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# The Mitsunobu reaction in preparing 3-deazapurine carbocyclic nucleosides

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**Abstract**—The coupling reaction of 4-chloro-1*H*-imidazo[4,5-*c*]pyridine (6-chloro-3-deazapurine, **3**) with several cyclopentyl derivatives under Mitsunobo reaction conditions provides an efficient entry into N-7 and N-9 substituted 3-deazapurine carbocyclic nucleosides of antiviral potential. The versatility of this procedure is illustrated with a new and efficient synthesis of (−)-3-deazaaristeromycin, a formal preparation of 3-deazaneplanocin A, and a route to 3-deaza-5′-homoaristeromycin.


## 1. Introduction

Nucleoside analogs based on the 3-deazapurine (1*H*-imidazo[4,5-*c*]pyridine) framework have found significant usefulness in antiviral agent design and biochemical investigations.[1,2] The carbocyclic nucleosides[3] 3-deazaristeromycin (**1**)[4] and 3-deazaneplanocin (**2**)[5] have been central to these studies (Fig. 1). In our efforts to further exploit the 3-deazapurine carbocyclic nucleoside platform as a source for new antiviral candidates, it was necessary to seek a more versatile synthetic means to this series that would give access to a number of structural variations. In this regard it was surprising to find that the Mitsunobu reaction,[6] which has been successfully employed to produce traditional carbocyclic nucleosides, had not been investigated in the 3-deazapurine genera. This paper describes the use of the Mitsunobu reaction in the preparation of such derivatives.[7]

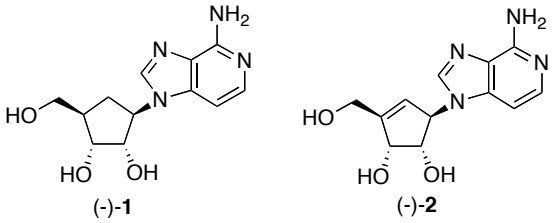
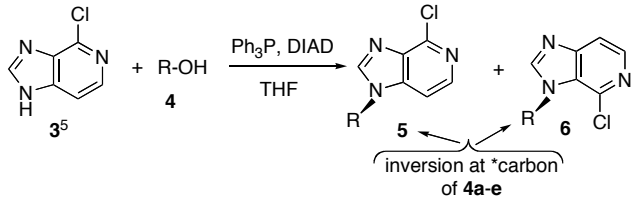
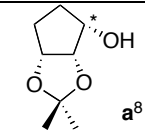
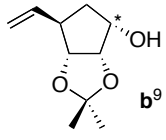
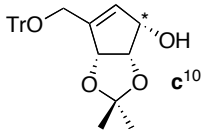
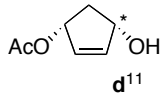
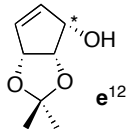



**Figure 1.**

**Table 1**. Mitsunubo reaction of 4-chloro-1*H*-imidazo[4,5-*c*]pyridine (3-deaza-6-chloropurine) with substituted cyclopentanols




| Entry | R-OH | Products (%) | |
|---|---|---|---|
| | | **5** | **6** |
| 1 |  **a**[8] | 86 | 0 |
| 2 |  **b**[9] | 70 | 0 |
| 3 |  **c**[10] | 42 | 53 |
| 4 |  **d**[11] | 38 | 57 |
| 5 |  **e**[12] | 32 | 43 |

*Keywords*: 4-Amino-1*H*-imidazo[4,5-*c*]pyridine; Carbocyclic nucleosides; Aristeromycin; Neplanocin.
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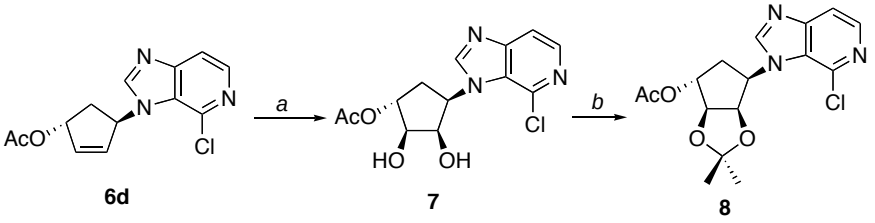



**Scheme 1.** Reagents: a, $OsO_4$, NMO, $CH_2Cl_2$; b, $(MeO)_2CMe_2$, acetone, *p*TSA, 83% (two steps).

## 2. Chemistry

Following standard Mitsunobu conditions (that is, triphenylphosphine and diisopropyl azodicarboxylate in tetrahydrofuran), the reaction of 4-chloro-1*H*-imidazo-[4,5-*c*]pyridine (**3**)[5] with various cyclopentanols gave the results presented in the Table 1. Thus, reacting **4a** with **3** cleanly gave **5a** as the only isomer. Likewise, compound **4b** provided **5b** as the only regioisomer. The more reactive allylic alcohols **4c–e**, however, yielded the N-1 (purine N-9) products **5c–e** along with the N-3 (purine N-7) isomers **6c–e**, which were the major products.

