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Synthesis of an Adenine Nucleoside Containing the (8′*R*) Epimeric Carbohydrate Core of Amipurimycin and Its Biological Study

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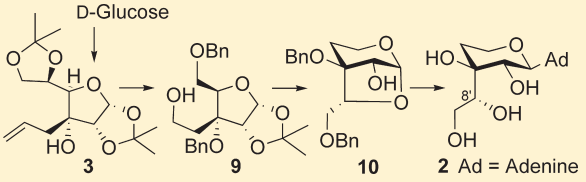
Supporting Information

ABSTRACT: The (8′*R*) epimeric carbohydrate core **2** of amipurimycin was synthesized from D-glucose derived allylic alcohol **3** in 11 steps and 13% overall yield. The key steps involve an acid-catalyzed acetonide ring opening of **9** with concomitant formation of an unprecedented pyranose ring skeleton to give 2,7-dioxabicyclo-[3.2.1]octane **10**. The α-orientation of the furan ring in **10** readily allows the stereoselective β-glycosylation and opening of the furanose ring that on removal of protecting groups affords the pyranosyl adenine nucleoside **2**. The antifungal and anticancer activities of **2** were studied.



The peptidyl nucleoside antibiotic amipurimycin **1** (Figure 1), isolated from *Streptomyces novoguineensis* sp. nov., shows activity against *Pyricularia oryzae*, a causative agent for rice blast disease.[1] On the basis of the chemical degradation, Goto et al.[2] have assigned the primary structure of amipurimycin that includes (a) a unique carbohydrate ring skeleton having a quaternary center at C-3′ bearing a hydroxy group and a branched 1,2-dihydroxyethyl side chain, (b) a glycosidic β-linked purine nucleobase at the anomeric carbon, and (c) an amino acid at C-5′ attached at its *N*-terminus to *cis*-pentacin with undefined absolute configurations at C-6′ and in the aminocyclopentane ring.[3] Different strategies for the synthesis of pyranosyl sugar cores of amipurimycin with/without C-3′ side chain, nucleobase, and peptidyl region at C-6′ are known.[4] As a part of our continuing efforts in the sugar chemistry,[5] we are now reporting the synthesis of the hitherto unknown (8′*R*) epimeric pyranosyl adenine nucleoside analogue **2**, representing a carbohydrate core of amipurimycin with C-3′ dihydroxyethyl side chain, and the study of its antifungal and anticancer activity.

Our retrosynthetic analysis (Scheme 1) suggested that acetylated 2,7-dioxabicyclo[3.2.1]octane **A** would allow the stereoselective β-glycosylation with concomitant opening of the furan ring to give pyranosyl nucleoside **2**. We envisaged the formation of the bridged bicyclic system **A** upon opening of the 1,2-acetonide functionality in **B** under acidic conditions, followed by addition of the alkoxy side chain at C-3 to the in situ generated oxocarbenium ion intermediate. Intermediate **B** could be obtained from the D-glucose derived homoallylic alcohol **3** by dihydroxylation, oxidation, and reduction protocol.

As shown in Scheme 2, D-glucose was converted to the known alcohol **3** having a well-defined quaternary center and requisite hydroxyl and allyl groups.[6] Selective 5,6-acetonide deprotection in **3** using 30% $HClO_4$ in THF gave triol **4**, which on treatment with $NaIO_4$ afforded aldehyde **5**. Reduction of aldehyde functionality in **5** with $NaBH_4$ gave diol **6**, which on protection using benzyl bromide and sodium hydroxide afforded dibenzylated product **7**.[7] Dihydroxylation of the double bond in **7** using $K_2OsO_4 \cdot 2H_2O$ (5 mol %) and *N*-methylmorpholine-*N*-oxide (NMO) as co-oxidant followed by oxidative cleavage of the intermediate diol with $NaIO_4$ gave aldehyde **8**. Reduction of **8** using $NaBH_4$ followed by hydrolysis of 1,2-acetonide group in **9** with TFA/water (3:1) provided **10** with the desired 2,7-dioxabicyclo[3.2.1]octane framework as a single product (overall 34% yield from **3**). Acetylation of **10** using Ac_2O and pyridine gave monoacetyl derivative **11**. The chemical shift assignments and coupling constant values in the ^1H NMR of **11** were obtained from the decoupling experiments. In the ^1H NMR spectrum of **11**, the H-1 and H-2 protons appeared as two singlets at δ 5.26 and δ 4.95, respectively. The absence of vicinal coupling constant between H-1 and H-2 requires the dihedral angle between these protons to be approximately 90°. As the absolute configuration (*R*) at the C-2 in **9** is retained in the bicyclic system **10**, the H-2 was given the axial position, and therefore the H-1 was assigned the equatorial orientation. This is in agreement with the attack of primary hydroxyl side chain at C-3 from the β-face forcing the H-1 into the equatorial position. The little twist in the chair conformation, due to the bridged system, arranges the dihedral angle between the H-1 and H-2 close to 90° accounting for the absence of a coupling constant.

