Studies Directed toward the Synthesis of (+)-Sesbanimide A: Construction of the AB-Ring System (A Formal Total Synthesis)

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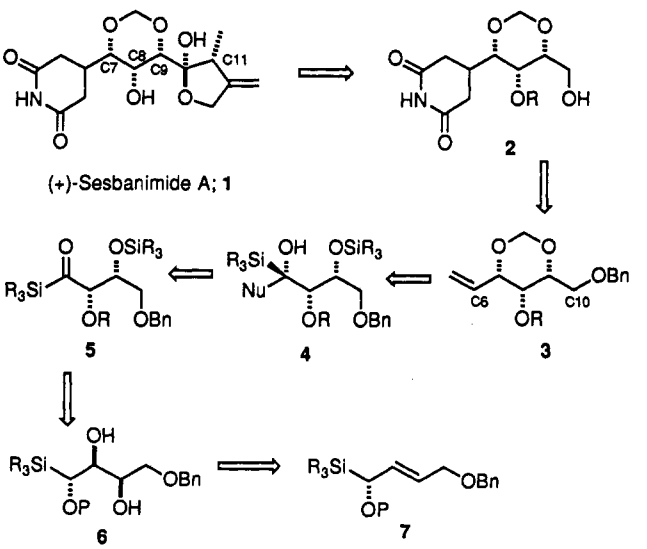
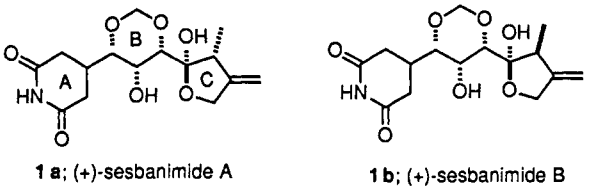
Complete details of a study leading to the asymmetric synthesis of the AB-ring system of (+)-sesbanimide A (1), a potent cytotoxic agent belonging to the class of sesbania alkaloids, are described. Key features of the synthesis include (a) the stereoselective introduction of the C8 and C9 hydroxyl groups through the use of a diastereoselective catalytic osmylation of enantiomerically enriched α-alkoxy allylsilanes and (b) a chelation-controlled nucleophilic addition of a vinyl Grignard reagent to a syn α-alkoxy β-(silyloxy) aldehyde for the introduction of the C7 stereocenter required for assembly of the B-ring.

Sesbanimides A (**1a**) and B (**1b**) are unique tricyclic metabolites isolated from the seeds of *Sesbania drummondii*[1] and *Sesbania punicea*.[2] Sesbanimide A is the most active member of the sesbania alkaloids and is present at only 0.5 ppm. One thousand pounds of seed provided less than 30 mg of pure agent. The structure of (+)-sesbanimide A and its relative stereochemistry were determined by X-ray diffraction analysis[1a] and subsequent synthetic efforts have confirmed that the absolute stereochemistry is the 7*S*,8*R*,9*S*,10*R*,11*R* stereoisomer.[3] This tricyclic metabolite is linked together by single bonds containing a glutarimide ring, a 1,3-dioxane ring, and a substituted tetrahydrofuran ring. The agent has exhibited excellent *in vitro* cytotoxicity (ED_{50} of 7.7×10^{-3} μg/mL against KB cells) and potent *in vivo* activity against P-388 murine leukemia (T/C values of 140 to 181 in the 8.0 to 32.0×10^{-2} mg/kg range). The significant antitumor activity associated with this structure has distinguished this molecule and related structures as excellent candidates for development as potential antineoplastic agents.[4] Research efforts from our laboratories have focused on the development of chiral α-alkoxy allylic silanes as versatile stereoselective reagents. We have shown that they can act as useful homoenolate equivalents for the stereoselective C-glycosidation of pyranoside derivatives,[5] as well as participate in fluoride ion promoted conjugate additions to α,β-enones.[6] In connection with our interest in utilizing these heterosubstituted allylic silanes for the synthesis of sesbania alkaloids, we wish to detail our studies that have led to the construction of the AB-ring system of (+)-sesbanimide A.

Scheme 1





Analysis of the Synthesis. A retrosynthetic analysis of our approach to (+)-sesbanimide A is illustrated in Scheme 1. Our first objective was the asymmetric construction of the 1,3-dioxane ring system **3** (B-ring) as an advanced synthon that is differentiated at the terminal C6 and C10 positions. A precursor to **3** is the differentially protected tetrol **4** in which the three contiguous secondary hydroxyls are *syn* with respect to each other. Our general approach to *syn*-1,2,3-triol derivatives uses two diastereoselective reactions. The C7 stereocenter is introduced via a nucleophilic addition reaction to an acylsilane **5** (or

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(1) (a) Powell, R. G.; Smith, C. R., Jr.; Weisleder, D.; Matsumoto, G. K.; Clardy, J.; Kozlowski, J. *J. Am. Chem. Soc.* **1983**, *105*, 3739–3741. (b) Powell, R. G.; Smith, C. R., Jr.; Weisleder, D. *Phytochemistry* **1984**, *23*, 2789–2796.

(2) Gorst-Allman, C. P.; Steyn, P. S.; Vleggaar, R. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1311–1314.

(3) Review: Matsuda, F.; Terashima, S. *J. Synth. Org. Chem. Jpn.* **1987**, *45*, 983–1012. Total synthesis: (a) Tomioka, K.; Hagiwara, A.; Koga, K. *Tetrahedron Lett.* **1988**, *29*, 3095–3096. (b) Matsuda, F.; Terashima, S. *Tetrahedron* **1988**, *44*, 4721–4736. (c) Wanner, M. J.; Willard, N. P.; Koomen, G.-J.; Pandit, U. K. *Tetrahedron* **1987**, *43*, 2549–2556. (d) Wanner, M. J.; Willard, N. P.; Koomen, G.-J.; Pandit, U. K. *J. Chem. Soc., Chem. Commun.* **1986**, 396–397. (e) Schlessinger, R. H.; Wood, J. L. *J. Org. Chem.* **1986**, *51*, 2621–2623. Synthetic studies: (f) Roush, W. R.; Michaelides, M. R. *Tetrahedron Lett.* **1986**, *27*, 3353–3356. (g) Rama Rao, A. V.; Yadav, J. S.; Naik, J. M.; Chaudhary, A. G. *Tetrahedron Lett.* **1986**, 27, 993–994. (h) Fleet, G. W. J.; Shing, T. K. M. *J. Chem. Soc., Chem. Commun.* **1984**, 835–837. (i) Tomioka, K.; Koga, K. *Tetrahedron Lett.* **1984**, *25*, 1599–1600. Synthesis of analogs: (j) Van den Bos, J. C.; Vloon, W. J.; Koomen, G.-J.; Pandit, U. K. *Tetrahedron* **1991**, *47*, 6787–6794.

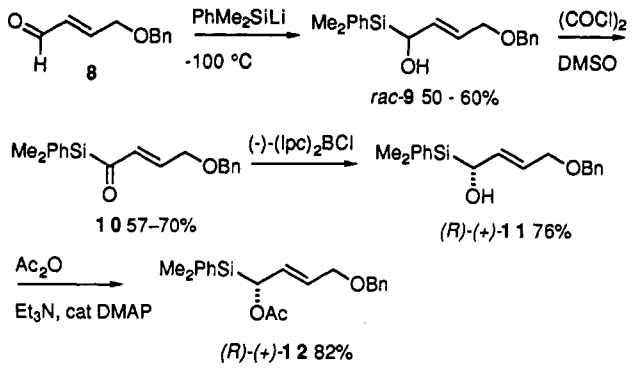
(4) A number of glutarimide antibiotics, such as streptovitacin A and cycloheximide, have been tested for effectiveness as protein synthesis inhibitors and are of interest as antitumor and antifungal agents. See: Sisler, H. D.; Siegel, M. R. *Antibiot. (Mech. Action)* **1967**, *1*, 283–307.

(5) Panek, J. S.; Sparks, M. A. *J. Org. Chem.* **1989**, *54*, 2034–2038.

(6) Panek, J. S.; Sparks, M. A. *Tetrahedron Lett.* **1987**, *28*, 4649–4652.

0022-3263/94/1959-3055$04.50/0

Scheme 2



the corresponding aldehyde) which possesses the C8 and C9 stereocenters at the α and β positions. These in turn can be introduced via an osmium tetraoxide catalyzed dihydroxylation on enantioenriched α-alkoxy allylic silane **7**.[7]

The development of heterosubstituted allylic metals as versatile and readily-available, chiral building blocks was crucial to the success of this approach to the stereoselective synthesis of the C7, C8, and C9 centers of sesbanimide A.[7d] In an earlier report we have shown that α-alkoxy allylic silanes of type **7** do undergo dihydroxylations catalyzed by osmium tetraoxide with useful levels of diastereoselectivity.[7a] Moreover, subsequent differentiation of the newly-formed hydroxyl groups in a protection scheme was easily carried out. Finally, the geminal silicon and oxygen functionalities can be manipulated to yield either an acylsilane or aldehyde, which subsequently undergoes highly diastereoselective chelation-controlled nucleophilic addition reactions to yield *syn,syn*-1,2,3 triol units which contain the general stereochemical features found in the target B-ring of **1** (Scheme 1).[7b,c]

Asymmetric synthesis of α,γ-Dialkoxy (*E*)-Crotylsilane 12. Several approaches to the asymmetric synthesis of (*R*)-(*E*)-4-(benzyloxy)-1-((dimethylphenyl)-silyl)-2-buten-1-yl acetate (**12**) were explored. The route that was ultimately chosen was based on an asymmetric hydride reduction of an acylsilane (Scheme 2). The synthesis of this material began with the generation of the racemic α-hydroxy silane **9** by the addition of lithio-(dimethylphenyl)silane to (*E*)-4-(benzyloxy)-2-butenal[8] (**8**; −100 °C, THF, 0.75 h), producing the 1,2-addition product in 48–62% yield. This α-hydroxy allylsilane was transformed into an acylsilane by a Swern oxidation in 57% yield.[9] The optically active acetoxy allylic silane was obtained from the α,β-unsaturated acylsilane **10** by a two-step sequence. Asymmetric reduction with (−)-chlorodiisopinocampheylborane [(−)-$(Ipc)_2BCl$][10] utilizing a modification of Buynak's[11] published procedure for the asymmetric reduction of acylsilanes afforded the (*R*)-alcohol **11** in 87–92% ee and in good yield.[12] Acylation of the derived α-hydroxy silane under standard conditions provided the optically active α,γ-dialkoxy (*E*)-crotylsilane **12** (Scheme 2).

