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The Ring Opening of Cyclopentene Oxides by Pyrimidines and Purines as a Pathway to Carbocyclic Nucleoside Analogues

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Summary. Various carbocyclic nucleosides with *xylo*-configuration have been synthesized using ring opening of 5-O-acetyl-1,2-anhydro-3-O-benzylcarba-α-*DL-xylo*-pentofuranose (**6**) by thymine, uracil, 4-N-benzoylcytosine, adenine, 6-N-benzoyladenine, and 2-amino-6-chloropurine in alkaline medium. For this purpose, the use of triethylaluminum is introduced into carbanucleoside chemistry. The new method proved to be superior over the application of sodium hydride and potassium or caesium carbonate.

Keywords. Nucleosides, carbocyclic; Carbanucleosides; Epoxides, opening of; Triethylaluminum.

Ringöffnung von Cyclopentenoxiden mit Pyrimidinen und Purinen als Syntheseweg zu carbocyclischen Nucleosidanalogen

Zusammenfassung. Ringöffnung von 5-O-Acetyl-1,2-anhydro-3-O-benzylcarba-α-*DL-xylo*-pentofuranose (**6**) mit Thymin, Uracil, 4-N-Benzoylcytosin, Adenin, 6-N-Benzoyladenin und 2-Amino-6-chlorpurin in alkalischem Medium ergab die entsprechenden *xylo*-konfigurierten carbocyclischen Nucleoside. Als Hilfsbase wurde Triethylaluminium verwendet, was deutliche Vorteile gegenüber der Verwendung von Natriumhydrid und Kalium- oder Cäsiumcarbonat bezüglich Produktreinheit und Ausbeute bietet.

Introduction

By formal substitution of the ring oxygen atom of nucleosides, carbocyclic counterparts are obtained which are more stable against hydrolysis due to the lack of an acetal moiety [1]. Due to their structural analogy to natural nucleosides, a variety of carbocyclic nucleosides with biological activities [2] have been prepared.

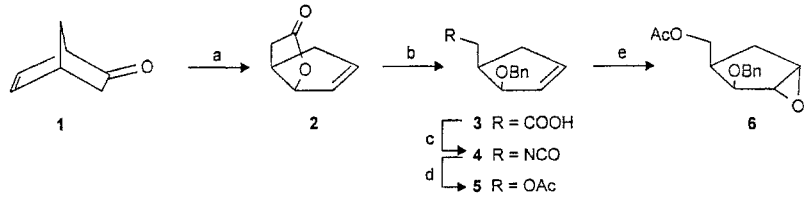
Several synthetic methods have been developped for this purpose, such as the construction of the heterocyclic base starting from an amino group on the cyclopentane ring [1, 3]. As an alternative, the aglycone can be linked to the carbasugar moiety by S_N2 type reactions [1, 4]. A versatile method is the nucleophilic opening of cyclopentene oxides by purines and pyrimidines, introducing regio- and stereoselectively a hydroxy group. By application of this methodology, various carbanucleosides have been obtained [5]. In our laboratory, several carbocyclic nucleosides with β-*xylo*-configuration have been synthesized

using the epoxide of the protected carbocyclic pentofuranose **6** as the central intermediate employing NaH, K_2CO_3, or Cs_2CO_3 to generate the nucleophile from the aglycone [6]. Meanwhile, Et_3Al proved to be superior for this purpose, as will be described here together with all experimental details. The isolated yields were always better when Et_3Al was employed, and the workup procedure was less complicated because no polar and high boiling solvents had to be removed.