The formation of anomeric anhydro sugar **10** can be explained as follows. Under acidic conditions, opening of the 1,2-acetonide

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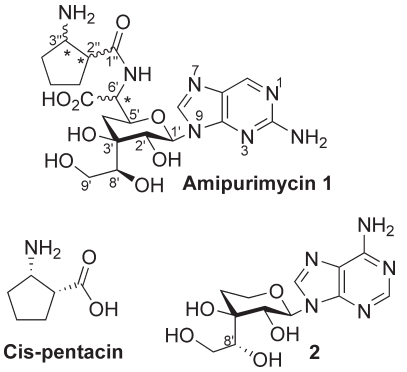
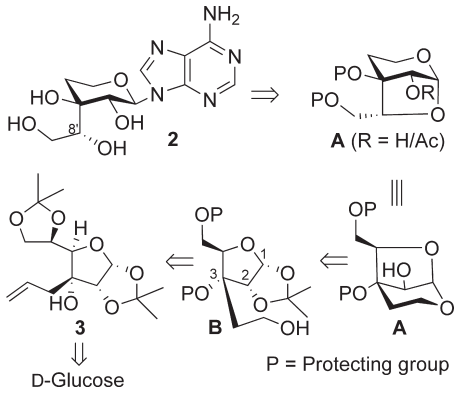


Figure 1. Structures of amipurimycin **1**, *cis*-pentacin, and pyranosyl nucleoside **2**.

Scheme 1. Retrosynthesis of 2

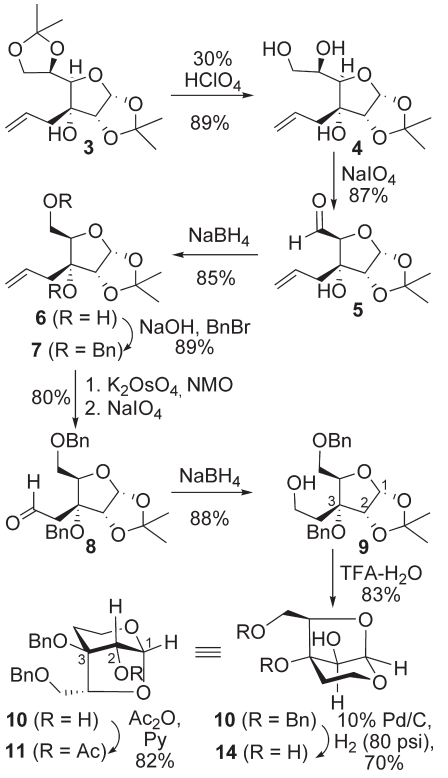


functionality in **9** results in the generation of an oxocarbenium ion **Y** (Scheme 3), which could be attacked either reversibly by water to give rise to a hemiacetal or irreversibly by the primary alcohol to yield **10**. We suggest that the attack of the primary alcohol to the C-1 position of the oxocarbenium ion **Y** in an intramolecular and irreversible manner gives rise to a stable pyranose ring shifting the equilibrium in favor of the bridged bicyclic system **10**.

In the next step, the acetyl derivative **11** was glycosylated using a protocol developed by Zou and Robins[8] (Scheme 4). This one-pot process involves the stereoselective formation of the β-oriented adenine nucleoside with concomitant opening of the furan ring unmasking the 1,2-dihydroxyethyl side chain to give **12**. The large coupling constant between the H-1′ and H-2′ (J = 8.4 Hz) in the ^{1}H NMR spectrum of **12** indicated their diaxial orientation, confirming the stereoselective opening of the bridged system by the attack of the adenine nucleobase from the β-face, which is being assisted either by the α-orientated furanose ring at C-3′ or by the acetoxy group at C-2′.

