# The First Synthesis of Herbicidin B. Stereoselective Construction of the Tricyclic Undecose Moiety by a Conformational Restriction Strategy Using Steric Repulsion between Adjacent Bulky Silyl Protecting Groups on a Pyranose Ring†

**Satoshi Ichikawa, Satoshi Shuto, and Akira Matsuda***

*Contribution from the Graduate School of Pharmaceutical Sciences, Hokkaido University, Kita-12, Nishi-6, Kita-ku, Sapporo 060-0812, Japan*

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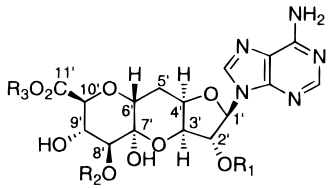
**Abstract:** The first total synthesis of the nucleoside antibiotic herbicidin B (**1b**) was achieved, where a novel aldol-type *C*-glycosidation reaction promoted by samarium diiodide ($SmI_2$) was used as a key step. Treatment of methyl 3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxanediyl)-1-phenylthio-2-ulos-$\beta$-D-glucuronate (**13**) with $SmI_2$ in THF regioselectively gave the corresponding 1-enolate, which was readily trapped with 1-$\beta$-D-xylosyladenine 5′-aldehyde derivative **7** to afford the product **19a**,**b** as an anomeric mixture. Dehydration of the 5′-hydroxyl in **19a**,**b** with using Burgess's inner salt gave the enone **20**, which was subsequently hydrogenated to give undeculofuranuronyl adenine derivative **21**. Deprotection of **21** gave a tricyclic sugar nucleoside, **23**. However, it was an epimer of herbicidin B at the 6′-position. Construction of the desired 6′-α-configuration was achieved by using a conformational restriction strategy based on repulsion between adjacent bulky protecting groups on the pyranose ring. Thus, when methyl 3-*O*-*tert*-butyldimethylsilyl-4-*O*-*tert*-butyldiphenylsilyl-1-phenylthio-2-ulos-D-glucuronate (**29c**), the conformation of which was restricted in an unusual $^1C_4$-like conformation, was used as a precursor for ulose 1-enolate in the $SmI_2$-promoted aldol reaction with **7**, the desired 6′-α-aldol product **30c** was predominantly obtained. Compound **30c** was dehydrated, followed by hydrogenation of the alkenyl bond and then deprotection to form an internal ketal linkage between the 3′- and 7′-positions, which spontaneously gave herbicidin B.

## Introduction

Nucleoside antibiotics are fascinating compounds that show a variety of biological activities.[1] They are not only used as medicines, lead compounds for the development of drugs, and biological tools but are also important as total synthetic targets.[2]

Herbicidins (**1a**−**f**),[3] aureonucleomycin (**2**),[4] and S12245 (**3**),[5] a series of adenine nucleoside antibiotics that have the same backbone structure (Figure 1), have been isolated from strains of *Streptomyces*. Herbicidin A (**1a**) and B (**1b**), as well as aureonuclemycin (**2**), efficiently inhibit the growth of *Xanthomonas oryzae*, which causes rice leaf blight, and are also selectively toxic toward dicotyledon. These compounds have some interesting structural features: (1) adenine is glycosylated at the 1$\beta$-position of an unusual sugar, undecose, which has a tricyclic furano-pyrano-pyran structure; (2) there is an internal hemiketal linkage between the C-3′- and -7′-positions which forms a trans junction for a pyrano-pyran ring; and (3) all of the substituents at the C-7′-, -8′-, -9′-, and -10′-positions on the second pyranose are fixed in axial positions due to the tricyclic structure of the undecose. Although considerable effort has been devoted to the total synthesis of herbicidins because of their unique and complex structures,[6,7] none of these attempts has yet been successful.



| | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|
| Herbicidin A (**1a**) | Me | $CH_3CH=C(CH_2OH)CO$ | Me |
| Herbicidin B (**1b**) | Me | H | Me |
| Herbicidin C (**1c**) | H | H | Me |
| Herbicidin E (**1d**) | Me | $(CH_3)_2CHCO$ | Me |
| Herbicidin F (**1e**) | Me | $CH_3CH=C(CH_3)CO$ | Me |
| Herbicidin G (**1f**) | H | $CH_3CH=C(CH_3)CO$ | H |
| Aureonuclemycin (**2**) | Me | $CH_3CO$ | Me |
| SI2245 (**3**) | H | H | H |

**Figure 1.** Structures of herbicidins.

In this paper, we describe the synthesis of herbicidin B (**1b**), in which a novel samarium diiodide ($SmI_2$)-promoted aldol-

* To whom correspondence and reprint requests should be addressed. Phone: +81-11-706-3228. Fax: +81-11-706-4980. E-mail: matuda@pharm.hokudai.ac.jp.

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(1) (a) Isono, K. *J. Antibiot.* **1988**, *41*, 1711−1739. (b) Isono, K. *Pharmacol. Ther*. **1991**, *52*, 296−286.

(2) Knapp, S. *Chem. Rev*. **1995**, *95*, 1859−1876.

(3) (a) Arai, M.; Haneishi, T.; Kitahara, N.; Enokita, R.; Kawakubo, K.; Kondo, Y. *J. Antibiot.* **1976**, *29*, 863−869. (b) Haneishi, T.; Terahara, A.; Kayamori, H.; Yabe, J.; Arai, M. *J. Antibiot.* **1976**, *29*, 870−875. (c) Taguchi, Y.; Yoshikawa, H.; Terahara, A.; Torikata, A.; Terao, M. *J. Antibiot.* **1979**, *32*, 857−861. (d) Takiguchi, Y.; Yoshikawa, H.; Terahara, A. *J. Antibiot.* **1979**, *32*, 862−867. (e) Terahara, A.; Haneishi, T.; Arai, M. *J. Antibiot.* **1982**, *35*, 1711−1714.

(4) Dai, X.; Li, G.; Wu, Z.; Lu, D.; Wang, H.; Li, Z.; Zhou, L.; Chen, X.; Chen, W. *Chem. Abstr*. **1989**, *111*, 230661f.

(5) Tsuzuki, M.; Suzuki, G. *Chem. Abstr*. **1988**, *109*, 53206x.

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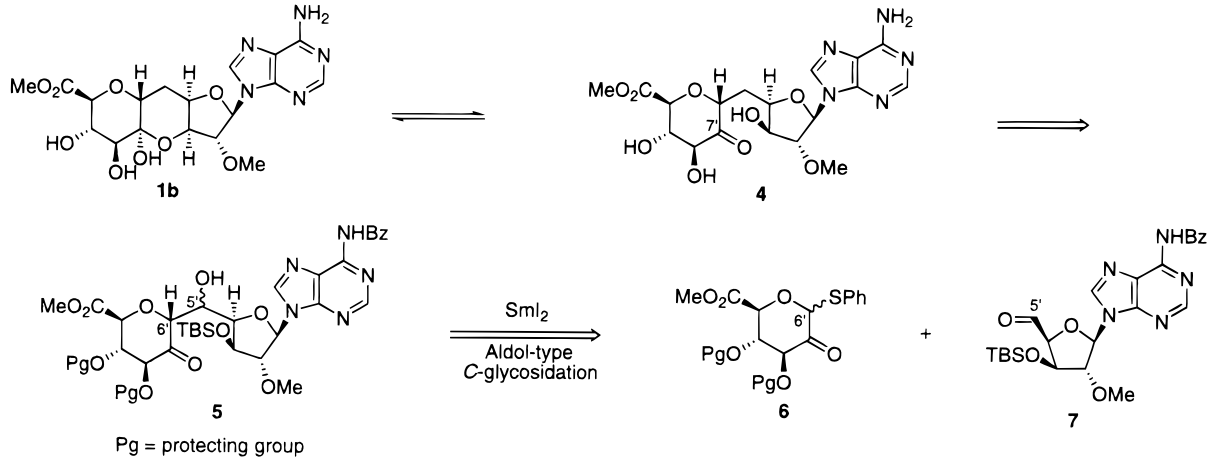
**Scheme 1**



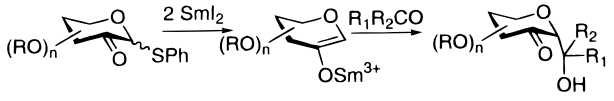

type *C*-glycosidation reaction with 1-phenylthio-2-ulose derivatives, as a precursor for generating ulose-1-enolate,[8] is effectively used as a key step. This is the first total synthesis of a herbicidin congener.

## Results and Discussion

**Retrosynthetic Analysis and Strategy.** Our retrosynthetic analysis and synthetic strategy for herbicidin B (**1b**) are shown in Scheme 1. Herbicidin B can be considered the equivalent of a ring-opened 7′-keto compound, **4**, and appropriate protection of the hydroxyl groups and the introduction of a hydroxyl group at the C-5′ of **4** leads to aldol product **5**. This aldol product **5** is then retrosynthetically disassembled by an aldol-type reaction to the phenylthioulose **6** as a precursor of enolate and 1-$\beta$-D-xylosyladenine 5′-aldehyde derivative **7** as an acceptor. Compounds **6** and **7** can be synthesized from D-glucose and adenosine, respectively.

In this retrosynthetic analysis and synthetic strategy, the following two steps are considered key steps: (a) formation of the tricyclic structure with the desired stereochemistry, namely 6′-α-(6′,7′-*trans*)-configuration, in the second pyranose ring in which the substituents at the *C*-8′-, -9′-, and -10′-positions are all in axial positions, and (b) a stereoselective *C*-glycosidation which gives the 6′-α-configuration by an aldol-type reaction between a ulose derivative and an adenine nucleoside 5′-aldehyde. In the former step, we expected that spontaneous cyclization by the formation of a ketal linkage between the 3′- and 7′-positions would be achieved in a stereoselective manner to give the desired herbicidin B when the protecting groups of the hydroxyls are removed. In the latter step, we planned to use a $SmI_2$-promoted aldol-type *C*-glycosidation reaction, which we recently developed (Scheme 2).[8] This reaction is very useful because (1) phenylthio-2-ulose derivatives, the precursor for generating enolates, are stable and easy to prepare, (2) regioselective enolization at the anomeric position of the ulose

**Scheme 2**




derivative is possible by $SmI_2$-promoted reductive cleavage of a C−S bond at the anomeric position,[9] (3) substrates such as nucleoside 5′-aldehydes, which are unstable under basic and/or acidic conditions,[10] can be used, since the reaction proceeds under neutral conditions at −78 °C, and (4) the reaction gives the corresponding α-*C*-glycosides as a major product in high yields. Based on these findings, we expected that the 6′-α-aldol product **5** could be obtained by the $SmI_2$-promoted condensation reaction between **6** and **7**.

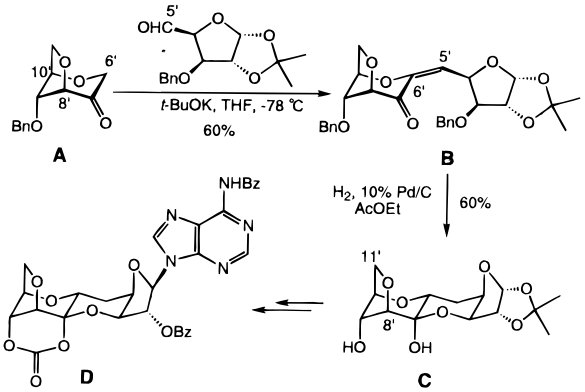
**Preparation of the 1-Phenylthio-2-ulose Unit.** We first selected **13** as a precursor for ulose 1-enolate, in which the 3,4-*trans* hydroxyls were protected by a 1,1,3,3-tetraisopropyldisiloxane (TIPDS) group. Scheme 3 shows its preparation. Protection of the 4- and 6-hydroxyls of phenyl 1-thio-$\beta$-D-glucoside (**8**) by a TIPDS group, followed by acid-catalyzed

(6) (a) Beader, J. R.; Dewis, M. L.; Whiting, D. A. *J. Chem. Soc., Perkin Trans. 1* **1995**, 227−233. (b) Fairbanks, A. J.; Perrin, E.; Sinay, P. *Synlett* **1996**, 679−681. (c) Emery, F.; Vogel, P. *J. Org. Chem.* **1995**, *60*, 5843−5854. (d) Emery, F.; Vogel, P. *Tetrahedron Lett.* **1994**, *34*, 4209−4212.

(7) (a) Binch, H. M.; Griffin, A. M.; Gallagher, T. *Pure Appl. Chem.* **1996**, *68*, 589−592. (b) Newcombe, N. J.; Mahon, M. F.; Molloy, K. C.; Alker, D.; Gallagher, T. *J. Am. Chem. Soc.* **1993**, *115*, 6430−6431. (c) Binch, H. M.; Gallagher, T. *J. Chem. Soc., Perkin Trans. 1* **1996**, 401−402.

