Total Synthesis of Vancomycin—Part 4: Attachment of the Sugar Moieties and Completion of the Synthesis

K. C. Nicolaou,* Helen J. Mitchell, Nareshkumar F. Jain, Toshikazu Bando, Robert Hughes, Nicolas Winssinger, Swaminathan Natarajan, Alexandros E. Koumbis[a]

Abstract: The total synthesis of vancomycin (**1**, Figure 1) is described. The successful plan for this synthesis involves sequential and stereoselective coupling of vancomycin aglycon acceptor **6** and glycosyl donors, trichloroacetimidate **50** and glycosyl fluoride **27** (Scheme 8). Acceptor **6** was synthesized from vancomycin aglycon (**2**) (Scheme 1), which was derived both by total synthesis and by semisynthesis from vancomycin itself (**1**) (Scheme 2). The vancosamine derivative **27** was obtained by total synthesis (Scheme 3) while the glycosyl derivative **50** was prepared from glucal (**46**) (Scheme 6). A number of glycosidation model studies, carried out in order to establish the final route to vancomycin (**1**), are also described and so are a number of failed attempts to secure the target molecule (**1**).

Keywords: amino acids · antibiotics · synthetic methods · total synthesis · vancomycin

Introduction

In the preceding papers,[1–3] we delineated chemistry leading to the total synthesis of vancomycin's aglycon[4] (**2**, Figure 1). In this article, we present the completion of the synthesis[5] of vancomycin (**1**)[6] by attachment of the carbohydrate moieties onto the aglycon, followed by final deprotections.

Results and Discussion

The plan

The plan for the final stages of the total synthesis of vancomycin (**1**, Figure 1) was layed out according to the retrosynthetic analysis shown in Figure 2. Thus, it was envisioned that a suitably protected vancomycin aglycon acceptor would react with appropriately functionalized glucose and vancosamine derivatives to afford the entire vancomycin network. From our experience in the vancomycin

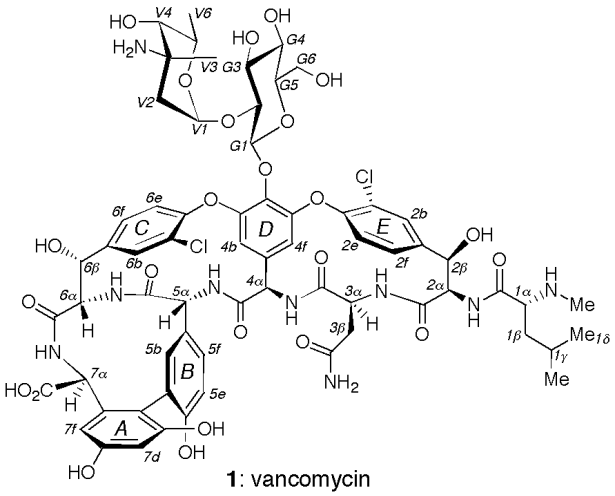

Figure 1. Molecular structures of vancomycin (**1**) and vancomycin aglycon (**2**).

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field, we felt that the aglycon derivative **6** (Figure 2) would be the most suitable precursor in that it exposed only the desired functionality towards glycosidation, and its protecting groups appeared compatible with the projected coupling and deprotection operations. With regards to the sugar moieties, the plan called for either a sequential attachment using activated systems of the two sugars, such as **3** (e.g. X = trichloroacetimidate) and **4** (e.g. Y = F), or a block-type glycosidation employing a suitable disaccharide, such as **5** (e.g. X = trichloroacetimidate). In addition to aiming for efficiency in the glycosidation, our objective was to achieve high stereoselectivity with regards to the glycoside bonds. To this end, we had to rely on a participating protecting group at C2 of the glucose moiety in order to facilitate β-glycosidation, and on the anomeric effect to deliver the required α-glycoside bond, linking the two sugar units. To test the implementation of this strategy we needed efficient routes to key building blocks **3**–**6**.

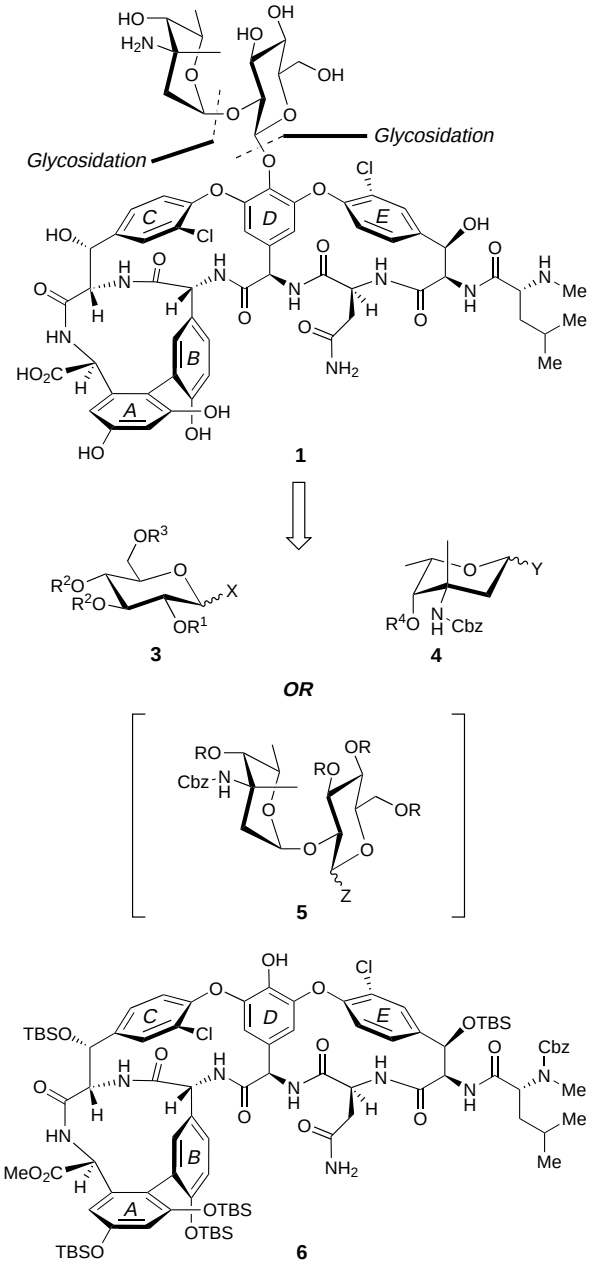


Figure 2. Retrosynthetic analysis of vancomycin (**1**).

Abstract in Greek:

Σε αυτο το αρθρο περιγραφεται η ολικη συνθεση της βανκομυκινης (**1**, Φιγουρα 1). Το επιτυχες σχεδιο για τη συνθεση αυτη περιλαμβανει τη διαδοχικη και στερεοεκλεκτικη συζευξη του δεκτη **6** με τους γλυκοζιδικους δοτες, τον τριχλωροακετιμιδικο εστερα **50** και το γλυκοζυλο–φθοριδιο **27** (Σχημα 8). Ο δεκτης **6** συντεθηκε απο το αγλυκο της βανκομυκινης (**2**) (Σχημα 1) το οποιο προηρθε απο την ολικη συνθεση και απο την ημισυνθετικη οδο, απο την ιδια τη βανκομυκινη (**1**) (Σχημα 2). Το βανκοζαμινικο παραγωγο **27** παρασκευαστηκε μεσω ολικης συνθεσης (Σχημα 3) ενω το γλυκοζιτικο παραγωγο **50** συντεθηκε απο τη γλυκαλη (**46**) (Σχημα 6). Επισης, περιγραφηκαν διαφοροι μεθοδοι γλυκοσυλιωσης που μελετηθηκαν με σκοπο να προσδιορισθει η τελικη οδος συνθεσης της βανκομυκινης (**1**), οπως επισης και διαφορες αποτυχημενες προσπαθειες που αφορουν τη συνθεση αυτη.

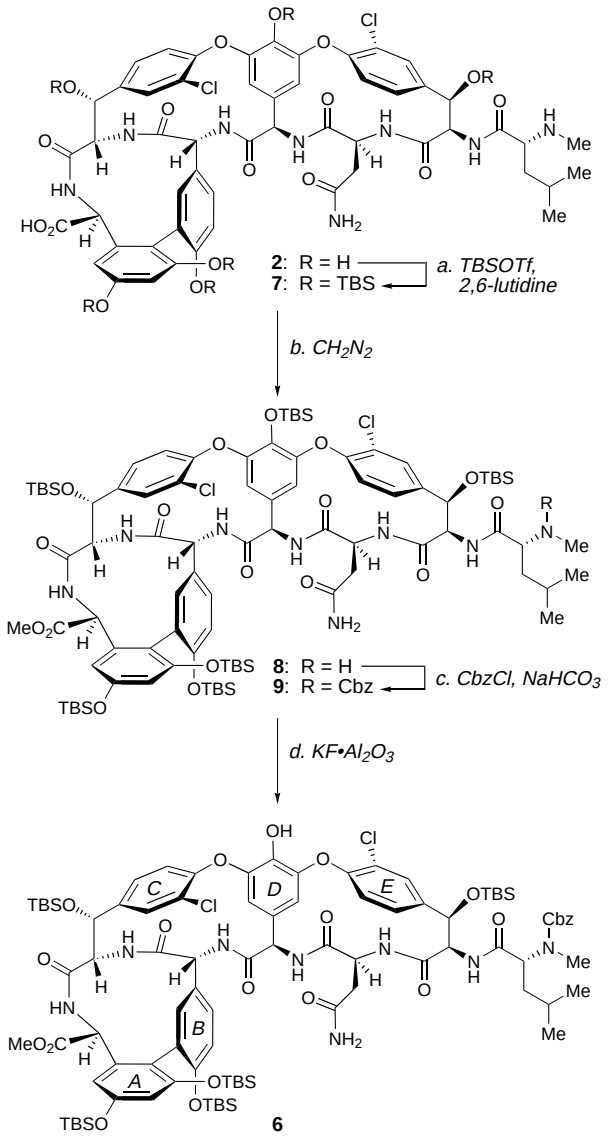
Synthesis of the vancomycin aglycon carbohydrate acceptor

The design of pentasilylated vancomycin's aglycon derivative **6** as a suitable carbohydrate acceptor was based on the premise that deprotection after glycosidation would be possible, since the silyl groups could potentially be removed by fluoride ion, the Cbz group by mild hydrogenolysis, and the methyl ester by selective, base-induced hydrolysis. The synthesis of **6** was, of course, the most crucial prerequisite for the success of the designed plan towards vancomycin (**1**).

Persilylation of vancomycin aglycon (**2**) with excess TBSOTf in the presence of 2,6-lutidine, followed by aqueous workup, furnished hexa-TBS derivative **7** in 72% yield (Scheme 1). Exposure of **7** to excess diazomethane in ether led to methyl ester **8** (91% yield), whose treatment with CbzCl in dioxane and aqueous $NaHCO_3$ gave the Cbz derivative **9** (92% yield). It was after some experimentation that we found $KF \cdot Al_2O_3$[7] to be a suitable reagent for selectively removing the more sensitive silyl group from the phenolic hydroxyl of ring D. Thus, exposure of the pentasilyl ether **9** to this reagent in MeCN at 0 °C for 2 h, furnished the desired hexasilyl phenol **6** in 60% yield.

The same intermediate (**6**) was obtained more conveniently from vancomycin (**1**) itself (Scheme 2). Thus, vancomycin (**1**) was persilylated with excess TBSOTf and 2,6-lutidine in CH_2Cl_2/DMF (10:1) furnishing, after aqueous workup, nonasilyl ether **10** in 65% yield. Prolonged aqueous exposure during workup was necessary to ensure complete rupture of the N–Si and C(O)O–Si bonds in this step. Exposure of **10** to excess diazomethane in ether led to methyl ester **11** (90% yield), which was treated with excess CbzCl in aqueous $NaHCO_3$ providing di-Cbz derivative **12** in 80% yield. Finally, and fortunately, hydrolysis of the sugar moieties from the aglycon proceeded smoothly in TFA/Me_2S/CH_2Cl_2 (1:1:1) at ambient temperature, and under carefully controlled conditions, to afford the required acceptor phenol **6** in 60% yield.

Scheme 2 also summarizes the conversion of vancomycin (**1**) to compound **13** [di-Cbz-vancomycin methyl ester] which was encountered as a key intermediate in the total synthesis of vancomycin (**1**) (vide infra, see Scheme 8). These degradation studies provided important comparison stages and, by enriching our supplies of the key intermediates, facilitated the eventual total synthesis of vancomycin (**1**). In addition, the readily available intermediate so obtained (**13**) provides

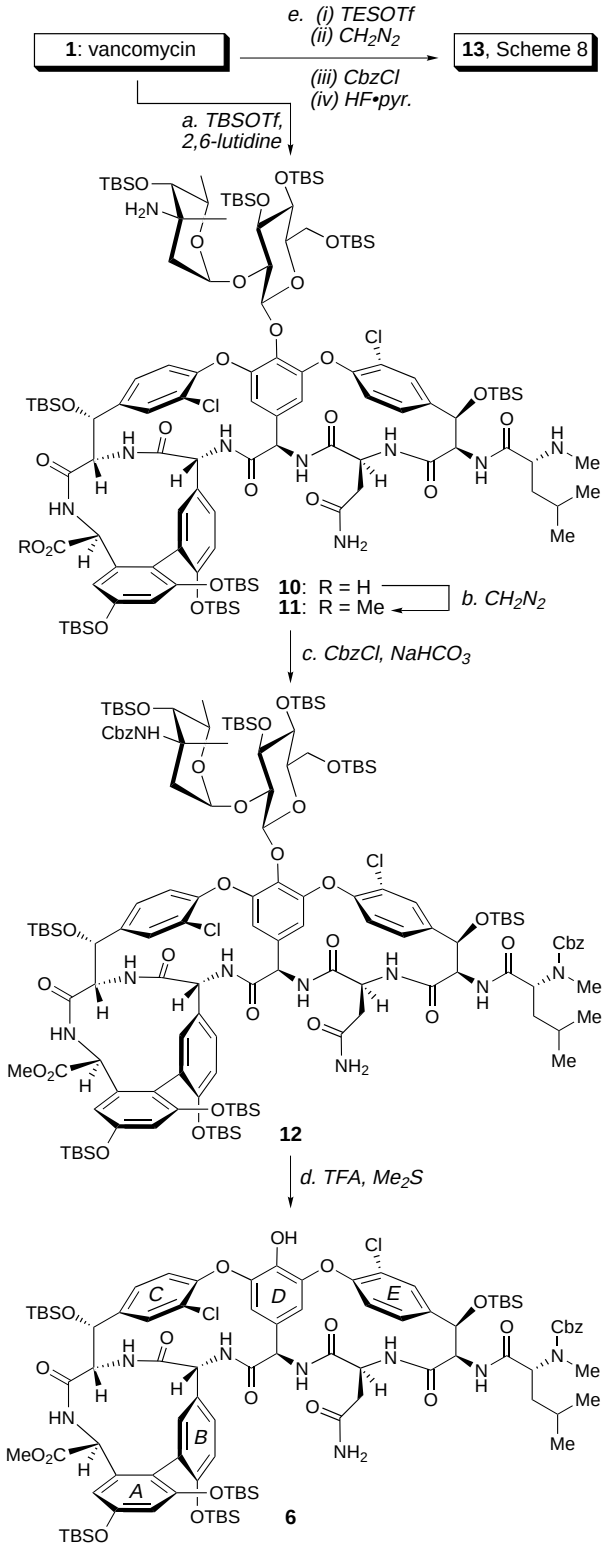


Scheme 1. Synthesis of phenol **6** from vancomycin aglycon (**2**). a) 20 equiv of TBSOTf, 60 equiv of 2,6-lutidine, CH_2Cl_2/DMF (10:1), 0 → 25 °C, 7 h, 72 %; b) CH_2N_2 (excess), Et_2O, 0 °C, 0.5 h, 91 %; c) 5.0 equiv of CbzCl, 10.0 equiv of $NaHCO_3$, 1,4-dioxane/H_2O (10:1), 0 °C, 0.5 h, 92 %; d) 1.0 equiv of $KF \cdot Al_2O_3$, MeCN, 0 °C, 2 h, 60 %. TBS = *tert*-butyldimethylsilyl; DMF = dimethylformamide; Cbz = benzyloxycarbonyl; Tf = trifluoromethanesulfonyl.

opportunities for the construction of combinatorial libraries of vancomycin analogs for biological screening.

Synthesis of vancosamine donors

In order to explore the chemistry of the projected glycosidations, we required a flexible sequence towards potential vancosamine and glucose donors by which we could vary the protecting groups on these sugars. To this end, we embarked on a rapid and stereoselective synthesis[8] of vancosamine in order to gain access to such intermediates as they were needed (Scheme 3). In our planning, we envisioned a stereoselective *anti* addition[9] of an acyl anion equivalent to an aldehyde derived from L-lactic acid as a means to install the C4



Scheme 2. Degradation of vancomycin (**1**) and synthesis of intermediates **6** and **13**. a) 60 equiv of TBSOTf, 180 equiv of 2,6-lutidine, CH_2Cl_2/DMF (10:1), 0 → 25 °C, 18 h; saturated aq. $NaHCO_3$, 25 °C, 60 h, 65 %; b) CH_2N_2 (excess), Et_2O, 0 °C, 0.5 h, 90 %; c) 6.0 equiv of CbzCl, 10.0 equiv of $NaHCO_3$, 1,4-dioxane/H_2O (10:1), 0 °C, 0.5 h, 80 %; d) TFA, Me_2S, CH_2Cl_2 (1:1:1, 0.01M), 25 °C, 3 h, 60 %; e) (i) 60 equiv of TESOTf, 180 equiv of 2,6-lutidine, CH_2Cl_2/DMF (10:1), 0 → 25 °C, 18 h; sat. aq. $NaHCO_3$, 25 °C, 60 h; (ii) CH_2N_2 (excess), Et_2O, 0 °C, 0.5 h; (iii) 5.0 equiv of CbzCl, 10.0 equiv of $NaHCO_3$, 1,4-dioxane/H_2O (10:1), 0 °C, 0.5 h; (iv) HF · pyr./pyr. (1:1), THF, 0 → 25 °C, 12 h, 40 % overall yield. TES = triethylsilyl; TFA = trifluoroacetic acid.

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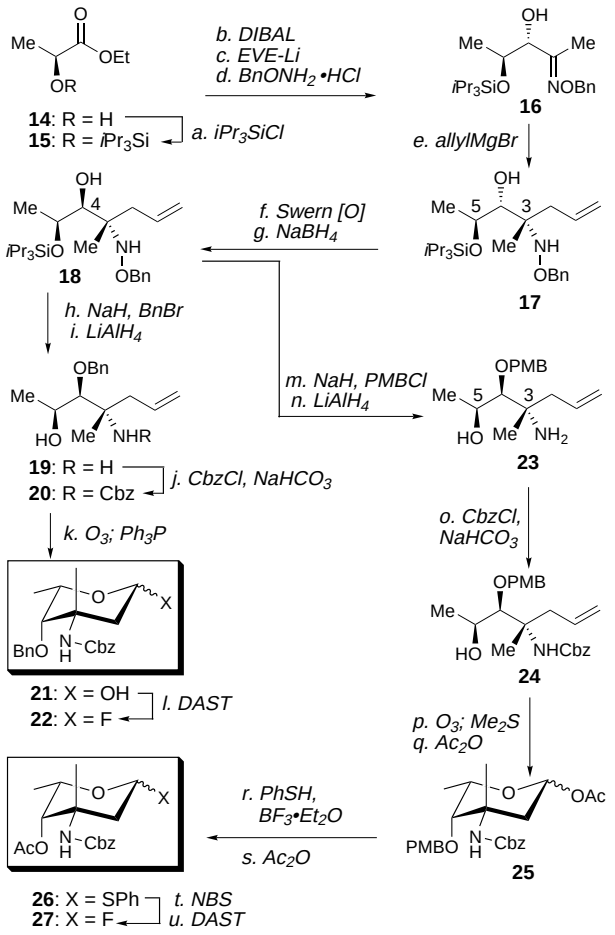


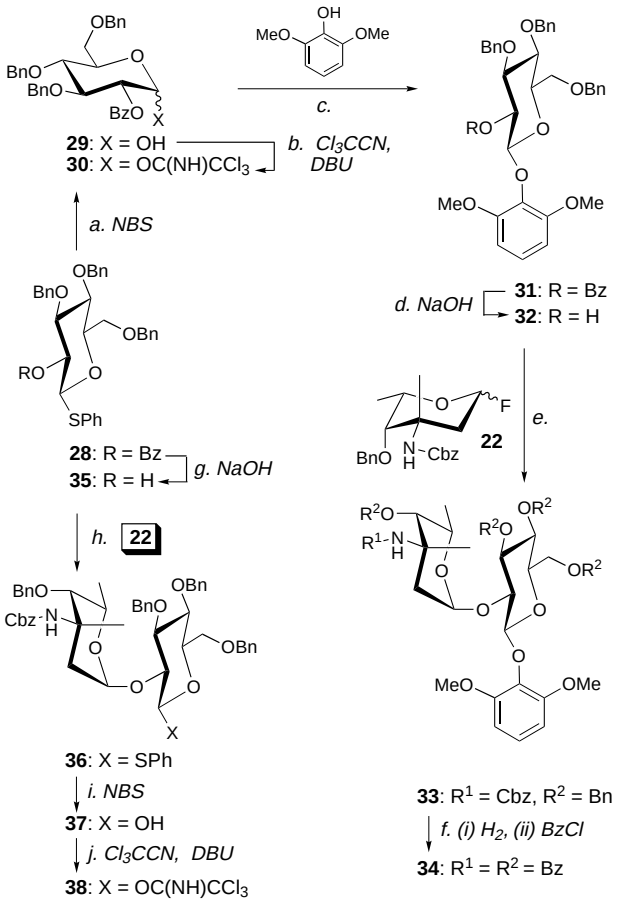
Scheme 3. Synthesis of vancosamine donors **22** and **27**. a) 1.1 equiv of iPr$_3$SiCl, 2.0 equiv of imidazole, DMF, 0 →25 °C, 10 h, 99 %; b) 1.6 equiv of DIBAL, CH_2Cl_2, −78 °C, 45 min; c) 1.8 equiv of EVE-Li, THF, −100 °C, 5 min; then 5 % aq HCl, THF/H_2O (4:1), 65 % for three steps, 85 % *de*; d) 1.1 equiv of $BnONH_2 \cdot HCl$, pyr., 0 →25 °C, 2 h, 97 % (*E*:*Z* ca. 4:1); e) 2.5 equiv of allylMgBr, Et_2O, −35 °C, 1 h, 95 % based on 50 % conversion; f) 2.0 equiv of $(COCl)_2$, 2.5 equiv of DMSO, −78 °C, 2 h; 4.0 equiv of Et_3N, −78 →0 °C, 2 h, 91 %; g) 3.0 equiv of $NaBH_4$, Et_2O/MeOH (5:1), 25 °C, 0.5 h, 90 %, 92 % *de* ; h) 1.1 equiv of NaH, 1.2 equiv of BnBr, 0.2 equiv of nBu$_4$NI, DMF, 0 →25 °C, 2 h, 88 %; i) 1.6 equiv of $LiAlH_4$, Et_2O, 25 °C, 24 h; j) 3.0 equiv of CbzCl, 10.0 equiv of $NaHCO_3$, H_2O/THF (1:5), 0 →25 °C, 0.5 h, 78 % for two steps; k) (i) O_3, CH_2Cl_2, −78 °C, 1 h; (ii) 2.0 equiv of Ph_3P, −78 →25 °C, 12 h, 95 %, α:β ca. 1.8:1; l) 1.4 equiv of DAST, CH_2Cl_2, 0 °C, 20 min, 85 %; m) 1.1 equiv of NaH, 1.3 equiv of PMBCl, THF, 0 →25 °C, 4 h, 93 %; n) 4.0 equiv of $LiAlH_4$, Et_2O, reflux, 5 h; o) 1.5 equiv of CbzCl, 2.0 equiv of $NaHCO_3$, 1,4-dioxane/H_2O (4:1), 0 →25 °C, 18 h, 81 % for two steps; p) O_3 (excess), CH_2Cl_2, −78 °C, 1 h; Me_2S, −78 →25 °C, 6 h, 92 %; q) 2.0 equiv of Ac_2O, 3.0 equiv of Et_3N, 0.1 equiv of 4-DMAP, CH_2Cl_2, 25 °C, 2 h, 96 %; r) 4.0 equiv of PhSH; 4.0 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, −20 °C, 1 h, 91 %; s) 2.0 equiv of Ac_2O, 3.0 equiv of Et_3N, 0.1 equiv of 4-DMAP, CH_2Cl_2, 25 °C, 2 h, 97 %; t) 1.5 equiv of NBS, acetone/H_2O (9:1), 0 °C, 0.5 h, 87 %; u) 1.5 equiv of DAST, CH_2Cl_2, 0 °C, 20 min, 100 %. NBS = *N*-bromosuccinimide; DAST = diethylaminosulfur trifluoride; DIBAL = diisobutylaluminum hydride; 4-DMAP = 4-dimethylaminopyridine; allyl = CH_2=CHCH$_2$; EVE-Li = CH_2=C(OEt)Li; Bn = benzyl; DMSO = dimethyl sulfoxide; PMB = *p*-methoxybenzyl.

stereocenter (numbering based on the final carbohydrate ring) and a nucleophilic addition to an oxime[10] to craft the C3 functionality. Thus, ethyl L-lactate (**14**, Scheme 3) was protected with a bulky silicon group (iPr$_3$Si) under standard conditions, furnishing silyl ether **15** in 99 % yield. Sequential reduction of **15** with DIBAL and addition of EVE-Li[11] to the resulting aldehyde at −100 °C, followed by acidic hydrolysis, afforded the corresponding hydroxy ketone as a mixture of diastereoisomers (85 % *de*, 65 % combined yield for three steps). After chromatographic separation, the desired *anti* isomer (major) was condensed with *O*-benzylhydroxylamine in pyridine, to afford the two readily separable oxime ethers **16** (97 % yield, *E*:*Z* ca. 4:1). Pleasantly, chain extension of the *E* isomer of **16** by addition of allylmagnesium bromide at −35 °C afforded hydroxylamine **17** as a single diastereoisomer (95 % yield based on ca. 50 % conversion). Interestingly, despite considerable experimentation and the excellent overall recovery of materials, this reaction could not be pushed to completion. Since the C4 configuration of **17** is opposite to the one required for vancosamine, an inversion at this center was necessary. To this end, alcohol **17** was oxidized under Swern conditions [$(COCl)_2$, DMSO, Et_3N] to afford the corresponding ketone (91 % yield), which was subjected to chelation-controlled reduction with $NaBH_4$ in Et_2O/MeOH (5:1) affording the desired hydroxy compound **18** (92 % *de*, 90 % yield). While other methods may have provided the desired C4 stereoisomer directly, we should recall[8] that the objective of this lactate sequence was a broader one, namely the synthesis of both vancosamine and evernitrose, the latter being accessible directly from diastereoisomer **17**, which served as a common intermediate for both syntheses. At the stage of intermediate **18**, we could vary the protecting group at C4. Thus, for our first-generation glycosidation studies we chose a benzyl ether at this position and proceeded towards vancosamine donor **22** as follows. The hydroxy group in **18** was benzylated (NaH, BnBr, nBu$_4$NI cat., 88 % yield) and the resulting product was subjected to the action of $LiAlH_4$ which cleaved both the N-O and O−Si bonds,[12] furnishing amino alcohol **19**. Selective formation of the *N*-Cbz derivative by exposure of **19** to CbzCl in aqueous $NaHCO_3$ led to compound **20** in 78 % yield for the two steps. Finally, cleavage of the terminal olefin in **20** by ozonolysis, followed by exposure of the resulting ozonide to Ph_3P, furnished an approximate 1:1.8 mixture of α:β lactols **21** in 95 % yield. Fluoride **22**, our favorite choice as a vancosamine donor, was prepared smoothly by reacting **21** with DAST[13] in CH_2Cl_2 at 0 °C (85 % yield, α:β ca. 16:1). As matters transpired, we needed a second vancosamine donor, fluoride **27** (Scheme 3), equipped with an acetate group at C4. While we will save the discussion for the rationale of its design for later, we will discuss here its synthesis from intermediate **18**. Thus, the hydroxy group of the latter compound (**18**) was temporarily protected as a PMB ether (NaH, PMBCl, 93 % yield), and the resulting compound was exposed to $LiAlH_4$, furnishing amino alcohol **23** by cleavage of the N−O and O−Si bonds as before. The amino group of **19** was selectively engaged by treatment with CbzCl in aqueous $NaHCO_3$, furnishing hydroxy Cbz derivative **24** in 81 % yield (two steps). Cleavage of the terminal olefin in **24** by ozonolysis, followed by reaction with Me_2S and acetylation (Ac_2O, Et_3N, 4-DMAP cat.), led to vancosamine derivative **25** in 88 % overall yield. Exposure of **25** to excess PhSH and $BF_3 \cdot Et_2O$ in CH_2Cl_2 at −20 °C removed cleanly, both the PMB and acetate groups (91 % yield), leading, after acetylation of the C4 hydroxyl group as

above (97% yield), to phenylthioglycoside **26**. Formation of vancosamine fluoride **27** required cleavage of the PhS group with NBS in acetone/H_2O (9:1) (87% yield) and exposure of the resulting mixture of α/β lactol anomers to DAST in CH_2Cl_2 at 0 °C (100% yield, α:β ca. 16:1).

