Supporting Information for
Mannich-type C-nucleosidations in the 5,8-diaza-7,9-dicarba-purine family

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Procedures Referring to Scheme 2:

N-formyl-glycyl-guanidine (**5**). This compound was prepared according to Hoffmann's procedure for the synthesis of N-formyl-L-valyl-guanidine.[1] Guanidine hydrochloride (15.00 g, 157 mmol) was added to a turbid suspension of NaOMe (8.48 g, 157 mmol) in 200 ml of anhydrous MeOH. The resulting suspension was stirred at rt for 40 min. The formed precipitate, NaCl was filtered off via celite and washed with 50 ml of MeOH. To the colorless filtrate thus obtained was added N-formylglycine ethyl ester[2] (41.14 g, 314 mmol, 2.0 eq) in 20 ml of MeOH. The reaction mixture was stirred at rt for 6 hrs, during which a white precipitate appeared within minutes. After cooling at 4°C for 2 hrs, the white solid was filtered, washed with 50 ml of cold MeOH, dried (HV, rt, overnight) to give 15.60 g of guanidine **5** as white solid. Yield: 69%; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.67 (2H, d, J = 5.1Hz, NHC$\underline{H}_2$), 6.20-8.40 (5H, m, NH × 5), 8.03 (1H, s, CHO); ^{13}C NMR (75 MHz, DMSO-d_6): δ 44.05, 161.07, 162.23, 179.40; ESI MS: m/e 145.3 (28, M+H$^+$), 167.2 (20, M+Na$^+$), 289.2 (52, 2M+H$^+$), 311.2 (100, 2M+Na$^+$).

2-Amino-4-formylaminomethyl-6-trichloromethyl-s-triazine **(6)**[3]. To a suspension of guanidine **5** (14.4 g, 0.1 mol) in 100 ml of DMF was added dropwise of Cl_3CCN (28.8 g, 0.2 mol, 2eq). After adding, the reaction mixture was stirred at r.t. for 30 min until the solution became clear. After heating at 80°C (bath temperature) for 1 hr, the light brown solution was evaporated to dryness. The white solid thus obtained was washed with H_2O (200 ml), dried under HV over P_2O_5 to give 26.5 g of triazine **6** as white solid.[4] Yield: 98%; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.29 (2H, d, J = 6.0 Hz, CH_2), 8.15 (1H, d, J = 1.2 Hz, CHO), 8.23 (1H, br, NH_2), 8.27 (1H, br, NH_2), 8.51 (1H, t, J = 5.7 Hz, N$\underline{H}$CHO); ^{13}C NMR (75 MHz, DMSO-d_6): δ 42.89, 95.99, 161.28, 166.87, 172.06, 176.65; ESI MS (negative): m/e 268.0 (100, [M-H]$^-$), 270.0 (96), 272.0 (30).

4-Amino-6-formylaminomethyl-1H-[1,3,5]triazin-2-one **(7**). Triazine **6** (13.5 g, 50 mmol) was suspended in 250 ml of 0.8 M aq. Na_2CO_3 solution. The reaction mixture was stirred at 80°C for 2 hrs, at which time **6** was gradually dissolved and a clear light yellow solution was obtained. TLC ($CHCl_3$/MeOH, 25% aq. NH_3) showed the consumption of **6** (Rf 0.86) and the formation of a major product (Rf 0.22). The reaction mixture was cooled to 0°C, and neutralized with conc. aq. HCl to pH7. The white precipitate was filtered, washed with H_2O (2× 100 ml), MeOH (2× 100 ml), and diethyl ether (2× 100 ml) to give 7.1 g of 4-amino-6-formylaminomethyl-1*H*-[1,3,5]triazin-2-one **7** as white solid.[5] Yield: 83%; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.05 (2H, d, J = 6.0 Hz, CH_2), 7.38 (1H, br, NH_2), 7.51 (1H, br, NH_2), 8.10 (1H, s, CHO), 8.36 (1H, t, J = 5.7 Hz, N$\underline{H}$CHO), 11.54 (1H, br, NH); ^{13}C NMR (75 MHz, DMSO-d_6, 60°C): δ 40.48, 156.00, 161.61, 165.06, 168.85; ESI MS (positive): m/e 191.9 (100, M+Na$^+$).

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[1] Hoffmann, E.; Diller, D. *Can. J. Chem.* **1965**, *43*, 3103.

[2] Martin, P. K.; Matthews, H. R.; Rapoport, H.; Thyagarajan, G. *J. Org. Chem.* **1968**, *33*, 3758.

[3] Trichloroacetonitrile has been used for the synthesis of 2-amino-4-alkyl-6-trichloromethyl-s-[1,3,5]triazine. Kelarev, V. I.; Ammar Dibi; Lunin, A. F. *Chem. Heterocycl. Compd. (New York)*, **1985**, *21*, 1284, Engl. Transl. From Khim. Geterotsikl. Soedin. (Russion) 1985, *21*,1557.

[4] Triazine **6** can be dissolved well in MeOH. It is sparingly soluble in H_2O.

[5] Triazin-2-one **7** is soluble in DMSO, and non-soluble in CH_2Cl_2, MeOH, and H_2O.

2-amino-6-oxo-5, 8-diaza-7, 9-dicarbapurine (**2**)[6]. Triazin-2-one **7** (4.23 g, 25 mmol) was dissolved in 40 ml of 98% H_2SO_4, and the resulting light brown solution was stirred at 100°C for 5 hrs. After cooling to rt, the acid solution was carefully poured into 500 ml of rapid stirred ether. The ether was decanted and fresh ether was added; this sequence was repeated twice. The precipitated salt was suspended in 100 ml of H_2O and the solution was made basic (pH=9) by adding 25% aq. NH_3. To the clear light brown solution thus obtained was added dropwise AcOH until pH=6.5. The light brown precipitate formed was filtered, washed with 50 ml of cold H_2O, and dried under HV over P_2O_5 to give 3.21 g of purine **2** as light brown solid.[7] Yield: 85%; Rf: 0.33 (CH_2Cl_2/MeOH, 4/1); ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.46 (2H, s, NH_2), 6.52 (1H, d, ^4J = 0.9 Hz, H-9), 7.93 (1H, d, ^4J = 0.9 Hz, H-7), 11.17 (1H, br, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 111.66 (C-9), 125.37 (C-7), 137.79, 145.08, 149.45; ESI MS (positive): 152.1 (100, $M+H^+$), 303.1 (20, $2M+H^+$), 325.1 (24, $2M+Na^+$); ESI MS (negative): m/e 150.0 (100, $[M-H]^-$), 301.0 (32, $[2M-H]^-$), 452.0 (4, $[3M-H]^-$). UV (C = 2.50×10^{-4}M in pH =7 0.1 M phosphate buffer): ε (220nm) = 10200; λ_{max} = 261nm (ε = 7300).

