Simple Designs for the Construction of Complex Trans-Fused Polyether Toxin Frameworks. A Convergent Strategy Based on Hydroxy Ketone Cyclization of C-Linked Oxacycles

Eleuterio Alvarez, Ricardo Pérez, Milagros Rico, Rosa M. Rodríguez, and Julio D. Martín*

Centro de Productos Naturales Orgánicos Antonio González, Universidad de La Laguna−CSIC, Carretera de la Esperanza, 2, 38206 La Laguna, Tenerife, Spain

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A single, unified convergent strategy for the stereocontrolled synthesis of *trans*-fused polyethers was developed. It was demonstrated that the epimerization and reductive intramolecular coupling of hydroxy ketones in reactions with silane−Lewis acids (SI−LA) to generate ethers in C-linked oxacycles is affected by its conformational preference in a predictable manner. The obtained results make evident that the influence of hydrogen bonding between a hemiketal hydroxyl and a 1,3-diaxial C−O bond is regular and predictable and that convergent synthesis of *trans*-fused polyethers may confidently be conducted on driving ring closure to oxane rings under thermodynamic conditions

Introduction

Trans-fused polyether toxins[1] from marine microorganisms are probably the most intriguing of all the marine substances under investigation at the present time. Although much effort has been expended over the last few years in developing a valid synthetic methodology to prepare these substances,[2,3] the synthesis of the lowest MW natural *trans*-fused polyether, hemibrevetoxin-B, has been achieved thanks to a linear strategy.[2p−q,w] Substances such as ciguatoxin (**1**)[4] (Figure 1) or related compounds on the same scale, however, are practically impossible to synthesize without a convergent methodology[3] to achieve the coupling of appropriate oxacyclic subunits and at the same time generate the *trans*,*syn*,*trans* stereochemistry present in this type of molecule.

The following generalizations can be drawn from a convergent design founded on the two detachments shown in Scheme 1: (i) the **2** ⇒ **3** simplification (C−C disconnection) relates the process to the convergent synthesis of O-linked oxacyclic subunits, **3**, in which all the stereogenic centers of the target molecule must be generated prior to the final cyclization step; (ii) the **2** ⇒ **4** simplification (C−O disconnection) involves the convergent synthesis of C-linked oxacyclic substructures, **4**, in which at least one of the stereogenic centers has to be originated during the last stage of the synthetic operation.

As a part of a larger project to synthesize *trans*-fused polyethers related to ciguatoxin (**1**) and congeners,[5] both possibilities outlined in Scheme 1 are being investigated. In this paper, we report results related to the **2** ⇒ **4** disconnection approach based on very simple models.[6]

Background and Problem

Reductive coupling of hydroxy ketones in reactions with silane−Lewis acids (SI−LA) to generate ethers[7] is

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S0022-3263(95)00547-0 CCC: $12.00

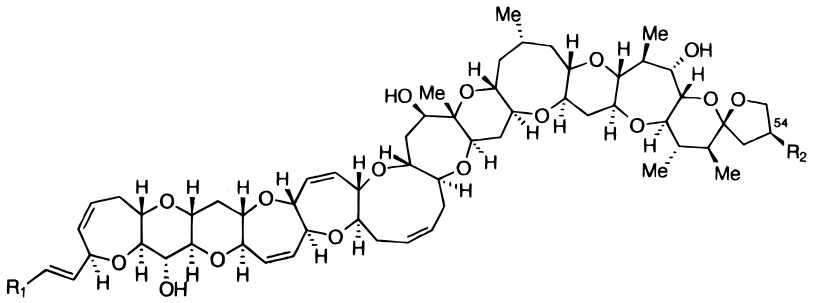

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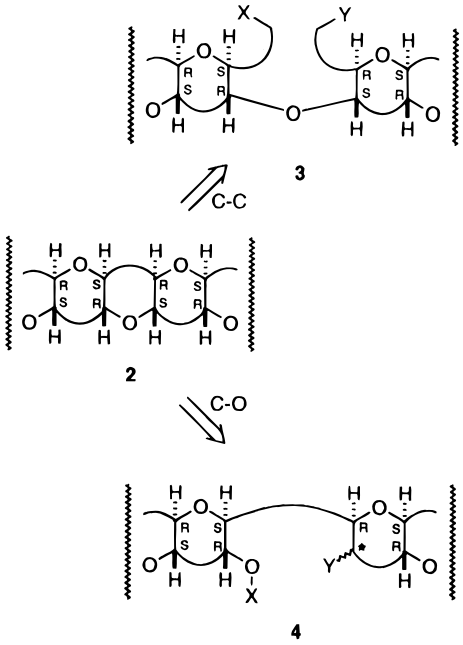
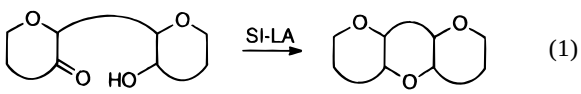
Figure 1. Structure of ciguatoxin. Example of *trans*-fused polyether toxin from marine origin.

Scheme 1. General Retrosynthetic Analysis for a Convergent Approach



a tried and tested methodology in the convergent synthesis of oxacyclic *ortho*-condensed model polyethers[3e] (eq 1). However, in the case of *trans*-fused polyethers of



(1)

marine origin, the strict *R*/*S* alternation of the stereogenic centers in the carbon skeleton of these substances (see general structure **2**) limits the applicability of this reaction[2q] due to the difficulty in directing stereoselectivity toward the required *trans*,*syn*,*trans* epimer. With a view to analyzing in greater detail the results reported,[2q] the two-carbon linked dioxanyl compounds **12** and **13** were synthesized by an expeditious route (Scheme 2). Oxidation of the readily available[3h] tosyl derivative **5** under Swern[8] conditions gave the labile α,*β*-unsaturated ketone **6** which dimerized[9] to afford the adduct **7** (racemic sample; 76%). Reduction of the carbonyl group in **7** with $NaBH_4$ took place from the more accessible face to give the alcohol **8** (97%). Protection of the hydroxyl group in **8** to afford the benzyl ether **9** followed by treatment with $Et_3SiH/TiCl_4$[10] in CH_2Cl_2 gave an inseparable mixture of benzyloxy ketones **10** and **11** in a 1:1 ratio albeit in modest yield (29%).[11] Debenzylation of the **10**:**11** (1:1) mixture under standard conditions gave a 1:1 mixture of hydroxy ketones **12** and **13** (85%) which was subjected to SI−LA-induced reductive coupling (Ph_2MeSiH−TMSOTf) to furnish the *ortho*-condensed oxatricyclic compound **14** in 77% yield. The manner of fusion and stereochemistry of the ether ring in **14** were clarified by 1D ^{1}HNOE difference measurements (Figure 2) and $J_{H,H}$ (Table 1) data. Prominent enhancements in the NOE diff spectra of **14** were observed on H_{1a}/H_5, H_5/H_4, H_4/H_9, and H_8/H_{12a}. Coupling constants between angular methines H_5/H_4, J = 2.1 Hz, and H_8/H_9, J = 10.2 Hz, were typical values for interaction between synclinal and antiperiplanar oxymethines, respectively, indicating a *cis*,*syn*,*trans* fusion for the ether rings.

Although separation of the 1:1 mixture of hydroxy ketones **12** and **13** was very difficult by means of column chromatography, we could conduct the independent coupling reaction of **13** by virtue of the large differences in reactivity. For example, when a 1:1 mixture of **12** and **13** was allowed to react with Ph_2MeSiH−TMSOTf, in dry nitromethane at 0 °C for 1 h, the unreacted hydroxy ketone **13** was almost quantitatively recovered in an enriched stereochemical state. The failure of **13** to respond to a favorable cyclization to give **15** and the large differences in reactivity with **12** in the formation of **14** cannot exclude the intermediacy of **12** ⇄ **13** epimerization.

To overcome the limitations of the synthesis of pure **12** via **9**, we examined a different strategy (Schemes 3 and 4) with the purpose of carrying out independent SI−LA coupling reactions on each isomer. Syntheses of key intermediates **18** and **24** are briefly summarized in Scheme 3. Thus, diol **16**, X = H,[3h] was converted into aldehyde **17** by silylation of both hydroxy groups with excess of TBDMSCl in DMF and selective deprotection at the primary position by removal of the TBDMS group with 0.2 equiv of CSA in MeOH at 0 °C to furnish the alcohol which was oxidized under Swern conditions to give **17**. Dibromoolefination[12] of **17** gave the vinyl dibromide **18** in 76% yield. For the synthesis of the *δ*-lactone **24**, diol **16**, X = H, was selectively protected involving 1,3-benzylidene ketalization followed by DIBAH reduction to give **20**. Oxidation of **20** under

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(11) Interestingly, a 1:1 mixture of the *cis* and *trans* hydrogenation products of **9** was also obtained (46%), a reaction that, at least theoretically, should require protic/hydride conditions (see ref 3h).

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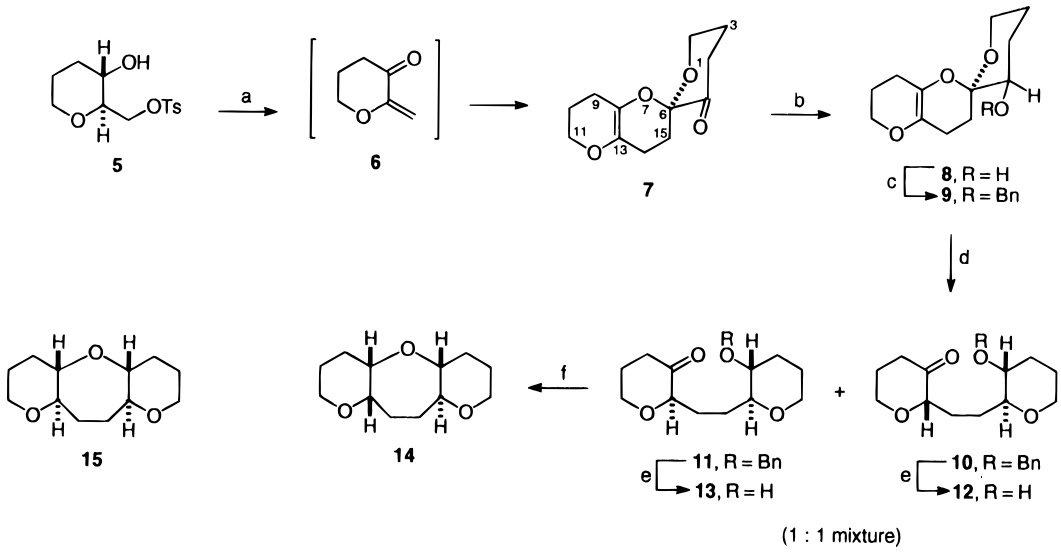
Scheme 2. Synthesis of 14[a]



[a] Reagents and conditions: (a) 3.0 equiv of oxalyl chloride, 9.0 equiv of DMSO, 15.0 equiv of Et_3N, CH_2Cl_2, −78 °C, 36 h, 76%; (b) 2.0 equiv of $NaBH_4$, MeOH, 0 °C, 30 min, 97%; (c) 1.1 equiv of BnBr, 1.1 equiv of NaH, TBAI catalyst, THF, 0 °C, 12 h, 85%; (d) 4.0 equiv of Et_3SiH, 0.5 equiv of $TiCl_4$, CH_2Cl_2, −78 °C, 10 min, 29%; (e) 10% Pd−C catalyst, H_2, EtOAc, 25 °C, 2 h, 85%. (f) 3.2 equiv of Ph_2MeSiH, 3.0 equiv of TMSOTf, CH_3NO_2, 0 °C, 18 h, 77%.

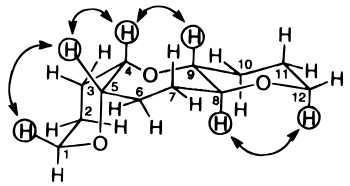


Figure 2. Structure of **14**. Arrows indicating the protons giving NOEs around the ether linkages by 1DNOE difference spectra in $CDCl_3$ or C_6D_6.

Swern conditions gave the aldehyde **21** which was further treated with *m*-chloroperbenzoic acid to yield, afterbase hydrolysis, the hemiketal **23** (42% yield from **20**). PCC oxidation of **23** gave the lactone **24** in 68% yield.

The coupling of intermediates **18** and **24** and elaboration of the resulting product to compound **d-12** is summarized in Scheme 4. The lithium acetylide obtained from *n*-butyllithium addition to **18** (*n*-BuLi, THF, −78 to −40 °C) was quenched with lactone **24** to afford **25** as an inseparable mixture of diastereomers at C-1 in 90% yield. Reduction of the hemiketal (Et_3SiH, $BF_3{\cdot}Et_2O$, CH_3CN, 0 °C) resulted in isomerically pure **26** with none of the α-isomer being detected by ^1H NMR. Desylilation followed by catalytic hydrogenation[13] gave the alcohol **27** which was further oxidized under Swern conditions to give pure **d-10**. Debenzylation of **d-10** afforded the hydroxy ketone **d-12** which was submitted to SI−LA coupling reactions (Ph_2MeSiH-TMSOTf, CH_3NO_2, 0 °C, 15 min) to give **d-14** in 83% overall yield.

Mechanistically, these reductive couplings can be viewed as occurring by the stepwise process illustrated in Scheme 5, in which it is proposed that both isomers (**12** and **13**) are converted into **14** either by direct stereoselective reduction of the common hemiketal **29** or by loss of trimethylsilanol from **29**, which would give **30**, subsequently axially reduced to yield the exclusively observed *cis,syn,trans* isomer **14**. Thus, a strategy for the synthesis of *trans,syn,trans* epimers via reductive hydroxy ketone coupling reactions remained to be developed.

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Synthetic Strategy

The proposed intermediacy of a cyclic hemiketal (**29**) in this mechanism should provide the necessary basis for stereochemical control. Indeed, taking a six-atom subunit as the disconnection nucleus in the polyether, a convergent process such as that shown in the retrosynthetic development of Scheme 6 adequately generates the *R*/*S* alternation present in **31** if the postulated balances shown in Scheme 6 enter into operation: (i) the greater thermodynamic stability attributed to the isomer **32a** (*trans,syn,trans*) as opposed to its epimer, **32b**, should allow the absolute configuration *S* to be selectively induced in the stereogenic center **c** of the target substance **31**;[14] (ii) the equilibrium expected between the cyclic hemiketal **34a** and the "open" form **34b** which will favor **34a** should correctly orientate the reacting hydroxy ketone groups by cooperation of the anomeric and hydrogen-bonding effects so that the SI−LA-induced reductive coupling can take place stereoselectively and induce configuration *R* in the stereogenic center d of the target molecule **31**.[15] The convergent coupling process of substrates such as **35** and **36** should ensure the right groups for the whole process to take place with asymmetrical induction controlled from the stereogenic centers a and b which are present in the starting substance **36**, following the synthetic sequence **34a** → **33** → **32a** → **31**.

The implementation of these ideas is shown in Schemes 7 and 8. The *meso*-oxatricyclic molecules **54**, **56** (Scheme 7), and **59** (Scheme 8) were selected on the basis of the unequivocal spectroscopic simplification (^1H and ^{13}C NMR) which for the sake of symmetry must occur when the targeted *trans,syn,trans* stereochemistry is attained.

The vinylstannane **38** was prepared by deprotonation of the 3,4-dihydro-2*H*-pyran **37** with 1.2 equiv of *tert*-butyllithium and quenching with tri-*n*-butyltin chloride.[16] Tin−lithium exchange with *n*-butyllithium proceeded smoothly at low temperature to give **39** which was allowed to react with the optically active aldehyde **17** (prepared from tri-*O*-acetyl-D-glucal[3h]) at −78 °C over 2 h to give a 8:1 mixture of an alcohol **40** and its epimer **43** in 86% yield from the stannane. The diastereomers

Table 1. Selected ^{1}H and ^{13}C NMR Chemical Shifts (δ)[a] and Coupling Constants (Hz)[b] of 14

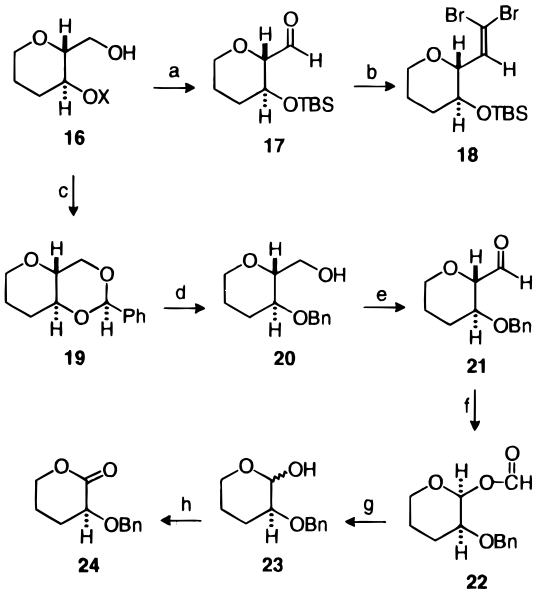
	$CDCl_3$		C_6D_6	
Positn	1H (pattern)	^{13}C (pattern)	1H (pattern)	^{13}C (patttern)
1	3.92 (11.3, 4.4, 2.3, 2.1) 3.46 (11.3, 11.2, 2.4)	67.3 (t)	3.85 (11.2, 4.1, 2.0, 2.0) 3.23 (11.2,11.2, 2.4)	66.9 (t)
2	1.88 (13.9, 12.8, 12.8, 4.1) 1.37 (m)[c]	21.3 (t)	2.04 (m)[c] 1.05 (m)[c]	21.4 (t)
3	1.88 (m)[c] 1.64 (m)[c]	29.7 (t)	1.90 (m)[c] 1.39 (13.1, 13.1, 4.2, 4.0)	30.1 (t)
4	3.51 (5.8, 3.5, 2.1)	76.7 (d)	3.18 (m)[c]	76.7 (d)
5	3.59 (7.2, 6.9, 2.1)	77.5 (d)	3.29 (7.0, 7.0, 2.1)	77.2 (d)
6	2.18 (13.6, 7.5, 7.2) 1.59 (m)[c]	28.4 (t)	2.04 (m)[c] 1.83 (11.4, 7.3, 7.0, 2.0)	28.6 (t)
7	1.94 (m)[c] 1.54 (m)[c]	28.9 (t)	2.20 (11.0, 7.0, 4.4, 1.7) 1.60 (11.0, 9.0, 8.0, 2.0)	28.9 (t)
8	3.04 (m)[c]	84.1 (d)	3.09 (m)[c]	84.1 (d)
9	3.04 (m)[c]	81.9 (d)	2.95 (10.2, 10.2, 4.2)	81.5 (d)
10	2.16 (13.8) 1.52 (m)[c]	31.4 (t)	2.04 (m)[c] 1.51 (m)[c]	31.9 (t)
11	1.64 (m)[c] 1.64 (m)[c]	26.0 (t)	1.51 (m)[c] 1.29 (m)[c]	26.2 (t)
12	3.86 (11.3, 3.9, 2.1, 1.8) 3.31 (11.3, 11.0, 3.5)	67.9 (t)	3.74 (11.1, 4.4, 2.0, 2.0) 3.06 (m)[c]	67.4 (t)

