Synthesis of the 2-Deoxy Trisaccharide Glycal of Antitumor Antibiotics Landomycins A and E

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Abstract: Synthesis of the 2-deoxy trisaccharide glycal of antitumor antibiotics landomycins A and E has been described. The synthesis involves an anomeric *O*-alkylation for the synthesis of 2-deoxy β -linked disaccharide, a *tert*-butyldimethylsilyl triflate-catalyzed α -selective L-rhodinosylation, and a lithium 4,4'-di-*tert*-butylbiphenyl-mediated reductive debenzoylation and concomitant reductive lithiation-elimination for the production of the 2-deoxy trisaccharide glycal.

Keywords: 2-deoxy sugars; glycal; anomeric *O*-alkylation; glycosylation

1. Introduction

The angucycline antibiotics are a class of secondary metabolites bearing angularly assembled tetracyclic framework and 2-deoxy sugar subunits (*cf.* **1** and **2**, **Figure 1**).¹⁻³ Besides their interesting structural features, the angucyclines possess various intriguing biological activities.¹⁻³ The landomycins are a subclass of angucycline antibiotics isolated from *Streptomyces* sp. (DSM 5087).⁴⁻⁶ Among the landomycins, landomycin A (**1**) exhibits broad spectrum antitumor activity against 60 cancer cell lines.^{4,7-8} Structurally, landomycin A contains an angular tetracyclic core and a hexasaccharide subunit consisting of two repeat units of trisaccharide (α -L-rhodinose-(1 $\rightarrow$ 3)- β -D-olivose-(1 $\rightarrow$ 4)- β -D-olivose), while landomycin E (**2**) bears one trisaccharide. Although landomycin A is known to inhibit DNA synthesis and G1/S cell cycle progression,⁹ the specific mechanism of action has not yet been determined. Structure and activity (SAR) studies suggested that cytotoxic activity of the landomycins depends on the length of the 2-deoxy sugar subunits. For instance, landomycin A with the longest sugar chain was found to be the most potent congener, while landomycins B, D, E, I, and J with shorter chains showed inferior cytotoxic activities.^{4,6,9} The initially proposed landomycin A structure⁴ was revised in 1994,¹⁰ and later unambiguously determined through synthetic studies by Roush¹¹ and total synthesis by Yu.¹² In addition, the hexasaccharide subunit of landomycin A has also been synthesized by three independent groups including Sulikowski,¹³ Roush,¹⁴ and Yu.¹⁵ Furthermore, the repeating trisaccharide has been prepared by Kirschning,¹⁶ O'Doherty,¹⁷ and, most recently from the Mong group.¹⁸ Moreover, Tanaka and co-workers have reported stereoselective synthesis of a combinatorial library of sixteen deoxyhexasaccharides related to landomycin A sugar moiety.¹⁹

Figure 1. Structures of landomycin A (1) and E (2).

During our synthetic studies of angucycline antitumor antibiotics, we have recently accomplished the total synthesis of derhodinosylurdamycin A.²⁰ In addition, we prepared S-linked hexasaccharide of landomycin A²¹ via Umpolung S-Glycosylation.^{22,23} To continue our studies on the landomycins, herein we wish to report a concise synthesis of O-linked trisaccharide of landomycin A/E.

2. Results and Discussion

2.1 Attempted synthesis of trisaccharide 7 of landomycin A/E

Our original approach was to prepare protected trisaccharide 7 which corresponds to the trisaccharide (α -L-rhodinose-(1 $\rightarrow$ 3)- β -D-olivose-(1 $\rightarrow$ 4)-D-olivose) of landomycin A/E. As shown in **Scheme 1**, disaccharide 5 was obtained from known D-olivose-derived diol 3 and triflate 4 via anomeric O-alkylation in 87% yield.²⁴ Since disaccharide 5 contains a free alcohol at C3', it was directly subjected to the glycosylation with L-rhodinose-derived acetate donor 6¹² in order to produce trisaccharide 7. However, subsequent *tert*-butyldimethylsilyl triflate (TBSOTf)-catalyzed glycosylation¹² of disaccharide 5 with donor 6 did not afford desired trisaccharide 7, probably due to the instability of 2,6-dideoxy glycosyl phenylsulfide toward the Lewis acid, such as TBSOTf.

