total synthesis of penicillins. The substitutionally inert Co(III) center protects both the amine and carboxylato functional groups through chelation and is a useful single substitute for the more conventional phthalamido and ester protecting groups used in the organic chemistry.

Apart from the reactions reported herein, the aldehyde complex has obvious synthetic potential, particularly in penicillin chemistry. We will be reporting on this later but note here that the metal center, in addition of functioning as a protecting group, can be modified by using the appropriate ligands (e.g., the chiral Λ or Δ $Co(en)_2$ in lieu of (p)- or (t)-Co(tren)) to impart a specificity in asymmetric synthesis involving the aldehyde center. Also, as this work has shown, the inner chiral methine center of the substituted glycine is readily mutarotated.

A useful property of the glycine aldehyde complex, from a synthetic viewpoint, is its relative stability in dilute base. It does not self-condense as readily as normal aldehydes (aldol condensation), presumably because this involves two positively charged (2+) cations, nor does it readily undergo intramolecular cyclization with the coordinated amine centers, e.g., cyclic imine formation. This is probably a steric constraint, although the similar complex $[Co(en)_2NH_2{\cdot}CN(C{\equiv}N)CO_2]^{2+}$ condenses intramolecularly in base to give a cyclic (albeit strained) amidine.[16]

Acknowledgment. We thank the Microanalytical Section (A.N.U.) for elemental analyses and Dr. N.J. Curtis for checking some of the results.

Registry No. 1, 76024-02-7; **7**, 84809-81-4; $[Co(tren)(ser)]S_2O_6$, 84847-59-6; $[Co(tren)B]ZnCl_4$ (B = (hydroxyethoxymethyl)glycinate), 84809-83-6.

Supplementary Material Available: Tables of final atomic coordinates, bond lengths and angles, hydrogen bonding parameters, an ORTEP drawing of the complex ion, thermal parameters, and observed and calculated structure factor amplitudes (15 pages). Ordering information is given on any current masthead page.

(15) Sheehan, J. C.; Henery-Logan, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 3089.

(16) Springborg, J.; Geue, R. J.; Sargeson, A. M.; Taylor, D.; Snow, M. R. *J. Chem. Soc., Chem. Commun.* **1978**, 647-649.

A Mild and General Method for the Synthesis of *O*-Glycosides

K. C. Nicolaou,*† S. P. Seitz, and D. P. Papahatjis

Contribution from the Department of Chemistry, University of Pennsylvania, Philadephia, Pennsylvania 19104. *Received April 22, 1982*

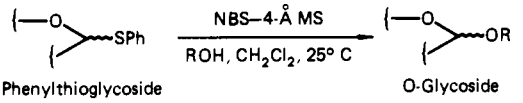
Abstract: A mild and general procedure for the synthesis of *O*-glycosides from phenyl thioglycosides (Scheme I) is described. The method involves treatment of the readily available phenyl thioglycosides with *N*-bromosuccinimide in the presence of various hydroxy components in organic solvents under anhydrous conditions at 25 °C to produce a series of *O*-glycosides in a few minutes. Applications to complex systems and intramolecular cases are included.

The widespread occurrence of the *O*-glycoside bond in nature and the importance of biomolecules containing this bond are becoming increasingly evident.[1] Methodology[2] for the construction of the *O*-glycoside linkage is, therefore, of paramount interest due to the central role of such reactions in organic synthesis and in assembling complex frameworks containing carbohydrate residues. Despite the great deal of work in this area, however, severe limitations and deficiencies still exist in the present technology.[3] One of the most widely used methods, for example, the utilization of 1-halo derivatives of carbohydrates, often suffers from the instability of the intermediates, the relative drastic conditions for their preparation, and the requirement of precious or other related heavy metal reagents as further activators.[2] In connection with our work in the total synthesis of complex and sensitive, carbohydrate-containing natural products from the macrolide area[4] we were faced with the problem of coupling carbohydrate units and of attaching them onto suitable aglycones efficiently and under extremely mild conditions. In this article we wish to report a mild and facile procedure that constitutes a convenient and general method for the construction of the *O*-glycoside bond and, furthermore, fulfills the above requirements.

Results and Discussion

Scheme I profiles this general method that employs the stable and readily available phenyl thioglycosides (*vide infra*) as starting materials. The phenyl thioglycoside is activated with *N*-bromosuccinimide (NBS, 1.1 equiv) in the presence of the hydroxy

Scheme I



component (stoichiometric or near stoichiometric amounts) and 4-Å molecular sieves (to ensure strict anhydrous and neutral conditions) in methylene chloride (CH_2Cl_2) at 25 °C leading to *O*-glycosides (α- and β-anomers) in good to excellent yields, the reaction being complete usually in less than 15 min.[5] Table I includes some of the examples of *O*-glycosides synthesized according to the above prescription and helps to illustrate the ef-

† Fellow of the A. P. Sloan Foundation, 1979-1983; recipient of a Camille and Henry Dreyfus Teacher-Scholar Award, 1980-1985.

(1) For some recent reviews see: (a) Hanessian, S.; Dixit, D. M.; Liak, T. J. *Pure Appl. Chem.* **1981**, *53*, 129 and references cited therein. (b) *Chem. Eng. News* **1981**, *59* (13) 21.

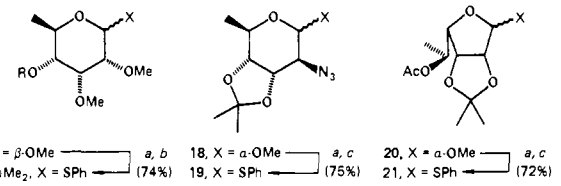
(2) For some recent reviews see: (a) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155. (b) Tsutsumi, H.; Ishido, Y. *Yuki Gosei Kagaku Kyokaiski* **1980**, *38*, 473. (c) Bochkov, A. F.; Zaikov, G. E. "Chemistry of the *O*-Glycosidic Bond: Formation and Cleavage"; Pergamon Press: Oxford, 1979. (d) Sinai, P. *Pure Appl. Chem.* **1978**, *50*, 1437. (e) Igarashi, K. *Adv. Carbohydr. Chem. Biochem.* **1977**, *34*, 243. (f) Hanessian, S.; Banoub, J. *Adv. Chem. Ser.* **1976**, *No. 39*, 36. (g) Iley, D. E.; Frazer-Reid, B. *J. Am. Chem. Soc.* **1975**, *97*, 2563. (h) Wulff, G., Rohl, G. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 157.

