Supporting Information

A Facile and Efficient Synthesis of (Purin-6-yl)alanines

Petr Čapek, Radek Pohl and Michal Hocek*

Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, CZ-16610, Prague 6, Czech Republic.

hocek@uochb.cas.cz

List of Contents:
1. General Methods S2
2. Starting Materials S2
3. Procedures and characterization of compounds 6a-6d, 7c, 7d, (S)-7d, 8a, 8b, 9a, 9b, 10c, 10d, (S)-10d, 11c, 11d, and (S)-11d S3
4. Deprotection of 6c under acidic conditions S14
5. References S15
**General methods.** Melting points were determined on a Kofler block and are uncorrected. NMR spectra were measured on a 400 MHz for $^1$H and 100.6 MHz for $^{13}$C nuclei or at 500 MHz for $^1$H and 125.8 MHz for $^{13}$C in CDCl$_3$ (TMS was used as internal standard), DMSO-$d_6$ (referenced to the solvent signal) or in D$_2$O (referenced to the solvent signal or dioxane as internal standard). Chemical shifts are given in ppm ($\delta$-scale), coupling constants ($J$) in Hz. Complete assignment of all NMR signals was performed using a combination of H,H-COSY, H,C-HSQC and H,C-HMBC experiments. DMF was degassed *in vacuo* and stored over molecular sieves under argon. Preparative HPLC separations were performed on a columns packed with 7 µm C18 reversed phase using a linear gradient H$_2$O / MeOH as eluent. Ligand-exchange chromatography on copper-loaded L-proline modified silica gel with 0.02M ammonia in MeCN/H$_2$O (81:19) as eluant was used for chiral analytical separations.

**Starting materials.** (R,S)-2-[(tert-butoxycarbonyl)amino]-3-iodopropanoate$^2$ (1), (R,S)- and (S)-2-[(benzylxycarbonyl)amino]-3-iodopropanoate$^3$ (2 and (S)-2), 9-benzyl-6-iodopurine$^4$ (5a), 6-iodo-9-(tetrahydropyran-2-yl)purine$^5$ (5b) and 6-iodo-9-(2,3,5-O-acetyl-β-D-ribofuranosyl)purine$^6$ (5c) were prepared according to published procedures. Unpublished 6-iodo-9-(2-deoxy-3,5-di-O-toluoyl-β-D-erythro-pentofuranosyl)purine (5d) was prepared as described below. Zinc dust <10 micron, Aldrich, was used for preparation of organozinc reagents.

9-(3,5-Di-O-$p$-toluoyl-2-deoxy-β-D-erythro-pentofuranosyl)-6-iodopurine (5d)

6-Iodopurine (11.1 g, 45 mmol) was added to NaH (50%, 2.4 g, 50 mmol) in acetonitrile and suspension was stirred for 30 min at ambient temperature. Then 3,5-di-p-toluoyl-2-deoxy-β-D-erythro-pentofuranosyl chloride (19.4 g, 50 mmol) was added and string continued for 18h at ambient temperature. Solvent was evaporated *in vacuo* and residue was codistilled with toluene, chromatographed on a silica gel column (ethyl acetate / hexane, 1:2) and crude product recrystallized from ethyl acetate / hexane to give 16.4 g (61%) of 5d as white crystals, m.p. 139-140 °C. MS (FAB): 599 (6, M + 1); 353 (6); 247 (19); 185 (10); 119 (82); 91 (38); 81 (100). HRMS (FAB): for C$_{26}$H$_{24}$InN$_4$O$_5$ calculated 599.0791; found 599.0787. $^1$H NMR (500 MHz, CDCl$_3$): 2.41 (s, 3H, CH$_3$); 2.45 (s, 3H, CH$_3$); 2.89 (ddd, 1H, $J$ = 2.2, 5.9 and 14.2, H-2’a); 3.19 (ddd, 1H, $J$ = 6.4, 8.0 and 14.2, H-2’b); 4.66 (m, 2H, H-4’ + H-5’b); 4.79 (m, 1H, H-5’a); 5.84 (m, 1H, $J$ = 2.0, 2.2 and 6.4, H-3’); 6.55 (dd, 1H, H-4’ + H-5’b); 6.65 (dd, 1H, $J$ = 5.9 and 8.0, H-1’); 7.21 (d, 2H, $J$ = 8.0, arom.); 7.28 (d, 2H, $J$ = 8.0, arom.); 7.85 (d, 2H, $J$ = 8.2, arom.); 7.97 (d, 2H, $J$ = 8.2, arom.);
arom.); 8.30 (s, 1H, H-8); 8.55 (s, 1H, H-2). $^{13}$C NMR (100 MHz, CDCl$_3$): 21.69 (CH$_3$); 21.72 (CH$_3$); 37.90 (CH$_2$-2'); 63.74 (CH$_2$-5'); 74.99 (CH-3'); 83.41 (CH-4'); 85.44 (CH-1'); 122.42 (C-6); 126.30 and 126.48 (2 × C-1-arom.); 129.29, 129.55 and 129.80 (3 × CH-arom.); 139.22 (C-5); 142.50 (CH-8); 144.26 and 144.61 (2 × C-4-arom.); 147.33 (C-4); 151.94 (CH-2); 165.90 and 166.05 (2 × CO). IR (CHCl$_3$): 3033, 3003, 1721, 1612, 1581, 1554, 1485, 1429, 1333, 1269, 1178, 1102, 1021, 914, 839, 691. Anal. calculated for C$_{26}$H$_{23}$IN$_4$O$_5$ (598.4): C 52.19%, H 3.87%, I 21.21%, N 9.36%, found: C 52.27%, H 4.00%, I 21.17%, N 9.26%.

**Preparation of Organozinc Reagents from Iodoalanines and their Cross-coupling Reactions with 6-Iodopurines - General Procedure**

Trimethylsilyl chloride (60 µl, 0.5 mmol) was added through septum to an argon purged flask containing suspension of zinc dust (1.95 g, 30 mmol) in DMF (3 ml). Mixture was sonicated at ambient temperature for 15 min. Then solution of protected 2-amino-3-iodopropanoate (6.0 mmol) in DMF (20 ml) prepared under argon was added through septum to the suspension of activated Zn and sonication continued for another 40 min at ambient temperature, then the zinc was allowed to settle. The supernatant was transferred through septum to a mixture of appropriate 6-iodopurine (4.5 mmol), Pd$_2$dba$_3$ (95 mg, 0.1 mmol) and tri(o-tolyl)phosphine (122 mg, 0.4 mmol) in DMF (15 ml) prepared under argon. Reaction mixture was stirred at ambient temperature for 8 h and allowed stand overnight and then solvent was evaporated in vacuo. Residue was diluted by ethyl acetate (90 ml) and washed with water (2 × 80 ml) and brine (80 ml). Organic phase was evaporated and residue chromatographed on a silica gel column (ethyl acetate / hexane) to give (purine-6-yl)alanines.