Scheme 1. Attempted synthesis of 2-deoxy trisaccharide of landomycin A/E.

2.2 Revised strategy

Based on this observation, we decided to slightly modify aforementioned synthetic strategy for the synthesis of trisaccharide glycal **8** of landomycin A/E. As shown in **Scheme 2**, the 2-deoxy trisaccharide glycal **8** may be prepared via glycosylation between donor **6** and disaccharide acceptor **9**. We speculated that the disaccharide **9** bearing 6-deoxy glycosyl phenylsulfide should be more stable towards Lewis acid than disaccharide **5** bearing 2,6-dideoxy glycosyl phenylsulfide. In turn, disaccharide acceptor **9** should be obtained via anomeric *O*-alkylation of lactol **10**²⁵ with D-fucose-derived C4-triflate **11** following our recently developed protocol.²⁴

Scheme 2. Retrosynthesis of 2-deoxy trisaccharide glycal of landomycin A/E.

2.3 Synthesis of 2-deoxy trisaccharide glycal of landomycin A/E

Starting from β -D-galactose pentaacetate **12**, D-fucose-derived C4-alcohol **13** was obtained in seven steps according to the known procedure.²⁶ Triflation of the C4-*axial* alcohol of **13** provided the corresponding triflate **11**. With this triflate acceptor **11** in hand, we next explored

the key β -selective glycosylation between known lactol **10**²⁵ and C4-triflate **11** via anomeric *O*-alkylation.²⁴ Under our optimal condition, β -selective anomeric *O*-alkylation of lactol **10** with C4-triflate **11** in 1,4-dioxane at room temperature afforded desired disaccharide **9** in 40% yield (56% based on recovered donor **10**) (**Scheme 3**). The β -configuration of newly formed 2-deoxy glycosidic linkage in **9** was unambiguously confirmed by the analysis of the coupling constant of H^{1'}_{ax} and H^{2'}_{ax} (J (H^{1'}, H^{2'}_{ax}) = 9.6 Hz). Disaccharide **9** was produced in relatively lower yield (40%), probably because of the lower reactivity of triflate **11** as compared to those 2-deoxy sugar-derived triflates.²⁴ Disaccharide **9** bearing a free alcohol at C3' was then directly subjected to TBSOTf-catalyzed glycosylation¹² with L-rhodinose-derived donor **6**. Gratifyingly, desired product trisaccharide **14** was obtained in 88% yield.

Scheme 3. Synthesis of trisaccharide **14**.

Next, trisaccharide **14** was treated with LiDBB (lithium di-*tert*-butylbiphenylide) to effect reductive debenzoylation and concomitant reductive lithiation-elimination^{27,28} to afford trisaccharide glycal **16** in 88% yield (**Scheme 4**). Presumably, trisaccharide **14** first underwent debenzoylation and concomitant reductive lithiation to furnish intermediate **15** which upon 1,2-elimination led to the formation of trisaccharide glycal **16**. Finally, tetra-*n*-butylammonium fluoride-mediated deprotection of *tert*-butyldimethylsilyl ether of **16** provided the desired target, trisaccharide glycal **8** in 61% yield (93% yield based on recovered starting material **16**).

Scheme 4. Synthesis of 2-deoxy trisaccharide glycal of landomycin A/E.

3. Conclusion

In conclusion, we have described a concise synthesis of the 2-deoxy trisaccharide glycal of antitumor antibiotics landomycins A and E. The synthesis features a β -selective anomeric *O*-alkylation for the preparation of 2-deoxy β -linked disaccharide, a *tert*-butyldimethylsilyl triflate-catalyzed α -selective L-rhodosylation, and a lithium 4,4'-di-*tert*-butylbiphenyl-mediated reductive debenzoylation and concomitant reductive lithiation-elimination for the production of the 2-deoxy trisaccharide glycal. This effort will facilitate our comparative chemical and biological studies of *O*-linked and *S*-linked 2-deoxy glycosides.