2-(N,N-dimethylaminomethyleneamino)-6-oxo-5,8-diaza-7,9-dicarbapurine (**8**). To a solution of purine **2** (225 mg, 1.5 mmol) in 25 ml of MeOH was added dimethylformamide dimethylacetal (1.79 g, 15.0 mmol, 10 eq) in one portion. The reaction solution was stirred at rt for 12hrs. TLC (CH_2Cl_2/MeOH, 4/1) showed the consumption of starting compd. 2 (Rf 0.29) and the formation of two new spots (Rf 0.41, 0.73). The clear yellow solution was evaporated under reduced pressure at 35 °C to dryness. The yellow oil residue was dissolved in CH_2Cl_2/MeOH (10/1) and loaded onto a silica gel column. Chromatography was conducted using CH_2Cl_2/MeOH (10/1) as eluent. Fractions containing the fast moving product were combined, evaporated, and dried to give 245 mg of **8** as white solid. Yield 79%; Rf 0.52 (CH_2Cl_2/MeOH, 10/1); ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.05 (3H, s, CH_3), 3.16 (3H, s, CH_3), 6.75 (1H, s, H-7), 8.04 (1H, s, H-9), 8.61 (1H, s, -N=CH-), 11.61 (1H, br, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 34.79, 40.74, 114.71, 125.92, 138.08, 145.05, 152.74, 158.17; ESI MS: m/e 207.2 (52, $M+H^+$), 435.1 (100, $2M+Na^+$); Colorless crystals were obtained after crystallization of 6 in MeOH. A colorless, cubic crystal was mounted to collect X-ray data. m.p.(MeOH) >179°C (decomp.).

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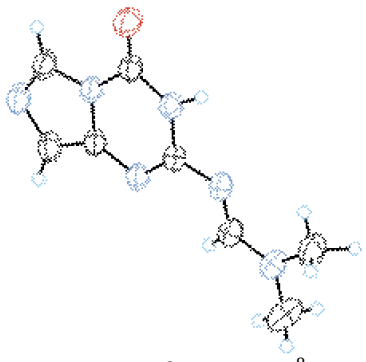
[6] Conc. H_2SO_4 has been successfully used in the cyclization of 2-amino-4-(2-hydroxyvinyleneamino)-*s*-triazin-4-one to give 5-aza-7-carbaguanine. Kim, S.H.; Bartholomew, D.G.; Allen, L.B.; Robins, R.K.; Revankar, G.R.; Dea, P. *J. Med. Chem.* **1978**, 21, 883.

[7] Purine **2** can be dissolved in DMF, DMSO, hot H_2O and hot MeOH. It is not soluble in ether, CH_2Cl_2. It is thermally stable for 10 hrs at 190°C, and underwent slow sublimation.



X-ray of Purine 8.[8]

Fractions containing the slow moving product were combined, evaporated, and dried to give 36 mg of 2-(N,N-dimethylaminomethyleneamino)-9-(N,N-dimethylaminomethylene)-6-oxo-5,8-diaza-7,9-dicarbapurine[9] as yellow solid. Yield 9%; Rf 0.19 (CH_2Cl_2/MeOH, 10/1); ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.01 (3H, s, H-16), 3.14 (3H, s, H-16), 3.48 (3H, s, H-12), 3.74 (3H, s, H-12), 8.19 (1H, s, H-7), 8.25 (1H, s, H-10), 8.74 (1H, s, H-14); ^{13}C NMR (125 MHz, DMSO-d_6): δ 34.58 (C-16), 40.59 (C-16), 40.82 (C-12), 47.26 (C-12), 115.85 (C-9), 131.88 (C-7), 147.96 (C-10), 150.04 (C-6), 158.51 (C-4), 159.54 (C-14), 169.25 (C-2) (assignment of ^{1}H and ^{13}C were based on difference-NOE and HMBC); ESI MS (positive): m/e 262.3 (100, M+H^+), 284.2 (40, M+Na^+), 300.0 (12, M+K^+), 523.2 (5, 2M+H^+), 545.1 (80, 2M+Na^+), 561.1 (8, 2M+K^+).

4,6-diamino-2-formylaminomethyl-s-triazine (**9**)[10]**.** Triazine **6** (540mg, 2 mmol) was dissolved in 50 ml of saturated NH_3 in MeOH. The reaction solution was left 48 hrs at rt without stirring. The formed colorless needles were filtered, washed with ether and dried under HV at rt overnight to give 276 mg of 4,6-diamino-2-formylaminomethyl-s-triazine **9**. Yield 82%; m.p. >275°C (decomp.); ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.19 (1H, br, NH), 8.09 (1H, s, CHO), 6.68 (4H, br, 2 × NH_2), 3.97 (2H, d, J = 6.0 Hz, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6): δ 42.59 (CH_2), 161.19 (CHO), 166.93 (C-4, C-6), 174.01 (C-2).

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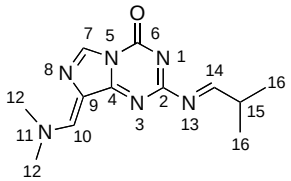
[8]) x-ray structure analysis of **8** was carried out by Dr. Bernd Schweizer, ETH-Z. Crystallographic data for the structure has been deposited with the Cambridge Crystallographic Data Center as deposition no. CCDC 242452. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 union Road, Cambridge CB12 1EZ, UK (fax +44 (1233) 336 0333; e-mail: deposit@ccdc.cam.ac.uk).

[9] Structure of 2-(N,N-dimethylaminomethyleneamino)-9-(N,N-dimethylaminomethylene)-6-oxo-5,8-diaza-7,9-dicarbapurine:



[10] Triazine **9**, the precursor compd. for the synthesis of 2,6-Diamino-5,8-diaza-7,9-dicarba-purine, has been reported by Wang et al. using the reaction of N-formylglycine ethyl ester with biguanide. Wang, Z.; Huynh, H. K.; Han, B.; Krishnamurthy, R.; Eschenmoser, A. *Org. Lett*. **2003**, *5*, 2067. The present method offered another convenient route to the synthesis of **9**.

Procedures Referring to Scheme 3:

N-cyano-isocyanate-dimethylacetal[11]. Cyanamide (Aldrich 99%, 15.5 g, 0.37 mol) was dissolved in tetramethyl orthocarbonate (50.0 g, 0.37 mol, 1eq), and the reaction was heated at 95 °C before removing MeOH (ca 21 g) by distillation under atmospheric pressure. After evaporated at 90 °C (bath temperature) under reduced pressure (0.2 mmHg), the light yellow liquid residue was left at 4 °C for 4 hrs. After adding 10 ml of cold ether, the colorless solid was filtered and dried under vacuum (60 mmHg) to give 31.3 g of N-cyano-isocyanate-dimethylacetal as colorless crystal. Yield: 76%; m.p. 56-58 °C (lit.[12] 52-56°C); ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.93 (6H, 2 × CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 58.46 (CH_3), 113.00 (>CH=), 164.36 (CN); EI MS: m/e 114.0 (54, $M^{\bullet+}$), 69.0 (100).

