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Synthesis of 2′-Substituted Derivatives of Neplanocin A (Nucleosides and Nucleotides. XLIV)[1]

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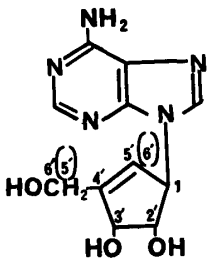
Neplanocin A (**1**) and N^6-benzoylneplanocin A (**2**) were converted to the corresponding 3′,6′-*O*-(tetraisopropyldisiloxane-1,3-diyl)-neplanocin A's (**3**, **4**). The 2′-hydroxy group in **3** and **4** was triflated (**5**, **6**). Nucleophilic displacement of **5** and **6** with a number of nucleophiles (I^-, Br^-, Cl^-, N_3^-, AcO^-, AcS^-) in hexamethylphosphoric triamide afforded the corresponding 2′(*R*)-substituted derivatives in high yields. The 2′(*S*)-azido derivatives were obtained in a similar manner from arabinoneplanocin A prepared by this method. Adenosine was also converted to 2′(*R*)-substituted derivatives, including arabinofuranosyladenine, as well as 2′(*S*)-substituted adenosines. The physical properties of these 2′-substituted derivatives of neplanocin A and adenosine, including nuclear magnetic resonance and circular dichroism spectra, are presented.

Keywords——neplanocin A; adenosine; nucleoside antibiotic; triflates; nucleophilic substitution; silyl protecting group; NMR; CD

Neplanocin A (**1**) is an antitumor nucleoside antibiotic isolated as a component of neplanocins from the culture filtrate of *Ampullariella regularis* A11079.[3] The structure of neplanocin A, [1*R*-(1α, 2α, 3β)]-3-(6-amino-9*H*-purin-9-yl)-5-hydroxymethyl-4-cyclopentene-1,2-diol, has been elucidated by instrumental analyses including X-ray crystallography.[4] There has been considerable interest in the synthesis of 2′-modified nucleosides, stemming primarily from the antitumor or antiviral activities of arabinofuranosyl-cytosine and -adenine,[5] and 2′-amino-2′-deoxyguanosine.[6] It was therefore hoped that the 2′-substituted derivatives **1** of might exhibit better chemotherapeutic indices than the mother compound.



neplanocin A (1)

Due to the unique cyclopentenediol structure of **1**, the conventional procedures[7] for introducing halogeno functions in place of the hydroxyl groups of nucleosides met with little success. In a previous communication we developed and reported a versatile procedure for derivatization at the 2′-position of neplanocin A.[8] This paper describes the synthesis of 2′-substituted 2′-deoxyneplanocin A's in detail, and also reports the conversion of adenosine to 2′-substituted derivatives by a similar process.

Neplanocin A (**1**) was treated with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane[9] in the presence of imidazole to give a derivatives simultaneously protected at the 3-and 6′-hydroxyls, 3′,6′-*O*-(tetraisopropyldisiloxane-1,3-diyl)neplanocin A (**3**)[10] as monoclinic crystals in 82% yield. The structure of **3** was elucidated by analysis of the nuclear magnetic resonance (NMR) spectrum. The 2′-hydroxyl proton of **3** appeared as a doublet at δ 3.59 (disappeared on addition of D_2O) and the 2′-proton appeared as a triple doublet at δ 4.32 (collapsed to a double doublet on addition of D_2O) which showed that the silyl protection had occurred between the 6′- and 3′-hydroxyls (Fig. 1). X-Ray crystallography of **3** also confirmed the structure.[11]

With the structure of **3** established, the conversion at the 2′-position was undertaken. Treatment of **3** with *p*-toluenesulfonyl chloride in pyridine afforded two major spots on thin layer chromatography (TLC); these were tentatively assigned on the basis of NMR measure-

ments as the N^6,2′-*O*-di-tosylate and N^6,N^6,2′-*O*-tri-tosylate respectively. The expected 2′-*O*-tosylate was not obtained. The result indicated the necessity for protection of the amino function of adenine moiety of **3**. Therefore N^6-benzoyl-neplanocin A (**2**) was prepared and converted to the silyl-protected derivative (**4**). Treatment of **4** with trifluoromethanesulfonyl chloride in pyridine at elevated temperature gave two major products. These were separated and characterized as the 2′-*O*-triflate (**6**) and 2′-chloro-2′-deoxy derivative (**8c**). These results showed that the triflation had occurred,but the reaction conditions were such that the product **6** was further converted to **8c** by the attack of chloride ion. Reaction at room temperature or at −20—50°C failed to improve the results. However, the addition of 4-dimethylaminopyridine (DMAP) in this system greatly improved the yield of **6** to 86%. The effective catalytic action of DMAP for acylation in general has been well documented by Vorbrüggen and coworkers.[12] Nucleophilic displacement at the 2′-position of **6** with a number of nucleophiles (LiI, LiCl, LiN_3, and NaOAc) proceeded smoothly at room temperature in hexamethylphosphoric triamide (HMPA) to afford the corresponding products (**8a, c, d, f**).

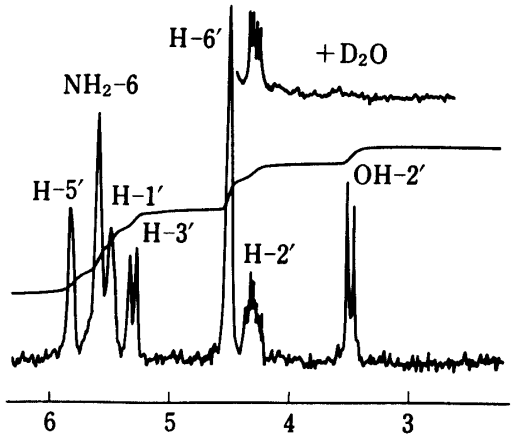


Fig. 1. The NMR Spectrum of **3** in $CDCl_3$ and Effect of Addition of D_2O

The effectiveness of addition of DMAP for the triflation was further demonstrated in the reaction of **3**. Treatment of **3** with trifluoromethanesulfonyl chloride in pyridine or CH_2Cl_2 in the presence of DMAP afforded the 2′-*O*-triflate (**5**) as a foam in 89% yield. The instrumental analyses of **5** confirmed the structure. This finding facilitates the overall conversion of **1**, since the prior protection of the amino group of **1** is no longer necessary.

Treatment of **5** with a number of nucleophiles (LiI, LiBr, LiCl, LiN_3, NaOAc, and KSAc) in HMPA at room temperature for 3—36 h also gave the corresponding 2′(*R*) derivatives (**7a—d, f, h**) in high yields.

A characteristic feature of the arabino configuration of the products **7** is apparent in the NMR spectra of the 2′-*O*-acetyl derivatives (**7f** and **8f**). The chemical shifts of the acetyl-

TABLE I. Reaction Conditions for Nucleophilic Displacement of 2′-*O*-Triflyl-3′, 6′-*O*-(tetraisopropyldisiloxane-1,3-diyl) neplanocin A (**5**) and N^6-Benzoyl-2′-*O*-triflyl-3′,6′-*O*-(tetraisopropyldisiloxane-1,3-diyl) neplanocin A (**6**) in HMPA at Room Temperature

Starting material	Nucleophile	h	Product	Yield (%)
5	LiI	36	**7a**	66
5	LiBr	2.5	**7b**	98
5	LiCl	20	**7c**	86
5	LiN3	10	**7d**	81
5	NaOAc	36	**7f**	82[a]
5	KSAc	3	**7h**	92
6	LiI	10[b]	**8a**	79
6	LiCl	6	**8c**	72
6	LiN3	0.5	**8d**	68
6	NaOAc	18	**8f**	77

a) Treatment of **5** with NaOAc in DMF in the same manner afforded **7f** in 37% yield together with unknown products.
b) The reaction was carried out at 70 °C.