In the final steps, hydrolysis of the acetyl and *N*-benzoyl protecting groups in **12** using 1 N NaOH yielded nucleoside **13** in good yield. Hydrogenation of **13** with 10% Pd/C at 80 psi in methanol at room temperature for 12 h unexpectedly afforded compound **14** (Scheme 2) and not the desired pyranosyl nucleoside **2**. This one-pot three-step process involves cleavage of the benzyl groups and restoration of the bridged bicyclic system **14** with concurrent cleavage of the glycosidic bond.[9] To confirm the

Scheme 2. Synthesis of 11 and 14



structure of **14**, it was alternatively obtained from the previously synthesized **10** by hydrogenation (10% Pd/C, 80 psi, methanol) (Scheme 2). Alternatively, hydrogenation of **13** with 10% Pd-$(OH)_2$ in methanol under balloon pressure afforded the fully deprotected pyranosyl nucleoside **2** in 77% yield.

The antifungal activity of the pyranosyl nucleoside **2** against seven different pathogenic fungi, *Candida tropicalis*, *Candida albicans*, *Fusarium oxysporum*, *Phoma exigua*, *Aspergillus oryzae*, *Helminthosporium graminium*, *Trichoderma resei*, and *Cladosporium herbarum*, was determined. Nystatin, a known antifungal drug, was used as reference.[10] Compound **2** did not exhibit significant antifungal activity against any of the fungal pathogens as compared to Nystatin, pointing toward the *cis*-pentacin core as the active principle for the antifungal activity found in **1**. Indeed, *cis*-pentacin has pronounced antifungal activity[3] and has been an important lead structure for the development of novel antifungal agents. The in vitro cytotoxicity of the pyranosyl nucleoside **2** against HeLa (human epithelial cervical cancer) cell lines was determined at a concentration range of 2.5−100 μM at different times (24−96 h).[11] The 3-(4,5-dimethyl-thiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT) colorimetric assay was used to determine growth inhibition[12] and percentage of inhibition was calculated and statistically analyzed.[5a] As shown in Figure 2, compound **2** exhibited maximum activity during 96 h, highest being 72.8 ± 1.7% at 100 μM. Our results were compared with the Mitomycin C, a known anticancer drug as standard reference, which showed 50% inhibition at 5 μM. As compound **2** showed 52.63% inhibition at 20 μM, it was found to be four times less active than the Mitomycin C.

In conclusion, we have exploited the carbon skeleton of D-glucose to construct the pyranose ring skeleton with a C-3

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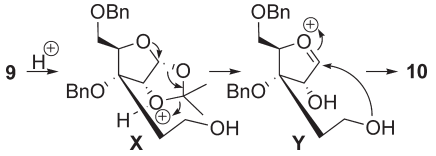
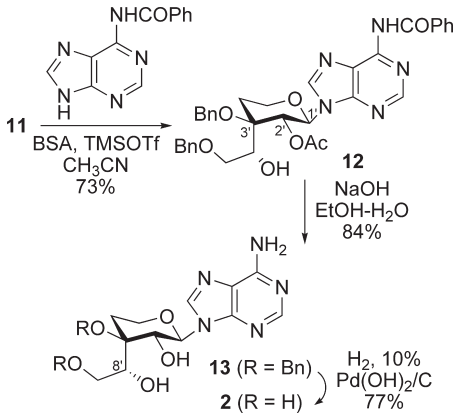
Scheme 3. Formation of 10



Scheme 4. Synthesis of 2



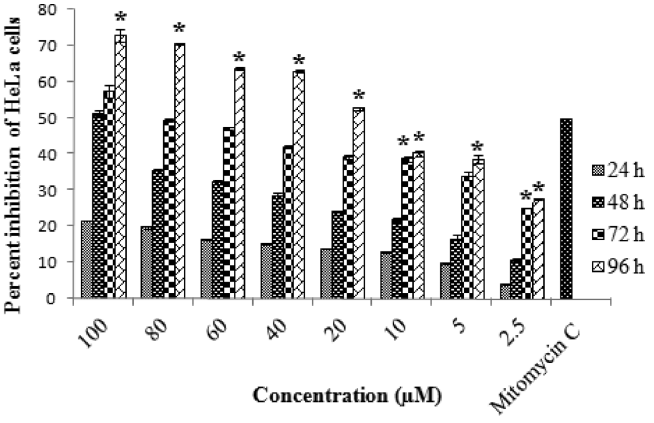


Figure 2. Anti-proliferative activity of compound **2** against HeLa cells incubated with different concentrations at different times (24−96 h). The data are expressed as a percentage of the control MTT reduction (always taken as 100%) and represent the average ± SEM (n = 3). * denotes more significant value ($P < 0.05$).[13]

