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Note

# Synthesis, the crystal structure, and high-resolution NMR spectroscopy of methyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-6-iodo-α-D-*arabino*-hexopyranoside

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**Abstract**

Selective tosylation followed by acetylation of methyl 3-azido-2,3-dideoxy-α-D-*arabino*-hexopyranoside (**1**) in pyridine at room temperature affords a mixture of methyl 4-*O*-acetyl-3-azido-2,3-dideoxy-6-di-*O*-*p*-tolylsulfonyl-α-D-*arabino*-hexopyranoside (**4**) and methyl 3-azido-2,3-dideoxy-4,6-di-*O*-*p*-tolylsulfonyl-α-D-*arabino*-hexopyranoside (**3**). Compound **4** undergoes nucleophilic displacement with sodium iodide in acetic anhydride to give methyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-6-iodo-α-D-*arabino*-hexopyranoside (**7**), whose crystal structure and $^{1}H$ and $^{13}C$ NMR data are reported. This compound adopts the $^{4}C_{1}$ conformation.


*Keywords:* Methyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-6-iodo-α-D-*arabino*-hexopyranoside; Synthesis, X-ray diffraction; $^{1}H$ and $^{13}C$ NMR spectroscopy

## 1. Introduction

In a previous paper, we reported on the synthesis of **1**, a useful intermediate for synthesis of 3-amino derivatives of 2,3-dideoxy sugars.[1] Here we show that this compound can be converted into methyl 3-azido-2,3,6-trideoxy-6-iodo-α-D-*arabino*-hexopyranoside (**5**) or methyl 4-*O*-acetyl-3-azido-6-iodo-2,3,6-trideoxy-α-D-*arabino*-hexopyranoside (**7**) in good yields. Both **5** and **7** can serve as useful intermediates in the synthesis of the diastereoisomers of 3-amino-2,3,6-trideoxy-hexose derivatives—glycoside-type antibiotics useful in clinical practice. Acosamine, with the arabino configuration, has been found both in L and D forms. L-Acosamine was isolated from the antibiotic actinodine and their D enantiomer was obtained from the basic antibiotic *N*-acetylsporaciridine.[2] L-Daunosamine is the glycosidic component of a number of important anthracycline antibiotics that exhibit impressive activity against a broad range of solid tumors and soft tissue sarcomas.[2] Changing L-daunosamine to its 4-epimer, L-acosamine, was reported to suppress the cardiotoxicity of semisynthetic anthracycline antibiotics while retaining antitumor activity.[3]

## 2. Results and discussion

Methyl 3-azido-2,3-dideoxy-α-D-*arabino*-hexopyranoside[1] (**1**) was treated with 3 mol of *p*-toluenesulfonyl chloride in pyridine at room temperature to gave a mixture of methyl 3-azido-2,3-dideoxy-6-*O*-*p*-tolylsulfonyl-α-D-*arabino*-hexopyranoside (**2**) as the major product and methyl 3-azido-2,3-dideoxy-4,6-di-*O*-*p*-tolylsulfonyl-α-D-*arabino*-hexopyranoside (**3**) as a minor product (Scheme 1). The reason for the lower susceptibility for tosylation at O-4 is thought to be due

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to the steric effect of the equatorial azide group at C-3 preventing the access of the reagent from the other side. The conformation and configuration of **2** and **3** was ascertained on the basis of IR and $^1$H NMR spectroscopy. In the IR spectrum of **2**, the broad band centered at 3500 cm$^{-1}$ indicated that the hydroxyl group is present. The values of the $^1$H NMR coupling constants ($J_{2a,3} = J_{3,4} = J_{4,5} \sim 10$ Hz) indicate that these 6-*O*-sulfonyl derivatives **2** and **3** adopt the $^4C_1$ conformation and the coupling values clearly indicated the arabino configuration. The positive sign of optical rotation additionally confirmed that both compounds are the α anomers.