Diastereoselection in the Catalytic Osmylation Reaction of chiral α-Alkoxy Allylsilanes: Introduction of the C8 and C9 Stereocenters. Studies on electrophilic addition reactions to π systems adjacent to stereogenic carbon atoms have been the subject of considerable experimental and theoretical interest.[13] A fascinating aspect of this chemistry is the manner by which the asymmetric center can alter the relative rates of additions to either face (k_{anti}/k_{syn}) of the π system. Reports have documented that chiral allylic metals can participate in and direct the regio- and diastereochemical outcome of many addition reactions.[14] In this regard, Vedejs[15] and Fleming[16] have shown that allylic silanes participate in osmylations with useful levels of diastereoselectivity. Initial investigations by Kishi and co-workers[17] have demonstrated that chiral allylic alcohols and ethers undergo diastereoselective osmylation reactions preferentially anti to the oxygen function. The osmylation of 1,1-disubstituted olefins possessing an allylic, oxygen-bearing stereocenter also proceeds with useful levels of stereoselectivity.[18] In preliminary experiments relevant to the synthesis of (+)-sesbanimide A, we have examined the vicinal dihydroxylation of racemic α-alkoxy allylic silanes containing (*E*)- and (*Z*)-1,2-disubstituted olefins.[7a] These experiments have shown that the anti stereoisomer is favored and diastereoselection is enhanced by maximizing the size difference between the geminal allylic substitutents OP and SiR_3 (eq 1). Representative examples of these experiments are shown in Table 1.

The strategy represented a simple way in which the double-bond configuration helps to transform one stereocenter into *anti*-1,2-*syn*-2,3- and *anti*-1,2-*anti*-2,3-tetrol derivatives that are differentiated at each terminus.[19] Thus the C8 and C9 stereocenters of (+)-sesbanimide were introduced by an osmium tetraoxide promoted dihy-

(7) (a) Panek, J. S.; Cirillo, P. F. *J. Am. Chem. Soc.* **1990**, *112*, 4873–4878. (b) Cirillo, P. F.; Panek, J. S. *J. Org. Chem.* **1990**, *55*, 6071–6073. (c) Cirillo, P. F.; Panek, J. S. *Tetrahedron Lett.* **1991**, *32*, 457–460. (d) Cirillo, P. F.; Panek, J. S. *Org. Prep. Proc. Intl.* **1992**, 561–590.

(8) Danishefsky, S.; Regan, J. *Tetrahedron Lett.* **1981**, *22*, 3919–3922.

(9) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480–2482.

(10) Chandrasekharan, J.; Ramachandran, P. V.; Brown, H. C. *J. Org. Chem.* **1985**, *50*, 5446–5448. (b) Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Org. Chem.* **1986**, *51*, 3394–3396.

(11) (a) Buynak, J. D.; Strickland, J. B.; Lamb, G. W.; Khasnis, D.; Modi, S.; Williams, D.; Zhang, H. *J. Org. Chem.* **1991**, *56*, 7076–7083. (b) Soderquist, J. A.; Anderson, C. L.; Miranda, E. I.; Rivera, I.; Kabalka, G. W. *Tetrahedron Lett.* **1990**, *31*, 4677–4680.

(12) Assignment of absolute stereochemistry is based on analogy with published results and on comparison of rotation with alcohols that were resolved by column chromatography as their (*R*)-mandelate derivatives. See: Panek, J. S.; Sparks, M. A. *Tetrahedron: Asymmetry* **1990**, *1*, 801–816. The enantiomeric excess was measured by integration of the crude ^1H NMR spectrum after coupling with *O*-acetylmandelic acid of >99% ee (DCC, cat. DMAP, 0 °C, CH_2Cl_2).

(13) See, *inter alia*: (a) Symposia in print, *Control of Acyclic Stereoselectivity;* Mukaiyama, T. *Tetrahedron* **1984**, *40*, 2197–2343. (b) Khan, D. S.; Pau, C. F.; Chamberlin, A. R.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 650–663. (c) Solladie, G.; Frechou, C.; Demailly, G. *Tetrahedron Lett.* **1986**, *27*, 2867–2870. (d) McGarvey, G. J.; Williams, J. M. *J. Am. Chem. Soc.* **1985**, *107*, 1435–1437. (e) Labelle, M.; Guindon, Y. *J. Am. Chem. Soc.* **1989**, *111*, 2204–2210.

(14) Organosilanes in synthesis, see *inter alia*: (a) Colvin, E. *Silicon in Organic Synthesis*; Butterworths: London, 1981. (b) Sakurai, H. *Organosilicon and Bioorganosilicon Chemistry*; Ellis Horwood: Chichester, 1985. (c) Symposia in print, *Organosilicon Chemisty in Organic Synthesis*: Fleming, I. *Tetrahedron* **1988**, *44*, 3760. (d) Fleming, I. *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1992; Vol. 2, pp 563–593. (e) Fleming, I.; Dunogues, J.; Smithers, R. *Org. React. (N.Y.)* **1989**, 37, 57–588.

(15) Vedejs, E.; McClure, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 1094–1096.

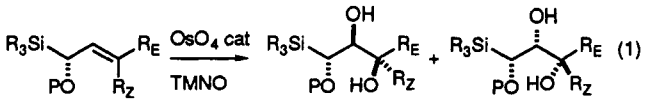
(16) (a) Fleming, I; Sarkar, A. S.; Thomas, A. P. *J. Chem. Soc., Chem. Commun.* **1987**, 157–159.

(17) Christ, W. J.; Cha, J. K.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247–2255.

(18) Evans, D. A.; Kaldor, S. W. *J. Org. Chem.* **1990**, *55*, 1698–1700.

(19) Particularly worthy of note is the great enhancement in diastereoselectivity with unprotected α-hydroxy allylic silanes. This selectivity jumps from an order of 4–10:1 to >100:1 on going from the acetate-protected derivatives to the free hydroxyls, albeit with a price in yield. Synthetically we could not take advantage of this feature because of the subsequent problem of differentiation during protection of the resulting triol.

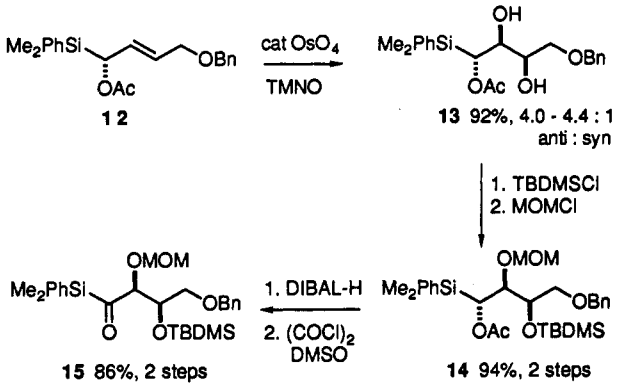
Table 1. Diastereoselective Osmium-Catalyzed Vicinal Hydroxylations of Chiral α-Alkoxy Allylic Silanes[a]



entry	R_3Si	P	R_E	R_Z	ratio *anti/syn*[b]	yield (%)[c,d]
1	$SiMe_3$	Ac	H	H	6.5:1	57
2	$SiMe_2Ph$	Ac	H	H	7.0:1	70
3	Si^tBuMe_2	Ac	H	H	11.3:1	70
4	$SiMe_3$	H	H	H	>97:3	65[e]
5	$SiMe_3$	Ac	CH_3	H	4.5:1	63
6	Si^tBuMe_2	Ac	CH_3	H	7.0:1	61
7	Si^tBuMe_2	Ac	H	CH_3	1.4:1	94
8	Si^tBuMe_2	H	CH_3	H	120–147:1	62[e]
9	Si^tBuMe_2	H	H	CH_3	4.7:1	45[e]

[a] The reactions were run in acetone/water [8:1; 5.0 mol % OsO_4; TMNO (2.2 equiv) 0.2–0.4 M in substrate, and hydrolysis was carried out with an aqueous 10% $NaHSO_3$ solution. [b] All products were isolated as *anti/syn* diastereomers, and ratios were determined by integration of the C1 methine protons at 400 MHz (^1H NMR) or by capillary GC analysis after peracetylation. [c] All products exhibited the expected ^1H NMR, IR, and MS characteristics. [d] All yields are based on pure materials isolated by chromatography on SiO_2. [e] Crude yield, obtained without aqueous workup.

Scheme 3



droxylation of the α-alkoxy allylsilane **12**. Catalytic osmylation (OsO_4) of α-acetoxy (*E*)-crotylsilane **12** with trimethylamine *N*-oxide (TMNO) as the secondary oxidant provided the *anti*-1,2-*syn*-2,3-tetrol derivative **13** in good yield with useful diastereoselection favoring the *anti* isomer (*anti/syn* 4.0–4.4:1) (Scheme 3).

Diastereoselectivity in Nucleophilic Additions to *syn*-α,β-Dialkoxy Acylsilane 15 and *syn*-α,β-Dialkoxy Aldehyde 16: Introduction of the C7 Stereocenter and Construction of the B-Ring. The stereoselective construction of the C7 center was envisioned to take place via substrate control during a nucleophilic addition reaction after conversion of **13** to an α,β-dialkoxy carbonyl derivative.[20] The nucleophilic addition reactions of chiral α-methyl acylsilanes have been examined by Ohno and co-workers. These studies have shown that enhanced levels of Cram-type selectivity can be achieved under nonchelate-controlled reaction conditions (eq 2).[21] On the basis of that precedent, chelation-controlled additions to α-alkoxy-β-(silyloxy) acylsilanes were investigated with the hope that similarly high levels of diastereoselection favoring the Cram product would be obtained (eq 3).

(20) Cram, D. J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 2748–2755.

(21) Nakada, M.; Urano, Y.; Kobayashi, S.; Ohno, M. *J. Am. Chem. Soc.* **1988**, *110*, 4826–4827.