[a] ^{1}H and ^{13}C NMR spectra were measured with a 400 MHz spectrometer. [b] Multiplicity (s, singlet; d, doublet; t, triplet; m, multiplet). [c] Coupling could not be assigned due to heavy signal overlapping.

could be separated and their relative configurations were initially established by ^{1}H NMR. The magnitude of the H-5, H-6 coupling constants (in **40**, $J_{5,6} = 1.8$ Hz; in **43**, $J_{5,6} = 7.0$ Hz) unambiguously showed the proton at C-6 to be gauche of H-5 in **40** and anti to H-5 in **43**. As was to be expected, both epimers (**40** and **43**) had a single unique conformation in which each C−C linking bond adopted the exoanomeric conformation.[17]

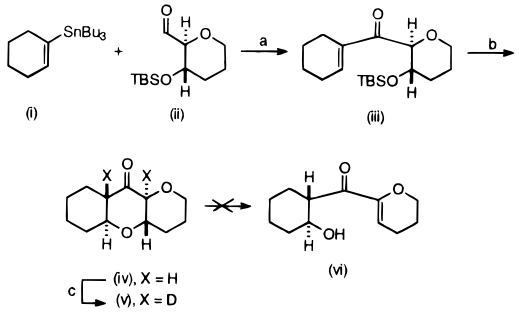
Oxidation of the mixture of **40** and **43** (SO_3·py complex) gave the α,β-unsaturated ketone **42** in an S-*cis* conformation in which the C=O and the dihydropyrane C−O dipoles were antiparallel. Nucleophilic addition to the preferred conformation shown in **42** was expected to be highly stereoselective and to take place mainly from the less sterically hindered side of the carbonyl. Reduction of **42** with $NaBH_4$ gave alcohol **43** as the only product due to the easier access of the hydride from the "back side" of the carbonyl. The silyloxy substituent at C-4 in **42** clearly contributed to this selectivity. Benzylation of **43** under standard conditions afforded the benzyl ether **44** in high yield (97%), which was then hydroborated (BH_3·Me_2S) and oxidatively converted to a mixture of alcohols **45** and **46** in 75% and 8% yields, respectively. Analysis of the vicinal coupling constants around each oxane ring affirmed the expected chair conformation, while analysis of the coupling constants of the interannular (benzyloxy)methine link provided information about

Scheme 3. Preparation of Key Intermediates 18 and 24[a]



[a] Reagents and conditions: (a) From **16**, X = TBS,[3h] 4.0 equiv of SO_3·pyridine, 7.0 equiv of Et_3N, 6:1 CH_2Cl_2:DMSO, 25 °C, 4 h, 84%; (b) 4.0 equiv of Ph_3P, 2.0 equiv of CBr_4, CH_2Cl_2, 0 °C, 20 min, 76%; (c) from **16**, X = H,[3h] 1.5 equiv of $PhCH(OMe)_2$, 0.01 equiv of CSA, DMF, 50 °C, 4 h, 92%; (d) 10.0 equiv of DIBAH, CH_2Cl_2, 0 °C, 30 h, 94%; (e) 3.0 equiv of oxalyl chloride, 9.0 equiv of DMSO, 15.0 equiv of Et_3N, CH_2Cl_2, −78 °C, 30 min, 77%; (f) 4.0 equiv of *m*-CPBA, CH_2Cl_2, 0 °C, 3 h, 77%; (g) 1.0 equiv of Na_2CO_3, MeOH, 25 °C, 30 min, 71%; (h) 1.5 equiv of PCC, 0.2 equiv of NaOAc, CH_2Cl_2, 25 °C, 12 h, 68%.

(14) Subsequent investigations in these laboratories have shown that the compound **iv** can incorporate deuterium by treatment with potassium carbonate in methanol-d_4 without unwanted retro-Michael fragmentation to give **vi** [reagents and conditions: (a) (i) *n*-BuLi, THF; (ii) SO_3·pyridine, Et_3N, DMSO, CH_2Cl_2; (b) *n*-Bu_4NF, THF; (c) K_2CO_3, CD_3OD].

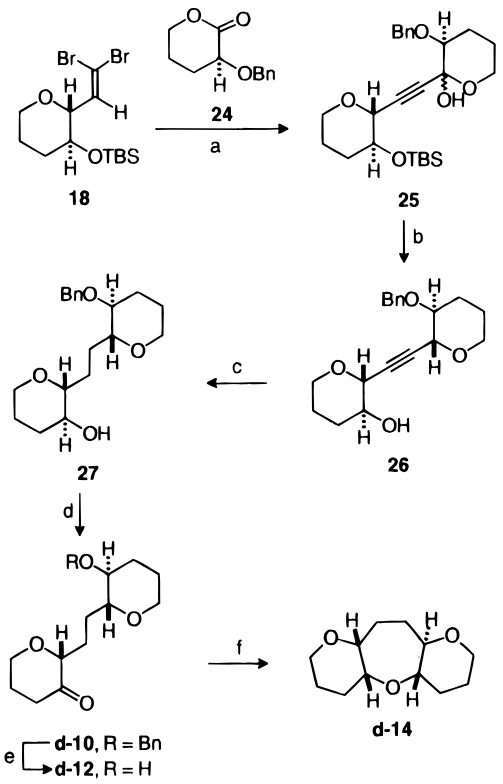


(15) It was hoped that stereochemical control would be achieved by hydride addition to the pyran oxonium ion derived from the hemiketal which would preferentially accept nucleophiles from the axial direction of the oxane ring due to the anomeric effect. (For examples, see: *Anomeric Effect: Origin and Consequences*; Szarek, W. A., Horton, D., Eds.; ACS Symposium Series 87, American Chemical Society: Washington, D.C., 1979. Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: New York, 1983. Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: New York, 1983).

(16) Friesen, R. W.; Sturino, C. F.; Daljeet, A. K.; Kolaczewska, A *J. Org. Chem.* **1991**, *56*, 1944.

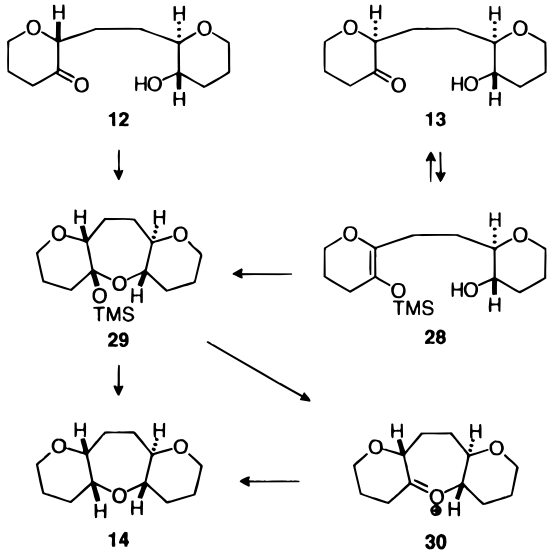
(17) For conformational analysis of the C-trehalose analog, see: Wei, A.; Kishi, Y. *J. Org. Chem.* **1994**, *59*, 88. Duda, C. A.; Stevens, E. S. *J. Am. Chem. Soc.* **1993**, *115*, 8487.

Scheme 4. Synthesis of d-14[a]



[a] Reagents and conditions: (a) 2.0 equiv of *n*-BuLi, THF, −78 to −35 °C, 1 h, then 0.96 equiv of **24**, 25 °C, 1.5 h, 90%; (b) 3.2 equiv of Et_3SiH, 1.4 equiv of $BF_3{\cdot}OEt_2$, CH_3CN, 0 °C, 1.5 h, 88%; (c) 5% Pd−C catalyst, H_2, EtOAc, 25 °C, 2 h, 88%; (d) 3.0 equiv of oxalyl chloride, 5.0 equiv of DMSO, 10.0 equiv of Et_3N, CH_2Cl_2, −78 °C, 1 h, 92%; (e) 10% Pd−C catalyst, H_2, EtOAc, 25 °C, 2 h, 91%; (f) 3.2 equiv of Ph_2MeSiH, 3.2 equiv of TMSOTf, CH_3NO_2, 0 °C, 15 min, 91%.

Scheme 5. Presumed Stepwise Process for the Reductive (R_3SiH−TMSOTf) Coupling Reaction of 16 or 17 To Give 14



each exocyclic bond. The coupling constants of the equatorial C-linked bonds in the major isomer **45** ($J_{5,6}$ = 3.0 Hz, $J_{6,7}$ = 3.0 Hz) suggest that the molecule exists either as a conformer that is somewhat distorted from the exoanomeric position or as a mixture of staggered conformers.

Swern oxidation[8] of the hydroxy group in **45** gave the ketone **47** in 89% yield. Fluoride-induced silyl deprotection in **47** yielded the hemiketal **48** with a single configuration in which the hemiketal hydroxy group is axially oriented and exhibits a strong intramolecular hydrogen bonding with the 1,3-diaxial C−O bond of the benzyloxy group. The SI−LA reduction using Et_3SiH−TMSOTf of hemiketal **48** proceeded exclusively with retention to afford the trioxane system **49**. It is assumed that the axial attack of the hydride takes place predominantly on the oxocarbenium ion intermediate for stereoelectronic reasons.[15]

Compound **49** was debenzylated by hydrogenolysis to afford alcohol **50** which was further oxidized under Swern conditions to give the ketone **51** (90% overall yield). Treatment of **51** with DBU in benzene at 25 °C for 2.4 h led to the quantitative epimerization to the *meso*-ketone **52** with *trans,syn,trans* stereochemistry. Compound **52** was finally converted to the oxatricyclic product **54** *via* reduction (Ni-Raney/EtOH) of the dithioketal **53** in 30% overall yield. Reduction of the ketone **52** with $NaBH_4$ in the presence of $CeCl_3$[18] occurred exclusively via axial attack to give **55** further benzylated to **56**.

Isomerization of the 7β-ketone **47** to the 7α-epimer **57** was effected in quantitative yield by treatment with DBU in benzene (Scheme 8). Ketone **57** was also obtained by Swern oxidation of alcohol **46** in high yield (89%). Fluoride-induced silyl deprotection in **57** gave the hemiketal **58** which was further subjected to reductive SI−LA conditions to afford the *trans,syn,trans* oxatricycle **59** in 87% overall yield from **57**.[15] ^1H and ^{13}C NMR spectral analysis clearly showed that **59** was *meso*-symmetrical.

The importance of intramolecular hydrogen bonding in stabilizing hemiketal conformations and consequently in affecting the ratio of products in SI−LA reductive reactions is evident from the reaction sequence outlined in Scheme 9. Ketone **62** was prepared from **45** by protecting group manipulation followed by oxidation of the alcohol **61** (77% overall yield from **45**). Base-induced acetate hydrolysis in **62**, after workup, gave the mixed hemiketal **63** in which intramolecular hydrogen bonding was frustrated by the forced equatorial orientation of the benzyloxy group. Treatment of **63** under SI−LA conditions (Et_3SiH−TMSOTf) afforded a separable mixture of oxacyclic compounds **64**, **66**, and **56** (9:0.5:1) in 91% yield. The stereochemistry of the major epimer **64** was determined by debenzylation which gave the alcohol **65** which was further oxidized, affording ketone **51**.

The ^1H NMR spectra of the minor compounds **66** and **56** show well-resolved resonances which were assigned by homonuclear decoupling. The vicinal coupling constants around the oxane rings indicated that they adopted chair conformations in a *trans*-fused form. The ^1H and ^{13}C NMR spectra of **56** clearly showed its *meso*-symmetry, all the methine protons having an axial orientation.

Conclusion

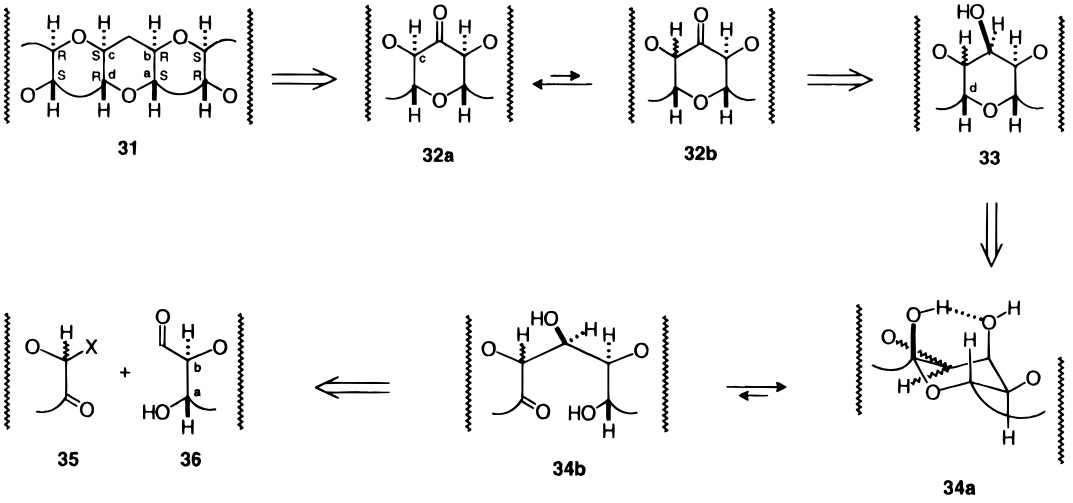
The above results demonstrate that the influence of hydrogen bonding, frequently found between a hemiketal hydroxyl and a 1,3-diaxial C−O bond, is regular and predictable and that synthesis of *trans*-fused polyethers may confidently be based on driving ring closure to oxane rings under thermodynamic conditions.

Experimental Section

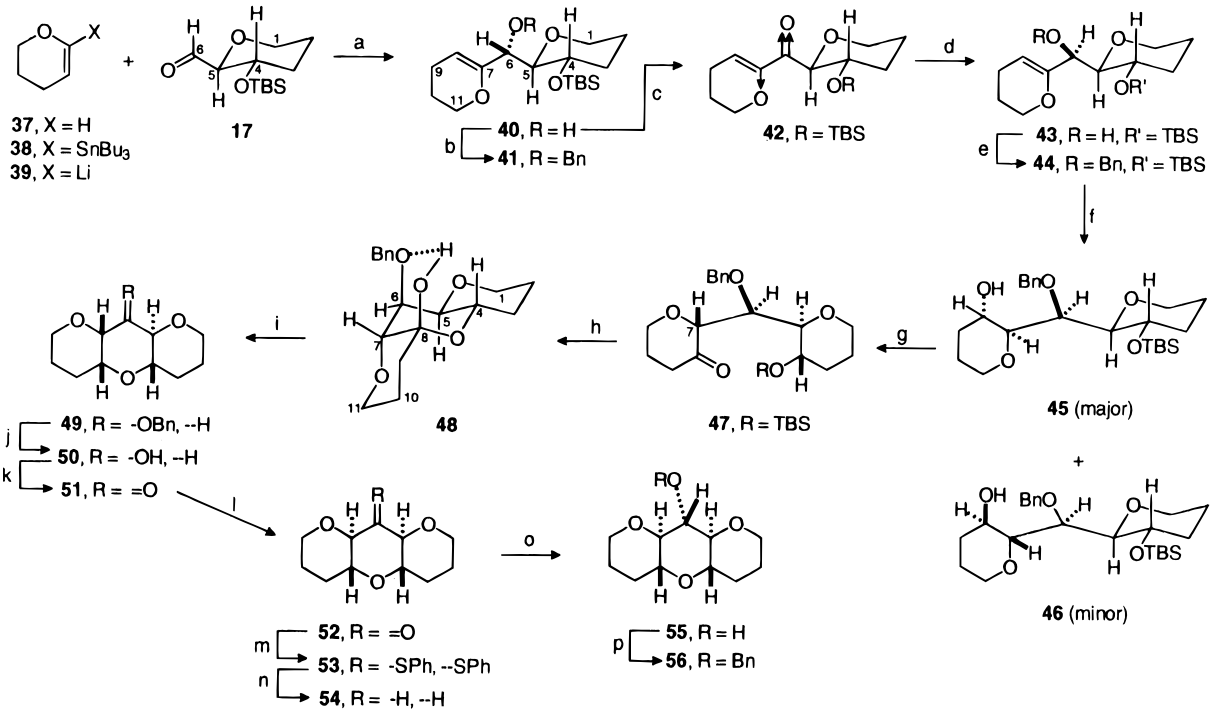
General Experimental Procedures. Reagent grade chemicals were used as purchased unless stated otherwise. The general experimental procedures were recently described elsewhere.[5] Only selected spectral data are presented.

(18) Luche, J.-L.; Gemal, A. L. *J. Am. Chem. Soc.* **1979**, *101*, 5848.

Scheme 6. General concept for stereoselective convergent coupling to oxane rings.



Scheme 7. Synthesis of Compounds 54 and 56[a]



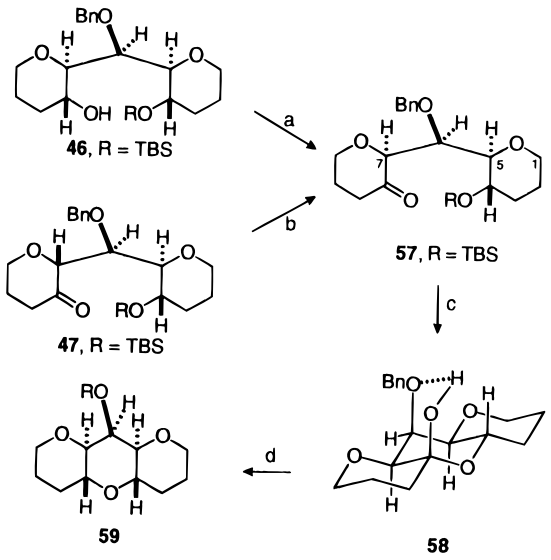
[a] Reagents and Conditions: (a) 1.0 equiv of *n*-BuLi, THF, −78 °C, 2 h, 86%; (b) 5.0 equiv of BnBr, 1.2 equiv of NaH, TBAI catalyst, THF, 25 °C, 12 h, 80%; (c) 5.0 equiv of SO_3·pyridine, 5.0 equiv of Et_3N, 4:1 CH_2Cl_2:DMSO, 0 °C, 2 h, 63%; (d) 2.0 equiv of $NaBH_4$, MeOH, 0 °C, 30 min, 80%; (e) 5.0 equiv of BnBr, 1.2 equiv of NaH, TBAI catalyst, THF, 25 °C, 10 h, 97%; (f) 3.0 equiv of BH_3·Me_2S, THF, 0 to 25 °C, 12 h then add excess H_2O, 3.0 equiv of 3 N NaOH, 1.0 equiv of 30% H_2O_2, 30 min, 83%; (g) 3.0 equiv of oxalyl chloride, 9.0 equiv of DMSO, 15.0 equiv of Et_3N, CH_2Cl_2, −60 to 0 °C, 30 min, 25 °C, 1 h, 89%; (h) 1.3 equiv of *n*-Bu_4NF, THF, 25 °C, 12 h, 89%; (i) 3.0 equiv of Et_3SiH, 1.5 equiv of TMSOTf, CH_3NO_2, 0 °C, 2 h, 99%; (j) $Pd(OH)_2$ (20% Pd), catalyst, H_2, MeOH, 25 °C, 12 h, 98%; (k) 3.0 equiv of oxalyl chloride, 9.0 equiv of DMSO, 15.0 equiv of Et_3N, CH_2Cl_2, −60 to 0 °C, 30 min, 25 °C, 92%; (l) 10.0 equiv of DBU, benzene, 25 °C, 12 h, 97%; (m) 2.5 equiv of thiophenol, 0.15 equiv of $TiCl_4$, CH_2Cl_2, 25 °C, 12 h, 50%; (n) W-2 Raney nickel, EtOH, reflux, 24 h, 60%; (o) 1.0 equiv of $CeCl_3$, 2.5 equiv of $NaBH_4$, MeOH:THF (1:1), −20 °C, 15 min, 93%; (p) 1.1 equiv of BnBr, 1.1 equiv of NaH, TBAI catalyst, THF, 0 °C, 12 h, 88%.