First-generation glycosidation studies

With the C4-benzyl protected vancosamine donor **22** ready, we turned our attention to model glycosidation studies directed at exploring a strategy for an eventual coupling of the vancomycin aglycon and the sugar moieties.[8] For these studies, we required a suitable glucose donor. We initially chose trichloroacetimidate[14] **30** (Scheme 4), in which the C2 position was occupied by a benzoate group and the remaining three hydroxy groups were carrying benzyl groups for protection. The C2 benzoyl group was expected to direct the glycosidation reaction in the β direction by the well-known neighboring group participation, as required. Thus, phenylthioglucoside **28** (readily available form tribenzyl glucal by dihydroxylation, dibenzoylation, and reaction with PhSH/$BF_3 \cdot Et_2O$, see Experimental Section) was treated with NBS in acetone/H_2O (10:1) to afford lactol **29** in 87% yield (ca. 10:1 mixture of α:β anomers). Conversion to imidate **30** was smoothly effected by treatment with trichloroacetonitrile and DBU (90% yield).



Scheme 4. Synthesis of first-generation vancomycin disaccharides **34** and **38**. a) 2.0 equiv of NBS, acetone/H_2O (10:1), 0 °C, 0.5 h, 87%, α:β ca. 10:1; b) 10.0 equiv of Cl_3CCN, 0.05 equiv of DBU, CH_2Cl_2, −30 °C, 0.5 h, 90%; c) 1.6 equiv of **30**, 0.6 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, 4 Å MS, −30 → 25 °C, 24 h, 95%, β:α ca. 13:1; d) 2.5 equiv of NaOH, MeOH, 25 °C, 3 h, 90%; e) 2.0 equiv of **22**, 0.4 equiv of $BF_3 \cdot Et_2O$, 0.4 equiv of Me_3SiOTf, CH_2Cl_2, 4 Å MS, −30 → 25 °C, 72 h, 89% based on 90% conversion, α:β ca. 10:1; f) (i) H_2, 10% Pd/C, EtOAc, 25 °C, 12 h; (ii) 7.0 equiv of BzCl, pyr., 0 °C, 6 h, 85% for two steps; g) 1% aq. NaOH, MeOH, 25 °C, 3 h, 90%; h) 1.3 equiv of **22**, 1.9 equiv of $SnCl_2$, CH_2Cl_2, 4 Å MS, −10 °C, 2 h, 85%, α:β ca. 3.3:1; i) 1.5 equiv of NBS, acetone/H_2O (10:1), 0 °C, 0.5 h, 85%; j) 20 equiv of Cl_3CCN, 0.05 equiv of DBU, CH_2Cl_2, 0 °C, 15 min, 90%, α:β ca. 20:1. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene; Bz = benzoyl.

Using 2,6-dimethoxyphenol as a phenol representative of the bulky vancomycin aglycon, we found that its coupling with trichloroacetimidate donor **30** proceeded smoothly in the presence of $BF_3 \cdot Et_2O$ at −30 → 25 °C to afford the desired glucoside **31** in excellent yield (95%) and high anomeric stereoselectivity (β:α ca. 13:1). Debenzoylation at C2 under basic conditions (NaOH, 90%) gave direct access to acceptor **32**, setting the stage for an attempt at the second glycosidation utilizing vancosamine donor **22**. A combination of $BF_3 \cdot Et_2O$ and TMSOTf was found, in this instance, to be highly effective for the attachment of **22** to **32**, furnishing the desired α-glycoside **33** as the major product (89% yield based on 90% conversion, α:β ca. 10:1). Hydrogenolysis of the Cbz and benzyl groups from **33** (H_2, 10% Pd/C), followed by benzoylation of the resulting amino-tetraol gave disaccharide **34**. The spectroscopic data of **34** matched those reported by Danishefsky et al., who had previously developed an independent route to this vancomycin model.[15] Of particular value in confirming the stereochemistry of the glycosidic linkages were the coupling constants $J_{1,2ax} = 4.5$ Hz for vancosamine, and $J_{1,2} = 7.5$ Hz for glucose.

In order to explore the ground for the possibility of a block-type installation of the two sugar units onto the vancomycin aglycon, we proceeded to synthesize the disaccharide trichloroacetimidate **38**, as outlined in Scheme 4. Thus, debenzoylation of **28** (NaOH) gave acceptor **35** in 90% yield. Coupling of **35** with vancosamine donor **22** in CH_2Cl_2 at −10 °C in the presence of $SnCl_2$, proceeded in excellent yield (85%), but led to only modest anomeric selectivity in favor of the desired α-glycoside **36** (α:β ca. 3.3:1). Varying the temperature of the reaction, or the catalyst, did not improve significantly this result. On the other hand, these studies revealed that a major controlling factor in terms of reactivity and diastereoselectivity was the size and electronic nature of the glucose anomeric substituent: the smaller the substituent, the faster the coupling with the vancosamine donor, but the lower the anomeric selectivity. After separation of the isomers, the desired α-anomer **36** was treated with NBS in acetone/H_2O (10:1), releasing disaccharide lactol **37** (85% yield), which was converted to its trichloroacetimidate **38** by exposure to CCl_3CN in the presence of DBU in CH_2Cl_2 at 0 °C (90% yield, α:β ca. 20:1).

The successful synthesis of disaccharides **34** and **36** (Scheme 4) established the feasibility of attaching, stereoselectively, the carbohydrate units onto vancomycin's aglycon, either stepwise or in a block-type fashion. Early experimentation with the benzoyl-containing glucose donor **30** and the pentasilylated aglycon derivative **6** indicated that basic removal of the C2 benzoate from the glucose moiety would be problematic due to significant TBS cleavage from some of

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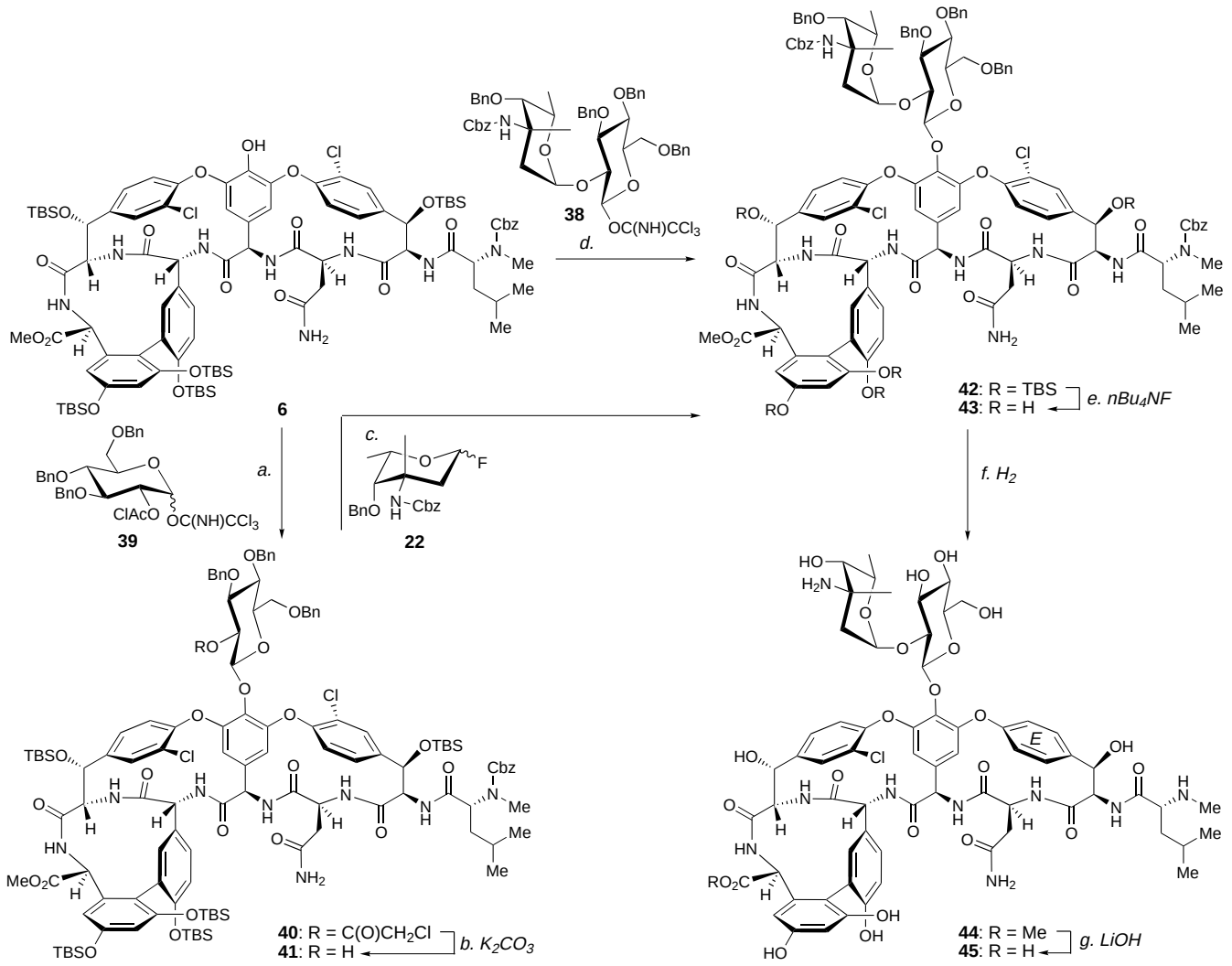


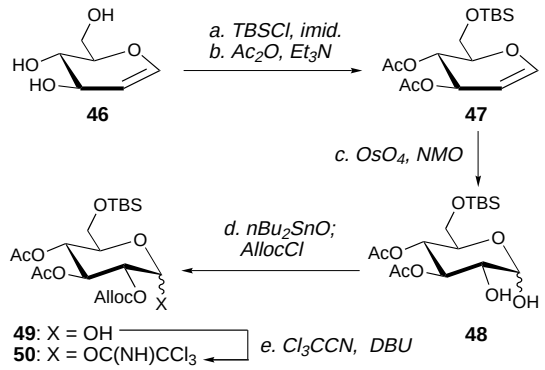
Scheme 5. First-generation approach to vancomycin (**1**). a) 1.7 equiv of **39**, 4.0 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, $-78 \rightarrow -30\,^{\circ}C$, 18 h, 70%; b) 3.0 equiv of K_2CO_3,THF/MeOH (2:1), 25 °C, 10 min, 75%; c) 10.0 equiv of **22**, 5.0 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 24 h, 5%; d) 5.0 equiv of **38**, 10.0 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, $-78 \rightarrow -30\,^{\circ}C$, 24 h, 70%; e) 30 equiv of nBu$_4$NF, THF, $-10\,^{\circ}C$, 2 h; f) H_2, 10% Pd/C, MeOH, 25 °C, 16 h; g) 5.0 equiv of LiOH, THF/H_2O (1:1), 0 °C, 20 min. ClAc = C(O)CH_2Cl.

the phenolic groups under the required basic conditions. Anticipating a more selective C2 deprotection of the chloroacetate group, trichloroacetimidate **39** (Scheme 5) [prepared by an analogous route to its benzoate counterpart (**29**) as shown in Scheme 4] was, therefore, utilized in our first attempt to install the glucose moiety onto the aglycon. Reaction of the aglycon derivative **6** with carbohydrate donor **39** in the presence of $BF_3 \cdot Et_2O$ in CH_2Cl_2 at $-78 \rightarrow -30\,^{\circ}C$ furnished the desired glycoside **40** in 70% yield. The chloroacetate group was then removed from the C2 carbohydrate position by controlled reaction with K_2CO_3 in THF/MeOH, providing acceptor **41** (75% yield). However, the second glycosidation step with vancosamine donor **22** proceeded sluggishly, and furnished only poor yields of the desired disaccharide, even after prolonged reaction times. Thus, reaction of **41** with excess **22** in CH_2Cl_2 and in the presence of $BF_3 \cdot Et_2O$ at $0 \rightarrow 23\,^{\circ}C$ resulted in only 5% yield of the desired compound (**42**). Confronted with these disappointing results, we opted for the more convergent, block-type attachment of the disaccharide domain onto the aglycon acceptor (**6**). This strategy, of course, could potentially suffer from the absence of a β-directing group to control the anomeric stereochemistry of the newly generated glycosidic linkage (joining the disaccharide to the aglycon), but, at this point, we counted on the bulkiness of the glucose C2 substituent to provide some degree of selectivity. Indeed, the coupling of disaccharide donor **38** with phenol **6** proceeded smoothly in CH_2Cl_2 at $-78 \rightarrow -30\,^{\circ}C$, affording a single coupling product, which was presumed to be the desired β-glycoside. Stereochemical assignment of the newly formed glycoside bond, however, was not possible at this stage and had to await deprotection and comparison with authentic vancomycin methyl ester. To this end, the TBS groups were cleaved from **42** by exposure to TBAF, furnishing pentahydroxy vancomycin derivative **43**, which was subjected to hydrogenolysis (H_2, 10% Pd/C, MeOH, 25 °C) and saponification (LiOH, THF/H_2O, 1:1, 0 °C) to remove the benzyl ethers and the methyl ester, respectively. Spectroscopic analysis, however, clearly indicated that the hydrogenolysis of the benzyl ethers was accompanied by scission of the C–Cl

bond of ring E, and that compounds **44** and **45** lacking one chlorine substituent were the products, rather than the expected vancomycin and its methyl ester. Other methods for removing the benzyl ethers from **43** were attempted; however, none were successful. It was, therefore, decided to abandon the benzyl groups and search for different protecting groups as part of second-generation glycosidation studies.

Second-generation glycosidation studies

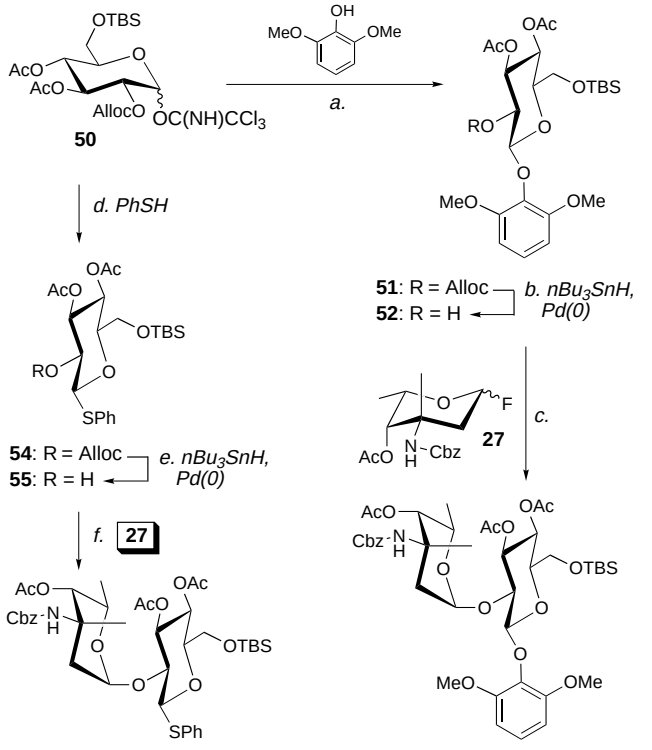
With the decision to move away from benzyl protecting groups on the sugars, we were faced with the option of using silyl and/or acetate groups for the protection of the hydroxy groups of these moieties. Fully silylated (e.g. TBS) mono- and disaccharide systems were synthesized and proved to be poor candidates as glycosidation donors. On the other hand, fully acetylated systems were considered to be too deactivated for the projected glycosidations. We, therefore, chose to explore a combination of silyl and acetyl groups as a possible scenario for the construction of the vancomycin system. Our own experiences demonstrated that silyl groups could be removed successfully from vancomycin and, drawing comfort from the recent work of Kahne et al.,[16] we projected that cleavage of acetate and alloc (allyloxycarbonyl) groups would be compatible with the molecule. For a glucose donor, therefore, we designed trichloroacetimidate **50** (Scheme 6) with a TBS



Scheme 6. Synthesis of glucose donor **50**. a) 1.0 equiv of TBSCl, 2.2 equiv of imidazole, DMF, 0→25 °C, 1 h, 82 %; b) 2.5 equiv of Ac_2O, 4.0 equiv of Et_3N, 0.1 equiv of 4-DMAP, CH_2Cl_2, 0→25 °C, 1 h, 97 %; c) 0.05 equiv of OsO_4, 1.5 equiv of NMO, acetone/H_2O (9:1), 25 °C, 12 h, 84 %; d) 1.2 equiv of nBu$_2$SnO, toluene, reflux, 6 h; 1.1 equiv of AllocCl, 0 °C, 0.5 h, 67 %; e) 20 equiv of Cl_3CCN, 0.05 equiv of DBU, CH_2Cl_2, −10 °C, 20 min, 89 %, α:β ca. 14:1. NMO = 4-methylmorpholine *N*-oxide; Alloc = allyloxycarbonyl.

group at C6, acetate groups at C4 and C3, and an alloc group at C2. As a vancosamine donor, we chose the 4-acetoxy glycosyl fluoride **27** (Scheme 3). The synthesis of the latter intermediate (**27**) has already been described above (see Scheme 3), whereas the construction of trichloroacetimidate **50** is summarized in Scheme 6. Thus, **46** (obtained from commercially available glucal triacetate by deacetylation with K_2CO_3, MeOH, 100 %), was selectively monosilylated (C6, TBSCl, imidazole, 82 % overall yield) and acetylated (C4 and C3, Ac_2O, Et_3N, 4-DMAP, 97 % yield) to afford **47**. Dihydroxylation of **47** with NMO/OsO_4 cat. in acetone/H_2O (9:1) furnished diol **48** in 84 % yield. The selective allylcarbonylation of the C2 hydroxy group in **48** was accomplished by reaction with nBu$_2$SnO, followed by quenching with AllocCl, leading to compound **49** (67 % yield). Exposure of **49** to CCl_3CN in CH_2Cl_2 in the presence of DBU gave the desired trichloroacetimidate **50** in 89 % yield (α:β ca. 14:1).

With the newly designed carbohydrate donors now available, and before attempting the real task of constructing vancomycin (**1**), we proceeded to test their coupling and loading onto a model phenolic acceptor as shown in Scheme 7.



Scheme 7. Synthesis of second-generation vancomycin model disaccharides **53** and **56**. a) 1.7 equiv of **50**, 0.2 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, 4 Å MS, −78 °C, 20 min, 95 %; b) 0.05 equiv of $Pd(Ph_3P)_4$, 1.5 equiv of nBu$_3$SnH, CH_2Cl_2, 25 °C, 0.5 h, 83 %; c) 1.6 equiv of **27**, 1.1 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, 4 Å MS, −30 °C, 2 h, 91 %, α:β ca. 9:1; d) 1.2 equiv of PhSH, 0.3 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, 4 Å MS, −78 °C, 45 min, 95 %, β:α > 99:1; e) 0.05 equiv of $Pd(Ph_3P)_4$, 1.5 equiv of nBu$_3$SnH, CH_2Cl_2, 25 °C, 0.5 h, 87 %; f) 1.6 equiv of **27**, 1.1 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, 4 Å MS, −30 °C, 2 h, 98 %, α:β ca. 3:2.

Stability of protecting groups, reactivity of donors, and stereoselectivity were the issues to be explored. To this end, glucose donor **50** was treated with 2,6-dimethoxyphenol in CH_2Cl_2 and in the presence of $BF_3 \cdot Et_2O$ at −78 °C, affording, rapidly and in 95 % yield, the desired β-glycoside **51** as a single stereoisomer. Liberation of the C2 hydroxy group from **51** proceeded selectively in the presence of nBu$_3$SnH and a catalytic amount of $Pd(Ph_3P)_4$,[17] yielding acceptor **52** in 83 % yield. The coupling of **52** with vancosamine donor **27** proceeded smoothly in CH_2Cl_2 at −30 °C and in the presence of $BF_3 \cdot Et_2O$, furnishing disaccharide **53** in high yield and excellent anomeric diastereoselectivity (91 %, α:β ca. 10:1). Starting again from glucose donor **50**, and repeating the sequence with thiophenol instead of 2,6-dimethoxyphenol,

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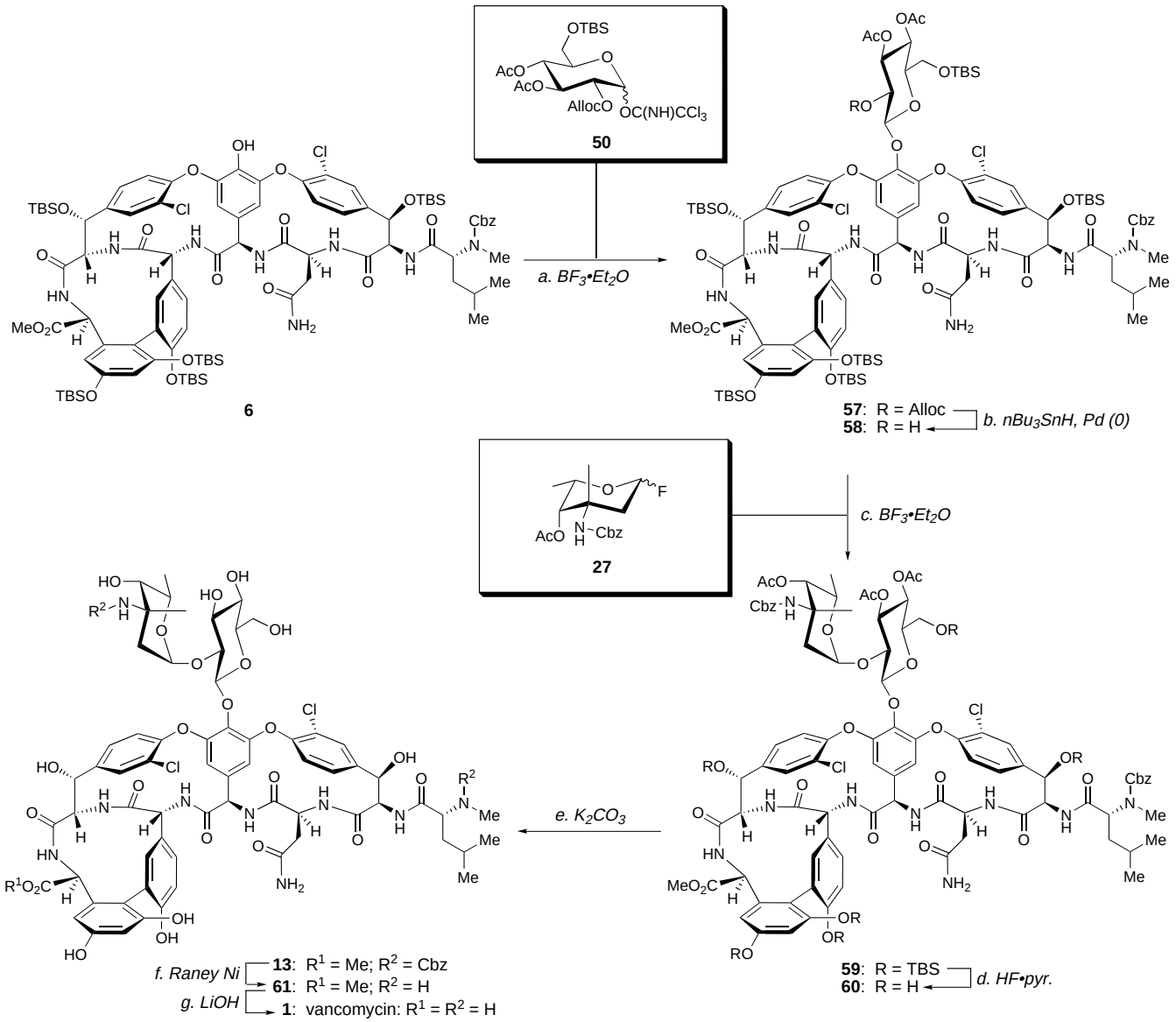

Scheme 8. Synthesis of vancomycin (**1**). a) 5.0 equiv of **50**, 10.0 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, $-78\,^{\circ}C$, 6 h, 82 %; b) 4.0 equiv of nBu$_3$SnH, 0.1 equiv of $Pd(Ph_3P)_4$, CH_2Cl_2, $25\,^{\circ}C$, 0.5 h, 85 %; c) 4.0 equiv of **27**, 3.0 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, $-35\,^{\circ}C$, 2 h, 84 %; d) HF · pyr./pyr. (1:1), THF, $0 \rightarrow 25\,^{\circ}C$, 12 h, 80 %; e) 5.0 equiv of K_2CO_3, MeOH, $25\,^{\circ}C$, 4 h, 95 %; f) Raney Ni, nPrOH/H_2O (2:1), $25\,^{\circ}C$, 0.5 h; g) 5.0 equiv of LiOH, THF/H_2O (1:1), $0\,^{\circ}C$, 20 min, 85 % from **13**.

intermediates **54** (95 % yield, β:$\alpha > 99$:1), **55** (87 % yield), and finally disaccharide **56** (98 %, α:β ca. 3:2) were obtained in excellent yield (Scheme 7). Thus, while the stereoselectivity of the first glycosidation was excellent, that of the second coupling was only modest, pointing to the overriding effect of the size and electronic nature of the glucose C1 substituent. The C4 acetate group of vancosamine, apparently, did not influence the outcome of this glycosidation reaction, even at lower temperatures. It was with this knowledge at hand that we proceeded to apply this strategy to the real case, being cautiously confident of the outcome.

Completion of the synthesis

The model studies described above helped shape the final plan for the completion of the total synthesis of vancomycin (**1**): a stepwise glycosidation approach utilizing acceptor **6** and donors **50** and **27** as shown in Scheme 8. Glycosidation of phenol **6** with excess trichloroacetimidate **50** in CH_2Cl_2 and in the presence of $BF_3 \cdot Et_2O$ at $-78\,^{\circ}C$ proceeded smoothly to afford monosaccharide **57** in 82 % yield, together with a minor product, presumed to be the undesired α-anomer. The β-stereochemistry of the major product (**57**) was tentatively assigned at this stage based solely on the results of the model studies described above, and was later confirmed by NMR spectroscopy and conversion to vancomycin (**1**). Proceeding with the synthesis, the C2 hydroxy group of the glucose moiety of **57** was liberated by reaction with nBu$_3$SnH/$Pd(Ph_3P)_4$ in wet CH_2Cl_2, leading to the new glycoside acceptor **58** (85 % yield). At this stage we were also pleased to observe in the ^{1}H NMR spectrum of **58** a revealing coupling constant ($J_{1,2} =$ 7.7 Hz) associated with the anomeric position, characteristic of a β-glycoside linkage.

