The integrity of the Keggin polyoxometalates $K_4SiW_{12}O_{40}$ and $K_5PV_2Mo_{10}O_{40}$ under the reaction conditions was also proven by IR spectroscopy and X-ray diffraction studies. A finely powdered sample of the polyoxometalate was treated under the reaction conditions (0.5 g of benzophenone, 50 mg of polyoxometalate, 23 atm H_2, $T = 300\,^{\circ}C$, $t = 200$ min). After cooling, the autoclave was opened and the polyoxometalate was isolated by filtration. The catalyst first appeared brown-blue, but after exposure to air the color turned lighter. The IR spectra and X-ray powder patterns before and after the reaction were identical, indicating that the structure of the polyoxometalates was unchanged. A room-temperature ESR spectrum of the $PV_2Mo_{10}O_{40}^{5-}$ catalyst after reaction showed the typical eight-line spectrum of the two-electron-reduced compound.[8] That no leaching of the polyoxometalate from the support occurred was indicated by atomic absorption measurements of the organic phase after extraction with water.

We have demonstrated a new application of Keggin polyoxometalates as deoxygenation and hydrogenation catalysts for the reduction of carbonyl compounds. The $[PV_2Mo_{10}O_{40}]^{5-}$ polyoxometalate, which is most active for the activation (oxidation) of H_2, is the most active catalyst. The product selectivity shows that the reduced polyoxometalates deoxygenate ketones and aldehydes; carbinols are not intermediates. Use of $[PV_2Mo_{10}O_{40}]^{5-}$ tends to lead to formation of saturated compounds, whereas for $[SiW_{12}O_{40}]^{4-}$ alkenes are preferred initial products.

Experimental Section

Solutions of $H_3PW_{12}O_{40}$, $H_3PMo_{12}O_{40}$, $H_4SiW_{12}O_{40}$, and $H_5PV_2Mo_{10}O_{40}$[9] were treated on an Amberlyst 120 (K^+ form) ion-exchange column to prepare the polyoxometalates $K_3PW_{12}O_{40}$, $K_3PMo_{12}O_{40}$, $K_4SiW_{12}O_{40}$, and $K_5PV_2Mo_{10}O_{40}$. $K_6SiM(H_2O)W_{11}O_{39}$ ($M = Co^{II}$, Cu^{II}, Ni^{II}) and $K_5SiCr^{III}(H_2O)W_{11}O_3$ were prepared by the literature procedure.[10] The polyoxometalates were wet impregnated from water on γ-alumina at a 5 wt% loading and dried at 100 °C overnight. Reactions were run in a stirred Parr autoclave at 300 °C and 23–54 atm H_2. Specific conditions are given in the Table legends. The reaction products were analyzed by GC and GC-MS using an apolar methylsilicone column.

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Total Synthesis of Everninomicin 13,384-1—Part 1: Synthesis of the $A_1B(A)C$ Fragment**

K. C. Nicolaou,* Helen J. Mitchell, Hideo Suzuki, Rosa Maria Rodríguez, Olivier Baudoin, and Konstantina C. Fylaktakidou

Dedicated to Dr. A. K. Ganguly on the occasion of his 65th birthday

Drug-resistant bacteria are currently causing considerable concern because of the serious and constant threat they pose to human health and their potential to cause widespread epidemics. Even vancomycin,[1] whose effectiveness against such resistant bacterial strains provided the last line of defense, is showing signs of weakness in the face of the evolution of aggressive bacteria. Everninomicin 13,384-1 (Ziracin) (**1**),[2] a member of the orthosomicin class of antibiotics[3] and currently in clinical trials, is a promising new weapon against drug-resistant bacteria, including methicillin-resistant staphylococci and vancomycin-resistant streptococci and enterococci.[4] Isolated from *Micromonospora carbonacea var. africana* (found in a soil sample collected from the banks of the Nyiro River in Kenya), everninomicin 13,384-1 (**1**) possesses a novel oligosaccharide structure containing two sensitive orthoester moieties and terminating with two highly substituted aromatic esters. In addition, **1** contains a $1 \rightarrow 1'$-disaccharide bridge, a nitrosugar (everni-

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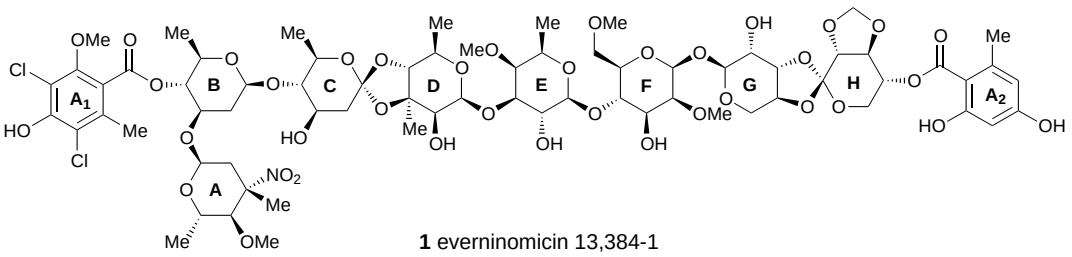

1 everninomicin 13,384-1

trose), thirteen rings, and thirty five stereogenic centers within its structure.[5] Certainly, **1** constitutes a formidable challenge to organic synthesis[6] because of its unusual connectivity and polyfunctional and sensitive nature. In this and the following two communications[7, 8] we report the total synthesis of everninomicin 13,384-1 (**1**) through a number of novel synthetic strategies and methods. Herein we lay out the overall strategy and describe the construction of the $A_1B(A)C$ fragment of the target molecule.

