Synthesis of 2-Substituted Polyhydroxytetrahydropyrimidines (*N*-Hydroxy Cyclic Guanidino-Sugars): Transition-State Mimics of Enzymatic Glycosidic Cleavage

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The synthesis of 2-substituted polyhydroxytetrahydropyrimidines as transition-state mimics of enzymatic glycosidic cleavage has been achieved by using guanylation and cyclization methodologies. The D-galacto type *N*-hydroxy cyclic guanidino-sugar **21** was synthesized in six steps from amine **7** and thiourea **14** in an overall yield of 59%. To further derivatize compound **21** to incorporate the leaving group moiety, we have synthesized 2-methylsulfanyl compounds **26**−**29** as key intermediates. The 2-methylsulfanyl group in **29** was displaced with amines, assisted by silver tetrafluoroborate as Lewis acid, to give protected cyclic guanidines **30**−**32** in moderate yields (60−67%). Removal of the protecting groups in **32** gave the D-galacto-type *N*-hydroxy cyclic guanidino-sugar **34**. The key steps in the synthesis of the 6-deoxy-DL-galacto type *N*-hydroxy cyclic guanidino-sugars **49**, **54**, and **64**−**66** involve cyclization of the appropriate acetal intermediates (**45**, **50**, and **58**−**60**) followed by removal of the protecting groups.

Introduction

Inhibitors of glycosidases are useful for the study of the biological functions of oligosaccharides.[1] They are also potential as drugs for the treatment of a variety of carbohydrate-mediated diseases;[2] for example, some glycosidase inhibitors are finding clinical application as anti-HIV,[3] anticancer,[4] antidiabetic,[5] and antiviral agents.[6] Development of new novel structures as glycosidase inhibitors is thus of considerable interest to synthetic chemists.[7]

Polyhydroxylated azaheterocycles having a resonance-stabilized π-system of the amidine[8] or cyclic guanidine type[9] have been developed as glycosidase inhibitors, as these compounds mimic the electronic character and conformation of the transition state of enzymatic glycoside hydrolysis. These enzymatic reactions are thought to proceed through a flattened half-chair (or twisted-boat) transition state with substantial sp^2 character at the anomeric position[10] (Figure 1). We and others[11] have shown that transition-state analogues that are neutral at physiological pH and protonated upon binding are effective inhibitors of glycosidases. Ichikawa and another group[12] have demonstrated that 1-*N*-iminosugars **1** (nitrogen atom at the anomeric position) are highly potent and specific inhibitors of β-glycosidases, whereas DNJ-type iminosugars **2** (nitrogen atom replacing the ring oxygen) are potent inhibitors of α-glycosidases[13] (Figure 2).

In an effort to develop new transition-state analogue inhibitors of glycosidases, we have reported a study of cyclic guanidino-sugars.[11a] We have demonstrated that these inhibitors (**4**−**6**) are pH dependent and that the

(1) (a) Albein, A. D. *Annu. Rev. Biochem*. **1987**, *56*, 497−534. (b) Dwek, R. A. *Chem. Rev*. **1996**, *96*, 683−720.

(2) Hughs, A. B.; Rudge, A. J. *Nat. Prod. Rep*. **1994**, 35−162.

(3) (a) Karpas, A.; Fleet, G. W. J.; Dwek, R. A.; Petursson, S.; Namgoog, S. K.; Ramsden, N. G.; Jacob, G. S.; Rademacher, T. W. *Proc. Natl. Acad. Sci. U.S.A*. **1988**, *85*, 9229−9233. (b) Fleet, G. W. J.; Karpas, A.; Dwek, R. A.; Fellows, L. E.; Tyms, A. S.; Petursson, S.; Namgoong, S. K.; Ramsden, N. G.; Smith, P. W.; Son, J. C.; Wilson, F.; Witty, D. R.; Jacob, G. S.; Rademacher, T. W. *FEBS Lett*. **1988**, *237*, 128−132. (c) Wikler, D. A.; Holan, G. *J. Med. Chem*. **1989**, *32*, 2084−2089. (d) Ratner, L.; Heyden, N. V.; Dedera, D. *Virology* **1991**, *181*, 180−192.

(4) For review on glycosidase inhibitor as anticancer agents, see: Gross, P. E.; Baker, M. A.; Carver, J. P.; Dennis, J. W. *Clin. Cancer Res*. **1995**, *1*, 935−944.

(5) (a) Joubert, P. H.; Venter, C. P.; Joubert, H. F.; Hillebran, I. *Eur. J. Pharmacol*. **1985**, *28*, 705−708. (b) Anzeveno, P. B.; Creemer, L. J.; Daniel, J. K.; King, C.-H.; Liu, P. S. *J. Org. Chem*. **1989**, *54*, 2539−2542. (c) Balfour, J. A.; McTavish, D. *Drugs*, **1993**, *46*, 1025−1054. (d) Truscheit, E.; Frommer, W.; Junge, B.; Müller, L.; Schmidt, D. D.; Wingender, W. *Angew. Chem., Int. Ed. Engl*. **1981**, *20*, 744−761. For reviews on the synthesis of DNJ-based iminosugar inhibitor, see: (e) Look, G. C.; Fotsch, C. H.; Wong, C.-H. *Acc. Chem. Res*. **1993**, *26*, 182−190. (f) Ganem, B. *Acc. Chem. Res*. **1996**, *29*, 340−347. (g) Gijsen, H. J. M.; Qiao, L.; Fitz, W.; Wong, C.-H. *Chem. Rev*. **1996**, *96*, 443−473. (h) Wong, C.-H.; Halcomb, R. L.; Ichikawa, Y.; Kajimoto, Y. *Angew. Chem., Int. Ed. Engl*. **1995**, *34*, 412−432 and 521−546.

(6) (a) Kim, C. U.; Lew, W.; Williams, M. A.; Liu, H.; Zhang, L.; Swaminathan, S.; Bischofberger, N.; Chen, M. S.; Mendel, D. B.; Tai, C. Y.; Laver, W. G.; Stevens, R. C. *J. Am. Chem. Soc*. **1997**, *119*, 681−690. (b) von Itzstein, M.; Wu, W.-Y.; G. B. Kok, G. B.; Pegg, M. S.; Dyason, J. C.; Jin, B.; Phan, T. V.; Smythe, M. L.; White, H. F.; Oliver, S. W.; Colman, P. M.; Varghese, J. N.; Ryan, D. M.; Woods, J. M.; Bethell, R. C.; Hotham, V. J.; Cameron, J. M.; Penn, C. R. *Nature* **1993**, *363*, 418−423.

(7) For some potent designed glycosidase inhibitors and reviews, see: (a) Heightman, T. D.; Vasella, A. T. *Angew. Chem., Int. Ed. Engl*. **1999**, *38*, 750−770. (b) Heightman, T. D.; Ermert, P.; Klein, D.; Vasella, A. *Helv. Chim. Acta* **1995**, *78*, 514−532. (c) Pan, Y.-T.; Kanshal, G. P.; Papandreou, G.; Ganem, B.; Elbein, A. D. *J. Biol. Chem*. **1992**, *267*, 8313−8318.

(8) (a) Hoos, R.; Vasella, A.; Rupitz, K.; Withers, S. G. *Carbohydr. Res*. **1997**, *298*, 291−298. (b) Blériot, Y.; Dintinger, T.; Guillo, N.; Tellier, C. *Tetrahedron Lett*. **1995**, *36*, 5175−5178.

(9) (a) Chan, A. W.-Y.; Ganem, B. *Tetrahedron Lett*. **1995**, *36*, 811−814. (b) Lehmann, J.; Rob, B. *Tetrahedron*: *Asymmetry* **1994**, *5*, 2255. (c) Fotsch, C. H.; Wong, C.-H. *Tetrahedron Lett*. **1994**, *35*, 3481−3484. (10) Schramm, V. L.; Horenstein, B. A.; Klein, P. C. *J. Biol. Chem*. **1994**, *269*, 18259.

(11) (a) Jeong, J.-H.; Murray, B. W.; Takayama, S.; Wong, C.-H. *J. Am. Chem. Soc*. **1996**, *118*, 4227−4234. (b) Legler, G.; Finken, M.-T. *Carbohydr. Res*. **1996**, *292*, 103−115. (c) Blériot, Y.; Genre-Grandpierre, A.; Imberty, A.; Tellier, C. *J. Carbohydr. Chem*. **1996**, *15*, 985−1000. (d) Ermert, P.; Vasella, A.; Weber, M.; Ruoitz, K.; Withers, S. G. *Carbohydr. Res*. **1993**, *250*, 31−43.

(12) (a) Ichikawa, Y.; Igarashi, Y.; Ichikawa, M.; Suhara, Y. *J. Am. Chem. Soc*. **1998**, *120*, 3007−3018. (b) Bols, M. *Acc. Chem. Res*. **1998**, *31*, 1−8.

(13) Legler, G. *Adv. Carbohydr. Chem. Biochem*. **1990**, *48*, 319−384.

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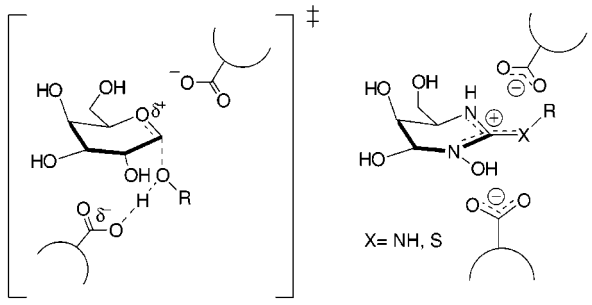


Figure 1. Expected transition state (left) and its mimic (right) in an α-galactosidase reaction. It is proposed that the neutral form of the cyclic guanidino-sugar is accepted by the enzyme followed by protonation from one of the two carboxyl groups to form a tight charge complex.

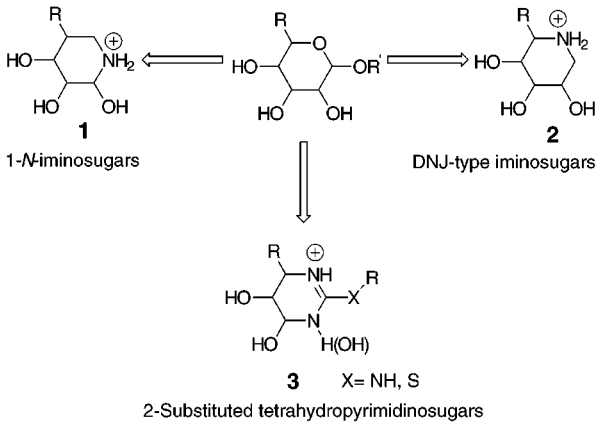


Figure 2. General design strategy of glycosidase inhibitor.

neutral, tetrahydropyrimidine form is the most potent form of the guanidino sugars (Chart 1). 2-Deoxy- and 3-deoxyguanidino-sugars have been reported;[9b,11a] however, these compounds may have an insufficient hydroxyl topography for the targeting of specific glycosidases. A proper transition-state analogue should mimic both the steric and electrostatic properties of the transition state. Here, we describe the synthesis of guanidino sugar **3** (X = NH, see Figure 2) with an extra hydroxyl group on the 3-N-position of the pyrimidyl ring. This extra hydroxyl group may play an important role in mimicking both the steric and electrostatic properties of the transition-state. We also describe the synthesis of other 2-substituted pyrimidino sugars, notably the sulfur analogues (**3**, X = S).

Results and Discussion

First Attempt at the Synthesis of Cyclic 3-*N*-Hydroxyguanidino Sugar (Scheme 1). We began our investigation on the regio- and stereoselectivity of the cyclization reaction of compound **11**. The isothiocyanate **8**, which was made from the amine **7**,[14] was transformed into thiourea **9** by heating it with benzylamine in toluene. Guanylation of the thiourea **9** with *O*-benzylhydroxylamine followed by desilylation of the guanidine **10** with TBAF gave the alcohol **11** in 82% overall yield. Oxidation of this alcohol **11** under Swern conditions gave a complex mixture as visualized by TLC, and no identifiable products were isolated. Using Ley's oxidation protocol,[15] the cyclization proceeded smoothly to the undesired lactam **12** in moderate yield; however, none of the desired product **13** was observed (Scheme 1). The structure of **12** was confirmed by crystal structure analysis (Figure 3).

Synthesis of the D-Galacto-Type Pyrimidino Sugars 21, 34, and 40 (Schemes 2−4). To avoid cyclization through the nitrogen atom, which is attached to the benzyl group, we have synthesized compound **16**, a carbamate derivative of **11**. Guanylation of thiourea **14**[16] with amine **7** under standard conditions, followed by removal of the TBDPS group in **15** with TBAF, gave the alcohol **16**. Dess−Martin oxidation[17] of the alcohol **16** at room temperature for 6 h gave the hemiaminal **17** as a single isomer (J_{4-5} = 2.5 Hz). No lactam was observed. The relative configuration of **17** was not readily determined from the ^{1}H NMR coupling constants due to the presence of flattened chair conformations. We therefore determined the structure of **17** by X-ray structural analysis (Figure 3). Protection of **17** with an acetyl or a TES group gave compounds **18** and **19** in 82% and 79% yield, respectively. An attempt to remove the CBz group in **18** or **19** without affecting the benzyl group by hydrogenolysis in a mixture of ethyl acetate/Et_3N was unsuccessful. The reaction was slow, and the starting material was recovered in moderate yield. However, when EtOAc or AcOH was used as the solvent, both of the benzyl and CBz groups in **17** were removed to give the acetonide **20** as a single isomer (J_{4-5} = 2.4 Hz). Attempts to derivatize **20** by alkylation were unsuccessful; there was no reaction between benzyl bromide and the guanidine **20** at room temperature or at reflux.[18a,b] The isopropylidene group in **20** was removed with aqueous HCl in methanol to give the D-galacto-type pyrimidino sugar **21** in 59% yield (Scheme 2).