2-methoxy-6-amino-5,8-diaza-7,9-dicarbapurine (**10**). A suspension of 4-nitroimidazole (11.3 g, 0.1 mol, ACROS 98%) and 10% Pd/C (4.5 g, 40% w/w, Fluka) in 250 ml dried 1,4-dioxane (distilled over sodium) was stirred vigorously under atomospheric pressure of H_2 for 12 hrs until TLC showed the total disappearance of 4-nitroimidazole (Rf 0.50, CH_2Cl_2/MeOH/25% aq NH_3, 5/1/0.1) and the formation of 4-amino-imidazole (Rf 0.30, CH_2Cl_2/MeOH/25% aq NH_3, 5/1/0.1). Under Ar, the catalyst was filtered off (closed two branched flask). At r.t., N-cyano-isocyanate-dimethylacetal (11.4 g, 0.1 mol, 1eq) was then added dropwise as pure solid to the filtrate. After adding, the reaction mixture was heated at 80 °C for 3 hrs until TLC showed the consumption of 4-amino-imidazole and the formation of a major new UV active spot (Rf 0.57, CH_2Cl_2/MeOH/25% aq NH_3, 5/1/0.1). After adding silica gel (25 g), the reaction mixture was evaporated at 40°C under reduced pressure to dryness. The resulting silica gel containing product was loaded onto silica gel column and eluted with CH_2Cl_2/MeOH (8/1). Fractions containing product were collected and evaporated to dryness to give 3.49 g of purine **10** as white solid. Yield: 21%; Rf: 0.51 (CH_2Cl_2/MeOH, 6/1); ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.79 (3H, s, CH_3), 6.86 (1H, d, J = 0.6 Hz, H-7), 8.22 (1H, d, J = 0.6 Hz, H-9), 8.49 (2H, br, NH_2); ^{13}C NMR (75 MHz, DMSO-d_6): δ 53.80, 112.51, 122.51, 139.15, 149.53, 159.97; ESI MS: m/e 166.1 (100, $M+H^+$); EI MS: m/e 165.0 (100, M^{+}), 135.0 (11), 108.99 (32), 107.99 (73).

2-oxo-6-amino-5,8-diaza-7,9-dicarbapurine (**3**). Purine **10** (1.65 g, 10mmol) was suspended in 50 ml of 33% HBr/AcOH (Fluka). The reaction mixture was stirred at r.t. for 12 hrs. After evaporation of the excess HBr and AcOH under HV (liquid N_2 trap) at r.t., the resulting light yellow solid residue was stirred in 80 ml of MeOH for 20 min. The white solid was filtered, washed with MeOH (20 ml), ether (50 ml), and dried at r.t. under HV to give 1.63 g 2-oxo-6-amino-5,8-diaza-7,9-dicarbapurine hydrobromides which was neutralized directly with 25% aq ammonia. Thus to a suspension of 1.60 g of 2-oxo-6-amino-5,8-diaza-7,9-dicarbapurine hydrobromides in 50 ml of H_2O (pH 1.7) was added dropwise 25% aq ammonia until pH = 10. The suspension was sonicated (ultra sound bath) for 30 min at rt. The white precipitate was filtered, washed with H_2O (25 ml), and dried under HV at rt to give 998 mg of purine **3** as white

[11] Tetramethyl orthocarbonate was used instead tetraethyl orthocarbonate in order to avoid the formation of a mixture of O- and N- ethylated isomers. Kantlehner, W.; Maier, T.; Löffler, W.; Kapassakalidis J.J. *Liebigs Ann. Chem* **1982**, 507.

[12] Heitke, B. T.; McCarty, C. G. *J. Org. Chem.* **1974**, *39*, 1522.

solid. [13]Yield 66%; ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.31 (1H, s, H-7), 8.08 (1H, s, H-9), 8.26 (2H, br, NH_2), 10.84 (1H, br, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 104.44, 124.12, 132.31, 148.55, 153.28; ESI MS: m/e 152.0 (61, $M+H^+$), 184.0 (100, $M+MeOH+H^+$), 302.9 (59, $2M+H^+$); UV (C = 2.52×10^{-4}M in pH =7 0.1 M phosphate buffer): ε (220nm) = 24400; λ_{sh} = 240nm (ε = 5200); ε (ca 290nm) = 1000.

4-(imidazol-4'-yl)-allophanic acid phenyl ester (**11**). A suspension of 4-nitroimidazole (11.3 g, 0.1 mol, ACROS 98%) and 10% Pd/C (4.5g, 40% w/w, Fluka) in 250 ml dried 1,4-dioxane (distilled over sodium) was stirred vigorously under atomospheric pressure of H_2 for 12 hrs until TLC showed the total disappearance of 4-nitroimidazole (Rf 0.51, CH_2Cl_2/MeOH/25% aq NH_3, 5/1/0.1) and the formation of 4-amino-imidazole (Rf 0.28, CH_2Cl_2/MeOH/25% aq NH_3, 5/1/0.1). Under Ar, the catalyst was filtered off (closed two branched flask) and phenoxycarbonyl-isocyanate[14] (16.3g, 0.1 mol, 1.0 eq) was added dropwise as pure liquid to the filtrate. The reaction mixture was stirred at rt for 2 hrs. TLC showed the formation of a major new compd. (Rf 0.68, CH_2Cl_2/MeOH/25% aq NH_3, 5/1/0.1). After adding silica gel (5.0 g), the reaction mixture was evaporated at 30°C under reduced pressure to dryness. The resulting silica gel containing product was loaded onto silica gel column and eluted with CH_2Cl_2/MeOH (8/1). Fractions containing product (Rf 0.30, CH_2Cl_2/MeOH, 8/1) were collected and evaporated at 30°C under reduced pressure to give 7.9 g of ester **11** as white solid. Yield: 32%; Rf 0.58 (CH_2Cl_2/MeOH, 6/1); 1H NMR (300 MHz, DMSO-d_6): δ 7.04 (1H, s, =CH- of imidazole), 7.23-7.47 (6H, m, C_6H_5 and =CH- of imidazole), 9.62 (1H, br, NH), 10.85 (1H, br, NH), 11.91 (1H, br, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 102.43, 121.88, 126.19, 129.61, 136.04, 148.94, 149.80, 13.09; ESI MS: m/e 247.1 (7, $M+H^+$), 269.1 (41, $M+Na^+$), 515.1 (100, $2M+Na^+$); HR ESI: Anal. Calcd. for $C_{10}H_{11}N_4O_3Na$ 269.0645. Found: 269.0648.