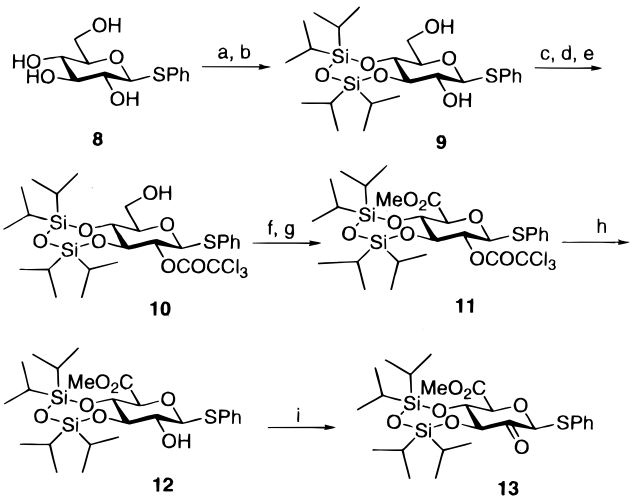
(8) Ichikawa, S.; Shuto, S.; Matsuda, A. *Tetrahedreon Lett.* **1998**, *39*, 4525−4528. $SmI_2$-promoted *C*-glycosidation reaction with mannosyl pyridylsulfones as substrates were also reported: Jarreton, O.; Skrydstrup, T.; Beau J.-M. *Tetrahedron Lett.* **1997**, *38*, 1767−1770.

(9) Gallagher et al. reported that the generation of the 1-enolate was successful when 3,6-anhydro-ulose **A** was used as a substrate. Compound **B** was further glycosylated with adenine to give nucleoside derivative **D**. However, hydrolysis of the 8′,11′-ether linkage on **D** was unsuccessful; see ref 7c.




(10) Gallagher et al. tried to prepare an aldol condensation product between **A** (footnote 9) and adenosine 5′-aldehyde derivative which was almost the same as **7**, but this was unsuccessful due to the instability of adenosine 5′-aldehyde under the basic conditions used. Therefore, reductive coupling using ulosyl bromides as enolates was developed. However, ulosyl bromides are not very stable, and the substrates that can be synthesized are limited: Binch, H. M.; Griffin, A. M.; Schwidetzky, S.; Ramsay, M. V. J.; Gallagher, T.; Lichtenthaler, F. W. *J. Chem. Soc., Chem. Commun.* **1995**, 967−968.

**Scheme 3**[a]



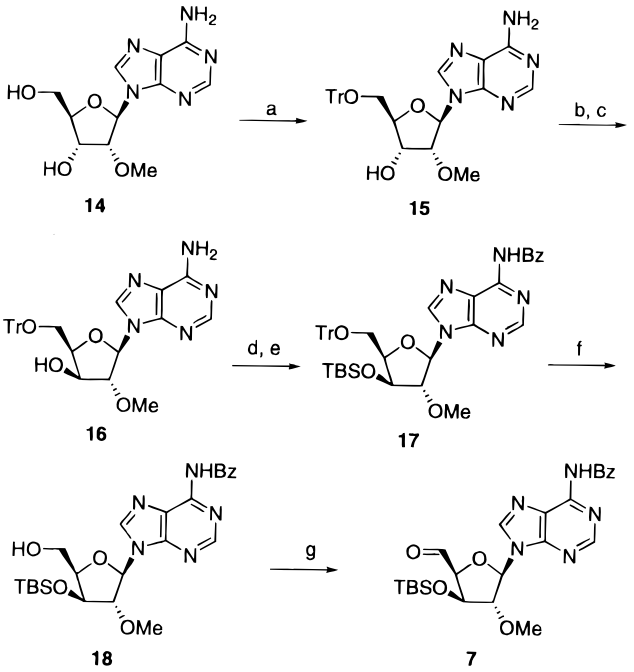

[a] Reagents: (a) $TIPDSCl_2$, pyridine; (b) *p*-TsOH, DMF; (c) TrCl, pyridine; (d) $Cl_3COCl$; (e) TFA, $CH_2Cl_2$; (f) DCC, TFA, DMSO; (g) PDC, MeOH, DMF; (h) $K_2CO_3$, MeOH; (i) $(COCl)_2$, DMSO, $Et_3N$, $CH_2Cl_2$.

isomerization,[11] gave **9** in 59% yield in two steps. After protection of the 2-hydroxyl of **9** by a trichloroacetyl group, it was successively treated by Moffatt oxidation conditions and PDC in the presence of MeOH[12] to give methyl ester derivative **11** in 61% yield. Removal of the trichloroacetyl group at the 2-position of **11** with $K_2CO_3$/MeOH, followed by Swern oxidation of the resulting secondary alcohol, gave 1-phenylthio-2-ulose derivative **13** in excellent yield. The compound **13** was sufficiently stable to be purified by silica gel column chromatography.

**Preparation of the 1-*β*-D-Xylosyladenine 5′-Aldehyde Unit.** 1-*β*-D-Xylosyladenine 5′-aldehyde derivative **7** was prepared as shown in Scheme 4. After the 5′-primary hydroxyl of 2′-*O*-methyladenosine **14** (prepared by a known method[13]) was protected by a triphenylmethyl (Tr) group, the 3′-hydroxyl was inverted by a successive oxidation−reduction procedure with $CrO_3/Ac_2O$/pyridine and $NaBH_4$/AcOH systems[14] to give xylonucleoside **16** in 78% yield. Protection of the resulting 3′-hydroxyl and 6-amino groups of **16** with *tert*-butyldimethysilyl (TBS) and benzoyl groups, respectively, by usual procedures gave **17** in 83% yield. Removal of the Tr group of **17** under acidic conditions, followed by oxidation with Dess−Martin periodinane, gave **7**, an acceptor of the aldol reaction. The aldehyde **7** was used for the next reaction without further purification because of its instability.

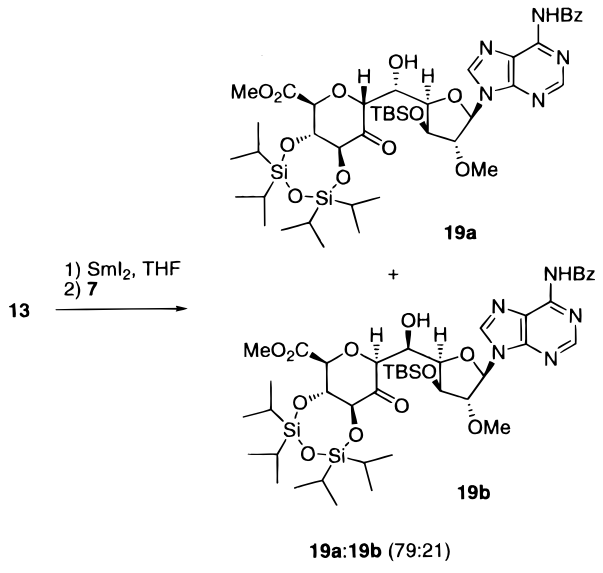
**Synthesis of 6′-*epi*-Herbicidin B Using a $SmI_2$-Promoted Aldol-Type *C*-Glycosidation Reaction as a Key Step.** We examined the $SmI_2$-promoted aldol-type *C*-glycosidation reaction with **13** and **7** (Scheme 5). When a solution of **13** in THF was added dropwise to a stirring solution of $SmI_2$ (2.0 equiv) in THF at −78 °C, the corresponding samarium 1-enolate was successfully generated, to which a solution of **7** (1.0 equiv) in THF was added to give the desired aldol products in 75% yield as an anomeric mixture (**19a**/**19b** = 79/21). NOE experiments of the mixture revealed their 6′-stereochemistries; correlation

**Scheme 4**[a]




[a] Reagents: (a) TrCl, pyridine; (b) $CrO_3$, pyridine, $Ac_2O$, 4-Å molecular sieves, $CH_2Cl_2$; (c) $NaBH_4$, AcOH; (d) TBSCl, imidazole; (e) BzCl, pyridine; (f) TFA, $CH_2Cl_2$; (g) Dess−Martin periodinane, $CH_2Cl_2$.

**Scheme 5**




between H-6′ and H-9′ for the α-anomer **19a** and correlations between H-6′ and H-8′, and between H-6′ and H-10′, for the *β*-anomer **19b** were observed (Figure 2).[15]

Radical deoxygenation of the 5′-hydroxyl group of the anomeric mixture **19a**,**b** via the corresponding 5′-*O*-methyl oxalate[16] or 5′-thiocarbonylimidazolidate[17] was tried but was

(11) van Boeckel, C. A. A.; van Boom, J. H. *Tetrahedron* **1985**, *41*, 4545−4555.

(12) Garegg, P. J.; Olsson, L.; Oscarson, S. *J. Org. Chem.* **1995**, *60*, 2200−2204.

(13) Yano, J.; Kan, L. S.; Ts'o, P. O. P. *Biochim. Biophys. Acta* **1980**, *629*, 178−183.

(14) Robins, M. J.; Samano, V.; Johnson, M. D. *J. Org. Chem.* **1990**, *55*, 410−412.

(15) The 5′-configurations of **19a** and **19b** were suggested to be 5′*R* and 5′*S*, respectively, on the basis of the possible six-membered-ring chelation transition state in the $SmI_2$-mediated aldol reaction. In fact, the 5′*R*-configuration of **19a** was confirmed as shown below. During the treatment of **19a** with $SmI_2$ in MeOH, an isomerization of the configuration at the 6′-position was observed.

(16) (a) Matsuda, A.; Takenuki, K.; Itoh, H.; Sasaki, T.; Ueda, T. *Chem. Pharm. Bull.* **1987**, *35*, 3967−3970. (b) Matsuda, A.; Takenuki, K.; Sasaki, T.; Ueda, T. *J. Med. Chem.* **1991**, *34*, 235−239. (c) Dolan, S. C.; MacMillan, J. *J. Chem. Soc., Chem. Commun.* **1985**, 1588−1589.

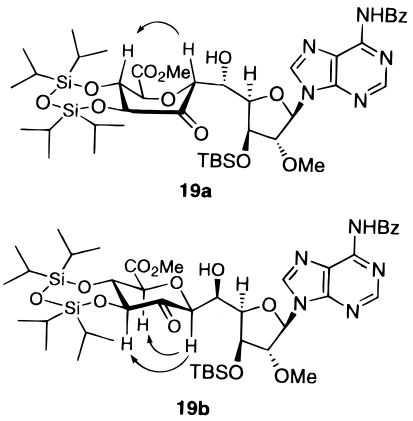
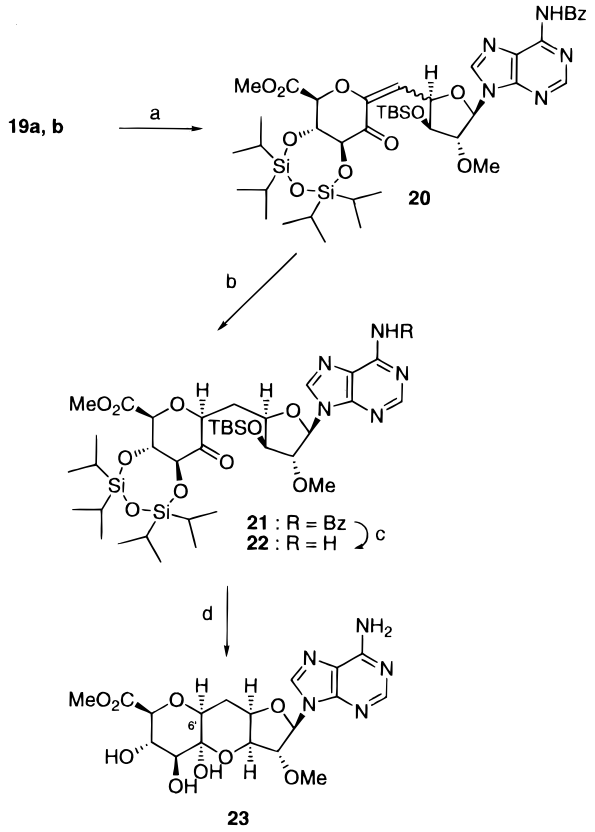



**Figure 2.** Determination of stereochemistry at the 6′-position of **19a** and **19b** by NOE experiments.

**Scheme 6**[a]




[a] Reagents: (a) $MeO_2CNSO_2NEt_3$, toluene; (b) $H_2$, Pd/C, EtOAc; (c) Sm, $I_2$, MeOH; (d) TBAF, THF.

unsuccessful.[18] We next sought to dehydrate it by elimination of the 5′-hydroxy of **19a**,**b**, followed by hydrogenation of the resulting alkenyl bond. Thus, **19a**,**b** was converted to the corresponding 5′-*O*-mesylate and -triflate. However, treatment of these 5′-*O*-sulfonates with a base led only to their decomposition, and the desired elimination product **20** was not obtained. On the other hand, as shown in Scheme 6, when **19a**,**b** was treated with $MeO_2CNSO_2NEt_3$ (Burgess's inner salt)[19] in toluene, the desired elimination reaction proceeded to give the enone **20** in 49% yield as a mixture of inseparable isomers due to a *cis*/*trans* geometry at the 5′-position. The enone **20** was hydrogenated with $H_2$ in the presence of palladium-on-carbon in EtOAc to give **21** quantitatively, the anomeric configuration of which was determined to be the undesired $\beta$ by NOE experiments; correlations between H-6′ and H-8′, and between H-6′ and H-10′, were observed.[20] However, we expected that isomerization at the 6′-position, which was adjacent to the 7′-carbonyl, into the desired α-configuration might occur in the following stages.