**Benzyl (R,S)-3-(9-benzylpurin-6-yl)-2-[(tert-butoxycarbonyl)amino]propanoate (6a)**

Prepared from 1 (2.1g, 5.2 mmol) and 5a (1.35 g, 4 mmol): yield 1.85 g (95%) of 6a as colorless amorphous solid. MS (FAB): 488 (6, M+1); 432 (5); 252 (8); 225 (9); 147 (14); 91 (Bn). HRMS (FAB): for C$_{27}$H$_{30}$N$_5$O$_4$ calculated 488.2298; found 488.2290. $^1$H NMR (500 MHz, CDCl$_3$): 1.40 (s, 9H, 3 × CH$_3$ – Boc); 3.62 (dd, 1H, $J = 4.6$ and 15.8, PuCH$_2$); 3.89 (dd, 1H, $J = 5.7$ and 15.8, PuCH$_2$); 4.98 (m, 1H, CHCO); 5.05 and 5.14 (d, 2H, $J = 11.9$, OCH$_2$Ph); 5.40 (s, 2H, NCH$_2$Ph); 6.16 (d, 1H, $J = 8.5$, NH); 7.20-7.38 (m, 10H, arom.); 7.97 (s, 1H, H-8); 8.80 (s, 1H, H-2). $^{13}$C NMR (125.8 MHz, CDCl$_3$): 28.25 (CH$_3$); 34.58 (Pu-CH$_2$); 47.26 (NCH$_2$Ph); 51.73 (CHCO); 66.93 (OCH$_2$Ph); 79.71 (C(CH$_3$)$_3$); 127.86, 128.00, 128.04, 128.26, 128.62 and 129.13 (CH-arom.); 132.69 (C-5); 134.96 and 135.44 (C-arom.); 143.90
(CH-8); 150.75 (C-4); 152.19 (CH-2); 155.53 (CO – Boc); 157.72 (C-6); 171.57 (COOBn). IR (CHCl₃): 3436, 3096, 3033, 3011, 2983, 1744, 1710, 1598, 1499, 1456, 1406, 1368, 1334, 1230, 1193, 1163, 1057, 1028.

**Benzy l (R,S)-3-[9-(tetrahydropyran-2-yl)purin-6-yl]-2-[(tert-butoxycarbonyl)amino]-propanoate (6b)**

Prepared from 1 (2.4 g, 6 mmol) and 5b (1.5 g, 4.5 mmol): product was crystallized from dichloromethane – heptane after chromatography, yield 1.92 g (88%) of 6b as white crystals, m.p. 101-103 °C. MS (EI): 481 (1, M); 397 (3, M – THP + H); 346 (10, M – COOBn); 262 (17); 218 (10); 206 (28); 188 (20); 162 (100); 134 (54); 91 (66, Bn). HRMS (EI): for C₂₅H₃₁N₅O₅ calculated 481.2325; found 481.2323. ¹H NMR (500 MHz, CDCl₃): 1.41 (s, 9H, 3 × CH₃ – Boc); 1.67-1.87 (m, 3 H, CH₂ from THP); 2.03-2.15 (m, 3H, CH₂ from THP); 3.62 (dd, 1H, J = 4.6 and 16.4, CH₆H₆ from alanine); 3.79 (m, 1H, H-5’); 3.90 (dd, 1H, J = 5.4 and 16.4, CH₆H₆ from alanine); 4.19 (m, 1H, H-5’); 4.97 (dt, 1H, J = 4.6, 5.4 and 8.6, CHNH); 5.10 (m, 2H, CH₂Ph); 5.77 (d, 1H, J = 10.5, H-1’); 6.10 (d, 1H, J = 8.6, NH); 7.24 (m, 5H, arom.); 8.22 (s, 1H, H-8); 8.77 (s, 1H, H-2). ¹³C NMR (125.8 MHz, CDCl₃): 22.74 (CH₂ – THP); 24.84 (CH₂ – THP); 28.29 (CH₃ – tBu); 31.79 (CH₂ – THP); 34.53 (CH₂ from alanine); 51.79 (CH from alanine); 66.99 (CH₂Ph); 68.83 (CH₂-5’); 79.75 (C – tBu); 81.98 (CH-1’); 128.07, 128.10 and 128.32 (3 × CH arom.), 132.95 (C-5); 135.49 (C arom.); 141.92 (CH-8); 149.98 (C-4); 152.05 (CH-2); 155.54 (CO – Boc); 157.80 (C-6); 171.60 (COOBn). IR (CHCl₃): 3436, 2983, 2867, 1735, 1710, 1599, 1584, 1498, 1456, 1369, 1335, 1250, 1163, 1086, 1046, 913. Anal. calculated for C₂₅H₃₁N₅O₅ (481.5): C 62.36%, H 6.49%, N 14.54%; found: C 62.04%, H 6.79 %, N 14.15%.

**Benzy l (R,S)-3-[9-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)purin-6-yl]-2-[(tert-butoxycarbonyl)amino]propanoate (6c)**

Prepared from 1 (2.1 g, 5.2 mmol) and 5c (2.02 g, 4 mmol): yield 1.96 g (75%) of 6c as yellow amorphous solid. MS (FAB): 656 (47, M + 1); 600 (25); 298 (35); 281 (66). HRMS (FAB): for C₃₁H₃₈N₅O₁₁ calculated 656.2568; found 656.2549. ¹H NMR (500 MHz, CDCl₃): 1.43 (s, 9H, 3 × CH₃ – Boc); 2.10 (s, 3H, CH₃); 2.14 (s, 3H, CH₃); 2.18 (s, 3H, CH₃); 3.62 and 3.66 diastereomeric (dd, 1H, J = 4.6 and 16.0, PuCH₂H₆); 3.89 and 3.92 diastereomeric (dd, 1H, J = 5.8 and 16.0, PuCH₆H₆); 4.38-4.51 (m, 3H, H-4’ + H-5’); 5.00 (dt, 1H, J = 4.6, 5.8 and 8.0, CH from alanine); 5.08 and 5.11 (d, 1H, J = 12.0, CH₂Ph); 5.16 and
5.17 (d, 1H, J = 12.0, CH2Ph); 5.69 and 5.70 diastereomeric (t, 1H, J = 4.5 and 5.2, H-3’); 5.95 and 5.99 diastereomeric (t, 1H, J = 5.2 and 5.4, H-2’); 6.06 and 6.07 diastereomeric (br d, 1H, J = 8.0, NH); 6.24 (t, 1H, J = 5.4, H-1’); 7.26 (m, 5H, arom.); 8.177 and 8.184 diastereomeric (s, 1H, H-8); 8.78 and 8.79 (s, 1H, H-2). 13C NMR (125.8 MHz, CDCl3): 20.38, 20.48 and 20.70 (3 × CH3CO); 28.23 (CH3 – tBu); 34.47 and 34.59 diastereomeric (CH2 from alanine); 51.61 and 51.66 diastereomeric (CH from alanine); 62.98 (CH2-5’); 67.03 (CH2Ph); 70.53 (CH-3’); 72.92 and 73.05 diastereomeric (CH-2’); 79.80 (C – tBu); 80.32 (CH-4’); 86.33 and 86.41 diastereomeric (CH-1’); 128.12 and 128.30 (CH-arom.); 133.42 and 133.48 diastereomeric (C-5); 135.35 (C-arom.); 142.42 and 142.53 diastereomeric (CH-8); 150.21 and 150.24 diastereomeric (C-4); 152.25 (CH-2); 155.48 (CO – Boc); 158.32 (C-6); 169.28, 169.51 and 170.24 (3 × COCH3); 171.48 (COOBn). IR (CHCl3): 3436, 3029, 3011, 2983, 1749, 1711, 1599, 1498, 1456, 1399, 1336, 1235, 1205, 1163, 1097, 1050, 911, 645, 698. Anal. calculated for C31H37N5O11 (655.6): C 56.79%, H 5.69%, N 10.68%; found: C 57.06%, H 6.04 %, N 10.32%.