2,6-dioxo-5,8-diaza-7,9-dicarbapurine (**4**)[15]. Ester **11** (7.15 g, 29 mmol) was suspended in 150 ml of EtOH. The reaction mixture was heated under reflux for 3 hrs, in which time starting material was dissolved within 10 min, and a white precipitate was produced there after. After cooling at 4°C overnight, the white precipitate was filtered, washed with dry ether to give 3.81 g of 2,6-dioxo-5,8-diaza-7,9-dicarbapurine **4** as white solid.[16] Yield: 86%; Rf: mp > 250 °C (decomp.); ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.40 (1H, d, J = 0.9 Hz, H-9), 7.99 (1H, d, J = 0.9 Hz, H-7), 11.50 (2H, br, 2 × NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 107.12, 127.20, 129.19, 144.32, 148.23; EI MS: m/e 152.0 (31, $M^{+\bullet}$), 109.0 (68), 54.1 (100); UV (C = 2.33×10^{-4}M in pH =7, 0.1 M phosphate buffer): ε (220nm) = 4300; λ_{max} = 237nm (ε = 5900). Colorless crystals were obtained by crystallization of **4** in EtOH. A colorless, cubic crystal was mounted to collect X-ray data.

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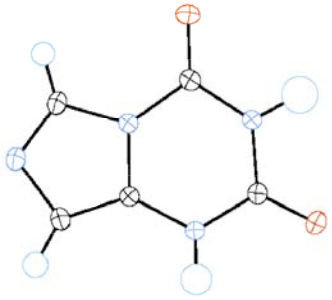
[13] Purine **3** is sparingly dissolved in DMSO and not soluble in MeOH, H_2O. It is thermally stable at 190 °C for 10 hrs. ^{1}H, ^{13}C NMR sample was obtained by filtration of the suspension of **3** in DMSO-d_6.

[14] Ramirez, F.; Telefus, C. D.; and Prasad, V. A. V. *Tetrahedron*, **1975**, *31*, 2007.

[15] Phenoxycarbonyl-isocyanate has been used for the synthesis of 5-aza-7-carbaxanthine. Rao, P.; Benner S. A. *J. Org. Chem.* **2001**, *66*, 5012.

[16] Purine **4** is soluble in DMSO, hot H_2O and hot MeOH. It is partially dissolved in DMF.



X-ray of purine **4**.[17]

Procedures Referring to Scheme 4:

2-amino-6-oxo-9-[N-(tert-butyloxycarbonyl)-(2'R,3'S)-2',3'-di(tert-butyloxycarbonylamino)-(1'R)-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine (**13α**) and *2-amino-6-oxo-9-[N-(tert-butyloxycarbonyl)-(2'R,3'S)-2',3'-di(tert-butyloxycarbonylamino)-(1'S)-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine* (**13β**). Into the solution of 2-animo-6-oxo-5,8-diaza-7,9-dicarbapurine **2** (302 mg, 2.0 mmol) and pyrroline **12**[18] (660 mg, 2.2 mmol, 1.1 eq) in 10 ml of DMF was added p-toluenesulfonic acid monohydrate (380 mg, 2.0 mmol, 1.0 eq). The reaction mixture was stirred at room temperature for 2 hrs. T.L.C (CH_2Cl_2/MeOH, 4/1) revealed the total consumption of **5** (Rf 0.34) and formation of a new spot (Rf 0.10). Then Et_3N (1.01, 10.0 mmol, 5.0 eq) added in one portion to the reaction mixture, followed by the dropwise adding of Boc_2O (480 mg, 2.2 mmol, 1.1 eq) in 2 ml of CH_2Cl_2. The reaction mixture was stirred at room temperature for 2 hrs, after which TLC (CH_2Cl_2/MeOH, 4/1) showed the spot with the Rf 0.10 was consumed with the formation of another main spot (Rf 0.86). The reaction solution was evaporated till dryness gave light yellow foam, upon which 150 ml of ethyl acetate was added. The whole solution was washed with water (3 × 50 ml), dried over Na_2SO_4, and concentrated under reduced pressure at 30 ^{0}C to yield a pale yellow foam. The crude product was purified by column chromatography on silica gel using CH_2Cl_2/MeOH (100/3 to 100/5) gave 765 mg (70%) of pure α-epimer **13α** and 240mg (22%) of pure β-epimer **13β** in the molecular ratio of α/β =3.2/1.

13α: colorless solid, Rf 0.30 (CH_2Cl_2/MeOH, 10/1); ^{1}H NMR (300MHz, 100°C, DMSO-d_6): δ 1.19 (9H, s, 3× CH_3), 1.32 (9H, s, 3× CH_3), 1.40 (9H, s, 3× CH_3), 3.23 (1H, dd, ^{3}J = 7.2 Hz, ^{2}J = 10.5 Hz, *Re*-H-4'), 3.75 (1H, dd, ^{3}J = 5.9 Hz, ^{2}J = 10.5 Hz, *Si*-H-4'), 3.98 (2H, m, H-2', H-3'), 4.64 (1H, d, J = 5.3 Hz, H-1'), 6.22 (2H, br, NH_2), 6.78 (1H, br, NHBoc), 7.08 (1H, br, NHBoc), 7.89 (1H, s, H-7), 10.83 (1H, br, H-1); MALDI MS: m/e 573.3(80, M+Na^+), 551.3 (12, M+H^+), 473.2 (100, M-Boc+Na^+), 451.2 (42, M-Boc +H^+), 373.2 (46, M-2Boc+Na^+), 351.2 (34, M-2Boc +H^+), 273.0 (6, M-3Boc+Na^+), 251.1 (10, M-3Boc +H^+); HRMALDI MS: m/e (M+Na^+) found 573.2764, $C_{24}H_{38}N_8O_7Na$ requires 573.2756; UV (C = 9.53×10^{-5} M in MeOH): ε (220nm) = 6000, λmax = 266 nm (ε = 11000).

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[17] X-ray structure analysis of **4** was carried out by Dr. Bernd Schweizer, ETH-Z. Crystallographic data for the structure has been deposited with the Cambridge Crystallographic Data Center as deposition no. CCDC 242453. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 union Road, Cambridge CB12 1EZ, UK (fax +44 (1233) 336 0333; e-mail: deposit@ccdc.cam.ac.uk).

[18] Han, B.; Wang, Z.; Krishnamurthy, R., Jaun, B., Eschenmoser, A. *Org. Lett.* **2003**, *5*, 2071.