We were now in a position to attempt the second glycosidation with vancosamine donor **27**. Reaction of **58** with glycosyl fluoride **27** in CH_2Cl_2 and in the presence of $BF_3 \cdot Et_2O$ at $-35\,^{\circ}C$ gave the fully protected vancomycin derivative **59** in 84% yield and about 8:1 α:β stereoselectivity. Chromatographically separated **59** was then subjected to desilylation (excess HF·pyr./pyr.), furnishing hexahydroxy compound **60** in 80% yield. Exposure of **60** to the action of K_2CO_3 in MeOH at ambient temperature removed the three acetate groups, leading to di-Cbz vancomycin methyl ester **13** (95% yield). The latter compound (**13**) was found to be identical with a sample derived from vancomycin (**1**) as summarized in Scheme 2 [(i) TESOTf, 2,6-lutidine, 65%; (ii) CH_2N_2; (iii) CbzCl, $NaHCO_3$, 80% for two steps; (iv) HF·pyr./pyr., 80%]. Finally, treatment of **13** with Raney-Ni in *n*PrOH/H_2O (2:1) led in clean removal of the Cbz groups without dechlorination (as occasionally observed under hydrogenolysis conditions using H_2-Pd/C systems) and saponification of the resulting vancomycin methyl ester with LiOH in THF/H_2O (1:1) at 0 °C, furnished vancomycin (**1**) in 85% yield from **13**. Synthetic vancomycin (**1**) was identical with an authentic sample by the usual criteria (HPLC, ^{1}H NMR, mixed ^{1}H NMR, MS).[18] Kahne's group has also accomplished a synthesis of vancomycin (**1**) from vancomycin-derived derivatives of a pseudoaglycon (containing the glucose residue only)[16] and an aglycon derivative.[20]

Conclusion

In this and the preceding three articles,[1–3] we described the total synthesis of vancomycin (**1**). During this campaign a number of new synthetic technologies and strategies were designed and developed, among which the triazene-driven biaryl ether synthesis is perhaps the most prominent. The successful strategy employed modern catalytic asymmetric reactions for the construction of the required amino acid building blocks which were then assembled to appropriate peptide fragments, whose cyclization in the order C-O-D → AB/C-O-D → AB/C-O-D-O-E led to the framework of vancomycin's aglycon. While both the C-O-D and D-O-E macrocycles were constructed by the triazene-driven cyclization process, the AB-containing ring system was formed by a sequential Suzuki coupling–macrolactamization procedure. The latter cyclization became possible only after formation of the C-O-D ring system which provided the necessary preorganization for ring closure. Interestingly, while the unnatural atropisomer of the D-O-E ring system equilibrated at 130 °C to a 1:1 mixture of both, the natural and the unnatural isomers, the AB and C-O-D macrocycles maintained their natural integrity. The catalytic asymmetric Suzuki coupling based synthesis of biaryl systems, developed during this program, is also worth noting since it allows the stereoselective and efficient construction of this important moiety. Furthermore, this reaction played a crucial role in the eventual construction of the vancomycin aglycon.

Finally, sequential attachment of the sugar moieties onto a suitably protected aglycon derivative (phenol **6**), followed by deprotection, allowed a stereoselective total synthesis of vancomycin (**1**). Well designed degradation studies on vancomycin (**1**) opened additional avenues to certain key synthetic intermediates rendering them readily available for semisynthetic studies. In conjunction with solid-phase and combinatorial chemistry, such studies may prove extremely valuable in delivering vancomycin libraries for biological screening. Thus, the chemistry developed during this program enriched our knowledge in the field of chemical synthesis and set the stage for possible contributions to the chemical biology and medicine of the glycopeptide antibiotics.

Experimental Section

General techniques: See paper 1 in this series.[1]

Hexa-TBS-aglycon 7: TBSOTf (20.1 mL, 8.7 mmol) was added dropwise to a solution of vancomycin aglycon (**2**) (500 mg, 0.437 mmol) and 2,6-lutidine (30.5 mL, 26.2 mmol) in CH_2Cl_2/DMF (10:1, 40 mL) at 0 °C. The reaction mixture was slowly warmed to 25 °C and stirred for 7 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (30 mL) and stirred at 25 °C for 10 h. The organic layer was separated and the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), concentrated and the residue was purified by flash column chromatography (silica gel, 1 → 5% MeOH in CH_2Cl_2, gradient elution) to afford hexa-TBS-aglycon **7** (574 mg, 72%) as a white foam. **7**: $R_f = 0.22$ (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]_D^{22} = -19.3$ ($c = 0.89$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3403$, 2927, 2856, 1675, 1498, 1471, 1256, 1175, 1105, 1060, 1021, 916, 838, 782 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD, 330 K): $\delta = 7.65$ (s, 1H), 7.55–7.52 (m, 2H), 7.43 (s, 1H), 7.23 (d, $J = 8.5$ Hz, 1H), 7.18–7.16 (m, 1H), 7.05 (d, $J = 2.5$ Hz, 1H), 6.98 (dd, $J = 8.5$, 2.5 Hz, 1H), 6.75 (d, $J = 8.5$ Hz, 1H), 6.58 (br. s, 1H), 6.39 (d, $J = 2.0$ Hz, 1H), 5.72 (br. s, 1H), 5.67–5.64 (m, 1H), 5.42 (d, $J = 4.0$ Hz, 1H), 5.37 (s, 1H), 5.33 (br. s, 1H), 4.90 (s, 1H), 4.83 (d, $J = 4.0$ Hz, 1H), 4.63–4.61 (m, 1H), 4.59 (s, 1H), 4.53 (s, 1H), 4.09 (s, 1H), 3.13–3.11 (m, 1H), 2.52–2.49 (m, 1H), 2.40 (s, 3H), 1.83–1.80 (m, 1H), 1.62–1.59 (m, 1H), 1.53–1.50 (m, 1H), 1.06 (s, 9H), 1.01 (s, 9H), 0.96 (d, $J = 6.5$ Hz, 3H), 0.95 (d, $J = 6.5$ Hz, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.73 (s, 9H), 0.61 (s, 9H), 0.36 (s, 3H), 0.35 (s, 3H), 0.23 (s, 3H), 0.23 (s, 3H), 0.16 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H), −0.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$:CD_3OD (9:1), 310 K): $\delta = 173.9$, 173.8, 171.2, 168.8, 168.3, 156.3, 155.4, 154.5, 152.6, 151.9, 151.3, 141.2, 139.3, 136.4, 134.2, 130.1, 129.5, 129.3, 129.2, 128.6, 128.0, 127.6, 126.9, 125.1, 117.2, 113.7, 111.7, 107.5, 105.5, 74.1, 73.1, 71.0, 67.8, 64.0, 63.3, 60.9, 56.2, 54.9, 53.1, 52.5, 42.3, 37.3, 35.2, 30.4, 29.6, 26.7, 26.5, 26.0, 26.0, 25.8, 23.6, 22.9, 22.3, 19.6, 19.1, 19.0, 2.0, 1.7, −3.3, −3.5, −3.7, −3.8, −4.0, −4.1, −4.3, −4.6; HRMS (FAB) calcd for $C_{89}H_{136}Cl_2N_8O_{17}Si_6Cs$ [$M + Cs^+$] 1959.7071, found 1959.6976.

Hexa-TBS-aglycon methyl ester 8: A solution of hexa-TBS-aglycon **7** (400 mg, 0.218 mmol) in ether (5.0 mL) was treated with CH_2N_2 (solution in ether, excess) at 0 °C. The reaction mixture was stirred for 0.5 h, argon was then bubbled through for 5 min, and then the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 20 → 60% EtOAc in benzene, gradient elution) to afford hexa-TBS-aglycon methyl ester **8** (367 mg, 91%) as a yellow foam. **8**: $R_f = 0.24$ (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]_D^{22} = +9.0$ ($c = 0.92$, $CHCl_3$); IR (film) $\tilde{\nu}_{max} = 3403$, 2956, 2929, 2858, 1676, 1508, 1473, 1425, 1255, 1176, 1110, 1061, 1022, 919, 838, 782 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD, 330 K): $\delta = 7.60$ (d, $J = 2.0$ Hz, 1H), 7.54 (dd, $J = 8.5$, 2.0 Hz, 1H), 7.52 (dd, $J = 8.5$, 2.0 Hz, 1H), 7.42 (d, $J = 2.0$ Hz, 1H), 7.24 (d, $J = 8.5$ Hz, 1H), 7.10 (br. d, $J = 8.5$ Hz, 1H), 7.04 (d, $J = 2.5$ Hz, 1H), 6.99 (dd, $J = 8.5$, 2.5 Hz, 1H), 6.76 (d, $J = 8.5$ Hz, 1H), 6.41 (d, $J = 2.0$ Hz, 1H), 6.32 (d, $J = 2.0$ Hz, 1H), 5.73 (d, $J = 2.0$ Hz, 2H), 5.42 (d, $J = 4.0$ Hz, 1H), 5.36 (s, 1H), 5.34 (s, 1H), 4.92 (s, 1H), 4.83 (d, $J = 4.0$ Hz, 1H), 4.64 (t, $J = 5.5$ Hz, 1H), 4.59 (s, 1H), 4.47 (s, 1H), 4.10 (s, 1H), 3.75 (s, 3H), 3.12 (dd, $J = 8.5$, 5.5 Hz, 1H), 2.54–2.47 (m, 1H), 2.39 (s, 3H), 1.84–1.79 (m, 1H), 1.65–1.58 (m, 1H), 1.53–1.48 (m, 1H), 1.11 (s, 9H), 1.01 (s, 9H), 0.96 (d, $J = 6.0$ Hz, 3H), 0.95 (d, $J = 6.0$ Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.73 (s, 9H), 0.61 (s, 9H), 0.36 (s, 3H), 0.35 (s, 3H), 0.23 (s, 6H), 0.17 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H), −0.08 (s, 3H);

0947-6539/99/0509-2656 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 9

^{13}C NMR (150 MHz, CD_3OD, 330 K): δ = 177.9, 174.4, 172.8, 171.9, 171.4, 170.2, 169.4, 157.2, 156.4, 155.2, 153.5, 152.8, 152.4, 152.1, 142.1, 140.0, 137.3, 134.8, 132.1, 130.4, 129.3, 129.0, 128.7, 128.6, 128.0, 127.7, 126.8, 125.7, 125.1, 121.1, 113.6, 112.2, 108.1, 106.3, 75.0, 74.5, 64.9, 64.7, 61.3, 58.3, 56.5, 55.8, 53.3, 52.6, 43.4, 37.8, 35.7, 26.6, 26.5, 26.4, 26.2, 26.1, 23.6, 22.7, 19.8, 19.3, 19.2, 18.8, −3.5, −3.6, −3.8, −3.9, −4.0, −4.2, −4.4, −4.5, −4.6, −4.7; HRMS (FAB) calcd for $C_{90}H_{138}Cl_2N_8O_{17}Si_6Cs$ [M + Cs^+] 1976.7239, found 1976.7397.

***N*-Cbz-hexa-TBS-aglycon methyl ester 9:** A solution of hexa-TBS-aglycon methyl ester **8** (350 mg, 0.191 mmol) in dioxane/H_2O (10:1, 3.0 mL) was treated with $NaHCO_3$ (160 mg, 1.91 mmol) and CbzCl (136 μL, 0.948 mmol) at 0 °C. After stirring for 0.5 h, the reaction mixture was diluted with EtOAc (200 mL) and washed with saturated aqueous $NaHCO_3$ (30 mL) and brine (30 mL). The organic layer was dried (Na_2SO_4), concentrated, and the residue was purified by flash column chromatography (silica gel, 10 → 50 % EtOAc in hexanes, gradient elution) to afford *N*-Cbz-hexa-TBS-aglycon methyl ester **9** (347 mg, 92 %) as a viscous oil. **9**: R_f = 0.36 (silica gel, 5 % MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ = +7.4 (c = 2.51, $CHCl_3$); IR (film) $\tilde{\nu}_{max}$ = 3403, 2954, 2928, 2856, 1677, 1507, 1472, 1419, 1255, 1173, 1109, 1060, 1020, 918, 838, 782 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD, 330 K): δ = 7.57 (s, 1H), 7.53 (dd, J = 8.5, 2.0 Hz, 1H), 7.38 (br.d, J = 8.0 Hz, 1H), 7.37 (s, 1H), 7.32–7.26 (m, 6H), 7.06 (d, J = 2.5 Hz, 1H), 7.01 (dd, J = 8.5, 2.5 Hz, 1H), 7.00 (br.s, 1H), 6.75 (d, J = 8.5 Hz, 1H), 6.37 (d, J = 2.0 Hz, 1H), 6.33 (d, J = 2.0 Hz, 1H), 5.84–5.82 (m, 1H), 5.70 (s, 1H), 5.46 (d, J = 4.5 Hz, 1H), 5.37 (s, 1H), 5.35 (br.s, 1H), 5.19–5.17 (m, 2H), 4.96–4.93 (m, 1H), 4.93 (s, 1H), 4.89–4.85 (m, 1H), 4.79–4.74 (m, 1H), 4.62 (s, 1H), 4.11 (s, 1H), 3.75 (s, 3H), 2.94 (s, 3H), 2.49–2.42 (m, 2H), 1.89–1.83 (m, 1H), 1.53–1.45 (m, 2H), 1.13 (s, 9H), 1.01 (s, 9H), 0.92 (s, 9H), 0.89–0.87 (m, 6H), 0.87 (s, 9H), 0.74 (s, 9H), 0.62 (s, 9H), 0.39 (s, 3H), 0.38 (s, 3H), 0.23 (s, 6H), 0.18 (s, 3H), 0.12 (s, 3H), 0.10 (s, 6H), 0.08 (s, 6H), 0.02 (s, 3H), −0.09 (s, 3H); ^{13}C NMR (150 MHz, CD_3OD, 330 K): δ = 174.0, 173.5, 172.7, 171.8, 169.4, 157.1, 156.3, 155.2, 153.6, 152.8, 152.3, 151.8, 142.8, 142.1, 139.7, 137.8, 137.2, 137.0, 134.8, 131.7, 130.6, 130.4, 129.7, 129.3, 129.0, 128.5, 128.2, 128.0, 127.7, 126.7, 125.8, 125.0, 121.0, 113.6, 112.2, 106.1, 74.9, 73.9, 69.1, 65.3, 64.8, 60.9, 58.3, 58.2, 56.4, 55.7, 53.0, 52.6, 30.7, 26.5, 26.4, 26.4, 26.3, 26.0, 26.0, 25.8, 23.8, 22.1, 19.8, 19.3, 19.1, 18.8, −3.6, −3.7, −3.9, −4.0, −4.1, −4.2, −4.6, −4.6, −4.8, −4.9; HRMS (FAB) calcd for $C_{98}H_{144}Cl_2N_8O_{19}Si_6Cs$ [M + Cs^+] 2107.7595, found 2107.7462.

Aglycon acceptor 6: A mixture of potassium fluoride (18.5 g) and basic alumina (63.0 g) in water (100 mL) was stirred for 0.5 h at 25 °C. The resulting solution was concentrated in vacuo and dried at 85 °C under vacuum. A solution of *N*-Cbz-hexa-TBS-aglycon methyl ester **9** (600 mg, 0.303 mmol) in MeCN (2.0 mL) was treated with the above activated KF·Al_2O_3 (600 mg, 1.0 wt. equiv) at 0 °C, and the reaction mixture was stirred for 2 h. After diluting with EtOAc (150 mL), the reaction mixture was filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 10 → 50 % EtOAc in hexanes, gradient elution) to afford aglycon acceptor **6** (338 mg, 60 %) as a white foam. **6**: R_f = 0.31 (silica gel, 5 % MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ = −14.0 (c = 1.21, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 3403, 2995, 2857, 1751, 1676, 1670, 1658, 1508, 1472, 781 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD, 330 K): δ = 7.49 (br.s, 2H, H-6b and H-6f), 7.38 (br.d, J = 8.0 Hz, 1H, H-2f), 7.37 (s, 1H, H-2b), 7.35–7.30 (m, 6H, Cbz(ArH) and H-2e), 7.08 (d, J = 2.0 Hz, 1H, H-5b), 7.01 (dd, J = 8.5, 2.0 Hz, 1H, H-5f), 6.77 (d, J = 8.5 Hz, 1H, H-6e), 6.65 (br.s, 1H, H-5e), 6.41 (d, J = 2.0 Hz, 1H, H-7d), 6.35 (d, J = 2.0 Hz, 1H, H-7f), 6.05-6.02 (m, 1H, H-1α), 5.72 (s, 1H, H-4f), 5.49 (d, J = 4.5 Hz, 1H, H-2β), 5.37 (s, 2H, H-6β and H-4b), 5.20–5.17 (m, 2H, CH_2 of Cbz), 4.97 (br.s, 1H, H-2α), 4.94 (s, 1H, H-4α), 4.90–4.86 (m, 1H, H-3α), 4.85–4.80 (m, 1H, H-7α), 4.64 (s, 1H, H-5α), 4.11 (s, 1H, H-6α), 3.75 (s, 3H, OCH_3), 2.94 (s, 3H, NCH_3), 2.45–2.39 (m, 2H, H-3β), 1.84–1.81 (m, 1H, H-1β), 1.53–1.45 (m, 2H, H-1β and H-1γ), 1.01 (s, 9H, *t*BuSi), 0.94 (s, 9H, *t*BuSi), 0.93–0.90 (m, 6H, H-1γ), 0.86 (s, 9H, *t*BuSi), 0.75 (s, 9H, *t*BuSi), 0.64 (s, 9H, *t*BuSi), 0.23 (s, 6H, CH_3Si), 0.18 (s, 3H, CH_3Si), 0.12 (s, 3H, CH_3Si), 0.10 (s, 3H, CH_3Si), 0.09 (s, 3H, CH_3Si), 0.09 (s, 3H, CH_3Si), 0.08 (s, 3H, CH_3Si), 0.02 (s, 3H, CH_3Si), −0.09 (s, 3H, CH_3Si); ^{13}C NMR (150 MHz, CD_3CN, 330 K): δ = 172.2, 171.8, 171.4, 171.1, 170.6, 169.1, 167.9, 156.4, 155.8, 154.3, 151.7, 151.6, 149.4, 147.7, 141.5, 139.7, 138.0, 136.7, 136.5, 135.4, 130.6, 129.9, 129.3, 129.2, 129.0, 128.8, 128.0, 127.2, 126.9, 126.4, 125.3, 124.7, 121.3, 113.1, 112.1, 106.1, 105.5, 74.4, 73.6, 68.1, 64.3, 60.4, 57.7, 57.6, 55.3, 55.2, 52.7, 52.5, 38.9, 37.3, 30.3, 26.2, 26.1, 26.0, 25.6, 25.5, 25.3, 23.5, 22.1, 18.9, 18.8, 18.7, 18.3, 18.3, −3.9, −4.0, −4.2, −4.3, −4.5, −4.6, −4.7, −4.7, −5.0, −5.0; HRMS (FAB) calcd for $C_{92}H_{130}Cl_2N_8O_{19}Si_5Cs$ [M + Cs^+] 1993.6730, found 1993.6606.

Nona-TBS-vancomycin 10: TBSOTf (47.6 mL, 207 mmol) was added dropwise to a solution of vancomycin free base (**1**) (5.00 g, 3.45 mmol) and 2,6-lutidine (72.4 mL, 621 mmol) in CH_2Cl_2/DMF (10:1, 340 mL) at 0 °C. The reaction mixture was slowly warmed to 25 °C and was stirred for 18 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (200 mL) and stirred at 25 °C for 60 h. The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 400 mL). The combined organic layers were dried (Na_2SO_4), concentrated, and the residue was purified by flash column chromatography (silica gel, 1 → 8 % MeOH in CH_2Cl_2, gradient elution) to afford nona-TBS-vancomycin **10** (5.56 g, 65 %) as a white foam. **10**: R_f = 0.17 (silica gel, 5 % MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ = −27.2 (*c* = 0.90, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 3406, 2956, 2930, 2858, 1677, 1490, 1473, 1256, 1109, 1060, 837, 780 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD, 295 K): δ = 7.80 (s, 1H), 7.53 (br.d, J = 8.5 Hz, 1H), 7.50 (dd, J = 8.5, 2.0 Hz, 1H), 7.43 (s, 1H), 7.23 (d, J = 8.5 Hz, 2H), 7.08 (d, J = 2.5 Hz, 1H), 6.95 (dd, J = 8.5, 2.5 Hz, 1H), 6.75 (s, 1H), 6.73–6.71 (m, 1H), 6.35 (d, J = 2.5 Hz, 1H), 6.00 (d, J = 5.5 Hz, 1H), 5.80 (s, 1H), 5.72–5.70 (m, 1H), 5.41 (d, J = 4.5 Hz, 1H), 5.39 (s, 1H), 5.38 (s, 1H), 5.20 (d, J = 4.5 Hz, 1H), 4.70–4.64 (m, 1H), 4.62 (s, 1H), 4.53–4.51 (m, 1H), 4.27 (br.s, 1H), 4.17 (d, J = 5.5 Hz, 1H), 4.10 (s, 1H), 4.03–3.99 (m, 2H), 3.90–3.86 (m, 2H), 3.40 (s, 1H), 3.17–3.15 (m, 1H), 2.49–2.45 (m, 1H), 2.38 (s, 3H), 2.06–2.02 (m, 1H), 1.86–1.82 (m, 1H), 1.73–1.71 (m, 1H), 1.62–1.50 (m, 2H), 1.50 (s, 3H), 1.28 (d, J = 6.5 Hz, 3H), 1.01 (s, 9H), 0.98 (s, 9H), 0.97–0.96 (m, 6H), 0.95 (s, 9H), 0.90 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.87 (s, 9H), 0.73 (s, 9H), 0.59 (s, 9H), 0.24 (s, 6H), 0.20 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.13 (s, 6H), 0.12 (s, 3H), 0.11 (s, 6H), 0.09 (s, 3H), 0.08 (s, 3H), 0.05 (s, 6H), 0.01 (s, 3H), 0.00 (s, 3H), −0.12 (s, 3H); ^{13}C NMR (150 MHz, CD_3OD, 330 K): δ = 177.1, 174.2, 172.2, 172.0, 171.3, 170.2, 168.4, 156.8, 155.8, 155.2, 153.7, 153.6, 151.3, 143.2, 140.2, 139.6, 137.8, 135.6, 135.3, 130.6, 130.2, 129.1, 129.0, 128.8, 127.7, 127.4, 126.8, 125.9, 125.2, 121.0, 115.2, 111.6, 106.8, 102.3, 95.9, 83.1, 79.5, 76.2, 76.0, 74.7, 74.5, 71.2, 65.6, 65.5, 64.7, 64.4, 60.8, 56.6, 56.1, 55.2, 53.6, 42.7, 38.9, 36.3, 35.0, 30.8, 26.9, 26.7, 26.6, 26.5, 26.4, 26.2, 26.1, 25.9, 24.6, 23.5, 22.9, 19.6, 19.3, 19.3, 19.1, 19.0, 18.8, 18.6, −3.1, −3.7, −3.8, −3.9, −4.0, −4.3, −4.5, −4.7, −4.8, −4.8; HRMS (FAB) calcd for $C_{120}H_{201}Cl_2N_9O_{24}Si_9Cs$ [M + Cs^+] 2607.1139, found 2607.1324.

Nona-TBS-vancomycin methyl ester 11: A solution of nona-TBS-vancomycin **10** (2.00 g, 0.800 mmol) in ether (20 mL) was treated with CH_2N_2 (solution in ether, excess) at 0 °C. After stirring the mixture for 0.5 h, argon was bubbled through for 5 min, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 20 → 80 % EtOAc in hexanes, gradient elution) to afford nona-TBS-vancomycin methyl ester **11** (1.79 g, 90 %) as a yellow foam. **11**: R_f = 0.24 (silica gel, 5 % MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ = −14.9 (c = 1.33, $CHCl_3$); IR (film) $\tilde{\nu}_{max}$ = 3406, 2929, 2856, 1685, 1490, 1473, 1256, 1112, 1061, 838, 780 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD, 330 K): δ = 7.64 (d, J = 2.0 Hz, 1H), 7.53-7.49 (m, 2H), 7.43 (d, J = 2.0 Hz, 1H), 7.23 (d, J = 8.5 Hz, 1H), 7.20 (d, J = 8.5 Hz, 1H), 7.03 (d, J = 2.5 Hz, 1H), 7.00 (dd, J = 8.5, 2.5 Hz, 1H), 6.77 (d, J = 8.5 Hz, 1H), 6.41 (d, J = 2.0 Hz, 1H), 6.32 (d, J = 2.0 Hz, 1H), 6.04 (d, J = 5.0 Hz, 1H), 5.81 (s, 1H), 5.63 (s, 1H), 5.41 (d, J = 4.5 Hz, 1H), 5.36 (s, 1H), 5.35 (d, J = 2.0 Hz, 1H), 5.14 (d, J = 4.0 Hz, 1H), 4.91 (s, 1H), 4.83 (d, J = 4.5 Hz, 1H), 4.61 (d, J = 5.5 Hz, 1H), 4.60 (s, 1H), 4.50 (s, 1H), 4.46–4.43 (m, 1H), 4.25 (br.s, 1H), 4.17 (d, J = 5.0 Hz, 1H), 4.10 (s, 1H), 4.06–4.02 (m, 2H), 3.91–3.89 (m, 2H), 3.75 (s, 3H), 3.19 (s, 1H), 3.10 (dd, J = 8.5, 5.5 Hz, 1H), 2.49–2.47 (m, 1H), 2.37 (s, 3H), 1.85-1.80 (m, 2H), 1.59–1.47 (m, 3H), 1.31 (s, 3H), 1.05 (d, J = 6.5 Hz, 3H), 1.01 (s, 9H), 0.96 (s, 9H), 0.97–0.96 (m, 6H), 0.94 (s, 9H), 0.91 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.86 (s, 9H), 0.73 (s, 9H), 0.60 (s, 9H), 0.23 (s, 6H), 0.19 (s, 3H), 0.17 (s, 3H), 0.15 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H), 0.00 (s, 3H), −0.01 (s, 3H), −0.08 (s, 3H); ^{13}C NMR (150 MHz, CD_3OD, 320 K): δ = 177.8, 174.1, 172.6, 172.1, 171.7, 171.0, 170.0, 169.3, 157.0, 156.3, 155.0, 153.9, 153.6, 153.3, 151.5, 142.3, 139.9, 137.2, 135.7, 135.0, 130.4, 130.2, 129.1, 129.0, 128.8, 128.5, 127.8, 127.7, 127.6, 126.6, 125.8, 125.1, 121.0, 113.4, 112.1, 110.2, 106.9, 102.2, 96.8, 82.8, 79.4, 78.7, 76.3, 74.7, 74.3, 71.4, 66.3, 65.7, 64.7, 64.6, 61.0, 58.1, 56.5, 55.7, 53.0, 52.6, 52.0, 43.3, 39.1, 37.9, 35.5, 30.6, 26.7, 26.5, 26.5, 26.5, 26.4, 26.3, 26.3, 26.2, 25.9, 25.9, 23.4, 22.7, 19.5, 19.2, 19.1, 19.0, 18.9, 18.7, 18.7, −3.3, −3.4, −3.8, −3.9, −4.0,

−4.1, −4.2, −4.4, −4.5, −4.6, −4.7, −4.8, −4.9; HRMS (FAB) calcd for $C_{121}H_{203}Cl_2N_9O_{24}Si_9Cs$ [$M+Cs^+$] 2624.1321, found 2624.1503.