**Benzyl (R,S)-3-[9-(3,5-di-O-p-toluoyl-2-deoxy-β-D-erythro-pentofuranosyl)purin-6-yl]-2-[(tert-butoxycarbonyl)amino]propanoate (6d)**

Prepared from 1 (1.66g, 4.1 mmol) and 5d (1.88 g, 3.14 mmol): yield 2.22 g (94%) of 6d as yellow amorphous solid. MS (FAB): 750 (10, M+ 1); 398 (18); 342 (100); 298 (36); 281 (66); 252 (25). HRMS (FAB): for C41H43N5O9 calculated 750.3139; found 750.3140. 1H NMR (500 MHz, CDCl3): 1.43 (s, 9H, tBu); 2.43 and 2.47 (2 × s, 6H, 2 × CH3 from toluoyl); 2.83 and 2.84 diastereomeric (ddd, 1H, J = 2.2, 5.8 and 14.0, H-2’); 3.14 and 3.15 diastereomeric (ddd, 1H, J = 6.4, 8.4 and 14.0, H-2’); 3.58 and 3.62 diastereomeric (dd, 1H, J = 4.7 and 15.4, PuCH3H); 3.85 and 3.89 diastereomeric (dd, 1H, J = 5.7 and 15.4, PuCH3H); 4.65-4.70 (m, 2H, H-4’ + H-5’); 4.75-4.80 (m, 1H, H-5’); 4.99 (m, 1H, CH from alanine); 5.04 and 5.06 diastereomeric (d, 1H, J = 12.1, CH2Ph); 5.12 and 5.13 diastereomeric (d, 1H, J = 12.1, CH2Ph); 5.85 (m, 1H, H-3’); 6.06 and 6.10 diastereomeric (d, 1H, J = 8.8, NH); 6.59 (dd, 1H, J = 5.8 and 8.4, H-1’); 7.21-7.32 (m, 9H, arom.); 7.91 and 7.93 (m, 2H, o-H-toluoyl); 8.00 (m, 2H, o-H-toluoyl); 8.20 (s, 1H, H-8); 8.74 and 8.75 diastereomeric (s, 1H, H-2). 13C NMR (125.8 MHz, CDCl3): 21.69 and 21.75 (2 × CH3 from toluoyl); 28.29 (C(CH3)3); 34.52 and 34.63 diastereomeric (CH2 from alanine); 37.76 and 37.84 diastereomeric (CH2-2’); 51.74 (CH from alanine); 63.97 (CH2-5’); 67.03 and 67.05 diastereomeric (CH2Ph); 75.06 (CH-3’); 79.81 (C(CH3)3); 83.08 and 83.11 diastereomeric (CH-4’); 84.79 (CH-1’); 126.35 and 126.62 (2 × C-
\( p \)-arom.); 128.13, 128.33, 129.31, 129.64 and 129.82 (5 × CH-arom.); 133.47 (C-5); 135.40 (C-4); 142.32 (CH-8); 144.23 and 144.59 (2 × C-i-arom.); 150.21 (C-4); 152.09 (CH-2); 155.55 (CO from Boc); 158.10 (C-6); 165.94 and 166.16 (CO from toluoyl); 171.52 (COOBn). IR (CHCl₃): 3435, 3020, 2983, 1719, 1612, 1599, 1498, 1456, 1369, 1335, 1269, 1179, 1163, 1102, 1021. Anal. calculated for C₄₁H₄₃N₅O₉ (749.8): C 65.68%, H 5.78%, N 9.34%; found: C 65.80%, H 6.06%, N 8.96%.

**Benzyl \((R,S)-3-[9-(2,3,5-tri-O-acetyl-\beta-D-ribofuranosyl)purin-6-yl]-2-[(benzyloxy-carbonyl)amino]propanoate (7c)**

Prepared from 2 (1.54g, 3.5 mmol) and 5c (1.26 g, 2.5 mmol): yield 1.39 g (80%) of 7c as yellowish amorphous solid. MS (FAB): 690 (58, M + 1); 430 (96, M – AcRf + 2); 303 (52); 281 (100). HRMS (FAB): for C₃₄H₃₆N₅O₁₁ calculated 690.2411; found 690.2466. \(^1\)H NMR (500 MHz, CDCl₃): 2.08 (s, 3H, CH₃); 2,11 (s, 3H, CH₃); 2.16 (s, 3H, CH₃); 3.63 and 3.67 diastereomeric (dd, 1H, \( J = 4.4 \) and 15.8, PuCH₂H₃); 3.91 and 3.95 diastereomeric (dd, 1H, \( J = 5.6 \) and 15.8, PuCH₂H₃); 4.36-4.48 (m, 3H, H-4' + H-5'); 5.05 (dt, 1H, \( J = 4.4, 5,6 \) and 8.6, CH from alanine); 5.09 and 5.13 (d, 4H, \( J = 13.1, 2 \times CH₂Ph \)); 5.66 and 5.67 diastereomeric (t, 1H, \( J = 4.8 \) and 5.4, H-3'); 5.92 and 5.96 diastereomeric (t, 1H, \( J = 5.4 \) and 5.5, H-2'); 6.20 and 6.22 diastereomeric (d, 1H, \( J = 5.5, H-1' \)); 6.45 and 6.46 diastereomeric (d, 1H, \( J = 8.6, NH \)); 7.20–7.34 (m, 10H, arom.); 8.166 and 8.173 diastereomeric (s, 1H, H-8); 8.72 and 8.74 diastereomeric (s, 1H, H-2). \(^1\)C NMR (125.8 MHz, CDCl₃): 20.32, 20.46 and 20.67 (3 × CH₃CO); 34.30 and 34.42 diastereomeric (CH₂ from alanine); 52.12 (CH from alanine); 62.98 (CH₃-5'); 66.93 and 67.03 (2 × CH₂Ph); 70.55 (CH-3'); 72.98 and 73.11 diastereomeric (CH-2'); 80.38 (CH-4'); 86.38 and 86.46 diastereomeric (CH-1'); 128.04, 128.18, 128.36 and 128.43 (CH-arom.); 133.23 and 133.29 diastereomeric (C-5); 135.31 and 136.31 (2 × C-arom.); 142.55 and 142.66 diastereomeric (CH-8); 150.30 (C-4); 152.25 (CH-2); 156.10 (NCO); 158.07 (C-6); 169.26, 169.49 and 170.23 (3 × COCH₃); 171.08 (COOBn). IR (CHCl₃): 3430, 3030, 3013, 1750, 1599, 1500, 1456, 1410, 1375, 1336, 1229, 909, 645, 603. Anal. for C₃₄H₃₅N₅O₁₁ calculated C 59.21%, H 5.12%, N 10.15%; found C 58.84%, H 5.30%, N 9.78%.

**Benzyl \((R,S)-3-[9-(2,3,5-di-O-p-toluoyl-2-deoxy-\beta-D-erythro-pentofuranosyl)purin-6-yl]-2-[(benzyloxy-carbonyl)amino]propanoate (7d)**