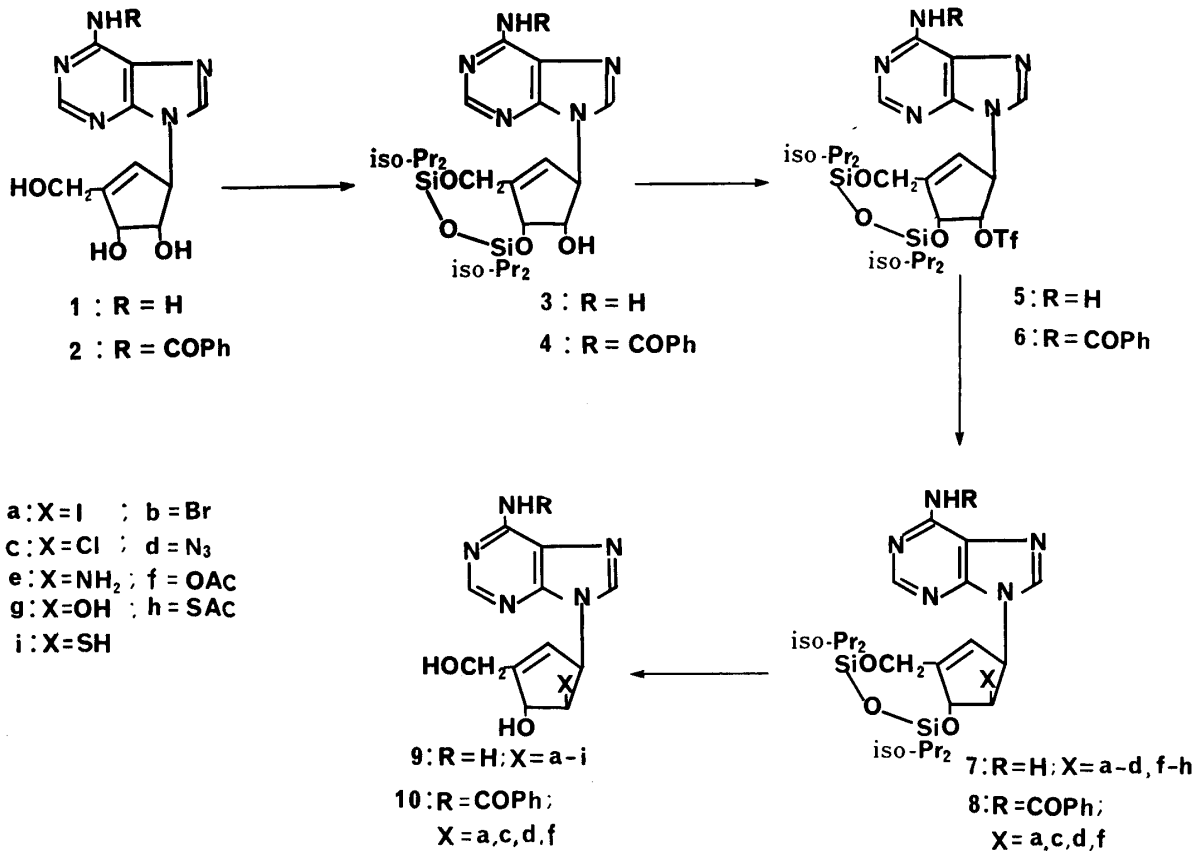


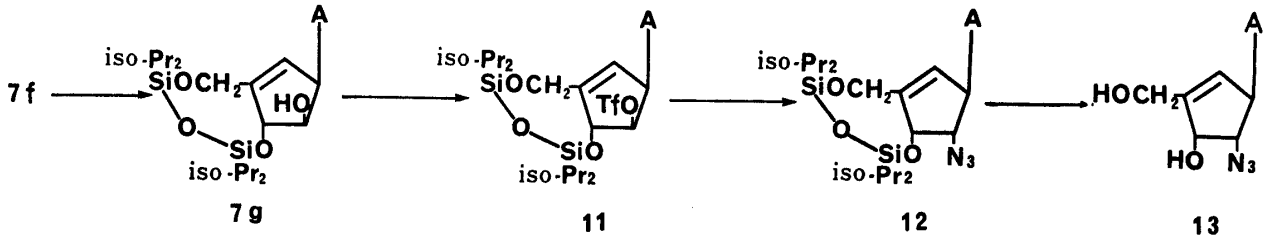
Chart 1

methyl groups of **7f** and **8f** are shifted to unusually highfield (1.61 and 1.60 ppm) as compared with those of the corresponding 2′-*ribo*-acetoxy derivatives (2.09 and 2.12) or usual acetoxy functions in the sugar portions of ribonucleosides. This upfield shift of the 2′-*ara*-substituted acetoxy protons is due to the anisotropic effect of the pyrimidine moiety of the adenine portion. Such an effect would not occur at the 2′-acetoxy group of nucleosides of *ribo*-configuration (Table II).

Deprotection of the silyl group of **7a—c** and **8a, c** with tetra-*n*-butylammonium fluoride proceeded in tetrahydrofuran at room temperature and afforded the corresponding products (**9a—c, 10a, c**) without affecting the *trans*-halohydrin systems in these compounds. Desilylation of **7d** to **9d** followed by reduction of the azido group by bubbling of hy drogen sulfide in aqueous pyridine gave the 2′-amino-2′-deoxy compound (**9e**) in 72% yield. The unsaturated system at 4′-5′ in **9d** was not affected by this treatment. Deprotection of **7f** (and **8f**) by the same procedure gave **9f** (and **10f**) which was deacetylated to furnish *ara*-neplanocin A (**9g**), an analog of arabinofuranosyladenine, a known antiviral agent.[5] The paper chromatography of **1** and **9g** in a system containing boric acid distinguishes them clearly, since the former *ribo*-isomer (**1**) forms a cyclic borate ester while **9g** does not. Desilylation and deacetylation of **7h** gave the 2′-mercapto derivative (**9i**). The thiol **9i** was fairly stable as compared with the reported 2′mercaptans of *ribo* configuration.[13] The X-ray analysis of **9i** confirmed the structure.[14]

The physical properties of the 2′(*R*)-substituted neplanocin A's prepared in this study are summarized in Table III. It should be noted that the bulkiness of the 2′-substituents strongly affected the molecular ellipticities in the CD spectra, which may be due to the preference for the *anti* conformations around the "glycosyl" bond with the bulkier 2′-*ara*-substituents.

For the synthesis of 2′(*S*)-substituted derivatives of **1**, compound **7f** was used. Treatment of **7f** with triethylamine in methanol at room temperature afforded the deacetylated compound



A=adenine-9-yl

Chart 2

(**7g**). Triflation of **7g** to **11** followed by substitution with lithium azide gave, after desilylation, 2′(*S*)-azido-2′-deoxyneplanocin A (**12**). Other 2′-substitutions may well be possible in a similar manner (Chart 2).

The procedure for conversion of the 2′-hydroxyl group of **1** so far described should be readily applicable to common ribonucleosides or arabinonucleosides, and this was confirmed to be the case. The 3′,5′-biprotected adenosine[9] (**14**) was readily converted to the 2′-*O*-triflate (**15**) which was reacted with various nucleophiles (LiI, LiBr, LiCl, LiN_3, NaOAc, KSAc) to give the corresponding 2′-substituted derivatives (**16**). Desilylation of **16** gave the 2′(*R*)-substituted adenosines (**17**) in high yields. (Chart 3, Table IV and V). It should be noted that the present route for the preparation of araA (**17f**) from adenosine is the shortest among several reported methods.[15-20] Starting from the silylated araA(**16f**), 2′-azido-2′-deoxyadenosine (**20**) was likewise prepared.