Figure 1 outlines, in retrosynthetic format, the strategy utilized in the present total synthesis. As a consequence of its extreme sensitivity to acidic conditions[2] the CD orthoester moiety was disassembled first, leading to phenylseleno fluoride **2** (the $A_1B(A)C$ fragment) and diol **3** (the DEF-GHA_2 fragment). The larger fragment **3** was further disconnected at the EF glycosidic bond to give fragments **4** (DE) and **5** ($FGHA_2$) as potential key intermediates for its construction. Returning to fragment **2**, disconnection at the indicated sites (two glycosidic and one ester bonds) defined building blocks **6**–**9** as the requisite starting materials. Crucial to this plan were the 1,2-phenylseleno and 1,2-phenylthio migrations[9] that set the stage for the stereocontrolled constructions of the CD and GH orthoesters and β-2-deoxy B-C glycoside bonds. The stereocontrolled synthesis of building blocks **6**–**9** and their assembly to the $A_1B(A)C$ fragment **2** is described below.

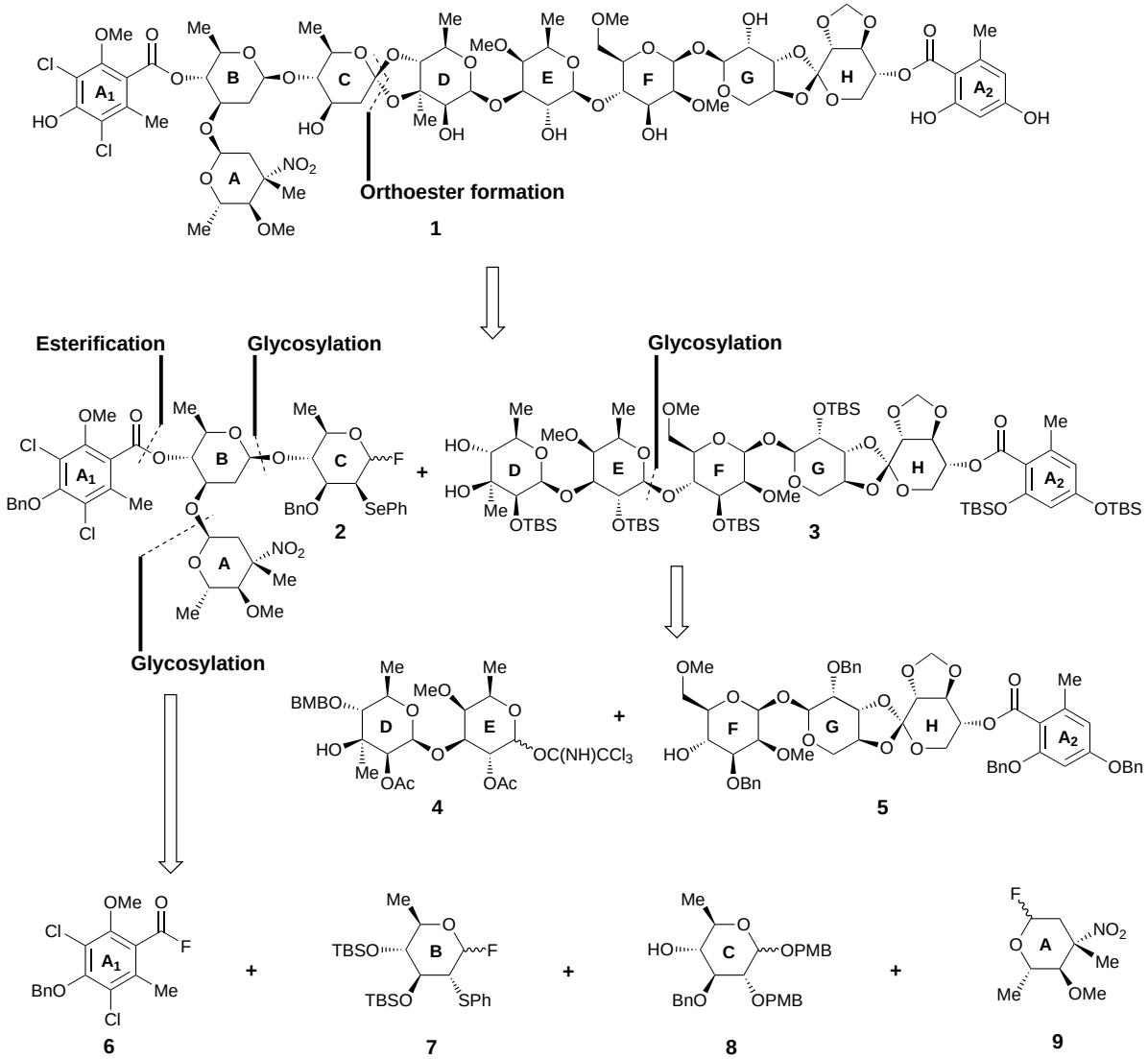

Figure 1. Retrosynthetic analysis of everninomicin 13,384-1 (**1**). Ac = acetyl; Bn = benzyl; PMB = *p*-methoxybenzyl; TBS = *tert*-butyldimethylsilyl.

