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Development of the Carboxamide Protecting Group, 4-(*tert*-Butyldimethylsiloxy)-2-methoxybenzyl

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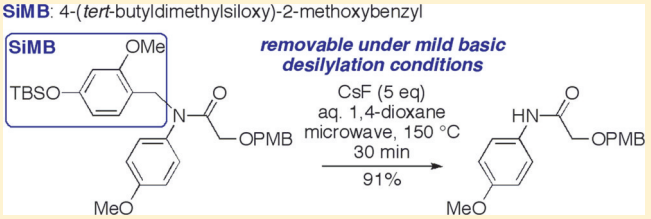
Supporting Information

ABSTRACT: The new carboxamide protecting group, 4-(*tert*-butyldimethylsiloxy)-2-methoxybenzyl (SiMB), has been developed. While this SiMB group can be removed using mild basic desilylation methods, it can also be deprotected under strongly acidic or oxidative conditions. An application of this group to simple carboxamide groups, as well as to more complex and acid-sensitive adenosine derivatives containing a cyclophane scaffold, was also demonstrated.



INTRODUCTION

The essential role of protecting groups is to prevent functional groups from unwanted reactions during a synthesis.[1] Therefore, it is preferable if these protecting groups possess additional functions, such as the ability to induce selectivity in reactions, a conformational change of the molecules, or functionalization of neighboring chemical entities.[2] Consequently, their contribution in organic synthesis is considerable. *N*-Protection of a carboxamide to induce a conformational change is an established strategy to improve the yields of certain intramolecular cyclization reactions, especially those providing highly strained macrocycles.[3] We have recently reported the synthesis of an adenosine analogue containing a 14-membered cyclophane as a potential Hsp90 inhibitor (**4**, Scheme 1).[4] A key reaction in the synthesis of **4** is the highly efficient ring-closing metathesis (RCM) assisted by the 2,4-dimethoxybenzyl (DMB) group. The conversion to the highly strained 14-membered cyclophane **2** containing two olefins within the macrocycle was nearly quantitative, indicating that the impact of the newly introduced DMB group on the RCM was considerable, since no cyclization products were obtained when the nitrogen atom of the carboxamide moiety was unprotected. However, it turned out that the DMB group was relatively stable under the acidic deprotection conditions (TFA, Et_3SiH, CH_2Cl_2, room temperature, 24 h), during the course of which the 14-membered cyclophane derivatives gradually decomposed partly because of depurination. As a result, the chemical yields of **4** were low. Protection of a carboxamide is an area of protecting group chemistry that has received little attention compared to that of other functional groups, and as a consequence, few good methods exist.[1] Herein, we describe the development of a new carboxamide protecting group, the 4-(*tert*-butyldimethylsiloxy)-2-methoxybenzyl (SiMB) group, which helps cyclization reactions and can be removed under conditions other than strong acid. An application of the SiMB group to a more complex system was also demonstrated by an improved synthesis of **4** and its derivative **46**.

Several substituted *N*-benzylcarboxamide protecting groups[5] have been reported in the literature; however, most of them are ultimately removed by strongly acidic or oxidative conditions.[6] Less attention has been paid to developing substituted *N*-benzylcarboxamide protecting groups cleavable under mildly basic conditions. Recently, the 4-(*tert*-butyldimethylsiloxy)-3-fluorobenzyl group has been developed as a sugar hydroxyl protecting group by Crich's group.[7] This protecting group was removed by tetrabutylamonium fluoride (TBAF) under microwave irradiation or conventional heating. We simply designed the 4-siloxy-2-methoxybenzyl group **6** as a carboxamide protective group by replacing one of the methoxy substituents of the DMB group with a siloxy group (Scheme 2). Upon treatment of **6** under typical desilylation conditions, the liberated 4-hydroxy-2-methoxybenzyl group could be removed to give the secondary carboxamide **8** in addition to the 3-methoxy-*p*-quinonemethide (**9**). To ensure chemical stability during the synthesis, we chose a TBS group as the capping group at the 4-position.[8]

RESULTS AND DISCUSSION

The model carboxamides protected with an SiMB group were prepared as shown in Scheme 3.[9] Reductive amination of 4-(*tert*-butyldimethylsiloxy)-2-methoxybenzaldehyde (**11**), which was prepared by conventional TBS protection of commercially available 4-hydroxy-2-methoxybenzaldehyde (**10**), with *p*-anisidine gave the *N*-SiMB-protected amine **12**. The amine was acylated with benzoyl chloride in the presence of Et_3N in CH_2Cl_2 to give the corresponding carboxamide **13** in 94%. First, we attempted to optimize the conditions to deprotect the SiMB group (Table 1). Exposure of **13** to TBAF in THF at room temperature resulted only in removal of the TBS group

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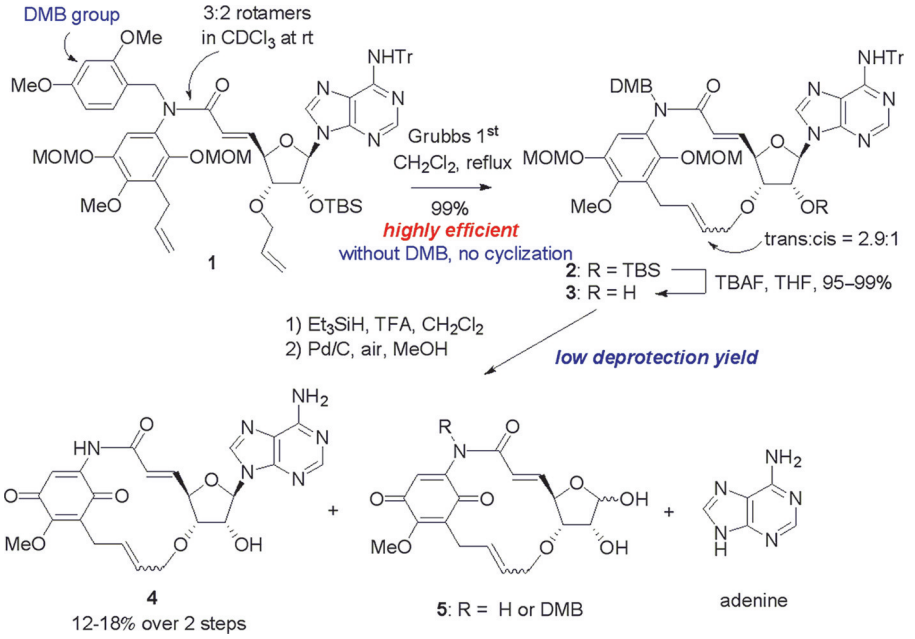
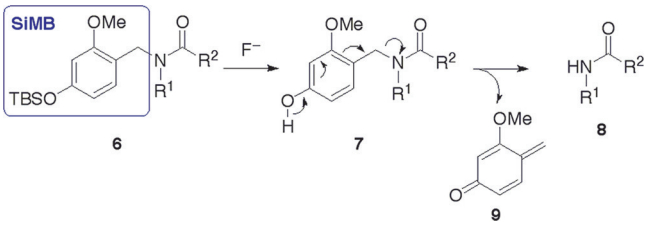
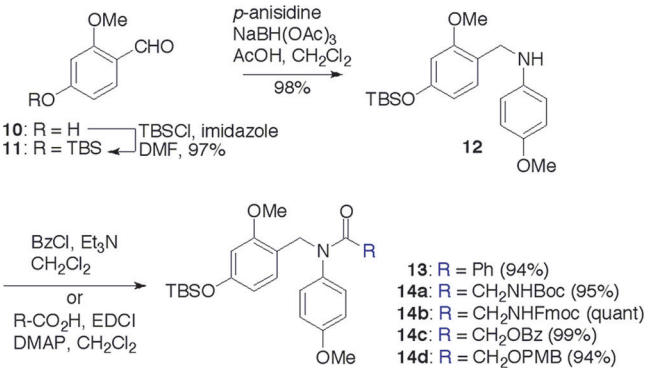
Scheme 1. Previous Study for the Synthesis of Cyclophane-Type Adenosine Derivatives



Scheme 2. 4-(*tert*-Butyldimethylsiloxy)-2-methoxybenzyl (SiMB) Group

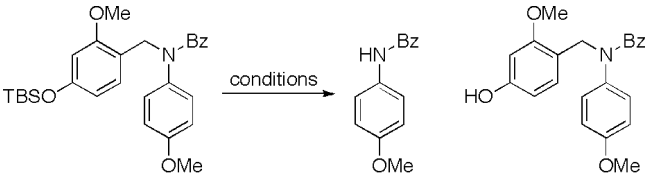


Scheme 3. Preparation of *N*-SiMB Carboxamides



to give *N*-(4-hydroxy-2-methoxybenzyl)-*p*-benzanisidide (**16**) in 98% yield (entry 1). Since a careful TLC analysis indicated that a trace amount of the desired *p*-benzanisidide (**15**) was formed in this reaction, we then examined the reaction using higher temperatures. When the reaction was conducted at 150 °C under microwave irradiation (70 W, 5 bar), further cleavage of the resulting 4-hydroxy-2-methoxybenzyl group proceeded within 10 min to afford **15** in 97% yield (entry 2). From these results, we confirmed the feasibility of the deprotection of the SiMB group under basic conditions. Next, other basic desilylation conditions were tested. Treatment of **13** with CsF in refluxing aqueous 1,4-dioxane for 12 h

Table 1. Deprotection of SiMB Group



entry	conditions	time	yield[a] (%)
1	TBAF, THF, rt	24 h	trace (98)[b]
2	TBAF, THF, MW, 150 °C	10 min	97
3	CsF, aq 1,4-dioxane, reflux	12 h	93
4	CsF, aq 1,4-dioxane, MW, 150 °C	20 min	95
5	K_2CO_3, MeOH, reflux	9 h	90
6	K_2CO_3, MeOH, MW, 100 °C	10 min	93
7	80% aq TFA, rt	30 min	84
8	DDQ, CH_2Cl_2–H_2O, rt	30 h	83
9[c]	DDQ, CH_2Cl_2–H_2O, rt	20 min	95
10	CAN, MeCN–H_2O, rt	1 h	29

[a]Isolated yield. [b]TLC analysis. The yield shown in parentheses is an isolated yield of **16** to which the removal of the TBS group occurred. [c]**16** was used as a substrate.

gave **15** in 93% yield (entry 3). When a microwave reactor with a higher temperature was used, the reaction time was dramatically shortened to 20 min (entry 4). Since the deprotection is an oxidative process, the deprotection under O_2 atmosphere was also investigated. However, promotion of the reaction time was not observed, and **15** was obtained in 90% in entry 3 and 91% in entry 4 under O_2 atmosphere (1 atm), respectively. Treatment of **13** with K_2CO_3 in MeOH under thermal and microwave conditions afforded **15** in 90% and 93% yield, respectively (entries 5 and 6). Compared to the 4-(*tert*-butyldimethylsiloxy)-3-fluorobenzyl group as a protective group of the alcohol,[7] the SiMB group was easily removed from the carboxamide in high chemical conversion under these conditions. Acidic and oxidative conditions, which are generally used to remove an *N*-DMB group,[1] were also

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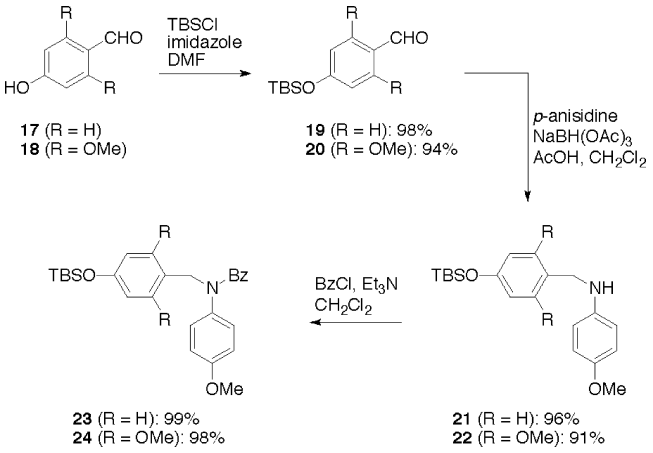
examined (entries 7 and 8). In the case of oxidative conditions using DDQ in wet CH_2Cl_2, a long reaction time was required to complete the reaction (entry 8). However, the oxidation of the free phenol **16**, which was obtained by TBAF treatment (entry 1), with DDQ proceeded very smoothly to provide **15** in 95% yield (entry 9). This two-step procedure provides an opportunity to deprotect the SiMB group without having to deal with high temperature. In addition, the 4-(*tert*-butyldimethylsiloxy)-3-fluorobenzyl group was resistant to DDQ oxidation.[7] On the other hands, the SiMB group can be removed by DDQ by modulating the susceptibility to the oxidative conditions. Although not fitting into our stated goal of finding a carboxamide protecting group which is not removed with strong acid or oxidative conditions, the feasibility of using such a two-step approach as a room temperature method for deprotection would expand the scope of this new protecting group. When **13** was treated with CAN, **13** completely consumed within 1 h. However, the yield of **15** was poor (29%) because of further removal of the *N*-4-methoxyphenyl group (entry 10).

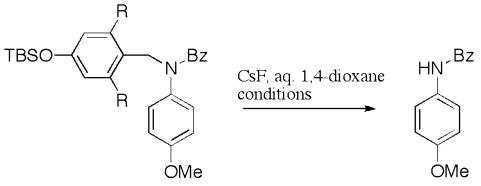
Since it is likely that electron-donating substituents increase the rate of formation of the *p*-quinonemethide, the deprotection efficiency of the 4-siloxybenzyl group might be enhanced by increasing the number of methoxy substituents. Therefore, we next compared the reactivity of the 4-*tert*-butyldimethylsiloxybenzyl (SiB) group and the 4-(*tert*-butyldimethylsiloxy)-2,6-dimethoxybenzyl (SiDMB) group, which possess two electron-donating methoxy substituents at the *o*-positions or none. The SiB- and SiDMB-protected substrates **23** and **24** were prepared from the corresponding 4-hydroxybenzaldehydes **17** and **18** in a manner similar to the synthesis of **13** (Scheme 4). The deprotection conditions using

Scheme 4. Preparation of 23 and 24



CsF were selected to compare the reactivity of the different *N*-4-siloxybenzyl groups, and the results are summarized in Table 2. When the *N*-SiB-protected carboxamide **23** was treated with CsF under thermal conditions (entry 1), the deprotection was not complete even after 72 h and gave the secondary carboxamide **15** in only 31% yield along with *N*-(4-hydroxybenzyl)-*p*-benzanisidide in 57% yield. In order to accelerate this reaction, we next used a microwave reactor (entry 2). However, the time to obtain **15** was much longer than that for the SiMB deprotection (20 min for **13** vs 9 h for **23**). On the other hand, deprotection of the SiDMB-protected carboxamide **24** under thermal or microwave irradiation

Table 2. Comparison of the Reactivity of Substituted *N*-Benzyl Group under Basic Conditions



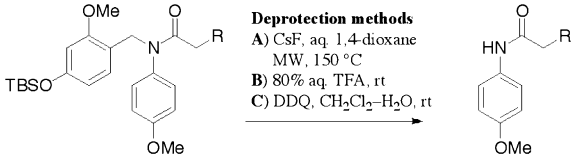
entry	substrates	conditions	time	yield[a] (%)
1	**23** (R = H)	reflux	72 h	31 (57)[b]
2	**23** (R = H)	MW, 150 °C	9 h	88
3	**24** (R = OMe)	reflux	8 h	94
4	**24** (R = OMe)	MW, 150 °C	15 min	97

[a]Isolated yield. [b]The yield shown in parentheses is an isolated yield of *N*-(4-hydroxybenzyl)-*p*-benzanisidide to which the removal of the TBS group occurs.

conditions proceeded very smoothly to give **15** in excellent yields (entries 3 and 4). The deprotection of the SiDMB group was slightly faster than that of the SiMB group, and increasing the number of the electron-donating methoxy group resulted in an increase rate of deprotection. Considering the cost of 4-hydroxybenzaldehyde derivatives (4-hydroxy-2-methoxybenzaldehyde, Wako Chemicals, 5 g, ¥19500 vs 4-hydroxy-2,6-dimethoxybenzaldehyde, Aldrich, 1 g, ¥25700), the SiMB group would be the best choice as the carboxamide protecting group since there was very little difference between the two groups with regard to the ease of deprotection.

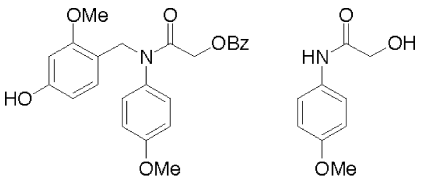
Next, the orthogonality of the SiMB group with other protecting groups, which are labile under acidic, basic, or oxidative conditions, was examined (Table 3). We prepared the

Table 3. Selective Deprotection of the SiMB Group in the Presence of Other Protective Groups



entry	substrates	methods	products	time	yield[a] (%)
1	**14a** (R = NHBoc)	A	**25a**	30 min	93
2	**14a** (R = NHBoc)	C	**25a**	21 h	54
3	**14b** (R = NHFmoc)	B	**25b**	1.5 h	95
4	**14b** (R = NHFmoc)	C	**25b**	35 h	43
5	**14c** (R = OBz)	A	**25c**	20 min	14[b]
6	**14c** (R = OBz)	B	**25c**	22 h	87
7	**14c** (R = OBz)	C	**25c**	12 h	96
8	**14d** (R = OPMB)	A	**25d**	30 min	91

[a]Isolated yield. [b]Besides **25c**, compounds **26** and **27** were obtained in 31% and 49% yield, respectively.