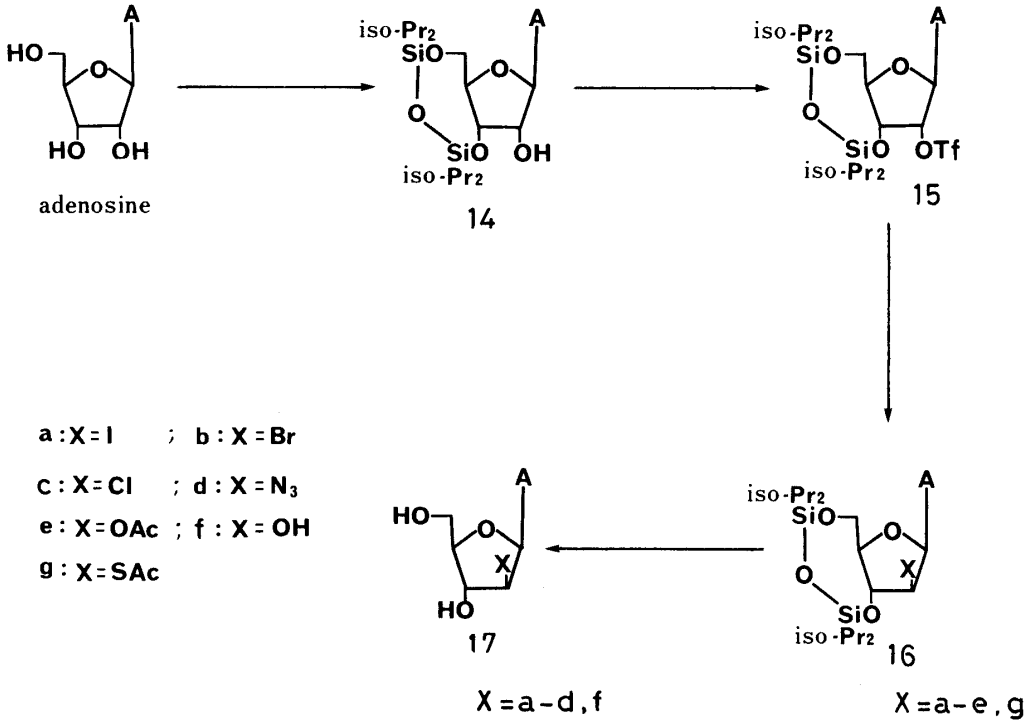


Chart 3

An attempt to synthesize 2′-substituted pyrimidine nucleosides by the present procedure was unsuccessful, because of the formation of 2,2′-*O*-cyclonucleoside at the step of triflation of the 3′,5′-*O*-silylnucleoside in the case of uridine.

In conclusion, the method described here is advantageous for practical preparation of

2′-substituted purine nucleosides from ribo- as well as arabinonucleosides. The biological activities of neplanocin A derivatives prepared in the present work will be reported in a forthcoming paper.

Experimental

All melting points were determined on a Yanagimoto micromelting point apparatus (MP-3) and are uncorrected. The ^{1}H NMR spectra were recorded with a JEOL FX-100-FT or FX-200-FT spectrometer in $CDCl_3$ or DMSO-d_6 as the solvent with tetramethylsilane as an internal standard. Chemical shifts are reported in ppm (δ), and signals are described as s(singlet), d(doublet), t(triplet), q(quartet), sex (sextet), br(broad) or m(multiplet). All exchangeable protons were confirmed by addition of D_2O. Ultraviolet (UV) spectra were recorded with a Shimadzu UV-300 spectrophotometer and infrared (IR) spectra with a Hitachi 215 spectrophotometer. Mass spectra (MS) were measured on a JEOL JMS-D-300 spectrometer. Circular dichroism (CD) spectra were recorded with a JASCO J-40 spectropolarometer at room temperature. TLC was carried out on Merck pre-coated plate $60F_{254}$. Silica gel column chromatography was performed on Wako-gel C-200.

3′,6′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)neplanocin A (3)——Neplanocin A (**1**, 263 mg, 1 mmol) and imidazole (0.3 g, 4.4 eq) were dissolved in 3 ml of dimethylformamide (DMF), and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane[9] (0.35 g) was added to the solution at room temperature. The mixture was stirred at room temperature for 40 min and the reaction was quenched by addition of H_2O. The resulting oil was separated by decantation and partitioned between $CHCl_3$ and water. The organic layer was separated, washed with water, passed through phase separating paper (Whatman 1PS), and concentrated under reduced pressure. The residue was crystallized and recrystallized from EtOH to afford **3**: 414 mg (82%); mp 185—186°C. MS *m/e*: 505 (M^+), 463 (M^+—iso-Pr), 136 (B+2), 135 (B+1). NMR (FX-100 in $CDCl_3$): 1.1 (28H, iso-Pr×4), 3.59 (1H, d, OH-2′), 4.32 (1H, sex, H-2′), 4.52 (2H, slightly br, H-6′a, b), 5.32 (1H, d, H-3′), 5.50 (1H, dd, H-1′), 5.60 (2H, br, NH_2-6), 5.83 (1H, d, H-5′), 7.76 (1H, s, H-2), 8.36 (1H, s, H-8). *Anal.* Calcd for $C_{23}H_{39}N_5O_4Si_2$: C, 54.62; H, 7.77; N, 13.85. Found: C, 54.57; H, 7.79; N, 13.81.

N^6-Benzoyl-3′,6′-*O*-(tetraisopropyldisiloxane-1,3-diyl)neplanocin A (4)——Neplanocin A (**1**) was perbenzoylated, and treatment of the perbenzoylated neplanocin A with 2 N NaOH for 5 min gave **2** in 80% yield: mp 180—183°C. NMR (FX-100 in DMSO-d_6): 4.16 (2H, m, H-6′a, b), 4.36 (1H, dd, H-2′), 4.44 (1H, d, H-3′), 4.94 (1H, t, OH-6′), 5.02, 5.21 (1H 1H, each d, OH-2′ and OH-3′), 5.50 (1H, dd, H-1′), 5.76 (1H, d, H-5′), 7.4—8.1 (5H, m, Ph), 8.40 (1H, s, H-2), 8.70 (1H, s, H-8), 10.38 (1H, br, NH-6). **2** was converted to **4** in a similar manner. Purification through silica gel chromatography with $CHCl_3$: MeOH (20: 1) as an eluent gave **4** in 82% yield. NMR (FX-100 in $CDCl_3$): 1.1 (28H, iso-Pr×4), 3.48 (1H, d, OH-2′), 4.34 (1H, sex, H-2′), 4.50 (2H, slightly br, H-6′a, b), 5.34 (1H, d, H-3′), 5.55 (1H, dd, H-1′), 5.82 (1H, d, H-5′), 7.4—8.1 (6H, m, Ph and H-2 or H-8), 8.78 (1H, s, H-2 or H-8), 8.96 (1H, br, NH-6). MS *m/e*: 609 (M^+), 566 (M^+—iso-Pr). UV λ_{max}^{MeOH} nm: 282.

N^6-Benzoyl-2′-*O*-triflyl-3′,6′-*O*-(tetraisopropyldisiloxane-1,3-diyl)neplanocin A (6)——Triethylamine (13 μl, 1.1 eq) and DMAP (10 mg, 1 eq) were added to a solution of **4** (52 mg) in pyridine or CH_2Cl_2 (1 ml), then the mixture was cooled in an ice bath. To this solution, Tf-Cl (10 μl) was added with exclusion of moisture. After being stirred for 30 min at room temperature, the mixture was poured into ice water and extracted with $CHCl_3$ several times. The organic layer was washed, passed through Whatman 1PS and concentrated to dryness under reduced pressure. The residue was purified by a silica gel chromatography with $CHCl_3$: MeOH (30: 1) as an eluent to give **6**: 48 mg (86%). NMR (in $CDCl_3$): See the next section. MS *m/e*: 636 (M^+—COPh). UV λ_{max}^{MeOH} nm: 280.

