33. Highly Stereoselective Total Syntheses of 2,5-Anhydro-4-deoxy-D-*ribo*-hexonic Acid and of (1*S*)-1-*C*-(6-Amino-7*H*-purin-8-yl)-1,4-anhydro-3-deoxy-D-*erythro*-pentitol (= Cordycepin C)[1][2]

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Dedicated to Prof. *Hans Dahn* on the occasion of his 70th birthday

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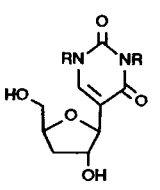
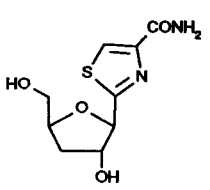
Highly regio- and stereoselective monohydroxylation of the C=C bond of (+)-7-oxabicyclo[2.2.1]hept-5-en-2-one (**8**) was achieved *via* $LiAlH_4$ reduction of the corresponding 5,6-*exo*-epoxy dimethyl acetal **9**. The reaction gave exclusively (−)-(1*R*,2*R*,4*S*)-6,6-dimethoxy-7-oxabicyclo[2.2.1]heptan-2-*exo*-ol (**10**) which was transformed into 2,5-anhydro-3-*O*-benzyl-4-deoxy-D-*ribo*-hexonic acid (**15**) and 2,5-anhydro-4-deoxy-D-*ribo*-hexonic acid (**6**) *via* ozonolysis of (−)-(1*R*,4*S*,6*R*)-6-*exo*-benzyloxy-2-{[(*tert*-butyl)dimethylsilyl]oxy}-7-oxabicyclo[2.2.1]hept-2-ene (**14**). Cordycepin C (**5**) was derived from **6** and 4,5,6-triaminopyrimidine using CsF/DMF to generate the adenine heterocycle.

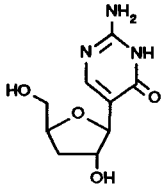
Introduction. – *C*-Nucleosides have attracted a wide interest because of their biological activity; some members possess antitumor and/or antiviral properties [3] [4]. In general, they are β-*C*-glycosides derived from D-ribose [3] [5]. The need for new antiviral agents for human immunodeficiency virus has stimulated a regain of interest in the



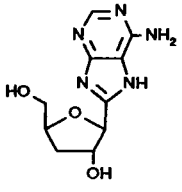
1 R=Me [6] [7c]
2 R=H [7a]



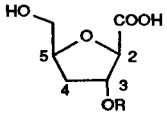
3 [7b]



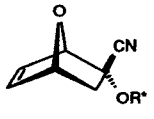
4 [7c]



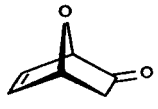
5 [8]



6 R=H
15 R=CH_2Ph = Bn



7 R*= (1*S*)-Camphanoyl



8 (1*R*)

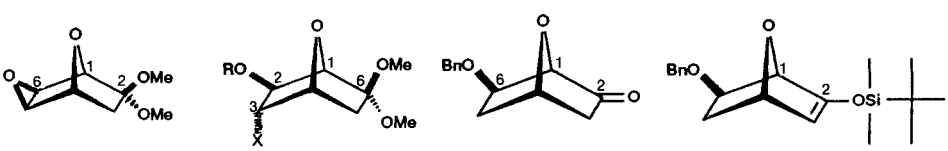
[1] Enantiomerically pure 7-oxabicyclo[2.2.1]hept-5-en-2-yl derivatives ('naked sugars') as synthetic intermediates, Part V. Part III: [1]. Part IV: [2].

[2] Part of the planned Ph.D. thesis of *F. G.*, University of Lausanne.

synthesis of new nucleosides and *C*-nucleosides [6]. *C*-Nucleosides **1**–**5** are rare examples of 3′-deoxy-*β*-D-*erythro*-pentofuranosyl derivatives [3] [4] [6–8]. Compounds **1**–**4** were prepared by reduction of the corresponding *C*-(*β*-D-*ribo*-pentofuranosyl) derivatives or analogues. The *C*-nucleoside analogue of cordycepine, cordycepine C (= (1*S*)-1-*C*-(6-amino-7*H*-purin-8-yl)-1,4-anhydro-3-deoxy-D-*erythro*-pentitol; **5**) whose synthesis was first reported by *El Khadem* and *El Ashry* [8] was obtained by condensation of 4,5,6-triaminopyrimidine with 2,5-anhydro-4-deoxy-*β*-D-*ribo*-hexonic acid (**6**). Acid **6** was derived from D-xylose in 13 steps in less than 16% yield [8].