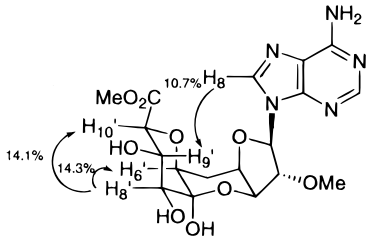



**Figure 3.** Structure determination of 6′-*epi*-herbicidin B (**23**) by NOE experiments.

Therefore, removal of the protecting groups was examined next. When **21** was treated with NaOMe or $K_2CO_3$ in MeOH to remove the benzoyl group at the $N^6$-position, it decomposed and did not give any of the debenzoylated **22**. However, exposure of **21** to samarium and $I_2$ in MeOH[21] successfully gave the debenzoylated product **22**. When **22** was treated with tetrabutylammonium fluoride (TBAF) in THF, all of the silyl protecting groups were removed simultaneously to give a tricyclic sugar product by spontaneously forming an internal ketal linkage between the 3′- and 7′-positions, as expected. However, the product was not herbicidin B, but rather 6′-*epi*-herbicidin B (**23**), an epimer of herbicidin B at the 6′-position. The structure of **23** was confirmed by $^1$H NMR and NOE experiments. As shown in Figure 3, the coupling constants, $J_{8',9'} = J_{9',10'} = 9.5$ Hz, suggested its $^{9'}C_{6'}$-structure, and NOE correlations between H-6′ and H-8′, H-8′ and H-10′, and H-9′ and H-8 at the adenine moiety suggested a $\beta$-configuration at the 6′-position. Although isomerization of **23** into herbicidin B was investigated by treating it under acidic and basic conditions, such isomerization was not observed.[22]

**Conformation-Flip Strategy.** Based on the above results, we recognized that it would be essential to provide the 6′-α-*C*-glycosidic structure before forming the 3′,7′-ketal linkage to construct the desired tricyclic structure of the sugar moiety of herbicidin B. Therefore, stereoselective hydrogenation from the α-face of the 5′,6′-alkenyl bond in the enone system was required. The $^1$H NMR spectrum of **20** showed that the substituents at 8′, 9′, and 10′ were in equatorial positions; both

(17) Pankiewicz, K.; Matsuda, A.; Watanabe, K. A. *J. Org. Chem.* **1982**, *47*, 485−488.

(18) It has been reported that deoxygenation of the 5-hydroxyl group in undecose derivatives was very difficult, possibly because of the instability of the aldol products and significant steric hindrance around the hydroxyl: Cox, P. J.; Griffin, A. M.; Newcombe, N. J.; Lister, S.; Ramsay, M. V. J.; Alker, D.; Gallgher, Y. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1443−1447.

(19) Burgess, E. M.; Penton, H. R.; Taylar, E. A. *J. Org. Chem.* **1973**, *38*, 26−31.

(20) $^1$H NMR analysis of the reaction mixture suggested that the hydrogenation product was a mixture of anomers, and the α-anomer readily isomerized during the workup to give the $\beta$-anomer as the sole product.

(21) Yanada, R.; Negoro, N.; Bessho, K.; Yanada, K. *Synlett* **1995**, 1261−1263.

(22) Molecular modeling of both herbicidin B (**1b**) and its 6′-epimer **23** was carried out using Macromodel (version 4.5) software. Preferred conformations were determined from the results of Monte Carlo conformer searches starting from previously minimized structures of the two compounds. Minimization employed the MM2* force field. Sets of conformers close to minimum were found for **1b** and **23**, respectively. The minimum-energy conformation for **23** was consistent with that suggested from the coupling constants and NOE relationships of **23**. The minimum-energy conformer of 6′-*epi*-herbicidin B (**23**) was approximately 3.0 kcal/mol more stable than that of herbicidin B.

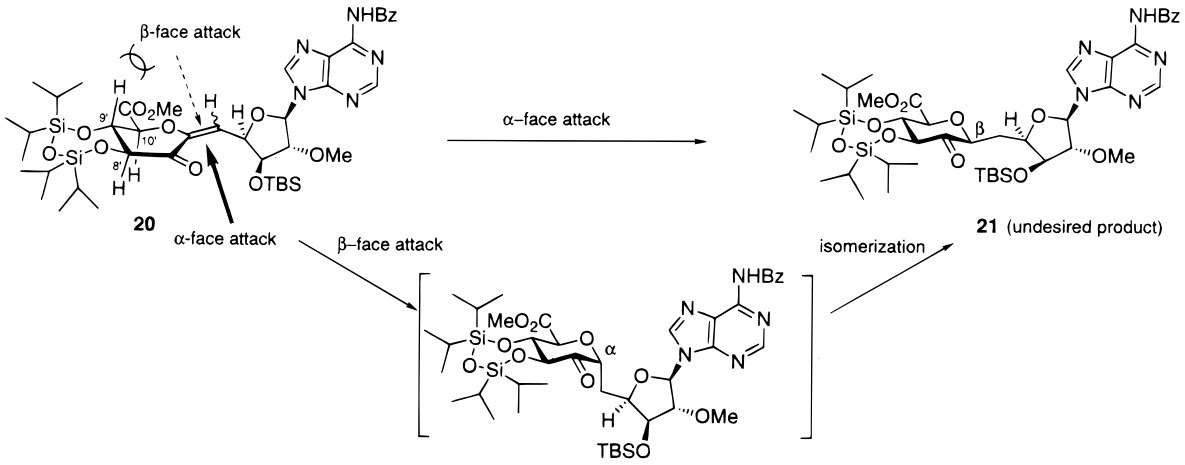



**Figure 4.**

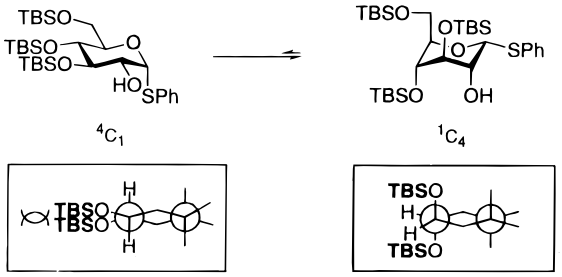



**Figure 5.**

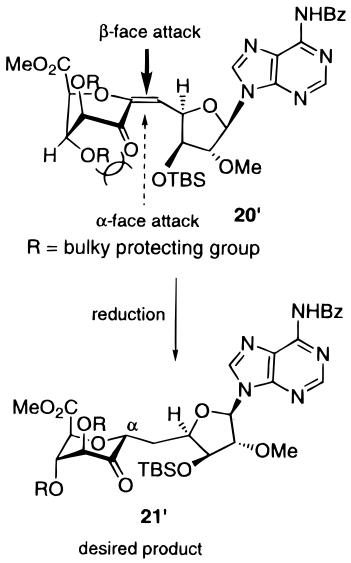
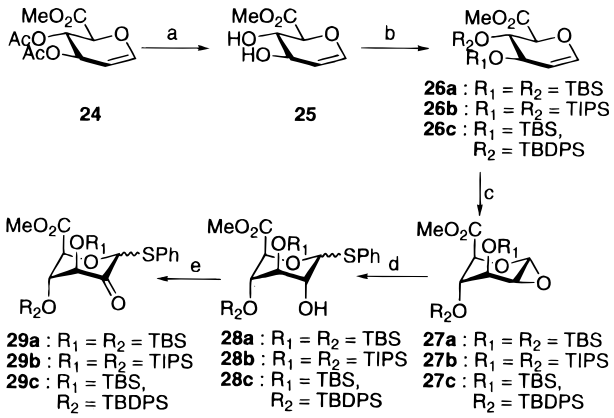



**Figure 6.**

$J_{8',9'}$ and $J_{9',10'}$ were ca. 9−10 Hz. Accordingly, **20** preferentially adopts a half-chair conformation, as shown in Figure 4. Since hydrogenation from the $\beta$-face of the alkenyl bond of **20** would be disfavored probably due to steric repulsion for the 9′-axial proton, α-face attack proceeded to give the undesired 6′-$\beta$-*C*-glycosidic product **21** as the major product. It is also possible that isomerization at the anomeric 6′-position into the undesired $\beta$-configuration might occur if the hydrogenation product was the desired α-*C*-glycoside. $^1$H NMR analysis of 6′-$\beta$-*C*-glycoside **21** suggested that it adopts a $^{9'}C_{6'}$-like conformation in which all of the substituents on the ulose moiety are in equatorial positions. 6′-$\beta$-*C*-Glycoside **21** would be more thermodynamically stable than the corresponding α-*C*-glycoside, which has a very bulky 6′-substituent in an axial position, and therefore the undesired isomerization might occur.

**Scheme 7**[a]

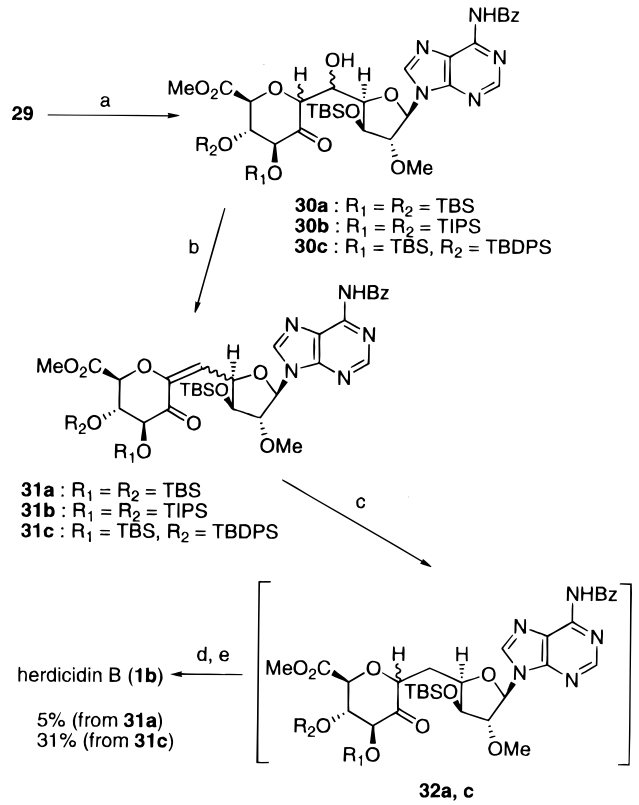



[a] Reagents: (a) $K_2CO_3$, MeOH; (b) TBSCl, TIPSCl, or TBDPSCl, imidazole, DMF; (c) dimethyldioxirane, acetone; (d) PhSH, $BF_3Et_2O$, $CH_2Cl_2$; (e) Dess−Martin periodinane, $CH_2Cl_2$.

Recently, it was reported that introducing significantly bulky protecting groups at vicinal hydroxyl groups on pyranoses caused a flip of their conformation from the usual $^4C_1$-form into an unusual $^1C_4$-form, where the substituents were in axial orientations due to steric repulsion between the bulky protecting groups (Figure 5).[23] We expected that enone **20′**, which has bulky protecting groups at both the 8′- and 9′-hydroxyls, would adopt a $^{6'}C_{9'}$-like conformation, as shown in Figure 6, due to steric repulsion between the bulky protecting groups. If so, hydrogenation of **20′** would selectively occur from the $\beta$-face to give the desired α-product **21′**, due to a significant steric repulsion for the 9′-axial protecting group when the catalyst accesses the alkenyl bond from the α-face. In addition, the desired α-glycoside **21′** would be more thermodynamically stable than the corresponding $\beta$-*C*-glycoside, since the substituent at the 6′-position of **21′** is in an equatorial position. Thus, isomerization from a $\beta$- to an α-configuration at the 6′-position would occur if the hydrogenation does not proceed selectively from the $\beta$-face. Based on these considerations, we designed phenylthiouloses **29a**−**c** (Scheme 7), which had bulky silyl protecting groups at both the 8′- and 9′-positions, as alternative substrates for the aldol reaction.

(23) (a) Walford, C.; Jackson, R. F. W.; Rees, N. H.; Clegg, W.; Heath, S. L. *Chem. Commun.* **1997**, 1855−1856. As for reactions: (b) Hosoya, T.; Ohashi, Y.; Matsumoto, T.; Suzuki, K. *Tetrahedron Lett.* **1996**, *37*, 663−666. (c) Roush, W. R.; Sebesta, S. P.; Bennett, C. E. *Tetrahedron* **1997**, *53*, 8825−8836. (d) Roush, W. R.; Sebesta, D. P.; James, R. A. *Tetrahedron* **1997**, *53*, 8837−8852.

**Scheme 8**[a]




[a] Reagents: (a) $SmI_2$, THF, then **7**; (b) $MeO_2CNSO_2NEt_3$, toluene; (c) Pd/C, $HCO_2NH_4$, MeOH; (d) Sm, $I_2$, MeOH; (e) TBAF, THF.

