Carbohydrate Research, 111 (1982) 59–66
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

SYNTHETIC APPROACHES TO 6-SUBSTITUTED 9-(3-AZIDO-3,4-DIDEOXY-β-D,L-*erythro*-PENTOPYRANOSYL)PURINES*

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(Received November 19th, 1981; accepted for publication in revised form, March 8th, 1982)

ABSTRACT

Methyl 3-azido-2-*O*-benzoyl-3,4-dideoxy-β-DL-*erythro*-pentopyranoside (**6**) was synthesized through two routes in five steps from methyl 2,3-anhydro-4-deoxy-β-DL-*erythro*-pentopyranoside (**1**). The first route proceeded *via* selective azide displacement of the 3-tosyloxy group of methyl 4-deoxy-2,3-di-*O*-tosyl-α-DL-*threo*-pentopyranoside, followed by detosylation and benzoylation. The second route consisted, with a better overall yield, in the azide displacement of the mesyloxy group of methyl *O*-benzoyl-4-deoxy-3-*O*-methylsulfonyl-α-DL-*threo*-pentopyranoside (**10**), obtained by benzylate opening of **1**, followed by benzoylation, debenzylation, and mesylation. Compound **6** was transformed into its glycosyl chloride, further treated by 6-chloropurine to give the nucleoside 9-(3-azido-2-*O*-benzoyl-3,4-dideoxy-β-DL-*erythro*-pentopyranosyl)-6-chloropurine (**13**). When treated with propanolic ammonia, **13** yielded 9-(3-azido-3,4-dideoxy-β-DL-*erythro*-pentopyranosyl)adenine.

INTRODUCTION

Recently, various 2′- and 3′-azido- and -aminodeoxyribonucleosides have been shown to exhibit antiviral and antitumor properties[1]. As part of our program on development of nucleosides of potential chemotherapeutical value, we described previously the synthesis and the biological activities of 9-(3-azido- and 3-amino-3,4-dideoxy-α-DL-*threo*-pentopyranosyl)adenine[2]. The azidonucleoside was active against *Vaccinia* DNA virus. In continuation of these studies, we report herein the synthesis of the *erythro* isomer and the ways of access to its precursor, 9-(3-azido-2-*O*-benzoyl-3,4-dideoxy-β-DL-*erythro*-pentopyranosyl)-6-chloropurine (**13**)**. This chloro compound is also the intermediate for the synthesis of the corresponding purine nucleosides having such groups as methylamino, dimethylamino, methoxyl, thiomethyl, etc. at C-6. Ribonucleosides having these substituents at the 6-position of purine residues have been proved to be active antimetabolites[3].

*Presented at the 4th International Round Table on Nucleosides, Antwerp, Belgium, February, 1981.
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**For simplicity, only the D series is depicted in the schemes.

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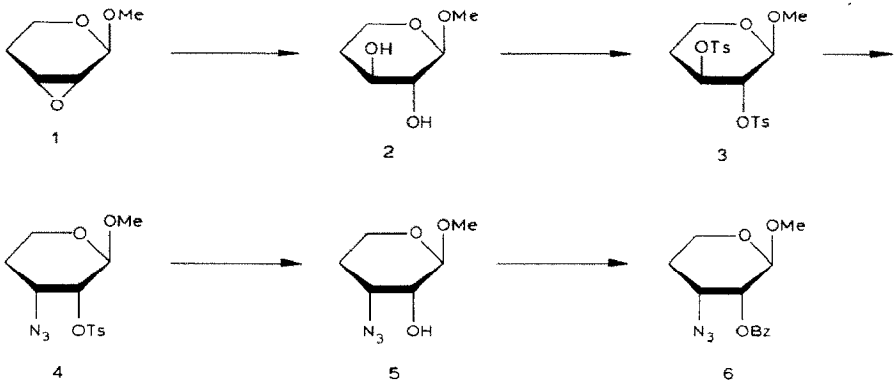
RESULTS AND DISCUSSION