4. Experimental

4.1 Materials and Methods

Proton and carbon nuclear magnetic resonance spectra (^1H NMR and ^{13}C NMR) were recorded on either Bruker 600 (^1H NMR-600 MHz; ^{13}C NMR 150 MHz) at ambient temperature with CDCl_3 as the solvent unless otherwise stated. Chemical shifts are reported in parts per million relative to residual protic solvent internal standard CDCl_3 : ^1H NMR at δ 7.26, ^{13}C NMR at δ 77.36. Data for ^1H NMR are reported as follows: chemical shift, integration, multiplicity (app = apparent, par obsc = partially obscure, ovrlp = overlapping, s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartet, m = multiplet) and coupling constants in Hertz. All ^{13}C NMR spectra were recorded with complete proton decoupling. Low resolution mass spectra (LRMS) were acquired on a Waters Acuity Premiere XE TOF LC-MS by electrospray ionization. Optical rotations were measured with Autopol-IV digital polarimeter; concentrations are expressed as g/100 mL.

All reagents and chemicals were purchased from Acros Organics, Sigma Aldrich, Fisher Scientific, Alfa Aesar, and Strem Chemicals and used without further purification. THF, methylene chloride, toluene, and diethyl ether were purified by passing through two packed columns of neutral alumina (Innovative Technology). Anhydrous DMF and benzene were purchased from Acros Organics and Sigma-Aldrich and used without further drying. All reactions were carried out in oven-dried glassware under an argon atmosphere unless otherwise

noted. Analytical thin layer chromatography was performed using 0.25 mm silica gel 60-F plates. Flash column chromatography was performed using 200-400 mesh silica gel (Scientific Absorbents, Inc.). Yields refer to chromatographically and spectroscopically pure materials, unless otherwise stated.

4.2 Synthesis of phenyl 2,3-di-*O*-benzyl-4-*O*-trifluoromethanesulfonyl-1-thio- β -D-fucopyranoside (11).

To a mixture of known phenyl 2,3-di-*O*-benzyl-1-thio- β -D-fucopyranoside **13**²⁶ (1.0 g, 2.29 mmol) in 12 mL methylene chloride and pyridine (1.9 mL, 22.9 mmol) cooled at 0°C was added triflic anhydride (0.8 mL, 4.6 mmol) dropwise. The resulting mixture was stirred at 0°C for 1 hour and then quenched with ice water. The organic layer was separated and the aqueous layer was extracted with methylene chloride. The combined organic layer was washed sequentially with saturated aqueous copper sulfate solution and water, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo to afford 1.21 g (93% yield) of phenyl 2,3-di-*O*-benzyl-4-*O*-trifluoromethanesulfonyl-1-thio- β -D-fucopyranoside (**11**). ¹H NMR (600 MHz, CDCl₃) δ 7.61 - 7.58 (m, 2 H, aromatic of SPh), 7.40 - 7.30 (m, 13 H, aromatic), 5.08 (d, *J* = 2.1 Hz, 1 H, H⁴), 4.90 (d, *J* = 11.4 Hz, 1 H, benzylic), 4.81 (d, *J* = 10.2 Hz, 1 H, benzylic), 4.75 (d, *J* = 10.2 Hz, 1 H, benzylic), 4.68 - 4.62 (ovrlp, 2 H, one benzylic and H¹), 3.78 (q, *J* = 6.6 Hz, 1 H, H⁵), 3.72 - 3.68 (ovrlp, 2 H, H² and H³), 1.43 (d, *J* = 6.6 Hz, 1 H, CH₃). ¹³C NMR (150 MHz, CDCl₃) δ 137.8, 136.9, 133.0, 132.3, 129.0, 128.53, 128.48, 128.4, 128.3, 128.2, 128.1, 127.98, 127.95, 127.9, 121.7, 119.6, 117.5, 115.4, 87.6, 85.7, 79.9, 75.9, 75.8, 73.1, 72.3, 53.5, 17.1.

4.3 Synthesis of phenyl 4-*O*-benzyl-2,6-dideoxy- β -D-arabino-hexapyranosyl-(1 $\rightarrow$ 4)-2,3-di-*O*-benzyl-1-thio- β -D-fucopyranoside (**9**).