dihydroxyethyl side chain. A unique feature of our strategy is (a) the acid-catalyzed closing of the pyran ring utilizing a hydroxyethyl residue of the sugar furanose ring in **9** to get the bicyclic ring system **10** and (b) β-selective opening of the sugar furanose ring in **10** with adenine nucleobase, giving the (8′R) epimeric carbohydrate core **2** of amipurimycin. The pyranosyl adenine nucleoside **2** showed potent anticancer activity against HeLa cells.

EXPERIMENTAL SECTION

(1*S*,5*R*,6*R*,8*R*)-5-*O*-Benzyl-6-benzyloxymethyl-8-hydroxy-2,7-dioxabicyclo[3.2.1]octane (10)[14]**.** A solution of **9** (0.40 g, 0.94 mmol) in TFA−water (5 mL, 3:1) was stirred for 3 h at 0 °C to rt. TFA was coevaporated with toluene. Purification by column chromatography (n-hexane/ethyl acetate = 7/3) furnished **10** (0.30 g, 83%) as a viscous liquid: R_f 0.61 (n-hexane/ethyl acetate = 3/2); $[\alpha]^{25}_D$ +8.1 (c 0.5, $CHCl_3$); IR ($CHCl_3$) 3500−3000 (br) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.60 (br s, 1H), 1.77 (dd, J = 13.2, 4.8 Hz, 1H), 2.05−2.20 (m, 1H), 3.75−3.96 (m, 5H), 4.40−4.45 (m, 1H), 4.48 (d, J = 11.4 Hz, 1H), 4.58 (ABq, J = 12.0 Hz, 2H), 4.63 (d, J = 11.4 Hz, 1H), 5.24 (s, 1H), 7.20−7.40 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.3, 59.0, 66.7, 67.5, 73.3, 80.0, 80.1, 81.2, 102.6, 127.4 (strong), 127.6 (strong), 127.7 (strong), 128.0 (strong), 128.4 (strong), 128.6 (strong), 137.8, 137.9. Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79. Found: C, 70.92; H, 6.93.

(1*S*,5*R*,6*R*,8*R*)-5-*O*-Benzyl-6-benzyloxymethyl-8-acetoxy-2,7-dioxabicyclo[3.2.1]octane (11)[14]**.** To a solution of **10** (0.20 g, 0.56 mmol) in pyridine (2 mL) was added Ac_2O (0.10 mL, 1.12 mmol), and the mixture was stirred for 6 h. After concentration, residue was purified by column chromatography (n-hexane/ethyl acetate = 9/1) to give **11** (0.18 g, 82%) as a solid: mp 72−74 °C; R_f 0.81 (n-hexane/ethyl acetate = 7/3); $[\alpha]^{25}_D$ +15.5 (c 1.4, $CHCl_3$); IR ($CHCl_3$) 1739 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.76 (dd, J = 12.9, 4.8 Hz, 1H), 2.10 (s, 3H), 2.24−2.38 (m, 1H), 3.70−4.00 (m, 4H), 4.42−4.48 (m, 1H), 4.43 (ABq, J = 11.1, 2H), 4.56 (ABq, J = 12.3, 2H), 4.95 (s, 1H), 5.26 (s, 1H), 7.18−7.38 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 29.8, 58.8, 67.0, 67.2, 73.2, 76.0, 80.0, 80.6, 101.1, 127.2 (strong), 127.5 (strong), 127.6 (strong), 128.2 (strong), 137.7, 169.8. Anal. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.58; H, 6.76.