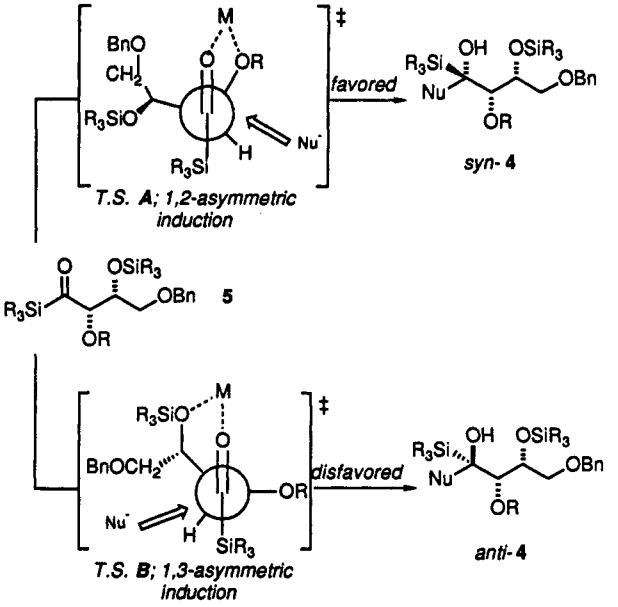
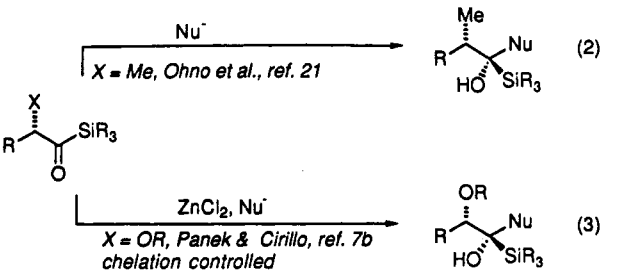


Figure 1.

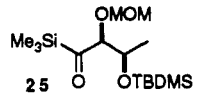
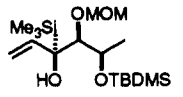
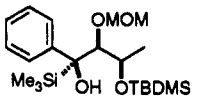
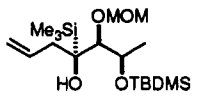
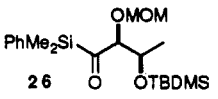
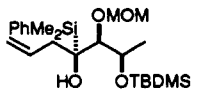
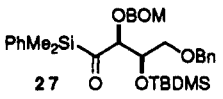


Selective differentiation between the three oxygens of the derived 1,2-*anti*-2,3-*syn*-triol **13** was needed to determine if the α,β-dialkoxy acylsilanes would serve as useful substrates in chelation-controlled addition reactions. The protecting group arrangement of acylsilane **5** (Scheme 1) is illustrated with the substrate possessing a bulky trialkylsilicon group at the C3 position and an ether protecting group at C2. During the nucleophilic addition reaction, this arrangement was expected to promote chelation with the C2 oxygen to facilitate the formation of transition state **A**, leading to the *syn* product **4**. The formation of the alternative transition state **B**, which leads to the production of the undesired *anti*-**4** via 1,3-asymmetric induction, should be disfavored due to the poor chelating ability of the bulky trialkylsilyl ether (Figure 1).[7b]

Scheme 3 describes the reaction sequence for the conversion of triol **13** to acylsilane **15**. Selective silylation with *tert*-butyldimethylsilyl chloride [TBDMSCl (1.1 equiv)/imidazole (2.0 equiv)/DMF/rt] of the C3 hydroxyl was followed by protection of the C2 hydroxyl as the MOM or BOM ether.[22] Following conversion of the C1 acetate to the acylsilane [i. DIBAL, 2.0 equiv, −78 °C, 5 h; ii. $(COCl)_2$, DMSO, Et_3N], compound **15** was obtained in a typical yield of 46% from **12**.

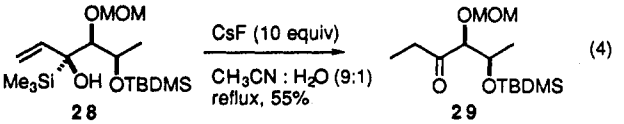
Preliminary studies conducted in our laboratory concerning chelation-controlled nucleophilic additions to α,β-dialkoxy acylsilanes have demonstrated that good levels of selectivity can be obtained favoring the Cram-type products. These studies also resulted in a successful synthesis of the 2,6-dideoxyhexopyranoside β-D-boivinose.[7b] Examples from that study are summarized in Table 2. The allylation with allyltri-*n*-butyltin worked well if zinc

Table 2.[a] Diastereoselectivity in Nucleophilic Additions to *syn*-α,β-Dialkoxy Acylsilanes

entry	acylsilane	conditions[a]	major diastereomer[b]	yield (%)[c]	ratio[d]
1	 25	vinyl-MgBr[e] -78 °C		88	6.7 : 1
2	25	PhMgBr -78 °C		86	>50 : 1
3	25	allyl-SnBu3, $ZnCl_2$ -30 °C		96	10 : 1
4	 26	vinyl-MgBr -78 °C	-	82	1.2 : 1
5	26	allyl-MgBr -78 °C	-	85	1.3 : 1
6	26	allyl-SnBu3, $ZnCl_2$ -30 °C		86	2.8 : 1
7	 27	allyl-SnBu3, $ZnCl_2$ 0 °C	-	85	~1 :1

[a] All reactions were run in dry CH_2Cl_2 at 0.15–0.2 M in substrate, unless otherwise stated. [b] All products exhibited the expected ^1H NMR (270 MHz), ^{13}C NMR (67.5 MHz), IR, MS, and HRMS characteristics. [c] All yields are based on pure materials isolated by chromatography on SiO_2. [d] All products were isolated as *anti/syn* mixtures of diastereomers and ratios were determined by integration of the crude ^1H NMR spectrum. [e] 0.03 M in substrate, at 0.18 M concentration, the ratio is 4:1.

halide salts were used as Lewis acids (entry 3).[23] Whereas vinyl and phenyl Grignard reagents worked well (entries 1 and 2), allylmagnesium bromide failed to achieve good diastereoselectivity.[24] At this point the construction of 1,2,3-*syn*-triol systems using this methodology seemed well in hand. The bis-desilylation of the derived hydroxysilane on both carbon and oxygen was expected to be stereospecific[25] and provide the desired 1,2,3-*syn*-triol with the desired protecting group arrangement (namely on the C2 hydroxyl only) to allow the construction of the B-ring of sesbanimide A. The introduction of a vinyl substituent was viewed as being a most advantageous way of introducing functionality that could then be manipulated into the glutarimide A-ring. However, the addition of vinyl Grignard reagent was found to be nonselective for the (dimethylphenyl)acylsilane derivative, giving a 1.2:1 ratio of diastereomers (entry 4). Thus diastereoselectivity seemed to depend on the size of the acylsilane moiety. Furthermore, the fluoride ion promoted desilylation of the derived allylsilane inevitably produced the undesired ethyl ketone derivative **29** and in moderate yields (eq 4).[26] Nucleophilic addition reactions to acylsilanes containing the C4-benzyloxy substituent were also found to be nondiastereoselective (entry 7).



(4)

The combination of these problems led us to consider the possibility of performing the nucleophilic addition reactions on the corresponding α,β-dialkoxy aldehydes. Efficient methods for the conversion of acylsilanes to aldehydes were unknown. β-Alkoxy acylsilanes have been shown to preferentially undergo elimination to provide α,β-unsaturated aldehydes when treated with catalytic amounts of quaternary ammonium salts.[27] It was however known from single-crystal X-ray analysis performed on

(22) It is important to highlight here the sensitive and hindered nature of the C2 hydroxyl group. Silylation with TBDMSCl is completely selective for the C3 hydroxyl, no trace of C2 protection being detected by ^1H NMR, even if 2 equiv of silyl chloride were used. Protection of the C2 hydroxyl group after silylation of C3 is difficult, the MOMylation requiring 5 days to reach completion at rt at 0.5–0.8 M concentrations. Also the use of Hünig's base is essential for the success of this reaction, the use of triethylamine failing to bring about protection. Using more forcing conditions, such as generation of the alkoxide at C2 with sodium hydride, is to be avoided as this leads to decomposition of the starting material, possibly via a Peterson-like elimination pathway. Benzylation with benzyl trichloroacetimidate (Iversen, T.; Bundle, D. R. *J. Chem. Soc., Chem. Commun.* **1981**, 1240–1241) also failed, returning unchanged starting material even after prolonged reaction times.

(23) Other Lewis acids that were examined include: BF_3-OEt_2, $TiCl_4$, $MgBr_2$-OEt_2, $SnCl_4$ at various temperatures. These either failed to provide the desired product or complicated the product mixture because of partial loss of the acid-sensitive protecting groups.

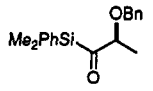
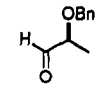
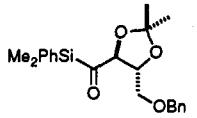
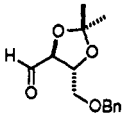
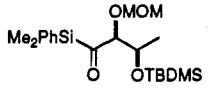
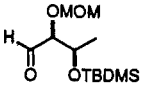
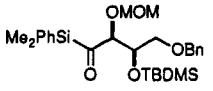
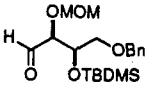
(24) The use of other Grignard reagents such as *n*-butylmagnesium bromide or isopropylmagnesium bromide resulted in the formation of significant amounts of the reduction product α-hydroxy silane, arising from hydride addition.

(25) The fluoride-promoted bis-desilylation was well solved in most cases by the use of excess cesium fluoride in a refluxing wet acetonitrile solution. It has been well documented and further demonstrated in our experiments that the protiodesilylation proceeds with complete retention of stereochemistry at the carbon center. For examples of stereospecific desilylations on carbon, see: (a) Hudrlik, P. F.; Hudrlik, A. M.; Kulkarni, A. K. *J. Am. Chem. Soc.* **1982**, *104*, 6809–6811. (b) Reich, H. J.; Holtan, R. C.; Borkowski, S. L. *J. Org. Chem.* **1987**, *52*, 312–314. References 21 and 3a.

(26) This transformation probably takes places via a Brook rearrangement. A similar observation has been previously reported: Koreeda, M.; Koo, S. *Tetrahedron Lett.* **1990**, *31*, 831–834.

(27) Sato, T.; Arai, M.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 5827–5829.