***N,N′*-diCbz-nona-TBS-vancomycin methyl ester 12:** A solution of nona-TBS-vancomycin methyl ester **11** (2.91 g, 1.16 mmol) in dioxane/H_2O (10:1, 60 mL) was treated sequentially with $NaHCO_3$ (487 mg, 5.80 mmol) and CbzCl (1.1 mL, 5.8 mmol) at 0 °C. After stirring the reaction mixture for 0.5 h, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (10 mL), extracted with EtOAc (2 × 50 mL), and washed with brine (25 mL). The combined organic layers were dried (Na_2SO_4), concentrated, and the residue was purified by flash column chromatography (silica gel, 5 →40 % EtOAc in hexanes, gradient elution) to provide *N,N′*-diCbz-nona-TBS-vancomycin methyl ester **12** (2.55 g, 80 %) as a white foam. **12**: R_f = 0.36 (silica gel, 5 % MeOH in CH_2Cl_2); $[\alpha]_D^{22} = -13.9$ (c = 0.77, $CHCl_3$); IR (film) $\tilde{\nu}_{max}$ = 3404, 2954, 2923, 2886, 2857, 1684, 1490, 1472, 1256, 1108, 1060, 837, 780 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD, 330 K): δ = 7.63 (s, 1H), 7.53 (br. d, J = 8.5 Hz, 1H), 7.36 – 7.28 (m, 12H), 7.25 (d, J = 8.5 Hz, 1H), 7.22 (d, J = 8.5 Hz, 1H), 7.04 (s, 1H), 7.00 (br. d, J = 8.5 Hz, 1H), 6.77 (d, J = 8.5 Hz, 1H), 6.41 (d, J = 2.0 Hz, 1H), 6.32 (d, J = 2.0 Hz, 1H), 6.03 (d, J = 4.5 Hz, 1H), 5.80 (s, 1H), 5.64 (s, 1H), 5.44 (s, 1H), 5.37 (s, 1H), 5.36 (s, 1H), 5.13 (br. s, 1H), 5.05 – 5.00 (m, 4H), 4.95 – 4.92 (m, 1H), 4.91 (s, 1H), 4.87 – 4.85 (m, 1H), 4.71 – 4.69 (m, 1H), 4.62 (s, 1H), 4.37 – 4.34 (m, 1H), 4.28 – 4.20 (m, 1H), 4.22 – 4.20 (m, 1H), 4.11 (s, 1H), 4.08 (d, J = 11.0 Hz, 1H), 4.04 (d, J = 3.5 Hz, 1H), 3.94 – 3.90 (m, 2H), 3.75 (s, 3H), 3.62 (s, 1H), 2.92 (s, 3H), 2.46 – 2.38 (m, 2H), 2.09 – 2.06 (m, 1H), 1.83 – 1.80 (m, 2H), 1.60 (s, 3H), 1.58 – 1.47 (m, 2H), 1.03 (d, J = 6.5 Hz, 3H), 1.01 (s, 9H), 0.93 (s, 9H), 0.96 – 0.92 (m, 6H), 0.90 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.85 (s, 9H), 0.84 (s, 9H), 0.74 (s, 9H), 0.62 (s, 9H), 0.23 (s, 6H), 0.17 (s, 3H), 0.14 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 6H), 0.06 (s, 3H), 0.05 (s, 6H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), −0.01 (s, 3H), −0.03 (s, 3H), −0.09 (s, 3H); ^{13}C NMR (150 MHz, CD_3COCD_3, 300 K): δ = 172.0, 171.5, 171.3, 170.6, 169.1, 168.3, 156.6, 156.0, 155.2, 154.3, 153.2, 152.9, 151.0, 143.4, 142.1, 139.8, 138.3, 137.8, 137.3, 136.4, 135.0, 134.6, 130.2, 129.4, 129.3, 129.2, 129.1, 128.9, 128.7, 128.5, 128.5, 128.3, 127.9, 127.7, 127.5, 127.4, 127.3, 127.0, 126.3, 125.7, 124.9, 120.5, 113.4, 111.9, 109.2, 106.2, 102.1, 96.0, 82.0, 78.5, 75.4, 75.1, 74.4, 73.8, 70.7, 68.1, 67.0, 66.0, 65.9, 65.5, 65.3, 64.7, 63.8, 59.9, 57.8, 57.6, 56.1, 55.3, 54.9, 52.7, 52.2, 39.0, 37.4, 36.6, 35.4, 26.7, 26.6, 26.4, 26.3, 26.2, 26.1, 25.7, 25.7, 25.4, 24.4, 23.6, 22.6, 19.3, 19.2, 19.0, 18.9, 18.9, 18.7, 18.7, 18.6, 18.3, −3.4, −3.8, −3.9, −4.0, −4.1, −4.2, −4.3, −4.5, −4.6, −4.8, −5.0; HRMS (FAB) calcd for $C_{137}H_{215}Cl_2N_9O_{28}Si_9Cs$ [$M+Cs^+$] 2889.2032, found 2889.2237.

Aglycon acceptor 6 [from vancomycin (**1**)]: A solution of *N,N′*-diCbz-nona-TBS-vancomycin methyl ester **12** (1.12 g, 0.406 mmol) in trifluoroacetic acid/dimethyl sulfide/CH_2Cl_2 (1:1:1, 12 mL) was stirred at 25 °C for 3 h. The reaction mixture was then diluted with EtOAc (50 mL), and concentrated in vacuo (× 4). The residue was purified by flash column chromatography (silica gel, 5 →30 % EtOAc in hexanes, gradient elution) to afford aglycon acceptor **6** (454 mg, 60 %) as a white foam (spectroscopically identical to **6** derived from the aglycon **2**).

Silylated ethyl lactate 15: Triisopropylsilyl chloride (19.1 mL, 0.089 mol) was added dropwise to a solution of (S)-ethyl lactate (**14**) (9.60 g, 0.081 mol) and imidazole (11.1 g, 0.162 mol) in DMF (160 mL) at 0 °C. The reaction mixture was allowed to warm to 25 °C and stirred for 10 h. The reaction mixture was diluted with hexanes (1 L) and washed with H_2O (3 × 75 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 0 →4 % ether in hexanes, gradient elution) to provide ester **15** (22.2 g, 99 %) as a colorless oil. **15**: R_f = 0.68 (silica gel, 40 % ether in hexanes); $[\alpha]_D^{22} = -19.5$ (c = 2.6, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 2943, 2867, 1755, 1464, 1371, 1273, 1147, 1062, 1017, 971, 883, 682 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.38 (q, J = 6.7 Hz, 1H, H-2), 4.14 (q, J = 7.1 Hz, 2H, OCH_2), 1.39 (d, J = 6.7 Hz, 3H, H-3), 1.24 (t, J = 7.1 Hz, 3H, CH_3), 1.04-1.01 (m, J = 6.5 Hz, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.1, 68.4, 68.4, 60.5, 21.7, 17.7, 14.1, 12.0; HRMS (FAB) calcd for $C_{14}H_{31}O_3Si$ [$M+H^+$] 275.2042, found 275.2048.

Oxime alcohol 16: Ethyl ester **15** (8.00 g, 0.029 mol) was dissolved in ether (150 mL) and cooled to −78 °C. Diisobutylaluminum hydride (48.0 mL, 1 M solution in CH_2Cl_2, 0.041 mol) was added dropwise by cannula, and the reaction mixture was stirred at −78 °C for 45 min. Methanol (10 mL) was added at −78 °C, followed by the addition of ether (250 mL) and saturated aqueous sodium potassium tartrate solution (60 mL). The reaction mixture was then allowed to warm to 25 °C and stirred for 1 h. The organic layer was separated, and the aqueous phase was extracted with ether (3 × 50 mL). The combined organic phase was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude aldehyde was azeotroped with benzene (2 × 10 mL) and then used directly in the next reaction. Ethyl vinyl ether (10.6 mL, 0.111 mol, distilled from calcium hydride) was dissolved in THF (100 mL), cooled to −78 °C, and then *tert*-butyllithium (31.0 mL, 1.7 M in pentane, 0.052 mol) was added by cannula. The dark orange solution was allowed to warm to 0 °C over 1 h, during which time the solution became pale yellow. The anion solution was cooled to −100 °C and to it was added the crude aldehyde [dissolved in THF (50 mL) and cooled to −78 °C] by fast addition by cannula. After stirring for 5 min, the reaction mixture was poured into saturated aqueous NH_4Cl (100 mL), and diluted with ether (200 mL). Aqueous HCl (5 %, 50 mL) was added and the mixture was stirred for 0.5 h. The reaction mixture was further diluted with ether (300 mL) and washed with H_2O (50 mL). The combined organic fractions were dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 1 →10 % ether in hexanes, gradient elution) to afford the *anti*-alcohol and the *syn*-alcohol in a ratio of about 10:1 as colorless oils. *anti*-Alcohol: (4.36 g, 59 %): R_f = 0.40 (silica gel, 25 % ether in hexanes); $[\alpha]_D^{22} = +39.7$ (c = 1.0, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 3474, 2943, 2867, 1715, 1463, 1381, 1356, 1140, 1103, 883 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.23 (dq, J = 6.5, 3.5 Hz, 1H, H-4), 4.11 (br. s, 1H, H-3), 3.22 (br. d, 1H, OH), 2.23 (s, 3H, H-1), 1.18 (d, J = 6 Hz, 3H, H-5), 1.06 – 1.03 (m, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 209.2. 81.6, 70.6, 27.8, 18.9, 18.1, 12.5; HRMS (FAB) calcd for $C_{14}H_{31}O_3Si$ [$M+H^+$] 275.2042, found 275.2047; *syn*-Alcohol: (460 mg, 6 %): R_f = 0.52 (silica gel, 25 % ether in hexanes); $[\alpha]_D^{22} = -76.5$ (c = 0.70, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 3472, 2943, 2867, 1713, 1463, 1382, 1360, 1239, 1107, 1009, 883 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.25 (dq, J = 6.5, 3.5 Hz, 1H, H-4), 4.10 (br. s, 1H, H-3), 3.60 (br. s, 1H, OH), 2.30 (s, 3H, H-1), 1.10 (d, J = 6.0 Hz, 3H, H-5), 1.08 – 1.04 (m, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 209.8, 80.8, 69.9, 27.6, 18.7, 18.2, 18.1, 12.5; HRMS (FAB) calcd for $C_{14}H_{31}O_3Si$ [$M+H^+$] 275.2042, found 275.2047. The *anti*-alcohol (6.60 g, 0.024 mol) was dissolved in pyridine (100 mL), cooled to 0 °C, and *O*-benzyl hydroxylamine · HCl (4.22 g, 0.026 mol) was added. The reaction mixture was stirred at 0 °C for 1 h and then at 25 °C for 1 h. The reaction mixture was diluted with hexanes (800 mL), and washed with H_2O (100 mL) and brine (100 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 2 →10 % ether in hexanes, gradient elution) to afford a 4:1 mixture of *E* and *Z* oximes (9.1 g, 97 %) as colorless oils. Separation (flash column chromatography, silica gel, 2 →10 % ether in hexanes, gradient elution) of an analytical sample of the oximes yielded the pure oximes. *E*-oxime **16a**: R_f = 0.50 (silica gel, 25 % ether in hexanes); $[\alpha]_D^{22} = +5.2$ (c = 0.56, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 3416, 2913, 2866, 1463, 1367, 1145, 1053, 1014, 883, 764, 698, 679 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 – 7.30 (m, 5H, ArH), 5.11 (s, 2H, CH_2Ar), 4.15 – 4.08 (m, 2H, H-3, H-4), 2.86 (br. d, J = 5.0 Hz, 1H, OH), 1.93 (s, 3H, H-1), 1.13 (d, J = 6.0 Hz, 3H, H-5), 1.11 – 1.04 (m, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.1, 138.0, 128.3, 128.0, 127.7, 76.6, 75.6, 70.9, 18.4, 18.1, 12.4, 12.1; HRMS (FAB) calcd for $C_{21}H_{38}NO_3Si$ [$M+H^+$] 380.2621, found 380.2633; *Z*-oxime **16b**: R_f = 0.63 (silica gel, 25 % ether in hexanes); $[\alpha]_D^{22} = -31.3$ (c = 0.50, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 2942, 2866, 1464, 1381, 1208, 1139, 1096, 1029, 969, 883, 754, 678 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 – 7.26 (m, 5H, ArH), 5.03 and 4.98 (AB, J = 11.5 Hz, 2H, CH_2Ar), 4.90 (br. s, 1H, H-3), 4.40 (dq, J = 6.0, 3.5 Hz, 1H, H-4), 1.26 (br. s, 1H, OH), 1.94 (s, 3H, H-1), 1.08 (d, J = 6.5 Hz, 3H, H-5), 0.99 – 0.98 (m, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.2, 137.3, 128.4, 128.3, 127.9, 76.0, 72.1, 67.6, 17.9, 17.2, 16.7, 12.1; HRMS (FAB) calcd for $C_{21}H_{38}O_3NSi$ [$M+H^+$] 380.2621, found 380.2633.

Olefinic alcohol 17: Oxime **16a** (235 mg, 0.62 mmol) was dissolved in ether (5.0 mL) and cooled to −35 °C. Allylmagnesium bromide (1.56 mL, 1 M solution in ether, 1.56 mmol) was added dropwise and the reaction mixture was stirred for 1 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with ether (30 mL), and washed with H_2O (5 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 15 % ether in hexanes) to yield alcohol **17** (130 mg, 50 %) as a single diastereoisomer and recovered oxime **16a** (110 mg, 47 %). Alcohol **17**: R_f = 0.61 (silica gel, 25 % ether in hexanes); $[\alpha]_D^{22} = -20.0$ (c = 0.56, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 3576, 3071, 2942, 2866, 1463, 1384, 1368, 1248, 1140, 1091, 1049, 1013, 913, 883, 749, 697, 679 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ =

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7.34 – 7.26 (m, 5H, ArH), 5.91 – 5.88 (m, 1H, H-1), 5.73 (br. s, 1H, NH), 5.13 (d, $J = 17.0$ Hz, 1H, H-1*Z*), 5.12 (d, $J = 10.0$ Hz, 1H, H-1*E*), 4.70 (s, 2H, CH_2Ar), 4.09 (dq, $J = 6.3$, 3.8 Hz, 1H, H-5), 3.75 (dd, $J = 3.5$, 2.5 Hz, 1H, H-4), 2.76 (br. s, 1H, OH), 2.53 (dd, $J = 13.5$, 7.0 Hz, 1H, H-2a), 2.32 (dd, $J = 13.5$, 8.0 Hz, 1H, H-2b), 1.28 (br. s, 1H, OH), 1.28 (d, $J = 6.0$ Hz, 3H, H-6), 1.07 – 1.05 (m, 21H, *i*Pr_3Si), 0.99 (s, 3H, H-3(CH_3)); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 138.0$, 134.3, 128.3, 128.2, 127.7, 118.3, 77.0, 76.7, 69.8, 62.0, 39.1, 19.5, 18.2, 18.2, 17.4, 12.7; HRMS (FAB) calcd for $C_{24}H_{44}NO_3Si$ $[M + H^+]$ 422.3090, found 422.3097.

Inverted olefinic alcohol 18: Dimethyl sulfoxide (328 μL, 4.62 mmol) was added dropwise to a solution of oxalyl chloride (322 μL, 3.69 mmol) in CH_2Cl_2 (10 mL) at −78 °C and the resulting mixture was stirred for 10 min. Alcohol **17** (779 mg, 1.85 mmol) was dissolved in CH_2Cl_2 (10 mL) and added to the reaction mixture by cannula over 5 min. The reaction mixture was stirred at −78 °C for 2 h, and then triethylamine (1.03 mL, 7.39 mmol) was added and the reaction mixture was allowed to warm to 0 °C over 2 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with H_2O (15 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 3% ether in hexanes) to yield the corresponding ketone (705 mg, 91%) as a white foam. Ketone: $R_f = 0.26$ (silica gel, 10% ether in hexanes); $[\alpha]_D^{22} = -7.5$ ($c = 2.7$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3020$, 2944, 2866, 1710, 1640, 1454, 1368, 1258, 1159, 1097, 1062, 996, 918, 884, 779, 750, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.34 – 7.28$ (m, 5H, ArH), 6.73 (br. s, 1H, NH), 5.81 – 5.73 (m, 1H, H-1), 5.11 (br. d, $J = 16.0$ Hz, 1H, H-1*Z*), 5.10 (d, $J = 11.5$ Hz, 1H, H-1*E*), 4.75 (q, $J = 7.0$ Hz, 1H, H-5), 4.69 (s, 2H, CH_2Ar), 2.54 (dd, $J = 14.0$, 7.0 Hz, 1H, H-2a), 2.50 (dd, $J = 14.0$, 7.3 Hz, 1H, H-2b), 1.43 (d, $J = 7.0$ Hz, 3H, H-6), 1.29 (s, 3H, CH_3(H-3)), 1.09 – 1.05 (m, 21H, *i*Pr_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 213.2$, 137.5, 133.1, 128.3, 128.2, 128.1, 127.7, 127.6, 118.5, 76.9, 74.9, 69.4, 38.7, 21.6, 21.6, 19.4, 18.2, 18.1, 12.7; HRMS (FAB) calcd for $C_{24}H_{41}NO_3SiCs$ $[M + Cs^+]$ 552.1910, found 552.1894. To a solution of the above ketone (705 mg, 1.68 mmol) in ether/MeOH (5:1) (21 mL) at 25 °C was added sodium borohydride (109 mg, 5.04 mmol) and the reaction mixture was stirred for 0.5 h. Saturated aqueous NH_4Cl (5 mL) was added and the reaction mixture was stirred for 10 min. The reaction mixture was diluted with ether (150 mL) and washed with brine (10 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 2% ether in hexanes) to afford alcohol **18** (636 mg, 90%, 92% *de*) as a colorless oil. **18**: $R_f = 0.28$ (silica gel, 7% ether in hexanes); $[\alpha]_D^{22} = -8.1$ ($c = 1.6$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3522$, 3071, 3031, 2943, 2866, 1638, 1464, 1454, 1372, 1256, 1133, 1057, 1014, 945, 915, 883, 748, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.36 – 7.29$ (m, 5H, ArH), 5.87 – 5.82 (m, 2H, H-1, NH), 5.10 (d, $J = 11.5$ Hz, 1H, H-1*E*), 5.09 (br. d, $J = 16.0$ Hz, 1H, H-1*Z*), 4.65 and 4.62 (AB, 2H, $J = 11.5$ Hz, CH_2Ar), 4.37 (dq, $J = 6.0$, 2.0 Hz, 1H, H-5), 3.32 (br. dd, $J = 7.5$, 2.0 Hz, 1H, H-4), 3.11 (d, $J = 7.5$ Hz, 1H, OH), 2.89 (dd, $J = 14.0$, 8.5 Hz, 1H, H-2b), 2.28 (dd, $J = 13.5$, 7.0 Hz, 1H, H-2a), 1.30 (d, $J = 6.5$ Hz, 3H, H-6), 1.07 – 1.04 (m, 21H, *i*Pr_3Si), 1.05 (s, 3H, CH_3(H-3)); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 138.0$, 134.3, 128.3, 128.2, 127.6, 118.2, 77.2, 76.7, 67.4, 62.5, 38.7, 23.1, 18.3, 18.2, 18.1, 18.0, 13.1; HRMS (FAB) calcd for $C_{24}H_{43}NO_3SiCs$ $[M + Cs^+]$ 554.2067, found 554.2083.

Hydroxylamine 19: Sodium hydride (122 mg, 3.06 mmol) was added to a solution of alcohol **18** (1.17 g, 2.71 mmol) in DMF (14 mL) at 0 °C. After 2 min, benzyl bromide (400 μL, 3.23 mmol) and tetra-*n*-butylammonium iodide (205 mg, 0.56 mmol) were added. After stirring for 2 h, the reaction was quenched by the addition of saturated aqueous NH_4Cl (10 mL), diluted with ether (200 mL), washed with H_2O (20 mL) and then brine (20 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 3% ether in hexanes) to provide the benzyl ether (1.25 g, 88%) as a colorless oil. Benzyl ether: $R_f = 0.50$ (silica gel, 10% ether in hexanes); $[\alpha]_D^{22} = -23.0$ ($c = 2.8$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3065$, 3031, 2943, 2866, 1639, 1497, 1463, 1367, 1308, 1249, 1209, 1163, 1106, 1057, 1028, 1014, 910, 883, 732, 697, 682 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.33 – 7.27$ (m, 10H, ArH), 5.99 – 5.92 (m, 2H, H-1, NH), 5.03 (d, $J = 11.5$ Hz, 1H, H-1*E*), 5.03 (br. d, $J = 16.0$ Hz, 1H, H-1*Z*), 4.77 and 4.62 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.69 and 4.65 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.33 (dq, $J = 6.2$, 3.7 Hz, 1H, H-5), 3.57 (d, $J = 4.0$ Hz, 1H, H-4), 2.42 – 2.41 (m, 2H, H-2), 1.36 (d, $J = 6.5$ Hz, 3H, H-6), 1.20 (s, 3H, CH_3(H-3)), 1.09 – 1.06 (m, 21H, *i*Pr_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 139.4$, 138.2, 135.5, 128.3, 128.2, 127.5, 127.2, 116.9, 84.1, 76.7, 74.7, 69.2, 63.6, 39.0, 22.1, 19.6, 18.3, 18.2, 18.2, 12.9; HRMS (FAB) calcd for $C_{31}H_{50}NO_3Si$ $[M + H^+]$ 512.3560, found 512.3595. Lithium aluminum hydride (148 mg, 3.90 mmol) was added to a solution of the above benzyl ether (1.25 g, 2.44 mmol) in dry ether (35 mL) at 25 °C. The reaction mixture was heated to reflux for 24 h, cooled to 0 °C, and quenched by the addition of saturated aqueous NH_4Cl (10 mL). The reaction mixture was diluted with CH_2Cl_2 (200 mL) and washed with H_2O (20 mL). The aqueous layer was further extracted with CH_2Cl_2 (2 × 40 mL) and EtOAc (2 × 40 mL). The combined organic layers were dried ($MgSO_4$), filtered, and the solvents were removed under reduced pressure. The crude mixture was taken to the next step. Flash column chromatography (silica gel, 20% MeOH in CH_2Cl_2) gave an analytically pure sample of amino alcohol **19** as a colorless oil. **19**: $R_f = 0.45$ (silica gel, 20% MeOH in CH_2Cl_2); $[\alpha]_D^{22} = -23.6$ ($c = 2.4$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3282$, 3068, 3030, 2976, 2926, 1652, 1580, 1496, 1455, 1398, 1346, 1249, 1209, 1184, 1064, 996, 918, 856, 799, 738 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.39 – 7.25$ (m, 5H, ArH), 5.83 – 5.75 (m, 2H, H-1), 5.15 (br. d, $J = 15.5$ Hz, 1H, H-1*Z*), 5.14 (d, $J = 11.0$ Hz, 1H, H-1*E*), 4.72 and 4.58 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.22 (dq, $J = 6.5$ Hz, 1H, H-5), 3.52 (br. s, 3H, NH_2, OH), 2.96 (br. d, $J = 1.5$ Hz, 1H, H-4), 2.32 (dd, $J = 13.0$, 7.5 Hz, 1H, H-2a), 2.25 (dd, $J = 13.5$, 8.0 Hz, 1H, H-2b), 1.27 (d, $J = 6.5$ Hz, 3H, H-6), 1.20 (s, 3H, CH_3(H-3)); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 138.0$, 132.7, 128.2, 127.6, 119.3, 85.3, 76.6, 74.7, 67.3, 56.8, 43.0, 27.2, 20.4; HRMS (FAB) calcd for $C_{15}H_{23}NO_2Na$ $[M + Na^+]$ 272.1626, found 272.1619.

Cbz-protected hydroxylamine 20: To a solution of the above crude amino alcohol **19** and $NaHCO_3$ (2.58 g, 24.4 mmol) in THF/H_2O (5:1) (25 mL) at 0 °C was added CbzCl (1.03 mL, 7.20 mmol). After stirring for 0.5 h at 25 °C, the reaction mixture was diluted with CH_2Cl_2 (200 mL) and washed with H_2O (20 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 50% ether in hexanes) to afford amine **20** (705 mg, 78% over two steps) as a colorless oil. **20**: $R_f = 0.30$ (silica gel, 60% ether in hexanes); $[\alpha]_D^{22} = -39.3$ ($c = 1.8$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3346$, 3065, 3032, 2976, 2936, 1732, 1640, 1538, 1456, 1373, 1242, 1072, 1002, 914, 737, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.38 – 7.31$ (m, 10H, ArH), 5.85 – 5.77 (m, 2H, H-1), 5.19 (br. s, 1H, NH), 5.12 (br. d, $J = 10.5$ Hz, 1H, H-1*E*), 5.09 (d, $J = 19.0$ Hz, 1H, H-1*Z*), 5.12 and 5.02 (AB, $J = 12.5$ Hz, 2H, CH_2Ar), 4.74 and 4.66 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.69 (br. d, $J = 4.0$ Hz, 1H, H-4), 4.00 (dq, $J = 8.5$, 7.0 Hz, 1H, H-5), 3.88 (br. s, 3H, OH), 2.91 (dd, $J = 13.5$, 7.0 Hz, 1H, H-2b), 2.42 (dd, $J = 13.5$, 7.0 Hz, 1H, H-2a), 1.37 (d, $J = 6.5$ Hz, 3H, H-6), 1.24 (s, 3H, CH_3(H-3)); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 154.8$, 137.9, 136.6, 133.5, 128.5, 128.4, 128.0, 127.9, 127.6, 127.5, 126.9, 118.9, 84.2, 76.7, 66.2, 65.7, 65.2, 58.6, 40.4, 23.5, 20.9; HRMS (FAB) calcd for $C_{23}H_{30}NO_4$ $[M + H^+]$ 384.2175, found 384.2164.

Benzyl-protected vancosamine lactols 21: Ozone was bubbled through a solution of alcohol **20** (159 mg, 0.410 mmol) in CH_2Cl_2 (25 mL) at −78 °C for 1 h. Triphenylphosphane (107 mg, 0.82 mmol) was added at −78 °C, and then the reaction mixture was warmed to 25 °C and stirred for 12 h. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 75% ether in hexanes) to yield lactols **21** (150 mg, 95%) as a white foam. **21**: $R_f = 0.12$; (silica gel, 60% ether in hexanes); $[\alpha]_D^{22} = -56.8$ ($c = 0.5$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3410$, 3064, 3032, 2930, 1713, 1517, 1453, 1380, 1350, 1280, 1240, 1208, 1160, 1068, 962, 885, 821, 753, 699, 585, 552, 486 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, mixture of α:β anomers ca. 1.8:1): $\delta = 7.32 – 7.27$ (m, 10H, ArH), 5.34 (br. s, 0.4H, H-V1α), 5.03 and 4.99 (AB, $J = 12.5$ Hz, 2H, CH_2Ar), 4.92 (br. s, 1H, NH), 4.95 – 4.85 (m, 2.5H, H-V1β, NH, CH_2Ar), 4.64 and 4.54 (AB, $J = 11.0$ Hz, 0.8H, CH_2Ar), 4.62 and 4.50 (AB, $J = 11.0$ Hz, 1.2H, CH_2Ar), 4.29 (br. q, $J = 6.5$ Hz, 0.4H, H-V5α), 3.82 (br. q, $J = 6.5$ Hz, 0.6H, H-V5β), 3,56 (br. s, 0.4H, H-V4α), 3.52 (br. s, 0.6H, H-V4β), 3.15 (d, $J = 8.0$ Hz, 0.6H, OHβ), 2.61 (dd, $J = 8.0$, 1.5 Hz, 0.4H, OHβ), 1.96 (dd, $J = 13.0$, 4.5 Hz, 0.6H, H-V2αa), 1.81 (br. d, $J = 11.0$ Hz, 0.4H, H-V2βa), 1.78 (br. d, $J = 13.5$ Hz, 0.6H, H-V2αb), 1.73 (s, 1.2H, H-V3α), 1.61 (dd, $J = 12.0$, 11.0 Hz, 1H, H-V2βb), 1.55 (s, 1.8H, H-V3β), 1.30 (d, $J = 6.5$ Hz, 0.8H, H-V6α), 1.30 (d, $J = 6.5$ Hz, 1.2H, H-V6β); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 154.8$, 154.8, 137.9, 136.6, 136.4, 128.5, 128.4, 128.2, 128.2, 128.1, 128.1, 127.8, 92.7, 91.4, 80.1, 78.8, 75.8, 75.6, 70.1, 66.3, 66.2, 64.8, 55.3, 53.6, 40.5, 36.3, 29.7, 24.0, 22.0, 17.7, 17.5; HRMS (FAB) calcd for $C_{22}H_{27}NO_5Na$ $[M + Na^+]$ 408.1787, found 408.1780.