Structural assignments for the N-1 (N-9) and N-3 (N-7) isomers were possible because the proton on the cyclopentyl carbon bearing the heterocyclic ring in the N-3 product is downfield in the proton NMR spectrum compared to the N-1 product (by correlating the data of Ref. 5 with the data found in this study that is supported by the X-ray structural confirmation of **8**, vide infra). A characteristic carbon-13 NMR peak ($\delta = \sim 106$ ppm) was observed for the carbon (possibly C-2) in the heterocyclic ring of all N-1 products (**5**) while the peak moves to ($\delta = 115$ ppm) in all N-3 products (**6**). Supporting these NMR assignments for N-3 products was the conversion of **6d** to **8** (Scheme 1), whose structure was confirmed by X-ray crystallography (Fig. 2) and whose NMR spectrum fit the diagnostic peaks used for isomer distinction.

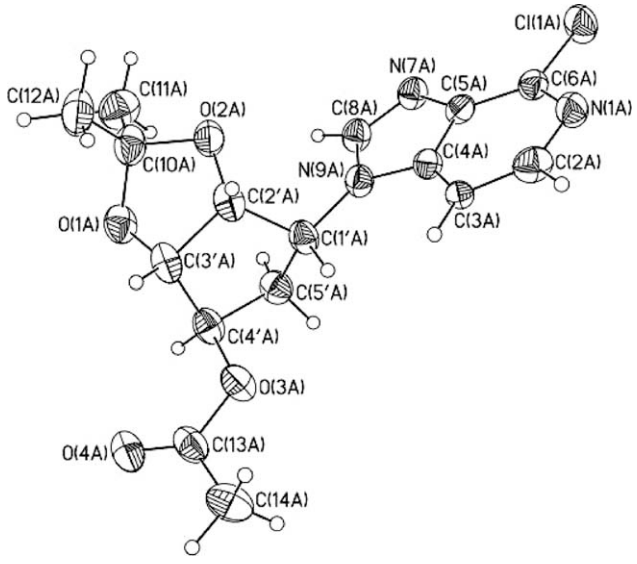
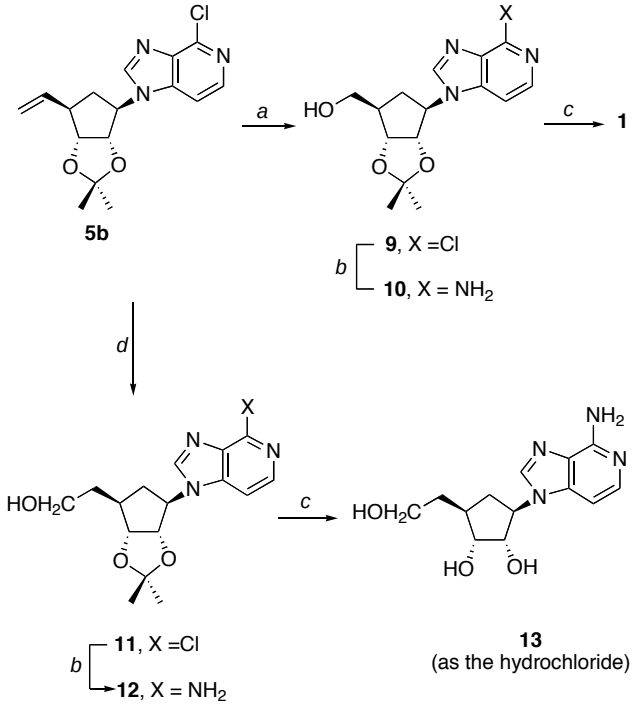



**Figure 2.** X-ray structure for compound **8**.

Further transformations of the coupled products **5b** and **5c** were sought for additional structural confirmation and to demonstrate extended synthetic versatility by their conversion into two important 3-deazapurine carbocyclic nucleosides, 3-deazaaristeromycin (**1**) and 3-deazaneplanocin (**2**). Whereas compound **2** was obtained from **5c** by modifying a known procedure,[5] manipulation of the vinyl group in **5b** to a hydroxymethyl moiety following our recently reported procedure[9a] furnished (−)-**1** in good overall yield (Scheme 2).[13] Compound **5b** also provided access to 3-deaza-5′-homoaristeromycin (**13**), which is a compound of potentially significant activity toward the orthopox viruses.[14]




**Scheme 2.** Reagents: a, (i) $OsO_4$, $NaIO_4$, MeOH; (ii) $NaBH_4$, MeOH, 81%; b, (i) $NH_2NH_2$, THF; (ii) Ra-Ni, MeOH/$H_2O$, 75% (two steps for **9**); 80% (two steps) for **12**; c, HCl/MeOH, 89% for **1**; 78% for **13**; d, (i) 9-BBN, THF; (ii) NaOH, $H_2O_2$, 80% (two steps).