Pyranosyl Nucleoside (12). *N*,*O*-Bis(trimethylsilyl)acetamide (0.74 mL, 3.01 mmol) was added to a solution of *N*-benzoyl adenine (0.25 g, 1.05 mmol) in dry acetonitrile (4 mL), the reaction mixture was stirred for 20 min and cooled to 0 °C, a solution of **11** (0.40 g, 1.00 mmol) in dry acetonitrile (3 mL) and TMSOTf (0.19 mL, 1.00 mmol) was added dropwise at 0 °C, and the resulting solution was stirred for 10 h at 50 °C. The reaction mixture was cooled to 0 °C, and chloroform (10 mL) and then saturated aq $NaHCO_3$ solution (5 mL) were added. The reaction mixture was extracted with chloroform (20 mL × 3), and the combined organic layers were extracted with brine and concentrated. Purification by column chromatography (n-hexane/ethyl acetate = 1/4) gave nucleoside **12** (0.47 g, 73%) as a viscous oil: R_f 0.56 (n-hexane/ethyl acetate = 1/9); $[\alpha]^{25}_D$ +12.2 (c 0.2, $CHCl_3$); IR ($CHCl_3$) 3300 (br), 1745 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.77 (s, 3H), 1.80−2.00 (br s, 1H), 2.10−2.23 (m, 1H), 2.23−2.35 (m, 1H), 3.55 (dd, J = 9.9, 6.3 Hz, 1H), 3.90 (dd, J = 9.9, 2.4 Hz, 1H), 3.95−4.07 (m, 1H), 4.28−4.65 (m, 6H), 5.76 (d, J = 8.4 Hz, 1H), 6.45 (d, J = 8.4 Hz, 1H), 7.08−7.38 (m, 10H), 7.42−7.67 (m, 3H), 8.02 (d, J = 7.2 Hz, 2H), 8.25 (s, 1H), 8.82 (s, 1H), 9.11 (br s, 1H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 30.0, 63.6, 64.5, 71.6, 72.7, 73.3, 75.0, 77.5, 81.4, 122.4, 127.5 (strong), 127.6 (strong), 127.7 (strong), 128.3 (strong), 128.7 (strong), 132.6, 133.7, 137.8, 141.1, 149.3, 151.8, 152.8, 164.5, 169.2. Anal. Calcd for $C_{35}H_{35}N_5O_7$: C, 65.92; H, 5.53. Found: C, 66.07; H, 5.66.

Pyranosyl Nucleoside (13). A solution of nucleoside **12** (0.5 g, 0.78 mmol) in ethanol−water (7:3, 10 mL) and NaOH (0.12 g, 3.13 mmol) was stirred at room temperature. After 24 h, the reaction mixture was neutralized with 1 N HCl, and the volume of the reaction mixture was reduced to half by evaporation at reduced pressure. The mixture was extracted with chloroform (10 mL × 3), and the combined organic layers were concentrated. Purification of the residue by column chromatography (n-hexane/ethyl acetate = 1/9) gave nucleoside **13** (0.32 g, 84%) as a white solid: mp 94−96 °C; R_f 0.38 (ethyl acetate); $[\alpha]^{25}_D$ −36.7 (c 0.5, $CHCl_3$); IR 3650−3050 (br) ($CHCl_3$) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.95−2.18 (m, 1H), 2.20−2.38 (br d, J = 12.9 Hz, 1H), 3.68−3.82 (m, 1H), 3.90−4.10 (m, 2H), 4.22−4.40 (m, 1H), 4.48−4.72 (m, 4H), 4.75−4.94 (m, 2H), 5.40−6.00 (br s, 2H), 6.12 (br s, 2H), 6.29 (d, J = 8.7 Hz, 1H), 7.18−7.38 (m, 10H), 7.79 (s, 1H), 8.12 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.6, 64.0, 65.3, 70.0, 72.1, 73.3,

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73.9, 78.1, 84.0, 118.3, 127.1 (strong), 127.3, 127.7, 127.8 (strong), 128.3 (strong), 128.4 (strong), 137.8, 138.8, 139.4, 149.3, 152.8, 154.6. Anal. Calcd for $C_{26}H_{29}N_5O_5$: C, 63.53; H, 5.95. Found: C, 63.79; H, 6.16.