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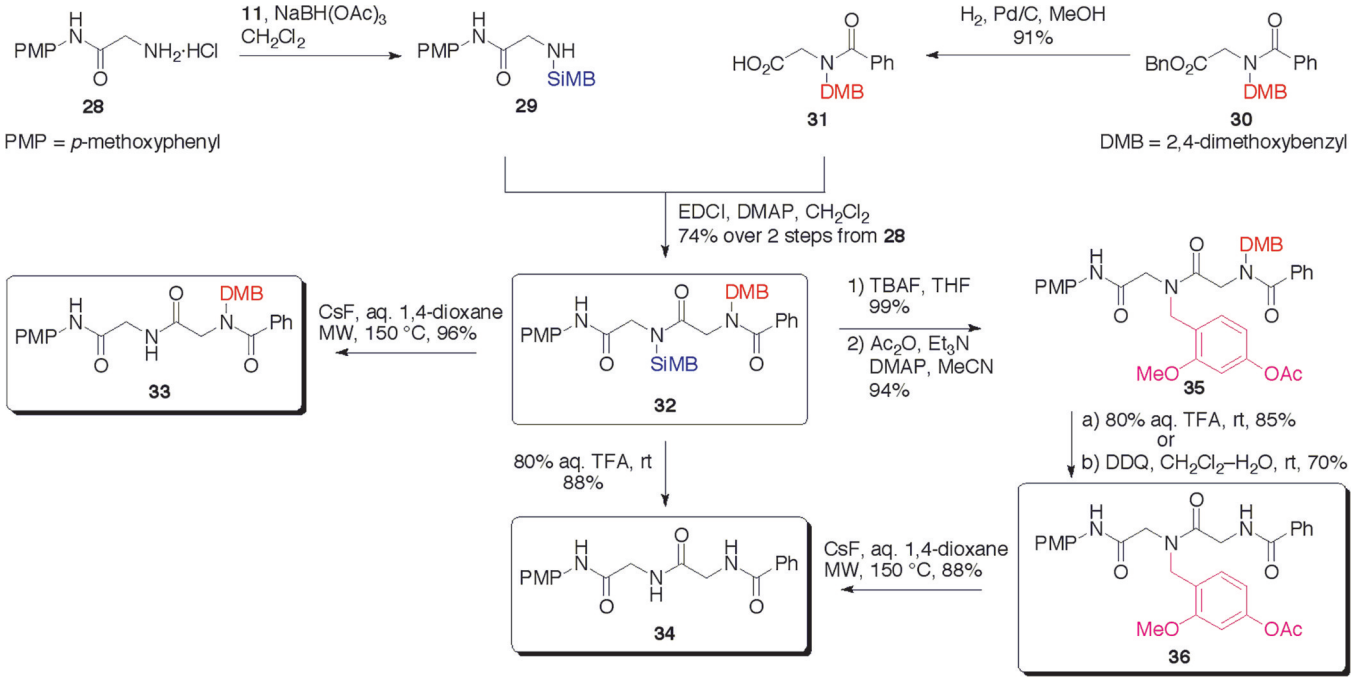
Scheme 5. Orthogonality between the SiMB and the DMB Groups and Reversible Modification of the SiMB Group



N-protected *p*-glycylanisidide derivatives (**14a** and **14b**) and the *O*-protected *p*-glycolanisidide derivatives (**14c** and **14d**) by the simple condensation of the amine **12** with the corresponding carboxylic acid derivatives (EDCI, DMAP, CH_2Cl_2, 94% to quantitative yield) as shown in Scheme 3. When CsF-promoted deprotection conditions (method A) were applied to **14a**, which possesses an acid-labile *N*-Boc protecting group, the *N*-Boc-*p*-glycylanisidide (**25a**) was cleanly obtained in 93% yield (entry 1), while DDQ oxidation in wet CH_2Cl_2 (method C) resulted in a moderate yield of **25a** due to incomplete reaction with concomitant byproducts (entry 2). When the base-sensitive *N*-Fmoc-protected carboxamide **14b** was treated with aqueous 80% TFA (method B), the deprotected **25b** was obtained in 95% yield (entry 3). Under the oxidative conditions, a byproduct, which might have occurred by oxidation of the Fmoc group, was observed, and the isolated yield of **25b** was moderate (entry 4). Next, the glycolamide **14c** containing an *O*-benzoyl substituent was treated with method A. The desired **25c** was obtained in 14% yield along with the des-TBS product **26** and the fully deprotected compound **27** in 31% and 49% yield, respectively (entry 5). Treatment of **14c** with method B or C proceeded to give **25c** in high yield (entries 6 and 7). The most remarkable example is the *O*-*p*-methoxybenzyl-*N*-SiMB-*p*-glycolanisidide (**14d**). Deprotection of the SiMB group of **14d** with method A proceeded smoothly to give **25d** without cleavage of the PMB ether. If the carboxamide nitrogen atom had been protected with a DMB group, **25d** could not have been obtained because the PMB ether would be easily cleaved under acidic and oxidative conditions, which are generally used for the removal of an *N*-DMB group.[1] As discussed above, the SiMB group is very useful for the protection of a carboxamide nitrogen atom when the target molecules contain acid- or oxidation-labile moieties and is the first example of an *N*-benzyl-type protective group cleavable under mildly basic conditions.

We further verified the orthogonality of the SiMB group with a DMB group with a glycylglycine derivative **32** bearing both *N*-benzyl-type protecting groups as the substrate (Scheme 5). Reductive alkylation of the glycyl-*p*-anisidide hydrochloride (**28**)[10] with **11** gave the *N*-SiMB-protected amine **29**. The resulting amine **29** was acylated with the carboxylic acid **31**, which was prepared from **30**[11] by catalytic hydrogenation, using EDCI and DMAP in CH_2Cl_2 to give **32** in 74% over two steps from **28**. First, treatment of **32** with CsF in aqueous 1,4-dioxane under microwave irradiation, in order to effect selective deprotection of the SiMB group, proceeded to give **33** in 96% yield. When **32** was treated with 80% aqueous TFA, the removal of both the SiMB and the DMB groups proceeded cleanly to provide **34** in 88% yield. We also planned to remove the DMB group of **32** selectively in the presence of the SiMB group. This was accomplished by substituent manipulation from a TBS group to an electron-withdrawing acetyl group prior to treatment with 80% aqueous TFA. Namely, the electron-withdrawing substituent was intended to enhance stability under acidic and oxidative conditions, in much the same way that a 2-acetoxy substituent enhances the stability of *N*-(4-methoxybenzyl)carboxamide under acidic conditions.[6e] Removal of the TBS group of **32** by brief treatment with TBAF at room temperature followed by acylation of the resulting hydroxyl moiety with acetic anhydride afforded the *N*-(4-acetoxy-2-methoxybenzyl)-protected carboxamide **35** in nearly quantitative yield over two steps. When **35** was treated with TFA or DDQ, selective cleavage of the DMB group proceeded to give the desired carboxamide **36** in 85% and 70% yield, respectively. Thus, stability to acidic and oxidative conditions could be imparted to the SiMB group by facile conversion of the TBS capping group to the electron-withdrawing acetyl group. In addition, simple deprotection of the 4-acetoxy-2-methoxybenzyl group by treatment with CsF gave **34** in 88% yield.

Having developed the SiMB group, we next evaluated its potency in the synthesis of **4** (Scheme 6). The *N*-SiMB-protected RCM precursor **41a** was prepared in a manner similar to the synthesis of **1**.[4] The SiMB group was introduced

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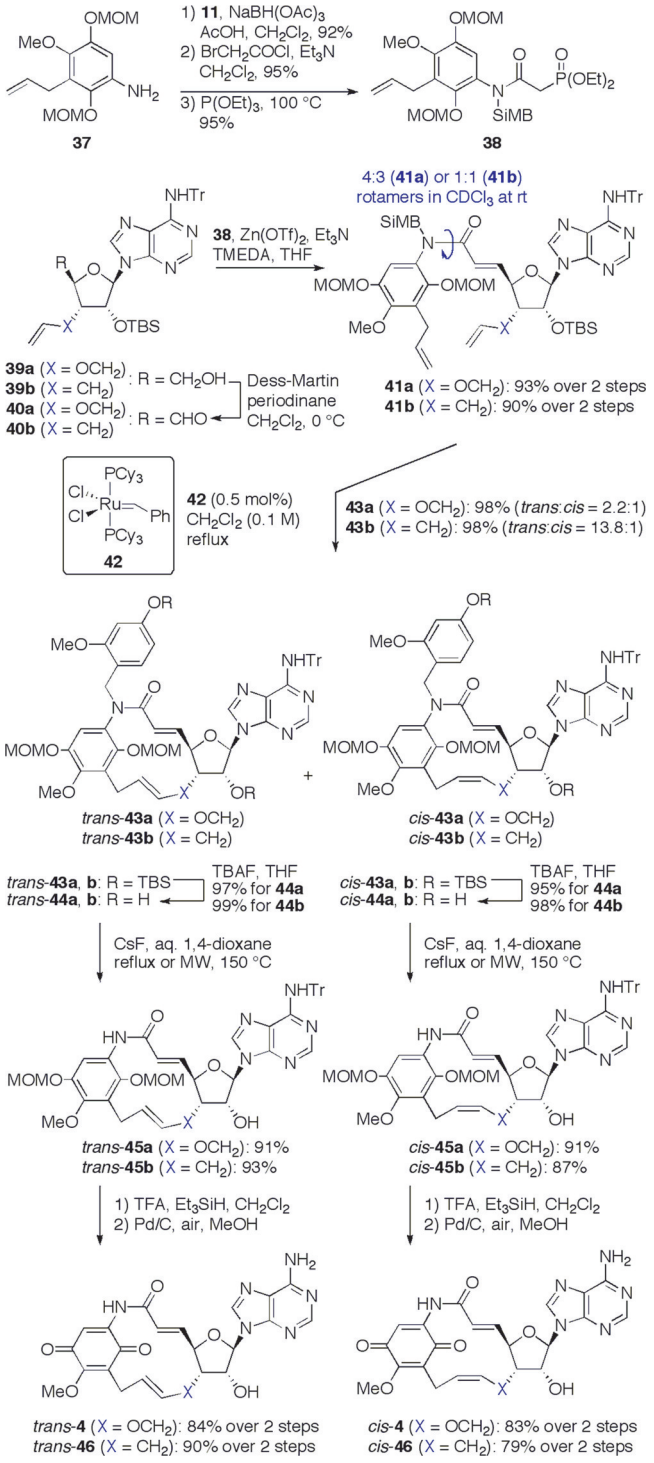
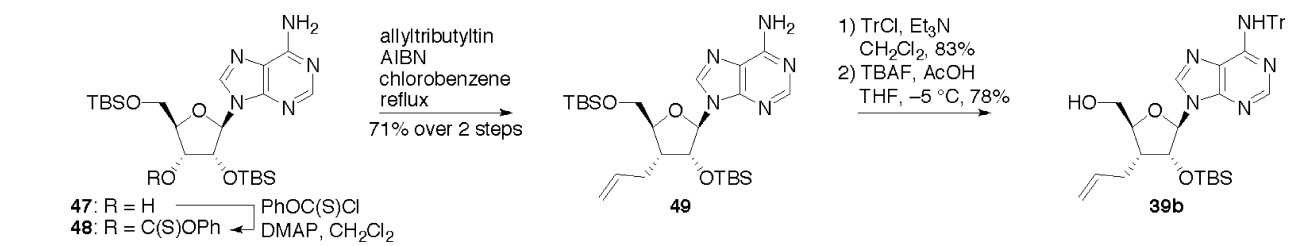
Scheme 6. Improved Synthesis of 4 and 13-Membered Cyclophane Derivatives 46



into **37** by reductive alkylation of **11** to give an *N*-SiMB amine in 92% yield. Bromoacetylation of the amine followed by the Arbuzov reaction with triethyl phosphite provided the *N*-SiMB-*N*-arylphosphonoacetamide **38**. The mild Horner–Wadsworth–Emmons (HWE) olefination[12] of **38** with the adenosine 5′-aldehyde derivative **40a**, which was prepared by the oxidation of the alcohol of **39a**[4] with Dess–Martin periodinane,[13] was conducted, and the *N*-SiMB-protected unsaturated *E*-carboxamide **41a** was obtained in 93% yield over two steps. The RCM precursor **41a** existed in an approximate 4:3 mixture of rotamers in $CDCl_3$ observed by ^1H NMR at room temperature. A similar observation was noted in the case of the *N*-DMB-protected carboxamide **1**.[4] Treatment of **41a** with the first-generation Grubbs' catalyst **42**[14] in CH_2Cl_2 gave the desired 14-membered cyclophane **43a** in nearly quantitative yield as a mixture of *trans*- and *cis*-isomers.[15] As expected, the efficiency of the SiMB group in the RCM was similar to that of the DMB group. In addition, it was found that this RCM was scalable because the reaction proceeded smoothly even with low catalyst loading (0.5 mol % of **42**) and high concentration (0.1 M). After removal of TBS groups of *trans*-**43a** at both the SiMB moiety and the 2′-hydroxyl group, treatment of the resulting *trans*-**44a** with CsF afforded the secondary carboxamide *trans*-**45a** in 91% yield. Although direct conversion of *trans*-**43a** to *trans*-**45a** by the treatment with CsF should be straightforward, it turned out to be difficult to distinguish by TLC analysis between the desired product *trans*-**45a** and the compound, in which only the TBS group on the SiMB moiety of *trans*-**43a** had been removed. Since monitoring of the progress of the deprotection reaction was difficult, the stepwise deprotection method worked well. Finally, brief treatment of *trans*-**45a** with TFA to deprotect the Tr and the two MOM groups followed by air oxidation of the resulting hydroquinone moiety successfully afforded *trans*-**4** in 84% yield over two steps. Similarly, *cis*-**4** was synthesized in satisfactory yield (83% over two steps). In order to demonstrate further applicability, the synthesis of the more rigid derivative **46**, which consisted of a 13-membered cyclophane framework, was conducted. The synthesis of **46** started from the 3′-deoxy-3′-α-allyladenosine derivative **39b**, the preparation of which is described in Scheme 7. Stereoselective radical allylation of adenosine 3′-phenoxy thionocarbonate derivative **48**[16] afforded **49** in good yield.[17] We prepared **39b** by protection of **49** with a Tr group followed by selective removal of the TBS-protecting group at the 5′-hydroxy group with TBAF in the presence of acetic acid in THF at low temperature. Dess–Martin oxidation of **39b** gave the aldehyde **40b**, and the subsequent HWE olefination of **40b** with **38** afforded the *N*-SiMB carboxamide **41b**, which is the RCM precursor, in 90% yield over two steps (Scheme 6). Compound **41b** existed as a 1:1 mixture of rotamers in $CDCl_3$. Treatment of **41b** with the RCM catalyst **42** in CH_2Cl_2 under reflux afforded the desired 13-membered

Scheme 7. Preparation of 39b



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cyclophane **43b** in 98% yield. The cyclophane **43b** was obtained as *trans*- and *cis*-isomers (*trans*/*cis* = 13.8:1),[15] and the geometric selectivity of this RCM reaction was rather high compared with the case of the synthesis of the 14-membered derivative **43a** (2.2:1). After successfully constructing the desired 13-membered cyclophane, we carried out the stepwise conversion of **43b** to **46**, including desilylation, removal of the *N*-(4-hydroxy-2-methoxybenzyl) group, deprotection of the Tr and the two MOM groups, followed by air oxidation of the hydroquinone moiety, as in the synthesis of **4**. All of the reactions proceeded smoothly, and the desired *trans*- and *cis*-**46** were obtained in good yields (90% for *trans*-**46**, 79% for *cis*-**46**). As discussed above, this synthetic strategy using the *N*-SiMB group as the carboxamide protecting group, which helps the cyclization, is quite effective and enabled us to prepare **4** and **46** in 65−68% and 59−73% yields over seven steps from the corresponding adenosine derivatives **39a** and **39b**, respectively.

■ CONCLUSION

A new carboxamide protecting group, the 4-(*tert*-butyldimethylsiloxy)-2-methoxybenzyl (SiMB) group, has been developed. The SiMB group can be removed under conditions other than strong acid. An application of the SiMB group to a complex and acid-sensitive molecule was also demonstrated. The SiMB group is very useful for the protection of the carboxamide nitrogen atom when the target molecules contain acid- or oxidation-labile moieties and is the first example of an *N*-benzyl-type protective group cleavable under mildly basic conditions. In this study, we have investigated the deprotection of the SiMB group with only two types of *N*-substituted carboxamides, which are *N*-*p*-methoxyphenyl and *N*-carbamoylmethyl carboxamides. Further study will be necessary to determine the versatility of this protecting group, and its application of the SiMB group is underway.

■ EXPERIMENTAL SECTION

General Experimental Methods. NMR spectra were reported in parts per million (δ) relative to tetramethylsilane (0.00 ppm) for proton and carbon and H_3PO_4 (0.00 ppm) for phosphorus as internal or external standard. Coupling constants (J) are reported in hertz (Hz). Abbreviations of multiplicity are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Assignment was based on ^{1}H−^{1}H COSY, HMQC, and HMBC NMR spectra. Experiments conducted using microwave irradiation were carried out in sealed vials with temperature determination by means of infrared sensor. All reactions except for the aqueous-phase reactions and the deprotection reactions were carried out under the argon gas atmosphere unless otherwise noted. Isolated yields were calculated by weighing products, and the weights of starting materials and products were not calibrated.[19]

4-*tert*-Butyldimethylsiloxy-2-methoxybenzaldehyde (11). A solution of 4-hydroxy-2-methoxybenzaldehyde (**10**) (1.0 g, 6.6 mmol) in DMF (10 mL) was treated with imidazole (1.1 g, 16 mmol) and TBSCl (1.2 g, 7.9 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 min. The reaction was quenched with H_2O (10 mL), and the mixture was extracted with AcOEt (50 mL). The organic layer was washed with H_2O (30 mL × 2), 0.1 N aqueous HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL), and brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (3 × 5 cm, hexane/AcOEt = 15/1) to give **11** (1.7 g, 97%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.29 (s, 1H, CHO), 7.73 (d, 1H, H-6, J = 8.6 Hz), 6.46 (dd, 1H, H-5, J = 2.3, 8.6 Hz), 6.39 (d, 1H, H-3, J = 2.3 Hz), 3.88 (s, 3H, OMe), 0.99 (s, 9H, ^{t}Bu), 0.25 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.6, 163.8, 163.1, 130.6, 119.5, 112.6, 103.5, 55.7, 25.7, 18.4, −4.2; ESIMS-LR m/z = 289 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{14}H_{22}O_3NaSi$ 289.1236, found 289.1232.

***N*-(4-*tert*-Butyldimethylsiloxy-2-methoxybenzyl)-*p*-anisidine (12).** A mixture of *p*-anisidine (250 mg, 2.0 mmol), **11** (590 mg, 2.2 mmol), and AcOH (0.57 mL, 10 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 10 min. The mixture was treated with $NaBH(OAc)_3$ (1.7 g, 8.0 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 20 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (50 mL), and the mixture was extracted with AcOEt (80 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 10 cm, hexane/AcOEt = 9/1) to give **12** (730 mg, 98%) as a slightly yellow syrup: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, 1H, SiMB-6, J = 8.0 Hz), 6.77 (d, 2H, H-2, J = 8.6 Hz), 6.63 (d, 2H, H-3, J = 8.6 Hz), 6.37 (m, 2H, SiMB-3 and SiMB-5), 4.18 (s, 2H, SiMB-CH_2), 3.81 (s, 3H, OMe), 3.80 (br s, 1H, NH), 3.74 (s, 3H, OMe), 0.99 (s, 9H, ^{t}Bu), 0.20 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 156.2, 152.2, 143.0, 129.8, 120.5, 114.9, 114.6, 111.5, 103.6, 55.9, 55.5, 44.5, 25.8, 18.3, −4.2; ESIMS-LR m/z = 396 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{21}H_{31}O_3NNaSi$ 396.1971, found 396.1971.

***N*-(4-*tert*-Butyldimethylsiloxy-2-methoxybenzyl)-*p*-benzanisidide (13).** A solution of **12** (110 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was treated with benzoyl chloride (45 μL, 0.36 mmol) and Et_3N (0.10 mL, 0.72 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 10 min. The reaction was quenched with H_2O, and the mixture was extracted with AcOEt (30 mL). The organic layers were washed with 0.1 N aqueous HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 5 cm, hexane/AcOEt = 5/1) to give **13** (135 mg, 94%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (m, 2H, Bz), 7.23−7.10 (m, 4H, Bz and SiMB-6), 6.79 (d, 2H, H-2′, J = 8.0 Hz), 6.59 (d, 2H, H-3′, J = 8.0 Hz), 6.39 (dd, 1H, SiMB-5, J = 1.8, 8.0 Hz), 6.29 (d, 1H, SiMB-3, J = 1.8 Hz), 5.05 (s, 2H, SiMB-CH_2), 3.65 (s, 3H, OMe), 3.60 (s, 3H, OMe), 0.98 (s, 9H, ^{t}Bu), 0.19 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 158.3, 157.8, 156.1, 136.6, 130.4, 129.2, 129.1, 128.6, 128.3, 127.7, 18.5, 113.7, 111.6, 103.3, 55.2, 55.1, 48.0, 25.7, 18.3, −4.3; ESIMS-LR m/z = 500 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{28}H_{35}O_4NNaSi$ 500.2233, found 500.2235.

