Identification of NAE inhibitors exhibiting potent activity in K562 Leukemia cells: Exploring the structural determinants of NAE Specificity

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Supporting Information

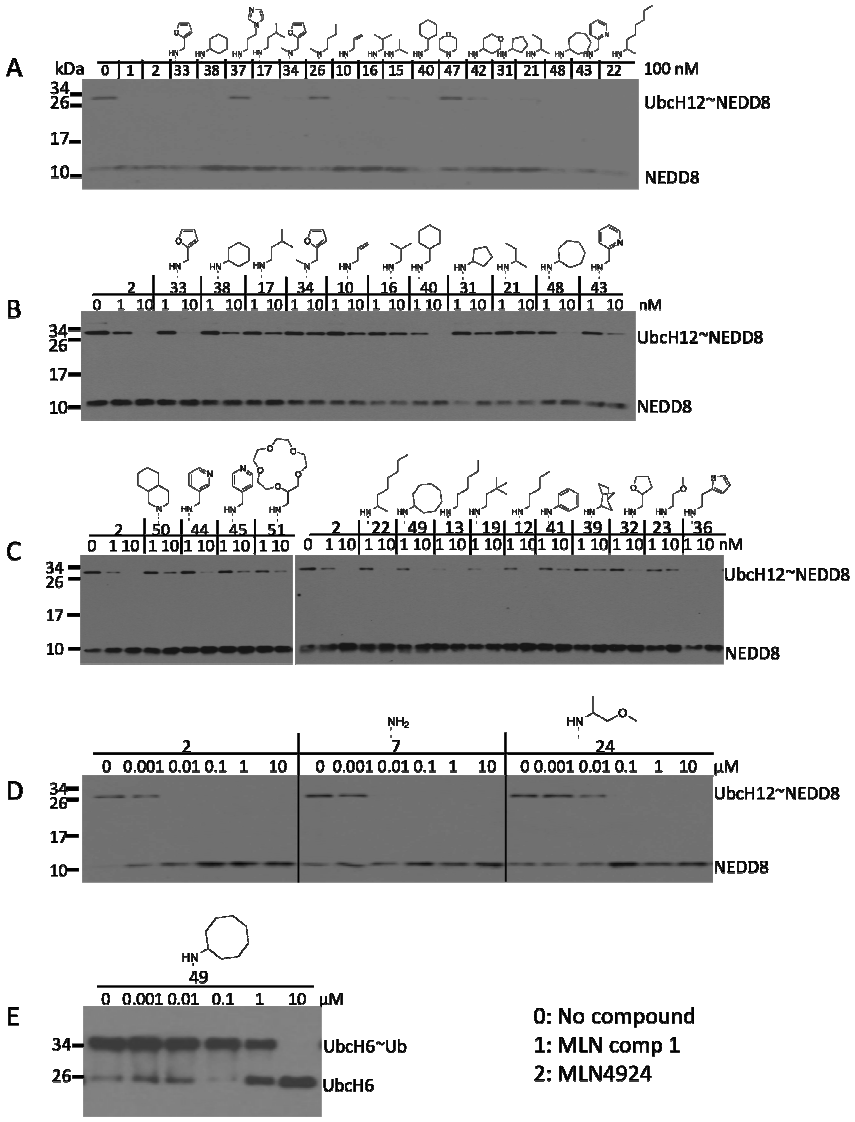


Figure 1. Representative assays for the evaluation of compounds **7-51** against (A) UBA3 and (B) UBA1. Millennium: The Takeda Oncology Company's compound 1 (**1**), MLN4924 (**2**).

Table 1. Evaluating non-specific kinase activity of lead NAE inhibitors

Kinase	% Enzyme Activity (relative to DMSO controls)		IC50 (nM) of Staurosporine
	Trial 1	Trial 2	
ABL	103.24	101.73	50.11
CAMK2b	102.66	101.08	<1.0
CDK1/cyclin B	112.51	113.98	<1.0
DAPK1	97.42	88.52	6.53
EGFR	99.36	98.91	163.40
IGF1R	99.36	100.44	33.97
JAK1	98.94	99.28	<1.0
JAK3	91.81	94.04	<1.0
MEK1	121.61	122.89	3.82
TRKA	109.43	109.09	1.69

Percent kinase activity (relative to DMSO control) was measured in the presence of 0.1 μM of compound **13** and 10 μM ATP (in duplicate) using a radiolabeled kinase profiling assay. Kinases tested include: Abelson tyrosine kinase (ABL), Calcium/calmodulin-dependent protein kinase type II beta chain (CAMK2b), Cyclin dependent kinase 1/cyclin B (CDK1/cyclin B), Death-associated protein kinase 1 (DAPK1), Epidermal growth factor receptor (EGFR), Insulin growth factor 1 receptor (IGF1R), Janus kinase 1 (JAK1), Janus kinase 3 (JAK3), Mitogen-activated protein kinase kinase 1 (MEK1), and Tyrosine kinase receptor A (TRKA). Kinase profiling was conducted at Reaction Biology; see full assay details at www.reactionbiology.com.

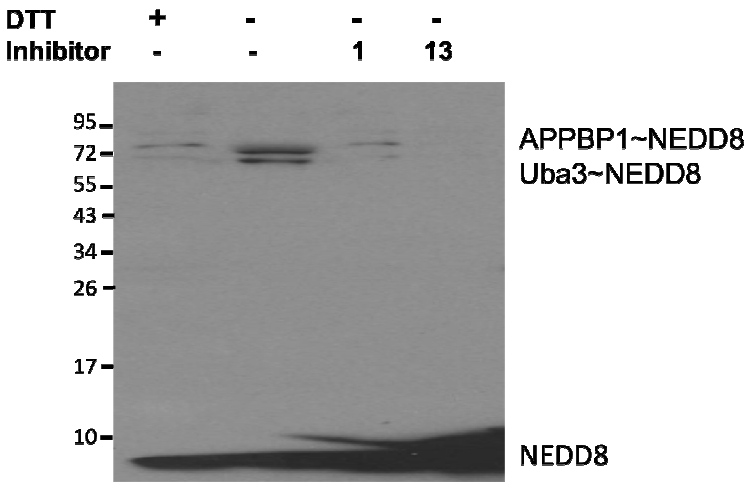


Figure 2. NAE inhibitors disrupt NEDD8 activation of Uba3. Putative Uba3 inhibitors 1 and 13 (10mM) were incubated with Uba3, (1mM), NEDD8 (2.5mM), and ATP (1 mM) with and without DTT (10mM) for 1.5 hours at room temperature. Products were fractionated on non-denaturing SDS-PAGE followed by Western Blot analysis with anti-NEDD8.

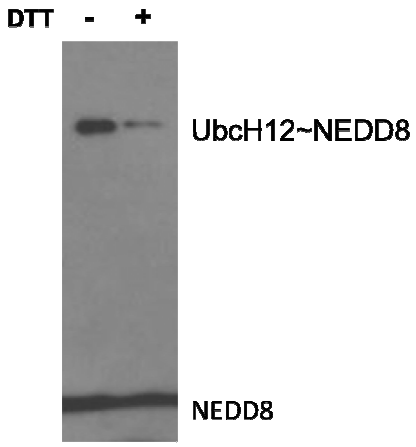


Figure 3. The UbcH12-NEDD8 linkage is sensitive to reducing agents. Uba3, (10nM), NEDD8 (500nM), UbcH12 (500 nM), and ATP (20mM) were incubated with and without DTT (10mM) for 1.5 hours at room temperature. Products were fractionated on non-denaturing SDS-PAGE followed by Western Blot analysis with anti-NEDD8.

S.1.0 Chemical Methods

Acetone, trifluoroacetic acid (TFA), dimethyl sulfoxide (DMSO), anhydrous tetrahydrofuran (THF) and the deuterated solvents (chloroform 99.8 atom %D, methanol-d_4 99.8+ atom % D, DMSO-d_6 99.9 atom % D) were purchased from Sigma Aldrich and used as received. With the exception of 6-chloropurine riboside which was purchased from 3B-Scientific Corporation, all of the reactants/reagents used were purchased from Sigma-Aldrich. Microwave reactions were carried out using a Biotage Initiator 2.5 microwave reactor. During all reactions, product formation was monitored using silica gel thin-layer chromatography (TLC), which was visualized by UV light or developed by treatment with $KMnO_4$ stain. ^1H and ^{13}C NMR spectra were acquired using a Bruker 400MHz spectrometer, samples were dissolved in $CDCl_3$, MeOD-d_4 or DMSO-d_6. Chemical shifts (δ) were reported in parts per million (ppm), proceeding calibration to residual isotopic solvent peak, and coupling constants (*J*) were reported in Hz. Low resolution mass spectrometry of the intermediates was carried out using a Waters Micromass ZQ equiped with an ESI source. An AB/Sciex QStar mass spectrometer equiped with an ESI source and MS/MS was utilized for accurate mass determination of the final molecules **7**-**51**. The purity of the final was evaluated using reverse-phase high performance liquid chromatography (*rp*-HPLC). Analysis was done using a MicroSorb-MV 300 A C18 250 mm x 4.6 mm column, run at 1 ml/min with gradient mixtures of (A) water with 0.1 M CH_3COONH_4, and (B) methanol. Overall a total of four different methods were utilized for analyzing **7**-**51**, each beginning with an initial 2-minute period of 90% A and 10% B followed by a change in gradient to: 1) 50% A and 50% B at a rate of change of (I) 3.6% per minute or (II) 6.7% per minute, at a UV detection of 254 nm or a change in gradient to 0 % A and 2) 100% B at a rate of change of either (III) 8.2% per minute, or (IV) 15% per minute, at a UV detection of 254 nm. Compound purity was

confirmed by running samples of the final molecules under two of the four previously described conditions. Percentage purity from HPLC data is reported in parentheses after the retention time for each condition. All compounds were >95% chemically pure, as measured by HPLC.

S.1.1 Experimental Procedure - Synthesis of C6 amino-substituted 5'-sulfamate nucleosides

General Procedure A. Nucleophilic aromatic substitution at C6 with amine: The protected starting material (**4**) (100 mg, 3.1×10^{-4}, 1.0 eq) was placed in a microwave vial and dissolved in DMSO (1.5 ml). To this solution was added the amine (2.0 eq) and DIPEA (119 mg, 9.3×10^{-3} moles, 3.0 eq). The vial was then sealed, placed under an atmosphere of nitrogen, and irradiated in a Biotage Initiator microwave reactor for 40 minutes, at 105 °C. Once the reaction was complete, the solution was extracted three times with ethyl acetate. The ethyl acetate layers were combined, extracted with distilled water, washed with brine, and dried over anhydrous sodium sulfate. The ethyl acetate was removed using a rotary evaporator, and the resulting product residue was purified by silica gel column using a Biotage Isolera One automated column set with a gradient of ethyl acetate and hexanes.