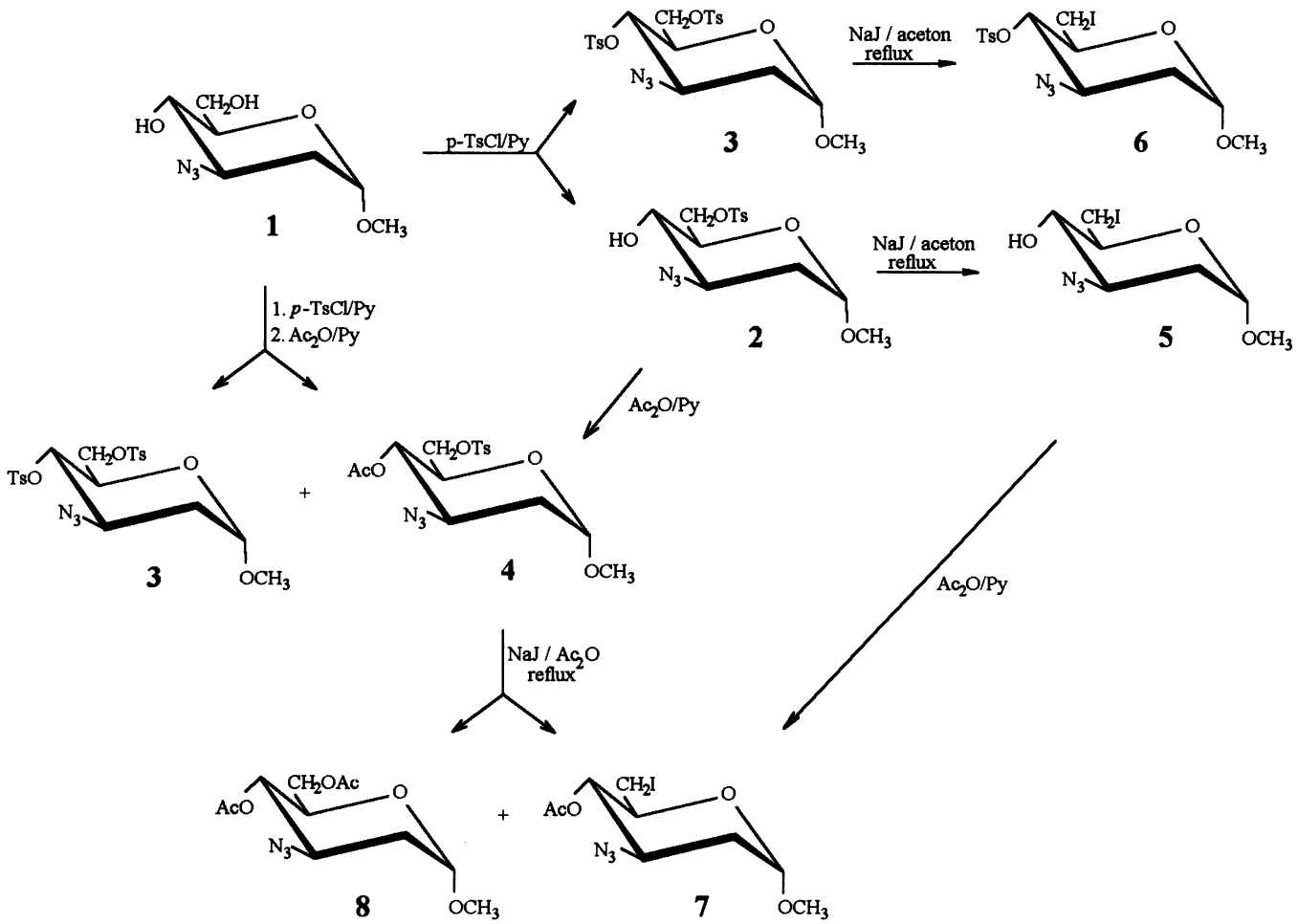
Acetylation of **2** using acetic anhydride in pyridine gave methyl 4-*O*-acetyl-3-azido-2,3-dideoxy-6-*O*-*p*-tolylsulfonyl-α-D-*arabino*-hexopyranoside (**4**) in 85% yield.

Compounds **2**, **3**, and **4** underwent selective nucleophilic displacement[4] at C-6, when refluxed for 24 h with sodium iodide in acetone. Under these conditions, **2** was converted into methyl 3-azido-6-iodo-2,3,6-trideoxy-α-D-*arabino*-hexopyranoside (**5**) in 52% yield, **3** into 3-azido-2,3-dideoxy-6-iodo-4-*O*-*p*-tolylsulfonyl-α-D-*arabino*-hexopyranoside (**6**) in 65% yield, and **4** into **7** in 47% yield. The H-6 signal in the $^1$H NMR spectrum of **6** was shifted to a higher field by 0.88 ppm as compared to that of compound **3**, indicating replacement of the OTs group.

The reaction of **4** with sodium iodide in acetic anhydride gave improved yields of the 6-iodo derivative: **4** was converted into **7** in 83% yield, and methyl 4,6-di-*O*-acetyl-3-azido-2,3-dideoxy-α-D-*arabino*-hexopyranoside[1] (**8**) was obtained as a minor byproduct in 2% yield.

Acetylation of the unseparated mixture of **2** and **3** obtained in an optimized run afforded **4** with 90% yield and unchanged **3** in 6% yield. After extraction of **3** + **4** with dichloromethane and removing solvents, this mixture was subjected to reaction with sodium iodide in acetic anhydride. After chromatographic separation, pure **6**, **7**, and **8** were obtained with yields of 4, 63, and 5%, respectively.

Comparison of coupling constants calculated for hydrogen atoms of sugar moiety in the crystal of **7** with




Scheme 1.