Representative Procedures for Reductive Reactions of Hydroxy Ketones and Spiro- or Hemiketals with Silane−Lewis Acid (SI−LA**) To Generate Ethers. Method a**.[3e,6] A solution of 1 mmol of the substrate in CH_3NO_2 (or CH_2Cl_2) is stirred at 0 °C for 5−10 min under nitrogen. To this solution was slowly added via syringe Et_3SiH (3−10 mmol) and TMSOTf (3−10 mmol). The cold bath was then removed and the reaction allowed to stir at room temperature for 12−20 h and quenched with saturated NH_4Cl. Aqueous workup (Et_2O) and silica gel chromatography yielded ethers in yields varing from 60 to 90%. **Method b**. To a solution of 1 mmol of the substrate and Et_3SiH (3−15 mmol) in freshly distilled CH_3CN (or CH_2Cl_2) at −78 °C was dropwise added, under nitrogen, BF_3·OEt_2 (3−15 mmol) and the resulting solution further stirred at 0 °C for 1−2 h. The mixture was poured slowly into a cold saturated $NaHCO_3$ solution and submitted to aqueous workup and silica gel chromatography to isolate the ethers.

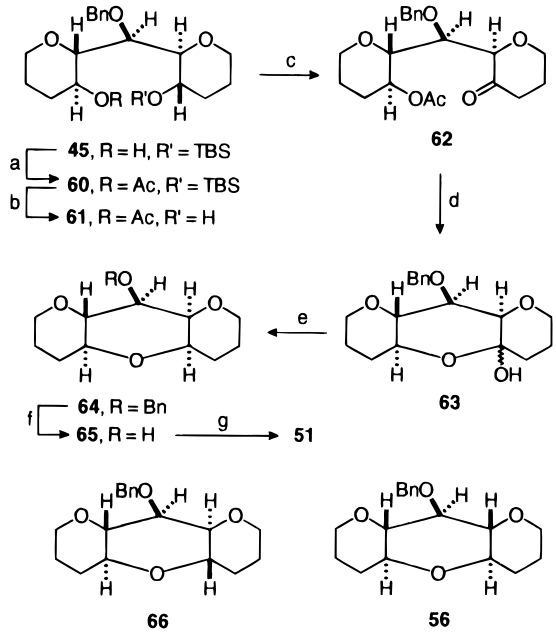
Other silane reagents effecting the same transformation include the following: Ph_3SiH, Ph_2MeSiH, Me_2PhSiH, and Ph_2SiH_2 in combination with other Lewis acids including $TiCl_4$, $SnCl_4$.

Spiro[2,3,4,6,7,8-hexahydropyrano[3,2-*b*]pyranyl-2,2′-tetrahydropyran-3-one] (7). To a cold (−78 °C) stirred solution of oxalyl chloride (6.0 mL, 69.0 mmol) in CH_2Cl_2 (153 mL) freshly distilled from CaH_2 under argon was added DMSO (14.6 mL, 207.0 mmol). After 10 min of stirring, the tosyl derivative **5** (6.2 g, 23.0 mmol) in CH_2Cl_2 (77 mL) was added

Scheme 8. Synthesis of Compound 59[a]



Scheme 9[a]



[a] Reagents and conditions: (a) 3.0 equiv of Ac_2O, 2.3 equiv of Et_3N, DMAP catalyst, CH_2Cl_2, 25 °C, 4 h, 94%; (b) 1.3 equiv of *n*-Bu_4NF, THF, 0 °C, 3 h, 98%; (c) 3.0 equiv of oxalyl chloride, 9.0 equiv of DMSO, 15.0 equiv of Et_3N, CH_2Cl_2, −78 to 0 °C, 2 h, 84%; (d) 0.1 equiv of K_2CO_3, MeOH, 25 °C, 30 min, 70%; (e) 15.0 equiv of Et_3SiH, 15.0 equiv of $BF_3{\cdot}Et_2O$, CH_3CN, 0 °C, 2 h, 87%; (f) $Pd(OH)_2$ (20% Pd) catalyst, H_2, MeOH, 25 °C, 12 h, 89%; (g) 3.0 equiv of oxalyl chloride, 9.0 equiv of DMSO, 15.0 equiv of Et_3N, CH_2Cl_2, −60 to 0 °C, 30 min, 25 °C, 91%.

dropwise at −78 °C, and the mixture was stirred at that temperature for 30 min. Et_3N (48.0 mL, 345.0 mmol) was then added and the reaction mixture stirred at room temperature for 36 h and quenched with saturated NH_4Cl. Aqueous workup (EtOAc) and silica gel chromatography (flash silica, 5−10% EtOAc/hexanes) yielded dimer ketone **7** (1.95 g, 76% yield) as a clear, colorless oil: R_f = 0.55 (silica, 10% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 3026, 2956, 2359, 1732, 1445, 1234, 1155, 1083, 1004, 976 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.14 (ddd, J = 12.1, 11.5, 3.0 Hz, 1H), 3.92 (ddd, J = 10.5, 4.7, 4.2 Hz, 1H), 3.80 (ddd, J = 11.4, 6.0, 4.5 Hz, 1H), 3.70 (dddd, J = 11.4, 4.9, 1.8, 1.8 Hz, 1H), 2.95 (ddd, J = 14.2, 13.2, 6.7 Hz, 1H), 2.45 (dddd, J = 14.2, 4.6, 2.6, 1.9 Hz, 1H), 2.14 (m, 6H), 2.00 (m, 1H), 1.92 (m, 2H), 1.81 (ddd, J = 13.4, 6.6, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 203.4 (s), 134.2 (s), 128.0 (s), 96.9 (s), 65.9 (t), 60.5 (t), 36.1 (t), 29.1 (t), 25.7 (t), 23.3 (t), 23.2 (t), 19.9 (t); MS *m*/*e* (rel intensity) 244 (M^+, 13), 196 (4), 154 (34), 126 (15), 113 (11), 84 (2); HRMS calcd for $C_{12}H_{16}O_4$ (M^+) 224.104 86, found 224.103 91. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.29; H, 7.14. Found: C, 64.23; H, 7.11.

Spiro[2,3,4,6,7,8-hexahydropyrano[3,2-*b*]pyranyl-2(*R*)-*,2′(*R*)*-tetrahydropyran-3(*R*)*-ol] (8). To a stirred solution of ketone **7** (700.0 mg, 2.43 mmol) in MeOH (24.3 mL) at 0 °C was added $NaBH_4$ (136.0 mg, 4.86 mmol). After 30 min, the reaction mixture was quenched with water, concentrated, and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated, and the residue was subjected to flash chromatography (silica, 20% EtOAc/hexanes) to give the alcohol **8** (686.0 mg, 97%). **8**: amorphous solid; R_f = 0.40 (silica, 30% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 3577, 3016, 2949, 2852, 1226, 1208, 1169, 1157, 1093, 1059, 1038, 992, 956 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.93 (ddd, J = 11.5, 6.2, 1.8 Hz, 1H), 3.84 (m, 1H), 3.80 (ddd, J = 12.0, 11.7, 3.1 Hz, 1H) 3.62 (ddd, J = 11.5, 3.0, 2.7 Hz, 1H), 3.52 (m, 1H), 2.16 (m, 4H), 1.92 (m, 4H), 1.70 (m, 3H), 1.27 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 133.4 (s), 127.7 (s), 96.5 (s), 71.6 (d), 65.4 (t), 60.5 (t), 28.3 (t), 27.7 (t), 25.2 (t), 22.9 (t), 19.7 (t), 19.6 (t); MS *m*/*e* (rel intensity) 226 (M^+, 100), 208 (37), 180 (30), 163 (13), 150 (18) 136 (17), 126 (35), 114 (69), 87 (34); HRMS calcd for $C_{12}H_{18}O_4$ (M^+) 226.120 51, found 226.121 33. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63,72; H, 7.96. Found: C, 63.69; H, 7.98.

Spiro[2(*R*)*,3,4,6,7,8-hexahydropyrano[3,2-*b*]pyranyl-2,2′-tetrahydro-3(*R*)*-(benzyloxy)pyran] (9). To a suspension of NaH (117.0 mg, 60% dispersion, 2.9 mmol) in THF (20 mL) at 0 °C were added alcohol **8** (600.0 mg, 2.65 mmol) in THF (6 mL), benzyl bromide (0.35 mL, 2.9 mmol), and a catalytic amount of TBAI. The reaction mixture was stirred at room temperature for 12 h. The mixture was quenched with water, concentrated, and extracted with ether, and the extract was dried with $MgSO_4$. Following solvent removal, the crude product was purified by chromatography (silica, 10% EtOAc/hexanes) to give **9** (717.0 mg, 85%). **9**: colorless oil; R_f = 0.65 (silica, 20% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 2954, 2881, 2359, 1599, 1454, 1273, 1227, 1175, 1069, 987 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 5H), 4.68 (d, J = 12.3 Hz, 1H), 4.51 (d, J = 12.3 Hz, 1H), 3.92 (m, 1H), 3.81 (ddd, J = 11.1, 7.7, 3.7 Hz, 1H), 3.67 (m, 1H), 3.52 (m, 1H), 3.26 (dd, J = 8.2, 8.0 Hz, 1H), 2.26 (m, 3H), 2.13 (m, 1H), 1.91 (m, 5H), 1.62 (m, 1H), 1.52 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 139.7 (s), 133.6 (s), 128.7 (2C, d), 128.6 (2C, d), 128.4 (s), 128.1 (d), 96.5 (s), 78.7 (d), 71.6 (t), 65.8 (t), 60.8 (t), 28.3 (t), 25.7 (t), 23.9 (t), 23.4 (t), 23.3 (t), 20.3 (t); MS *m*/*e* (rel intensity) 316 (M^+, 17), 263 (2), 187 (0.5), 154 (14); HRMS calcd for $C_{19}H_{24}O_4$ (M^+) 316.167 46, found 316.167 10.

(2*R/2*S**)-[2-[3(*R*)*-(Benzyloxy)tetrahydropyran-2(*S*)-*-yl]ethyl]tetrahydropyran-3-one (10 and 11)**. $TiCl_4$ (1 M in CH_2Cl_2, 0.46 mmol) was added dropwise to a solution of **13** (290.0 mg, 0.92 mmol) and Et_3SiH (0.6 mL, 3.7 mmol) in CH_2Cl_2 (9.2 mL) at −78 °C, and the reaction mixture was stirred at this temperature for 10 min. Dilution with ether (150 mL), sequential washing with a saturated aqueous solution of $NaHCO_3$ (2 × 20 mL) and brine (20 mL), drying ($MgSO_4$), and concentration yielded, after chromatographic purification (silica, 20% EtOAc/hexanes), an unseparable diastereomeric mixture of the compounds **10** and **11** (2S*:2R*1:1) (87.0 mg, 29%). The data for **10** and **11** were determined from the mixture. **10** and **11**: R_f = 0.45 (silica, 20% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 3011, 2942, 2860, 1726, 1246, 1090, 1043 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (m, 5H), 4.61 (d, J = 11.6 Hz, 1H), 4.48 (d, J = 11.6 Hz, 1H), 4.04 (dddd, J = 11.7, 3.2, 2.8, 1.5 Hz, 1H), 3.83 (ddd, J = 11.4, 4.3, 1.7 Hz, 1H), 3.81 (ddd, J = 7.9, 4.5, 3.5 Hz, 1H), 3.65 (dddd, J = 11.7, 9.8, 3.4, 2.0 Hz, 1H), 3.30 (dddd, J = 11.3, 11.1, 4.5, 3.0 Hz, 1H), 3.14 (m, 2H), 2.53 (m, 1H), 2.42 (ddd, J = 16.0, 9.5, 6.7 Hz, 1H), 2.24 (ddd, J = 12.3, 1.9, 1.4 Hz, 1H), 2.11 (m, 1H), 2.02 (m, 2H), 1.87 (m, 1H), 1.66 (m, 2H), 1.60 (m, 1H), 1.41 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 209.5 (s), 209.3 (s), 138.9 (s), 138.6 (s), 128.7 (2C, d), 128.3 (2C, d), 127.9 (d), 127.7 (d), 83.9 (d), 83.3 (d), 81.4 (d), 80.9 (d), 77.7 (d), 77.3 (d), 71.2 (t), 71.2 (t), 67.9 (t), 67.7 (t), 65.5 (t), 65.4 (t), 37.9 (t), 37.8 (t), 29.7 (t), 29.3 (t), 28.3 (t), 28.0 (t), 27.6 (t), 26.4 (t), 26.4 (t), 26.1 (t), 25.8 (t), 25.8 (t); MS *m*/*e* (rel intensity) 318 (M^+, 0.2), 247 (1), 226 (0.6), 209 (1.3), 139

(2), 107 (1), 98 (5), 91 (100), 86 (1); HRMS calcd for $C_{19}H_{26}O_4$ (M^+) 318.183 11, found 318,182 96.

(2*S/2*R**,2″*S**,3″*R**)-2-[2′-(3″-Hydroxytetrahydropyran-2″-yl)ethyl]tetrahydropyran-3-one (12 and 13)**. 10% Pd/C catalyst (7.0 mg) was added to a stirred solution of the mixture **10** and **11** (1:1) (70.0 mg, 0.22 mmol) in EtOAc (2.2 mL) at 25 °C under H_2 atmosphere. When monitoring of the reaction by TLC indicated that all starting material has been consumed (2 h), the reaction mixture was filtered through Celite and rinsed thoroughly with EtOAc. Following the solvent removal, the crude product was purified by chromatography (silica, 50% EtOAc/hexanes) to give a mixture of compounds **12** and **13** (2S*:2R*1:1) (59.0 mg, 85%). The data for **12** and **13** were determined from the mixture. **12** and **13**: oil; $R_f = 0.30$ (silica, 50% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 2990, 2944, 2857, 1724, 1262, 1224, 1215, 1092, 1045, 1027, 937, 908 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.05 (m, 1H), 3.82 (m, 2H), 3.50 (dddd, J = 13.3, 10.0, 3.4, 1.8 Hz, 1H), 3.28 (m, 2H), 2.99 (m, 1H), 2.55 (ddd, J = 15.8, 5.7, 5.2 Hz, 1H), 2.41 (ddd, J = 15.9, 9.8, 6.8 Hz, 1H), 2.10 (m, 4H), 1.87 (m, 2H), 1.65 (m, 3H), 1.37 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 209.4 (s), 209.3 (s), 83.8 (d), 83.4 (d), 82.8 (d), 82.3 (d), 70.7 (d), 70.5 (d), 67.9 (t), 67.8 (t), 65.8 (t), 65.7 (t), 38.0 (t), 37.9 (t), 33.1 (t), 33.1 (t), 28.0 (t), 27.6 (t), 26.7 (t), 26.5 (t), 26.0 (t), 25.9 (t), 25.8 (t), 25.5 (t); MS m/e (rel intensity) 228 (M^+, 8), 210 (4), 181 (0.1), 157 (0.1), 154 (1), 111 (11), 97 (27); HRMS calcd for $C_{12}H_{20}O_4$ (M^+) 228.136 16, found 228.137 00.

(4a*S,5a*R**,9a*S**,11a*S**)-Dodecahydropyrano[3,2-*b*]pyrano[3′,2′-*f*]oxepin (14)**. To a stirred solution of **12** and **13** (1:1 mixture, 2*S**:2*R**) (30.0 mg, 0.12 mmol) and Ph_2MeSiH (80 μL, 0.38 mmol) in dry CH_3NO_2 (12 mL) at 0 °C was added TMSOTf (66 μL, 0.36 mmol). After 18 h at room temperature, the reaction mixture was quenched with a saturated solution of $NaHCO_3$ (5 mL), concentrated, and extracted with ether (3 × 25 mL). The organic layer was dried ($MgSO_4$) and concentrated in vacuo. Chromatography of the residue on silica gel (40% EtOAc/hexanes) gave **14** as a single diastereoisomer (21.6 mg, 77%). **14**: oil; $R_f = 0.60$ (silica, 50% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 3015, 2946, 2854, 1250, 1207, 1085, 1032, 991 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.92 (dddd, J = 11.3, 4.4, 2.3, 2.1 Hz, 1H), 3.86 (dddd, J = 11.3, 3.9, 2.1, 1.8 Hz, 1H), 3.59 (ddd, J = 7.2, 6.9, 2.1 Hz, 1H), 3.51 (ddd, J = 5.8, 3.5, 2.1 Hz, 1H), 3.46 (ddd, J = 11.3, 11.2, 2.4 Hz, 1H), 3.31 (ddd, J = 11.3, 11.0, 3.5 Hz, 1H), 3.04 (m, 2H), 2.18 (ddd, J = 13.6, 7.5, 7.2 Hz, 1H), 2.16 (br d, J = 13.8 Hz, 1H), 1.96 (br d, J = 11.2 Hz, 1H), 1.94 (m, 1H), 1.88 (dddd, J = 13.9, 12.8, 12.8, 4.1 Hz, 1H), 1.64 (m, 3H), 1.59 (m, 1H), 1.54 (m, 1H), 1.52 (m, 1H), 1.37 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 84.1 (d), 81.9 (d), 77.5 (d),-76.7 (d), 67.9 (t), 67.3 (t), 31.4 (t), 29.7 (t), 28.9 (t), 28.4 (t), 26.0 (t), 21.3 (t); ^1H NMR (400 MHz, C_6D_6) δ 3.85 (dddd, J = 11.2, 4.1, 2.0, 2.0 Hz, 1H), 3.74 (dddd, J = 11.1, 4.4, 2.0, 2.0 Hz, 1H), 3.29 (ddd, J = 7.0, 7.0, 2.1 Hz, 1H), 3.23 (ddd, J = 11.2, 11.2, 2.4 Hz, 1H), 3.18 (m, 1H), 3.09 (m, 1H), 3.06 (m, 1H), 2.95 (ddd, J = 10.2, 10.2, 4.2 Hz, 1H), 2.20 (dddd, J = 11.0, 7.0, 4.4, 1.7 Hz, 1H), 2.04 (m, 3H), 1.90 (m, 1H), 1.83 (dddd, J = 11.4, 7.3, 7.0, 2.0 Hz, 1H), 1.60 (dddd, J = 11.0, 9.0, 8.0, 2.0 Hz, 1H), 1.51 (m, 2H), 1.39 (dddd, J = 13.1, 13.1, 4.2, 4.0 Hz, 1H), 1.29 (m, 1H), 1.05 (br d, J = 13.1 Hz, 1H); ^{13}C NMR (C_6D_6) δ 84.1 (d), 81.5 (d), 77.2 (d), 76.7 (d), 67.4 (t), 66.9 (t), 31.9 (t), 30.1 (t), 28.9 (t), 28.6 (t), 26.2 (t), 21.4 (t); HRMS calcd for $C_{12}H_{20}O_3$ (M^+) 212.141 24, found 212.141 11. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.92; H, 9.43. Found: C, 67.88; H, 9.44.