## 3. Experimental

### 3.1. General

Melting points were recorded on a Meltemp II melting point apparatus and the values are uncorrected. The combustion analyses were performed at Atlantic Microlab, Norcross, GA. $^1H$ and $^{13}C$ NMR spectra were recorded on either a Bruker AC 250 spectrometer (250 MHz for proton and 62.9 MHz for carbon) or a Bruker AV 400 spectrometer (400 MHz for proton and 100 MHz for carbon), referenced to internal tetramethylsilane (TMS) at 0.0 ppm. The X-ray

crystal structure was determined using a Bruker APEX CCD single crystal X-ray diffractometer. The HRMS measurements were obtained using a VG 70S magnetic sector mass spectrometer. The reactions were monitored by thin-layer chromatography (TLC) using 0.25 mm Whatman Diamond silica gel 60-$F_{254}$ precoated plates with visualization by irradiation with a Mineralight UVGL-25 lamp. Column chromatography was performed on Whatman silica, 230–400 mesh and 60 Å using elution with the indicated solvent system. Yields refer to chromatographically and spectroscopically ($^1$H and $^{13}$C NMR) homogeneous materials.

**3.1.1. (3a*S*,4*S*,6a*R*)-Tetrahydro-2,2-dimethyl-3a*H*-cyclopenta[*d*][1,3]dioxol-4-ol (4a).** A mixture of (3a*R*,6a*R*)-2,2-dimethyl-3a*H*-cyclopenta[*d*][1,3]dioxol-4(6a*H*)-one (**i**)[8,9a] (2.0 g, 13.0 mmol), Pd/C and MeOH (30 mL) was shaken under 18 psi of $H_2$. The reaction was run until TLC monitoring indicated no UV-active starting material was present. After filtration, concentration of the filtrate gave an oily product that was purified by silica gel chromatography (EtOAc/hexanes, 1:2) to provide 1.9 g (93.8%) of (3a*R*,6a*R*)-dihydro-2,2-dimethyl-3a*H*-cyclopenta[*d*][1,3]-dioxol-4(5*H*)-one (**ii**)[8]as a white solid.[9b]

To a stirred solution of ketone **ii** (0.50 g, 3.20 mmol) in MeOH (30 mL) at 0 °C $NaBH_4$ (0.18 g, 4.76 mmol) was added portion wise. After stirring at room temperature for 1 h, the mixture was quenched with $H_2O$. Most of solvent was removed under reduced pressure and the aqueous layer exacted with $CH_2Cl_2$; the combined organic layers were washed with $H_2O$, dried ($Na_2SO_4$), concentrated, and purified by flash chromatography to give **4a** as colorless oil (0.46 g, 88.8%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.61 (t, $J$=5.2 Hz, 1H), 4.41 (t, $J$=5.6 Hz, 1H), 3.84 (m, 1H), 2.40 (d, $J$=9.8 Hz, 1H), 1.83 (m, 2H), 1.64 (m, 1H), 1.49 (s, 3H), 1.43 (m, 1H), 1.35 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 110.6, 79.6, 78.7, 73.5, 30.3, 27.7, 26.0, 24.3. Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.74; H, 9.17.

### 3.2. General procedure for the Mitsunobu reaction of 6-chloro-3-deazapurine (4-chloro-1*H*-imidazo [4,5-*c*]pyridine) with cyclopentanols

To a solution of cyclopentanol **4a–e** (10 mmol) and triphenylphosphine (15 mmol) in THF (50 mL) was added 4-chloro-1*H*-imidazo[4,5-*c*]pyridine (**3**) (10 mmol). This suspension was cooled by ice to 0 °C and DIAD (15 mmol) was added dropwise. After completion of the addition, the reaction mixture was warmed to room temperature and stirred at this temperature for 12 h and 50 °C for another 12 h. The solvent was removed under reduced pressure and the residue purified by column chromatography ($CH_2Cl_2$/EtOAc, 3:1 or $CH_2Cl_2$/acetone, 4:1) to afford the coupled product.