General Procedure B. Sulfonamide formation at 5'-OH: Under an atmosphere of nitrogen, the product of the nucleophilic aromatic substitution (1.0 eq), described in general procedure **A** was dissolved in 15 ml of anhydrous THF. The resulting solution was cooled in an ice-water bath and NaH (1.5 eq) was added. The reaction mixture was stirred for 30 minutes with continued cooling. Next, the sulfamoyl chloride (1.5 eq) was added, the reaction mixture was allowed to warm to room temperature and then stirred for 2 hours (the synthesis of sulfamoyl chloride is described below). Once the reaction was complete, the reaction mixture was once again cooled in an ice bath and any residual NaH was quenched through the dropwise addition of methanol. The reaction mixture was then concentrated using a rotary evaporator. The resultant residue was

dissolved in water and extracted three times with ethyl acetate. The combined ethyl acetate layers were washed with brine, and dried over anhydrous sodium sulfate. The ethyl acetate was removed using a rotary evaporator, and the product residue was purified by adsorption onto silica gel using dichloromethane with a small about of methanol and then run through a silica gel column using a Biotage Isolera One automated column device, set with a gradient of dichloromethane (CH_2Cl_2) and methanol (MeOH).

Synthesis of Sufamoyl Chloride

The sulfamoyl chloride was prepared according to the procedure reported previously[30] with some minor modifications. Chlorosulfonyl isocyanate was placed in a round bottom flask (732 μL, 8.4 x 10^{-3} moles) and cooled in an ice water bath. Formic acid (324 μL, 8.4 x 10^{-3} moles) was added dropwise and the reaction mixture was stirred. Gas evolution was observed as foaming of the mixture. The reaction was then stirred overnight under an atmosphere of nitrogen and used without purification for the synthesis of the sulfonamides.

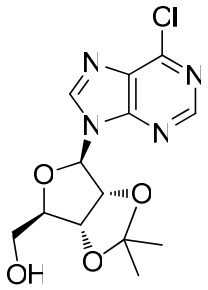
General Procedure C. Deprotection of 2', 3'-acetal: To a round-bottom flask containing the products of general procedure **B** (1.0 eq) was added TFA (1.5 ml) and distilled water (0.5 ml). The reaction mixture was stirred for 1 hour at room temperature. The water and TFA were then removed using a rotary evaporatory and the product residue was azeotroped three times with methanol followed by three times with chloroform and then adsorbed onto silica gel using methanol. The product was purified by silica gel column using a Biotage Isolera One automated column with a solvent gradient that consisted of CH_2Cl_2 and CH_2Cl_2/MeOH/NH_4OH (25/7/1).

General Procedure D. *In vitro* enzymatic assays: Ubiquitin protein was taken from bovine red blood cells, while other Ubl's were human recombinant, purified proteins. Enzymatic assays were carried out following the method described previously,[31] with slight modifications. To

determine the effects of inhibitors on Ub/Ubl-E2 loading, His6-tagged and untagged E1 proteins (25 nM His6-UBA1 [in-house]; 100 nM SAE1/SAE2 [Boston BioChem]; 10 nM APPBP1/UBA3 [Boston BioChem]; 200 nM His6-UBA5 [in-house]) were incubated with their respective Ub/Ubl's (1 μM Ub [Boston BioChem]; 500 nM SUMO-1 [Boston BioChem], 500 nM NEDD8 [Boston BioChem]; 500 nM His6-UFM1 [in-house]) and E2 proteins (300 nM His6-UbcH6 [in-house]; 500 nM UbcH9 [Boston BioChem]; 500 nM NEDD8 [Boston BioChem]; 500 nM His6-UFC1 [in-house]) and various concentrations of ATP (Sigma-Aldrich; 1 μM, 5 μM, 20 μM, 1 μM, respectively) in 10 μL assay buffer (50 mM HEPES, 5 mM $MgCl_2$, 0.5% BSA, pH 7.4) for 1.5 hours, in the presence and absence of compounds **7-51**. The generated protein-protein complexes were separated on a 15% non-degenerating SDS-PAGE, followed by Western blot analysis. The His6-tagged Ub-UbcH6 complex was resolved using a mouse monoclonal primary antibody (1:2500, BD Sciences) specific for His6. Rabbit polyclonal primary antibodies were used for the detection of other E2-Ubl complexes (anti-SUMO-1 [1:500, Boston BioChem] for SAE1/SAE2, anti-NEDD8 [1:500, Boston BioChem] for APPBP1-UBA3, and anti-UMF1 [1:1000, Boston BioChem] for UBA5). All Ub/Ubl-E2 complex formation was revealed using enhanced chemiluminescent detection (GE Healthcare). Densitometry measurements were carried out using ImageJ software. Percent inhibition was calculated using the following equations: Percent activity = (100 x E2~Ubl band intensity with compound)/(E2~Ubl band intensity without compound); Percent inhibition = 100 - percent activity.

General Procedure E. Cell viability assays: A K562 leukemia cell line was grown in RPMI 1640 supplemented with 10% fetal bovine serum (HyClone) and antibiotics. Cells were seeded in 96-well white-walled plates (Greiner Bio-One) at $3x10^5$ cells/well and treated with increasing

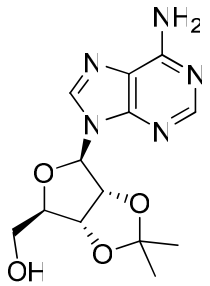
concentrations of compounds for 72 hours. After incubation, cell viability was assessed using the CellTiter-Glo luminescent cell viability assay (Promega) on a SpectraMax M5 multi-mode microplate reader (Molecular Devices) according to the manufacturer's instructions. Cell viability was calculated relative to sham-treated control wells on each plate. Values of EC_{50} were calculated using the data fitting program BioDataFit (www.changbioscience.com).



((3aR,4R,6R,6aR)-6-(6-chloro-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (4)

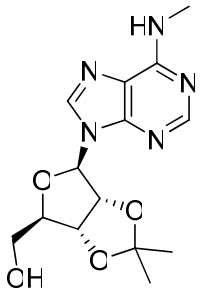
6-chloropurine riboside (2.0 g, 7.0×10^{-3} moles), *p*-toluene sulfonic acid (13.3 g, 7.0×10^{-2} moles) and acetone (300 mL) were combined and stirred at room temperature for 3 hours. Next, while cooling in an ice bath, a saturated sodium bicarbonate solution (300 mL) was added in 10 mL portions, until the pH of the solution was slightly basic. Then the acetone was evaporated off using a rotary evaporator, and the remaining aqueous layer was extracted three times with ethyl acetate. The combined ethyl acetate layers were washed with brine and dried over anhydrous sodium sulfate. The ethyl acetate was removed using a rotary evaporator, and the product was dried under high-powered vaccum for 15 minutes yielding **4** as a white solid (93%): m.p. = 132-137 °C; δ_H (400 MHz, $CDCl_3$) 1.39 (s, 3H, $C(C\underline{H}_3)_2$), 1.66 (s, 3H, $C(C\underline{H}_3)_2$), 3.79-3.86 (m, 1H, 5'H_2), 3.98 (dt, *J* = 12.7 Hz and 2.0 Hz, 1H, 5'H_2), 4.56 (q, *J* = 1.8 Hz, 1H, 4'H), 4.93 (dd, *J* = 10.7 Hz and 2.4 Hz, 1H, OH), 5.12 (dd, *J* = 5.9 Hz, 1H, 3'H), 5.21 (dd, *J* = 5.9 Hz,

1H, 2'H), 5.97 (d, J = 4.6 Hz, 1H, 1'H), 8.26 (s, 1H, H-2), 8.76 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{13}H_{15}ClN_4O_4Na]^+$ m/z = 349.07, obsd 349.19.



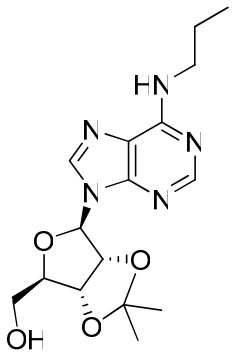
((3aR,4R,6R,6aR)-6-(6-amino-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5a)

The protection of the 2',3'-diol of adenosine was carried out according to the procedure described for (**4**) but adenosine was used in place of 6-chloropurine riboside. The product (**5b**) was obtained as a white solid (75%): m.p. = 190-200 °C; δ_H (400 MHz, $CDCl_3$) 1.26 (s, 3H C(C<u>H</u>$_3$)$_2$), 1.53 (s, 3H, C(C<u>H</u>$_3$)$_2$), 3.65 (d, J = 12.5 Hz, 1H, 5'H_2), 3.82 (d, J = 13.4 Hz, 1H, 5'H_2), 4.38-4.42 (m, 1H, 4'H), 4.94-4.99 (m, 1H, 3'H), 5.04-5.09 (m, 1H, 2'H), 5.80-5.84 (m, 1H, 1'H), 6.17 (vbs, 1H, OH), 6.43 (bs, 2H, NH_2), 7.86 (bs, 1H, H-2), 8.17 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{13}H_{17}N_5O_4Na]^+$ m/z = 330.12, obsd 330.03.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(methylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5b)

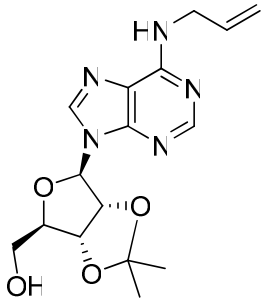
The protected purine riboside (**4**) was reacted with methylamine as outlined in general procedure **A** with a minor modification: the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and MeOH. The product (**5b**) was obtained as a white solid (98%): m.p. = 54-67 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 3.18 (bs, 3H, $HNC\underline{H}_3$), 3.79 (d, J = 12.8 Hz, 1H, 5'H_2), 3.98 (dd, J = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.10 (d, J = 5.9 Hz, 1H, 3'H), 5.19 (t, J = 5.4 Hz, 1H, 2'H), 5.85 (bs, 1H, 1'H), 6.00 (bs, 1H, NH), 5.76 (vbs, 1H, OH), 7.79 (s, 1H, H-2), 8.35 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{14}H_{19}N_5O_4Na]^+$ m/z = 344.13, obsd 344.33.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(propylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5c)

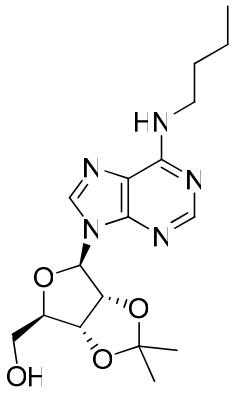
The protected purine riboside (**4**) was reacted with *n*-propylamine as outlined in general procedure **A**, yielding **5c** as a white solid (79%): m.p. = 35-44 °C; δ_H (400 MHz, $CDCl_3$) 1.01 (t, J = 7.4 Hz, 3H, $HNCH_2CH_2C\underline{H}_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.64 (s, 3H, $C(CH_3)_2$), 1.71 (sextet, J = 7.3 Hz, 2H, $HNCH_2C\underline{H}_2CH_3$), 3.59 (bs, 2H, $HNC\underline{H}_2CH_2CH_3$), 3.78 (d, J = 12.8 Hz, 1H, 5'H_2), 3.98 (dd, J = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.11 (dd, J = 5.9 Hz and 0.7 Hz, 1H, 3'H), 5.20 (t, J = 5.3 Hz, 1H, 2'H), 5.84 (d, J = 5.0 Hz, 1H, 1'H), 5.88 (bs, 1H, NH),

6.82 (bs, 1H, OH), 7.77 (s, 1H, H-2), 8.32 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{16}H_{24}N_5O_4]^+$ *m/z* = 350.19, obsd 350.24.