(3) These deficiencies include both low yields and low stereoselectivities. See, for example: (a) Tatsuta, K.; Tanaka, A.; Fujimoto, K.; Kinoshita, M.; Umezawa, S. *J. Am. Chem. Soc.* **1977**, *99*, 5826. (b) *Ibid.*, ref 6c.

(4) (a) Nicolaou, K. C.; Pavia, M. R.; Seitz, S. P. *J. Am. Chem. Soc.* **1982**, *104*, 2027. (b) Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R. *Ibid.* **1982**, *104*, 2030. (c) Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R. *Ibid.* **1981**, *103*, 1222. (d) Nicolaou, K. C.; Pavia, M. R.; Seitz, S. P. *Ibid.* **1981**, *103*, 1224.

0002-7863/83/1505-2430$01.50/0

Scheme II



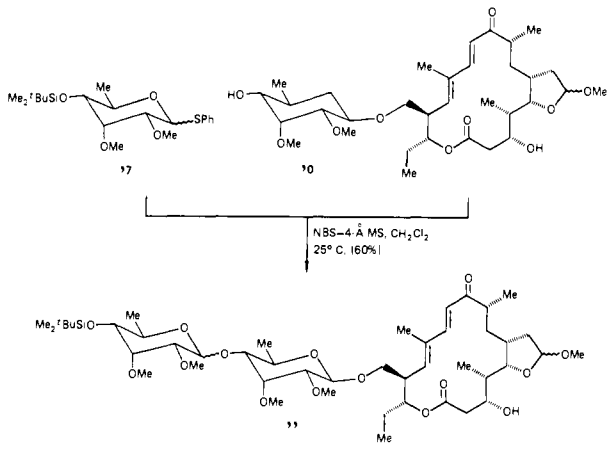
a, 5.0 equiv $PhSSiMe_3$, 1.2 equiv $TfOSiMe_3$, CH_2Cl_2, 0–25 °C; b, 1.2 equiv *t*-$BuMe_2SiCl$, 1.2 equiv imidazole, DMF, 25 °C; c, excess 2,2-dimethoxypropane, camphorsulfonic acid, acetone, 25 °C

ficiency, mildness, applicability, and scope of this reaction. The following comments also help evaluate this technique and highlight certain advantages over existing methods in this area. The generality of the method is illustrated by the considerable variation possible in both the thioglycoside and hydroxy components. Thus, furanosides, pyranosides, 2-deoxycarbohydrates, and azidocarbohydrates enter comfortably in this reaction as the phenyl thioglycoside partner, while primary, secondary, and even tertiary alcohols serve well as the hydroxy component. The efficiency of this coupling reaction even with stoichiometric or near stoichiometric amounts of the two main reactants makes it attractive in cases where advanced and valuable intermediates are involved, particularly for small scale operations. Furthermore, the extremely mild conditions utilized (ambient or lower temperatures, neutrality, convenient and inert solvents) should make this procedure the method of choice in complex and sensitive cases. Finally, one of the most important features of the present methodology is the ready availability and stability of phenyl thioglycosides translating into a highly convenient glycosidation method even on a small scale. This later property of the thioglycosides allows for easy manipulation, purification, and storage until activation is initiated with NBS.

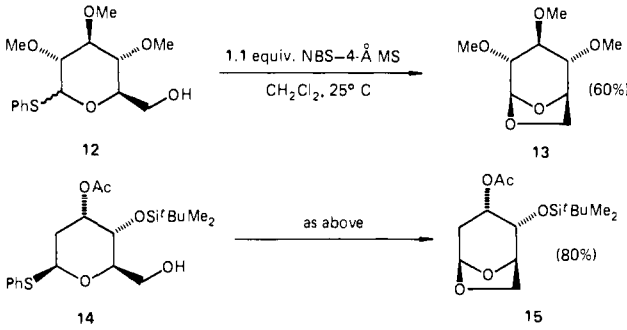
Thioglycosides can be obtained from carbohydrates by a variety of methods[6-8] including the use of free carbohydrates[6] and 1-halo derivatives[7] and the recent and highly useful procedure of Hanessian[8] utilizing *O*-glycosides, (trimethylsilyl)thiophenol ($PhSSiMe_3$), zinc iodide (ZnI_2), and tetrabutylammonium iodide (n-Bu_4NI). To make these intermediates even more readily available and abundant, we introduced yet another general procedure involving reaction of methyl glycosides with $PhSSiMe_3$ in the presence of trimethylsilyl triflate ($TfOSiMe_3$) as illustrated in Scheme II with examples from the pyranoside and furanoside types of carbohydrate derivatives.[4a] Note, however, the loss of the acid sensitive *tert*-butyldimethylsilyl protecting group under these conditions (**16** → **17**).

The stereochemical consequences in this *O*-glycoside bond forming reaction are interesting and could prove synthetically useful since often considerable stereocontrol can be exerted by a simple change of solvent. Entries 5 and 6 (Table I) demonstrate a rather dramatic change in stereoselectivity by going from CH_2Cl_2 (α:β ratio ca. 1:1) to CH_3CN (α:β ratio ca 9:1) which is presumed to be due to the reverse anomeric effect as discussed extensively by Schuerch.[9] The stereochemistry of the thioglycoside bond, however, does not appear to be always crucial to the final stereochemical outcome of the glycosidation reaction since it has been demonstrated that in the case of entry 2 (Table I) either isomer of the thio sugar resulted in comparable ratio of α- and β-anomers in the product. This observation is consistent with a mechanism for this glycoside bond forming reaction that involves initial electrophilic activation of sulfur generating a reactive sulfonium species which must be losing, at least partially, its stereochemical integrity prior to final *O*-glycoside bond formation.[10]

Scheme III



Scheme IV



For a demonstration of the applicability of the present glycosidation reaction to complex instances a novel and polyfunctional tylosin derivative **11** was constructed as shown in Scheme III.[11] Finally, the intramolecular version of this new reaction has been demonstrated to be a facile process leading to internal acetals (**12** → **13**; **14** → **15**) as illustrated in Scheme IV, adding another dimension to the scope and applicability of this method.