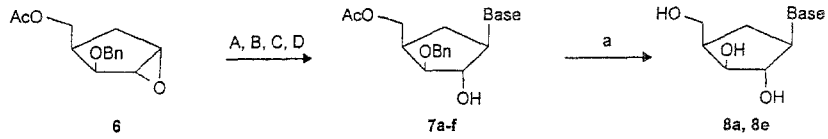
Results and Discussion

Racemic lactone **2** is prepared from (±)-norborn-5-en-2-one (**1**), which is also easily available enantiomerically pure [7], if enantiopure compounds have to be synthesized, by *Baeyer-Villiger* oxidation in acidic medium [8] (71% yield). Opening of the lactone ring using potassium hydroxide in 1,4-dioxane and subsequent protection of the secondary hydroxy group with benzyl bromide yields carboxylic acid **3**, which can be converted into isocyanate **4** by *Curtius* degradation. For the transformation into acetate **5**, the best procedure (a one pot reaction) was to convert **4** into a carbamic acid derivative using anhydrous acetic acid followed by nitrosation and smooth further conversion by stirring at room temperature [9]. Reaction of **5** with *m-CPBA* in toluene proceeds in a stereospecific manner to give epoxide **6** as a central precursor for the introduction of the heterocyclic base [10].

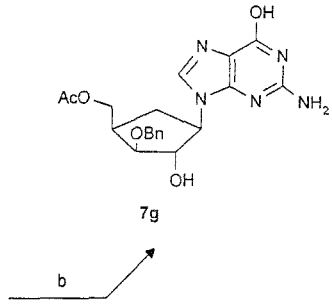
The introduction of purine and pyrimidine rings *via* opening of an epoxide to give carbanucleosides can be accomplished by several different methods as shown in Scheme 2. For comparison, all these reactions were performed with thymine first. Treatment of the heterocyclic base with sodium hydride in N,N-dimethylformamide at room temperature followed by reaction with **6** at reflux temperature [11] afforded the desired nucleoside analogues in 44–47% yield. When sodium hydride was replaced by potassium carbonate [10], the results were similar. Employing caesium carbonate allowed the reactions to be performed at lower temperature (80 °C) and to use even heterocyclic bases with unblocked amino groups (*e.g.* adenine). However, dark coloured by-products are formed, and purification by column chromatography is difficult. A completely novel method can be developped by application of the results of *Overman* [12], *i.e.* the use of triethylaluminum, to nucleoside chemistry. In this case, epoxide opening is



Scheme 1. Reagents and conditions: (a) diethyl ether/water/H_2SO_4/H_2O_2 (35%); (b) (i) KOH/1,4-dioxane/reflux, (ii) benzyl bromide/reflux; (c) (i) ethyl chloroformate/Et_3N/acetone, (ii) NaN_3/H_2O, (iii) toluene/reflux; (d) $NaNO_2$/acetic acid/CH_2Cl_2; (e) *m-CPBA*/toluene/reflux; all compounds are racemic, only one enantiomer is shown



Base	Method	Time	Yield	Product
thymine	A	48 h	44%	**7a**
	B	24 h	41%	**7a**
	C	48 h	41%	**7a**
	D	48 h	51%	**7a**
uracil	A	48 h	44%	**7b**
	D	48 h	65%	**7b**
4-N-benzoylcytosine	D	48 h	57%	**7c**
6-N-benzoyladenine	A	48 h	46%	**7d**
	D	48 h	52%	**7d**
adenine	C	48 h	45%	**7e**
2-amino-6-chloropurine	C	48 h	43%	**7f**
	D	48 h	60%	**7f**



Scheme 2. Reagents and conditions: method *A*: NaH/base/refluxing *DMF*; method *B*: K_2CO_3/base/refluxing *DMF*; method *C*: Cs_2CO_3/base/*DMF*/80°C; method *D*: Et_3Al/base/*THF*/r.t.; (a) (i) CH_3ONa/CH_3OH, (ii) H_2/Pd-C(10%)/CH_3OH; (b) HOAc (80%)/reflux; all compounds are racemic, only one enantiomer is shown

possible at room temperature in tetrahydrofuran which can be removed during workup much more easily than the high-boiling N,N-dimethyl formamide.

Employing these four methods, thymine, uracil, 4-N-benzoylcytosine, adenine, and 6-N-benzoyladenine could be transformed easily to give **7a–e**, but no reaction occurred with guanine derivatives (*e.g.* 2-N-acetylguanine). In this case, the synthesis could be achieved starting with 2-amino-6-chloropurine as the aglycone and replacing the chlorine atom of **7f** by a hydroxy group using 80% acetic acid in 35% overall yield to give **7g**. Deprotection of **7a** and **7d** was performed by methanolysis and subsequent hydrogenation to yield the carbocylic nucleosides 1-(carba-*β-DL-xylo*-pentofuranosyl)-5-methyl-(1*H*,3*H*)-pyrimidine-2,4-dione (**8a**) and 9-(carba-*β-DL-xylo*-pentofuranosyl)-6-amino-9*H*-purine (**8e**).

