.3; HRMS calcd for $C_{38}H_{58}O_7Si$ (M + Cs) 787.3006, found 787.3006.

68-α-epimer: colorless oil; R_f = 0.40 (silica, 60% ether in petroleum ether); $[\alpha]^{25}_D$ –32.83° (c = 0.86, $CHCl_3$); IR (neat) ν_{max} 3449, 2932, 2856, 1462, 1453, 1370, 1255, 1096, 1029, 835, 835, 776, 735, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25–7.36 (m, 10 H, Ar), 4.74 (d, J = 12.5 Hz, 1 H, CH_2Ar), 4.53–4.57 (m, 3 H, CH_2Ar), 4.01–4.08 (m, 2 H, HCO), 3.79 (m, 1 H, HCO), 3.52–3.79 (series of multiplets, 5 H, HCO), 3.27–3.32 (m, 2 H, HCO), 3.22 (dd, J = 11.8, 4.7 Hz, 1 H, HCO), 1.78–1.99 (s, 3 H, CH_2), 1.43–1.73 (m, 9 H, CH_2), 1.24 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.04 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.29 (CH_2Ar), 138.50 (CH_2Ar), 128.29 (Ar), 128.15 (Ar), 127.75 (Ar), 127.52 (Ar), 127.13 (Ar), 126.97 (Ar), 82.58 (CO), 77.12 (CO), 76.74 (CO), 73.13 (CO), 72.94 (CO), 72.84 (CO), 72.43 (CO), 71.62 (CO), 71.39 (CO), 70.10 (CO), 64.01 (CO), 63.15 (CO), 40.31, 33.93, 32.83, 32.17, 31.88, 31.04, 25.97, 22.82, 15.64, –5.27; HRMS calcd for $C_{38}H_{58}O_7Si$ (M + Cs) 787.3006, found 787.2967.

Compound 69. Acetylation procedure was followed as described for compound **35**. **69**: R_f = 0.26 (silica, 60% ether in petroleum ether); $[\alpha]^{25}_D$ +14.06° (c 0.32, $CHCl_3$); IR (neat) ν_{max} 2928, 2856, 1734, 1466, 1453, 1369, 1247, 1090, 835, 776, 734, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26–7.33 (m, 10 H, Ar), 4.91 (d, J = 6.2 Hz, 1 H, HCO), 4.81 (d, J = 12.1 Hz, 1 H, CH_2Ar), 4.52–4.57 (m, 3 H, CH_2Ar), 4.04–4.07 (m, 2 H, HCO), 3.82 (m, 1 H, HCO), 3.67–3.72 (m, 1 H, HCO), 3.60 (t, J = 6.3 Hz, 2 H, HCO), 3.51–3.54 (m, 2 H, HCO), 3.32–3.36 (m, 2 H, HCO), 2.08 (s, 3 H, CH_3CO), 1.88–2.05 (m, 4 H, CH_2), 1.37–1.77 (m, 10 H, CH_2), 1.22 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.04 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.05 (OC=O), 139.60 (CH_2Ar), 138.00 (CH_2Ar), 128.26 (Ar), 128.12 (Ar), 127.82 (Ar), 127.49 (Ar), 127.09 (Ar), 126.98 (Ar), 83.31 (CO), 78.26 (CO), 77.60 (CO), 73.23 (CO), 72.94 (CO), 72.66 (CO), 71.45 (CO), 70.01 (CO), 64.16 (CO), 63.02 (CO), 35.47, 34.51, 32.99, 32.50, 31.36, 25.96, 23.65, 21.95, 21.36, 15.35, –5.28; HRMS calcd for $C_{40}H_{60}O_8Si$ (M + Cs) 829.3112, found 829.3120. Anal. Calcd C, 68.92; H, 8.67. Found: C, 68.94; H, 8.71.

Tricyclic Acetate 70. Acetate **69** (5.3 g, 7.60 mmol) was dissolved in CH_2Cl_2–MeOH (150 mL, 1:1) and treated with CSA (1.10 g, 4.70 mmol) at 0 °C. The reaction was stirred at room temperature for 30 min and quenched with Et_3N (1.4 mL). Ether (500 mL) was added, and the solution was washed with water (3 × 200 mL) and brine (200 mL), dried over $MgSO_4$, and concentrated under vacuum. Flash column chromatography on silica gel with ether gave 4.20 g (95%) of alcohol **70**: colorless oil; R_f = 0.32 (silica, 100% ether); $[\alpha]^{25}_D$ +28.72° (c 0.19, $CHCl_3$); IR (neat) ν_{max} 3459, 2941, 2867, 1732, 1453, 1370, 1245, 1110, 1088, 911, 734, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26–7.36 (m, 10 H, Ar), 4.91 (d, J = 6.3 Hz, 1 H, HCO), 4.81 (d, J = 12.2 Hz, 1 H, CH_2Ar), 4.55 (m, 3 H, CH_2Ar), 4.04–4.09 (m, 2 H, HCO), 3.82 (m, 1 H, HCO), 3.68–3.73 (m, 1 H, HCO), 3.64 (t, J = 6.4 Hz, 2 H, HCO), 3.51–3.56 (m, 2 H, HCO), 3.33–3.37 (m, 2 H, HCO), 2.08 (s, 3 H, CH_3CO), 1.89–2.05 (m, 4 H, CH_2), 1.44 (m, 10 H, CH_2), 1.22 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.05 (OC=O), 139.60 (CH_2Ar), 138.50 (CH_2Ar), 128.29 (Ar), 128.14 (Ar), 127.83 (Ar), 127.51 (Ar), 127.13 (Ar), 127.00 (Ar), 83.31 (CO), 78.34 (CO), 77.53 (CO), 73.23 (CO), 72.96 (CO), 72.68 (CO), 71.45 (CO), 70.04 (CO), 64.15 (CO), 62.79 (CO), 34.37, 33.03, 32.38, 31.36, 23.67, 21.89, 21.39, 15.38; HRMS calcd for $C_{34}H_{46}O_8$ (M + Cs) 715.2247, found 715.2268.