**Preparation of Conformation-Flipped 1-Phenylthio-2-ulose Units.** The preparation of 1-phenylthio-2-uloses **29a**−**c** is summarized in Scheme 7. Glycal **24**, derived from D-glucurono-3,6-lactone, was treated with NaOMe in MeOH to give **25**.[24] The 3,4-diol of **25** was silylated by usual methods to afford **26a** and **26b**, which have TBS or TIPS groups at both the 3- and 4-hydroxyls, respectively. Glycal **26c** was prepared by successive treatment of **25** with TBSCl and TBDPSCl in the presence of imidazole in DMF. Epoxidation of **26a** with dimethyldioxirane[25] gave the gluco-type epoxide **27a** selectively in quantitative yield.[26] Next, ring-opening of the epoxide was examined. When **27a** was treated with PhSH and $Et_3N$, only a trace of the desired phenylthioglycoside **28a** was obtained. Treatment with 10 equiv of PhSH in the presence of a catalytic amount of $BF_3{\cdot}OEt_2$ gave **28a** in good yield as an anomeric mixture. Oxidation of **28a** with Dess−Martin periodinane[27] gave an anomeric mixture of 1-phenylthio-2-ulose (**29a**) in 80% yield. Similarly, other aldol substrates **29b** and **29c** were prepared from **26b** and **26c**, respectively. The conformations of these phenylthiouloses **29a**−**c** were investigated by their $^1H$ NMR spectra. The large coupling constants ($J_{3,4}$ = 5.8, $J_{4,5}$ = 12.8 Hz) of **29a** showed that it adopted an undesired $^4C_1$-like conformation, similar to that of 3,4-*O*-TIPDS-phenylthioulose **13**. This result suggested that a TBS group would be not bulky enough to flip the conformation. On the other hand, a preference for the desired $^1C_4$ conformations in **29b** and **29c**, where the substituents at the 3- and 4-positions are in axial positions, was suggested on the basis of their coupling constants between H-3 and H-4, and between H-4 and H-5 ($J_{3,4}$, $J_{4,5}$ = 0−4.3 Hz).

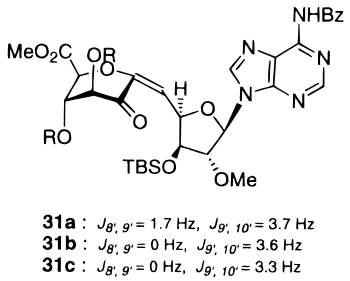



**Figure 7.** Conformation of the pyranose ring on the enones.

**Synthesis of Herbicidin B.** The total synthesis of herbicidin B was achieved as shown in Scheme 8. $SmI_2$-promoted aldol reactions[8] with phenylthioulose **29a**−**c** and aldehyde **7** were examined. When **29a** was treated with $SmI_2$ at −78 °C, the samarium enolate was not generated efficiently,[28] and the yield of the coupling product was low. However, the condensation reaction proceeded effectively at −40 °C, and the desired coupling product **30a** was obtained in 65% yield as a mixture of two diastereoisomers.[29] By similar condensation reactions, the aldol products **30b** and **30c** were obtained from **29b** and **29c**, respectively. Treatment of **30a**−**c** with Burgess's inner salt gave the corresponding enones **31a**−**c** in 66−79% yields as a single isomer, respectively, while the alkene geometry was unknown.

The conformations of enones **31a**−**c** were investigated by their $^1H$ NMR spectra. Small coupling constants between the protons on the pyranose ring, $J_{8',9'}$ = 0−2 Hz and $J_{9',10'}$ = 3−4 Hz, suggested that they had flipped conformations where the 8′- and 9′-*O*-silyl substituents were in axial positions (Figure 7). Reduction of the enones under a variety of conditions was investigated next. Enone **31b**, which has a pair of significantly bulky TIPS groups at the 8′- and 9′-hydroxyls, was resistant to all of the reduction conditions examined.[30] However, when enone **31a**, which has less bulky TBS groups instead of TIPS groups, was treated with $HCO_2NH_4$ as a hydrogen donor in the presence of Pd−C in MeOH,[31] the desired reduced product **32a** was obtained.[32,33] Compound **32a** was then successively treated with $SmI_2$/MeOH and TBAF/TFH to form an internal ketal linkage between the 3′- and 7′-positions, to spontaneously give a tricyclic sugar compound, the $^1H$ NMR spectrum of which was consistent with that of herbicidin B (**1b**), while the yield was low (5% from **31a**).

The yield was improved when **31c**, which had a TBS group and a TBDPS group at the 8′- and 9′-hydroxyls, respectively, was used as a substrate. Thus, treatments of **31c** with $HCO_2NH_4$/Pd−C/MeOH,[33] $SmI_2$/MeOH, and TBAF/THF gave herbicidin B (**1b**) in 31% yield after preparative silica gel TLC purification. In this reaction, production of 6′-*epi*-herbicidin B (**23**) was not observed at all. This completes the first synthesis of herbicidin B. Its spectroscopic and analytical data are in full agreement with those of the authentic sample.

(24) Nishimura, S.; Nomura, S.; Yamada, K. *Chem. Commun*. **1998**, 617−618.

(25) Adam, W.; Chan, Y. Y.; Cremer, D.; Gauss, J.; Scheutzow, D.; Schindler, M. *J. Org. Chem*. **1987**, *52*, 2800−2803.

(26) Friesen, R.; Danishefsky, S. J. *J. Am. Chem. Soc*. **1989**, *111*, 6656−6660.

(27) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc*. **191**, *113*, 7277−7279.

(28) Remaining starting material **29a** was observed on TLC.

(29) The stereochemistries of the two diastereomers were not confirmed.

(30) For example, catalytic hydrogenations with Pd−C, PtO, Raney-Ni, or Pd-black and hydride reductions with DIBAL/HMPA, $NaBH_4/NiCl_2$, or $Bu_3SnH$ were tried.

(31) Bieg, T.; Szeja, W. *Synthesis* **1985**, 76−77.

(32) The $^1H$ NMR spectrum of the crude reduction product suggested that it was an anomeric mixture ($\alpha/\beta$ = 3/1).

(33) A byproduct, the structure of which has not been determined, was also obtained in the hydrogenation of **31a**, and it made the yield of **32a** low. On the other hand, production of such a byproduct was not observed in the hydrogenation of **31c**.

## Conclusions

Using a novel aldol-type *C*-glycosidation reaction promoted by $SmI_2$ as a key step and a strategy involving the axial orientation of vicinal substituents, we completed the first total synthesis of the nucleoside antibiotic herbicidin B (**1b**). This aldol-type *C*-glycosidation reaction promoted by $SmI_2$ was very effective for constructing the undecose nucleoside **19** and **30** using 1-*β*-D-xylosyladenine 5′-aldehyde derivative as an acceptor, which was very unstable under either acidic or basic conditions. The fact that the reactions promoted by $SmI_2$ proceeded under mild and neutral conditions made this result possible, and since phenylthiouloses as the enolate source are readily synthesized and stable, this approach can be applied to a variety of compounds. Thus, the aldol-type *C*-glycosidation reaction promoted by $SmI_2$ may be a powerful tool for synthesizing other higher carbon sugar nucleosides. Reduction followed by the deprotection of **20**, in which the conformation of the pyranose ring was $^{9'}C_{6'}$, gave selectively 6′-*epi*-herbicidin B, which is an analogue of herbicidin B. On the other hand, similar conversion of enones **31**, which adopted a $^{O,8'}$B-type conformation on the pyranose ring, by the introduction of bulky protecting groups gave herbicidin B (**1b**). This work is the first total synthesis of herbicidin congeners, and our methods should be applicable to the synthesis of other herbicidin congeners and their analogues.

## Experimental Section

**9-(2-*O*-Methyl-5-*O*-trityl-*β*-D-ribofuranosyl)adenine (15).** A mixture of **14** (12.9 g, 40 mmol) and TrCl (11.2 g, 44 mmol) in pyridine (100 mL) was stirred for 12 h at 60 °C. After MeOH (10 mL) was added, the solution was evaporated under reduced pressure, and the residue was partitioned between $CHCl_3$ (500 mL) and $H_2O$ (200 mL). The organic layer was washed with brine (200 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography ($SiO_2$, 6% MeOH/$CHCl_3$) to give **15** (19.2 g, 92% as a white foam): $[\alpha]_D$ +0.29° (*c* 1.14, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.30 (s, 1H), 8.02 (s, 1H), 7.45−7.23 (m, 15H), 6.14 (d, 1H, $J$ = 3.7 Hz), 5.59 (br s, 2H, exchanged with $D_2O$), 4.50 (dd, 1H, $J$ = 5.5, 11.1 Hz), 4.42 (dd, 1H, $J$ = 3.8, 5.3 Hz), 4.20 (ddd, 1H, $J$ = 3.3, 4.5, 11.1 Hz), 3.57 (s, 3H), 3.52 (dd, 1H, $J$ = 3.3, 10.7 Hz), 3.43 (dd, 1H, $J$ = 4.5, 10.7 Hz), 2.74 (d, 1H, $J$ = 6.3 Hz, exchanged with $D_2O$); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 155.8, 153.4, 149.8, 143.8, 139.2, 128.9, 128.8, 128.8, 128.2, 127.5, 120.3, 87.4, 86.9, 84.0, 83.6, 77.5, 77.3, 77.0, 70.0, 63.5, 59.0, 58.5; MS (EI) *m*/*z* 523 ($M^+$). Anal. Calcd for $C_{30}H_{29}N_5O_4 \cdot 1.2H_2O$: C, 66.09; H, 5.80; N, 12.85. Found: C, 66.03; H, 5.56; N, 12.64.

**9-(2-*O*-Methyl-5-*O*-trityl-*β*-D-xylofuranosyl)adenine (16).** To a mixture of $CrO_3$ (11.2 g, 112 mmol) and 4-Å molecular sieves (28 g) in $CH_2Cl_2$ (250 mL) was added pyridine (18.0 mL, 224 mmol) at 0 °C. The mixture was stirred for 30 min at 0 °C, and then $Ac_2O$ (10.6 mL, 112 mmol) was added at the same temperature, and the whole was stirred for additional 15 min. To the resulting mixture was added **15** (14.6 g, 27.9 mmol) in $CH_2Cl_2$ (100 mL), and the mixture was stirred for 30 min at room temperature. The solution was diluted with EtOAc (1 L) and filtered through a Celite pad, and the filtrate was concentrated to about 500 mL under reduced pressure. The solution was washed with $H_2O$ (3 × 200 mL) and brine (200 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. A mixture of the residue and $NaBH_4$ (6.87 g, 181 mmol) in AcOH (300 mL) was stirred for 12 h at 4 °C. The mixture was evaporated under reduced pressure, and the residue was coevaporated with EtOH (3 × 30 mL). The residue was partitioned between $CHCl_3$ (500 mL) and $H_2O$ (2 × 200 mL), and the organic layer was washed with saturated $NaHCO_3$ (200 mL) and brine (200 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. The residue was crystallized from EtOAc to give **16** (11.3 g, 78%): mp 205−206 °C; $[\alpha]_D$ −38.8° (*c* 0.82, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.23 (s, 1H), 7.92 (s, 1H), 7.44 (d, 6H, $J$ = 7.4 Hz), 7.26−7.18 (m, 9H), 6.86 (d, 1H, $J$ = 10.6 Hz), 5.80 (br s, 2H, exchanged with $D_2O$), 5.77 (d, 1H, $J$ = 1.5 Hz), 4.27 (dd, 1H, $J$ = 5.6, 8.7 Hz), 4.21 (dd, 1H, $J$ = 3.0, 10.5 Hz), 4.18 (d, 1H, $J$ = 1.5 Hz), 3.45 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 152.6, 144.0, 140.9, 128.9, 127.9, 127.2, 127.1, 126.7, 91.9, 90.9, 87.3, 82.9, 73.9, 62.4, 58.3; MS (EI) *m*/*z* 523 ($M^+$). Anal. Calcd for $C_{30}H_{29}N_5O_4$: C, 68.82; H, 5.58; N, 13.38. Found: C, 68.61; H, 5.74; N, 13.19.

***N*$^6$-Benzoyl-9-(3-*O*-*tert*-butyldimethylsily-2-*O*-methyl-5-*O*-trityl-*β*-D-xylofuranosyl)adenine (17).** A mixture of **16** (1.48 g, 2.82 mmol), TBSCl (852 mg, 5.62 mmol), and imidazole (767 mg, 11.3 mmol) in DMF (30 mL) was stirred for 15 h at room temperature. After MeOH (5 mL) was added, the mixture was stirred for an additional 12 h and evaporated under reduced pressure. The residue was partitioned between EtOAc (200 mL) and $H_2O$ (100 mL), and the organic layer was washed with brine (50 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. A mixture of the residue and BzCl (0.72 mL, 6.2 mmol) in pyridine (30 mL) was stirred for 3 h at room temperature. After $NH_4$-OH (28%, 10 mL) was added to the mixture, the resulting mixture was stirred for a further 20 min and evaporated under reduced pressure. The residue was partitioned between EtOAc (200 mL) and $H_2O$ (100 mL), and the organic layer was washed with brine (50 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography ($SiO_2$, 33% EtOAc/hexane) to give **17** (1.73 g, 83% as a white foam): $[\alpha]_D$ −27.3° (*c* 1.10, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.23 (br s, 1H, exchanged with $D_2O$), 9.00 (s, 1H), 8.30 (s, 1H), 8.19 (d, 2H, $J$ = 7.5 Hz), 7.98 (d, 1H, $J$ = 7.5 Hz), 7.66−7.40 (m, 17H), 6.50 (s, 1H), 4.81 (dd, 1H, $J$ = 3.3, 3.7 Hz), 4.36 (s, 1H), 4.09 (s, 1H), 3.81 (dd, 1H, $J$ = 3.7, 10.5 Hz), 3.80 (s, 3H), 3.43 (dd, 1H, $J$ = 3.3, 10.3 Hz), 0.73 (s, 9H), −0.76 (s, 3H), −0.89 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 152.9, 144.0, 141.9, 132.9, 132.2, 129.1, 128.9, 128.8, 128.1, 128.0, 127.6, 127.4, 90.8, 88.9, 87.4, 84.3, 63.5, 58.6, 25.6, 18.0, −4.9, −5.3; MS (EI) *m*/*z* 498 ($M^+$ − Tr). Anal. Calcd for $C_{43}H_{47}N_5O_5Si \cdot 0.5H_2O$: C, 68.77; H, 6.44; N, 9.33. Found: C, 69.06; H, 6.43; N, 9.37.