In conclusion, the isolated yields of carbocyclic nucleoside analogues were always better when aluminum salts of the aglycone in *THF* were used instead of alkali salts in aprotic polar solvents (*e.g. DMF*). The less complicated workup and purification procedure will credit Et_3Al in *THF* solution for the nucleophilic opening of epoxides with heterocyclic bases as method of choice, too.

Experimental

Melting points were determined on a Tottoli apparatus and are uncorrected. NMR spectra were recorded on a Bruker MSL 300 spectrometer (^1H NMR: 300.13 MHz, ^{13}C NMR: 75.47 MHz); chemical shifts are given in ppm relative to internal *TMS*. IR spectra were recorded on a Bomem

Michelson 100 spectrometer as films on KBr. Mass spectra were obtained from a Kratos Profile. Flash chromatography was performed on Merck silica gel 60 (230–400 mesh), and anhydrous solvents were used. For nomenclature, carbocyclic nucleosides are considered to be carbohydrate derivatives [13]. The elemental analyses were performed at the Institute of Organic Chemistry, University of Graz.

*(±)-cis-(2-Hydroxy-3-cyclopentenyl)acetic acid lactone (**2**) [8]*

210 ml of H_2O_2 (35%) were added dropwise to a cooled solution (−10°C) of 149 g (1.38 mol) of **1** and 2 ml of conc. H_2SO_4 in 1200 ml of diethyl ether with vigorous stirring. Stirring was continued for 2 h at room temperature. The reaction mixture was neutralized in a 5 l *Erlenmeyer* flask with saturated aqueous $NaHCO_3$ solution, and excess H_2O_2 was reacted very cautiously at 0°C with small portions of $Na_2S_2O_5$ over a period of 3 h. The ethereal solution was separated, and the aqueous layer reextracted with dichloromethane (5 × 150 ml). The combined organic extracts were dried (Na_2SO_4), and evaporation *in vacuo* yielded the crude lactone **2** as a yellow liquid. Distillation under reduced pressure afforded 121 g (71%) of **2** as a colourless oil.

$Bp_{0.1}$= 84°C (Ref. [8]: bp_{29} = 131–132°C); ^{1}H NMR ($CDCl_3$): δ = 2.16–2.18 (m, 1H), 2.21–2.23 (m, 1H), 2.62–2.70 (m, 1H), 2.73 (dd, J = 18.4, 10.4 Hz, 1H), 2.99–3.11 (m, 1H), 5.40–5.42 (m, 1H), 5.75 (ddd, J = 6.0, 4.1, 2.0 Hz, 1H), 5.97 – 6.99 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 34.83, 35.74, 39.34, 89.37, 128.67, 136.88, 176.90; IR (KBr): ν = 2941, 1767, 1448, 1416, 1361, 1337, 1169, 1012, 956, 914, 763, 718 cm^{-1}; EIMS: *m/z* (rel.int.%) = 124 ($M^{+\cdot}$, 26), 95 (14), 79 (100), 67 (15), 53 (11), 39 (16); $C_7H_8O_2$ (124.14); calcd.: C 67.73, H 6.50; found: C 68.22, H 6.41.

(±)-cis-2-Benzyloxycyclopent-3-enylacetic acid (**3**)

A mixture of 70 g (0.56 mol) of lactone **2** and 190 g (3.40 mol) of powdered KOH in 400 ml of 1,4-dioxane was refluxed for 1 h. After cautious addition of 200 ml (1.89 mol) of benzyl bromide in four 50 ml portions, refluxing was continued overnight. Water was added, and the reaction mixture was extracted with diethyl ether (4 × 100 ml) to remove benzyl alcohol and dibenzyl ether. The aqueous layer was acidified with conc. HCl (*pH* 1) and extracted with diethyl ether (5 × 100 ml). The combined latter organic extracts were dried (Na_2SO_4) and evaporated *in vacuo* to yield 126 g (96%) of carboxylic acid **3** as a red oil.