(1*S*,5*R*,6*R*,8*R*)-5,8-Dihydroxy-6-hydroxymethyl-2,7-dioxabicyclo[3.2.1]octane (14)[14]**.** To a solution of **10** (0.50 g, 1.40 mmol) in methanol (15 mL) was added 10% Pd/C (0.20 g), and the solution was hydrogenated at 80 psi for 12 h. The catalyst was filtered off and washed with methanol, and the filtrate was concentrated. Purification by column chromatography (methanol/chloroform = 3/2) furnished **14** (0.17 g, 70%) as a viscous liquid: R_f 0.31 (methanol); $[\alpha]^{25}_D$ +6.9 (*c* 0.2, MeOH); IR (neat) 3500−2900 (br) cm^{-1}; ^1H NMR (300 MHz, D_2O) δ 1.88−2.08 (m, 2H), 3.72 (s, 1H), 3.84−3.95 (m, 3H), 4.03 (dd, *J* = 12.3, 9.0 Hz, 1H), 4.22 (br d, *J* = 8.4 Hz, 1H), 5.28 (s, 1H).; ^{13}C NMR (75 MHz, D_2O) δ 31.6, 58.6, 59.3, 75.2, 77.8, 80.5, 101.9. Anal. Calcd for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.97; H, 6.96.

Pyranosyl Nucleoside (2). To a stirred solution of nucleoside **13** (0.4 g, 0.80 mmol) in dry methanol (10 mL) was added 10% $Pd(OH)_2$ on carbon (0.05 g). The reaction mixture was flushed with hydrogen three times and stirred under a hydrogen atmosphere at balloon pressure. After 12 h, the catalyst was filtered through Celite, the filtrate was evaporated under reduced pressure, and the residue was purified by column chromatography (methanol/chloroform = 4/1) to give nucleoside **2** (0.18 g, 77%) as a viscous liquid: R_f 0.15 (methanol); $[\alpha]^{25}_D$ −13.7 (*c* 0.3, H_2O); IR (neat) 3600−2900 (br) cm^{-1}; ^1H NMR (300 MHz, D_2O) δ 1.94−2.05 (m, 1H), 2.36 (br d, *J* = 14.4 Hz, 1H), 3.78 (dd, *J* = 11.7, 8.1 Hz, 1H), 3.98−4.10 (m, 2H), 4.15 (br d, *J* = 10.8 Hz, 1H), 4.20 (dd, *J* = 8.1, 2.4 Hz, 1H), 4.32 (d, *J* = 9.3 Hz, 1H), 6.16 (d, *J* = 9.3 Hz, 1H), 8.21 (s, 1H), 8.38 (s, 1H); ^{13}C NMR (75 MHz, D_2O) δ 35.6, 65.2, 66.1, 74.7, 76.6, 77.8, 85.5, 121.0, 143.1, 151.3, 155.2, 158.0. Anal. Calcd for $C_{12}H_{17}N_5O_5$: C, 46.30; H, 5.50. Found: C, 46.57; H, 5.95.

■ ASSOCIATED CONTENT

Supporting Information. General experimental methods, experimental procedure, spectral and analytical data for compounds **4**, **5**, **6**, **7**, **8**, and **9** and copies of ^1H and ^{13}C NMR spectrum of compounds **4**, **5**, **6**, **7**, **8**, **9**, **10**, **11**, **12**, **13**, **14** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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DISCLOSURE

[⊥]Part of this work was carried out with Prof. Oliver Reiser, Institut fur Organische Chemie, Universität Regensburg, 93053 Regensburg, Germany under the INDIGO programme.

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■ REFERENCES

(1) (a) Iwasa, T.; Kishi, T.; Matsuura, K.; Wakae, O. *J. Antibiot.* **1977**, *30*, 1–10. (b) Harada, S.; Kishi, T. *J. Antibiot.* **1977**, *30*, 11–16.

(2) (a) Goto, T.; Toya, Y.; Ohgi, T.; Kondo, T. *Tetrahedron Lett.* **1982**, *23*, 1271–1274.

(3) (a) Iwamoto, T.; Tsujii, E.; Ezaki, M.; Fujie, A.; Hashimoto, S.; Okuhara, M.; Kohsaka, M.; Imanaka, H.; Kawabata, K. *J. Antibiot.* **1990**, *43*, 1–7. (b) Kawabata, K.; Inamoto, Y.; Sakane, K.; Iwamoto, T.; Hashimoto, S. *J. Antibiot.* **1990**, *43*, 513–518.