***N*$^6$-Benzoyl-9-(3-*O*-*tert*-butyldimethylsily-2-*O*-methyl-*β*-D-xylofuranosyl)adenine (18).** A mixture of **17** (7.31 g, 9.86 mmol) and 80% aqueous TFA (5 mL) in $CHCl_3$ (100 mL) was stirred for 1 h at room temperature. The mixture was washed with $H_2O$ (2 × 50 mL), saturated $NaHCO_3$ (50 mL), and brine (30 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography ($SiO_2$, 75% EtOAc/hexane) to give **18** (3.99 g, 81% as a white foam): $[\alpha]_D$ −42.3° (*c* 1.28, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.09 (br s, 1H, exchanged with $D_2O$), 8.83 (s, 1H), 8.39 (s, 1H), 8.03 (d, 2H, $J$ = 7.5 Hz), 7.61 (t, 1H, $J$ = 7.5 Hz), 7.53 (t, 2H, $J$ = 7.4 Hz), 6.20 (d, 1H, $J$ = 1.9 Hz), 4.39−4.37 (m, 2H), 4.15 (d, 1H, $J$ = 1.9 Hz), 4.06 (dd, 1H, $J$ = 4.6, 11.3 Hz), 3.99 (dd, 1H, $J$ = 3.2, 11.3 Hz), 3.55 (s, 3H), 2.75 (br s, 1H, exchanged with $D_2O$), 0.81 (s, 9H), 0.11 (s, 3H), −0.03 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 152.9, 149.7, 142.0, 134.0, 132.9, 129.0, 128.1, 127.6, 90.5. 88.3, 61.6, 58.8, 25.8, 18.2, −4.7, −5.0; MS (EI) *m*/*z* 499 ($M^+$). Anal. Calcd for $C_{24}H_{33}N_5O_5Si$: C, 57.69; H, 6.66; N, 14.02. Found: C, 57.73; H, 6.56; N, 14.05.

***N*$^6$-Benzoyl-9-(3-*O*-*tert*-butyldimethylsily-2-*O*-methyl-*β*-D-xylofuranos-5-urosyl)adenine (7).** Trifluoroacetic acid (1.09 mL, 4.5 mmol) was added to a solution of **18** (4.51 g, 9.05 mmol), DCC (5.63 g, 27.2 mmol), and pyridine (0.91 mL, 9.1 mmol) in DMSO (50 mL) at room temperature, and the mixture was stirred for 2 h. The mixture was filtered to remove dicyclohexylurea, and the filtrate was washed with hexane (3 × 50 mL) and partitioned with EtOAc (200 mL) and $H_2O$ (200 mL). The organic layer was washed with brine (20 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. The residue was coevaporated with toluene (3 × 50 mL) under reduced pressure to give crude **7** (4.77 g as a syrup, quantitative). This compound was used in the next reaction without further purification, because it was too unstable to be isolated: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.78 (s, 1H), 9.16 (br s, 1H, exchanged with $D_2O$), 8.81 (s, 1H), 8.50 (s, 1H), 8.01 (d, 2H, $J$ = 7.5 Hz), 7.59 (t, 1H, $J$ = 7.5 Hz), 7.51 (t, 2H, $J$ = 7.4 Hz), 6.39 (s, 1H), 4.79 (d, 1H, $J$ = 3.7 Hz), 4.68 (d, 1H, $J$ = 3.8 Hz), 4.13 (s, 1H), 3.62 (s, 3H), 0.68 (s, 9H), 0.04 (s, 3H), −0.15 (s, 3H).

**Methyl Glucuronate-D-glycal (25).** A mixture of **24** (258 mg, 1.00 mmol) in MeOH (10 mL) containing NaOMe (28% in MeOH, 10 $\mu$L) was stirred for 1 h at room temperature. The mixture was neutralized

with AcOH and evaporated under reduced pressure. The resulting syrup was partitioned between EtOAc (50 mL) and $H_2O$ (50 mL), and the organic layer was washed with $H_2O$ (50 mL) and brine (20 mL). The organic layer was dried ($Na_2SO_4$) and evaporated under reduced pressure. The residue was purified by silica gel column chromatography ($SiO_2$, 4% MeOH/$CHCl_3$) to give **25** (150 mg, 86% as a white solid), which was crystallized from MeOH/$CHCl_3$: mp 148−151 °C; $[\alpha]_D$ −13.5° (*c* 1.00, MeOH); $^1$H NMR (DMSO-$d_6$, 500 MHz) $\delta$ 6.37 (d, 1H, $J$ = 6.2 Hz), 5.43 (d, 1H, $J$ = 5.0 Hz, exchanged with $D_2O$), 4.98 (d, 1H, $J$ = 4.0 Hz, exchanged with $D_2O$), 4.72 (t, 1H, $J$ = 5.0, 6.2 Hz), 4.40 (d, 1H, $J$ = 5.1 Hz), 3.82 (ddd, 1H, $J$ = 5.1, 4.6, 4.0 Hz), 3.74 (ddd, 1H, $J$ = 5.0, 4.6, 5.0 Hz), 3.61 (s, 3H).

**Methyl (3,4-Di-*O*-*tert*-butyldimethylsilyl-D-glucuronate)glycal (26a).** A mixture of **25** (1.74 g, 10.0 mmol), TBSCl (4.51 g, 30.0 mmol), and imidazole (4.08 g, 60.0 mmol) in DMF (50 mL) was stirred for 4 h at 100 °C. After being cooled to room temperature, MeOH (10 mL) was added. The reaction mixture was partitioned between EtOAc (200 mL) and $H_2O$ (200 mL), and the organic layer was washed with $H_2O$ (200 mL) and brine (50 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography ($SiO_2$, 10% EtOAc/hexane) to give **26a** (3.97 g, 99% as a colorless syrup): $[\alpha]_D$ −27.2° (*c* 1.05, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 6.50 (d, 1H, $J$ = 6.6 Hz), 4.81 (m, 1H), 4.53 (br s, 1H), 4.23 (dd, 1H, $J$ = 2.0, 4.0 Hz), 3.77 (m, 1H), 3.71 (s, 3H), 0.90 (s, 9H),0.83 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H); $^{13}$C NMR ($CDCl_3$,125 MHz) $\delta$ 169.7, 144.3, 101.6, 75.8, 64.5, 52.2, 25.9, 25.8, −4.4, −4.7, −4.8, −4.9; MS (FAB) *m*/*z* 402 ($MH^+$). Anal. Calcd for $C_{19}H_{38}O_5Si_2$: C, 56.67; H, 9.51. Found: C, 56.55; H, 9.67.

**Methyl (3,4-Di-*O*-triisopropylsilyl-D-glucuronate)glycal (26b).** In a manner similar to that described for **26a**, reaction of **25** (2.00 g, 11.4 mmol) with TIPSCl (7.38 mL, 34.2 mmol) and imidazole (4.66 g, 68.4 mmol) in DMF (50 mL) and purification by column chromatography ($SiO_2$, 10% EtOAc/hexane) gave **26b** (5.24 g, 95% as a colorless syrup): $[\alpha]_D$ −24.8° (*c* 1.12, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 6.52 (d, 1H, $J$ = 6.4 Hz), 4.90 (m, 1H), 4.64 (br s, 1H), 4.47 (dd, 1H, $J$ = 2.0, 4.0 Hz), 3.95 (ddd, 1H, $J$ = 1.2, 2.0, 4.0 Hz), 3.70 (s, 3H), 1.87−1.04 (m, 42H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 168.8, 143.5, 101.1, 75.5, 70.7, 64.2, 52.2, 18.3, 18.2, 18.2, 18.1, 18.1, 17.9, 12.8, 12.7, 12.6, 12.6, 12.4, 12.3, 12.1; MS (FAB) *m*/*z* 443 ($MH^+$ − *i*-Pr). Anal. Calcd for $C_{25}H_{50}O_5Si_2$: C, 61.68; H, 10.35. Found: C, 61.31; H, 10.11.

**Methyl (3-*O*-*tert*-Butyldimethylsilyl-4-*O*-*tert*-butyldiphenylsilyl-D-glucuronate)glycal (26c).** A mixture of **25** (107 mg, 0.61 mmol), TBSCl (110 mg, 0.73 mmol), and imidazole (99.7 mg, 1.46 mmol) in DMF (5 mL) was stirred for 2 h at room temperature. After MeOH (2 mL) was added, the mixture was partitioned between EtOAc (50 mL) and $H_2O$ (50 mL), and the organic layer was washed with $H_2O$ (20 mL) and brine (20 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. A mixture of the above residue, TBDPSCl (238 $\mu$L, 0.92 mmol), and imidazole (125 mg, 1.80 mmol) in DMF (5 mL) was stirred for 4 h at 100 °C. After MeOH (2 mL) was added, the reaction mixture was partitioned between EtOAc (50 mL) and $H_2O$ (50 mL), and the separated organic layer was washed with $H_2O$ (20 mL) and brine (20 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography ($SiO_2$, 10% EtOAc/hexane) to give **26c** (298 mg, 93% as a colorless syrup): $[\alpha]_D$ −8.15° (*c* 1.34, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.72−7.38 (m, 10H), 6.51 (d, 1H, $J$ = 6.3 Hz), 4.85 (m, 1H), 4.52 (br s, 1H), 4.32 (dd, 1H, $J$ = 1.2, 5.6 Hz), 3.77 (m, 1H), 3.56 (s, 3H), 1.05 (s, 9H), 0.72 (s, 9H), −0.14 (s, 3H), −0.17 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 168.6, 143.8, 136.0, 135.9, 133.7, 133.5, 130.2, 128.1, 128.0, 101.2, 74.9, 71.0, 63.6, 52.0, 27.1, 25.9, −4.5, −4.9; MS (FAB) *m*/*z* 469 ($MH^+$ − *t*-Bu). Anal. Calcd for $C_{29}H_{42}O_5Si_2$: C, 66.12; H, 8.04. Found: C, 66.32; H, 7.97.

**Methyl (3,4-Di-*O*-*tert*-butyldimethylsilyl-2,3-anhydro)-D-glucuronate (27a).** A solution of **26a** (200 mg, 0.40 mmol) in $CH_2Cl_2$ (4 mL) was added dropwise to an acetone solution of dimethyldioxirane (ca. 0.05 M, 10 mL, 0.50 mmol), and the mixture was stirred for 2 h at room temperature. After most of the acetone was removed under reduced pressure, the residue was dissolved in $CH_2Cl_2$, dried ($Na_2SO_4$), and filtered, and the filtrate was evaporated under reduced pressure to give **27a** (210 mg, quantitative): $[\alpha]_D$ −34.1° (*c* 1.00, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 5.07 (d, 1H, $J$ = 2.4 Hz), 4.18 (d, 1H, $J$ = 4.5 Hz), 4.09 (dd, 1H, $J$ = 2.7, 8.9 Hz), 3.97 (t, 1H, $J$ = 2.4 Hz), 3.74 (s, 3H), 2.92 (t, 1H, $J$ = 2.4 Hz), 0.91 (s, 9H), 0.90 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H), 0.11 (s, 3H), 0.07 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 170.8, 76.6, 74.5, 72.8, 69.6, 54.1, 52.5, 25.9, −1.1, −4.6, −4.7, −4.9; MS (FAB) *m*/*z* 419 ($MH^+$). Anal. Calcd for $C_{19}H_{38}O_6Si_2$: C, 54.51; H, 9.15. Found: C, 54.28; H, 9.02.

**Methyl (3,4-Di-*O*-triisopropylsilyl-2,3-anhydro)-D-glucuronate (27b).** In a manner similar to that described for **27a**, the reaction of **26b** (1.94 g, 4.00 mmol) with an acetone solution of dimethyldioxirane (ca. 0.05 M, 100 mL, 5.00 mmol) gave **27b** (2.03 g, quantitative as a foam): $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 5.30 (s, 1H), 4.33 (s, 1H), 4.31 (br s, 2H), 3.72 (s, 3H), 3.09 (br s, 1H), 1.18−1.04 (m, 42H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 169.8, 132.5, 130.8, 129.0, 128.8, 125.3, 75.5, 73.1, 67.4, 53.2, 52.0, 18.8, 18.7, 18.6, 18.3, 17.9, 14.0, 12.8, 12.7, 12.4, 12.3, 12.1; MS (FAB) *m*/*z* 503 ($MH^+$).