^{1}H NMR ($CDCl_3$): δ = 2.25 (m, 1H), 2.46–2.59 (m, 2H), 2.70–2.85 (m, 2H), 4.50–4.61 (m, 3H), 6.00 (m, 1H), 6.06 (m, 1H), 7.36 (m, 5H), 9.4–10.3 (bs, 1H); ^{13}C NMR ($CDCl_3$): δ = 34.3, 37.4, 37.9, 71.6, 83.5, 127.67, 127.80, 128.48, 138.8, 130.6, 135.5, 179.80; IR (KBr): ν = 3045, 2926, 1710, 1495, 1453, 1410, 1357, 1282, 1218, 1118, 1061, 1027, 930, 738, 699 cm^{-1}; $C_{14}H_{16}O_3$ (232.28); calcd.: C 72.39, H 6.94; found: C 72.24, H 7.19.

(±)-cis-2-Benzyloxycyclopent-3-enylmethyl isocyanate (**4**)

To a stirred solution of 16.2 g (70 mmol) of carboxylic acid **3** and 11.7 ml (84 mmol) of triethylamine in 150 ml of acetone, 8.7 ml (91 mmol) of ethyl chloroformate were added drop by drop at −30°C. The reaction mixture was allowed to warm to −5°C and was stirred for additional 15 minutes. 6.80 g (105 mmol) of NaN_3 in 40 ml of water were added at −5°C, and stirring was continued for 30 min. The reaction mixture was poured into ice/water (100 ml) and extracted with toluene (3 × 150 ml). The combined organic layers were dried (Na_2SO_4), concentrated under reduced pressure to a volume of approximately 200 ml, dropped into a flask with boiling toluene equipped with a condenser, and refluxed for 1 h. After the liberation of nitrogen has ceased, the solution was evaporated *in vacuo* to afford 14.2 g (89%) of crude isocyanate **4** as a colourless oil after bulb-to-bulb distillation.

^{1}H NMR ($CDCl_3$): δ = 2.29 (ddq, J = 16.4, 6.3, 2.0 Hz, 1H), 2.49 (ddt, J = 16.4, 7.8, 1.7 Hz, 1H), 2.60 (sextett, J = 7.1 Hz, 1H), 3.39 (dd, J = 12.9, 7.7 Hz, 1H), 3.67 (dd, J = 12.9, 7.7 Hz, 1H), 4.57 (m, 1H), 4.59–4.66 (AB, J = 11.6 Hz, 2H), 6.02–6.10 (m, 2H), 7.32–7.43 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 35.22, 42.77, 43.16, 71.41, 82.53, 122.85, 127.61, 127.69, 128.20, 130.67, 135.10, 138.73; IR (KBr): ν = 3050, 2898, 2271, 1733, 1542, 1452, 1360, 1236, 1120, 1060, 1119, 866, 736, 698 cm^{-1}; EIMS: *m/z* (rel.int.%) = 229 ($M^{+\cdot}$, 0.7), 210 (0.6), 138 (13), 123 (38), 107 (82), 91 (100), 79 (49), 65 (31), 56 (19), 51 (10), 39 (20); $C_{14}H_{15}NO_2$ (229.28); calcd.: C 73.34, H 6.59, N 6.11; found: C 73.07, H 6.63, N 5.94.

(±)-cis-2-Benzyloxycyclopent-3-enylmethyl acetate (**5**)

To a solution of 5.70 g (248 mmol) of isocyanate **4** in 150 ml of dichloromethane, 22 ml of glacial acetic acid and afterwards 17.3 g (250 mmol) of $NaNO_2$ in small portions (caution: NO_2 generation) were added at 0°C with stirring. Stirring was continued at room temperature overnight. The resulting mixture was evaporated *in vacuo*, the residue dissolved in water (80 ml), and extracted with dichloromethane (3 × 100 ml). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution, dried (Na_2SO_4), evaporated under reduced pressure, and purified on a silica gel column (toluene/ethyl acetate 9/1 v/v) to afford 2.4 g (40%) of **5** as a yellow oil.