We report here on the total synthesis of acid **6** which makes use of the readily available, optically pure 7-oxabicyclo[2.2.1]hept-5-en-2-yl derivatives **7** and **8** derived from furane and 1-cyanovinyl (1*S*)-camphanate in 93 and 89% yield, respectively (taking into account the recovered dienophile) [9]. We disclose a method for the stereo- and regioselective monohydroxylation of the double bond in 7-oxatrinorbornenone **8**[3]). Since the method of *El Khadem* and *El Ashry* [8] for the convertion of **16** into cordycepin C (**5**) failed in our hands, we have developed an improved technique featuring CsF in DMF as a mean to induce smooth H_2O elimination [10] [11] during the formation of the adenine moiety of **5** without epimerization of the anomeric center [12].

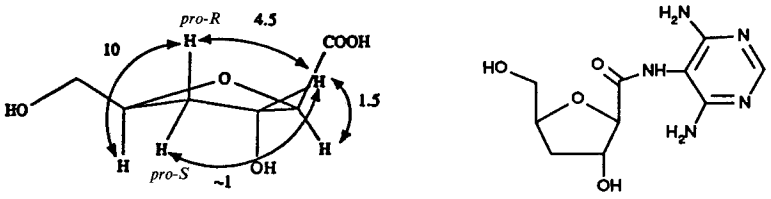
Results and Discussion. – Following the method of *Le Drian* and *Vogel* [13], optically pure 7-oxatrinorbornenone **8** was transformed in two steps into the epoxy acetal **9** (78% overall yield). Heating **9** with an excess of $LiAlH_4$ in THF (sealed *Pyrex* tube, 85°, 3 days) gave alcohol **10** (83%). No trace of any isomeric compound could be detected by 360-MHz ^{1}H-NMR of the crude reaction mixture. The structure of **10** was established unambiguously by its ^{1}H-NMR spectrum and double-irradiation experiments. Typical were the signals of the bridgehead protons H–C(1) and H–C(4) which resonated at 4.3 (*s*, ^3J(H–C(1), H_{endo}–C(2)) = 0 Hz [14]) and 4.67 ppm (*t*, ^3J(H–C(4), H_{exo}–C(3)) $\approx$ ^3J(H–C(4), H_{exo}–C(5)) = 5 Hz [14]), respectively. The isomeric 6,6-dimethoxy-7-oxabicyclo[2.2.1]heptan-2-*exo*-ol showed two *d* for H–C(1) and H–C(4). The high regioselectivity of reduction **9**→**10** can be attributed to steric hindrance of the *endo* MeO group at C(2) in **9** which impedes the competitive attack of the hydride agent onto the C(5) *endo* position. This hypothesis was consistent with the exclusive formation of the 3-*endo*-deuterio derivative **11**, when the reduction of **9** was carried out with $LiAlD_4$. The absence of *Wagner-Meerwein* rearrangement products in that reaction is also noteworthy [15].



9 **10** R=H, X=H; **11** R=H, X=D; **12** R=Bn, X=H **13** **14**

[3]) The hydroboration of 5,5-dimethoxy-7-oxabicyclo[2.2.1]hept-2-ene ($BH_3 \cdot Me_2S$, THF; $NaOH/H_2O_2$) led to a 3:2 mixture of the two regioisomeric 5,5-dimethoxy- and 6,6-dimethoxy-7-oxabicyclo[2.2.1]heptan-2-*exo*-ols in 60% yield.

After benzylation of **10** (NaH/DMF, BnBr; →**12**) and hydrolysis (*Nafion*, acetone/H_2O, reflux, 4 h), the protected 6-*exo*-benzyloxy-7-oxatrinorbornan-2-one **13** was obtained in 81% yield (**10**→**13**). The corresponding (*tert*-butyl)dimethylsilyl enol ether **14** was prepared in 93% yield following the technique of *House et al.* [16]. Ozonolysis (3% O_3 in O_2, MeOH/CH_2Cl_2 4:1, −78°) followed by treatment with $NaBH_4$ [17] afforded the hexonic-acid derivative **15** (80%). Hydrogenolysis (H_2, Pd/C, EtOH) furnished **6** (90%) with physical characteristics (m.p. 83–85°, $[\alpha]_D^{25} = -44$ (c = 1.25, 95% EtOH))[4]) different from those reported by *El Khadem* and *El Ashry* [8] for that product (oil, $[\alpha]_D^{25} = +24.9$ (c = 1.16, 95% EtOH)). The 360-MHz ^{1}H-NMR spectrum (and other spectral data, see *Exper. Part*) were in agreement with the structure of **6**. In particular, the *trans* relationship between H–C(2) and H–C(3) was established by the value for J(2,3) of 1.5 Hz (*ca.* 0 Hz in **15**; dihedral angle approaching 90°) [18]. The other vicinal coupling constants (application of the *Karplus* rule [19]) suggested the puckered conformation shown in the *Figure* for **6** in CD_3OD. Compounds **15**, **16**, and **5** must have similar conformations for their tetrahydrofuran rings (see *Exper. Part*).