Conclusion

We have demonstrated that the readily accessible phenyl thioglycosides serve as stable intermediates for further elaboration in carbohydrate related areas. Specifically, the described methodology offers a very convenient and efficient approach to the construction of the *O*-glycoside bond and related acetals with considerable stereocontrol. Research in carbohydrate chemistry and the total synthesis of complex natural products containing these linkages is expected to benefit from the present technology, and efforts in these directions are under way in these laboratories.[12]

Experimental Section

General Data. ^1H NMR spectra were recorded on a Bruker 250-MHz NMR spectrometer in $CDCl_3/Me_4Si$ and are reported in δ values from

(5) For some related but synthetically less attractive glycosidation reactions utilizing various thioglycoside derivatives see: (a) Hanessian, S.; Bacquet, C.; Lehong, N. *Carbohydr. Res.* **1980**, *80*, C17. (b) Mukaiyama, T.; Nakatsuka, T.; Shoda, S. *Chem. Lett.* **1969**, 487. (c) Ferrier, R. J.; Hay, R. W.; Vethaviyasar, N. *Carbohydr. Res.* **1973**, *27*, 55. (d) VanCleve, J. W. *Ibid.* **1979**, *70*, 161. Particularly inspiring and instrumental to the present development were Hanessian's recent and elegant glycosidations by remote activation.[5a]

(6) For some examples starting with carbohydrates and thiophenol see: (a) Zissis, E.; Glingman, A. L.; Richtmyer, N. K. *Carbohydr. Res.* **1966**, *2*, 461. (b) Reference 5c (c) For related examples involving free lactol-type sugars, 2-mercaptopyrimidine, diethyl diazocarboxylate, and tributylphosphine, or dipyridyl disulfide, and tributylphosphine, see: Woodward, R. B., et al. J. Am. Chem. Soc. **1981** *103*, 3215. We found that the former method is also applicable to the synthesis of phenyl thioglycosides.

(7) For some examples utilizing 1-halocarbohydrate derivatives and thiols see: ref 5a and references cited therein.

(8) Hanessian, S.; Guindon, Y. J. Carbohydr. Res. **1980**, *86*, C3.

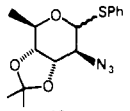
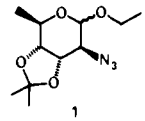
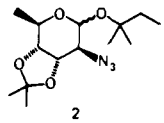
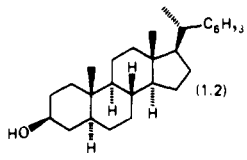
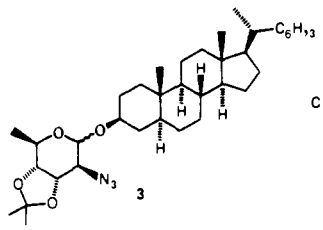
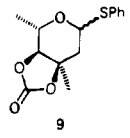
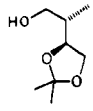
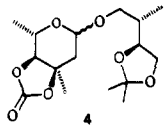
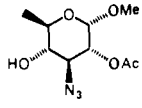
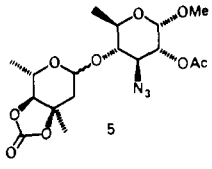
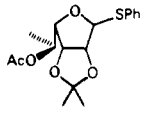
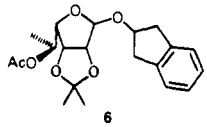
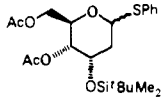
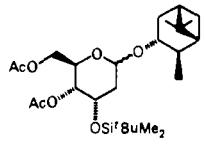
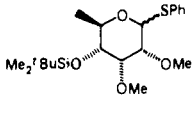
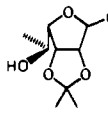
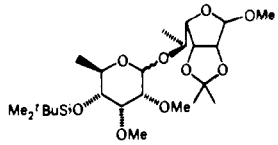
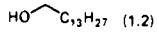
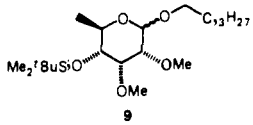
(9) West, A. C.; Schuerch, C. *J. Am. Chem. Soc.* **1973**, *95*, 1333. See also: Lemieux, R. V.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2205.

(10) It is presumed that initial activation of sulfur by bromination is followed by oxygen-assisted departure of this group, which may be reversible. and finally interception of the oxonium species and/or activated sulfur-containing species by the oxygen nucleophile to give the O-glycoside.

(11) Intermediates **17** and **10** were synthesized as described in ref 4a. The *O*-glycoside bond in **10** was also constructed by the present method, see ref 4a.

(12) This work was financially supported by NIH (Grant GM-26879), Merck, Sharp and Dohme, the Camille and Henry Dreyfus Foundation, and the Sloan Foundation.

Table I. Formation of *O*-Glycosides from Phenyl Thioglycosides and Alcohols by Activation with N8S

Entry	Phenylthioglycoside	Alcohol (equiv.)	O-Glycoside	Solvent	Yield (percent)	α : β ratio[a]
1	 19	 (5.0)	 1	CH_2Cl_2	78	1 : 1
2		 (2.0)	 2	CH_2Cl_2	73	1 : 1.8
3		 (1.2)	 3	CH_2Cl_2	55	1 : 1.5
4	 9	 (1.2)	 4	MeCN	75	3 : 1
5		 (1.2)	 5	CH_2Cl_2	72	1 : 1
6		(1.2)		MeCN	72	9 : 1
7	 21	 (1.2)	 6	CH_2Cl_2	54	1 : 0
8	 22	 (1.3)	 7	CH_2Cl_2	82	2 : 1
9	 17	 (1.2)	 8	MeCN	57	1 : 2.3
10		 (1.2)	 9	CH_2Cl_2	65	3 : 1

[a] α:β ratios were determined by ^1H NMR spectroscopy and/or isolation of pure anomers. The anomers were separated chromatographically in all cases except in 1 and 4 where such separation was difficult.

Me_4Si. IR spectra were obtained with a Perkin-Elmer Model 281B spectrophotometer, and the IR figures reported are ν_{max} in cm^{-1}. Mass spectra data were provided by the Mass Spectrometry Center of the Chemistry Department, University of Pennsylvania, and are within acceptable limits unless otherwise stated. Optical rotations were recorded on a Perkin-Elmer Model 241 polarimeter at the sodium D line and ambient temperatures.