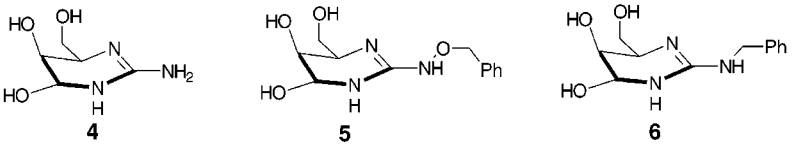
Because of the difficulty of derivatizing the guanidine **20**, we decided to seek a different method (Scheme 3). The isothiocyanate **8** was converted into its thiourea **22**, followed by S-alkylation with iodomethane, to give compound **23** in 97% yield. Removal of the TBDPS group in **23** with TBAF followed by oxidation of the alcohol **24** with Dess−Martin reagent gave the cyclic hemiaminal **25**. The ^{1}H NMR spectrum of **25** shows small $J_{4,5}$ and $J_{5,6}$ values (2.5−3.0 Hz), which is indicative of a gauche disposition for the corresponding protons. The (4*R*)-^{5}E configuration of **25** (Figure 4) was supported by the ^{1}H NMR spectrum in $CDCl_3$ that showed the H-4 signal as a doublet at δ_H 4.70 with a coupling constant of 2.5 Hz, similar to that of cyclic hemiaminal **17** (δ 4.72, J 2.5 Hz).

Treatment of **25** with acetic anhydride in pyridine gave the acetate **26** in 77% yield. Guanylation of **26** with 2-methoxyethylamine in the presence of silver tetrafluoroborate only gave a trace of the desired product. A similar observation was obtained with the MOM derivative **27**. Interestingly, starting with the triethylsilyl derivative **29**, guanylation with 2-methoxyethylamine proceeded smoothly to give the protected guanidine **32**

(14) Compound **7** was prepared in five steps from 2-butene-1,4-diol; see ref 11a.

(15) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639.
(16) Jirgensons, A.; Kums, I.; Kauss, V.; Kalvins, I. *Synth. Commun.* **1997**, *27*, 315−322.
(17) Dess, D. B.; Martin. J. C. *J. Org. Chem.* **1983**, *48*, 4156.
(18) (a) Stähle, H.; Daniel, H. *J. Med. Chem.* **1980**, *23*, 1217−1222. (b) Augstein, J.; Green, S. M.; Monro, A. M.; Potter, G. W. H.; Worthing, C. R.; Wrigley, T. I. *J. Med. Chem.* **1965**, *8*, 446. (c) Ritter, J.; Gleiter, R.; Irngartinger, H.; Oeser, T. *J. Am. Chem. Soc.* **1997**, *119*, 10599−10607. (d) Lehmann, J.; Rob, B.; Wagenknecht, H.-A. *Carbohydr. Res.* **1995**, *278*, 167−180.

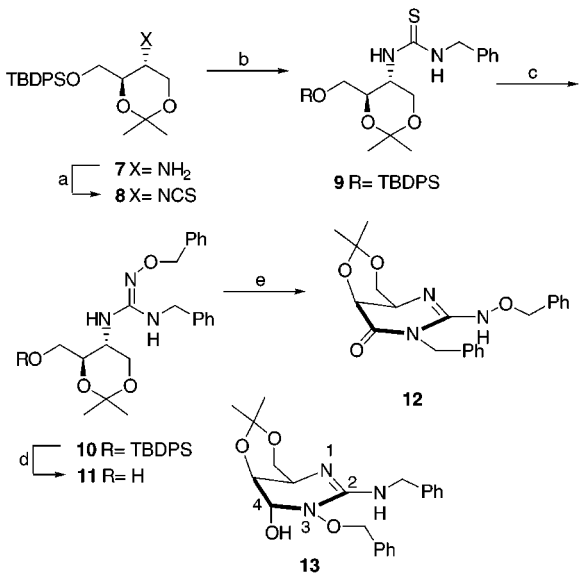
Chart 1. Inhibition of α- and β-Galactosidases with Known Guanidino-Sugars



		4	**5**	**6**
α-Galactosidase	K_i (μM)	480[a]	6.4[b]	4.9[b]
β-Galactosidase	K_i (μM)	N.D	24.7[b]	62.0[b]

[a] See ref 9c. [b] See ref 11a.

Scheme 1[a]



[a] Reagents and conditions: (a) 1,1′-thiocarbonyldiimidazole, EtOAc, rt/12 h; (b) $BnNH_2$, $PhCH_3$, 90 °C/6 h; (c) $BnONH_2HCl$, $HgCl_2$, TEA, DMF, rt/12 h; (d) TBAF, THF, rt/1 h; (e) TPAP, NMO, CH_2Cl_2, rt/4 h.

in 65% yield. Similar yields of **30** and **31** were obtained when benzylamine and ethanolamine were used as nucleophiles. Debenzylation of **32** under standard conditions gave the *N*-hydroxy compound **33**. Finally, removal of both TES and isopropylidene groups in **33** with trifluoroacetic acid gave the D-galacto-type pyrimidino sugar **34** in 71% yield (Scheme 3).

The synthesis of 2-substituted pyrimido sugar **40** began with conversion of the azide **35**[11a] to the amine, which without purification was treated with benzoyl isothiocyanate to give thiourea **36**. The benzoyl-protecting group in **36** was removed with KOH in methanol and reprotected with the BOC group to give **38** in 77% yield. Alkylation of thiourea **38** with iodomethane followed by cyclization with trifluoroacetic acid gave the pyrimindo sugar **40** in good yield (two steps, 79%, Scheme 4). A gauche arrangement of the hydrogen atoms at C-4 and C-5 with a coupling constant $J_{4,5}$ of 3.0 Hz proves the ^5E conformation in compound **40**, with pseudoanomeric 4-OH in an axial disposition. This is in agreement with Gleiter et al.,[18c] who have postulated that the axial orientation of the nitrogen lone pair orbital increases the axial preferences for the pseudoanomeric hydroxyl group at C-4 in a six membered azaheterocycles.

Synthesis of the 6-Deoxy-DL-galacto-Type Pyrimidino Sugars 49, 54, and 64−66 (Scheme 5). The synthesis of **49** began with the alcohol **41**, which was prepared by a known procedure.[19] Protection of the alcohol **41** with TBDMS followed by reduction of the azide **42** gave amine **43**. Without purification, **43** was subjected to benzoyl isothiocyanate, from which thiourea **44** was formed. Guanylation of **44** with *O*-benzylhydroxylamine and mercuric chloride[11a] in DMF gave protected guanidine **45** in excellent yield (93%). Cyclization of **45** to cyclic guanidine **46** was achieved with trifluoroacetic acid and desilylation of compound **46** with TBAF gave diol **47**. An attempt to remove the benzyl group from **47** by hydrogenolysis gave a complex mixture, and no identifiable products were isolated. However, when the diol **47** was converted to the acetate **48**, the benzyl group was easily be removed. Finally, the acetyl group was removed with ammonia in methanol to give the 6-deoxy-DL-galacto-type pyrimidino sugar **49** (Scheme 5). The ^1H NMR spectrum of **49** confirmed that the configuration was 4,5-trans. The coupling constant *J* (4, 5) was small (2.5 Hz), indicating a trans-diequatorial configuration.

The synthesis of **54** began with guanylation of thiourea **14**[16] with amine **43** to give the protected guanidine **50**. Cyclization of this compound with trifluoroacetic acid gave the hemiaminal **51** in 78% yield. The regio- and stereochemistry of **51** was confirmed by X-ray analysis (Figure 3). Protection of the secondary alcohol in **51** with the TES group followed by debenzylation gave the *N*-hydroxy compound **53** in 58% yield. Finally, both of the silyl protecting groups in **53** were removed with aqueous HF in acetonitrile to afford the 6-deoxy-DL-galacto-type pyrimidino sugar **54** in 75% yield (Scheme 6).

The synthesis of **64−66** began with isothiocyanate **55**, which was prepared from the amine **43** in two steps (Scheme 7). Compound **55** was heated to reflux with ammonium hydroxide in ethanol to yield thiourea **56**, which was then protected with the BOC group to give **57** in 79% yield. Alkylation of thiourea **57** with iodomethane, 1-iodopropane, and benzyl bromide gave the corresponding S-alkylated compounds **58−60**. Treatment of these compounds with trifluoroacetic acid for 12 h gave the cyclized products **61−63** in moderate yield (54−76%). Finally, removal of the TBDMS group from **61−63** using aqueous HF in acetonitrile gave the 6-deoxy-DL-galacto-type pyrimidino sugars **64−66** (52−62%) as water-soluble solids. The stereochemical assignment of hemiaminals **64−66** was confirmed by comparing the NMR spectra of other hemi-aminals (**12**, **17**, and **51**) that have been determined by X-ray structural analysis. The ^1H NMR spectra of **64−66** showed small coupling constants (2.5−3.0 Hz) between H4, H5, and H6, indicating that H4 and H5 protons are equatorial and H6 is axial.

A preliminary biological evaluation was carried out on compounds **21**, **34**, **40**, **49**, **54**, and **64−66**. The com-

(19) Straub, A.; Effenberger, F.; Franz, P. *J. Org. Chem.* **1990**, *55*, 3926−3932.

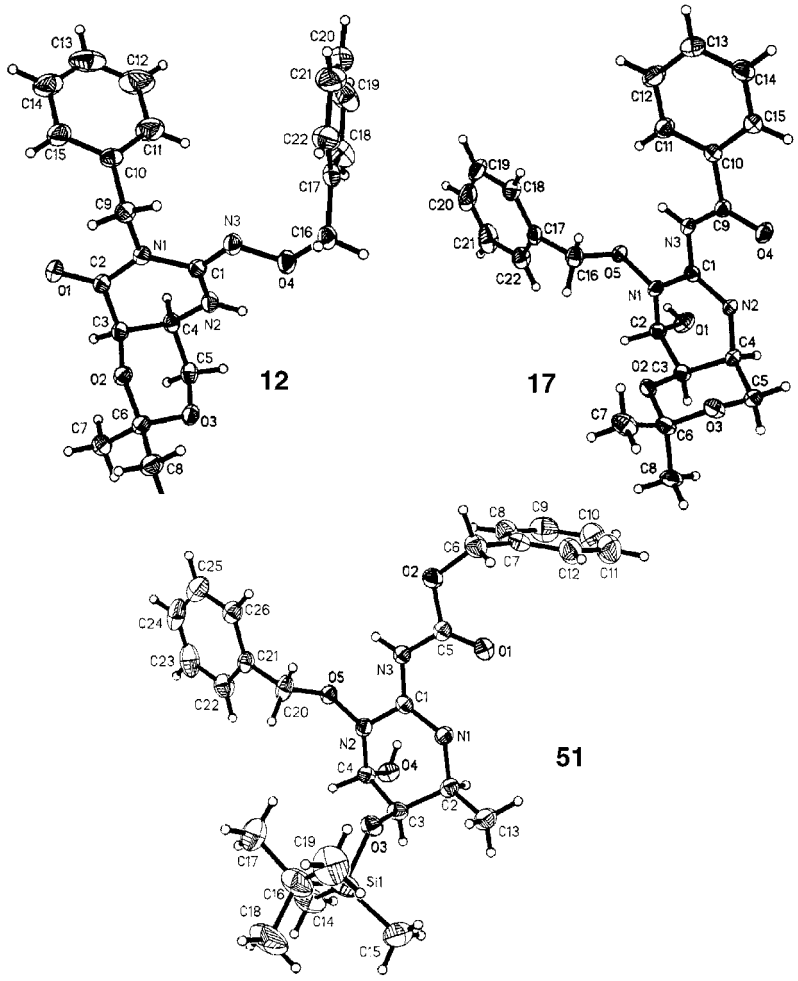
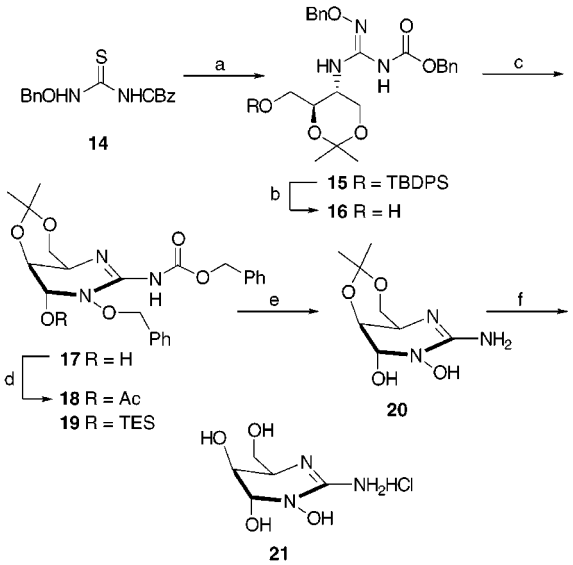


Figure 3. ORTEP diagram of compounds **12**, **17**, and **51**.