**Methyl (3-*O*-*tert*-Butyldimethylsilyl-4-*O*-*tert*-butyldiphenylsilyl-2,3-anhydro)-D-glucuronate (27c).** In a manner similar to that described for **27a**, the reaction of **26c** (2.10 g, 4.00 mmol) with an acetone solution of dimethyldioxirane (ca. 0.05 M, 100 mL, 5.00 mmol) gave **27c** (2.21 g, quantitative): $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.74−7.36 (m, 10H), 5.12 (d, 1H, $J$ = 2.4 Hz), 4.18 (br s, 2H), 4.07 (dd, 1H, $J$ = 1.9, 3.8 Hz), 3.57 (s, 3H), 3.01 (d, 1H, $J$ = 1.4 Hz), 1.09 (s, 9H), 0.74 (s, 9H), −0.09 (s, 3H), −0.14 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 169.8, 132.5, 130.8, 129.0, 128.8, 125.3, 75.5, 73.1, 67.4, 53.2, 52.0, 18.8, 18.7, 18.6, 18.3, 17.9, 14.0, 12.8, 12.7, 12.4, 12.3, 12.1; MS (FAB) *m*/*z* 543 ($MH^+$). Anal. Calcd for $C_{29}H_{42}O_6Si_2$: C, 64.17; H, 7.80. Found: C, 64.68; H, 7.76.

**Methyl 3,4-Di-*O*-*tert*-butyldimethylsilyl-1-phenylthio-D-glucuronate (28a).** Boron trifluoride diethyl ether complex (49 $\mu$L, 0.4 mmol) was added dropwise to a mixture of **27a** (1.67 g, 4.00 mmol) and PhSH (4.11 mL, 40.0 mmol) in $CH_2Cl_2$ (40 mL), and the mixture was stirred for 30 min at −40 °C. The mixture was washed with saturated aqueous $NaHCO_3$ (40 mL), $H_2O$ (50 mL), and brine (50 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography ($SiO_2$, 75% benzene/hexane) to give **28a** as an inseparable anomeric mixture (1.44 g, 80% as a colorless syrup, the ratio of $\alpha/\beta$ = 39/61): MS (FAB) *m*/*z* 528 ($M^+$). Anal. Calcd for $C_{25}H_{44}O_6SSi_2$: C, 56.78; H, 8.39. Found: C, 56.93; H, 8.09. For $\beta$-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.57 (d, 2H, $J$ = 7.5 Hz), 7.33−7.18 (t, 3H), 5.16 (d, 1H, $J$ = 5.8 Hz), 4.30 (t, 1H, $J$ = 3.8 Hz), 4.27 (d, 1H, $J$ = 3.1 Hz), 3.85 (t, 1H, $J$ = 4.3 Hz), 3.67 (s, 3H), 3.22 (d, 1H, $J$ = 7.7 Hz, exchanged with $D_2O$), 0.89 (s, 9H), 0.88 (s, 9H), 0.18 (s, 3H), 0.17 (s, 3H), 0.15 (s, 3H), 0.11 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 169.9, 135.5, 133.1, 129.4, 129.0, 87.1, 72.8, 71.8, 70.7, 64.4, 52.1, 26.2, 25.9, 18.6, 18.1, −4.1, −4.2, −4.8, −4.9. For $\alpha$-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.71 (d, 2H, $J$ = 7.7 Hz), 7.33−7.18 (t, 3H), 5.94 (s, 1H), 4.48 (s, 1H), 4.20 (t, 1H, $J$ = 1.4 Hz), 3.98 (t, 1H, $J$ = 3.4 Hz), 3.95 (s, 1H), 3.73 (m, 2H), 3.72 (s, 3H), 0.94 (s, 9H), 0.85 (s, 9H), 0.18 (s, 3H), 0.17 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 169.7, 143.7, 133.1, 127.3, 126.4, 81.7, 77.8, 75.6, 73.1, 72.2, 69.9, 26.0, 25.8, 18.2, 11.7, −4.3, −4.5, −4.5, −4.6.

**Methyl 3,4-Di-*O*-triisopropylsilyl-1-phenylthio-D-glucuronate (28b).** In a manner similar to that described for **28a**, reaction of **27b** (2.03 g, 4.00 mmol) with $BF_3{\cdot}OEt_2$ (49 $\mu$L, 0.4 mmol) and PhSH (4.11 mL, 40.0 mmol) in $CH_2Cl_2$ (40 mL) and purification by column chromatography ($SiO_2$, 75% benzene/hexane) gave **28b** as an inseparable anomeric mixture (1.53 g, 63% as a colorless syrup, the ratio of $\alpha/\beta$ = 60/40): MS (FAB) *m*/*z* 613 ($M^+$). Anal. Calcd for $C_{31}H_{56}O_6SSi_2$: C, 60.74; H, 9.21. Found: C, 60.42; H, 9.53. For $\alpha$-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.59 (d, 2H, $J$ = 7.3 Hz), 7.32−7.19 (m, 3H), 5.35 (d, 1H, $J$ = 5.8 Hz), 4.68 (d, 1H, $J$ = 2.3 Hz), 4.54 (s, 1H), 4.12 (d, 1H, $J$ = 6.5 Hz), 3.82 (m, 1H), 3.66 (s, 3H), 3.20 (d, 1H, $J$ = 8.8 Hz, exchanged with $D_2O$), 1.12−1.04 (m, 42H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 171.1, 136.6, 132.4, 130.0, 127.4, 87.0, 74.6, 73.6, 72.3, 71.2, 53.1, 19.5, 19.3, 19.2, 19.1, 13.6, 13.4. For $\beta$-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.70 (d, 2H, $J$ = 7.0 Hz), 7.31−7.22 (m, 3H), 5.99 (s, 1H), 4.58 (s, 1H), 4.43 (m, 1H), 4.20 (t, 1H, $J$ = 3.3 Hz), 4.05 (d, 1H, $J$ = 10.1 Hz, exchanged with $D_2O$), 3.82 (m, 1H), 3.69 (s,

3H), 1.12−1.00 (m, 42H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 170.7, 144.6, 136.9, 130.6, 130.0, 128.2, 102.2, 82.9, 76.6, 73.5, 71.8, 65.2, 19.3, 19.2, 19.1, 18.9, 13.7, 13.5.

**Methyl 3-*O*-*tert*-Butyldimethylsilyl-4-*O*-*tert*-butyldiphenylsilyl-1-phenylthio-D-glucuronate (28c).** In a manner similar to that described for **28a**, reaction of **27c** (2.71 g, 4.00 mmol) with $BF_3$·$OEt_2$ (49 $\mu$L, 0.4 mmol) and PhSH (4.11 mL, 40.0 mmol) in $CH_2Cl_2$ (40 mL) and purification by column chromatography ($SiO_2$, 75% benzene/hexane) gave **28c** as an inseparable anomeric mixture (1.96 g, 75% as a colorless syrup, the ratio of $\alpha/\beta$ = 72/28): MS (FAB) *m*/*z* 652 ($M^+$). Anal. Calcd for $C_{35}H_{48}O_6SSi_2$·0.5benzene: C, 65.95; H, 7.42. Found: C, 65.98; H, 7.41. For α-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.89−7.46 (m, 15H), 5.67 (d, 1H, $J$ = 5.0 Hz), 4.64 (d, 1H, $J$ = 1.7 Hz), 4.55 (s, 1H), 4.17 (t, 1H, $J$ = 3.0 Hz), 3.99 (m, 1H), 3.72 (d, 1H, $J$ = 7.8 Hz, exchanged with $D_2O$), 3.64 (s, 3H), 1.23 (s, 9H), 0.94 (s, 9H), 0.40 (s, 3H), 0.00 (s, 3H); $^{13}$C NMR ($CDCl_3$,125 MHz) $\delta$ 169.7, 1362−126.3, 86.5, 73.1, 72.4, 71.4, 51.8, 27.2, 27.2, 25.9, 19.3, 19.2, 18.3, −5.0, −5.1. For $\beta$-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.89−7.46 (m, 15H), 6.10 (s, 1H), 4.57 (s, 1H), 4.37 (t, 1H, $J$ = 1.6 Hz), 4.24 (d, 1H, $J$ = 11.9 Hz, exchanged with $D_2O$), 4.20 (t, 1H, $J$ = 3.4 Hz), 3.99 (m, 1H), 3.68 (s, 3H), 1.30 (s, 9H), 0.89 (s, 9H), 0.05 (s, 3H), −0.03 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 169.4, 1362−126.3, 81.6, 76.1, 72.2, 71.2, 70.0, 26.8, 25.8, 19.3, 18.1, −5.0, −5.2.

**Methyl 3,4-Di-*O*-*tert*-butyldimethylsilyl-1-phenylthio-2-ulos-D-glucuronate (29a).** A mixture of **28a** (1.31 g, 2.48 mmol, the ratio of $\alpha/\beta$ = 39/61) and Dess−Martin periodinane (1.26 g, 2.98 mmol) in $CH_2Cl_2$ (25 mL) was stirred for 3 h at room temperature. After a mixture of saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ (5:1) was added, the mixture was vigorously stirred until the organic layer turned clear. The separated organic layer was washed with $H_2O$ (50 mL) and brine (50 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography ($SiO_2$, 50% benzene/hexane) to give **29a** as an inseparable anomeric mixture (1.23 g, 94% as a colorless syrup, the ratio of $\alpha/\beta$ = 39/61): MS (FAB) *m*/*z* 527 ($MH^+$). Anal. Calcd for $C_{25}H_{42}O_6SSi_2$: C, 57.00; H, 8.04. Found: C, 56.81; H, 7.80. For $\beta$-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.50 (d, 2H, $J$ = 7.0 Hz), 7.23−7.15 (m, 3H), 5.47 (s, 1H), 4.45 (dd, 1H, $J$ = 3.3, 5.4 Hz), 4.33 (d, 1H, $J$ = 3.3 Hz), 3.96 (d, 1H, $J$ = 5.4 Hz), 3.69 (s, 3H), 0.79 (s, 9H), 0.76 (s, 9H), 0.01 (s, 3H), 0.00 (s, 3H), −0.01 (s, 3H), −0.08 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 199.2, 169.1, 133.4, 132.2, 128.9, 128.1, 127.7, 86.9, 78.9, 76.3, 74.0, 52.5, 26.0, 25.8, −4.8, −4.9, −5.1. For α-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.45 (d, 2H, $J$ = 7.0 Hz), 7.23−7.15 (m, 3H), 5.75 (s, 1H), 4.68 (d, 1H, $J$ = 5.8 Hz), 4.17 (dd, 1H, $J$ = 5.8, 12.8 Hz), 4.17 (d, 1H, $J$ = 12.8 Hz), 3.70 (s, 3H), 0.84 (s, 9H), 0.80 (s, 9H), 0.03 (s, 3H), −0.04 (s, 3H), −0.05 (s, 3H), −0.09 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 198.1, 169.1, 132.8, 132.1, 129.2, 128.3, 88.2, 78.1, 75.5, 75.4, 52.4, 25.8, 25.7, −3.8, −4.1, −4.5.

**Methyl 3,4-Di-*O*-triisopropylsilyl-1-phenylthio-2-ulos-D-glucuronate (29b).** In a manner similar to that described for **29a**, the reaction of **28b** (1.39 g, 2.28 mmol, the ratio of $\alpha/\beta$ = 60/40) with Dess−Martin periodinane (1.16 g, 2.74 mmol) in $CH_2Cl_2$ (25 mL) and purification by column chromatography ($SiO_2$, 50% benzene/hexane) gave **29b** as an inseparable anomeric mixture (1.12 g, 81% as a colorless syrup, the ratio of $\alpha/\beta$ = 60/40): MS (FAB) *m*/*z* 611 ($M^+$). Anal. Calcd for $C_{31}H_{54}O_6SSi_2$: C, 60.94; H, 8.91. Found: C, 60.83; H, 8.83. For α-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.62 (d, 2H, $J$ = 7.0 Hz), 7.31−7.22 (m, 3H), 5.65 (s, 1H), 4.92 (d, 1H, $J$ = 4.3 Hz), 4.6 (s, 1H), 4.15 (d, 1H, $J$ = 4.3 Hz), 3.79 (s, 3H), 1.12−1.00 (m, 42H); $^{13}$C NMR ($CDCl_3$,125 MHz) $\delta$ 199.2, 169.1, 133.4, 132.2, 129.2, 128.3, 127.7, 86.9, 78.9, 76.3, 74.0, 52.5, 25.9, 25.8. For $\beta$-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.64 (d, 2H, $J$ = 7.0 Hz), 7.31−7.22 (m, 3H), 6.42 (s, 1H), 4.85 (d, 1H, $J$ = 4.1 Hz), 4.70 (s, 1H), 4.19 (d, 1H, $J$ = 4.1 Hz), 3.78 (s, 3H), 1.12−1.00 (m, 42H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 198.0, 169.0, 132.8, 132.1129.2, 128.3, 128.1, 88.2, 78.1, 75.5, 75.4, 52.4, 25.8, 25.7.