Thin layer chromatography (TLC) was carried out on 0.25-mm E. Merck precoated silica gel plates (60F-254) using UV light and/or 7% polyphosphomolybdic acid in ethanol–heat as developing agent. Prepa-

rative layer chromatography (PLC) was performed on 0.25, 0.5, 1, and 2 mm × 20 cm × 20 cm E. Merck precoated silica gel plates-60 (60F-254). For flash column chromatography silica silica gel-60 (230–400 mesh) was used.

All reactions were carried out under an argon atmosphere by using dry, freshly distilled solvents under anhydrous conditions unless otherwise stated. Etherial and hydrocarbon solvents were dried and distilled under argon from sodium benzophenone ketyl. Methylene chloride and acetonitrile were distilled under argon from calcium hydride. Reaction temperatures were measured externally. NMR multiplicities are reported by using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad; *J*, coupling constant (hertz). Only the strongest and/or structurally most important peaks are reported for the IR and mass spectra. Low-resolution mass data were obtained from electron-impact (EI) spectra and high-resolution mass spectra (HRMS) were obtained by the chemical-ionization (CI) technique. Yields refer to chromatographically and spectroscopically pure compounds.

Phenyl Thioglycoside Preparation. Method A (Hanessian et al.). Methyl α-pyranoside (or furanoside; 1.0 mmol) was dissolved in $ClCH_2CH_2Cl$ (5 mL) containing Me_3SiSPh (5.0 mmol). ZnI_2 (3.0 mmol) and n-Bu_4NI (1.20 mmol) were added, and the mixture was heated under argon at 60 °C, with stirring. After 1–2 h, the mixture was filtered and diluted with CH_2Cl_2, and the filtrate was washed with 10% $Ba(OH)_2$ (3 times) and processed as usual to give a yellow syrup. Flash column chromatography gave pure 1-thiopyranosides (or furanosides) as α/β mixture in 65–75% yields. Compounds **9**, **12**, **14**, **17**, **19**, **21**, and **22** were prepared according to this method; their physical properties are recorded in the supplementary material.

Phenyl Thioglycoside Preparation. Method B. Methyl α-pyranoside (or furanoside; 1.0 mmol) was dissolved in CH_2Cl_2 (3 mL) containing Me_3SiSPh (5.0 mmol) under argon, and the solution was cooled to 0 °C. $Me_3SiOSO_2CF_3$ (1.2 mmol) was added, and the mixture was allowed to warm to room temperature. After 1–2 h of stirring, the mixture was worked up and purified as in method A. Pure 1-thiopyranosides (or furanosides) were obtained as α/β anomeric mixtures in 60–70% yields. Compounds **17**, **19**, and **21** were prepared by this method; their physical properties are recorded in the supplementary material.

***O*-Glycoside Synthesis. General Procedure.** The hydroxy component (1.2–5.0 mmol) and the thioglycoside (1.0 mmol) were combined and azeotropically dried with benzene (3 times). CH_2Cl_2 (or CH_3CN; 10 mL) and pulverized 4-Å molecular sieves (250–500 mg) were added, and an argon atmosphere was secured. The mixture was allowed to stir for 10 min before recrystallized *N*-bromosuccinimide (1.1 mmol) was added. The solution gradually turned bright orange, the color usually fading with the completion of the reaction the progress of which was followed by TLC (usually 15–30 min). Dilution with ether or CH_2Cl_2 followed by filtration by successive washes with (i) 10% $NaHSO_3$, (ii) water, and (iii) brine, drying ($MgSO_4$), filtration, and evaporation furnished the crude products, which were purified by either preparative layer chromatography (PLC) or flash column chromatography. The following *O*-glycosides were prepared according to this method.

1: 320 mg (1.0 mmol) of **19** and 230 mg (5.0 mmol) of alcohol gave 200 mg of **1**, 78% yield (mixture of α- and β-anomers); oil; R_f 0.33 (silica, 10% ether in petroleum ether); IR (neat) ν_{max} 2987, 2940, 2910, 2110, 1450, 1385, 1375, 1255, 1215, 1165 ,1115, 1060, 980, 870 cm^{-1}; ^1H NMR δ 4.86 (d, J = 1 Hz, 0.5 H, H-1), 4.53 (d, J = 7 Hz, 0.5 H, H-1), 4.37 (t, J = 5 Hz, 0.5 H, CHO), 4.10–3.48 (m, 5.5 H, CH_2O, CHO, CHN), 1.54–1.2 (m, 12 H); mass spectrum m/e (relative intensity) 212 (M^+ – OEt, 0.8), 169 (4.0), 149 (4.4), 113 (18.1), 99 (11.6), 85 (20.5), 59 (base peak); HRMS calcd for $C_{11}H_{19}N_3O_4$ (M^+) 257.1376, found 257.1335.

2: 320 mg (1.0 mmol) of **19** and 180 mg (2.0 mmol) of alcohol gave 217 mg of **2**, 73% yield.

2a (**α-anomer**): oil; R_f 0.40 (silica, 10% ether in petroleum ether); α_D^{25} –59.05° (c 0.63, $CHCl_3$); IR (neat) ν_{max} 2985, 2940, 2890, 2110, 1465, 1387, 1375, 1250, 1220, 1170, 1070, 1000, 950, 865 cm^{-1}; ^1H NMR δ 5.06 (d, J = 2.4 Hz, 1 H, H-1), 4.33, 3.88, 3.60, 3.48 (multiplets, 1 H each, CHO, CHN), 1.56 (q, J = 7.5 Hz, 2 H, CH_2), 1.48, 1.38, 1.26, 1.24 (singlets, 3 H each, CH_3), 1.28 (d, J = 7.5 Hz, 3 H, CH_3), 0.92 (t, J = 7.0 Hz, 3 H, CH_3); mass spectrum m/e (relative intensity), 299 (M^+, 1.3), 284 (0.6), 257 (0.3), 262 (0.9), 212 (1.0), 202 (2.9), 184 (3.5), 157 (5.9), 115 (13.3), 85 (13), 71 (base peak); HRMS calcd for $C_{14}H_{26}N_3O_4$ (M^+ + 1) 300.1914, found 300.1900.