Benzyl-protected vancosamine glycosyl fluoride 22: Diethylaminosulfur trifluoride (10 μL, 0.076 mmol) was added to a solution of lactols **21** (21.0 mg, 0.054 mmol) in CH_2Cl_2 (1.0 mL) at 0 °C. After stirring for 20 min,

the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (2.0 mL), diluted with CH_2Cl_2 (10 mL), and stirred for 5 min. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and the solvents were removed under reduced pressure. The residue was azeotroped with benzene (2 mL), dried under vacuum for 1 h, and used directly in the next reaction. **22**: crude ^{1}H NMR (500 MHz, $CDCl_3$, α:β ca. 16:1): $\delta = 7.33-7.26$ (m, 10H, ArH), 5.69 (dd, $J = 53.0$, 3.0 Hz, 1H, H-V1), 5.05 and 4.99 (AB, $J = 12.5$ Hz, 2H, CH_2Ar), 4.88 (s, 1H, NH), 4.67 and 4.53 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.27 (br. q, $J = 6.5$ Hz, 1H, H-V5), 3.56 (s, 1H, H-V4), 2.03 (dd, $J = 14.0$, 7.0 Hz, 1H, H-V2a), 1.90 (ddd, $J = 53.0$, 14.0, 3.2 Hz, 1H, H-V2b), 1.71 (s, 3H, H-V3), 1.31 (d, $J = 6.0$ Hz, 3H, H-V6).

Cbz-protected amine 24: Sodium hydride (457 mg, 60% in mineral oil, 11.94 mmol) was added to a solution of alcohol **18** (4.20 g, 9.95 mmol), *p*-methoxybenzyl chloride (1.75 mL, 12.9 mmol), and tetra-*n*-butylammonium iodide (367 mg, 0.99 mmol) in DMF (52 mL) at 0 °C. After stirring the reaction mixture for 4 h at 25 °C, the reaction was quenched by the careful addition of saturated aqueous NH_4Cl (10 mL), the solution was diluted with ether (300 mL), and washed with brine (30 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography to afford the PMB-ether (6.2 g, 93%). PMB-ether: $R_f = 0.66$ (silica gel, 20% ether in hexanes); $[\alpha]_D^{22} = -41.7$ ($c = 1.1$, $CHCl_3$); IR (thin flim) $\tilde{\nu}_{max} = 2942$, 2865, 1607, 1513, 1463, 1366, 1248, 1171, 1082 cm^{-1}; ^{1}H NMR (500 MHz $CDCl_3$): $\delta = 7.33-7.25$ (m, 5H, ArH), 7.23 (d, $J = 9.0$ Hz, 2H, ArH), 6.83 (d, $J = 9.0$ Hz, 2H, ArH), 5.97–5.90 (m, 2H, H-1, NH), 5.03–4.99 (m, 2H, H-1*Z*, H-1*E*), 4.68–4.64 (m, 3H, CH_2Ar), 4.51 (d, $J = 11.0$ Hz, 1H, CH_2Ar), 4.31–4.26 (m, 1H, H-5), 3.79 (s, 3H, OCH_3), 3.54 (d, $J = 3.7$ Hz, 1H, H-4), 2.38 (d, $J = 7.0$ Hz, 2H, H-2a, H-2b), 1.33 (d, $J = 7.0$ Hz, 3H, H-6), 1.17 (s, 3H, CH_3(H-3)), 1.05 (s, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 158.8$, 138.2, 135.2, 131.4, 128.9, 128.8, 128.8, 128.7, 128.2, 128.1, 128.1, 128.0, 128.0, 127.4, 116.8, 113.5, 110.0, 83.7, 74.3, 69.2, 63.5, 55.2, 38.9; HRMS (FAB) calcd for $C_{32}H_{51}NO_4SiCs$ [$M + Cs^+$] 674.2642, found 674.2619. Lithium aluminum hydride (640 mg, 16.1 mmol) was added to a solution of the above PMB-ether (2.44 g, 4.60 mmol) in ether (46 mL), at 0 °C. The reaction mixture was refluxed for 5 h, cooled to 0 °C, and then quenched by the addition of saturated aqueous NH_4Cl (10 mL). The reaction mixture was diluted with CH_2Cl_2 (200 mL) and washed with H_2O (20 mL). The aqueous layer was further extracted with CH_2Cl_2 (2 × 80 mL) and EtOAc (2 × 80 mL). The combined organic layers were dried ($MgSO_4$), filtered, and the solvents were removed under reduced pressure. To a solution of the above crude amino-alcohol and $NaHCO_3$ (3.85 g, 45.8 mmol) in dioxane/H_2O (4:1) (55 mL) at 0 °C was added CbzCl (5.39 mL, 37.7 mmol). After stirring for 18 h at 25 °C, the reaction mixture was diluted with CH_2Cl_2 (200 mL), and washed with H_2O (20 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 50% ether in hexanes) to afford Cbz-protected amine **24** (1.54 g, 81% over two steps) as a colorless oil. **24**: $R_f = 0.40$ (silica gel, 50% ether in hexanes); $[\alpha]_D^{22} = -38.0$ ($c = 0.83$, $CHCl_3$); IR (film) $\tilde{\nu}_{max} = 3354$, 2932, 1714, 1613, 1514, 1247, 1075, 1031 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.34-7.28$ (m, 5H, ArH), 7.23 (d, $J = 9.0$ Hz, 2H, ArH), 6.87 (d, $J = 8.5$ Hz, 2H, ArH), 5.81–5.74 (m, 1H, H-1), 5.14–4.99 (m, 4H, H-1*E*, H-1*Z*, CH_2Ar), 4.64 (d, $J = 10.6$ Hz, 1H, CH_2Ar), 4.56 (d, $J = 10.3$ Hz, 1H, CH_2Ar), 3.96 (br. s, 1H, H-4), 3.83 (br. s, 1H, H-5), 3.80 (s, 3H, OCH_3), 2.89–2.85 (m, 1H, H-2b), 2.41–2.39 (m, 1H, H-2a), 1.33 (s, 3H, CH_3(H-3)), 1.21 (d, $J = 6.5$ Hz, 3H, CH_3(H-6)); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.4$, 155.0, 137.0, 133.5, 130.1, 129.5, 128.5, 128.1, 118.9, 113.8, 83.9, 66.2, 65.7, 58.7, 55.3, 40.4, 23.6, 20.9; HRMS (FAB) calcd for $C_{24}H_{31}NO_5Na$ [$M + Na^+$] 436.2100, found 436.2109.

Vancosamine anomeric acetate 25: Ozone was bubbled through a solution of alcohol **24** (1.10 g, 2.52 mmol) in CH_2Cl_2 (35 mL) at −78 °C for 1 h. Dimethyl sulfide (5.0 mL) was added and the solution was allowed to warm to 25 °C over 6 h. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography to afford the anomeric mixture of lactols (1.00 g, 92%). Lactols: $R_f = 0.50$ (silica gel, ether); IR (thin film): $\tilde{\nu}_{max} = 3404$, 1716, 1612, 1513, 1454, 1247, 1064 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 1:1 mixture of α:β anomers): $\delta = 7.32-7.28$ (m, 4H, ArH), 7.20 (d, $J = 8.5$ Hz, 1H, ArH), 7.16 (d, $J = 8.0$ Hz, 2H, ArH), 6.82-6.78 (m, 2H, ArH, H-1α), 5.29 (br. s, 1H, H-V1α), 5.07–4.98 (m, 4H, CH_2Ar), 4.93 (s, 1H), 4.83 (s, 1H, H-1Vβ), 4.79 (d, $J = 9.5$ Hz, 1H, CH_2Ar), 4.67 (s, 1H), 4.59 (d, $J = 11.0$ Hz, 1H), 4.50 (d, $J = 11.0$ Hz, 1H), 4.45 (d, $J = 11.0$ Hz), 4.39 (d, $J = 10.6$ Hz, 1H), 4.25 (q, $J = 6.2$ Hz, 1H, H-V5), 3.74 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 3.49 (br. s, 1H), 3.46 (br. s, 1H), 1.92–1.89 (m, 1H, H-V2), 1.75–1.66 (m, 4H, H-V3, H-V2), 1.57–1.49 (m, 4H, H-V3, H-V2), 1.25 (d, $J = 6.2$ Hz, 3H, H-V6), 1.21 (d, $J = 7.0$ Hz, 3H, H-V6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.0$, 154.8, 136.4, 130.0, 129.8, 128.5, 128.4, 128.2, 128.1, 128.1, 128.0, 113.8, 113.7, 92.7, 91.4, 79.7, 78.5, 75.4, 75.1, 70.0, 66.2, 66.1, 64.7, 55.2, 53.5, 40.4, 36.3, 23.9, 21.9, 17.7, 17.5; HRMS (FAB) calcd for $C_{23}H_{29}NO_6Na$ [$M + Na^+$] 438.1893, found 438.1879. To a solution of the above lactols (850 mg, 2.04 mmol), triethylamine (1.42 mL, 10.2 mmol), and 4-DMAP (10 mg, 0.08 mmol) in CH_2Cl_2 (4.0 mL) at 0 °C was added acetic anhydride (580 μL, 6.12 mmol). After stirring the reaction mixture for 2 h at 25 °C, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (10 mL), and the aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography to afford acetate **25** (940 mg, 96%, β:α ca. 3.5:1 mixture of anomers) as a white foam. **25**: $R_f = 0.30$ (silica gel, 40% EtOAc in hexanes); IR (thin film): $\tilde{\nu}_{max} = 3372$, 1722, 1607, 1514, 1453, 1370, 1240, 1038 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.32-7.31$ (m, 5H, ArH), 7.20 (d, $J = 8.5$ Hz, 2H, ArH), 6.80 (d, $J = 8.8$ Hz, 2H, ArH), 6.15 (br. d, $J = 3.6$ Hz, 1H, H-V1α), 5.81 (dd, $J = 11.7$, 2.5 Hz, 1H, H-V1β), 5.05–5.02 (m, 3H, CH_2Ar, NH), 4.61 (d, $J = 11.4$ Hz, 1H, CH_2Ar), 4.41 (d, $J = 11.4$ Hz, 1H, CH_2Ar), 3.91 (q, $J = 6.2$ Hz, 1H, H-V5), 3.74 (s, 3H, OCH_3), 3.52 (br. s, 1H, H-V4α), 3.41 (br. s, 1H, H-V4β), 2.05 (s, 3H, $COCH_3$), 1.89–1.80 (m, 2H, H-V2a, H-V2b), 1.68 (s, 3H, H-3Vα), 1.58 (s, 3H, H-V3β), 1.28 (d, $J = 6.6$ Hz, 3H, H-V6β), 1.26 (d, $J = 6.2$ Hz, 3H, H-V6α); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 169.3$, 159.3, 154.8, 136.3, 128.7, 128.4, 128.1, 113.9, 113.8, 91.5, 90.8, 79.3, 78.6, 75.3, 70.5, 66.9, 66.2, 66.2, 55.1, 54.9, 53.1, 36.8, 35.0, 23.4, 21.8, 21.3, 17.6; HRMS (FAB) calcd for $C_{25}H_{31}NO_7Na$ [$M + Na^+$] 480.1998, found 480.1983.

Acetate-protected vancosamine thioglycoside 26: To a solution of anomeric acetates **25** (700 mg, 1.25 mmol) and thiophenol (630 μL, 6.11 mmol) in CH_2Cl_2 (15 mL) at −20 °C was added $BF_3 \cdot Et_2O$ (390 μL, 3.05 mmol). After 1 h at −20 °C, the reaction mixture was diluted with CH_2Cl_2 (100 mL), and washed with $NaHCO_3$ (25 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 30% EtOAc in hexanes) to afford the thioglycosides (560 mg, 95%, 1:1 mixture of α:β anomers) as a white foam. Thioglycosides: $R_f = 0.29$ (silica gel, 50% ether in hexanes); IR (thin film): $\tilde{\nu}_{max} = 3045$, 1713, 1498, 1453, 1274, 1220, 1006 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 1:1 mixture of α:β anomers): $\delta = 7.49$ (d, $J = 7.0$ Hz, 1H, ArH), 7.45 (d, $J = 7.3$ Hz, 1H, ArH), 7.35–7.25 (m, 9H, ArH), 5.54 (d, $J = 7.0$ Hz, 1H, H-V1), 5.51 (d, $J = 6.0$ Hz, 1H, H-V1), 5.07–5.03 (m, 2H, CH_2Ar), 4.81 (dd, $J = 14.2$, 2.0 Hz, 2H, CH_2Ar), 4.56 (q, $J = 6.6$ Hz, 1H, H-V5), 3.89 (q, $J = 6.5$ Hz, 1H, H-V5), 3.80 (s, 3H, OCH_3), 3.38 (br. s, 1H, H-V4), 3.23 (br. s, 1H, H-V4), 2.45–2.42 (m, 1H, H-V2), 2.30 (d, $J = 7.0$ Hz, 1H, H-V2), 2.13 (br. s, 1H, H-V2), 2.04 (br. s, 1H, H-V2), 1.74 (s, 3H, H-V3), 1.54 (s, 3H, H-V3), 1.31 (d, $J = 6.5$ Hz, 3H, H-V6), 1.27 (d, $J = 6.6$ Hz, 3H, H-V6); ^{13}C NMR (500 MHz, $CDCl_3$): $\delta = 155.0$, 136.4, 136.3, 135.8, 133.8, 131.5, 131.0, 128.9, 128.6, 128.5, 128.1, 128.0, 127.5, 127.1, 83.2, 81.7, 73.2, 72.5, 71.9, 66.3, 64.3, 54.9, 53.7, 37.2, 36.8, 23.2, 20.6, 17.5, 17.1; HRMS (FAB) calcd for $C_{21}H_{25}NO_4SNa$ [$M + Na^+$] 410.1402, found 410.1417. To a solution of the above thioglycosides (550 mg, 1.41 mmol), triethylamine (0.99 mL, 7.05 mmol), and 4-DMAP (10 mg, 0.08 mmol) in CH_2Cl_2 (4.0 mL) at 25 °C was added acetic anhydride (401 μL, 4.25 mmol). After the reaction mixture was stirred 2 h, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (10 mL), and the aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography to give **26** (600 mg, 97%) as a white foam. **26**: $R_f = 0.38$ (silica gel, 50% ether in hexanes); IR (thin film): $\tilde{\nu}_{max} = 1745$, 1520, 1455, 1372, 1230, 1062, 1025 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.51$ (d, $J = 9.0$ Hz, 1H, ArH), 7.41 (d, $J = 7.0$ Hz, 1H, ArH), 7.35–7.24 (m, 8H, ArH), 5.58 (dd, $J = 9.1$, 2.5 Hz, 1H, H-V1), 5.08 (d, $J = 11.7$ Hz, 2H, H-V1), 5.00–4.93 (m, 5H, CH_2Ar), 4.87 (br. s, 1H), 4.75 (br. s, 1H), 4.50 (q, $J = 6.6$ Hz, 1H, H-V5), 3.90 (q, $J = 6.0$ Hz, 1H, H-V5), 2.53 (dd, $J = 7.0$, 2.2 Hz, 1H, H-V2), 2.24–2.16 (m, 2H, H-V2), 2.09 (s, 3H, $COCH_3$), 2.06 (s, 3H, $COCH_3$), 1.90 (t, $J = 12.5$ Hz, 1H), 1.76 (s, 3H, H-V3), 1.63 (s, 3H, H-V3), 1.19 (d, $J = 6.2$ Hz, 3H, H-V6), 1.15 (d, $J = 6.6$ Hz, 3H, H-V6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 137.0$, 136.0, 133.5, 131.5, 131.0, 128.9, 128.8, 126.5, 128.3, 128.3, 128.2, 127.5, 127.1, 82.9, 81.0, 73.8, 72.3, 71.2, 66.2, 54.5, 53.4, 37.8, 36.8, 23.7, 21.2, 20.7, 17.8, 16.9; HRMS (FAB) calcd for $C_{23}H_{28}NO_5S$ [$M + H^+$] 430.1188, found 430.1702.

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Acetate-protected vancosamine fluoride donor 27: To a solution of the thioglycoside **26** (160 mg, 0.24 mmol) in acetone/H_2O (9:1) (5.5 mL) at 0 °C was added *N*-bromosuccinimide (70 mg, 0.37 mmol). After stirring for 0.5 h, the reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (25 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography to afford the lactols (120 mg, 87 %). Lactols: $R_f = 0.20$ (silica gel, 70 % ether in hexanes); IR (thin film): $\tilde{\nu}_{max} = 3362, 3033, 3020, 2983, 2969, 2942, 1738, 1734, 1718, 1714, 1538, 1508, 1453, 1372, 1251, 1131, 1060, 1025\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$, mixture of α:β anomers ca. 1.6:1): $\delta = 7.35-7.30$ (m, 10 H, ArH), 5.39 (br. s, 1 H, H-V1β), 5.10 (br. s, 1 H, NH), 5.08 (br. s, 1.6 H, NH), 5.00–4.93 (m, 6.2 H, H-V1α, 2 × CH_2Ar), 4.83 (s, 1.6 H, H-V4α), 4.79 (s, 1 H, H-V4β), 4.36 (br. q, $J = 6.2$ Hz, 1 H, H-V5α), 3.89 (br. q, $J = 6.5$ Hz, 1.6 H, H-V5β), 3.82 (d, $J = 7.0$ Hz, 1.6 H, OHβ), 2.10–2.05 (m, 3.6 H, H-V2aα, H-V2aβ, H-V2bβ), 2.07 (s, 3 H, $COCH_3$), 2.05 (s, 4.8 H, $COCH_3$), 1.96 (br. d, $J = 10.7$ Hz, 1.6 H, H-V2bα), 1.77 (s, 4.8 H, H-V3α), 1.59 (s, 3 H, H-V3β), 1.18 (d, $J = 6.4$ Hz, 4.8 H, H-V6α), 1.12 (d, $J = 6.4$ Hz, 3 H, H-V6β); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 171.0, 170.7, 136.4, 136.3, 128.5, 128.5, 128.3, 128.3, 128.2, 128.1, 128.1, 92.7, 91.6, 73.7, 72.2, 68.7, 63.1, 54.5, 53.0, 39.7, 35.6, 30.3, 29.5, 24.0, 22.2, 20.7, 20.6, 17.3$; HRMS (FAB) calcd for $C_{17}H_{23}NO_6Na$ $[M + Na^+]$: 360.1423, found 360.1415. Diethylaminosulfur trifluoride (65 μL, 0.49 mmol) was added to a solution of the lactols (110 mg, 0.32 mmol) in CH_2Cl_2 (2 mL) at 0 °C. After the reaction mixture was stirred for 20 min, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (3 mL), diluted with CH_2Cl_2 (20 mL), and stirred for 5 min. The layers were separated, the aqueous layer was extracted with CH_2Cl_2 (20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and the solvents were removed under reduced pressure. The residue was azeotroped with benzene (2 mL), dried under vacuum for 1 h, and used directly in the next reaction. **27**: (crude) ^1H NMR (500 MHz, $CDCl_3$, α:β ca. 16:1): $\delta = 7.37-7.26$ (m, 5 H, ArH), 5.69 (br. d, $J = 53.0$ Hz, 1 H, H-V1), 5.08 and 4.95 (AB, $J = 12.0$ Hz, 2 H, CH_2Ar), 5.00 (s, 1 H, NH), 4.82 (s, 1 H, H-V4), 4.32 (br. q, $J = 6.5$ Hz, 1 H, H-V5), 2.40–2.37 (m, 1 H, H-V2a), 2.09 (s, 3 H, $COCH_3$), 1.90 (dd, $J = 53.0$, 14.0 Hz, 1 H, H-V2b), 1.70 (s, 3 H, H-V3), 1.17 (d, $J = 6.5$ Hz, 3 H, H-V6).

Glucose thioglycoside 28: Osmium tetroxide (200 μL, 2.5 % solution in *tert*-butyl alcohol) was added to a solution of tribenzylglucal (4.30 g, 10.3 mmol) and 4-methylmorpholine *N*-oxide (1.57 g, 13.4 mmol) in acetone/H_2O (10:1) (110 mL) at 25 °C. After stirring for 12 h, the reaction mixture was concentrated, diluted with CH_2Cl_2 (100 mL), and washed with saturated aqueous $NaHCO_3$ (5 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 80 % ether in hexanes) to provide the diol (4.23 g, 91 %). To a solution of the above diol (4.24 g, 9.2 mmol) in pyridine (20 mL) at 0 °C was added benzoyl chloride (2.66 mL, 23.0 mmol) and 4-DMAP (0.224 g, 1.86 mmol), and the resulting reaction mixture was warmed to 25 °C and stirred for 12 h. The reaction mixture was diluted with ether (500 mL), and washed with saturated aqueous NH_4Cl (2 × 100 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 40 % ether in hexanes) to afford the dibenzoate (5.92 g, 98 %). To a solution of the above dibenzoate (241 mg, 0.37 mmol) and thiophenol (80 μL, 0.73 mmol) in CH_2Cl_2 (2 mL) at −10 °C was added $BF_3 \cdot Et_2O$ (9.0 μL, 0.070 mmol). After 1 h, the reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with saturated aqueous $NaHCO_3$ (25 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 35 % ether in hexanes) to yield β-thioglycoside **28** (0.20 g, 84 %) as a white foam. **28**: $R_f = 0.47$ (silica gel, 50 % ether in hexanes); $[\alpha]_D^{22} = +21.7$ ($c = 1.1$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3047, 3031, 2987, 2865, 1722, 1602, 1584, 1496, 1454, 1365, 1316, 1285, 1071, 1027, 908, 739, 710\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.05$ (d, $J = 7.5$ Hz, 2 H, ArH), 7.59 (t, $J = 7.5$ Hz, 1 H, ArH), 7.50 (d, $J = 7.5$ Hz, 2 H, ArH), 7.46 (t, $J = 7.5$ Hz, 2 H, ArH), 7.36–7.11 (m, 18 H, ArH), 5.30 (t, $J = 9.5$ Hz, 1 H, H-G2), 4.83 and 4.60 (AB, $J = 10.9$ Hz, 2 H, CH_2Ar), 4.80 (d, $J = 9.9$ Hz, 1 H, H-G1), 4.74 and 4.65 (AB, $J = 11.0$ Hz, 2 H, CH_2Ar), 4.63 and 4.57 (AB, $J = 11.9$ Hz, 2 H, CH_2Ar), 3.86 (t, $J = 9.0$ Hz, 1 H, H-G3), 3.83 (br. d, $J = 9.1$ Hz, 1 H, H-G6a), 3.78 (dd, $J = 10.0$, 5.2 Hz, 1 H, H-G6b), 3.75 (t, $J = 9.0$ Hz, 1 H, H-G4), 3.67–3.60 (m, 1 H, H-G5); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.0, 138.2, 137.9, 137.6, 133.2, 132.9, 132.5, 129.8, 128.8, 128.4, 128.4, 128.3, 128.2, 128.0, 128.0, 127.8, 127.7, 127.7, 127.6, 86.1, 84.3, 79.4, 77.8, 75.3, 75.1, 73.5, 72.4, 68.9$; HRMS (FAB) calcd for $C_{40}H_{38}O_6SCs$ $[M + Cs^+]$ 779.1443, found 779.1455.

Benzyl-protected glucose lactols 29: To a solution of thioglycoside **28** (160 mg, 0.24 mmol) in acetone/H_2O (10:1) (5.5 mL) at 0 °C was added *N*-bromosuccinimide (90 mg, 0.49 mmol). After stirring for 0.5 h, the reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (25 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 50 % ether in hexanes) to afford lactols **29** (120 mg, 87 %) as a white foam. **29**: $R_f = 0.50$ (silica gel, 70 % ether in hexanes); IR (thin film): $\tilde{\nu}_{max} = 3363, 3063, 3031, 2922, 2874, 1775, 1715, 1603, 1494, 1452, 1362, 1314, 1282, 1175, 1154, 1119, 1096, 1068, 1012, 1026, 918, 856, 745, 697\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.03$ (d, $J = 7.5$ Hz, 2 H, ArH), 7.54 (t, $J = 7.5$ Hz, 2 H, ArH), 7.41 (t, $J = 7.5$ Hz, 2 H, ArH), 7.32–7.19 (m, 15 H, ArH), 6.94 (t, $J = 8.5$ Hz, 1 H, ArH), 6.45 (d, $J = 8.5$ Hz, 2 H, ArH), 5.56 (d, $J = 3.5$ Hz, 1 H, H-G1), 5.16 (dd, $J = 10.0$, 3.5 Hz, 1 H, H-G2), 4.87 and 4.53 (AB, $J = 12.0$ Hz, 2 H, CH_2Ar), 4.87-4.84 (m, 2 H, CH_2Ar), 4.61 and 4.53 (AB, $J = 12.0$ Hz, 2 H, CH_2Ar), 4.29 (t, $J = 9.0$ Hz, 1 H, H-G3), 4.22 (ddd, $J = 10.0$, 5.0, 2.0 Hz, 1 H, H-G5), 3.72–3.66 (m, 3 H, H-G4, H-G6a, H-G6b); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 178.4, 166.0, 138.2, 138.0, 137.7, 130.0, 129.7, 128.5, 128.5, 128.4, 128.3, 128.0, 128.0, 127.8, 127.7, 90.5, 90.4, 79.8, 79.7, 78.3, 78.2, 77.4, 75.6, 73.4, 70.2$; HRMS (FAB) calcd for $C_{34}H_{34}O_7Cs$ $[M + Cs^+]$ 687.1359, found 687.1373.

2,6-Dimethoxyphenolic glucoside 31: DBU (5.0 μL, 0.033 mmol) was added to a solution of glucose lactols **29** (0.42 g, 0.76 mmol) and trichloroacetonitrile (0.60 mL, 7.4 mmol) in CH_2Cl_2 at −30 °C. After 0.5 h, the solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 35 % ether in hexanes) to afford imidate **30** (470 mg, 90 %). A mixture of 2,6-dimethoxyphenol (17 mg, 0.11 mmol) and imidate **30** (118 mg, 1.85 mmol) was azeotroped with benzene (3 × 3 mL), and then dried under high vacuum for 1 h. CH_2Cl_2 (0.5 mL) and 4 Å MS were added, and the mixture was stirred for 15 min at ambient temperature. The resulting mixture was cooled to −30 °C and $BF_3 \cdot Et_2O$ (60 μL, 0.38 M solution in CH_2Cl_2, 0.020 mmol) was added dropwise. After 1 h and 2 h, a second and third 60 μL of $BF_3 \cdot Et_2O$ solution were added. The reaction mixture was warmed slowly to 25 °C, and then stirred for 22 h. The reaction mixture was diluted with EtOAc (150 mL), washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), concentrated, and the residue was purified by flash column chromatography (silica gel, (1:1:3) ether/CH_2Cl_2/hexanes) to yield β-glucoside **31** (72 mg, 95 %, β:α ca. 13:1) as a white foam. **31**: $R_f = 0.26$ (silica gel, (1:1:3) ether/CH_2Cl_2/hexanes); $[\alpha]_D^{22} = +13.6$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3030, 2923, 2854, 1730, 1600, 1496, 1478, 1456, 1365, 1259, 1111, 1027, 735, 702\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.03$ (d, $J = 7.5$ Hz, 2 H, ArH), 7.54 (t, $J = 7.5$ Hz, ArH), 7.41 (t, $J = 7.5$ Hz, 2 H, ArH), 7.32–7.12 (m, 15 H, ArH), 6.94 (t, $J = 8.5$ Hz, 1 H, ArH), 6.45 (d, $J = 8.5$ Hz, 2 H, ArH), 5.60 (br. t, $J = 8.0$ Hz, 1 H, H-G2), 5.07 (d, $J = 7.5$ Hz, 1 H, H-G1), 4.84 and 4.57 (AB, $J = 11.0$ Hz, 2 H, CH_2Ar), 4.76 and 4.70 (AB, $J = 11.0$ Hz, 2 H, CH_2Ar), 4.65 and 4.62 (AB, $J = 12.0$ Hz, 2 H, CH_2Ar), 3.89–3.86 (m, 2 H, H-G3, H-G4), 3.80 (dd, $J = 11.3$, 2.0 Hz, 1 H, H-G6a), 3.75 (dd, $J = 11.5$, 5.0 Hz, 1 H, H-G6b), 3.57 (s, 7 H, OCH_3, H-G5); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 165.1, 153.3, 138.4, 138.0, 137.9, 135.0, 132.7, 130.4, 129.8, 128.4, 128.2, 128.2, 128.1, 128.0, 127.8, 127.7, 127.5, 127.4, 124.3, 105.3, 102.2, 82.9, 77.8, 75.9, 74.9, 74.8, 74.3, 73.7, 69.0, 55.9$; HRMS (FAB) calcd for $C_{42}H_{42}O_9Cs$ $[M + Cs^+]$ 823.1883, found 823.1913.