Scheme 2[a]



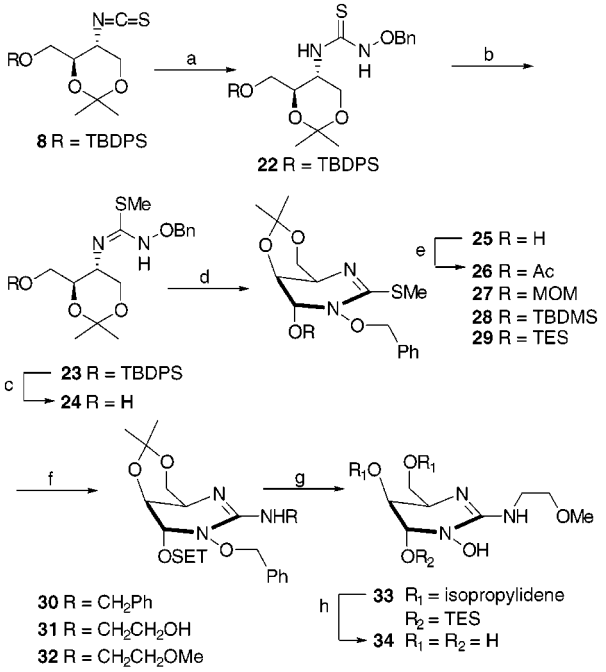
[a] Reagents and conditions: (a) **7**, $HgCl_2$, TEA, DMF, rt/24 h; (b) TBAF, THF, rt/30 min; (c) Dess−Martin, CH_2Cl_2, rt/6 h; (d) Ac_2O, Py, rt/12 h or TESOTf, 2,6-lutidine, CH_2Cl_2, rt/1 h; (e) H_2/Pd−C, AcOH, H_2O, rt/2 h; (f) 2.5 *N* HCl, MeOH, rt/24 h.

pounds were tested as inhibitors of α- and β-galactosidases and α-fucosidase, but none of them exhibited any significant activity. Compound **40** and compounds **64**−**66** showed moderate activity against the α-fucosidase from bovine kidney (compound **40**, IC_{50} 500 μM; compound **64**, IC_{50} 46 μM; compound **65**, IC_{50} 140 μM and compound **66**, IC_{50} 230 μM). Even though these guanidino sugars have sufficient hydroxyl topography for targeting specific glycosidases and they have proper conformation as transition-state analogue,[18d] it is unclear why they are weak inhibitors. One possibility is that they are either highly charged or lack an appropriate leaving group. Work is in progress to further investigate this issue. The chemistry described here is, however, useful for the synthesis of this series of structures.

Experimental Section

General Methods. Tetrahydrofuran (THF), toluene, and diethyl ether (Et_2O) were distilled over sodium/benzophenone, methylene chloride (CH_2Cl_2), and acetonitrile (CH_3CN) over calcium hydride. Reagentsof commercial quality were purchased and used without further purification unless otherwise stated. All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel 60 F_{254} glass plates using UV light (254 nm) as visualizing agent and a yellow solution containing $Ce(NH_4)_2(NO_3)_6$ (0.5 g) and $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (24.0 g) in 6% H_2SO_4 (500 mL) and heat as developing agent. Column chromatography was performed on silica gel 60 Geduran (35−75 μm, EM Science) or reversed-phase silica gel LiChroprep RP-18 (EM Science). Inhibition studies were carried out on coffee bean (CB) α-galactosidase, *Aspergillus niger* α-galactosidase, *A. niger* β-galactosidase, and bovine kidney α-fucosidase. Libera-

Scheme 3[a]



[a] Reagents and conditions: (a) $BnONH_2$, $PhCH_3$, 90 °C/6 h; (b) MeI, NaH, EtOH, rt/30 min; (c) TBAF, THF, rt/30 min; (d) Dess−Martin, CH_2Cl_2, rt/4 h; (e) Ac_2O, Py, rt/12 h; MOMCl, NaH, THF, rt/12 h; TBDMSOTf or TESOTf, 2,6-lutidine, CH_2Cl_2, rt/1 h; (f) $BnNH_2$ or 2-aminoethanol or 2-methoxethylamine, $AgBF_4$, TEA, CH_3CN, rt/2 days; (g) H_2/Pd−C, EtOAc, rt/2 h; (h) TFA, H_2O, CH_2Cl_2, rt/12 h.

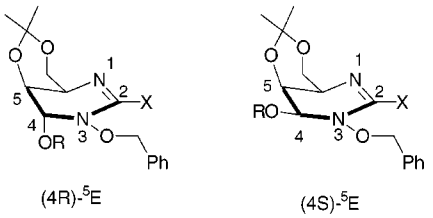


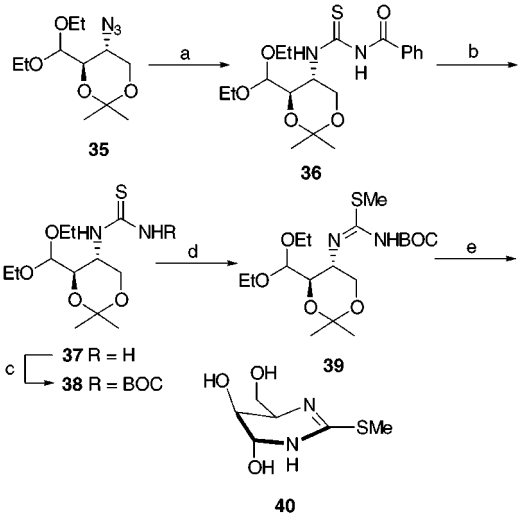
Figure 4. Flattened-chair or envelope conformers for 2-substituted tetrahydropyrimidines.

tion of *p*-nitrophenolate was monitored at 400 nm on a Beckman DU-6 spectrophotometer.

Compound 8. To a solution of 1,1′-thiocarbonyldiimidazole (77 mg, 0.43 mmol) in EtOAc (2 mL) was added a solution of amine **7**[14] (172 mg, 0.43 mmol) in EtOAc (2 mL). The reaction mixture was stirred at room temperature for 12 h. After dilution with EtOAc (10 mL), the reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (9:1) as an eluent to give **8** (160 mg, 84%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (s, 9H), 1.40 (s, 3H), 1.41 (s, 3H), 3.59 (q, J = 1.8 Hz, 1H), 3.67−3.76 (m, 2H), 4.00 (dd, J = 12.2 Hz, 1.7 Hz, 1H), 4.04 (m, 1H), 4.08 (dd, J = 12.4 Hz, 1.8 Hz, 1H), 7.39−7.44 (m, 6H), 7.65−7.68 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.5, 19.2, 26.8, 28.9, 52.6, 62.8, 63.9, 71.1, 99.2, 127.8, 127.9, 129.8, 129.9, 132.6, 133.0, 135.5, 135.6; HRMS calcd for $C_{24}H_{31}NO_3SSiCs$ 574.0848, found 574.0830.

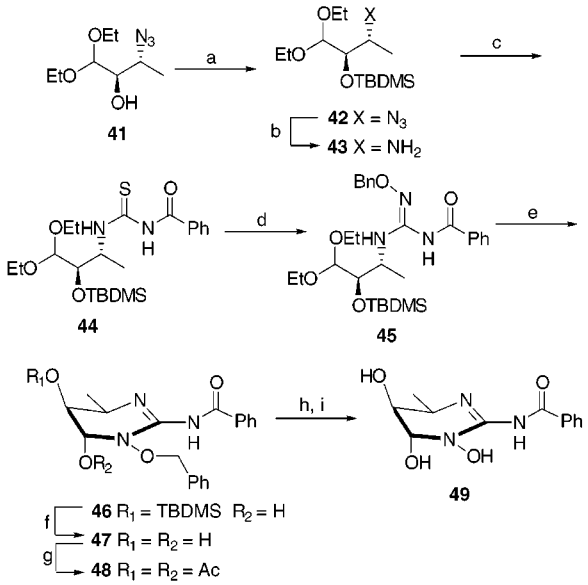
Compound 9. To a solution of benzylamine (79μL, 0.72 mmol) in EtOAc (1 mL) was added isothiocyanate **8** (154 mg, 0.36 mmol) in $PhCH_3$ (1 mL). The reaction mixture was stirred at 90 °C for 6 h. The reaction mixture was allowed to cool to room temperature, washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (8:2) as an eluent to give **9** (157 mg, 82%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 9H), 1.26 (s, 3H), 1.33 (s, 3H), 3.45 (m, 1H), 3.59 (m, 1H), 3.82 (dd, J = 12.0 Hz, 1.5 Hz, 1H), 3.90 (d, J = 11.0 Hz, 1H), 4.42 (m, 2H), 7.18−7.24 (m, 4H), 7.34−7.43 (m, 7H), 7.65−7.66 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.3, 19.0, 26.7, 47.8, 49.0, 60.3, 63.3, 64.3, 71.9, 99.2, 127.4, 127.5, 127.6, 128.7, 129.6, 133.1, 135.5, 135.6, 181.8; HRMS (FAB) calcd for $C_{31}H_{40}N_2O_3SSiCs$ 681.1583, found 681.1558.

Scheme 4[a]



[a] Reagents and conditions: (a) H_2/Pd−C, EtOH, rt/6 h, PhCONCS, EtOAc, rt/12 h; (b) KOH, MeOH, rt/1 h; (c) BOC_2O, DMAP, Et_3N, CH_2Cl_2, rt/2 h; (d) MeI, NaH, EtOH, rt/12 h; (e) TFA, CH_2Cl_2, H_2O, rt/12 h.

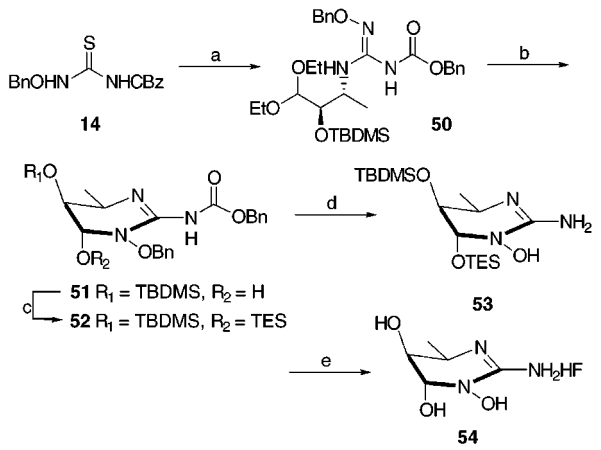
Scheme 5[a]



[a] Reagents and conditions: (a) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, rt/1 h; (b) H_2/Pd−C, EtOAc, rt/2 h; (c) PhCONCS, rt/4 h; (d) $BnONH_2HCl$, $HgCl_2$, TEA, DMF, rt/24 h; (e) TFA, H_2O, CH_2Cl_2, rt/12 h; (f) TBAF, THF, rt/30 min; (g) Ac_2O, Py, rt/12 h; (h) H_2/Pd−C, EtOH, rt/2 h; (i) NH_3, MeOH, rt/6 h.

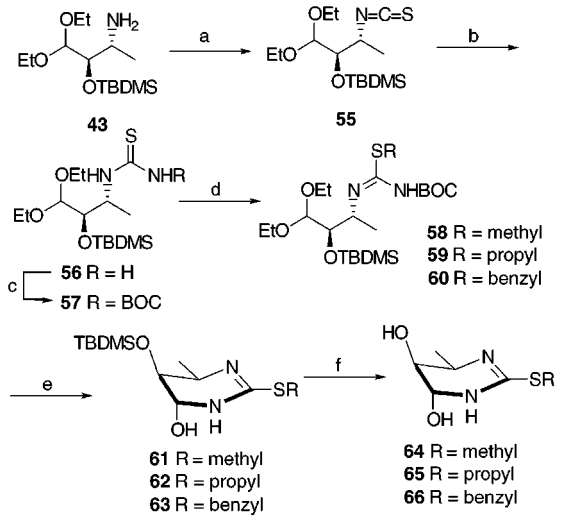
Compound 10. Mercuric chloride (241 mg, 0.89 mmol) was added in one portion to a solution of thiourea **9** (442 mg, 0.81 mmol), triethylamine (560 μL, 3.19 mmol), and *O*-benzylhydroxylamine hydrochloride (227 mg, 1.43 mmol) in DMF (6 mL) at 0 °C. The color of the reaction mixture changed to dark yellow, and the reaction was then warmed to room temperature. After 12 h, a combination of brine solution and EtOAc were added to the reaction. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with

Scheme 6[a]



[a] Reagents and conditions: (a) **43**, $HgCl_2$, TEA, DMF, rt/24 h; (b) TFA, H_2O, CH_2Cl_2, rt/24 h; (c) TESOTf, 2,6-lutidine, CH_2Cl_2, rt/1 h; (d) H_2/Pd−C, EtOAc, rt/2 h; (e) HF (49% in water), CH_3CN, rt/2 h.