2b (**β-anomer**): oil; R_f 0.35 (silica, 10% ether in petroleum ether); α_D^{25} +13.69° (c 1.03, $CHCl_3$); IR (neat) ν_{max} 2980, 2940, 2880, 2105, 1463, 1385, 1370, 1260, 1212, 1180, 1165, 1095, 1070, 1035, 980, 870 cm^{-1}; ^1H NMR δ 4.79 (d, J = 7 Hz, 1 H, H-1), 3.94 (3 H) and 3.54 (1 H) (multiplets, 4 H, CHO, CHN), 1.56 (m, 2 H, CH_2), 1.53, 1.38, 1.23, 1.21 (singlets, 3 H each, CH_3), 1.30 (d, J = 6.0 Hz, 3 H, CH_3), 0.92 (t, J = 7.0 Hz, 3 H, CH_3); mass spectrum, m/e (relative intensity) 299 (M^+, 5.0), 257 (1.4), 253 (1.9), 220 (21.3), 199 (15.4), 167 (13.2), 149 (41.7), 109 (10.7), 81 (30.2); HRMS calcd for $C_{14}H_{26}N_3O_4$ (M^+ + 1) 300.1914, found 300.1926.

3: 320 mg (1.0 mmol) of **19** and 460 mg (1.2 mmol) of alcohol gave 490 mg of **3**, 55% yield.

3a (**α-anomer**): oil; R_f 0.37 (silica, 10% ether in petroleum ether); α_D^{25} –28.57° (c 1.12, $CHCl_3$); IR (neat) ν_{max} 2930, 2870, 2100, 1470, 1450, 1385, 1375, 1350, 1335, 1265, 1250, 1210, 1160, 1145, 1115, 1080, 1065, 1025, 950, 920, 870, 790, 740, 700 cm^{-1}; ^1H NMR δ 5.01 (d, J = 1 Hz, 1 H, H-1), 4.36 (t, J = 5 Hz, 1 H), 3.92 (dd, J = 9.6 Hz, 1 H), 3.73–3.43 (m, 3 H, CHO, CHN), 2.00–0.60 (m, 55 H, CH, CH_2, CH_3); mass spectrum, m/e (relative intensity) 463 (1.1), 423 (8.9), 422 (20.9), 371 (14.3), 355 (9.5), 316 (5.6), 231 (19.2), 217 (27.2), 215 (40.7), 212 (0.6), 189 (6.8), 159 (11.5), 149 (29.3), 135 (26.3), 121 (38.1), 107 (57.6), 93 (54.4), 81 (77.5), 69 (56.6), 55.1 (base peak); HRMS calcd for $C_{36}H_{60}N_3O_4$ (M^+ – 1) 598.4566; found 598.4631. Anal. Calcd for $C_{36}H_{61}N_3O_4$: C, 72.12; H, 10.26. Found: C, 72.04; H, 10.47.

3b (**β-anomer**): oil; R_f 0.33 (silica, 10% ether in petroleum ether); α_D^{25} +22.86° (c 1.4, $CHCl_3$); IR (neat) ν_{max} 2935, 2870, 2110, 1470, 1450, 1385, 1370, 1310, 1265, 1213, 1150, 1100, 1050, 980, 930, 870, 800, 740 cm^{-1}; ^1H NMR δ 4.67 (d, J = 7.5 Hz, 1 H, H-1), 4.04–3.44 (m, 5 H, CHO, CHN), 2.00–0.60 (m, 55 H, CH, CH_2, CH_3); mass spectrum, m/e (relative intensity) 584 (M^+ – Me, 2.7), 429 (31.5), 371 (63.7), 257 (10.2), 217 (14), 201 (21.1), 163 (28.6), 149 (39.3), 135 (31.6), 123 (30.9), 109 (66.2), 95 (base peak); HRMS calcd for $C_{36}H_{60}N_3O_4$ (M^+ – 1) 598.4566; found 498.4527.

4: 280 mg (1.0 mmol) of **9** and 190 mg (1.2 mmol) of alcohol gave 250 mg of **4**, 75% yield (mixture of α- and β-anomers): oil; R_f 0.30 (silica, 50% ether in petroleum ether); IR (neat) ν_{max} 2980, 2935, 2880, 1810, 1455, 1380, 1370, 1310, 1240, 1210, 1185, 1160, 1115, 1060, 1040, 990, 892, 850, 760 cm^{-1}; ^1H NMR δ 4.81 (t, J = 6 Hz, 0.5 H, H-1), 4.74 (dd, J = 8, 3 Hz, 0.5 H, H-1), 3.35–4.06 (m, 7 H, CH_2O, CHO), 2.42 (dd, J = 14, 3 Hz, 0.5 H, CH_2), 2.17 (d, J = 6 Hz, 1 H, CH_2), 1.85 (dd, J = 14, 8 Hz, 0.5 H, CH_2), 1.86 (m, 1 H, CH), 1.50 (s, 3 H, CH_3), 1.35 and 1.42 (singlets, 3 H each, acetonide), 1.38 (d, J = 7 Hz, 3 H, CH_3), 0.93 (d, J = 7 Hz, 3 H, CH_3); mass spectrum, m/e (relative intensity) 331 (M^+ + 1, 0.3), 246 (1.3), 205 (3.3), 181 (5.4), 145 (41.5), 123 (5), 121 (6.4), 85 (base peak); HRMS calcd for $C_{16}H_{27}O_7$ (M^+ + 1) 331.1749, found 331.1762. Anal. Calcd for $C_{16}H_{26}O_7$: C, 58.20; H: 7.94. Found: C, 57.91; H, 8.09.

5: 280 mg (1.0 mmol) of **9** and 150 mg (1.2 mmol) of alcohol gave 298 mg of **5**, 72% yield.