Glucose acceptor 32: NaOH (10 mg, 0.25 mmol, powdered) was added to a solution of glucoside **31** (72 mg, 0.10 mmol) in MeOH (3.0 mL) at 25 °C. After the mixture was stirred for 3 h, saturated aqueous NH_4Cl (5 mL) was added, and the reaction mixture was extracted with CH_2Cl_2 (100 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 30 % ether in hexanes) to provide alcohol **32** (53 mg, 90 %) as a white foam. **32**: $R_f = 0.18$ (silica gel, (1:1:3) ether/CH_2Cl_2/hexanes); $[\alpha]_D^{22} = -11.3$ ($c = 0.60$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3504, 3062, 3030, 2901, 1600, 1497, 1478, 1455, 1298, 1257, 1112, 1070, 1037, 984, 733, 698\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.44$ (d, $J = 7.5$ Hz, 2 H, ArH), 7.54–7.19 (m, 13 H, ArH), 7.07 (t, $J = 8.5$ Hz, 1 H, ArH), 6.61 (d, $J = 8.5$ Hz, 2 H, ArH), 5.09 and 4.58 (AB, $J = 11.0$ Hz, 2 H, CH_2Ar), 4.88 and 4.84 (AB, $J = 11.5$ Hz, 2 H, CH_2Ar), 4.63 and 4.60 (AB, $J = 11.5$ Hz, 2 H, CH_2Ar), 4.57 (d, $J = 7.5$ Hz, 1 H, H-G1), 3.99 (br. s, 1 H, OH), 3.93 (t, $J = 8.5$ Hz, 1 H, H-G3), 3.85 (s, 6 H, OCH_3), 3.81 (dd, $J = 11.0$, 2.0, 1 H, H-G6a), 3.75 (dd, $J = 11.0$, 5.5, 1 H, H-G6b), 3.66-3.62 (m, 2 H, H-G2, H-G4), 3.53-3.51 (m, 1 H, H-G5); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 153.0$,

138.8, 138.4, 138.1, 135.8, 128.3, 128.3, 128.2, 127.9, 127.9, 127.7, 127.7, 127.5, 124.9, 106.3, 105.4, 84.8, 77.2, 75.9, 75.6, 75.0, 74.9, 73.5, 69.4, 56.3; HRMS (FAB) calcd for $C_{35}H_{38}O_8Cs$ $[M+Cs^+]$ 719.1621, found 719.1598.

Benzyl-protected disaccharide 33: Vancosamine fluoride **22** (30 mg, 0.06 mmol) and alcohol **32** (20 mg, 0.03 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (0.5 mL) and 4 Å MS were added, and the mixture was stirred for 15 min. The resulting mixture was cooled to −30 °C and $BF_3 \cdot Et_2O$ (40 μL, 0.4 M solution in CH_2Cl_2, 0.010 mmol) and TMSOTf (80 μL, 0.2 M solution in CH_2Cl_2, 0.010 mmol) were added dropwise. The reaction mixture was warmed to 25 °C and stirred for 72 h. The reaction mixture was diluted with EtOAc (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 30% ether in hexanes) to afford disaccharide **33** (26 mg, 80%) (α:β ca. 10:1) as a white foam and recovered alcohol **32** (2 mg, 10%). **33**: $R_f = 0.18$ (silica gel, 50% ether in hexanes); $[\alpha]_D^{22} = -43.8$ ($c = 0.24$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3409$, 3031, 2931, 1723, 1599, 1497, 1478, 1455, 1363, 1297, 1256, 1215, 1111, 1062, 735, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.31-7.18$ (m, 25H, ArH), 7.02 (t, $J = 8.5$ Hz, 2H, ArH), 6.57 (d, $J = 8.5$ Hz, 2H, ArH), 5.32 (br. d, $J = 4.5$ Hz, 1H, H-V1), 5.08 (d, $J = 7.5$ Hz, 1H, H-G1), 5.01 and 4.98 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.90 (s, 1H, NH), 4.87 and 4.78 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.77 and 4.47 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.64 and 4.61 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.53-4.49 (m, 1H, H-V5), 4.45 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 3.94 (t, $J = 8.0$ Hz, 1H, H-G3), 3.77 (s, 6H, OCH_3), 3.72–3.65 (m, 3H, H-G2, H-G4, H-G6a), 3.61 (dd, $J = 12.0$, 5.5 Hz, 1H, H-G6b), 3.41 (s, 1H, H-V4), 3.39–3.37 (m, 1H, H-G5), 1.84 (s, 3H, H-V3), 1.83 (d, $J = 13.0$ Hz, 1H, H-V2a), 1.78 (dd, $J = 13.0$, 4.5 Hz, 1H, H-V2b), 1.09 (d, $J = 6.5$ Hz, 3H, H-V6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 154.9$, 153.9, 138.6, 138.4, 138.1, 136.6, 134.0, 130.0, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 124.1, 105.5, 100.7, 97.7, 86.0, 80.9, 78.2, 75.8, 75.8, 75.7, 75.3, 74.7, 73.6, 68.8, 66.0, 64.3, 56.1, 53.7, 36.6, 29.7, 23.4, 17.4; HRMS (FAB) calcd for $C_{57}H_{63}NO_{12}Cs$ $[M+Cs^+]$ 1086.3405, found 1086.3450.

Benzoyl-protected disaccharide 34: A mixture of disaccharide **33** (20 mg, 0.021 mmol) and 10% Pd/C (ca. 10 mg) in EtOAc (2.0 mL) was stirred under an atmosphere of H_2 for 12 h at 25 °C. The reaction mixture was then filtered through a pad of celite, concentrated, and azeotroped with benzene (2 mL). The residue was dissolved in pyridine (1.0 mL), cooled to 0 °C and treated with benzoyl chloride (21 μL, 0.15 mmol) for 6 h. The reaction mixture was diluted with ether (100 mL) and washed with saturated aqueous NH_4Cl (3 × 10 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 50% ether in hexanes) to yield disaccharide **34** (19 mg, 85% for two steps) as a white foam. **34**: ^1H NMR (500 MHz, $CDCl_3$): $\delta =$ 8.08 (d, $J = 7.0$ Hz, 2H, ArH), 7.99 (d, $J = 7.0$ Hz, 2H, ArH), 7.90 (d, $J =$ 7.0 Hz, 2H, ArH), 7.80 (d, $J = 7.0$ Hz, 2H, ArH), 7.63–7.23 (m, 17H, ArH), 7.04 (t, $J = 8.5$ Hz, 1H, ArH), 6.59 (s, 1H, NH), 6.57 (d, $J = 8.0$ Hz, 2H, ArH), 5.85 (t, $J = 9.0$ Hz, 1H, H-G3), 5.76 (t, $J = 10.0$ Hz, 1H, H-G4), 5.43 (d, $J = 7.0$ Hz, 1H, H-G1), 5.26 (d, $J = 4.5$ Hz, 1H, H-V1), 5.12 (s, 1H, H-V4), 4.80 (q, $J = 6.5$ Hz, 1H, H-V5), 4.50 (dd, $J = 11.5$, 3.6 Hz, 1H, H-G6a), 4.40 (dd, $J = 8.0$, 7.5 Hz, 1H, H-G2), 4.37 (dd, $J = 11.5$, 6.0 Hz, 1H, H-G6b), 4.05-3.98 (m, 1H, H-G5), 3.81 (s, 6H, OCH_3), 2.70 (d, $J = 14.0$ Hz, 1H, H-V2a), 2.03 (s, 3H, H-V3), 2.00 (dd, $J = 14.0$, 4.5 Hz, 1H, H-V2b), 1.11 (d, $J = 6.0$ Hz, 3H, H-V6); HRMS (FAB) calcd for $C_{56}H_{53}NO_{16}Cs$ $[M+Cs^+]$ 1122.2464, found 1112.2441.

Glucose alcohol 35: NaOH (10 mg, powdered) was added to a solution of thioglycoside (300 mg, 0.46 mmol) in MeOH (5.0 mL) at 25 °C. After stirring for 3 h, the reaction mixture was diluted with ether (150 mL) and washed with saturated aqueous NH_4Cl (25 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 30% ether in hexanes) to provide alcohol **35** (220 mg, 90%) as a white foam. **35**: $R_f = 0.41$ (silica gel, 50% ether in hexanes); $[\alpha]_D^{22} = -11.1$ ($c = 2.9$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3444$, 3062, 3030, 2868, 1584, 1496, 1453, 1440, 1360, 1285, 1209, 1058, 911, 818, 738, 697 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.62-7.22$ (m, 20H, ArH), 4.95 and 4.87 (AB, $J = 11.2$ Hz, 2H, CH_2Ar), 4.87 and 4.62 (AB, $J = 10.5$ Hz, 2H, CH_2Ar), 4.65 and 4.58 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.54 (d, $J = 9.6$ Hz, 1H, H-G1), 3.83 (d, $J = 10.2$ Hz, 1H, H-G6a), 3.78 (dd, $J = 10.9$, 4.5 Hz, 1H, H-G6b), 3.66–3.60 (m, 2H, H-G3, H-G4), 3.58–3.51 (m, 2H, H-G2, H-G5), 2.50 (s, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 138.4$, 138.2, 138.0, 132.8, 131.8, 128.9, 128.4, 128.3, 128.3, 127.0, 127.9, 127.9, 127.7, 127.6, 127.5, 88.0, 85.9, 79.3, 77.3, 75.3, 75.0, 73.4, 72.5, 68.9; HRMS (FAB) calcd for $C_{33}H_{34}O_5SCs$ $[M+Cs^+]$ 675.1181, found 675.1198.

Benzyl-protected thio-disaccharide 36: Vancosamine fluoride **22** (100 mg, 0.26 mmol) and alcohol **35** (120 mg, 0.21 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (0.5 mL) and 4 Å MS were added and the mixture was stirred for 15 min. The resulting reaction mixture was cooled to −10 °C and tin dichloride (93 mg, 0.49 mmol) was added. After stirring for 2 h, the reaction mixture was diluted with EtOAc (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 30% ether in hexanes) to afford disaccharide **36** (162 mg, 85%, α:β ca. 3.3:1) as a white foam and recovered alcohol **35** (11 mg, 10%). **36**: $R_f = 0.53$ (silica gel, 50% ether in hexanes); $[\alpha]_D^{22} = -51.2$ ($c = 0.38$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3032$, 2925, 1720, 1584, 1497, 1454, 1360, 1270, 1212, 1129, 1056, 738, 696 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.55-7.16$ (m, 30H, ArH), 5.43 (d, $J = 4.4$ Hz, 1H, H-V1), 5.01 and 4.95 (AB, $J = 12.2$ Hz, 2H, CH_2Ar), 4.90–4.47 (AB, $J =$ 11.0, 12.0 Hz, 10H, CH_2Ar), 4.86 (s, 1H, NH), 4.68 (q, $J = 6.5$ Hz, 1H, H-V5), 4.61 (d, $J = 9.7$ Hz, 1H, H-G1), 3.76 (t, $J = 8.5$ Hz, 1H, H-G3), 3.73 (dd, $J = 10.9$, 1.7 Hz, 1H, H-G6a), 3.66 (dd, $J = 11.3$, 5.3 Hz, 1H, H-G6b), 3.63 (t, $J = 8.5$ Hz, 1H, H-G4), 3.59 (t, $J = 9.3$ Hz, 1H, H-G2), 3.55 (br. s, 1H, H-V4), 3.52–3.48 (m, 1H, H-G5), 1.83 (dd, $J = 11.4$, 4.8 Hz, 1H, H-V2a), 1.73 (d, $J = 11.4$ Hz, 1H, H-V2b), 1.55 (s, 3H, H-V3), 1.28 (d, $J =$ 6.5 Hz, 3H, H-V6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 154.7$, 138.2, 138.0, 137.9, 136.6, 134.4, 131.7, 128.9, 128.5, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.4, 127.3, 125.5, 98.0, 87.9, 87.4, 80.5, 79.1, 78.2, 76.2, 75.8, 75.5, 74.9, 73.4, 69.0, 66.1, 65.4, 53.4, 36.4, 30.3, 29.7, 23.6, 21.2, 17.5; HRMS (FAB) calcd for $C_{55}H_{59}NO_9SCs$ $[M+Cs^+]$ 1042.2965, found 1042.2919.

Benzyl-protected disaccharide lactols 37: To a solution of thioglycoside **36** (125 mg, 0.14 mmol) in acetone/H_2O (10:1) (5.5 mL) at 0 °C was added *N*-bromosuccinimide (40 mg, 0.21 mmol). After stirring for 0.5 h, the reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (25 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 60% ether in hexanes) to afford lactols **37** (97 mg, 85%, α:β ca. 5:1) as a white foam. **37**: $R_f = 0.38$ (silica gel, 70% ether in hexanes); IR (thin film): $\tilde{\nu}_{max} = 3410$, 3088, 3064, 3031, 2929, 2870, 1723, 1714, 1538, 1514, 1504, 1360, 1270, 1243, 1212, 1129, 1065, 912, 737, 698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.34-7.16$ (m, 25H, ArH), 5.36 (br. d, $J = 3.1$ Hz, 1H, H-G1), 5.10 (br. d, $J = 3.1$ Hz, 1H, H-V1), 5.05 and 4.99 (AB, $J =$ 12.2 Hz, 2H, CH_2Ar), 4.92 (s, 1H, NH), 4.85 and 4.80 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.65–4.50 (AB, $J = 11.0$, 12.0 Hz, 6H, CH_2Ar), 4.22 (br. q, $J =$ 6.3 Hz, 1H, H-V5), 4.05 (ddd, $J = 10.0$, 2.6, 2.6 Hz, 1H, H-G5), 3.96 (t, $J =$ 9.4 Hz, 1H, H-G3), 3.67–3.62 (m, 2H, H-G6a, H-G6b), 3.59–3.56 (m, 1H, H-G2), 3.57 (t, $J = 9.5$ Hz, 1H, H-G4), 3.09 (br. s, 1H, H-V4), 2.01 (dd, $J =$ 13.4, 4.6 Hz, 1H, H-V2a), 1.77 (d, $J = 14.0$ Hz, 1H, H-V2b), 1.76 (s, 3H, H-V3), 1.28 (d, $J = 6.5$ Hz, 3H, H-V6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 154.8, 138.6, 138.2, 138.0, 137.9, 137.8, 136.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 99.2, 92.9, 84.6, 83.4, 81.2, 80.2, 80.0, 77.8, 75.6, 75.6, 74.9, 73.4, 70.1, 68.8, 66.2, 65.1, 53.6, 36.5, 23.9, 17.5; HRMS (FAB) calcd for $C_{49}H_{55}NO_{10}Cs$ $[M+Cs^+]$ 950.2880, found 950.2848.

Benzyl-protected disaccharide imidate 38: DBU (5.0 μL, 0.033 mmol) was added to a solution of the disaccharide lactols **37** (133 mg, 0.16 mmol) and trichloroacetonitrile (200 μL, 3.2 mmol) in CH_2Cl_2 at 0 °C. After 15 min, the solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 30% ether in hexanes) to yield imidate **38** (136 mg, 90%). **38**: ^1H NMR (500 MHz, $CDCl_3$): $\delta =$ 8.65 (s, 1H, NH), 7.32–7.13 (m, 25H, ArH), 6.47 (d, $J = 3.5$ Hz, 1H, H-G1), 5.12 (d, $J = 4.0$ Hz, 1H, H-V1), 5.01 and 4.96 (AB, $J = 12.5$ Hz, 2H, CH_2 of Cbz), 4.85 (s, 1H, NH), 4.85–4.45 (AB, $J = 12.0$, 11.0 Hz, 8H, CH_2Ar), 4.08 (q, $J = 6.5$ Hz, 1H, H-V5), 4.01 (t, $J = 9.5$ Hz, 1H, H-G3), 3.97–3.94 (m, 1H, H-G5), 3.81 (dd, $J = 8.5$, 3.5 Hz, 1H, H-G2), 3.97 (t, $J = 9.5$ Hz, 1H, H-G4), 3.77 (dd, $J = 11.0$, 3.0 Hz, 1H, H-G6a), 3.65 (dd, $J = 11.0$, 1.5 Hz, 1H, H-G6b), 3.51 (s, 1H, H-V4), 1.86 (dd, $J = 13.5$, 4.5 Hz, 1H, H-V2a), 1.75 (d, $J = 13.0$ Hz, 1H, H-V2b), 1.66 (s, 3H, H-V3), 1.20 (d, $J = 6.5$ Hz, 3H, H-V6).

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Chloroacetate-protected glucose imidate 39: Chloroacetyl chloride (440 μL, 5.5 mmol) was added to a solution of 3,4,6-tri-*O*-benzyl glucose (825 mg, 1.85 mmol) and pyridine (0.74 mL, 9.2 mmol) in ether (10 mL) at −78 °C. After warming to 25 °C and stirring for 18 h, the reaction mixture was diluted with ether (200 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and saturated aqueous NH_4Cl (3 × 15 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 50% ether in hexanes) to yield the di-chloroacetate (720 mg, 65%). *n*-Butylamine (150 μL, 1.5 mmol) was added to a solution of the above di-chloroacetate (720 mg, 1.3 mmol) in THF (4.0 mL) at 25 °C. After stirring for 0.5 h, the reaction mixture was diluted with CH_2Cl_2 (200 mL) and washed with saturated aqueous NH_4Cl (3 × 15 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 70% ether in hexanes) to afford the lactols (540 mg, 80%) as a white foam. Lactols: $R_f = 0.22$ (silica gel, 50% ether in hexanes); IR (thin film): $\tilde{\nu}_{max} = 3306$, 2995, 2945, 2872, 1725, 1659, 1538, 1495, 1454, 1361, 1313, 1260, 1198, 1151, 1092, 1048, 827, 741, 710 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.31-7.16$ (m, 15H, ArH), 5.38 (br. t, $J = 3.2$ Hz, 1H, H-G2), 4.87 (br. d, $J = 3.4$ Hz, 1H, H-G1), 4.82 and 4.72 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.79 and 4.50 (AB, $J = 10.9$ Hz, 2H, CH_2Ar), 4.56 and 4.48 (AB, $J = 12.1$ Hz, 2H, CH_2Ar), 4.07-4.05 (m, 1H, H-G3), 3.96 and 3.81 (AB, $J = 15.2$ Hz, 2H, CH_2Cl), 3.69-3.58 (m, 4H, H-G4, H-G5, H-G6a, H-G6b); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.9$, 138.3, 137.8, 137.5, 128.4, 128.3, 128.3, 128.3, 128.3, 127.9, 127.8, 127.7, 127.6, 127.5, 95.0, 89.8, 79.6, 78.0, 75.4, 75.2, 74.9, 73.3, 69.8, 69.5, 40.6; HRMS (FAB) calcd for $C_{29}H_{31}ClO_7Cs$ $[M + Cs^+]$ 659.0813, found 659.0828. DBU (5.0 μL, 0.033 mmol) was added to a solution of the above glucose lactols (420 mg, 0.76 mmol) and trichloroacetonitrile (0.60 mL, 7.4 mmol) in CH_2Cl_2 at −30 °C. After the reaction mixture was stirred for 0.5 h, the solvents were removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel, 35% ether in hexanes) to afford imidate **39** (470 mg, 90%).

Benzyl-protected vancomycin monosaccharide 40: Aglycon acceptor **6** (125 mg, 0.07 mmol) and imidate **39** (320 mg, 0.48 mmol) were azeotroped with benzene (3 × 3 mL), and then dried under high vacuum for 1 h. CH_2Cl_2 (0.5 mL) and 4 Å MS were added, and the mixture was stirred for 15 min. The resulting mixture was cooled to −78 °C and $BF_3 \cdot Et_2O$ (253 μL, 1.06 M solution in CH_2Cl_2, 0.28 mmol) was added dropwise. The reaction mixture was warmed slowly to −30 °C, and then stirred for 18 h. The reaction mixture was diluted with EtOAc (150 mL), and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 4% MeOH in CH_2Cl_2) to afford *β*-glucoside **40** (116 mg, 70%) as an oil. **40**: $R_f = 0.20$ (silica gel, 4% MeOH in CH_2Cl_2); ^1H NMR (600 MHz, CD_3OD, 330 K): $\delta = 7.55-7.03$ (m, 28H), 6.81 (d, $J = 8.5$ Hz, 1H), 6.43 (s, 1H), 6.37 (s, 1H), 5.80–4.36 (m, 20H), 4.26-3.50 (m, 8H), 3.76 (s, 3H), 2.96 (s, 3H), 2.42–2.40 (m, 2H), 1.85–1.82 (m, 1H), 1.60–1.50 (m, 2H), 1.02 (s, 9H), 0.98 (s, 9H), 0.93 (s, 6H), 0.88 (s, 9H), 0.76 (s, 9H), 0.67 (s, 9H), 0.24 (s, 6H), 0.20 (s, 3H), 0.14 (s, 6H), 0.12 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), −0.08 (s, 3H); HRMS (FAB) calcd for $C_{121}H_{159}Cl_3N_8O_{25}Si_5Na$ $[M + Na^+]$ 2391.9225, found 2391.9144.

Benzyl-protected vancomycin monosaccharide acceptor 41: K_2CO_3 (8.0 mg, 0.06 mmol) was added to a solution of **40** (45 mg, 0.020 mmol) in THF/MeOH (2:1) (1.0 mL) at 25 °C. After stirring for 10 min, the reaction mixture was diluted with CH_2Cl_2 (150 mL), and washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 4% MeOH in CH_2Cl_2) to yield alcohol **41** (34 mg, 75%) as an oil. **41**: $R_f = 0.20$ (silica gel, 4% MeOH in CH_2Cl_2); ^1H NMR (600 MHz, CD_3OD, 330 K): $\delta = 7.54-7.04$ (m, 28H), 6.81 (d, $J = 8.4$ Hz, 1H), 6.44 (s, 1H), 6.37 (s, 1H), 5.83–4.38 (m, 20H), 4.26–3.64 (m, 6H), 3.76 (s, 3H), 2.95 (s, 3H), 2.47–2.44 (m, 2H), 1.84–1.82 (m, 1H), 1.56–1.53 (m, 2H), 1.02 (s, 9H), 0.96 (s, 9H), 0.92 (s, 6H), 0.88 (s, 9H), 0.76 (s, 9H), 0.65 (s, 9H), 0.24 (s, 6H), 0.20 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 6H), 0.10 (s, 3H), 0.05 (s, 3H), −0.07 (s, 3H); HRMS (FAB) calcd for $C_{119}H_{158}Cl_2N_8O_{24}Si_5Cs$ $[M + Cs^+]$ 2427.8690, found 2427.8494.

Benzyl-protected vancomycin 42 (from monosaccharide coupling)**:** Vancosamine fluoride **22** (20 mg, 0.05 mmol) and alcohol **41** (10 mg, 0.004 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (0.3 mL) and 4 Å MS were added, and the mixture was stirred for 15 min. The resulting mixture was cooled to 0 °C and $BF_3 \cdot Et_2O$ (40 μL, 0.5 M solution in CH_2Cl_2, 0.020 mmol) was added dropwise. After warming to 25 °C and stirring for 24 h, the reaction mixture was diluted with EtOAc (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 4% MeOH in CH_2Cl_2) to afford disaccharide **42** (0.7 mg, 5%) as an oil. **42**: $R_f = 0.30$ (silica gel, 4% MeOH in CH_2Cl_2); ^1H NMR (600 MHz, CD_3OD, 330 K): $\delta = 7.47-7.04$ (m, 38H), 6.80 (d, $J = 8.4$ Hz, 1H), 6.43 (s, 1H), 6.39 (s, 1H), 5.87–4.63 (m, 24H), 4.40–4.10 (m, 6H), 3.76 (s, 3H), 2.94 (s, 3H), 2.53–2.45 (m, 2H), 1.95–1.77 (m, 3H), 1.51–1.48 (m, 2H), 1.28 (s, 3H), 1.03–1.00 (m, 12H), 0.95–0.89 (m, 6H), 0.89 (s, 9H), 0.86 (s, 9H), 0.76 (s, 9H), 0.67 (s, 9H), 0.24 (s, 12H), 0.19 (s, 3H), 0.14 (s, 6H), 0.09 (s, 6H), 0.03 (s, 3H), −0.06 (s, 3H); HRMS (FAB) calcd for $C_{141}H_{183}Cl_2N_9O_{28}Si_5Cs$ $[M + Cs^+]$ 2793.0450, found 2793.0253.

Benzyl-protected vancomycin 42 (from disaccharide coupling): Aglycon acceptor **6** (17 mg, 0.010 mmol) and imidate **38** (34 mg, 0.040 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (0.5 mL) and 4 Å MS were added, and the mixture was stirred for 15 min. The resulting mixture was cooled to −78 °C and $BF_3 \cdot Et_2O$ (460 μL, 0.40 mmol) was added dropwise. The reaction mixture was warmed slowly to −30 °C, stirred for 24 h, and then diluted with EtOAc (150 mL), and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 4% MeOH in CH_2Cl_2) to provide disaccharide **42** (19 mg, 70%) as an oil (spectroscopically identical with **42** as described above).

Benzylsilyl-protected vancomycin 43: Tetra-*n*-butylammonium fluoride (50 μL, 1 M solution in THF) was added to a solution of disaccharide **42** (5.0 mg, 0.002 mmol) in THF (300 μL) at −10 °C. After stirring for 2 h, the reaction mixture was diluted with EtOAc (50 mL), washed with saturated aqueous $NaHCO_3$ (2 mL) and brine (2 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 4% MeOH in CH_2Cl_2) to yield disaccharide **43** as an oil.

Dechloro-vancomycin methyl ester 44: A mixture of disaccharide **43** (2.0 mg, 0.002 mmol) and 10% palladium on carbon (ca. 5.0 mg) in MeOH (1.0 mL) was stirred under an atmosphere of H_2 (1 atm) for 24 h. The reaction mixture was filtered through a pad of celite and taken directly to the next step. HRMS (MALDI) calcd for $C_{67}H_{77}ClN_9O_{24}Na$ $[M + Na^+]$ 1448.9826, found 1448.9809.

Dechloro-vancomycin 45: Lithium hydroxide (5.0 mg, excess) was added to a solution of **44** (2.0 mg, 0.001 mmol) THF/H_2O (1:1) (0.5 mL) at 0 °C. After the reaction mixture was stirred for 20 min, the reaction was quenched by the addition of saturated aqueous NH_4Cl (1 mL), filtered, and then the solvents were removed under reduced pressure. The residue was purified by HPLC [(C18 reverse-phase column (HP-LiChroCART 4 × 250 mm), gradient solvent system 0–15 min, 5–100% MeCN (0.1% TFA) in H_2O, flow rate 1.5 mL min^{-1}, 25 °C, retention time 5 min 38 s) to yield dechloro-vancomycin **45**. HRMS (MALDI) calcd for $C_{66}H_{75}ClN_9O_{24}Na$ $[M + Na^+]$ 1434.9670, found 1434.9701.