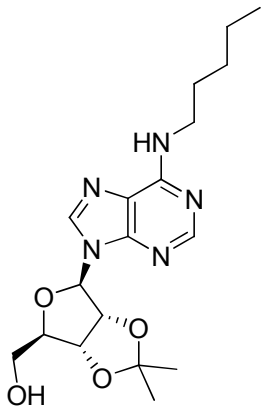
((3aR,4R,6R,6aR)-6-(6-(allylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5d)

The protected purine roboside (**4**) was reacted with allyl amine as outlined in general procedure **A**, yielding **5d** as a white solid (91%): m.p. = 47-50 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 3.79 (dd, *J* = 12.7 Hz and 1.3 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.5 Hz, 1H, 5'H_2), 4.29 (vbs, 2H, $HNC\underline{H}_2CHCH_2$), 4.53-4.55 (m, 1H, 4'H), 5.11 (dd, *J* = 5.9 Hz and 0.7 Hz, 1H, 3'H), 5.18-5.22 (m, 2H, $HNCH_2CHC\underline{H}_2$), 5.30 (dd, *J* = 17.1 Hz and 1.0 Hz, 1H, 2'H), 5.85 (d, *J* = 5.0 Hz, 1H, 1'H), 5.94-6.04 (m, 1H, $HNCH_2C\underline{H}CH_2$), 6.09 (vbs, 1H, $\underline{H}NCH_2CHCH_2$), 6.73 (vbs, 1H, $\underline{OH}$), 7.80 (s, 1H, H-2), 8.33 (s, 1H, H-8); LRMS (ESI+) calcd for $[C_{16}H_{21}N_5O_4Na]^+$ *m/z* = 370.15, obsd 370.26.



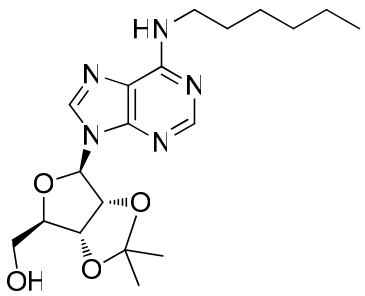
((3aR,4R,6R,6aR)-6-(6-(butylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5e)

The protected purine riboside (**4**) was reacted with *n*-butylamine as outlined in general procedure **A**, yielding **5e** as a colourless oil (96%): δ_H (400 MHz, $CDCl_3$) 0.96 (t, J = 7.3 Hz, 3H, $HN(CH_2)_3C\underline{H}_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.45 (sextet, J = 7.4 Hz, 2H, $HN(CH_2)_2C\underline{H}_2CH_3$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 1.67 (p, 7.3 Hz, 2H, $HNCH_2C\underline{H}_2CH_2CH_2$), 3.62 (bs, 2H, $HNC\underline{H}_2(CH_2)_2CH_3$), 3.79 (d, J = 12.8 Hz, 1H, 5'H_2), 3.97 (dd, J = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.11 (d, J = 5.9 Hz, 1H, 3'H), 5.10 (t, J = 5.3 Hz, 1H, 2'H), 5.80-5.93 (m, 2H, 1'H, NH), 6.82 (bs, 1H, OH), 7.77 (s, 1H, H-2), 8.33 (s, 1H, H-8); LRMS calcd for $[C_{17}H_{26}N_5O_4]^+$ m/z = 364.20, obsd 364.39.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(pentylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5f)

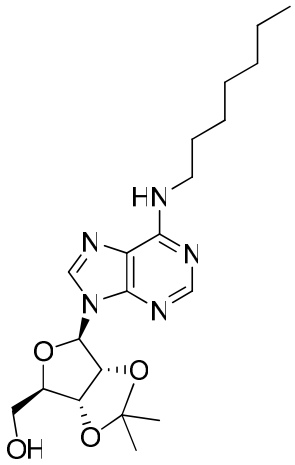
The protected purine riboside (**4**) was reacted with *n*-pentylamine as outlined in general procedure **A**, yielding **5f** as a golden-yellow oil (97%): δ_H (400 MHz, $CDCl_3$) 0.90 (t, J = 7.2 Hz, 3H, $HN(CH_2)_4C\underline{H}_3$), 1.31-1.44 (m, 4H, $HN(CH_2)_2(C\underline{H}_2)_2CH_3$), 1.37 (s, 3H, $C(CH_3)_2$), 1.64 (s, 3H, $C(CH_3)_2$), 1.68 (p, J = 7.2 Hz, 2H, $HNCH_2C\underline{H}_2(CH_2)_2CH_3$), 3.61 (bs, 2H, $HNC\underline{H}_2(CH_2)_3CH_3$), 3.78 (d, J = 12.8 Hz, 1H, 5'H_2), 3.97 (dd, J = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.11 (dd, J = 5.9 Hz and 0.9 Hz, 1H, 3'H), 5.19 (t, J = 5.4 Hz, 1H, 2'H), 5.83 (d, J = 5.0 Hz, 1H, 1'H), 5.91 (bs, 1H, NH), 6.85 (bs, 1H, OH), 7.77 (bs, 1H, H-2), 8.32 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{18}H_{27}N_5O_4Na]^+$ m/z = 400.20, obsd 400.36.



((3aR,4R,6R,6aR)-6-(6-(hexylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5g)

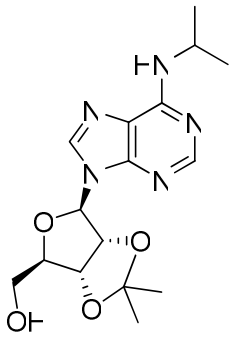
The protected purine riboside (**4**) was reacted with *n*-hexylamine as outlined in general procedure **A**, yielding **5g** a colourless oil (72%): δ_H (400 MHz, $CDCl_3$) 0.89 (t, J = 7.1 Hz, 3H, $HN(CH_2)_5C\underline{H}_3$), 1.29-1.34 (m, 4H, $HN(CH_2)_3(C\underline{H}_2)_2CH_3$), 1.38 (s, 3H, $C(C\underline{H}_3)_2$), 1.42 (p, J = 7.12 Hz, 2H, $HN(CH_2)_4C\underline{H}_2CH_3$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 1.68 (p, J = 1.69 Hz, 2H, $HNCH_2C\underline{H}_2(CH_2)_3CH_3$), 3.62 (bs, 2H, $HNC\underline{H}_2(CH_2)_4CH_3$), 3.75-3.83 (bm, 1H, 5'H), 3.98 (dd, J = 12.89 Hz and 1.36 Hz, 1H, 5'H), 4.53-4.55 (m, 1H, 4'H), 5.11 (dd, J = 5.86 Hz and 0.75 Hz,

1H, 3'H), 5.19 (t, J = 5.38, 1H, 2'H), 5.80-5.88 (m, 2H, 1'H and NH), 6.83 (s, 1H, OH), 7.77 (s, 1H, H-2), 8.33 (s, 1H, H-8); LRMS (ESI+) calcd for $[C_{19}H_{29}N_5O_4Na]^{1+}$ *m/z* = 414.21, obsd 414.28.



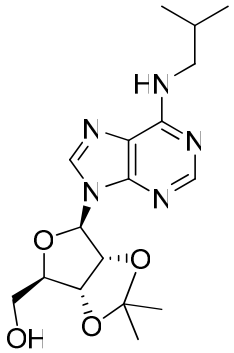
((3aR,4R,6R,6aR)-6-(6-(heptylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5h)

The protected purine riboside (**4**) was reacted with *n*-heptylamine as outlined in general procedure **A** with a minor modification: the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and MeOH. The product (**5h**) was obtained as a colourless oil (92%): δ_H (400 MHz, $CDCl_3$) 0.87 (t, J = 7.8 Hz, 3H, $HN(CH_2)_6C\underline{H}_3$), 1.23-1.46 (m, 8H, $HN(CH_2)_2(C\underline{H}_2)_4CH_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 1.68 (p, 2H, J = 7.1 Hz, $HNCH_2C\underline{H}_2(CH_2)_4CH_3$), 3.62 (bs, 2H, $HNC\underline{H}_2CH_2(CH_2)_4CH_3$), 3.79 (d, J = 12.6 Hz, 1H, 5'H_2), 3.97 (dd, J = 12.8 Hz and 0.9 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.10 (d, J = 5.6 Hz, 1H, 3'H), 5.19 (t, J = 5.3 Hz, 1H, 2'H), 5.80-5.95 (m, 2H, 1'H, NH), 6.82 (bs, 1H, OH), 7.78 (bs, 1H, H-2), 8.33 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{20}H_{31}N_5O_4Na]^+$ *m/z* = 428.23, obsd 428.39.



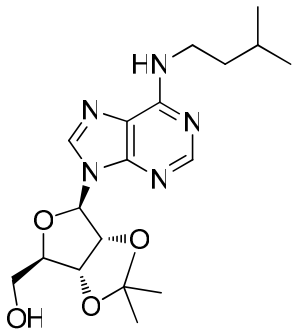
((3aR,4R,6R,6aR)-6-(6-(isopropylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5i)

The protected purine riboside (**4**) was reacted with isopropylamine as outlined in general procedure **A**, with a final microwave-assisted reaction time of 70 mins at 105 °C, yielding **5i** as a white solid (89%): m.p.=120-130 °C; δ_H (400 MHz, $CDCl_3$) 1.31 (d, *J* = 2.6 Hz, 3H, HNCH(C<u>H</u>$_3$)$_2$), 1.33 (d, *J* = 2.6 Hz, 3H, HNCH(C<u>H</u>$_3$)$_2$), 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.64 (s, 3H, C(C<u>H</u>$_3$)$_2$), 3.78 (d, *J* = 12.8 Hz, 1H, 5'H$_2$), 3.97 (dd, *J* = 12.8 Hz and 1.3 Hz, 1H, 4'H), 4.49 (vbs, 1H, HNC<u>H</u>(C<u>H</u>$_3$)$_2$), 4.52-4.54 (m, 1H, 3'H), 5.11 (dd, *J* = 5.9 Hz and 0.9 Hz, 1H, 3'H), 5.19 (t, *J* = 5.4 Hz, 1H, 2'H), 5.71 (vbs, 1H, <u>H</u>NCH(CH$_3$)$_2$), 5.84 (d, *J* = 4.8 Hz, 1H), 6.83 (vbs, 1H, <u>OH</u>), 7.78 (s, 1H, H-2), 8.31 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{16}H_{24}N_5O_4]^+$ *m/z* = 350.19, obsd 350.35.