13β: colorless solid, Rf 0.25 (CH_2Cl_2/MeOH, 10/1); ^{1}H NMR (300MHz, 100°C, DMSO-d_6): δ 1.25 (9H, s, 3× CH_3), 1.30 (9H, s, 3× CH_3), 1.40 (9H, s, 3× CH_3), 3.13 (1H, dd, ^{3}J = 8.4 Hz, ^{2}J = 10.0 Hz, *Re*-H-4'), 3.73 (1H, dd, ^{3}J = 8.7 Hz, ^{2}J = 10.0 Hz, *Si*-H-4'), 4.09 (1H, q, J ≈ 8.7 Hz, H-2'), 4.48 (1H, br. qi, J ≈ 8.7 Hz, H-3'), 5.03 (1H, d, J = 7.5 Hz, H-1'), 5.28 (1H, br, NHBoc), 6.18 (2H, br, NH_2), 6.67 (1H, d, J = 7.2 Hz, NHBoc), 7.90 (1H, s, H-7), 10.81 (1H, br, H-1); MALDI MS: m/e 573.3(100, M+Na^+), 552.3 (18, M+H^+), 473.2 (76, M-Boc+Na^+), 451.2 (65, M-Boc +H^+), 373.2 (39, M-2Boc+Na^+), 351.2 (54, M-2Boc +H^+), 273.0 (6, M-3Boc+Na^+), 251.1 (14, M-3Boc +H^+); HRMALDI MS: m/e (M+Na^+) found 573.2763, $C_{24}H_{38}N_8O_7Na$ requires 573.2756. UV (C = 8.42×10^{-5} M in MeOH): ε (220nm) = 5500, λmax = 266 nm (ε = 10200).

2-amino-6-oxo-9-[(2'R,3'S)-2',3'-diamino-(1'R)-pyrrolidinyl]-5,8-diaza-7,9-dicarba-purine hydrochlorides (**14α**) Nucleoside **13α** (150 mg, 0.27 mmol) was added in one portion to 20 ml of saturated HCl in MeOH. After the reaction solution was stirred at rt for 30 min, solvent and excess of HCl was evaporated to dryness. The white solid residue was co-evaporated twice with toluene and dried under HV at rt overnight to give 102 mg of 2-amino-6-oxo-9-[(2'R,3'S)-2',3'-diamino-(1'R)-pyrrolidinyl]-5,8-diaza-7,9-dicarba-purine hydrochlorides **14α** as white solid. Yield: 95% (calculated according to the corresponding tetrahydrochlorides); ^{1}H NMR (300MHz, AcOH-d_4/D_2O, 5/2): δ 4.00 (1H, dd, J = 6.0, 13.6 Hz, *Re*-H-4'), 3.80 (1H, dd, J = 9.3, 13.6 Hz, *Si*-H-4'), 4.54 (1H, ddd, $J_{H2',\ H3'}$=5.8 Hz, $J_{H3',\ Si\text{-}H4'}$=8.8 Hz, $J_{H3',Re\text{-}H4'}$=6.0Hz, H-3'), 5.06 (1H, dd, $J_{H1',\ H2'}$= 7.4 Hz, $J_{H3',\ H2'}$ = 5.8 Hz, H-2'), 5.52 (1H, d, J = 7.4 Hz, H-1'), 8.37 (1H, s, H-7); ^{13}C NMR (300MHz, AcOH-d_4/D_2O, 5/2): δ 46.98 (C-4'), 51.96 (C-3'), 55.97 (C-2'), 74.43 (C-1'), 110.50 (C-9), 128.18 (C-7), 137.89, 144.41, 151.30; ESI MS: m/e 251.1 (M+H^+, 100).

2-amino-6-oxo-9-[(2'R,3'S)-2',3'-diamino-(1'S)-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine hydrochlorides (**14β**). Following the procedure for the preparation of **14α**, from **13α**, **14β** was prepared from **13β**; Yield: 100% (calculated according to the corresponding tetrahydrochlorides); ^{1}H NMR (300MHz, AcOH-d_4/D_2O, 5/2): δ 3.98 (1H, dd, J = 6.0, 13.5 Hz, *Re*-H-4'), 4.36 (1H, dd, J = 9.3 13.0 Hz, *Si*-H-4'), 4.98 (1H, dd, $J_{H1',\ H2'}$= 7.9 Hz, $J_{H3',\ H2'}$ = 6.7 Hz, H-2'), 5.15 (1H, ddd, $J_{Si\text{-}H4',\ H3'}$= 9.3 Hz, $J_{Re\text{-}H4',\ H3'}$ = 6.0 Hz, $J_{H2',\ H3'}$ = 6.7 Hz, H-3'), 5.87 (1H, d, J = 7.9 Hz, H-1'), 8.32(1H, s, H-7); ^{13}C NMR (300MHz, AcOH-d_4/D_2O, 5/2): δ 46.50 (C-4'), 52.46 (C-3'), 54.65 (C-2'), 55.91 (C-1'), 110.02 (C-9), 128.79 (C-7), 137.18, 144.48, 151.49; ESI MS: m/e 251.0 (M+H^+, 100).

Procedures Referring to Scheme 5:

9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-dibenzoyloxy-1'-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurines (**16-19**)[19]. General procedure: Into a solution of 5,8-diaza-7,9-dicarbapurine (2.0

[19] The assignment of the configuration of the anomeric center in the epimeric pairs **16α/β**, **17α/β**, **18α/β**, and **19α/β** (**Scheme 5**) is based on the following observations: Due to slow rotamer interconversion at room temperature, the ^{1}H-NMR spectra (DMSO-d_6, 300-500 MHz) of all N-Boc protected compounds showed broad lines, whereas at 70°C, the signals were sharp. In each pair, coupling constants $J_{1',2'}$ and $J_{2',3'}$ were small in the α-isomer and large for the β-isomer. Compared to the α-isomer, the signals of H1' and H3' were shifted to low field by ca. 0.2 ppm in β-isomer. On the basis of this consistent pattern, the configuration of the two isomers was determined for **18α**/**18β** from the coupling constants and DPFGSE-NOE build-up curves at 70°C and was carried over to the other pairs by analogy.

mmol) and (3S, 4S)-3, 4-dibenzoyloxypyrroline trimer **15**[16](1.85 g, 2.0 mmol, 1.0 eq) in 20 ml of DMSO was added p-toluenesulfonic acid monohydrate (380 mg, 2.0 mmol, 1.0 eq). The reaction mixture was stirred at room temperature until T.L.C revealed the consumption of 5,8-diaza-7,9-dicarbapurine (6 hr for **2** and **3**, 24 hr for **4**, 72 hr for 2-deamino-**1**). Then Et_3N (1.01 g, 10.0 mmol, 5.0 eq) in 2 ml of CH_2Cl_2 was added in one portion to the reaction mixture, followed by the dropwise adding of Boc_2O (480 mg, 2.2 mmol, 1.1 eq) in 2 ml of CH_2Cl_2. The reaction mixture was stirred at room temperature for 2 hrs. The reaction solution was evaporated at 50°C under HV till dryness to give light brown oil. Column chromatography (AcOEt/iPrOH/10/1 for **16**; CH_2Cl_2/MeOH/10/1 for **17**; AcOEt/hexane/1/1 to 2/1 for **18**; AcOEt/hexane/9/1 for **19**) gave **16-19** as epimeric mixtures.