Mono-TBS-glucal 47: Potassium carbonate (100 mg, 0.7 mmol) was added to a solution of triacetyl-glucal (15.0 g, 55.1 mmol) in MeOH (100 mL) at 25 °C and the resulting mixture was stirred for 12 h. The solvents were removed under reduced pressure, the residue was azeotroped with toluene (2 × 50 mL), and then dried under high vacuum for 2 h. The residue was dissolved in dry DMF (100 mL), cooled to 0 °C, and imidazole (8.0 g, 121 mmol) and TBSCl (8.3 g, 55.1 mmol) were added. After stirring for 1 h, the reaction mixture was diluted with CH_2Cl_2 (500 mL) and washed with H_2O (50 mL). The organic layer was dried (Na_2SO_4), concentrated, and the residue was purified by flash column chromatography (silica gel, ether) to afford the diol (11.7 g, 82%) as a white foam. Diol: $R_f = 0.39$ (silica gel, ether); $[\alpha]_D^{22} = +2.22$ ($c = 1.6$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3363$, 2953, 2929, 2857, 1650, 1471, 1463, 1390, 1361, 1254, 1106, 1075, 1053, 940, 878, 836, 778, 672 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 6.31$ (dd, $J = 6.0$, 1.5 Hz, 1H, H-G1), 4.72 (dd, $J = 6.0$, 2.0 Hz, 1H, H-G2), 4.30–4.25 (m, 1H, H-G3), 3.99 (dd, $J = 11.0$, 3.0 Hz, 1H, H-G6a), 3.91 (dd, $J = 11.0$, 4.0 Hz,

1H, H-G6b), 3.82–3.78 (m, 2H, H-G4, OH), 3.32 (s, 1H, H-G5), 2.69 (br. s, 1H, OH), 0.90 (s, 9H, *t*BuSi), 0.10 (s, 6H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 144.2, 102.4, 76.6, 72.3, 69.2, 63.8, 25.8, 17.4, -5.4, -5.5$; HRMS (FAB) calcd for $C_{12}H_{24}O_4SiNa$ $[M+Na^+]$ 283.1342, found 283.1336. Acetic anhydride (11.1 mL, 118 mmol) was added to a solution of the above diol (12.3 g, 47.3 mmol), triethylamine (26.3 mL, 189 mmol) and 4-DMAP (0.58 g, 4.7 mmol) in CH_2Cl_2 (500 mL) at 0 °C. After stirring 1 h at 25 °C, the reaction mixture was washed with saturated aqueous $NaHCO_3$ (100 mL), the organic layer was dried (Na_2SO_4), and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 30% ether in hexanes) to provide glucal **47** (15.8 g, 97%) as a colorless oil. **47**: $R_f = 0.53$ (silica gel, 50% ether in hexanes); $[\alpha]_D^{22} = -9.4$ ($c = 5.1$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 2954, 2943, 2857, 1742, 1650, 1599, 1472, 1372, 1242, 1105, 1045, 962, 837, 778, 679, 602\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 6.44$ (dd, $J = 6.3$, 1.5 Hz, 1H, H-G1), 5.30–5.29 (m, 1H, H-G3), 5.24 (dd, $J = 7.3$, 5.6 Hz, 1H, H-G4), 4.75 (dd, $J = 6.2$, 3.3 Hz, 1H, H-G2), 4.06 (ddd, $J = 9.6$, 4.6, 4.6 Hz, 1H, H-G5), 3.79–3.77 (m, 2H, H-G6), 2.03 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 0.86 (s, 9H, *t*BuSi), 0.03 (s, 6H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.5, 169.4, 145.9, 98.3, 76.6, 67.5, 61.2, 25.7, 21.0, 20.8, 18.2, -5.5$; HRMS (FAB) calcd for $C_{12}H_{24}O_4SiNa$ $[M+Na^+]$ 283.1342, found 283.1336.

Mono-TBS-glucose diol 48: Osmium tetroxide (0.5 mL, 2.5% solution in *tert*-butyl alcohol) was added dropwise to a solution of glucal **47** (6.0 g, 22.6 mmol) and 4-methylmorpholine *N*-oxide (4.00 g, 33.9 mmol) in acetone/H_2O (9:1) (200 mL) at 25 °C and the resulting mixture was stirred for 12 h. Saturated aqueous $NaHCO_3$ (50 mL) was added and the solvents were removed under reduced pressure. The residue was diluted with CH_2Cl_2 (200 mL) and washed with brine (15 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 75% ether in hexanes) to yield diol **48** (7.2 g, 84%) as a colorless oil. **48**: $R_f = 0.15$ (silica gel, 70% ether in hexanes); IR (thin film): $\tilde{\nu}_{max} = 3435, 2958, 2924, 2857, 1753, 1463, 1432, 1366, 1251, 1151, 1087, 837, 778\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$, major anomer): $\delta = 5.29$ (t, $J = 6.5$ Hz, 1H, H-G1), 5.25 (t, $J = 9.7$ Hz, 1H, H-G3), 4.97 (t, $J = 9.7$ Hz, 1H, H-G4), 4.15 (br. s, 1H, OH), 4.03 (ddd, $J = 10.1$, 3.5, 3.5 Hz, 1H, H-G5), 3.72–3.62 (m, 3H, H-G2, H-G6a, H-G6b), 2.66 (br. s, 1H, OH), 2.06 (s, 3H, $COCH_3$), 2.03 (s, 3H, $COCH_3$), 0.88 (s, 9H, *t*BuSi), 0.04 (s, 6H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$, major anomer): $\delta = 171.6, 169.6, 96.7, 92.2, 76.8, 75.0, 74.8, 73.7, 73.4, 71.0, 70.2, 68.9, 68.6, 62.6, 62.4, 25.9, 25.9, 20.9, 20.7, 18.4, -5.4$; HRMS (FAB) calcd for $C_{18}H_{30}O_5SiNa$ $[M+Na^+]$ 401.1608, found 401.1621.

Alloc-protected lactol 49: Di-*n*-butyltin oxide (960 mg, 3.9 mmol) was added to a solution of diol **48** (1.21 g, 3.2 mmol) in toluene (150 mL) at 25 °C and the resulting solution was refluxed with removal of H_2O with a Dean–Stark apparatus for 6 h. The reaction mixture was cooled to 0 °C, and Alloc-Cl (360 μL, 3.3 mmol) was added dropwise. After stirring for 0.5 h, the reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with brine (15 mL). The organic layer was dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, 35% ether in hexanes) to afford the lactol **49** (840 mg, 67%,) as a white foam. **49**: $R_f = 0.27$ (silica gel, 50% ether in hexanes); IR (thin film): $\tilde{\nu}_{max} = 3468, 2945, 2930, 2885, 2857, 1759, 1462, 1432, 1367, 1233, 1157, 1055, 1007, 970, 837, 784\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$, α:β ca. 3:1): $\delta = 5.94-5.87$ (m, 1.3H, $OCH_2CH{=}CH_2$), 5.52 (t, $J = 9.6$ Hz, 1H, H-G3), 5.49 (t, $J = 3.6$ Hz, 1H, H-G1), 5.34 (br. dd, $J = 15.8$, 1.3 Hz, 1.3H, $OCH_2CH{=}CH_2$-*Z*), 5.26 (br. dd, $J = 10.4$, 1.0 Hz, 1.3H, $OCH_2CH{=}CH_2$-*E*), 5.24 (t, $J = 9.6$ Hz, 0.3H, H-G3), 5.09 (t, $J = 9.6$ Hz, 0.3H, H-G4), 5.05 (t, $J = 9.6$ Hz, 1H, H-G4), 4.76 (t, $J = 8.0$ Hz, 0.3H, H-G2β), 4.73 (dd, $J = 10.3$, 3.6 Hz, 1H, H-G2a), 4.66–4.56 (m, 2.6H, $OCH_2CH{=}CH_2$), 4.10 (ddd, $J = 10.1$, 3.4, 3.4 Hz, 1.3H, H-G5), 3.75–3.70 (m, 0.3H, OH), 3.70-3.68 (m, 2.6H, H-G6), 3.57 (ddd, $J = 9.9$, 4.6, 2.4 Hz, 0.3H, H-G5b), 3.45 (d, $J = 3.7$ Hz, 1H, OH), 2.01 (s, 3.9H, $COCH_3$), 2.00 (s, 3.9H, $COCH_3$), 0.88 (s, 11.7H, *t*BuSi), 0.04 (s, 3.9H, CH_3Si), 0.03 (s, 3.9H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$, α:β ca. 3:1): $\delta = 170.3, 170.2, 169.6, 169.4, 154.8, 154.1, 131.1, 131.1, 119.2, 119.1, 95.2, 89.9, 76.8, 74.8, 74.3, 72.4, 70.2, 69.8, 69.0, 68.9, 62.2, 62.1, 25.9, 25.8, 20.7, 20.6, 18.4, 4.0, -5.4, -5.5, -5.7$; HRMS (FAB) calcd for $C_{20}H_{34}O_{10}SiNa$ $[M+Na^+]$ 485.1819, found 485.1805.

Mono-TBS-glucose imidate 50: DBU (5.0 μL, 0.033 mmol) was added to a solution of lactol **49** (950 mg, 2.1 mmol) and trichloroacetonitrile (3.3 mL, 41.1 mmol) in CH_2Cl_2 (50 mL) at −10 °C. After stirring for 20 min, the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 35% ether in hexanes) to afford imidate **50** (1.05 g, 89%) as a colorless oil. **50**: $R_f = 0.35$ (silica gel, 30% ether in hexanes); ^1H NMR (600 MHz, $CDCl_3$, α:β ca. 14:1): $\delta = 8.64$ (s, 1H, NH), 6.63 (d, $J = 3.6$ Hz, 1H, H-G1), 5.93–5.85 (m, 1H, $OCH_2CH{=}CH_2$), 5.55 (t, $J = 9.9$ Hz, 1H, H-G3), 5.32 (dd, $J = 17.0$, 1.4 Hz, 1H, $OCH_2CH{=}CH_2$-*Z*), 5.25 (dd, $J = 10.4$, 1.1 Hz, 1H, $OCH_2CH{=}CH_2$-*E*), 5.21 (t, $J = 9.9$ Hz, 1H, H-G4), 4.94 (dd, $J = 10.2$, 3.6 Hz, 1H, H-G2), 4.62–4.60 (m, 2H, $OCH_2CH{=}CH_2$), 4.06 (ddd, $J = 10.2$, 4.1, 2.2 Hz, 1H, H-G5), 3.79 (dd, $J = 11.7$, 2.2 Hz, 1H, H-G6a), 3.69 (dd, $J = 11.7$, 4.2 Hz, 1H, H-G6b), 2.02 (s, 3H, $COCH_3$), 0.86 (s, 9H, *t*BuSi), 0.02 (s, 3H, CH_3Si), 0.01 (s, 3H, CH_3Si); ^{13}C NMR (150 MHz, $CDCl_3$, α:β ca. 14:1): $\delta = 170.0, 169.4, 160.8, 154.0, 131.1, 119.1, 92.9, 73.2, 72.7, 70.1, 69.0, 68.2, 61.5, 25.8, 20.7, 18.2, -5.5$.

Mono-TBS-protected-2,6-dimethoxyphenolic glucoside 51: 2,6-Dimethoxyphenol (25 mg, 0.16 mmol) and imidate **50** (180 mg, 0.27 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (0.5 mL) and 4 Å MS were added, and the mixture was stirred for 15 min. The resulting mixture was cooled to −78 °C and $BF_3 \cdot Et_2O$ (21 μL, 0.16 mmol) was added dropwise. After stirring for 20 min, the reaction mixture was diluted with EtOAc (150 mL), and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), concentrated, and the residue was purified by flash column chromatography (silica gel, 20% ether in hexanes) to afford β-glucoside **51** (92 mg, 95%) as a white foam. **51**: $R_f = 0.22$ (silica gel, 50% ether in hexanes); $[\alpha]_D^{22} = +13.7$ ($c = 0.60$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 2931, 2856, 1759, 1734, 1601, 1480, 1366, 1296, 1259, 1234, 1113, 1062, 971, 832, 779\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 6.99$ (t, $J = 8.5$ Hz, 1H, ArH), 6.53 (d, $J = 8.5$ Hz, 2H, ArH), 5.91–5.84 (m, 1H, $OCH_2CH{=}CH_2$), 5.30 (br. dd, $J = 11.0$, 1.3 Hz, 1H, $OCH_2CH{=}CH_2$-*Z*), 5.28 (t, $J = 9.5$ Hz, 1H, H-G3), 5.20 (br. dd $J = 10.5$, 7.2 Hz, 1H, $OCH_2CH{=}CH_2$-*E*), 5.13 (t, $J = 10.0$ Hz, 1H, H-G4), 5.11 (d, $J = 8.0$ Hz, 1H, H-G1), 5.03 (dd, $J = 9.0$, 7.5 Hz, 1H, H-G2), 4.65–4.59 (m, 2H, $OCH_2CH{=}CH_2$), 3.78 (s, 6H, OCH_3), 3.67–3.65 (m, 2H, H-G6), 3.48–3.44 (m, 1H, H-G5), 2.01 (s, 3H, $COCH_3$), 1.98 (s, 3H, $COCH_3$), 0.79 (s, 9H, *t*BuSi), −0.01 (s, 3H, CH_3Si), −0.09 (s, 3H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.3, 169.4, 154.0, 153.1, 134.2, 131.3, 124.7, 118.5, 105.3, 101.1, 75.8, 74.8, 68.7, 68.6, 62.2, 56.1, 56.0, 25.6, 20.6, 18.1, 15.1, -5.7, -5.8$; HRMS (FAB) calcd for $C_{28}H_{42}O_{12}SiCs$ $[M+Cs^+]$ 731.1500, found 731.1526.

Mono-TBS-alcohol 52: A catalytic amount of palladium tetrakistriphenylphosphane (ca. 10 mg, 0.01 mmol) was added to a solution of β-glucoside **51** (110 mg, 0.18 mmol) and tri-*n*-butyltin hydride (74 μL, 0.27 mmol) in wet CH_2Cl_2 (5.0 mL) at 25 °C. After the reaction mixture was stirred for 0.5 h, the solvents were removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel, 30% ether in hexanes) to afford **52** (79 mg, 83%) as a white foam. **52**: $R_f = 0.2$ (silica gel, 70% ether in hexanes); $[\alpha]_D^{22} = +14.0$ ($c = 4.7$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3453, 2929, 2860, 2856, 1755, 1734, 1718, 1600, 1480, 1474, 1444, 1367, 1299, 1256, 1113, 998, 838, 777\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.03$ (t, $J = 8.4$ Hz, 1H, ArH), 6.58 (d, $J = 8.4$ Hz, 2H, ArH), 5.15 (t, $J = 9.5$ Hz, 1H, H-G3), 5.04 (t, $J = 9.5$ Hz, 1H, H-G4), 4.68 (d, $J = 7.8$ Hz, 1H, H-G1), 3.92–3.90 (m, 1H, OH), 3.85–3.83 (m, 7H, OCH_3, H-G2), 3.74–3.67 (m, 2H, H-G6), 3.50–3.44 (m, 1H, H-G5), 2.07 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 0.85 (s, 9H, *t*BuSi), 0.03 (s, 3H, CH_3Si), −0.02 (s, 3H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.7, 169.5, 152.8, 135.2, 125.0, 105.5, 105.4, 105.4, 105.3, 75.3, 74.8, 72.5, 68.9, 66.7, 65.8, 62.6, 56.2, 56.2, 30.2, 27.7, 26.7, 25.7, 20.8, 20.7, 18.2, 17.4, 13.5, -5.6, -5.7$; HRMS (FAB) calcd for $C_{24}H_{38}O_{10}SiNa$ $[M+Na^+]$ 537.2132, found 537.2148.

Mono-TBS-disaccharide 53: Vancosamine fluoride **27** (82 mg, 0.22 mmol) and alcohol **52** (79 mg, 0.15 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (0.6 mL) and 4 Å MS were added, and the mixture was stirred for 15 min. The resulting mixture was cooled to −30 °C and $BF_3 \cdot Et_2O$ (18 μL, 0.13 mmol) was added dropwise. After stirring for 2 h, the reaction mixture was diluted with EtOAc (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), concentrated, and the residue was purified by flash column chromatography (silica gel, 30% ether in hexanes) to give disaccharide **53** (116 mg, 91%, α:β ca. 9:1) as a white foam. **53**: $R_f = 0.2$ (silica gel, 70% ether in hexanes); $[\alpha]_D^{22} = -54.8$ ($c = 1.3$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3379, 2935, 2871, 1747, 1600, 1514, 1495, 1480, 1372, 1255, 1219, 1113, 1061, 1032, 912, 838, 777, 734\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.36-7.30$ (m, 5H, ArH), 6.99 (t, $J =$

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8.4 Hz, 1H, ArH), 6.55 (d, $J = 8.4$ Hz, 2H, ArH), 5.28 (d, $J = 7.4$ Hz, 1H, H-G1), 5.25 (t, $J = 9.1$ Hz, 1H, H-G3), 5.09 (br. d, $J = 4.6$ Hz, 1H, H-V1), 5.08 and 4.95 (AB, $J = 12.2$ Hz, 2H, CH_2Ar), 5.07 (t, $J = 9.6$ Hz, 1H, H-G4), 4.89 (s, 1H, H-V4), 4.72 (s, 1H, NH), 4.51 (br. q, $J = 6.3$ Hz, 1H, H-V5), 3.99 (dd, $J = 8.9$, 7.5 Hz, 1H, H-G2), 3.78 (s, 6H, OCH_3), 3.60–3.58 (m, 2H, H-G6), 3.47–3.42 (m, 1H, H-G5), 2.10 (d, $J = 13.4$ Hz, 1H, H-V2a), 2.04 (s, 3H, $COCH_3$), 2.03 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 1.94 (dd, $J = 13.5$, 4.6 Hz, 1H, H-V2b), 1.79 (s, 3H, H-V3), 0.95 (d, $J = 6.4$ Hz, 3H, H-V6), 0.76 (s, 9H, *t*BuSi), −0.06 (s, 3H, CH_3Si), −0.19 (s, 3H, CH_3Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 171.2$, 171.1, 169.7, 153.4, 136.6, 133.3, 128.5, 128.2, 128.1, 128.0, 124.2, 105.4, 99.9, 97.7, 76.1, 74.8, 74.1, 69.2, 63.3, 62.6, 55.9, 55.8, 53.1, 33.8, 30.3, 25.7, 20.8, 20.8, 20.7, 18.1, 16.7, −5.8; HRMS (FAB), calcd for $C_{41}H_{59}NO_{15}SiCs$ $[M + Cs^+]$ 966.2708, found 966.2746.

Mono-TBS-thioglucoside 54: Thiophenol (32 μL, 0.31 mmol) was added to a solution of imidate **50** (120 mg, 0.21 mmol) in CH_2Cl_2 (0.5 mL) containing 4 Å MS and the mixture was stirred at ambient temperature for 15 min. The resulting mixture was cooled to −78 °C and $BF_3 \cdot Et_2O$ (8.0 μL, 0.062 mmol) was added dropwise. After stirring for 45 min, the reaction mixture was diluted with EtOAc (150 mL), and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 30% ether in hexanes) to afford *β*-thioglucoside **54** (110 mg, 95%) as a white foam. **54**: $R_f = 0.30$ (silica gel, 50% ether in hexanes); $[\alpha]_D^{22} = +15.7$ ($c = 1.3$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 2954$, 2930, 2884, 2857, 1760, 1462, 1440, 1369, 1259, 1230, 1052, 1005, 967, 912, 837, 781, 748, 692 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.55–7.20$ (m, 5H, ArH), 5.95–5.85 (m, 1H, $OCH_2CH{=}CH_2$), 5.36 (ddd, $J = 17.0$, 2.8, 1.3 Hz, 1H, $OCH_2CH{=}CH_2$-*Z*), 5.26 (ddd $J = 10.3$, 2.4, 1.1 Hz, 1H, $OCH_2CH{=}CH_2$-*E*), 5.25–5.22 (m, 1H, H-G2), 5.02 (t, $J = 9.8$ Hz, 1H, H-G3), 4.73 (d, $J = 6.4$ Hz, 1H, H-G1), 4.73–4.68 (m, 1H, H-G4), 4.65–4.64 (m, 2H, $OCH_2CH{=}CH_2$), 3.73 (dd, $J = 11.5$, 2.2 Hz, 1H, H-G6a), 3.68 (dd, $J = 11.5$, 5.1 Hz, 1H, H-G6b), 3.57 (ddd, $J = 9.9$, 5.0, 2.2 Hz, 1H, H-G5), 1.99 (s, 3H, $COCH_3$), 1.97 (s, 3H, $COCH_3$), 0.88 (s, 9H, *t*BuSi), 0.06 (s, 3H, CH_3Si), 0.03 (s, 3H, CH_3Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 170.0$, 169.2, 153.7, 132.9, 131.7, 131.2, 128.8, 128.2, 118.8, 85.4, 78.8, 74.1, 73.7, 68.8, 68.5, 62.2, 25.8, 20.6, 18.2, 15.2, −5.5; HRMS (FAB) calcd for $C_{26}H_{38}O_9SSiNa$ $[M + Na^+]$ 577.1904, found 577.1922.

Mono-TBS-alcohol 55: A catalytic amount of palladium tetrakistriphenylphosphane (ca. 10 mg, 0.01 mmol) was added to a solution of *β*-glucoside **54** (90 mg, 0.16 mmol) and tri-*n*-butyltin hydride (65 μL, 0.24 mmol) in wet CH_2Cl_2 (5.0 mL) at 25 °C. After the reaction mixture was stirred for 0.5 h, the solvents were removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel, 30% ether in hexanes) to provide **55** (66 mg, 87%) as a white foam. **55**: $R_f = 0.30$ (silica gel, 70% ether in hexanes); $[\alpha]_D^{22} = +6.2$ ($c = 3.3$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3478$, 3061, 2929, 2857, 1760, 1733, 1714, 1584, 1470, 1441, 1372, 1254, 1043, 914, 835, 776 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.59–7.25$ (m, 5H, ArH), 5.10 (t, $J = 9.3$ Hz, 1H, H-G3), 4.96 (t, $J = 9.8$ Hz, 1H, H-G4), 4.96 (d, $J = 9.7$ Hz, 1H, H-G1), 3.74 (dd, $J = 11.4$, 2.2 Hz, 1H, H-G6a), 3.67 (dd, $J = 11.5$, 5.1 Hz, 1H, H-G6b), 3.56 (ddd, $J = 10.0$, 5.1, 2.2 Hz, 1H, H-G5), 3.48–3.44 (m, 1H, H-G2), 2.65 (d, $J = 3.2$ Hz, 1H, OH), 2.03 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 0.89 (s, 9H, *t*BuSi), 0.06 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 170.9$, 169.5, 133.1, 131.0, 129.0, 128.3, 87.8, 78.9, 76.2, 70.1, 68.4, 62.3, 25.8, 20.8, 20.6, 18.2, 17.5, 15.2, 13.5, −5.4; HRMS (FAB) calcd for $C_{22}H_{34}O_7SSiNa$ $[M + Na^+]$ 493.1692, found 493.1681.

Mono-TBS-disaccharide 56: Vancosamine fluoride **27** (76 mg, 0.22 mmol) and alcohol **55** (66 mg, 0.162 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (0.6 mL) and 4 Å MS were added, and the mixture was stirred at ambient temperature for 15 min. The resulting mixture was cooled to −30 °C and $BF_3 \cdot Et_2O$ (16 μL, 0.12 mmol) was added dropwise. After stirring for 2 h, the reaction mixture was diluted with EtOAc (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 30% ether in hexanes) to afford disaccharide **56** (109 mg, 98%, *α*:*β* ca. 3:2) as a white foam. **56**: $R_f = 0.24$ (silica gel, 70% ether in hexanes); IR (thin film): $\tilde{\nu}_{max} = 3369$, 2931, 2857, 1734, 1520, 1462, 1448, 1372, 1240, 1058, 913, 839, 778, 775 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, *α*:*β* ca. 3:2): $\delta = 7.53–7.26$ (m, 17H, ArH), 5.21 (t, $J = 9.0$ Hz, 1H, H-G3), 5.14–4.73 (m, 9.9H, H-V1, H-V1, NH, H-G3, H-G4, H-V4, H-V4, CH_2Ar), 4.93 (t, $J = 9.0$ Hz, 1H, H-G4), 4.75–4.73 (m, 2.7H, H-V5, H-V5), 4.67 (d, $J = 9.7$ Hz, 1H, H-G1), 4.62 (d, $J = 9.9$ Hz, 1H, H-G1), 3.78 (dd, $J = 9.0$, 8.8 Hz, 1H, H-G2), 3.73 (dd, $J = 9.0$, 8.8 Hz, 1.7H, H-G2), 3.69–3.64 (m, 3.4H, H-G6a, H-G6b, H-G6a, H-G6b), 3.56–3.50 (m, 2.7H, H-G5, H-G5), 2.02 (s, 3H, $COCH_3$), 2.01 (s, 2.1H, $COCH_3$), 2.01 (s, 2.1H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 2.10-1.92 (m, 2H, H-V2), 1.67 (s, 3H, H-V3), 1.60 (s, 3H, H-V3), 1.53 (dd, $J = 12.3$, 10.0 Hz, 0.7H, H-V2a), 1.38 (d, $J = 6.4$ Hz, 3H, H-V6), 1.06 (d, $J = 6.4$ Hz, 2.1H, H-V6), 0.90 (s, 6.3H, *t*BuSi), 0.87 (s, 9H, *t*BuSi), 0.06 (s, 2.1H, CH_3Si), 0.04 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si), 0.04 (s, 2.1H, CH_3Si), 0.01 (s, 3H, CH_3Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 170.8$, 170.4, 170.3, 169.8, 169.6, 169.4, 136.5, 133.6, 133.1, 131.7, 131.5, 129.0, 129.0, 128.4, 128.3, 128.1, 128.1, 128.0, 127.7, 128.6, 98.8, 97.9, 87.3, 87.1, 78.8, 78.6, 77.3, 76.5, 75.4, 74.6, 73.8, 72.1, 68.8, 68.4, 68.1, 64.3, 62.5, 62.3, 62.3, 54.04, 52.7, 30.3, 25.8, 23.9, 20.9, 20.7, 20.6, 20.5, 18.2, 17.4, 16.9, 13.5, −5.5; HRMS (FAB) calcd for $C_{39}H_{55}NO_{12}SSiCs$ $[M + Cs^+]$ 922.2269, found 922.2239.