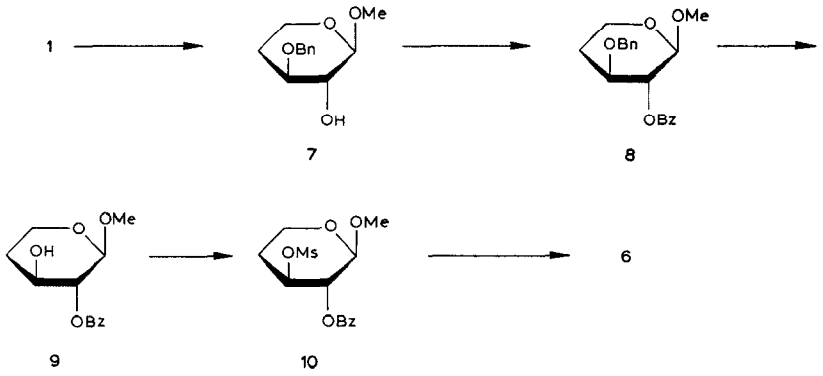
The starting compound of this synthesis, methyl 3-azido-2-*O*-benzoyl-3,4-dideoxy-β-DL-*erythro*-pentopyranoside (**6**), was prepared by two routes from the oxirane methyl 2,3-anhydro-4-deoxy-β-DL-*erythro*-pentopyranoside (**1**), obtained either by a new procedure of oxiranation[4], or by the improved procedure of Sweet and Brown[5].



Hydroxide opening of the epoxide group of **1** resulted in methyl 4-deoxy-α-DL-*threo*-pentopyranoside (**2**), previously obtained beside the β isomer by opening of the mixture of α- and β-oxiranes with sulfuric acid[6]. Treatment of the di-*O*-(*p*-tolylsulfonyl) derivative **3** with sodium azide in *N*,*N*-dimethylformamide displaced the sulfonyloxy group at C-3 with inversion of configuration. The resulting azide **4** was detosylated into **5** by treatment with methanolic potassium hydroxyde, and then benzoylated to give **6**. It is of interest that no azidolysis occurred by identical treatment of the di-*O*-(*p*-tolylsulfonyl) derivative of the β anomer of **2**, obtained by hydrolysis of the α-oxirane. The nucleophilic displacement-reaction was inhibited, presumably because of an unfavorable 1,3-diaxial interaction between the entering azide ion and the anomeric methoxyl group, which is axial in this case. The five steps of this first route were carried out in a 41% overall-yield from epoxide **1**.

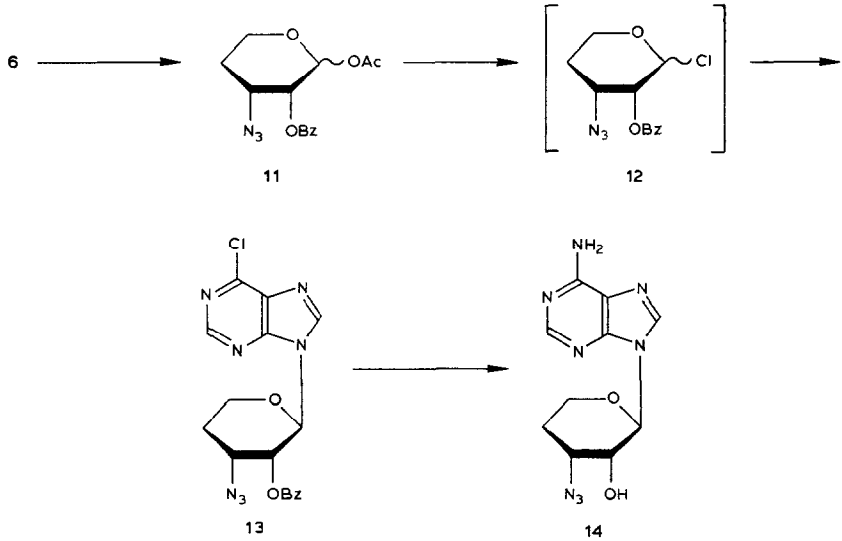
Conceivably, an alternative and direct synthesis of **6** could be achieved by selective tosylation at O-3 of **2** or of the β anomer with a stoichiometric amount of tosyl chloride, followed by nucleophilic substitution of the tosyloxy group with sodium azide, and benzoylation. An attempt at this route showed that **2** is preferentially *p*-toluenesulfonylated at O-3 and the β anomer at O-2. The mixture of 3- and 2-α-sulfonates obtained in the ratio 4:1 was not easy to separate, and the inversion reaction of the mixture of compounds, used as such, gave a mixture too difficult to resolve. Consequently, this approach was abandoned.