**3.2.1. Compound 5a (86%).** White solid, mp 131–133 °C: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.24 (d, $J$=5.6 Hz, 1H), 7.94 (s, 1H), 7.47 (d, $J$=5.6 Hz, 1H), 4.88 (m, 1H), 4.69 (m, 2H), 2.59 (m, 1H), 2.17 (m, 3H), 1.57 (s, 3H), 1.35 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 143.5, 142.1, 141.8, 140.3, 138.4, 112.2, 106.3, 85.7, 80.5, 63.2, 31.5, 28.6, 26.9, 24.6. HRMS calcd for $C_{14}H_{16}ClN_3O_2$ ($M^+$) 293.0931, found 293.0936.

**3.2.2. Compound 5b (70%).** Colorless oil: $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 8.23 (d, $J$=5.7 Hz, 1H), 8.04 (s, 1H), 7.60 (d, $J$=5.7 Hz, 1H), 5.94 (m, 1H), 5.22 (m, 2H), 4.67 (m, 2H), 4.58 (m, 1H), 2.92 (m, 1H), 2.68 (m, 1H), 2.33 (m, 1H), 1.64 (s, 3H), 1.33 (s, 3H). $^{13}$C NMR (62.9 MHz, $CDCl_3$) $\delta$ 143.2, 142.0, 141.8, 140.2, 138.3, 137.0, 117.0, 114.8, 106.6, 84.9, 83.9, 62.3, 47.7, 35.7, 27.5, 25.1. Anal. Calcd for $C_{16}H_{18}ClN_3O_2$: C, 60.09; H, 5.67; N, 13.14. Found: C, 60.06; H, 5.60; N, 12.79.

**3.2.3. Compound 5c (42%).** White foam: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.25 (d, $J$=5.6 Hz, 1H), 7.89 (s, 1H), 7.50 (m, 15H), 7.45 (d, $J$=5.6 Hz, 1H), 6.16 (m, 1H), 5.48 (m, 1H), 5.22 (d, $J$=5.8 Hz, 1H), 4.58 (d, $J$=5.8 Hz, 1H), 4.08 (d, $J$=15.6 Hz, 1H), 3.92 (d, $J$=15.6 Hz, 1H), 1.50 (s, 3H), 1.35 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 151.1, 143.8, 143.4, 142.6, 141.9, 139.7, 138.6, 128.7, 128.2, 127.5, 121.3, 113.3, 105.8, 87.6, 84.8, 83.9, 67.1, 61.5, 27.5, 26.0. Anal. Calcd for $C_{34}H_{30}ClN_3O_3$: C, 72.40; H, 5.36; N, 7.45. Found: C, 72.06; H, 5.67; N, 7.19.

**3.2.4. Compound 6c (53%).** White foam: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.24 (d, $J$=5.7 Hz, 1H), 7.86 (s, 1H), 7.66 (d, $J$=5.7 Hz, 1H), 7.53 (m, 15H), 6.30 (m, 1H), 6.19 (m, 1H), 5.17 (d, $J$=5.4 Hz, 1H), 4.67 (d, $J$=5.4 Hz, 1H), 4.11 (d, $J$=15.5 Hz, 1H), 3.93 (d, $J$=15.5 Hz, 1H), 1.47 (s, 3H), 1.35 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 152.0, 151.7, 144.6, 143.8, 143.7, 141.6, 134.3, 128.7, 128.2, 127.5, 121.4, 115.2, 112.9, 87.5, 85.1, 83.7, 66.3, 61.4, 27.7, 26.3. Anal. Calcd for $C_{34}H_{30}ClN_3O_3$: C, 72.40; H, 5.36; N, 7.45. Found: C, 72.13; H, 5.60; N, 7.28

**3.2.5. Compound 5d (38%).** Colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.17 (d, $J$=5.8 Hz, 1H), 8.00 (s, 1H), 7.30 (d, $J$=5.8 Hz, 1H), 6.42 (ddd, $J$=5.6, 2.7, 2.7 Hz, 1H), 6.26 (m, 1H), 5.95 (m, 1H), 5.78 (m, 1H), 2.60 (ddd, $J$=14.9, 7.8, 2.6 Hz, 1H), 2.39 (ddd, $J$=14.9, 7.3, 4.8 Hz, 1H), 2.08 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.7, 143.1, 142.9, 141.4, 139.1, 138.1, 136.4, 134.4, 105.7, 78.0, 61.2, 38.3, 21.0. Anal. Calcd for $C_{13}H_{12}ClN_3O_2$: C, 56.22; H, 4.36; N, 15.13. Found: C, 56.59; H, 4.01; N, 15.36.

