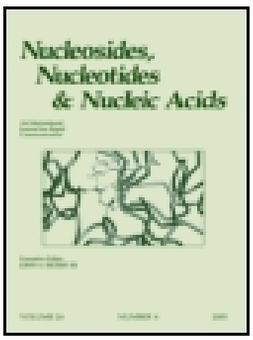

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6-CHLOROXANTHOSINE, A USEFUL INTERMEDIATE FOR THE EFFICIENT SYNTHESES OF [6-^{15}N]-ISOGUANOSINE, ISOINOSINE AND OTHER PURINE NUCLEOSIDE ANALOGUES

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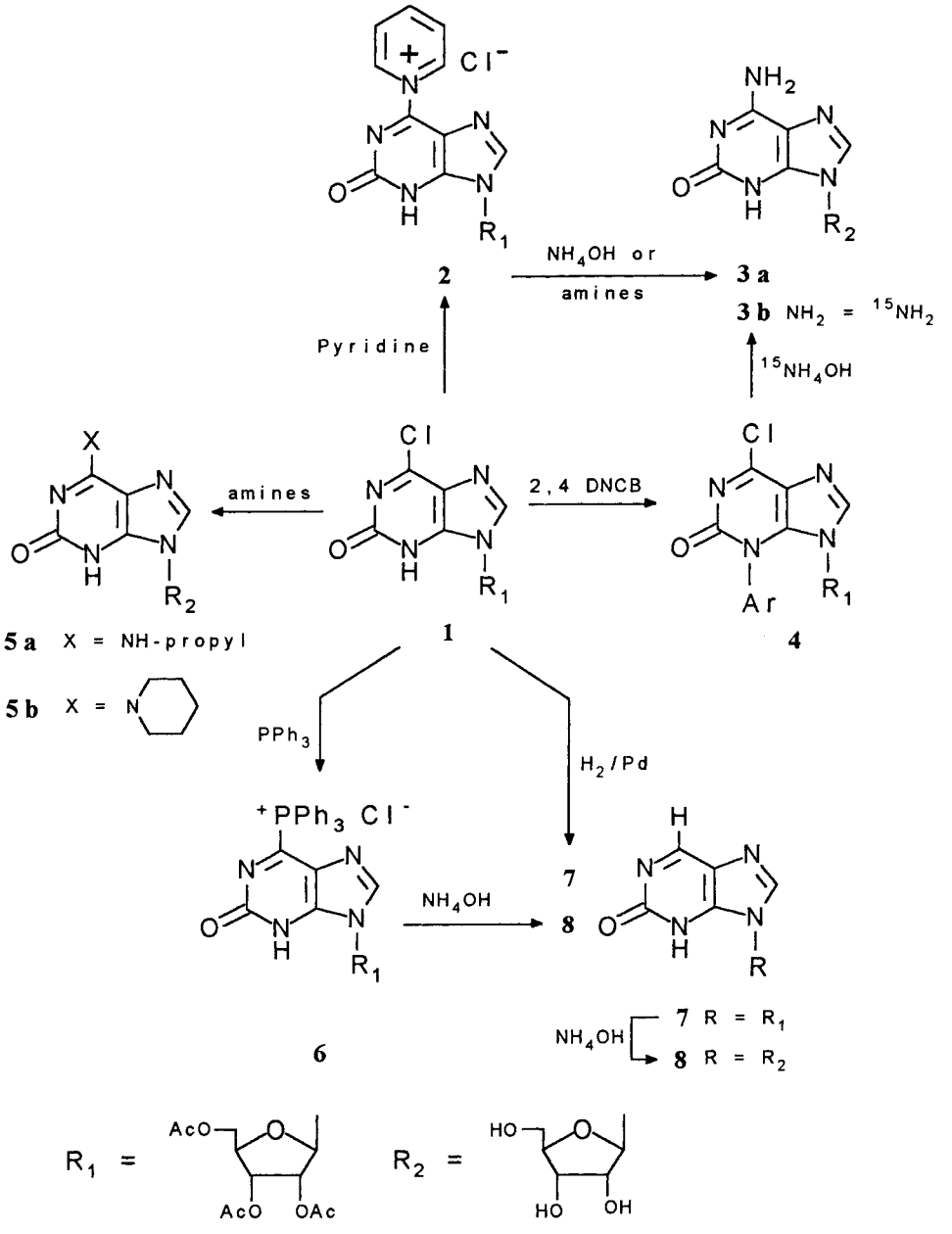
ABSTRACT. 6-Chloroxanthosine **1**, when activated towards nucleophilic displacement at the 6-C position by conversion into the corresponding 3-N-(2,4-dinitrophenyl) derivative **4**, reacted with aq. $^{15}NH_3$ to afford [6-^{15}N]-isoguanosine **3b** in 81 % overall yield. Catalytic hydrogenation (Pd/C) of **1** led in 60 % yield to isoinosine **8**; alternatively, this could be obtained in 88 % overall yield through alkaline hydrolysis of triphenylphosphonium salt **6**, synthesized from **1** by reaction with PPh_3. The reactivity of **1** was further explored by treating it with primary and secondary amines: the 6-N propylamino and the 6-N piperidinyl derivatives (**5a** and **5b**, respectively) could thus both be prepared in more than 90 % yield.