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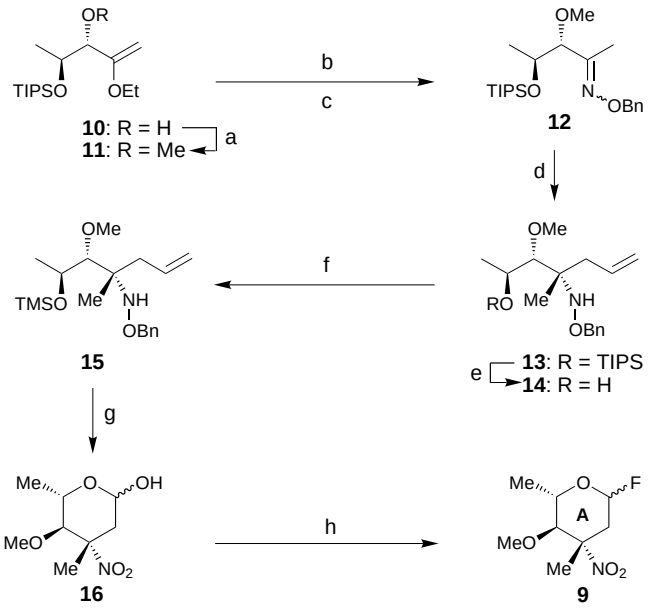
The construction of the evernitrose donor **9** (Scheme 1) involved an improved sequence along the lines of our original synthesis[10] of both evernitrose and vancosamine. Thus, methylation of alcohol **10** with NaH and MeI gave, in 96% yield, the methoxy compound **11**, which was hydrolyzed to the

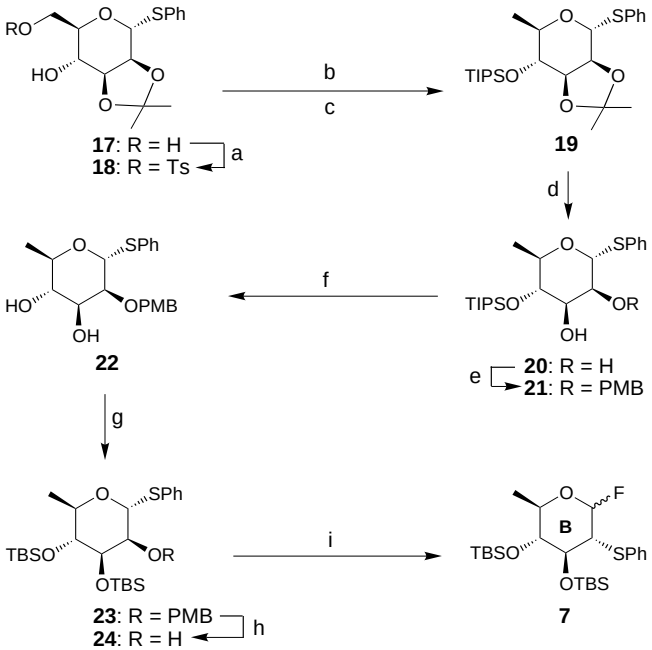


Scheme 1. Synthesis of nitrosugar A (**9**). a) 1.1 equiv NaH, 1.3 equiv MeI, THF, 0 →25 °C, 4 h, 96%; b) 0.1N HCl, THF/H_2O (4/1), 25 °C, 0.5 h, 100%; c) 1.1 equiv $BnONH_2 \cdot HCl$, py, 0 →25 °C, 2 h, 91% (*E*:*Z* ca. 4:1); d) 2.5 equiv allylMgBr, Et_2O, −35 °C, 1 h, 87%; e) 1.1 equiv nBu$_4$NF, THF, 25 °C, 1 h, 92%; f) 5.0 equiv $(TMS)_2NH$, 0.1 equiv TMSCl, 25 °C, 0.5 h, 100%; g) 1. O_3, iC$_8$H$_8$/CCl_4 (2/1), −78 °C, 1 h; 2. 2.0 equiv TFA, −78 →25 °C, 1 h; 3. 2.0 equiv Ph_3P, −78 →25 °C, 12 h, 82% over three steps (α:β ca. 1.8:1); h) 1.5 equiv DAST, CH_2Cl_2, 0 °C, 20 min, 100%. DAST = (diethylamino)sulfur trifluoride; py = pyridine; TFA = trifluoroacetic acid; TIPS = triisopropylsilyl; TMS = trimethylsilyl.

corresponding ketone with aqueous HCl and converted into oxime **12** by condensation with *O*-benzylhydroxylamine (ratio of *E*:*Z* isomers approximately 4:1; 91% over 2 steps). Addition of allylmagnesium bromide to **12** in diethyl ether at −35 °C afforded **13** (87% yield), which after an exchange of silyl groups (nBu$_4$NF, 92%; $(TMS)_2NH$, TMSCl, 100%) gave the more labile trimethylsilyl ether **15** via the hydroxy compound **14**. Ozonolysis of **15** followed by sequential exposure to TFA and Ph_3P resulted in aldehyde and nitro group formation, desilylation, and ring closure and the generation of lactol **16**. Finally, treatment of lactol **16** with DAST[11] led to its rapid conversion into glycosyl fluoride **9** in quantitative yield (an approximate 8:1 mixture of α- and β-anomers).

Despite our original model studies[12] and success in constructing rings B and C from a common intermediate, we now required a more demanding orchestration of protecting groups and glycosylation tactics for an eventual total synthesis. After considerable design and experimentation, we finally discovered the winning combination of TBS and PMB groups on rings B and C, respectively.