((3aR,4R,6R,6aR)-6-(6-(isobutylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5j)

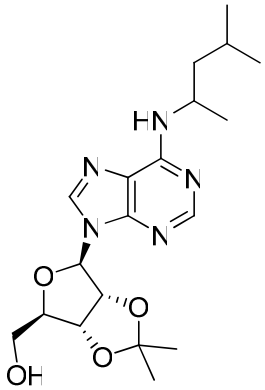
The protected purine riboside (**4**) was reacted with isobutylamine as outlined in general procedure **A**, yielding **5j** as a white solid (92%): m.p. = 41-46 °C; δ_H (400 MHz, $CDCl_3$) 1.01 (d, 6H, 6.6 Hz, $HNCH_2CH(C\underline{H}_3)_2$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 1.97 (septet, *J* = 6.8 Hz, 1H, $HNCH_2C\underline{H}(CH_3)_2$), 3.46 (bs, 2H, $HNC\underline{H}_2CH(CH_3)_2$), 3.79 (d, *J* = 12.3 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.11 (d, *J* = 5.9 Hz, 1H, 3'H), 5.19 (t, *J* = 5.3 Hz, 1H, 2'H), 5.84 (d, *J* = 3.7 Hz, 1H, 1'H), 5.94 (vbs, 1H, $\underline{H}NCH_2CH(CH_3)_2$), 6.82 (vbs, 1H, OH), 7.77 (s, 1H, H-2), 8.32 (s, 1H, H-8); LRMS (ESI+) calcd for $[C_{17}H_{26}N_5O_4]^+$ *m/z* = 364.20, obsd 364.38.



((3aR,4R,6R,6aR)-6-(6-(isopentylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5k)

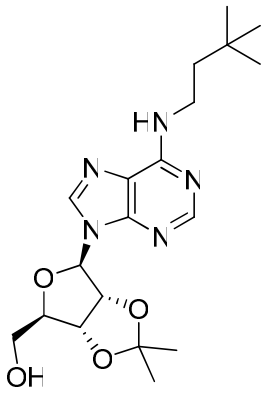
The protected purine riboside (**4**) was reacted with isoamylamine as outlined in general procedure **A** for a total of 40 minutes at 115 °C, yielding **5k** as an off-white solid (83%): m.p. = 40-47 °C; δ_H (400 MHz, $CDCl_3$) 0.96 (d, *J* = 6.6 Hz, 6H, $HN(CH_2)_2CHC(C\underline{H}_3)_2$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.57 (q, *J* = 7.2 Hz, 2H, $HNCH_2C\underline{H}_2CHC(CH_3)_2$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), (septet, *J* = 6.7 Hz, 1H, $HN(CH_2)_2C\underline{H}C(CH_3)_2$), 3.64 (bs, 2H, $HNC\underline{H}_2CH_2CHC(CH_3)_2$), 3.78 (t, *J* = 12.3 Hz,

1H, 5'H_2), 3.97 (d, 12.9 Hz, 1H, 5'H_2), 4.53-4.54 (m, 1H, 4'H), 5.11 (dd, *J* = 5.9 Hz and 0.87 Hz, 1H, 3'H), 5.20 (t, *J* = 5.4 Hz, 1H, 2'H), 5.79 (bs, 1H, HN), 5.83 (d, *J* = 5.0 Hz, 1H, 1'H), 6.81 (d, *J* = 11.9 Hz, 1H, OH), 7.76 (s, 1H, H-2), 8.33 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{18}H_{27}N_5O_4Na]^+$ *m/z* = 400.20, obsd 400.34.



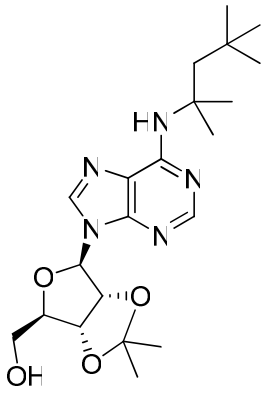
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((4-methylpentan-2-yl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5l)

The protected purine riboside (**4**) was reacted with 1,3-dimethylbutylamine as outlined in general procedure **A**, yielding **5l** as a white solid (85%): m.p. = 117-123 °C; δ_H (400 MHz, $CDCl_3$) 0.90-0.94 (m, 6H, HNCH(CH_3)CH_2CH(CH_3)$_2$), 1.25-1.28 (m, 3H, HNCH(CH_3)CH_2CH(CH_3)$_2$), 1.35-1.43 (m, 1H, HNCH(CH_3)CH_2CH(CH_3)$_2$), 1.37 (s, 3H, C(CH_3)$_2$), 1.48-1.57 (m, 1H, HNCH(CH_3)CH_2CH(CH_3)$_2$), 1.64 (s, 3H, C(CH_3)$_2$), 1.67-1.77 (m, 1H, HNCH(CH_3)CH_2CH(CH_3)$_2$), 3.78 (t, *J* = 12.5 Hz, 1H, 5'H_2), 3.97 (d, *J* = 12.8 Hz, 1H, 5'H_2), 4.51 (bs, 1H, HNCH(CH_3)CH_2CH(CH_3)$_2$), 4.52-4.55 (m, 1H, 4'H), 5.11 (d, *J* = 5.7 Hz, 1H, 3'H), 5.20 (t, *J* = 5.2 Hz, 1H, 2'H), 5.60 (bs, 1H, NH), 5.83 (d, *J* = 5.0 Hz, 1H, 1'H), 5.85 (d, *J* = 11.7 Hz, 1H, OH), 7.76 (s, 1H, H-2), 8.31 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{19}H_{30}N_5O_4]^+$ *m/z* = 392.23, obsd 392.31.



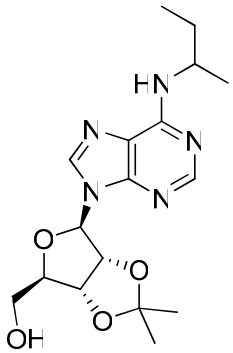
((3aR,4R,6R,6aR)-6-(6-(3,3-dimethylbutylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5m)

The protected purine riboside (**4**) was reacted with 3,3-dimethyl butylamine as outlined in general procedure **A**, yielding **5m** an off-white solid (97%): m.p. = 62-75 °C; δ_H (400 MHz, $CDCl_3$) 0.99 (s, 9H, $HN(CH_2)_2C(C\underline{H}_3)_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.57-1.65 (m, 2H, $HNCH_2C\underline{H}_2C(CH_3)_3$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 3.63 (bs, 2H, $HNC\underline{H}_2CH_2C(CH_3)_3$), 3.79 (d, J = 12.7 Hz, 1H, 5'H_2), 3.98 (dd, J = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.10 (d, J = 5.9 Hz, 1H, 3'H), 5.19 (t, J = 5.3 Hz, 1H, 2'H), 5.73 (bs, 1H, NH), 5.84 (bs, 1H, 1'H), 6.82 (bs, 1H, OH), 7.77 (bs, 1H, H-2), 8.34 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{19}H_{29}N_5O_4Na]^+$ *m/z* = 414.21, obsd 414.40.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(2,4,4-trimethylpentan-2-ylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5n)

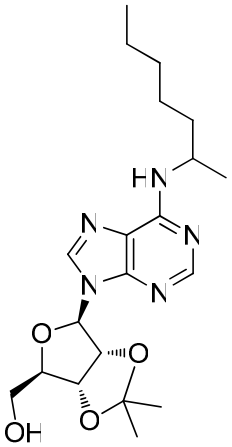
The protected purine riboside (**4**) was reacted with *tert*-octylamine as outlined in general procedure **A** for a total microwave-assisted reaction time of 4 hours 20 minutes at 135 °C, yielding **5n** as a clear yellow solid (70%): m.p. = 62-70 °C; δ_H (400 MHz, $CDCl_3$) 0.98 (s, 9H, $HNC(CH_3)_2CH_2C(C\underline{H}_3)_3$), 1.37 (s, 3H, $C(CH_3)_2$), 1.60 (bs, 6H, $HNC(C\underline{H}_3)_2CH_2C(CH_3)_3$), 1.64 (s, 3H, $C(CH_3)_2$), 2.00-2.03 (m, 2H, $HNC(CH_3)_2C\underline{H}_2C(CH_3)_3$), 3.78 (d, J = 12.8 Hz, 1H, 5'H_2), 3.98 (dd, J = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.11 (d, J = 5.9 Hz, 1H, 3'H), 5.20 (t, J = 5.4 Hz, 1H, 2'H), 5.78 (bs, 1H, NH), 5.82 (d, J = 5.0 Hz, 1H, 1'H), 6.95 (bs, 1H, OH), 7.73 (s, 1H, H-2), 8.29 (s, 1H, H-8); LRMS [ESI+] calcd for [$C_{21}H_{33}N_5O_4Na$] *m/z* = 442.24, obsd 442.43.



((3aR,4R,6R,6aR)-6-(6-(sec-butylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5o)

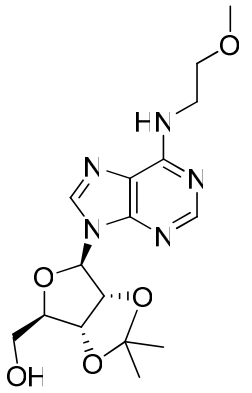
The protected purine riboside (**4**) was reacted with *sec*-butylamine as outlined in general procedure **A**, yielding **5o** as off-white solid (92%): m.p. = 43-47 °C; δ_H (400 MHz, $CDCl_3$) 0.98 (t, J = 7.5 Hz, 3H, $NHCH(CH_3)CH_2C\underline{H}_3$), 1.24-1.32 (m, 3H, $HNCH(C\underline{H}_3)CH_2CH_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.60-1.69 (m, 2H, $HNCH(CH_3)C\underline{H}_2CH_3$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 3.78 (d, J = 12.7 Hz,

1H, 5'H_2), 3.97 (dd, *J* = 12.7 Hz and 1.2 Hz, 1H, 5'H_2), 4.34 (vbs, 1H, HNC<u>H</u>(CH_3)CH_2CH_3), 4.53-4.55 (m, 1H, 4'H), 5.10 (d, *J* = 5.9 Hz, 1H, 3'H), 5.19 (t, *J* = 5.4 Hz, 1H, 2'H), 5.72 (bs, 1H, NH), 5.84 (d, *J* = 4.2 Hz, 1H, 1'H), 6.85 (vbs, 1H, OH), 7.77 (bs, 1H, H-2), 8.31 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{17}H_{26}N_5O_4]^+$ *m/z* = 364.20, obsd 364.28.