Table 1
Selected torsion angles and their coupling constants in the $^1$H NMR spectrum of compound **7**

| | $\Theta$ (°) | $J_{calc}$ | $J_{found}$ | $\Delta J$ |
|---|---|---|---|---|
| H-1A–C-1–C-2–H-2A(e) | −78 | $J_{1,2e}$ 0.07 | $J_{1,2e}$ 1.47 | 1.4 |
| H-1A–C-1–C-2–H-2B(a) | 39 | $J_{1,2a}$ 4.83 | $J_{1,2a}$ 3.66 | −1.17 |
| H-2A(e)–C-2–C-3–H-3A | −41 | $J_{2e,3}$ 4.54 | $J_{2e,3}$ 4.94 | 0.40 |
| H-2B(a)–C-2–C-3–H-3A | −159 | $J_{2a,3}$ 7.98 | $J_{2a,3}$ 8.78 | 0.80 |
| H-3A–C-3–C-4–H-4A | 173 | $J_{3,4}$ 9.06 | $J_{3,4}$ 9.71 | 0.65 |
| H-4A–C-4–C-5–H-5A | −177 | $J_{4,5}$ 9.17 | $J_{4,5}$ 9.88 | 0.71 |
| H-5A–C-5–C-6–H-6A(a) | 176 | $J_{5,6a}$ 9.15 | $J_{5,6a}$ 9.15 | 0.00 |
| H-5A–C-5–C-6–H-6B(e) | 67 | $J_{5,6e}$ 0.99 | $J_{5,6e}$ 2.56 | 1.57 |

those found in the $^1$H NMR spectrum (Table 1) shows that conformations in the crystal, as well as in the solution are very similar.

The crystal structure of **7** was solved by the SHELXS program and refined by SHELXL-97.[5,6] A summary of crystallographic data, data collection, and structure refinement is presented in Table 2. A view of **7** and molecular packing in the crystal are presented in Figs. 1 and 2, respectively.[7,8] The coordinates of atoms and their isotropic temperature factors are presented in Table 3, and a selection of important geometric parameters of **7** is tabulated in Table 4.

In the crystal, **7** adopts a $^4C_1$ chair conformation with puckering parameters $Q = 0.046(7)$ and $\Theta = 4.6(7)°$. The values of bond lengths and angles determined in this work for **7** agree well with the expected ones.[9] An interesting, nearby linear contact of 4.691(7) Å between the iodine atom and the outer N atom of the azido group of neighboring molecules was not found in the Cambridge Structural Database (CSD).[10]

## 3. Experimental

*General methods.*—Melting points were uncorrected. Optical rotations were determined with a Hilger–Watt polarimeter in 1-dm tubes at the D line of sodium and rt. Infrared spectra were recorded in Nujol mulls with a Perkin–Elmer 257 spectrophotometer. NMR spectra were measured with a Varian XL-100 spectrometer at 500 MHz in $CDCl_3$ (unless otherwise stated) with $Me_4Si$ as the internal standard. Mass spectra were recorded with a Varian Mat 711 spectrometer with the field-desorption ionization mode. Progress of the reaction was monitored by thin-layer chromatography (TLC) using aluminum plates precoated with Silica Gel 60 (0.08 mm, E. Merck, Darmstadt, Germany) using the following eluent systems (v/v): (A) 20:1 $CCl_4$–acetone; (B) 2:1 $CCl_4$–ether; (C) 10:1 $CCl_4$–ether; (D) 2:1 heptane–EtOAc; (E) 4:1 $CCl_4$–ether; (F) 20:1 petroleum ether–EtOAc; (G) 3:1 heptane–EtOAc; components were detected by heating at ca 200 °C. Flash chromatography was performed on Silica Gel 60 (0.08 mm, E. Merck). Evaporations were carried out under diminished pressure at 35–40 °C. Some elementary analyses for the syrupy products are not satisfactory within accepted limits, but all other spectral data confirms unambiguously the structures of obtained compounds.

*Methyl 3-azido-2,3-dideoxy-6-*O*-p-tolylsulfonyl-α-*D*-arabino-hexopyranoside* (**2**) *and methyl 3-azido-2,3-dideoxy-4,6-di-*O*-p-tolylsulfonyl-α-*D*-arabino-hexopyranoside* (**3**).—To a solution of methyl 3-azido-2,3-dideoxy-α-D-*arabino*-hexopyranoside[1] (**1**) (0.2 g, 0.98

Table 2
Crystal data and structure refinement for **7**

| | |
|---|---|
| Empirical formula | $C_9H_{14}IN_3O_4$ |
| Formula weight | 355.13 |
| Temperature (K) | 293(2) |
| Wavelength (Å) | 0.71073 |
| Crystal system | orthorhombic |
| Space group | $P2_12_12_1$ |
| Unit cell dimensions | |
| $a$ (Å) | 7.331(1) |
| $b$ (Å) | 8.928(2) |
| $c$ (Å) | 20.652(4) |
| $V$ (Å$^3$) | 1351.7(4) |
| Z | 4 |
| $D_{calcd}$ (Mg m$^{-3}$) | 1.745 |
| Absorption coefficient (mm$^{-1}$) | 2.377 |
| $F(000)$ | 696 |
| Crystal size (mm) | $0.4 \times 0.4 \times 0.5$ |
| $\Theta$ Range for data collection (°) | 1.97–30.13 |
| Limiting indices | $0 \le h \le 10$, $0 \le k \le 12$, $0 \le l \le 28$ |
| Reflections collected/unique | 2194/2192 [$R_{int} = 0.6977$] |
| Completeness to $2\Theta = 60.26$ (%) | 95.3 |
| Refinement method | full-matrix least-squares on $F^2$ |
| Data/restraints/parameters | 2192/0/156 |
| Goodness-of-fit on $F^2$ | 1.016 |
| Final $R$ indices [$I > 2\sigma(I)$] | $R_1 = 0.0484$ $wR_2 = 0.1158$ |
| $R$ indices (all data) | $R_1 = 0.1097$ $wR_2 = 0.1447$ |
| Absolute structure parameter | −0.05(6) |
| Largest difference peak and hole (e Å$^{-3}$) | 0.862 and −1.103 |