In the course of our studies on the synthesis of purine nucleoside analogues[1-3] we have proposed an easy and one step procedure to 6-chloroxanthosine (**1**) which was used in the preparation of isoguanosine[2,4] (**3a**). In this paper, we have further explored the reactivity of **1** in a number of functional group transformations resulting in efficient routes to synthesize [6-^{15}N]-isoguanosine (**3b**), isoinosine (**8**) and other base modified nucleosides.

The synthesis of ^{15}N-labelled nucleosides is of considerable interest because of their high potential, after incorporation in an oligonucleotide chain, as probes in NMR studies aimed at the elucidation of nucleic acids structures and

nucleic acid-protein interactions. Recently, several papers dealing with the synthesis of ^{15}N-labelled nucleosides have appeared in the literature[5-8]. In the case of guanosine, adenosine and cytidine, the introduction of the ^{15}N atom in the exocyclic amino function is not troublesome, generally requiring only a nucleophilic displacement with $^{15}NH_3$ or other ^{15}N reagents on the appropriate activated nucleoside bases[5-8]. In the case of isoguanosine, however, a direct conversion of chloride **1** into isoguanosine **3a** by treatment with aq. ammonia (10 M) was unsuccessful (only 20 % of the target compound could be recovered even after 3 days at 55 °C)[2,9]. Using more dilute aqueous NH_3 solution lower yields were obtained. This is particularly detrimental when $^{15}NH_3$, as commercially available 3.3 M solution, has to be used. The synthetic pathway previously described[2] to obtain **3a** in high yields required the preparation of the 6-pyridinyl derivative **2**, which, when treated with ammonia or amines, led to the target compound **3a** through a nucleophilic attack of the reagent on the pyridinium α-carbons, followed by opening of the ring (Zincke reaction)[10-12]. In these cases, the exocyclic amino group of isoguanosine is generated by the nitrogen atom of the pyridinium residue. The preparation of labelled [6-^{15}N]-isoguanosine could be accomplished in this manner, but only by reacting **2** with expensive ^{15}N-labelled pyridine.

In order to render the 6-C of **1** more reactive towards aq. ammonia we introduced into the heterocyclic ring a strong electron-withdrawing group, such as 2,4-dinitrophenyl. The efficacy of such a substituent in rendering the purine base moiety more prone to nucleophilic attack had already been tested in previous work[3] in which the 1-N-(2-nitrophenyl) derivative of inosine was shown to react with ^{15}N-ammonia on the purine 2-C, giving [1-^{15}N]-inosine in good yields. In the case of chloride **1**, the reaction with 2,4-dinitrochlorobenzene in DMF solution (1.5 h, 80 °C) afforded derivative **4** in 95 % yield. On the other hand, when **1** was treated with 4-nitrochloro- (or fluoro-) benzene, under the same reaction conditions, the corresponding 3-N-(4-nitrophenyl) nucleoside could not be obtained. As expected, **4** reacted satisfactorily with $^{15}NH_3$ (aq., 3.3 M), yielding [6-^{15}N]-isoguanosine (**3b**), which was purified by reversed phase HPLC (85 % yield of isolated product). The isolation from the reaction mixtures of [1-^{15}N]-2,4-dinitroaniline in 1:1 ratio with respect to **3b** confirmed that the formation of isoguanosine **3b** resulted from a nucleophilic attack of the ammonia on the purine 6-C, followed by a fast, analogous reaction on the 1-C of the 2,4-dinitrophenyl ring.