**Methyl 3-*O*-*tert*-Butyldimethylsilyl-4-*O*-*tert*-butyldiphenylsilyl-1-phenylthio-2-ulos-D-glucuronate (29c).** In a manner similar to that described for **28a**, the reaction of **28c** (1.78 g, 2.74 mmol, the ratio of $\alpha/\beta$ = 72/28) with Dess−Martin periodinane (1.39 g, 3.29 mmol) in $CH_2Cl_2$ (30 mL) and purification by column chromatography ($SiO_2$, 50% benzene/hexane) gave an inseparable anomeric mixture of **29c** (1.75 g, 99% as a colorless syrup, the ratio of $\alpha/\beta$ = 74/26): MS (FAB) *m*/*z* 651 ($MH^+$). Anal. Calcd for $C_{35}H_{46}O_6SSi_2$·1/6benzene: C, 65.12; H, 7.13. Found: C, 65.22; H, 7.26. For α-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.73−7.26 (m, 15H), 5.74 (s, 1H), 4.70 (d, 1H, $J$ = 4.0 Hz), 4.56 (s, 1H), 3.87 (d, 1H, $J$ = 4.0 Hz), 3.65 (s, 3H), 0.95 (s, 9H), 0.89 (s, 9H), −0.18 (s, 3H), −0.19 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 199.0, 168.6, 136.1, 135.9, 135.7, 132.2, 130.1, 129.0, 127.8, 127.7, 86.4, 77.9, 74.1, 73.3, 52.1, 26.8, 26.7. For $\beta$-anomer: $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.73−7.26 (m, 15H), 6.41 (s, 1H), 4.66 (s, 1H), 4.58 (d, 1H, $J$ = 4.0 Hz), 3.89 (d, 1H, $J$ = 4.0 Hz), 3.62 (s, 3H), 0.93 (s, 9H), 0.91 (s, 9H), −0.14 (s, 3H), −0.21 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 193.4, 164.7, 135.8, 135.7, 135.6, 133.9, 132.2, 131.9, 129.8, 127.6, 127.5, 86.3, 76.2, 76.6, 76.1, 50.9, 26.7, 26.5.

***N*$^6$-Benzoyl-9-[methyl 6,10-Anhydro-3,8,9-tri-*O*-(*tert*-butyldimethylsilyl)-2-*O*-methyl-α-D-*arabino*-L-*ido*-7-undeculofuranuronyl]adenine (30a-α) and *N*$^6$-Benzoyl-9-[methyl 6,10-Anhydro-3,8,9-tri-*O*-(*tert*-butyldimethylsilyl)-2-*O*-methyl-*β*-D-*arabino*-D-*gluco*-7-undeculofuranuronate]adenine (30a-*β*).** A THF solution of $SmI_2$ (0.1 M, 7.0 mL, 0.70 mmol) was cooled to −40 °C, and then **29a** (168 mg, 0.32 mmol) in THF (3 mL) was added dropwise to the mixture. After the TLC analysis indicated the disappearance of **29a**, oxygen gas was passed through the mixture. Then, **7** (160 mg, 0.32 mmol) in THF (3 mL) was added dropwise to the above mixture, and the whole was stirred for 15 min at the same temperature. After the mixture was allowed to warm to room temperature, saturated aqueous $NH_4Cl$ was added. The mixture was filtrated through a Celite pad, the filtrate was partitioned between EtOAc (50 mL) and $H_2O$ (50 mL), and the separated organic layer was washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (30 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. The residue was purified by flash column chromatography ($SiO_2$, 40% EtOAc/hexane) to give **30a-α** (22.8 mg, 16% as a white foam) and **30a-*β*** (123 mg, 42% as a white foam). For α-anomer: $[\alpha]_D$ −45.0° (*c* 1.10, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.02 (br s, 1H, exchanged with $D_2O$), 8.83 (s, 1H), 8.40 (s, 1H), 8.03 (d, 2H, $J$ = 7.6 Hz), 7.61 (t, 1H, $J$ = 7.4 Hz), 7.53 (t, 2H, $J$ = 7.6 Hz), 6.23 (s, 1H), 4.56 (m, 2H), 4.52 (m, 3H), 3.99 (br s, 1H), 3.86 (d, 1H, $J$ = 2.8 Hz), 3.80 (s, 3H), 3.71 (d, 1H, $J$ = 5.1 Hz), 3.61 (s, 3H), 0.89 (s, 9H), 0.85 (s, 9H), 0.74 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.07 (s, 3H), 0.02 (s, 3H), −0.08 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 203.0, 170.1, 152.4, 150.7, 149.1, 141.9, 133.8, 132.6, 132.5, 128.7, 127.8, 122.8, 90.6, 88.5, 82.1, 80.7, 77.9, 75.7, 75.1, 73.4, 69.9, 58.2, 52.4, 25.7, 25.6, 25.5, 18.3, 18.0, −4.7, −4.8, −4.9, −5.1; MS (FAB) *m*/*z* 917 ($MH^+$); exact MS (FAB) calcd for $C_{43}H_{70}N_5O_{11}Si_3$ 916.4379, found 916.4398. Anal. Calcd for $C_{43}H_{69}N_5O_{11}Si_3$: C, 56.36; H, 7.59; N, 7.64. Found: C, 55.90; H, 7.47; N, 7.69. For $\beta$-anomer: $[\alpha]_D$ +5.08° (*c* 1.15, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.00 (br s, 1H, exchanged with $D_2O$), 8.82 (s, 1H), 8.65 (s, 1H), 7.92 (d, 2H, $J$ = 7.5 Hz), 7.61 (t, 1H, $J$ = 7.2 Hz), 7.53 (t, 2H, $J$ = 7.3 Hz), 6.23 (s, 1H, $J$ = 3.6 Hz), 4.97 (d, 1H, $J$ = 7.1 Hz), 4.47 (d, 1H, $J$ = 7.1 Hz), 4.56 (dd, 2H, $J$ = 3.2, 6.6 Hz), 4.37 (m, 2H), 4.26 (d, 1H, $J$ = 4.5 Hz), 3.72 (s, 3H), 3.64 (d, 1H, $J$ = 4.4 Hz), 3.44 (s, 3H), 0.89 (s, 9H), 0.85 (s, 9H), 0.84 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 205.6, 169.0, 152.2, 151.0, 149.1, 142.0, 133.5, 132.3, 128.5, 127.7, 122.7, 89.2, 86.7, 80.3, 77.3, 77.2, 77.0, 76.7, 76.5, 76.1, 75.8, 75.3, 74.2, 68.0, 58.4, 52.0, 25.6, 25.5, 25.4, 18.1, 17.8, 17.7, −4.8, −4.8, −5.0, −5.0, −5.1, −5.2; MS (FAB) *m*/*z* 917 ($MH^+$); exact MS (FAB) calcd for $C_{43}H_{70}N_5O_{11}Si_3$ 916.4379, found 916.4352. Anal. Calcd for $C_{43}H_{69}N_5O_{11}Si_3$: C, 56.36; H, 7.59; N, 7.64. Found: C, 56.36; H, 7.50; N, 7.61.

***N*$^6$-Benzoyl-9-[methyl 6,10-Anhydro-3-*O*-(*tert*-butyldimethylsilyl)-2-*O*-methyl-8,9-di-*O*-(triisopropylsilyl)-α-D-*arabino*-L-*ido*-7-undeculofuranuronyl]adenine (30b-α) and *N*$^6$-Benzoyl-9-[methyl 6,10-Anhydro-3-*O*-(*tert*-butyldimethylsilyl)-2-*O*-methyl-8,9-di-*O*-(triisopropylsilyl)-*β*-D-*arabino*-D-*gluco*-7-undeculofuranuronate]adenine (30b-*β*).** In a manner similar to that described for **30a**, from **29b** (196 mg, 0.32 mmol), **30b-α** (122 mg, 38% as a white foam) and **30b-*β*** (103 mg, 33% as a white foam) were obtained after purification by flash column chromatography ($SiO_2$, 40% EtOAc/hexane). For α-anomer: $[\alpha]_D$ −32.7° (*c* 1.06, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$

9.08 (br s, 1H, exchanged with $D_2O$), 8.83 (s, 1H), 8.39 (s, 1H), 8.03 (d, 2H, $J = 7.5$ Hz), 7.61 (t, 1H, $J = 7.4$ Hz), 7.53 (t, 2H, $J = 7.8$ Hz), 6.22 (s, 1H), 4.84 (d, 1H, $J = 4.3$ Hz), 4.61 (s, 1H), 4.58 (br s, 3H), 4.54 (s, 1H), 4.03 (d, 1H, $J = 4.3$ z), 3.93 (br s, 1H), 3.79 (s, 3H), 3.61 (s, 3H), 3.57 (br s, 1H, exchanged with $D_2O$), 1.05−1.01 (m, 42H), 0.73 (s, 9H), 0.13 (s, 3H), −0.96 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 203.4, 169.9, 164.5, 152.5, 149.0, 141.9, 133.8, 132.5, 128.7, 127.7, 90.5, 88.6, 82.1, 80.3, 77.9, 77.2, 75.1, 74.1, 69.8, 58.2, 52.3, 25.5, 17.9, 17.7, 12.1, −5.1, −5.2; MS (FAB) *m*/*z* 1001 ($MH^+$); exact MS (FAB) calcd for $C_{49}H_{82}N_5O_{11}Si_3$ 1000.5318, found 1000.5320. Anal. Calcd for $C_{49}H_{81}N_5O_{11}Si_3$: C, 58.83; H, 8.16; N, 7.00. Found: C, 58.62; H, 8.09; N, 6.75. For $\beta$-anomer: $[\alpha]_D$ 1 + 12.1° (*c* 0.94, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.01 (br s, 1H, exchanged with $D_2O$), 8.82 (s, 1H), 8.72 (s, 1H), 8.02 (d, 2H, $J = 7.1$ Hz), 7.61 (t, 1H, $J = 7.4$ Hz), 7.53 (t, 2H, $J = 7.4$ Hz), 6.24 (s, 1H, $J = 4.9$ Hz), 5.16 (d, 1H, $J = 7.9$ Hz), 4.82 (dd, 1H, $J = 1.7$, 4.0 Hz), 4.62 (dd, 1H, $J = 1.4$, 6.8 Hz), 4.54 (d, 1H, $J = 6.2$ Hz), 4.39 (br s, 1H), 4.32 (m, 2H), 4.10 (d, 1H, $J = 4.0$ z), 3.70 (s, 3H), 3.37 (s, 3H), 3.29 (br s, 1H, exchanged with $D_2O$), 1.06−1.00 (m, 42H), 0.87 (s, 9H), 0.11 (s, 3H), 0.06 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 206.0, 168.9, 164.4, 152.5, 151.3, 149.1, 142.3, 133.8, 132.5, 128.7, 127.7, 122.7, 88.8, 86.4, 78.9, 76.5, 76.2, 75.6, 75.5, 72.1, 67.6, 58.7, 52.0, 25.6, 17.9, 17.8, 17.7, 17.6, 12.2, 12.0, −4.8, −5.0; MS (FAB) *m*/*z* 1001 ($MH^+$); exact MS (FAB) calcd for $C_{49}H_{82}N_5O_{11}Si_3$ 1000.5318, found 1000.5390. Anal. Calcd for $C_{49}H_{81}N_5O_{11}Si_3$: C, 58.83; H, 8.16; N, 7.00. Found: C, 58.74; H, 8.02; N, 6.99.