To a solution of known lactol donor **10**²⁵ (93.5 mg, 0.39 mmol) in 1.0 mL 1, 4-dioxane was added NaH (60 % dispersion in mineral oil, 47 mg, 1.17 mmol) and the resulting mixture was stirred for 10 minutes. A solution of triflate **11** (446 mg, 0.78 mmol) in 2.0 mL 1, 4-dioxane was added followed by addition of 15-crown-5 (0.12 mL, 0.59 mmol). The reaction mixture was stirred at room temperature for 24 hours. After removing most of the 1,4-dioxane by air flow, the crude residue was diluted with dichloromethane and purified by preparative thin layer chromatography (Hexanes:EtOAc = 2:1) to furnish 103 mg (40% yield) of phenyl 4-*O*-benzyl-2,6-dideoxy- β -D-arabino-hexapyranosyl-(1 $\rightarrow$ 4)-2,3-di-*O*-benzyl-1-thio- β -D-fucopyranoside (**9**). During the purification, 27 mg of unreacted lactol donor **10** was recovered (yield of **9** based on recovered lactol donor **10** was 56%). $[\alpha]_D^{22} = 7.9^\circ$ (*c* = 1.0, CHCl₃). ¹H NMR (600 MHz, CDCl₃) δ 7.58 - 7.54 (m, 2 H, aromatic of SPh), 7.43 - 7.29 (m, 18 H, aromatic), 5.07 (d, *J* = 10.8 Hz, 1 H, benzylic), 4.85 (d, *J* = 10.1 Hz, 1 H, benzylic), 4.82 - 4.77 (m, 2 H, benzylic), 4.75 (d, *J* = 10.1 Hz, 1 H, benzylic), 4.73 (dd, *J* = 1.8, 9.6 Hz, 1 H, H¹), 4.69 (d, *J* = 11.4 Hz, 1 H, benzylic), 4.67 (d, *J* = 9.9 Hz, 1 H, H¹), 3.72 - 3.65 (m, 1 H, H³), 3.64 (t, *J* = 9.9 Hz, 1H, H³), 3.48 (t, *J* = 9.9 Hz, 1H, H²), 3.46 - 3.40 (m, ovrlp, 2 H, H⁴ and H⁵), 3.34 - 3.24 (m, 1 H, H⁵), 2.98 (t, *J* = 9.0 Hz, 1 H, H⁴), 2.26 (ddd, *J* = 1.8, 4.8, 12.3 Hz, 1 H, H² eq), 2.13 (br, s, 1 H, OH), 1.70 - 1.57 (m, 1 H, H² ax), 1.37 (d, *J* = 5.5 Hz, 3 H, C⁶-CH₃), 1.30 (d, *J* = 5.5 Hz, 4 H, C⁶-CH₃). ¹³C NMR (150 MHz, CDCl₃) δ 138.9, 138.1, 133.7, 132.0, 128.9, 128.8, 128.4, 128.3, 128.24, 128.19, 128.0, 127.8, 127.76, 127.5, 127.49, 100.3, 87.4, 85.9, 85.3, 82.0, 80.8, 77.3, 77.1, 76.8, 75.6, 75.5, 75.47, 75.2, 71.6, 71.0, 39.2, 18.3, 18.29. FT-IR (thin film): 3559, 2875, 1733, 1481, 1454, 1362, 1128, 1094, 1066, 734 cm⁻¹. ESI-LRMS [M+Na]⁺ calculated for C₃₉H₄₄NaO₇S 679.28, found 679.20.

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4.4 Synthesis of phenyl 4-*O*-*tert*-butyldimethylsilyl- α -L-rhodinosyl-(1 $\rightarrow$ 3)-4-*O*-benzyl-2,6-dideoxy- β -D-*arabino*-hexapyranosyl-(1 $\rightarrow$ 4)-2,3-di-*O*-benzyl-1-thio- β -D-fucopyranoside (14).