While unreactive towards aq. ammonia, **1** gave in high yields 6-N-alkylisoguanosine derivatives by treatment with amines. Either primary amines, such as *n*-propylamine, or secondary amines, such as piperidine, reacted smoothly (neat, 2.5 h, 50 °C) with substrate **1**, giving respectively **5a** (91 %) and **5b** (93 %). The same products could be obtained, as expected, more rapidly and in almost quantitative yields, starting from compound **4**.

6-Chloroxanthosine **1** was recognized as a useful precursor of the rare isoinosine **8**, a fluorescent nucleoside whose interest is related to its ability to form base pairs with all the four common nucleosides in duplex oligonucleotide structures[13]. The previously reported syntheses of **8**[14] are based on the ribosylation of 2-hydroxypurine or on the deamination of 9-(β-D-ribofuranosyl)-2-aminopurine. However, the reduction of halogenated purines is a well known method[15,16] for introducing a C-H bond in the purine ring. We reasoned therefore that the reduction of **1** could result in a straightforward and unprecedented synthesis of isoinosine. When **1** underwent a catalytic hydrogenation with Pd/C in EtOH, only very low yields of isoinosine, in its triacetylated form (**7**), were observed, even after prolonged treatments. The reaction was optimized using water as solvent in the presence of MgO (1 eq, 8 h, r.t.) and, after deacetylation, isoinosine **8** could be obtained in 60 % overall yield. An alternative route was tested, which proved to be more efficient. **1** was first converted, by reaction with triphenylphosphine in benzene, into phosphonium salt **6** (93 % yield), which was successively hydrolyzed in alkaline conditions[17] (NH_4OH, 4 h, 50 °C, 95 % yield after purification), thus affording, through cleavage of the C-P bond, **8** in 88 % overall yield.

Unless otherwise stated, all the synthesized compounds were purified by silica gel chromatography (experimental).

The structures of all the cited compounds were confirmed by spectroscopic data (^1H and ^{13}C NMR, FAB MS and UV), which agreed, for the known products, with the literature values. Particularly, in the case of **4**, the position of the 2,4-dinitrophenyl group was proved by selective nOe experiments, which showed a nOe effect between the anomeric proton and the 3-H of the phenyl ring. This evidence indicated **4** to be the most plausible structure, where the protons at issue, by inspection of molecular models, are within nOe proximity, while excluding the alternative regioisomer having the 2,4-dinitrophenyl ring linked to the 1-N purine atom.

EXPERIMENTAL

General. TLC plates (Merck, silica gel 60, F254) were developed in solvent systems: A [$CHCl_3$-MeOH (97:3, v/v)]; B [butan-1-ol-acetic acid-water (60:15:25, v/v)]; C [$CHCl_3$-MeOH (9:1, v/v)]; D [$CHCl_3$-MeOH (8:2, v/v)]. HPLC analyses were carried out on a Lichrosorb RP-18 column (Merck, 7 μm, 250-10). Column chromatographies were performed on silica gel (Merck, Kieselgel 60, 0.063-0.200 mm). PPh_3 was dried under reduced pressure at 50 °C for 15 h. The ^1H and ^{13}C NMR spectra were recorded on a Bruker WM 270 instrument (270 MHz); *J* values are given in Hz. FAB mass spectra (positive) were determined on a ZAB 2SE spectrometer. High resolution mass data were recorded on a VG 70-250S spectrometer. UV spectra were taken on a Perkin-Elmer lambda 7 spectrophotometer. Melting points were determined on a Reichert Thermovar apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 141 polarimeter at 25° C and are quoted in 10^{-1} deg cm^2 g^{-1}.