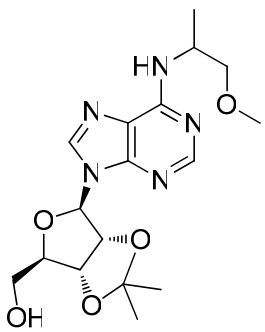
((3aR,4R,6R,6aR)-6-(6-(heptan-2-ylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5p)

The protected purine riboside (**4**) was reacted with 2-aminoheptane as outlined in general procedure **A**, yielding **5p** as a yellow oil (68%): δ_H (400 MHz, $CDCl_3$) 0.86 (t, *J* = 6.10, 3H, HNCH(CH_3) $(CH_2)_4C\underline{H}_3$), 1.23-1.32 (m, 9H, HNCH($C\underline{H}_3$)$CH_2(C\underline{H}_2)_3CH_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.53-1.61 (m, 2H, HNCH(CH_3)$C\underline{H}_2(CH_2)_3CH_3$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 3.71-3.82 (m, 2H, 5'H_2), 3.97 (dt, *J* = 12.84 Hz and 1.48 Hz, 1H, 4'H), 4.40 (bs, 1H, HNC<u>H</u>(CH_3)$(CH_2)_4CH_3$), 5.11 (d, *J* = 5.79 Hz, 1H, 3'H), 5.20 (t, *J* = 5.39, 1H, 2'H), 5.64 (bs, 1H, NH), 5.83 (d, *J* = 4.94 Hz, 1H, 1'H), 6.85 (d, *J* = 11.68 Hz, 1H, OH), 7.76 (s, 1H, H-2), 8.31 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{20}H_{31}N_5O_4Na]^+$ *m/z* = 428.23, obsd 428.32.



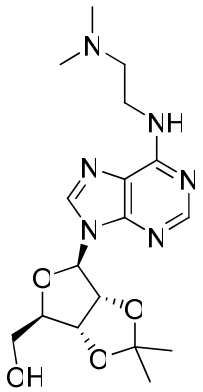
((3aR,4R,6R,6aR)-6-(6-(2-methoxyethylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5q)

The protected purine riboside (**4**) was reacted with 2-methoxyethylamine as outlined in general procedure **A** with a minor modification: the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and MeOH. The product (**5q**) was obtained as a colourless oil (90%): δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.64 (s, 3H, C(CH_3)$_2$), 3.39 (s, 3H, HNCH$_2$CH$_2$OC$\underline{H}_3$), 3.62 (t, *J* = 5.1 Hz, 2H, HNCH$_2$C$\underline{H}_2$OCH$_3$), 3.78 (d, *J* = 12.8 Hz, 1H, 5'H$_2$), 3.83 (bs, 2H, HNC$\underline{H}_2$CH$_2$OCH$_3$), 3.97 (dd, *J* = 12.8 Hz and 1.3 Hz, 1H, 5'H$_2$), 4.53-4.54 (m, 1H, 4'H), 5.10 (d, *J* = 5.9 Hz, 1H, 3'H), 5.19 (t, *J* = 5.4 Hz, 1H, 2'H), 5.84 (d, *J* = 5.0 Hz, 1H, 1'H), 6.27, (bs, 1H, NH), 6.77 (bs, 1H, OH), 7.79 (s, 1H, H-2), 8.32 (s, 1H, H-8); LRMS [ESI+] calcd for [$C_{16}H_{23}N_5O_5Na$] *m/z* = 388.16, obsd 388.33.



((3aR,4R,6R,6aR)-6-(6-((1-methoxypropan-2-yl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5r)

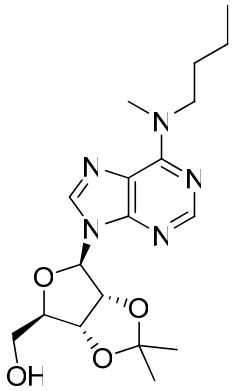
The protected purine riboside (**4**) was reacted with 1-methoxy-2-propylamine as outlined in general procedure **A**, yielding **5r** as a colourless solid (91%): m.p. = 34-44 °C; δ_H (400 MHz, $CDCl_3$) 1.31-1.36 (m, 3H, HNCH($C\underline{H}_3$)CH_2OCH_3), 1.37 (s, 3H, C($C\underline{H}_3$)$_2$), 1.64 (s, 3H, C(CH_3)$_2$), 3.38 (d, *J* = 2.4 Hz, 3H, HNCH(CH_3)$CH_2OC\underline{H}_3$), 3.49-3.52 (m, 2H, HNCH(CH_3)$C\underline{H}_2OCH_3$), 3.79 (d. *J* = 12.8 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.5 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 4.61 (bs, 1H, HN$C\underline{H}$(CH_3)CH_2OCH_3), 5.10 (d, *J* = 5.9 Hz, 1H, 3'H), 5.19 (d, *J* = 5.3 Hz, 1H, 2'H), 5.85 (d, *J* = 4.4 Hz, 1H, 1'H), 6.08 (bs, 1H, NH), 6.79 (bs, 1H, OH), 7.81 (bs, 1H, H-2), 8.31 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{17}H_{25}N_5O_5Na]^+$ *m/z* = 402.18, obsd 402.37.



((3aR,4R,6R,6aR)-6-(6-(2-(dimethylamino)ethylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5s)

The protected purine riboside (**4**) was reacted with *N,N*-dimethylethylenediamine as outlined in general procedure **A** with a minor modification: the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and CH_2Cl_2/MeOH/NH_4OH (92/7/1).

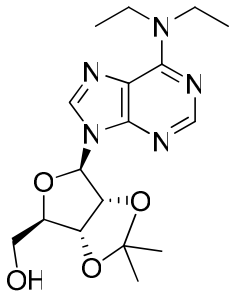
The product (**5s**) was obtained as a colourless solid (55%): m.p. = 1-4-109 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.64 (s, 3H, C(C<u>H</u>$_3$)$_2$), 2.36 (s, 6H, HN(CH$_2$)$_2$N(C<u>H</u>$_3$)$_2$), 2.66-2.73 (m, 2H, HNCH$_2$C<u>H</u>$_2$N(CH$_3$)$_2$), 3.76 (bs, 2H, HNC<u>H</u>$_2$CH$_2$N(CH$_3$)$_2$), 3.78 (d, *J* = 13.0 Hz, 1H, 5'H$_2$), 3.97 (dd, *J* = 12.9 Hz and 1.3 Hz, 1H, 5'H$_2$), 4.53-4.55 (m, 1H, 4'H), 5.11 (dd, *J* = 5.8 Hz and 0.8 Hz, 1H, 3'H), 5.19 (t, *J* = 5.4 Hz, 1H, 2'H), 5.85 (d, *J* = 4.9 Hz, 1H, 1'H), 6.62 (bs, 1H, <u>H</u>N(CH$_2$)$_2$N(CH$_3$)$_2$), 6.80 (bs, 1H, OH), 7.81 (s, 1H, H-2), 8.32 (s, 1H, H-8). LRMS [ESI+] calcd for $[C_{17}H_{26}N_6O_4Na]^+$ 401.19, obsd 401.36.



((3aR,4R,6R,6aR)-6-(6-(butyl(methyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5t)

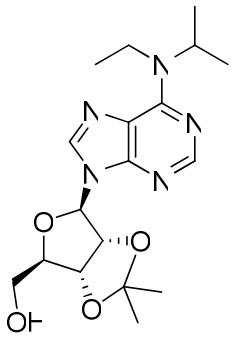
The protected purine riboside (**4**) was reacted with *N*-methylbutan-1-amine as outlined in general procedure **A**, yielding **5t** as a colourless oil (93%): δ_H (400 MHz, $CDCl_3$) 0.94 (t, *J* = 7.3 Hz, 3H, CH$_3$N(CH$_2$)$_3$C<u>H</u>$_3$), 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.38 (sextet, *J* = 7.4 Hz, 2H, CH$_3$N(CH$_2$)C<u>H</u>$_2$CH$_3$), 1.64 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.66 (p, *J* = 7.5 Hz, 2H, CH$_3$NCH$_2$C<u>H</u>$_2$CH$_2$CH$_3$), 3.19-3.83 (vbm, 3H, C<u>H</u>$_3$N(CH$_2$)$_3$CH$_3$), 3.78 (d, *J* = 12.7 Hz, 1H, 5'H$_2$), 3.97 (dd, *J* = 12.8 Hz and 1.4 Hz, 1H, 5'H$_2$), 4.01-4.38 (vbs, 2H, CH$_3$NC<u>H</u>$_2$(CH$_2$)$_2$CH$_3$), 4.52-4.54 (m, 1H, 4'H), 5.12 (dd, *J* = 5.9 Hz and 0.9 Hz, 1H, 3'H), 5.24 (t, *J* = 5.5 Hz, 1H, 2'H), 5.81 (d, 5.1 Hz, 1H, 1'H), 6.96 (bs, 1H, OH), 7.72

(s, 1H, H-2), 8.26 (s, 1H, H-8); LRMS (ESI+) calcd for $[C_{18}H_{27}N_5O_4Na]^+$ *m/z* = 400.20, obsd 400.34.



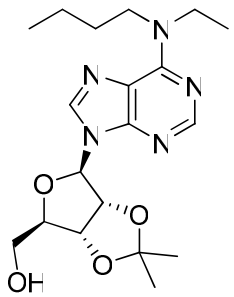
((3aR,4R,6R,6aR)-6-(6-(diethylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5u)

The protected purine riboside (**4**) was reacted with diethylamine as outlined in general procedure **A** for a microwave-assisted reaction time of 3 hours 40 minutes at 135 °C, yielding **5u** as a white solid (86%): m.p. = 75-85 °C; δ_H (400 MHz, $CDCl_3$) 1.28 (t, *J* = 7.0 Hz, 6H, $(C\underline{H}_3CH_2)_2N$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 3.68-4.32 (vbm, 4H, $(CH_3C\underline{H}_2)_2N$), 3.79 (d, *J* = 12.8 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.5 Hz, 1H, 5'H_2), 4.52-4.54 (m, 1H, 4'H), 5.12 (dd, *J* = 5.9 Hz and 0.9 Hz, 1H, 3'H), 5.25 (t, *J* = 5.4 Hz, 1H, 2'H), 5.82 (d, *J* = 5.1 Hz, 1H, 1'H), 7.00 (bs, 1H, OH), 7.73 (s, 1H, H-2), 8.27 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{17}H_{26}N_5O_4]^+$ *m/z* = 364.20, obsd 364.39.