Table 1, Entry 1. A mixture of **13** (48 mg, 0.10 mmol) in THF (2 mL) was treated with TBAF (1.0 M solution in THF, 0.15 mL, 0.15 mmol) at room temperature for 24 h. The mixture was concentrated, and the residue was purified by silica gel column chromatography (1 × 5 cm, hexane/AcOEt = 1/1) to give *N*-(4-hydroxy-2-methoxybenzyl)-*p*-benzanisidide (**16**) (36.0 mg, 98%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (br s, 1H, HMB-4-OH), 7.30 (m, 2H, Bz), 7.20−7.15 (m, 4H, Bz and HMB-6), 6.81 (d, 1H, H-2′, J = 8.0 Hz), 6.60 (d, 2H, H-3′, J = 8.0 Hz), 6.33 (d, 1H, HMB-5, J = 7.4 Hz), 6.32 (d, 1H, HMB-3), 5.03 (s, 2H, HMB-CH_2), 3.68 (s, 3H, OMe), 3.51 (s, 3H, OMe); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 158.0, 157.3, 136.3, 130.5, 129.6, 129.0, 128.7, 127.9, 116.6, 113.9, 107.3, 99.0, 55.4, 55.2, 48.7; ESIMS-LR m/z = 386 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{22}H_{21}O_4NNa$ 386.1368, found 386.1360.

Table 1, Entry 2. A mixture of **13** (48 mg, 0.10 mmol) and TBAF (1.0 M solution in THF, 0.20 mL, 0.20 mmol) in THF (2 mL) was stirred at 150 °C under microwave irradiation for 10 min. The mixture was concentrated, and the residue was purified by silica gel column chromatography (1 × 6 cm, hexane/AcOEt = 4/1) to give **15** (22.0 mg, 0.097 mmol, 97%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (br s, 1H, CONH), 7.85 (d, 2H, Bz, J = 7.4 Hz), 7.53 (d, 2H, H-2′, J = 8.6 Hz), 7.51 (t, 1H, Bz, J = 7.4 Hz), 7.45 (t, 2H, Bz, J = 7.4 Hz), 6.88 (d, 2H, H-3′, J = 8.6 Hz), 3.80 (s, 3H, OMe); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 156.7, 135.1, 131.8, 131.1, 128.8, 127.1, 122.3, 114.3, 55.6. This is a known compound reported in the literature.[19]

Table 1, Entry 3. A mixture of **13** (48 mg, 0.10 mmol) and CsF (75 mg, 0.50 mmol) in 1,4-dioxane−H_2O (3:1 (v/v), 1 mL) was refluxed

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at 120 °C for 12 h. The mixture was partitioned between AcOEt (20 mL) and H_2O (10 mL). The organic layers were washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 6 cm, hexane/AcOEt = 4/1) to give **15** (21.0 mg, 93%) as a white solid.

Table 1, Entry 4. A mixture of **13** (48 mg, 0.10 mmol) and CsF (75 mg, 0.50 mmol) in 1,4-dioxane−H_2O (3:1 (v/v), 1 mL) was stirred at 150 °C under microwave irradiation for 20 min. The mixture was partitioned between AcOEt (20 mL) and H_2O (10 mL). The organic layers were washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 6 cm, hexane/AcOEt = 4/1) to give **15** (21.5 mg, 95%) as a white solid.

Table 1, Entry 5. A mixture of **13** (48 mg, 0.10 mmol) and K_2CO_3 (69 mg, 0.50 mmol) in MeOH (2 mL) was refluxed for 9 h. The residue was partitioned between AcOEt (20 mL) and H_2O (10 mL), and the organic layer was washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 7 cm, hexane/AcOEt = 4/1) to give **15** (20.5 mg, 90%) as a white solid.

Table 1, Entry 6. A mixture of **13** (48 mg, 0.10 mmol) and K_2CO_3 (69 mg, 0.50 mmol) in MeOH (2 mL) was stirred at 100 °C under microwave irradiation for 10 min. The residue was partitioned between AcOEt (20 mL) and H_2O (10 mL), and the organic layer was washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified by silica gel column chromatography (1 × 7 cm, hexane/AcOEt = 4/1) to give **15** (21.0 mg, 93%) as a white solid.

Table 1, Entry 7. Compound **13** (48 mg, 0.10 mmol) was treated with 80% aqueous TFA (1 mL) at room temperature for 30 min. The mixture was concentrated, and the residue was purified by silica gel column chromatography (1 × 6 cm, hexane/AcOEt = 4/1) to give **15** (19.0 mg, 84%) as a white solid.

Table 1, Entry 8. A solution of **13** (48 mg, 0.10 mmol) in CH_2Cl_2−H_2O (10:1 (v/v), 1 mL) was treated with DDQ (34 mg, 0.15 mmol) at room temperature for 30 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (2 mL), and the mixture was extracted with AcOEt (20 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (10 mL × 3) and brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 7 cm, hexane/AcOEt = 4/1) to give **15** (18.8 mg, 83%) as a white solid.

Table 1, Entry 9. A solution of **13** (36 mg, 0.10 mmol) in CH_2Cl_2−H_2O (10:1 (v/v), 1 mL) was treated with DDQ (34 mg, 0.15 mmol) at room temperature for 20 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (2 mL), and the mixture was extracted with AcOEt (20 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (10 mL × 3) and brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 7 cm, hexane/AcOEt = 4/1) to give **15** (21.5 mg, 95%) as a white solid.

Table 1, Entry 10. A solution of **13** (48 mg, 0.10 mmol) in MeCN−H_2O (3/1 (v/v), 2 mL) was treated with ceric ammonium nitrate (220 mg, 0.40 mmol) at room temeperature for 1 h. The mixture was partitioned between AcOEt (30 mL) and H_2O (20 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (20 mL × 2) and brine (20 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by preparative TLC (hexane/AcOEt = 2/1 × 2) to give **15** (6.5 mg, 29%) as a white solid.

4-*tert*-Butyldimethylsiloxybenzaldehyde (19). A solution of 4-hydroxybenzaldehyde (**17**) (5.0 g, 41 mmol) in DMF (50 mL) was treated with imidazole (7.2 g, 106 mmol) and TBSCl (8.0 g, 53 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O (20 mL) at 0 °C, and the mixture was extracted with AcOEt (200 mL). The organic layer was washed with H_2O (100 mL × 3), 0.1 N aqueous HCl (100 mL), saturated $NaHCO_3$ (100 mL), and brine (100 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (3 × 10 cm, hexane/AcOEt = 4/1) to give **19** (9.4 g, 98%) as a colorless syrup: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.89 (s, 1H, CHO), 7.78 (d, 2H, H-2, J = 8.6 Hz), 6.94 (d, 2H, H-3, J = 8.6 Hz), 0.99 (s, 9H, ^{t}Bu), 0.25 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.1, 161.6, 132.1, 130.5, 120.6, 25.7, 18.4, −4.2. This is a known compound reported in the literature.[20]

***N*-(4-*tert*-Butyldimethylsiloxybenzyl)-4-methoxyaniline (21).** A solution of *p*-anisidine (180 mg, 1.4 mmol), **19** (400 mg, 1.6 mmol), and AcOH (0.28 mL, 7.0 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 20 min. $NaBH(OAc)_3$ (590 mg, 2.8 mmol) was added to the solution at 0 °C, and the mixture was stirred at room temperature for 30 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL) at 0 °C, and the mixture was extracted with AcOEt (50 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (30 mL × 2) and brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 10 cm, hexane/AcOEt = 8/1) to give **21** (460 mg, 96%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, 2H, SiB-2, J = 8.6 Hz), 6.80 (d, 2H, SiB-3, J = 8.6 Hz), 6.78 (d, 2H, H-2, J = 9.2 Hz), 6.61 (d, 2H, H-3, J = 9.2 Hz), 4.19 (s, 2H, SiB-CH_2), 3.74 (s, 4H, OMe and NH), 0.99 (s, 9H, ^{t}Bu), 0.20 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 152.3, 142.7, 132.4, 128.9, 120.3, 115.0, 114.2, 56.0, 49.0, 25.8, 18.3, −4.3; ESIMS-LR m/z = 366 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{20}H_{29}O_2NNaSi$ 366.1865, found 366.1857.

***N*-(4-*tert*-Butyldimethylsiloxybenzyl)-*N*-(4-methoxyphenyl)-benzamide (23).** A solution of **21** (480 mg, 1.4 mmol) in CH_2Cl_2 (5 mL) was treated with benzoyl chloride (0.20 mL, 1.7 mmol) and Et_3N (0.47 mL, 3.4 mmol) at 0 °C, and the mixture was stirred at room temperature for 10 min. The reaction was quenched with H_2O (5 mL) at 0 °C, and the mixture was extracted with AcOEt (50 mL). The organic layers were washed with 0.1 N aqueous HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL × 2), and brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 10 cm, hexane/AcOEt = 5/1) to give **23** (620 mg, 99%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, 2H, SiB-2, J = 7.5 Hz), 7.21−7.13 (m, 5H, Bz), 6.75 (m, 4H, SiB-3 and H-2′), 6.62 (d, 2H, H-3′, J = 9.2 Hz), 5.00 (s, 2H, SiB-CH_2), 3.69 (s, 3H, OMe), 0.97 (s, 9H, ^{t}Bu), 0.18 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 158.0, 155.0, 136.4, 136.1, 130.5, 130.1, 129.4, 129.3, 128.7, 127.8, 120.1, 114.1, 55.3, 53.4, 25.8, 18.3, −4.3; ESIMS-LR m/z = 470 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{27}H_{33}O_3NNaSi$ 470.2122, found 470.2116.

4-*tert*-Butyldimethylsiloxy-2,6-dimethoxybenzaldehyde (20). A solution of 4-hydroxy-2,6-dimethoxybenzaldehyde (**18**) (730 mg, 4.0 mmol) in DMF (5 mL) was treated with imidazole (650 mg, 9.6 mmol) and TBSCl (730 mg, 4.8 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O (5 mL), and the mixture was extracted with AcOEt (50 mL). The organic layer was washed with H_2O (50 mL × 2) and brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 8 cm, hexane/AcOEt = 4/1) to give **20** (1.1 g, 94%) as a pale yellow syrup: ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.30 (s, 1H, CHO), 5.98 (s, 2H, H-3 and H-5), 3.81 (s, 6H, OMe × 2), 0.96 (s, 9H, ^{t}Bu), 0.22 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.0, 164.0, 163.3, 109.1, 96.2, 56.0, 25.6, 18.3, −4.2; ESIMS-LR m/z = 319 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{15}H_{24}O_4NaSi$ 319.1342, found 319.1334.

***N*-(4-*tert*-Butyldimethylsiloxy-2,6-dimethoxybenzyl)-4-methoxyaniline (22).** A mixture of **20** (360 mg, 1.2 mmol), *p*-anisidine (160 mg, 1.3 mmol), and AcOH (0.34 mL, 6.0 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 10 min. $NaBH(OAc)_3$ (380 mg, 1.8 mmol) was added to the mixture at 0 °C, and the resulting mixture was stirred at room temperature for 30 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL), and the mixture was extracted with AcOEt (50 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (30 mL) and brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 10 cm, hexane/AcOEt = 5/1) to give **22** (440 mg, 91%) as an yellow syrup: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (d, 2H, H-2, J = 8.6 Hz), 6.71 (d, 1H, H-3, J = 8.6 Hz), 6.05 (s, 2H, SiDMB-3 and SiDMB-5), 4.22 (s, 2H, SiDMB-CH_2), 3.78 (s, 6H, SiDMB-OMe × 2), 3.74 (s, 3H, OMe), 0.99 (s, 9H, ^{t}Bu), 0.21

(s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 156.6, 152.2, 143.4, 115.2, 114.7, 108.8, 96.6, 55.9, 55.8, 37.8, 25.8, 18.3, −4.2; ESIMS-LR m/z = 426 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{22}H_{33}O_4NNaSi$ 426.2077, found 426.2070.

***N*-(4-*tert*-Butyldimethylsiloxy-2,6-dimethoxybenzyl)-*N*-(4-methoxyphenyl)benzamide (24).** A solution of **22** (380 mg, 0.94 mmol) in CH_2Cl_2 (5 mL) was treated with benzoyl chloride (0.13 mL, 1.1 mmol) and Et_3N (0.31 mL, 2.2 mmol) at 0 °C for 10 min. The reaction was quenched with H_2O (5 mL), and the mixture was extracted with AcOEt (50 mL). The organic layers were washed with 0.1 N aqueous HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL), and brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 10 cm, hexane/AcOEt = 4/1) to give **24** (470 mg, 98%) as a pale yellow syrup: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (br s, 2H, Bz), 7.13 (br s, 3H, Bz), 6.65 (br s, 2H, H-2′), 6.47 (br s, 2H, H-3′), 5.89 (s, 2H, SiDMB-3 and SiDMB-5), 5.09 (s, 2H, SiDMB-CH_2), 3.63 (s, 3H, OMe), 3.61 (s, 6H, OMe × 2), 0.95 (s, 9H, ^{t}Bu), 0.15 (s, 6H, Me × 2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 157.8, 157.0, 137.6, 130.1, 128.8, 128.4, 127.6, 113.0, 106.3, 96.4, 55.6, 55.2, 25.8, 18.4, −4.3; ESIMS-LR m/z = 530 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{29}H_{37}O_5NNa$ 530.2339, found 530.2324.

***N*-(4-*tert*-Butyldimethylsiloxy-2-methoxybenzyl)-*N*-(4-methoxyphenyl)-*tert*-butoxycarbonylaminoacetamide (14a).** A mixture of **12** (80 mg, 0.20 mmol), *N*-Boc-glycine (46 mg, 0.26 mmol), and DMAP (1 mg) in CH_2Cl_2 (2 mL) was treated with EDCI (77 mg, 0.40 mmol) at room temperature for 10 min. The reaction was quenched with H_2O, and the mixture was extracted with AcOEt (30 mL). The organic layers were washed with 0.1 N aqueous HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 8 cm, hexane/AcOEt = 3/1) to give **14a** (100 mg, 95%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (d, 1H, SiMB-6, J = 8.0 Hz), 6.83 (d, 2H, H-2′, J = 8.6 Hz), 6.73 (d, 2H, H-3′, J = 8.6 Hz), 6.31 (dd, 1H, SiMB-5, J = 2.3, 8.0 Hz), 6.23 (d, 1H, SiMB-3, J = 2.3 Hz), 5.48 (br s, 1H, BocNH), 4.81 (s, 2H, SiMB-CH_2), 4.73 (s, 3H, OMe), 3.56 (d, 2H, C(O)CH_2, J = 4.6 Hz), 3.51 (s, 3H, OMe), 1.38 (s, 9H, ^{t}Bu), 0.94 (s, 9H, ^{t}Bu), 0.15 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 159.2, 158.5, 156.4, 155.8, 132.9, 131.2, 129.5, 117.8, 114.6, 111.6, 103.3, 79.4, 55.4, 55.1, 47.3, 43.3, 28.4, 25.7, 18.3, −4.3; ESIMS-LR m/z = 553 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{28}H_{42}O_6N_2NaSi$ 553.2710, found 553.2705.

***N*-(4-*tert*-Butyldimethylsiloxy-2-methoxybenzyl)-*N*-(4-methoxyphenyl)-9-fluorenylmethyloxycarbonylaminoacetamide (14b).** A mixture of **12** (80 mg, 0.20 mmol), *N*-Fmoc-glycine (77 mg, 0.26 mmol), and DMAP (1 mg) in CH_2Cl_2 (2 mL) was treated with EDCI (77 mg, 0.40 mmol) at room temperature for 30 min. The reaction was quenched with H_2O, and the mixture was extracted with AcOEt (30 mL). The organic layers were washed with 0.1 N aqueous HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 7 cm, hexane/AcOEt = 3/1) to give **14b** (130 mg, quant) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, 2H, Fmoc-aromatic, J = 7.4 Hz), 7.62 (d, 2H, Fmoc-aromatic, J = 7.4 Hz), 7.39 (t, 2H, Fmoc-aromatic, J = 7.4 Hz), 7.31 (t, 2H, Fmoc-aromatic, J = 7.4 Hz), 7.05 (d, 1H, SiMB-6, J = 8.0 Hz), 6.88 (d, 2H, H-2′, J = 8.6 Hz), 6.78 (d, 2H, H-3′, J = 8.6 Hz), 6.37 (d, 1H, SiMB-5, J = 8.0 Hz), 6.29 (s, 1H, SiMB-3), 5.91 (br s, 1H, FmocNH), 4.88 (s, 2H, SiMB-CH_2), 4.34 (d, 2H, Fmoc-CH_2, J = 7.5 Hz), 4.22 (t, 1H, Fmoc-9, J = 7.5 Hz), 3.76 (s, 3H, OMe), 3.70 (d, 2H, C(O)CH_2, J = 4.0 Hz), 3.56 (s, 3H, OMe), 0.99 (s, 9H, ^{t}Bu), 0.21 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 159.3, 158.5, 156.5, 156.2, 144.0, 141.3, 132.7, 131.3, 129.5, 127.7, 127.1, 125.2, 120.0, 117.7, 114.6, 111.7, 103.4, 67.0, 55.4, 55.2, 47.4, 47.1, 43.6, 25.7, 18.3, −4.3; ESIMS-LR m/z = 675 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{38}H_{44}O_6N_2NaSi$ 675.2866, found 675.2850.

***O*$^\alpha$-Benzoyl-*N*-(4-*tert*-butyldimethylsiloxy-2-methoxybenzyl)-*N*-(4-methoxyphenyl)glycolamide (14c).** A mixture of **12** (150 mg, 0.40 mmol), O^α-benzoylglycolic acid[21] (95 mg, 0.52 mmol), and DMAP (1 mg) in CH_2Cl_2 (4 mL) was treated with EDCI (150 mg, 0.80 mmol) at room temperature for 10 min. The reaction was quenched with H_2O (10 mL), and the mixture was partitioned between AcOEt (50 mL) and H_2O (30 mL). The organic layers were washed with 1 N aqueous HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL), and brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 6 cm, hexane/AcOEt = 4/1) to give **14c** (210 mg, 99%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, 2H, Bz, J = 6.9 Hz), 7.53 (t, 1H, Bz, J = 7.5 Hz), 7.41 (t, 2H, Bz, J = 7.5 Hz), 7.09 (d, 1H, SiMB-6, J = 8.0 Hz), 6.97 (d, 2H, H-2′, J = 8.5 Hz), 6.79 (d, 2H, H-3′, J = 8.5 Hz), 6.35 (dd, 1H, SiMB-5, J = 2.3, 8.0 Hz), 6.25 (d, 1H, SiMB-3, J = 2.3 Hz), 4.87 (s, 2H, SiMB-CH_2), 4.58 (s, 2H, C(O)CH_2), 0.97 (s, 9H, ^{t}Bu), 0.18 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 166.3, 159.3, 158.6, 156.4, 133.1, 132.8, 131.4, 130.0, 129.7, 129.6, 128.3, 117.9, 114.5, 111.7, 103.3, 62.4, 55.4, 55.1, 47.2, 25.7, 18.3, −4.3; ESIMS-LR m/z = 558 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{30}H_{37}O_6NNaSi$ 558.2288, found 558.2279.