Data for *2-amino-6-oxo-9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-dibenzoyloxy-1'-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine* **16α, β** (**16α/β** = 1.2/1, ^{1}H NMR from epimeric mixture): 858 mg brown solid; yield 77%; Rf 0.72 (CH_2Cl_2/MeOH/25% aq. NH_3= 5/1/0.1), 0.44 (CH_2Cl_2/iPrOH=10/1); ^{1}H NMR (300Mz, DMSO-d_6, 80°C); δ 1.28, 1.30 (s, s, 9H, 3 × CH_3), 3.54 (0.45H, dd, ^{2}J = 5.0, 11.9 Hz, *Re*-H-4'-β), 3.76 (0.55H, dd, ^{2}J = 4.4, 11.9Hz, *Re*-H-4'-α), 4.23 (1H, m, *Si*-H-4'), 5.12 (0.55H, d, J = 2.5 Hz, H-1'-α), 5.43 (0.45H, d, J = 7.2 Hz, H-1'-β), 5.56 (0.55H, dt, J = 6.0, 4.0 Hz, H-3'-α), 5.76 (0.45H, dd, J = 5.3, 2.5 Hz, H-2'-β), 5.77 (0.55H, t, J = 7.0 Hz, H-2'-α), 5.96 (0.45H, ddd, J = 6.0, 6.0, 7.0 Hz, H-3'-β), 6.20, 6.24 (br, br, 2H, NH_2), 7.20-8.20 (m, 11H, 2 × C_6H_5, H-7), 10.80 (br, 1H, NH); MALDI MS: m/e 583.1 (26, M+Na^+), 561.2 (10, M+H^+), 483.1 (31, M-Boc+Na^+), 461.1 (100, M-Boc+H^+); HRMALDI: m/e (M+Na^+) found 583.1919, $C_{28}H_{28}N_6O_7Na$ requires 583.1912; UV (C = 9.39 × 10^{-5} M in MeOH): ε(231 nm) = 29900, λmax = 267 nm (ε =11900).

Data for *2-oxo-6-amino-9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-dibenzoyloxy-1'-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine* **17α, β** (**17α/β** = 1.7/1, ^{1}H NMR from epimeric mixture): 920 mg brown solid; yield 82%; Rf 0.78 (CH_2Cl_2/MeOH/25% aq. NH_3= 5/1/0.1), 0.33 (CH_2Cl_2/MeOH= 10/1); ^{1}H NMR (300Mz, DMSO-d_6, 70°C); δ 1.29 ((9H, br s, 3 × CH_3), 3.61 (0.37H, dd, J = 4.5, 11.7 Hz, *Re*-H-4'-β), 3.73 (0.63H, dd, J = 5.1, 12.7 Hz, *Re*-H-4'-α), 4.14 (0.37 H, dd, J = 6.0, 11.4 Hz, *Si*-H-4'-β), 4.19 (0.63H, dd, J = 6.9, 12.0 Hz, *Si* -H-4'-α), 5.19 (0.63H, d, J = 3.3 Hz, H-1'-α), 5.53 (0.37H, d, J = 6.9 Hz, H-1'-β), 5.57 (0.63H, m, H-3'-α), 7.39-8.12 (13H, m, 2 × C_6H_5, H-7, NH_2), 5.70-5.84 (2.37H, m, H-2'-α, H-2'-β, H-3'-β), 11.70 (1H, br, NH-2); HRMALDI: m/e (M+Na^+) found 583.1908, $C_{28}H_{28}N_6O_7Na$ requires 583.1912. UV (C = 7.23 × 10^{-5}M in MeOH): ε(224 nm) = 41700, λmax = 274 nm (ε = 3200).

2,*6-dioxo-9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-dibenzoyloxy-1'-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine* **18α, β (18α/β** = 1.1/1, ^{1}H NMR from epimeric mixture): 833 mg brown solid; yield 74%; Rf 0.71 (CH_2Cl_2/MeOH/25% aq. NH_3= 5/1/0.1), 0.23, 0.30 (AcOEt/Hex=1/1). Preparative HPLC separation (VERTEX COLUMN, Spherisorb SW, JL280, eluted with

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NMR data of **18α**: $J_{1',2'}$=3.1 Hz, $J_{2',3'}$=3.4 Hz, $J_{3',Si\text{-}4'}$=7.0 Hz, $J_{3',Re\text{-}4'}$=5.1 Hz. Estimated distances from NOE build up rates (calibrated on *Si*-H4'-*Re*-H4'=1.8Å): d(H1'-H2')=2.75Å, d(H1'-H3')=3.2Å, d(H1'-*Si*-H4')=3.6Å, d(H3'-*Re*-H4')=3.9Å.

NMR data of **18β**: $J_{1',2'}$=6.9 Hz, $J_{2',3'}$=5.9 Hz, $J_{3',Si\text{-}4'}$=6.7 Hz, $J_{3',Re\text{-}4'}$=4.7 Hz. Estimated distances from NOE build up rates (calibrated on *Si*-H4'-*Re*-H4'=1.8Å): d(H1'-H2')=2.4Å, d(H1'-H3')=3.4Å, d(H1'-*Si*-H4')=3.7Å, d(H3'-*Re*-H4')=3.8Å. These data are consistent with the distances and dihedral angles for a nearly planar five membered ring (in the time average) and the configurations at C1' as indicated.

AcOEt/hexane/2/3, UV 254 detection, flow rate 5 ml/min) of 180 mg of epimeric mixture gave 82 mg of fast moving product and 73 mg of slow moving product.

Data for *2,6-dioxo-9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-dibenzoyloxy-(1'S)-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine* **18α**: fast moving product, t_R 35.0 min; yield 45%; ^{1}H NMR (300Mz, DMSO-d_6, 70°C); δ 1.31 (9H, br s, 3 × CH_3), 3.74 (1H, dd, J = 5.1, 11.8Hz, *Re*-H-4'), 4.21 (1H, dd, J = 7.0, 11.8 Hz, *Si*-H-4'), 5.17 (1H, d, J = 3.1 Hz, H-1'), 5.58 (1H, ddd, $J_{Si\text{-}H\text{-}4'\text{-}H\text{-}3'}$ = 7.0 Hz, $J_{Re\text{-}H\text{-}4'\text{-}H\text{-}3'}$ = 5.1 Hz, $J_{H\text{-}2'\text{-}H\text{-}3'}$ = 3.7 Hz, H-3'), 7.50-8.05 (11H, m, H-7, 2 × C_6H_5), 5.71 (1H, dd, $J_{H\text{-}1',H2'} \approx J_{H\text{-}3',\ H\text{-}2'} \approx$ 3.3 Hz, H-2'), 11.41 (2H, br, 2 × NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 27.66 (CH_3), 49.76 (C-4'), 56.78 (C-1'), 74.44 (C-3'), 78.96 (CMe_3), 80.38 (C-2'), 117.55, 125.07, 126.41, 128.07, 128.26, 128.32, 128.83, 128.89, 128.98, 129.13, 132.30, 133.13, 133.22, 143.61, 147.74, 152.95, 164.34 (PhCO), 164.78(PhCO); ESI MS: m/e 583.9 ($M+Na^+$, 100), 562.0 ($M+H^+$, 26), 506.0 ($M-C_4H_8+H^+$, 50), 484.0 (M-Boc+Na^+, 100), 462.1 (M-Boc+H^+, 76); HR MALDI: m/e ($M+Na^+$) found 584.1749, $C_{28}H_{27}N_5O_8Na$ requires 584.1757; UV (C = 6.89 × 10^{-5}M in MeOH): ε(231 nm) =35600, λs = 274 nm (ε =6000), λs = 282 nm (ε =4900).