(2*S*,3*S*)-3-(*tert*-Butyldimethylsiloxy)tetrahydropyran-2-carbaldehyde (17). To a stirred mixture of the silyl alcohol **16**, X = TBS[3h] (1.41 g, 5.9 mmol), Et_3N (5.7 mL, 41.0 mmol), dry DMSO (3.9 mL, 55 mmol), and CH_2Cl_2 (23 mL) at 0 °C was added SO_3·py complex (3.74 g, 23.0 mmol). After 4 h, the reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with H_2O (2 × 20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was subjected to flash chromatography (silica, 5% EtOAc/hexanes) to give the aldehyde **17** (1.20 g, 84%). **17**: oil; $R_f = 0.40$ (silica, 10% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +58.8° (*c* 0.67, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2950, 2858, 1730, 1472, 1406, 1253, 1100, 1079, 1026, 960 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 3.95 (br d, J = 11.3 Hz, 1H), 3.69 (ddd, J = 9.2, 9.0, 4.4 Hz, 1H), 3.65 (m, 1H), 3.35 (ddd, J = 11.4, 6.6, 3.9 Hz, 1H), 2.04 (m, 1H), 1.61 (m, 2H), 1.22 (m, 1H), 0.86 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 199.9 (s), 85.9 (d), 68.2 (d), 67.7 (t), 33.9 (t), 26.1 (q), 24.8 (t), 18.0 (s), −3.7 (q), −4.6 (q); MS m/e (rel intensity) 215 ([M − CHO]$^+$, 17), 187 (100), 185 (59), 173 (57).

2(*R*)-(2′,2′-Dibromovinyl)-3(*S*)-(*tert*-butyldimethylsiloxy)tetrahydropyran (18). Triphenylphosphine (8.6 g, 32.8 mmol) was added to a stirred solution of carbon tetrabromide (5.44 g, 16.4 mmol) in dry CH_2Cl_2 (30 mL) at 0 °C. After 1 h the bright orange solution was cooled to −78 °C and treated dropwise with the aldehyde **17** (2.0 g, 8.2 mmol) in CH_2Cl_2 (10 mL) over a 2-min period. After 20-min at 0 °C, the reaction was treated with Et_3N (5.9 mL, 42.6 mmol) and then poured into stirring hexanes (200 mL). The solids were removed by filtration, the filtrate was concentrated, and the residue was chromatographed (silica, 10% EtOAc/hexanes) to afford the vinyl dibromide **18** (2.47 g, 76%). **18**: oil; R_f = 0.75 (silica, 10% EtOAc/*n*-hexane); $[\alpha]^{25}_D = -5.0°$ (*c* 3.2, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2940, 2929, 2858, 1474, 1464, 1259, 1226, 1221, 1207, 1117, 1103, 977 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.34, (d, J = 8.7 Hz, 1H), 3.88 (dddd, J = 11.3, 3.5, 1.6, 1.3 Hz, 1H), 3.78 (dd, J = 8.7, 8.7 Hz, 1H), 3.40 (ddd, J = 8.7, 8.3, 5.1 Hz, 1H), 3.39 (ddd, J = 11.3, 8.6, 4.6 Hz, 1H), 2.04 (br dd, J = 12.4, 3.2 Hz, 1H), 1.65 (m, 2H), 1.50 (m, 1H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.8 (d), 94.5 (t), 83.1 (d), 70.8 (d), 67.9 (t), 33.7 (t), 26.1 (q), 25.6 (t), 18.3 (s), −4.0 (q), −4.3 (q); MS m/e (rel intensity) 402 (M^+, 0.4), 400 (0.1), 398 (0.2), 386 (0.4), 345 (1.5), 344 (10), 341 (2), 340 (12), 263 (20), 262 (11); HRMS calcd for $C_{13}H_{25}{}^{81}Br_2O_2Si$ (M + H)$^+$ 402.994 96, found 402.991 30.

(2*R*,4a*R*,8a*S*)-2-Phenylhexahydropyrano[3,2-*d*]-1,3-dioxin (19). A mixture of diol **16** (4.0 g, 30.0 mmol), benzaldehyde dimethyl acetal (6.7 mL, 45.0 mmol), and CSA (69.5 mg, 0.3 mmol) in DMF (30 mL) was stirred for 4 h at 50 °C. The reaction mixture was quenched with Et_3N (3 mL) and concentrated and the residue subjected to flash chromatography (silica, 10% EtOAc/hexanes) to afford benzylidene **19** (6.13 g, 92%). **19**: crystalline solid; mp 135−136 °C (CH_2Cl_2/*n*-hexane); $R_f = 0.60$ (silica, 10% EtOAc/*n*-hexane); $[\alpha]^{25}_D = -3.9°$ (*c* 1.17, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3013, 2948, 2872, 1456, 1382, 1236, 1222, 1144, 1101, 1008, 978 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (m, 2H), 7.36 (m, 3H), 5.58 (s, 1H), 4.26 (dd, J = 10.5, 4.9 Hz, 1H), 3.97 (dddd, J = 11.5, 4.5, 1.5, 1.3 Hz, 1H), 3.70 (dd, J = 10.5, 10.3 Hz, 1H), 3.58 (ddd, J = 11.2, 8.9, 4.3 Hz, 1H), 3.51 (ddd, J = 11.8, 11.8, 3.1 Hz, 1H), 3.36 (ddd, J = 10.1, 9.0, 4.9 Hz, 1H), 2.14 (ddd, J = 12.0, 4.2, 3.6 Hz, 1H), 1.82 (ddd, J = 8.6, 3.9, 3.6 Hz, 1H), 1.80 (m, 1H), 1.71 (ddd, J = 12.1, 11.2, 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 137.7 (s), 128.9 (d), 128.3 (2 × d), 126.2 (2 × d), 101.8 (d), 78.6 (d), 74.1 (d), 69.4 (t), 68.1 (t), 28.8 (t), 25.6 (t); MS m/e (rel intensity) 220 (M^+, 1.5), 132 (3.5), 121 (6), 144 (15), 105 (11); HRMS calcd for $C_{13}H_{16}O_3$ (M^+) 220.109 94, found 220.109 94.

(2*R*,3*S*)-[3-(Benzyloxy)tetrahydropyran-2-yl]methanol (20). DIBAH (182.0 mL, 182.0 mmol, 1 M in hexanes) was added dropwise to a stirred solution of benzylidene **19** (4.0 g, 18.2 mmol) in CH_2Cl_2 (40 mL) at 0 °C over a 30-min period. The mixture was then warmed to 25 °C, and stirring was continued for 30 h. Upon recooling to 0 °C, methanol (7.4 mL, 182.0 mmol) was added carefully, followed by removal the cooling bath and continued stirring for 20 min. The reaction mixture was cooled to 0 °C, treated dropwise with 3 N NaOH (25.0 mL, 75.0 mmol), and then poured into stirring hexanes (200 mL). The white solid was removed by filtration, the filtrate was concentrated, and the residue was chromatographed (silica, 20% EtOAc/*n*-hexane) to afford compound **20** (3.7 g, 94%). **20**: oil, $R_f = 0.3$ (silica, 30% EtOAc/*n*-hexane); $[\alpha]^{25}_D = +65°$ (*c* 2.7, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3501, 3012, 2944, 1495, 1454, 1357, 1220, 1101, 1077, 1029, 984 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 5H), 4.64 (d, J = 11.6 Hz, 1H), 4.47 (d, J = 11.6 Hz, 1H), 3.92 (dddd, J = 11.4, 4.2, 1.7, 1.4 Hz, 1H), 3.88 (ddd, J = 11.8, 11.5, 2.9 Hz, 1H), 3.70 (ddd, J = 11.7, 6.4, 5.3 Hz, 1H), 3.38 (ddd, J = 11.8, 11.5, 2.9 Hz, 1H), 3.35 (ddd, J = 10.5, 9.1, 4.4 Hz, 1H), 3.26 (ddd, J = 8.9, 5.1, 3.2 Hz, 1H), 2.37 (dd, J = 6.3, 6.3 Hz, 1H, D_2O-exchangeable), 2.29 (ddd, J = 13.2, 4.4, 3.3 Hz, 1H), 1.68 (m, 1H), 1.62 (m, 1H), 1.43 (dddd, J = 12.3, 12.3, 10.7, 5.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 183.3 (s), 128.4 (2 × d), 127.7 (3 × d), 80.8 (d), 74.0

(d), 70.8 (d), 67.7 (t), 63.1 (t), 29.1 (t), 25.2 (t); MS *m*/*e* (rel intensity) 222 (M^+, 1), 204 (0.1), 191 (1.2), 160 (1), 116 (12), 97 (3), 91 (100); HRMS calcd for $C_{13}H_{18}O_3$ (M^+) 222.125 59, found 222.126 13.

(2*R*,3*S*)-3-(Benzyloxy)tetrahydropyran-2-carbaldehyde (21). A solution of alcohol **20** (2.0 g, 9.0 mmol) in CH_2Cl_2 (10 mL) was added dropwise to a mixture of oxalyl chloride (2.3 mL, 27.0 mmol) and DMSO (5.7 mL, 81.0 mmol) in CH_2Cl_2 (80 mL) at −78 °C over 25 min. After 30 min Et_3N (19.0 mL, 135.0 mmol) was added slowly and the cooling bath removed. When the reaction mixture reached 0 °C, it was diluted with ether (200 mL), washed with saturated aqueous ammonium chloride (100 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (silica, 20% EtOAc/hexanes) gave the aldehyde **21** (1.53 g, 77%). **21**: oil; R_f = 0.40 (silica, 30% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +66.3° (*c* 1.8, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3011, 2945, 2862, 1732, 1464, 1440, 1359, 1274, 1144, 1082, 1029 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.35 (m, 5H), 4.65 (d, *J* = 11.6 Hz, 1H), 4.50 (d, *J* = 11.6 Hz, 1H), 3.99 (ddd, *J* = 11.3, 3.9, 3.2 Hz, 1H), 3.82 (d, *J* = 8.8 Hz, 1H), 3.55 (m, 1H), 3.47 (ddd, *J* = 11.4, 11.0, 2.4 Hz, 1H), 2.26 (m, 1H), 1.77 (m, 1H), 1.62 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 199.7 (s), 137.7 (s), 128.5 (2 × d), 127.9 (d), 127.8 (2 × d), 83.4 (d), 73.2 (d), 70.8 (t), 67.3 (t), 28.9 (t), 23.8 (t); MS *m*/*e* (rel intensity) 220 (M^+, 0.8), 191 (0.6), 150 (12), 132 (0.5), 114 (3.5), 91 (100); HRMS calcd for $C_{13}H_{16}O_3$ (M^+) 220.109 58, found 220.109 94.

(2*S*,3*S*)-3-(Benzyloxy)tetrahydropyranyl 2-Formate (22). *m*-Chloroperoxybenzoic acid (*m*-CPBA, 10.4 g, 75%, 36.4 mmol) was added to a cold (0 °C) and stirred solution of aldehyde **21** (2.0 g, 9.1 mmol) in CH_2Cl_2 (91 mL). After being stirred for 3 h at 0 °C, the reaction mixture was quenched with an aqueous solution of Na_2SO_3 (3.74 g, 36.4 mmol). The mixture was washed with 3 N NaOH (50 mL), H_2O (2 × 20 mL), and brine (20 mL) and then dried ($MgSO_4$). Concentration followed by flash column chromatography (silica, 10% EtOAc/hexanes) gave **22** (1.65 g, 77%). **22**: oil; R_f = 0.65 (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +32.6° (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2953, 2864, 1732, 1230, 1209, 1173, 1144, 1060 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.33 (m, 5H), 5.95 (d, *J* = 3.3 Hz, 1H), 4.63 (s, 2H), 3.87 (ddd, *J* = 11.5, 9.5, 3.3 Hz, 1H), 3.71 (ddd, *J* = 11.5, 4.4, 3.6 Hz, 1H), 3.43 (ddd, *J* = 6.5, 3.4, 3.1 Hz, 1H), 2.01 (m, 1H), 1.95 (m, 1H), 1.82 (m, 1H), 1.46 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 159.8 (s), 138.0 (s), 128.4 (2 × d), 127.8 (d), 127.6 (2 × d), 93.3 (d), 72.4 (d), 71.4 (t), 63.2 (t), 24.4 (t), 20.8 (t); MS *m*/*e* (rel intensity) 235 (M^+, 0.4), 191 (2), 148 (0.1); HRMS calcd for $C_{12}H_{15}O_2$ [M − CO_2H]$^+$ 191.107 20, found 191.107 48.

(2*R*/2*S*,3*S*)-3-(Benzyloxy)tetrahydropyran-2-ol (23). A mixture of formate **22** (1.5 g, 6.36 mmol), Na_2CO_3 (736.0 mg, 6.0 mmol), and methanol (32 mL) was stirred at 25 °C for 30 min. Dilution with ether (100 mL) and petroleum ether (50 mL) followed by filtration through a Celite pad and concentration gave the 1:1 mixture **23** (1.32 g, 71%). **23**: oil; R_f = 0.33 (silica, 30% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 3396, 3010, 2949, 2862, 1496, 1466, 1454, 1356, 1274, 1080 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$:D_2O) δ 7.34 (m, 10 H), 4.94 (d, *J* = 2.2 Hz, 1H), 4.76 (d, *J* = 5.3 Hz, 1H), 4.68 (m, 2H), 4.67 (d, *J* = 11.7 Hz, 1H), 4.53 (d, *J* = 11.9 Hz, 1H), 3.94 (m, 2H), 3.54 (m, 3H), 3.25 (ddd, *J* = 9.0, 4.8, 3.3 Hz, 1H), 2.06 (m, 1H), 1.95 (m, 1H), 1.62 (m, 4H), 1.54 (m, 1H), 1.50 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 138.6 (s), 138.1 (s), 128.5 (2 × d), 128.3 (2 × d), 127.8 (2 × d), 127.7 (2 × d), 127.6 (d), 127.5 (d), 96.5 (d), 92.3 (d), 77.5 (d), 74.6 (d), 71.7 (t), 70.7 (t), 63.4 (t), 61.6 (t), 26.3 (t), 24.2 (t), 23.1 (t), 22.6 (t); MS *m*/*e* (rel intensity) 208 (M^+, 0.01), 117 (2), 91 (100); HRMS calcd for $C_{12}H_{16}O_3$ (M^+) 208.109 94, found 108.109 90.

3(*S*)-(Benzyloxy)tetrahydropyran-2-one (24). To a stirred mixture of pyridinium chlorochromate (PCC, 1.56 g, 7.2 mmol), dry CH_2Cl_2 (50 mL), and sodium acetate (79.0 mg, 0.96 mmol) was added a solution of **23** (1.0 g, 4.8 mmol) and CH_2Cl_2 (15 mL) dropwise over ca. 5 min. After 12 h, the reaction was diluted with 50 mL of dry pentane−Et_2O (2:1, v/v, from Na_2SO_4), and the supernatent was filtered through a plug of silica gel. The chromiun salts were washed with additional pentane−Et_2O, and the washing were passed through the plug of silica gel. Concentration afforded **24** (673.0 mg, 68%). **24**: oil; R_f = 0.42 (silica, 30% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = −35.2° (*c* 1.42, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3020, 2965, 2866, 1748, 1455, 1399, 1309, 1272, 1253, 1161, 1132, 1114, 1067 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 5H), 4.93 (d, *J* = 11.8 Hz, 1H), 4.64 (d, *J* = 11.8 Hz, 1H), 4.38 (ddd, *J* = 11.3, 4.9, 4.8 Hz, 1H), 4.26 (ddd, *J* = 11.5, 7.7, 4.4 Hz, 1H), 4.05 (dd, *J* = 8.0, 7.2 Hz, 1H), 2.23 (m, 1H), 1.98 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 171.4 (s), 137.4 (s), 128.5 (2 × d), 128.0 (2 × d), 127.9 (d), 72.7 (d), 72.5 (t), 67.9 (t), 26.1 (t), 20.8 (t); MS *m*/*e* (rel intensity) 206 (M^+, 0.1), 179 (0.5), 105 (43), 91 (100); HRMS calcd for $C_{12}H_{13}O_3$ [M − H]$^+$ 205.086 47, found 205.086 72.

(2*R*,3*S*,2′*R*,3′*S*)-[2-[3′-(Benzyloxy)tetrahydropyran-2′-yl]ethynyl]tetrahydropyran-3-ol (26). The vinyl dibromide **18** (1.0 g, 2.5 mmol) in a stirred solution of dry THF (25 mL) at −78 °C was treated dropwise with *n*-BuLi (2.94 mL, 5.0 mmol, 1.7 M in THF). The mixture was then warmed to −35 °C, and stirring was continued for 1 h. The solution was cooled to −78 °C, and the compound **24** (500.0 mg, 2.4 mmol) in dry THF (3 mL) was added dropwise over a 5-min period. After 1.5 h at 25 °C, the reaction was carefully quenched with saturated NH_4Cl (10 mL) and diluted with ether (100 mL). The ethereal portion was dried ($MgSO_4$) and concentrated and the residue subjected to flash chromatography (silica, 30% EtOAc/hexanes) to give **25** (980.0 mg, 90%). The condensed compound **25** (500.0 mg, 1.12 mmol) was dissolved in dry CH_3CN (150 mL), and Et_3SiH (0.58 mL, 3.6 mmol) and $BF_3{\cdot}Et_2O$ (0.2 mL, 1.6 mmol) were added at 0 °C. After being stirred for 1.5 h, the reaction mixture was diluted with ether (100 mL) and then washed with aqueous saturated NH_4Cl solution (2 × 50 mL), H_2O (2 × 50 mL), and brine (50 mL). Drying ($MgSO_4$), concentration, and flash column chromatography (silica, 30% EtOAc/hexanes) gave pure **26** (340.0 mg, 88%). **26**: oil; R_f = 0.5 (silica, 30% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +29.0° (*c* 1.25, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3009, 2949, 2859, 1266, 1224, 1208, 1005, 948 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 5H), 4.69 (d, *J* = 11.9 Hz, 1H), 4.64 (d, *J* = 11.9 Hz, 1H), 4.29 (dd, *J* = 6.3, 1.3 Hz, 1H), 4.28 (dd, *J* = 6.9, 1.4 Hz, 1H), 3.93 (m, 2H), 3.62 (m, 1H), 3.51 (ddd, *J* = 11.3, 8.1, 3.2 Hz, 1H), 3.43 (ddd, *J* = 8.8, 8.7, 3.1 Hz, 1H), 2.41 (br s, 1H, D_2O-exchangeable), 2.12 (dddd, *J* = 11.4, 7.0, 3.6, 3.1 Hz, 2H), 1.83 (m, 1H), 1.74 (m, 2H), 1.62 (m, 2H), 1.54 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 138.2 (s), 128.4 (2 × d), 127.7 (2 × d), 127.6 (d), 84.6 (s), 83.3 (s), 75.8 (d), 72.6 (d), 71.5 (t), 69.9 (d), 69.5 (d), 66.2 (t), 65.8 (t), 29.4 (t), 27.4 (t), 23.4 (t), 23.1 (t); MS *m*/*e* (rel intensity) 225 [(M − C_7H_7)$^+$, 0.5], 208 (1), 179 (2), 151 (16), 137 (93), 123 (35). Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.15; H, 7.59. Found: C, 72.20; H, 7.61.