***O*$^\alpha$-(4-Methoxybenzyl)-*N*-(4-*tert*-butyldimethylsiloxy-2-methoxybenzyl)-*N*-(4-methoxyphenyl)glycolamide (14d).** A mixture of **12** (190 mg, 0.50 mmol), O^α-*p*-methoxybenzylglycolic acid[22] (120 mg, 0.60 mmol), and DMAP (1 mg) in CH_2Cl_2 (5 mL) was treated with EDCI (192 mg, 1.0 mmol) at room temperature for 20 min. The reaction was quenched with H_2O (10 mL), and the mixture was partitioned between AcOEt (50 mL) and H_2O (30 mL). The organic layers were washed with 1 N aqueous HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL), and brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 7 cm, hexane/AcOEt = 5/2) to give **14d** (260 mg, 94%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, 2H, PMB-2, J = 8.6 Hz), 7.06 (d, 1H, SiMB-6, J = 8.6 Hz), 6.81 (d, 2H, PMB-3, J = 8.6 Hz), 6.79 (d, 2H, H-2′, J = 9.1 Hz), 6.71 (d, 2H, H-3′, J = 9.1 Hz), 6.33 (dd, 1H, SiMB-5, J = 2.3, 8.6 Hz), 6.23 (d, 1H, SiMB-3, J = 2.3 Hz), 4.84 (s, 2H, benzyl-CH_2), 4.50 (s, 2H, benzyl-CH_2), 3.80 (s, 2H, C(O)CH_2), 3.77 (s, 3H, OMe), 3.74 (s, 3H, OMe), 3.51 (s, 3H, OMe), 0.96 (s, 9H, ^{t}Bu), 0.17 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 159.3, 159.0, 158.5, 156.3, 133.3, 131.3, 129.8, 129.7, 129.5, 118.2, 114.2, 113.7, 111.7, 103.3, 72.7, 67.9, 55.4, 55.3, 55.2, 46.8, 25.8, 18.3, −4.3; ESIMS-LR m/z = 574 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{31}H_{41}O_6NNaSi$ 574.2601, found 574.2596.

Table 3. General Procedure for the Removal of the SiMB Group under Basic Conditions Using a Microwave Reactor (Method A). A mixture of the substrate (0.10 mmol) and CsF (75 mg, 0.50 mmol, 5 equiv) in 1,4-dioxane−H_2O (3:1 (v/v), 1 mL) was stirred at 150 °C under microwave irradiation until the reaction was complete (checked by TLC). The mixture was partitioned between AcOEt and H_2O. The organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography, eluting with hexane/AcOEt mixtures, to afford the corresponding carboxamides.

General Procedure for the Removal of the SiMB Group under Acidic Conditions (Method B). The substrate (0.10 mmol) was treated with 80% aqueous TFA (1 mL) at room temperature until the reaction was complete (checked by TLC). The mixture was concentrated, and the residue was purified by silica gel column chromatography, eluting with hexane/AcOEt mixtures, to afford the corresponding carboxamides.

General Procedure for the Removal of the SiMB Group under Oxidative Conditions (Method C). A solution of the substrate (0.10 mmol) in CH_2Cl_2−H_2O (10:1 (v/v), 1 mL) was treated with DDQ (34 mg, 0.15 mmol, 1.5 equiv) at room temperature until the reaction was complete (checked by TLC). The reaction was quenched with saturated aqueous $NaHCO_3$, and the mixture was extracted with AcOEt. The organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography, eluting with hexane/AcOEt mixtures, to afford the corresponding carboxamides.

2-[*N*-Benzoyl-*N*-(2,4-dimethoxybenzyl)]aminoacetic Acid (31). A mixture of **30** (960 mg, 2.3 mmol) and 10% Pd/C (290 mg) in MeOH (30 mL) was vigorously stirred under H_2 atmosphere at

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room temperature for 1 h. The insoluble was filtered off through a Celite pad, and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (2 × 6 cm, 10% MeOH in $CHCl_3$) to give **31** (690 mg, 91%) as a colorless syrup: ^{1}H NMR (500 MHz, $CDCl_3$, 20 °C, 4:1 mixture of rotamers, data for major rotamer) δ 7.53 (d, 2H, Bz, J = 6.9 Hz), 7.40 (m, 3H, Bz), 6.99 (d, 1H, DMB-6, J = 8.0 Hz), 6.44 (d, 1H, DMB-5, J = 8.0 Hz), 6.41 (s, 1H, DMB-3), 4.52 (s, 2H, DMB-CH_2), 4.17 (s, 2H, CH_2), 3.79 (s, 3H, OMe), 3.71 (s, 3H, OMe); ^{13}C NMR (125 MHz, $CDCl_3$, 20 °C, 4:1 mixture of rotamers, observed peaks were described) δ 173.7, 173.5, 161.1, 158.7, 135.4, 130.2, 129.9, 128.7, 128.5, 127.4, 126.7, 116.0, 104.2, 98.7, 55.5, 55.2, 49.7, 46.8; ESIMS-LR (negative) m/z = 328 [(M − H)$^-$]; ESIMS-HR calcd for $C_{18}H_{18}O_5N$ 328.1185, found 328.1198.

2-[*N*-[2-[*N*-Benzoyl-*N*-(2,4-dimethoxybenzyl)]aminoacetyl]-*N*-[4-*tert*-butyldimethylsiloxy-2-methoxybenzyl]]amino-*N*-(4-methoxyphenyl)acetamide (32). A mixture of **28** (430 mg, 2.0 mmol) and **11** (550 mg, 2.1 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 20 min. $NaBH(OAc)_3$ (640 mg, 3.0 mmol) was added to the mixture at 0 °C, and the resulting mixture was stirred at room temperature for 30 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (30 mL), and the mixture was extracted with AcOEt (100 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (60 mL), dried (Na_2SO_4), filtered, and concentrated to give a crude *N*-SiMB amine **29**. Compound **29** was dissolved in CH_2Cl_2 (20 mL), and the solution was treated with **31** (660 mg, 2.0 mmol), DMAP (24 mg, 0.20 mmol), and EDCI (580 mg, 3.0 mmol) at room temperature for 1 h. The reaction was quenched with H_2O (20 mL), and the mixture was extracted with AcOEt (150 mL). The organic layers were washed with 0.1 N aqueous HCl (100 mL × 2), saturated aqueous $NaHCO_3$ (100 mL × 2), and brine (100 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 14 cm, hexane/AcOEt = 2/1) to give **32** (1.1 g, 74% over two steps) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$, 20 °C, 7.1:1.6:1 mixture of rotamers, data for major rotamer) δ 8.51 (br s, 1H, CONH), 7.53 (m, 4H, H-2′and Bz), 7.40 (m, 3H, Bz), 7.19 (d, 1H, SiMB-6, J = 8.6 Hz), 6.99 (d, 1H, DMB-6, J = 8.9 Hz), 6.77 (d, 2H, H-3′, J = 9.1 Hz), 6.48 (dd, 1H, SiMB-5, J = 2.3, 8.6 Hz), 6.42 (d, 1H, SiMB-3, J = 2.3 Hz), 6.38 (dd, 1H, DMB-5, J = 2.3, 8.9 Hz), 6.30 (d, 1H, DMB-3, J = 2.3 Hz), 4.65 (s, 2H, SiMB-CH_2), 4.58 (s, 2H, DMB-CH_2), 4.31 (s, 2H, CH_2), 4.16 (s, 2H, CH_2), 3.80 (s, 3H, OMe), 3.75 (s, 3H, OMe), 3.70 (s, 3H, OMe), 3.67 (s, 3H, OMe), 0.96 (s, 9H, ^{t}Bu), 0.17 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$, 20 °C, 7.1:1.6:1 mixture of rotamers, observed peaks were described) δ 173.4, 172.8, 170.1, 168.5, 166.8, 160.7, 158.8, 158.6, 158.5, 157.3, 157.0, 156.4, 156.1, 135.6, 131.9, 131.6, 131.1, 130.2, 130.1, 130.0, 129.7, 129.5, 129.4, 129.2, 128.6, 128.4, 127.3, 126.7, 122.0, 121.6, 121.5, 117.1, 116.8, 116.7, 116.0, 114.2, 113.9, 113.8, 111.9, 111.7, 104.1, 103.6, 103.4, 98.7, 55.5, 55.2, 52.0, 50.7, 50.4, 50.3, 49.7, 48.4, 47.0, 46.5, 45.4, 25.7, 18.3, −4.3; ESIMS-LR m/z = 764 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{41}H_{51}O_8N_3NaSi$ 764.3343, found 764.3344.

2-[*N*-[2-[*N*-Benzoyl-*N*-(2,4-dimethoxybenzyl)]aminoacetyl]]-amino-*N*-(4-methoxyphenyl)acetamide (33). A mixture of **32** (74 mg, 0.10 mmol) and CsF (75 mg, 0.50 mmol) in 1,4-dioxane−H_2O (3/1 (v/v), 2 mL) was stirred at 150 °C under microwave irradiation for 30 min. The mixture was extracted with AcOEt (30 mL), and the organic layers were washed with H_2O (20 mL) and brine (20 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 10 cm, 2% MeOH in $CHCl_3$) to give **33** (47 mg, 96%) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.88 (br s, 1H, CONH), 7.50 (m, 4H, H-2′and Bz), 7.39 (m, 3H, Bz), 7.29 (br s, 1H, CONH), 7.03 (d, 1H, DMB-6, J = 8.6 Hz), 6.73 (d, 2H, H-3′, J = 9.2 Hz), 6.40 (dd, 1H, DMB-5, J = 2.3, 8.6 Hz), 6.38 (d, 1H, DMB-3, J = 2.3 Hz), 4.58 (s, 2H, DMB-CH_2), 4.03 (s, 2H, CH_2), 3.98 (d, 2H, CH_2, J = 5.7 Hz), 3.74 (s, 3H, OMe), 3.72 (s, 3H, OMe), 3.67 (s, 3H, OMe); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 169.6, 167.0, 161.1, 158.6, 156.2, 135.2, 131.2, 130.3, 128.5, 127.3, 121.6, 115.9, 114.0, 104.3, 98.7, 55.4, 55.3, 55.1, 50.7, 49.7, 43.8; ESIMS-LR m/z = 514 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{27}H_{29}O_6N_3Na$ 514.1954, found 514.1952.

2-[*N*-[2-(*N*-Benzoyl)aminoacetyl]]amino-*N*-(4-methoxyphenyl)acetamide (34). From 32. Compound **32** (74 mg, 0.10 mmol) was treated with 80% aqueous TFA (2 mL) at room temperature for 4 h. The mixture was concentrated in vacuo, and the residue was triturated with $CHCl_3$−MeOH to give **34** (30 mg, 88%) as a white solid. **From 36.** A mixture of **36** (26 mg, 0.050 mmol) and CsF (38 mg, 0.25 mmol) in 1,4-dioxane−H_2O (3/1 (v/v), 1 mL) was stirred at 150 °C under microwave irradiation for 1 h. The mixture was concentrated and the residue was purified by silica gel column chromatography (1 × 9) cm, 6% MeOH in $CHCl_3$) to give **34** (16 mg, 88%) as a white solid: ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.62 (s, 1H, CONH), 8.92 (t, 1H, CONH, J = 5.7 Hz), 8.33 (t, 1H, CONH, J = 5.7 Hz), 7.90 (d, 2H, Bz, J = 7.5 Hz), 7.53 (d, 2H, H-2′, J = 8.6 Hz), 7.48 (m, 3H, Bz), 6.88 (d, 2H, H-3′, J = 8.6 Hz), 3.92 (d, 2H, CH_2, J = 5.7 Hz), 3.86 (d, 2H, CH_2, J = 5.7 Hz), 3.71 (s, 3H, OMe); ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.5, 167.1, 166.9, 155.2, 133.8, 131.9, 131.5, 128.3, 127.4, 120.7, 113.9, 55.2, 43.0, 42.6; ESIMS-LR m/z = 364 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{18}H_{19}O_4N_3Na$ 364.1273, found 364.1272.

2-[*N*-[2-[*N*-Benzoyl-*N*-(2,4-dimethoxybenzyl)]aminoacetyl]-*N*-[4-hydroxy-2-methoxybenzyl]]amino-*N*-(4-methoxyphenyl)-acetamide. A solution of **32** (150 mg, 0.20 mmol) in THF (3 mL) was treated with TBAF (1.0 M solution in THF, 0.24 mL, 0.24 mmol) at room temperature for 10 min. The mixture was concentrated, and the residue was purified by silica gel column chromatography (1 × 7 cm, 2% MeOH in $CHCl_3$) to give the titled compound (125 mg, 99%) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$, 20 °C, 8.3:1.9:1 mixture of rotamers, data for major rotamer) δ 8.62 (br s, 1H, CONH), 8.18 (br s, 1H, HMB-4-OH), 7.55 (d, 2H, Bz, J = 6.9 Hz), 7.45 (d, 2H, H-2′, J = 9.2 Hz), 7.40 (m, 3H, Bz), 7.14 (d, 1H, HMB-6, J = 8.0 Hz), 6.87 (d, 1H, DMB-6, J = 8.0 Hz), 6.75 (d, 2H, H-3′, J = 9.2 Hz), 6.47 (dd, 1H, HMB-5, J = 2.3, 8.0 Hz), 6.42 (d, 1H, HMB-3, J = 2.3 Hz), 6.30 (m, 2H, DMB-3 and DMB-5), 4.63 (s, 2H, benzyl-CH_2), 4.48 (s, 2H, benzyl-CH_2), 4.38 (s, 2H, CH_2), 4.13 (s, 2H, CH_2), 3.83 (s, 3H, OMe), 3.76 (s, 3H, OMe), 3.69 (s, 3H, OMe), 3.56 (s, 3H, OMe); ^{13}C NMR (125 MHz, $CDCl_3$, 20 °C, 8.3:1.9:1 mixture of rotamers, observed peaks were described) δ 173.7, 169.9, 167.5, 160.9, 158.8, 158.7, 158.6, 156.4, 135.5, 131.1, 130.7, 130.2, 129.5, 128.5, 127.4, 127.3, 122.2, 122.0, 116.7, 114.0, 113.7, 107.4, 104.2, 99.4, 98.8, 55.5, 55.3, 55.2, 50.3, 50.0, 48.2, 46.6; ESIMS-LR m/z = 650 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{35}H_{37}O_8N_3Na$ 650.2478, found 650.2479.

2-[*N*-]2-[*N*-Benzoyl-*N*-(2,4-dimethoxybenzyl)]aminoacetyl]-*N*-[4-acetoxy-2-methoxybenzyl (AcMB)]]amino-*N*-(4-methoxyphenyl)acetamide (35). A solution of 2-[*N*-]2-[*N*-benzoyl-*N*-(2,4-dimethoxybenzyl)]aminoacetyl]-*N*-[4-hydroxy-2-methoxybenzyl]]amino-*N*-(4-methoxyphenyl)acetamide (120 mg, 0.19 mmol), DMAP (2.3 mg, 0.019 mmol), and Et_3N (64 mL, 0.46 mmol) in MeCN (3 mL) was treated with Ac_2O (22 mL, 0.23 mmol) at 0 °C, and the mixture was stirred at the same temperature for 10 min. The reaction was quenched with H_2O (5 mL), and the mixture was extracted with AcOEt (30 mL). The organic layers were washed with 0.1 N aqueous HCl (15 mL), saturated aqueous $NaHCO_3$ (15 mL), and brine (15 mL), dried (Na_2SO_4), filtered, and concentrated to give **35** (120 mg, 94%) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$, 20 °C, 6.7:2:1 mixture of rotamers, data for major rotamer) δ 8.65 (br s, 1H, CONH), 7.53 (m, 5H, H-2′and Bz), 7.38 (m, 3H, AcMB-6 and Bz), 7.16 (d, 1H, DMB-6, J = 8.6 Hz), 6.76 (d, 2H, H-3′, J = 9.2 Hz), 6.65 (dd, 1H, AcMB-5, J = 2.3, 8.0 Hz), 6.58 (d, 1H, AcMB-3, J = 2.3 Hz), 6.47 (dd, 1H, DMB-5, J = 2.3, 8.6 Hz), 6.42 (d, 1H, DMB-3, J = 2.3 Hz), 4.66 (s, 2H, DMB-CH_2), 4.64 (s, 2H, AcMB-CH_2), 4.23 (s, 2H, CH_2), 4.16 (s, 2H, CH_2), 3.78 (s, 3H, OMe), 3.74 (s, 3H, OMe), 3.72 (s, 3H, OMe), 3.68 (s, 3H, OMe), 2.27 (s, 3H, Ac); ^{13}C NMR (125 MHz, $CDCl_3$, 20 °C, 6.7:2:1 mixture of rotamers, observed peaks were described) δ 173.3, 172.8, 170.2, 169.3, 168.6, 166.7, 166.1, 160.7, 158.5, 158.4, 158.0, 156.3, 156.1, 151.7, 151.4, 135.5, 131.5, 131.0, 130.1, 130.0, 129.5, 129.3, 129.2, 128.7, 128.6, 128.4, 128.3, 127.3, 127.2, 126.6, 122.0, 121.9, 121.6, 121.5, 121.0, 116.6, 114.1, 13.9, 113.6, 113.5, 104.9, 104.6, 104.1, 98.7, 98.5, 55.6, 55.4, 55.2, 52.1,

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50.7, 50.3, 50.2, 48.2, 46.7, 46.3, 45.3, 25.7, 21.2; ESIMS-LR m/z = 692 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{37}H_{39}O_9N_3Na$ 692.2584, found 692.2583.

2-[*N*-(2-*N*-Benzoylaminoacetyl)-*N*-(4-acetoxy-2-methoxybenzyl)]amino-*N*-(4-methoxyphenyl)acetamide (36). **(a) Acidic Conditions.** Compound **35** (67 mg, 0.10 mmol) was treated with 80% aqueous TFA at room temperature for 30 min. The mixture was concentrated in vacuo, and the residue was purified by silica gel column chromatography (1 × 8 cm, 1% MeOH in $CHCl_3$) to give **36** (44 mg, 85%) as a white foam. **(b) Oxidative Conditions.** A mixture of **35** (67 mg, 0.10 mmol) and DDQ (34 mg, 0.15 mmol) in CH_2Cl_2−H_2O (10:1 (v/v), 1 mL) was stirred at room temperature for 48 h. The mixture was diluted with AcOEt (20 mL), and the organic layers were washed wih saturated aqueous $NaHCO_3$ (20 mL × 3) and brine (20 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (1 × 7 cm, 2% MeOH in $CHCl_3$) to give **36** (36 mg, 70%) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$, 20 °C, 3.4:1 mixture of rotamers, data for major rotamer) δ 8.25 (br s, 1H, CONH), 7.80 (d, 2H, Bz, J = 7.5 Hz), 7.46 (t, 1H, CONH, J = 4.0 Hz), 7.38 (d, 2H, H-2′, J = 8.6 Hz), 7.35 (m, 3H, Bz), 7.15 (d, 1H, AcMB-6, J = 8.0 Hz), 6.78 (d, 2H, H-3′, J = 8.6 Hz), 6.69 (dd, 1H, AcMB-5, J = 2.3, 8.0 Hz), 6.62 (d, 1H, AcMB-3, J = 2.3 Hz), 4.63 (s, 2H, AcMB-CH_2), 4.45 (d, 2H, C(O)CH_2, J = 4.0 Hz), 4.11 (s, 2H, C(O)CH_2), 3.79 (s, 3H, OMe), 3.74 (s, 3H, OMe), 2.30 (s, 3H, Ac); ^{13}C NMR (125 MHz, $CDCl_3$, 20 °C, 3.2:1 mixture of rotamers, observed peaks were described) δ 170.6, 169.6, 169.5, 169.4, 167.8, 166.4, 165.9, 158.4, 158.3, 156.4, 151.9, 151.4, 133.5, 131.8, 131.1, 130.9, 130.7, 129.6, 128.6, 127.2, 122.1, 121.8, 121.7, 114.0, 113.7, 105.1, 104.7, 55.7, 55.5, 50.8, 50.3, 47.9, 45.8, 42.0, 41.7, 29.8, 21.2; ESIMS-LR m/z = 542 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{28}H_{29}O_7N_3Na$ 542.1903, found 542.1902.