Tricyclic Carboxylic Acid 71. Alcohol **70** (4.18 g, 7.17 mmol) was dissolved in dry DMF (50 mL) and cooled to 0 °C. PDC (9.44 g, 25.10 mmol) was added in one portion. The mixture was warmed to room temperature and stirred for 16 h. The reaction was diluted with ether (250 mmol) and saturated NaCl solution (500 mL). The mixture was extensively extracted with ether (4 × 300 mL), and the combined extract was washed with 5% tartaric acid (200 mL), water (500 mL), and brine (200 mL), filtered through $MgSO_4$, and concentrated under vacuum. Flash column chromatography on silica gel with 80% ether in ethyl acetate yielded acid **71** (4.03 g, 94%) as an oil: R_f = 0.32 (silica, ether); $[\alpha]^{25}_D$ +10.33° (c 0.33, $CHCl_3$); IR (neat) ν_{max} 3086, 2941, 1732, 1453, 1370, 1242, 1089, 1027, 734, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26–7.36 (m, 10 H, Ar), 4.89 (d, J = 6.2 Hz, 1 H, HCO), 4.80 (d, J = 12.1 Hz, 1 H, CH_2Ar), 4.55 (m, 3 H, CH_2Ar), 4.03–4.08 (m, 2 H, HCO), 3.82 (m, 1 H, HCO), 3.67–3.73 (m, 1 H, HCO), 3.56–3.58 (m, 1 H, HCO), 3.53 (dd, J = 9.4, 4.1 Hz, 1 H, HCO), 3.33–3.37 (m, 2 H, HCO), 2.37 (t, J = 7.4 Hz, 2 H, CH_2C=O), 2.08 (s, 3 H, OCH_3), 1.89–2.04 (m, 4 H, CH_2), 1.49–1.78 (m, 8 H, CH_2), 1.22 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.00 (COOH), 170.07 (OC=O), 139.58 (CH_2-Ar), 138.51 (CH_2Ar), 128.25 (Ar), 128.11 (Ar), 128.00 (Ar), 127.80 (Ar), 127.09 (Ar), 126.96 (Ar), 82.89 (CO), 78.24 (CO), 77.48 (CO), 73.18 (CO), 72.92 (CO), 72.63 (CO), 71.40 (CO), 69.99 (CO), 64.10 (CO), 35.40, 33.81, 33.29, 32.91, 32.29, 23.59, 21.32, 20.95, 15.33; HRMS calcd for $C_{34}H_{44}O_9$ (M + Cs) 729.2040, found 729.2018.

Hydroxy Acid 72. A solution of acetate **71** (4.00 g, 6.70 mmol) in methanol (100 mL) was treated with potassium carbonate (2.20 g, 26.8 mmol) at room temperature for 3 h. The mixture was diluted with ether (500 mL) and acidified with 5% tartaric acid aqueous solution (500 mL). The aqueous layer was extracted with ether (4 × 200 mL). The combined organic solution was washed with water (2 × 300 mL) and brine (300 mL), dried over $MgSO_4$, and concentrated under vacuum. Flash chromatography and silica gel with ethyl acetate gave 3.7 g (quantitative) of hydroxy acid **72** as colorless oil: R_f = 0.20 (silica, 100% ether); $[\alpha]^{25}_D$ +0.95° (c 0.42, $CHCl_3$); IR (neat) ν_{max} 3435, 2927, 2871, 1712, 1453, 1371, 1213, 1087, 996, 910, 734, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.24–7.36 (m, 10 H, Ar), 4.77 (d, J = 12.0 Hz, 1 H, CH_2Ar), 4.51–4.57 (m, 3 H, CH_2Ar), 4.03–4.08 (m, 2 H, HCO), 3.80 (m, 2 H, HCO), 3.71–3.81 (m, 1 H, HCO), 3.47–3.70 (m, 2 H, HCO), 3.42 (dd, J = 12.1, 4.3 Hz, 1 H, HCO), 3.34 (dd, J = 9.9, 2.5 Hz, 1 H, HCO), 2.36–2.39 (m, 2 H, CH_2C=O), 1.93–2.05 (m, 4 H, CH_2), 1.67–1.82 (m, 4 H, CH_2), 1.43–1.60 (m, 4 H, CH_2), 1.20 (s, 3 H, CH_3); ^{13}C NMR (500 MHz, $CDCl_3$) δ 177.80 (COOH), 139.60 (CH_2Ar), 138.50 (CH_2Ar), 128.19 (Ar), 128.03 (Ar), 127.75 (Ar), 127.45 (Ar), 126.93 (Ar), 85.47 (CO), 78.89 (CO), 74.82 (CO), 73.13 (CO), 72.94 (CO), 72.49 (CO), 71.41 (CO), 69.93 (CO), 64.10 (CO), 34.88, 33.88, 33.34, 32.79, 31.21, 27.43, 21.01, 15.46; HRMS calcd for $C_{34}H_{42}O_8$ (M + Cs) 687.1934, found 687.1968.

Tetracyclic Lactone 73. Experimental procedure was followed as described for compound **65**. **73**: colorless oil; R_f = 0.31 (silica, 100% ether in petroleum ether); $[\alpha]^{25}_D$ –9.15° (c 0.29, $CHCl_3$); IR (neat) ν_{max} 2933, 2866, 1733, 1452, 1332, 1268, 1197, 1108, 1086, 1066, 1019, 734, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26–7.36 (m, 10 H, Ar), 4.74 (d, J = 12.3 Hz, 1 H, CH_2Ar), 4.53–4.56 (m, 3 H, CH_2Ar), 4.36–4.39 (m, 1 H, HCO), 4.03–4.09 (m, 2 H, HCO), 3.82 (m, 1 H, HCO), 3.74 (dt, J = 11.0, 4.9 Hz, 1 H, HCO), 3.49 (dd, J = 9.5, 4.1 Hz, 1 H, HCO), 3.43 (dd, J = 9.9, 2.3 Hz, 1 H, HCO), 3.40 (m, 1 H, HCO), 3.25 (dd, J = 12.4, 3.7 Hz, 1 H, HCO), 2.64 (t, J = 4.5 Hz, 2 H, CH_2C=O), 1.92–2.19 (m, 9 H, CH_2), 1.63–1.75 (m, 3 H, CH_2), 1.22 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6 (OC=O), 139.2 (CH_2Ar), 138.5 (CH_2Ar), 128.3 (Ar), 128.2 (Ar), 127.9 (Ar), 127.6 (Ar), 127.2 (Ar), 127.0 (Ar), 86.5 (CO), 85.4 (CO), 82.8 (CO), 76.9 (CO), 73.6 (CO), 73.3 (CO), 73.1 (CO), 72.7 (CO), 71.7 (CO), 69.9 (CO), 64.6 (CO), 36.2, 36.0, 33.6, 32.9, 31.4, 27.8, 21.2, 14.7; HRMS calcd for $C_{32}H_{40}O_7$ (M + Cs) 669.1828, found 669.1861. Anal. Calcd: C, 71.60; H, 7.51. Found: C, 71.63; H, 7.57.