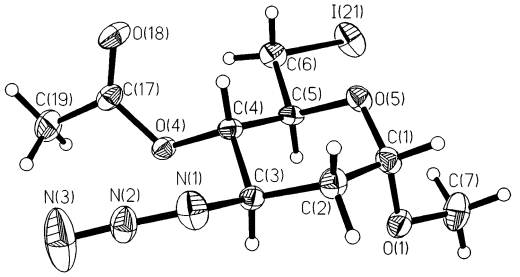



Fig. 1. Structure of methyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-6-iodo-α-D-*arabino*-hexopyranoside (**7**) showing 50% probability displacements for ellipsoids.

mmol) in $CH_2Cl_2$ (5 mL), dry pyridine (0.5 mL) and *p*-toluenesulfonyl chloride (0.57 g, 3 mmol) were added. After stirring at rt for 20 h the mixture was diluted with $CH_2Cl_2$ (10 mL), washed with aq $NaHCO_3$ and water. The resulting solution was dried with $Na_2SO_4$, concentrated to a syrup (0.5 g), and then submitted to column chromatography (A) to give **2** as a syrup (0.22 g, 62%); $[\alpha]_D^{20}$ +90° (*c* 0.9, $CHCl_3$); $R_f$ 0.32 (B); IR (Nujol); *v* 3280–3140, 2960–2840, 2100, 1600, 1370, 1170, 815 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.69 (dd, 4 H, *J* 8 Hz, $CH_3C_6H_4SO_3$), 4.82 (d, 1 H, $J_{1,2a}$ 4, $J_{1,2e}$ 1.5 Hz, H-1), 4.5 (dd, 1 H, $J_{6,6'}$ 12 Hz, H-6), 4.28 (dd, 1 H, $J_{5,6'}$ 4 Hz, H-6′), 4.23 (t, 1 H, $J_{4,5}$ 10 Hz, H-4), 3.86 (m, 1 H, $J_{3,4}$ 10 Hz, H-3), 3.64 (m, 1 H, $J_{5,6}$ 2 Hz, H-5), 3.35 (s, 3 H, $OCH_3$), 2.84 (ps. 1 H, O*H*), 2.5 (s, 3 H, $CH_3C_6H_4$), 2.19 (m, 1 H, $J_{2a,2e}$ 13 Hz, H-2e), 1.7 (m, 1 H, $J_{3,2a}$ 13, $J_{3,2e}$ 5 Hz, H-2a); FDMS: *m*/*z* 357 [$M^+$]. Anal. Calcd for $C_{14}H_{19}N_3O_6S$ (357.38): C, 47.05; H, 5.36; N, 11.76; S, 8.97. Found: C, 46.18; H, 5.50, N, 11.20; S, 9.02.Compound **3** was isolated as a syrup (0.1 g, 20%); $[\alpha]_D^{20}$ +105° (*c* 1.1, $CHCl_3$); $R_f$ 0.44 (B); IR (Nujol); *v* 2960–2840, 2100, 1600, 1450, 1375, 1175, 1000, 820 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.65 (dd, 8 H, *J* 8 Hz,

Table 3
Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **7**

| Atom | *x* | *y* | *z* | $U_{eq}$ |
|---|---|---|---|---|
| I-21 | −725(1) | 6147(1) | 2027(1) | 86(1) |
| O-1 | −5059(10) | 2448(6) | 1571(3) | 61(2) |
| O-4 | −3111(7) | 4997(5) | −162(2) | 47(1) |
| O-5 | −4717(7) | 5047(6) | 519(2) | 51(1) |
| O-1 | −3313(10) | 7462(6) | −351(3) | 70(2) |
| N-1 | −6940(10) | 4014(10) | −293(3) | 71(2) |
| N-2 | −6274(11) | 4033(9) | −817(3) | 67(2) |
| N-3 | −5832(15) | 4030(19) | −1315(5) | 154(6) |
| C-1 | −5959(10) | 3816(10) | 1502(3) | 53(2) |
| C-2 | −7010(10) | 3798(10) | 877(3) | 55(2) |
| C-3 | −5750(9) | 3816(8) | 292(3) | 44(1) |
| C-4 | −4401(10) | 5114(7) | 363(3) | 42(1) |
| C-5 | −3400(10) | 5000(8) | 1015(3) | 43(2) |
| C-6 | −2105(10) | 6275(9) | 1107(4) | 55(2) |
| C-7 | −4267(16) | 2241(13) | 2207(4) | 86(3) |
| C-17 | −2698(11) | 6260(9) | −495(4) | 53(2) |
| C-19 | −1423(17) | 5961(12) | −1031(5) | 85(3) |
| H-1A | −6813 | 3969 | 1848 | 63 |
| H-2A | −7534 | 2813 | 875 | 65 |
| H-2B | −7986 | 4513 | 851 | 65 |
| H-3A | −5098 | 2889 | 250 | 53 |
| H-4A | −5004 | 6069 | 351 | 50 |
| H-5A | −2731 | 4077 | 1034 | 52 |
| H-6A | −2859 | 7154 | 1117 | 66 |
| H-6B | −1234 | 6420 | 765 | 66 |
| H-7A | −3978 | 1202 | 2269 | 129 |
| H-7B | −5123 | 2556 | 2531 | 129 |
| H-7C | −3174 | 2828 | 2242 | 129 |
| H-19A | −1179 | 6875 | −1259 | 127 |
| H-9B | −1955 | 5246 | −1322 | 127 |
| H-9C | −304 | 5566 | −860 | 127 |