Data for *2,6-dioxo-9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-dibenzoyloxy-(1'R)-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine* **18β**: slow moving product, t_R 43.4 min; yield 40%; ^{1}H NMR (300Mz, DMSO-d_6, 70°C); δ 1.29 (9H, br s, 3 × CH_3), 3.60 (1H, dd, J = 4.7, 11.5 Hz, *Re*-H-4'), 4.21 (1H, dd, J = 6.7, 11.5 Hz, *Si*-H-4'), 5.17 (1H, d, J = 6.9 Hz, H-1'), 5.84 (2H, m, H-2' and H-3'), 7.40-8.02 (11H, m, H-7, 2 × C_6H_5), 11.46 (2H, br, 2 × NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 27.63 (CH_3), 48.28 (C-4'), 52.91 (C-1'), 73.95 (C-2'), 75.15 (C-3'), 78.77 (CMe_3), 115.52, 125.75, 126.43, 128.07, 128.19, 128.37, 128.65, 128.71, 128.83, 128.86, 128.99, 133.09, 133.25, 143.46, 147.57, 152.92, 164.29 (PhCO), 164.87 (PhCO). ESI MS: m/e 583.9 ($M+Na^+$, 100), 562.0 ($M+H^+$, 20), 506.0 ($M-C_4H_8+H^+$, 39), 484.0 (M-Boc+Na^+, 76), 462.1 (M-Boc+H^+, 60); HR MALDI: m/e ($M+Na^+$) found 584.1750, $C_{28}H_{27}N_5O_8Na$ requires 584.1757; UV (C = 6.46 × 10^{-5}M in MeOH): ε(231 nm)=36100, λs = 274 nm (ε =4400), λs = 282 nm (ε =3500).

Data for *6-amino-9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-dibenzoyloxy-1'-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine* **19α, β** (**19α/β** =1.5/1, ^{1}H NMR from epimeric mixture) : 702 mg brown solid; yield 64%; Rf 0.32 (AcOEt/hexane=9/1); ^{1}H NMR (300Mz, DMSO-d_6, 70°C); δ 1.22 (9H, br s, 3 × CH_3), 3.60 (0.4H, dd, J = 5.6, 11.5 Hz, *Re*-H-4'-β), 3.78 (0.6H, dd, J = 3.5, 12.4 Hz, *Re*-H-4'-α), 4.21-4.31 (1H, m, *Si*-H-4'-α and *Si*-H-4-β'), 5.34 (0.6 H, d, J = 1.9 Hz, H-1'-α), 5.58 (0.6H, ddd, J = 6.6, 3.0, 3.0 Hz, H-3'-α), 5.66 (0.4H, d, J = 7.5 Hz, H-1'-β), 5.84 (1H, m, H-2'-α and H-2'-β), 5.95 (0.4H, m, H-3'-β), 7.32-8.03 (11H, m, 2 × C_6H_5, -CH=N-), 8.30 (2H, br, NH_2), 8.31(0.4H, s, -CH=N-β), 8.37 (0.6H, s, -CH=N-α); ESI MS: m/e 567.1 ($M+Na^+$, 34), 545.0 ($M+H^+$, 100), 489.1 ($M-C_4H_8+H^+$, 56), 445.1 (M-Boc+H^+, 76); UV (C = 5.76 × 10^{-5}M in MeOH): ε(225 nm) =34700, λmax = 273 nm (ε =11300), λs = 283 nm (ε = 9100), ε (316 nm) = 5600.

2-Amino-6-oxo-9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-hydroxy-(1'S)-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine (**20α**) and *2-Amino-6-oxo-9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-hydroxy-(1'R)-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine* (**20β**). 560 mg (1.0 mmol) of epimeric mixture **16α, β** (**16α/β** = 1.2/1) was dissolved in 300 ml of saturated methanoic ammonia. The reaction mixture was stirred at rt. for 4 days. TLC (CH_2Cl_2/MeOH, 4/1) showed the consumption

of starting material **16α, β** (Rf 0.95) and the formation of two new spots (Rf 0.55, 0.25). After the adding of 5 g of silica gel, the reaction mixture was concentrated to dryness. The resulting brown solid was loaded on a silica gel column (50 g). Elution was conducted using CH_2Cl_2/MeOH (5/1). Fractions contained **20α** and **20β**, respectively, were collected, evaporated and dried under HV gave 169 mg (48%) of **20α** and 155 mg (44%) of **20β**, in the total yield of 92%.

Data for **20α**:[20] white solid; fast moving product, Rf 0.55 (CH_2Cl_2/MeOH, 4/1); yield 48%; ^{1}H NMR (300Mz, DMSO-d_6, 70°C): δ 1.21 (9H, br s, 3 × CH_3), 3.45 (1H, dd, J = 3.1, 11.2 Hz, *Re*-H-4'), 3.68 (1H, dd, J = 5.6, 11.5Hz, *Si*-H-4'), 3.88 (1H, m, H-3'), 3.95 (1H, br s, H-2'), 4.63 (1H, d, J = 1.8 Hz, H-1'), 5.21 (1H, d, J = 3.3 Hz, OH), 6.01 (1H, br, OH), 6.34 (2H, br, NH_2), 7.96 (1H, s, H-7), 10.98 (1H, br, NH); ^{13}C NMR (75Mz, DMSO-d_6, 65°C): δ 28.15, 53.33, 59.89, 74.32, 78.08, 80.71, 122.98, 124.37, 133.35, 144.88, 149.08, 153.78; MALDI MS: m/e 375.1 ($M+Na^+$, 46), 353.2 ($M+H^+$, 47), 297.1 ($M-C_4H_8+H^+$, 60), 253.1 (M-Boc+H^+, 100); HR MALDI: m/e ($M+H^+$) found 353.1571, $C_{14}H_{21}N_6O_5$ requires 353.1568; UV (C = 8.49× 10^{-5} M in MeOH): ε(220nm) = 7600, λmax = 265 nm (ε = 10200).