Scheme 7[a]



[a] Reagents and conditions: (a) 1,1′-thiocarbonyldiimidazole, EtOAc, rt/12 h; (b) NH_4OH, EtOH, reflux/6 h; (c) BOC_2O, DMAP, TEA, CH_2Cl_2, rt/2 h; (d) MeI or PrI or BnBr, NaH, THF, rt/12 h; (e) TFA, H_2O, CH_2Cl_2, rt/12 h; (f) HF (49% in water), CH_3CN, rt/2 h.

an aqueous solution of $NaHCO_3$, filtered through Celite, dried with $MgSO_4$, and concentrated in vacuo to afford a pale yellow oil. The crude product was purified by flash chromatography on silica gel using hexanes/EtOAc (2:1) as an eluent to give **10** (350 mg, 68%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.26 (s, 3H), 1.30 (s, 3H), 3.52 (dd, J = 8.0 Hz, 4.8 Hz, 1H), 3.59 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 3.67−3.73 (m, 2H), 3.81 (dd, J = 9.6 Hz, 1.2 Hz, 1H), 3.89 (dd, J = 9.2 Hz, 1.2 Hz, 1H), 4.00−4.02 (m, 1H), 4.05−4.10 (m, 1H), 4.75 (d, J = 8.8 Hz, 1H), 4.82 (d, J = 8.8 Hz, 1H), 5.41 (t, J = 4.8 Hz, 1H), 7.13−7.43 (m, 14H), 7.53−7.57 (m, 2H), 7.66−7.69 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 19.1, 26.8, 29.3, 44.5, 45.5, 63.5, 63.8, 72.3, 75.4, 98.8, 126.6, 127.5, 127.6, 127.8, 128.2, 128.5, 128.7, 129.5, 129.6, 129.8, 130.0, 133.6, 135.4, 135.5, 135.7, 138.7, 155.1; HRMS (FAB) calcd for $C_{38}H_{48}N_3O_4Si$ 638.3414, found 638.3436.

Compound 11. A solution of silyl ether **10** (166 mg, 0.26 mmol) in dry THF (2 mL) was treated with *n*-Bu_4NF (TBAF, 520 μL of a 1 M solution in THF, 0.52 mmol) and stirred at 25 °C for 1 h. After dilution with EtOAc (10 mL), water (5 mL) was added. The organic layer was separated, washed with brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (2:8) as an eluent to give **11** (86 mg, 82%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.10 (s, 3H), 1.37 (s, 3H), 3.19 (dd, J = 11.5, 9.5 Hz, 1H), 3.36 (dd, J = 11.5, 5.0 Hz, 1H), 3.59 (dt, J = 21.0, 12.5, 2.0 Hz, 2H), 3.96 (dq, J = 15.0, 9.5, 5.0, 1.0 Hz, 1H), 4.01 (dd, J = 12.0, 2.5 Hz, 1H), 4.05 (d, J = 10.0 Hz, 1H), 4.26 (dd, J = 15.5, 5.5 Hz, 1H), 4.30 (dd, J = 15.5, 6.5 Hz, 1H), 4.79 (d, J = 11.0 Hz, 1H), 4.82 (d, J = 11.0 Hz, 1H), 5.59 (t, J = 6.0 Hz, 1H), 7.25−7.27 (m, 3H), 7.32−7.40 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 29.2, 44.2, 45.5, 60.2, 65.3, 71.5, 75.6, 98.5, 126.6, 127.7, 127.8, 128.3, 128.6, 128.9, 137.6, 138.1, 156.1; HRMS (FAB) calcd for $C_{22}H_{30}N_3O_4$ 400.2236, found 400.2247.

Compound 12. To a solution of the alcohol **11** (57 mg, 0.14 mmol) and NMO (25 mg, 0.21 mmol) in dry dichloromethane (1 mL) was added TPAP (3 mg, 0.05 equiv.). The reaction mixture was stirred at room temperature for 4 h. After dilution with EtOAc (5 mL), water (5 mL) was added. The organic layer was separated, washed with brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (1:1) as an eluent to give **12** (32 mg, 57%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 3H), 1.49 (s, 3H), 3.31 (t, J = 1.5 Hz, 1H), 3.78 (dd, J = 13.0, 2.0 Hz, 1H), 4.07 (dd, J = 13.0, 2.5 Hz, 1H), 4.50 (t, J = 2.0 Hz, 1H), 4.92 (d, J = 14.0 Hz, 1H), 4.94 (d, J = 12.0 Hz, 1H), 4.97 (d, J = 15.0 Hz, 1H), 4.98 (d, J = 11.5 Hz, 1H), 5.22 (s, 1H), 7.21−7.23 (m, 4H), 7.26−7.34 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1, 28.5, 43.8, 44.3, 61.1, 67.9, 76.0, 99.4, 127.2, 127.8, 128.1, 128.3, 128.5, 128.6, 137.0, 137.9, 147.8, 163.8; HRMS (FAB) calcd for $C_{22}H_{26}N_3O_4$ 396.2080, found 396.2090.

Compound 15. Mercuric chloride (176 mg, 0.65 mmol) was added in one portion to a solution of thiourea **14**[16] (186 mg, 0.59 mmol), triethylamine (24 μL,1.76 mmol), and the crude amine **7** (235 mg, 0.59 mmol) in DMF (14 mL) at 0 °C. The color of the reaction mixture changed to dark yellow, and the reaction was then warmed to room temperature. After 24 h, a combination of brine solution and EtOAc was added to the reaction. The aqueous layer was extracted with EtOAc. The combined organic layers were wash with 1 M sodium bicarbonate solution, filtered through Celite, dried with $MgSO_4$, and concentrated in vacuo to afford a pale yellow foam. The crude product was purified by flash chromatography on silica gel using hexanes/EtOAc (1:1) as an eluent to give **15** (350 mg, 87%) as a colorless foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.40 (s, 3H), 1.43 (s, 3H), 3.65 (dd, J = 10.1, 5.8 Hz, 1H), 3.73−3.80 (m, 2H), 3.91 (ABq, J = 21.3, 11.8 Hz, 2H), 4.12 (t, J = 5.9 Hz, 1H), 4.73 (d, J = 11.4 Hz, 1H), 4.80 (d, J = 11.4 Hz, 1H), 5.10 (ABq, J = 15.0, 2.8 Hz, 1H), 6.93 (bs, 1H), 7.24−7.42 (m, 16H), 7.64−7.70 (m, 4H), 7.88 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.6, 19.1, 26.8, 29.4, 44.4, 63.2, 63.3, 67.5, 71.7, 75.7, 98.9, 127.5, 127.5, 127.6, 127.8, 128.2, 128.5, 128.6, 128.6, 129.5, 129.6, 133.4, 135.0, 135.4, 135.6, 135.7, 137.6, 147.6, 152.4; HRMS (FAB) calcd for $C_{39}H_{47}N_3O_6SiCs$ 814.2288, found 814.2256.

Compound 16. A solution of silyl ether **15** (420 mg, 0.61 mmol) in dry THF (10 mL) was treated with *n*-Bu_4NF (TBAF, 1.22 mL of a 1 M solution in THF, 1.22 mmol) and stirred at 25 °C for 30 min. After dilution with EtOAc (10 mL), water (10 mL) was added. The organic layer was separated, washed with brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (3:7) as an eluent to give **16** (160 mg, 59%) as a colorless foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 3H), 1.46 (s, 3H), 3.37 (dq, J = 21.0, 11.5, 9.5, 4.5 Hz, 1H), 3.47 (dt, J = 22.0, 11.5, 5.5 Hz, 1H), 3.61 (dd, J = 9.0, 1.5 Hz, 1H), 3.81 (dd, J = 12.0, 1.5 Hz, 1H), 4.05 (dq, J = 14.5, 9.0, 5.6 Hz, 1.0 Hz, 1H), 4.11 (d, J = 2.0 Hz, 1H), 4.13 (d, J = 2.0 Hz, 1H), 4.58 (dd, J = 10.5, 5.0 Hz, 1H), 4.80 (ABq, J = 17.5, 11.0 Hz, 2H), 5.16 (ABq, J = 14.5, 12.0 Hz, 2H), 7.30−7.40 (m, 10H), 7.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.5, 29.5, 44.8, 60.7, 64.5, 67.9, 71.7, 75.9, 98.8, 128.1, 128.4, 128.6, 128.7, 128.7, 134.8, 136.9, 149.5, 152.6; HRMS (FAB) calcd for $C_{23}H_{30}N_3O_6$ 444.2135, found 444.2120.

Compound 17. To a solution of the alcohol **16** (160 mg, 0.36 mmol) in dry dichloromethane (3 mL) was added Dess−Martin

reagent (183 mg, 0.43 mmol). The reaction mixture was stirred at room temperature for 6 h. After dilution with EtOAc (20 mL), water (10 mL) was added. The organic layer was separated, washed with aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (1:1) as an eluent to give **17** (120 mg, 75%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (s, 3H), 1.40 (s, 3H), 2.72 (bs, 1H), 3.68 (d, J = 13.0 Hz, 1H), 3.89 (dd, J = 13.0, 2.0 Hz, 1H), 4.00 (t, J = 2.5 Hz, 1H), 4.63 (d, J = 10.0 Hz, 1H), 4.72 (d, J = 2.5 Hz, 1H), 4.94 (d, J = 10.0 Hz, 1H), 5.09 (d, J = 13.0 Hz, 1H), 5.29 (d, J = 13.0 Hz, 1H), 7.20−7.30 (m, 5H), 7.34−7.37 (m, 3H), 7.47−7.48 (m, 2H), 8.80 (bs, 1H).

Compound 18. A solution of compound **17** (20 mg, 0.05 mmol) in dry pyridine (0.5 mL) was treated with acetic anhydride (0.5 mL) and stirred at room temperature for 12 h. Evaporation of the reaction mixture, followed by purification of the crude product using hexanes/EtOAc (6:4) as an eluent, gave acetate **18** (18 mg, 82%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 3H), 1.42 (s, 3H), 2.02 (s, 3H), 3.36 (m, 1H), 3.85 (dd, J = 13.0, 2.0 Hz, 1H), 4.03 (t, J = 2.5 Hz, 1H), 4.06 (dd, J = 13.0, 2.0 Hz, 1H), 5.04 (ABq, J = 25.5, 11.0 Hz, 2H), 5.18 (ABq, J = 24.5, 12.5 Hz, 2H), 5.94 (d, J = 3.5 Hz, 1H), 7.33−7.37 (m, 6H), 7.44−7.48 (m, 4H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 20.9, 29.0, 42.9, 61.7, 63.6, 66.9, 78.2, 80.5, 98.9, 127.6, 127.9, 128.3, 128.6, 130.1, 134.8, 137.2, 158.7, 164.5, 169.0; HRMS (FAB) calcd for $C_{25}H_{30}N_3O_7$ 484.2084, found 484.2069.

Compound 19. A solution of the alcohol **17** (100 mg, 0.23 mmol) and 2,6-lutidine (132 μL, 1.13 mmol) in dichloromethane (3 mL) at 0 °C was treated with triethylsilyl trifluoromethanesulfonate (205 μL, 0.91 mmol). The reaction mixture was allowed to warm to 25 °C and stirred for 1 h. After dilution with EtOAc (10 mL), the reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (1:1) as an eluent to give **19** (100 mg, 79%) as a colorless foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.58 (m, 6H), 0.87 (t, J = 8.0 Hz, 9H), 1.41 (s, 3H), 1.42 (s, 3H), 3.41 (d, J = 2.0 Hz, 1H), 3.85 (dd, J = 13.0, 1.5 Hz, 1H), 3.86 (d, J = 3.5 Hz, 1H), 4.06 (dd, J = 13.0, 2.0 Hz, 1H), 4.60 (d, J = 3.5 Hz, 1H), 4.94 (d, J = 11.5 Hz, 1H), 5.11 (d, J = 11.0 Hz, 1H), 5.17 (ABq, J = 20.0, 12.5 Hz, 2H), 7.26−7.29 (m, 1H), 7.31−7.36 (m, 5H), 7.44−7.47 (m, 4H), 9.31 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.5, 6.6, 18.5, 29.1, 42.5, 62.2, 66.4, 66.7, 78.1, 81.6, 98.3, 127.5, 127.9, 128.2, 128.2, 128.4, 130.3, 135.2, 137.5, 158.5, 164.6; HRMS (FAB) calcd for $C_{29}H_{41}N_3O_6SiCs$ 688.1819, found 688.1844.

Compound 20. A mixture of silyl ether **19** (94 mg, 0.17 mmol) and palladium on carbon (10%, 10 mg) in acetic acid/water (9:1, 1 mL) was vigorously stirred under an atmosphere of H_2 at room temperature for 2 h, the reaction mixture was filtered through a Celite pad, and the filter cake was washed with methanol. The combined filtrates were concentrated to give compound **20** (25 mg, 68%) as a white solid: ^{1}H NMR (400 MHz, CD_3OD) δ 1.31 (s, 3H), 1.49 (s, 3H), 3.32 (m, 1H), 3.82 (dd, J = 12.9, 1.6 Hz, 1H), 4.17 (m, 1H), 4.18 (dd, J = 12.9, 1.7 Hz, 1H), 4.76 (d, J = 2.4 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 18.8, 29.6, 43.4, 62.5, 67.8, 83.4, 99.8, 151.2; HRMS (FAB) calcd for $C_8H_{16}N_3O_4$ 218.1141, found 218.1138.