Mono-TBS-protected vancomycin monosaccharide 57: Glucose imidate **50** (310 mg, 0.54 mmol) and aglycon acceptor **6** (200 mg, 0.11 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (1.5 mL) and 4 Å MS were added, and the mixture was stirred at ambient temperature for 15 min. The resulting mixture was cooled to −78 °C and $BF_3 \cdot Et_2O$ (160 μL, 1.1 mmol) was added dropwise. After stirring for 6 h at −78 °C, the reaction mixture was diluted with EtOAc (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 10→30% acetone in CH_2Cl_2, gradient elution), followed by preparative TLC (silica gel, 3% MeOH in CH_2Cl_2) to afford *β*-glucoside **57** (203 mg, 82%) as a white foam. **57**: $R_f = 0.33$ (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]_D^{22} = +7.9$ ($c = 0.3$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3550$, 2956, 2929, 2874, 2857, 1760, 1691, 1667, 1644, 1599, 1504, 1471, 1416, 1362, 1307, 1234, 1172, 1111, 1062, 948, 923, 837, 781 cm^{-1}; ^{1}H NMR (500 MHz, CD_3CN, 330 K): $\delta = 7.57–7.54$ (m, 2H), 7.50–7.31 (m, 9H), 7.27 (s, 2H), 7.10 (s, 1H), 6.94 (s, 3H), 6.46 (d, $J = 2.2$ Hz, 1H), 6.34 (d, $J = 2.2$ Hz, 1H), 6.32 (br. s, 1H), 6.10–6.02 (m, 2H), 5.79 (s, 2H), 5.56 (s, 2H), 5.48 (t, $J = 9.5$ Hz, 1H), 5.49–5.42 (m, 3H), 5.35 (t, $J = 9.5$ Hz, 1H), 5.32-5.16 (m, 5H), 5.01 (dd, $J = 17.3$, 1.4 Hz, 1H), 4.96 (d, $J = 10.6$ Hz, 1H), 4.95–4.80 (m, 4H), 4.57 (s, 1H), 4.45 (dd, $J = 12.9$, 6.0 Hz, 1H), 4.27 (dd, $J = 12.8$, 5.4 Hz, 1H), 3.96–3.94 (m, 1H), 3.83–3.80 (m, 1H), 3.73 (s, 3H), 3.73–3.70 (m, 1H), 3.66 (dd, $J = 10.3$, 1.9 Hz, 1H), 2.92 (s, 3H), 2.41–2.31 (m, 2H), 2.01 (s, 3H), 1.99 (s, 3H), 1.78 (br. t, $J = 10.2$ Hz, 1H), 1.61–1.40 (m, 2H), 1.02 (s, 9H), 0.96 (s, 9H), 0.94–0.91 (m, 6H), 0.88 (s, 9H), 0.76 (s, 9H), 0.74 (s, 9H), 0.61 (s, 9H), 0.24 (s, 6H), 0.19 (s, 3H), 0.15 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.04 (s, 3H), −0.5 (s, 3H), −0.10 (s, 3H), −0.15 (s, 3H); ^{13}C NMR (150 MHz, CD_3CN, 330 K): $\delta = 172.2$, 172.1, 171.8, 171.3, 171.1, 171.0, 170.7, 170.3, 170.1, 169.1, 167.9, 167.8, 156.5, 155.7, 154.8, 154.5, 154.3, 153.1, 151.8, 151.5, 141.4, 139.6, 137.9, 137.4, 136.7, 136.7, 136.5, 135.6, 132.3, 129.3, 129.3, 128.9, 128.9, 128.9, 128.9, 128.8, 128.8, 128.2, 127.3, 126.9, 126.4, 126.0, 125.5, 124.5, 121.3, 118.7, 113.1, 112.1, 106.2, 105.1, 76.7, 74.5, 74.4, 74.1, 73.6, 70.2, 69.2, 68.2, 66.0, 64.5, 63.5, 60.4, 60.1, 57.7, 57.6, 57.6, 55.3, 55.3, 55.2, 52.6, 52.5, 37.1, 30.2, 26.3, 26.3, 26.1, 26.1, 26.1, 26.1, 26.1, 26.0, 26.0, 25.7, 25.7, 25.7, 25.7, 25.7, 25.7, 25.3, 23.6, 22.1, 21.0, 20.8, 19.0, 18.9, 18.8, 18.8, 18.4, 18.3, −3.9, −4.0, −4.2, −4.3, −4.5, −4.5, −4.7, −4.7, −4.9, −4.9, −5.4, −5.5; HRMS (FAB) calcd for $C_{112}H_{162}Cl_2N_8O_{28}Si_6Cs$ $[M + Cs^+]$ 2440.8874, found 2440.8738.

Mono-TBS-protected vancomycin monosaccharide acceptor 58: A catalytic amount of palladium tetrakistriphenylphosphane (ca. 10 mg, 0.01 mmol) was added to a solution of the *β*-glucoside **57** (100 mg, 0.040 mmol) and tri-*n*-butyltin hydride (44 μL, 0.16 mmol) in wet CH_2Cl_2 (0.5 mL) at 25 °C. After the reaction mixture was stirred for 0.5 h, the solvents were removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel, 10→30% acetone in CH_2Cl_2), followed by preparative TLC (silica gel, 3% MeOH in CH_2Cl_2) to provide alcohol **58** (76 mg, 85%) as a white foam. **58**: $R_f = 0.34$ (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]_D^{22} = -4.0$ ($c = 1.5$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} =$ 3306, 2956, 2876, 2858, 1755, 1682, 1651, 1599, 1504, 1491, 1470, 1416, 1299, 1254, 1175, 1112, 1051, 1026, 838, 781cm^{-1}; ^{1}H NMR (600 MHz, CD_3CN, 340 K): $\delta = 7.55–7.52$ (m, 2H), 7.46–7.38 (m, 7H), 7.35 (d, $J = 7.2$ Hz, 1H), 7.30 (s, 1H), 7.26 (br. s, 2H), 7.11 (s, 2H), 6.96 (s, 2H), 6.87 (br. s, 2H), 6.62 (br. s, 1H), 6.47 (d, $J = 2.2$ Hz, 1H), 6.35 (d, $J = 2.2$ Hz, 1H), 6.35–6.33 (m,

2H), 6.02 (br. s, 1H), 5.85 (s, 1H), 5.56 (s, 1H), 5.45 (d, $J = 4.5$ Hz, 1H), 5.34 (t, $J = 9.6$ Hz, 1H, H-G3), 5.33 (s, 1H), 5.25 (d, $J = 7.7$ Hz, 1H, H-G1), 5.20 (t, $J = 9.7$ Hz, 1H, H-G4), 4.95 – 4.84 (m, 6H), 4.61 (s, 1H), 4.03 (br. t, $J =$ 7.7 Hz, 1H, H-G2), 3.99 – 3.95 (m, 1H), 3.87 – 3.86 (m, 1H, H-G5), 3.82 (s, 1H), 3.74 (s, 3H, OCH_3), 3.75 – 3.73 (m, 1H, H-G6a), 3.68 (dd, $J = 11.0$, 3.2 Hz, 1H, H-G6b), 2.92 (s, 3H, NCH_3), 2.49 – 2.23 (m, 2H, H-3β), 2.06 (s, 3H, $COCH_3$), 2.02 (s, 3H, $COCH_3$), 1.78 – 1.75 (m, 1H, H-1β), 1.57 – 1.51 (m, 2H, H-1β, H-1γ), 1.03 (s, 9H, *t*BuSi), 0.96 (s, 9H, *t*BuSi), 0.94 – 0.92 (m, 6H, H-1δ), 0.89 (s, 9H, *t*BuSi), 0.77(s, 9H, *t*BuSi), 0.75 (s, 9H, *t*BuSi), 0.63 (s, 9H, *t*BuSi), 0.25 (s, 6H, CH_3Si), 0.20 (s, 3H, CH_3Si), 0.15 (s, 3H, CH_3Si), 0.13 (s, 3H, CH_3Si), 0.12 (s, 3H, CH_3Si), 0.12 (s, 3H, CH_3Si), 0.09 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si), -0.05 (s, 3H, CH_3Si), -0.10 (s, 3H, CH_3Si), -0.12 (s, 3H, CH_3Si); ^{13}C NMR (150 MHz, CD_3CN, 340 K): $\delta = 172.3$, 172.2, 171.8, 171.4, 171.2, 171.1, 170.2, 169.1, 167.8, 167.8, 156.5, 155.8, 154.4, 152.9, 151.5, 151.4, 141.6, 139.9, 138.0, 137.1, 136.8, 136.7, 136.5, 136.3, 136.3, 135.5, 132.6, 132.6, 130.6, 130.2, 129.4, 129.3, 129.3, 129.3, 129.2, 128.7, 128.7, 128.7, 128.2, 128.1, 127.4, 126.9, 126.4, 126.3, 125.2, 124.5, 121.3, 113.1, 112.1, 107.0, 106.3, 81.3, 76.2, 75.0, 74.4, 73.6, 73.5, 70.3, 68.2, 63.6, 60.7, 57.8, 57.7, 57.6, 55.3, 52.6, 52.4, 30.6, 30.3, 26.3, 26.3, 26.3, 26.2, 26.2, 26.2, 26.1, 26.1, 26.1, 26.0, 26.0, 26.0, 25.6, 25.6, 25.6, 25.4, 23.3, 22.1, 21.1, 20.9, 18.9, 18.9, 18.8, 18.7, 18.3, 18.3, -3.9, -4.0, -4.3, -4.3, -4.5, -4.5, -4.7, -4.8, -4.9, -4.9, -5.3, -5.3; HRMS (MALDI) calcd for $C_{108}H_{158}C_{12}N_8O_{26}Si_6Cs$ [$M + Cs^+$] 2243.9178, found 2243.9198.

Fully protected vancomycin 59: Vancosamine fluoride **27** (40 mg, 0.13 mmol) and alcohol **58** (70 mg, 0.030 mmol) were azeotroped with benzene (3×3 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (0.5 mL) and 4 Å MS were added, and the mixture was stirred at ambient temperature for 15 min. The resulting mixture was cooled to $-35\,^\circ C$ and $BF_3 \cdot Et_2O$ (10 μL, 0.012 mmol) was added dropwise. After stirring for 2 h, the reaction mixture was diluted with EtOAc (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 10 → 30 % acetone in CH_2Cl_2), followed by preparative TLC (silica gel, 3 % MeOH in CH_2Cl_2) to furnish fully protected vancomycin **59** (65 mg, 84 %) as a white foam and a trace of the other anomer. **59**: $R_f = 0.36$ (silica gel, 5 % MeOH in CH_2Cl_2); $[\alpha]_D^{22} = -9.0$ ($c = 0.30$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3550$, 2928, 2856, 1755, 1718, 1682, 1654, 1504, 1470, 1458, 1416, 1298, 1252, 1062, 837 cm^{-1}; ^1H NMR (600 MHz, CD_3CN, 340 K): $\delta = 7.60 - 7.50$ (m, 2H), 7.46 – 7.20 (m, 16H), 7.11 (s, 3H), 6.97 (s, 2H), 6.90 – 6.84 (m, 2H), 6.65-6.55 (m, 2H), 6.47 (d, $J = 2.2$ Hz, 1H), 6.35 (d, $J = 2.2$ Hz, 1H), 6.10-6.01 (m, 1H), 5.85 (s, 1H), 5.60 – 5.50 (m, 2H), 5.47 (d, $J = 4.5$ Hz, 1H), 5.34 – 5.13 (m, 4H), 4.98 and 4.80 (AB, $J = 12.6$ Hz, 2H), 4.93 – 4.80 (m, 7H), 4.61 (s, 1H), 4.60 (s, 1H), 4.01 – 3.97 (m, 3H), 3.87 – 3.84 (m, 1H), 3.75-3.67 (m, 2H), 3.74 (s, 3H), 2.91 (s, 3H), 2.35 – 2.25 (m, 2H), 2.02 (s, 3H), 2.02 – 1.90 (m, 1H), 1.97 (s, 3H), 1.95 (s, 3H), 1.79 – 1.75 (m, 2H), 1.53 – 1.48 (m, 2H), 1.45 (s, 3H), 1.06 (d, $J = 6.2$ Hz, 3H), 1.03 (s, 9H), 0.98 (s, 9H), 0.93 – 0.92 (m, 6H), 0.89 (s, 9H), 0.79 (s, 9H), 0.72 (s, 9H), 0.62 (s, 9H), 0.24 (s, 6H), 0.20 (s, 3H), 0.15 (s, 3H), 0.13 (s, 3H), 0.12 (s, 6H), 0.06 (s, 3H), -0.04 (s, 3H), -0.09 (s, 3H), -0.11 (s, 3H), -0.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.2$, 171.7, 171.3, 171.1, 171.0, 170.6, 170.2, 169.1, 167.9, 156.5, 156.5, 155.8, 155.5, 154.4, 154.4, 152.9, 151.4, 151.4, 141.7, 139.7, 138.4, 138.0, 136.8, 136.4, 136.4, 130.0, 130.0, 129.5, 129.3, 129.3, 129.3, 129.2, 129.2, 129.2, 128.9, 128.8, 128.8, 128.8, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 127.3, 126.9, 126.4, 125.0, 124.8, 121.3, 113.1, 112.1, 106.4, 99.9, 74.4, 74.3, 73.6, 68.1, 66.2, 66.2, 64.7, 64.5, 60.7, 57.7, 57.7, 55.3, 53.6, 52.7, 52.4, 37.1, 36.9, 30.6, 30.2, 26.3, 26.3, 26.3, 26.3, 26.3, 26.3, 26.2, 26.2, 26.1, 26.1, 26.1, 26.0, 26.0, 26.0, 25.6, 25.6, 25.6, 25.6, 25.6, 25.3, 24.2, 23.5, 22.1, 22.1, 21.2, 20.9, 20.9, 18.9, 18.8, 18.8, 18.3, 18.3, 18.3, -4.0, -4.0, -4.3, -4.3, -4.4, -4.7, -4.7, -4.7, -4.9, -4.9, -5.3, -5.3; HRMS (FAB) calcd for $C_{125}H_{179}Cl_2N_9O_{31}Si_6Cs$ [$M + Cs^+$] 2676.1712, found 2676.1552.

Triacetylated-vancomycin 60: HF · pyr. (40 μL) was added dropwise to a solution of the protected vancomycin **59** (10 mg, 0.004 mmol) and freshly distilled pyridine (40 μL) in THF (0.5 mL) at 0 °C. The reaction mixture was slowly warmed to 25 °C and stirred for 12 h. The reaction was quenched by the careful addition of saturated aqueous $NaHCO_3$ (5 mL), diluted with 5 % MeOH in EtOAc (100 mL), and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 15 % MeOH in CH_2Cl_2) to afford triacetate **60** (6.0 mg, 80 %) as a white solid. **60**: $R_f = 0.22$ (silica gel, 15 % MeOH in CH_2Cl_2); $[\alpha]_D^{22} = -3.94$ ($c = 0.33$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} =$ 3401, 3290, 2943, 1725, 1713, 1678, 1666, 1642, 1501, 1455, 1419, 1396, 1372, 1320, 1226, 1063, 1032 cm^{-1}; ^1H NMR (600 MHz, CD_3CN/D_2O (20:1), 340 K): $\delta = 7.62$ (s, 1H, H-6b), 7.50 – 7.45 (m, 1H), 7.41 – 7.27 (m, 13H), 7.13 (d, $J = 8.3$ Hz, 1H), 7.10 (d, $J = 2.2$ Hz, 1H), 6.97 (dd, $J = 8.5$, 2.3 Hz, 1H), 6.88 (d, $J = 8.6$ Hz, 1H), 6.51 (d, $J = 2.2$ Hz), 6.24 (d, $J = 2.2$ Hz, 1H), 5.79 (s, 1H), 5.65 (s, 1H), 5.53 (d, $J = 7.6$ Hz, 1H), 5.40 (s, 1H), 5.33 (s, 2H), 5.21 – 5.17 (m, 2H), 5.18 (t, $J = 9.2$ Hz, 1H), 5.11 (d, $J = 4.3$ Hz, 1H), 4.98 and 4.85 (AB, $J = 12.5$ Hz, 2H), 4.98 (s, 1H), 4.88 – 4.86 (m, 1H), 4.80-4.77 (m, 3H), 4.69 (s, 1H), 4.56 (s, 1H), 4.24 (dd, $J = 12.2$, 4.2 Hz, 1H), 4.20 (dd, $J = 11.9$, 2.0 Hz, 1H), 4.06 (s, 1H), 3.91 (bt, $J = 8.8$ Hz, 1H), 3.80 (s, 3H, OCH_3), 3.78 – 3.74 (m, 1H), 2.89 (s, 3H, NCH_3), 2.56 – 2.54 (m, 1H), 2.32 (dd, $J = 15.9$, 6.7 Hz, 1H), 2.09 (s, 3H, $COCH_3$), 1.96 (s, 3H, $COCH_3$), 1.94 – 1.91 (m, 2H), 1.90 (s, 3H, $COCH_3$), 1.69-1.61 (m, 3H), 1.49 (s, 3H), 0.99 (d, $J = 6.4$ Hz, 3H), 0.91-0.85 (m, 6H); ^{13}C NMR (150 MHz, CD_3CN/D_2O (20:1), 340 K): $\delta = 173.3$, 172.9, 172.3, 171.9, 171.9, 171.8, 171.0, 170.7, 169.1, 158.5, 157.2, 156.0, 155.6, 153.7, 153.4, 150.4, 141.9, 139.8, 138.1, 137.7, 136.7, 132.7, 130.1, 129.4, 129.4, 129.4, 129.4, 129.3, 129.3, 129.3, 129.3, 129.2, 128.9, 128.7, 128.7, 128.7, 128.6, 128.5, 128.5, 128.1, 127.8, 127.4, 127.3, 127.3, 121.9, 112.7, 107.7, 107.5, 105.7, 104.2, 102.3, 99.2, 78.7, 78.2, 74.6, 74.4, 72.3, 71.8, 69.1, 68.4, 66.5, 64.5, 64.3, 64.1, 64.0, 60.0, 58.4, 58.3, 57.8, 56.0, 55.3, 53.4, 53.3, 52.2, 36.7, 30.9, 26.0, 25.4, 24.1, 23.2, 21.9, 21.1, 20.8, 20.7, 17.8; HRMS (MALDI) calcd for $C_{89}H_{95}Cl_2N_9O_{31}Na$ [$M + Na^+$] 1878.5409, found 1878.5450.

***N,N′*-di-Cbz-vancomycin methyl ester 13:** Potassium carbonate (3.0 mg, 0.020 mmol) was added to a solution of the protected vancomycin **60** (10 mg, 0.005 mmol) in dry MeOH (0.5 mL) at 25 °C. The reaction mixture was stirred for 4 h, filtered, and then the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 50 % MeOH in CH_2Cl_2) to yield *N,N′*-di-Cbz-vancomycin methyl ester **13** (8.0 mg, 95 %) as a white solid. **13**: $R_f = 0.46$ (silica gel, 30 % MeOH in CH_2Cl_2); $[\alpha]_D^{22} = -10.0$ ($c = 0.12$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} =$ 3542-3119, 2931, 2872, 1719, 1684, 1655, 1590, 1496, 1466, 1431, 1378, 1226, 1149, 1067, 1020, 903, 732, 656, 591 cm^{-1}; ^1H NMR (600 MHz, $CD_3CN/[D_7]DMF$ (3:1), 340 K): $\delta = 8.47$ (br. s, 1H), 8.19 (d, $J = 5.9$ Hz, 1H), 8.12 (bs 1H), 7.96 (s, 1H), 7.79 (d, $J = 1.7$ Hz, 2H), 7.46 – 7.29 (m, 14H), 7.19 (d, $J = 2.0$ Hz, 1H), 7.17 (d, $J = 8.4$ Hz, 1H), 6.96 (dd, $J = 8.5$, 2.0 Hz, 1H), 6.91 (br. d, $J = 7.4$ Hz, 1H), 6.88 (d, $J = 8.5$ Hz, 1H), 6.85 – 6.80 (m, 2H), 6.64 (br. d, $J = 11.4$ Hz, 1H), 6.61 (d, $J = 2.1$ Hz, 1H), 6.30 (d, $J = 2.1$ Hz, 1H), 5.90 (br. d, $J =$ 8.1 Hz, 2H), 5.77 (s, 1H), 5.64 (s, 1H), 5.54 (d, $J = 7.2$ Hz, 1H), 5.43 (s, 1H), 5.39 (s, 1H), 5.36 (d, $J = 3.9$ Hz, 1H), 5.32 (d, $J = 4.4$ Hz, 1H), 5.25 – 5.20 (m, 2H), 5.01 (s, 2H), 4.88 (dd, $J = 7.8$, 4.2 Hz, 1H), 4.82 (bq, $J =$ 6.2 Hz, 1H), 4.79 – 4.77 (m, 1H), 4.73 (d, $J = 6.0$ Hz, 1H), 4.57 – 4.55 (m, 1H), 4.35 (br. d, $J = 12.3$ Hz, 1H), 3.79 (s, 3H), 3.76 – 3.67 (m, 3H), 3.56 – 3.53 (m, 3H), 2.93 (s, 3H), 2.70 – 2.66 (m, 1H), 2.65 – 2.20 (m, 6H), 2.33 – 2.30 (m, 1H), 2.18 (d, $J = 12.0$ Hz, 1H), 1.92 (dd, $J = 12.4$, 4.4 Hz, 1H), 1.74 – 1.68 (m, 3H), 1.53 (s, 3H), 1.18 (d, $J = 6.4$ Hz, 3H), 0.94 (br. d, $J =$ 6.6 Hz, 3H), 0.89 (br. d, $J = 6.2$ Hz, 3H); ^{13}C NMR (150 MHz, $CD_3CN/[D_7]DMF$ (3:1), 340 K): $\delta = 172.9$, 172.1, 171.9, 171.3, 170.5, 169.7, 168.4, 168.2, 158.6, 157.5, 155.8, 155.3, 153.4, 153.0, 151.1, 150.0, 142.2, 140.0, 138.1, 137.6, 137.1, 136.3, 135.6, 133.3, 129.3, 128.9, 128.9, 128.7, 128.3, 128.3, 128.0, 128.0, 127.9, 127.6, 127.1, 127.0, 125.0, 124.7, 124.1, 121.6, 107.6, 107.3, 106.9, 105.9, 105.4, 104.7, 103.5, 102.3, 98.5, 79.1, 78.0, 77.4, 77.3, 76.5, 75.2, 73.3, 72.6, 71.8, 71.4, 71.2, 67.6, 65.7, 64.0, 63.4, 62.4, 62.3, 59.9, 57.9, 57.4, 56.2, 55.9, 55.1, 54.0, 52.1, 52.0, 49.3, 36.9, 35.6, 25.1, 23.5, 22.8, 21.5, 17.3; HRMS (MALDI) calcd for $C_{88}H_{89}Cl_2N_9O_{28}Cs$ [$M + Cs^+$] 1864.4260, found 1864.4373.

Vancomycin methyl ester (61): Raney Ni (W-2) (ca. 100 mg, slurry in H_2O) was added to a solution of the Cbz-protected vancomycin methyl ester **13** (10 mg, 0.006 mmol) in *n*PrOH/H_2O (2:1) (3 mL) at 25 °C. The reaction mixture was stirred for 0.5 h, filtered through a pad of celite, and then the solvents were removed under reduced pressure. The residue was purified by HPLC [(C18 reverse-phase column (HP-LiChroCART 4×250 mm), gradient solvent system 0 – 15 min, 5 – 100 % MeCN (0.1 % TFA) in H_2O, flow rate 1.5 mL min^{-1}, 25 °C, retention time 8 min 29 s)] to yield vancomycin methyl ester **61**. **61**: $[\alpha]_D^{22} = -27.3$ ($c = 0.3$, H_2O); IR (KBr): $\tilde{\nu}_{max} = 3500$, 1731, 1666, 1649, 1596, 1555, 1502, 1414, 1384, 1337, 1302, 1220, 1114, 1061, 1032, 967, 803, 761 cm^{-1}; ^1H NMR (500 MHz, CD_3OD, 330 K): $\delta = 7.70$ (s, 1H), 7.61 (s, 1H), 7.57 (br. d, $J = 6.6$ Hz, 2H), 7.20 – 7.18 (m, 1H), 7.11 (s, 2H), 6.89 (br. s, 2H), 6.56 (d, $J = 1.9$ Hz, 1H), 6.28 (d, $J = 1.9$ Hz, 1H), 5.92 (br. s, 1H), 5.79 (br. s, 1H), 5.48 (br. s, 2H), 5.33 (br. s, 4H), 4.84 –

0947-6539/99/0509-2666 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 9

4.81 (m, 1H), 4.73 (s, 1H), 4.68 (s, 1H), 4.22 (s, 1H), 4.11–4.03 (m, 1H), 3.85 (s, 3H), 3.80–3.78 (m, 3H), 3.76-3.75 (m, 1H), 3.67-3.65 (m, 1H), 3.50–3.48 (m, 1H), 3.43 (s, 1H), 3.33 (s, 2H), 2.77 (s, 3H), 2.20–2.15 (m, 2H), 1.84–1.80 (m, 1H), 1.70–1.68 (m, 1H), 1.63–1.58 (m, 1H), 1.49 (s, 3H), 1.24–1.20 (m, 1H), 1.16 (d, $J = 6.4$ Hz, 3H), 0.89 (br. s, 3H), 0.84 (br. s, 3H); ^{13}C NMR (150 MHz, CD_3OD, 330 K): $\delta = 173.6$, 171.6, 171.0, 171.0, 169.6, 157.1, 157.1, 155.9, 155.9, 154.9, 154.9, 153.0, 152.3, 151.5, 151.2, 149.5, 141.0, 135.9, 135.5, 128.9, 128.7, 128.2, 127.0, 124.7, 124.0, 121.1, 119.4, 119.2, 119.2, 118.1, 118.1, 118.0, 117.5, 115.5, 113.6, 107.3, 105.4, 103.7, 98.1, 79.7, 76.7, 76.3, 72.1, 71.7, 71.2, 69.9, 64.2, 60.9, 57.4, 55.2, 54.9, 53.5, 51.8, 39.2, 36.8, 36.5, 33.3, 32.0, 24.2, 22.5, 22.2, 22.0, 21.7, 17.1, 16.5; HRMS (MALDI) calcd for $C_{67}H_{77}Cl_2N_9O_{24}Na$ $[M + Na^+]$ 1484.4356, found 1484.4339.

Vancomycin (1): Lithium hydroxide (1.0 mg, 0.034 mmol) was added to a solution of vancomycin methyl ester (10 mg, 0.006 mmol) in THF/H_2O (1:1) (0.5 mL) at 0 °C. The reaction mixture was stirred for 20 min, and then quenched by the addition of saturated aqueous NH_4Cl (1 mL). The reaction mixture was filtered and the solvents were removed under reduced pressure. The residue was purified by HPLC [C18 reverse-phase column (HP-LiChroCART 4×250 mm), gradient solvent system 0–15 min, 5–100% MeCN (0.1% TFA) in H_2O, flow rate 1.5 mL min^{-1}, 25 °C, retention time 5 min 38 s] to yield vancomycin **1** (7.4 mg, 85% for two steps). **1**: $[\alpha]_D^{22} = -25.6$ ($c = 0.30$, H_2O); IR (KBr): $\tilde{\nu}_{max} = 3676–2940$, 1718, 1684, 1654, 1638, 1584, 1491, 1390, 1232, 1120, 1067, 1020, 991, 714, 615 cm^{-1}; ^{1}H NMR (600 MHz, D_2O, 330 K): $\delta = 8.03$ (s, 1H), 7.96 (s, 1H), 7.91–7.88 (m, 2H), 7.79–7.78 (m, 2H), 7.42 (s, 1H), 7.34–7.32 (m, 1H), 7.28 (s, 1H), 6.91 (s, 1H), 6.82 (s, 1H), 6.14 (br. s, 1H), 6.06 (br. s, 1H), 5.86 (s, 1H), 5.82 (d, $J = 6.5$ Hz, 1H), 5.75 (d, $J = 4.0$ Hz, 1H), 5.71 (s ,1H), 5.67 (s, 1H), 5.23 (br. s, 1H), 5.17 (q, $J = 6.6$ Hz, 1H), 5.03–5.00 (m, 2H), 4.55 (s, 1H), 4.41 (t, $J = 7.4$ Hz, 1H), 4.18–4.16 (m, 1H), 4.14–4.07 (m, 1H), 3.94 (t, $J = 8.8$ Hz, 1H), 3.87–3.84 (m, 1H), 3.78 (s, 1H), 3.40–3.39 (m, 1H), 3.15–3.14 (m, 1H), 3.11 (s, 1H), 2.72–2.70 (m, 1H), 2.42–2.40 (m, 1H), 2.38–2.34 (m, 1H), 2.16–2.13 (m, 1H), 2.06–2.02 (m, 1H), 1.99–1.94 (m, 1H), 1.76 (s, 3H), 1.49 (d, $J = 6.6$ Hz, 3H), 1.24 (d, $J = 6.5$ Hz, 3H), 1.20 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (150 MHz, D_2O, 330 K): $\delta = 177.8$, 175.7, 172.5, 171.8, 170.5, 169.7, 169.3, 157.9, 156.4, 155.6, 154.1, 150.5, 141.7, 140.0, 138.7, 136.4, 136.3, 134.1, 130.2, 129.6, 129.6, 129.3, 128.6, 127.9, 127.7, 127.7, 125.8, 125.0, 122.7, 119.4, 119.0, 118.9, 109.6, 106.8, 104.5, 102.9, 98.9, 80.6, 77.7, 77.3, 73.3, 72.7, 72.1, 72.1, 70.6, 65.2, 62.1, 62.0, 62.0, 60.6, 59.1, 56.3, 56.0, 55.4, 52.8, 39.9, 39.9, 37.0, 34.3, 33.2, 25.3, 25.6, 23.1, 23.1, 17.6; HRMS (MALDI) calcd for $C_{66}H_{75}Cl_2N_9O_{24}Na$ $[M + Na^+]$: 1470.4200/1472.4170, found 1470.4231/1472.4240.

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