(2*R*,3*S*,2″*R*,3″*S*)-2-[2′-[3″-(Benzyloxy)tetrahydropyran-2″-yl]ethyl]tetrahydropyran-3-ol (27). Pd catalyst (5% Pd−C, 10.0 mg) was added in one portion to a solution of compound **26** (150.0 mg, 0.34 mmol) in EtOAc (10 mL) under a H_2 atmosphere at 25 °C. The reaction mixture was stirred for 2 h at room temperature before the catalyst was removed by filtration. Concentration followed by flash chromatography (silica, 30% EtOAc/hexanes) gave the reduced product **27** (133.0 mg, 88%). **27**: oil; R_f = 0.22 (silica, 30% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +48.6° (*c* 1.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 5H), 4.61 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 3.87 (br dd, *J* = 10.9, 1.7 Hz, 2H), 3.32 (m, 3H), 3.12 (m, 2H), 3.03 (m, 1H), 2.24 (br dd, *J* = 12.1, 2.2 Hz, 2H), 2.04 (m, 2H), 1.88 (m, 1H), 1.64 (m, 6H), 1.40 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 138.5 (s), 128.3 (2 × d), 127.8 (2 × d), 127.6 (d), 82.1 (d), 81.0 (d), 77.5 (d), 70.9 (t), 69.8 (d), 67.6 (t), 67.5 (t), 32.4 (t), 29.3 (t), 27.4 (t), 26.9 (t), 25.7 (t), 25.4 (t); MS *m*/*e* (rel intensity) 320 (M^+, 0.02), 302 (0.05), 212 (8), 196 (4), 184 (1), 141 (11), 112 (20), 91 (100); HRMS calcd for $C_{19}H_{28}O_4$ (M^+) 320.198 76, found 320.196 34. Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.25; H, 8.75. Found: C, 71.30; H, 8.73.

(2*R*,2″*R*,3″*S*)-2-[2′[3″-(Benzyloxy)tetrahydropyran-2″-yl]ethyl]tetrahydropyran-3-one (d-10). Oxalyl chloride (0.10 mL, 1.2 mmol) was slowly added to a cold (−78 °C) and stirred solution of DMSO (0.14 mL, 2.0 mmol) in dry CH_2Cl_2 (5 mL) under argon. After the solution was stirred for 10 min, the alcohol **27** (130.0 mg, 0.4 mmol) in CH_2Cl_2 (5 mL) was dropwise added at −78 °C, and stirring was continued at that temperature for 1 h. Et_3N (0.56 mL, 4.0 mmol) was then added

at −78 °C. The mixture was allowed to warm to 25 °C over a 1-h period, diluted with CH_2Cl_2 (10 mL), and washed with brine (2 × 10 mL). The organic solution was dried ($MgSO_4$) and concentrated to afford a crude product that was purified by flash column chromatography (silica, 20% EtOAc/hexanes) to yield the ketone **d-10** (120.8 mg, 92%). **d-10**: oil; $R_f = 0.45$ (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D = +18.2°$ (*c* 1.12, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3011, 2942, 2860, 1726, 1246, 1044 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (m, 5H), 4.61 (d, $J = 11.6$ Hz, 1H), 4.48 (d, $J = 11.6$ Hz, 1H), 4.04 (dddd, $J = 11.6$, 5.1, 5.1, 1.2 Hz, 1H), 3.87 (ddd, $J = 11.4$, 4.4, 1.8 Hz, 1H), 3.85 (m, 1H), 3.70 (ddd, $J = 11.6$, 9.7, 3.7 Hz, 1H), 3.29 (ddd, $J = 11.4$, 11.4, 3.2 Hz, 1H), 3.14 (m, 2H), 2.56 (ddd, $J = 15.9$, 4.6, 4.6 Hz, 1H), 2.42 (ddd, $J = 15.9$, 9.0, 7.0 Hz, 1H), 2.24 (ddd, $J = 12.3$, 2.0, 1.5 Hz, 1H), 2.11 (m, 1H), 2.02 (m, 2H), 1.87 (m, 2H), 1.66 (m, 2H), 1.60 (m, 1H), 1.41 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 209.2 (s), 138.6 (s), 128.3 (2 × d), 127.7 (2 × d), 127.6 (d), 83.1 (d), 80.5 (d), 77.3 (d), 70.8 (t), 67.5 (t), 65.0 (t), 37.5 (t), 29.3 (t), 27.6 (t), 26.1 (t), 25.5 (t), 25.4 (t); MS *m*/*e* (rel intensity) 318 (M^+, 0.3), 247 (1.2), 226 (1), 209 (1.5), 139 (2), 98 (5), 91 (100); HRMS calcd for $C_{19}H_{26}O_4$ (M^+) 318.183 11, found 318.183 18.

(4a*R*,5a*S*,9a*R*,11a*R*)-Dodecahydropyrano[3,2-*b*]pyrano-[3′,2′-*f*]oxepin (d-14). 10% Pd/C catalyst (8.0 mg) was added to a stirred solution of the compound **d-10** (106.0 mg, 0.33 mmol) in EtOAc (5 mL) at 25 °C under H_2 atmosphere. When monitoring of the reaction by TLC indicated that all starting material had been consumed (2 h), the reaction mixture was filtered through a Celite pad and rinsed thoroughly with EtOAc. Following the solvent removal, the crude product was purified by flash column chromatography (silica, 45% EtOAc/hexanes) to give **d-12** (70.7 mg, 91%), $[\alpha]^{25}_D = +26.3°$ (*c* 1.2, $CHCl_3$). To a solution of **d-12** (70.7 mg, 0.31 mmol) in CH_3NO_2 (10 mL) at 0 °C was added Ph_2MeSiH (0.2 mL, 1.0 mmol) and then TMSOTf (0.2 mL, 1.0 mmol), and the resulting solution was stirred for 15 min. The reaction mixture was then diluted with ether (30 mL) and washed with saturated $NaHCO_3$ (2 × 30 mL) and brine (30 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 40% EtOAc/hexanes) gave cyclized product **d-14** (57.2 mg, 87%). **d-14**: $[\alpha]^{25}_D = +37°$ (*c* 1.62, $CHCl_3$), showing identical IR, NMR and MS spectra as those of racemate **14**.

6-[(Benzyloxy)[(2*R*,3*S*)-3-(*tert*-butyldimethylsiloxy)tetrahydropyran-2-yl]-(*R*)-methyl]-3,4-dihydro-2*H*-pyran (41) and 6-[(benzyloxy)[(2*R*,3*S*)-3-(*tert*-butyldimethylsiloxy)-tetrahydropyran-2-yl]-(*S*)-methyl]-3,4-dihydro-2*H*-pyran (44). A stirred solution of **38** (3.13 g, 8.4 mmol) in 1.5 mL of dry THF was treated at −78 °C with *n*-BuLi (8.0 mL, 8.8 mmol of 1.1 M solution in cyclohexane). After being stirred for 15 min a solution of **17** (2.15 g, 8.8 mmol) in THF (2 mL) was added dropwise. The reaction mixture was stirred for 2 h and then diluted with Et_2O and quenched with H_2O. Aqueous workup (Et_2O) and a quick pass through a short silica gel column (flash silica, 20−30% EtOAc/hexanes) yielded a mixture of allylic alcohols **40** and **43** (2.1 g, 6.4 mmol, 86%) which was used without further purification in the following sequence of reactions. A stirred solution of the alcohols **40** and **43** (111.5 mg, 0.34 mmol) in dry THF (3.4 mL) at 0 °C under N_2 was treated with NaH (16.4 mg of a 60% dispersion in oil, 0.41 mmol). The reaction was stirred at room temperature for 15 min and then treated with BnBr (0.62 mL, 89.0 mg, 1.7 mmol) and tetrabutylammonium iodide (TBAI) (3.7 mg, 0.01 mmol), stirred for 12 h, and then quenched with saturated NH_4Cl. Aqueous workup (Et_2O) and silica gel chromatography (flash silica, 10−15% EtOAc/hexanes) yielded the benzyl ether **41** (100.2 mg, 0.24 mmol, 71%) and its epimer **44** (12.5 mg, 0.03 mmol, 9%). **41**: crystalline solid; mp 65−66 °C (ether/*n*-hexane); $R_f = 0.60$ (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D = +36.3°$ (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3003, 2950, 2930, 2856, 1497, 1471, 1362, 1258, 1066, 884 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 5H), 4.89 (dd, $J = 3.6$, 3.6 Hz, 1H), 4.73 (d, $J = 11.5$ Hz, 1H), 4.42 (d, $J = 11.5$ Hz, 1H), 4.11 (br s, 1H), 4.07 (ddd, $J = 10.5$, 5.4, 4.3 Hz, 1H), 3.94 (m, 2H), 3.87 (ddd, $J = 10.2$, 8.6, 4.7 Hz, 1H), 3.30 (ddd, $J = 11.2$, 11.2, 2.9 Hz, 1H), 3.25 (dd, $J = 8.6$, 1.8 Hz, 1H), 2.07 (m, 3H), 1.84 (m, 2H), 1.64 (m, 2H), 1.45 (m, 1H), 0.87 (s, 9H), 0.06 (s, 3H), 0.01 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 151.5 (s), 139.2 (s), 128.5 (d), 128.5 (d), 128.1 (d), 128.1 (d), 127.6 (d), 97.8 (d), 83.3 (d), 77.0 (d), 72.5 (t), 68.3 (t), 67.2 (d), 66.5 (t), 33.9 (t), 26.3 (q), 25.4 (t), 23.0 (t), 20.4 (t), 18.4 (s), −3.1 (q), −4.3 (q); MS *m*/*e* (rel intensity) 418 (M^+, 1), 361 ($[M - {}^tBu]^+$, 8), 255 (52), 215 (99), 204 (67), 179 (68), 145 (39), 91 (100), 83 (88), 75 (99), 73 (100), 71 (46), 55 (45); HRMS calcd for $C_{24}H_{38}O_4Si$ (M^+) 418.253 94, found 418.254 66; calcd for $C_{20}H_{29}O_4Si$ ($M - {}^tBu)^+$ 361.183 52, found 361.187 42. **44**: white solid; mp 30−31 °C (ether/*n*-hexane); $R_f = 0.66$ (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D = -22.8°$ (*c* 0.38, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3003, 2955, 2930, 2856, 1676, 1496, 1463, 1362, 1258, 1219, 1136, 1068, 916, 862, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 5H), 4.88 (dd, $J = 3.6$, 3.6 Hz, 1H), 4.71 (d, $J = 12.5$ Hz, 1H), 4.45 (d, $J = 12.5$ Hz, 1H), 4.04 (m, 1H), 4.01 (d, $J = 2.7$ Hz, 1H), 3.93 (dd, $J = 9.3$, 2.7 Hz, 1H), 3.61 (ddd, $J = 13.2$, 9.3, 4.6 Hz, 1H), 3.39 (dd, $J = 9.3$, 2.7 Hz, 1H), 3.35 (ddd, $J = 10.9$, 10.9, 2.8 Hz, 1H), 2.09 (m, 2H), 1.94 (m, 1H), 1.84 (m, 2H), 1.61 (m, 2H), 1.34 (m, 1H), 0.78 (s, 9H), 0.01 (s, 3H), −0.03 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 150.7 (s), 139.0 (s), 128.6 (d), 128.6 (d), 128.4 (d), 128.4 (d), 127.7 (d), 100.1 (d), 84.2 (d), 77.1 (d), 71.2 (t), 67.7 (t), 67.6 (d), 66.1 (t), 33.5 (t), 26.2 (q), 25.0 (t), 23.0 (t), 20.5 (t), 18.3 (s), −3.4 (q), −4.6 (q); MS *m*/*e* (rel intensity) 361 ($[M - {}^tBu]^+$, 4), 215 (33), 179 (27), 149 (30), 117 (16), 97 (14), 91 (100); HRMS calcd for $C_{24}H_{38}O_4Si$ (M^+) 418.253 94, found 418.252 83; calcd for $C_{20}H_{29}O_4Si$ ($M - {}^tBu)^+$ 361.183 51, found 361.184 36.

(5,6-Dihydro-4*H*-pyran-2-yl)[(2*S*,3*R*)-3-(*tert*-butyldimethylsiloxy)tetrahydropyran-2-yl]methanone (42). SO_3·py complex (5.92 g, 37.2 mmol) was added to a stirred crude mixture of the alcohols **40** and **43** (prepared from 7.44 mmol of **38**), Et_3N (5.18 mL, 37.2 mmol), dry DMSO (4.7 mL, 66.9 mmol), and CH_2Cl_2 (17.7 mL) at 0 °C. After 2 h, the reaction mixture was diluted with ether (80 mL), washed with H_2O (3 × 20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated. Chromatography of the residue on silica gel (20% EtOAc/hexanes) yielded the ketone **42** (1.2 g, 3.7 mmol, 50% overall yield from **38**). **42**: colorless oil; $R_f = 0.54$ (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D = +60.6°$ (*c* 2.32, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3016, 2954, 2886, 2858, 1738, 1681, 1471, 1464, 1441, 1290, 1254, 1126, 952, 933, 913 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.14 (dd, $J = 4.3$, 4.3 Hz, 1H), 4.23 (d, $J = 8.6$ Hz, 1H), 4.09 (m, 2H), 3. 97 (ddd, $J = 11.5$, 3.0, 1.5 Hz, 1H), 3.83 (br ddd, $J = 10.4$, 8.6, 4.5 Hz, 1H), 3.38 (ddd, $J = 11.5$, 11.5, 2.6 Hz, 1H), 2.24 (m, 2H), 2.06 (m, 1H), 1.84 (m, 2H), 1.75 (m, 1H), 1.66 (m, 1H), 1.54 (m, 1H), 0.82 (s, 9H), 0.02 (s, 3H), −0.05 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 193.9 (s), 151.7 (s), 114.4 (d), 80.6 (d), 69.6 (d), 68.2 (t), 66.6 (t), 33.7 (t), 26.0 (q), 25.1 (t), 21.8 (t), 21.4 (t), 18.2 (s), −4.1 (q), −4.8 (q); MS *m*/*e* (rel intensity) 326 (M^+, 3), 269 (100), 185 (58), 117 (41), 155 (58), 129 (58), 111 (32), 101 (31), 83 (88), 75 (100), 73 (100), 59 (64), 55 (100); HRMS calcd for $C_{13}H_{21}O_4Si$ ($M - {}^tBu)^+$ 269.120 91, found 269.118 98.

(*S*)-(5,6-Dihydro-4H-pyran-2-yl)[(2*R*,3*S*)-3-(*tert*-butyldimethylsiloxy)tetrahydropyran-2-yl]methanol (43) from 42. To a stirred solution of ketone **42** (1.22 g, 3.75 mmol) in MeOH (37 mL) at 0 °C was added $NaBH_4$ (283.0 mg, 7.5 mmol). After 30 min of vigorous stirring the solvent was removed by vacuum evaporation. Dilution with ether (60 mL), followed by washing with H_2O (2 × 30 mL) and brine (25 mL), drying ($MgSO_4$), concentration, and flash chromatography (silica, 10% EtOAc/hexanes containing 1 mL/L of pyridine) produced the alcohol **43** (984.0 mg, 3.0 mmol, 80%). **43**: colorless oil; $R_f = 0.30$ (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D = +37.6°$ (*c* 0.41, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3460, 3025, 2954, 2858, 1678, 1391, 1257, 1224, 1168, 1098 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.85 (dd, $J = 3.7$, 3.7 Hz, 1H), 4.08 (dd, $J = 6.4$, 4.2 Hz, 1H), 4.03 (m, 2H), 3.94 (ddd, $J = 13.2$, 2.4, 2.0 Hz, 1H), 3.66 (ddd, $J = 10.5$, 9.0, 4.5 Hz, 1H), 3.58 (d, $J = 4.2$ Hz, 1H), 3.33 (m, 1H), 3.28 (dd, $J = 9.0$, 6.4 Hz, 1H), 2.06 (m, 3H), 1.83 (m, 2H), 1.65 (m, 2H), 1.52 (m, 1H), 0.88 (s, 9H), 0.12 (s, 3H), 0.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 152.9 (s), 100.7 (d), 82.2 (d), 75.2 (d), 72.3 (d), 68.5 (t), 66.6 (t), 34.2 (t), 26.1 (q), 25.7 (t), 22.8 (t), 20.5 (t), 18.3 (s), −3.11 (q), −4.4 (q); MS *m*/*e* (rel intensity) 328 (M^+, 1), 271 ($[M - {}^tBu]^+$, 12), 215 (72), 214 (87), 201 (41), 197 (79), 173 (55), 145 (95), 83 (98), 75 (100), 73 (100); HRMS calcd for $C_{17}H_{32}O_4Si$ (M^+) 328.206 99, found 328.206 70.

Benzylation of **43** (525.0 mg, 1.6 mmol) to give **44** (650.0 mg, 1.55 mmol, 97%) was performed according to an earlier procedure (cf. benzylation of **40** and **41** mixture).