In the second route, opening of the epoxide group of **1** with benzyl alcohol and sodium hydride in *N*,*N*′,*N*″-hexamethylphosphoric triamide afforded **7**, in a yield of 87%; this yield is improved over that obtained by treatment of **1** with benzyl



alcohol and sodium[7]. Benzoylation of **7**, followed by debenzylation of **8**, and methanesulfonylation of **9** gave the methanesulfonate **10**, which was converted into **6** when treated with sodium azide in *N,N*-dimethylformamide. This second route was preferred to the first one because of its 66% overall yield from epoxide **1** in five steps.

For the preparation of **8**, we have just reported[8] a third pathway that involves trifluoromethanesulfonylation of the *threo* isomer[2] of the azidodeoxy derivative **5**, and benzoate displacement of the resulting triflate. This route is, unfortunately, not applicable to large-scale preparation.



Compound **6** was hydrolyzed, and then acetylated to give the mixture of anomers **11** in the ratio of 3:17, based on ^{1}H-n.m.r. data. Conversion of **11** into the glycosyl chloride **12**, followed by condensation with 6-chloropurine in the presence of mercuric cyanide, according to the method of Yamaoka *et al.*[9], gave the

6-chloropurine nucleoside **13**. Its treatment with propanolic ammonia afforded the adenine nucleoside **14**. The assignment of the β configuration is consistent with the value of the coupling constant ($J_{1',2'}$ 9.3 Hz).

EXPERIMENTAL

General. — Melting points were determined with a Kofler melting-point apparatus and are uncorrected. ^{1}H-N.m.r. spectra were recorded with a Brucker WP-80 spectrometer and are reported relative to the tetramethylsilane signal. I.r. spectra were recorded with a Beckman Acculab-4 spectrophotometer, and u.v. spectra with a Beckman DBG spectrophotometer. Column chromatography was performed on Silica Gel 60 F_{254} (Merck), and t.l.c. on Silica Gel 60 F_{254} aluminum sheets (Merck); substances were made visible by spraying with the phosphomolybdic acid reagent and heating at 120°. Elemental analyses were performed by the Service Central d'Analyse du C.N.R.S.

*Methyl 4-deoxy-α-*DL-threo-*pentopyranoside* (**2**). — A solution of epoxide **1** (8 g, 60 mmol) in 10% sodium hydroxide (145 mL) was boiled under reflux until complete absence of **1** (monitored by t.l.c.). The solution was made neutral with aqueous sulfuric acid and evaporated *in vacuo*. Removal of any moisture by azeotrope distillation with toluene gave a slurry that was filtered. The filter pad was washed with hot toluene. The filtrate and the toluene washings were concentrated, and the solid formed was collected by filtration to give crystalline diol **2** (8.2 g, 90%), m.p. 105°; ν_{max}^{KBr} 3600–3100 and 3000–2800 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 4.10 (d, 1 H, $J_{1,2}$ 7 Hz, H-1), 3.45 (s, 3 H, OCH_3), 4.00–3.25 (m, 4 H, H-2, -3, -5a, and -5e), and 2.20–1.50 (m, 2 H, H-4a and -4e).