$U_{eq}$ is defined as one third of the trace of the orthogonalized $U_{ij}$ tensor.

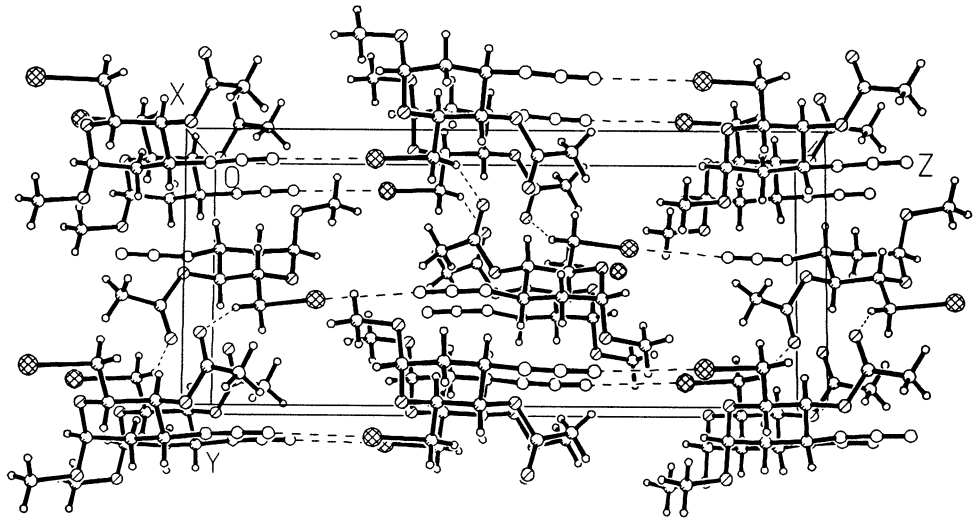



Fig. 2. Molecular packing of **7** (view along *x* axis).

Table 4
Selected bond lengths (Å), valence angles (°) and torsion angles (°) for **7**

| | |
|---|---|
| *Bond lengths* | |
| I-21–C-6 | 2.156(7) |
| O-1–C-1 | 1.396(10) |
| O-1–C-7 | 1.448(11) |
| O-4–C-17 | 1.356(9) |
| O-4–C-4 | 1.442(8) |
| O-5–C-5 | 1.421(8) |
| O-5–C-1 | 1.428(9) |
| N-1–N-2 | 1.186(10) |
| N-1–C-3 | 1.502(9) |
| N-2–N-3 | 1.079(11) |
| C-1–C-2 | 1.504(10) |
| C-2–C-3 | 1.521(9) |
| C-3–C-4 | 1.531(9) |
| C-4–C-5 | 1.537(10) |
| C-5–C-6 | 1.495(10) |
| *Valence angles* | |
| C-1–O-1–C-7 | 113.1(7) |
| C-17–O-4–C-4 | 117.9(5) |
| C-5–O-5–C-1 | 113.1(5) |
| N-2–N-1–C-3 | 119.8(7) |
| N-3–N-2–N-1 | 173.1(10) |
| C-1–C-2–C-3 | 111.7(6) |
| N-1–C-3–C-2 | 106.7(6) |
| N-1–C-3–C-4 | 111.3(6) |
| C-2–C-3–C-4 | 108.9(6) |
| C-3–C-4–C-5 | 110.0(5) |
| C-6–C-5–C-4 | 111.3(6) |
| C-5–C-6–I-21 | 111.7(5) |
| *Torsion angles* | |
| C-5–O-5–C-1–C-2 | −60.6(8) |
| O-5–C-1–C-2–C-3 | 54.2(9) |
| C-1–C-2–C-3–C-4 | −52.0(9) |
| C-2–C-3–C-4–C-5 | 54.4(7) |
| C-3–C-4–C-5–O-5 | −59.4(7) |
| C-1–O-5–C-5–C-4 | 62.8(7) |