3-N-(2,4-dinitrophenyl)-6-chloro-9-(2',3',5'-tri-O-acetyl-β-D-ribofuranosyl)-2,3-dihydropurin-2-one 4.- A mixture of 300 mg (0.7 mmol) of **1**, 350 mg (1.7 mmol) of 2,4-dinitrochlorobenzene and 240 mg (1.7 mmol) of K_2CO_3 was suspended in anhydrous DMF (2.5 ml) at 80 °C under stirring for 1.5 h. After cooling, the mixture was filtered and the solid washed with $CHCl_3$. The filtrate and washings, concentrated under reduced pressure, were purified on a silica gel column eluting with increasing amounts of MeOH in $CHCl_3$ (from 0 to 6 %) to give pure chloride **4** (395 mg, 95 %), R_f 0.5 (system A); m.p. 81-83 °C (from $CHCl_3$/MeOH); $[\alpha]_D$ -1.3 (c 0.06 in $CHCl_3$); λ_{max} ($CHCl_3$)/nm 276 (21500) and 242 (18400); MS (FAB) m/z 595 (MH^+), 471 and 259; HRMS (EI) m/z 594.0747 (M^+. $C_{22}H_{19}ClN_6O_{12}$ requires 594.0749); δ_H ($CDCl_3$): 8.98 (1H, d, *J* = 2.7, 3-H dinitrophenyl); 8.57 (1H, dd, *J* = 2.7 and 9.0, 5-H dinitrophenyl); 8.21 (1H, s, 8-H); 7.63 (1H, d, *J* = 9.0, 6-H dinitrophenyl); 6.03 (1H, d, *J* = 4.7, 1'-H); 5.75 (1H, dd, *J* = 4.7 and 5.1, 2'-H); 5.25 (1H, dd, *J* = 5.1 and 5.1, 3'-H); 4.38 (1H, m, 4'-H); 4.18 (2H, m, 5'-H_2); 2.08, 2.07 and 2.05 (3H each, s, Ac); δ_C ($CDCl_3$): 169.9, 169.2, 169.0 (3 $CH_3\underline{C}O$); 158.1 (2-C); 152.7, 152.3 (6-C and 4-C); 143.6 (8-C); 131.7 (5-C); 149.8, 144.7, 141.5 (3 C dinitrophenyl); 129.3, 126.3, 121.8 (3 CH dinitrophenyl); 86.8 (1'-C); 79.7 (4'-C); 72.3 (3'-C); 69.9 (2'-C); 62.5 (5'-C); 20.3, 20.1 and 20.1 (3 $\underline{C}H_3CO$).

[6-^{15}N]-isoguanosine 3b.- Compound **4** (100 mg, 0.17 mmol) was treated with 1 ml of aq. $^{15}NH_3$ (3.3 N, 99 % ^{15}N) and the mixture was heated at 50 °C for 12 h under stirring. The resulting solution was evaporated under reduced pressure and the residue, dissolved in water, was purified by HPLC on a reversed-phase C_{18}

column eluted with increasing amounts of MeOH in water from 20 to 100%. Fractions eluted with 50 % MeOH gave [6-^{15}N]-isoguanosine **3b** (41 mg, 0.14 mmol, 85 %); fractions eluted with 90 % MeOH gave [1-^{15}N]-2,4-dinitroaniline (26 mg, 0.14 mmol), identified by ^{1}H and ^{13}C NMR. δ_C (CD_3OD): 151.4 (d, J_{C-15N} = 18.3, 1-C); 137.9; 131.9; 130.6; 124.7; 120.7.

3b, R_f 0.3 (system B); m.p. 236-240 °C (from MeOH); $[\alpha]_D$ -66 (c 0.020 in water); λ_{max} (water)/nm 292 (10500) and 246 (8600); HRMS (FAB) m/z 285.0967 (MH^+. $C_{10}H_{14}{}^{14}N_4{}^{15}NO_5$ requires 285.0965); δ_H (DMSO-d_6): 7.94 (1H, s, 8-H); 7.25 (2H, d, J_{H-15N} = 89.0, $^{15}NH_2$); 5.64 (1H, d, J = 5.7, 1'-H); 4.51 (1H, br dd, J = 5.7 and 5.5, 2'-H); 4.08 (1H, br m, 3'-H); 3.93 (1H, m, 4'-H); 3.58 (2H, ddd, J = 12.2, 2.2, 2.2, 5'-H_2); δ_C (DMSO-d_6): 155.5 (d, J_{C-15N} = 18.6, 6-C); 155.4 (2-C); 152.9 (4-C); 138.4 (8-C); 109.4 (5-C); 87.7 (1'-C); 86.0 (4'-C); 73.0 (2'-C); 70.8 (3'-C); 61.8 (5'-C). Anal. calcd. for $C_{10}H_{13}{}^{14}N_4{}^{15}NO_5 \cdot 0.5H_2O$: C 40.96; H 4.81; N 24.23. Found: C 41.01; H 4.90; N 24.27.