Furthermore, the adopted constructions of rings B (**7**) and C (**8**) took independent paths and started from thioglycoside **17** (Scheme 2) and glucal **25** (Scheme 3), respectively. The synthesis of building block **7** is summarized in Scheme 2. Thus, tosylation of the primary hydroxyl group of the known intermediate **17**[13] with TsCl/py furnished tosylate **18** (93%), which was silylated (TIPSOTf/2,6-lutidine, 90%) and reduced with LAH (90%) to afford compound **19**. Acidic methanolysis (TsOH/MeOH) of the acetonide group in **19** gave diol **20** (80%), whose exposure to nBu$_2$SnO[14] and subsequent



Scheme 2. Synthesis of carbohydrate building block B (**7**). a) 1.1 equiv TsCl, py, 0 →25 °C, 12 h, 93%; b) 1.1 equiv TIPSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, 0 →25 °C, 0.5 h, 90%; c) 2.5 equiv LAH, THF, 0 →45 °C, 6 h, 90%; d) 0.5 equiv TsOH, 2.5 equiv $(CH_2OH)_2$, MeOH, 25 °C, 10 h, 80%; e) 1.1 equiv nBu$_2$SnO, toluene, 110 °C, 3 h; 1.5 equiv PMBCl, 0.2 equiv nBu$_4$NI, 25 →110 °C, 83%; f) 2.5 equiv nBu$_4$NF, THF, 25 °C, 2 h, 91%; g) 2.2 equiv TBSOTf, 4.0 equiv 2,6-lutidine, CH_2Cl_2, 0 →25 °C, 0.5 h, 93%; h) 1.5 equiv DDQ, CH_2Cl_2/H_2O (10/1) 0 →25 °C, 1 h, 91%; i) 1.5 equiv DAST, CH_2Cl_2, 0 °C, 20 min, 100% (α:β ca. 10:1). DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone; LAH = lithium aluminum hydride; Tf = trifluoromethanesulfonyl; Ts = *p*-toluenesulfonyl.

reaction with PMBCl/nBu$_4$NI furnished **21** in 83% overall yield. Removal of the TIPS group was induced by nBu$_4$NF to give diol **22** (91%), whose treatment with TBSOTf and 2,6-lutidine furnished the bis-TBS derivative **23** (93%). Finally, DDQ deprotection of **23** gave hydroxy compound **24** (91%), which on exposure to DAST resulted in the desired 1,2-migration[9] of the thiophenyl group (with inversion of the C2 stereochemistry) and inplantation of the fluoride group at C1 (100%, approximate 10:1 mixture of α- and β-anomers) leading to the targeted glycosyl fluoride **7**.

Building block **8** was constructed in five steps from the readily available glucal **25**[15] as shown in Scheme 3. Thus, tin acetal mediated benzylation of **25** (nBu$_2$SnO, BnBr/nBu$_4$NI) resulted in the selective protection at C3 in 83% yield. Further protection, now at C4, with TBSCl/imidazole led to compound **27** whose exposure to OsO_4/NMO furnished diol **28** in 97% yield (approximate 1:1 mixture of anomers). Protection of both hydroxyl groups of **28** as PMB ethers

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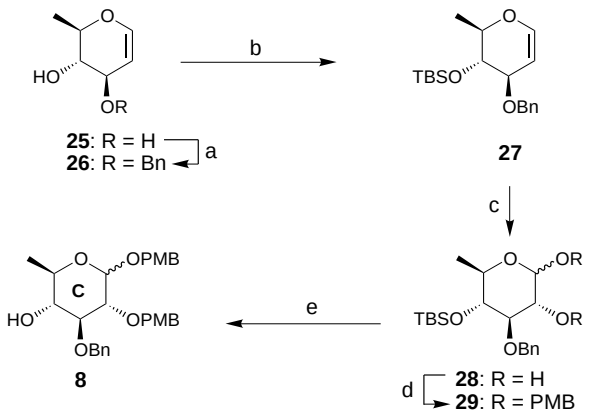
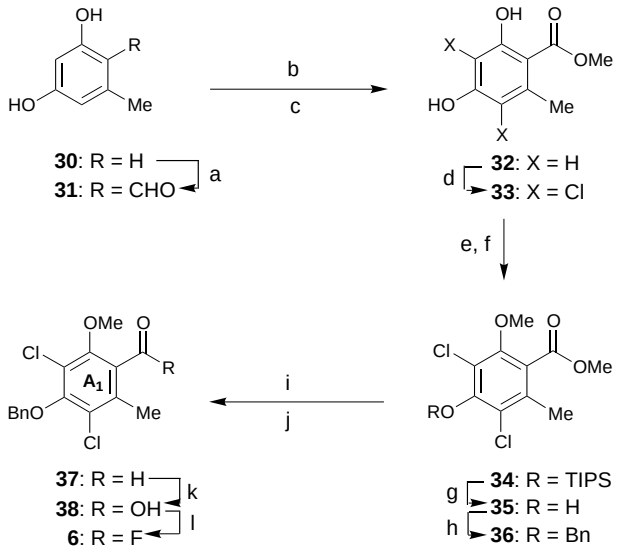


Scheme 3. Synthesis of carbohydrate building block C (**8**). a) 1.1 equiv nBu$_2$SnO, toluene, 110 °C, 3 h, 1.5 equiv BnBr, 0.2 equiv nBu$_4$NI, 25 → 110 °C, 5 h, 83 %; b) 1.5 equiv TBSCl, 2.5 equiv imidazole, 0 → 25 °C, 3 h, 93 %; c) 1.1 equiv NMO, 0.05 equiv OsO_4, Me_2CO/H_2O (10/1), 25 °C, 8 h, 97 %; d) 2.4 equiv NaH, 3.0 equiv PMBCl, 0.2 equiv nBu$_4$NI, DMF, 0 → 25 °C, 3 h, 95 %; e) 1.1 equiv nBu$_4$NF, THF, 25 °C, 1 h, 95 % (α:β ca. 1:1). NMO = *N*-methylmorpholine *N*-oxide.