$CH_3C_6H_4SO_3$), 4.74 (d, 1 H, $J_{1,2a}$ 4, $J_{1,2e}$ 1.5 Hz, H-1), 4.45 (dd, 1 H, $J_{6,6'}$ 12 Hz, H-6), 4.41 (t, 1 H, $J_{4,5}$ 10 Hz, H-4), 4.21 (dd, 1 H, $J_{5,6'}$ 10 Hz, H-6′), 4.12 (m, 1 H, $J_{5,6}$ 3 Hz, H-5), 3.79 (m, 1 H, $J_{3,4}$ 10 Hz, H-3), 3.3 (s, 3 H, $OCH_3$), 2.5 (s, 6 H, $CH_3C_6H_4$), 2.17 (m, 1 H, $J_{2a,2e}$ 13 Hz, H-2e), 1.69 (m, 1 H, $J_{3,2a}$ 13, $J_{3,2e}$ 5 Hz, H-2a); FDMS: $m/z$ 511 [$M^+$]. Anal. Calcd for $C_{21}H_{25}N_3O_8S_2$ (511.56): C, 49.31; H, 4.93; N, 8.21; S, 12.53. Found: C, 48.90; H, 4.94, N, 7.61; S, 11.25.

*Methyl 3-azido-2,3-dideoxy-4,6-di*-O-p-*tolylsulfonyl*-α-D-arabino-*hexopyranoside* (**3**) *and methyl 4*-O-*acetylo-3-azido-2,3-dideoxy-6*-O-p-*tolylsulfonyl*-α-D-arabino-*hexopyranoside* (**4**)

*Method A*. To a solution of **1**[1] (0.2 g, 0.98 mmol) in $CH_2Cl_2$ (6 mL), a solution of *p*-toluenesulfonyl chloride (0.58 g, 3 mmol) in pyridine (0.6 mL) was added dropwise for 15 min. The mixture was then stored at rt overnight and the resulting solution was then extracted with $CH_2Cl_2$. The organic layer was washed with aq $NaHCO_3$ and water, dried over $Na_2SO_4$, and concentrated to a syrup yielding 1.3 g of a mixture of **2** and **3**. This mixture was then diluted with $CH_2Cl_2$ (70 mL), and acetylated in pyridine (10 mL), using $Ac_2O$ (10 mL) at rt to the point when all the starting compounds (TLC, D) had disappeared (about 2 h). In this way, 0.52 g of the crude syrupy product was obtained, which after chromatographic separation with the eluent system (A) gave two syrupy products **3** (0.10 g, 20%) and **4** (0.25 g, 63%).

*Method B*. To a solution of **1**[1] (0.2 g, 1 mmol) in $CH_2Cl_2$ (6 mL), a solution of *p*-toluenesulfonyl chloride (0.58 g, 3 mmol) in pyridine (0.6 mL) was added dropwise for 15 min. The mixture was then stored at rt overnight. The resulting solution was then acetylated in pyridine (2 mL), using $Ac_2O$ (2 mL) at rt for 2 h, whereupon TLC (D) indicated that all the starting compound had disappeared. The mixture was then diluted with $Et_2O$ (5 mL) and the supernatant layer decanted. The filtrate was concentrated to dryness, and the syrupy residue was dissolved in $CHCl_3$ (100 mL). The solution was washed with aq $NaHCO_3$ and water, dried over $Na_2SO_4$, and evaporated to dryness to give 0.6 g of crude syrupy product containing a mixture of **3** and **4** [TLC, $R_f$ 0.44 and 0.52 (B)]. Column chromatography with the eluent system (A) gave **3** as a syrup (0.03 g, 6%) and **4** as a syrup (0.36 g, 91%).

*Methyl 4*-O-*acetyl-3-azido-2,3-dideoxy-6*-O-p-*tolylsulfonyl*-α-D-arabino-*hexopyranoside* (**4**).—To a solution of **2** (0.22 g, 0.6 mmol) in $CH_2Cl_2$ (20 mL), pyridine (2 mL), $Ac_2O$ (2 mL) and catalytic amount of DMAP was added. The mixture was kept at rt for 2 h (TLC, C), and then poured on to ice–water and extracted with $CH_2Cl_2$. The organic layer was washed with aq $NaHCO_3$ and water, dried over $Na_2SO_4$, and concentrated to a syrup yielding **4** (0.21 g, 85%); $[\alpha]_D^{20}$ +118° (*c* 0.9, $CHCl_3$); $R_f$ 0.52 (B); IR (Nujol); $\nu$ 2960–2880, 2110, 1770, 1620, 1385, 1245, 1200, 850 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 7.63 (dd, 4 H, *J* 8 Hz, $CH_3C_6H_4SO_3$), 4.78 (t, 1 H, $J_{4,5}$ 10 Hz, H-4), 4.77 (d, 1 H, $J_{1,2a}$ 4, $J_{1,2e}$ 1.5 Hz, H-1), 4.03 (dd, 1 H, $J_{6,6'}$ 13 Hz, H-6), 3.98 (m, 1 H, $J_{3,4}$ 10 Hz, H-3), 3.93 (m, 1 H, $J_{5,6}$ 2 Hz, H-5), 3.81 (dd, 1 H, $J_{5,6'}$ 5 Hz, H-6′), 3.375 (s, 3 H, $OCH_3$), 2.47 (s, 3 H, $CH_3C_6H_4$), 2.15 (m, 1 H, $J_{2a,2e}$ 13 Hz, H-2e), 2.12 (s, 3 H, $CH_3CO$), 1.67 (m, 1 H, $J_{3,2a}$ 13, $J_{3,2e}$ 5 Hz, H-2a); FDMS: $m/z$ 399 [$M^+$]. Anal. Calcd for $C_{16}H_{21}N_3O_7S$ (399.42): C, 48.11; H, 5.30; N, 10.52; S, 8.03. Found: C, 48.01; H, 5.02, N, 9.12; S, 9.02.