***N*$^6$-Benzoyl-9-[methyl 6,10-Anhydro-3,8-*O*-(*tert*-butyldimethylsilyl)-2-*O*-methyl-9-*O*-(*tert*-butyldiphenylsilyl)-α-D-*arabino*-L-*ido*-7-undeculofuranuronyl]adenine (30c-α) and *N*$^6$-Benzoyl-9-[methyl 6,10-Anhydro-3,8-*O*-(*tert*-butyldimethylsilyl)-2-*O*-methyl-9-*O*-(*tert*-butyldiphenylsilyl)-*β*-D-*arabino*-D-*gluco*-7-undeculofuranuronate]adenine (30c-*β*).** In a manner similar to that described for **30a**, from **29c** (300 mg, 0.46 mmol), **30c-α** (198 mg, 41% as a white foam) and **30c-*β*** (135 mg, 29% as a white foam) were obtained after purification by flash column chromatography ($SiO_2$, 40% EtOAc/hexane). For α-anomer: $[\alpha]_D$ −36.3° (*c* 1.15, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.06 (br s, 1H, exchanged with $D_2O$), 8.84 (s, 1H), 8.43 (s, 1H), 8.03 (d, 2H, $J = 7.3$ Hz), 7.65−7.39 (m, 13H), 6.26 (s, 1H), 4.74 (d, 1H, $J = 2.1$ Hz), 4.57 (m, 5H), 3.98 (br s, 2H), 3.68 (d, 1H, $J = 4.2$ z), 3.64 (s, 3H), 3.60 (s, 3H), 1.02 (s, 9H), 0.74 (s, 9H), 0.68 (s, 9H), 0.14 (s, 3H), −0.08 (s, 3H),- 0.17 (s, 3H), −0.23 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 203.3, 170.2, 152.5, 150.7, 149.1, 141.9, 135.7, 133.8, 132.5, 132.1, 132.0, 130.3, 130.1, 128.7, 127.9, 127.8, 127.7, 122.8, 90.7, 88.5, 82.1, 80.8, 77.2, 75.0, 73.3, 73.1, 70.2, 58.2, 52.2, 26.8, 25.6, 25.4, 19.1, 18.1, 18.0, −5.1, −5.2, −5.6; MS (FAB) *m*/*z* 1041 ($MH^+$); exact MS (FAB) calcd for $C_{53}H_{74}N_5O_{11}Si_3$ 1040.4692, found 1040.4700. Anal. Calcd for $C_{53}H_{73}N_5O_{11}Si_3$·EtOAc: C, 60.66; H, 7.23; N, 6.21. Found: C, 60.35; H, 7.05; N, 6.25. For $\beta$-anomer: $[\alpha]_D$ +11.4° (*c* 1.06, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.03 (br s, 1H, exchanged with $D_2O$), 8.82 (s, 1H), 8.72 (s, 1H), 8.02 (d, 2H, $J = 7.3$ Hz), 7.60−7.38 (m, 13H), 6.25 (d, 1H, $J = 4.4$ Hz), 5.06 (d, 1H, $J = 7.9$ Hz), 4.69 (d, 1H, $J = 6.5$ Hz), 4.55 (m, 3H), 4.41 (d, 1H, $J = 6.7$ Hz), 4.32 (br s, 2H), 3.84 (d, 1H, $J = 4.0$ Hz), 3.57 (s, 3H), 3.39 (s, 3H), 1.06 (s, 9H), 0.88 (s, 9H), 0.69 (s, 9H), 0.15 (s, 3H), 0.07 (s, 3H), − 0.16 (s, 3H), −0.17 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 206.1, 168.8, 152.5, 151.4, 149.2, 142.3, 135.6, 135.5, 133.8, 132.5, 132.2, 130.2, 130.1, 128.7, 127.9, 127.8, 127.7, 122.6, 89.0, 86.6, 79.3, 76.7, 75.7, 75.5, 75.0, 67.8, 58.7, 51.9, 89.0, 86.6, 79.3, 77.3, 77.0, 76.7, 75.7, 75.5, 75.0, 72.5, 67.8, 58.7, 51.9, 26.8, 25.7, 25.4, 19.2, 18.0, 17.9, −4.7, −4.8, −5.2, −5.3; MS (FAB) *m*/*z* 1041 ($MH^+$); exact MS (FAB) calcd for $C_{53}H_{74}N_5O_{11}Si_3$ 1040.4692, found 1040.4680. Anal. Calcd for $C_{53}H_{73}N_5O_{11}Si_3$·EtOAc: C, 60.66; H, 7.23; N, 6.21. Found: C, 60.47; H, 6.97; N, 6.50.

***N*$^6$-Benzoyl-9-[methyl 6,10-Anhydro-3,8,9-tri-*O*-(*tert*-butyldimethylsilyl)-6-dehydro-5-deoxy-2-*O*-methyl-α-D-*arabino*-L-*ido*-7-undeculofuranuronyl]adenine (31a).** A mixture of **30a** (60 mg, 66 $\mu$mol) and Burgess's inner salt (96 mg, 396 $\mu$mol) in toluene (5 mL) was heated under reflux for 1 h. After being cooled to room temperature, the mixture was evaporated under reduced pressure. The residue in EtOAc (30 mL) was washed with $H_2O$ (3 × 20 mL) and brine (10 mL). The organic layer was dried ($Na_2SO_4$) and evaporated under reduced pressure. The residue was purified by flash column chromatography ($SiO_2$, 40% EtOAc/hexane) to give **31a** (28 mg, 66% as a pale yellow foam): $[\alpha]_D$ −7.55° (*c* 1.02, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.04 (br s, 1H, exchanged with $D_2O$), 8.84 (s, 1H), 8.41 (s, 1H), 8.03 (d, 2H, $J = 7.5$ Hz), 7.61 (t, 1H, $J = 7.5$ Hz), 7.54 (t, 2H, $J = 7.5$ Hz), 6.32 (s, 1H), 6.08 (d, 1H, $J = 8.1$ Hz), 5.36 (dd, 1H, $J = 2.9$, 8.1 Hz), 4.65 (d, 1H, $J = 1.7$ Hz), 4.56 (dd, 1H, $J = 1.7$, 3.8 Hz), 4.28 (d, 1H, $J = 2.8$ Hz), 4.12 (d, 1H, $J = 1.7$ Hz), 3.99 (d, 1H, $J = 3.9$ Hz), 3.77 (s, 3H), 3.61 (s, 3H), 0.89 (s, 9H), 0.86 (s, 9H), 0.76 (s, 9H), 0.15 (s, 3H), 0.13 (s, 3H), 0.10 (s, 3H), 0.07 (s, 3H), 0.02 (s, 3H), −0.09 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 189.2, 168.5, 152.5, 150.8, 149.2, 147.5, 141.9, 133.8, 132.6, 128.7, 127.8, 122.6, 111.3, 91.4, 88.1, 79.6, 76.5, 76.4, 72.8, 72.5, 58.4, 52.4, 25.6, 25.6, 25.5, 18.4, 18.0, −4.8, −4.9, −5.0, −5.0, −5.1, −5.2; MS (FAB) *m*/*z* 899 ($MH^+$); exact MS (FAB) calcd for $C_{43}H_{68}N_5O_{10}Si_3$ 898.4273, found 898.4302. Anal. Calcd for $C_{43}H_{67}N_5O_{10}Si_3$·$H_2O$: C, 56.36; H, 7.59; N, 7.64. Found: C, 56.16; H, 7.39; N, 7.68.

***N*$^6$-Benzoyl-9-[methyl 6,10-Anhydro-3-*O*-(*tert*-butyldimethylsilyl)-6-dehydro-5-deoxy-8,9-di-*O*-(triisopropylsilyl)-2-*O*-methyl-α-D-*arabino*-L-*ido*-7-undeculofuranuronyl]adenine (31b).** In a manner similar to that described for **31a**, the reaction of **30b** (60 mg, 60 $\mu$mol) with Burgess's inner salt (87 mg, 360 $\mu$mol) in toluene (5 mL) and purification by flash silica gel column chromatography ($SiO_2$, 40% EtOAc/hexane) gave **31b** (41 mg, 70% as a pale yellow foam): $[\alpha]_D$ −13.6° (*c* 1.02, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.04 (br s, 1H, exchanged with $D_2O$), 8.84 (s, 1H), 8.40 (s, 1H), 8.03 (d, 2H, $J = 7.6$ Hz), 7.61 (t, 1H, $J = 7.5$ Hz), 7.53 (t, 2H, $J = 7.6$ Hz), 6.31 (s, 1H), 6.04 (d, 1H, $J = 8.2$ Hz), 5.39 (dd, 1H, $J = 2.9$, 8.2 Hz), 4.83 (dd, 1H, $J = 1.7$, 3.6 Hz), 4.75 (s, 1H), 4.26 (d, 1H, $J = 2.9$ Hz), 4.13 (d, 1H, $J = 3.9$ Hz), 3.99 (s, 1H), 3.76 (s, 3H), 3.63 (s, 3H), 1.14−1.02 (m, 42H), 0.76 (s, 9H), 0.04 (s, 3H), −0.10 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 189.2, 168.5, 152.5, 150.8, 149.2, 147.5, 141.9, 133.8, 132.6, 128.7, 127.8, 122.6, 111.3, 91.4, 88.1, 79.6, 76.5, 76.4, 72.8, 72.5, 58.4, 52.4, 25.6, 25.6, 25.5, 18.4, 18.0, −4.8, −4.9, −5.0, −5.0, −5.1, −5.2; MS (FAB) *m*/*z* 983 ($MH^+$); exact MS (FAB) calcd for $C_{49}H_{80}N_5O_{10}Si_3$ 982.5212, found 982.5192. Anal. Calcd for $C_{49}H_{79}N_5O_{10}Si_3$·0.5EtOAc: C, 59.67; H, 8.15; N, 6.82. Found: C, 59.26; H, 7.76; N, 7.16.

***N*$^6$-Benzoyl-9-[methyl 6,10-Anhydro-3,8-di-*O*-(*tert*-butyldimethylsilyl)-6-dehydro-5-deoxy-9-*O*-(*tert*-butyldiphenylsilyl)-2-*O*-methyl-α-D-*arabino*-L-*ido*-7-undeculofuranuronyl]adenine (31c).** In a manner similar to that described for **31a**, the reaction of **30c** (60 mg, 66 $\mu$mol) with Burgess's inner salt (96 mg, 396 $\mu$mol) in toluene (5 mL) and purification by flash silica gel column chromatography ($SiO_2$, 40% EtOAc/hexane) gave **31c** (28 mg, 79% as a pale yellow foam): $[\alpha]_D$ −22.0° (*c* 0.68, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 9.12 (br s, 1H, exchanged with $D_2O$), 8.84 (s, 1H), 8.43 (s, 1H), 8.03 (d, 2H, $J = 7.5$ Hz), 7.61 (t, 1H, $J = 7.5$ Hz), 7.54 (t, 2H, $J = 7.5$ Hz), 7.49−7.40 (m, 10H), 6.33 (s, 1H), 6.11 (d, 1H, $J = 8.3$ Hz), 5.42 (dd, 1H, $J = 2.9$, 8.3 Hz), 4.68 (d, 1H, $J = 1.4$ Hz), 4.55 (dd, 1H, $J = 2.0$, 3.6 Hz), 4.32 (d, 1H, $J = 2.9$ Hz), 4.01 (s, 1H), 3.83 (d, 1H, $J = 3.6$ Hz), 3.65 (s, 3H), 3.64 (s, 3H), 1.06 (s, 9H), 0.78 (s, 9H), 0.69 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H), −0.14 (s, 3H), −0.15 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 181.3, 169.6, 169.3, 163.0, 139.7, 134.6, 132.0, 129.3, 128.1, 111.4, 102.4, 101.7, 100.1, 88.6, 87.2, 84.9, 76.4, 76.2, 75.9, 71.9, 69.5, 68.4, 63.8, 36.0, 30.3, 27.9, 26.0, 21.4, 20.9, −4.0, −4.2, −4.5, −4.8; MS (FAB) *m*/*z* 1023 ($MH^+$); exact MS (FAB) calcd for $C_{53}H_{72}N_5O_{10}Si_3$ 1022.4586, found 1022.4579. Anal. Calcd for $C_{53}H_{71}N_5O_{10}Si_3$: C, 62.26; H, 7.00; N, 6.85. Found: C, 62.54; H, 6.77; N, 6.32.

**Herbicidin B (1b).** A mixture of **31c** (50 mg, 55 $\mu$mol), $HCO_2NH_4$ (173 mg, 5.5 mmol), and Pd-on-carbon (20%, 15 mg) in MeOH (5 mL) was stirred for 24 h at room temperature. The mixture was filtrated through a Celite pad, and the filtrate was evaporated under reduced pressure. The residue was partitioned between EtOAc (5 mL) and $H_2O$ (2 mL), and the separated organic layer was washed with $H_2O$ (3 mL) and brine (3 mL). The organic layer was dried ($Na_2SO_4$) and evaporated under reduced pressure. A mixture of the residue in MeOH (5 mL) containing Sm (9.2 mg, 59 $\mu$mol) and $I_2$ (15 mg, 59 $\mu$mol) was stirred for 15 min at room temperature. The mixture was evaporated under reduced pressure, and the residue was partitioned between EtOAc (5

mL) and $H_2O$ (2 mL). The organic layer was washed with $H_2O$ (3 mL) and brine (3 mL), dried ($Na_2SO_4$), and evaporated under reduced pressure. A solution of the residue in THF (5 mL) containing TBAF (1 M THF solution, 50 $\mu$L, 50 $\mu$mol) was stirred for 30 min at 0 °C. The mixture was evaporated under reduced pressure, and the residue was purified by preparative TLC (17% MeOH/$CHCl_3$) to give herbicidin B (7.3 mg, 31%): $[\alpha]_D$ +55.1° (*c* 0.61, MeOH), lit.[3b] $[\alpha]_D$ +63° (*c* 1, MeOH); $^1$H NMR ($CD_3OD$, 500 MHz) $\delta$ 8.59 (s, 1H), 8.11 (s, 1H), 6.08 (s, 1H), 4.58 (t, 1H, $J$ = 8.6 Hz), 4.35 (s, 1H), 4.33 (d, 1H, $J$ = 2.3 Hz), 4.27 (s, 1H), 4.25 (d, 1H, $J$ = 3.3 Hz), 3.90 (s, 1H), 3.62 (s, 3H), 3.37 (t, 1H, $J$ = 9.5 Hz), 3.44 (s, 3H), 2.14 (br s, 1H), 2.12 (s, 1H); $^{13}$C NMR ($CD_3OD$, 125 MHz) $\delta$ 171.8, 154.0, 142.4, 94.6, 92.2, 89.1, 79.7, 78.0, 74.4, 73.8, 71.3, 65.5, 58.4, 26.4; MS (FAB) *m*/*z* 454 ($MH^+$). Anal. Calcd for $C_{18}H_{23}N_5O_9$: C, 47.68; H, 5.11; N, 15.45. Found: C, 47.89; H, 5.09; N, 14.78.

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**Supporting Information Available:** General experimental methods, experimental details for the synthesis of **9**−**13**, **19a**,**b**, and **20**−**23**, and complete $^1$H NMR spectral information for **22**, **23**, **25**, **27b**, and synthetic and natural herbicidin B (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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