Prepared from 2 (1.54g, 3.5 mmol) and 5d (1.5 g, 2.5 mmol): yield 1.87 g (96%) of 7d as yellowish amorphous solid. MS (FAB): 784 (8, M + 1); 432 (23); 321 (8); 281 (11); 154 (21);
119 (82); 91 (100%). HRMS (FAB): for C_{44}H_{42}N_{5}O_{9} calculated 784.2983; found 784.2955. ^1H NMR (500 MHz, CDCl3): 2.40 (s, 3H, CH₃); 2.45 (s, 3H, CH₃); 2.83 and 2.84 diastereomeric (ddd, 1H, J = 5.6, 8.2 and 14.2, H-2'b); 3.14 and 3.16 diastereomeric (ddd, 1H, J = 4.4 and 16.0, PuCH₂H₂); 3.91 and 3.94 diastereomeric (dd, 1H, J = 5.6 and 16.0, PuCH₂H₂); 4.65–4.70 (m, 2H, H-4' + H-5'b); 4.75–4.79 (m, 1H, H-5'a); 5.06 (dt, 1H, J = 4.4, 5.6 and 8.5, CH from alanine); 5.10 and 5.13 (2 × d, 2 × 2H, J = 12.6, 2 × CH₂Ph); 5.83 (m, 1H, H-3'); 6.48 and 6.51 diastereomeric (dd, 1H, J = 8.5, NH); 6.56 (dd, 1H, J = 5.6 and 8.4, H-1'); 7.18-7.34 (m, 14H, arom.); 7.91 and 7.92 (m, 2H, o-H-toluoyl); 8.18 (s, 1H, H-8); 8.69 and 8.70 diastereomeric (s, 1H, H-2). ^13C NMR (125.8 MHz, CDCl3): 21.64 and 21.72 (2 × CH₃); 34.35 (PuCH₂); 37.70 (CH₂-2'); 52.12 (CH from alanine); 63.91 (CH₂-5'); 66.88 and 67.08 ((2 × CH₂Ph); 74.99 (CH-3'); 83.03 and 83.06 diastereomeric (CH-4'); 84.76 and 84.79 diastereomeric (CH-1'); 126.31 and 126.58 (2 × C-p-arom.); 128.03, 128.14, 128.30, 128.32, 128.42, 129.26, 129.59 and 129.78 (8 × CH-arom.); 133.38 and 133.43 (C-5); 135.27 and 136.28 (2 × C-i-arom.); 142.39 and 144.24 diastereomeric (CH-8); 144.16 and 144.53 (2 × C-i-arom.); 150.18 and 150.22 diastereomeric (C-4); 151.99 (CH-2); 156.07 and 156.09 diastereomeric (NCO); 157.75 (C-6); 165.88 and 166.10 (CO from toluoyl); 171.10 (COOBn). IR (CHCl₃): 3429, 3032, 3013, 1721, 1612, 1599, 1500, 1456, 1408, 1387, 1335, 1269, 1102, 1021, 938, 841, 646. Anal. calculated for C_{44}H_{41}N_{5}O_{9} (783.8): C 67.42%, H 5.27%, N 8.93%; found: C 67.07%, H 5.46%, N 8.71%.

**Benzyl (S)-3-[9-(3,5-di-O-p-toluoyl-2-deoxy-β-D-erythro-pentofuranosyl)purin-6-yl]-2-[(benzyloxy carbonyl)amino]propanoate ((S)-7d)**

Prepared from (S)-2 (1.43g, 3.25 mmol) and 5d (1.5 g, 2.5 mmol): yield 1.87 g (95%) of (S)-7d as yellowish amorphous solid. MS (FAB): 784 (14, M + 1); 432 (100, M - diTol(dRf) + 2); 281 (72). ^1H NMR (500 MHz, CDCl₃): 2.41 (s, 3H, CH₃); 2.46 (s, 3H, CH₃); 2.83 (ddd, 1H, J = 1.6, 5.7 and 14.1, H-2'b); 3.16 (ddd, 1H, J = 6.4, 8.3 and 14.1, H-2'a); 3.65 (dd, 1H, J = 4.5 and 16.0, PuCH₂H₂); 3.92 (dd, 1H, J = 5.6 and 16.0, PuCH₂H₂); 4.67 (m, 2H, H-4' + H-5'b); 4.77 (dd, 1H, J = 3.4 and 11.4, H-5'a); 5.05 (dt, 1H, J = 4.5, 5.6 and 8.7, CH from alanine); 5.11 (s, 2H, CH₂Ph); 5.12 (s, 2H, CH₂Ph); 5.83 (dt, 1H, J = 1.6, 2.2 and 6.4, H-3'); 6.47 (d, 1H, J = 8.7, NH); 6.56 (dd, 1H, J = 5.7 and 8.3, H-1'); 7.20-7.35 (m, 14H, arom.); 7.92 (m, 2H, o-H-toluoyl); 7.99 (m, 2H, o-H-toluoyl); 8.18 (s, 1H, H-8); 8.70 (s, 1H, H-2). ^13C NMR (125.8 MHz, CDCl₃): 21.64 and 21.72 (2 × CH₃); 34.35 (PuCH₂); 37.70 (CH₂-2'); 52.12 (CH from alanine).
alanine); 63.93 (CH$_2$-5’); 66.91 and 67.10 (2 × CH$_2$Ph); 75.00 (CH-3’); 83.05 (CH-4’); 84.80 (CH-1’); 126.32 and 126.59 (2 × C-$_p$-arom.); 128.06, 128.08, 128.14, 128.34, 128.43, 129.27, 129.61 and 129.79 (8 × CH-arom.); 133.45 (C-5); 135.31 and 136.29 (2 × C-$_i$-arom.); 142.41 (CH-8); 144.18 and 144.55 (2 × C-$_i$-arom.); 150.24 (C-4); 152.01 (CH-2); 156.08 (NCO); 157.77 (C-6); 165.89 and 166.12 (2 × CO from toluoyl); 171.12 (COOBN). [α]$_D^{20}$ = -23.8 (c = 6.71, CHCl$_3$). Anal. calculated for C$_{44}$H$_{41}$N$_5$O$_9$ (783.8): C 67.42%, H 5.27%, N 8.93%; found: C 67.13%, H 5.35%, N 8.73%.

(R,S)-3-(9-Benzylpurin-6-yl)-2-[(tert-butoxycarbonyl)amino]propanoic acid (8a)

Compound 6a (1.9 g, 3.9 mmol) was hydrogenated in ethanol (140 ml) under slight overpressure of hydrogen in the presence of Pd/C catalyst (10 wt %, 180 mg) for 6 h (progress was monitored by TLC). The catalyst was filtered off on Celite pad and the filtrate evaporated in vacuo. Product was crystallized from ethanol to yield 8a (1.38 g, 89%) as white crystals, m.p. 172-175 °C. MS (FAB): 398 (16, M + 1); 342 (19); 281 (7, M - NHBoc); 252 (19); 225 (23); 135 (6); 91 (100, Bn). HRMS (FAB): for C$_{20}$H$_{23}$N$_5$O$_4$ calculated 398.1828, found 398.1840. ¹H NMR (200 MHz, DMSO-$d_6$): 1.28 (s, 9H, 3 × CH$_3$ – Boc); 3.42 (dd, 1H, $J$ = 7.8 and 14.9, PuC$\_H$A$\_H$B); 3.57 (dd, 1H, $J$ = 6.9 and 14.9, PuCH$\_A$B$\_H$); 4.75 (dt, 1H, $J$ = 6.9, 7.8 and 8.4, CH$_2$); 5.50 (s, 2H, CH$_2$Ph); 6.85 (d, 1H, $J$ = 8.4, NH); 7.20-7.33 (m, 5H, arom.); 8.73 (s, 1H, H-8); 8.86 (s, 1H, H-2). ¹³C NMR (50.3 MHz, DMSO-$d_6$): 28.29 (CH$_3$); 34.48 (CH$_2$CH); 46.71 (CH$_2$Ph); 52.00 (CHCH$_2$); 78.32 (C(CH$_3$)); 127.89, 128.18 and 128.98 (3 × CH-arom.); 132.51 (C-5); 136.71 (C-arom.); 146.20 (CH-8); 150.72 (C-4); 151.67 (CH-2); 155.40 (COO-$_{t}$Bu); 157.73 (C-6); 173.27 (COOH). IR (KBr): 3210, 2980, 2932, 1726, 1701, 1653, 1599, 1532, 1504, 1455, 1406, 1368, 1335, 1161, 1050. Anal. calculated for C$_{20}$H$_{23}$N$_5$O$_4$ (397.4): C 60.44%, H 5.83%, N 17.62%; found: C 60.22%, H 5.92%, N 17.36%.