Anal. Calc. for $C_6H_{12}O_4$: C, 48.64; H, 8.11. Found: C, 48.78; H, 8.38.

*Methyl 4-deoxy-2,3-di-*O-p-*tolylsulfonyl-α-*DL-threo-*pentopyranoside* (**3**). — To a stirred solution of diol **2** (14.8 g, 0.1 mol) in dry pyridine (60 mL), cooled to −5°, was added portionwise freshly purified *p*-toluenesulfonyl chloride (48.6 g, 255 mmol). The mixture was stirred at room temperature for 3 days, and then poured into cold 10M aqueous hydrochloric acid (200 mL). The solution was extracted with chloroform. The organic phase was washed with saturated sodium hydrogencarbonate and then water, dried (sodium sulfate), and evaporated. The residue crystallized from methanol or toluene to give **3** (43.3 g, 95%) as white crystals, m.p. 140–141°; ν_{max}^{KBr} 3060–2800, 1600, and 1180–1170 cm^{-1}; ^{1}H-n.m.r.* ($CDCl_3$): δ 7.74 and 7.32 (2 m, 8 H, aryl), 4.54 (m, 1 H, H-3), 4.35 (q, 1 H, $J_{2,3}$ 6.75 Hz, H-2), 4.19 (d, 1 H, $J_{1,2}$ 5 Hz, H-1), 3.93 (m, 1 H, H-5e), 3.38 (m, 1 H, H-5a), 3.16 (s, 3 H, OCH_3), 2.45 (s, 3 H, CH_3 of Ts), 2.22 (m, 1 H, $J_{3,4e}$ 4.75 Hz, H-4e), and 1.79 (m, 1 H, $J_{3,4a}$ 8.25 Hz, H-4a).

*This n.m.r. spectrum was recorded with a Cameca-250 spectrometer of the Service Interuniversitaire de R.M.N. à Haut Champ de la Faculté de Pharmacie de Marseille: the observed 1,2-diaxial coupling constant is weak because of the strong electronegativity of the tosyl substituents which decreases the value of ^3J.

Anal. Calc. for $C_{20}H_{24}O_8S_2$: C, 52.63; H, 5.26; O, 28.07; S, 14.03. Found: C, 52.59; H, 5.23; O, 28.11; S, 13.80.

*Methyl 3-azido-3,4-dideoxy-2-*O*-p-tolylsulfonyl-β-*DL*-erythro-pentopyranoside* (**4**). — To a solution of **3** (5 g, 11 mmol) in dry *N,N*-dimethylformamide (50 mL) was added sodium azide (1.17 g, 18 mmol). The resultant suspension was heated for 24 h at 90°, after monitoring the reaction by t.l.c. After the mixture had been cooled, the solvent was evaporated, the residue was taken up with a minimal amount of water, and the resultant solution was extracted with ether. The organic layer was dried (sodium sulfate) and evaporated, and the crude product crystallized from methanol–water to give **4** (3.05 g, 85%), m.p. 83°; ν_{max}^{KBr} 3200–2800, 2120, 1600, and 1180–1170 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 7.90–7.18 (m, 4 H, C_6H_4), 4.75 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 4.45 (t, 1 H, $J_{2,3}$ 3 Hz, H-2), 3.70 (m, 3 H, H-3, -5a, and -5e), 3.35 (s, 3 H, OCH_3), 2.45 (s, 3 H, CH_3 of Ts), and 2.25–1.50 (m, 2 H, H-4a and -4e).

Anal. Calc. for $C_{13}H_{17}N_3O_5S$: C, 47.70; H, 5.20; O, 24.46; S, 9.78. Found: C, 47.83; H, 5.23; O, 24.63; S, 9.93.