6 **16**

Figure. *Coupling constants* (J(H,H)[Hz]) *and conformation of* **6**

Condensation of **6** with 4,5,6-triaminopyrimidine [8] gave the corresponding anhydrous amide **16** (30–45%) whose characteristics ($[\alpha]_D^{25} = +127$ (c = 0.33, MeOH)) were similar to those reported by *El Khadem* and *El Ashry* [8] for **16**·1.5 H_2O ($[\alpha]_D^{25} = +94$ (c = 0.23, MeOH)). In our hands, pyrolysis [11] (215–220°) of **16** and of **16**·1.5 H_2O failed to afford **5** [8]. Addition of a base or acid catalyst led exclusively to the decomposition of **16**. We found, however, that heating **16** in anh. DMF containing CsF to 110–120° (instead of 220°) for 55 h led to the smooth formation of **5**, isolated in 55% yield. Its characteristics (m.p. 222–225° (dec.), $[\alpha]_D^{25} = -6.2$ (c = 0.32, H_2O)) differred somewhat from those reported in [8] for this *C*-nucleoside (m.p. 165°, $[\alpha]_D^{25} = -11.1$ (c = 0.32 (H_2O)). All the spectral data recorded for **5**, **6**, and **14** confirmed their structures.

The (2*R*) configuration of **6** was confirmed by its circular dichroism (CD) spectrum which showed a negative *Cotton* effect (CE) at 215 nm ($\Delta\varepsilon_{215} = -0.97$, 95% EtOH) as in the case of 2,5-anhydro-D-*allo*- and 2,5-anhydro-D-*gluco*-hexonic acids [20]. Positive CE's were reported for 2,5-anhydro-4-deoxy-D-*lyxo*- and 2,5-anhydro-D-*manno*-hexonic acids [20]. The (1*S*) configuration of the *C*-nucleoside **5** was also confirmed by its CD spectrum

[4]) Oxidative anodic decarboxylation of **6** (MeOH, graphite electrodes, 110 mA/cm^2, 6 F/mol) led to an anomeric mixture of methyl 3-deoxy-D-*erythro*-pentofuranosides in 76% yield. Hydrolysis (0.25M H_2SO_4 in H_2O, 2 h, reflux) of this product afforded cordycepose (= 3-deoxy-D-*erythro*-pentose) in 79% yield whose characteristics were similar to those of the literature [23].

which showed a typical positive CE at 258 nm ($\Delta\varepsilon_{258} = +5.8$, MeOH) [12a][5]). For the related (1*R*)-1-*C*-(6-amino-7*H*-purin-8-yl)-1,4-anhydro-2-deoxy-D-*erythro*-pentitol[5]), a positive CE was recorded near 260 nm, whereas a negative CE was found for its (1*S*) isomer [12a]. The differences in the melting points and $[\alpha]_D$'s between our sample of **5** and that of *El Khadem* and *El Ashry* remain unexplained at this moment.

Conclusion. – *C*-Glycosides and *C*-nucleosides of ribose have already been prepared from furan [21] [22]. With the stereo- and regioselective monohydroxylation of optically pure (+)-7-oxabicyclo[2.2.1]hept-5-en-2-one (**8**) and its further transformation (8 steps, 36% overall yield, or 10 steps, 32% based on 1-cyanovinyl (1*S*)-camphanate) into 2,5-anhydro-4-deoxy-D-*ribo*-hexonic acid (**6**), we have demonstrated the possibility for that route to obtain optically pure 3′-deoxy-β-D-*erythro*-pentofuranosyl derivatives. The partially protected derivative **15** of **6** was also obtained selectively. A smooth technique using CsF in DMF is presented for the transformation of **6** into cordycepin C (**5**). Compounds **6** and **15** are potential precursors for the stereoselective synthesis [3–5] [25] of further 3-deoxy-β-D-*erythro*-pentofuranosyl derivatives. The new route presented here for the preparation of **6** and **15** should make the *C*-nucleosides derived from 3-deoxy-ribose better accessible. Starting from (1*S*)-7-oxabicyclo[2.2.1]hept-5-en-2-one (derived from furan and 1-cyanovinyl (1*R*)-camphanate [26]), 2,5-anhydro-4-deoxy-L-*ribo*-hexonic acid (enantiomer of **6**) and the corresponding *C*-nucleosides can be obtained as readily as their D-enantiomers.

We are grateful to *F. Hoffmann-La Roche & Co. AG*, Basel, *E.I. du Pont de Nemours & Co.*, Wilmington, Delaware, USA, the *Fonds Herbette*, Lausanne, and the *Swiss National Science Foundation* for financial support.