***N*-(4-*tert*-Butyldimethylsiloxy-2-methoxybenzyl)-3-allyl-4-methoxy-2,5-dimethoxymethoxyaniline.** A mixture of **37** (2.1 g, 7.4 mmol), **11** (2.1 g, 8.1 mmol), and AcOH (2.1 mL, 37 mmol) in CH_2Cl_2 (50 mL) was stirred at room temperature for 10 min. The mixture was treated with $NaBH(OAc)_3$ (6.4 g, 30 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 20 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (100 mL), and the mixture was extracted with AcOEt (250 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (200 mL) and brine (200 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 20 cm, hexane/AcOEt = 10/1) to give the titled compound (3.6 g, 92%) as a red oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (d, 1H, SiMB-6, J = 8.6 Hz), 6.48 (s, 1H, H-6), 6.40 (m, 2H, SiMB-3 and SiMB-5), 6.00 (ddt, 1H, H-2′, J = 6.3, 9.2, 16.7 Hz), 5.15 (s, 2H, MOM-CH_2), 5.02 (dd, 1H, H-3′-*trans*, J = 1.7, 16.7 Hz), 5.00 (dd, 1H, H-3′-*cis*, J = 1.7, 9.2 Hz), 4.89 (s, 2H, MOM-CH_2), 4.73 (br s, 1H, NH), 4.22 (s, 2H, SiMB-CH_2), 3.81 (s, 3H, OMe), 3.76 (s, 3H, OMe), 3.52 (s, 3H, OMe), 3.50 (s, 3H, OMe), 3.42 (d, 2H, H-1′, J = 6.3 Hz), 1.00 (s, 9H, ^{t}Bu), 0.22 (s, 6H, Me × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.3, 156.0, 147.6, 138.9, 138.8, 137.9, 137.6, 129.7, 127.2, 120.3, 114.8, 111.4, 103.4, 99.8, 99.7, 95.8, 61.2, 57.3, 56.1, 55.3, 43.0, 29.3, 25.7, 18.3, −4.3; ESIMS-LR m/z = 556 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{28}H_{43}O_7NNaSi$ 556.2706, found 556.2707.

***N*-(3-Allyl-4-methoxy-2,5-dimethoxymethoxyphenyl)-*N*-(4-*tert*-butyldimethylsiloxy-2-methoxybenzyl)bromoacetamide.** A solution of *N*-(4-*tert*-butyldimethylsiloxy-2-methoxybenzyl)-3-allyl-4-methoxy-2,5-dimethoxymethoxyaniline (2.0 g, 3.7 mmol) in CH_2Cl_2 (20 mL) was treated with bromoacetyl chloride (0.37 mL, 4.5 mmol) and Et_3N (1.3 mL, 8.9 mmol) at 0 °C, and the mixture was stirred at room temperature for 20 min. The reaction was quenched with H_2O (10 mL), and the mixture was extracted with AcOEt (80 mL). The organic layers were washed with 0.1 N aqueous HCl (40 mL), saturated aqueous $NaHCO_3$ (40 mL), and brine (40 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 15 cm, hexane/AcOEt = 5/1) to give the titled compound (2.3 g, 95%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, 1H, SiMB-6, J = 8.0 Hz), 6.58 (s, 1H, H-6), 6.27 (dd, 1H, SiMB-5, J = 2.3, 8.0 Hz), 6.19 (d, 1H, SiMB-3, J = 2.3 Hz), 5.94 (ddt, 1H, H-2′, J = 5.7, 10.3, 17.1 Hz), 5.45 (d, 1H, SiMB-CH_2, J = 13.7 Hz), 4.99 (dd, 1H, H-3′-*cis*, J = 1.7, 10.3 Hz), 4.97 (d, 1H, MOM-CH_2, J = 6.9 Hz), 4.89 (dd, 1H, H-3′-*trans*, J = 1.7, 17.1 Hz), 4.86 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.85 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.80 (d, 1H, MOM-CH_2, J = 6.9 Hz), 4.24 (d, 1H, SiMB-CH_2, J = 13.7 Hz), 3.77 (s, 3H, OMe), 3.76 (d, 1H, $BrCH_2$, J = 11.4 Hz), 3.70 (d, 1H, $BrCH_2$, J = 11.4 Hz), 3.53 (s, 3H, OMe), 3.46 (s, 3H, OMe), 3.41 (dd, 1H, H-1′, J = 5.7, 14.9 Hz), 3.35 (dd, 1H, H-1′, J = 5.7, 14.9 Hz), 3.34 (s, 3H, OMe), 0.92 (s, 9H, ^{t}Bu), 0.13 (s, 3H, Me), 0.12 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 158.6, 156.5, 148.7, 147.5, 146.5, 136.6, 131.5, 130.0, 128.2, 117.7, 116.1, 115.3, 111.4, 103.0, 100.2, 95.4, 61.0, 57.4, 56.0, 55.0, 46.3, 29.3, 28.8, 25.7, 18.2, −4.4; ESIMS-LR m/z = 676 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{30}H_{44}O_8BrNNaSi$ 676.1917, found 676.1912.

***N*-(3-Allyl-4-methoxy-2,5-bis-methoxymethoxyphenyl)-*N*-(4-*tert*-butyldimethylsiloxy-2-methoxybenzyl)-diethylphosphonoacetamide (38).** A mixture of *N*-(3-allyl-4-methoxy-2,5-dimethoxymethoxyphenyl)-*N*-(4-*tert*-butyldimethylsiloxy-2-methoxybenzyl)bromoacetamide (1.8 g, 2.8 mmol) and triethyl phosphite (15 mL) was stirred at 100 °C for 4 h. The mixture was concentrated, and the residue was purified by silica gel column chromatography (2 × 5 cm, hexane/AcOEt = 1/1) to give **38** (1.9 g, 95%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$, 20 °C, 99:1 mixture of rotamers) δ 7.10 (d, 1H, SiMB-6, J = 8.6 Hz), 6.67 (s, 1H, H-6), 6.25 (dd, 1H, SiMB-5, J = 2.3, 8.6 Hz), 6.14 (d, 1H, SiMB-3, J = 2.3 Hz), 5.89 (ddt, 1H, H-2′, J = 5.8, 10.3, 17.5 Hz), 5.39 (d, 1H, SiMB-CH_2, J = 14.5 Hz), 4.97 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.94 (dd, 1H, H-3′-*cis*, J = 1.7, 10.3 Hz), 4.86 (dd, 1H, H-3′-*trans*, J = 1.7, 17.5 Hz), 4.85 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.80 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.76 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.22 (d, 1H, SiMB-CH_2, J = 14.5 Hz), 4.04 (m, 4H, OCH_2 × 2), 3.73 (s, H, OMe), 3.48 (s, 3H, OMe), 3.44 (s, 3H, OMe), 3.37 (dd, 1H, H-1′, J = 5.8, 14.9 Hz), 3.30 (dd, 1H, H-1′, J = 5.8, 14.9 Hz), 3.29 (s, 3H, OMe), 2.91 (dd, 1H, C(O)CH_2, J = 15.4, 19.4 Hz), 2.77 (dd, 1H, C(O)CH_2, J = 14.9, 22.9 Hz), 1.24 (m, 6H, Me × 2), 0.88 (s, 9H, ^{t}Bu), 0.09 (s, 3H, Me), 0.08 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 158.5, 156.3, 148.6, 147.2, 146.7, 136.8, 131.1, 1310, 128.3, 118.0, 116.6, 115.3, 111.4, 103.0, 100.2, 95.5, 62.7, 62.6, 62.2, 61.0, 57.5, 56.2, 55.1, 46.0, 34.2, 33.1, 29.4, 25.8, 18.3, 16.6, 16.5, 16.4, −4.4; ^{31}P NMR (202 MHz, $CDCl_3$) δ 23.1; ESIMS-LR m/z = 734 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{34}H_{54}O_{11}NNaPSi$ 734.3101, found 734.3095.

***N*-(3-Allyl-4-methoxy-2,5-bis-methoxymethoxyphenyl)-*N*-(4-*tert*-butyldimethylsiloxy-2-methoxybenzyl) (*E*)-3-*O*-Allyl-1-(6-amino-*N*^{6}-trityl-9*H*-purin-9-yl)-2-*O*-*tert*-butyldimethylsilyl-5,6-dideoxy-*β*-D-*ribo*-5-eneheptofuranuronamide (41a).** A solution of **39a** (500 mg, 0.75 mmol) in CH_2Cl_2 (5 mL) was treated with Dess−Martin periodinane (470 mg, 1.1 mmol) at 0 °C for 1 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL) and saturated aqueous $NaHCO_3$ (10 mL), and the mixture was stirred at 0 °C for 15 min. The mixture was extracted with AcOEt (40 mL), and the organic layers were washed with saturated aqueous $NaHCO_3$ (20 mL × 2) and brine (20 mL), dried (Na_2SO_4), filtered, and concentrated to give crude aldehyde **40a** as a white foam. Compound **40a** (500 mg, 0.75 mmol) was added to a mixture of **38** (530 mg, 0.75 mmol), $Zn(OTf)_2$ (330 mg, 0.90 mmol), Et_3N (0.42 mL, 3.0 mmol), and TMEDA (0.14 mL, 0.90 mmol) in THF (7 mL) at room temperature, and the resulting mixture was stirred at the same temperature for 16 h. The mixture was partitioned between AcOEt (100 mL) and H_2O (60 mL). The organic layers were washed with 0.1 N aqueous HCl (80 mL), saturated aqueous $NaHCO_3$ (80 mL), and brine (60 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash silica gel column chromatography (2 × 20 cm, hexane/AcOEt = 3/1) to give **41a** (850 mg, 93%) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$, 20 °C, 4:3 mixture of rotamers) data for major rotamer; δ 7.99 (s, 1H, H-2), 7.69 (s, 1H, H-8), 7.36−7.22 (m, 15H, Tr), 7.15 (d, 1H, SiMB-6, J = 8.6 Hz), 7.06 (dd, 1H, H-5′, J = 5.1, 15.4 Hz), 6.93 (br s, 1H, NHTr), 6.38 (s, 1H, H-6″), 6.32 (dd, 1H, SiMB-5, J = 2.3, 8.6 Hz), 6.28 (dd, 1H, H-6′, J = 1.7, 15.4 Hz), 6.19 (d, 1H, SiMB-3, J = 2.3 Hz), 6.01 (d, 1H, H-1′, J = 5.1 Hz), 5.97 (m, 1H, H-8′), 5.85 (m, 1H, H-11′), 5.50 (d, 1H, SiMB-CH_2, J = 14.3 Hz), 5.25

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(dd, 1H, H-12′-*trans*, J = 1.2, 17.2 Hz), 5.17 (dd, 1H, H-12′-*cis*, J = 1.2, 10.3 Hz), 5.00 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.95 (m, 2H, H-9′), 4.90 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.84 (d, 1H, MOM-CH_2, J = 5.9 Hz), 4.81 (d, 1H, MOM-CH_2, J = 5.9 Hz), 4.70 (dt, 1H, H-4′, J = 1.7, 4.6 Hz), 4.60 (t, 1H, H-2′, J = 4.6 Hz), 4.42 (d, 1H, SiMB-CH_2, J = 14.3 Hz), 4.14 (dd, 1H, H-10′a, J = 5.7, 12.6 Hz), 4.01 (dd, 1H, H-10′b, J = 5.7, 12.6 Hz), 3.86 (t, 1, H-3′, J = 4.6 Hz), 3.66 (s, 3H, OMe), 3.50 (s, 3H, OMe), 3.49 (s, 3H, OMe), 3.45 (m, 2H, H-7′), 3.20 (s, 3H, OMe), 0.95 (s, 9H, ^{t}Bu), 0.77 (s, 9H, ^{t}Bu), 0.16 (s, 3H, Me), 0.15 (s, 3H, Me), −0.01 (s, 3H, Me), −0.16 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$, 20 °C, 4:3 mixture of rotamers, observed peaks were described) δ 165.2, 158.6, 156.4, 154.2, 152.5, 149.0, 148.7, 148.5, 147.3, 147.2, 146.6, 146.5, 145.2, 145.1, 140.8, 138.4, 138.0, 136.9, 134.1, 134.0, 131.8, 131.7, 130.3, 130.2, 129.1, 128.7, 128.5, 128.0, 127.0, 124.3, 123.2, 121.7, 121.3, 118.2, 117.7, 116.8, 115.2, 111.5, 103.0, 99.9, 99.8, 95.6, 95.3, 89.9, 88.1, 81.8, 81.5, 80.9, 74.4, 74.3, 71.8, 71.5, 71.4, 61.1, 60.9, 57.4, 56.2, 56.0, 55.1, 45.8, 29.6, 29.3, 25.8, 25.7, 25.6, 18.3, 18.1, 18.0, −4.3, −4.8, −4.9, −5.0, −5.1; ESIMS-LR m/z = 1242 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{68}H_{86}O_{11}N_6NaSi_2$ 1241.5791, found 1241.5792.

Cyclophanes 43a. A mixture of **41a** (530 mg, 0.43 mmol) and Grubbs' first catalyst (1.7 mg, 2.1 μmol) in CH_2Cl_2 (4.3 mL) was refluxed for 5 h. The solvent was removed in vacuo, and the residue was purified by flash silica gel column chromatography (2 × 20 cm, hexane/AcOEt = 3/1) to give (+)-*trans*-**43a** (131 mg, 25%) as a white foam and a mixture of (−)-*trans*-**43a** and *cis*-**43**. The mixture was further purified by flash silica gel column chromatography (2 × 20 cm, hexane/$CHCl_3$/MeOH = 2/3/0.01) to give (−)-*trans*-**43a** (214 mg, 42%) as a white foam and *cis*-**43a** (155 mg, 31%) as a white foam (total 98% yield, *trans*/*cis* = 2.2:1). Data for (+)-*trans*-**43a**: R_f = 0.65 (hexane/AcOEt = 2/1 × 2); $[\alpha]^{21}_D$ +54.4 (c 1.08, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (s, 1H, H-2), 7.51 (s, 1H, H-8), 7.32−7.22 (m, 16H, Tr and SiMB-6), 6.86 (br s, 1H, NHTr), 6.76 (dd, 1H, H-5′, J = 4.6, 15.4 Hz), 6.67 (s, 1H, H-6″), 6.39 (dd, 1H, SiMB-5, J = 2.3, 8.0 Hz), 6.30 (d, 1H, SiMB-3, J = 2.3 Hz), 6.08 (dd, 1H, H-6′, J = 1.1, 15.4 Hz), 5.77 (d, 1H, H-1′, J = 2.3 Hz), 5.71 (ddd, 1H, H-8′, J = 4.6, 8.0, 14.9 Hz), 5.47 (ddd, 1H, H-9′, J = 6.9, 8.0, 14.9 Hz), 5.24 (d, 1H, SiMB-CH_2, J = 14.3 Hz), 4.95 (d, 1H, MOM-CH_2, J = 6.8 Hz), 4.79 (d, 1H, MOM-CH_2, J = 6.8 Hz), 4.67 (d, 1H, MOM-CH_2, J = 5.8 Hz), 4.65 (d, 1H, MOM-CH_2, J = 5.8 Hz), 4.58 (ddd, 1H, H-4′, J = 1.1, 4.6, 8.0 Hz), 4.53 (d, 1H, SiMB-CH_2, J = 14.3 Hz), 4.50 (dd, 1H, H-2′, J = 2.3, 4.6 Hz), 4.13 (dd, 1H, H-10′a, J = 6.9, 13.2 Hz), 3.89 (dd, 1H, H-3′, J = 4.6, 8.0 Hz), 3.78 (s, 3H, OMe), 3.61 (s, 3H, OMe), 3.55 (dd, 1H, H-10′b, J = 8.0, 13.2 Hz), 3.48 (s, 3H, OMe), 3.47 (dd, 1H, H-7′a, J = 4.6, 13.8 Hz), 3.33 (dd, 1H, H-7′b, J = 8.0, 13.8 Hz), 3.30 (s, 3H, OMe), 0.98 (s, 9H, ^{t}Bu), 0.86 (s, 9H, ^{t}Bu), 0.19 (s, 3H, Me), 0.18 (s, 3H, Me), 0.01 (s, 3H, Me), −0.09 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 158.5, 156.5, 154.1, 152.4, 148.3, 147.2, 147.0, 146.8, 145.1, 138.4, 136.8, 134.9, 132.1, 131.8, 129.1, 128.0, 127.0, 126.0, 125.2, 121.7, 118.5, 113.7, 111.9, 103.4, 100.0, 95.7, 90.5, 79.4, 76.1, 73.7, 71.4, 69.8, 61.5, 57.8, 56.3, 55.3, 46.8, 29.8, 27.3, 25.8, 25.7, 18.3, 18.1, −4.3, −4.7, −4.8; ESIMS-LR m/z = 1213 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{66}H_{82}O_{11}N_6NaSi_2$ 1213.5478, found 1213.5452. Data for (−)-*trans*-**43a**: R_f = 0.55 (hexane/AcOEt = 2/1 × 2) or 0.80 (5% MeOH in $CHCl_3$ × 2); $[\alpha]^{22}_D$ −118.8 (c 0.80, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (s, 1H, H-2), 7.83 (s, 1H, H-8), 7.35−7.22 (m, 16H, Tr and SiMB-6), 7.07 (dd, 1H, H-5′, J = 6.4, 15.9 Hz), 6.90 (br s, 1H, NHTr), 6.71 (s, 1H, H-6″), 6.40 (dd, 1H, SiMB-5, J = 2.2, 8.1 Hz), 6.30 (d, 1H, SiMB-3, J = 2.2 Hz), 5.96 (dd, 1H, H-8′, J = 5.0, 15.8 Hz), 5.85 (d, 1H, H-1′, J = 6.8 Hz), 5.84 (dd, 1H, H-6′, J = 1.8, 15.9 Hz), 5.26 (d, 1H, SiMB-CH_2, J = 14.5 Hz), 5.01 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.96 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.86 (br t, 1H, H-9′, J = 12.6 Hz), 4.80 (t, 1H, H-2′, J = 6.4 Hz), 4.60 (d, 1H, MOM-CH_2, J = 5.9 Hz), 4.55 (ddd, 1H, H-4′, J = 1.8, 2.9, 6.4 Hz), 4.54 (d, 1H, SiMB-CH_2, J = 14.5 Hz), 4.52 (d, 1H, MOM-CH_2, J = 5.9 Hz), 4.29 (br d, 1H, H-10′a, J = 13.2 Hz), 3.95 (dd, 1H, H-10′b, J = 10.0, 13.2 Hz), 3.92 (dd, 1H, H-3′, J = 2.9, 5.1 Hz), 3.82 (s, 3H, OMe), 3.60 (s, 3H, OMe), 3.55 (dd, 1H, H-7′a, J = 2.2, 16.3 Hz), 3.45 (s, 3H, OMe), 3.40 (s, 3H, OMe), 3.26 (dd, 1H, H-7′b, J = 6.4, 16.3 Hz), 0.97 (s, 9H, ^{t}Bu), 0.75 (s, 9H, ^{t}Bu), 0.19 (s, 3H, Me), 0.18 (s, 3H, Me), −0.10 (s, 3H, Me), −0.38 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 158.6, 156.6, 154.3, 152.5, 149.0, 148.1, 147.0, 145.2, 141.4, 138.9, 135.1, 131.8, 131.7, 129.1, 128.8, 128.0, 127.1, 127.0, 123.8, 121.8, 118.5, 114.0, 112.0, 103.5, 99.8, 95.7, 88.5, 84.1, 79.2, 74.5, 71.6, 71.0, 61.6, 57.4, 56.4, 55.3, 46.7, 26.3, 25.8, 25.6, 18.3, 18.0, −4.3, −4.9, −5.4; ESIMS-LR m/z = 1213 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{66}H_{82}O_{11}N_6NaSi_2$ 1213.5478, found 1213.5486. Data for *cis*-**43a**: R_f = 0.55 (hexane/AcOEt = 2/1 × 2) or 0.85 (5% MeOH in $CHCl_3$ × 2); $[\alpha]^{22}_D$ −95.5 (c 1.35, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H, H-2), 7.91 (s, 1H, H-8), 7.38−7.24 (m, 16H, Tr and SiMB-6), 6.97 (dd, 1H, H-5′, J = 6.8, 15.8 Hz), 6.96 (br s, 1H, NHTr), 6.68 (s, 1H, H-6″), 6.40 (dd, 1H, SiMB-5, J = 2.3, 8.2 Hz), 6.29 (d, 1H, SiMB-3, J = 2.3 Hz), 6.11 (dd, 1H, H-6′, J = 1.4, 15.8 Hz), 6.10 (m, 1H, H-8′), 5.79 (s, 1H, H-1′), 5.55 (dt, 1H, H-9′, J = 4.6, 10.4 Hz), 5.23 (d, 1H, SiMB-CH_2, J = 14.5 Hz), 4.98 (d, 1H, MOM-CH_2, J = 6.4 Hz), 4.94 (d, 1H, MOM-CH_2, J = 6.4 Hz), 4.88 (d, 1H, H-2′, J = 5.0 Hz), 4.58 (t, 1H, H-4′, J = 6.8 Hz), 4.53 (d, 1H, SiMB-CH_2, J = 14.5 Hz), 4.51 (d, 1H, MOM-CH_2, J = 5.9 Hz), 4.45 (d, 1H, MOM-CH_2, J = 5.9 Hz), 4.42 (t, 1H, H-10′a, J = 10.0 Hz), 4.00 (dd, 1H, H-3′, J = 5.0, 8.6 Hz), 3.92 (s, 3H, OMe), 3.79 (dd, 1H, H-10′b, J = 4.6, 9.9 Hz), 3.59 (m, 1H, H-7′a), 3.58 (s, 3H, OMe), 3.44 (s, 3H, OMe), 3.43 (s, 3H, OMe), 3.06 (dd, 1H, H-7′b, J = 7.7, 12.7 Hz), 0.98 (s, 9H, ^{t}Bu), 0.89 (s, 9H, ^{t}Bu), 0.19 (s, 3H, Me), 0.18 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 158.6, 156.6, 154.2, 152.3, 148.2, 147.9, 146.8, 145.2, 145.1, 141.2, 138.6, 131.8, 131.6, 131.4, 129.6, 129.1, 128.0, 127.2, 127.0, 125.0, 121.9, 118.7, 113.7, 111.9, 103.4, 100.3, 95.5, 92.3, 82.1, 81.2, 73.8, 71.5, 67.1, 61.0, 58.0, 56.4, 55.2, 47.0, 25.9, 25.8, 23.2, 18.3, 18.2, −4.3, −4.6, −4.7; ESIMS-LR m/z = 1213 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{66}H_{82}O_{11}N_6NaSi_2$ 1213.5478, found 1213.5488.