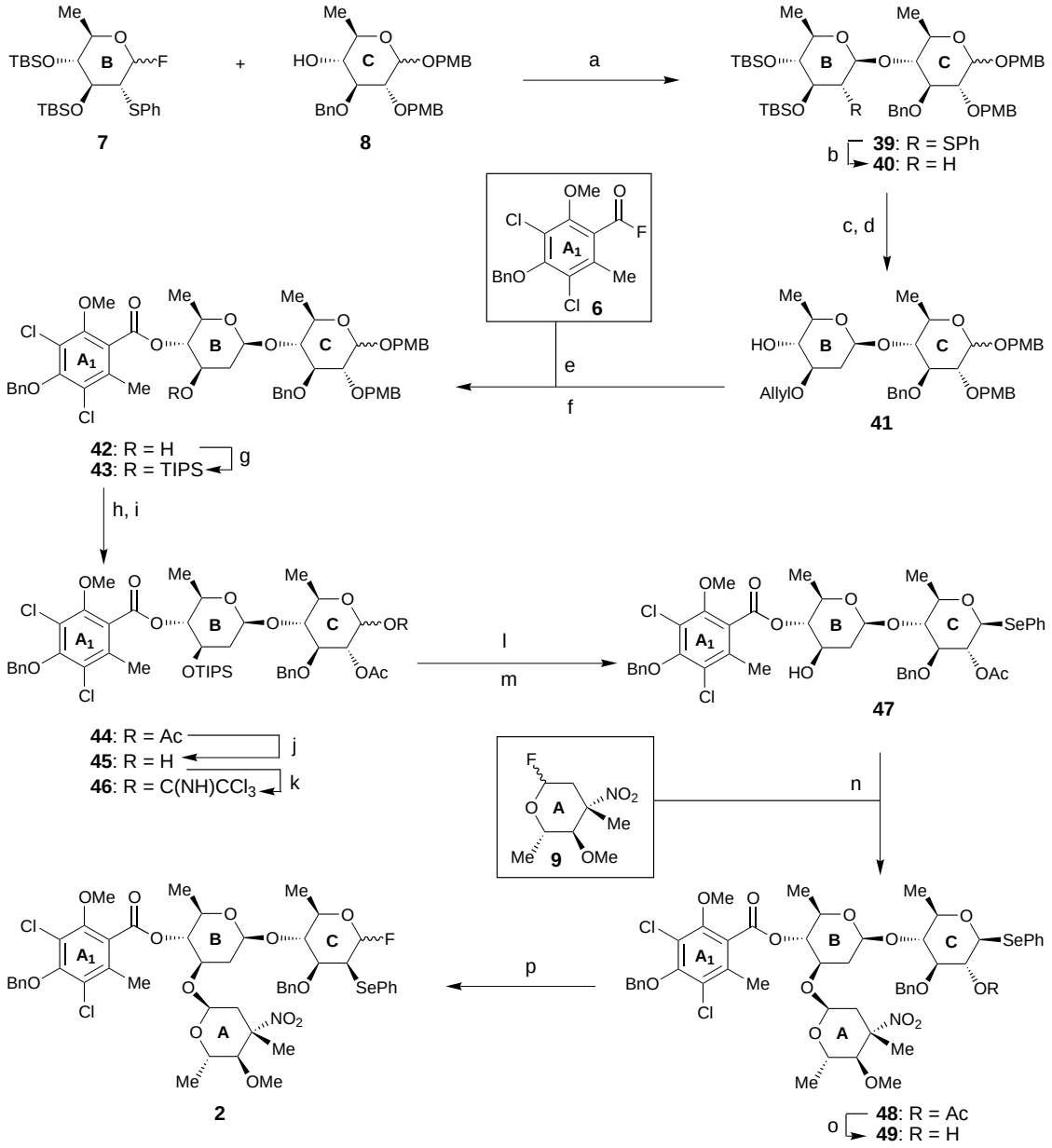
(NaH/PMBCl/nBu$_4$NI, 95 %) led to **29** (approximate 1:1 mixture of anomers) and exposure to nBu$_4$NF generated the desired building block **8** in 95 % yield. The stereochemistry at C1 is inconsequential as it will be destroyed at a later stage.

A more efficient synthesis than the one previously reported[12] for the aromatic fragment **6** was developed and is summarized in Scheme 4. Thus, Gatterman formylation of orcinol (**30**) with $Zn(CN)_2/AlCl_3$ gave aldehyde **31** (92 %), which was oxidized to the corresponding carboxylic acid ($NaClO_2$, 80 %) and methylated ($MeOH/NaHCO_3$) to give methyl ester **32** (90 %). Chlorination of **32** with SO_2Cl_2 led to dichloride **33** in 95 % yield, while sequential protection of the phenolic groups proceeded smoothly and regioselectively upon treatment with TIPSOTf/2,6-lutidine (90 %) and Ag_2O/MeI (91 %) to furnish compound **34**. The TIPS group was then exchanged for a Bn group (nBu$_4$NF, 96 %; K_2CO_3/BnBr, 92 %) to give **36** via **35**. The resistance of the methyl ester in **36** towards hydrolysis led to a three-step protocol for its conversion into carboxylic acid **38** (DIBAL reduction, 90 %; PDC oxidation, 90 %; $NaClO_2$ oxidation, 95 %) involving aldehyde **37** as an intermediate. Finally, exposure[16] of **38** to $(Me_2N)_2CF^+PF_6^-$ gave the desired acyl fluoride **6**, which withstood chromatographic purification on silica gel (97 % yield).