Experimental Part

General. See [1]. Synthesis of (±)-**6** and (±)-**10** to (±)-**16** follow the same procedures as those given below for the optically pure enantiomers, the starting material being (±)-**9** [13]. The spectral data were the same as for the optically pure derivatives; for crystalline compounds, the m.p. will be given.

*(–)-(1R,2R,4S)-6,6-Dimethoxy-7-oxabicyclo[2.2.1]heptan-2-*exo*-ol* (**10**). $LiAlH_4$ (595 mg, 15.6 mmol) was added portionwise to a stirred soln. of **9** [13] (1.35 g, 7.84 mmol) in anh. THF (20 ml). The flask was sealed and heated to 80–85° for 3 days (until disappearance of **9**, TLC control). After cooling to 20°, a soln. of 2,2′,2″-nitrilotris(ethanol) (2.3 ml, 17.2 mmol) in anh. THF (5 ml) was added dropwise under stirring. After 1 h at 20°, H_2O (0.56 ml, 31.2 mmol) was added and the mixture stirred overnight. The suspension was filtered *(Büchner)* and the precipitate washed with THF (30–40 ml). The solvent was evaporated and the residue filtered through a short column of silica gel (50 × 3 cm, SiO_2 *Merck 40–63*, AcOEt) yielding 1.12 g (83%) of **10** as colourless oil ((±)-**10**: white crystals, m.p. 44–46°). $[\alpha]_{365}^{25} = -10.3$, $[\alpha]_{436}^{25} = -5.2$, $[\alpha]_{546}^{25} = -3.4$, $[\alpha]_{578}^{25} = -2.0$, $[\alpha]_{589}^{25} = -1.8$, (*c* = 1.78, CH_2Cl_2). IR (KBr): 3600, 3400 (br.), 3000, 2960, 2850, 1770, 1720, 1450, 1400, 1335, 1290, 1180, 1130, 1085, 1050, 980, 915, 890, 870. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.67 (*t*, ^3J = 5, H–C(4)); 4.36 (*dd*, ^3J = 6.5, 2, H–C(2)); 4.3 (*s*, H–C(1)); 3.27, 3.24 (2*s*, 2 MeO); 2.12 (*dd*, ^2J = 13, ^3J = 7, H_{endo}–C(3)); 1.95 (*ddd*, ^2J = 12.5, ^3J = 5, ^4J = 2.5, H_{exo}–C(5)); 1.9 (br. *s*, OH); 1.64 (*dm*, ^2J = 13, H_{exo}–C(3)); 1.46 (*d*, ^2J = 12.5, H_{endo}–C(5)). ^{13}C-NMR (90 MHz, $CDCl_3$): 108.4 (*s*); 85.8 (*d*, ^1J(C,H) = 157); 76.4 (*d*, ^1J(C,H) = 155); 68.9 (*d*, ^1J(C,H) = 150); 51.2, 48.8 (2*q*, ^1J(C,H) = 140); 42.3, 40.7 (2*t*, ^1J(C,H) = 135). MS (70 eV): 174 (5, $M^{+\cdot}$), 143 (16), 142 (15), 133 (6), 130 (4), 129 (2), 124 (10), 116 (100), 110 (14). Anal. calc. for $C_8H_{14}O_4$ (174.20): C 55.16, H 8.10; found: C 55.07, H 8.04.

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[5]) We have repeated the synthesis of (1*R*)-1-*C*-(6-amino-7*H*-purin-8-yl)-1,4-anhydro-2-deoxy-D-*erythro*-pentitol using 2,5-anhydro-3-deoxy-β-D-*ribo*-hexonic acid and our method (CsF/DMF, 120°) for the formation of the heterocycle. It did not lead to isomerization at C(1) [24].

*(1RS,2RS,3RS,4SR)-6,6-Dimethoxy(3-*endo-^2H*)-7-oxabicyclo[2.2.1]heptan-2-*exo-*ol* ((±)-**11**). Same procedure as for (±)-**10** with $LiAlD_4$ instead of $LiAlH_4$. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.64 (*t*, ^3J = 5.5, H–C(4)); 4.34 (br. *s*, H–C(2)); 4.28 (*s*, H–C(1)); 3.25, 3.22 (2*s*, 2 MeO); 2.84 (br. *s*, OH); 1.94 (*ddd*, ^2J = 12.5, ^3J = 5.5, ^4J = 2.5, H_{exo}–C(5)); 1.62 (*m*, H_{exo}–C(3)); 1.43 (*d*, ^2J = 12.5, H_{endo}–C(5)).