(2*S*,3*S*)-2-[(Benzyloxy)(2*R*,3*S*)-3-(*tert*-butyldimethylsiloxy)tetrahydropyran-2-yl]-(*R*)-methyl]dihydropyran-3-ol (45) and (2*R*,3*R*)-2-[(Benzyloxy)(2*R*,3*S*)-3-(*tert*-butyldimethylsiloxy)tetrahydropyran-2-yl]-(*R*)-methyl]dihydropyran-3-ol (46). To a stirred solution of the vinyl ether **44** (536.0 mg, 1.28 mmol) in dry THF (13 mL) at 0 °C was added BH_3-Me_2S (1.9 mL, 3.83 mmol 2 M in THF) dropwise over a 5-min period. Then the mixture was stirred for 12 h at 25 °C, and the excess borane was quenched carefully with cold H_2O (0.57 mL). Dropwise addition of a mixture of 3 N NaOH (1.3 mL, 4.02 mmol) and 30% H_2O_2 (1.15 mL) and continued stirring for 30 min resulted in a white heterogeneous mixture. Dilution with ether (100 mL), followed by washing with H_2O (2 × 80 mL) and brine (80 mL), drying ($MgSO_4$), concentration, and flash chromatography (silica, 15−30% EtOAc/hexanes) produced the alcohols **45** (418.6 mg, 0.96 mmol, 75%) and its less polar diastereomer **46** (43.6 mg, 0.10 mmol, 8%). **45**: white solid; mp 71−73 °C; R_f = 0.23 (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +9.7° (*c* 0.47, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3674, 3506, 3088, 2949, 2857, 1602, 1496, 1471, 1254, 1094, 1007, 923, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 5H), 4.66 (d, *J* = 12.4 Hz, 1H), 4.66 (d, *J* = 12.4 Hz, 1H), 3.95 (dd, *J* = 3.0, 3.0 Hz, 1H), 3.89 (m, 4H), 3.57 (dd, *J* = 8.7, 3.0 Hz, 1H), 3.44 (br s, 1H), 3.36 (dd, *J* = 9.3, 3.0 Hz, 1H), 3.30 (m, 2H), 2.09 (m, 1H), 1.97 (m, 1H), 1.61 (m, 4H), 1.38 (m, 2H), 0.82 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.3 (s), 128.3 (d), 128.3 (d), 128.0 (d), 128.0 (d), 127.5 (d), 82.8 (d), 82.6 (d), 78.0 (d), 72.2 (t), 68.0 (d), 67.9 (t), 67.5 (t), 66.4 (d), 33.5 (t), 32.4 (t), 25.8 (q), 25.5 (t), 24.7 (t), 17.9 (s), −4.2 (q), −4.9 (q); MS *m*/*e* (rel intensity) 379 ([M − ^{t}Bu]$^+$, 1), 271 (8), 187 (27), 129 (22), 107 (29), 101 (62), 97 (39), 92 (41), 91 (100), 71 (100); HRMS calcd for $C_{24}H_{41}O_5Si$ (M + H)$^+$ 437.272 33, found 437.271 89; calcd for $C_{20}H_{31}O_5Si$ (M − ^{t}Bu)$^+$ 379.19408, found 379.19376. **46**: colorless oil; R_f = 0.4 (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +13.2° (*c* 0.61, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3385, 3019, 2930, 2857, 1602, 1463, 1253, 1212, 1140, 1094, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 5H), 4.75 (d, *J* = 12.0 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 3.98 (dd, *J* = 4.3, 2.0 Hz, 1H), 3.97 (m, 1H), 3.88 (ddd, *J* = 10.9, 2.0, 2.0 Hz, 1H), 3.66 (m, 2H), 3.37 (m, 3H), 3.24 (ddd, *J* = 10.9, 10.9, 3.6 Hz, 1H), 2.14 (br dd, *J* = 12.6, 3.2 Hz, 1H), 2.04 (br d, *J* = 12.4, 3.2 Hz, 1H), 1.64 (m, 4H), 1.40 (m, 2H), 0.86 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.1 (s), 128.3 (d), 128.3 (d), 128.1 (d), 128.1 (d), 127.7 (d), 82.6 (d), 81.7 (d), 80.3 (d), 73.3 (t), 68.1 (t), 67.5 (t), 67.4 (d), 66.7 (d), 33.8 (t), 31.7 (t), 25.8 (q), 25.1 (t), 25.1 (t), 17.8 (s), −4.0 (q), −5.0 (q); MS *m*/*e* (rel intensity) 379 ([M − ^{t}Bu]$^+$, 1), 187 (20), 171 (21), 145 (24), 129 (18), 105 (23), 97 (62), 91 (100), 75 (100), 71 (100), 57 (72), 53 (56); HRMS calcd for $C_{20}H_{31}O_5Si$ (M − ^{t}Bu)$^+$ 379.194 08, found 379.195 42.

(2*R*)-2-[(Benzyloxy)(2*R*,3*S*)-3-(*tert*-butyldimethylsiloxy)tetrahydropyran-2-yl]-(*S*)-methyl]dihydropyran-3-one (47). The alcohol **45** was oxidized to the ketone by the usual Swern procedure.[8] Oxalyl chloride (1.6 mL, 18.0 mmol) in 30 mL of CH_2Cl_2 was cooled to −60 °C, DMSO (3.83 mL, 54.0 mmol) was added, and the reaction mixture was stirred for 15 min. Alcohol **45** (2.62 g, 6.0 mmol) in 6 mL of CH_2Cl_2 was added. After 30 min, Et_3N (12.5 mL, 90.0 mmol) was added dropwise. The mixture was allowed to warm to rt over a 1-h period, diluted with CH_2Cl_2 (90 mL), and washed with brine (90 mL). The organic solution was dried over anhydrous $MgSO_4$ and concentrated to afford a crude product that was purified by flash chromatography (silica, 20% EtOAc/hexanes) to yield the ketone **47** (2.32 g, 89%). **47**: colorless oil; R_f = 0.54 (silica, 30% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +58.1° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3019, 2952, 2857, 1723, 1471, 1362, 1253, 1136, 1099, 1007, 946, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 5H), 4.55 (d, *J* = 11.8 Hz, 1H), 4.54 (d, *J* = 11.8 Hz, 1H), 4.29 (dd, *J* = 3.8, 3.0 Hz, 1H), 4.19 (d, *J* = 3.0 Hz, 1H), 4.16 (ddd, *J* = 10.7, 5.0, 5.0 Hz, 1H), 3.85 (dd, *J* = 10.7, 4.0, 3.8 Hz, 1H), 3.69 (m, 2H), 3.50 (dd, *J* = 7.4, 3.8 Hz, 1H), 3.35 (ddd, *J* = 11.3, 11.3, 3.0 Hz, 1H), 2.64 (ddd, *J* = 16.2, 6.7, 6.7 Hz, 1H), 2.45 (ddd, *J* = 16.2, 8.5, 7.4 Hz, 1H), 2.21 (dddd, *J* = 15.0, 13.7, 8.5, 6.7 Hz, 1H), 1.97 (m, 2H), 1.71 (m, 1H), 1.56 (m, 1H), 1.43 (m, 1H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 210.4 (s), 138.8 (s), 128.5 (d), 128.5 (d), 128.3 (d), 128.3 (d), 127.8 (d), 82.5 (d), 81.8 (d), 77.4 (d), 73.5 (t), 67.6 (d), 67.3 (t), 65.6 (t), 38.0 (t), 32.7 (t), 26.2 (q), 25.0 (t), 24.4 (t), 18.3 (s), −3.5 (q), −4.3 (q); MS *m*/*e* (rel intensity) 377 ([M − ^{t}Bu]$^+$, 3), 355 (35), 285 (38), 269 (24), 229 (10), 215 (15), 203 (31), 199 (23), 190 (88), 185 (91), 173 (17), 157 (27), 145 (74), 129 (35), 114 (33), 91 (100); HRMS calcd for $C_{20}H_{29}O_5Si$ (M − ^{t}Bu)$^+$ 377.178 43, found 377.179 77.

(9*S*,4a*R*,8a*R*,10a*S*)-9-(Benzyloxy)octahydro-1,8,10-trioxaanthracen-4a-ol (48). A mixture of **47** (2.3 g, 5.3 mmol), *n*-Bu_4NF (2.17 g, 6.9 mmol), and THF (53 mL) was stirred at 25 °C for 12 h. The reaction was diluted with CH_2Cl_2, washed with a saturated NaCl solution (150 mL) and H_2O (150 mL), and dried ($MgSO_4$). Concentration followed by flash chromatography (silica, 20% EtOAc/hexanes) afforded **48** (1.51 g, 4.72 mmol, 89%). **48**: crystalline solid; mp 71−73 °C (ether/*n*-hexane); R_f = 0.33 (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +5.15° (*c* 0.66, acetone); IR ($CHCl_3$) ν_{max} 3458, 3030, 3009, 2951, 2856, 1636, 1209, 1157, 1102, 1032, 974, 950, 859 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 5H), 5.52 (s, 1H), 4.95 (d, *J* = 11.7 Hz, 1H), 4.67 (d, *J* = 11.7 Hz, 1H), 3.99 (dd, *J* = 10.9, 4.5 Hz, 1H), 3.93 (m, 3H), 3.52 (d, *J* = 3.6 Hz, 1H), 3.46 (dd, *J* = 10.1, 2.7 Hz, 1H), 3.43 (ddd, *J* = 11.5, 11.5, 3.0 Hz, 1H), 3.35 (ddd, *J* = 13.0, 11.0, 2.1 Hz, 1H), 2.08 (br dd, *J* = 12.0, 3.4 Hz, 1H), 2.01 (br dd, *J* = 13.4, 1.6 Hz, 1H), 1.86 (m, 1H), 1.74 (m, 2H), 1.58 (m, 2H), 1.46 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 138.1 (s), 129.0 (d), 128.9 (d), 128.4 (d), 128.2 (d), 127.4 (d), 93.4 (s), 77.7 (d), 77.5 (d), 76.9 (d), 74.9 (t), 68.9 (t), 68.3 (t), 64.9 (d), 35.3 (t), 29.8 (t), 26.0 (t), 23.3 (t); ^1H NMR (400 MHz, C_6D_6) δ 7.19 (m, 5H), 5.73 (s, 1H), 4.86 (d, *J* = 11.8 Hz, 1H), 4.55 (d, *J* = 11.8 Hz, 1H), 4.25 (ddd, *J* = 10.2, 10.2, 4.5 Hz, 1H), 4.09 (dd *J* = 3.6, 3.1 Hz, 1H), 3.75 (dd, *J* = 10.2, 3.1 Hz, 1H), 3.75 (m, 2H), 3.58 (d, *J* = 3.6 Hz, 1H), 3.11 (ddd, *J* = 12.2, 12.2, 2.2 Hz, 1H), 3.05 (ddd, *J* = 13.1, 11.5, 2.2 Hz, 1H), 2.32 (br d, *J* = 13.1 Hz, 1H), 2.06 (m, 1H), 2.00 (ddddd, *J* = 13.5, 13.5, 11.5, 4.5, 4.3 Hz, 1H), 1.66 (ddd, *J* = 13.5, 13.5, 4.5 Hz, 1H), 1.56 (br dddd, *J* = 11.8, 10.2, 10.2, 4.0 Hz, 1H), 1.47 (br ddddd, *J* = 13.5, 12.2, 10.2, 4.5, 4.0 Hz, 1H), 1.20 (br d, *J* = 13.5 Hz, 1H), 1.09 (ddddd, *J* = 13.5, 4.5, 2.0, 2.0, 2.0 Hz, 1H); ^{13}C NMR (C_6D_6) δ 138.5 (s), 128.9 (d), 128.8 (d), 128.4 (d), 128.2 (d), 128.0 (d), 93.5 (s), 78.1 (d), 77.8 (d), 77.5 (d), 74.8 (t), 68.6 (t), 68.0 (t), 64.9 (d), 35.7 (t), 30.1 (t), 25.9 (t), 23.4 (t); MS *m*/*e* (rel intensity) 302 ([M − H_2O]$^+$, 3), 212 (76), 126 (100), 113 (60), 98 (91), 91 (97), 71 (65); HRMS calcd for $C_{18}H_{22}O_4$ (M − H_2O)$^+$ 302.151 81, found 302.146 83. Anal. Calcd for $C_{18}H_{24}O_5$: C, 67.50; H, 7.50. Found: C, 67.49; H, 7.52.

(9*S*,4a*R*,8a*R*,9a*R*,10a*S*)-9-(Benzyloxy)decahydro-1,8,10-trioxaanthracene (49). To a solution of **48** (1.22 g, 3.81 mmol) in CH_3CN (38 mL) at −78 °C were added Et_3SiH (9.13 mL, 57.2 mmol) and then $BF_3{\cdot}OEt_2$ (7.21 mL, 57.2 mmol). The resulting solution was stirred for 2 h at 0 °C. The reaction mixture was then diluted with ether (100 mL) and washed with saturated $NaHCO_3$ (2 × 50 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$) and concentrated under vacuum. Flash column chromatography (silica, 20% EtOAc/hexanes) afforded **49** (822.4 mg, 2.7 mmol, 71%). **49**: crystalline solid; mp 62−63 °C (*n*-hexane); R_f = 0.65 (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +7.1° (*c* 0.68, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3005, 2855, 1603, 1497, 1464, 1264, 1215, 1103, 978, 898 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 5H), 4.89 (d, *J* = 12.2 Hz, 1H), 4.62 (d, *J* = 12.2 Hz, 1H), 3.97 (m, 2H), 3.80 (br s, 1H), 3.76 (dd, *J* = 3.3, 3.0 Hz, 1H), 3.72 (ddd, *J* = 10.8, 10.0, 4.5 Hz, 1H), 3.49 (d, *J* = 3.3 Hz, 1H), 3.41 (m, 3H), 2.06 (m, 1H), 1.97 (m, 2H), 1.72 (m, 2H), 1.55 (m, 2H), 1.29 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 139.5 (s), 128.6 (d), 128.6 (d), 127.8 (d), 127.8 (d), 127.7 (d), 78.5 (d), 76.7 (d), 76.2 (d), 73.7 (t), 71.1 (d), 68.7 (t), 68.7 (t), 68.4 (d), 30.1 (t), 28.4 (t), 25.8 (t), 21.3 (t); ^1H NMR (400 MHz, C_6D_6) δ 7.30 (m, 5H), 5.02 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.03 (dd, *J* = 3.0, 3.0 Hz, 1H), 3.93 (ddd, *J* = 10.2, 9.7, 5.0 Hz, 1H), 3.90 (br s, 1H), 3.86 (br d, *J* = 11.3 Hz, 1H), 3.79 (br d, *J* = 11.3 Hz, 1H), 3.75 (dd, *J* = 9.7, 3.0 Hz, 1H), 3.50 (d, *J* = 3.0 Hz, 1H), 3.17 (ddd, *J* = 11.3, 11.3, 3.2 Hz, 2H), 2.16 (ddddd, *J* = 13.5, 11.3, 11.3, 4.5, 4.5 Hz, 1H), 2.09 (br d, *J* = 14.5 Hz, 1H), 1.97 (br d, *J* = 13.8 Hz, 1H), 1.50 (m, 2H), 1.29 (dddd, *J* = 13.8, 11.3, 4.3, 3.5 Hz,

1H), 1.21 (br d, J = 12.2 Hz, 1H), 0.97 (br dd, J = 13.5, 3.5 Hz, 1H); ^{13}C NMR (C_6D_6) δ 140.1 (s), 128.6 (d), 128.4 (d), 128.1 (d), 127.9 (d), 127.6 (d), 79.3 (d), 77.3 (d), 76.4 (d), 74.0 (t), 71.3 (d), 68.5 (d), 68.4 (t), 68.3 (t), 30.3 (t), 28.4 (t), 25.9 (t), 21.4 (t); MS m/e (rel intensity) 304 (M^+, 50), 198 (26), 154 (20), 139 (42), 113 (47), 111 (25), 101 (26), 97 (34), 91 (100), 84 (51), 83 (32), 71 (100), 67 (30), 65 (58), 57 (56), 55 (75); HRMS calcd for $C_{18}H_{24}O_4$ (M^+) 304.167 46, found 304.166 57.

When TMSOTf (29 μL, 33.4 mg, 0.15 mmol) was used as catalyst in CH_3NO_2, **48** (32.2 mg, 0.1 mmol) was converted to **49** (30.1 mg, 99%).

(9*S*,4a*R*,8a*R*,9a*R*,10a*S*)-Decahydro-1,8,10-trioxaanthracen-9-ol (50). $Pd(OH)_2$ (20% Pd) catalyst (10.0 mg) was added to a stirred solution of **49** (800.0 mg, 2.63 mmol) in MeOH (3.0 mL) at 25 °C under H_2 atmosphere. After the mixture was stirred for 12 h at 25 °C, the catalyst was filtered off and the solvent was removed under vacuum to give essentially pure **50**. Chromatography of the crude residue on silica gel (eluant 75% EtOAc/hexanes) gave **50** (551.0 mg, 2.58 mmol, 98%). **50**: white solid; mp 128−130 °C (ether/*n*-hexane); R_f = 0.18 (silica, 20% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = −4.4° (*c* 0.34, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3584, 3020, 2856, 1464, 1213, 1107, 1045, 958, 900 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (br d, J = 11.4 Hz, 1H), 3.96 (br d, J = 3.0 Hz, 1H), 3.93 (br d, J = 11.0 Hz, 1H), 3.79 (br s, 1H), 3.56 (ddd, J = 10.8, 9.9, 4.5 Hz, 1H), 3.51 (br d, J = 3.0 Hz, 1H), 3.46 (ddd, J = 12.3, 11.5, 2.0 Hz, 1H), 3.32 (dd, J = 9.9, 3.0 Hz, 1H), 2.31 (br s, 1H), 2.06 (br d, J = 12.1 Hz, 1H), 2.01 (br d, J = 10.3 Hz, 1H), 1.96 (m, 1H), 1.63 (m, 4H), 1.34 (br d, J = 13.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 77.6 (d), 77.5 (d), 71.0 (d), 69.0 (d), 69.0 (d), 68.8 (t), 68.7 (t), 29.7 (t), 28.2 (t), 26.0 (t), 21.4 (t); MS m/e (rel intensity) 214 (M^+, 20), 196 (12), 113 (44), 101 (32), 100 (27), 85 (20), 84 (100), 71 (92); HRMS calcd for $C_{11}H_{18}O_4$ (M^+) 214.12051, found 214.12019; calcd for $C_{11}H_{16}O_3$ ($M - H_2O$)$^+$ 196.109 94, found 196.110 65. Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.68; H, 8.41. Found: C, 61.72; H, 8.39.

(4a*R*,8a*S*,9a*S*,10a*S*)-Octahydro-1,8,10-trioxaanthracen-9-one (51). Prepared from **50** as described for **47** from **45**, using 0.348 mL (3.93 mmol) of oxalyl chloride in 6.5 mL of CH_2Cl_2, 0.836 mL (11.8 mmol) of DMSO, 280.0 mg (1.31 mmol) of **50** in 1 mL of CH_2Cl_2, and 2.74 mL (19.65 mmol) of Et_3N. Chromatography on silica gel (80% EtOAc/hexanes) furnished **51** (255 mg, 1.2 mmol, 92%), more polar than **50**. **51**: crystalline solid; mp 171−173 °C (*n*-hexane); R_f = 0.43 (silica, EtOAc); $[\alpha]^{25}_D$ = +6.6° (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3020, 2953, 2858, 1738, 1464, 1441, 1214, 1114, 1057, 994, 964 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.25 (d, J = 9.7 Hz, 1H), 4.01 (ddd, J = 10.0, 2.4, 2.0 Hz, 1H), 3.96 (ddd, J = 11.5, 2.5, 2.0 Hz, 1H), 3.80 (br s, 1H), 3.61 (br s, 1H), 3.39 (ddd, J = 11.5, 11.5, 2.5 Hz, 1H), 3.37 (ddd, J = 10.0, 9.3, 3.0 Hz, 1H), 3.26 (ddd, J = 10.0, 9.7, 4.5 Hz, 1H), 2.14 (m, 1H), 2.04 (m, 2H), 1.69 (m, 4H), 1.34 (br d, J = 11.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 201.2 (s), 83.8 (d), 82.6 (d), 79.1 (d), 74.8 (d), 68.3 (t), 68.2 (t), 30.6 (t), 27.5 (t), 25.1 (t), 20.5 (t); MS m/e (rel intensity) 212 (M^+, 28), 168 (17), 100 (24), 84 (100), 71 (45), 55 (42); HRMS calcd for $C_{11}H_{16}O_4$ (M^+) 212.104 86, found 212.105 66.