A mixture of donor **6** (52 mg, 0.18 mmol), disaccharide **9** (59 mg, 0.09 mmol), and 4 Å molecular sieves (160 mg) in 2 mL dry methylene chloride was stirred at room temperature for 10 minutes before being cooled to -78 °C. *tert*-Butyldimethylsilyl triflate (TBSOTf) (1.6 μ L, 0.01 mmol) was added and the mixture was stirred at -78 °C for one hour before being quenched with Et₃N (0.6 mL) at -78 °C and diluted with ethyl acetate. Molecular sieves were filtered off and the reaction mixture was concentrated under vacuo. The crude mixture was purified by column chromatography (Hexanes:EtOAc = 20:1 to 10:1) to furnish 70.0 mg (88% yield) of phenyl 4-*O*-*tert*-butyldimethylsilyl- α -L-rhodinosyl-(1 $\rightarrow$ 3)-4-*O*-benzyl-2,6-dideoxy- β -D-*arabino*-hexapyranosyl-(1 $\rightarrow$ 4)-2,3-di-*O*-benzyl-1-thio- β -D-fucopyranoside (**14**). $[\alpha]_D^{22} = -8.8^\circ$ ($c = 1.0$, CHCl₃). ¹H NMR (600 MHz, CDCl₃) δ 7.57 - 7.54 (td, $J = 1.5, 6.8$ Hz, 2 H, aromatic of SPh), 7.42-7.27 (m, 18 H, aromatic), 5.07 (d, $J = 10.2$ Hz, 1 H, benzylic), 5.02 (br, 1 H, H^{1''}), 4.91 (d, $J = 11.1$ Hz, 1 H, benzylic), 4.83 (d, $J = 10.8$ Hz, 1 H, benzylic), 4.77 (d, $J = 10.5$ Hz, 1 H, benzylic), 4.73 (d, $J = 10.2$ Hz, 1 H, benzylic), 4.70 (d, $J = 10.2$ Hz, 1 H, benzylic), 4.68 (dd, $J = 1.2, 9.6$ Hz, 1 H, 1 H, H^{1'}), 4.65 (d, $J = 9.9$ Hz, 1 H, H^{1'}), 3.94- 3.85 (m, 2 H, H^{3'}, H^{5''}), 3.61 (t, $J = 8.7$ Hz, 1 H, H^{3'}), 3.50 - 3.43 (m, 2 H, H^{2'} and H^{4'}), 3.42-3.38 (m, 2 H, H^{4''} and H^{5'}), 3.34 - 3.30 (m, 1 H, H^{5''}), 3.11 - 3.06 (t, $J = 9.0$ Hz, 1 H, H^{4'}), 2.46 - 2.41 (m, 1 H, H^{2'}ax), 2.13 - 2.06 (m, 1 H, H^{2''}), 2.00 - 1.93 (m, 1 H, H^{3''}), 1.65 - 1.58 (m, 1 H, H^{3''}), 1.49 - 1.41 (m, 2 H, H^{2'}eq, H^{2''}), 1.36 - 1.33 (d, $J = 6.0$ Hz, 3 H, C^{6'}-CH₃), 1.25 - 1.22 (d, $J = 6.0$ Hz, 3 H, C^{6''}-CH₃), 1.03 - 1.00 (d, $J = 6.4$ Hz, 3 H, C^{6''}-CH₃), 0.94 (s, 9 H, ^tBu-TBS), 0.06 (s, 3 H, CH₃-TBS), 0.05 (s, 3 H, CH₃-TBS). ¹³C NMR (150 MHz, CDCl₃) δ 138.9, 138.5, 138.2, 133.7, 132.0, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 127.5, 127.4, 100.2, 91.7, 87.4, 85.3, 83.0, 81.8, 80.7, 75.6, 75.5, 75.3, 72.5, 71.7, 67.6, 66.8, 35.9, 26.4, 25.9, 23.5, 18.4, 18.2, 17.6, -4.61, -4.93. FT-IR (thin film): 2931, 2861, 1750, 1454, 1362, 1213, 1077 cm⁻¹. ESI-LRMS [M+Na]⁺ calculated for C₅₁H₆₈NaO₉SSi 907.43, found 907.30.