*(1R,4S,6R)-6-*exo-*(Benzyloxy)-2,2-dimethoxy-7-oxabicyclo[2.2.1]heptane* (**12**). A soln. of **10** (540 mg, 3.1 mmol) in anh. DMF (4 ml) was added dropwise to a stirred suspension of NaH (103 mg, 3.4 mmol) in anh. DMF (1.2 ml) cooled to −14°. The temp. was allowed to reach 20° and the mixture stirred until the end of H_2 evolution. After cooling to −14°, a soln. of benzyl bromide (0.4 ml, 3.4 mmol) in anh. DMF (1 ml) was added dropwise. The mixture was then stirred at 25° until disappearance of **10** (TLC control). After 12–14 h, MeOH (2 ml) was added to the homogeneous soln. and the mixture allowed to stand for 1 h at 20°. The solvent was evaporated and the residue dissolved in AcOEt (25 ml). The soln. was washed with H_2O (5 ml) and sat. aq. NaCl soln. (5 ml), the combined aq. phase extracted with AcOEt (5 ml, twice), the combined org. phase dried ($MgSO_4$) and evaporated, and the residue purified by column chromatography on silica gel (*Lobar B, Merck 40–60*, AcOEt/petroleum ether 2:1) yielding 720 mg (88%) of **12**. Colourless oil. $[\alpha]_{436}^{25} = -6.5$, $[\alpha]_{546}^{25} = -3.7$, $[\alpha]_{578}^{25} = -3.4$, $[\alpha]_{589}^{25} = -3.1$ (*c* = 1.755, CH_2Cl_2). IR ($CHCl_3$): 3050, 3000, 2960, 2840, 1490, 1450, 1350, 1330, 1310, 1290, 1240, 1180, 1130, 1090, 1060, 1020. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.44–7.31 (*m*, Ph); 4.72 (*t*, ^3J = 6, H–C(4)); 4.62, 4.57 (2*d*, ^2J = 13, PhCH_2O); 4.5 (*s*, H–C(1)); 4.24 (*dd*, ^3J = 7, 2.5, H–C(6)); 3.27, 3.23 (2*s*, 2 MeO); 2.05 (*dd*, ^2J = 12.5, ^3J = 7, H_{endo}–C(5)); 2.02 (*ddd*, ^2J = 12.5, ^3J = 6, ^4J = 2.5, H_{exo}–C(3)); 1.88 (*dm*, ^2J = 12.5, H_{exo}–C(5)); 1.48 (*d*, ^2J = 12.5, H_{endo}–C(3)). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 138.1 (*s*); 128.3, 127.7, 127.5 (3*d*, ^1J(C,H) = 160); 180.7 (*s*); 82.7, 76.3 (2*d*, ^1J(C,H) = 160); 76.7 (*d*, ^1J(C,H) = 150); 51.0, 48.7 (2*q*, ^1J(C,H) = 140); 70.9, 40.8, 39.3 (3*t*, ^1J(C,H) = 140). MS (70 eV): 264 (15, $M^{+\cdot}$), 233 (3), 189 (4), 158 (6), 157 (6), 117 (3), 116 (7), 115 (100), 105 (14), 91 (60). Anal. calc. for $C_{15}H_{20}O_4$ (264.2): C 68.19, H 7.63; found: C 68.21, H 7.55.

*(+)-(1R,4S,6R)-6-*exo-*(Benzyloxy)-7-oxabicyclo[2.2.1]heptan-2-one* (**13**). A mixture of **12** (430 mg, 1.62 mmol), acetone (5 ml), H_2O (3 ml) and *Nafion* (100 mg) was refluxed for 4 h. The mixture was filtered and the solvent evaporated yielding 330 mg (93%) of **13**, colourless oil ((±)-(**13**): m.p. 35–37°). $[\alpha]_{365}^{25} = +258$, $[\alpha]_{426}^{25} = +105$, $[\alpha]_{546}^{25} = +50$, $[\alpha]_{578}^{25} = +43$, $[\alpha]_{589}^{25} = +40$ (*c* = 2.17, CH_2Cl_2). IR ($CHCl_3$): 3020, 3000, 2960, 2900, 2880, 1770, 1490, 1450, 1400, 1350, 1310, 1280, 1240, 1150, 1080, 1040, 1010. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.38–7.25 (*m*, Ph); 5.04 (*t*, ^3J = 6, H–C(4)); 4.6, 4.5 (2*d*, ^2J = 12, PhCH_2O); 4.4 (*s*, H–C(1)); 4.0 (*dd*, ^3J = 7, 3, H_{endo}–C(6)); 2.43 (*ddd*, ^2J = 17, ^3J = 6, ^4J = 2, H_{exo}–C(3)); 2.11 (*dd*, ^2J = 14, ^3J = 7, H_{endo}–C(5)); 2.04 (*m*, H_{exo}–C(5)); 1.91 (*d*, ^2J = 17, H_{endo}–C(3)). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 221.2, 137.2 (2*s*); 128.5, 127.9, 127.7 (3*d*, ^1J(C,H) = 155); 84 (*d*, ^1J(C,H) = 175); 77, 76.2 (2*d*, ^1J(C,H) = 150); 71.5 (*t*, ^1J(C,H) = 145); 43.8, 38.7 (2*t*, ^1J(C,H) = 125). MS (70 eV): 218 (1, $M^{+\cdot}$), 172 (1.4), 146 (1.3), 127 (1.5), 120 (2.5), 105 (4), 92 (10), 91 (100), 77 (13). Anal. calc. for $C_{13}H_{14}O_3$ (218.25): C 71.54, H 6.46; found: C 71.53, H 6.53.