***meso*-(4a*R*,8a*S*,9a*S*,10a*S*)-Octahydro-1,8,10-trioxaanthracen-9-one (52)**. To a stirred solution of ketone **51** (109.0 mg, 0.52 mmol) in dry benzene (5.5 mL) at 25 °C was added dropwise DBU (0.8 mL, 5.14 mmol). After being stirred for 12 h, the solvent was evaporated. Flash column chromatography (silica, 75% EtOAc/hexanes) afforded **52** (107.0 mg, 0.50 mmol, 97%). **52**: crystalline solid; mp 202−204 °C (*n*-hexane); R_f = 0.41 (silica, EtOAc); IR ($CHCl_3$) ν_{max} 3024, 2941, 2860, 1740, 1466, 1445, 1219, 1119, 1096, 1056, 996, 955 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.09 (br d, J = 11.6 Hz, 2H), 3.77 (d, J = 9.2 Hz, 2H), 3.44 (ddd, J = 10.0, 9.2, 4.2 Hz, 2H), 3.40 (m, 2H), 2.25 (br d, J = 11.6 Hz, 2H), 1.68 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 198.5 (s), 83.7 (d), 79.5 (d), 68.4 (t), 30.6 (t), 25.1 (t); ^{1}H NMR (400 MHz, C_6D_6) δ 3.76 (br dd, J = 11.4, 4.0 Hz, 2H), 3.31 (d, J = 9.3 Hz, 2H), 3.10 (ddd, J = 9.6, 9.3, 4.2 Hz, 2H), 2.92 (br dd, J = 11.4, 11.4 Hz, 2H), 1.87 (m, 2H), 1.31 (m, 4H), 1.08 (m, 2H); ^{13}C NMR (C_6D_6) δ 159.9 (s), 83.9 (d), 79.0 (d), 67.6 (t), 30.6 (t), 25.1 (t); MS m/e (rel intensity) 212 (M^+, 34), 168 (27), 123 (45), 113 (17), 100 (40), 85 (49), 84 (100), 71 (94), 69 (51), 57 (82), 56 (68), 55 (97); HRMS calcd for $C_{11}H_{16}O_4$ (M^+) 212.104 86, found 212.104 37.

***meso*-(4a*R*,8a*S*,9a*R*,10a*S*)-9,9-Bis(phenylsulfanyl)-decahydro-1,8,10-trioxaanthracene (53)**. A solution of ketone **52** (61.0 mg, 0.29 mmol) in CH_2Cl_2 (1 mL) freshly distilled from CaH_2 under argon was treated with thiophenol (0.074 mL, 0.72 mmol) at 0 °C. The reaction mixture was stirred for 5 min under N_2, 0.005 mL (0.045 mmol) of $TiCl_4$ was added dropwise, and then the reaction was allowed to warm to rt. After 12 h the reaction mixture was poured onto a saturated aqueous $NaHCO_3$ solution (0.5 mL) and extracted with CH_2Cl_2. The combined organic layers were washed with H_2O (2 × 0.5 mL) and brine (0.5 mL) and dried ($MgSO_4$). Evaporation of the solvent under vacuum and flash chromatography (silica, 20% EtOAc/hexanes) gave **53** (60.0 mg, 50%). **53**: crystalline solid; mp 125−127 °C (EtOAc/*n*-hexane); R_f = 0.66 (silica, 30% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 3060, 3002, 2948, 2853, 1582, 1487, 1439, 1215, 1122, 1091, 1025, 992, 955 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.0 Hz, 2H), 7.55 (d, J = 7.0 Hz, 2H), 7.32 (m, 6H), 3.99 (ddd, J = 11.3, 9.0, 4.6 Hz, 2H), 3.94 (br d, J = 11.5 Hz, 2H), 3.16 (ddd, J = 11.5, 11.5, 3.0 Hz, 2H), 2.75 (d, J = 9.0 Hz, 2H), 2.06 (br d, J = 10.3 Hz, 2H), 1.67 (m, 4H), 1.23 (dddd, J = 11.3, 10.3, 9.0, 4.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 138.9 (d), 138.9 (d), 138.5 (d), 138.5 (d), 130.9 (s), 130.7 (s), 130.0 (d), 129.3 (d), 129.1 (d), 129.1 (d), 128.1 (d), 128.1 (d), 81.1 (d), 72.9 (d), 68.4 (t), 67.6 (t), 30.0 (t), 25.4 (t); MS m/e (rel intensity) 305 ([M − SC_6H_5]$^+$, 100), 287 (19), 205 (97), 195 (83), 109 (64), 87 (25), 71 (97); HRMS calcd for $C_{17}H_{21}O_3S$ (M − SC_6H_5)$^+$ 305.121 14, found 305.124 61. Anal. Calcd for $C_{23}H_{26}O_3S_2$: C, 66.67; H, 6.28; S, 15.46. Found: C, 66.58; H, 6.18; S, 15.50.

***meso*-(4a*R*,8a*R*,9a*S*,10a*S*)-Decahydro-1,8,10-trioxaanthracene (54)**. A mixture of **53** (50.0 mg, 0.12 mmol), W-2 Raney nickel (1 g), and absolute EtOH (1 mL) was heated to reflux for 24 h. The nickel was removed by filtration and rinsed with ethanol. The combined filtrates were evaporated and flash chromatographied (silica, 30% EtOAc/hexanes) to yield **54** (14.3 mg, 0.07 mmol, 60%). **54**: crystalline solid; mp 81−83 °C; R_f = 0.29 (silica, 30% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 3020, 2931, 2856, 1464, 1439, 1215, 1100, 1076, 1022, 998, 975, 886 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.91 (ddd, J = 11.5, 2.0, 1.5 Hz, 2H), 3.38 (ddd, J = 11.5, 10.5, 4.0 Hz, 2H), 3.06 (m, 4H), 2.27 (ddd, J = 11.3, 4.0, 4.0 Hz, 1H), 2.06 (br dd, J = 12.0, 3.5 Hz, 2H), 1.74 (m, 4H), 1.52 (ddd, J = 11.3, 10.5, 10.5 Hz, 1H), 1.44 (ddd, J = 12.0, 11.5, 5.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 78.2 (d), 77.4 (d), 67.9 (t), 36.0 (t), 29.3 (t), 25.6 (t); MS m/e (rel intensity) 198 (M^+, 10), 175 (20), 111 (35), 101 (33), 99 (26), 97 (30), 91 (80), 84 (33), 83 (39), 81 (36), 71 (84), 70 (23), 69 (46), 57 (57), 55 (100); HRMS calcd for $C_{11}H_{18}O_3$ (M^+) 198.125 59, found 198.126 63. Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.67; H, 9.09. Found: C, 66.63; H, 9.15.

***meso*-(9*S*,4a*R*,8a*R*,9a*S*,10a*S*)-9-(Benzyloxy)decahydro-1,8,10-trioxaanthracene (56)**. Cerium(III) chloride (49.3 mg, 0.2 mmol) was added in one portion to a stirred solution of **52** (42.4 mg, 0.2 mmol) in MeOH:THF (1:1) (10 mL). The mixture was cooled to −20 °C, and then $NaBH_4$ (19.0 mg, 0.5 mmol) was added in one portion. Stirring was continued for 15 min. Excess $NaBH_4$ was destroyed with acetone (2 mL), and the mixture was then diluted with ether (20 mL) and extracted with saturated NH_4Cl aqueous solution (10 mL), H_2O (2 × 10 mL), and brine (10 mL). Drying ($MgSO_4$), concentration, and flash column chromatography (silica, 20% EtOAc/hexanes) gave pure **55** (39.8 mg, 93%). Benzylation of **55** (39.8 mg, 0.19 mmol) to give **56** (51.0 mg, 88%) was performed according to an earlier procedure (cf. benzylation of **8**). **56**: crystalline solid; mp 101−102 °C (EtOAc/*n*-hexane); R_f = 0.61 (silica, 40% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 3006, 2947, 2857, 1602, 1496, 1454, 1439, 1374, 1343, 1228, 1086, 984 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 5H), 4.85 (s, 2H), 3.97 (br d, J = 11.5 Hz, 2H), 3.50 (dd, J = 8.7, 8.7 Hz, 1H), 3.36 (ddd, J = 11.5, 11.0, 4.0 Hz, 2H), 3.17 (ddd, J = 10.4, 9.3, 4.2 Hz, 2H), 3.12 (dd, J = 9.3, 8.7 Hz, 2H), 2.08 (br d, J = 12.0 Hz, 2H), 1.72 (m, 4H), 1.47 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 139.7 (s), 128.5 (d), 128.5 (d), 128.1 (d), 128.1 (d), 127.6 (d), 83.1 (d), 83.1 (d), 76.3 (d), 74.8 (t), 68.2 (t), 29.7 (t), 25.7 (t); MS m/e (rel intensity) 304 (M^+, 12), 198 (23), 154 (21), 97 (99), 91 (100);

HRMS calcd for $C_{18}H_{24}O_4$ (M^+) 304.167 46, found 304.168 98. Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.05; H, 7.90. Found: C, 71.00; H, 7.94.

(2*S*)-2-[(Benzyloxy)[(2*R*,3*S*)-3-(*tert*-butyldimethylsiloxy)tetrahydropyran-2-yl]-(*S*)-methyl]dihydropyran-3-one (57). To a stirred solution of ketone **47** (520.0 mg, 1.2 mmol) in dry benzene (12 mL) at rt was added dropwise DBU (1.79 mL, 12.0 mmol). After being stirred for 12 h, the solvent was evaporated and the residue subjected to flash chromatography (silica, 20% EtOAc/hexanes) to give **57** (514.8 mg, 1.2 mmol, 99%). **57**: colorless oil; $R_f = 0.68$ (silica, 30% EtOAc/*n*-hexane); $[\alpha]^{25}_D = -19.7°$ (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3007, 2955, 2942, 2857, 1728, 1463, 1371, 1252, 1136, 1085, 1073, 1020, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 5H), 4.69 (d, $J = 11.4$ Hz, 1H), 4.59 (d, $J = 11.4$ Hz, 1H), 4.19 (d, $J = 6.2$ Hz, 1H), 4.12 (dd, $J = 6.2$, 4.1 Hz, 1H), 4.02 (ddd, $J = 10.0$, 4.5, 4.5 Hz, 1H), 3.84 (ddd, $J = 8.0$, 6.8, 3.5 Hz, 1H), 3.69 (m, 2H), 3.58 (dd, $J = 6.8$, 4.1 Hz, 1H), 3.32 (ddd, $J = 11.4$, 11.4, 2.3 Hz, 1H), 2.54 (m, 1H), 2.43 (m, 1H), 2.14 (m, 1H), 2.02 (m, 1H), 1.74 (m, 2H), 1.45 (m, 2H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 207.4 (s), 138.6 (s), 128.7 (d), 128.6 (d), 128.6 (d), 128.5 (d), 127.9 (d), 81.7 (d), 80.8 (d), 77.1 (d), 72.7 (t), 67.4 (d), 66.6 (t), 65.7 (t), 38.4 (t), 32.2 (t), 27.1 (t), 26.3 (s), 24.0 (t), 18.4 (q), −3.92 (q), −4.07 (q); MS *m*/*e* (rel intensity) 377 ($[M - {}^tBu]^+$, 6), 285 (18), 269 (15), 195 (20), 187 (20), 185 (43), 129 (17), 92 (22), 91 (100), 75 (37), 73 (55), 71 (56); HRMS calcd for $C_{20}H_{29}O_5Si$ $(M - {}^tBu)^+$ 377.17843, found 377.17855.

(2*S*)-2-[(Benzyloxy)[(2*R*,3*S*)-3-(*tert*-butyldimethylsiloxy)tetrahydropyran-2-yl]-(*S*)-methyl]dihydropyran-3-one (57) from (2*R*,3*R*)-2-[(Benzyloxy)(2*R*,3*S*)-3-(*tert*-butyldimethylsiloxy)tetrahydropyran-2-yl]-(*R*)-methyl]-dihydropyran-3-ol (46). **57** was prepared from **46** as described above for **47** from **45**, using 0.18 mL (1.98 mmol) of oxalyl chloride in 3.32 mL of CH_2Cl_2, 0.42 mL (5.94 mmol) of DMSO, 288 mg (0.66 mmol) of alcohol **46**, and 1.45 mL (9.9 mmol) of Et_3N. Flash column chromatography (silica, 10−20% EtOAc/hexanes) afforded **57** (255.0 mg, 0.59 mmol, 89%).

(9*S*,4a*R*,8a*R*,9a*S*,10a*S*)-9-(Benzyloxy)octahydro-1,8,10-trioxaanthracen-4a-ol (58). Compound **58** was prepared from **57** (200.0 mg, 0.46 mmol) by the same procedure used to convert **47** to **48** described above. Flash column chromatography (silica, 10% EtOAc/$CHCl_3$) afforded **58** (131.2 mg, 0.41 mmol, 89%). **58**: crystalline solid; mp 115−117 °C (ether/*n*-hexane); $R_f = 0.44$ (silica, 10% EtOAc/$CHCl_3$); $[\alpha]^{25}_D = -19.1°$ (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3684, 3450, 3019, 2855, 2400, 1522, 1476, 1425, 1212, 1087, 1062, 982, 929, 849 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 5H), 5.81 (d, $J = 1.9$ Hz, 1H), 4.88 (d, $J = 11.5$ Hz, 1H), 4.80 (d, $J = 11.5$ Hz, 1H), 4.16 (dd, $J = 2.4$, 2.4 Hz, 1H), 4.08 (dd, $J = 11.2$, 4.8 Hz, 1H), 3.99 (m, 2H), 3.46 (ddd, $J = 13.0$, 11.5, 2.5 Hz, 1H), 3.39 (ddd, $J = 11.5$, 11.5, 3.3 Hz, 1H), 3.17 (d, $J = 2.4$ Hz, 1H), 3.13 (dd, $J = 9.6$, 2.4 Hz, 1H), 2.14 (m, 2H), 1.91 (br d, $J = 12.3$ Hz, 1H), 1.73 (m, 2H), 1.52 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 138.4 (s), 128.7 (d), 128.7 (d), 128.6 (d), 128.1 (d), 128.1 (d), 95.5 (s), 80.7 (d), 78.4 (d), 78.0 (d), 75.2 (t), 69.4 (t), 68.7 (t), 65.1 (d), 35.1 (t), 29.6 (t), 25.8 (t), 24.3 (t); MS *m*/*e* (rel intensity) 303 ($[M - OH]^+$, 1), 212 (51), 126 (100), 113 (41), 98 (63), 91 (93), 71 (51); HRMS calcd for $C_{18}H_{23}O_4$ $(M - OH)^+$ 303.159 63, found 303.159 66; calcd for $C_{11}H_{16}O_4$ $(M - OH - C_7H_7)^+$ 212.104 86, found 212.106 88.

***meso*-(9*R*,4a*R*,8a*R*,9aS,10a*S*)-9-(Benzyloxy)decahydro-1,8,10-trioxa anthracene (59)**. The transformation of **58** (548.0 mg, 1.72 mmol) to **59** (391.0 mg, 1.22 mmol, 71%) was performed according to an earlier procedure (cf. compound **49**). **59**: crystalline solid; mp 144−146 °C (*n*-hexane); $R_f = 0.35$ (silica, 10% EtOAc/$CHCl_3$); IR ($CHCl_3$) ν_{max} 3008, 2948, 2856, 1602, 1464, 1439, 1338, 1216, 1177, 1086, 1028, 992 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 5H), 4.87 (br s, 2H), 4.05 (br s, 1H), 3.96 (ddd, $J = 11.5$, 2.3, 2.0 Hz, 2H), 3.73 (ddd, $J = 11.2$, 9.4, 4.6 Hz, 2H), 3.35 (ddd, $J = 11.5$, 11.3, 3.1 Hz, 2H), 3.05 (dd, $J = 9.4$, 2.3 Hz, 2H), 2.10 (br dd, $J = 12.0$, 3.5 Hz, 2H), 1.68 (m, 4H), 1.41 (dddd, $J = 12.0$, 12.0, 11.2, 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 141.4 (s), 128.9 (d), 128.5 (d), 127.9 (d), 127.7 (d), 127.3 (d), 81.2 (d), 76.1 (d), 74.1 (t), 71.5 (d), 68.5 (t), 29.9 (t), 25.6 (t); MS *m*/*e* (rel intensity) 304 (M^+, 35), 212 (23), 198 (30), 100 (23), 97 (26), 91 (100), 84 (92), 71 (97), 65 (29), 57 (28), 55 (58); HRMS calcd for $C_{18}H_{24}O_4$ (M^+) 304.167 46, found 304.168 28.

When TMSOTf (0.30 μL, 33.5 mg, 0.15 mmol) was used as the catalyst in CH_3NO_2, **58** (32.1 mg, 0.1 mmol) was converted to **59** (29.8 mg, 98%).