Compound 21. A solution of the acetonide **20** (25 mg, 0.12 mmol) in MeOH (1 mL) was treated with 2.5 N HCl (0.5 mL). The reaction mixture was stirred at room temperature for 24 h. Removal of excess solvent to dryness affords compound **21** (12 mg, 59%) as a pale yellow solid: ^{1}H NMR (500 MHz, CD_3OD) δ 3.60−3.63 (m, 1H), 3.72 (dd, J = 10.5, 8.0 Hz, 1H), 3.79 (dd, J = 11.0, 5.5 Hz, 1H), 3.90 (t, J = 3.0 Hz, 1H), 4.92 (d, J = 3.0 Hz, 1H); HRMS (FAB) calcd for $C_5H_{12}N_3O_4$ 178.0828, found 178.0826.

Compound 22. A mixture of isothiocyanate **8** (839 mg, 1.90 mmol) and *O*-benzylhydroxylamine (234 mg, 1.90 mmol) in dry toluene (6 mL) was stirred at 90 °C for 6 h. The reaction mixture was allowed to cooled to room temperature, and the solvent was removed in vacuo to dryness. The residue was purified by flash chromatography on silica gel using hexanes/EtOAc (8:2) as an eluent to give **22** (950 mg, 89%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.37 (s, 3H), 1.46 (s, 3H), 3.53 (dd, J = 13.3, 7.8 Hz, 1H), 3.62 (dd, J = 13.4, 7.7 Hz, 1H), 3.86 (dd, J = 15.1, 2.0 Hz, 1H), 4.04 (dd, J = 15.1, 1.2 Hz, 1H), 4.16 (dt, J = 7.7, 1.8 Hz, 1H), 4.54 (dd, J = 11.4, 1.3 Hz, 1H), 4.68 (ABq, J = 18.7, 14.0 Hz, 2H), 7.28−7.42 (m, 11H), 7.49 (d, J = 11.6 Hz, 1H), 8.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.5, 19.1, 26.8, 29.5, 48.4, 63.4, 64.1, 71.9, 78.3, 99.3, 127.6, 127.7, 128.8, 129.1, 129.2, 129.7, 133.1, 133.2, 134.3, 135.7, 135.8, 181.7; HRMS (FAB) calcd for $C_{31}H_{40}N_2O_4SSiCs$ 697.1532, found 697.1554.

Compound 23. A solution of thiourea **22** (8.94 g, 15.9 mmol) in ethanol (120 mL) was added dropwise to a stirred suspension of sodium hydride (0.64 g of a 95% dispersion in mineral oil, 25.4 mmol) in ethanol (20 mL) at 25 °C. After 30 min, iodomethane was added dropwise to the reaction mixture and stirred for 1 h. Excess of solvent was removed in vacuo, and the residue was dissolved in water (20 mL). The aqueous solution was extracted with EtOAc, and the combined organic extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel using hexanes/EtOAc (8:2) as an eluent gives **23** (8.90 g, 97%) as a colorless foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.33 (s, 3H), 1.39 (s, 3H), 2.31 (s, 3H), 3.53−3.58 (m, 2H), 3.74 (m, 1H), 3.76 (d, J = 10.0 Hz, 1H), 3.96 (d, J = 12.0 Hz, 1H), 4.02 (m, 1H), 4.99 (s, 2H), 6.09 (d, J = 10.5 Hz, 1H), 7.23−7.30 (m, 4H), 7.33−7.37 (m, 5H), 7.38−7.40 (m, 2H), 7.63−7.67 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 18.5, 19.1, 26.8, 29.4, 4.0, 62.9, 65.2, 71.9, 75.4, 99.0, 127.4, 127.6, 128.0, 128.1, 129.6, 129.7, 133.2, 133.4, 135.6, 135.6, 138.3, 153.5; HRMS (FAB) calcd for $C_{32}H_{42}N_2O_4SiCs$ 711.1689, found 711.1712.

Compound 24. A solution of silyl ether **23** (9.66 g, 16.7 mmol) in dry THF (140 mL) was treated with *n*-Bu_4NF (TBAF, 33 mL of a 1 ***M*** solution in THF, 33.4 mmol) and stirred at 25 °C for 30 min. After dilution with EtOAc (100 mL), water (100 mL) was added. The organic layer was separated, washed with brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (1:1) as an eluent to give **24** (4.20 g, 74%) as a colorless foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 3H), 1.47 (s, 3H), 2.33 (s, 3H), 3.42 (d, J = 11.0 Hz, 1H), 3.45 (d, J = 6.5 Hz, 2H), 3.71 (d, J = 12.5 Hz, 1H), 4.03 (d, J = 12.0 Hz, 1H), 4.07 (t, J = 6.0 Hz, 1H), 5.01 (s, 2H), 6.13 (d, J = 10.5 Hz, 1H), 7.26−7.39 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 18.5, 29.4, 47.3, 62.4, 64.9, 72.0, 75.5, 99.2, 127.5, 128.1, 128.2, 138.1, 153.0; HRMS (FAB) calcd for $C_{16}H_{25}N_2O_4S$ 341.1535, found 341.1528.

Compound 25. To a solution of the alcohol **24** (445 mg, 1.31 mmol) in dry dichloromethane (10 mL) was added Dess−Martin reagent (776 mg, 1.83 mmol). The reaction mixture was stirred at room temperature for 4 h. After dilution with EtOAc (20 mL), water (10 mL) was added. The organic layer was separated, washed with aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (1:1) as an eluent to give **25** (370 mg, 84%) as a colorless foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (s, 3H), 1.43 (s, 3H), 2.33 (s, 3H), 3.31 (q, J = 3.0 Hz, 1H), 4.05 (dd, J = 11.5, 3.0 Hz, 1H), 4.14 (dd, J = 11.5, 3.5 Hz, 1H), 4.17 (t, J = 3.0 Hz, 1H), 4.70 (d, J = 2.5 Hz, 1H), 4.89 (d, J = 10.5 Hz, 1H), 4.97 (d, J = 10.5 Hz, 1H), 7.36−7.41 (m, 3H), 7.46−7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.8, 19.3, 28.6, 48.7, 64.2, 68.4, 78.2, 81.8, 98.2, 128.5, 128.8, 129.6, 135.1, 157.1; HRMS (FAB) calcd for $C_{16}H_{23}N_2O_4S$ 339.2689, found 339.2612.

Compound 26. A solution of the alcohol **25** (2.30 g, 6.80 mmol) in dry pyridine (6 mL) was treated with acetic anhydride (6 mL) and stirred at room temperature for 12h. Evaporation of the reaction mixture to dryness followed by purification of the crude product using hexanes/EtOAc (6:4) as eluent gives acetate **26** (1.90 g, 77%) as a colorless foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 3H), 1.45 (s, 3H), 2.06 (s, 3H), 2.33 (s, 3H), 3.28 (ddd, J = 6.0, 3.4, 2.6 Hz, 1H), 4.06 (dd, J = 11.8, 2.6 Hz, 1H), 4.16 (dd, J = 11.9, 3.6 Hz, 1H), 4.17 (t, J = 3.2 Hz, 1H), 4.89 (s, 2H), 6.01 (d, J = 3.2 Hz, 1H), 7.34−7.40 (m, 3H), 7.43−7.48 (m, 2H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 12.8, 19.2, 21.1, 28.7, 48.6, 64.1, 66.7, 77.9, 79.7, 98.4, 128.4, 128.7, 129.9, 134.4, 156.1, 169.8; HRMS (FAB) calcd for $C_{18}H_{25}N_2O_5S$ 381.1484, found 381.1474.

Compound 27. A solution of the alcohol **25** (79 mg, 0.23 mmol) in dry THF (0.6 mL) was added dropwise to a stirred suspension of sodium hydride (10 mg of an 95% dispersion in mineral oil, 0.37 mmol) in THF (0.6 mL) at 25 °C. After 30 min, MOMCl (30μL, 0.37 mmol) was added dropwise to the reaction mixture and the resulting mixture stirred for 12 h. Excess solvent was removed in vacuo, and the residue was dissolved in water (1 mL). The aqueous solution was extracted with EtOAc, and the combined organic extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel using hexanes/EtOAc (6:4) as eluent gives **27** (65 mg, 73%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 3H), 1.46 (s, 3H), 2.32 (s, 3H), 3.20 (m, 1H), 3.56 (s, 3H), 4.06 (dd, J = 12.0, 2.5 Hz, 1H), 4.16 (dd, J = 11.5, 3.5 Hz, 1H), 4.18 (m, 1H), 4.67 (d, J = 6.5 Hz, 1H), 4.73 (d, J = 3.0 Hz, 1H), 4.84 (d, J = 10.0 Hz, 1H), 4.90 (d, J = 6.5 Hz, 1H), 4.94 (d, J = 10.5 Hz, 1H), 7.34−7.38 (m, 3H), 7.45−7.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.7, 19.3, 28.7, 48.9, 55.8, 64.3, 68.0, 78.0, 84.6, 95.5, 98.1, 128.4, 128.6, 129.7, 134.9, 156.1; HRMS (FAB) calcd for $C_{18}H_{27}N_5O_3S$ 383.1641, found 383.1635.

Compound 28. A solution of the alcohol **25** (122 mg, 0.36 mmol) and 2,6-lutidine (84 μL, 0.72 mmol) in dichloromethane (4 mL) at 0 °C was treated with *tert*-butyldimethylsilyl trifluoromethanesulfonate (165 μL, 0.72 mmol). The reaction mixture was allowed to warm to 25 °C and stirred for 1 h. After dilution with EtOAc (10 mL), the reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (8:2) as an eluent to give **28** (120 mg, 74%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.84 (s, 9H), 1.40 (s, 3H), 1.46 (s, 3H), 2.31 (s, 3H), 3.26 (q, J = 6.0, 3.0 Hz, 1H), 4.05 (t, J = 3.0 Hz, 1H), 4.07 (dd, J = 11.5, 2.5 Hz, 1H), 4.16 (dd, J = 12.0, 3.5 Hz, 1H), 4.70 (d, J = 3.0 Hz, 1H), 4.82 (d, J = 10.0 Hz, 1H), 4.94 (d, J = 10.0 Hz, 1H), 7.34−7.37 (m, 3H), 7.45−7.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.4, −4.6, 12.7, 17.9, 19.3, 25.6, 25.7, 28.8, 48.8, 64.5, 70.2, 77.9, 98.0, 128.3, 128.5, 129.7, 135.0, 153.2; HRMS (FAB) calcd for $C_{22}H_{37}N_2O_4SSi$ 453.2243, found 453.2253.

Compound 29. A solution of the alcohol **25** (227 mg, 0.67 mmol) and 2,6-lutidine (313 μL, 2.69 mmol) in dichloromethane (4 mL) at 0 °C was treated with triethylsilyl trifluoromethanesulfonate (290 μL, 1.34 mmol). The reaction mixture was allowed to warm to 25 °C and stirred for 1 h. After dilution with EtOAc (10 mL), the reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (8:2) as an eluent to give **29** (260 mg, 86%) as a colorless foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.52−0.63 (m, 6H), 0.88 (s, 9H), 1.40 (s, 3H), 1.45 (s, 3H), 2.31 (s, 3H), 3.33 (q, J = 3.2, 2.7 Hz, 1H), 4.05 (t, J = 3.3 Hz, 1H), 4.07 (dd, J = 12.3, 2.4 Hz, 1H), 4.16 (dd, J = 11.8, 3.6 Hz, 1H), 4.71 (d, J = 3.1 Hz, 1H), 4.82 (d, J = 10.3 Hz, 1H), 4.95 (d, J = 10.3 Hz, 1H), 7.33−7.37 (m, 3H), 7.45−7.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.6, 6.6, 12.7, 19.2, 28.8, 48.7, 64.5, 70.1, 78.0, 81.4, 97.9, 128.2, 128.4, 129.7, 135.0, 156.6; HRMS (FAB) calcd for $C_{22}H_{37}N_2O_4SSi$ 453.2243, found 453.2253.

General Procedure for the Synthesis of Protected Guanidines 30−32. To a mixture of silyl ether **29** (0.05−0.05 mmol), $AgBF_4$ (1.6 equiv), and triethylamine (2 equiv) in dry acetonitrile (1 mL) was added amine (3.8 equiv). The reaction mixture was stirred at room temperature for 2 days. After dilution with EtOAc (2 mL), the reaction mixture was filtered through a pad of Celite. The filtrate was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (1:9) as an eluent to give protected guanidine as a colorless oil.

Compound 30. According to the general procedure, **29** (21 mg, 0.05 mmol), $AgBF_4$ (15 mg, 0.08 mmol), triethylamine (13μL, 0.10 mmol), and benzylamine (21 μL, 0.19 mmol) gave protected guanidine **30** (16 mg, 67%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.66 (q, J = 7.9 Hz, 6H), 0.96 (t, J = 7.9 Hz, 9H), 1.48 (s, 3H), 1.50 (s, 3H), 3.65 (m, 1H), 4.08 (dd, J = 13.3, 2.1 Hz, 1H), 4.14 (t, J = 3.1 Hz, 1H), 4.22 (d, J = 13.9 Hz, 1H), 4.22−4.23 (m, 1H), 4.37 (d, J = 13.9 Hz, 1H), 4.78 (d, J = 11.8 Hz, 1H), 4.81 (d, J = 11.2 Hz, 1H), 4.99 (d, J = 3.4 Hz, 1H), 7.26−7.45 (m, 10H); HRMS (FAB) calcd for $C_{28}H_{42}N_3O_4Si$ 512.2945, found 512.2938.