Tetracyclic Thionolactone 74. Thionation procedure was followed as described for compound **66**. **72**: R_f = 0.20 (silica, 80% ether in petroleum ether); $[\alpha]^{25}_D$ –6.77° (c 1.92, $CHCl_3$); IR (neat) ν_{max} 2932, 2866, 1452, 1317, 1270, 1088 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.19–7.26 (m, 10 H, Ar), 4.65 (d, J = 12.4 Hz, 1 H, CH_2Ar), 4.55–4.58 (m, 1 H, HCO), 4.47 (d, J = 11.3 Hz, 1 H, CH_2Ar), 4.46 (s, 2 H, CH_2Ar), 3.96–4.01 (m, 2 H, HCO), 3.74 (d, J = 2.6 Hz, 1 H, HCO), 3.65–3.68 (m, 1 H, HCO), 3.41 (dd, J = 8.9, 3.5 Hz, 2 H, HCO), 3.33–3.39 (m, 2 H, HCO), 3.18 (dd, J = 12.4, 3.6 Hz, 1 H), 2.79 (t, 2 H), 1.57 2.02 (series of m, 11 H), 1.13 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 225 (OC=S), 139.1 (Ar), 138.3 (Ar), 128.2 (Ar), 128.1 (Ar), 127.8 (Ar), 127.4 (Ar), 127.1 (Ar), 126.9 (Ar), 87.9 (CO), 86.6 (CO), 84.2 (CO), 76.7 (CO), 73.5 (CO), 73.1 (CO), 73.0 (CO), 72.5 (CO), 71.6 (CO), 69.8 (CO), 64.4 (CO), 44.9, 36.1, 35.5, 32.7, 31.3, 27.6, 22.9, 14.4; HRMS calcd for $C_{32}H_{40}O_6S$ (M + Cs) 685.1600, found 685.1588.

Cuprate Addition and Hydroboration Product 76. Experimental procedure was followed as described for compound **68**. **76**: R_f = 0.20 (silica, 80% ether in petroleum ether); IR (neat) ν_{max} 3447, 2928, 2856, 1453, 1254, 1090, 1027, 835, 776, 733, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.24–7.36 (m, 10 H, Ar), 4.75 (d, J = 12.3 Hz, 1 H, CH_2Ar), 4.52–4.54 (m, 3 H, CH_2Ar), 4.02–4.08 (m, 2 H, HCO), 3.79 (m, 1 H,