Table 3. Palladium-Catalyzed Hydrogenolysis of Acylsilanes

entry	acylsilane	time (h)[a]	aldehyde[b]	yield (%)[c]
1	 **30**	10		80
2	 **24**	24		82
3	 **26**	10		75
4	 **15**	12	 **16**	84

[a] The reactions were run in ethanol, 0.1 M in substrate, at rt, 1 atm H_2 and 20% by weight of Pd on activated carbon (Aldrich). [b] All products exhibited the expected ^1H NMR, IR, MS, and HRMS characteristics. [c] All yields are based on pure materials isolated by chromatography on SiO_2.

acetyltriphenylsilanes that the silicon–carbonyl σ bond lengths are abnormally long. This lead us to expect that this bond ought to be considerably weaker than normal C–Si bonds, perhaps arising from poor orbital overlap. Since systems that possess relatively weak, elongated C–C σ bonds such as those in cyclopropane derivatives are susceptible to cleavage under catalytic hydrogenation conditions, we subjected a selected number of our acylsilanes to these reaction conditions (eq 5). We were

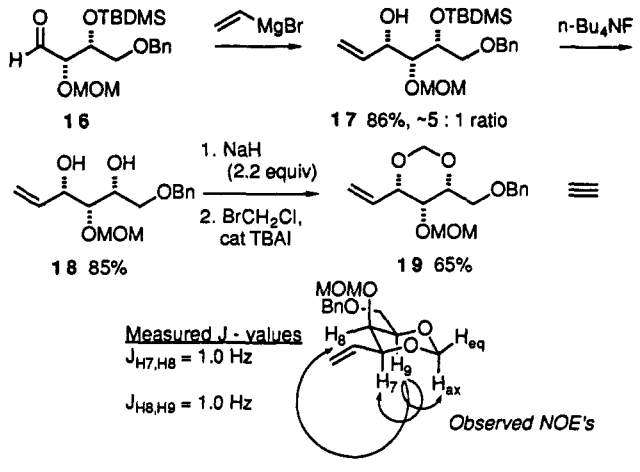
$$Me_2PhSiCOR \xrightarrow{H_2,\ Pd\text{-}C} RCHO \quad (5)$$

gratified to discover that not only does hydrogenolysis of acyldimethylphenylsilanes cleave this silicon–carbonyl bond, but the cleavage occurs faster than that of O–Bn bonds and other acid-sensitive groups are retained. Several examples illustrating this process are shown in Table 3.[7c] Thus, conversion of acylsilane **15** to the aldehyde **16** was achieved in good yield (entry 4). Vinyl Grignard addition (Scheme 4) to the aldehyde was found to take place diastereoselectively to afford a 5–6:1 ratio of diastereomers, favoring the desired 1,2,3-*syn*-triol.[28]

Having thus completed the introduction of the C7, C8, and C9 stereocenters, the B-ring of sesbanimide A was constructed (Scheme 4). Deprotection of the C3 hydroxyl with *n*-Bu_4NF and closure of the ring with bromochloromethane after generation of the dialkoxide proceeded cleanly to produce the desired 1,3-dioxane **19**, which possesses the differentiated termini at the C6 and C10 positions. The relative stereochemistry of the B-ring at the C7, C8, and C9 positions was further confirmed by difference NOE experiments and measurement of the vicinal coupling constants $J_{H7,H8}$ and $J_{H8,H9}$, which are within the expected range for the required axial–equatorial relationships in similar systems.[2,3b]

Assembly of the AB-Ring System. A variety of methods were explored for the construction of the A ring. Scheme 5 illustrates the route that was chosen, which follows the method utilized first by the Pandit[3c] and

Scheme 4



Roush[3f] groups. Ozonolysis of the double bond followed immediately by Wittig olefination with (carbethoxymethylene)triphenylphosphorane afforded the α,β-unsaturated ester **20** as a mixture of *E* and *Z* double-bond isomers (1.5–2:1), which was not separated. Conjugate addition of the *tert*-butyl acetamidoacetate anion and *in situ* cyclization assembled the A-ring as a mixture of diastereomers, which were subjected to the Krapcho decarboxylation (DMSO, NaCl, 160 °C)[29] to complete the assembly of the AB-ring system in good yield.[30] A simple, three-step manipulation of the protecting group arrangement leads to the silyl ether **24**, which is identical in all respects to an advanced intermediate in Terashima's synthesis of sesbanimide A.[3b] We have thus achieved a formal total synthesis of the alkaloid.

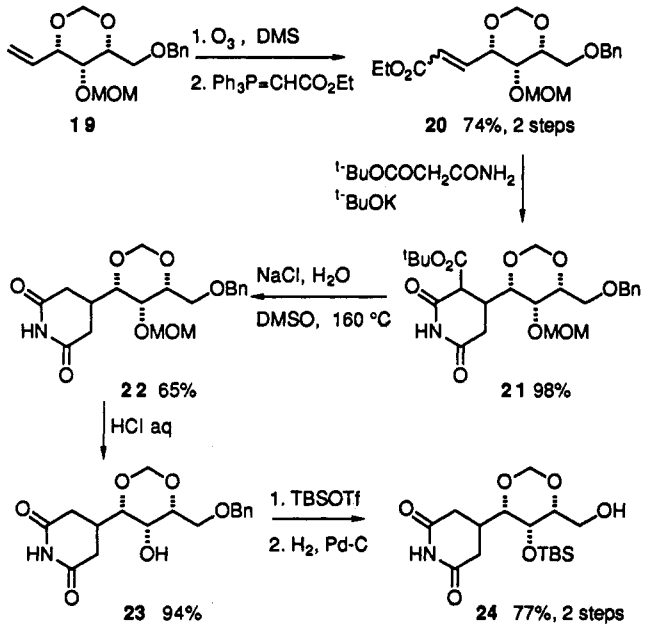
Conclusion. We have demonstrated that chiral α-alkoxy allylic silanes can have utility in acyclic diaster-

(28) Diastereoselection was found to depend on concentration and rate of addition of the Grignard reagent, best results being obtained at high dilution (<0.2 M) and fast addition times (<1 min).

(29) (a) Krapcho, A. P.; Jahngen, E. G. F.; Lovey, A. J. *Tetrahedron Lett.* **1974**, 1091–1094. (b) Liotta, C. L.; Cook, F. L. *Tetrahedron Lett.* **1974**, 1095–1098.

(30) The decarboxylation was attempted with trifluoroacetic acid, however competing loss of the MOM protecting group was observed. Compound **22** was also found to be contaminated by traces of a compound which is likely to be the 7-*epi* diastereomer derived from the minor product of the Grignard addition to aldehyde **16**. This impurity was extremely difficult to remove by column chromatography.

Scheme 5



eoselective reactions for the synthesis of polyoxygenated natural products as illustrated with the AB-ring system of (+)-sesbanimide A. Reviewing our approach to the A,B-ring system, one can conclude that geminally-substituted alkoxy and silicon functionalities exhibit a high degree of flexibility in synthesis. Incorporation of these functionalities at an allylic position has led to a π-face-selective osmylation. Subsequent protective differentiation of the two newly introduced hydroxyl groups is made possible by the geminal substitution at C1. Having served its purpose, the α-alkoxy silane functionality is converted to the aldehyde and a proper choice of protecting groups leads to a diastereoselective nucleophilic addition reaction. The selectivity of these additions is highly dependent upon the nature of the nucleophile and the nature of the oxygen protecting groups. Work is now in progress for the assembly of the C-ring of sesbanimide A, which possesses the C11 stereocenter. Progress in the search for a more satisfactory solution to this problem will be reported in due course.

Experimental Section

General. Unless otherwise noted, commercial reagents were purchased and used without further purification. THF and diethyl ether (Et_2O) were distilled from sodium and benzophenone prior to use. CH_2Cl_2, DMSO, DMF, Hunig's base, and triethylamine (NEt_3) were distilled from CaH_2 prior to use. All ^1H NMR spectra were recorded at 400 or 270 MHz and ^{13}C NMR spectra were recorded at 67.5 MHz field strengths, at rt in $CDCl_3$. TLC plates used for determining reaction progress were plastic sheets precoated with SiO_2 60F_{254} and flash chromatography was peformed on 230–400-mesh silica gel as previously described.[31]

(*E*)-4-(Benzyloxy)-1-(dimethylphenylsilyl)but-2-en-1-ol (9). Dimethylphenylsilyl chloride (18.0 mL, 120 mmol) was dissolved in 150 mL of dry THF and treated with excess lithium shot at rt. The mixture was vigorously stirred at rt for 18 h under N_2, during which time a dark brown color developed. 4-(Benzyloxy)-2-butenal (8, 21.1 g, 120 mmol) was dissolved in 150 mL of dry THF and cooled under nitrogen to below −100 °C (Et_2O/liquid nitrogen bath). The silyllithium solution was then added dropwise via syringe to the aldehyde solution, care being taken to keep the temperature below −100 °C. Forty-five minutes after the addition was complete the flask was removed from the −100 °C bath and saturated aqueous NH_4Cl (200 mL) was added carefully to the reaction mixture. Water (100 mL) and Et_2O (100 mL) were added, and the layers were separated. The aqueous layer was extracted twice with Et_2O (2 × 150 mL). The combined organic extracts were washed with water and brine and dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The product mixture contains both aldehyde starting material and 1,2-addition product. To facilitate the isolation of the latter desired material, the mixture was dissolved in 200 mL of dry methanol, cooled to 0 °C, and treated with $NaBH_4$ (1.90 g, 50 mmol). After the solution was stirred at 0 °C for 0.5 h under N_2, 3% aqueous HCl (300 mL) was added and the mixture was stirred for 10 min before extractive isolation with Et_2O as before. Column chromatography (SiO_2; 10% ethyl acetate/petroleum ether) afforded 17.97 g (48% yield) of the desired product.[7a]