(R,S)-2-(tert-Butoxycarbonyl)amino-3-(9H-purin-6-yl)propanoic acid (8b)

Compound 6b (867 mg, 1.8 mmol) was hydrogenated in ethanol (120 ml) under slight overpressure of hydrogen in the presence of Pd/C catalyst (10 wt %, 90 mg) for 6 h. The catalyst was filtered off on Celite pad and the filtrate evaporated in vacuo. Product was crystallized from methanol / ethyl acetate to yield 8b (465 mg, 84%) as white crystals, m.p. 186-189 °C (dec.). MS (FAB): 308 (21, M + 1); 252 (50); 208 (23, M – Boc + 2H); 191 (35); 162 (47); 135 (76). HRMS (FAB): for C$_{13}$H$_{18}$N$_2$O$_4$ calculated 308.1359; found 308.1352. ¹H NMR (500 MHz, DMSO-$d_6$): 1.30 (s, 9H, 3 × CH$_3$ from tBu); 3.40 (dd, 1H, $J$ = 8.1 and 14.5,
\[ CH_3H_b \); 3.50 (dd, 1H, \( J = 3.5 \) and 14.5, \( CH_3H_b \)); 4.70 (br, 1H, CH from alanine); 7.19 (d, 1H, \( J = 8.3 \), NH); 8.55 (br s, 1H, H-8); 8.79 (s, 1H, H-2); 13.48 (v br, 1H, COOH). \[ 13C \text{ NMR} \) (125.8 MHz, DMSO-\( d_6 \)): 28.07 (CH \( 3 \)); 34.62 (CH \( 2 \) from alanine); 51.81 (CH from alanine); 78.09 (C from \( tBu \)); 151.29 (C-4, HMBC experiment); 151.55 (CH-2); 155.17 (CO-\( tBu \)); 157.08 (C-6, HMBC experiment); 173.13 (COOH). \[ \text{IR (KBr):} \) 3257, 3978, 2815, 2557, 1928, 1735, 1711, 1625, 1573, 1532, 1447, 1383, 1328, 1298, 1250, 1164, 1045, 809, 640.

(\( R,S \))-2-Amino-3-(9-benzylpurin-6-yl)propanoic acid trifluoracetate (9a-TFA)

TFA (0.8 ml) was added at 0 °C to the solution of 8a (120 mg, 0.3 mmol) in CH\(_2\)Cl\(_2\) (8 ml). The reaction mixture was stirred at ambient temperature for 1 h. Then the solvents were evaporated \textit{in vacuo} and residue was codistilled with CH\(_2\)Cl\(_2\). The crude product was recrystallized from ethyl acetate / methanol to give product 9a-TFA (95 mg, 72 %) as white crystals, m.p. 243-244 °C. MS (FAB): 298 (100, M + 1); 252 (17, M - COOH); 225 (33); 157 (12); 135 (10); 91 (98, Bn). HRMS (FAB): for C\(_{15}\)H\(_{16}\)N\(_5\)O\(_2\) calculated 298.1304; found 298.1307. \[ \text{1H NMR (200 MHz, DMSO-\( d_6 \)):} \) 3.61 (dd, 1H, \( J = 6.7 \) and 16.4, \( CH_3H_b \)); 3.75 (dd, 1H, \( J = 5.7 \) and 16.4, \( CH_3H_b \)); 4.64 (t, 1H, \( J = 5.7 \) and 6.7, \( CHCH_2 \)); 5.52 (s, 2H, CH\(_2\)Ph); 7.29-7.38 (m, 5H, arom.); 8.44 (v br, NH\(_3^+\)); 8.78 (s, 1H, H-8); 8.87 (s, 1H, H-2). \[ \text{13C NMR (50.3 MHz, DMSO-\( d_6 \)):} \) 32.44 (CH\(_2\)CH); 46.80 (CH\(_2\)Ph); 50.35 (CH\(_2\)CH); 127.96, 128.24 and 129.02 (3 × CH arom.); 132.41 (C-5); 136.68 (C arom.); 146.50 (CH-8); 150.84 (C-4); 151.93 (CH-2); 155.49 (C-6); 170.43 (CH\(_2\)O). \[ \text{IR (KBr):} \) 1732, 1692, 1603, 1530, 1506, 1465, 1359, 1264, 1197, 1183, 1131. Anal. calculated for C\(_{17}\)H\(_{16}\)F\(_3\)N\(_5\)O\(_4\) (411.3): C 49.64%, H 3.92%, N 17.03%; found C 49.38%, H 3.97%, N 16.77%.

(\( R,S \))-2-Amino-3-(9-benzylpurin-6-yl)propanoic acid hydrochloride (9a-HCl)

Compound 8a (398 mg, 1 mmol) was stirred in ethyl acetate saturated with hydrochloride (aprox. 1.7M) at ambient temperature for 8 h, then precipitate was filtered and recrystallized from ethanol to give product 9a-HCl (280 mg, 84%) as white crystals, m.p. 231-235 °C. MS (FAB): 298 (100, M + 1). \[ \text{1H NMR (200 MHz, DMSO-\( d_6 \)):} \) 3.68 (dd, 1H, \( J = 6.4 \) and 16.4, \( CH_3H_b \)); 3.80 (dd, 1H, \( J = 6.2 \) and 16.4, \( CH_3H_b \)); 4.64 (br s, 1H, \( CHCH_2 \)); 5.53 (s, 2H, \( CH_2\)Ph); 7.27-7.39 (m, 5H, arom.); 8.68 (br s, 3H, NH\(_3^+\)); 8.81 (s, 1H, H-8); 8.86 (s, 1H, H-2). \[ \text{13C NMR (50.3 MHz, DMSO-\( d_6 \)):} \) 32.40 (CH\(_2\)CH); 46.79 (CH\(_2\)Ph); 50.18 (CH\(_2\)CH); 127.96, 128.23 and 129.02 (3 × CH arom.); 132.36 (C-5); 136.71 (C arom.); 146.51 (CH-8); 150.82 (C-...
4); 151.90 (CH-2); 155.60 (C-6); 170.31 (COO). Anal. calculated for C$_{15}$H$_{16}$ClN$_{5}$O$_{2}$ (333.8): C 53.98%, H 4.83%, N 20.98%, Cl 10.62%; found: C 53.79%, H 4.91%, N 20.62%, Cl 10.85%.

**($R,S$)-2-Amino-3-(9H-purin-6-yl)propanoic acid trifluoracetate (9b-TFA)**

TFA (0.7 ml) was added at 0 °C to the solution of 8b (100 mg, 0.33 mmol) in CH$_2$Cl$_2$ (7 ml). The reaction mixture was stirred at ambient temperature for 1 h. Then the solvents were evaporated in vacuo and residue was codistilled with CH$_2$Cl$_2$. The crude product was recrystallized from ethyl acetate / methanol to give product 9b-TFA (90 mg, 86 %) as white crystals, m.p. 163-166 °C. MS (FAB): 208 (100, M + 1); 181 (36); 162 (33); 149 (18); 135 (65); 133 (45); 36 (110). HRMS (FAB): for C$_8$H$_{10}$F$_3$N$_5$O$_4$ calculated 208.0835; found 208.0848. $^1$H NMR (500 MHz, DMSO-$d_6$): 3.62 (dd, 1H, $J = 6.8$ and 16.5, CH$_A$H$_B$); 3.73 (dd, 1H, $J = 5.3$ and 16.5, CH$_A$H$_B$); 4.64 (dd, 1H, $J = 5.3$ and 6.8, CHCH$_2$); 8.46 (v br, NH$_3^+$); 8.60 (s, 1H, H-8); 8.83 (s, 1H, H-2). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$): 32.35 (CH$_2$); 50.09 (CH from alanine); 145.20 (CH-8); 151.51 (CH-2); 153.33 (C-6, HMBC experiment); 170.22 (CO). IR (KBr): 3424, 3183, 3159, 2853, 2698, 2632, 1698, 1685, 1608, 1517, 1491, 1425, 1399, 1338, 1264, 1224, 1196, 1133, 836, 796, 723, 637. Anal. calculated for C$_{10}$H$_{10}$F$_3$N$_5$O$_4$ (321.2): C 37.39%, H 3.14%, N 21.80%; found C 37.44%, H 3.22%, N 21.43%.