HCO), 3.73 (td, J = 11.2, 4.8 Hz, 1 H, HCO), 3.48–3.54 (m, 2 H, HCO), 3.14–3.42 (series of multiplets, 5 H, HCO), 2.04–2.13 (m, 2 H, CH_2), 1.74–1.94 (m, 9 H, CH_2), 1.54–1.67 (m, 4 H, CH_2), 1.36–1.39 (m, 1 H, CH_2), 1.20 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.06 (s, 6 H, Me_2Si); HRMS calcd for $C_{41}H_{62}O_8Si$ (M + Cs) 843.3268, found 843.3251.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-10-one, 2-[(Benzyloxy)methyl]-4-(benzyloxy)-9-[1-[(*tert*-butyldimethylsilyl)oxy]propanyl]-hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aβ,9α(*Z*),12aα,-13aα,14aα]]- (78). Procedure for Swern oxidation was followed as described for **44** and isomerization as given for compound **41**. **78**: R_f = 0.29 (silica, 40% ether in petroleum ether); $[\alpha]^{25}_D$ 56.52° (*c* 1.35, $CHCl_3$); IR (neat) ν_{max} 2929, 2856, 1715, 1461, 1372, 1255, 1090, 1068, 1027, 835, 775, 734, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.34 (m, 10 H, Ar), 4.76 (d, J = 12.3 Hz, 1 H, CH_2Ar), 4.53–4.56 (m, 3 H, CH_2Ar), 4.03–4.09 (m, 2 H, CHO), 3.76–3.81 (m, 2 H, CHO), 3.73 (td, J = 11.2, 4.9 Hz, 1 H, HCO), 3.59–3.64 (m, 2 H, HCO), 3.49–3.54 (m, 2 H, HCO), 3.44 (dd, J = 12.2, 4.0 Hz, 1 H, HCO), 3.34 (dd, J = 9.9, 2.4 Hz, 1 H, HCO), 3.04 (m, 1 H, HCO), 2.86 (td, J = 14.1, 2.3 Hz, 1 H, CHC=O), 2.30–2.32 (m, 1 H, CHC=O), 2.21–2.29 (m, 1 H, CH_2), 1.91–2.20 (m, 6 H, CH_2), 1.54–1.77 (m, 7 H, CH_2), 1.19 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.04 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 216.5 (C=O), 139.5 (CH_2Ar), 138.6 (CH_2Ar), 128.4 (Ar), 128.3 (Ar), 127.9 (Ar), 127.6 (Ar), 127.3 (Ar), 127.1 (Ar), 86.9 (CO), 86.6 (CO), 84.6 (CO), 80.5 (CO), 73.8 (CO), 73.5 (CO), 73.1 (CO), 72.8 (CO), 71.7 (CO), 70.0 (CO), 64.6 (CO), 62.8, 38.1, 36.8, 32.8, 31.5, 30.5, 29.2, 28.8, 26.0, 17.2, –5.2; HRMS calcd for $C_{41}H_{60}O_8Si$ (M + Cs) 841.3112, found 841.3112.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin, 2-[(Benzyloxy)-methyl]-4-(benzyloxy)-10-hydroxy-9-[1-[(*tert*-butyldimethylsilyl)oxy]-propyl]hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aβ,9α(*Z*),-10β,12aα,13aα,14aα]]- (79). To a solution of ketone **78** (1.12 g, 1.58 mmol) in ether (25 mL) at –78 °C was added 1.4 M MeMgI solution in ether (1.24 mL, 1.74 mmol). The mixture was allowed to warm to –10 °C over 4 h. The reaction was diluted with ether (125 mL) and washed with saturated NH_4Cl solution (2 × 25 mL) and water (2 × 30 mL). The organic layer was dried and concentrated under vacuum. Flash column chromatography (silica, 60 → 70% ether in petroleum ether) gave **79** (650 mg, 56%) and **79**-α-methyl isomer (430 mg, 37%). **79**: colorless oil; R_f = 0.32 (silica, 70% ether in petroleum ether); $[\alpha]^{25}_D$ +27.0° (*c* 0.10, $CHCl_3$); IR (neat) ν_{max} 3458, 2930, 2856, 1454, 1373, 1256, 1096, 835, 775, 735, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25–7.33 (m, 10 H, Ar), 4.75 (d, J = 12.3 Hz, 1 H, CH_2Ar), 4.52–4.54 (m, 3 H, CH_2Ar), 4.02–4.07 (m, 2 H, HCO), 3.79 (m, 1 H, HCO), 3.73 (dt, J = 10.9, 4.8 Hz, 1 H, HCO), 3.62–3.67 (m, 2 H, HCO), 3.51 (dd, J = 9.1, 3.9 Hz, 1 H, HCO), 3.30–3.4 (m, 3 H, HCO), 3.23 (dd, J = 12.5, 3.6 Hz, 2 H, HCO), 2.04–2.16 (m, 2 H, CH_2), 1.49–1.92 (series of multiplets, 11 H, CH_2), 1.25–1.43 (m, 3 H, CH_2), 1.20 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.06 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.4 (CH_2Ar), 138.6 (CH_2Ar), 128.2 (Ar), 127.9 (Ar), 127.6 (Ar), 127.2 (Ar), 127.1 (Ar), 88.2 (CO), 86.3 (CO), 84.9 (CO), 82.2 (CO), 77.5 (CO), 74.6 (CO), 73.4 (CO), 73.2 (CO), 73.1 (CO), 72.7 (CO), 71.6 (CO), 70.1 (CO), 64.5 (CO), 63.5 (CO), 38.2, 37.7, 33.0, 31.4, 30.2, 29.7, 29.5, 29.0, 27.0, 26.1, 26.0, 23.5, 18.5, 16.2, –5.2; HRMS calcd for $C_{42}H_{64}O_8Si$ (M + Cs) 857.3425, found 857.3442. **79-α-Me-isomer**: colorless oil; R_f = 0.35 (silica, 60% ether in petroleum ether); $[\alpha]^{25}_D$ +24.70° (*c* 1.78, $CHCl_3$); IR (neat) ν_{max} 3468, 2932, 2857, 1461, 1373, 1254, 1089, 1045, 1013, 909, 835, 775, 732, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24–7.35 (m, 10 H, Ar), 4.75 (d, J = 12.4 Hz, 1 H, CH_2Ar), 4.51–4.56 (m, 3 H, CH_2Ar), 4.02–4.08 (m, 2 H, HCO), 3.79 (m, 1 H, HCO), 3.74 (td, J = 11.3, 4.7 Hz, 1 H, HCO), 3.59–3.67 (m, 2 H, HCO), 3.44–3.52 (m, 2 H, HCO), 3.29–3.36 (m, 2 H, HCO), 3.16–3.23 (m, 2 H, HCO), 2.17 (m, 1 H, CH_2), 2.05 (m, 2 H, CH_2), 1.45–2.20 (m, 13 H, CH_2), 1.19 (s, 3 H, CH_3), 1.13 (s, 3 H, CH_3Si), 0.89 (s, 9 H, ^{t}BuSi), 0.05 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2 (CH_2Ar), 138.4 (CH_2Ar), 128.2 (Ar), 128.0 (Ar), 127.7 (Ar), 127.4 (Ar), 127.0 (Ar), 126.9 (Ar), 89.3 (CO), 85.6 (CO), 83.8 (CO), 82.4 (CO), 77.3 (CO), 74.6 (CO), 73.2 (CO), 73.0 (CO), 73.0 (CO), 72.5 (CO), 71.5 (CO), 69.9 (CO), 64.3, 63.1, 37.3, 36.9, 32.8, 31.2, 29.7, 29.0, 25.9, 25.5, 15.7, –5.4; HRMS calcd for $C_{42}H_{64}O_8Si$ (M + Cs) 857.3425, found 857.3459.