Scheme 4. Synthesis of aromatic ring A_1 (**6**). a) 1. 1.5 equiv $Zn(CN)_2$, 2.4 equiv $AlCl_3$, HCl(g), 0 °C, 3 h; 2. H_2O, 0 → 100 °C, 30 min, 92 %; b) 2.4 equiv $NaClO_2$, 2.5 equiv NaH_2PO_4, DMSO, 0 °C, 12 h, 80 %; c) 2.0 equiv MeI, 1.2 equiv $NaHCO_3$, CH_2Cl_2, 25 °C, 12 h, 90 %; d) 2.5 equiv SO_2Cl_2, CH_2Cl_2, 35 °C, 3 h, 95 %; e) 1.1 equiv TIPSOTf, 1.3 equiv 2,6-lutidine, CH_2Cl_2, −78 °C, 0.5 h, 90 %; f) 4.0 equiv Ag_2O, 4.0 equiv MeI, Et_2O, 30 °C, 12 h, 91 %; g) 1.3 equiv nBu$_4$NF, THF, 25 °C, 2 h, 96 %; h) 1.5 equiv BnBr, 3.0 equiv K_2CO_3, Me_2CO, 70 °C, 92 %; i) 1.2 equiv DIBAL, CH_2Cl_2, −78 °C, 1 h, 90 %; j) 3.0 equiv PDC, 3 Å MS, CH_2Cl_2, 25 °C, 3 h, 90 %; k) 3.0 equiv $NaClO_2$, 3.0 equiv NaH_2PO_4, 2-methyl-2-butene (2.0 M in THF, 4.0 equiv), tBuOH, H_2O, 25 °C, 3 h, 95 %; l) 1.5 equiv $(Me_2N)_2CF^+PF_6^-$, 2.0 equiv iPr$_2$NEt, CH_2Cl_2, 0 → 25 °C, 2 h, 97 %. DIBAL = diisobutylaluminum hydride; DMSO = dimethylsulfoxide; PDC = pyridinium dichromate.

Having constructed all four requisite building blocks (**6**–**9**), their assembly became the next task at hand. Scheme 5 summarizes their stereoselective coupling to form the $A_1B(A)C$ fragment **2**. Thus, the $SnCl_2$-mediated coupling of glycosyl fluoride **7** with alcohol **8** under mild conditions (4 Å MS, $CH_2Cl_2/Et_2O/Me_2S$ (1/1/1), −10 °C)[9] gave disaccharide **39** in 71 % yield and as a single stereoisomer. Having performed its β-directing duty, thus ensuring the desired stereochemical outcome in this glycosylation reaction, the 2-thiophenyl group was now ready for reductive cleavage with Raney-nickel. This procedure led smoothly from **39** to **40**. The latter intermediate (**40**) was then modified for its coupling with acyl fluoride **6** by bis-desilylation (nBu$_4$NF, 78 % over two steps) and selective monoallylation (nBu$_2$SnO/allyl bromide, 93 %) to convert it into **41** (Table 1). Upon activation of the hydroxyl group of **41** (nBuLi, THF, −78 → 0 °C) followed by addition of acyl fluoride **6**, the corresponding ester was formed in 99 % yield, from which the allyl group was removed with Wilkinson's catalyst/DABCO and OsO_4/NMO to afford **42** (81 % yield). A TIPS group was then installed on ring B (TIPSOTf/2,6-lutidine, 93 %) to afford compound **43**. These particular choices of protecting groups were necessary for optimum esterification yields and subsequent chemistry. Experimentation with future steps in the total synthesis dictated the introduction of the selenium group before the attachment of the evernitrose fragment, and therefore the following sequence was adopted. Thus, the PMB groups were removed from **43** by exposure to PhSH and $BF_3 \cdot Et_2O$ (83 %) and acetate groups were installed in their place (Ac_2O/Et_3N/4-DMAP, 98 %) to afford diacetate **44**. Exposure of **44** to nBuNH$_2$ led to the selective cleavage of the C1 acetate and the liberation of lactol **45** (91 %), which was then converted into trichloroacetimidate **46**[17] by treatment with CCl_3CN in the presence of DBU. Addition of PhSeH[18] to **46** in the presence of $BF_3 \cdot Et_2O$ gave the desired β-phenylseleno glycoside as expected with participation of the C2 acetate (α:β approximately 1:9, 78 % over two steps). Removal of the TIPS group from this product with nBu$_4$NF furnished the phenylseleno glycoside **47** (91 % yield), which was ready for the next coupling. Indeed, attachment of the evernitrose fragment **9** onto the A_1BC chain **47** proceeded smoothly under the influence of $SnCl_2$ to furnish the desired