(4) (a) Stauffer, C. S.; Datta, A. *J. Org. Chem.* **2008**, *73*, 4166–4174. (b) Xue, J.; Guo, Z. *J. Carbohydr. Chem.* **2007**, *27* (2), 51–69. (c) Bhaket, P.; Stauffer, C. S.; Datta, A. *J. Org. Chem.* **2004**, *69*, 8594–8601. (d) Garner, P.; Yoo, J. U.; Sarabu, R.; Kennedy, V. O.; Youngs, W. J. *Tetrahedron* **1998**, *54*, 9303–9316. (e) Czernecki, S.; Franco, S.; Valery, J.-M. *J. Org. Chem.* **1997**, *62*, 4845–4847. (f) Czernecki, S.; Valery, J.-M.; Wilkens, R. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 1347–1351. (g) Rauter, A. P.; Fernandes, A. C.; Czernecki, S.; Valery, J.-M. *J. Org. Chem.* **1996**, *61*, 3594–3598. (h) Casiraghi, G.; Colombo, L.; Rassu, G.; Spanu, P. *J. Org. Chem.* **1991**, *56*, 6523–6527. (i) Hara, K.; Fujimoto, H.; Sato, K. I.; Hashimoto, H.; Yoshimura, J. *Carbohydr. Res.* **1987**, *159*, 65–79.

(5) (a) Sanap, S. P.; Ghosh, S.; Jabgunde, A. M.; Pinjari, R. V.; Gejji, S. P.; Singh, S.; Chopade, B. A.; Dhavale, D. D. *Org. Biomol. Chem.* **2010**, *14*, 3307–3315. (b) Jadhav, V. H.; Bande, O. P.; Pinjari, R. V.; Gejji, S. P.; Puranik, V. G.; Dhavale, D. D. *J. Org. Chem.* **2009**, *74*, 6486–6494. (c) Bhujbal, N. N.; Bande, O. P.; Dhavale, D. D. *Carbohydr. Res.* **2009**, *344*, 734–738. (d) Bande, O. P.; Jadhav, V. H.; Puranik, V. G.; Dhavale, D. D. *Synlett* **2009**, *12*, 1959–1963. (e) Bande, O. P.; Jadhav, V. H.; Puranik, V. G.; Dhavale, D. D. *Tetrahedron lett* **2009**, *50*, 6906–6908.

(6) (a) Mane, R. S.; Ajish Kumar, K. S.; Dhavale, D. D. *J. Org. Chem.* **2008**, *73*, 3284–3287. (b) Hotha, S.; Maurya, S. K.; Gurjar, M. K. *Tetrahedron Lett.* **2005**, *46*, 5329–5332.

(7) Wengel et al. have reported the synthesis of compound **7** using different methodology; see: Nielsen, P.; Pfundheller, H. M.; Olsen, C.; Wengel, J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3423–3433.

(8) Zou, R.; Robins, M. J. *Can. J. Chem.* **1987**, *65*, 1436–1437.

(9) (a) Analogous results were obtained with 10% Pd/C or 10% $Pd(OH)_2$, ammonium formate, methanol reflux conditions. (b) Wengel et al. have also observed glycosidic bond cleavage under various debenzylation methods (20% $Pd(OH)_2$)/C, H_2, ethanol; 10% Pd/C, H_2, methanol; 10% Pd/C, 1,4-cyclohexadiene, methanol; BCl_3, dichloromethane, hexane; 20% $Pd(OH)_2$, ammonium formate, methanol; BBr_3, dichloromethane; sodium, ethanol; CrO_3/CH_3COOH; iodotrimethylsilane); see: Singh, S. K.; Kumar, R.; Wengel, J. *J. Org. Chem.* **1998**, *63*, 6078–6079.

(10) (a) Gazim, Z. C.; Rezende, C. M.; Fraga, S. R.; Svidzinski, T. I. E.; Cortez, D. A. G. *Braz. J. Microbiol.* **2008**, *39*, 61–63. (b) Kumbhar, A. S.; Padhye, S. B.; Saraf, A. P.; Mahajani, H. B.; Chopade, B. A.; West, D. K. *Biometals* **1991**, *4*, 141–143.

(11) (a) Liu, Y.; Xing, H.; Han, X.; Shi, X.; Liang, F.; Cheng, G.; Lu, Y.; Ma, D. *J. Huazhong Univ. Sci. Technolog. Med. Sci.* **2008**, *28*, 197–199.

(12) Mosmann, T. *J. Immunol. Meth.* **1983**, *65*, 55–63.

(13) The general procedure and statistical analysis for anticancer assay is discussed in Supporting Information.

(14) The names of the sugars **10**, **11**, and **14** are given according to the von Baeyer nomenclature; however, the assignments of the protons and carbons in the figures follow standard carbohydrate nomenclature.