5a (**α-anomer**): oil; R_f 0.47 (silica, 75% ether in petroleum ether); α_D^{25} +83.07° (c 1.5, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3030, 2980, 2950, 2938, 2920, 2879, 2840, 2110, 1811, 1747, 1460, 1449, 1426, 1408, 1382, 1370, 1347, 1329, 1317, 1308, 1293, 1272, 1233, 1184, 1163, 1138, 1120, 1115, 1089, 1065, 1045, 996, 975, 970, 940, 928, 905, 892, 858, 845 cm^{-1}; ^1H NMR δ 5.02 (dd, J = 8.6, 2.6 Hz, 1 H, H-1″), 4.82 (d, J = 3.4 Hz, 1 H, H-1′), 4.69 (dd, J = 10.7, 3.6 Hz, 1 H, H-2′), 3.90 (d, J = 8.6 Hz, 1 H, H-4″), 3.88 (t, J = 10.3 Hz, 1 H, H-4′), 3.70 (m, 1 H, H-5″), 3.53 (m, 1 H, H-5′), 3.39 (s, 3 H, OCH_3), 3.24 (t, J = 9.6 Hz, 1 H, H-4′), 2.52 (dd, J = 14.5, 2.5 Hz, 1 H, H-2″ (equatorial)), 2.17 (s, 3 H, $C(O)CH_3$), 1.81 (dd, J = 14.5, 8.5 Hz, 1 H, H-2″ (axial)), 1.53 (s, 3 H, C-3″-CH_3), 1.38 (d, J = 6.5 Hz, 3 H, CH_3), 1.28 (d, J = 6.5 Hz, 3 H, CH_3); mass spectrum, m/e (relative intensity) 400 (M^+ – Me, 0.3), 370 (0.7), 205 (16.3), 171 (31.6), 109 (33.3), 99 (23.6), 85 (26.8), 83 (base peak); HRMS calcd for $C_{16}H_{22}N_3O_8$ (M^+ – OMe) 384.1407, found 384.1408.

5b (**β-anomer**): oil; R_f 0.32 (silica, 75% ether in petroleum ether); α_D^{25} –6.3° (c 0.38, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2980, 2936, 2105, 1805, 1745, 1458, 1446, 1382, 1367, 1360, 1348, 1312, 1287, 1273, 1230, 1218, 1205, 1176, 1158, 1152, 1138, 1118, 1100, 1068, 1055, 1048, 1034, 1003, 977, 898, 830, 718, 634 cm^{-1}; ^1H NMR 4.92 (dd, J = 8.1, 6.3 Hz, 1 H, H-1″), 4.82 (d, J = 3.8 Hz, 1 H, H-1′), 4.72 (dd, J = 10.8, 3.8 Hz, 1 H, H-2′), 4.10 (m, 1 H, H-5″), 3.93 (d, J = 8.7 Hz, 1 H, H-4″), 3.77 (m, 2 H, H-3′, H-5′), 3.38 (s, 3 H, OCH_3), 3.25 (t, J = 9.6 Hz, 1 H, H-4′), 2.28 (dd, J = 14.5, 6.3 Hz, 1 H, H-2″) (equatorial)), 2.17 (s, 3H, $C(O)CH_3$), 2.15 (dd, J = 14.5, 8.1 Hz, 1 H, H-2″ (axial)), 1.57 (s, 3 H, C-3″-CH_3), 1.40 (d, J = 6.0 Hz, 3 H, CH_3), 1.25 (d, J = 6.5 Hz, 3 H, CH_3); mass spectrum, m/e (relative intensity) 400 (M^+ – Me, 0.3), 370 (0.7), 205 (16.3), 171 (31.6), 109 (33.3), 99 (23.4); HRMS calcd for $C_{16}H_{22}N_3O_8$ (M^+ – OMe) 384.1407, found 384.1409.

6: 338 mg (1.0 mmol) of **21** and 160 mg (1.2 mmol) of alcohol gave 196 mg of **6**, 54% yield; oil; R_f 0.41 (silica, 50% ether in petroleum ether); α_D^{25} –57.41° (c 0.27, $CHCl_3$); IR (neat) ν_{max} 3060, 2980, 2940, 1745, 1580, 1480, 1450, 1370, 1240, 1208, 1160, 1120, 1080, 1020, 975, 937, 880, 850, 740 cm^{-1}; ^1H NMR δ 7.18 (m, 4 H, aromatic), 5.18 (s, 1 H, H-1), 5.16 (m, 1 H, H-5), 4.69 (dd, J = 7.0, 4.5 Hz, 1 H, H-3), 4.60 (m, CHO), 4.54 (d, J = 7 Hz, 1 H, H-2), 3.94 (dd, J = 8, 4.5 Hz, 1 H, H-4), 3.17 (m, 2 H, CH_2), 2.96 (m, 2H, CH_2), 2.07 (s, 3 H, $C(O)CH_3$), 1.45 and 1.28 (singlets, 3 H each, acetonide), 1.40 (d, J = 7 Hz, 3 H, CH_3);

mass spectrum, *m/e* (relative intensity) 347 (M^+ – Me, 0.3), 250 (1.6), 231 (6.8), 171 (3.7), 159 (2.4), 153 (3), 143 (2.4), 142 (4.6), 141 (3.4), 134 (8.0), 131 (10.7), 117 (57.2), 116 (base peak); HRMS calcd for $C_{20}H_{27}O_6$ (M^+ + 1) 363.1800; found 363.1770.

7: 454 mg (1.0 mmol) of **22** and 200 mg (1.3 mmol) of alcohol gave 410 mg of **7**, 82% yield.

7a (α-anomer): oil; R_f 0.30 (silica, 30% ether in petroleum ether); α_D^{25} + 41.55° (*c* 1.8, $CHCl_3$); IR (neat) ν_{max} 2960, 2930, 2900, 2860, 1745, 1473, 1463, 1450, 1367, 1245, 1140, 1114, 1045, 990, 970, 835, 800, 775, 670 cm^{-1}; ^1H NMR δ 4.95 (b s, 1 H, H-1), 4.77–3.77 (m, 6 H, CH_2O, CHO), 2.54–1.00 (m, 9 H, CH_2, CH), 2.06 and 2.04 (singlets, 3 H each, C(O) CH_3), 1.19 and 0.90 (singlets, 3 H each, CH_3), 1.04 (d, *J* = 8 Hz, 3 H, CH_3), 0.90 (s, 9 H, Si-*t*-Bu), 0.06 and 0.00 (singlets, 3 H each, $Si(CH_3)_2$); mass spectrum, *m/e* (relative intensity) 441 (M^+ – *t*-Bu, 0.1), 346 (1.9), 345 (7.3), 213 (25.7), 153 (41.5), 137 (37.8), 117 (41.7), 81 (base peak); HRMS calcd for $C_{26}H_{47}O_7Si$ (M^+ + 1) 499.3078, found 499.3129.