*Methyl 3-*O*-benzyl-4-deoxy-α-*DL*-threo-pentopyranoside* (**7**). — To a magnetically stirred suspension of sodium hydride (14.4 g, 0.3 mol) in freshly distilled *N,N',N''*-hexamethylphosphoric triamide (100 mL) was added dropwise at room temperature benzyl alcohol (35.3 mL, 0.34 mol). After evolution of hydrogen had ceased, epoxide **1** (13 g, 0.1 mol) was added in a single portion, and the stirring continued for 50 h at room temperature. After being cooled, the reaction mixture was made acid, under vigourous stirring, with glacial acetic acid (20 mL), and then diluted with sufficient water to dissolve the precipitated salts. The product was extracted with ether. After evaporation to dryness under reduced pressure (13 Pa, 90°), the residue was chromatographed on a column of silica gel, being eluted with 4:5 (v/v) ethyl acetate–hexane, to give **7** (20.9 g, 87.6%) as a pale-yellow oil that was homogeneous in t.l.c.; the physical characteristics were identical with those previously reported[7].

*Methyl 2-*O*-benzoyl-3-*O*-benzyl-4-deoxy-α-*DL*-threo-pentopyranoside* (**8**). — A stirred solution of **7** (20 g, 84 mmol) in pyridine (160 mL) was cooled to 0° and treated with benzoyl chloride (12 mL, 104 mmol). The solution was kept for 30 min at 0°, and for 4 h at room temperature, then poured into ice–10M hydrochloric acid, and extracted with chloroform. The organic layer was washed consecutively with saturated sodium hydrogencarbonate and water, dried, and evaporated, leaving a pale-yellow oil that solidified. It crystallized from ether–pentane to give **8** (27.6 g, 96%), m.p. 66–67°; $\nu_{max}^{CHCl_3}$ 1720, 1260, and 710 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 8.30–7.00 (m, 10 H, Ar), 5.15 (q, 1 H, $J_{2,3}$ 7.2 Hz, H-2), 4.60 (s, 2 H, CH_2 of benzyl), 4.36 (d, 1 H, $J_{1,2}$ 6.4 Hz, H-1), 4.20–3.10 (m, 3 H, H-3, -5a, and -5e), 3.42 (s, 3 H, OCH_3), and 2.3–1.4 (m, 2 H, H-4a and -4e).

Anal. Calc. for $C_{20}H_{22}O_5$: C, 70.17; H, 6.43; O, 23.39. Found: C, 70.01; H, 6.53; O, 23.53.

*Methyl 2-*O*-benzoyl-4-deoxy-α-*DL*-threo-pentopyranoside* (**9**). — A mixture of **8** (20 g, 58 mmol), palladium-on-charcoal (5%, 2 g), and glacial acetic acid (20 mL) in ethyl alcohol (200 mL) was hydrogenated at ambient pressure and temperature

for 3 h. The catalyst was filtered off, the filtrate was evaporated, and the residue crystallized from cyclohexane to yield **9** (14.4 g, 98%), m.p. 78–79°; $\nu_{max}^{CHCl_3}$ 3520, 1720, and 710 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 8.1–7.1 (m, 4 H, phenyl), 4.87 (q, 1 H, $J_{2,3}$ 5.7 Hz, H-2), 4.57 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 4.20–3.50 (m, 3 H, H-3, -5a, and -5e), 3.42 (s, 3 H, OCH_3), 3.27 (s, 1 H, OH), and 2.40–1.42 (m, 2 H, H-4a and -4e).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.90; H, 6.35; O, 31.75. Found: C, 61.80; H, H, 6.295; O, 31.59.