**3.2.6. Compound 6d (57%).** Colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.22 (d, $J$=5.5 Hz, 1H), 8.05 (s, 1H), 7.66 (d, $J$=5.5 Hz, 1H), 6.46 (m, 1H), 6.41 (m, 1H), 6.35 (m, 1H), 5.91 (m, 1H), 2.67 (ddd, $J$=14.7, 7.8, 3.3 Hz, 1H), 2.39 (ddd, $J$=14.7, 7.3, 3.8 Hz, 1H), 2.09 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.7, 151.4, 143.8, 141.2, 137.3, 133.6, 133.5, 127.9, 115.0, 77.9, 61.6, 40.7, 21.1. Anal. Calcd for $C_{13}H_{12}ClN_3O_2$: C, 56.22; H, 4.36; N, 15.13. Found: C, 56.13; H, 4.60; N, 14.98.

**3.2.7. Compound 5e (32%).** White solid, mp 96–98 °C: $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 8.25 (d, $J$=5.6 Hz, 1H), 7.90 (s, 1H), 7.50 (d, $J$=5.6 Hz, 1H), 6.44 (m, 1H), 6.10 (dd, $J$=5.8, 2.3 Hz, 1H), 5.43 (m, 2H), 4.56 (d, $J$=5.8 Hz, 1H), 1.52 (s, 3H), 1.36 (s, 3H). $^{13}$C NMR (62.9 MHz, $CDCl_3$) $\delta$ 143.4, 142.3, 141.9, 139.7, 139.0, 138.5, 129.0, 113.0, 105.8, 84.4, 84.2, 67.9, 27.3, 25.6. HRMS calcd for $C_{14}H_{14}ClN_3O_2$ ($M^+$) 291.0775, found 291.0773.

**3.2.8. Compound 6e (43%).** Colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.22 (d, $J$=5.5 Hz, 1H), 7.92 (s, 1H), 7.52 (d, $J$=5.5 Hz, 1H), 6.44 (dd, $J$=5.7, 1.5 Hz, 1H), 6.27 (s, 1H), 6.10 (dd, $J$=5.7, 1.1 Hz, 1H), 5.38 (dd, $J$=5.3, 1.3 Hz, 1H), 4.66 (d, $J$=5.4 Hz, 1H), 1.50 (s, 3H), 1.35 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 152.0, 144.5, 141.7, 140.0, 134.5, 129.4, 128.4, 115.3, 112.8, 84.7, 84.4, 67.4, 27.8, 26.3. HRMS calcd for $C_{14}H_{14}ClN_3O_2$ ($M^+$) 291.0775, found 291.0776.

**3.2.9. (1*R*,2*R*,3*R*,4*R*)-4-(4-Chloro-3*H*-imidazo[4,5-*c*]-pyridin-3-yl)-2,3-dihydroxycyclopent-1-yl acetate (7).** Methylmorpholine-*N*-oxide (2.13 g, 18.2 mmol) was added to a solution of **6d** (2.67 g, 9.64 mmol) in $CH_2Cl_2$ (50 mL) containing a small amount of $H_2O$ (0.8 mL). After the solution was cooled to 0 °C, a catalytic amount of solid $OsO_4$ (90 mg, 0.36 mmol) was added and the solution stirred for 12 h at room temperature. The reaction mixture was quenched by addition of sodium bisulfite. The solvent was removed and the residue purified by flash column chromatography (EtOAc) to afford **7** as white solid (2.55 g, 85%), mp 209–210 °C: $^1$H NMR (250 MHz, DMSO-$d_6$) $\delta$ 8.75 (s, 1H), 8.15 (d, $J$=5.5 Hz, 1H), 7.73 (d, $J$=5.5 Hz, 1H), 5.64 (m, 1H), 5.38 (d, $J$=3.0 Hz, 1H, OH), 5.37 (d, $J$=4.1 Hz, 1H, OH), 5.07 (m, 1H), 4.16 (m, 1H), 4.08 (m, 1H), 3.00 (m, 1H), 2.16 (m, 1H), 2.09 (s, 3H). $^{13}$C NMR (62.9 MHz, DMSO-$d_6$) $\delta$ 171.2, 151.8, 148.8, 141.2, 133.5, 128.8, 115.6, 78.4, 76.8, 73.6, 56.1, 34.3, 21.8. Anal. Calcd for $C_{13}H_{14}ClN_3O_4$: C, 50.09; H, 4.53; N, 13.48. Found: C, 49.84; H, 4.54; N, 13.31.