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin, 2-(Hydroxymethyl)-4,10-dihydroxy-9-[1-[(*tert*-butyldimethylsilyl)oxy]propyl]hexadeca-hydro-5a,10-dimethyl-, [2*R*[2α,4α,4aβ,5aβ,7aβ,9α(*Z*),10β,12aα,13aα,-14aα]]- (80). To a solution of benzyl ether **79** (640 mg, 0.88 mmol) in ethyl acetate (10 mL) was added $Pd(OH)_2$/C (65 mg), and the mixture was shaken at 40 psi hydrogen pressure on a Parr hydrogenation apparatus for 4 h. The catalyst was filtered off, and solvent was removed under vacuum. Flash column chromatography (silica, ethyl acetate) gave 430 mg (89%) of triol **80**: colorless oil; R_f = 0.23 (silica, 100% ethyl acetate); $[\alpha]^{25}_D$ +24.70° (*c* 1.78, $CHCl_3$); IR (neat) ν_{max} 3418, 2930, 2857, 1462, 1380, 1255, 1088, 1004, 910, 835, 776, 733 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.13 (dd, J = 12.0, 8.4 Hz, 1 H, HCO), 4.03 (m, 1 H, HCO), 3.95 (td, J = 8.0, 3.9 Hz, 1 H, HCO), 3.78–3.83 (m, 1 H, HCO), 3.62–3.69 (m, 2 H, HCO), 3.55 (dd, J = 12.1, 3.9 Hz, 1 H, HCO), 3.30–3.38 (m, 2 H, HCO), 3.22–3.27 (m, 3 H, HCO), 2.15 (m, 1 H, CH_2), 2.08 (m, 2 H, CH_2), 1.50–1.90 (series of multiplets, 12 H, CH_2), 1.25–1.49 (m, 1 H, CH_2), 1.24 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 0.90 (s, 9 H, ^{t}BuSi), 0.06 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 88.11 (CO), 86.0 (CO), 85.1 (CO), 82.0 (CO), 74.0 (CO), 72.5 (CO), 71.7 (CO), 65.8 (CO), 63.7 (CO), 63.4 (CO), 62.8 (CO), 38.0, 37.5, 32.1, 31.2, 30.1, 29.4, 28.8, 27.4, 26.0, 23.5, 16.8, –5.4; HRMS calcd for $C_{28}H_{52}O_8Si$ (M + Cs) 677.2486, found 677.2486. Anal. Calcd: C, 61.72; H, 9.62. Found: C, 61.74; H, 9.65.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin, 2-[(2,2,2-Trimethylacetoxy)methyl]-4,10-dihydroxy-9-[1-[(*tert*-butyldimethylsilyl)oxy]-propyl]hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aβ,9α(*Z*),-10β,12aα,13aα,14aα]]- (81). To a solution of triol **80** (430 mg, 0.79 mmol) in dichloromethane (15 mL) at 0 °C was added 4-(dimethylamino)-pyridine (136 mg, 1.1 mmol) followed by 2,2,2-trimethylacetyl chloride (0.1 mL, 0.948 mmol). The reaction mixture was allowed to warm to room temperature, stirred for 1 h, and then diluted with dichloromethane (60 mL). The organic layer was washed with water (2 × 15 mL) and saturated sodium bicarbonate solution (2 × 10 mL) and dried ($MgSO_4$). Solvent was concentrated under vacuum. Flash column chromatography gave **81** (460 mg, 90%): colorless oil; R_f = 0.33 (silica, 80% ether in petroleum ether); $[\alpha]^{25}_D$ +39.12° (*c* 0.34, $CHCl_3$); IR (neat) ν_{max} 3474, 2932, 2857, 1729, 1461, 1379, 1283, 1154, 1089, 835, 774 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.99 (dd, J = 12.0, 10.2 Hz, 1 H, HCO), 3.95–4.00 (m, 2 H, HCO), 3.77 (dd, J = 12.2, 3.9 Hz, 1 H, HCO), 3.72 (m, 1 H, HCO), 3.56–3.62 (m, 2 H, HCO), 3.31 (m, 2 H, HCO), 3.22 (dd, J = 11.9, 4.0 Hz, 1 H, HCO), 3.16–3.18 (m, 2 H, HCO), 2.50 (br s, 1 H, OH), 1.46–2.12 (series of multiplets, 15 H, CH_2), 1.23 (m, 1 H, CH_2), 1.17 (s, 3 H, CH_3), 1.16 (s, 9 H, $C(CH_3)_3$), 1.15 (s, 3 H, CH_3), 0.85 (s, 9 H, ^{t}BuSi), 0.01 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2 (C=O), 88.0 (CO), 85.8 (CO), 84.6 (CO), 82.0 (CO), 77.9 (CO), 74.3 (CO), 71.8 (CO), 70.4 (CO), 65.6 (CO), 65.2 (CO), 63.3 (CO), 63.3 (CO), 62.9, 38.6, 37.9, 37.3, 32.4, 31.4, 30.1, 29.3, 28.7, 27.1, 27.0, 26.8, 25.9, 23.3, 18.2, 16.5, 15.1, –5.4; HRMS calcd for $C_{33}H_{60}O_9Si$ (M + Cs) 761.3061, found 761.3076.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin, 2-[(2,2,2-Trimethylacetoxy)methyl]-4,10-bis[(*tert*-butyldimethylsilyl)oxy]-9-[1-(*tert*-butyldimethylsiloxy)propyl]hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,-4aβ,5aβ,7aβ,9α(*Z*),10β,12aα,13aα,14aα]]- (82). Experimental procedure was followed as described for compound **15**. **82**: R_f = 0.37 (silica, 10% ether in petroleum ether); $[\alpha]^{25}_D$ +29.64° (*c* 0.56, $CHCl_3$); IR (neat) ν_{max} 2930, 2856, 1732, 1462, 1360, 1254, 1154, 1090, 1016, 938, 835, 774 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.01 (dd, J = 11.7, 9.7 Hz, 1 H, HCO), 4.00 (m, 2 H, HCO), 3.78–3.82 (m, 2 H, HCO), 3.57–3.66 (m, 2 H, HCO), 3.33 (m, 2 H, HCO), 3.13–3.22 (m, 3 H, HCO), 2.12 (m, 1 H, CH_2), 1.50–1.98 (m, 15 H, CH_2), 1.19 (s, 9 H, $C(CH_3)_3$), 1.17 (s, 3 H, CH_3), 1.07 (s, 3 H, CH_3), 0.88 (s, 9 H, ^{t}BuSi), 0.87 (s, 9 H, ^{t}BuSi), 0.80 (s, 9 H, ^{t}BuSi), 0.05 (s, 6 H, Me_2Si), 0.04 (s, 6 H, Me_2Si), 0.03 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3 (C=O), 88.4 (CO), 86.4 (CO), 84.8 (CO), 82.4 (CO), 77.3 (CO), 72.4 (CO), 70.9 (CO), 66.8 (CO), 64.0 (CO), 63.6 (CO), 38.7, 37.6, 37.5, 34.1, 32.6, 30.5, 29.4, 28.8, 27.2, 27.2, 26.9, 26.0, 26.0, 25.8, 25.8, 25.7, 25.7, 25.7, 23.9, 18.4, 18.2, 18.0, 16.1, –2.2, –2.3, –2.9, –4.2, –5.1, –5.2; HRMS calcd for $C_{45}H_{88}O_9Si_3$ (M + Cs) 989.4791, found 989.4761.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin, 2-(Hydroxymethyl)-4,10-bis[(*tert*-butylmethylsilyl)oxy]-9-[1-(*tert*-butyldimethylsiloxy)propyl]hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aβ,9α-(*Z*),10β,12aα,13aα,14aα]]- (83). Experimental procedure was followed as described for compound **52**. **83**: colorless oil; R_f = 0.29 (silica, 60% ether in petroleum ether); $[\alpha]^{25}_D$ +29.23° (*c* 0.19, $CHCl_3$); IR (neat) ν_{max} 3465, 2927, 2855, 1471, 1386, 1360, 1255, 1089, 1060, 1015, 937, 834, 773, 707, 658 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.25 (t, J = 9.4 Hz, 1 H, HCO), 4.02 (m, 1 H, HCO), 3.92–3.96 (m, 1 H, HCO), 3.79–3.83 (m, 1 H, HCO), 3.59–3.68 (m, 2 H, HCO), 3.31–3.42 (m, 3 H, HCO), 3.18–3.21 (m, 3 H, HCO), 2.50 (br s, 1 H, OH), 2.04–2.16 (m, 3 H, CH_2), 1.49–1.93 (series of multiplets, 13 H, CH_2), 1.20 (s, 9 H, CH_3), 1.09 (s, 3 H, CH_3), 0.90 (s, 9 H, ^{t}BuSi), 0.88 (s, 9 H, ^{t}BuSi), 0.82 (s, 9 H, ^{t}BuSi), 0.06 (s, 6 H, Me_2Si), 0.05 (s, 12 H, Me_2Si); ^{13}C NMR