^{1}H NMR ($CDCl_3$): δ = 2.07 (s, 3H), 2.28 (ddq, J = 16.6, 6.8, 2.0 Hz, 1H), 2.42 (ddt, J = 16.6, 7.8, 2.0 Hz, 1H), 2.60 (sextett, J = 7.3 Hz, 1H), 4.19 (dd, J = 10.9, 7.6 Hz, 1H), 4.43 (dd, J = 10.9, 7.5 Hz, 1H), 4.51 (dt, J = 6.8, 1.8 Hz, 1H), 4.56 (s, 2H), 5.95 (m, 1H), 6.04 (m, 1H), 7.26 – 7.34 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 21.15, 34.96, 41.04, 64.36, 71.71, 83.06, 127.64, 128.49, 138.99, 130.97, 135.17, 171.18; IR (KBr): ν = 2906, 1736, 1452, 1363, 1240, 1119, 1047, 736, 698, 606 cm^{-1}; EIMS: *m/z* (rel.int.%) = 246 (1, $M^{+\cdot}$), 202 (1), 186 (4), 155 (3), 138 (13), 117 (4), 107 (28), 91 (100), 80 (85), 66 (26), 51 (13), 43 (47); $C_{15}H_{18}NO_3$ (246.31); calcd.: C 73.15, H 7.37; found: C 73.24, H 7.51.

5-O-Acetyl-1,2-anhydro-3-O-benzylcarba-α-DL-xylo-pentofuranose (**6**)

A mixture of 10.8 g (43.8 mmol) of acetate **5** and 22.7 g (65.8 mmol) of *m*-chloroperbenzoic acid (*m-CPBA*) in 120 ml of toluene was refluxed for 30 min. The resulting suspension was washed with saturated aqueous $NaHCO_3$ solution (150 ml), and the aqueous layer was reextracted with dichloromethane (3 × 150 ml). The combined organic extracts were dried (Na_2SO_4), evaporated under reduced pressure, and the residue purified on silica gel (toluene/ethyl acetate 9/1 v/v) to yield 9.24 g (79%) of **6** as a slightly yellow oil.

^{1}H NMR and ^{13}C NMR: see Ref. [6]; IR (KBr): ν = 3031, 2935, 1736, 1454, 1366, 1244, 1109, 1048, 842, 745, 699, 606 cm^{-1}; EIMS: *m/z* (rel.int.%) = 262 ($M^{+\cdot}$, 1), 219 (1), 202 (19), 156 (5), 107 (13), 96 (28), 91 (100), 81 (11), 65 (13), 55 (6), 43 (36); $C_{15}H_{18}O_4$ (262.30); calcd.: C 68.69, H 6.92; found: C 68.35, H 6.84.

General Procedures for the Introduction of the Bases

Method A

A suspension of 9.1 mmol of the heterocyclic base in 50 ml of N,N-dimethyl formamide was treated with 0.22 g (9.1 mmol) of NaH and stirred vigorously for 1 h at room temperature. 1.00 g (3.8 mmol) of epoxide **6** was added, and the mixture was refluxed for 48 h.

Workup: The reaction mixture was quenched with 0.5 ml of glacial acetic acid, diluted with water (100 ml), and extracted with dichloromethane (3 × 100 ml). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution (50 ml) and evaporated *in vacuo*. Purification of the residue was accomplished by flash chromatography on silica gel and/or recrystallization.

Method B

A suspension of 9.1 mmol of the heterocyclic base, 4.50 g (45 mmol) of K_2CO_3 and 1.00 g (4.5 mmol) of epoxide **6** in 50 ml of N,N-dimethyl formamide was refluxed for 24 h. After cooling to room temperature, the reaction mixture was diluted with water (100 ml) and worked up as described for method *A*.

Method C

To a solution of 1.00 g (4.5 mmol) of epoxide **6** in 50 ml of N,N-dimethyl formamide, 3.05 g (9.1 mmol) of Cs_2CO_3 and 9.1 mmol of the heterocyclic base were added. The suspension was stirred at 80 °C for 48 h. After dilution with water (100 ml), workup was performed as described above for method *A*.