Compound 31. According to the general procedure, **29** (39 mg, 0.09 mmol), $AgBF_4$ (34 mg, 0.17 mmol), triethylamine (36 μL, 0.26 mmol), and ethanolamine (30 μL, 0.43 mmol) gave protected guanidine **31** (24 mg, 60%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.63 (q, J = 7.9 Hz, 6H), 0.96 (t, J = 7.9 Hz, 9H), 1.39 (s, 3H), 1.46 (s, 3H), 2.81 (ddd, J = 26.0, 8.4, 2.6 Hz, 1H), 3.37 (d, J = 1.8 Hz, 1H), 3.49 (dt, J = 10.7, 2.3 Hz, 1H), 3.75 (dd, J = 12.8, 1.5 Hz, 1H), 3.99 (dt, J = 21.8, 10.9, 1.5 Hz, 1H), 4.08 (dd, J = 12.8, 2.0 Hz, 1H), 4.12 (q, J = 2.3 Hz, 1H), 4.21 (m, 1H), 4.49 (d, J = 2.8 Hz, 1H), 4.82 (ABq, J = 16.6, 5.2 Hz, 2H), 5.08 (bs, 1H), 5.45 (s, 1H), 7.27−7.30 (m, 1H), 7.32−7.35 (m, 2H), 7.39−7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.1, 6.6, 18.7, 29.3, 42.0, 51.6, 60.1, 63.1, 64.7, 75.5, 81.3, 98.5, 127.5, 128.2, 128.4, 138.6, 151.2; HRMS (FAB) calcd for $C_{23}H_{40}N_3O_5Si$ 466.2737, found 466.2747.

Compound 32. According to the general procedure, **29** (70 mg, 0.15 mmol), $AgBF_4$ (48 mg, 0.25 mmol), triethylamine (43 μL, 0.31 mmol), and 2-methoxethylamine (54 μL, 0.62 mmol) gave protected guanidine **32** (48 mg, 65%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.64 (q, J = 7.8 Hz, 6H), 0.93 (t, J = 7.9 Hz, 9H), 1.47 (s, 3H), 1.49 (s, 3H), 3.28 (m, 1H), 3.34 (s, 3H), 3.41−3.48 (m, 2H), 3.54 (m, 2H), 4.07 (t, J = 2.9 Hz, 1H), 4.10 (bs, 2H), 4.90 (d, J = 3.4 Hz, 1H), 4.91 (d, J = 11.4 Hz, 1H), 4.97 (d, J = 11.5 Hz, 1H), 6.60 (bs, 1H), 7.40−7.45 (m, 3H), 7.47−7.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.4, 6.5, 18.5, 29.0, 41.6, 43.4, 58.8, 61.0, 67.0, 70.6, 78.6, 80.5, 98.9, 128.9, 129.9, 130.8, 132.8, 154.0; HRMS (FAB) calcd for $C_{24}H_{42}N_3O_5Si$ 480.2894, found 480.2812.

Compound 33. A mixture of protected guanidine **32** (27 mg, 0.06 mmol) and palladium on carbon (10%, 4 mg) in EtOAc (2 mL) was vigorously stirred under an atmosphere of H_2 at room temperature for 2 h, the reaction mixture was filtered through a Celite pad, and the filter cake was washed with EtOAc. The combined filtrates were concentrated to give compound **33** (17 mg, 85%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.67−0.72 (m, 6H), 0.96 (t, J = 7.8 Hz, 9H), 1.39 (s, 3H), 1.48 (s, 3H), 3.43 (s, 3H), 3.45−3.47 (m, 1H), 3.50−3.55 (m, 1H), 3.59−3.66 (m, 2H), 3.70−3.73 (m, 1H), 3.94 (dd, J = 13.0, 1.5 Hz, 1H), 4.02 (q, J = 2.0 Hz, 1H), 4.17 (dd, J = 13.0, 1.5 Hz, 1H), 4.92 (d, J = 2.5 Hz, 1H), 7.22 (t, J = 6.0 Hz, 1H), 7.63 (bs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.4, 6.5, 18.2, 28.9, 42.7, 42.9, 59.2, 61.2, 67.3, 72.7, 82.6, 99.3, 154.5; HRMS (FAB) calcd for $C_{17}H_{36}N_3O_5Si$ 355.2650, found 355.2676.

Compound 34. Trifluoroacetic acid (0.5 mL) and water (100μL) were added to a solution of *N*-hydroxy compound **33** (17 mg, 0.05 mmol) in dichloromethane (0.5 mL). The reaction mixture was stirred at room temperature for 12 h, and excess solvent was removed in vacuo. The residue was purified by passing through a C-18 column using water as an eluent to give **34** (8 mg, 71%) as a white solid: ^{1}H NMR (400 MHz, D_2O) δ 3.38 (s, 3H), 3.48 (d, J = 4.0 Hz, 1H), 3.49 (d, J = 4.3 Hz, 1H), 3.62 (t, J = 4.8 Hz, 2H), 3.66−3.70 (m, 1H), 3.75−3.86 (m, 2H), 4.08 (t, J = 2.7 Hz, 1H), 5.05 (d, J = 3.0 Hz, 1H); ^{13}C NMR (125 MHz, D_2O) δ 43.8, 53.1, 60.8, 61.9, 67.6, 73.5, 86.0, 156.0; HRMS (FAB), calcd for $C_8H_{18}N_3O_5$ 236.1246, found 236.1240.

Compound 36. A mixture of azide **35**[11a] (200 mg, 0.77 mmol) and palladium on carbon (10%, 93 mg) in EtOH (6 mL) was vigorously stirred under an atmosphere of H_2 at room temperature for 6 h, the reaction mixture was filtered through a Celite pad, and the filter cake was washed with EtOH. The combined filtrates were concentrated to give crude amine. This was employed for the next step without further purification.To a solution of the above amine in EtOAc (4 mL) was added benzoyl isothiocyanate (0.10 mL, 0.77 mmol). The reaction mixture was stirred at room temperature for 4 h. The reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (9:1) as eluent to give **36** (0.22 g, 72%)

as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, J = 7.0 Hz, 3H), 1.22 (t, J = 7.0 Hz, 3H), 1.52 (s, 3H), 1.54 (s, 3H), 3.49−3.56 (m, 1H), 3.61−3.71 (m, 2H), 3.73−3.78 (m, 1H), 4.06−4.10 (m, 3H), 4.42 (d, J = 7.2 Hz, 1H), 4.64 (dq, J = 8.7, 5.0 Hz, 1.6 Hz, 1H), 7.50−7.54 (m, 2H), 7.60−7.64 (m, 1H), 7.86−7.88 (m, 2H), 9.04 (s, 1H), 9.74 (d, J = 8.6 Hz, 1H);^{13}C NMR (125 MHz, $CDCl_3$) δ 15.0, 15.4, 29.5, 50.4, 62.0, 63.4, 64.0, 71.4, 99.5, 100.8, 127.4, 129.0, 131.8, 133.4, 166.5, 179.1; HRMS (FAB), calcd for $C_{19}H_{29}N_2O_5S$ 397.1797, found 397.1801.

Compound 37. To a solution of thiourea **36** (0.2 g, 0.51 mmol) in methanol (6 mL) was added K_2CO_3 (70 mg). The reaction mixture was stirred at room temperature for 30 min. After dilution with ethyl acetate, the mixture was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel using hexanes/EtOAc (1:1) as an eluent gives **37** (98 mg, 66%) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (t, J = 7.0 Hz, 6H), 1.50 (s, 3H), 1.56 (s, 3H), 3.44 (m, 1H), 3.56−3.94 (m, 4H), 4.06−4.10 (m, 2H), 4.43 (d, J = 6.4 Hz, 1H), 4.61 (m, 1H), 6.34 (s, 2H), 6.48 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.0, 15.4, 29.2, 49.6, 60.4, 62.1, 64.4, 64.8, 71.0, 72.4, 100.1, 183.2; HRMS (FAB) calcd for $C_{12}H_{25}N_2O_4S$ 293.1535, found 293.15321.

Compound 38. To a mixture of thiourea **37** (50 mg, 0.17 mmol), DMAP (21 mg, 0.17 mmol), and Et_3N (0.095 mL, 0.68 mmol) in CH_2Cl_2 (2 mL) was added a solution of BOC_2O (45 mg, 0.21 mmol) in CH_2Cl_2 (0.5 mL). The reaction mixture was stirred at room temperature for 1 h. After dilution with EtOAc (5 mL), the reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (8:2) as eluent to give **38** (52 mg, 77%) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (t, J = 6.5 Hz, 3H), 1.21 (t, J = 7.0 Hz, 3H), 1.49 (s, 3H), 1.50 (s, 9H), 1.55 (s, 3H), 3.48−3.77 (m, 4H), 3.95−4.08 (m, 3H), 4.39 (dd, J = 7.3, 1.6 Hz, 1H), 4.61 (dt, J = 8.6, 3.2, 1.6 Hz, 1H), 8.03 (s, 1H), 10.40 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.0, 15.3, 18.3, 27.5, 27.9, 29.4, 49.9, 60.7, 63.6, 64.0, 70.9, 99.4, 100.3, 151.3, 178.9; HRMS (FAB) calcd for $C_{17}H_{32}N_2O_6SNa$ 415.1879, found 415.1867.

Compound 39. A solution of BOC derivative **38** (33 mg, 0.08 mmol) in dry THF (1 mL) was added dropwise to a stirred suspension of sodium hydride (5 mg of an 95% dispersion in mineral oil, 0.17 mmol) in THF (1 mL) at 25 °C. After 10 min, iodomethane (10 μL, 0.16 mmol) was added dropwise to the reaction mixture and stirred for 6 h. Excess of solvent was removed in vacuo, and the residue was dissolved in water (1 mL). The aqueous solution was extracted with EtOAc, and the organic extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel using hexanes/EtOAc (6:4) as eluent affords **39** (24 mg, 70%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.18 (t, J = 7.0 Hz, 3H), 1.20 (t, J = 7.0 Hz, 3H), 1.47 (s, 3H), 1.49 (s, 3H), 1.52 (s, 9H), 2.47 (s, 3H), 3.44−3.47 (m, 1H), 3.56−3.62 (m, 1H), 3.65−3.70 (m, 1H), 3.72−3.78 (m, 2H), 3.82−3.84 (m, 1H), 3.97−4.03 (m, 2H), 4.38 (d, J = 7.0 Hz, 1H); HRMS (FAB) calcd for MH^+ $C_{18}H_{35}N_2O_6S$ 407.2216, found 407.2204.

Compound 40. Trifluoroacetic acid (1 mL) and water (100 μL) were added to a solution of **39** (24 mg, 0.06 mmol) in dichloromethane (1 mL). The reaction mixture was stirred at room temperature for 12 h, and excess solvents were removed in vacuo to give **40** (10 mg, 88%) as a white solid: ^{1}H NMR (500 MHz, D_2O) δ 2.49 (s, 3H), 3.66 (dt, J = 13.5, 6.5, 2.5 Hz, 1H), 3.71 (dd, J = 11.0, 7.0 Hz, 1H), 3.77 (dd, J = 11.5, 6.5 Hz, 1H), 3.99 (t, J = 3.0 Hz, 1H), 4.86 (d, J = 3.0 Hz, 1H); 13C NMR (125 MHz, D2O) δ 15.2, 55.0, 61.4, 64.6, 77.3, 167.9; HRMS (FAB) calcd for $C_6H_{13}N_2O_3S$ 193.0647, found 193.0645.

Compound 42. A solution of alcohol **41**[19] (3.09 g, 15.2 mmol) and 2,6-lutidine (3.90 mL, 33.5 mmol) in dichloromethane (60 mL) at 0 °C was treated with *tert*-butyldimethylsilyl trifluoromethanesulfonate (3.85 mL, 16.8 mmol). The reaction mixture was allowed to warm to 25 °C and stirred for 1 h. After dilution with ether (80 mL), the reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (95:5) as eluent to give **42** (4.10 g, 85%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.09 (s, 3H), 0.12 (s, 3H), 0.93 (s, 9H), 1.21 (t, J = 7.06 Hz, 3H), 1.24 (t, J = 7.05 Hz, 3H), 1.35 (d, J = 6.92 Hz, 3H), 3.44 (dq, J = 6.89, 2.07 Hz, 1H), 3.51 (dd, J = 6.76, 2.13 Hz, 1H), 3.78−3.54 (m, 4H), 4.43 (d, J = 6.70 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.7, −3.9, 15.1, 15.4, 16.0, 18.3, 25.9, 56.8, 64.7, 77.3, 104.3; HRMS (FAB) calcd for $C_{14}H_{31}N_2O_3SiNa$ 340.2032, found 340.2025.