Cyclophane (+)-*trans*-44a. A solution of (+)-*trans*-**43a** (19 mg, 0.016 mmol) in THF (0.5 mL) was treated with TBAF (1.0 M solution in THF, 48 μL, 0.048 mmol) at room temperature for 10 min. The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography (0.5 × 10 cm, 2% MeOH in $CHCl_3$) to give (+)-*trans*-**44a** (15 mg, 97%) as a white solid: $[\alpha]^{21}_D$ +55.5 (c 1.11, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 1H, H-2), 7.73 (s, 1H, H-8), 7.65 (br s, 1H, HMB-4-OH), 7.33−7.21 (m, 15H, Tr), 7.16 (d, 1H, HMB-6, J = 8.0 Hz), 7.13 (br s, 1H, NHTr), 6.67 (s, 1H, H-6″), 6.65 (dd, 1H, H-5′, J = 5.2, 16.0 Hz), 6.32 (dd, 1H, HMB-5, J = 2.3, 8.0 Hz), 6.26 (d, 1H, HMB-3, J = 2.3 Hz), 6.12 (dd, 1H, H-6′, J = 1.1, 16.0 Hz), 5.80 (d, 1H, H-1′, J = 3.4 Hz), 5.79 (ddd, 1H, H-8′, J = 5.2, 8.0, 15.5 Hz), 5.53 (ddd, 1H, H-9′, J = 6.3, 8.0, 15.5 Hz), 5.23 (d, 1H, HMB-CH_2, J = 14.3 Hz), 4.84 (d, 1H, MOM-CH_2, J = 6.9 Hz), 4.72 (d, 1H, MOM-CH_2, J = 6.9 Hz), 4.68 (d, 1H, MOM-CH_2, J = 5.7 Hz), 4.65 (d, 1H, MOM-CH_2, J = 5.7 Hz), 4.52 (d, 1H, HMB-CH_2, J = 14.3 Hz), 4.47 (t, 1H, H-4′, J = 5.8 Hz), 4.40 (br s, 1H, H-2′), 4.24 (t, 1H, H-3′, J = 6.3 Hz), 4.22 (dd, 1H, H-10′a, J = 6.3, 12.6 Hz), 3.98 (br s, 1H, 2′−OH), 3.80 (s, 3H, OMe), 3.70 (dd, 1H, H-10′b, J = 8.0, 12.6 Hz), 3.57 (s, 3H, OMe), 3.48 (s, 3H, OMe), 3.46 (m, 1H, H-7′a), 3.34 (dd, 1H, H-7′b, J = 8.0, 13.1 Hz), 3.26 (s, 3H, OMe); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 158.7, 157.4, 154.1, 152.2, 148.1, 147.3, 146.9, 146.4, 144.9, 138.6, 136.3, 135.9, 132.1, 131.7, 129.2, 129.1, 127.9, 127.0, 125.9, 125.5, 121.2, 116.9, 113.3, 107.4, 100.1, 99.0, 95.5, 90.6, 80.3, 75.3, 73.4, 71.4, 70.2, 61.5, 57.8, 56.3, 55.3, 47.1, 27.4, 25.8; ESIMS-LR m/z = 985 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{54}H_{54}O_{11}N_6Na$ 985.3748, found 985.3738.

Cyclophane (+)-*trans*-45a. A mixture of (+)-*trans*-**44a** (5.0 mg, 5.2 μmol) and CsF (3.2 mg, 0.021 mmol) in 1,4-dioxane−H_2O (3/1 (v/v), 1 mL) was refluxed for 16 h. The mixture was extracted with $CHCl_3$ (20 mL), and the organic layer was washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by preparative TLC (5% MeOH in $CHCl_3$) to give (+)-*trans*-**45a** (3.9 mg, 91%) as a white solid: $[\alpha]^{21}_D$ +51.3 (c 1.60, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1H, H-2), 7.70 (s, 1H, H-8), 7.33−7.22 (m, 15H, Tr), 6.92 (br s, 1H, CONH), 6.85 (br s, 1H, NHTr), 6.79 (s, 1H, H-6″), 6.58 (dd, 1H, H-5′, J = 5.1, 16.0 Hz), 6.11 (dd, 1H, H-6′, J = 1.1, 16.0 Hz), 5.84 (ddd, 1H, H-8′, J = 3.4, 8.6, 14.9 Hz), 5.81 (d, 1H, H-1′, J = 2.3 Hz), 5.56 (ddd, 1H, H-9′, J = 6.3, 8.1, 14.9 Hz), 5.03 (d, 1H, 5″-MOM-CH_2, J = 6.9 Hz), 4.93 (d, 1H,

2″-MOM-CH_2, J = 6.3 Hz), 4.89 (d, 1H, 2″-MOM-CH_2, J = 6.3 Hz), 4.87 (d, 1H, 5″-MOM-CH_2, J = 6.9 Hz), 4.48 (m, 1H, H-4′), 4.45 (m, 2H, H-2′ and 2′-OH), 4.25 (dd, 1H, H-10′a, J = 6.3, 12.6 Hz), 3.82 (s, 3H, 4″-OMe), 3.77 (d, 1H, H-3′, J = 2.9 Hz), 3.71 (dd, 1H, H-10′b, J = 8.1, 12.6 Hz), 3.54 (s, 3H, 2″-MOM-OMe), 3.52 (dd, 1H, H-7′a, J = 3.4, 14.3 Hz), 3.37 (s, 3H, 5″-MOM-OMe), 3.35 (dd, 1H, H-7′b, J = 8.6, 14.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 154.2, 152.1, 148.0, 147.6, 146.9, 146.0, 145.0, 139.0, 137.7, 135.5, 129.7, 129.1, 128.0, 127.0, 126.5, 125.7, 124.0, 121.6, 112.6, 99.8, 95.3, 90.7, 81.0, 75.9, 73.4, 71.4, 70.4, 61.5, 58.2, 56.5, 27.2; ESIMS-LR m/z = 849 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{46}H_{46}O_9N_6Na$ 849.3224, found 849.3209.

***trans*-4.** A solution of (+)-*trans*-**45a** (100 mg, 0.12 mmol) in CH_2Cl_2 (0.6 mL) was treated with Et_3SiH (0.19 mL, 1.2 mmol) and TFA (1.4 mL) at 0 °C, and the mixture was stirred at room temperature for 2 h. The mixture was concentrated to give a crude hydroquinone. A mixture of the crude hydroquinone and Pd/C (60 mg) in MeOH (3 mL) was stirred at room temperature for 1 h. The insolubles were filtered off through a Celite pad and washed with hot MeOH. The filtrate was concentrated, and the residue was purified by silica gel column chromatography (1 × 7 cm, 6% MeOH in $CHCl_3$) to give *trans*-**4** (49 mg, 84% over two steps) as a yellow solid: ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 9.85 (s, 1H, CONH), 8.22 (s, 1H, H-2), 8.13 (s, 1H, H-8), 6.98 (br s, 2H, 6-NH_2), 6.50 (m, 1H, H-5′), 6.26 (s, 1H, H-6″), 5.88 (m, 1H, H-6′), 5.84 (d, 1H, H-1′, J = 5.1 Hz), 5.82 (m, 1H, H-8′), 5.54 (m, 1H, H-9′, J = 14.3 Hz), 5.27 (d, 1H, 2′−OH, J = 5.8 Hz), 4.80 (m, 1H, H-2′), 4.45 (br s, 1H, H-4′), 4.20 (dd, 1H, H-10′a, J = 4.0, 12.6 Hz), 4.07 (m, 1H, H-3′), 4.00 (s, 3H, OMe), 3.91 (dd, 1H, H-10′b, J = 9.1, 12.6 Hz), 3.25 (br d, 1H, H-7′a, J = 14.9 Hz), 3.16 (dd, 1H, H-7′b, J = 6.3, 12.6 Hz); ^{13}C NMR (125 MHz, DMSO-d_6, 80 °C) δ 183.2, 182.3, 166.2, 154.9, 154.6, 150.6, 148.9, 143.0, 140.0, 132.0, 128.1, 127.3, 119.0, 87.8, 80.9, 76.8, 71.7, 68.8, 60.8, 24.7; ESIMS-LR m/z = 517 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{23}H_{22}O_7N_6Na$ 517.1448, found 517.1442.

***cis*-44a.** A solution of *cis*-**43a** (27 mg, 0.022 mmol) in THF (1 mL) was treated with TBAF (1.0 M solution in THF, 66 μL, 0.066 mmol) at room temperature for 30 min. The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography (1 × 10 cm, 2% MeOH in $CHCl_3$) to give *cis*-**44a** (20 mg, 95%) as a white solid: $[\alpha]^{22}_D$ −107.3 (*c* 0.87, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H, H-2), 7.89 (s, 1H, H-8), 7.50 (br s, 1H, HMB-4-OH), 7.35−7.22 (m, 15H, Tr), 7.18 (d, 1H, HMB-6, J = 8.0 Hz), 7.13 (br s, 1H, NHTr), 6.91 (dd, 1H, H-5′, J = 6.8, 16.0 Hz), 6.68 (s, 1H, H-6″), 6.32 (dd, 1H, HMB-5, J = 2.3, 8.0 Hz), 6.26 (d, 1H, HMB-3, J = 2.3 Hz), 6.17 (dt, 1H, H-8′, J = 8.0, 10.3 Hz), 6.02 (d, 1H, H-6′, J = 16.0 Hz), 5.89 (d, 1H, H-1′, J = 1.2 Hz), 5.55 (dt, 1H, H-9′, J = 4.6, 10.3 Hz), 5.23 (d, 1H, HMB-CH_2, J = 14.3 Hz), 4.97 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.92 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.67 (d, 1H, H-2′, J = 4.0 Hz), 4.59 (d, 1H, MOM-CH_2, J = 5.8 Hz), 4.53 (t, 1H, H-10′a, J = 10.3 Hz), 4.51 (d, 1H, MOM-CH_2, J = 5.8 Hz), 4.46 (d, 1H, HMB-CH_2, J = 14.3 Hz), 4.39 (m, 2H, H-3′ and H-4′), 3.91 (s, 3H, OMe), 3.90 (m, 1H, H-10′b), 3.60 (dd, 1H, H-7′a, J = 8.0, 13.2 Hz), 3.54 (s, 3H, OMe), 3.45 (s, 3H, OMe), 3.41 (s, 3H, OMe), 3.07 (dd, 1H, H-7′b, J = 7.5, 13.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 158.8, 157.5, 154.2, 152.3, 148.1, 146.9, 145.2, 144.9, 140.5, 138.8, 132.4, 132.0, 131.2, 129.4, 129.1, 128.0, 127.0, 126.5, 125.3, 121.5, 117.0, 114.0, 107.4, 100.5, 99.1, 95.6, 91.4, 81.9, 81.8, 72.9, 71.5, 67.5, 61.0, 58.0, 56.4, 55.2, 47.3, 23.2; ESIMS-LR m/z = 985 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{54}H_{54}O_{11}N_6Na$ 985.3748, found 985.3741.

***cis*-45a.** A mixture of *cis*-**44a** (8.0 mg, 8.6 μmol) and CsF (15 mg, 0.086 mmol) in 1,4-dioxane−H_2O (3/1 (v/v), 1 mL) was refluxed for 21 h. The mixture was extracted with $CHCl_3$ (20 mL), and the organic layer was washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (0.5 × 5 cm, 3% MeOH in $CHCl_3$) to give *cis*-**45a** (6.5 mg, 91%) as a white solid: $[\alpha]^{22}_D$ −104.6 (*c* 0.92, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1H, H-2), 7.84 (s, 1H, H-8), 7.36−7.22 (m, 15H, Tr), 6.99 (dd, 1H, H-5′, J = 6.3, 16.0 Hz), 6.98 (s, 1H, NHTr), 6.94 (br s, 1H, CONH), 6.88 (s, 1H, H-6″), 6.17 (q, 1H, H-8′, J = 9.2 Hz), 6.08 (dd, 1H, H-6′, J = 1.1, 16.0 Hz), 5.90 (d, 1H, H-1′, J = 1.2 Hz), 5.57 (dt, 1H, H-9′, J = 4.0, 10.3 Hz), 5.17 (d, 1H, MOM-CH_2, J = 6.8 Hz), 5.15 (d, 1H, MOM-CH_2, J = 6.8 Hz), 4.85 (d, 1H, MOM-CH_2, J = 5.8 Hz), 4.82 (d, 1H, MOM-CH_2, J = 5.8 Hz), 4.70 (d, 1H, H-2′, J = 5.1 Hz), 4.66 (br t, 1H, H-10′a, J = 10.3 Hz), 4.56 (dd, 1H, H-3′, J = 5.1, 8.1 Hz), 4.46 (t, 1H, H-4′, J = 6.3 Hz), 3.94 (s, 3H, OMe), 3.93 (overlapping, 1H, H-10′b), 3.67 (dd, 1H, H-7′a, J = 9.2, 13.8 Hz), 3.54 (s, 3H, OMe), 3.52 (s, 3H, OMe), 3.27 (br s, 1H, 2′−OH), 3.14 (dd, 1H, H-7′b, J = 7.5, 13.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.7, 154.3, 152.3, 148.1, 148.0, 147.2, 145.0, 144.7, 142.3, 139.2, 132.5, 130.0, 129.1, 128.1, 127.1, 126.2, 125.9, 122.9, 121.8, 113.3, 100.2, 95.5, 91.6, 82.2, 81.4, 72.7, 71.6, 67.4, 61.1, 58.5, 56.6, 23.0; ESIMS-LR m/z = 849 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{46}H_{46}O_9N_6Na$ 849.3224, found 849.3221.

***cis*-4.** A solution of *cis*-**45a** (9.0 mg, 0.010 mmol) in CH_2Cl_2 (0.5 mL) was treated with Et_3SiH (16 mL, 0.10 mmol) and TFA (0.6 mL) at 0 °C, and the mixture was stirred at room temperature for 3 h. The mixture was concentrated in vacuo to give a crude hydroquinone. A mixture of the crude hydroquinone and Pd/C (20 mg) in MeOH (1 mL) was vigorously stirred under air at room temperature for 30 min. The insolubles were filtered off through a Celite pad and washed with hot MeOH. The filtrate was concentrated, and the residue was purified by flash silica gel column chromatography (0.5 × 6 cm, 6% MeOH in $CHCl_3$) to give *cis*-**4** (4.1 mg, 83% over two steps) as a yellow solid: ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.10 (br s, 1H, CONH), 8.34 (s, 1H, H-2), 8.16 (s, 1H, H-8), 7.33 (br s, 2H, 6-NH_2), 6.62 (dd, 1H, H-5′, J = 6.3, 15.5 Hz), 6.21 (s, 1H, H-6″), 5.89 (d, 1H, H-1′, J = 2.3 Hz), 5.82 (d, 1H, H-6′, J = 15.5 Hz), 5.77 (dt, 1H, H-8′, J = 6.9, 10.3 Hz), 5.65 (dt, 1H, H-9′, J = 5.1, 10.3 Hz), 5.54 (d, 1H, 2′−OH, J = 5.2 Hz), 4.66 (dt, 1H, H-2′, J = 2.3, 5.2 Hz), 4.39 (t, 1H, H-4′, J = 6.9 Hz), 4.22 (t, 1H, H-10′a, J = 9.7 Hz), 4.06 (t, 1H, H-3′, J = 5.2 Hz), 4.04 (s, 3H, OMe), 3.95 (dd, 1H, H-10′b, J = 5.1, 10.3 Hz), 3.51 (br t, 1H, H-7′a, J = 10.9 Hz), 2.83 (dd, 1H, H-7′b, J = 6.3, 12.6 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 182.9, 182.7, 166.6, 155.3, 152.8, 148.4, 142.2, 141.2, 128.8, 127.5, 127.4, 119.2, 119.1, 117.6, 115.2, 90.0, 81.6, 80.3, 71.8, 65.3, 61.2, 20.3; ESIMS-LR m/z = 517 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{23}H_{22}O_7N_6Na$ 517.1448, found 517.1443.