*Methyl 3-azido-6-iodo-2,3,6-trideoxy*-α-D-arabino-*hexopyranoside* (**5**).—A solution of the 6-sulfonate **2** (0.22 g, 0.6 mmol) in acetone (5.5 mL) containing NaI (0.55 g, 0.01 mol) was refluxed for 10 h. TLC (E)

indicated a fast-moving product. The mixture was then cooled, precipitated sodium *p*-toluenesulfonate was filtered off, and the filtrate concentrated to dryness. The residue was partitioned between water and $CHCl_3$, and the organic layer washed with aq $Na_2S_2O_3$ and water, dried over $Na_2SO_4$, and concentrated to give the crude product (0.13 g) which, after column chromatography (C), gave the 6-iodo derivative **5** as a syrup (0.1 g, 52%); $[\alpha]_D^{20}$ +83° (*c* 1.1, $CHCl_3$); $R_f$ 0.45 (E); IR (Nujol); *v* 3280–3160, 2960-2840, 2100, 1725, 1430, 1230, 1040, 930, 820, 760 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 4.9 (d, 1 H, $J_{1,2a}$ 3.5, $J_{1,2e}$ 1.5 Hz, H-1), 4.13 (t, 1 H, $J_{4,5}$ 12 Hz, H-4), 3.85 (dd, 1 H, $J_{6,6'}$ 13 Hz, H-6), 3.74 (dd, 1 H, $J_{5,6'}$ 10 Hz, H-6′), 3.57 (m, 1 H, $J_{3,4}$ 10 Hz, H-3), 3.24 (m, 1 H, $J_{5,6}$ 5 Hz, H-5), 3.44 (s, 3 H, OC*H*$_3$), 2.72 (ps, 1 H, O*H*), 2.22 (m, 1 H, $J_{2a,2e}$ 14 Hz, H-2e), 1.74 (m, 1 H, $J_{3,2a}$ 8, $J_{3,2e}$ 5 Hz, H-2a); FDMS: *m*/*z* 313 [$M^+$]. Anal. Calcd for $C_7H_{12}IN_3O_3$ (313.10): C, 26.85; H, 3.86; N, 13.42. Found: C, 27.01; H, 3.54, N, 12.7.

*Methyl 3-azido-6-iodo-2,3,6-trideoxy-4*-O-p-*tolylsulfonyl-α*-D-arabino-*hexopyranoside* (**6**).—A solution of the 4,6-disulfonate **3** (0.1 g, 0.2 mmol) in acetone (2 mL) containing NaI (0.2 g, 1.3 mmol) was refluxed for 24 h. The reaction was processed as described previously to give **6** as a syrup (0.06 g, 65%); $[\alpha]_D^{20}$ +168° (*c* 1.0, $CHCl_3$); $R_f$ 0.64 (E); IR (Nujol); *v* 2960–2840, 2100, 1600, 1370, 1180, 1130, 1050, 1000, 885. 830, 770 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 7.68 (dd, 4 H, *J* 8 Hz, $CH_3C_6H_4SO_3$), 4.86 (d, 1 H, $J_{1,2a}$ 3.5, $J_{1,2e}$ 1.5 Hz, H-1), 4.3 (t, 1 H, $J_{4,5}$ 12 Hz, H-4), 3.85 (dd, 1 H, $J_{6,6'}$ 13 Hz, H-6), 3.79 (m, 1 H, $J_{3,4}$ 10 Hz, H-3), 3.74 (dd, 1 H, $J_{5,6'}$ 10 Hz, H-6′), 3.44 (s, 3 H, OC*H*$_3$), 3.24 (m, 1 H, $J_{5,6}$ 5 Hz, H-5), 2.48 (s, 3 H, C*H*$_3$C$_6$H$_4$), 2.22 (m, 1 H, $J_{2a,2e}$ 14 Hz, H-2e), 1.74 (m, 1 H, $J_{3,2a}$ 8, $J_{3,2e}$ 5 Hz, H-2a); FDMS: *m*/*z* 467 [$M^+$]. Anal. Calcd for $C_{14}H_{18}IN_3O_5S$ (467.28): C, 35.99; H, 3.88; N, 8.99; S, 6.86. Found: C, 36.68; H, 4.23, N, 8.7; S, 6.04.