**3.2.10. (3a*R*,4*R*,6*R*,6a*S*)-4-(4-Chloro-3*H*-imidazo[4,5-*c*]-pyridin-3-yl)-tetrahydro-2,2-dimethyl-3a*H*-cyclopenta-[*d*][1,3]dioxol-6-yl acetate (8).** To a solution of **7** (3.12 g, 10.0 mmol) and 2,2-dimethoxypropane (15 mL) in dry acetone (20 mL) was added a catalytic amount of *p*-toluenesulfonic acid (50 mg). After the reaction mixture was stirred at room temperature for 12 h, the solvent was removed and the residue dissolved in $CH_2Cl_2$ (40 mL). This solution was washed with saturated $NaHCO_3$ solution, $H_2O$ and brine. The organic phase was dried ($MgSO_4$) and concentrated. The residue was purified by flash column chromatography (EtOAc/hexanes, 1:2) to afford **8** as a white solid, mp 142–143 °C: $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 8.29 (s, 1H), 8.23 (d, $J$=5.5 Hz, 1H), 7.68 (d, $J$=5.5 Hz, 1H), 5.81 (ddd, $J$=10.4, 5.5, 5.5 Hz, 1H), 5.17 (d, $J$=4.4 Hz, 1H), 4.89 (dd, $J$=4.8, 4.9 Hz, 1H), 4.65 (dd, $J$=5.4, 1.5 Hz, 1H), 2.69 (ddd, $J$=13.1, 4.5, 4.5 Hz, 1H), 2.37 (dd, $J$=13.1, 5.8 Hz, 1H), 2.16 (s, 3H), 1.52 (s, 3H), 1.29 (s, 3H). $^{13}$C NMR (62.9 MHz, $CDCl_3$) $\delta$ 169.9, 151.4, 146.2, 141.3, 133.3, 128.2, 115.4, 112.3, 83.5, 78.5, 74.7, 56.5, 33.2, 26.0, 24.0, 21.2. Anal. Calcd for $C_{16}H_{18}ClN_3O_4$: C, 54.63; H, 5.16; N, 11.94. Found: C, 54.83, H, 5.11, N, 11.85.

**3.2.11. ((3a*S*,4*R*,6*R*,6a*R*)-4-(4-Chloro-1*H*-imidazo[4,5-*c*]-pyridin-1-yl)-tetrahydro-2,2-dimethyl-3a*H*-cyclopenta-[*d*][1,3]dioxol-6-yl)methanol (9).** To a solution of **5b** (1.00 g, 3.13 mmol) in MeOH (20 mL), $H_2O$ (8 mL) and $NaIO_4$ (1.39 g, 6.48 mmol) were added. After the mixture was cooled to 0 °C, $OsO_4$ (20 mg) was added. This reaction mixture was stirred at the same temperature for 1 h and then at room temperature for 2 h. The resulting white solid was obtained by filtration and the filtrate cooled to 0 °C. To this $NaBH_4$ (0.80 g, 20 mmol) was added portion wise. After the reaction was stirred at room temperature for 0.5 h, the solvent was removed and the product obtained by short column chromatography (EtOAc/MeOH, 10:1) to give **9** as a white foam (0.82 g, 81%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.63 (s, 1H), 8.20 (d, $J$=5.6 Hz, 1H), 7.81 (d, $J$=5.6 Hz, 1H), 4.86 (m, 2H), 4.80 (t, $J$=6.5 Hz, 1H), 4.57 (dd, $J$=4.5, 7.0 Hz, 1H), 3.55 (t, $J$=5.5 Hz, 2H), 2.46 (m, 1H), 2.21 (m, 1H), 2.19 (m, 1H), 1.58 (s, 3H), 1.26 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 145.3, 142.0, 141.7, 140.9, 138.2, 113.7, 108.2, 84.9, 81.8, 62.9, 62.8, 46.1, 33.7, 28.2, 26.0. Anal. Calcd for $C_{15}H_{18}ClN_3O_3$: C, 55.64; H, 5.60; N, 12.98. Found: C, 55.87; H, 5.67; N, 12.79.