**($R,S$)-2-Amino-3-(9H-purin-6-yl)propanoic acid dihydrochloride (9b-2HCl)**

Compound 8b (100 mg, 0.33 mmol) was stirred in ethyl acetate saturated with hydrochloride (aprox. 1.7M) at ambient temperature for 3 h, then precipitate was filtered and recrystallized from ethanol to give product 9b-2HCl (89 mg, 96 %) as white crystals, m.p. more than 280 °C. MS (FAB): 208 (100, M + 1). $^1$H NMR (200 MHz, DMSO-$d_6$): 3.74 (dd, 1H, $J = 6.4$ and 16.4, CH$_A$H$_B$); 3.85 (dd, 1H, $J = 5.9$ and 16.4, CH$_A$H$_B$); 4.69 (br s, 1H, CHCH$_2$); 5.90 (v br, NH$_2^+$); 8.71 (br s, NH$_3^+$); 8.88 (s, 1H, H-8); 8.94 (s, 1H, H-2). $^{13}$C NMR (50.3 MHz, DMSO-$d_6$): 32.40 (CH$_2$); 50.12 (CH from alanine); 128.79 (C-5); 146.11 (CH-8); 151.29 (CH-2); 153.01 and 153.67 (C-6 and C-4); 170.14 (CO). Anal. calculated for C$_{10}$H$_{11}$Cl$_2$N$_5$O$_4$ (280.1): C 34.30%, H 3.96%, N 25.00%, Cl 25.31%; found: C 34.46%, H 4.05%, N 24.62%, Cl 24.93%.

**($R,S$)-3-[9-(β-D-ribofuranosyl)purin-6-yl]-2-[(benzyloxycarbonyl)amino]propanoic acid (10c)**

Aqueous solution of NaOH (0.59 M, 10 ml) was slowly added at 0 °C to the solution of 7c (1.36 g, 1.97 mmol) in THF (20 ml) / methanol (15 ml) and reaction mixture was stirred at
ambient temperature for 25 min. pH was adjusted to 7 by aqueous HCl (3%) and solvents were evaporated in vacuo. Crude product was purified by preparative HPLC on C18 column with water / methanol as mobile phase to give 908 mg (97%) of 10c as colorless amorphous solid. MS (FAB): 474 (100, M + 1); 342 (81, M – RF + 2). HRMS (FAB): for C21H24N5O8 calculated 474.1625; found 474.1630. \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): 3.46 and 3.47 diastereomeric (dd, 1H, \(J_{\text{gem}} = 15.0\), \(J_{\text{CH2bCH}} = 8.2\), CH2-b); 3.57 (bdd, 1H, \(J_{\text{gem}} = 12.0\), \(J_{5^b'4^b} = 4.1\), H-5’b); 3.61 and 3.62 diastereomeric (dd, 1H, \(J_{\text{gem}} = 15.0\), \(J_{\text{CH2aCH}} = 5.7\), CH2-a); 3.69 (bdd, 1H, \(J_{\text{gem}} = 12.0\), \(J_{5^a'4^a} = 4.2\), H-5’a); 3.98 (q, 1H, \(J_{4^a'5^a} = 4.2\), \(J_{4^b'5^b} = 4.1\), \(J_{4^a'3^a'} = 3.6\), H-4’a); 4.19 (dd, 1H, \(J_{3^a'2^a'} = 4.9\), \(J_{3^a'4^a'} = 3.6\), H-3’a’); 4.65 (m, 1H, H-2’); 4.87 (m, 1H, CH); 4.98 (s, 2H, CH2-Ph); 6.02 and 6.03 diastereomeric (d, 1H, \(J_{1^a'2^a'} = 5.8\), H-1’); 7.22-7.38 (m, 5H, Ph); 7.70 (bd, 1H, \(J_{\text{NHCH}} = 9.1\), NH); 8.79 (s, 1H, H-8); 8.84 (s, 1H, H-2). \(^{13}\)C NMR (125 MHz, DMSO-\(d_6\)): 34.22 (CH2-Pu); 52.08 (CHCO); 61.29 (CH2-5’); 70.32 (CH-3’); 73.50 and 73.55 diastereomeric (CH-2’); 85.70 (CH-4’); 87.55 (CH-1’); 127.50, 127.68 and 128.23 (3 × CH arom.); 132.86 (C-5); 136.89 (C arom.); 144.26 (CH-8); 150.31 (C-4); 151.55 (CH-2); 155.80 (NCO); 157.87 (C-6); 172.77 (COOH). IR (KBr): 3421, 2931, 1706, 1603, 1499, 1456, 1410, 1338, 1213, 1123, 1082, 1055, 737, 697, 646.

(R,S)-3-[9-(2-deoxy-\(\beta\)-D-erythro-pentofuranosyl)purin-6-yl]-2-[(benzyloxycarbonyl)-amino]propanoic acid (10d)

Aqueous solution of NaOH (0.45 M, 10 ml) was slowly added at 0 °C to the solution of 7d (1.76 g, 2.25 mmol) in THF (30 ml) / methanol (30 ml) and reaction mixture was stirred at ambient temperature for 40 min. pH was adjusted to 7 by aqueous HCl (2%) and solvents were evaporated in vacuo to final volume 6 ml. After diluting by water (12 ml) excluded oil was taken away and solution evaporated in vacuo. Crude product was purified by preparative HPLC on C18 column with water / methanol as mobile phase to give 870 mg (85%) of 10d as colorless amorphous solid. MS (FAB): 458 (53, M + 1); 342 (100, M – DRf + 2). HRMS (FAB): for C21H24N5O7 calculated 458.1676; found 458.1642. \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): 2.34 (ddd, 1H, \(J_{\text{gem}} = 13.3\), \(J_{2^b'1^b'} = 6.3\), \(J_{2^b'3^b} = 3.4\), H-2’b); 2.79 and 2.80 diastereomeric (ddd, 1H, \(J_{\text{gem}} = 13.3\), \(J_{2^a'1^a'} = 7.7\), \(J_{2^a'3^a'} = 5.9\), H-2’a); 3.40 – 3.67 (m, 4H, CH2 and H-5’); 3.89 (dt, 1H, \(J_{4^a'5^a} = 4.6\), \(J_{4^b'5^b} = 4.6\), \(J_{4^a'3^a'} = 2.9\), H-4’a); 4.45 (bm, 1H, H-3’a’); 4.86 and 4.87 diastereomeric (dt, 1H, \(J_{\text{CHNH}} = 8.4\), \(J_{\text{CHCH2b}} = 8.2\), \(J_{\text{CHCH2a}} = 6.0\), CH); 4.98 (s, 2H, CH2-Ph); 5.00 (bm, 1H, OH-5’); 5.36 (bs, 1H, OH-5’); 6.47 (dd, 1H, \(J_{1^b'2^b} = 7.7\), \(J_{1^b'2^a} = 6.3\), H-1’); 7.23-7.37 (m, 5H, Ph); 7.71 (bd, 1H, \(J_{\text{NHCH}} = 8.4\), NH); 8.75 (s, 1H, H-8); 8.83 (s, 1H, H-2). \(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)): 34.21 (CH2-Pu); 39.40 (CH-2’, overlaid by DMSO, read from
HMOC); 52.06 (CHCO); 61.56 (CH₂-5'); 65.28 (CH₂Ph); 70.63 (CH-3'); 83.66 (CH₂-1'); 87.95 (CH-4'); 127.50, 127.67 and 128.23 (3 × CH arom.); 132.87 (C-5); 136.90 (C arom.); 144.16 (CH-8); 150.00 (C-4); 151.47 (CH-2); 155.79 (NCO); 157.74 (C-6); 172.75 (COOH).