Scheme 5. Construction of $A_1B(A)C$ fragment **2**. a) 1.0 equiv **7**, 1.1 equiv **8**, 1.8 equiv $SnCl_2$, 4 Å MS, $CH_2Cl_2/Et_2O/Me_2S$ (1/1/1), $-10\,^{\circ}C$, 3 h, 71%; b) ca. 1.0 equiv Raney-Ni (w/w), EtOH/THF (1/1), $90\,^{\circ}C$, 8 h; c) 2.2 equiv nBu_4NF, $25\,^{\circ}C$, 2 h, 78% over two steps; d) 1.1 equiv nBu_2SnO, toluene, $110\,^{\circ}C$, 3 h; 1.5 equiv allylBr, 0.2 equiv nBu_4NI, $25 \rightarrow 110\,^{\circ}C$, 93%; e) 1.1 equiv nBuLi, THF, $-78 \rightarrow 0\,^{\circ}C$, 1 h; 1.2 equiv **6**, THF, $25\,^{\circ}C$, 99%; f) 1. 1.5 equiv DABCO, 0.05 equiv $[(Ph_3P)_3RhCl]$, EtOH/H_2O (10/1), $90\,^{\circ}C$, 2 h; 2. 1.1 equiv NMO, 0.05 equiv OsO_4, Me_2CO/H_2O (10/1), $25\,^{\circ}C$, 8 h, 81%; g) 1.2 equiv TIPSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 1 h, 93%; h) 8.0 equiv PhSH, 4.0 equiv $BF_3 \cdot Et_2O$, CH_2Cl_2, $-30\,^{\circ}C$, 2 h, 83%; i) 2.5 equiv Ac_2O, 4.0 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 1 h, 98%; j) 1.3 equiv nBuNH$_2$, THF, $25\,^{\circ}C$, 5 h, 91%; k) 5.0 equiv CCl_3CN, 0.05 equiv DBU, CH_2Cl_2, $0\,^{\circ}C$, 0.5 h; l) ca. 2.0 equiv PhSeH, 0.2 equiv $BF_3 \cdot Et_2O$, CH_2Cl_2, $-78 \rightarrow 0\,^{\circ}C$, 1 h, 78% over two steps (α:β ca. 1:9); m) 1.2 equiv nBu_4NF, THF, $25\,^{\circ}C$, 1 h, 91%; n) 2.0 equiv **9**, 1.2 equiv $SnCl_2$, CH_2Cl_2/Et_2O (1/1), $0 \rightarrow 25\,^{\circ}C$, 1 h, 80%; o) 0.3 equiv NaOH, MeOH, $25\,^{\circ}C$, 1 h, 91%; p) 1.5 equiv DAST, CH_2Cl_2, $0\,^{\circ}C$, 20 min, 90% (α:β ca. 8:1). DABCO = 1,4-diazabicyclo[2.2.2]octane; DBU = 1,8-diazabicyclo[5. 4.0]undec-7-ene; 4-DMAP = 4-dimethylaminopyridine.

assembly **48** (80%) in which the newly formed glycoside bond ($A \rightarrow B$, α-anomer) was fully controlled by the anomeric effect.

Finally, basic hydrolysis (NaOH/MeOH) of the acetate group from **48** led to the C2 hydroxy compound **49** (91% yield), whose treatment with DAST produced the targeted 2-phenylselenoglycosyl fluoride **2** in excellent yield (90%) and with an inversion of the stereochemistry at C2 of ring C (approximate 8:1 mixture of α- and β-fluoride anomers).[19] In the following communication[7] we describe the construction of the desired $FGHA_2$ fragment of everninomicin 13,384-1 (**1**).

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Table 1. Selected physical and spectroscopic data of compounds **41**, **42**, and **49**.

41: $R_f = 0.25$ (silica, 70 % Et_2O in hexanes); $\alpha_D^{22} = -23.4$ ($c = 0.80$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3387, 2955, 2908, 2861, 1608, 1584, 1455, 1355, 1302, 1249, 1173, 1091, 1044, 926, 814, 732\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.41-7.24$ (m, 7H, ArH), 7.17 (d, $J = 8.5$ Hz, 2H, PMB), 6.88 (d, $J = 8.5$ Hz, 2H, PMB), 6.79 (d, $J = 8.5$ Hz, 2H, PMB), 5.90 (dddd, $J = 17.0, 10.5, 6.0, 5.5$ Hz, 1H, OCH_2CHCH_2), 5.28 (dd, $J = 17.0, 1.5$ Hz, 1H, OCH_2CHCH_2), 5.19 (dd, $J = 10.5, 1.0$ Hz, 1H, OCH_2CHCH_2), 4.92 and 4.83 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.88 and 4.59 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.81 and 4.61 (AB, $J = 10.5$ Hz, 2H, CH_2Ar), 4.70 (dd, $J = 9.5, 2.0$ Hz, 1H, B-1), 4.47 (d, $J = 8.0$ Hz, 1H, C-1), 4.11 (dd, $J = 12.5, 5.5$ Hz, 1H, OCH_2CHCH_2), 3.94 (dd, $J = 12.5, 6.0$ Hz, 1H, OCH_2CHCH_2), 3.80 (s, 3H, OMe (PMB)), 3.77 (s, 3H, OMe (PMB)), 3.54 (t, $J = 8.5$ Hz, 1H, C-3), 3.44 (t, $J = 8.5$ Hz, 1H, C-2), 3.41 – 3.35 (m, 2H, C-4, C-5), 3.30 – 3.22 (m, 1H, B-3), 3.21 – 3.10 (m, 2H, B-4, B-5), 2.64 (d, $J = 2.0$ Hz, 1H, OH), 2.30 (ddd, $J = 12.5, 4.5, 2.0$ Hz, 1H, B-2), 1.46 (td, $J = 12.5, 9.5$ Hz, 1H, B-2), 1.35 (d, $J = 5.0$ Hz, 3H, C-6), 1.24 (d, $J = 5.5$ Hz, 3H, B-6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.2, 159.0, 138.9, 134.5, 130.5, 130.0, 129.7, 129.7, 129.5, 129.5, 129.4, 128.1, 127.5, 127.2, 117.3, 113.7, 113.5, 102.1, 100.0, 94.8, 83.1, 82.0, 81.8, 81.6, 80.4, 79.4, 78.5, 75.4, 75.2, 71.8, 70.8, 69.8, 55.1, 36.2, 18.0, 17.8$; HR-MS (FAB), calcd for $C_{38}H_{48}O_{10}Cs$ $[M + Cs^+]$: 797.3202, found: 797.2287