(*E*)-4-(Benzyloxy)-1-(dimethylphenylsilyl)-1-oxobut-2-ene (10). Freshly distilled oxalyl chloride (4.2 mL, 47.4 mmol) was dissolved in 200 mL of dry CH_2Cl_2, stirred, and cooled to −78 °C under N_2. Dry DMSO (7.4 mL, 105 mmol) was then added dropwise by syringe. After 20 min a solution of (*E*)-1-(phenyldimethylsilyl)-4-(benzyloxy)but-2-en-1-ol (9, 13.44 g, 43.08 mmol) in 100 mL of dry CH_2Cl_2 was added slowly by syringe. After the solution was stirred at −78 °C for 1 h, dry NEt_3 (15.5 mL, 110 mmol) was added via syringe and the cold bath was removed. The solution was allowed to warm to rt. After the mixture was stirred for 0.5 h, water was added (400 mL). The aqueous fraction was extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with saturated brine and dried ($MgSO_4$), and the solvent was evaporated under reduced pressure to yield a yellow oil. Column chromatography (5% ethyl acetate/petroleum ether) afforded 7.57 g (57% yield) of the desired acylsilane: ^1H NMR (270 MHz) δ 7.52–7.10 (m, 10 H), 6.58 (dt, 1 H, $J_{H2,H3}$ = 16.1, $J_{H3,H4}$ = 4.4 Hz), 6.45 (d, 1 H, $J_{H2,H3}$ = 16.1 Hz), 4.41 (s, 2 H), 4.07 (d, 2H, $J_{H3,H4}$ = 4.4 Hz), 0.48 (s, 6 H); ^{13}C NMR (67.5 MHz) δ 234.3, 143.3, 134.6, 134.0, 129.8, 128.4, 128.2, 127.8, 127.7, 72.6, 68.9, −3.7; IR (neat) (cm^{-1}) 1950 (w), 1880 (w), 1810 (w), 1740, 1640 (m), 1590 (s), 1430 (m); CIMS (NH_3) 311.1, 293.1, 277.1, 234.1, 219.1, 203.1, 189.1, 155.0, 135.0, 91.0; CIHRMS M$^+$ (calcd for $C_{19}H_{23}SiO_2$) 311.1467, found 311.1458.

(*R*)-(*E*)-4-(Benzyloxy)-1-(dimethylphenylsilyl)but-2-en-1-ol (11). To a solution of (−)-DIP-chloride (Aldrich, 16.80 g, 52.35 mmol) in dry THF (100 mL) under N_2 and at −78 °C was added by syringe a solution of acylsilane 10 (10.82 g, 34.90 mmol) in 35 mL of dry THF. The reaction mixture was allowed to slowly warm to −35 °C and was stirred at that temperature for 2 h, at the end of which time the yellow color of the acylsilane had disappeared completely. Diethanolamine was then added (14.3 mL, 150.1 mmol) and the reaction flask was removed from the cold bath. After the mixture was stirred overnight at rt, dry Et_2O was added (100 mL). The reaction mixture was cooled back to 0 °C and vacuum filtered through Celite. The filtrate was washed with more Et_2O and the solvent was then removed under reduced pressure. Another portion of Et_2O (~150 mL) was added to the residue and the mixture was refiltered through Celite to afford a murky, light yellow oil. Chromatography on silica gel column (10% ethyl acetate/petroleum ether) yielded 8.25 g (76% yield) of the (*R*)-alcohol, which was determined to be of 92% ee after conversion of a small portion to the *O*-acetylmandelate. 11: ^1H NMR (400 MHz) δ 7.61–7.59 (m, 2 H), 7.44–7.31 (m, 8 H), 5.92 (dd, 1 H, $J_{H2,H1}$ = 5.6, $J_{H3,H2}$ = 15.6 Hz), 5.68 (dtd, 1 H, $J_{H1,H3}$ = 1.9, $J_{H4,H3}$ = 6.2 Hz), 4.50 (s, 2 H), 4.25 (d, 1 H), 4.06, 4.04 (2 s, 2 H), 2.05 (br s, 1 H), 0.40, 0.38 (2 s, 6 H); ^{13}C NMR (67.5 MHz) δ 139.8, 138.4, 135.9, 135.2, 134.2, 133.9, 129.5, 129.3, 128.4 (2C), 127.8 (2C), 127.6 (2 C), 122.7, 71.7, 70.5, 67.4, −5.6, −5.9; IR ($CHCl_3$) (cm^{-1}) 3400, 3080, 3040, 2960, 2900, 2860, 1500, 1460, 1430; CIMS (NH_3) 330.2, 210.2, 52.1; CIHRMS M$^+$ (calcd for $C_{19}H_{28}NO_2Si$) 330.1889, found 330.1903; $[\alpha]^{24}_D$ = +10.6° (*c* 2.64; $CHCl_3$).

(*R*)-(*E*)-1-(Acetyloxy)-4-(benzyloxy)-1-(dimethylphenylsilyl)-2-butene (12). (*R*)-(*E*)-1-(Phenyldimethylsilyl)-4-(benzyloxy)but-2-en-1-ol (11, 8.25 g, 26.44 mmol) was dissolved in 100 mL of dry CH_2Cl_2 and cooled to 0 °C while stirring under N_2. A catalytic amount of DMAP (~100 mg) was added. Acetic anhydride (5.0 mL, 52.9 mmol) and NEt_3 (14 mL, 100 mmol) were then added by syringe. The reaction mixture was allowed

(31) Still, W. C.; Khan, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

to reach rt and was stirred for 2 h, after which time it was quenched with water (100 mL) and saturated aqueous NH_4Cl (100 mL). Extractive isolation with CH_2Cl_2 (3 × 75 mL) followed. The combined organic extracts were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. Chromatography on a silica gel column afforded the desired (*R*)-acetate (7.70 g, 82% yield): ^{1}H NMR (400 MHz) δ 7.57–7.53 (m, 2 H), 7.40–7.28 (m, 8 H), 5.75 (ddd, 1 H, J = 0.9, $J_{H1,H2}$ = 5.9, $J_{H3,H2}$ = 15.4 Hz), 5.58 (dt, 1 H, J = 5.2 Hz), 5.47 (d, 1 H), 4.46 (s, 2 H), 4.04 (d, 2 H, J = 5.2 Hz), 2.09 (s, 3 H) 0.40 (s, 6 H); ^{13}C NMR (67.5 MHz) δ 170.5, 138.3, 135.2, 134.1 (2 C), 130.0 (2 C), 129.6, 128.3, 127.8 (2 C), 127.7, 127.5, 124.5, 71.6, 70.2, 68.9, 21.0, –5.4, –5.5; IR ($CHCl_3$) (cm^{-1}) 3020, 2830, 1730, 1370, 1230; CIMS (NH_3) 372.1, 135.2, 91.1; CIHRMS M^+ (calcd for $C_{21}H_{25}O_3Si$) 354.1651, found 354.1649; $[\alpha]^{24}_D$ = +28.4° (*c* 2.89; $CHCl_3$).

(*1R,2S,3R*)-1-(Acetyloxy)-4-(benzyloxy)-1-(dimethylphenylsilyl)butane-2,3-diol (13). (*R*)-(*E*)-1-(Phenyldimethylsilyl)-1-(acetyloxy)-4-(benzyloxy)-2-butene (**12**, 7.30 g, 20.62 mmol) was dissolved in 160 mL of acetone and 10 mL of water and was treated at rt with TMANO (5.04 g, 45.37 mmol) and catalytic OsO_4 (1.0 mL of a 0.1 M solution in toluene). The reaction mixture was stirred at rt overnight, and the solvent was removed under reduced pressure to afford a sticky brown oil. Chromatography on a silica gel column (20–25% ethyl acetate/petroleum ether) yielded 5.77 g (72% yield) of the major 1,2-*anti* diastereomer and 1.62 g (20% yield) of the minor 1,2-*syn* diastereomer.

(*1R,2S,3R*)-1,2-*anti*-Diastereomer: ^{1}H NMR (270 MHz) δ 7.56–7.52 (m, 2 H); 7.35–7.25 (m, 8 H), 4.87 (d, 1 H, $J_{H1,H2}$ = 9.3 Hz), 4.50 (s, 2 H), 3.72 (br d, 1 H, $J_{H1,H2}$ = 9.3 Hz), 3.56–3.52 (m, 1 H), 3.55 (s, 2 H), 2.80 and 2.45 (2 br s, 2 × 1 H), 1.92 (s, 3 H), 0.41 and 0.38 (2 s, 2 × 3 H); ^{13}C NMR (67.5 MHz) δ 171.5, 137.7, 136.1, 134.1 (2 C), 129.3 (2 C), 128.4 (2 C), 127.71 (2 C), 127.66, 73.1, 71.9, 71.8, 68.4, 66.9, 20.7, –4.12, –4.54; IR (neat) (cm^{-1}) 3450 (s, br), 2920, 2880, 1730 (s), 1370, 1240; $[\alpha]^{24}_D$ = +10.0° (*c* 2.25; $CHCl_3$).

(*1R,2R,3S*)-1,2-*syn*-Diastereomer: ^{1}H NMR (270 MHz) δ 7.59–7.56 (m, 2 H), 7.37–7.27 (m, 8 H), 5.09 (d, 1 H, $J_{H1,H2}$ = 2.5 Hz), 4.46 (AB q, 2 H, J_{AB} = 11.7 Hz), 3.80–3.65 (m, 2 H), 3.55–3.40 (m, 2 H), 2.90 (br s, 2 H), 2.02 (s, 3 H), 0.46 and 0.42 (2 s, 2 × 3 H); ^{13}C NMR (67.5 MHz) δ 171.2, 137.6, 135.7, 133.9 (2 C), 129.4 (2 C), 128.3 (2 C), 127.7, 127.6, 127.5, 73.2, 71.8, 71.4, 70.9, 69.6, 20.7, –4.28 (2 C); IR (neat) (cm^{-1}) 3460 (s, br), 3040, 2910, 2860, 1730 (s), 1370, 1240.