P-[2-Oxo-9-(2',3',5'-tri-O-acetyl-β-D-ribofuranosyl)-2,3-dihydropurin-6-yl]-triphenylphosphonium chloride 6.- Compound **1** (214 mg, 0.5 mmol) was treated in benzene (5 ml) with 196 mg (0.75 mmol) of triphenylphosphine and the solution was kept at reflux for 4 h. Then the mixture was dried under reduced pressure and purified on a silica gel column eluted with increasing amounts of MeOH in $CHCl_3$ (up to 7%) to afford pure phosphonium salt **6** (305 mg, 93 %), R_f 0.5 (system C); m.p. 141-144 °C (from benzene/$CHCl_3$); $[\alpha]_D$ 0.6 (c 0.03 in $CHCl_3$); λ_{max} ($CHCl_3$)/nm 381 (6000) and 241 (17000); HRMS (FAB) m/z 655.1962 ($[M\text{-}Cl^-]^+$. $C_{34}H_{32}N_4O_8P$ requires 655.1958); δ_H ($CDCl_3$): 7.80-7.35 (16H, complex signals, phosphonium and 8-H); 6.36 (1H, d, J = 5.4, 1'-H); 5.56 (1H, dd, J = 5.5 and 5.4, 2'-H); 5.43 (1H, dd, J = 5.5 and 5.1, 3'-H); 4.33 (3H, m, 3'-H and 5'-H_2); 2.11, 2.07 and 2.03 (3H each, s, Ac); δ_C ($CDCl_3$): 169.7, 169.1, 169.0 (3 $CH_3\underline{C}O$); 165.6 (d, J_{C-P} = 4.1, 2-C), 156.6 (d, J_{C-P} = 1.4, 4-C), 141.3 (d, J_{C-P} = 110.7, 6-C), 137.7 (8-C), 134.4 (d, J_{C-P} = 9.3, phenyl *ortho* C), 134.2 (phenyl *para* C), 129.2 (d, J_{C-P} = 12.9, phenyl *meta* C), 126.4 (d, J_{C-P} = 25.0, 5-C), 118.0 (d, J_{C-P} = 87.3, phenyl 1-C), 83.6 (1'-C); 79.10 (4'-C); 72.7 (3'-C); 70.2 (2'-C); 62.7 (5'-C); 20.3, 20.0 and 20.0 (3 $\underline{C}H_3CO$).

Isoinosine 8.

From chloride **1**. A mixture of **1** (160 mg, 0.37 mmol) and MgO (14 mg, 0.37 mmol) in H_2O (15 ml) was hydrogenated in the presence of 10 % Pd/C (150 mg) at atmospheric pressure and at r. t. After 8 h the mixture was filtered, dried and then purified on a silica gel column eluted with increasing amounts of MeOH in

$CHCl_3$ (up to 5 %) thus furnishing pure 2',3',5'-tri-O-acetylisoinosine **7**, which, treated with conc. NH_4OH (4 ml, 4 h, 50 °C), was then lyophilized twice to afford pure isoinosine **8** (60 mg, 60 %).

From phosphonium salt **6**. Compound **6** (200 mg, 0.31 mmol) was treated with conc. NH_4OH (4 ml) at 50 °C for 4 h. The mixture was filtered, dried under reduced pressure and then purified by HPLC on a reversed phase C_{18} column, eluted with increasing amounts of MeOH in water from 0 to 100 %. Fractions eluted with 58 % MeOH gave pure isoinosine **8** (79 mg, 95 %).

7, R_f 0.40 (system C); m.p. 98-101 °C (from MeOH); $[\alpha]_D$ 33.7 (c 0.02 in $CHCl_3$); $\lambda_{max}(CHCl_3)$/nm 324 (2800) and 241 (2600); MS (FAB) m/z 395 (MH^+), 259; HRMS (EI) m/z 394.1119 (M^+. $C_{16}H_{18}N_4O_8$ requires 394.1125); δ_H ($CDCl_3$): 8.31 (1H, s, 6-H); 8.04 (1H, s, 8-H); 6.19 (1H, d, J = 5.8, 1'-H); 5.69 (1H, dd, J = 5.8 and 5.5, 2'-H); 5.03 (1H, dd, J = 5.5 and 5.3, 3'-H); 4.41 (3H, m, 4'-H and 5'-H_2); 2.17, 2.15 and 2.08 (3H each, s, Ac); δ_C ($CDCl_3$): 170.1, 169.5, 169.4 (3 $CH_3\underline{C}O$); 159.5, 158.3 (2-C and 4-C); 144.2 (8-C); 138.2 (6-C); 124.4 (5-C); 84.5 (1'-C); 80.1 (4'-C); 73.0 (3'-C); 70.4 (2'-C); 63.0 (5'-C); 20.7, 20.4 and 20.3 (3 $\underline{C}H_3CO$).