((3aR,4R,6R,6aR)-6-(6-(ethyl(isopropyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5v)

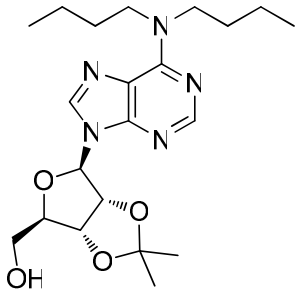
The protected purine riboside (**4**) was reacted with *N*-ethylisopropylamine as outlined in general procedure **A**, yielding **5v** as a yellow solid (70%): m.p. = 124-132 °C; δ_H (400 MHz, $CDCl_3$) 1.28-1.33 (m, 9H, $(C\underline{H}_3)_2CHNCH_2C\underline{H}_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_3$), 1.64 (s, 3H, $C(C\underline{H}_3)_3$), 3.87 (vbs, 3H, $(CH_3)_2C\underline{H}NC\underline{H}_2CH_3$), 3.79 (d, J = 12.8 Hz, 1H, 5'H_2), 3.97 (dd, J = 12.8 Hz and 1.4 Hz, 1H, 5'H_2), 4.52-4.54 (m, 1H, 4'H), 5.12 (dd, J = 5.9 Hz and 0.9 Hz, 1H, 3'H), 5.25 (t, J = 5.4 Hz, 1H, 2'H), 5.82 (d, J = 5.0 Hz, 1H, 1'H), 7.00 (vbs, 1H, OH), 7.74 (s, 1H, H-2), 8.25 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{18}H_{28}N_5O_4]^+$ m/z = 378.22, obsd 378.38.



((3aR,4R,6R,6aR)-6-(6-(butyl(ethyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5w)

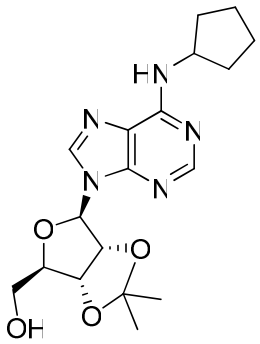
The protected purine riboside (**4**) was reacted with *N*-ethylbutylamine as outlined in general procedure **A**, yielding **5w** as a colourless oil (97%): δ_H (400 MHz, $CDCl_3$) 0.95 (t, J = 7.3 Hz,

3H, $CH_3CH_2N(CH_2)_3C\underline{H}_3$), 1.27 (t, *J* = 7.0 Hz, 3H, $C\underline{H}_3CH_2N(CH_2)_3CH_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.39 (sextet, *J* = 7.6 Hz, 2H, $CH_3CH_2NCH_2CH_2C\underline{H}_2CH_3$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 1.67 (p, *J* = 7.6 Hz, 2H, $CH_3CH_2NCH_2C\underline{H}_2CH_2CH_3$), 3.47-4.30 (vbm, 4H, $CH_3C\underline{H}_2NC\underline{H}_2CH_2CH_2CH_3$), 3.78 (d, *J* = 12.8 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.52-4.54 (m, 1H, 4'H), 5.12 (dd, *J* = 5.9 Hz and 0.7 Hz, 1H, 3'H), 5.25 (t, *J* = 5.4 Hz, 1H, 2'H), 5.81 (d, *J* = 5.0 Hz, 1H, 1'H), 7.04 (vbs, 1H, OH), 7.72 (s, 1H, H-2), 8.25 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{19}H_{29}N_5O_4Na]^+$ *m/z* = 414.21, obsd 414.40.



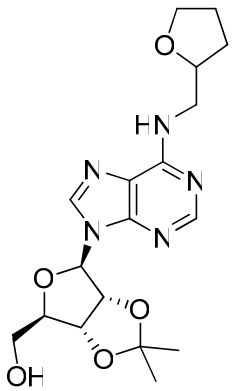
((3aR,4R,6R,6aR)-6-(6-(dibutylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5x)

The protected purine riboside (**4**) was reacted with dibutylamine as outlined in general procedure **A**, yielding **5x** as a light yellow oil (81%): δ_H (400 MHz, $CDCl_3$) 0.95 (t, *J* = 7.32 Hz, 6H, $C\underline{H}_3(CH_2)_3N(CH_2)_3C\underline{H}_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.39 (sextet, *J* = 7.49 Hz, 4H, $CH_3(C\underline{H}_2)_3N(C\underline{H}_2)_3CH_3$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 1.65 (p, *J* = 7.58 Hz, 4H, $CH_3(C\underline{H}_2)_3N(C\underline{H}_2)_3CH_3$), 3.75 (bs, 2H, $CH_3(C\underline{H}_2)_3N(CH_2)_3CH_3$), 3.79 (bd, *J* = 12.12 Hz, 1H, 5'H), 3.97 (dd, *J* = 12.78 Hz and 1.29 Hz, 1H, 5'H), 4.12 (bs, 2H, $CH_3(CH_2)_3N(C\underline{H}_2)_3CH_3$), 4.52-4.54 (bm, 1H, 4'H), 5.12 (dd, *J* = 5.86 Hz and 0.83 Hz, 1H, 3'H), 5.25 (t, *J* = 5.44 Hz, 1H, 2'H), 5.81 (d, *J* = 5.04, 1H, 1'H), 7.07 (bs, 1H, OH), 7.70 (s, 1H, H-2), 8.24 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{21}H_{33}N_5O_4Na]^+$ *m/z* = 442.24, obsd 442.43.



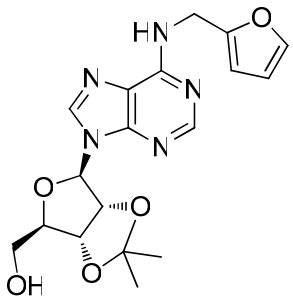
((3aR,4R,6R,6aR)-6-(6-(cyclopentylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5y)

The protected purine riboside (**4**) was reacted with cyclopentylamine as outlined in general procedure **A**, yielding **5y** as an off-white solid (83%): m.p. = 51-55 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.51-1.83 (m, 6H, cyclopentyl), 1.64 (s, 3H, C(C<u>H</u>$_3$)$_2$), 2.14 (sextet, *J* = 6.1 Hz, 2H, cyclopentyl), 3.79 (d, *J* = 12.5 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.54 (m, 1H, 4'H), 4.58 (bs, 1H, cyclopentyl), 5.10 (d, *J* = 5.9 Hz, 1H, 3'H), 5.19 (t, *J* = 5.4 Hz, 1H, 2'H), 5.80-5.92 (m, 2H, NH, 1'H), 6.83 (vbs, 1H, OH), 7.77 (bs, 1H, H-2), 8.33 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{18}H_{26}N_5O_4]^+$ *m/z* = 376.20, obsd 376.23.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((tetrahydrofuran-2-yl)methylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5z)

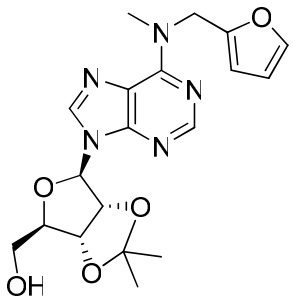
The protected purine riboside (**4**) was reacted with tetrahydrofurfurylamine as outlined in general procedure **A** with a minor modification: the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and MeOH. The product (**5z**) as a white solid (88%): m.p. = 75-80 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.59-1.69 (m, 1H, tetrahydrofuran), 1.64 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.87-1.96 (m, 2H, tetrahydrofuran), 1.98-2.08 (m, 1H, tetrahydrofuran), 3.63 (bs, 1H, tetrahydrofuran), 3.74-4.00 (m, 4H, 5'H_2, C<u>H</u>$_2$tetrahydrofuran) 4.10-4.17 (m, 1H, tetrahydrofuran), 4.53-4.55 (m, 1H, 4'H), 5.11 (d, *J* = 5.7 Hz, 1H, 3'H), 5.19 (t, *J* = 5.3 Hz, 1H, 2'H), 5.84 (d, *J* = 5.0 Hz, 1H, 1'H), 6.22 (bs, 1H, NH), 6.79 (bs, 1H, OH), 7.78 (s, 1H, H-2), 8.31 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{18}H_{25}N_5O_5Na]^+$ *m/z* = 414.18, obsd 414.34.



((3aR,4R,6R,6aR)-6-(6-((furan-2-ylmethyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5aa)

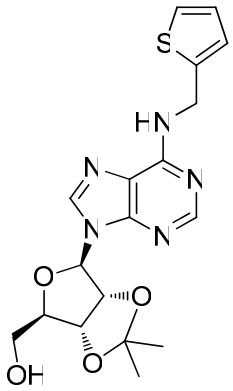
The protected purine riboside (**4**) was reacted with furfurylamine as outlined in general procedure **A**, yielding **5aa** as an off-white solid (96%): m.p. = 48-60 °C; δ_H (400 MHz, $CDCl_3$) 1.35 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.62 (s, 3H, C(C<u>H</u>$_3$)$_2$), 3.72-3.81 (bm, 1H, 5'H_2), 3.95 (dd, *J* = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.50-4.52 (bm, 1H, 4'H), 4.81 (bs, 2H, C<u>H</u>$_2$furan), 5.09 (dd, *J* = 5.9 Hz and 0.7 Hz, 1H, 3'H), 5.19 (t, *J* = 5.3 Hz, 1H, 2'H), 5.82 (d, *J* = 5.0 Hz, 1H, 1'H), 6.25-6.30 (m,

2H, furan), 6.68 (bs, 1H, NH), 6.79 (bs, 1H, OH), 7.31-7.34 (m, 1H, furan), 7.70 (s, 1H, H-2), 8.34 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{18}H_{22}N_5O_5]^+$ *m/z* = 388.16, obsd 388.28.



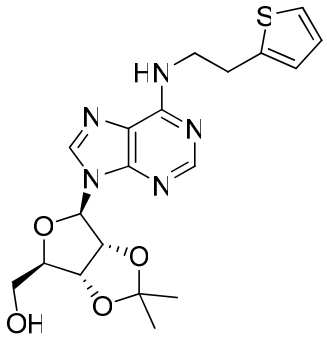
((3aR,4R,6R,6aR)-6-(6-((furan-2-ylmethyl)(methyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ab)

The protected purine riboside (**4**) was reacted with *N*-methylfurfurylamine as outlined in general procedure **A**, yielding **5ab** as a clear yellow solid (95%): m.p. = 45-48 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C$\underline{H}_3$)$_2$, 1.64 (s, 3H, C(C$\underline{H}_3$)$_2$, 3.17-3.90 (vbm, 3H, C$\underline{H}_3$Nfurfuryl), 3.79 (dd, *J* = 12.8 Hz and 1.7 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.5 Hz, 1H, 5'H_2), 4.53-4.54 (m, 1H, 4'H), 4.92-5.66 (vbm, 2H, CH_3NC$\underline{H}_2$furan), 5.12 (dd, *J* = 5.9 Hz and 0.92 Hz, 1H, 3'H), 5.24 (t, *J* = 5.4 Hz, 1H, 2'H), 5.83 (d, *J* = 5.0 Hz, 1H, 1'H), 6.28-6.31 (m, 2H, furan), 6.62-7.15 (vbs, 1H, OH), 7.34-7.35 (m, 1H, furan), 7.78 (s, 1H, H-2), 8.32 (s, 1H, H-8); LRMS (ESI+) calcd for $[C_{19}H_{24}N_5O_5]^+$ *m/z* = 402.18, obsd 402.32.