(*1R,2S,3R*)-1-(Acetyloxy)-4-(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-1-(dimethylphenylsilyl)-2-(methoxymethoxy)butane (14). 2,3-Diol **13** (5.77 g, 14.87 mmol), imidazole (29.74 mmol, 2.02 g), and *tert*-butyldimethylsilyl chloride (16.36 mmol, 2.47 g) were dissolved in 50 mL of dry DMF, and the solution was stirred at rt under N_2. After 8 h of stirring, water (75 mL) was added and the mixture was extracted with Et_2O (3 × 30 mL). The combined organic extracts were washed with water (25 mL) and saturated brine and then dried (Na_2SO_4). Evaporation of solvent and flash chromatography on a silica gel column (5–10% ethyl acetate/petroleum ether) yielded 7.36 g (99% yield) of the triprotected tetrol (*1R,2S,3R*)-1-(acetyloxy)-4-(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-1-(dimethylphenylsilyl)-2-butanol: ^{1}H NMR (270 MHz) δ 7.57–7.53 (m, 2 H), 7.33–7.24 (m, 8 H), 4.88 (d, 1 H, $J_{H1,H2}$ = 9.8 Hz), 4.45 (s, 2 H), 3.78 (t, 1 H, J = 9.3 Hz), 3.69 (distorted td, 1 H, J = 1.5, J = 6.4, J = 5.9 Hz), 3.41 (ABX, 2 H, J_{AX} = 5.9, J_{BX} = 6.4, J_{AB} = 15.6 Hz), 2.34 (br d, 1 H, J = 9.8 Hz), 1.88 (s, 3 H), 0.82 (s, 9 H), 0.40 and 0.36 (2 s, 2 × 3 H); 0.03 and –0.01 (2 s, 2 × 3 H); ^{13}C NMR (67.5 MHz) δ 170.2, 138.0, 136.9, 134.2 (2 C), 129.1 (2 C), 128.3 (2 C), 127.7 (2 C), 127.63, 127.60, 73.3, 71.9, 71.6, 70.3, 67.7, 25.9 (3 C), 20.8, 18.1, –4.14 (2 C), –4.17, –5.22; IR (neat) (cm^{-1}) 3540 (w), 2940, 2850, 1730 (s), 1370, 1240 (s); CIMS (NH_3) 520.3, 425.2, 335.2, 268.2, 193.1, 179.1, 173.1, 135.1, 91.1; CIHRMS M^+ (calcd for $C_{27}H_{46}NSi_2O_5$) 520.2915, found 520.2882; $[\alpha]^{24}_D$ = +5.6° (*c* 2.68; $CHCl_3$).

(*1R,2S,3R*)-1-(Acetyloxy)-4-(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-1-(dimethylphenylsilyl)-2-butanol (2.21 g, 4.402 mmol) was dissolved in 12 mL of dry CH_2Cl_2, and the solution was cooled to 0 °C while being stirred under N_2. A catalytic amount of tetrabutylammonium iodide was added (~20 mg, 0.05 mmol). Hunigs' base (30.8 mmol, 5.4 mL) and chloromethyl methyl ether (17.61 mmol, 1.4 mL) were added by syringe. The reaction mixture was allowed to stir at rt for 4 d before the reaction was quenched with water (50 mL), followed by extractive isolation with CH_2Cl_2 (3 × 25 mL). Drying (Na_2SO_4) and evaporation of the solvent under reduced pressure yielded an orange oil. Column chromatography on silica gel (5% ethyl acetate/petroleum ether) afforded the fully protected tetrol **14** as a colorless oil (2.28 g, 95% yield): ^{1}H NMR (270 MHz) δ 7.49–7.46 (m, 2 H), 7.35–7.25 (m, 8 H), 5.17 (d, 1 H, $J_{H1,H2}$ = 2.4 Hz), 4.58 (AB q, 2 H, J_{AB} = 6.8 Hz), 4.44 (AB q, 2 H, J_{AB} = 11.7 Hz), 3.74 (dd, 1 H, $J_{H1,H2}$ = 2.4, $J_{H2,H3}$ = 8.3 Hz), 3.61–3.55 (m, 1 H), 3.48 (dd, 1 H, J = 5.4, J = 9.8 Hz), 3.33–3.28 (buried m, 1 H, J = 4.4 Hz), 3.29 (s, 3 H), 2.00 (s, 3 H), 0.82 (9 H), 0.41 and 0.35 (2 s, 2 × 3 H), –0.03 and –0.10 (2 s, 2 × 3 H); ^{13}C NMR (67.5 MHz) δ 170.7, 138.3, 136.9, 134.4 (2 C), 129.2, 128.2 (2 C), 127.7 (2 C), 127.6 (2 C), 127.4, 97.6, 82.8, 73.4, 73.2, 72.6, 68.6, 55.6, 25.8 (3 C), 21.1, 18.0, –3.25, –3.52, –4.64, –5.00; IR (neat) (cm^{-1}) 2920, 2880, 2850, 1730, 1365, 1240; CIMS (NH_3) 564.9, 515.8, 485.8, 389.7, 385.6, 347.6, 335.6, 317.6, 285.5, 229.4, 187.3, 152.3, 91.2; CIHRMS M^+ (calcd for $C_{29}H_{50}NSi_2O_6$) 564.3176, found 564.3184; $[\alpha]^{24}_D$ = +46.3° (*c* 2.68; $CHCl_3$).

(*2S,3R*)-4-(Benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-1-(dimethylphenylsilyl)-2-(methoxymethoxy)-1-oxobutane (15). The acetate **14** (3.74 g, 6.875 mmol) was dissolved in 50 mL of dry CH_2Cl_2, and the solution was cooled to –78 °C under N_2. A solution of diisobutylaluminum hydride (1.0 M in THF, Aldrich) was added by syringe (13.75 mmol, 14 mL), and the reaction mixture was stirred at –78 °C overnight. The reaction flask was then removed from the cold bath and an aqueous saturated solution of potassium sodium tartrate (0.3 mL) was added by syringe. The reaction mixture was allowed to warm to rt and was then vacuum filtered through Celite. The gelatinous filtrate was washed repeatedly with CH_2Cl_2 (3 × 10 mL), and the solvent was evaporated from the collected mother liquor under reduced pressure. The resulting pale yellow oil was chromatographed on a silica gel column (5% ethyl acetate/petroleum ether) to yield 3.25 g (94%) of the desired (*1R,2S,3R*)-4-(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-1-(dimethylphenylsilyl)-2-(methoxymethoxy)-1-butanol: ^{1}H NMR (270 MHz) δ 7.57–7.53 (m, 2 H), 7.32–7.25 (m, 8 H), 4.47 (s, 2 H), 4.37 (AB q, 2 H, J_{AB} = 6.8 Hz), 3.98–3.94 (m, 1 H), 3.67–3.44 (m, 4 H), 3.22 (s, 3 H), 0.84 (9 H), 0.34 and 0.33 (2 s, 2 × 3 H), 0.01, –0.01 (2 s, 2 × 3 H); ^{13}C NMR (67.5 MHz) δ 138.3, 137.5, 134.3 (2 C), 129.0, 128.2 (2 C), 127.60 (2 C), 127.55 (2 C), 127.45, 98.4, 83.6, 74.7, 73.3, 71.7, 65.7, 55.7, 25.8 (3 C), 18.0, –4.07, –4.15, –4.75, –5.01; IR (neat) (cm^{-1}) 3480, 2940, 2860, 1250, 1110, 1040; CIMS (NH_3) 523.1, 443.9, 321.7, 311.6, 233.5, 187.4, 152.4, 91.3; CIHRMS M^+ (calcd for $C_{27}H_{48}NSi_2O_5$) 522.3071, found 522.3066; $[\alpha]^{24}_D$ = +5.6° (*c* 2.61; $CHCl_3$).

A 250-mL round-bottom flask was charged with 80 mL of dry CH_2Cl_2 and cooled to –78 °C under a nitrogen atmosphere. Freshly distilled oxalyl chloride (8.425 mmol, 0.74 mL) was added by syringe. Distilled, dry DMSO (18.382 mmol, 1.31 mL) was then added dropwise, and the reaction mixture was allowed to stir for 20 min at –78 °C. The above silyl alcohol (7.659 mmol, 3.86 g) dissolved in 25 mL of dry CH_2Cl_2 was added slowly by syringe. The reaction mixture was allowed to stir for 1 h. Distilled, dry NEt_3 was then added by syringe (19.15 mmol, 2.67 mL), and the flask was removed from the cold bath. The mixture was allowed to reach rt and was stirred 0.5 h before addition of water (100 mL) and extractive isolation with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. Chromatography on a silica gel column (first 100% petroleum ether to remove all sulfur impurities then 5% ethyl acetate/petroleum ether) afforded the required acylsilane **15** (3.50 g, 91%) as a pale green oil: ^{1}H NMR (270 MHz) δ 7.52–7.10 (m, 5 H), 4.41 (AB q, 2 H, J_{AB} = 6.6 Hz), 4.32 (s, 2 H), 4.05–3.95 (m, 1 H), 3.91 (d, 1 H, $J_{H1,H2}$ = 5.9 Hz), 3.30 (ABX, 2 H, J_{AB} = 9.9, J_{AX} = 5.1, J_{BX} = 6.6 Hz), 3.13 (s, 3 H), 0.81 (s, 9 H), 0.53 (s, 3 H), 0.41 (s, 3 H), –0.04 (s, 6 H); ^{13}C NMR (67.5 MHz) δ 244.9, 138.0, 135.0, 134.3 (2 C), 129.6, 128.3, 127.9, 127.8, 127.7 (2 C), 127.62, 127.57, 97.3, 88.7, 73.0, 71.8, 71.0, 55.8, 25.8 (3 C), 18.1, –3.72, –4.29, –4.45, –4.87; IR (neat) (cm^{-1}) 2920, 2860, 1640, 1460, 1360, 1250; CIMS (NH_3) 521.1, 471.9, 441.9, 395.8, 339.7, 303.6, 221.5, 187.4, 159.4, 152.4, 135.3, 91.3; CIHRMS M^+ (calcd for $C_{27}H_{46}NSi_2O_5$) 520.2914, found 520.2900; $[\alpha]^{24}_D$ = –51.8° (*c* 1.82; $CHCl_3$).