*Methyl 2-O-benzoyl-4-deoxy-3-O-methylsulfonyl-α-*DL-threo-*pentopyranoside* (**10**). — To a solution of **9** (14 g, 55.5 mmol) in pyridine (100 mL) cooled to −30° was added methanesulfonyl chloride (8.7 mL, 110 mmol). The reaction mixture was kept for 3 h at −30°, then for 1 h at 0°, and finally for 1 h at room temperature. The pyridine was evaporated under reduced pressure, and the residue extracted with a concentrated solution of sodium hydrogencarbonate. The suspension was filtered off, air-dried, and extracted with chloroform. Evaporation of the filtrates afforded **10** (16.3 g, 89%), m.p. 103–104°; $\nu_{max}^{CH_2Cl_2}$ 1725, 1170, and 1160 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 8.15–7.15 (m, 5 H, phenyl), 5.1 (q, 1 H, $J_{2,3}$ 7.8 Hz, H-2), 4.85 (m, 1 H, $J_{3,4e}$ 5.1, $J_{3,4a}$ 9 Hz, H-3), 4.45 (d, 1 H, $J_{1,2}$ 6 Hz, H-1), 4.15 (m, 1 H, $J_{5e,5a}$ 12.3, $J_{5e,4e} = J_{5e,4a}$ 4.8 Hz, H-5e), 3.50–3.40 (overlapping s and m, 4 H, $J_{5a,4a}$ 9.3, $J_{5a,4e}$ 3.3 Hz, OCH_3 and H-5a), 2.90 (s, 3 H, CH_3 of mesyl), and 2.50–1.70 (m, 2 H, H-4a and -4e).

Anal. Calc. for $C_{14}H_{18}O_7S$: C, 51.06; H, 5.17; O, 34.04; S, 9.725. Found: C, 51.23; H, 5.40; O, 34.29; S, 9.78.

*Methyl 3-azido-2-O-benzoyl-3,4-dideoxy-β-*DL-erythro-*pentopyranoside* (**6**). — (*a*) A solution of **4** (11.2 g, 34 mmol) in 10% methanolic potassium hydroxide (560 mL) was heated for 2 h at 60°. After addition of saturated sodium chloride and evaporation of the methanol, the residue was continuously extracted with ether for 18 h in a liquid–liquid extraction apparatus. The organic phase was separated and evaporated to give a pale-yellow oil, which was purified on a silica gel column with 1:1 (v/v) ethyl acetate–hexane as eluent to give **5** (3.97 g, 67%) as a colorless oil used without further purification. A solution of **5** (1.7 g, 10 mmol) and benzoic anhydride (4.52 g, 20 mmol) in dried pyridine (2.4 mL) was heated for 2 h at 120°. The temperature was then lowered to 80°, and methanol (5 mL) was added slowly. After the mixture had been further heated for 5 h at 80°, methanol was removed *in vacuo*. The residue was taken up in ice-cold hydrochloric acid and extracted with ether. The extract was stirred with saturated sodium hydrogencarbonate, washed with water, and dried (sodium sulfate). Evaporation to dryness under 130 Pa pressure afforded an oil that was purified by silica gel column chromatography with ethyl acetate as eluent to give **6** (2.28 g, 84%); $\nu_{max}^{CHCl_3}$ 3100–2800, 2120, 1720, and 1600 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 8.15–7.22 (m, 5 H, phenyl), 5.15 (q, 1 H, $J_{2,3}$ 2.7 Hz, H-2), 4.77 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1), 4.00–3.70 (m, 3 H, -5a, and -5e), 3.40 (s, 3 H, OCH_3), and 2.52–1.62 (m, 2 H, H-4a and -4e).

Anal. Calc. for $C_{13}H_{15}N_3O_4$: C, 56.32; H, 5.41; N, 15.16; O, 23.11. Found: C, 56.41; H, 5.45; N, 14.91; O, 23.32.

(*b*) To a solution of **10** (5 g, 15 mmol) in *N,N*-dimethylformamide (100 mL) were added sodium azide (1.5 g, 23 mmol) and molecular sieve 3A. The solution was stirred for 24 h at 90°. After evaporation of the solvent, the solid residue was dissolved in water, the suspension filtered, and the filtrate extracted with ether. Removal of ether afforded pure **6** (3.8 g, 90%) as a colorless oil identical (t.l.c., i.r., and n.m.r.) with the sample prepared by method (*a*).