6-Amino-9-[3-deoxy-3-*C*-allyl-2,5-*O*-bis(*tert*-butyldimethylsilyl)-β-D-pentofuranosyl]-9*H*-purine (49). A mixture of **47**[23] (3.7 g, 7.4 mmol) and DMAP (3.6 g, 30 mmol) in CH_2Cl_2 (50 mL) was treated with phenyl chlorothionoformate (1.2 mL, 8.2 mmol) at 0 °C for 2 h. The mixture was stirred at room temperature for 14 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (30 mL) at 0 °C, and the mixture was vigorously stirred for 15 min. The mixture was extracted with AcOEt (300 mL), and the organic layers were washed with H_2O (100 mL), 0.1 N aqueous HCl (150 mL × 3), saturated aqueous $NaHCO_3$ (200 mL), and brine (200 mL), dried (Na_2SO_4), filtered, and concentrated to give crude phenoxy thionocarbonate **48**.[17] A mixture of **48**, allyl tributyltin (9.2 mL, 30 mmol), and AIBN (0.60 g, 3.7 mmol) in chlorobenzene (14 mL) was refluxed for 1 h. The mixture was cooled to room temperature and directly purified by flash silica gel column chromatography (3 × 25 cm, hexane/AcOEt = 1:1) to give **49** (2.7 g, 71% over two steps) as a white solid: $[\alpha]^{20}_D$ −5.8 (*c* 1.15, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (s, 1H, H-2), 8.33 (s, 1H, H-8), 6.00 (s, 1H, H-1′), 5.73 (m, 1H, H-2″), 5.70 (br s, 2H, 6-NH_2), 5.06 (dd, 1H, H-3″-*trans*, J = 1.1, 15.5 Hz), 4.99 (dd, 1H, H-3″-*cis*, J = 1.1, 10.3 Hz), 4.50 (d, 1H, H-2′, J = 3.4 Hz), 4.13 (m, 2H, H-4′and H-5′a), 3.77 (dd, 1H, H-5′b, J = 2.3, 11.4 Hz), 2.39 (m, 2H, H-3′and H-1″a), 2.07 (m, 1H, H-1″b), 0.95 (s, 9H, ^{t}Bu), 0.94 (s, 9H, ^{t}Bu), 0.29 (s, 3H, Me), 0.15 (s, 3H, Me), 0.13 (s, 3H, Me), 0.12 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.3, 152.8, 149.5, 139.4, 136.0, 120.2, 116.6, 90.8, 85.1, 78.1, 62.5, 40.6, 29.1, 26.2, 26.0, 18.7, 18.2, −4.0, −5.1, −5.3; FABMS-LR m/z = 520 [(M + Na)$^+$]. Anal. Calcd for $C_{25}H_{45}N_5O_3Si_2$: C, 57.76; H, 8.73; N, 13.47. Found: C, 57.51; H, 8.62; N, 13.23.

6-Amino-9-[3-deoxy-3-*C*-allyl-2,5-*O*-bis(*tert*-butyldimethylsilyl)-β-D-pentofuranosyl]-*N*^{6}-trityl-9*H*-purine. A solution of **49** (1.0 g, 1.9 mmol) and Et_3N (0.80 mL, 5.8 mmol) in CH_2Cl_2 (10 mL) was treated with TrCl (800 mg, 2.9 mmol) at room temperature for 40 h. The reaction was quenched with H_2O (20 mL), and the mixture was

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extracted with AcOEt (100 mL). The organic layers were washed with brine (50 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (2 × 12 cm, hexane/AcOEt = 9/1) to give the titled compound (1.2 g, 83%) as a white foam: $[\alpha]^{20}_D$ −16.8 (*c* 0.94, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (s, 1H, H-2), 8.01 (s, 1H, H-8), 7.40−7.20 (m, 15H,Tr), 6.96 (br s, 1H, NHTr), 5.96 (s, 1H, H-1′), 5.75 (m, 1H, H-2″), 5.09 (dd, 1H, H-3″-*trans*, *J* = 1.2, 16.7 Hz), 5.02 (dd, 1H, H-3″-*cis*, *J* = 1.2, 10.3 Hz), 4.55 (d, 1H, H-2′, *J* = 2.9 Hz), 4.14 (m, 2H, H-4′ and H-5′a), 3.79 (dd, 1H, H-5′b, *J* = 2.3, 11.5 Hz), 2.43 (m, 2H, H-3′ and H-1″a), 2.11 (dt, 1H, H-1″b, *J* = 8.0, 9.2 Hz), 0.97 (s, 9H, ^{t}Bu), 0.93 (s, 9H, ^{t}Bu), 0.25 (s, 3H, Me), 0.17 (s, 3H, Me), 0.15 (s, 3H, Me), 0.11 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.0, 152.0, 148.4, 145.2, 144.0, 138.6, 136.1, 129.6, 129.2, 128.4, 128.1, 128.0, 127.9, 127.3, 126.9, 126.4, 121.4, 116.6, 90.7, 85.0, 77.9, 71.4, 62.7, 40.8, 29.2, 26.2, 26.0, 18.7, 18.2, −4.1, −5.1, −5.3; ESIMS-LR *m*/*z* = 784 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{44}H_{59}O_3N_5NaSi_2$ 784.4054, found 784.4049.

6-Amino-9-(3-deoxy-3-*C*-allyl-2-*O*-*tert*-butyldimethylsilyl-β-D-pentofuranosyl)-N^6-trityl-9*H*-purine (39b). A mixture of 6-amino-9-[3-deoxy-3-*C*-allyl-2,5-*O*-bis(*tert*-butyldimethylsilyl)-β-D-pentofuranosyl]-N^6-trityl-9*H*-purine (1.3 g, 1.7 mmol) and AcOH (0.20 mL, 3.4 mmol) in THF (10 mL) was treated with TBAF (1.0 M solution in THF, 1.7 mL, 1.7 mmol) at −20 °C for 1 h, and then the mixture was stirred at −5 °C for 10 h. The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography (1 × 10 cm, hexane/AcOEt = 3/1) to give **39b** (860 mg, 78%) as a white foam: $[\alpha]^{20}_D$ −68.3 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H, H-2), 7.80 (s, 1H, H-8), 7.35−7.20 (m, 15H, Tr), 7.06 (br s, 1H, NHTr), 6.38 (br s, 1H, 5′−OH), 5.80 (m, 1H, H-2″), 5.63 (d, 1H, H-1′, *J* = 6.3 Hz), 5.14 (d, 1H, H-3′-*trans*, *J* = 14.0 Hz), 5.11 (d, 1H, H-3′-*cis*, *J* = 9.1 Hz), 5.02 (t, 1H, H-2′, *J* = 6.8 Hz), 4.19 (d, 1H, H-4′, *J* = 1.3 Hz), 3.96 (dd, 1H, H-5′a, *J* = 1.3, 12.2 Hz), 3.49 (d, 1H, H-5′b, *J* = 12.2 Hz), 2.62 (m, 1H, H-3′), 2.55 (m, 1H, H-1′a), 2.13 (m, 1H, H-1′b), 0.79 (s, 9H, ^{t}Bu), −0.12 (s, 3H, Me), −0.37 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 151.9, 147.5, 144.9, 140.0, 136.1, 129.1, 128.0, 127.1, 122.5, 117.5, 92.5, 85.6, 77.4, 75.0, 71.8, 64.7, 41.9, 31.8, 25.7, 18.0, −5.1, −5.6; ESIMS-LR *m*/*z* = 670 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{38}H_{45}O_3N_5NaSi$ 670.3189, found 670.3184.

***N*-(3-Allyl-4-methoxy-2,5-bis-methoxymethoxyphenyl)-*N*-(4-*tert*-butyldimethylsiloxy-2-methoxybenzyl) (*E*)-3-*C*-Allyl-1-(6-amino-N^6-trityl-9*H*-purin-9-yl)-2-*O*-*tert*-butyldimethylsilyl-3,5,6-trideoxy-β-D-*ribo*-5-eneheptofuranuronamide (41b).** A solution of **39b** (150 mg, 0.23 mmol) in CH_2Cl_2 (5 mL) was treated with Dess−Martin periodinane (200 mg, 0.46 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 min. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) at 0 °C and stirred for 20 min. The mixture was extracted with AcOEt (40 mL), and the organic layers were washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL), dried (Na_2SO_4), filtered, and concentrated to give a crude aldehyde **40b**. Compound **40b** (150 mg, 0.23 mmol) was added to a mixture of **38** (160 mg, 0.23 mmol), $Zn(OTf)_2$ (100 mg, 0.28 mmol), Et_3N (0.14 mL, 0.92 mmol), and TMEDA (42 mL, 0.28 mmol) in THF (3 mL), and the mixture was stirred at room temperature for 4 h. The mixture was partitioned between AcOEt (50 mL) and H_2O (40 mL), and the organic layers were washed with 0.1 N aqueous HCl (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash silica gel column chromatography (1 × 25 cm, hexane/AcOEt = 3/1) to give **41b** (250 mg, 90% over two steps) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$, 20 °C, 1:1 mixture of rotamers) δ 7.99 (s, 0.5H, H-2), 7.98 (s, 0.5H, H-2), 7.81 (s, 0.5H, H-8), 7.80 (s, 0.5H, H-8), 7.37−7.21 (m, 15H, Tr), 7.19 (d, 0.5H, SiMB-6, *J* = 8.0 Hz), 7.18 (d, 0.5H, SiMB-6, *J* = 8.0 Hz), 7.02 (dd, 0.5H, H-5′, *J* = 5.7, 17.2 Hz), 7.00 (dd, 0.5H, H-5′, *J* = 6.9, 17.2 Hz), 6.96 (br s, 0.5H, NHTr), 6.95 (br s, 0.5H, NHTr), 6.49 (s, 0.5H, H-6″), 6.43 (s, 0.5H, H-6″), 6.35 (dd, 0.5H, SiMB-5, *J* = 2.3, 8.0 Hz), 6.33 (dd, 0.5H, SiMB-5, *J* = 2.3, 8.0 Hz), 6.25 (dd, 0.5H, H-6′, *J* = 1.1, 17.2 Hz), 6.23 (d, 0.5H, SiMB-3, *J* = 2.3 Hz), 6.21 (d, 0.5H, SiMB-3, *J* = 2.3 Hz), 6.17 (d, 0.5H, H-6′, *J* = 17.2 Hz), 5.97 (m, 1H, H-8′), 5.91 (s, 0.5H, H-1′), 5.89 (s, 0.5H, H-1′), 5.67 (m, 1H, H-11′), 5.51 (d, 0.5H, SiMB-CH_2, *J* = 14.3 Hz), 5.47 (d, 0.5H, SiMB-CH_2, *J* = 14.3 Hz), 5.06−4.87 (m, 7H, H-9′, H-12′ and MOM-CH_2), 4.83 (d, 0.5H, MOM-CH_2, *J* = 5.7 Hz), 4.81 (d, 0.5H, MOM-CH_2, *J* = 5.7 Hz), 4.67 (d, 0.5H, H-2′, *J* = 4.0 Hz), 4.59 (d, 0.5H, H-2′, *J* = 3.4 Hz), 4.52 (dd, 0.5H, H-4′, *J* = 5.7, 8.5 Hz), 4.47 (overlapping, 0.5H, H-4′), 4.45 (d, 0.5H, SiMB-CH_2, *J* = 14.3 Hz), 4.44 (d, 0.5H, SiMB-CH_2, *J* = 14.3 Hz), 3.79 (s, 1.5H, OMe), 3.75 (s, 1.5H, OMe), 3.53 (s, 1.5H, OMe), 3.52 (s, 1.5H, OMe), 3.51 (s, 1.5H, OMe), 3.49 (s, 1.5H, OMe), 3.45 (m, 2H, H-7′), 3.33 (s, 1.5H, OMe), 3.30 (s, 1.5H, OMe), 2.30 (m, 1H, H-10′a), 2.09 (m, 2H, H-3′ and H-10′b), 0.97 (s, 4.5H, ^{t}Bu), 0.96 (s, 4.5H, ^{t}Bu), 0.91 (s, 4.5H, ^{t}Bu), 0.90 (s, 4.5H, ^{t}Bu), 0.24 (s, 1.5H, Me), 0.22 (s, 1.5H, Me), 0.18 (s, 1.5H, Me), 0.17 (s, 1.5H, Me), 0.16 (s, 1.5H, Me), 0.15 (s, 1.5H, Me), 0.11 (s, 1.5H, Me), 0.11 (s, 1.5H, Me); ^{13}C NMR (125 MHz, $CDCl_3$, 20 °C, 1:1 mixture of rotamers, observed peaks were described) δ 165.3, 165.2, 158.6, 156.4, 156.3, 154.0, 152.2, 152.1, 148.5, 148.4, 148.2, 148.1, 147.4, 147.3, 146.6, 146.5, 145.2, 145.1, 141.2, 141.1, 137.8, 137.7, 136.8, 135.5, 135.4, 131.7, 130.3, 130.2, 129.1, 128.7, 128.5, 127.9, 126.9, 124.6, 123.6, 121.6, 121.4, 118.2, 118.1, 116.9, 116.7, 116.6, 116.4, 115.2, 111.5, 111.4, 103.1, 103.0, 100.0, 99.8, 95.5, 95.4, 92.0, 91.4, 83.9, 83.4, 71.3, 61.0, 60.9, 57.4, 57.3, 56.1, 56.0, 55.1, 55.0, 47.1, 47.0, 45.8, 45.7, 29.8, 29.5, 29.3, 28.4, 28.0, 25.9, 25.7, 18.3, 18.1, −4.0, −4.1, −4.3, −5.2; ESIMS-LR *m*/*z* = 1226 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{68}H_{86}O_{10}N_6NaSi_2$ 1225.5842, found 1225.5841.

Cyclophanes 43b. A mixture of **41b** (1.1 g, 0.91 mmol) and Grubbs' first-generation catalyst (3.7 mg, 4.6 μmol) in CH_2Cl_2 (10 mL) was refluxed for 7 h. The solvent was removed in vacuo, and the residue was purified by flash silica gel column chromatography (2 × 25 cm, hexane/AcOEt = 2/1) to give (−)-*trans*-**43b** (890 mg, 84%) as a white foam, (+)-*trans*-**43b** (75 mg, 7.0%) as a white foam, and *cis*-**43b** (70 mg, 6.6%) as a white foam (total 98% yield, *trans*/*cis* = 13.8:1). Data for (−)-*trans*-**43b**: R_f = 0.50 (hexane/AcOEt = 2/1 × 3); $[\alpha]^{18}_D$ −121.8 (*c* 1.07, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 1H, H-2), 7.98 (s, 1H, H-8), 7.37−7.23 (m, 16H, Tr and SiMB-6), 6.95 (br s, 1H, NHTr), 6.60 (s, 1H, H-6″), 6.40 (dd, 1H, SiMB-5, *J* = 2.3, 8.6 Hz), 6.37 (dd, 1H, H-5′, *J* = 9.2, 15.5 Hz), 6.34 (d, 1H, SiMB-3, *J* = 2.3 Hz), 5.73 (s, 1H, H-1′), 5.68 (d, 1H, H-6′, *J* = 15.5 Hz), 5.50 (dt, 1H, H-8′, *J* = 5.3, 14.9 Hz), 5.31 (d, 1H, SiMB-CH_2, *J* = 13.7 Hz), 5.01 (d, 1H, MOM-CH_2, *J* = 6.3 Hz), 4.98 (d, 1H, H-2′, *J* = 3.5 Hz), 4.95 (d, 1H, MOM-CH_2, *J* = 6.3 Hz), 4.77 (ddd, 1H, H-9′, *J* = 6.3, 8.0, 14.9 Hz), 4.63 (d, 1H, MOM-CH_2, *J* = 5.7 Hz), 4.61 (d, 1H, MOM-CH_2, *J* = 5.7 Hz), 4.39 (t, 1H, H-4′, *J* = 9.1 Hz), 4.30 (d, 1H, SiMB-CH_2, *J* = 13.7 Hz), 3.78 (s, 3H, OMe), 3.66 (s, 3H, OMe), 3.45 (s, 6H, OMe × 2), 3.44 (d, 1H, H-7′a, *J* = 16.0 Hz), 3.16 (dd, 1H, H-7′b, *J* = 5.3, 16.0 Hz), 2.22 (m, 3H, H-3′ and H-10′), 0.99 (s, 9H, ^{t}Bu), 0.87 (s, 9H, ^{t}Bu), 0.20 (s, 3H, Me), 0.19 (s, 3H, Me), 0.12 (s, 3H, Me), 0.09 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 158.8, 156.7, 154.1, 152.1, 148.5, 148.2, 147.6, 147.3, 145.2, 138.9, 138.6, 132.2, 131.7, 129.6, 129.1, 128.6, 128.0, 127.8, 127.0, 121.9, 118.6, 113.6, 111.8, 103.5, 100.1, 95.7, 92.4, 86.4, 78.8, 71.4, 61.6, 57.6, 56.4, 55.3, 48.3, 46.6, 31.2, 27.2, 25.9, 25.8, 18.3, 18.2, −4.3, −4.4, −4.9; ESIMS-LR *m*/*z* = 1198 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{66}H_{82}O_{10}N_6NaSi_2$ 1197.5523, found 1197.5512. Data for (+)-*trans*-**43b**: R_f = 0.55 (hexane/AcOEt = 2/1 × 3); $[\alpha]^{20}_D$ 54.6 (*c* 0.85, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1H, H-2), 7.78 (s, 1H, H-8), 7.34−7.21 (m, 16H, Tr and SiMB-6), 6.87 (br s, 1H, NHTr), 6.74 (s, 1H, H-6″), 6.70 (dd, 1H, H-5′, *J* = 4.6, 16.0 Hz), 6.41 (dd, 1H, SiMB-5, *J* = 2.3, 8.6 Hz), 6.31 (d, 1H, SiMB-3, *J* = 2.3 Hz), 5.77 (s, 1H, H-1′), 5.75 (dt, 1H, H-8′, *J* = 6.3, 14.9 Hz), 5.66 (dd, 1H, H-6′, *J* = 1.7, 16.0 Hz), 5.18 (d, 1H, SiMB-CH_2, *J* = 14.3 Hz), 5.04 (d, 1H, MOM-CH_2, *J* = 6.3 Hz), 4.97 (d, 1H, MOM-CH_2, *J* = 6.3 Hz), 4.67−4.60 (m, 4H, H-2′, H-4′, H-9′ and SiMB-CH_2), 4.46 (d, 1H, MOM-CH_2, *J* = 5.7 Hz), 4.44 (d, 1H, MOM-CH_2, *J* = 5.7 Hz), 3.78 (s, 3H, OMe), 3.62 (s, 3H, OMe), 3.44 (s, 3H, OMe), 3.40 (s, 3H, OMe), 3.35 (br d, 1H, H-7′a, *J* = 14.9 Hz), 3.19 (dd, 1H, H-7′b, *J* = 6.3, 14.9 Hz), 2.20 (m, 2H, H-3′ and H-10′a), 1.96 (m, 1H, H-10′b), 0.98 (s, 9H, ^{t}Bu), 0.89 (s, 9H, ^{t}Bu), 0.20 (s, 3H, Me), 0.19 (s, 3H, Me), 0.18 (s, 3H, Me), 0.08 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 158.6, 156.6, 154.0, 152.1, 148.1,