4.5 Synthesis of 4-*O*-*tert*-butyldimethylsilyl- α -L-rhodinosyl-(1 $\rightarrow$ 3)-2,6-dideoxy- β -D-*arabino*-hexapyranosyl-(1 $\rightarrow$ 4)-1,5-anhydro-2,6-dideoxy-D-*arabino*-hex-1-enitol (16).

To phenyl 4-*O*-*tert*-butyldimethylsilyl- α -L-rhodinosyl-(1 $\rightarrow$ 3)-4-*O*-benzyl-2,6-dideoxy- β -D-*arabino*-hexapyranosyl-(1 $\rightarrow$ 4)-2,3-di-*O*-benzyl-1-thio- β -D-fucopyranoside (**14**) (113 mg, 0.13 mmol) in 1.0 mL anhydrous THF cooled at -20 °C was added 0.4 M LiDBB in THF until the colour of the mixture became dark green (approximately 4.0 mL). The mixture was quenched with saturated NaHCO₃. THF was removed under vacuo and the crude mixture was extracted with EtOAc (20 mL) three times. The organic layer was combined, washed with brine, dried with sodium sulphate, filtered, and concentrated in vacuo. The crude mixture was purified by column chromatography (hexanes: ethyl acetate = 10:1 to 3:1) to furnish 55 mg (88% yield) of 4-*O*-*tert*-butyldimethylsilyl- α -L-rhodinosyl-(1 $\rightarrow$ 3)-2,6-dideoxy- β -D-*arabino*-hexapyranosyl-(1 $\rightarrow$ 4)-1,5-anhydro-2,6-dideoxy-D-*arabino*-hex-1-enitol (**16**). $[\alpha]_D^{22} = -31.2^\circ$ ($c = 1.0$, CHCl₃). ¹H NMR (600 MHz, CDCl₃) δ 6.32 (dd, $J = 1.8, 6.0$ Hz, 1 H, H^{1'}), 4.95 (b s, 1 H, H^{1''}), 4.79 (dd, $J = 2.4, 6.3$ Hz, 1 H, H^{2'}), 4.59 - 4.55 (m, 3 H, H^{1'}, C3-OH, C4'-OH), 4.28 (td, $J = 1.8, 7.2$ Hz, 1 H, H^{3'}), 4.05 (dq, $J = 1.8, 6.0$ Hz, 1 H, H^{5''}), 3.89 - 3.84 (m, 1 H, H^{5'}), 3.65 (b s, 1 H, H^{4''}), 3.55 - 3.51 (m, 1 H, H^{3'}), 3.43 - 3.38 (m, 1 H, H^{5'}), 3.31 (dd, $J = 7.2, 10.2$ Hz, 1 H, H^{4'}), 3.13 (t, $J = 8.7$ Hz, 1 H, H^{4'}), 2.28 (ddd, $J = 2.1, 5.4, 12.9$ Hz, 1 H, H^{2'}ax), 2.16 - 2.11 (m, 1 H, H^{2''}), 2.01-1.95 (m, 1 H,

H^{3''}), 1.74 – 1.69 (m, 1 H, H^{3''}), 1.68-1.63 (m, 1 H, H^{2'eq}), 1.55 – 1.49 (m, 1 H, H^{2''}), 1.42 (d, J = 6.0 Hz, 3 H, C^{6'}-CH₃), 1.35 (d, J = 6.0 Hz, 3 H, C⁶-CH₃), 1.18 (d, J = 6.0 Hz, 3 H, C^{6''}-CH₃), 0.94 (s, 9 H, ^tBu-TBS), 0.09 (s, 3 H, CH₃-TBS), 0.08 (s, 3 H, CH₃-TBS). ¹³C NMR (150 MHz, CDCl₃) δ 143.8, 102.4, 101.0, 97.6, 86.0, 80.5, 75.2, 72.7, 72.3, 68.7, 68.3, 67.6, 37.0, 25.9, 24.5, 18.2, 17.8, 17.4, 17.3, -4.6, -4.9. FT-IR (thin film): 3442, 2938, 2858, 1656, 1453, 1255, 1120 cm⁻¹. ESI-LRMS [M+Na]⁺ calculated for C₂₄H₄₄NaO₈Si 511.28, found 511.30.