IR (KBr): 3396, 2934, 2586, 1715, 1601, 1500, 1455, 1402, 1337, 1213, 1095, 1057, 940, 645.

(-S)-3-[9-(2-deoxy-β-D-erythro-pentofuranosyl)purin-6-yl]-2-[(benzyloxycarbonyl)-amino]propanoic acid ((S)-10d)

Aqueous solution of NaOH (0.45 M, 5 ml) was slowly added at 0 °C to the solution of (S)-7d (850 mg, 1.08 mmol) in THF (15 ml) / methanol (15 ml) and reaction mixture was stirred at ambient temperature for 40 min. pH was adjusted to 7 by aqueous HCl (2%) and solvents were evaporated in vacuo to final volume of 6 ml. After diluting by water (8 ml) the excluded oil was taken away and solution evaporated in vacuo. Crude product was purified by preparative HPLC on C18 column with water / methanol as mobile phase to give 468 mg (95%) of (S)-10d as white solid. MS (FAB): 458 (10, M + 1); 342 (32, M – dRf + 2); 130 (100). ¹H NMR (400 MHz, DMSO-d₆): 2.34 (ddd, 1H, J = 3.4, 6.3 and 13.2, H-2′b); 2.79 (ddd, 1H, J = 6.0, 7.3 and 13.2, H-2′a); 3.46 (dd, 1H, J = 8.1 and 15.0, PuCH₆H₆); 3.53 (dd, 1H, J = 4.5 and 11.7, H-5′); 3.60 (dd, 1H, J = 6.1 and 15.0, PuCH₆H₆); 3.62 (dd, 1H, J = 4.8 and 11.7, H-5′); 3.89 (dt, 1H, J = 3.0, 4.5 and 4.8, H-4′); 4.45 (dt, 1H, J = 3.0, 3.4 and 6.0, H-3′); 4.87 (dt, 1H, J = 6.1, 8.1 and 8.4, CHCO); 4.98 (s, 2H, CH₂Ph); 6.47 (t, 1H, J = 6.3 and 7.3, H-1′); 7.27-7.35 (m, 5H, arom.); 7.72 (d, 1H, J = 8.4, NH); 8.75 (s, 1H, H-8); 8.83 (s, 1H, H-2). ¹³C NMR (100 MHz, DMSO-d₆): 34.47 (CH₂Pu); 39.37 (CH-2); 52.31 (CHCO); 61.79 (CH₂-5′); 65.53 (CH₂Ph); 70.89 (CH-3′); 83.88 (CH₂-1′); 88.19 (CH-4′); 127.77, 127.95 and 128.49 (3 × CH arom.); 133.10 (C-5); 137.15 (C arom.); 144.44 (CH-8); 150.25 (C-4); 151.75 (CH-2); 156.06 (NCO); 158.00 (C-6); 173.08 (COOH). [α]D20 = -9.96 (c = 6.34, MeOH).

(R,S)-3-[9-(β-D-ribofuranosyl)purin-6-yl]-2-aminopropanoic acid mono hydrate (11c)

Hydrogen was bubbled through a solution of 10c (908 mg, 1.92 mmol) in water (50 ml), dioxane (50 ml) and acetic acid (0.4 ml) in the presence of Pd/C catalyst (10 wt %, 90 mg) for 4 h. The catalyst was filtered off on Celite pad and the filtrate evaporated in vacuo. Crude product was purified by preparative HPLC on C18 column with water / methanol as mobile phase. Product was lyophilized from water to give 550 mg (80%) of 11c as white solid. MS (FAB): 340 (7, M + 1); 201 (14); 110 (16). HRMS (FAB): for C₁₃H₁₅N₅O₆ calculated 340.1257; found 340.1275. ¹H NMR (500 MHz, D₂O): 3.76 (m, 2H, CH₂); 3.85 (dd, 1H, J_gem=
12.8, $J_{5'b4'} = 4.0$, H-5’b); 3.92 (dd, 1H, $J_{gem} = 12.8$, $J_{5'a4'} = 3.0$, H-5’a); 4.29 (q, 1H, $J_{4'3'} = 4.6$, $J_{4'5'b} = 4.0$, $J_{4'5'a} = 3.0$, H-4’); 4.36 (dd, 1H, $J = 7.2$ and 5.3, CH); 4.46 (t, 1H, $J_{3'2'} = 5.4$, $J_{3'4'} = 4.6$, H-3’); 4.82 and 4.83 diastereomeric (t, 1H, $J_{2'1'} = 5.6$, $J_{2'3'} = 5.4$, H-2’); 6.18 (d, 1H, $J_{1'2'} = 5.6$, H-1’); 6.58 (t, 1H, $J_{1'2'a} = 6.5$, H-1’); 8.65 (s, 1H, H-8); 8.86 (s, 1H, H-2). $^{13}$C NMR (125.8 MHz, D$_2$O, ref(dioxane) = 67.19 ppm): 33.00 (CH2-Pu); 39.52 (C-2’); 53.45 (CH); 62.14 (C-5’); 71.70 (C-3’); 85.35 (C-1’); 88.09 (C-4’); 133.16 (C-5); 145.51 (C-8); 150.65 (C-4); 152.30 (C-2); 157.54 (C-6); 173.65 (CO). IR (KBr): 3381, 3305, 2558, 1607, 1583, 1407, 1340, 1213, 1053, 646, 539. Anal. calculated for C$_{13}$H$_{19}$N$_{5}$O$_{7}$ (357.3): C 43.70%, H 5.36%, N 19.60%; found C 43.68%, H 5.22%, N 19.47%.