*(−)-(1R,4S,6R)-6-*exo-*(Benzyloxy)-2-*{[(tert-*butyl)dimethylsilyl]oxy}*-7-oxabicyclo[2.2.1]hept-2-ene* (**14**). A mixture of **13** (1.153 g, 5.3 mmol), *N*-[(*tert*-butyl)dimethylsilyl]-*N*-methyltrifluoroacetamide (10.35 g, 42.9 mmol), and Et_3N (6.8 ml, 48 mmol) in anh. DMF (12 ml) was heated to 60° for 4 days under Ar. The solvent was evaporated (10^{-2} Torr) and the residue filtered through a column of silica gel (35 × 3 cm, AcOEt/petroleum ether 1:3) yielding 1.64 g (93%) of **14**, unstable colourless oil which gives white crystals on sublimation. M.p. 51–52°. $[\alpha]_{365}^{25} = -131$, $[\alpha]_{436}^{25} = -74$, $[\alpha]_{546}^{25} = -40$, $[\alpha]_{578}^{25} = -34.2$, $[\alpha]_{589}^{25} = -33$ (*c* = 1.325, CH_2Cl_2). ^{1}H-NMR (360 MHz, $CDCl_3$): 7.32–7.21 (*m*, Ph); 5.93 (br. *d*, ^3J = 2, H–C(3)); 4.89 (*m*, H–C(4)); 4.58, 4.53 (2*d*, ^2J = 12, PhCH_2O); 4.45 (*d*, *J* = 0.8, H–C(1)); 3.94 (*dd*, ^3J = 6.5, 2.5, H–C(6)); 1.91 (*dd*, ^2J = 11.5, ^3J = 6.5, H_{endo}–C(5)); 1.77 (*ddd*, ^2J = 11.5, ^3J = 4.5, 2.5, H_{exo}–C(5)); 0.87 (*s*, *t*-Bu); 0.12, 0.08 (2*s*, 2 Me). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 160.2, 138.2 (2*s*); 128.4, 127.8, 127.6 (3*d*, ^1J(C,H) = 160); 107.7 (*d*, ^1J(C,H) = 170); 82.5 (*d*, ^1J(C,H) = 165); 78.8 (*d*, ^1J(C,H) = 160); 78.4 (*d*, ^1J(C,H) = 150); 71.6 (*t*, ^1J(C,H) = 145); 37.5 (*d*, ^1J(C,H) = 135); 25.5 (*q*, ^1J(C,H) = 125); 18.1 (*s*); −4.8, −5.0 (2*q*, ^1J(C,H) = 120).

*2,5-Anhydro-3-*O*-benzyl-4-deoxy-*D-ribo-*hexonic Acid* (**15**). A flux of O_2 containing 3% of O_3 was bubbled through a soln. of **14** (1.6 g, 4.8 mmol) in MeOH/CH_2Cl_2 4:1 (35 ml) at −78° until persistence of a blue colour. The excess of O_3 was eliminated by purging with N_2, and $NaBH_4$ (360 mg, 9.6 mmol) was added. After 30 min at −78°, the temp. was allowed to reach 20°, and $NaBH_4$ (360 mg, 9.6 mmol) was added and the mixture stirred for 3 h. After the addition of *Dowex 50W* × *8* resin (until pH 1–2), the mixture was filtered and the solvent evaporated. The residue was purified by column chromatography on silica gel (*Lobar C*, Et_2O/MeOH 85:15) yielding 1.064 g (80%) of **15**, colourless oil. $[\alpha]_{365}^{25} = -64$, $[\alpha]_{436}^{25} = -41$, $[\alpha]_{546}^{25} = -24$, $[\alpha]_{578}^{25} = -21$, $[\alpha]_{589}^{25} = -20$ (*c* = 1.6, CH_2Cl_2). IR (KBr): 3400 (br.), 1730, 1480, 1450, 1350, 1260, 1210, 1080, 1020. ^{1}H-NMR (360 MHz, CD_3OD): 7.43–7.3 (*m*, Ph); 5.4 (br. *s*, 2 OH); 4.84, 4.63 (2*d*, ^2J = 12, PhCH_2O); 4.65 (*s*, H–C(2)); 4.47 (*m*, H–C(5)); 4.37 (*d*, ^3J = 5.5, H–C(3)); 3.88 (*dd*, ^2J = 12, ^3J = 3.2, H–C(6)); 3.66 (*dd*, ^2J = 12, ^3J = 3.8, H–C(6)); 2.14 (*dd*, ^2J = 13.5, ^3J(H–C(4),H–C(5)) = 6, ^3J(H–C(3),H–C(4)) ≈ 0, $H_{pro\text{-}S}$–C(4)); 1.97 (*ddd*, ^2J = 13.5, ^3J(H–C(4),H–C(5))