7b (β-anomer): oil; R_f 0.39 (silica, 30% ether in petroleum ether); α_D^{25} –2.38° (*c* 0.8, $CHCl_3$); IR (neat) ν_{max} 2955, 2930, 2860, 1747, 1470, 1460, 1450, 1430, 1367, 1320, 1253, 1240, 1165, 1140, 1110, 1085, 1050, 990, 970, 910, 835, 810, 773, 700 cm^{-1}; ^1H NMR 4.96 (dd, 1 H, *J* = 10, 2.5 Hz, H-1), 4.80–4.10 (m, 6 H, CH_2O, CHO), 2.52–1.00 (m, 9 H, CH_2, CH), 2.07 and 2.05 (singlets, 3 H each, C(O)CH_3), 1.22 and 0.92 (singlets, 3 H each, CH_3), 1.12 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.92 (s, 9 H, Si-*t*-Bu), 0.08 and 0.04 (singlets, 3 H each, $Si(CH_3)_2$); mass spectrum, *m/e* (relative intensity) 441 (M^+ – *t*-Bu, 1.3), 345 (6.7), 213 (23.2), 153 (36.6), 137 (49.8), 111 (43.8), 81 (base peak); HRMS calcd for $C_{25}H_{43}O_7Si$ (M^+ – Me) 483.2766; found 483.2846.

8: 390 mg (1.0 mmol) of **17** and 256 mg (1.2 mmol) of alcohol gave 280 mg of **8**, 57% yield.

8a (α-anomer): oil; R_f 0.23 (silica, 50% ether in petroleum ether); α_D^{25} +39.05° (*c* 0.21, $CHCl_3$); IR (neat) ν_{max} 2955, 2930, 2860, 1460, 1370, 1320, 1225, 1210, 1140, 1090, 1035, 1013, 983, 960, 917, 900, 880, 870, 825, 785, 770, 706 cm^{-1}; ^1H NMR δ 5.04 (d, *J* = 5.0 Hz, 1 H, H-1″), 4.86 (dd, *J* = 6, 2.5 Hz, 1 H, H-3′), 4.81 (s, 1 H, H-1′), 4.47 (d, *J* = 6 Hz, 1 H, H-2′), 4.40–3.24 (m, 6 H, CHO), 3.56, 3.42, and 3.27 (singlets, 3 H each, OCH_3), 1.45 and 1.33 (singlets, 3 H each, acetonide), 1.30 and 1.14 (doublets, *J* = 6.0 Hz, 3 H each, CH_3), 0.92 (s, 9 H, Si-*t*-Bu), 0.13 and 0.10 (singlets, 3 H each, $Si(CH_3)_2$); mass spectrum, *m/e* (relative intensity) 491 (M^+ – Me, 0.5), 449 (3.4), 261 (10), 201 (55.5), 172 (22.7), 143 (18.4), 115 (78.6), 113 (37.8), 101 (53.3), 89 (base peak); HRMS calcd for $C_{24}H_{46}O_9Si$ (M^+) 506.2898, found 506.2873.

8b (β-anomer): oil; R_f 0.52 (silica, 50% ether in petroleum ether); α_D^{25} –37.14° (*c* 0.35, $CHCl_3$); IR (neat) ν_{max} 2960, 2935, 2900, 2860, 2830, 1460, 1380, 1373, 1335, 1256, 1200, 1170, 1100, 1085, 1065, 1025, 990, 965, 890, 860, 835, 773 cm^{-1}; ^1H NMR 4.91 (d, *J* = 8.0 Hz, 1 H, H-1″), 4.83 (s, 1 H, H-1′), 4.78 (dd, *J* = 7.0, 3.0 Hz, 1 H, H-3′), 4.51 (d, *J* = 7.0 Hz, 1 H, H-2′), 4.12 (m, 1 H, H-5′), 3.84–2.92 (m, 5 H, CHO), 3.60, 3.50, and 3.29 (singlets, 3 H each, OCH_3), 1.42 and 1.30 (singlets, 3 H each, acetonide), 1.37 and 1.18 (doublets, *J* = 6.0 Hz, 3 H, each CH_3), 0.90 (s, 9 H, Si-*t*-Bu), 0.12 and 0.10 (singlets, 3 H each, $Si(CH_3)_3$); mass spectrum, *m/e* (relative intensity) 491 (M^+ – Me, 0.4), 289 (5.5), 261 (10.3), 201 (58.4), 175 (4.9), 172 (17.7), 171 (12.7), 143 (11.7), 115 (50.8), 113 (18.7), 101 (28), 89 (49.4), 88 (base peak); HRMS calcd for $C_{24}H_{46}O_9Si$ (M^+) 506.2898, found 506.2838.

9: 390 mg (1.0 mmol) of **17** and 250 mg (1.2 mmol) of alcohol gave 320 mg of **9**, 65% yield.

9a (α-anomer): oil; R_f 0.23 (silica, 20% ether in petroleum ether); α_D^{25} +53.13° (c 0.57, $CHCl_3$); IR (neat) ν_{max} 2960, 2930, 2900, 2860, 1475, 1465, 1450, 1380, 1373, 1340, 1310, 1255, 1210, 1200, 1170, 1135, 1100, 1065, 1040, 1005, 965, 940, 915, 903, 865, 835, 775, 715, 692, 653 cm^{-1}; ^1H NMR δ 4.88 (d, *J* = 5 Hz, 1 H, H-1), 4.10 (m, 1 H, H-5), 3.77–3.22 (m, 5 H, CH_2O, CHO), 3.61 and 3.44 (singlets, 3 H each, OCH_3), 1.7–1.25 (m, 24 H, CH_2), 1.18 (d, *J* = 8 Hz, 3 H, CH_3), 0.94 (s, 9 H, Si-*t*-Bu), 0.90 (t, *J* = 7.0 Hz, 3 H, CH_3), 0.14 and 0.12 (singlets, 3 H each, $Si(CH_3)_2$); mass spectrum, *m/e* (relative intensity) 445 (M^+ – *t*-Bu, 0.9), 257 (1.1), 201 (86.3), 171 (16), 116 (8.2), 89 (94.1), 88 (base peak); HRMS calcd for $C_{28}H_{58}O_5Si$ (M^+) 502.4038, found 502.4024. Anal. Calcd for $C_{28}H_{58}O_5Si$: C, 66.93; H, 11.64. Found: C, 67.14; H, 11.67.