*1-O-Acetyl-3-azido-2-O-benzoyl-3,4-dideoxy-α- and -β-*DL-erythro-*pentopyranose* (**11**). — Compound **6** (4.34 g, 15.6 mmol) was hydrolyzed by heating its solution in glacial acetic acid (68 mL) with concentrated hydrochloric acid (16 mL) for 3 h at 60°. The solution was made neutral with sodium hydrogencarbonate (16 g) and evaporated to dryness (40°) under reduced pressure, and the residue used for the next reaction was suspended in pyridine (23 mL). After addition of acetic anhydride (23 mL), the suspension was stirred for 1 h at room temperature and evaporated (40°) *in vacuo*. The residue was diluted with ice–hydrochloric acid and extracted with chloroform. The organic layer was washed successively with 5% aqueous sodium hydrogencarbonate and water. After being dried (sodium sulfate), the chloroform extract was evaporated at 13 Pa. The residual syrup was chromatographed on a silica gel column with 2:7 (v/v) ethyl acetate–hexane as eluent to afford a mixture of the anomers of **11** (4 g, 84%). The n.m.r. signals for H-1, H-2, and OAc showed 85% of the α anomer; $\nu_{max}^{CHCl_3}$ 3100–2840, 2120, 1750, 1720, and 1600 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 8.12–7.22 (m, 5 H, phenyl), 6.12 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1 of α anomer), 6.05 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1 of β anomer), 5.40 (q, 1 H, $J_{2,3}$ 4.2 Hz, H-2 of β anomer), 5.17 (q, 1 H, $J_{2,3}$ 3 Hz, H-2 of α anomer), 4.15–3.77 (m, 3 H, H-3, -5a, and -5e), 2.6–1.7 (m, 2 H, H-4a and -4e), and 2.1 (s, 3 H, OAc).

Anal. Calc. for $C_{14}H_{15}N_3O_5$: C, 55.08; H, 4.92; N, 13.77; O, 26.23. Found: C, 55.23; H, 4.81; N, 13.67; O, 26.39.

*9-(3-Azido-2-O-benzoyl-3,4-dideoxy-β-*DL-erythro-*pentopyranosyl)-6-chloropurine* (**13**). — To a solution of **11** (2 g, 6.56 mmol) in anhydrous ether (68 mL) were added molecular sieve 3A (2 g) and acetyl chloride (2 mL, 25 mmol). Through this solution, cooled to −10°, was bubbled dry hydrogen chloride until the gas escaped from the drying tube. After monitoring the starting of the reaction by t.l.c. in 1:2 (v/v) ethyl acetate–hexane*, the mixture was kept for 1 h at 0°, and then for 10 h at room temperature. Evaporation of the mixture to dryness gave a pale-yellow oil, which was immediately dissolved in nitromethane (57 mL, distilled in the presence of phosphorus pentaoxide). To this solution were added molecular sieve 3A (2.4 g), 6-chloropurine (2 g, 12.9 mmol), and mercuric cyanide (2 g, 7.9 mmol), and the mixture was heated for 7 h at 120°. The reaction mixture was filtered hot, and the filter cake was washed with hot nitromethane. After evaporation of the combined filtrates under aspiration vacuum and then at 130 Pa at 50°, the remaining solid was extracted with chloroform, and the suspension filtered. The filtrate was washed with 50% potassium iodide in half-saturated sodium chloride (100 mL) and

*The chromatogram must be rapidly developed to avoid hydrolysis of the chloride.

saturated sodium chloride (2 × 100 mL), and dried. Evaporation of the dried organic layer gave **13** as a light-yellow lac that crystallized as urchins. Recrystallization from ethanol gave 2.1 g (80%) of **13**, m.p. 198°; λ_{max}^{EtOH} 205 nm (ε 23 600), 244 (ε 14 000), and 275 (ε 7 830); ν_{max}^{KBr} 2120, 1730, and 1590 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 8.62–8.25 (s, 2 H, H-2 and -8), 7.80–7.12 (m, 5 H, phenyl), 6.2 (d, 1 H, $J_{1',2'}$ 9.6 Hz, H-1'), 5.67 (q, 1 H, $J_{2',3'}$ 3 Hz, H-2'), 4.50 (q, 1 H, $J_{3',4'e} = J_{3',4'a}$ 3 Hz, H-3'), 4.05 (m, 2 H, H-5'a and -5'e), and 2.57–1.50 (m, 2 H, H-4'a and -4'e).