Data for **20β**: white solid, slow moving product, Rf 0.25 (CH_2Cl_2/MeOH, 4/1); yield 44%; ^{1}H NMR (300Mz, DMSO-d_6, 80°C): δ 1.18 (9H, s, 3 × CH_3), 3.15 (1H, dd, J = 4.4, 10.9 Hz, *Re*-H-4'), 3.69 (1H, dd, J = 6.2, 10.9 Hz, *Si*-H-4'), 3.94 ('t', 1H, J ≈ 5.6 Hz, H-2'), 4.22 (1H, ddd, J ≈ 5.0 Hz, H-3'), 4.80 (2H, br, 2 × OH), 4.90 (1H, d, J = 6.2Hz, H-1'), 8.32 (2H, br, NH_2), 7.87 (1H, s, H-7), 11.80 (1H, br, H-1); ^{13}C NMR (75Mz, DMSO-d_6, 80°C): δ 28.07, 51.59, 55.71, 72.71, 77.41, 77.84, 121.23, 124.09, 133.83, 145.21, 149.21, 153.93; MALDI MS: m/e 375.1 ($M+Na^+$, 14), 353.2 ($M+H^+$, 22), 297.1 ($M-C_4H_8+H^+$, 56), 253.1 (M-Boc+H^+, 100); HR MALDI: m/e ($M+H^+$) found 353.1566, $C_{14}H_{21}N_6O_5$ requires 353.1568. UV (C = 1.02× 10^{-4} M in MeOH): ε(220nm) = 8500, λmax = 265 nm (ε = 9000).

6-amino-9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-hydroxy-(1'S)-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine (**21α**) and *2-amino-6-oxo-9-[N-(tert-butyloxycarbonyl)-(2'S,3'S)-2',3'-hydroxy-(1'R)-pyrrolidinyl]-5,8-diaza-7,9-dicarbapurine* (**21β**). 444 mg (0.82 mmol) of epimeric mixture **19α, β** (1.5/1) was dissolved in 150 ml of saturated methanoic ammonia. The reaction mixture was stirred at rt. for 48 hr. TLC (CH_2Cl_2/MeOH, 5/1) showed the consumption of starting material **19** (Rf 0.98) and the formation of two new spots (Rf 0.42, 0.21). The reaction solution was evaporated at rt under reduced pressure to dryness to give a yellow oil, which was subject to column chromatography using CH_2Cl_2/MeOH (7/1 to 5/1) as elutant. Fractions contained **21α** and **21β** respectively, were collected, evaporated and dried under HV gave 160 mg (58%) of **21α**, and 90 mg (33%) of **21β** in the total yield of 91%.

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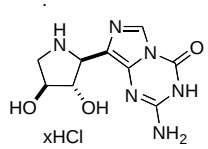
[20] Configuration of **20α** was further determined by NMR of its corresponding BOC-deprotected product: For 2-amino-6-oxo-9-[(2'S,3'S)-2',3'-dihydroxy-(1'S)-pyrrolidinyl]-5,8-diaza-7,9-dicarba- purine hydrochlorides, with coupling constants $J_{1',2'}$=3.7 Hz, $J_{2',3'}$=2.4 Hz, $J_{3', Si\text{-}4'}$=4.8 Hz, $J_{3', Re\text{-}4'}$=2.6 Hz, together with NOEs H1'-H2'(m), H1'-H3'(m), H1'-*Si*-H4' (w), H2'-*Re*-H4' (m), and H3'-*Si*-H4' (s), indicate a dominantly 3'-endo conformation of the five membered ring with H1' and H3' in *cis* orientation.



Debocylated compd of **20α**

Data for **21α**: fast moving product, Rf 0.42 (CH_2Cl_2/MeOH, 5/1); yield 58%; ^{1}H NMR (300Mz, DMSO-d_6, 80°C): δ 1.14 (9H, br s, 3 × CH_3), 3.37 (1H, dd, J = 5.1, 11.3 Hz, *Re*-H-4'), 3.74 (1H, dd, J = 5.9, 11.2 Hz, *Si*-H-4'), 3.94 (1H, m, H-3'), 4.00 (1H, dd, J = 3.4, 7.5 Hz, H-2'), 4.88 (1H, d, J = 2.8 Hz, H-1'), 5.17 (1H, d, J = 4.1 Hz, OH), 5.70 (1H, br d, J = 8.7 Hz, OH), 7.80 (1H, s, -N=CH-), 8.26 (2H, br, NH_2), 8.34 (1H, s, -N=CH-); ^{13}C NMR (100Mz, DMSO-d_6, 80°C): δ 27.65 (q, CH_3), 48.17 (t, C-4'), 59.80 (d, C-1'), 74.26 (d, C-3'), 77.48 (s, $\underline{C}Me_3$), 80.77 (d, C-2'), 121.13 (d, C-7), 127.42 (s) , 133.79 (s), 148.11 (s), 149.73 (d, C-2), 153.25 (s, C=O of Boc); UV (C = 7.38 × 10^{-5} M in MeOH): ε(217 nm) =13500), λmax = 273 nm (ε =6600), λs = 284 nm (ε = 5000), ε(320nm) = 4100; ESI MS (positive): m/e 695.0 (2M+Na^+, 100); HR ESI: m/e (M+H^+) found 359.1614, $C_{14}H_{21}N_6O_4$ requires 359.1619.

Data for **21β**: slow moving product, Rf 0.21 (CH_2Cl_2/MeOH, 5/1); yield 33%; ^{1}H NMR (300Mz, DMSO-d_6, 80°C): δ 1.11 (9H, br s, 3 × CH_3), 3.15 (1H, dd, J = 5.0, 10.9 Hz, *Re*-H-4'), 3.75 (1H, dd, J = 5.6, 10.6 Hz, *Si*-H-4'), 4.03 (1H, dd, J = 5.9, 11.8 Hz, H-2'), 4.29 (1H, ddd, J = 5.5, 5.4, 10.9 Hz, H-3'), 4.48 (1H, d, J = 4.9 Hz, OH), 4.89 (1H, d, J = 4.4 Hz, OH), 5.15 (1H, d, J = 6.5 Hz, H-1'), 7.76 (1H, s, -N=CH-), 8.18 (2H, br, NH_2), 8.29 (1H, s, -N=CH-); ^{13}C NMR (100Mz, DMSO-d_6, 80°C): δ 27.60 (q, CH_3), 50.86 (t, C-4'), 55.60 (d, C-1'), 72.43 (d, C-3'), 77.02 (d, C-2'), 77.26 (s, $\underline{C}Me_3$), 120.94 (d, C-7), 125.87 (s), 134.71 (s), 148.06 (s), 149.22 (d, C-2), 153.28 (s, C=O of Boc). UV (C = 6.75 × 10^{-5} M in MeOH): ε (217nm) =14800, λmax = 273 nm (ε =6700), λs = 285 nm (ε = 5000), ε(321 nm) = 4100; ESI MS (positive): m/e 695.0 (2M+Na^+, 100); HR ESI: m/e (M+Na^+) found 359.1434, $C_{14}H_{20}N_6O_4Na$ requires 359.1438.