Reaction of 4 with Tf-Cl in Pyridine (6 and 8c)——A solution of **4** (55 mg) in pyridine (1 ml) was treated with Tf-Cl (11 μl) at room temperature and the mixture was stirred overnight and then at 55°C for 2 h. The reaction mixture was concentrated under reduced pressure and the residue was separated and purified by preparative TLC (benzene: ethyl acetate, 1: 1) to give **6**. *Rf* (upper). Beilstein test (−). NMR (FX-100 in $CDCl_3$): 1.1 (28H, iso-Pr×4), 4.52 (2H, slightly br, H-6′a, b), 5.41 (1H, dd, H-2′), 5.58 (1H, d, H-3′), 5.76 (1H, dd, H-1′), 5.86 (1H, d, H-5′), 7.4—8.1 (6H, m, Ph+H-2 or H-8), 8.75 (1H, s, H-2 or H-8), 9.00 (1H, br, NH-6). From the band at *Rf* (lower), **8c** was obtained. Beilstein test (+). NMR (FX-100 in $CDCl_3$): 1.1 (28H, iso-Pr×4), 4.46 (2H, slightly br, H-6′a, b), 4.59 (1H, dd, H-2′), 5.28 (1H, d, H-3′), 5.84 (1H, dd, H-1′), 5.92 (1H, d, H-5′), 7.5—8.1 (6H, m, Ph+H-2 or H-8), 8.81 (1H, s, H-2 or H-8), 8.98 (1H, br, NH-6). These compounds were identical with products described later.

2′-*O*-Triflyl-3′,6′-*O*-(tetraisopropyldisiloxane-1,3-diyl)neplanocin A (5)——Compound **5** was obtained in 89% yield from **3** by the same procedure as described in the case of **6**. NMR (FX-100 in $CDCl_3$): 1.1 (28H, iso-Pr×4), 4.51 (2H, slightly br, H-6′a, b), 5.38 (1H, dd, H-2′), 5.58 (3H, NH_2-6 and H-3′), 5.69 (1H, dd, H-1′), 5.84 (1H, d, H-5′), 7.73 (1H, s, H-2), 8.32 (1H, s, H-8). MS *m/e*: 594 (M^+—iso-Pr). UV λ_{max}^{MeOH} nm: 262.

Nucleophilic Displacement of 5 and 6——General Procedure: An appropriate nucleophile was added to a solution of **6** in HMPA and the mixture was stirred at room temperature with exclusion of moisture.

TABLE II. Phydical Physical Properties of 2′(*R*)-Substituted 2′-Deoxy-3′, 6′*O*-(tetraisopropyldisiloxane-1, 3-diyl)nepianocin A's (**7** and **8**)

Compd No.	mp (°C)	MS (*m/e*)	NMR (in $CDCl_3$)
7a	150—152[a] (EtOH)	615 (M^+)	1.1 (28H, iso-Pr×4), 4.48 (2H, slightly br, H-6′a, b), 4.67 (1H, dd, H-2′), 5.42 (1H, d, H-3′), 5.71 (1H, dd, H-1′), 5.8—6.0 (3H, m, H-5′ and NH_2-6), 7.68 (1H, s, H-2), 8.38 (1H, s, H-8)
7b	175—178[b] (Cyclohexane)	569, 567 (M^+) 526, 524 (M^+−iso-Pr) 488 (M^+−Br)	1.1 (28H, iso-Pr×4), 4.46 (2H, s, H-6′), 4.59 (1H, dd, H-2′), 5.34 (1H, d, H-3′), 5.56 (2H, br, NH_2-6), 5.78 (1H, dd, H-1′), 5.90 (1H, d, H-5′), 7.69 (1H, s, H-2), 8.38 (1H, s, H-8)
7c	180—181[c] (EtOH)	525, 523 (M^+)	1.1 (28H, iso-Pr×4), 4.45 (2H, s, H-6′), 4.55 (1H, dd, H-2′), 5.25 (1H, d, H-3′), 5.7—5.9 (4H, m, NH_2-6, H-1′ and H-5′), 7.70 (1H, s, H-2), 8.38 (1H, s, H-8)
7d	189—191[d] (MeOH)	530 (M^+) 488 (M^+−N_3) 487 (M^+−iso-Pr)	1.1 (28H, iso-Pr×4), 4.27 (1H, dd, H-2′), 4.44 (2H, s, H-6′), 5.06 (1H, d, H-3′), 5.54 (2H, br, NH_2-6), 5.74 (1H, dd, H-1′), 5.84 (1H, d, H-5′), 7.64 (1H, s, H-2), 8.38 (1H, s, H-8)
7f	———[e]	547 (M^+) 504 (M^+−iso-Pr)	1.1 (28H, iso-Pr×4), 1.61 (3H, s, OAc), 4.45 (2H, slightly br, H-6′a, b), 5.32 (1H, d, H-3′), 5.44 (1H, dd, H-2′), 5.6—6.0 (4H, m, NH_2-6, H-1′ and H-5′), 7.69 (1H, s, H-2), 8.34 (1H, s, H-8)
7h	———[e]	563 (M^+) 523 (M^+−iso-Pr)	1.1 (28H, iso-Pr×4), 2.11 (3H, s, SAc), 4.38 (1H, d, H-3′), 4.46 (2H, slightly br, H-6′a, b), 5.38 (1H, dd, H-2′), 5.64 (2H, br, NH_2-6), 5.75 (1H, dd, H-1′), 5.85 (1H, d, H-5′), 7.59 (1H, s, H-2), 8.28 (1H, s, H-8)
8a	———[e,f]	676 (M^+−iso-Pr) 240 (B+2) 239 (B+1)	1.1 (28H, iso-Pr×4), 4.51 (2H, slightly br, H-6′a, b), 4.70 (1H, dd, H-2′), 5.46 (1H, d, H-3′), 5.78 (1H, dd, H-1′), 5.92 (1H, d, H-5′), 7.4—8.1 (5H, m, Ph), 7.88 (1H, s, H-2 or H-8), 8.83 (1H, s, H-2 or H-8), 8.98 (1H, br, NH-6)
8c	———[e,f]	———[g]	———[g]
8d	———[e,h]	651 (M^+) 591 (M^+−iso-Pr)	1.1 (28H, iso-Pr×4), 4.32 (1H, dd, H-2′), 4.46 (2H, slightly br, H-6′a, b), 5.10 (1H, d, H-3′), 5.74—5.96 (2H, m, H-1′ and H-5′), 7.4—8.1 (5H, m, Ph), 7.84 (1H, s, H-2 or H-8), 8.82 (1H, s, H-2 or H-8), 9.03 (1H, br, NH-6)
8f	———[e]	651 (M^+) 608 (M^+−iso-Pr)	1.1 (28H, iso-Pr×4), 1.60 (3H, s, OAc), 4.46 (2H, slightly br, H-6′a, b), 5.3—5.5 (2H, m, H-2′ and H-3′), 5.87 (2H, m, H-5′ and H-1′), 7.4—8.1 (6H, m, Ph and H-2 or H-8), 8.76 (1H, s, H-2 or H-8), 9.04 (1H, br, NH-6)

a) *Anal.* Calcd for $C_{23}H_{38}IN_5O_3Si_2$: C, 44.87; H, 6.22; N, 11.38; I, 20.62. Found. C, 44.55; H, 6.10; N, 10.36; I, 21.64. *b*) *Anal.* Calcd for $C_{23}H_{38}BrN_5O_3Si_2$: C, 48.58; H, 6,74; N, 12.32; Br, 14.05. Found. C, 48.56; H, 6.77; N,12.27; Br, 14,13. *c*) *Anal.* Calcd for $C_{23}H_{38}ClN_5O_3Si_2 \cdot H_2O$: C, 50.94; H, 7.44; N, 12.92; Cl, 6.54. Found. C, 50.75; H, 7.44; N, 12.72; Cl, 6.72. *d*) *Anal.* Calcd for $C_{23}H_{38}N_8O_3Si_2$: C, 52.04; H, 7.22; N, 21.11. Found. C, 51.81; H, 7.19; N, 20.95. IR $\nu_{N_3}^{KBr}$ cm^{-1}: 2110. *e*) Isolated as amorphous form. *f*) Beilstein test: positive. *g*) Identical with the product (R_f lower) of the reaction of **4** with Tf-Cl in pyridine. *h*) IR $\nu_{N_3}^{KBr}$ cm^{-1}: 2125.