4.6 Synthesis of α -L-Rhodinosyl-(1 $\rightarrow$ 3)-2,6-dideoxy- β -D-arabino-hexapyranosyl-(1 $\rightarrow$ 4)-1,5-anhydro-2,6-dideoxy-D-arabino-hex-1-enitol (**8**).

To 4-*O*-*tert*-Butyldimethylsilyl- α -L-rhodinosyl-(1 $\rightarrow$ 3)-2,6-dideoxy- β -D-arabino-hexapyranosyl-(1 $\rightarrow$ 4)-1,5-anhydro-2,6-dideoxy-D-arabino-hex-1-enitol (**16**) (43 mg, 0.088 mmol) in 1.0 mL THF was added tetra-*n*-butylammonium fluoride (1.0 M, 0.13 mL) and the mixture was stirred at room temperature overnight. Saturated NaHCO₃ was added and the mixture was extracted with ethyl acetate. The organic layer was combined, dried with sodium sulphate, filtered, and concentrated in vacuo. The crude mixture was purified by column chromatography (CH₂Cl₂: MeOH = 40:1 to 20:1) to furnish 20 mg (61%) of α -L-rhodinosyl-(1 $\rightarrow$ 3)-2,6-dideoxy- β -D-arabino-hexapyranosyl-(1 $\rightarrow$ 4)-1,5-anhydro-2,6-dideoxy-D-arabino-hex-1-enitol (**8**). During the purification, 15 mg unreacted starting material **16** was recovered (yield of **8** based on recovered starting material **16** was 93%). $[\alpha]_D^{22} = -36.7^\circ$ (c = 1.0, CHCl₃). ¹H NMR (600 MHz, CDCl₃) δ 6.32 (dd, J = 1.5, 6.0 Hz, 1 H, H¹), 4.98 (b s, 1 H, H^{1''}), 4.79 (dd, J = 2.2, 6.2 Hz, 1 H, H²), 4.58 (dd, J = 2.1, 10.2 Hz, 1 H, H¹), 4.56 (b, s, 1H, C3-OH), (4.42 (b s, 1 H, C4'-OH), 4.28 (td, J = 1.8, 7.2 Hz, 1 H, H³), 4.17 (ddd, J = 1.8, 6.6, 13.2 Hz, 1 H, H^{5''}), 3.90 – 3.84 (m, 1 H, H⁵), 3.67 (b s, 1 H, H^{4''}), 3.58 – 3.54 (m, 1 H, H^{3'}), 3.49 – 3.43 (m, 1 H, H^{5'}), 3.30 (dd, J = 7.2, 10.2 Hz, 1 H, H⁴), 3.15 (t, J = 8.7 Hz, 1 H, H^{4'}), 2.29 (ddd, J = 2.1, 5.4, 12.9 Hz, 1 H, H²ax), 2.12 – 2.01 (m, 2 H, H^{3''}, H^{2''}), 1.84-1.78 (m, 1 H, H^{3''}), 1.75 – 1.69 (m, 1 H, H^{2'eq}), 1.63 – 1.58 (m, 1 H, H^{2''}), 1.42 (d, J = 6.0 Hz, 3 H, C^{6'}-CH₃), 1.35 (d, J = 6.0 Hz, 3 H, C⁶-CH₃), 1.25 (d, J = 6.0 Hz, 3 H, C^{6''}-CH₃). ¹³C NMR (150 MHz, CDCl₃) δ 143.8, 102.4, 100.9, 97.6, 85.9, 80.5, 75.2, 72.7, 72.2, 68.3, 67.7, 67.1, 36.9, 25.5, 24.1, 17.8, 17.4, 17.3, 17.1. FT-IR (thin film): 3401, 2973, 2938, 2890, 1654, 1448, 1384, 1226, 1120, 1071. ESI-LRMS [M+Na]⁺ calculated for C₁₈H₃₀NaO₈ 397.19, found 397.20.

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Appendix: Supplementary material

Supplementary data to this article can be found online at XXXXXX.

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Synthesis of the 2-Deoxy Trisaccharide Glycal of Antitumor Antibiotics Landomycins A and E

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