**3.2.12. ((3a*S*,4*R*,6*R*,6a*R*)-4-(4-Amino-1*H*-imidazo[4,5-*c*]-pyridin-1-yl)-tetrahydro-2,2-dimethyl-3a*H*-cyclopenta-[*d*][1,3]dioxol-6-yl)methanol (10).** A solution of **9** (1.62 g, 5.00 mmol) in hydrazine (15 mL) and MeOH (6 mL) was brought to reflux for 6 h. After cooling to room temperature, the solution was concentrated. The residue was dissolved in MeOH (30 mL) and freshly prepared W2-Raney Ni (prepared from 40 g of alloy) was added to it. The reaction mixture was heated to reflux for 1 h. The hot reaction mixture was filtered and the solid recovered and washed with hot MeOH (3×15 mL). The combined filtrates were evaporated to dryness and the residue purified via column chromatography (EtOAc/MeOH, 10:1) to afford **10** as white solid (1.14 g, 75%), mp 203–205 °C: $^1$H NMR (250 MHz, DMSO-$d_6$) $\delta$ 8.22 (s, 1H), 7.66 (d, $J$=5.8 Hz, 1H), 6.87 (d, $J$=5.8 Hz, 1H), 6.38 (br, 2H), 4.74 (q, $J$=6.8 Hz, 1H), 4.69 (m, 1H), 4.55 (m, 1H), 3.51 (d, $J$=4.8 Hz, 2H), 2.39–2.17 (m, 3H), 1.50 (s, 3H), 1.23 (s, 3H). $^{13}$C NMR (62.9 MHz, DMSO-$d_6$) $\delta$ 152.4, 140.0, 139.9, 138.1, 126.9, 112.6, 97.3, 84.0, 80.9, 61.8, 61.6, 45.2, 32.9, 27.4, 25.1.[15]

**3.2.13. (1*R*,2*S*,3*R*,5*R*)-3-(4-Amino-1*H*-imidazo[4,5-*c*]-pyridin-1-yl)-5-(hydroxymethyl)cyclopentane-1,2-diol ((−)-3-deazaaristeromycin, 1).** Compound **10** (304 mg, 1.00 mmol) was dissolved in a mixture of MeOH (5 mL) and 1 N HCl (5 mL) and the resulting solution was stirred at room temperature for 5 h. Basic resin (Amberlite IR 67) was added to neutralize the solution. The mixture was filtered and the filtrate removed under vacuum. The residue was purified by column chromatography (EtOAc/MeOH/$NH_4OH$, 5:2:1) to afford **1** as a 1 mol HCl salt, white solid (89%), mp >231 °C (dec): $^1$H NMR (250 MHz, DMSO-$d_6$) $\delta$ 8.63 (s, 1H), 8.50 (br, 2H), 7.74 (d, $J$=7.0 Hz, 1H), 7.30 (d, $J$=7.0 Hz, 1H), 4.72 (q, $J$=9.5 Hz, 1H), 4.14 (dd, $J$=9.3, 5.4 Hz, 1H), 3.82 (dd, $J$=5.4, 2.8 Hz, 1H), 3.46 (d, $J$=5.3 Hz, 2H), 2.31 (dt, $J$=12.7, 8.8 Hz, 1H), 2.09 (m, 1H), 1.75 (m, 1H). $^{13}$C NMR (62.9 MHz, DMSO-$d_6$) $\delta$ 148.9, 143.5, 140.1, 129.0, 126.1, 99.3, 76.1, 72.0, 62.7, 61.0, 45.4, 28.9.[13]

**3.2.14. 2-((3a*S*,4*R*,6*R*,6a*R*)-4-(4-Chloro-1*H*-imidazo[4,5-*c*]-pyridin-1-yl)-tetrahydro-2,2-dimethyl-3a*H*-cyclopenta-[*d*][1,3]dioxol-6-yl)ethanol (11).** To a solution of **5b** (1.00 g, 3.13 mmol) in THF (20 mL) at 0 °C under $N_2$ was added 9-BBN-H (0.5 M in THF, 10.0 mL, 5.00 mmol), and the resultant mixture stirred for 3 h. To this, NaOH solution (1 M, 6 mL) followed by $H_2O_2$ (50% in $H_2O$, 3 mL) was added and the stirring continued an additional 30 min. The reaction mixture was diluted with $CH_2Cl_2$ (100 mL) and this

mixture washed with saturated $NaHCO_3$ solution (30 mL). The organic layer was dried ($MgSO_4$), filtered, and the filtrate concentrated in vacuo to give the crude product as a colorless oil, which was purified by flash column chromatography (EtOAc/hexane, 1:4) to afford **11** as a white solid (0.84 g, 80%), mp 190–191 °C: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.62 (s, 1H), 8.17 (d, $J$=5.6 Hz, 1H), 7.81 (d, $J$=5.6 Hz, 1H), 4.78 (m, 2H), 4.48 (t, $J$=5.1 Hz, 1H), 4.44 (dd, $J$=5.6, 6.6 Hz, 1H), 3.48 (dd, $J$=11.9, 6.6 Hz, 2H), 2.48 (dd, $J$=12.1, 6.1 Hz, 1H), 2.13 (m, 2H), 1.73 (ddd, $J$=13.4, 6.3, 6.3 Hz, 1H), 1.61 (ddd, $J$=13.6, 6.4, 6.4 Hz, 1H), 1.52 (s, 3H), 1.24 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 144.4, 141.0, 140.8, 140.0, 137.2, 113.0, 107.3, 84.2, 84.0, 61.6, 59.2, 40.0, 36.2, 35.9, 27.3, 25.1. Anal. Calcd for $C_{16}H_{20}ClN_3O_3$: C, 56.89; H, 5.97; N, 12.44. Found: C, 56.88; H, 6.09; N, 12.29.