(2S,3R)-4-(Benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-2-(methoxymethoxy)-1-butanal (16). A 250-mL round-bottom flask equipped with a magnetic stirrer bar was charged with acylsilane (3.17 g, 6.315 mmol), 80 mL of absolute ethanol, and 300 mg of 10% palladium on activated carbon catalyst. The mixture was then stirred overnight at rt under 1 atm of hydrogen gas. The suspension was then vacuum filtered through a Celite bed. The filtrate was washed twice with ethanol and the solvent was evaporated under reduced pressure to afford a colorless oil which was purified by columnn chromatography on silica gel (100% petroleum ether to remove dimethylphenylsilane and then 10% ethyl acetate/petroleum ether). The aldehyde was thus obtained as a colorless oil (1.96 g, 84% yield): ^{1}H NMR (270 MHz) δ 9.76 (s ,1 H), 7.40–7.26 (m, 5 H), 4.73 (AB q, J_{AB} = 6.6 Hz), 4.50 (AB q, 2 H, J_{AB} = 13.2 Hz), 4.22 (m, 1 H), 4.02 (d, 1 H, $J_{H2,H3}$ = 4.3 Hz), 3.54 (ABX, 2 H, J_{AB} = 9.8, J_{AX} = 4.9, J_{BX} = 5.9 Hz), 3.38 (s, 3 H), 0.85 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (67.5 MHz) δ 202.1, 137.8, 128.3 (2 C), 127.8, 127.6 (2 C), 97.1, 82.9, 73.3, 72.2, 70.2, 55.9, 25.7 (3 C), 18.0, -4.62, -5.16; IR (neat) (cm^{-1}) 2920, 2850, 1730, 1460, 1360, 1250, 1100, 1030; CIMS (NH_3) 385.9, 336.9, 260.9, 188.9, 128.9, 90.9; CIHRMS M$^+$ (calcd for $C_{19}H_{36}NSiO_5$) 386.2363, found 386.2361; $[\alpha]^{24}_D$ = -4.02° (*c* 2.07; $CHCl_3$).

(3S,4R,5R)-6-(Benzyloxy)-5-((*tert*-butyldimethylsilyl)oxy)-4-(methoxymethoxy)hex-1-en-3-ol (17). Aldehyde **16** (3.56 g, 9.674 mmol) was dissolved in ~100 mL of dry CH_2Cl_2, and the solution was cooled to -78 °C while being stirred under N_2. This solution was then treated with a vinylmagnesium chloride solution (1.0 M in THF, Aldrich; 12.0 mL, 12.0 mmol), the addition being performed quickly, via syringe. After the solution was stirred at -78 °C for 15 min, the reaction was quenched with 5% aqueous HCl and the solution was warmed to rt and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried (Na_2SO_4), and the solvent was evaporated under reduced pressure to afford 3.31 g of a colorless oil (86% yield). ^{1}H NMR spectrum analysis of the crude product reveals a ~5:1 ratio of diastereomers, which could be partially separated by careful column chromatography. The following spectral data apply to the major diastereomer only: ^{1}H NMR (270 MHz) δ 7.35–7.25 (m, 5 H), 5.85–5.98 (m, 1 H), 5.36 (d, 1 H, $J_{H1,H2}$ = 17.1 Hz), 5.16 (d, 1 H, $J_{H1,H2}$ = 10.3 Hz), 4.66 (AB q, 2 H, J = 6.8 Hz), 4.52 (AB q, 2 H, J = 12.2 Hz), 4.37–4.32 (m, 1 H), 4.05-3.95 (m, 1 H), 3.60 (d, 2 H, J = 4.9 Hz), 3.36 (s, 3 H), 0.87 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (67.5 MHz) δ 138.50, 137.96, 128.33, 127.65, 127.62, 115.40, 97.92, 82.55, 73.47, 72.23, 71.39, 70.35, 55.93, 25.82, 18.05, -4.35, -4.95; IR (neat) (cm^{-1}) 3470 (br), 2940, 2860, 1460, 1370, 1250; CIMS (NH_3) 409.2, 397.3, 379.2, 365.2, 307.2, 277.1, 257.2, 217.1; CIHRMS M$^+$ (calcd for $C_{21}H_{37}SiO_5$) 397.24103, found 397.2414; $[\alpha]^{24}_D$ = +0.10° (*c* 2.89; $CHCl_3$).

(3S,4R,5R)-6-(Benzyloxy)-4-(methoxymethoxy)hex-1-ene-3,5-diol (18). The alcohol **17** (910 mg, 2.298 mmol) was dissolved in 25 mL of THF and 1.5 mL of water and was treated while being stirred at rt with tetrabutylammonium fluoride hydrate (0.5745 mmol, 150 mg). The reaction mixture was stirred at rt for 15 h and the reaction was quenched with saturated aqueous $NaHCO_3$ (50 mL) solution and extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with saturated brine and dried (Na_2SO_4). Evaporation of solvent under reduced pressure and column chromatography on silica gel (25% ethyl acetate/petroleum ether) afforded 0.55 g of the desired diol (85% yield) as a colorless oil: ^{1}H NMR (270 MHz) δ 7.37–7.25 (m, 5 H), 5.95–5.82 (m, 1 H), 5.38 (d, 1 H, J = 17.1 Hz), 5.20 (d, 1 H, J = 10.7 Hz), 4.68 (AB q, 2 H, J = 6.3 Hz), 4.53 (s, 2 H), 4.32–4.25 (m, 1 H), 3.90–4.02 (m, 1 H), 3.65–3.50 (m, 2 H), 3.40 (s, 3 H), 3.07 (br s, 1 H), 2.67 (br s, 1 H); ^{13}C NMR (67.5 MHz) δ 137.65, 137.18, 128.46, 127.88 (2 C), 116.86, 98.51, 83.58, 73.53, 72.67, 70.94, 70.43, 70.34, 56.21; IR (neat) (cm^{-1}) 3440 (br), 2900, 1450, 1370, 1210; CIMS (NH_3); CIHRMS M$^+$ (calcd for $C_{15}H_{26}NO_5$) 300.1811, found 300.1823; $[\alpha]^{24}_D$ = -13.1° (*c* 1.50; $CHCl_3$).

(4R,5R,6S)-4-((Benzyloxy)methyl)-5-(methoxymethoxy)-6-vinyl-1,3-dioxane (19). Diol **18** (0.96 g, 3.404 mmol) was dissolved in 25 mL of dry DMF, cooled to 0 °C, and treated with NaH (8.510 mmol, 340 mg of a 60% dispersion in mineral oil). After 30 min, bromochloromethane (5.106 mmol, 0.33 mL) and a catalytic amount of tetrabutylammonium iodide (25 mg) were added. The reaction mixture was allowed to warm to rt and stir for 48 h before the reaction was quenched with saturated aqueous NH_4Cl (50 mL), followed by extractive isolation with Et_2O (3 × 30 mL). The organic extracts were combined and washed successively with water (50 mL) and saturated brine (50 mL). Drying (Na_2SO_4) and evaporation of solvent under reduced pressure afforded, after column chromatography on silica gel (20% ethyl acetate/petroleum ether), the desired dioxane as a translucent white solid (0.65 g, 65% yield): ^{1}H NMR (270 MHz) δ 7.36–7.26 (m, 5 H), 5.89 (ddd, 1 H, C=CH), 5.44 (dd, 1 H, C=CH, J = 1.5, 17.6 Hz), 5.25 (dd, 1 H, C=CH, J = 1.5, 10.8 Hz), 5.20 (d, 1 H, H2eq, J = 6.4 Hz), 4.83 (d, 1 H, H2ax, J = 6.4 Hz), 4.63 (s, 2 H, OCH_2Ph), 4.54 (AB q, 2 H, $-OCH_2O-$, J_{AB} = 11.7 Hz), 4.14 (dd, 1 H, H6, $J_{H6,H5}$ = 10, J = 5.4 Hz), 3.92 (ddd, 1 H, H4, $J_{H4,H5}$ = 1.0, J = 5.8, 5.4 Hz), 3.69–3.59 (m, 3 H, CH_2-OBn), 3.58 (br s, 1 H, H5), 3.34 (s, 3 H, OMe); ^{13}C NMR (67.5 MHz) δ 137.70, 134.51, 128.44, 127.91, 127.84, 117.09, 98.07, 93.48, 80.16, 78.33, 73.63, 73.35, 69.46, 56.55; IR (neat) (cm^{-1}) 3020, 2400, 1460, 1420, 1220; CIMS (NH_3) 401.7, 311.0, 267.8, 262.8, 232.8, 192.8, 162.8; CIHRMS M$^+$ (calcd for $C_{16}H_{26}NO_5$) 312.1811, found 312.1808; $[\alpha]^{24}_D$ = -32.0° (*c* 1.00; $CHCl_3$); mp = 68–70 °C.

(*E* and *Z*, 4′*S*,5′*R*,6′*R*)-Ethyl 3-(5′-(Methoxymethoxy)-6′-((benzyloxy)methyl)-1′,3′-dioxan-4′-yl)acrylate (20). Vinyl dioxane **19** (0.65 g, 2.21 mmol) was dissolved in 15 mL of dry CH_2Cl_2 and cooled to -78 °C. Ozone was bubbled through the solution for 5–10 min, then dimethyl sulfide (22.1 mmol, 1.6 mL) was added and the mixture was allowed to reach rt. After the solution was stirred for 4 h, the solvent was removed under reduced pressure to afford a light yellow solid which was immediately dissolved in 10 mL of dry toluene and treated with (carbethoxymethylene)triphenylphosphorane (3.32 mmol, 1.15 g) at rt. After the solution was stirred overnight, the solvent was removed under reduced pressure and the reaction mixture was chromatographed to yield a ~2:1 mixture of (*E*) and (*Z*) unsaturated ethyl esters **20** (20–25% ethyl acetate/petroleum ether) (0.60 g, 74% yield in 2 steps). **(*E*)-20** isomer: ^{1}H NMR (270 MHz) δ 8.05 (br s, 1 H), 7.30–7.20 (m, 5 H), 6.89 (dd, 1 H, C=CH, J = 18.0, 1.6 Hz), 6.17 (dd, 1 H, C=CH, J = 18.0, 0.9 Hz), 5.20 (AB q, 2 H), 4.75 (AB q, 2 H), 4.60–4.45 (m, 4 H), 4.31 (br s, 1 H), 4.22–4.10 (m, 3 H), 3.95–3.90 (m, 1 H), 3.70 (s, 1 H), 3.65–3.55 (m, 2 H), 3.28 (s, 3 H), 1.22 (t, 2 H). **(*Z*)-20** isomer: ^{1}H NMR (270 MHz) δ 8.00 (br s, 1 H), 7.35–7.20 (m, 5 H), 6.30 (dd, 1 H, C=CH, J = 11.3, 8.6 Hz), 5.89 (d, 1 H, C=CH, J = 11.3 Hz), 5.25–5.12 (m, 2 H), 4.87 (m, 1 H), 4.60–4.40 (m, 4 H), 4.25–4.10 (m, 3 H), 4.06–4.02 (m, 1 H), 3.91 (s, 1 H), 3.70–3.50 (m, 3 H), 3.28 (s, 3 H), 1.22 (t, 2 H); CIMS (NH_3) 474.2, 398.1, 321.1, 384.2, 335.1, 277.1, 245.1, 207.1, 129.1, 105.0, 91.1; CIHRMS M$^+$ (calcd for $C_{19}H_{30}NO_7$) 384.2022, found 384.2033.