**(R,S)-3-[9-(2-deoxy-$eta$-D-erythro-pentofuranosyl)purin-6-yl]-2-aminopropanoic acid mono hydrate (11d)**

Hydrogen was bubbled through solution of 10d (560 mg, 1.22 mmol) in water (35 ml), dioxane (35 ml) and acetic acid (0.3 ml) in the presence of Pd/C catalyst (10 wt %, 56 mg) for 16 h. The catalyst was filtered off on Celite pad and the filtrate evaporated in vacuo. Crude product was purified by preparative HPLC on C18 column with water / methanol as mobile phase. Product was lyophilized from water to give 303 mg (73%) of 11d as white solid. MS (FAB): 324 (36, M + 1); 208 (100), 201 (61). HRMS (FAB): for C$_{13}$H$_{18}$N$_{5}$O$_{5}$ calculated 324.1308; found 324.1303. $^1$H NMR (400 MHz, D$_2$O): 2.60 (ddd, 1H, $J_{gem} = 14.1$, $J_{2'b1'} = 6.5$, $J_{2'b3'} = 3.7$, H-2’b); 2.89 and 2.90 diastereomeric (dt, 1H, $J_{gem} = 14.1$, $J_{2'a1'} = 6.7$, $J_{2'a3'} = 6.2$, H-2’a); 3.73 (m, 2H, CH$_2$); 3.79 (dd, 1H, $J_{gem} = 12.6$, $J_{5'b4'} = 4.6$, H-5’b); 3.84 (dd, 1H, $J_{gem} = 12.6$, $J_{5'a4'} = 3.5$, H-5’a); 4.18 (q, 1H, $J_{4'5'b} = 4.6$, $J_{4'5'a} = 3.5$, H-4’); 4.36 (dd, 1H, $J = 7.3$ and 5.3, CH); 4.67 (dt, 1H, $J_{3'2'a} = 6.2$, $J_{3'2'b} = 3.7$, $J_{3'4'} = 3.5$, H-3’); 6.58 (t, 1H, $J_{1'2'a} = 6.7$, $J_{1'2'b} = 6.5$, H-1’); 8.65 (s, 1H, H-8); 8.86 (s, 1H, H-2). $^{13}$C NMR (100.6 MHz, D$_2$O, ref(dioxane) = 67.19 ppm): 33.00 (CH2-Pu); 39.52 (C-2’); 53.45 (CHCO); 62.14 (C-5’); 71.70 (C-3’); 85.35 (C-1’); 88.09 (C-4’); 133.16 (C-5); 145.51 (C-8); 150.65 (C-4); 152.30 (C-2); 157.54 (C-6); 173.65 (CO). IR (KBr): 3421, 3113, 2927, 1635, 1602, 1497, 1397, 1336, 1213, 1095, 1058, 939, 646, 539. Anal. calculated for C$_{13}$H$_{19}$N$_{5}$O$_{6}$ (341.3): C 45.75%, H 5.61%, N 20.52%; found C 46.12%, H 5.52%, N 20.39%.

**(S)-3-[9-(2-deoxy-$eta$-D-erythro-pentofuranosyl)purin-6-yl]-2-aminopropanoic acid mono hydrate ((S)-11d)**

Hydrogen was bubbled through solution of (S)-10d (410 mg, 0.90 mmol) in water (25 ml), dioxane (25 ml) and acetic acid (0.2 ml) in the presence of Pd/C catalyst (10 wt %, 40 mg) for
16 h. The catalyst was filtered off on Celite pad and the filtrate evaporated in vacuo. Crude product was purified by preparative HPLC on C18 column with water / methanol as mobile phase. Product was lyophilized from water to give 214 mg (70%) of (S)-11d as white solid. MS (FAB): 324 (53, M + 1); 208 (100, M – dRf + 2), 176 (96). 1H NMR (500 MHz, D2O): 2.62 (ddd, 1H, J = 3.8, 6.4 and 14.1, H-2′b); 2.91 (dt, 1H, J = 6.1, 7.0 and 14.1, H-2′a); 3.76 (dd, 1H, J = 7.3 and 16.4, PuCH3H6b); 3.80 (dd, 1H, J = 4.6 and 12.6, H-5′b); 3.81 (dd, 1H, J = 5.2 and 16.4, PuCH3H6b); 3.86 (dd, 1H, J = 3.5 and 12.6, H-5′a); 4.19 (q, 1H, J = 3.4, 3.5 and 4.6, H-4′); 4.38 (dd, 1H, J = 5.3 and 7.2, CHCO); 4.68 (dt, 1H, J = 3.4, 3.8 and 6.1, H-3′); 6.59 (t, 1H, J = 6.4 and 7.0, H-1′); 8.67 (s, 1H, H-8); 8.87 (s, 1H, H-2). 13C NMR (125.7 MHz, D2O, ref(dioxane) = 67.19 ppm): 32.99 (CH2-Pu); 39.55 (C-2′); 53.43 (CHCO); 62.15 (C-5′); 71.70 (C-3′); 85.35 (C-1′); 88.09 (C-4′); 133.15 (C-5); 145.50 (C-8); 150.64 (C-4); 152.30 (C-2); 157.54 (C-6); 173.65 (CO). [α]D20 = +6.0 (c = 8.52, H2O). Anal. calculated for C13H19N5O6 (341.3): C 45.75%, H 5.61%, N 20.52%; found C 45.34%, H 5.70%, N 20.14%.

Deprotection of 6c under acidic conditions: (R,S)-2-Amino-3-[9-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)purin-6-yl]propionic acid benzyl ester trifluoracetate
TFA (1.8 ml, 2.3 mmol) was slowly added at 0 °C to benzyl (R,S)-3-[9-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)purin-6-yl]-2-[(tert-butoxycarbonyl)amino]propanoate (6c) (1.4 g, 2.1 mmol) in CH2Cl2 (30 ml). The reaction mixture was stirred at ambient temperature overnight. Then the solvents was evaporated in vacuo and residue was codistilled with CH2Cl2. Crude product was chromatographed on a silica gel column (methanol/chloroform, 1:9) to give the product (R,S)-2-Amino-3-[9-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)purin-6-yl]propionic acid benzyl ester trifluoracetate (1.4 g, 97%) as yellowish amorphous solid. MS (FAB): 556 (14, M + 1); 298 (26, M – AcRf + 2); 259 (25); 162 (33); 139 (100); 97 (74); 91 (98, Bn). HRMS (FAB): for C28H30N5O9 calculated 556.2044, found 556.2057. 1H NMR (500 MHz, CDCl3): 2.06, 2.07, 2.08, 2.12, 2.17 and 2.18 (s, 3 × 3H, 3 × CH3CO); 3.88-4.04 (m, 2H, CH2 from alanine); 4.39-4.49 (m, 3H, H-4′ + H-5′); 4.70 (m, 1H, CH form alanine); 5.05 and 5.08 (d, 1H, J = 11.9, CHaH6Ph); 5.17 and 5.19 diastereomeric (d, 1H, J = 11.9, CHbH6Ph); 5.66 and 5.67 diastereomeric (t, 1H , J = 4.5 and 5.0, H-3′); 5.90 and 5.97 diastereomeric (t, 1H, J = 5.0 and 5.3, H-2′); 6.22 and 6.24 diastereomeric (d, 1H, J = 5.3, H-1′); 7.09-7.25 (m, 5H, arom.); 8.25 (s, 1H, H-8); 8.67 and 8.69 diastereomeric (s, 1H, H-2). 13C NMR (125.8 MHz, CDCl3): 20.22, 20.45 and 20.65 (3 × CH3); 30.91 (PuCH2); 51.13 and 51.17 diastereomeric (CH from alanine); 63.03 and 63.07 diastereomeric (CH2-5′); 68.42 and 68.46 diastereomeric (CH2Ph); 70.57 and
70.63 diastereomeric (CH-3’); 72.90 and 73.15 diastereomeric (CH-2’); 80.51 and 80.57
diastereomeric (CH-4’); 86.30 and 86.58 diastereomeric (CH-1’); 128.37, 128.41, 128.52,
128.55 and 128.65 (5 × CH-arom.); 132.32 and 132.40 diastereomeric (C-5); 134.08 and
134.11 (C-arom.); 143.32 (CH-8); 150.43 (C-4); 151.98 (CH-2); 156.15 (C-6); 168.19
(COOBn); 169.53, 169.66 and 170.51 (3 × COCH3). IR (CHCl3): 3031, 3009, 1751, 1680,
1603, 1499, 1457, 1374, 1338, 1226, 1206, 1143, 801, 644.

References:
(1) Foucault, A.; Caude, M.; Oliveros, L. J. Chromatogr. 1979, 185, 345-360.
1998, 63, 7875-7884.
(3) Walker, C. V.; Caravatti, G.; Denholm, A. A.; Egerton, J.; Faessler, A.; Furet, P.; Garcia-