9b (β-anomer): oil; R_f 0.58 (silica, 20% ether in petroleum ether); α_D^{25} –6.25° (*c* 0.16, $CHCl_3$); IR (neat) ν_{max} 2960, 2932, 2860, 1465, 1380, 1360, 1335, 1255, 1200, 1170, 1130, 1100, 1067, 1040, 1000, 965, 905, 865, 835, 772 cm^{-1}; ^1H NMR δ 4.64 (d, *J* = 9 Hz, 1 H, H-1), 3.92–2.96 (m, 6 H, CH_2O, CHO), 3.61 and 3.54 (singlets, 3 H each, OCH_3), 1.65–1.2 (m, 24 H, CH_2), 1.20 (d, *J* = 6 Hz, 3 H, CH_3), 0.93 (s, 9 H, Si-*t*-Bu), 0.89 (t, *J* = 7.0 Hz, 3 H, CH_3), 0.14 and 0.10 (singlets, 3 H each, $Si(CH_3)_2$); mass spectrum, *m/e* (relative intensity) 445 (M^+ – *t*-Bu, 0.8), 413 (1.5), 257 (11.8), 201 (54.3), 115 (35.2), 89 (48.2), 88 (base peak); HRMS calcd for $C_{28}H_{59}O_5Si$ (M^+ + 1) 503.4116, found 503.4121.

11: 390 mg (1.0 mmol) of **17** and 720 mg (1.2 mmol) of alcohol gave 530 mg of **11**, 60% yield (mixture of α- and β-anomers): oil; R_f 0.18 (silica, 10% acetone in CH_2Cl_2); IR (neat) ν_{max} 3500, 2960, 2930, 2890, 2860, 2830, 1710, 1680, 1630, 1600, 1460, 1407, 1375, 1360, 1320, 1255, 1175, 1100, 1000, 980, 960, 938, 915, 870, 835, 810, 775, 735, 700, 660 cm^{-1}; ^1H NMR δ 7.22 (d, *J* = 16 Hz, 1 H, H-11), 6.29 (d, *J* = 16 Hz, 1 H, H-10), 5.86 (d, *J* = 10.4 Hz, 1 H, H-13), 5.00 (m, 3 H, CHO), 4.65 (d, *J* = 7.8 Hz, 1 H, CHO), 4.10–2.90 (m, 12 H, CH_2O, CHO), 3.60, 3.57, 3.48, 3.44, and 3.36 (singlets, 3 H each, OCH_3), 2.60–1.00 (m, 13 H, CH, CH_2), 1.80 (s, 3 H, C-12-CH_3), 1.32 (d, *J* = 7 Hz, 3 H, CH_3), 1.23 (d, *J* = 8 Hz, 3 H, CH_3), 1.17 (d, *J* = 7 Hz, 3 H, CH_3), 1.02 (d, *J* = 8 Hz, 3 H, CH_3), 0.92 (s, 9 H, Si-*t*-Bu), 0.92 (t, *J* = 6 Hz, 3 H, CH_3), 0.13 and 0.11 (singlets, 3 H each, $Si(CH_3)_2$). mass spectrum, *m/e* (relative intensity) 870 (M^+ – OMe, 0.2), 805 (0.2), 705 (0.5), 695 (0.7), 679 (0.8), 581 (1.1), 563 (1.7), 531 (2.4), 462 (93.0), 405 (18.2), 289 (33.1), 257 (30.2), 231 (18.2), 175 (47.7), 157 (67.1), 133 (52.3), 125 (base peak). Anal. Calcd for $C_{46}H_{80}O_{15}Si$: C, 61.30; H, 8.94. Found: C, 59.96; H, 8.85.

Internal Acetal Synthesis. General Procedure. Preparation of internal acetals proceeded as in *O*-glycoside synthesis described above in 0.05 M CH_2Cl_2 solution. The following acetals were prepared.

13: 160 mg (0.5 mmol) of **12** gave 60 mg of **13**, 60% yield; oil; R_f 0.26 (silica, ether); α_D^{25} –49.29° (*c* 0.14, $CHCl_3$); IR (neat) ν_{max} 2930, 2900, 2820, 1455, 1375, 1325, 1285, 1185, 1100, 1025, 1005, 970, 925, 888, 790 cm^{-1}; ^1H NMR δ 5.51 (s, 1 H, H-1), 4.64 (d, *J* = 6 Hz, 1 H, CHO), 3.95 (d, *J* = 6 Hz, 1 H, CHO), 3.76 (t, *J* = 6 Hz, 1 H, CHO), 3.51, 3.48, and 3.44 (singlets, 3 H each, OCH_3), 3.33, 3.15, and 3.10 (singlets, 1 H each, CHO); mass spectrum *m/e* (relative intensity) 173 (M^+ – OMe, 0.2), 167 (1.8), 159 (5.5), 144 (3.8), 143 (5.2), 127 (11.4), 103 (14.5), 101 (92), 88 (base peak); HRMS calcd for $C_9H_{17}O_5$ (M^+ + 1) 205.1071, found 205.1085.

15: 200 mg (0.5 mmol) of **14** gave 120 mg of **15**, 80% yield; oil; R_f 0.18 (silica, 30% ether in petroleum ether); α_D^{25} –46.25° (*c* 0.24, $CHCl_3$); IR (neat) ν_{max} 2960, 2930, 2860, 1745, 1465, 1440, 1370, 1242, 1163, 1130, 1100, 1065, 1027, 970, 935, 905, 883, 860, 835, 777 cm^{-1}; ^1H NMR δ 5.52 (s, 1 H, H-1), 5.0 (dt, *J* = 9.0, 5.0 Hz, 1 H, H-3), 4.46–3.58 (m, 4 H, CHO), 2.04 (s, 3 H, C(O)CH_3), 2.02 (s, 1 H, H-2), 1.96 (d, *J* = 9.0 Hz, 1 H, H-2), 0.94 (s, 9 H, Si-*t*-Bu), 0.10 and 0.04 (singlets, 3 H each, $Si(CH_3)_2$); mass spectrum, *m/e* (relative intensity) 245 (M^+ – *t*-Bu, 2.3), 203 (2.0), 186 (3.5), 185 (23.5), 171 (7.3), 157 (14.1), 129 (67.6), 117 (base peak); HRMS calcd for $C_{14}H_{27}O_5Si$ (M^+ + 1) 303.1620, found 303.1646.

Supplementary Material Available: Selected physical properties (^1H NMR, IR, and mass spectra) for compounds **9**, **12**, **14**, **17**, **19**, **21**, and **22** (4 pages). Ordering information is given on any current masthead page.