= 10.5, ^3J(H–C(3),H–C(4)) = 5.5, $H_{pro\text{-}R}$–C(4)). ^{13}C-NMR (90.55 MHz, CD_3OD): 175.6, 139.2 (2*s*); 129.4, 128.9, 128.8 (3*d*, ^1J(C,H) = 160); 84.8 (*s*, ^1J(C,H) = 150); 83.5 (*d*, ^1J(C,H) = 155); 82.4 (*d*, ^1J(C,H) = 150); 72.2, 63.9 (2*t*, ^1J(C,H) = 140); 33.7 (*t*, ^1J(C,H) = 135). CI-MS (NH_3): 270 (5, $M^{+\cdot}$ + 18), 253 (13), 252 (94, $M^{+\cdot}$), 235 (8), 210 (11), 196 (9), 180 (8), 126 (100). Anal. calc. for $C_{13}H_{16}O_5$ (252.26): C 61.89, H 6.39; found: C 61.9, H 6.38.

2,5-Anhydro-4-deoxy-D-ribo-*hexonic Acid* (**6**). A mixture of **15** (65 mg, 0.25 mmol), EtOH (1.5 ml), and 10% Pd/C (10 mg) was pressurized with H_2 (1 atm) and stirred for 12 h at 20°. After filtration, the solvent was evaporated yielding 38 mg (90%) of **6**, white crystals. M.p. 83–85° ((±)-(**6**): m.p. 93–94°). $[\alpha]_{365}^{25} = -142.2$, $[\alpha]_{436}^{25} = -90.1$, $[\alpha]_{546}^{25} = -52.6$, $[\alpha]_{578}^{25} = -46.5$, $[\alpha]_{589}^{25} = -44.7$ (*c* = 1.25, 95% EtOH). IR (KBr): 3350 (br.), 2900, 2600 (br.), 1720, 1450, 1300, 1240, 1120, 1100, 1060, 1030, 970, 940, 870, 860. ^{1}H-NMR (360 MHz, CD_3OD): 4.66 (*ddd*, ^3J(H–C(3), $H_{pro\text{-}R}$–C(4)) = 4.5, ^3J(H–C(2), H–C(3)) = 1.5, ^3J(H–C(3), $H_{pro\text{-}S}$–C(4)) = 1.5, H–C(3)); 4.6 (*m*, H–C(5)); 4.51 (*d*, ^3J = 1.5, H–C(2)); 3.97 (*dd*, ^2J = 11.5, ^3J = 3.2, H–C(6)); 3.76 (*dd*, ^2J = 11.5, ^3J = 4.0, H–C(6)); 2.1 (*ddd*, ^2J = 13, ^3J(H–C(4),H–C(5)) = 10, ^3J(H–C(3),H–C(4)) = 4.5, $H_{pro\text{-}R}$–C(4)); 2.05 (*ddd*, ^2J = 13, ^3J(H–C(4), H–C(5)) = 6, ^3J(H–C(3),H–C(4)) = 1.5, $H_{pro\text{-}S}$–C(4)). ^{13}C-NMR (90.55 MHz, CD_3OD): 175.9 (*s*); 86.4, 82.1 (2*d*, ^1J(C,H) = 145); 77.2 (*d*, ^1J(C,H) = 150); 64.0 (*t*, ^1J(C,H) = 140); 35.9 (*t*, ^1J(C,H) = 130). CI-MS (NH_3): 180 (30, $M^{+\cdot}$ + 18), 162 (100, $M^{+\cdot}$), 148 (12), 136 (38). Anal. calc. for $C_6H_{10}O_5$ (162.14): C 44.44, H 6.25; found: C 44.53, H 6.15.