After confirmation of loss of the starting material by TLC, the reaction mixture was poured into ice water with stirring to give a precipitate, which was collected by filtration and washed with water. Further separation by silica gel chromatography or preparative TLC was carried out when required to give **7** or **8** (Tables I and II).

Deprotection of Bifunctional Silyl Group——General Procedure: Tetra-*n*-butylammonium fluoride (2 eq) was added to a solution of a 2′-substituted derivative **7** or **8** in tetrahydrofuran (THF) at room temperature, and the deprotection reaction was followed by TLC ($CHCl_3$: MeOH, 5: 1). The reaction was almost completed within 10 min. The reaction mixture was concentrated under reduced pressure and the residue was crystallized from an appropriate solvent or purified by silica gel chromatography when required to give **9** and **10** (Table III).

2′-*ara*-Amino-2′-deoxyneplanocin A (9e)——H_2S gas was bubbled into a solution of **9d** (80 mg) in 50% aqueous pyridine (5 ml), and the reaction was followed by TLC analysis with the ninhydrin test. After 6 h, the reaction mixture was neutralized with 2 N AcOH and concentrated under reduced pressure below 45°C. The residue was co-evaporated to dryness with EtOH several times, then dissolved in water. Insoluble sulfur was filtered off and the filtrate was evaporated to dryness under reduced pressure, followed by trituration with EtOH to give an amorphous powder **9e**.

***ara*-Neplanocin A (9g)**——**9f** (233 mg) was kept in 20 ml of NH_3–MeOH (presaturated at 0°C) at room

TABLE III. Physical Properties of 2′(*R*)-Substituted 2′-Deoxyneplanocin A's (**9**, **10**)

Compd No. / 2′(*R*)-substituent	Yield (%)	mp (°C)	Formula and analysis Calcd (Found) % C	H	N	X	MS (*m/e*)	CD $[\theta]^{H_2O}_{252}$	NMR (DMSO-d_6)
9a/-I	99	212—215 (dec.) (EtOH-H_2O)	$C_{11}H_{12}IN_5O_2$ 35.40 (35.45)	3.24 (3.28)	18.77 (19.13)	X=I 34.01 (33.02)	373 (M^+) 246 (M^+−I) 136 (B+2)	−19300	4.18 (2H, slightly br, H-6′a, b), 4.59 (1H, dd, H-2′), 4.97 (1H, t, OH-6′), 5.08 (1H, t, H-3′), 5.59 (1H, dd, H-1′), 5.78 (1H, d, OH-3′), 5.84 (1H, d, H-5′), 7.19 (2H, br, NH_2-6), 7.94 (1H, s, H-2), 8.14 (1H, s, H-8)[a]
9b/-Br	83	224—226 (dec.) (EtOH)	$C_{11}H_{12}BrN_5O_2$ 40.50 (40.57)	3.71 (3.63)	21.47 (21.26)	X=Br 24.50 (24.24)	327, 325 (M^+ 246 (M^+−Br) 136 (B+2)	−13000	4.17 (2H, slightly br, H-6′a, b), 4.60 (1H, dd, H-2′), 4.93—5.06 (2H, m, H-3′ and OH-6′), 5.70 (1H, dd, H-1′), 5.84 (1H, d, OH-3′), 5.86 (1H, d, H-5′), 7.20 (2H, dr, NH_2-6), 7.96 (1H, s, H-2), 8.14 (1H, s, H-8)
9c/-Cl	90	233—235 (dec.) (EtOH)	$C_{11}H_{12}ClN_5O_2$ 46.09 (46.88)	4.29 (4.32)	24.86 (24.79)	X=CL 12.59 (12.51)	283, 281 (M^+) 246 (M^+−Cl) 136 (B+2)	−11000	4.16 (2H, slightly br, H-6′a, b), 4.54 (1H, dd, H-2′), 4.91 (1H, dd, H-3′), 5.00 (1H, t, OH-6′), 5.74 (1H, dd, H-1′), 5.85 (1H, d, OH-3′), 5.86 (1H, d, H-5′), 7.21 (2H, br, NH_2-6), 7.96 (1H, s, H-2), 8.14 (1H, s, H-8)
9d/-N_3[b]	98	231—233 (dec.) (EtOH-H_2O)	$C_{11}H_{12}N_8O_2$ 45.83 (45.86)	4.20 (4.25)	38.87 (38.66)		288 (M^+) 246 (M^+−N3) 136 (B+2)	−19900	4.15 (2H, slightly br, H-6′a, b), 4.27 (1H, dd, H-2′), 4.81 (1H, dd, H-3′), 4.95 (1H, t, OH-6′), 5.64 (1H, dd, H-1′), 5.75 (1H, d, OH-3′), 5.77 (1H, d, H-5′), 7.21 (2H, br, NH_2-6), 7.88 (1H, s, H-2), 8.15 (1H, s, H-8)
9e/-NH_2	72[c]	——[d]	——[b]				262 (M^+) 244 (M^+−H_2O) 136 (B+2)	−10000	3.29 (br, NH-2′), 3.47 (1H, dd, H-2′), 4.14 (2H, s, H-6′), 4.49 (1H, d, H-3′), 4.85, 5.22 (1H×2,each br OH-3′ and OH-6′), 5.46 (1H, dd, H-1′), 5.71 (1H, d, H-5′), 7.17 (2H, br, NH_2-6), 7.84 (1H, s, H-2), 8.12 (1H, s, H-8)
9f/-OAc	80	195—197 (EtOH)	$C_{13}H_{15}N_5O_4$ 51.14 (51.12)	4.95 (4.98)	22.94 (22.74)		305 (M^+) 245 (M^+−AcOH) 136 (B+2)	−11900	1.52 (1H, s, OAc), 4.17 (2H, slightly br, H-6′a, b), 4.82 (1H, t, H-3′), 4.97 (1H, t, OH-6′), 5.18 (1H, dd, H-2′), 5.55 (1H, d, OH-3′), 5.64 (1H, dd, H-1′), 5.80 (1H, d, H-5′), 7.18 (2H, br, NH_2-6), 7.87 (1H, s, H-2), 8.11 (1H, s, H-8)
9g/-OH	92[e]	239—240.5 (EtOH-H_2O)	$C_{11}H_{13}N_5O_3$· 1/3 H_2O 49.13 (49.01)	5.00 (5.01)	26.04 (25.97)		263 (M^+) 245 (M^+−H_2O) 136 (B+2)	−9700	4.14 (3H, m, H-2′ and H-6′a, b), 4.56 (1H, dd, H-3′), 4.86 (1H, t, OH-6′), 5.18, 5.22 (1H×2 each d, OH-2′ and OH-3′), 5.52 (1H, dd, H-1′), 5.72 (1H, d, H-5′), 7.10 (2H, br, NH_2-6), 7.78 (1H, s, H-2), 8.12 (1H, s, H-8)
9h/-SAc	88	165—167 (EtOH)	$C_{13}H_{15}N_5O_3S$· 1/2H_2O 47.26 (47.18)	4.88 (4.94)	21.20 (21.58)	X=S 9.70 (9.61)	320 (M^+−1) 136 (B+2)	−41800	2.10 (3H, s, SAc), 4.12 (1H, dd, H-2′), 4.16 (2H, slightly br, H-6′a, b), 4.91 (2H, m, H-3′and OH-3′), 5.61 (2H, m, H-1′and OH-6′), 5.80 (1H, d, OH-5′), 7.17 (2H, br, NH_2-6), 7.87 (1H, s, H-2), 8.08 (1H, s, H-8)
9i/-SH	75[f]	−263 (dec.) (EtOH-H_2O)	$C_{11}H_{13}N_5O_2S$ 47.30 (47.37)	4.69 (4.53)	25.08 (25.05)	X=S 11.48 (11.31)	279 (M^+) 261 (M^+−H_2O) 245 (M^+−H_2S)	−16800	2.02 (1H, d, SH-2′), 3.60 (1H, m, H-2′), 4.16 (2H, slightly br, H-6′a, b), 4.71 (1H, dd, H-3′), 4.92 (1H, t, OH-6′), 5.88 (1H, d, OH-3′), 5.62 (1H, dd, H-1′), 5.79 (1H, d, H-5′), 7.19 (2H, br NH_2-6), 7.89 (1H, s, H-2), 8.14 (1H, s, H-8)