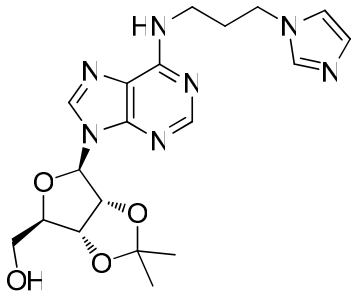
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((thiophen-2-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ac)

The protected purine riboside (**4**) was reacted with 2-thiophenemethylamine as outlined in general procedure **A**, yielding **5ac** as a light yellow solid (93%): m.p. = 47-60 °C; δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.64 (s, 3H, C(C<u>H</u>$_3$)$_2$), 3.79 (d, *J* = 12.8 Hz, 1H, 5'H$_2$), 3.98 (dd, *J* = 12.8 Hz and 0.9 Hz, 1H, 5'H$_2$), 5.02 (bs, 2H, C<u>H</u>$_2$thiophene), 4.53-4.55 (m, 1H, 4'H), 5.11 (d, *J* = 5.9 Hz, 1H, 3'H), 5.20 (t, *J* = 5.4 Hz, 1H, 2'H), 5.83 (d, *J* =5.0 Hz, 1H, 1'H), 6.32 (bs, 1H, NH), 6.71 (bs, 1H, OH), 6.96 (dd, *J* = 5.0 Hz and 3.5 Hz, 1H, thiophene), 7.05 (d, *J* = 3.1 Hz, 1H, thiophene), 7.22 (d, *J* = 5.1 Hz, 1H, thiophene), 7.74 (s, 1H, H-2), 8.39 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{18}H_{22}N_5O_4S]^+$ *m/z* = 404.14, obsd 404.26.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(2-(thiophen-2-yl)ethylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ad)

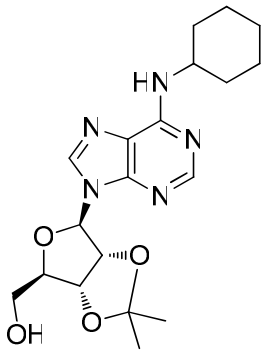
The protected purine riboside (**4**) was reacted with thiopheneethylamine as outlined in general procedure **A**, yielding **5ad** as a white solid (90%): m.p. = 45-51 °C; δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.64 (s, 3H, C(CH_3)$_2$), 3.21 (t, *J* = 6.6 Hz, 2H, HNCH_2C<u>H</u>$_2$thiophene), 3.79 (d, *J* = 12.5 Hz, 1H, 5'H_2), 3.93 (bs, 2H, HNC<u>H</u>$_2$CH_2thiophene), 3.98 (dd, *J* = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.11 (dd, *J* = 5.8 Hz and 0.8 Hz, 1H, 3'H), 5.20 (t, *J* = 5.4 Hz, 1H, 2'H), 5.83 (d, *J* = 5.0 Hz, 1H, 1'H), 6.10 (bs, 1H, NH), 6.76 (bs, 1H, OH), 6.87 (d, *J* = 2.8 Hz, 1H, thiophene), 6.94 (dd, *J* = 5.1 Hz and 3.5 Hz, 1H, thiophene), 7.16 (dd, *J* = 5.1 Hz and 1.1 Hz, 1H, thiophene), 7.75 (bs, 1H, H-2), 8.35 (bs, 1H, H-2); LRMS [ESI+] calcd for $[C_{19}H_{23}N_5O_4SNa]^+$ *m/z* = 440.14, obsd 440.29.



((3aR,4R,6R,6aR)-6-(6-((3-(1H-imidazol-1-yl)propyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ae)

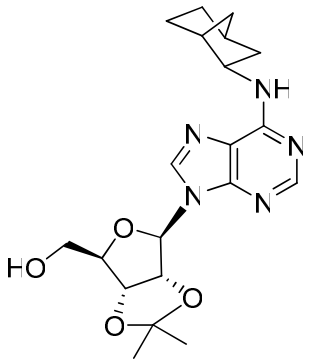
The protected purine riboside (**4**) was reacted with 1-(3-aminopropyl)imidazole as outlined in general procedure **A** with a minor modification: the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and CH_2Cl_2/MeOH/H_2O (70/12/1). The product (**5ae**) was obtained as a white solid (98%): δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.64 (s, 3H, C(CH_3)$_2$), 2.20 (p, *J* = 6.8 Hz, 2H, NHCH_2C<u>H</u>$_2$CH_2), 3.70 (bs, 2H, NC<u>H</u>$_2$(CH_2)$_2$), 3.78 (dd, *J* = 12.8 Hz and 2.1 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.4 Hz, 1H, 5'H_2), 4.10 (t, *J* = 7.0 Hz, 2H, NH(CH_2)$_2$C<u>H</u>$_2$), 4.53(vbs, 1H, N<u>H</u>CH_2(CH_2)$_2$), 4.52-4.54 (m,

1H, 4'H), 5.10 (dd, *J* = 5.9 Hz and 0.9 Hz, 1H, 3'H), 5.20 (t, *J* = 5.3 Hz, 1H, 2'H), 5.86 (d, *J* = 4.9 Hz, 1H, 1'H), 6.21-6.27 (m, 1H, O<u>H</u>), 6.98 (s, 1H, imidazole), 7.09 (s, 1H, imidazole), 7.74 (s, 1H, H-2), 7.80 (s, 1H, imidazole) 8.32 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{19}H_{26}N_7O_4]^+$ *m/z* = 416.21, obsd 416.29.



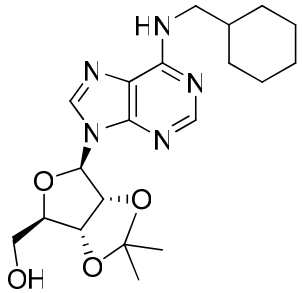
((3aR,4R,6R,6aR)-6-(6-(cyclohexylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5af)

The protected purine riboside (**4**) was reacted with cyclohexylamine as outlined in general procedure **A**, yielding **5af** as an off-white solid (96%): m.p. = 112-114 °C; δ_H (400 MHz, $CDCl_3$) 1.17-1.53 (m, 5H, cyclohexyl), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.64 (s, 3H, $C(CH_3)_2$), 1.66-1.71 (m, 1H, cyclohexyl), 1.74-1.83 (m, 2H, cyclohexyl), 2.04-2.12 (m, 2H, cyclohexyl), 3.78 (t, *J* = 12.3 Hz, 1H, 5'H_2), 3.97 (d, *J* = 12.9 Hz, 1H, 5'H_2), 4.16 (bs, 1H, cyclohexyl), 4.52-4.54 (m, 1H, 4'H), 5.11 (dd, *J* = 5.8 Hz and 0.72 Hz, 1H, 3'H) 5.19 (t, *J* = 5.4 Hz, 1H, 2'H), 5.73 (bs, 1H, N<u>H</u>), 5.82 (d, *J* = 5.0 Hz, 1H, 1'H), 6.84 (d, J = 11.5 Hz, 1H, O<u>H</u>), 7.75 (s, 1H, H-2), 8.30 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{19}H_{28}N_5O_4]^+$ *m/z* = 390.22, obsd 390.35.



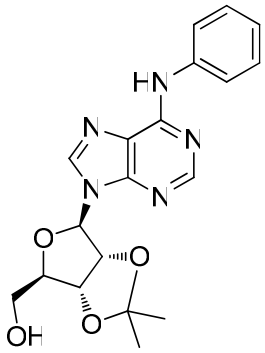
((3aR,4R,6R,6aR)-6-(6-((2R,4S)-bicyclo[2.2.1]heptan-2-ylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ag)

The protected purine riboside (**4**) was reacted with exo-2-aminonorborane as outlined in general procedure **A**, yielding **5ag** as a white solid (87%): m.p. = 77-88 °C; δ_H (400 MHz, $CDCl_3$) 1.16-1.28 (m, 2H, norborane), 1.32-1.41 (m, 2H, norborane), 1.37 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.46-1.62 (m, 3H, norborane), 1.64 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.91-1.98 (m, 1H, norborane), 2.33-2.38 (m, 2H, norborane), 3.78 (t, J = 10.6 Hz, 1H, 5'H_2), 3.97 (dd, J = 12.8 Hz and 1.1 Hz, 1H, 5'H_2), 4.08 (bs, 1H, norborane), 4.52-4.54 (m, 1H, 4'H), 5.11 (d, J = 5.9 Hz, 1H, 3'H), 5.19 (t, J = 5.3 Hz, 1H, 2'H), 5.76 (bs, 1H, NH), 5.83 (d, J = 5.0 Hz, 1H, 1'H), 6.85 (bs, 1H, OH), 7.76 (s, 1H, H-2), 8.32 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{20}H_{27}N_5O_4Na]^+$ *m/z* = 424.20, obsd 424.35.



((3aR,4R,6R,6aR)-6-(6-(cyclohexylmethylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ah)

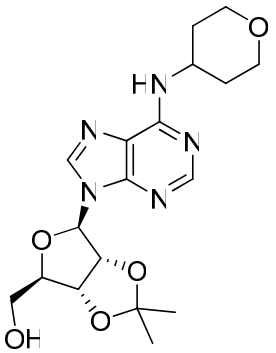
The protected purine riboside (**4**) was reacted with cyclohexanemethylamine as outlined in general procedure **A** yielding **5ah** as an off-white solid (90%): m.p. = 48-59 °C; δ_H (400 MHz, $CDCl_3$) 0.97-1.08 (m, 2H, cyclohexyl), 1.14-1.31 (m, 3H, cyclohexyl), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.64 (s, 3H, $C(C\underline{H}_3)_2$), 1.59-1.85 (m, 6H, cyclohexyl), 3.48 (bs, 2H, $HNC\underline{H}_2$cyclohexyl), 3.78 (d, J = 12.1 Hz, 1H, 5'H_2), 3.97 (dd, J = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.10 (d, J = 5.7 Hz, 1H, 3'H), 5.19 (t, J = 5.3 Hz, 1H, 2'H), 5.83 (d, J = 5.0 Hz, 1H, 1'H), 5.92 (vbs, 1H, $\underline{H}NCH_2$cyclohexyl), 6.83 (vbs, 1H, OH), 7.77 (s, 1H, H-2), 8.32 (s, 1H, H-8); LRMS (ESI+) calcd for $[C_{20}H_{30}N_5O_4]^+$ 404.23, obsd 404.37.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(phenylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ai)

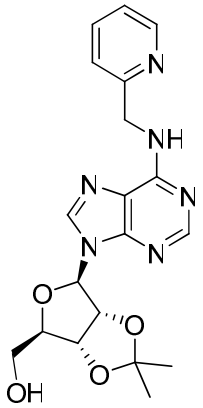
The protected purine riboside (**4**) was reacted with aniline as outlined in general procedure **A** with a couple of minor modifications: 1) a total microwave-assisted reaction time of 3 hours at 135 °C was utilized and 2) the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and MeOH. The product (**5ai)** was obtained as an orange solid (97%): m.p. = 167-175 °C; δ_H (400 MHz, $CDCl_3$) 1.39 (s, 3H, $C(C\underline{H}_3)_2$), 1.66 (s, 3H, $C(C\underline{H}_3)_2$), 3.81 (dd, J = 12.8 Hz and 1.8 Hz, 1H, 5'H_2), 4.01 (dd, J = 12.8 Hz and 1.4 Hz, 1H, 5'H_2), 4.57-4.59 (m, 1H, 4'H), 5.12 (dd, J = 5.9 Hz and 0.8 Hz, 1H, 3'H), 5.22 (t, J = 5.3 Hz,

1H, 2'H), 5.93 (d, *J* = 4.7 Hz, 1H, 1'H), 6.20 (vbs, 1H, OH), 7.16 (t, *J* = 7.4 Hz, 1H, phenyl), 7.40 (t, *J* = 7.9 Hz, 2H, phenyl), 7.82 (d, *J* = 7.9 Hz, 2H, phenyl), 8.07 (bs, 1H, H-2), 8.50 (s, 1H, H-8), 8.58 (bs, 1H, NH); LRMS [ESI+] calcd for $[C_{19}H_{22}N_5O_4]^+$ *m/z* = 384.17, obsd 384.28.