(4′*S*,5′*R*,6′*R*)-4-(5′-(Methoxymethoxy)-6′-((benzyloxy)methyl)-1′,3′-dioxan-4′-yl)-2,6-piperidinedione (22). Potassium *tert*-butoxide (119 mg, 1.06 mmol) was added to a solution of *tert*-butyl carbamoylacetate (203 mg, 1.27 mmol) in dry THF (4 mL) at 0 °C. When the solution has become homogeneous, ethyl acrylate (**20**, 426 mg, 1.16 mmol) was added slowly via syringe as a solution in THF (0.5 M). After 1 h, more *tert*-butoxide was added (~5 mg). The reaction mixture was left stirring at 0 °C for 5 h and then was quenched with glacial acetic acid (1.38 mmol, 79 μL). The mixture was then partitioned between water and ethyl acetate and the aqueous layer was extracted with ethyl acetate (3 × 3 mL portions). The combined organic extracts were washed once with saturated brine and dried ($MgSO_4$), and the solvent was removed under reduced pressure to yield a tan foam (550 mg, 98% crude) that appears to be a clean mixture of diastereomers **21** by ^{1}H NMR analysis. The crude product (400 mg, 0.833 mmol) was dissolved in 5 mL of DMSO. Water (2.5 mmol, 45 $\mu\Lambda$) and NaCl (1.67 mmol, 98 mg) were added, and the mixture was heated to 160–170 °C for 1 h. The mixture was then cooled down to rt and partitioned between water and Et_2O, and the aqueous layer was extracted with Et_2O (3 × 6 mL). After drying (brine and $MgSO_4$), the solvent was removed under reduced pressure to yield a white foam. Chromatography on an SiO_2 column (75–100% ethyl acetate/petroleum ether) afforded the desired piperidinedione **22** as a white solid (200 mg, 63%; 2 steps): ^{1}H NMR (270 MHz) δ 7.79 (br s, 1 H), 7.37–7.26 (m, 5 H), 5.13 (d, 1 H), 4.74–4.72 (m, 2 H), 4.64 (d, 1 H), 4.51 (s, 2 H), 3.83–3.77 (m, 1 H), 3.67–3.55 (m, 3 H), 3.35 (s, 3 H, OCH_3), 3.31–3.29 (m, 1 H), 3.00–2.87 (m, 2 H), 2.68–2.54 (m, 1 H), 2.50–2.15 (m, 2 H); ^{13}C NMR (67.5 MHz) δ 172.1, 171.5, 137.2, 129.6, 128.5,

128.0, 127.9, 98.0, 93.7, 81.0, 73.6, 70.8, 67.8, 56.4, 33.9, 32.9, 30.9; IR ($CHCl_3$) (cm^{-1}) 3280, 1720, 1700, 1420; CIMS (NH_3) 397.2, 348.1, 334.1, 258.0, 180.0, 104.9, 90.9; CIHRMS M^+ (calcd for $C_{19}H_{29}N_2O_7$) 397.1975, found 397.1972; $[\alpha]^{24}_D$ = +34.0° (*c* 0.97; $CHCl_3$); mp = 66–68 °C.

(4′*S*,5′*R*,6′*R*)-4-(5′-Hydroxy-6′-((benzyloxy)methyl)-1′,3′-dioxan-4′-yl)-2,6-piperidinedione (23). MOM ether **22** (46.2 mg; 0.122 mmol) was dissolved in 1.2 mL of a THF:H_2O:HCl (concd) solution (8:1:1) and stirred at rt for 1 h. Aqueous, saturated $NaHCO_3$ quench and extractive isolation with THF:ethyl acetate (1:1) followed, to afford 42.7 mg of a solid, which was chromatographed on SiO_2 column (5% ethyl alcohol in CH_2Cl_2); yield 38.3 mg (94%); ^1H NMR (270 MHz) δ 8.55 (br s, 1 H, N–H); 7.35–7.27 (m, 5 H), 5.09 (d, 1 H), 4.70 (d, 1 H), 4.54 (AB q; 2 H, *J* = 12.2 Hz), 3.78 (t, 1 H, *J* = 5.6 Hz), 3.64 (AB q, 2 H, *J* = Hz), 3.56 (br s, 1 H), 3.32 (d, 1 H, *J* = 8.3 Hz), 2.89 (ddd, 1 H, *J* = 16.6, 1.5, 4.0 Hz), 2.70 (ddd, 1 H, *J* = 17.2, 1.5, 4.0 Hz), 2.63–2.52 (m, 1 H), 2.40 (dd, 1 H, *J* = 17.2, 9.8 Hz), 2.28 (dd, 1 H, *J* = 16.6, 9.6); ^{13}C NMR (67.5 MHz) δ 172.2, 171.6, 137.4, 129.7, 128.4 (2 C), 127.9, 127.8, 93.7, 81.4, 78.5, 73.7, 69.5, 64.6, 33.8, 33.0, 30.9; CIMS (NH_3) 397.2, 348.1, 334.1, 258.0, 180.0; CIHRMS M^+ (calcd for $C_{17}H_{25}N_2O_6$) 353.1713, found 353.1732; $[\alpha]^{24}_D$ = +3.6° (*c* 0.45; $CHCl_3$); mp = 162–165 °C.

(4′*S*,5′*R*,6′*R*)-4-(5′-((*tert*-Butyldimethylsilyl)oxy)-6′-(hydroxymethyl)-1′,3′-dioxan-4′-yl)-2,6-piperidinedione (24). Alcohol **23** (28.6 mg; 0.0851 mmol) was dissolved in 0.8 mL of CH_2Cl_2 at rt under N_2 and treated with 2,6-lutidine (79 μL, 0.681 mmol) and TBSOTf (69 mL; 0.300 mmol). After 10 min the mixture was diluted with ethyl acetate and washed with saturated, aqueous $NaHCO_3$ and then brine. The mixture was dried ($MgSO_4$), the solvent was evaporated, and the product was chromatographed on an SiO_2 column (20% ethyl acetate in petroleum ether), to yield a colorless caramel: 35.4 mg (78.7 mmol; 92%); ^1H NMR (400 MHz) δ 7.35–7.27 (m, 5 H), 5.88 (br s, 1 H), 5.12 (d, 1 H, *J* = 6.2 Hz), 4.76 (d, 1 H, *J* = 6.3 Hz), 4.53 (AB q, 2 H, *J* = 2.1 Hz), 3.88 (m, 1 H), 3.65 (dd, 1 H, *J* = 10.2, 7.4 Hz), 3.54 (br s, 1 H), 3.51 (dd, 1 H, *J* = 10.2, 4.3 Hz), 3.39 (br s, 1 H), 2.63 (dd, 1 H, *J* = 18.6, 7.1 Hz), 2.47 (m, 1 H), 2.38 (dd, 1 H, *J* = 14.0, 1.7 Hz), 2.28 (br d, 1 H, *J* = 18.6 Hz), 1.70 (dd, 1 H, *J* = 12.5, 2.9 Hz), 0.86 (s, 9 H), 0.21 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (67.5 MHz) δ 170.4 (2 C), 137.6, 129.7, 128.5 (2 C), 127.9, 127.8, 101.3, 92.9, 73.9, 73.6, 69.4, 66.7, 32.1, 31.9, 25.4 (3 C), 17.6, –2.82, –3.52; CIMS (NH_3) 451.2, 450.2, 342.1, 336.1, 284.1, 256.1, 226.1, 108.1, 105.0, 92.0, 91.1, 73.0; CIHRMS M^+ (calcd for $C_{23}H_{36}NSiO_6$) 450.2312, found 450.2316.

This benzyl ether (20.5 mg, 0.0456 mmol) was dissolved in 1 mL of ethanol (96%) and treated at rt with palladium on activated charcoal catalyst (~5 mg) under an atmosphere of H_2. After 2 h, the mixture was filtered through Celite, the residue was washed with ethanol (2 × 2.5 mL portions), and the solvent was evaporated *in vacuo*. Chromatography on SiO_2 column (5% methanol in $CHCl_3$) afforded the desired alcohol **24** (13.4 mg, 82%): ^1H NMR (270 MHz) δ 6.16 (br s, 1 H), 5.17 (d, 1 H, *J* = 6.3 Hz), 4.81 (d, 1 H, *J* = 6.3 Hz), 3.90 (m, 1 H), 3.80 (m, 1 H), 3.70 (m, 1 H), 3.61 (br s, 1 H), 3.43 (br s, 1 H), 2.69 (dd, 1 H, *J* = 7.2, 18.6 Hz), 2.53 (m, 1 H), 2.42 (br d, 1 H, 12.5 Hz), 2.33 (br d, 1 H, *J* = 18.6 Hz), 2.13–2.21 (m, 1 H), 1.75 (dd, 1 H, *J* = 2.9 and 12.5 Hz), 0.90 (s, 9 H), 0.27 (s, 3 H), 0.20 (s, 3 H); ^{13}C NMR (67.5 MHz) δ 170.8 (2 C), 101.3, 92.9, 78.2, 73.9, 66.6, 62.2, 33.3, 32.0, 31.9, 25.4 (3 C), 17.6, –2.81, –3.49; IR ($CHCl_3$) (cm^{-1}) 3450, 3310, 1665; CIMS (NH_3) 362.1, 361.1, 360.1, 272.1, 256.1, 226.1, 73.0; CIHRMS M^+ (calcd for $C_{16}H_{30}NSiO_6$) 360.1842, found 360.1810; $[\alpha]^{24}_D$ = –10.2° (*c* 0.67; $CHCl_3$); mp = 175–177 °C [lit.[3b] $[\alpha]^{20}_D$ –10.4° (*c* 0.50, $CHCl_3$); mp 176–178 °C].

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Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of **10–22** (37 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.