2,5-Anhydro-4-deoxy-N-*(4′,6′-diaminopyrimidin-5′-yl)*-D-ribo-*hexonamide* (**16**). Same procedure as in [8]. The crude product was purified by chromatography on silica gel (*Lobar B*, CH_2Cl_2/MeOH 2:1; removal of the excess of 4,5,6-triaminopyrimidine). Yield 30–45%. Slightly yellow crystals. M.p. 208–210° (dec.). $[\alpha]_{436}^{25} = +283$, $[\alpha]_{546}^{25} = +153$, $[\alpha]_{578}^{25} = +133$, $[\alpha]_{589}^{25} = +127$ (*c* = 0.33, MeOH). UV (MeOH): 221 (20200), 260 (5050). IR (KBr): 3450, 3300 (br.), 3100, 1660, 1640, 1590, 1520, 1480, 1340, 1290, 1240, 1120, 1090, 1060, 1010. ^{1}H-NMR (250 MHz, CD_3OD): 7.9 (*s*, H–C(2′)); 4.69 (*ddd*, ^3J = 5, 1.5, 1, H–C(3)); 4.57 (*m*, H–C(5)); 4.54 (*d*, ^3J = 1, H–C(2)); 4.07 (*dd*, ^2J = 12, ^3J = 2.5, H–C(6)); 3.71 (*dd*, ^2J = 12, ^3J = 2, H–C(6)); 2.23 (*ddd*, ^2J = 13, ^3J = 10, 5, $H_{pro\text{-}R}$–C(4)); 1.94 (*ddd*, ^2J = 13, ^3J = 5.5, 1.5, $H_{pro\text{-}S}$–C(4)). ^{13}C-NMR (90.55 MHz, D_2O); 173.9, 160.5 (2*s*); 156.5 (*d*, ^1J(C,H) = 190); 95.4 (*s*); 87.9, 82.2, 77.1 (3*d*, ^1J(C,H) = 150); 62.5 (*t*, ^1J(C,H) = 140); 35.2 (*t*, ^1J(C,H) = 135). MS (70 eV): 269 (34, $M^{+\cdot}$), 251 (4), 220 (10), 164 (15), 152 (51), 125 (100). Anal. calc. for $C_{10}H_{15}N_5O_4$ (269.26): C 44.65, H 5.61, N 26.0; found: C 44.46, H 5.68, N 26.12.

*(1S)-1-C-(6′-Amino-7′*H*-purin-8′-yl)-1,4-anhydro-3-deoxy*-D-erythro-*pentitol* (= *Cordycepin C*; **5**). A mixture of **16** (31 mg, 0.115 mmol), anh. DMF (1 ml), and CsF (87 mg, 0.55 mmol) was heated to 110–120° for 55 h. The mixture was filtered through silica gel rinsing with MeOH, the solvent evaporated, and the residue purified by column chromatography on silica gel (*Lobar B*, CH_2Cl_2/MeOH 2:1), yielding 16 mg (55%) of **5**. Colourless crystals. M.p. 223–225° (dec.). $[\alpha]_{365}^{25} = +12.5$, $[\alpha]_{436}^{25} = -1.5$, $[\alpha]_{546}^{25} = -5$, $[\alpha]_{578}^{25} = -6.8$, $[\alpha]_{589}^{25} = -6.2$ (*c* = 0.32, H_2O). CD: $\Delta\varepsilon_{258} = +5.8$ (*c* = 0.095 g/100 ml, MeOH). UV (MeOH): 211 (13700), 265 (11600). IR (KBr): 3400 (br.), 1670, 1610, 1440, 1360, 1340, 1300, 1110, 1080, 1030, 800. ^{1}H-NMR (250 MHz, CD_3OD): 8.16 (*s*, H–C(2′)); 5.07 (*d*, ^3J = 2, H–C(1)); 4.6 (*m*, H–C(2)); 4.56 (*m*, H–C(4)); 4.02 (*dd*, ^2J = 12, ^3J = 3, H–C(5)); 3.75 (*dd*, ^2J = 12, ^3J = 3.5, H–C(5)); 2.24 (*dd*, ^2J = 13.5, ^3J = 9.5, 5.5, H–C(3)); 2.02 (*ddd*, ^2J = 13.5, ^3J = 6, 2, H–C(3)). ^{13}C-NMR (90.55 MHz, (D_6)DMSO): 155.5 (*s*); 152.3 (*d*, ^1J(C,H) = 195); 151.4 (*s*); 150.8 (*s*); 118.6 (*s*); 82.9, 80.2, 75.9 (3*d*, ^1J(C,H) = 150); 62.8 (*t*, ^1J(C,H) = 140); 35.6 (*t*, ^1J(C,H) = 125). MS (70 eV): 251 (15, $M^{+\cdot}$), 235 (2.5), 233 (2.3), 220 (3), 203 (22), 178 (41), 164 (100). Anal. calc. for $C_{10}H_{13}N_5O_3$ (251.24): C 47.8, H 5.21, N 27.87; found: C 47.51, H 5.30, N 27.8.

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