Compd. No. / 2′(*R*)-substituent	Yield (%)	mp (°C)	Formula and analysis Catcd (Found) % C	H	N	X	MS (*m/e*)	$CD[\theta]^{H_2O}_{252}$	NMR (DMSO-d_6)
10a/-I	85	——[d]	——[d]				477 (M^+)	——[g]	4.21 (2H, slightly br, H-6′a, b), 4.66 (1H, dd, H-2′), 5.02 (1H, t, OH-6′), 5.13 (1H, dd, H-3′), 5.78 (1H, dd, H-1′), 5.84 (1H, d, OH-3′), 5.90 (1H, d, H-5′), 7.5—8.1 (5H, m, Ph), 8.32 (1H, s, H-2 or H-8), 8.75 (1H, s, H-2 or H-8), 11.14 (1H, br, NH-6)
10d/-N_3	78	——[d]	——[d]				392 (M^+)	——[g]	4.19 (2H, slightly br, H-6′a, b), 4.40 (1H, dd, H-2′), 4.89 (1H, dd, H-3′), 5.02 (1H, t, OH-6′), 5.84 (3H, m, H-1′, H-5′ and OH-3′), 7.4—8.1 (5H, m, Ph), 8.24 (1H, s, H-2 or H-8), 8.76 (1H, s, H-2 or H-2), 11.17 (1H, br NH-6)
10f/-OAc	54	205—207 (EtOH)	$C_{20}H_{19}N_5O_5 \cdot 1/2H_2O$ 57.41 (57.55)	4.82 (4.78)	16.74 (16.70)		409 (M^+) 349 (M^+—AcOH)	——[g]	1.52 (3H, s, OAc), 4.20 (2H, slightly br, H-6′a, b), 4.88 (1H, dd, H-3′), 5.03 (1H, t, OH-6′), 5.26 (1H, dd, H-2′), 5.62 (1H, d, OH-3′), 5.87 (2H, m, H-1′ and H-5′), 7.4—8.1 (5H, m, Ph), 8.22 (1H, s, H-2 or H-8), 8.71 (1H, s, H-2 or H-8), 11.13 (1H, br, NH-6)

[a] NMR spectra were recorded for specimens dissolved in DMSO-d_6, and the FX-200 FT machine was employed. [b] IR $\nu^{KBr}_{N_3}$ cm^{-1}: 2125. [c] **9e** was obtained by the reduction of **9d**. [d] Amorphous powder. [e] **9g** was obtained by the deacylation of **9f**. [f] **9h** was converted to **9i** by deacylation with NH_3–MeOH. [g] Not measured.

temperature for 3.5 h. Evaporation of the solvent under reduced pressure to dryness then afforded crystalline **9g**, which was recrystallized from EtOH–H_2O to give 185 mg of pure **9g**. HPLC: column, Zorbax ODS (4.6 mm × 25 cm); mobile phase, 40% MeOH–H_2O: flow rate, 2.0 ml/min. Neplanocin A (**1**): 7.5 min, *ara*-neplanocin A (**9g**): 9.2 min.

2′-*ara*-Mercapto-2′-deoxyneplanocin A (9i)——9h (270 mg) was treated with NH_3–MeOH in the usual manner to give **9i**. 175 mg (75%).

3′,6′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)*ara*-neplanocin A (7g)——Triethylamine (2 ml) was added to a solution of **7f** (2.33 g) in 40 ml of MeOH, and the mixture was stirred for 2 d at room temperature. The reaction mixture was concentrated under reduced pressure and the residue was chromatographed on silica gel ($CHCl_3$: MeOH, 40: 1) to give **7g** (1.40 g, 65%) as a foam. NMR (FX-100 in $CDCl_3$): 1.1 (28H, iso-Pr × 4), 4.42 (2H, ABq, H-6′a, b), 4.55 (1H, dd, H-2′), 5.06 (1H, d, H-3′), 5.54 (1H, dd, H-1′), 5.80 (1H, d, H-5′), 5.95 (2H, br, NH_2-6), 7.73 (1H, s, H-2), 8.19 (1H, s, H-8). MS *m/e*: 505 (M^+).

2′-*O*-Triflyl-3′,6′-*O*-(tetraisopropyldisiloxane-1,3-diyl)*ara*-neplanocin A (11)——The 2′-*O*-triflate **11** (1.23 g, 70%) was obtained from **7g** (1.40 g) in the manner described above. NMR (FX-100 in $CDCl_3$): 1.1 (28H, iso-Pr × 4), 4.46 (2H, slightly br, H-6′), 5.36 (1H, dd, H-2′), 5.6—5.9 (5H, m, H-1′, H-3′, H-5′, NH_2-6), 7.73 (1H, s, H-2), 8.33 (1H, s, H-8). MS *m/e*: 637 (M^+).

2′-(*S*)-Azido-2′-deoxy-3′,6′-*O*-(tetraisopropyldisiloxane-1,3-diyl)neplanocin A (12)——Compound **11** (1.2 g), LiN_3 (200 mg), HMPA (6 ml), 3 h: 0.54 g (54% foam). IR $\nu^{KBr}_{N_3}$ cm^{-1}: 2110. NMR (FX-100 in $CDCl_3$): 1.1 (28H, iso-Pr × 4), 3.95 (1H, dd, H-2′), 4.52 (2H, slightly br, H-6′), 5.44 (1H, d, H-3′), 5.59 (1H, dd, H-1′), 5.70 (2H, br, NH_2-6), 5.84 (1H, d, H-5′), 7.75 (1H, s, H-2), 8.38 (1H, s, H-6). MS *m/e*: 530 (M^+).