Method D

To a suspension of 9.1 mmol of the heterocyclic base in 50 ml of freshly distilled tetrahydrofuran, 9.1 ml of triethylaluminum (1 *N* solution in hexane) were added with stirring. Stirring was continued for 1 h at room temperature. 1.0 g (4.5 mmol) of epoxide **6** was added, and the mixture was refluxed for 48 h. After quenching with glacial acetic acid and dilution with water (100 ml), the mixture was worked up as given for method *A*.

1-(5-O-Acetyl-3-O-benzylcarba-β-DL-xylo-pentofuranosyl)-5-methyl-(1H,3H)-pyrimidine-2,4-dione (**7a**)

The introduction of thymine was accomplished by methods *A*, *B*, *C*, and *D*. Flash chromatography (ethyl acetate) yielded 0.65 g (44%), 0.61 g (41%), 0.61 g (41%), and 0.76 g (51%) of **7a** as white crystals, respectively. An analytical sample was recrystallized from methanol; m.p.: 140–142°C.

^{1}H NMR and ^{13}C NMR: see Ref. [6]; $C_{20}H_{24}N_2O_6$ (388.42); calcd.: C 61.85, H 6.23, N 7.21; found: C 61.05, H 6.19, N 7.38.

1-(5-O-Acetyl-3-O-benzylcarba-β-DL-xylo-pentofuranosyl)-(1H,3H)-pyrimidine-2,4-dione (**7b**)

Methods *A* and *D* yielded 0.63 g (44%) and 0.93 g (65%), respectively, of **7b** as a colourless oil after column chromatography (ethyl acetate).

^{1}H NMR ($CDCl_3$): $\delta = 1.65$ (m, 1H), 2.00 (s, 3H), 2.25 (m, 1H), 2.62 (m, 1H), 3.85 (m, 1H), 4.10–4.38 (m, 3H), 4.44–4.71 (m, 2H), 4.95 (m, 1H), 5.61 (d, $J = 8$ Hz, 1H), 7.32 (m, 5H), 7.44 (d, $J = 8$ Hz, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 21.06$, 32.17, 40.48, 62.95, 63.34, 71.84, 80.49, 83.74, 103.21, 127.85, 128.23, 128.60, 128.74, 142.27, 152.28, 164.10, 171.14; $C_{19}H_{22}N_2O_6$ (374.39); calcd.: C 60.95, H 5.92, N 7.48; found; C 61.34, H 5.84, N 7.58.

1-(5-O-Acetyl-3-O-benzylcarba-β-DL-xylo-pentofuranosyl)-4-benzoylamino-1H-pyrimidin-2-one (**7c**)

4-N-Benzoylcytosine was introduced according to method *D*. Recrystallization from methanol afforded 1.04 g (57%) of **7c** as white crystals; m.p.: 185–186°C.

^{1}H NMR ($CDCl_3$): $\delta = 1.71$ (m, 1H), 2.01 (s, 3H), 2.12 (m, 1H), 3.82 (m, 1H), 4.13 (m, 1H), 4.20–4.38 (m, 2H), 2.82 (m, 3H), 5.63 (d, $J = 5$ Hz, 1H), 7.25–8.32 (m, 11H), 11.27 (s, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 20.93$, 31.51, 37.91, 63.23, 63.57, 71.04, 78.21, 83.34, 127.76, 128.50, 128.68, 132.93, 133.49, 138.60, 147.66, 162.60, 170.61; $C_{26}H_{27}N_3O_6$ (477.52); calcd.: C 65.40, H 5.70, N 8.80; found: C 66.23, H 5.43, N 8.47.

9-(5-O-Acetyl-3-O-benzylcarba-β-DL-xylo-pentofuranosyl)-6-benzoylamino-9H-purine (**7d**)

The introduction of 6-N-benzoyladenine was accomplished by methods *A* and *D*. Column chromatography (chloroform/acetone 19/1 v/v) yielded 0.88 g (46%) and 0.99 g (52%) of **7d** as white crystals, respectively; m.p.: 88–90°C.

^{1}H NMR and ^{13}C NMR: see Ref. [6]; $C_{27}H_{27}N_5O_5$ (501.54); calcd.: C 64.66, H 5.43, N 13.96; found: C 64.14, H 5.51, N 13.76.