(125 MHz, $CDCl_3$) δ 88.3 (CO), 86.3 (CO), 84.8 (CO), 85.0 (CO), 82.3 (CO), 77.3 (CO), 73.3 (CO), 72.2 (CO), 66.5 (CO), 63.5 (CO), 63.4 (CO), 37.5, 37.4, 34.0, 32.8, 30.4, 29.4, 28.7, 26.8, 25.9, 25.7, 25.7, 23.8, 18.3, 18.1, 17.9, 16.2, −2.2, −2.3, −4.3, −5.2, −5.3; HRMS calcd for $C_{40}H_{80}O_8Si_3$ (M + Cs) 905.4215, found 905.4224.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-prop-2-enoate, 4,-10-Bis[(*tert*-butyldimethylsilyl)oxy]-9-[1-[(*tert*-butyldimethylsilyl)oxy]-propyl]hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aβ,9a(*Z*),-10β,12aα,13aα,14aα]]-, Methyl Ester (84). Experimental procedure was followed as described for compound **44**. **84**: colorless oil; R_f = 0.25 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +22.28° (*c* 0.17, $CHCl_3$); IR (neat) ν_{max} 2950, 2928, 2855, 1728, 1471, 1374, 1255, 1165, 1088, 1061, 1014, 834, 773 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 15.9, 4.3 Hz, 1 H, vinyl), 5.90 (dd, *J* = 15.9, 1.9 Hz, 1 H, vinyl), 4.47 (m, 1 H, HCO), 4.05 (m, 1 H, HCO), 3.84 (td, *J* = 10.0, 6.6 Hz, 1 H, HCO), 3.71 (s, 3 H, OCH_3), 3.59–3.69 (m, 2 H, HCO), 3.31–3.35 (m, 2 H, HCO), 3.17–3.21 (m, 3 H, HCO), 2.05–2.13 (m, 3 H, CH_2), 1.49–1.92 (m, 13 H, CH_2), 1.19 (s, 3 H, CH_3), 1.09 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.84 (s, 9 H, ^{t}BuSi), 0.83 (s, 9 H, ^{t}BuSi), 0.07 (s, 3 H, CH_3Si), 0.05 (s, 3 H, CH_3Si), 0.84 (s, 9 H, ^{t}BuSi), 0.83 (s, 9 H, ^{t}BuSi), 0.07 (s, 3 H, CH_3Si), 0.05 (s, 3 H, CH_3Si), 0.04 (s, 6 H, Me_2Si), 0.03 (s, 3 H, CH_3Si), 0.02 (s, 3 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6 (OC=O), 149.8 (vinyl), 118.9 (vinyl), 88.4 (CO), 86.3 (CO), 85.0 (CO), 82.2 (CO), 72.1 (CO), 70.6 (CO), 66.8 (CO), 64.2 (CO), 63.5 (CO), 51.2 (CO), 37.7, 37.6, 37.4, 32.5, 30.4, 29.4, 28.7, 26.9, 26.0, 25.7, 25.6, 23.8, 18.3, 17.9, 16.1, −2.2, −2.4, −4.5, −5.0, −5.3; HRMS calcd for $C_{43}H_{82}O_9Si_3$ (M + Cs) 959.4321, found 959.4321.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanoate, 4,-10-Bis[(*tert*-butyldimethylsilyl)oxy]-9-[1-[(*tert*-butyldimethylsilyl)oxy]-propyl]hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aβ,9α(*Z*),-10β,12aα,13α,14aα]]-, Methyl Ester (85). Catalytic hydrogenation procedure was followed as described for compound **16**. **85**: colorless oil; R_f = 0.35 (silica, 30% ether in petroleum ether); $[\alpha]^{25}_D$ +36.58° (*c* 0.02, $CHCl_3$); IR (neat) ν_{max} 2950, 2855, 1742, 1471, 1360, 1254, 1088, 1059, 1015, 938, 834, 773 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 4.02 (m, 1 H HCO), 3.81 (m, 1 H, HCO); 3.67–3.71 (m, 2 H, HCO), 3.65 (s, 3 H, OCH_3), 3.59–3.65 (m, 1 H, HCO), 3.31–3.35 (m, 2 H, HCO), 3.19–3.22 (m, 2 H, HCO), 3.14 (dd, *J* = 9.7, 2.4 Hz, 1 H, HCO), 2.70 (m, 1 H, CH_2), 2.33–2.38 (m, 2 H, CH_2), 2.15 (m, 1 H, CH_2), 1.56–2.00 (m, 16 H, CH_2), 1.19 (s, 3 H, CH_3), 1.09 (s, 3 H, CH_3), 0.90 (s, 9 H, ^{t}BuSi), 0.88 (s, 9 H, ^{t}BuSi), 0.83 (s, 9 H, ^{t}BuSi), 0.06 (s, 6 H, Me_2Si), 0.05 (s, 6 H, Me_2Si), 0.04 (s, 6 H, Me_2Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0 (OC=O), 88.3 (CO), 86.3 (CO), 84.8 (CO), 82.3 (CO), 77.0 (CO), 76.7 (CO), 72.4 (CO), 71.9 (CO), 67.2 (CO), 63.5 (CO), 62.7 (CO), 51.3 (CO), 37.6, 37.4, 36.2, 32.7, 31.6, 30.4, 29.4, 28.7, 28.3, 26.8, 25.9, 25.7, 25.6, 23.8, 18.3, 18.1, 17.9, 16.1, −2.3, −2.4, −4.4, −5.2, −5.3; HRMS calcd for $C_{43}H_{84}O_9Si_3$ (M + Cs) 961.4478, found 961.4449. Anal. Calcd: for C, 62.27; H, 10.21. Found: C, 62.30; H, 10.22.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanoate, 4,-10-Bis[(*tert*-butylmethylsilyl)oxy]-9-(1-hydroxypropyl)hexadecahydro-5a,10-dimethyl-, 2*R*-[2α,4α,4aβ,5aβ,7aβ,9α(*Z*),10β,12aα,13aα,-14aα]]-, Methyl Ester (86). Selective desiylation procedure was followed as described in compound **70**. **86**: colorless oil; R_f = 0.29 (silica, 50% ether in petroleum ether); $[\alpha]^{25}_D$ +29.39° (*c* 0.24, $CHCl_3$); IR (neat) ν_{max} 3466, 2948, 2855, 1740, 1471, 1436, 1374, 1254, 1087, 1058, 1015, 939, 834, 774 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.02 (m, 1 H, HCO), 3.78–3.81 (m, 1 H, HCO), 3.69 (td, *J* = 11.1, 4.8 Hz, 1 H), 3.65 (s, 3 H, OCH_3), 3.62 (m, 2 H, HCO), 3.33–3.39 (m, 2 H, HCO), 3.18–3.23 (m, 2 H, HCO), 3.14 (dd, *J* = 9.7, 2.2 Hz, 1 H, HCO), 2.70 (m, 1 H, CH_2), 2.33–2.38 (m, 2 H, CH_2), 2.26 (m, 1 H, CH_2), 2.18 (m, 1 H, CH_2), 1.56–2.00 (series of multiplets, 14 H, CH_2), 1.30 (m, 1 H, CH_2), 1.18 (s, 3 H, CH_3), 1.09 (s, 3 H, CH_3), 0.89 (s, 9 H, ^{t}BuSi), 0.83 (s, 9 H, ^{t}BuSi), 0.07 (s, 3 H, CH_3Si), 0.06 (s, 3 H, CH_3Si), 0.05 (s, 3 H, CH_3Si), 0.04 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0 (OC=O), 88.3 (CO), 86.3 (CO), 84.6 (CO), 82.5 (CO), 77.1 (CO), 72.4 (CO), 71.9 (CO), 67.2, (CO), 62.8 (CO), 62.6 (CO), 51.4 (CO), 37.5, 37.4, 37.3, 36.2, 32.7, 31.6, 30.1, 29.3, 28.7, 28.3, 26.4, 25.7, 25.7, 23.8, 18.1, 17.9, 16.0, −2.2, −2.4, −4.3, −5.2; HRMS calcd for $C_{37}H_{70}O_9Si_2$ (M + Cs) 847.3613, found 847.3630.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanoate, 4,-10-Bis[(*tert*-butylmethylsilyl)oxy]-9-(1-formylpropyl)hexadecahydro-5a,-10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aβ,9α(*Z*),10β,12aα,13aα,14aα]]-, Methyl Ester (87). Swern oxidation procedure was followed as described for compound **44**. **87**: colorless oil; R_f = 0.28 (silica, 30% ether in petroleum ether); $[\alpha]^{25}_D$ + 21.82° (*c* 0.11, $CHCl_3$); IR (neat) ν_{max} 2927, 2855, 1737, 1732, 1462, 1375, 1254, 1104, 1090, 1058, 1014, 834, 773 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.74 (t, *J* = 1.9 Hz, 1 H, HC=O), 4.02 (m, 1 H, HCO), 3.78–3.82 (m, 1 H, HCO), 3.70 (td, *J* = 11.6, 4.9 Hz, 1 H, HCO), 3.66 (s, 3 H, OCH_3), 3.29–3.32 (m, 2 H, HCO), 3.16–3.19 (m, 2 H, HCO), 3.14 (dd, *J* = 9.8, 2.5 Hz, 1 H, HCO), 2.65–2.71 (m, 1 H, CH_2), 2.44–2.49 (m, 2 H, CH_2), 2.33–2.38 (m, 2 H, CH_2), 2.12 (m, 1 H, CH_2), 1.52–2.00 (series of multiplets, 14 H, CH_2), 1.17 (s, 3 H, CH_3), 1.13 (s, 3 H, CH_3), 0.88 (s, 9 H, ^{t}BuSi), 0.83 (s, 9 H, ^{t}BuSi), 0.07 (s, 6 H, CH_3Si), 0.06 (s, 3 H, CH_3Si), 0.03 (s, 3 H, CH_3Si).