**3.2.15. 2-((3a*S*,4*R*,6*R*,6a*R*)-4-(4-Amino-1*H*-imidazo[4,5-*c*]-pyridin-1-yl)-tetrahydro-2,2-dimethyl-3a*H*-cyclopenta-[*d*][1,3]dioxol-6-yl)ethanol (12).** A solution of **11** (1.69 g, 5.00 mmol) in hydrazine (20 mL) and MeOH (6 mL) was brought to reflux for 6 h. After cooling to room temperature, the solution was concentrated. The residue was dissolved in MeOH (40 mL) and freshly prepared W2-Raney Ni (prepared from 40 g of alloy) was added to it. The reaction mixture was heated to reflux for 2 h and the hot reaction mixture filtered and the solid washed with hot MeOH (3×15 mL). The combined filtrates were evaporated to dryness and the residue purified via column chromatography (EtOAc/MeOH, 10:1) to afford **12** as a white solid (1.29 g, 80%), mp 192–194 °C: $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.23 (s, 1H), 7.67 (d, $J$=5.8 Hz, 1H), 6.89 (d, $J$=5.8 Hz, 1H), 6.27 (br, 2H), 4.75 (m, 1H), 4.63 (m, 1H), 4.53 (br, 1H), 4.41 (m, 1H), 3.46 (m, 2H), 2.42 (m, 1H), 2.05 (m, 1H), 2.00 (m, 1H), 1.72 (m, 1H), 1.59 (m, 1H), 1.50 (s, 3H), 1.23 (s, 3H). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 153.2, 140.8, 140.7, 139.0, 127.7, 113.8, 98.1, 85.1, 84.9, 62.0, 60.1, 41.0, 37.1, 37.0, 28.2, 26.0. Anal. Calcd for $C_{16}H_{22}N_4O_3$: C, 60.36; H, 6.97; N, 17.60. Found: C, 60.16; H, 7.06; N, 17.49.

**3.2.16. (1*R*,2*S*,3*R*,5*R*)-3-(4-Amino-1*H*-imidazo[4,5-*c*]-pyridin-1-yl)-5-(2-hydroxyethyl)cyclopentane-1,2-diol (3-deaza-5′-homoaristeromycin, 13).** Compound **12** (0.64 g, 2.01 mmol) was dissolved in a mixture of MeOH (10 mL) and 1 N HCl (10 mL) and the resulting solution was stirred at room temperature for 5 h. Basic resin (Amberlite IR 67) was added for neutralization. The solution was filtered, the filtrate removed under vacuum and the residue purified by column chromatography (EtOAc/MeOH/$NH_4OH$, 6:2:1) to afford **13**·HCl as a white solid (436 mg, 78%), mp 205–206 °C: $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.19 (s, 1H), 7.64 (d, $J$=5.8 Hz, 1H), 6.81 (d, $J$=5.8 Hz, 1H), 6.18 (br, 2H), 5.00 (d, $J$=6.3 Hz, 1H), 4.80 (d, $J$=4.8 Hz, 1H), 4.48 (m, 2H), 4.14 (q, $J$=6.3 Hz, 1H), 3.67 (q, $J$=4.8 Hz, 1H), 3.46 (m, 2H), 2.30 (ddd, $J$=12.6, 7.8, 7.8 Hz, 1H), 1.96 (m, 1H), 1.76 (ddd, $J$=13.1, 6.8, 6.8 Hz, 1H), 1.52 (m, 2H). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 151.6, 139.4, 139.0, 137.5, 126.1, 96.4, 74.1, 74.0, 60.1, 58.6, 39.5, 36.5, 31.6. Anal. Calcd for $C_{13}H_{19}N_4O_3Cl$: C, 49.60; H, 6.08; N, 17.80. Found: C, 49.40; H, 5.84; N, 17.49.

### 2.3. X-ray data for compound 8

Crystallographic data (excluding structure factors) for **8** has been deposited with Cambridge Crystallographic Data Centre as supplementary number CCDC 267776. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033 or e mail: deposit@ccdc.cam.ac.uk].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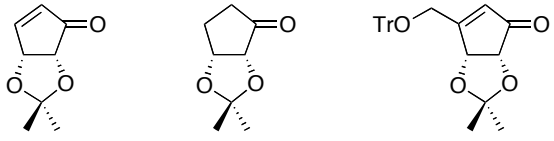


**i**[9a] **ii**[9b] **iii**

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