Compound 44. A mixture of azide **42** (280 mg, 0.87 mmol) and palladium on carbon (10%, 93 mg) in EtOAc (6 mL) was vigorously stirred under an atmosphere of H_2 at room temperature for 2 h, the reaction mixture was filtered through a Celite pad, and the filter cake was washed with EtOAc. The combined filtrates were concentrated to give crude amine **43**. This was employed for the next step without further purification.To a solution of the above amine **43** in EtOAc (4 mL) was added benzoyl isothiocyanate (0.12 mL, 0.87 mmol). After 4 h at room temperature, the reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (9:1) as eluent to give **44** (0.25 g, 63%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.02 (s, 3H), 0.09 (s, 3H), 0.9 (s, 9H), 1.24 (t, J = 7.05 Hz, 3H), 1.25 (t, J = 7.0 Hz, 3H), 1.33 (d, J = 6.76 Hz, 3H), 3.53 (m, 1H), 3.65 (m, 1H), 3.74 (m, 1H), 3.83 (m, 1H), 4.23 (dd, J = 6.61, 2.32 Hz, 1H), 4.36 (d, J = 6.62 Hz, 1H), 4.69 (m, 1H), 7.51 (t, J = 7.66 Hz, 2H), 7.62 (t, J = 7.52 Hz, 1H), 7.83 (d, J = 7.33 Hz, 2H), 8.90 (bs, 1H), 10.62 (bd, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0, −4.1, 13.5, 15.1, 18.2, 25.9, 53.8, 60.5, 63.3, 72.1, 102.8, 127.1, 129.1, 132.1, 133.7, 166.3, 178.4; HRMS (FAB) calcd for $C_{22}H_{38}N_2O_4SSiCs$ 587.1376, found 587.1362.

Compound 45. Mercuric chloride (208 mg, 0.76 mmol) was added in one portion to a solution of thiourea **44** (290 mg, 0.64 mmol), triethylamine (450μL, 3.19 mmol), and *O*-benzylhydroxylamine hydrochloride (204 mg, 1.28 mmol) in DMF (6 mL) at 0 °C. After 24 h at room temperature, a combination of brine solution and EtOAc was added to the reaction mixture. The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with 1 M sodium bicarbonate solution, filtered through Celite, dried with $MgSO_4$, and concentrated in vacuo to afford a pale yellow oil. The crude product was purified by flash chromatography on silica gel using hexanes/EtOAc (2:1) as an eluent to give **45** (324 mg, 93%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (3H, s), 0.02 (s, 3H), 0.85 (s, 9H), 1.10 (d, J = 7.0 Hz, 3H), 1.11 (t, J = 6.8 Hz, 6H), 3.41−3.62 (m, 4H), 3.47 (dd, J = 7.3 Hz, 1.6 Hz, 1H), 3.88 (m, 1H), 4.24 (d, J = 7.2 Hz, 1H), 4.81 (ABq, J = 22.0 Hz, 11.8 Hz, 2H), 7.16−7.31 (m, 8H), 7.38−7.46 (m, 1H), 7.58−7.60 (m, 2H), 9.04 (bs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.8, −4.0, 15.1, 15.3, 16.9, 18.2, 25.9, 46.9, 63.9, 64.4, 75.6, 75.7, 104.2, 127.1, 127.8, 128.2, 128.7, 132.4, 133.5, 137.9, 149.2, 165.3; HRMS (FAB) calcd for $C_{29}H_{45}N_3O_5SiCs$ 676.2183, found 676.2197.

Compound 46. Trifluoroacetic acid (1 mL) and water (100 μL) were added to a solution of compound **45** (300 mg, 0.55 mmol) in dichloromethane (1 mL). The reaction mixture was stirred at room temperature for 12 h, and the solvent was removed in vacuo to give **46** (200 mg, 77%) as a pale yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.01 (s, 3H), 0.02 (s, 3H), 0.84 (s, 9H), 1.14 (d, J = 6.7 Hz, 3H), 3.45 (m, 1H), 3.58 (bs, 1H), 4.84 (bs, 1H), 4.90 (d, J = 10.2 Hz, 1H), 5.33 (d, J = 10.2 Hz, 1H), 7.36−7.48 (m, 8H), 8.25 (d, J = 7.2 Hz, 2H), 10.3 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.1, −4.5, 15.9, 17.9, 25.6, 45.0, 68.2, 77.9, 83.0, 127.7, 128.6, 128.7, 129.1, 129.4, 131.1, 135.3, 138.5, 157.9, 178.2; HRMS (FAB) calcd for $C_{25}H_{36}N_3O_4$-Si 470.2475, found 470.2491.

Compound 47. A solution of silyl ether **46** (100 mg, 0.21 mmol) in dry THF (2 mL) was treated with *n*-Bu_4NF (TBAF, 426 μL of a 1 M solution in THF, 0.43 mmol) and stirred at 25 °C for 30 min. After dilution with EtOAc (10 mL), water (5 mL) was added. The organic layer was separated, washed with brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (2:8) as an eluent to give **47** (62 mg, 82%) as a white solid: ^{1}H NMR (500 MHz, CD_3OD) δ 1.35 (d, J = 6.8 Hz, 3H), 3.68 (m, 1H), 3.81−

3.85 (m, 1H), 5.10 (d, J = 10.0 Hz, 1H), 5.12 (m, 1H), 5.30 (d, J = 10.0 Hz, 1H), 7.35−7.41 (m, 5H), 7.45−7.48 (m, 1H), 7.56−7.57 (m, 2H), 8.15−8.17 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 15.8, 46.1, 69.2, 79.2, 84.5, 128.9, 129.5, 129.7, 130.1, 130.5, 132.4, 136.7, 139.8, 159.0, 179.4; HRMS (FAB) calcd for $C_{19}H_{22}N_3O_4$ 356.3998, found 356.3988.

Compound 48. A solution of the compound **47** (50 mg, 0.14 mmol) in dry pyridine (1 mL) was treated with acetic anhydride (1 mL) and stirred at room temperature for 12 h. Evaporation of the reaction mixture, followed by purification of the crude product using hexanes/EtOAc (1:1) as eluent gave acetate **48** (51 mg, 82%) as a colorless foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (d, J = 6.7 Hz, 3H), 2.06 (s, 3H), 2.08 (s, 3H), 3.95 (dq, J = 7.0, 2.0 Hz, 1H), 4.90 (m, 1H), 5.18 (d, J = 10.0 Hz, 1H), 5.25 (d, J = 10.0 Hz, 1H), 6.18 (d, J = 2.5 Hz, 1H), 7.39−7.51(m, 8H), 8.27 (m, 2H), 10.71 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 20.7, 20.9, 47.5, 61.9, 64.0, 78.4, 127.9, 128.2, 128.5, 128.9, 129.3, 129.7, 131.7, 134.7, 137.8, 158.0, 168.6, 169.1, 170.4, 179.0; HRMS (FAB) calcd for $C_{23}H_{26}N_3O_6$ 440.2324, found 440.2360.

Compound 49. A mixture of diacetate **48** (51 mg, 0.12 mmol) and palladium on carbon (10%, 5 mg) in ethanol (1 mL) was vigorously stirred under an atmosphere of H_2 at room temperature for 2 h, the reaction mixture was filtered through a Celite pad, and the filter cake was washed with ethanol. The combined filtrates were concentrated to give crude *N*-hydroxy derivative that was employed for the next step without further purification.To a solution of the above *N*-hydroxy compound in methanol (0.5 mL) was added NH_3 (2 M solution in methanol (1 mL). The reaction mixture was stirred for 6 h, and the solvent was removed in vacuo to give compound **49** (15 mg, 50%) as a pale yellow solid: ^{1}H NMR (500 MHz, CD_3OD) δ 1.36 (d, J = 6.9 Hz, 3H), 3.63 (t, J = 2.5 Hz, 1H), 3.81 (dq, J = 7.0, 2.5 Hz, 1H), 4.83 (d, J = 2.5 Hz, 1H), 7.37−7.40 (m, 2H), 7.44−7.48 (m, 1H), 8.03−8.05 (m, 2H); HRMS (FAB) calcd for $C_{12}H_{16}N_3O_4$ 266.2840, found 266.2852.

Compound 50. Mercuric chloride (1.68 g, 6.19 mmol) was added in one portion to a solution of thiourea **14**[16] (1.78 g, 5.62 mmol), triethylamine (2.34 mL, 16.9 mmol), and the crude amine **43** (1.64 g, 5.62 mmol) in DMF (14 mL) at 0 °C. The color of the reaction mixture changed to dark yellow, and the reaction was then warmed to room temperature. After 24 h, a combination of brine solution and EtOAc was added to the reaction. The aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with 1 M sodium bicarbonate solution, filtered through Celite, dried with $MgSO_4$, and concentrated in vacuo to afford a pale yellow foam. The crude product was purified by flash chromatography on silica gel using hexanes/EtOAc (2:1) as eluent to give **50** (2.24 g, 69%) as a colorless foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.01 (s, 3H), 0.03 (s, 3H), 0.87 (m, 9H), 1.12 (d, J = 6.7 Hz, 3H), 1.16 (t, J = 7.0 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H), 3.44−3.53 (m, 2H), 3.64−3.71 (m, 2H), 3.83 (dq, J = 7.0, 1.5 Hz, 1H), 4.00 (dd, J = 7.0, 2.0 Hz, 1H), 4.25 (d, J = 7.0 Hz, 1H), 4.82 (ABq, J = 23.0, 12.0 Hz, 2H), 5.11 (ABq, J = 30.5, 12.0 Hz, 2H), 6.18 (bd, J = 7.5 Hz, 1H), 7.28−7.38 (m, 10H), 7.89 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.1, −4.1, 13.9, 15.1, 15.4, 18.2, 26.0, 47.4, 59.0, 63.0, 67.4, 71.7, 75.6, 102.8, 127.7, 128.2, 1283, 128.4, 128.6, 128.7, 135.2, 138.0, 146.8, 152.5; HRMS (FAB) calcd for $C_{30}H_{48}N_3O_6Si$ 574.3312, found 574.3297.

Compound 51. Trifluoroacetic acid (8 mL) and water (800 μL) were added to a solution of compound **50** (1.82 g, 3.17 mmol) in dichloromethane (8 mL). The reaction mixture was stirred at room temperature for 12 h, and the solvent was removed in vacuo to give **51** (1.24 g, 78%) as a pale yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.06 (s, 3H), 0.85 (bs, 12H), 2.68 (dq, J = 6.7, 2.2 Hz, 1H), 3.57 (dd, J = 4.9, 2.3 Hz, 1H), 4.46 (d, J = 9.5 Hz, 1H), 4.90 (d, J = 3.2 Hz, 1H), 4.96 (d, J = 9.4 Hz, 1H), 5.02 (d, J = 12.7 Hz, 1H), 5.38 (d, J = 12.7 Hz, 1H), 7.05−7.13 (m, 4H), 7.22−7.29 (m, 2H), 7.37 (m, 2H), 7.54 (m, 2H), 8.19 (bs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.1, −4.4, 15.8, 17.9, 25.7, 44.8, 66.0, 68.1, 77.3, 82.1, 127.6, 127.7, 128.0, 128.2, 128.3, 129.8, 134.7, 138.4, 158.2, 163.6; HRMS (FAB) calcd for $C_{26}H_{38}N_3O_5Si_2$ 500.2581, found 500.2564.

Compound 52. A solution of the alcohol **51** (500 mg, 1.0 mmol) and 2,6-lutidine (580 μL, 5.0 mmol) in dichloromethane (20 mL) at 0 °C was treated with triethylsilyl trifluoromethanesulfonate (1.13 mL, 5.0 mmol). The reaction mixture was allowed to warm to 25 °C and stirred for 1 h. After dilution with EtOAc (20 mL), the reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (6:4) as an eluent to give **52** (490 mg, 80%) as a colorless foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 3H), 0.10 (s, 3H), 0.53−0.63 (m, 6H), 0.90 (t, J = 7.8 Hz, 9H), 0.92 (s, 9H), 1.22 (d, J = 6.8 Hz, 3H), 3.54 (dd, J = 5.2, 2.2 Hz, 1H), 3.80 (dq, J = 6.7, 2.1 Hz, 1H), 4.76 (d, J = 9.9 Hz, 1H), 4.95 (d, J = 3.2 Hz, 1H), 5.17 (d, J = 2.4 Hz, 1H), 5.26 (d, J = 9.9 Hz, 1H), 7.27−7.37 (m, 6H), 7.43−7.49 (m, 4H), 8.95 (bs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.0, −4.3, 4.6, 6.6, 16.2, 18.0, 25.7, 44.9, 66.6, 69.9, 77.8, 83.0, 127.4, 127.7, 128.2, 128.2, 128.3, 128.3, 129.3, 135.2, 137.6, 157.5, 164.5; HRMS (FAB) calcd for $C_{32}H_{52}N_3O_5Si_2$ 614.3446, found 614.3422.

Compound 53. A mixture of the compound **52** (206 mg, 0.34 mmol) and palladium on carbon (10%, 20 mg) in EtOAc (4 mL) was vigorously stirred under an atmosphere of H_2 at room temperature for 2 h, the reaction mixture was filtered through a Celite pad, and the filter cake was washed with EtOAc. The combined filtrates were concentrated to give compound **53** (77 mg, 58%) as a colorless foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.13 (s, 3H), 0.74 (m, 6H), 0.90 (m, 9H), 0.98 (m, 9H), 1.23 (d, J = 6.8 Hz, 3H), 3.51 (bs, 1H), 3.62−3.64 (m, 1H), 4.80 (d, J = 2.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.9, −4.3, 7.2, 7.4, 16.0, 19.0, 26.3, 45.8, 71.6, 85.6, 151.1; HRMS (FAB) calcd for $C_{17}H_{40}N_3O_3Si_2$ 390.2608, found 390.2602.