2′-(*S*)-Azido-2′-deoxyneplanocin A (13)——Compound **12** (0.41 g): 145 mg (70%), mp 204—206°C (dec) (EtOH). IR $\nu^{KBr}_{N_3}$ cm^{-1}: 2130. NMR (FX-100 in DMSO-d_6): 4.14 (2H, slightly br, H-6′), 4.13 (1H, dd, H-2′), 4.76 (1H, dd, H-3′), 5.00 (1H, t, H-6′), 5.5—5.7 (2H, m, H-1′, OH-3′), 5.79 (1H, d, H-5′), 7.25 (2H, br, NH_2-6), 8.08 (1H, s, H-2), 8.15 (1H, s, H-8). MS *m/e*: 288 (M^+), 135 (B+1). *Anal.* Calcd for $C_{11}H_{12}N_8O_2$: C, 45.83; H, 4.20; N, 38.87. Found: C, 45.50; H, 4.09; N, 38.73.

2′-*O*-Triflyl-3′,6′-*O*-(tetraisopropyldisiloxane-1,3-diyl)adenosine (15)——14[9] (4.25 g) was converted to the 2′-*O*-triflate **15** in 79% yield (4.21 g) in the manner described above mp 165—168°C (dec) (EtOH). NMR (FX-100 in $CDCl_3$), 1.1 (28H, iso-Pr × 4), 4.0—4.2 (3H, m, H-5′a, b, H-4′), 5.32 (1H, dd, H-3′), 5.59 (2H, br, NH_2-6), 5.82 (1H, d, H-2′), 6.12 (1H, s, H-1′), 7.96 (1H, s, H-2), 8.27 (1H, s, H-8). MS *m/e*: 598 (M^+—iso-Pr). UV λ^{EtOH}_{max} nm: 260. *Anal.* Calcd for $C_{23}H_{38}F_3N_5O_7SSi_2$: C, 43.04; H, 5.97; N, 10.91. Found: C, 43.05; H, 6.00; N, 11.01.

Nucleophilic Displacement of 15 and Deprotection of the Bifunctional Silyl Group of 16——The substitu-

TABLE IV. Reaction Conditions and Physical Properties of 2′-*ara*-substituted 2′-Deoxyadenosines(**16**) obtained from 2′-*O*-Trifly1-3′, 5′-*O*-(tetraisopropyldisiloxane-1, 3-diyl)adenosine (**15**) at Room Temperature in HMPA

Nucleophile	h	Yield (%)	Product	MS (*m/e*)	NMR(in $CDCl_3$)
LiI	38	85	**16a**[a]	619 (M^+), 576 (M^+−iso-Pr), 136 (B+2), 135 (B+1)	1.1(28H, iso-Pr×4), 3.90 (1H, m, H-4′), 4.20(2H, dq, H-5′a, b), 4.74 (1H, dd, H-3′), 4.98 (1H, dd, H-2′), 5.68 (2H, br, NH_2-6), 6.28 (1H, d, H-1′, J=6.3 Hz), 8.11 (1H, s, H-2), 8.36 (1H, s, H-8)
LiBr	6	97	**16b**[a]	573, 571 (M^+), 530, 528 (M^+−iso-Pr), 492 (M^+−Br), 136 (B+2), 135 (B+1)	1.1(28H, iso-Pr×4), 3.92 (1H, m, H-4′), 4.17 (2H, dq, H-5′a, b), 4.69 (1H, dd, H-3′), 4.90 (1H, dd, H-2′), 5.74 (2H, br, NH_2-6), 6.44 (1H, d, H-1′), 8.13 (1H, s, H-2), 8.35 (1H, s, H-8)
LiCl	5	63	**16c**[a]	5.29, 5.27 (M^+), 4.86, 4.87 (M^+−iso-Pr), 136 (B±2), 135 (B±1)	1.1(28H, iso-Pr×4), 3.97 (1H, m, H-4′), 4.15 (2H, dq, H-5′a, b), 4.66 (1H, dd, H-3′), 4.80 (1H, d, H-2′), 5.69 (2H, br, NH_2-6), 6.48 (1H, d, H-1′, J=5.8 Hz), 8.13 (1H, S, H-2), 8.35 (1H, s, H-8)
LiN_3	4	92	**16d**	543 (M^+), 491 (M^+−iso-Pr), 136 (B+2), 135 (B+1)	1.1(28H, iso-Pr×4), 3.90 (1H, m, H-4′), 4.12 (2H, dq, H-5′a, b), 4.45 (1H, dd, H-3′), 4.59 (1H, dd, H-2′), 5.75 (2H, br, NH_2-6), 6.44 (1H, d, H-1′), 8.08 (1H, s, H-2), 8.35 (1H, s, H-8)
NaOAc	6	82	**16e**	551 (M^+), 508 (M^+−iso-Pr), 136 (B+2), 135 (B+1)	1.1 (28H, ios-Pr×4), 1.70 (3H, s, OAc), 3.94 (1H, m, H-4′), 4.16 (2H, dq, H-5′b), 4.95 (1H, dd, H-3′), 5.56 (1H, dd, H-2′), 5.62 (2H, br, NH_2-6), 6.45 (1H, d, H-1′), 8.01 (1H, s, H-2), 8.39 (1H, s, H-8)
KSAc	3	69	**16g**	567 (M^+), 524 (M^+−iso-Pr), 136 (B+2), 135 (B+1)	1.1 (28H, ios-Pr×4), 2.17 (3H, s, SAc), 3.9—4.1 (2H, m, H-5′a, b), 4.26 (1H, m, H-4′b), 4.58 (1H, dd, H-3′), 5.03 (1H, dd, H-2′), 5.93 (2H, br, NH_2-6), 6.43 (1H, d, H-1′, J=7 Hz), 7.93 (1H, s, H-2), 8.27 (1H, s, H-8)

a) Beilstein test: positive.

TABLE V. Physical Properties of 2′-*ara*-substituted 2′-Deoxyadenosines (**17**)

Compd. No. / 2′-*ara*-substituted	Yield (%)	mp(°C)	Formula and analysis Calcd (Found) %				MS(*m/e*)	NMR(in DMSO-d_6)
			C	H	N	X		
17a/-I	83	206—209 (dec.) (EtOH)	$C_{10}H_{12}IN_5O_3$ 31.84 (31.94)	3.21 (3.15)	18.57 (18.40)	X=I 33.65 (33.69)	377(M^+) 250(M^+−I) 136(B+2) 135(B+1)	3.76 (3H, m, H-5′a, b, and H-4′), 4.6—4.8 (2H, m, H-2′ and H-3′), 5.25 (1H, t, OH-5′), 5.89 (1H, d, OH-3′), 6.29 (1H, d, H-1′, J=6 Hz), 7.30 (2H, br, NH_2-6), 8.14 (1H, s, H-2), 8.34 (1H, s, H-8)
17b/-Br	79	226—228[a] (dec.) (MeOH)	$C_{10}H_{12}BrN_5O_3 \cdot 1/2EtOH$[b] 37.46 (37.02)	4.14 (4.06)	19.86 (19.61)	X=Br 22.66 (22.53)	331,329(M^+) 250(M^+−Br) 136(B+2) 135(B+1)	3.6—3.9 (3H, m, H-5′a, b and H-4′), 4.58 (1H, dd, H-3′), 4.79 1H, d, H-2′), 5.24 (1H, t, OH-5′), 6.07 (1H, d, OH-3′), 6.43 (1H, d, H-1′), 7.30 (2H, br, NH_2-6), 8.14 (1H, s, H-2), 8.35 (1H, s, H-8)
17c/-Cl	82	241—244[c] (dec.) (EtOH-H_2O)	$C_{10}H_{12}ClN_5O_3$				287,285(M^+) 250(M^+−Cl) 136(B+2) 135(B+1)	3.6—3.9 (3H, m, H-5′a, b and H-4′), 4.48 (1H, oct, H-3′), 4.76 (1H, dd, H-2′), 5.23 (1H, t, OH-5′), 6.07 (1H, d, OH-3′), 6.48 (1H, d, H-1′), 7.30 (2H, br, NH_2-6), 8.14 (1H, s, H-2), 8.35 (1H, s, H-8)
17d/-N_3[d]	87	201—203[e] (dec.) (EtOH)	$C_{10}H_{12}N_8O_3$ 41.09 (41.06)	4.14 (4.03)	38.34 (37.98)		292(M^+) 250(M^+−N_3) 136(B+2) 135(B+1)	3.6—3.9 (3H, m, H-5′a, b and H-4′), 4.41 (1H, dd, H-3′), 4.60 (1H, dd, H-2′), 5.20 (1H, t, OH-5′), 6.00 (1H, d, OH-3′), 6.40 (1H, d, H-1′), 7.31 (2H, br, NH_2-6), 8.15 (1H, s, H-2), 8.32 (1H, s, H-8)
17f/-OH	90[f]	258—260[g] (dec.) (MeOH)	$C_{10}H_{13}N_5O_3$				267(M^+) 136(B+2) 135(B+1)	3.64 (2H, m, H-5′a, b), 3.77 (1H, m, H-4′), 4.12 (2H, m, H-2′ and H-1′), 5.10 (1H, t, OH-5′), 5.52, 5.62 (1H×2, each, d, OH-2′ and OH-3′), 6.25 (1H, d, H-1), 7.22 (2H, br, NH-2-6), 8.13 (1H, s, H-2), 8.17 (1H, s, H-8)