9-(5-O-Acetyl-3-O-benzylcarba-β-DL-xylo-pentofuranosyl)-6-amino-9H-purine (**7e**)

Adenine was introduced employing method *C*. Column chromatography (chloroform/acetone 19/1 v/v) yielded 0.68 g (45%) of **7e** as a colourless oil.

^{13}C NMR ($CDCl_3$): δ = 19.95, 31.52, 39.37, 60.05, 62.43, 70.40, 79.53, 82.57, 118.60, 137.30, 149.06, 151.55, 155.16, 169.66; $C_{20}H_{23}N_5O_4$ (397.43); calcd.: C 60.44, H 5.83, N 17.62; found: C 59.76, H 5.85, N 17.66.

9-(5-O-Acetyl-3-O-benzylcarba-β-DL-xylo-pentofuranosyl)-2-amino-6-chloro-9H-purine (**7f**)

Reaction of **6** with 2-amino-6-chloropurine employing methods *C* and *D* yielded 0.71 g (43%) and 0.99 g (60%), respectively, of **7f** as a slightly yellow oil after purification on silica gel (chloroform/acetone 19/1 v/v).

$C_{20}H_{22}ClN_5O_4$ (431.88); calcd.: C 55.62, H 5.13, Cl 8.21, N 16.22; found: C 56.02, H 5.26, Cl 8.09, N 16.41; NMR data were not determined.

9-(5-O-Acetyl-3-O-benzylcarba-β-DL-xylo-pentofuranosyl)-2-amino-1,9-dihydro-6-oxopurine (**7g**)

A solution of 0.71 g (1.6 mmol) of **7f** in 30 ml of acetic acid (80%) was heated under reflux overnight. The mixture was diluted with 50 ml of water and extracted with dichloromethane (3 × 100 ml). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (50 ml), dried (Na_2SO_4), evaporated *in vacuo*, and purified on silica gel (chloroform/acetone 19/1 v/v) to give 0.55 g (81%) of **7g** as a colourless oil.

^{1}H NMR ($CDCl_3$): δ = 2.03 (s, 3H), 2.24 (m, 1H), 2.46 (m, 1H), 2.64 (m, 1H), 3.95 (m, 1H), 4.28 (m, 3H), 4.35 (m, 1H), 4.57 (m, 1H), 4.69 (m, 1H), 3.30 (s, 5H), 7.42 (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 21.15, 31.18, 40.13, 63.04, 63.53, 71.16, 83.42, 83.57, 115.73, 127.84, 128.54, 128.77, 138.22, 133.95, 153.00, 155.72, 158.63, 171.15; $C_{20}H_{23}N_5O_5$ (413.43); calcd.: C 58.10, H 5.61, N 16.94; found: C 58.32, H 5.40, N 17.18.

1-(Carba-β-DL-xylo-pentofuranosyl)-5-methyl-(1H,3H)-pyrimidine-2,4-dione (**8a**) *and 9-(Carba-β-DL-xylo-pentofuranosyl)-6-amino-9H-purine* (**8e**)

0.5 g (1.3 mmol) of **7a** or 0.4 g (0.8 mmol) of **7e**, respectively, in 15 ml of dry methanol were treated with a solution of 20 mg of sodium in 2 ml of dry methanol overnight. The reaction mixture was acidified with trifluoroacetic acid and hydrogenated at 50 psi for 6 h with Pd-C (10%) as a catalyst. Removal of the catalyst by filtration, evaporation under reduced pressure, and recrystallization of the residue from methanol yielded 0.32 g (97%) of **8a** (m.p.: 206–207°C) or 0.19 g (88%) of **8e**, respectively, as white crystals.

8a: ^{1}H NMR and ^{13}C NMR: see Ref. [6]; $C_{11}H_{16}N_2O_5$ (256.26); calcd.: C 51.56, H 6.29, N 10.93; found: C 50.88, H 6.29, N 10.27.

8e: $C_{11}H_{15}N_5O_3$ (265.27); calcd.: C 49.81, H 5.70, N 26.40; found: C 49.45, H 5.89, N 26.10; all other physical data were in accordance with the literature [14].

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