42: $R_f = 0.24$ (silica, 70 % Et_2O in hexanes); $\alpha_D^{22} = +12.0$ ($c = 0.20$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3425, 2931, 2884, 1731, 1614, 1544, 1138, 1326, 1302, 1249, 1120, 1073, 938, 820, 749\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.57$ (d, $J = 6.9$ Hz, 2H, ArH), 7.43 – 7.28 (m, 10H, ArH), 7.16 (d, $J = 8.6$ Hz, 2H, PMB), 6.88 (d, $J = 8.6$ Hz, 2H, PMB), 6.79 (d, $J = 8.6$ Hz, 2H, PMB), 5.03 (br s, 2H, CH_2Ar (A_1)), 4.93 and 4.83 (AB, $J = 10.9$ Hz, 2H, CH_2Ar), 4.88 and 4.59 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.81 and 4.59 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.78 (t, $J = 9.4$ Hz, 1H, B-4), 4.74 (dd, $J = 9.7, 1.8$ Hz, 1H, B-1), 4.47 (d, $J = 7.9$ Hz, 1H, C-1), 3.87 (s, 3H, OMe), 3.85 – 3.72 (m, 1H, B-3), 3.81 (s, 3H, OMe), 3.78 (s, 3H, OMe), 3.55 (br t, $J = 9.0$ Hz, 1H, C-3), 3.43 (dd, $J = 9.0, 7.9$ Hz, 1H, C-2), 3.41 – 3.36 (m, 2H, C-4, C-5), 3.33 (dq, $J = 9.4, 6.2$ Hz, 1H, B-5), 2.66 (d, $J = 4.4$ Hz, 1H, OH), 2.36 (s, 3H, Me (A_1)), 2.40 – 2.30 (m, 1H, B-2), 1.72 (td, $J = 12.2, 9.7$ Hz, 1H, B-2), 1.35 (d, $J = 5.3$ Hz, 3H, C-6), 1.23 (d, $J = 6.2$ Hz, 3H, B-6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 166.4, 159.3, 159.1, 153.0, 151.8, 139.0, 138.9, 133.2, 130.5, 130.1, 129.8, 129.7, 129.6, 129.5, 129.2, 128.5, 128.2, 127.5, 127.3, 126.4, 125.5, 121.4, 113.8, 113.6, 102.2, 100.3, 84.2, 82.9, 81.9, 79.5, 75.3, 74.9, 74.5, 70.9, 70.8, 69.8, 69.6, 65.8, 62.4, 55.2, 39.3, 34.2, 30.3, 29.5, 21.1, 18.0, 17.6, 17.4, 15.2$; HR-MS (FAB), calcd for $C_{51}H_{56}Cl_2O_{13}Na$ $[M + Na^+]$: 969.2995, found: 969.2998

49: $R_f = 0.20$ (silica, 50 % Et_2O in hexanes); $\alpha_D^{22} = -36.1$ ($c = 0.40$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3476, 2939, 1732, 1542, 1453, 1391, 1251, 1128, 1032, 911, 736\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.64$ (d, $J = 7.0$ Hz, 2H, ArH), 7.57 (d, $J = 7.0$ Hz, 2H, ArH), 7.45 – 7.27 (m, 11H, ArH), 5.06 and 5.03 (AB, $J = 10.2$ Hz, 2H, CH_2Ar), 4.98 and 4.83 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.94 (br dd, $J = 5.0, 1.8$ Hz, 1H, A-1), 4.89 (t, $J = 9.4$ Hz, 1H, B-4), 4.72 (d, $J = 9.6$ Hz, 1H, C-1), 4.67 (dd, $J = 9.7, 1.8$ Hz, 1H, B-1), 3.89 – 3.83 (m, 1H, B-3), 3.86 (s, 3H, OMe (A)), 3.65 (d, $J = 9.4$ Hz, 1H, A-4), 3.53 – 3.32 (m, 6H, A-5, B-5, C-2, C-3, C-4, C-5), 3.36 (s, 3H, OMe (A_1)), 2.49 (br s, 1H, OH), 2.46 (dd, $J = 13.8, 5.0$ Hz, 1H, A-2), 2.39 (s, 3H, Me (A_1)), 2.29 (ddd, $J = 12.9, 5.1, 1.8$ Hz, 1H, B-2), 2.02 (dd, $J = 13.8, 1.8$ Hz, 1H, A-2), 1.72 – 1.65 (m, 1H, B-2), 1.68 (s, 3H, Me (A-3)), 1.34 (d, $J = 5.9$ Hz, 3H, B-6 or C-6), 1.33 (d, $J = 6.2$ Hz, 3H, B-6 or C-6), 0.84 (d, $J = 6.2$ Hz, 3H, A-6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.5, 153.2, 153.1, 138.7, 135.8, 135.1, 134.7, 129.0, 128.6, 128.5, 128.3, 128.2, 127.6, 127.5, 126.3, 125.9, 125.4, 99.7, 99.0, 92.4, 89.9, 84.3, 84.2, 83.0, 81.7, 76.7, 76.1, 75.0, 74.9, 73.1, 72.3, 71.0, 66.2, 61.9, 90.7, 40.0, 36.4, 31.5, 30.2, 22.6, 19.3, 18.3, 18.2, 18.0, 17.6, 14.1$; HR-MS (FAB), calcd for $C_{49}H_{57}Cl_2NO_{14}SeCs$ $[M + Cs^+]$: 1166.1378, found: 1166.1319

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