*Methyl 4*-O-*acetyl-3-azido-6-iodo-2,3,6-trideoxy-α*-D-arabino-*hexopyranoside* (**7**) *and methyl 4,6-di*-O-*acetyl-3-azido-2,3-dideoxy-α*-D-arabino-*hexopyranoside* (**8**).—A solution of **4** (0.61 g, 1.5 mmol) in $Ac_2O$ (6.2 mL) containing NaI (0.62 g, 4.1 mmol) was refluxed for 6 h. After cooling, precipitated sodium *p*-toluenesulfonate was filtered off, washed with $CHCl_3$ and the filtrate concentrated to dryness. The residue was partitioned between water and ether, and worked up as just described to give 0.54 g of a mixture of products. Column chromatography (F) gave the main product **7** (0.45 g, 83%); mp 77–78 °C; $[\alpha]_D^{20}$ +96° (*c* 1.1, $CHCl_3$); $R_f$ 0.54 (G); IR (Nujol); *v* 2960–2840, 2100, 1725, 1430, 1230, 1040 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 4.841 (d, 1 H, $J_{1,2a}$ 3.66, $J_{1,2e}$ 1.47 Hz, H-1), 4.701 (t, 1 H, $J_{4,5}$ 9.88 Hz, H-4), 3.883 (m, 1 H, $J_{3,4}$ 9.71 Hz, H-3), 3.727 (m, 1 H, $J_{5,6}$ 2.56 Hz, H-5), 3.438 (s, 3 H, OC*H*$_3$), 3.283 (dd, 1 H, $J_{6,6'}$ 10.98 Hz, H-6), 3.11 (dd, 1 H, $J_{5,6'}$ 9.15 Hz, H-6′), 2.173 (m, 1 H, $J_{2a,2e}$ 13.36 Hz, H-2e), 2.154 (s, 3 H, C*H*$_3$CO), 1.748 (m, 1 H, $J_{3,2a}$ 8.78, $J_{3,2e}$ 4.94 Hz, H-2a); $^{13}C$ NMR: $\delta$ 170.1 (CH$_3$*C*O), 97.716 (C-1), 74.472 (C-4), 70.01 (C-5), 57.668 (C-3), 55.501 (O*C*H$_3$), 35.272 (C-2), 21.052 (*C*H$_3$CO), 4.46 (C-6); FDMS: *m*/*z* 355 [$M^+$]. Anal. Calcd for $C_9H_{14}IN_3O_4$ (355.13): C, 30.40; H, 3.97; N, 11.80. Found: C, 30.59; H, 4.00; N, 11.80.

The byproduct **8** was a syrup (0.01 g, 2.3%); $[\alpha]_D^{20}$ +81° (*c* 1.0, $CHCl_3$); $R_f$ 0.26 (G); IR (Nujol); *v* 2960–2840, 2100, 1735, 1440, 1370, 1260–1220, 1130, 1050, 970 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 4.95 (t, 1 H, $J_{4,5}$ 10 Hz, H-4), 4.87 (dd, 1 H, $J_{1,2a}$ 4, $J_{1,2e}$ 1.5 Hz, H-1), 4.28 (dd, 1 H, $J_{6,6'}$ 12 Hz, H-6), 4.04 (dd, 1 H, $J_{5,6'}$ 2 Hz, H-6′), 3.95 (m, 1 H, $J_{3,4}$ 10 Hz, H-3), 3.88 (m, 1 H, $J_{5,6}$ 5 Hz, H-5), 3.37 (s, 3 H, OC*H*$_3$), 2.33 (m, 1 H, $J_{2a,2e}$ 13 Hz, H-2e), 2.02 (s, 3 H, C*H*$_3$CO), 2.01 (s, 3 H, C*H*$_3$CO), 1.77 (m, 1 H, $J_{3,2a}$ 12, $J_{3,2e}$ 5 Hz, H-2a); FDMS: *m*/*z* 287 [$M^+$]. Anal. Calcd for $C_{11}H_{17}N_3O_6$ (287.27): C, 45.99; H, 5.96; N, 14.62. Found: C, 45.83; H, 5.99; N, 14.69.

*Methyl 3-azido-6-iodo-2,3,6-trideoxy-4*-O-p-*tolylsulfonyl-α*-D-arabino-*hexopyranoside* (**6**), *methyl 4*-O-*acetyl-3-azido-6-iodo-2,3,6-trideoxy-α*-D-arabino-*hexopyranoside* (**7**), *and methyl 4,6-di*-O-*acetyl-3-azido-2,3-dideoxy-α*-D-arabino-*hexopyranoside* (**8**).—The crude mixture of compounds of **3** and **4** (0.6 g) (obtained by method B without final chromatography) in $Ac_2O$ (6.1 mL) containing NaI (0.61 g, 4.1 mmol) was refluxed for 6 h. TLC with solvent (G) showed three spots ($R_f$ 0.54, 0.43, and 0.27). After conventional processing, the crude product (0.4 g) was separated by a column chromatography with solvent (F). Three compounds were obtained: **6** (0.02 g, 4.3%), **7** (0.22 g, 63%), and **8** (0.015 g, 5.3%), identical with those obtained earlier, on the basis of their $^1H$ NMR spectra. (The yields of these compounds were calculated in regards to the starting substrate **1**.)

## 4. Supplementary material

Full crystallographic details, excluding structure features, have been deposited (deposition no. CCDC 168192) with the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Tel.: +44-1223-336408; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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