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147.3, 147.0, 146.3, 145.1, 138.4, 137.0, 132.3, 131.9, 130.7, 130.5, 129.6, 129.1, 128.0, 127.0, 125.7, 121.7, 118.6, 112.6, 112.0, 103.5, 99.9, 95.7, 91.0, 84.5, 79.9, 71.4, 61.6, 57.6, 56.4, 55.3, 46.3, 43.9, 30.7, 25.9, 25.8, 18.3, 18.1, −4.2, −4.3, −5.0; ESIMS-LR m/z = 1198 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{66}H_{82}O_{10}N_6NaSi_2$ 1197.5523, found 1197.5511. Data for *cis*-**43b**: R_f = 0.60 (hexane/AcOEt = 2/1 × 3); $[\alpha]^{18}_D$ 102.3 (*c* 1.11, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (s, 1H, H-2), 7.61 (s, 1H, H-8), 7.36−7.23 (m, 16H, Tr and SiMB-6), 6.87 (br s, 1H, NHTr), 6.72 (s, 1H, H-6″), 6.42 (dd, 1H, SiMB-5, J = 2.3, 8.1 Hz), 6.33 (d, 1H, SiMB-3, J = 2.3 Hz), 5.99 (d, 1H, H-6′, J = 16.0 Hz), 5.95 (dt, 1H, H-8′, J = 5.1, 10.3 Hz), 5.75 (s, 1H, H-1′), 5.54 (dd, 1H, H-5′, J = 8.6, 16.0 Hz), 5.32 (overlapping, 1H, H-9′), 5.30 (d, 1H, SiMB-CH_2, J = 14.9 Hz), 4.87 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.85 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.65 (d, 1H, H-2′, J = 4.6 Hz), 4.57 (d, 1H, MOM-CH_2, J = 5.8 Hz), 4.55 (d, 1H, MOM-CH_2, J = 5.8 Hz), 4.53 (d, 1H, SiMB-CH_2, J = 14.9 Hz), 4.22 (dd, 1H, H-4′, J = 8.6, 10.9 Hz), 3.63 (s, 3H, OMe), 3.60 (s, 3H, OMe), 3.52 (dd, 1H, H-7′a, J = 5.7, 15.3 Hz), 3.47 (s, 3H, OMe), 3.26 (s, 3H, OMe), 2.97 (dd, 1H, H-7′b, J = 9.2, 15.3 Hz), 2.01 (m, 2H, H-10′), 1.08 (m, 1H, H-3′), 0.99 (s, 9H, ^{t}Bu), 0.92 (s, 9H, ^{t}Bu), 0.20 (s, 3H, Me), 0.19 (s, 3H, Me), 0.18 (s, 3H, Me), 0.12 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 158.4, 156.5, 154.0, 152.2, 147.9, 147.6, 147.0, 145.1, 144.0, 137.9, 136.7, 133.5, 131.4, 131.3, 130.0, 129.1, 128.6, 128.0, 127.0, 126.5, 121.6, 118.7, 112.9, 112.0, 103.5, 100.4, 95.9, 93.0, 84.3, 75.8, 71.3, 60.7, 58.0, 56.5, 55.3, 48.3, 46.6, 25.9, 25.8, 23.1, 18.3, 18.1, −3.9, −4.2, −5.2; ESIMS-LR m/z = 1198 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{66}H_{82}O_{10}N_6NaSi_2$ 1197.5523, found 1197.5504.

(−)-*trans*-44b. A solution of (−)-*trans*-**43b** (580 mg, 0.49 mmol) in THF (10 mL) was treated with TBAF (1.0 M solution in THF, 1.2 mL, 1.2 mmol) at room temperature for 20 min. The mixture was concentrated, and the residue was purified by silica gel column chromatography (2 × 10 cm, 3% MeOH in $CHCl_3$) to give (−)-*trans*-**44b** (460 mg, 99%) as a white foam: $[\alpha]^{18}_D$ −93.1 (*c* 0.95, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H, H-2), 8.00 (br s, 1H, SiMB-4-OH), 7.95 (s, 1H, H-8), 7.35−7.17 (m, 17H, Tr, NHTr and SiMB-6), 6.60 (s, 1H, H-6″), 6.40 (dd, 1H, H-5′, J = 9.7, 15.5 Hz), 6.37 (dd, 1H, SiMB-5, J = 2.3, 8.1 Hz), 6.33 (d, 1H, SiMB-3, J = 2.3 Hz), 5.73 (s, 1H, H-1′), 5.66 (d, 1H, H-6′, J = 15.5 Hz), 5.50 (ddd, 1H, H-8′, J = 4.6, 5.7, 14.9 Hz), 5.30 (d, 1H, SiMB-CH_2, J = 14.3 Hz), 4.97 (d, 1H, MOM-CH_2, J = 6.9 Hz), 4.92 (d, 1H, MOM-CH_2, J = 6.9 Hz), 4.92 (overlapping, 1H, 2′−OH), 4.83 (dt, 1H, H-9′, J = 6.9, 14.9 Hz), 4.66 (s, 2H, MOM-CH_2), 4.65 (overlapping, 1H, H-2′), 4.34 (t, 1H, H-4′, J = 8.6 Hz), 4.30 (d, 1H, SiMB-CH_2, J = 14.3 Hz), 3.77 (s, 3H, OMe), 3.61 (s, 3H, OMe), 3.43 (s, 3H, OMe), 3.43 (overlapping, 1H, H-7′a), 3.37 (s, 3H, OMe), 3.16 (dd, 1H, H-7′b, J = 6.3, 15.4 Hz), 2.36 (t, 1H, H-10′a, J = 10.9 Hz), 2.22 (m, 2H, H-3′and H-10′b); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 159.2, 157.7, 154.4, 151.8, 148.6, 148.0, 147.8, 147.3, 145.1, 138.4, 138.3, 132.6, 131.6, 129.7, 129.2, 128.8, 128.2, 128.0, 127.0, 121.7, 117.3, 114.1, 107.6, 100.2, 99.5, 96.0, 92.7, 86.7, 77.9, 71.7, 61.5, 57.6, 56.4, 55.4, 47.7, 46.8, 31.7, 30.8, 27.3, 22.8, 14.2; ESIMS-LR m/z = 969 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{54}H_{54}O_{10}N_6Na$ 969.3799, found 969.3794.

(−)-*trans*-45b. A mixture of (−)-*trans*-**44b** (15 mg, 0.016 mmol) and CsF (12 mg, 0.080 mmol) in 1,4-dioxane−H_2O (3:1 (v/v), 2 mL) was stirred at 150 °C under microwave irradiation for 90 min. The mixture was concentrated, and the residue was partitioned between $CHCl_3$ (10 mL) and H_2O (5 mL). The organic layer was washed with brine (5 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatpgraphy (0.5 × 5 cm, 3% MeOH in $CHCl_3$) to give (−)-*trans*-**45b** (12 mg, 93%) as a white foam: $[\alpha]^{18}_D$ −144.7 (*c* 0.80, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1H, H-2), 7.94 (s, 1H, H-8), 7.34−7.21 (m, 15H, Tr), 7.06 (br s, 1H, NHTr), 7.04 (br s, 1H, CONH), 6.44 (dd, 1H, H-5′, J = 8.6, 16.0 Hz), 5.75 (d, 1H, H-6′, J = 16.0 Hz), 5.74 (d, 1H, H-1′, J = 2.8 Hz), 5.57 (dt, 1H, H-8′, J = 5.7, 15.5 Hz), 5.24 (br s, 1H, 2′−OH), 5.21 (d, 1H, MOM-CH_2, J = 6.8 Hz), 5.17 (d, 1H, MOM-CH_2, J = 6.8 Hz), 4.81 (overlapping, 1H, H-9′), 4.81 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.77 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.65 (br d, 1H, H-2′, J = 2.8 Hz), 4.42 (t, 1H, H-4′, J = 8.6 Hz), 3.80 (s, 3H, OMe), 3.53 (s, 3H, OMe), 3.49 (s, 6H, OMe × 2), 3.48 (overlapping, 1H, H-7′a), 3.12 (dd, 1H, H-7′b, J = 5.7, 15.5 Hz), 2.40 (t, 1H, H-10′a, J = 10.3 Hz), 2.25 (m, 2H, H-3′ and H-10′b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 154.3, 151.8, 148.7, 148.2, 147.7, 144.9, 139.7, 138.0, 129.1, 128.0, 127.7, 127.6, 127.1, 126.1, 121.6, 113.7, 99.9, 95.6, 92.4, 86.4, 77.6, 71.5, 61.7, 58.0, 56.6, 47.5, 30.8, 29.8, 27.1; ESIMS-LR m/z = 811 [(M + H)$^+$]; ESIMS-HR calcd for $C_{46}H_{47}O_8N_6$ 811.3455, found 811.3450.

***trans*-46.** A solution of *trans*-**45b** (140 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) was treated with Et_3SiH (0.13 mL, 0.85 mmol) and TFA (2 mL) at 0 °C, and the mixture was stirred at room temperature for 2 h. The mixture was concentrated in vacuo to give a crude hydroquinone. A mixture of the crude hydroquinone and Pd/C (100 mg) in MeOH (4 mL) was vigorously stirred under air atmosphere at room temperature for 1 h. The insolubles were filtered off through a Celite pad and washed with hot MeOH. The filtrate was concentrated, and the residue was triturated with MeOH to give *trans*-**46** (42 mg, 52% over two steps) as a yellow solid. The resulting residue was purified by silica gel column chromatography (1 × 6 cm, 8% MeOH in $CHCl_3$) to give *trans*-**46** (31 mg, 38% over two steps) as a yellow solid (total 90% over two steps): ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.03 (br s, 1H, CONH), 8.49 (s, 1H, H-2), 8.33 (s, 1H, H-8), 8.20 (br s, 2H, 6-NH_2), 6.20 (dd, 1H, H-5′, J = 9.2, 15.5 Hz), 6.17 (s, 1H, H-6″), 5.90 (d, 1H, H-1′, J = 1.7 Hz), 5.83 (d, 1H, H-6′, J = 15.5 Hz), 5.80 (br s, 1H, 2′−OH), 5.42−5.33 (m, 2H, H-8′and H-9′), 4.65 (dd, 1H, H-2′, J = 1.7, 6.3 Hz), 4.36 (t, 1H, H-4′, J = 8.6 Hz), 3.94 (s, 3H, OMe), 3.13 (d, 1H, H-7′a, J = 13.8 Hz), 3.01 (dd, 1H, H-7′b, J = 8.1, 13.8 Hz), 2.63 (m, 1H, H-3′), 2.39 (br d, 1H, H-10′a, J = 13.2 Hz), 2.20 (m, 1H, H-10′b); ^{13}C NMR (125 MHz, DMSO-d_6) δ 184.4, 182.9, 167.5, 154.1, 152.7, 148.5, 148.4, 144.5, 142.2, 140.8, 132.7, 128.6, 128.3, 125.4, 118.9, 118.8, 90.3, 85.1, 76.9, 61.3, 46.1, 31.1, 25.8; ESIMS-LR m/z = 477 [(M − H)$^-$]; ESIMS-HR calcd for $C_{23}H_{21}O_6N_6$ 477.1528, found 477.1541.

***cis*-44b.** A solution of *cis*-**43b** (40 mg, 0.034 mmol) in THF (1 mL) was treated with TBAF (1.0 M solution in THF, 85 μL, 0.085 mmol) at room temperature for 10 min. The mixture was concentrated, and the residue was purified by silica gel column chromatography (1 × 6 cm, 3% MeOH in $CHCl_3$) to give *cis*-**44b** (31 mg, 98%) as a white foam: $[\alpha]^{19}_D$ 138.4 (*c* 0.95, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.48 (br s, 1H, HMB-4-OH), 7.93 (s, 1H, H-2), 7.69 (s, 1H, H-8), 7.38 (br s, 1H, NHTr), 7.34−7.18 (m, 16H, Tr and HMB-6), 6.71 (s, 1H, H-6″), 6.37 (dd, 1H, HMB-5, J = 1.7, 8.0 Hz), 6.16 (d, 1H, HMB-3, J = 1.7 Hz), 6.00 (d, 1H, H-6′, J = 16.1 Hz), 5.93 (dt, 1H, H-8′, J = 5.7, 9.2 Hz), 5.89 (s, 1H, H-1′), 5.51 (dd, 1H, H-5′, J = 8.0, 16.1 Hz), 5.38 (d, 1H, HMB-CH_2, J = 14.3 Hz), 5.37 (m, 1H, H-9′), 5.24 (br s, 1H, 2′−OH), 4.87 (s, 2H, MOM-CH_2), 4.70 (d, 1H, MOM-CH_2, J = 5.7 Hz), 4.68 (d, 1H, MOM-CH_2, J = 5.7 Hz), 4.43 (d, 1H, HMB-CH_2, J = 14.3 Hz), 4.42 (overlapping, 1H, H-2′), 4.24 (t, 1H, H-4′, J = 8.6 Hz), 3.62 (s, 3H, OMe), 3.58 (s, 3H, OMe), 3.53 (dd, 1H, H-7′a, J = 5.7, 13.7 Hz), 3.50 (s, 3H, OMe), 3.30 (s, 3H, OMe), 2.97 (dd, 1H, H-7′b, J = 8.6, 13.7 Hz), 2.05 (m, 2H, H-10′), 0.83 (m, 1H, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 158.6, 157.5, 154.0, 152.0, 148.0, 147.2, 146.9, 144.8, 144.5, 136.9, 136.8, 133.7, 131.5, 131.3, 129.8, 129.1, 128.6, 127.9, 127.0, 126.5, 121.1, 117.3, 113.9, 107.6, 100.5, 99.3, 96.1, 93.4, 84.3, 75.1, 71.5, 60.7, 58.1, 56.4, 55.4, 47.7, 46.6, 25.8, 23.1, 21.0; ESIMS-LR m/z = 947 [(M + H)$^+$]; ESIMS-HR calcd for $C_{54}H_{55}O_{10}N_6$ 947.3980, found 947.3974.

***cis*-45b.** A mixture of *cis*-**44b** (30 mg, 0.031 mmol) and CsF (24 mg, 0.15 mmol) in 1,4-dioxane−H_2O (3:1 (v/v), 2 mL) was stirred at 150 °C under microwave irradiation for 60 min. The mixture was concentrated, and the residue was partitioned between $CHCl_3$ (10 mL) and H_2O (5 mL). The organic layer was washed with brine (5 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatpgraphy (0.5 × 5 cm, 3% MeOH in $CHCl_3$) to give *cis*-**45b** (22 mg, 87%) as a white foam. $[\alpha]_D^{18}$ 104.9 (*c* 0.61, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H, H-2), 7.63 (s, 1H, H-8), 7.37 (br s, 1H, CONH), 7.32−7.21 (m, 15H, Tr), 6.99 (br s, 1H, NHTr), 6.87 (s, 1H, H-6″), 5.98 (d, 1H, H-6′, J = 16.3 Hz), 5.95 (m, 1H, H-8′), 5.89 (s, 1H, H-1′), 5.58 (dd, 1H, H-5′, J = 8.2, 16.3 Hz), 5.40 (ddd, 1H, H-9′, J = 2.3, 5.0, 10.4 Hz), 5.10 (d, 1H, MOM-CH_2, J = 6.3 Hz), 5.02 (d, 1H, MOM-CH_2, J = 6.3 Hz), 4.92 (d, 1H, 2′-OH, J = 2.7 Hz), 4.87 (d, 1H, MOM-CH_2, J = 5.9 Hz), 4.82

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(d, 1H, MOM-CH_2, J = 5.9 Hz), 4.52 (t, 1H, H-2′, J = 3.7 Hz), 4.30 (dd, 1H, H-4′, J = 8.2, 10.4 Hz), 3.63 (s, 3H, OMe), 3.55 (overlapping, 1H, H-7′a), 3.54 (s, 3H, OMe), 3.39 (s, 3H, OMe), 3.00 (dd, 1H, H-7′b, J = 9.0, 14.0 Hz), 2.17−2.02 (m, 2H, H-10′), 0.95 (m, 1H, H-3′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 154.2, 152.0, 147.7, 147.5, 147.4, 144.9, 143.7, 137.9, 137.4, 132.1, 129.7, 129.0, 128.9, 128.1, 128.0, 127.1, 124.7, 121.7, 112.1, 100.3, 95.7, 93.5, 84.2, 75.2, 71.5, 60.7, 58.4, 56.6, 47.9, 29.9, 22.9, 21.1; ESIMS-LR m/z = 833 [(M + Na)$^+$]; ESIMS-HR calcd for $C_{46}H_{46}O_8N_6Na$ 833.3275, found 833.3271.

***cis*-46.** A solution of *cis*-**45b** (40 mg, 0.025 mmol) in CH_2Cl_2 (0.5 mL) was treated with Et_3SiH (20 μL, 0.12 mmol) and TFA (0.6 mL) at 0 °C, and the mixture was stirred at room temperature for 3 h. The mixture was concentrated in vacuo to give a crude hydroquinone. A mixture of the crude hydroquinone and Pd/C (20 mg) in MeOH (3 mL) was vigorously stirred under air atmosphere at room temperature for 30 min. The insolubles were filtered off through a Celite pad and washed with hot MeOH. The filtrate was concentrated, and the residue was purified by silica gel column chromatography (1 × 5 cm, 8% MeOH in $CHCl_3$) to give *cis*-**46** (9.6 mg, 79% over two steps) as a yellow solid: ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.0 (br s, 1H, CONH), 8.16 (s, 1H, H-2), 7.87 (s, 1H, H-8), 7.25 (br s, 2H, 6-NH_2), 6.24 (s, 1H, H-6″), 6.09 (dd, 1H, H-5′, J = 8.0, 16.1 Hz), 6.03 (d, 1H, H-6′, J = 16.1 Hz), 5.95 (d, 1H, 2′−OH, J = 5.2 Hz), 5.93 (s, 1H, H-1′), 5.80 (m, 1H, H-8′), 5.48 (br t, 1H, H-9′, J = 10.3 Hz), 4.36 (t, 1H, H-2′, J = 5.2 Hz), 4.20 (dd, 1H, H-4′, J = 8.0, 10.9 Hz), 3.92 (s, 3H, 4″-OMe), 3.38 (dd, 1H, H-7′b, J = 8.0, 13.8 Hz), 2.65 (dd, 1H, H-7′a, J = 8.0, 13.8 Hz), 2.22 (dt, 1H, H-3′, J = 5.2, 10.9 Hz), 2.03 (dt, 1H, H-10′a, J = 4.0, 13.2 Hz), 1.71 (br t, 1H, H-10′b, J = 12.0 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 183.9, 182.9, 168.6, 156.1, 156.0, 152.1, 148.5, 144.5, 139.9, 137.6, 130.6, 130.2, 129.9, 126.4, 119.6, 117.2, 93.2, 83.6, 74.8, 60.8, 47.7, 21.5, 20.0; ESIMS-LR m/z = 477 [(M−H)$^-$]; ESIMS-HR calcd for $C_{23}H_{21}O_6N_6$ 477.1528, found 477.1539.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H, ^{13}C, and ^{31}P NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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