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanoate, 4,-10-Bis[(*tert*-butyldimethylsilyl)oxy]-9-(3,5-hexadienyl)hexadecahydro-5a,10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7aβ,9α(*Z*),10β,12aα,13aα,-14aα]]-, Methyl Ester (89). To a dispersion of $PhSe(CH_2)_3P^+Ph_3Br^-$ (196 mg, 0.242 mmol) in THF (5 mL) at −78 °C was added 1.6 M ^{n}BuLi (0.16 mL, 0.26 mmol) dropwise. After stirring for 15 min the solution of aldehyde **87** (17 mg, 0.26 mmol) in THF was added followed by HMPA (45 μL, 0.26 mmol). The reaction was brought to room temperature over a period of 30 min, diluted with ether (30 mL), and washed with water (10 mL). The organic layer was dried and concentrated under reduced pressure.

To a solution of crude selenide in THF (5 mL) was added $NaHCO_3$ (235 mg, 2.8 mmol) and H_2O_2 (1 mL of 30% solution), and the reaction was stirred at room temperature for 4 h. The reaction mixture was then diluted with ether (25 mL) and washed with water (2 × 5 mL). The organic layer was dried and concentrated under vacuum. Flash column chromatography (silica, 20% ether in petroleum ether) gave 100 mg (56% overall two steps) of **89**: oil; R_f = 0.36 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +36.99° (*c* 0.27, $CHCl_3$); IR (neat) ν_{max} 2948, 2856, 1740, 1462, 1252, 1092, 834, 775 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.64 (ddd, *J* = 16.9, 11.0, 10.2 Hz, 1 H, HC=CH), 5.98 (t, *J* = 10.0 Hz, 1 H, HC=CH), 5.37–5.40 (m, 1 H, HC=CH), 5.15 (d, *J* = 16.9 Hz, 1 H, CH=CH), 5.05 (d, *J* = 10.2 Hz, 1 H, CH=CH), 3.98 (br s, 1 H, HCO), 3.74–3.78 (m, 1 H, HCO), 3.63–3.68 (m, 1 H, HCO), 3.61 (s, 3 H, OCH_3), 3.14–3.26 (series of m, 4 H), 3.09 (dd, *J* = 9.7, 2.3 Hz, 1 H), 2.62–2.67 (m, 1 H), 1.49–2.33 (series of m, 18 H), 1.21–1.37 (m, 1 H), 1.12 (s, 3 H, CH_3), 1.04 (s, 3 H, CH_3), 0.84 (s, 9 H, Si^tBu), 0.79 (s, 9 H, Si^tBu), 0.02 (s, 3 H, $SiMe_2$), 0.01 (s, 6 H, $SiMe_2$), 0.00 (s, 3 H, $SiMe_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2 (OC=O), 132.7 (C=C), 132.1 (C=C), 129.7 (C=C), 117.2 (C=C), 86.8 (CO), 86.2 (CO), 85.0 (CO), 85.0 (CO), 82.5 (CO), 77.3 (CO), 76.8 (CO), 72.6 (CO), 72.0 (CO), 67.4 (CO), 62.9 (CO), 51.5, 37.7, 37.5, 36.3, 32.9, 31.7, 30.0, 29.6, 29.5, 28.7, 28.4, 25.8, 25.7, 24.7, 24.0, 18.2, 18.1, 16.2, −2.1, −2.3, −4.2, −5.1; HRMS calcd for $C_{40}H_{72}O_8Si_2$ (M + Cs) 869.3814, found 869.3823. Anal. Calcd: C, 65.17; H, 9.84. Found: C, 65.31; H, 9.87.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanol, 4,10-Bis[(*tert*-butyldimethylsilyl)oxy]-9-(3,5-hexadienyl)hexadecahydro-5a,-10-dimethyl-, [2*R*-[2α,4α,4aβ,5aβ,7a,9α(*Z*),10β,12aα,13aα,14aα]]- (90), Procedure for DIBAL-H reduction was followed as described for compound **52**. **90**: colorless oil; R_f = 0.28 (50% ether in petroleum ether); $[\alpha]^{25}_D$ +28.90° (*c* = 0.55, $CHCl_3$); IR (thin film) ν_{max} 3405, 2934, 2855, 1612, 1513, 1247, 1098, 1033, 820 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.61 (dt, *J* = 16.9, 10.6 Hz, 1 H, HC=C), 6.00 (t, *J* = 10.9 Hz, 1 H, HC=C), 5.37–5.42 (m, 1 H, HC=C), 5.16 (d, *J* = 16.8 Hz, 1 H, HC=C), 5.05 (d, *J* = 10.1 Hz, 1 H, HC=C), 4.00 (br s, 1 H, HCO), 3.78–3.84 (m, 1 H, HCO), 3.67–3.74 (m, 1 H, HCO), 3.55–3.65 (m, 2 H, HCO), 3.22–3.32 (m, 2 H, HCO), 3.10–3.20 (m, 3 H, HCO), 1.25–2.32 (series of m, 20 H, CH_2), 1.13 (s, 3 H, CH_3), 1.05 (s, 3 H, CH_3), 0.85 (s, 9 H, ^{t}BuSi), 0.80 (s, 9 H, ^{t}BuSi), 0.03 (s, 3 H, CH_3Si), 0.01 (s, 6 H, CH_3Si), 0.00 (s, 3 H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.7 (C=C) 132.1 (C=C), 129.7 (C=C), 117.2 (C=C), 86.8 (CO), 86.2 (CO), 85.1 (CO), 85.0 (CO), 82.4 (CO), 72.9 (CO), 72.5 (CO), 68.1 (CO), 67.4 (CO), 62.9 (CO), 37.6, 37.5, 36.2, 32.8, 31.0, 30.7, 30.1, 30.0, 29.6, 29.5, 28.7, 25.8 (CH_3), 25.7 (CH_3), 24.6, 23.9, 18.2, 18.0, 16.2, −2.2 (CH_3), −2.4 (CH_3), −4.3 (CH_3), −5.1 (CH_3); HRMS calcd for $C_{39}H_{72}O_7Si_2$ (M + Cs) 841.3871, found 841.3888.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*f*]oxepin-2-propanal, 4,10-Bis[(*tert*-butyldimethylsilyl)oxy]-9-(3,5-hexadienyl)hexadecahydro-5a,-10-dimethyl-α-methylene-, [2*R*-[2α,4α,4aβ,5aβ,7aβ,9α(*Z*),10β,12aα,-13aα,14aα]]- (91). To a stirred solution of oxalyl chloride (16 μL, 0.18 mmol) in dichloromethane (2 mL) was added (26 μL, 0.36 mmol) at −70 °C, and the mixture was stirred for 15 min. The solution of alcohol **90** (66 mg, 0.09 mmol) in dichloromethane was added at the same temperature followed by addition of triethylamine (0.10 mL, 0.73 mmol). After warming to room temperature over a period of 1 h, methylenedimethylammonium chloride (33.3 mg, 0.18 mmol) was added to reaction mixture, and the stirring was continued for 15 h. The reaction was diluted with dichloromethane (30 mL), washed with saturated bicarbonate