8, R_f 0.36 (system B); TLC, UV data identical with authentic material[13]; m.p. > 200 °C decomp. (from MeOH); $[\alpha]_D$ 20 (c 0.04 in water); HRMS (FAB) m/z 269.0889 (MH^+. $C_{10}H_{13}N_4O_5$ requires 269.0886); δ_H (D_2O): 8.46 (1H, s, 6-H); 8.37 (1H, s, 8-H); 5.92 (1H, d, J = 5.6, 1'-H); 4.72 (1H, dd, J = 5.6 and 5.6, 2'-H); 4.39 (1H, dd, J = 5.6 and 5.4, 3'-H); 4.20 (1H, m, 4'-H); 3.83 (2H, ddd, J = 7.0, 3.0 and 3.3, 5'-H_2); δ_C (D_2O, 1,4-dioxane as internal reference, δ_C 67.4): 159.6, 159.0 (2-C and 4-C); 147.8 (8-C); 140.5 (6-C); 125.3 (5-C); 88.7 (1'-C); 86.3 (4'-C); 74.2 (3'-C); 71.2 (2'-C); 62.1 (5'-C).

6-(N-propylamino)-9-(β-D-ribofuranosyl)-2,3-dihydropurin-2-one 5a.
Compound **1** (100 mg, 0.23 mmol) was treated with propylamine (1.5 ml, 18 mmol) at 50 °C for 2.5 h. The resulting solution was dried under reduced pressure and purified on 3 silica gel plates (20x20 cm, 0.5 mm, Merck), developed in eluent system D. The band at R_f 0.2, scratched from the plates and eluted with $CHCl_3$/MeOH (1:1, v/v) afforded compound **5a** (66 mg, 91 %); m.p. 106-109 °C (from $CHCl_3$/MeOH); $[\alpha]_D$ -34.3 (c 0.038 in MeOH); λ_{max} (CH_3OH)/nm 276 (13400) and 249 (12200); HRMS (FAB) m/z 326.1468 (MH^+. $C_{13}H_{20}N_5O_5$ requires 326.1464); δ_H (CD_3OD): 7.91 (1H, s, 8-H); 5.79 (1H, d, J = 6.2, 1'-H); 4.57 (1H, br t, 2'-H); 4.29 (1H, dd, J = 3.5 and 2.5, 3'-H); 4.15 (1H, m, 4'-H); 3.82 (2H, ddd, J = 9.0, 2.0 and 1.0, 5'-H_2); 3.50 (2H, br t, NH-$C\underline{H}_2$); 1.70 (2H, m, $CH_2C\underline{H}_2CH_3$); 1.00 (3H, t, J = 7.4, $CH_2CH_2C\underline{H}_3$); δ_C (CD_3OD): 159.8, 153.7,

152.1 (2-C, 4-C and 6-C); 139.6 (8-C); 120.0 (5-C); 91.2 (1'-C); 88.2 (4'-C); 75.7 (3'-C); 72.9 (2'-C); 63.4 (1'-C); 42.7 ($NH\underline{C}H_2$); 22.2 ($CH_2\underline{C}H_2CH_3$); 11.7 (CH_3).