(2*R*,3*S*)-Acetic Acid 2-[(Benzyloxy)[(2*R*,3*S*)-3-(*tert*-butyldimethylsiloxy)tetrahydropyran-2-yl]-(*R*)-methyl]tetrahydropyran-3yl Ester (60). A mixture of **45** (2.33 g, 5.35 mmol), Ac_2O (1.52 mL, 16.05 mmol), Et_3N (2.98 mL, 12.4 mmol), and a catalytic amount of DMAP in dry CH_2Cl_2 (53 mL) was stirred at room temperature for 4 h. The mixture was quenched with aqueous saturated NH_4Cl solution and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic phases were washed with H_2O (2 × 50 mL) and then dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the residue chromatographed on a silica gel column (eluant 20% EtOAc/hexanes) to give **60** (2.4 g, 5.02 mmol, 94%). **60**: colorless oil; $R_f = 0.43$ (silica, 40% EtOAc/*n*-hexane); $[\alpha]^{25}_D = +58.2°$ (*c* 2.3, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3020, 2930, 2857, 1728, 1469, 1464, 1375, 1251, 1219, 1097, 1037, 948, 860, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 5H), 4.95 (ddd, $J = 10.2$, 10.2, 4.6 Hz, 1H), 4.57 (d, $J = 11.8$ Hz, 1H), 4.46 (d, $J = 11.8$, 1H), 3.98 (br dd, $J = 11.3$, 4.3 Hz, 1H), 3.88 (ddd, $J = 11.3$, 4.0, 3.5 Hz, 1H), 3.84 (dd, $J = 5.0$, 2.0 Hz, 1H), 3.71 (ddd, $J = 8.5$, 8.0, 4.0 Hz, 1H), 3.57 (m, 2H), 3.29 (br dd, $J = 11.3$, 11.0 Hz, 2H), 2.30 (m, 1H), 1.98 (m, 1H), 1.87 (s, 3H), 1.78 (br d, $J = 12.6$ Hz, 1H), 1.72 (m, 1H), 1.69 (m, 2H), 1.45 (m, 1H), 1.35 (m, 1H), 0.85 (s, 9H), 0.06 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 170.2 (s), 138.5 (s), 128.9 (d), 128.9 (d), 128.6 (d), 127.9 (d), 79.8 (d), 77.7 (d), 73.2 (d), 71.9 (t), 69.0 (t), 68.3 (t), 68.2 (t), 67.3 (t), 33.1 (t), 29.9 (t), 26.2 (q), 25.1 (t), 21.6 (q), 18.3 (s), −3.0 (q), −4.2 (q); MS *m*/*e* (rel intensity) 479 ($M^+ - H$, 1), 421 ($[M - {}^tBu]^+$, 6), 271 (21), 187 (55), 179 (32), 145 (22), 143 (35), 129 (22), 117 (25), 101 (26), 91 (100), 75 (50), 71 (98); HRMS calcd for $C_{22}H_{33}O_6Si$ $(M - {}^tBu)^+$ 421.204 64, found 421.205 34.

(2*R*,3*S*)-Acetic Acid 2-[(Benzyloxy)[(2*S*,3*S*)-3-hydroxytetrahydropyran-2-yl]-(*S*)-methyl]tetrahydropyran-3-yl Ester (61). To a stirred solution of **60** (2.4 g, 5.02 mmol) in THF (51 mL) at 0 °C was added *n*-$Bu_4F \times 3H_2O$ (2.06 g, 6.53 mmol). Concentration and flash chromatography (silica, 40% EtOAc/hexanes) gave the alcohol **61** (1.8 g, 4.92 mmol, 98%). **61**: colorless oil; $R_f = 0.24$ (silica, 40% EtOAc/*n*-hexane); $[\alpha]^{25}_D = +64.4°$ (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3392, 3023, 3008, 2948, 2863, 2358, 1733, 1602, 1496, 1455, 1376, 1243, 1221, 1090, 1070, 996, 974 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 5H), 4.78 (ddd, $J = 10.2$, 10.2, 4.6 Hz, 1H), 4.73 (d, $J = 11.0$ Hz, 1H), 4.60 (s, 1H), 4.55 (d, $J = 11.0$ Hz, 1H), 4.01 (br dd, $J = 11.1$, 3.7 Hz, 1H), 3.94 (br dd, $J = 11.5$, 1.6 Hz, 1H), 3.78 (br s, 1H), 3.73 (ddd, $J = 10.3$, 9.8, 5.0 Hz, 1H), 3.38 (m, 2H), 3.27 (ddd, $J = 11.3$, 11.3, 4.6 Hz, 1H), 3.25 (br d, $J = 9.8$ Hz, 1H), 2.32 (m, 1H), 2.20 (br d, $J = 12.4$ Hz, 1H), 1.86 (s, 3H), 1.82 (m, 1H), 1.65 (m, 3H), 1.38 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 169.9 (s), 137.7 (s), 129.5 (d), 129.5 (d), 128.8 (d), 128.8 (d), 128.3 (d), 85.2 (d), 80.8 (d), 78.5 (d), 74.8 (t), 69.0 (t), 68.5 (d), 68.4 (t), 65.8 (d), 31.9 (t), 29.6 (t), 25.5 (t), 24.8 (t), 21.5 (q); MS *m*/*e* (rel intensity) 364 (M^+, 1), 221 (28), 198 (68), 196 (40), 143 (64), 128 (20), 101 (29), 91 (100), 71 (93); HRMS calcd for $C_{20}H_{28}O_6$ (M^+) 364.188 59, found 364.190 12; calcd for $C_{18}H_{24}O_4$ $(M - AcOH)^+$ 304.16746, found 304.17029.

(2*R*,3*S*)-Acetic Acid 2-[(Benzyloxy)[(2*R*)-3-oxotetrahydropyran-2-yl]-(*R*)-methyl]tetrahydropyran-3-yl Ester (62). To a cold (−78 °C) stirred solution of oxalyl chloride (1.4 mL, 14.7 mmol) in CH_2Cl_2 (25 mL) freshly distilled from CaH_2 under argon was added DMSO (3.15 mL, 44.1 mmol). After the solution was stirred for 15 min, the alcohol **61** (1.8 g, 4.92 mmol) in CH_2Cl_2 (6 mL) was added dropwise at −78 °C, and the mixture was stirred at that temperature for 30 min. Et_3N (10.34 mL, 74.18 mmol) was then added dropwise, and the reaction mixture was allowed to warm to 0 °C while being stirred. After 2 h the reaction mixture was poured onto a mixture of saturated aqueous NH_4Cl solution (50 mL) and ether (100 mL). Shaking and separation of the organic layer were followed by washing with H_2O (2 × 50 mL) and brine (50 mL) and drying ($MgSO_4$). Evaporation of the solvent and purification by silica gel column chromatography (elution 40% EtOAc/hexanes) afforded **62** (1.5 g, 4.14 mmol, 84%). **62**:

white solid; mp 98−99 °C (EtOAc/*n*-hexane); R_f = 0.41 (silica, 40% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +82.7° (*c* 2.7, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3015, 2956, 2861, 1730, 1728, 1603, 1453, 1374, 1243, 1085, 1037, 912 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (m, 5H), 4.88 (ddd, *J* = 10.2, 10.2, 4.6 Hz, 1H), 4.83 (d, *J* = 10.2 Hz, 1H), 4.37 (d, *J* = 10.2 Hz, 1H), 4.06 (br d, *J* = 8.2 Hz, 1H), 4.06 (m, 1H), 3.95 (br d, *J* = 8.2 Hz, 1H), 3.95 (m, 1H), 3.77 (ddd, *J* = 11.0, 11.0, 3.4 Hz, 1H), 3.54 (br d, *J* = 10.2 Hz, 1H), 3.32 (ddd, *J* = 11.6, 10.2, 1.6 Hz, 1H), 2.56 (m, 2H), 2.35 (m, 1H), 2.15 (m, 2H), 2.02 (s, 3H), 1.75 (m, 1H), 1.61 (br d, *J* = 13.5 Hz, 1H), 1.41 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 207.8 (s), 170.3 (s), 138.3 (s), 129.1 (d), 129.1 (d), 128.6 (d), 128.6 (d), 128.0 (d), 81.2 (d), 78.0 (d), 74.5 (t), 74.4 (d), 68.5 (d), 68.5 (t), 67.4 (t), 39.7 (t), 29.8 (t), 29.1 (t), 25.3 (t), 21.6 (q); MS *m*/*e* (rel intensity) 344 ($[M - H_2O]^+$, 3), 203 (16), 143 (65), 97 (27), 92 (48), 91 (100), 71 (99), 65 (58); HRMS calcd for $C_{20}H_{24}O_5$ $(M - H_2O)^+$ 344.162 37, found 344.162 33.

(9*R*,4a*R*,8a*R*,9aξ, 10aξ)-9-(Benzyloxy)octahydro-1,8,10-trioxaanthracen-4a-ol (63). A mixture of acetate **62** (1.5 g, 4.14 mmol), K_2CO_3 (57.4 mg, 0.41 mmol), and MeOH (41 mL) was stirred at 25 °C for 30 min. Evaporation of the solvent followed by flash chromatography (silica, 40% EtOAc/hexanes) gave a mixture of hemiacetals **63** (927.0 mg, 2.9 mmol, 70%). **63a** (the major component from the mixture): oil; R_f = 0.17 (silica, 40% EtOAc/*n*-hexane); IR ($CHCl_3$) ν_{max} 3587, 3020, 2948, 2858, 2360, 1496, 1455, 1360, 1279, 1217, 1164, 1112, 1079, 1056, 1039, 984, 932 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 5H), 4.84 (d, *J* = 12.5 Hz, 1H), 4.69 (d, *J* = 12.5 Hz, 1H), 4.03 (ddd, *J* = 12.0, 2.8, 1.7 Hz, 1H), 3.99 (ddd, *J* = 11.5, 3.0, 2.2 Hz, 1H), 3.92 (dd, *J* = 9.8, 3.2 Hz, 1H), 3.68 (m, 1H), 3.58 (dd, *J* = 9.8, 9.6 Hz, 1H), 3.57 (d, *J* = 3.2 Hz, 1H), 3.43 (m, 1H), 3.25 (m, 1H), 1.92 (m, 3H), 1.73 (m, 2H), 1.61 (m, 2H), 1.47 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 139.4 (s), 128.6 (d), 128.6 (d), 128.2 (d), 128.1 (d), 127.7 (d), 94.3 (s), 79.3 (d), 77.8 (d), 75.9 (d), 72.7 (t), 69.8 (d), 68.4 (t), 68.1 (t), 37.4 (t), 29.5 (t), 26.1 (t), 23.9 (t); MS *m*/*e* (rel intensity) 320 (M^+, 3), 302 ($[M - H_2O]^+$, 9), 214 (14), 126 (68), 125 (23), 97 (32), 91 (100), 87 (73), 85 (56), 83 (83), 71 (100), 65 (67), 55 (79); HRMS calcd for $C_{18}H_{24}O_5$ (M^+) 320.162 37, found 320.163 26; calcd for $C_{18}H_{22}O_4$ $(M - H_2O)^+$ 302.151 81, found 302.151 81.

(9*R*,4a*S*,8a*R*,9a*R*,10a*R*)-9-(Benzyloxy)decahydro-1,8,10-trioxaanthracene (64),(4a*S*,8a*R*,9a*R*,10a*S*)-Decahydro-1,8,10-trioxaanthracene (66), and *meso*-(9*S*,4a*S*,-8a*S*,9a*R*,10a*R*)-Decahydro-1,8,10-trioxaanthracene (56). To a solution of **63** (mixture of isomers) (700.0 mg, 2.18 mmol) in freshly distilled CH_3CN (21 mL) at 0 °C were added Et_3SiH (5.2 mL, 32.5 mmol) and then $BF_3{\cdot}Et_2O$ (4.13 mL, 32.5 mmol). The resulting solution was stirred for 2 h at 0 °C. The reaction mixture was then diluted with ether (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, 30% EtOAc/hexanes) afforded **64** (352.0 mg, 1.16 mmol, 53%) and a mixture of **66** and **56** (226.0 mg of the mixture, 0.74 mmol, 34%). The mixture of **66** and **56** was separated by HPLC (elution 20% EtOAc/*n*-hexane) yielding **66** (159.0 mg, 0.52 mmol, 24%) and **56** (66.0 mg, 0.218 mmol, 10%). **64**: crystalline solid; mp 84−85 °C (Et_2O/*n*-hexane); R_f = 0.47 (silica, 40% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = +15.3° (*c* 1.3, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3023, 3006, 2949, 2856, 1602, 1496, 1454, 1347, 1280, 1227, 1100, 1040, 971 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 5H), 4.79 (d, *J* = 12.7 Hz, 1H), 4.71 (d, *J* = 12.7 Hz, 1H), 4.06 (br dd, *J* = 9.8, 2.9 Hz, 1H), 3.95 (br d, *J* = 11.5 Hz, 1H), 3.57 (d, *J* = 3.4 Hz, 1H), 3.51 (dd, *J* = 9.4, 9.2 Hz, 1H), 3.42 (dd, *J* = 9.4, 3.4 Hz, 1H), 3.37 (m, 3H), 3.04 (ddd, *J* = 10.5, 9.2, 4.2 Hz, 1H), 2.02 (m, 1H), 1.94 (m, 2H), 1.7 (m, 2H), 1.56 (m, 2H), 1.27 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 139.2 (s), 128.6 (d), 128.6 (d), 128.2 (d), 128.1 (d), 127.8 (d), 79.3 (d), 78.9 (d), 76.4 (d), 75.8 (d), 72.1 (t), 72.1 (d), 68.7 (t), 68.2 (t), 29.6 (t), 28.8 (t), 25.9 (t), 21.2 (t); MS *m*/*e* (rel intensity) 304 (M^+, 4), 198 (22), 180 (46), 154 (39), 139 (33), 111 (31), 97 (98), 91 (100), 71 (100), 65 (62), 57 (57); HRMS calcd for $C_{18}H_{24}O_4$ (M^+) 304.16746, found 304.16797. **66**: oil; R_f = 0.63 (silica, 40% EtOAc/*n*-hexane); $[\alpha]^{25}_D$ = −21.6° (*c* 1.9, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3006, 2947, 2857, 1602, 1496, 1454, 1439, 1374, 1343, 1226, 1212, 1163, 1086, 1055, 1028, 984, 946 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 5H), 4.87 (d, *J* = 12.5 Hz, 1H), 4.71 (d, *J* = 12.5 Hz, 1H), 4.02 (br dd, *J* = 11.3, 4.6 Hz, 1H), 3.86 (m, 3H), 3.68 (dd, *J* = 10.5, 5.4 Hz, 1H), 3.48 (m, 2H), 3.37 (ddd, *J* = 12.0, 11.3, 2.3 Hz, 1H), 3.32 (m, 1H), 2.15 (br dd, *J* = 12.1, 3.2 Hz, 1H), 2.06 (br d, *J* = 10.5, 1H), 1.68 (m, 4H), 1.83 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 139.3 (s), 128.5 (d), 128.5 (d), 128.1 (d), 128.1 (d), 127.7 (d), 84.4 (d), 77.3 (d), 77.3 (d), 73.2 (t), 68.7 (t), 68.3 (t), 67.9 (d), 67.6 (d), 31.7 (t), 31.3 (t), 25.4 (t), 25.0 (t); ^1H NMR (400 MHz, C_6D_6) δ 7.56 (d, *J* = 7.1 Hz, 2H), 7.35 (m, 3H), 5.10 (d, *J* = 12.1 Hz, 1H), 4.86 (d, *J* = 12.1 Hz, 1H), 4.05 (ddd, *J* = 10.5, 10.5, 4.8 Hz, 1H), 4.04 (dd, *J* = 4.7, 4.7 Hz, 1H), 3.77 (dddd, *J* = 11.3, 1.6, 1.5, 1.5 Hz, 1H), 3.70 (dddd, *J* = 12.0, 1.7, 1.5, 1.5 Hz, 1H), 3.65 (dd, *J* = 10.6, 4.7 Hz, 1H), 3.54 (dd, *J* = 10.5, 5.2 Hz, 1H), 3.40 (ddd, *J* = 10.6, 10.3, 4.5 Hz, 1H), 3.05 (ddd, *J* = 12.0, 11.3, 2.2 Hz, 2H), 2.09 (br dd, *J* = 12.0, 3.1 Hz, 1H), 1.99 (br d, *J* = 10.8 Hz, 1H), 1.39 (m, 5H), 1.15 (br dd, *J* = 13.1, 1.0 Hz, 1H); ^{13}C NMR (C_6D_6) δ 140.0 (s), 128.4 (d), 128.3 (d), 128.0 (d), 127.8 (d), 127.3 (d), 84.8 (d), 78.0 (d), 77.9 (d), 73.8 (t), 67.9 (t), 67.9 (t), 67.5 (d), 67.4 (d), 31.8 (t), 31.4 (t), 25.3 (t), 25.0 (t); MS *m*/*e* (rel intensity) 418 (M^+, 1), 361 ($[M - {}^tBu]^+$, 8), 255 (52), 215 (99), 204 (67), 179 (68), 91 (100), 83 (88), 75 (99), 73 (100); HRMS calcd for $C_{24}H_{38}O_4Si$ (M^+) 418.253 94, found 418.254 66; calcd for $C_{20}H_{29}O_4Si$ $(M - {}^tBu)^+$ 361.183 51, found 361.187 42.

When TMSOTf (30.0 μL, 33.4 mg, 0.15 mmol) was used as catalyst in CH_3NO_2, **63** (32.1 mg, 0.1 mmol) was converted to **64** (23.4 mg, 77%), **66** (1.3 mg, 5%), and **56** (2.7 mg, 9%).

(9*R*,4a*S*,8a*R*,9a*R*,10a*R*)-Decahydro-1,8,10-trioxaanthracen-9-ol (65). $Pd(OH)_2$ (20% Pd) catalyst (10 mg) was added to a stirred solution of **64** (250.0 mg, 0.82 mmol) in MeOH (1 mL) at 25 °C under H_2 atmosphere. After the mixture was stirred for 12 h at 25 °C, the catalyst was filtered off and the solvent was removed under vacuum to give essentially pure **65** (172.0 mg, 0.8 mmol, 89%). **65**: crystalline solid; mp 38−39 °C (*n*-hexane); R_f = 0.36 (silica, EtOAc); $[\alpha]^{25}_D$ = +53.5° (*c* 2.1, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3566, 3030, 2951, 2860, 1465, 1439, 1404, 1336, 1279, 1240, 1212, 1098, 1049 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.97 (br d, *J* = 10.3 Hz, 1H), 3.88 (br d, *J* = 11.4 Hz, 1H), 3.56 (d, *J* = 2.9 Hz, 1H), 3.50 (dd, *J* = 9.5, 3.5 Hz, 1H), 3.41 (br s, 1H), 3.33 (m, 2H), 3.18 (dd, *J* = 9.5, 9.5 Hz, 1H), 2.95 (dd, *J* = 11.0, 9.5 Hz, 1H), 2.91 (br s, 1H), 1.90 (m, 3H), 1.61 (m, 2H), 1.49 (m, 2H), 1.25 (br d, *J* = 13.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 79.9 (d), 77.1 (d), 75.8 (d), 72.6 (d), 71.9 (d), 68.6 (t), 68.2 (t), 29.4 (t), 28.5 (t), 25.8 (t), 21.3 (t); MS *m*/*e* (rel intensity) 214 (M^+, 4), 196 ($[M-H_2O]^+$, 8), 126 (94), 97 (61), 84 (97), 71 (100), 57 (43), 55 (94); HRMS calcd for $C_{11}H_{18}O_4$ (M^+) 214.120 51, found 214.120 04; calcd for $C_{11}H_{16}O_3$ $(M - H_2O)^+$ 196.109 94, found 196.109 62.

(4a*R*,8a*S*,9a*S*,10a*S*)-Octahydro-1,8,10-trioxaanthracen-9-one (51) from 65. The transformation of alcohol **65** (50.0 mg, 0.23 mmol) to the ketone **51** (44.5 mg, 0.21 mmol, 91%) was performed by the usual Swern oxidation[8] according to the procedure used to convert **50** to **51** described above.

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