solution (15 mL) and water (20 mL), and dried ($MgSO_4$). The solvent was removed under reduced pressure. Flash column chromatography (silica, 20% ether in petroleum ether) gave **91** (60 mg, 90%): colorless oil; R_f = 0.35 (silica, 20% ether in petroleum ether); $[\alpha]^{25}_D$ +49.65° (*c* 0.435, $CHCl_3$); IR (thin film) ν_{max} 2949, 2856, 1695, 1252, 1081, 1015, 833, 775 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.50 (s, 1 H, HC=O), 6.61 (dt, *J* = 16.8, 10.6 Hz, 1 H, HC=C), 6.30 (s, 1 H, HC=C), 6.04 (s, 1 H, HC=C), 6.00 (t, *J* = 10.9 Hz, 1 H, HC=C), 5.35–5.45 (m, 1 H, HC=C), 5.16 (d, *J* = 17.1 Hz, 1 H, HC=C), 5.05 (d, *J* = 10.1 Hz, 1 H, HC=C), 4.02 (br s, 1 H, HCO), 3.86–3.92 (m, 1 H, HCO), 3.75–3.81 (m, 1 H, HCO), 3.24–3.34 (m, 3 H, HCO), 3.17–3.22 (m, 1 H, HCO), 3.10–3.14 (m, 1 H, HCO), 1.30–2.32 (series of m, 18 H, CH_2), 1.13 (s, 3 H, CH_3), 1.05 (s, 3 H, CH_3), 0.87 (s, 9 H, ^{t}BuSi), 0.80 (s, 9 H, ^{t}BuSi), 0.04, 0.03, 0.02, 0.02 (4 s, 3 H each, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.6 (C=O), 148.2 (C=C), 135.8 (C=C), 132.8 (C=C), 132.1 (C=C), 129.7 (C=C), 117.2 (C=C), 86.8 (CO), 86.2 (CO), 85.0 (CO), 82.5 (CO), 72.5 (CO), 71.1 (CO), 67.4 (CO), 62.9 (CO), 37.7, 37.5, 36.6, 32.8, 31.7, 31.0, 30.1, 29.6, 28.8, 26.0 (CH_3), 25.9, 25.8, 25.7 (CH_3), 24.7, 24.0, 18.3, 18.1, 16.2, –2.1 (CH_3), –2.3 (CH_3), –4.2 (CH_3), –5.9 (CH_3); HRMS calcd for $C_{40}H_{70}O_7Si_2$ (M + Cs) 851.3714, found 851.3728.

Oxepino[3,2-*b*]pyrano[2′,3′:5,6[pyrano[2,3-*f*]oxepin-2-propanal, 9-(3,5-Hexadienyl)hexadecahydro-4,10-dihydroxy-5a,10-dimethyl-α-methylene-, [2*R*-[2α,4α,4aβ,5aβ,7aβ,9α(*Z*),10β,12aα,13aα,14aα]]- (Hemibrevetoxin B; 1). A 100-mL round-bottomed flask equipped with a balloon filled with SiF_4 gas was charged with a solution of disilyl ether **91** (27 mg, 0.037 mmol) in a 1:1 mixture of CH_3CN–CH_2Cl_2 (4 mL). After being stirred for 4 h at 0 °C, the reaction mixture was diluted with methylene chloride and washed successively with water, saturated sodium bicarbonate solution, and brine. The organic layer was dried and concentrated under reduced pressure. Flash column chromatography (silica, ether) gave **1** (15 mg, 82%): solid; R_f 0.33 (silica, ether); $[\alpha]^{25}_D$ +112° (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 3460, 3079, 2938, 2703, 1687, 1378, 1086, 922, 738 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ 9.51 (s, 1 H, HC=O), 6.69 (ddd, *J* = 16.9, 11.0, 10.2 Hz, 1 H, HC=CH), 6.37 (s, 1 H, C=CH_2), 6.09 (s, 1 H, C=CH_2), 6.04 (t, *J* = 11.0 Hz, 1 H, HC=CH), 5.46–5.50 (m, 1 H, CH=CH), 5.21 (d, *J* = 16.9 Hz, 1 H, C=CH_2), 5.10 (d, *J* = 10.2 Hz, 1 H, C=CH), 4.00 (br s, 1 H, HCO), 3.90–3.92 (m, 1 H, HCO), 3.73 (ddd, *J* = 10.8, 10.1, 4.6 Hz, 1 H, HCO), 3.32–3.33 (m, 2 H, HCO), 3.26 (dd, *J* = 12.0, 4.1 Hz, 1 H, HCO), 3.20 (dd, *J* = 10.1, 2.1 Hz, 1 H, HCO), 3.16 (dd, *J* = 14.4, 10.2, 1 H, HCO), 2.46 (dd, *J* = 14.5, 5.0 Hz, 1 H, HCO), 2.30–2.34 (m, 1 H, CH_2), 2.16–2.18 (m, 1 H, CH_2), 1.20–1.96 (series of m), 1.18 (s, 3 H, CH_3), 1.07 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 194.2 (HCO), 148.0 (=CHCO), 135.8 (H_2C=C), 132.3 (HC=CH), 131.8 (HC=CH), 129.2 (CH=CH), 116.6 (C=CH_2), 86.4 (CO), 85.5 (CO), 84.6 (CO), 81.8 (CO), 77.8 (CO), 74.6 (CO), 71.7 (CO), 70.3 (CO), 65.9 (CO), 62.2 (CO), 37.8, 37.1, 33.1, 32.4, 31.1, 29.9, 29.2, 28.5, 24.4, 23.0 (CH_3), 16.2 (CH_3); HRMS calcd for $C_{28}H_{42}O_7$ (M + Cs) 623.1985, found 623.1960.

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Supplementary Material Available: Experimental data for **4–11** and **19–31** and X-ray crystallographic data for compounds **45** and **54** (33 pages); observed and calculated structure factors (24 pages). Ordering information is given on any current masthead.