6-(N-piperidinyl)-9-(β-D-ribofuranosyl)-2,3-dihydropurin-2-one 5b.
Compound **1** (100 mg, 0.23 mmol) was reacted with piperidine (1.5 ml, 15 mmol) and the reaction mixture treated following the same procedure reported for **5a**, thus obtaining **5b** (76 mg, 93 %), R_f 0.35 (system D); m.p. 174-176 °C (from $CHCl_3$); $[\alpha]_D$ -43.0 (c 0.036 in MeOH); λ_{max} (MeOH)/nm 280 (13000) and 257 (12300); MS (FAB) m/z 352 (MH^+) and 277; HRMS (FAB) m/z 352.1622 (MH^+. $C_{15}H_{22}N_5O_5$ requires 352.1621); δ_H (CD_3OD): 7.84 (1H, s, 8-H); 5.78 (1H, d, J = 6.7, 1'-H); 4.51 (1H, dd, J = 6.7 and 5.3, 2'-H); 4.26 (1H, dd, J = 5.3 and 2.3, 3'-H); 4.16 (5H, m, 4'-H and piperidinyl α H_2); 3.82 (2H, ddd, J = 8.3, 2.4 and 1.3, 5'-H_2); 1.72 (6H, m, piperidinyl β and γ H_2); δ_C (pyridine-d_5): 162.2, 154.9, 152.8 (2-C, 4-C and 6-C); 136.8 (8-C); 116.7 (5-C); 90.7 (1'-C); 87.6 (4'-C); 75.3 (3'-C); 72.3 (2'-C); 62.9 (5'-C); 46.4 (2 α CH_2); 26.4 (2 β CH_2); 25.0 (γ CH_2).

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REFERENCES AND NOTES

1) De Napoli L; Messere A.; Montesarchio D.; Piccialli G.; Santacroce C.; Varra M.; *J. Chem. Soc., Perkin Trans. 1*, **1994**, 923-926.
2) De Napoli L.; Montesarchio D.; Piccialli G.; Santacroce C.; Varra M.; *J. Chem. Soc., Perkin Trans. 1*, **1995**, 15-18.
3) De Napoli L.; Messere A.; Montesarchio D.; Piccialli G.; *J. Org. Chem.*, **1995**, *60*, 2251-2253.
4) a) Davoll J.; *J. Am. Chem. Soc.*, **1951**, *73*, 3174-3176. b) Vorbrüggen H.; Krolikiewicz K.; *Liebigs Ann. Chem.* **1976**, 745-761. c) Chern J.W.; Lee H.Y.; Huang M.; Shish F.J.; *Tetrahedron Lett.* **1987**, *28*, 2151-2154. d) Divakar K. J.; Mottahedeh m.; Reese C.B.; Sanghvi Y. S.; Swift K.A.D.; *J. Chem. Soc., Perkin Trans. 1*, **1991**, 771-774.
5) Pagano A.R.; Lajewski W. M.; Jones R.A.; *J. Am. Chem. Soc.*, **1995**, *117*, 11669-11672.

6) Gao X.; Jones R.A.; *J. Am. Chem. Soc.*, **1987**, *109*, 1275-1278.
7) Acedo M.; Fàbrega C.; Avino A.; Goodman M.; Fagan P.; Wemmer D.; Eritja R.; *Nucleic Acids Res.*, **1994**, *22*, 2982-2989.
8) Kamaike K.; Takahashi M.; Utsugi K.; Tomizuka K.; Ishido Y.; *Tetrahedron Lett.*, **1995**, *36*, 91-94;
9) Similar results were found also in different reaction conditions; even treatments with NH_3 in $CHCl_3$, satd. soln., produced only traces of the target compound isoguanosine;
10) Zincke T.; *Liebigs Ann. Chem.*, **1903**, *330*, 361-374.
11) Krohnke F.; *Angew. Chem.*, **1963**, *75*, 317-329.
12) Lira E.P.; *J. Heterocycl. Chem.*, **1972**, *9*, 713-716.
13) Topal M.D.; Fresco J.R.; *Nature*, **1976**, *263*, 289-293.
14) Holy' A.; *Collect. Czech. Chem. Comm.*, **1979**, *44*, 2846-2853.
15) Iwamoto R.H.; Acton E.M.; Goodman L.; *J. Am. Chem. Soc.*, **1962**, *27*, 3949-3953.
16) Seela F.; Chen Y.; Bindig U.; Kazimierczuk Z.; *Helv. Chim. Acta*, **1994**, *77*, 194-202.
17) Cristau H.J.; Plénat F. in *The chemistry of organophosphorus compounds. Vol. 3: Phosphonium salts, ylides and phosphoranes*, Hartley F.R. Ed., Patai S. Series, Wiley-Interscience, Chichester, England, **1994**, pp.111-138.

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