Anal. Calc. for $C_{17}H_{14}N_7O_3Cl$: C, 51.06; H, 3.50; Cl, 8.89; N, 24.53. Found: C, 51.05; H, 3.51; Cl, 9.06; N, 24.51.

*9-(3-Azido-3,4-dideoxy-β-*D,L-erythro-*pentopyranosyl)adenine* (**14**). — A suspension of **13** (0.2 g, 0.5 mmol) in propanolic ammonia* (saturated at 0°, 7 mL) was stirred until dissolution in a sealed tube at room temperature, and then kept for 3 days. After evaporation of the solution to dryness, the residue was purified by silica gel column chromatography with 3:1 (v/v) ethyl acetate–ethyl alcohol as eluent to give **14** (125 mg, 90%) (for analytical purposes, a sample was crystallized from methyl alcohol), m.p. 254°; λ_{max}^{EtOH} 260 nm (ε 12 700); ν_{max}^{KBr} 3240, 3160, 2110, 2100, and 1600 cm^{-1}; ^{1}H-n.m.r. (Me_2SO-d_6): δ 8.25–8.10 (s, 2 H, H-2 and -8), 7.18 (s, 2 H, NH_2), 5.83 (d, 1 H, $J_{2',OH}$ 5.1 Hz, OH), 5.58 (d, 1 H, $J_{1',2'}$ 9.3 Hz, H-1'), 4.55 (d, 1 H, $J_{2',3'}$ 3.6 Hz, H-2'), 4.32 (m, 1 H, H-3'), 3.75 (m, 2 H, H-5'a and -5'e), and 2.15–1.65 (m, 2 H, H-4'a and -4'e).

Anal. Calc. for $C_{10}H_{12}N_8O_2$: C, 43.48; H, 4.35; N, 40.58; O, 11.59. Found: C, 43.74; H, 4.39; N, 40.45; O, 11.64.

ACKNOWLEDGMENTS

This investigation was supported, in part, by the Centre National de la Recherche Scientifique (ERA No. 560), and, in part, by the Institut National de la Santé et de la Recherche Médicale (U.205).

REFERENCES

1 E. De Clerq, J. Balzarini, J. Descamps, and F. Eckstein, *Biochem. Pharmacol.*, 29 (1980) 1849–1851.
2 D. Bouchu, M. Abou-Assali, A. Grouiller, G. Carret, and H. Pacheco, *Eur. J. Med. Chem.*, 16 (1981) 43–47.
3 M. Ikehara and Y. Takatsuka, *Chem. Pharm. Bull.*, 26 (1978) 985–988.
4 C. Gagnieu and A. Grouiller, *J. Chem. Soc., Perkin Trans 1*, (1982) 1009–1011.
5 F. Sweet and R. K. Brown, *Can. J. Chem.*, 46 (1968) 707–713; D. Picq and D. Anker, unpublished data.
6 C. Gagnieu and A. Grouiller, *Carbohydr. Res.*, 84 (1980) 61–69.
7 D. Descours, Dissertation No. I-DE-7904, Université Claude Bernard Lyon I, Lyon, 1979.
8 A. Grouiller, H. Bazin, and C. Gagnieu, *Nucleic Acids Res., Spec. Publ.*, 9 (1981) 111–114.
9 N. Yamaoka, K. Aso, and K. Matsuda, *J. Org. Chem.*, 30 (1965) 149–152.

*Methanol as solvent was avoided because of partial substitution of the chloro group of the base by a methoxyl group.