a) Lit.; 215—216.[21] *b*) From the NMR spectrum. *c*) Lit.; 245—247,[21] 225.[22] *d*) IR $\nu_{N_3}^{KBr}$ cm^{-1}: 2100. *e*) Lit.; 204—205.[7b] *f*) 270 mg of **16e** was treated with $n$$Bu_4NF$ in THF followed by ammonolysis to give 117 mg of **17f**. *g*) Lit.; 257—257.5.[16,18]

tion reaction (Table IV) and desilylation (Table V) were carried out as described in the case of neplanocin A to give **16** and **17**, respectively.

3′,5′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)*ara*-adenosine (16f)——**16e** (116 mg) was treated with triethylamine as described before to give **16f** as a foam after chromatographic purification. 95 mg (89%). NMR (FX-100 in $CDCl_3$): 1.1 (28H, iso-Pr×4), 3.86 (1H, m, H-4′), 4.03 (2H, m, H-5′a, b), 4.64 (2H, m, H-2′, H-3′), 5.28 (1H, br, OH-2′), 6.13 (2H, br, NH_2-6), 6.19 (1H, d, H-1′), 8.10 (1H, s, H-2), 8.18 (1H, s, H-8). MS *m/e*: 509 (M^+), 466 (M^+—iso-Pr), 136 (B+2), 135 (B+1).

2′-*O*-Triflyl-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)*ara*-adenosine (18)——**16f** (169 mg) was treated with TfCl in CH_2Cl_2 in the presence of DMAP as described before to afford **18**. 161 mg (77%). NMR (FX-100 in $CDCl_3$): 1.1 (28H, iso-Pr×4), 4.0 (1H, m, H-4′), 4.1 (2H, m, H-5′a, b), 5.4 (2H, m, H-2′, H-3′), 5.73 (2H, br, NH_2-6), 6.39 (1H, d, H-1′), 7.93 (1H, s, H-2), 8.33 (1H, s, H-8). MS *m/e*: 641 (M^+), 598 (M^+—iso-Pr), 136 (B+2), 135 (B+1). UV λ_{max}^{MeOH} nm: 260.

2′-*ribo*-Azido-2′-deoxy-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)adenosine (19)——Compound **18** (120 mg), LiN_3 (20 mg), HMPA (1 ml), 1 h: **19** (90 mg, 90%): mp 168—170°C (EtOH). IR ν_{max}^{KBr} cm^{-1}: 2110. NMR (FX-200 in $CDCl_3$): 1.1 (28H, iso-Pr×4), 4.1 (3H, m, H-4′, H-5′a, b), 4.61 (1H, d, H-2′), 5.19 (1H, dd, H-3′), 5.55 (2H, br, NH_2-6), 5.76 (1H, s, H-1′), 8.00 (1H, s, H-2), 8.32 (1H, s, H-8). MS *m/e*: 534 (M^+), 491 (M^+—iso-Pr), 136 (B+2), 135 (B+1). *Anal.* Calcd for $C_{22}H_{38}N_8O_4Si_2$: C, 49.41; H, 7.16; N, 20.96. Found: C, 49.53; H, 7.08; N, 20.98.

2′-*ribo*-Azido-2′-deoxyadenosine (20)——Compound **19** (70 mg): **20** (32 mg, 84%), mp 221—222.5°C (dec.) (EtOH) (lit: 205°C,[7a] 221—225°C,[23] 217—220°C[24]). IR $\nu_{N_3}^{KBr}$ cm^{-1}: 2110. NMR (FX-200 in DMSO-d_6): 3.64 (2H, m, H-5′a, b), 4.00 (1H, m, H-4′), 4.54 (1H, m, H-3′), 4.64 (1H, dd, H-2′), 5.30 (1H, t, OH-5′), 6.04 (1H, d, OH-3′), 6.05 (1H, d, H-1′), 7.38 (2H, br, NH_2-6), 8.16 (1H, s, H-2), 8.41 (1H, s, H-8). MS *m/e*: 292 (M^+), 250 (M^+-N_3), 136 (B+2), 135 (B+1). *Anal.* Calcd for $C_{10}H_{12}N_8O_3$: C, 41.09; H, 4.14; N, 38.34. Found: C, 41.16; H, 4.14; N, 38.56.

2,2′-*O*-Cyclo-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)uridine (21)——A solution of 3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)uridine[9] (91 mg), DMAP (23 mg), Et_3N (26 μl) in pyridine was treated with 22 μl of Tf-Cl at room temperature, and the mixture was stirred for 4 h. The reaction mixture was partitioned between $CHCl_3$ and H_2O. The organic layer was washed with water and passed through Whatman 1PS, then evaporated to dryness under reduced pressure. The residue was purified by preparative TLC ($CHCl_3$: MeOH, 15: 1) to give a crystalline product, which was recrystallized from ether. 62 mg (72%), mp 174—175.5°C (colorless needles). UV λ_{max}^{MeOH} nm: 225, 250. λ_{min}^{MeOH} nm: 238. NMR (FX-200 in $CDCl_3$): 1.1 (28H, iso-Pr×4), 3.8—4.1 (3H, m, H-4′, H-5′a, b), 5.29 (1H, dd, H-2′), 5.55 (1H, dd, H-3′), 5.97 (1H, d, H-1′, $J_{1',2'}$=6.4 Hz), 6.10 (1H, d, H-5), 7.31 (1H, d, H-6). MS *m/e*: 468 (M^+), 425 (M^+—iso-Pr). *Anal.* Calcd for $C_{21}H_{36}N_2O_6Si_2 \cdot 2/3H_2O$: C, 52.46; H, 7.83; N, 5.83. Found: C, 52.30; H, 7.51; N, 5.67.

2,2′-*O*-Cyclouridine (22)——mp 238—241°C (dec.) (lit: 244—245°C[7d]). NMR (FX-200 in DMSO-d_6): 3.1—3.3 (2H, m, H-5′a, b), 4.08 (1H, m, H-4′), 4.39 (1H, dd, H-3′), 4.97 (1H, t, OH-5′), 5.19 (1H, d, H-2′), 5.90 (2H, each d, H-5, OH-3′), 6.31 (1H, d, H-1′, J=5.9 Hz), 7.83 (1H, d, H-6). UV $\lambda_{max}^{H_2O}$ nm: 225, 250. $\lambda_{min}^{H_2O}$ nm: 238. MS *m/e*: 226 (M^+), 208 (M^+-H_2O).

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