Compound 54. To a solution of the compound **53** (77 mg, 0.20 mmol) in acetonitrile (2 mL) was added aqueous HF (50% in water, 0.2 mL). The reaction mixture was stirred for 2 h, and the solvent was removed in vacuo to give **54** (24 mg, 75%) as a pale yellow solid: ^{1}H NMR (500 MHz, D_2O) δ 1.32 (d, J = 6.8 Hz, 3H), 3.65 (t, J = 2.6 Hz, 1H), 3.86 (dq, J = 7.0, 2.5 Hz, 1H), 4.76 (d, J = 2.5 Hz, 1H); HRMS (FAB) calcd for $C_5H_{11}N_3O_3$ 162.0879, found 162.0874.

Compound 55. To a solution of 1,1′-thiocarbonyldiimidazole (1.28 g, 7.19 mmol) in EtOAc (20 mL) was added a solution of the crude amine **43** (2.09 g, 7.19 mmol) in EtOAc (5 mL). The reaction mixture was stirred at room temperature for 12 h. After dilution with EtOAc (10 mL), the reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (8:2) as eluent to give **55** (1.20 g, 50%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.08 (s, 3H), 0.11 (s, 3H), 0.93 (s, 9H), 1.22 (t, J = 7.0 Hz, 3H), 1.23 (t, J = 7.0 Hz, 3H), 1.36 (d, J = 6.5 Hz, 3H), 3.47 (dd, J = 6.5, 2.0 Hz, 1H), 3.54−3.59 (m, 1H), 3.63−3.67 (m, 1H), 3.70−3.77 (m, 2H), 3.92 (dq, J = 13.5, 6.5, 2.0 Hz, 1H), 4.35 (d, J = 6.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.8, −3.9, 15.1, 15.4, 19.3, 25.8, 55.1, 64.3, 64.9, 76.0, 104.0; HRMS (FAB) calcd for $C_{15}H_{31}NO_3SSiNa$ 356.1692, found 356.1695.

Compound 56. A mixture of isothiocyanate **49** (268 mg, 0.80 mmol) and aqueous ammonia (4 mL) in ethanol (2 mL) was refluxed for 6 h. The reaction mixture was allowed to cool to room temperature and was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give a pale yellow oil. The crude product was purified by flash chromatography on silica gel using EtOAc as an eluent to afford **56** (200 mg, 74%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 3H), 0.08 (s, 3H), 0.87 (s, 9H), 1.19 (t, J = 6.9 Hz, 6H), 1.20 (d, J = 6.9 Hz, 3H), 3.50−3.71 (m, 6H), 4.29 (d, J = 6.0 Hz, 1H), 5.87 (bs, 1H), 6.31 (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.7, −4.2, 15.4, 18.2, 25.9, 50.9, 62.7, 64.5, 75.5, 103.2, 181.5; HRMS (FAB) calcd for $C_{15}H_{35}N_2O_3SSi$ 351.2138, found 351.2132.

Compound 57. To a mixture of thiourea **56** (156 mg, 0.44 mmol), DMAP (60 mg, 0.49 mmol), and triethylamine (250 μL, 1.78 mmol) in dichloromethane (2 mL) was added a solution of BOC_2O (120 mg, 0.53 mmol) in CH_2Cl_2 (0.5 mL). The reaction mixture was stirred at room temperature for 2 h. After

dilution with EtOAc (10 mL), the reaction mixture was washed with water and brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography on silica gel using hexanes/EtOAc (6:4) as eluent to give **57** (190 mg, 79%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.14 (s, 6H), 0.93 (s, 9H), 1.23 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.9 Hz, 3H), 1.28 (d, J = 7.0 Hz, 3H), 1.47 (s, 9H), 3.57−3.66 (m, 3H), 3.70−3.75 (m, 2H), 4.24 (d, J = 7.0 Hz, 1H), 4.70 (1H, m), 7.89 (s, 1H), 10.15 (d, J = 5.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.7, −4.1, 15.1, 15.2, 16.3, 18.2, 25.8, 27.9, 52.7, 64.2, 64.8, 75.1, 83.0, 104.0, 151.1, 178.0; HRMS (FAB) calcd for $C_{20}H_{42}N_2O_5SSiCs$ 583.1638, found 583.1621.

General Procedure for the Synthesis of Compounds 58−60. A solution of BOC derivative **57** (0.18−0.29 mmol) in dry THF (1 mL) was added dropwise to a stirred suspension of sodium hydride (95% dispersion in mineral oil, 2.1 equiv) in THF (1 mL) at 25 °C. After 10 min, alkyl halide (1.6 equiv) was added dropwise to the reaction mixture and the resulting mixture stirred for 2−12 h. Excess solvent was removed in vacuo, and the residue was dissolved in water (1 mL). The aqueous solution was extracted with EtOAc (3 × 2 mL), and the combined organic extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel using hexanes/EtOAc (6:4) as eluent affords *S*-alkylated compound as a colorless oil.

Compound 58. According to the general procedure, **57** (128 mg, 0.29 mmol), sodium hydride (14 mg of an 95% dispersion in mineral oil, 0.57 mmol), and iodomethane (28 μL, 0.46 mmol) gave methylsulfanyl compound **58** (98 mg, 74%):. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.05 (s, 3H), 0.08 (s, 3H), 0.89 (s, 9H), 1.18 (t, J = 7.1 Hz, 3H), 1.19 (d, J = 7.3 Hz, 3H), 1.20 (t, J = 7.0 Hz, 3H), 1.44 (s, 9H), 2.40 (s, 3H), 3.48 (d, J = 6.9 Hz, 1H), 3.52 (q, J = 7.1 Hz, 2H), 3.65 (q, J = 7.1 Hz, 2H), 3.95 (m, 1H), 4.19 (d, J = 7.0 Hz, 1H), 10.05 (d, J = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.8, −4.0, 13.5, 15.1, 15.3, 18.2, 18.3, 25.8, 28.1, 51.0, 64.3, 64.5, 75.7, 78.8, 103.8, 161.5, 171.4; HRMS (FAB) calcd for $C_{21}H_{45}N_2O_5SSi$ 465.2818, found 465.2810.

Compound 59. According to the general procedure, **57** (82 mg, 0.18 mmol), sodium hydride (9 mg of an 95% dispersion in mineral oil, 0.36 mmol), and iodopropane (26 μL, 0.29 mmol) gave propylsulfanyl compound **59** (65 mg, 73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.13 (s, 3H), 0.94 (s, 9H), 1.00 (t, J = 7.5 Hz, 3H), 1.20−1.26 (m, 6H), 1.23 (d, J = 7.0 Hz, 3H), 1.48 (s, 9H), 1.65 (m, 2H), 3.10 (t, J = 7.0 Hz, 1H), 3.51 (m, 4H), 3.67−3.75 (m, 3H), 4.04 (m, 1H), 4.24 (d, J = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.8, −4.0, 15.1, 15.3, 18.2, 22.2, 25.8, 28.2, 32.5, 54.0, 64.3, 64.7, 74.5, 75.7, 78.7, 103.5, 161.6, 171.3; HRMS (FAB) calcd for $C_{23}H_{48}N_2O_5SSi$ 493.3131, found 493.3114.

Compound 60. According to the general procedure, **57** (100 mg, 0.22 mmol), sodium hydride (11 mg of an 95% dispersion in mineral oil, 0.44 mmol), and benzyl bromide (12 μL, 0.10 mmol) gave benzylsulfanyl compound **60** (68 mg, 57%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 3H), 0.10 (s, 3H), 0.94 (s, 9H), 1.16−1.26 (m, 9H), 1.52 (s, 9H), 3.49−3.61 (m, 3H), 3.66−3.77 (m, 2H), 3.98 (m, 1H), 4.23 (d, J = 7.0 Hz, 1H), 4.35 (s, 2H), 7.26−7.36 (m, 5H), 10.10 (d, J = 8.5 Hz, 1H); HRMS (FAB) calcd for $C_{27}H_{48}N_2O_5SSiCs$ 673.2108, found 673.2128.

General Procedure for the Synthesis of Compounds 61−63. Trifluoroacetic acid (1 mL) and water (100 μL) were added to a solution of compounds **58**−**60** (0.06−0.14 mmol) in dichloromethane (1 mL). The reaction mixture was stirred at room temperature for 12 h, and excess solvents were removed in vacuo to give compounds **61**−**63** as a colorless foam.

Compound 61 (32 mg, 76%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.09 (s, 6H), 0.87 (s, 9H), 1.32 (d, J = 7.5 Hz, 3H), 2.58 (3H, s), 3.77 (bs, 1H), 3.82 (bs, 1H), 4.91 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.1, −4.8, 13.4, 14.6, 17.8, 25.4, 48.2, 66.2, 76.3, 163.8; HRMS (FAB) calcd for $C_{12}H_{27}N_2O_2SSi$ 291.1563, found 291.1559.

Compound 62 (12 mg, 62%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.09 (s, 3H), 0.10 (s, 3H), 0.87 (s, 9H), 1.01 (t, J = 7.4 Hz, 3H), 1.32 (d, J = 6.6 Hz, 3H), 1.70 (m, 2H), 3.01−3.07 (m, 1H), 3.11−3.17 (m, 1H), 3.78 (m, 1H), 3.86 (m, 1H), 4.91 (d, J = 3.0 Hz, 1H), 8.26 (m, 1H), 10.73 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.0, −4.7, 12.8, 14.8, 22.3, 25.5, 29.3, 33.2, 48.3, 66.2, 76.4, 162.8; HRMS (FAB) calcd for $C_{14}H_{31}N_2O_2SSi$ 319.1876, found 319.1871.

Compound 63 (19 mg, 54%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.81 (s, 9H), 1.23 (d, J = 6.7 Hz, 3H), 3.74 (m, 1H), 3.80 (m, 1H), 4.33 (s, 2H), 4.90 (m, 1H), 7.25−7.36 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.1, −4.8, 14.6, 25.5, 29.7, 35.6, 48.3, 66.2, 76.4, 128.5, 129.0, 129.1, 133.2, 162.3; HRMS (FAB) calcd for $C_{18}H_{31}N_2O_2SSi$ 367.1876, found 367.1871.

General Procedure for the Synthesis of Compounds 64−66. To a solution of silyl ether **61**−**63** (0.04−0.11 mmol) in acetonitrile (1 mL) was added aqueous HF (49% in water, 0.2 mL). The reaction mixture was stirred for 2 h, and the solvent was removed in vacuo. The residue was purified by passing through a short C-18 column using water as an eluent to afford compounds **64**−**66** as white solids.

Compound 64 (12 mg, 62%): ^{1}H NMR (500 MHz, D_2O) δ 1.22 (d, J = 7.0 Hz, 3H), 2.47 (s, 3H), 3.71 (dq, J = 14.0, 7.0, 2.6 Hz, 1H), 3.77 (t, J = 2.6 Hz, 1H), 4.83 (d, J = 3.0 Hz, 1H); ^{13}C NMR (100 MHz, D_2O) δ 13.5, 14.3, 48.0, 65.5, 75.6, 165.7; HRMS (FAB) calcd for $C_6H_{13}N_2O_2S$ 177.0698, found 177.0700.

Compound 65 (4 mg, 52%): ^{1}H NMR (500 MHz, D_2O) δ 0.87 (t, J = 7.4 Hz, 3H), 1.23 (d, J = 6.9 Hz, 3H), 1.58 (m, 2H), 3.00 (m, 2H), 3,73 (dd, J = 7.0, 2.5 Hz, 1H), 3.79 (t, J = 2.5 Hz, 1H), 4.83 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, D_2O) δ 12.9, 14.2, 22.7, 33.8, 48.1, 65.4, 75.6, 164.5; HRMS (FAB) calcd for $C_8H_{17}N_2O_2S$ 205.1011, found 205.1008.

Compound 66 (8 mg, 61%): ^{1}H NMR (500 MHz, D_2O) δ 1.17 (d, J = 6.8 Hz, 3H), 3.60 (q, J = 7.1, 3.9 Hz, 1H), 3.70 (m, 1H), 4.28 (s, 2H), 4.76 (m, 1H), 7.24−7.32 (m, 5H); HRMS (FAB) calcd for $C_{12}H_{17}N_2O_2S$ 253.1011, found 253.1010.

Crystallographic Data.[20] Compounds **12**, **17**, and **51** crystallized as thin, colorless plates. X-ray data were collected and recorded with a Rigaku AFC6R diffractometer. Compounds **12** and **51** formed monoclinic crystals, space group $P2_1/c$ with Z = 4. Compounds **17** formed orthorhombic crystals, space group $P2_12_12_1$ with Z = 4. The structures were solved by means of the SHELXS86[21] direct methods package and refined on F by the full-matrix least-squares method, allowing anisotropic displacement parameters for non-hydrogen atoms. Hydrogen atoms were introduced in calculated positions and were refined.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for compounds **9**, **11**, **12**, **15**−**40**, **42**, **44**−**53**, and **55**−**66**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100368. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (Fax: Int. code +(1223)-336-033; e-mail: deposit@chemcrys.cam.ac.uk).

(21) Sheldrick, G. M. *Acta Crystallogr.* **1990**, *A46*, 467−473.