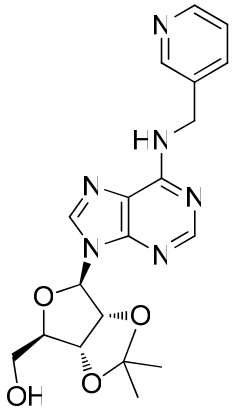
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(tetrahydro-2H-pyran-4-ylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5aj)

The protected purine riboside (**4**) was reacted with 4-aminotetrahydropyran as outlined in general procedure **A** with a minor modification**:** the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and MeOH. The product (**5aj**) was obtained as an off-white solid (98%): m.p. = 55-67 °C; δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.59-1.73 (m, 2H, tetrahydropyran), 1.64 (s, 3H, C(C$\underline{H}_3$)$_2$), 2.04-2.11 (m, 2H, tetrahydropyran), 3.58 (td, *J* = 11.5 Hz and 2.1 Hz, 2H, tetrahydropyran), 3.79 (d, *J* = 12.3 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.5 Hz, 1H, 5'H_2), 4.00-4.06 (m. 2H, tetrahydropyran), 4.41 (vbs, 1H, tetrahydropyran), 4.53-4.55 (m, 1H, 4'H), 5.10 (d, *J*, 5.9 Hz, 1H, 3'H), 5.19 (t, *J* = 5.4 Hz, 1H, 2'H), 5.78-5.90 (m, 2H, 1'H, NH), 6.70 (vbs, 1H, OH), 7.82 (bs, 1H, H-2), 8.32 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{18}H_{26}N_5O_5]^+$ 392.20, obsd 392.24.



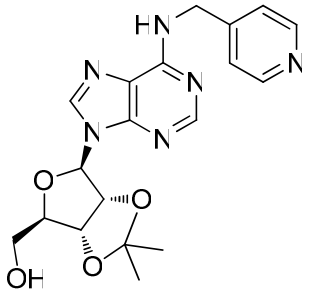
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((pyridin-2-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ak)

The protected purine riboside (**4**) was reacted with 2-aminomethylpyridine as outlined in general procedure **A**, with a minor modification: the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and MeOH. The product (**5ak**) was obtained as a white solid (95%): m.p. = 62-74 °C; δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.65 (s, 3H, C(C$\underline{H}_3$)$_2$), 2.69 (vbs, 1H, NH), 3.79 (dd, *J* = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 3.98 (dd, *J* = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 4.99 (bs, 2H, C$\underline{H}_2$pyridine), 5.11 (dd, *J* = 5.9 Hz and 0.9 Hz, 1H, 3'H), 5.20 (t, *J* = 5.4 Hz, 1H, 2'H), 5.86 (d, *J* = 5.0 Hz, 1H, 1'H), 6.72 (vbs, 1H, OH), 7.28 (d, *J* = 5.0 Hz, 1H, pyridine), 7.41 (d, *J* = 7.9 Hz, 1H, pyridine), 7.74 (td, *J* = 7.7 Hz and 1.7 Hz, 1H, pyridine), 7.83 (s, 1H, H-2), 8.36 (s, 1H, H-8), 8.58-8.62 (m, 1H, pyridine); LRSM [ESI+] calcd for $[C_{19}H_{22}N_6O_4Na]^+$ *m/z* = 421.16, obsd 421.25.



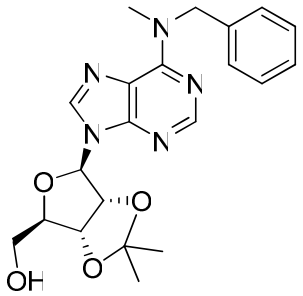
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((pyridin-3-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5al)

The protected purine riboside (**4**) was reacted with 3-(aminomethyl) pyridine as outlined in general procedure **A**, with a couple of minor modifications: 1) an oil bath was used as the source of heat instead of a microwave reactor, the reaction proceded at 75 °C for 16 hours, and 2) the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and MeOH. The product (**5al**) was obtained as a yellow solid (97%): m.p. = 47-58 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, $C(CH_3)_2$), 1.64 (s, 3H, $C(CH_3)_2$), 2.90 (vbs, 1H, OH), 3.79 (dd, *J* = 12.8 Hz and 1.9 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.5 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 4.90 (bs, 2H, C$\underline{H}_2$pyridine), 5.11 (dd, *J* = 5.9 Hz and 1.1 Hz, 1H, 3'H), 5.20 (t, *J* = 5.4 Hz, 1H, 2'H), 5.85 (d, *J* = 5.0 Hz, 1H, 1'H), 6.44-6.52 (bm, 1H, NH), 7.31 (dd, *J* = 7.9 Hz and 5.0 Hz, 1H, pyridine), 7.78 (d, *J* = 7.9 Hz, 1H, pyridine), 7.80 (s, 1H, pyridine), 8.36 (bs, 1H, H-2), 8.54 (d, *J* = 4.0 Hz, 1H, pyridine), 8.67 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{19}H_{23}N_6O_4]^+$ *m/z* = 399.18, obsd 399.35.



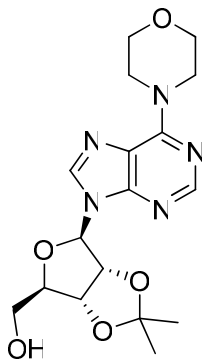
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((pyridin-4-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5am)

The protected purine riboside (**4**) was reacted with 4-(aminomethyl) pyridine as outlined in general procedure **A** with some minor modifications: 1) an oil bath was used as the source of heat instead of a microwave reactor, the reaction proceded at 75 °C for 17.5 hours and 2) the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and CH_2Cl_2/MeOH/NH_4OH (25/7/1). The product (**5am**) was obtained as a yellow solid (98%): m.p. = 54-67 °C; δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.65 (s, 3H, C(C$\underline{H}_3$)$_2$), 3.22 (vbs, 1H, OH), 3.79 (dd, *J* = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 3.97 (dd, *J* = 12.8 Hz and 1.5 Hz, 1H, 5'H_2), 4.54-4.56 (m, 1H, 4'H), 4.94 (bs, 2H, C$\underline{H}_2$pyridine), 5.11 (dd, *J* = 5.9 Hz and 1.1 Hz, 1H, 3'H), 5.20 (t, *J* = 5.4 Hz, 1H, 2'H), 5.86 (d, *J* = 5.0 Hz, 1H, 1'H), 6.48 (t, *J* = 6.2 Hz, 1H, NH), 7.38 (d, *J* = 6.1 Hz, 2H, pyridine), 7.82 (s, 1H, H-2), 8.34 (s, 1H, H-8), 8.57 (dd, *J* = 4.8 Hz and 1.6 Hz, 2H, pyridine); LRMS [ESI+] calcd for $[C_{19}H_{22}N_6O_4Na]^+$ *m/z* = 421.16, obsd 421.33.



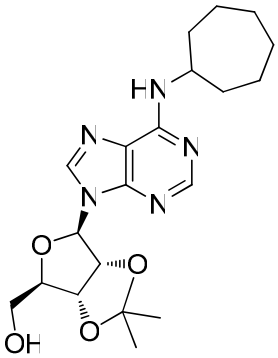
((3aR,4R,6R,6aR)-6-(6-(benzyl(methyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5an)

The protected purine riboside (**4**) was reacted with *N*-benzylmethylamine as outlined in general procedure **A** for a total reaction time of 1 hour at 135 °C, yielding **5an** as a yellow oil (93%): δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, $C(C\underline{H}_3)_2$), 1.65 (s, 3H, $C(C\underline{H}_3)_2$), 3.06-3.83 (bm, 3H, $C\underline{H}_3NCH_2$phenyl), 3.80 (dd, *J* = 12.8 Hz and 1.4 Hz, 1H, 5'H_2), 3.99 (dd, *J* = 12.8 Hz and 1.5 Hz, 1H, 5'H_2), 4.54-4.56 (m, 1H, 4'H), 5.13 (dd, *J* = 5.9 Hz and 0.9 Hz, 1H, 3'H), 5.26 (t, *J* = 5.4 Hz, 1H, 2'H), 4.91-5.72 (bm, 2H, $CH_3NC\underline{H}_2$phenyl), 5.83 (d, *J* = 5.1 Hz, 1H, 1'H), 6.88 (vbs, 1H, OH), 7.24-7.34 (m, 5H, phenyl), 7.75 (s, 1H, H-2), 8.33 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{21}H_{26}N_5O_4]^+$ *m/z* = 412.20, obsd 412.37.



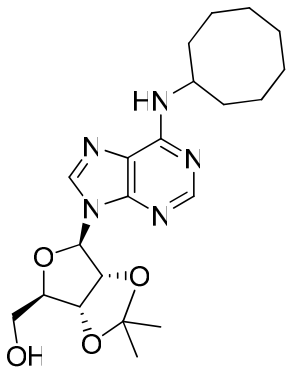
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-morpholino-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ao)

The protected purine riboside (**4**) was reacted with morpholine as outlined in general procedure **A**, yielding **5ao** as a colourless oil (85%): δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.64 (s, 3H, C(C$\underline{H}_3$)$_2$), 3.77-3.85 (m, 4H, C$\underline{H}_2$OC$\underline{H}_2$ morpholine, 1H, 5'H_2), 3.97 (dd, *J* = 12.7 Hz and 1.5Hz, 1H, 5'H_2), 4.33 (vbs, 4H, C$\underline{H}_2$NC$\underline{H}_2$ morpholine), 4.53-4.54 (m, 1H, 4'H), 5.12 (dd, *J* = 5.9 Hz and 0.9 Hz, 1H, 3'H), 5.22 (t, *J* = 5.5 Hz, 1H, 2'H), 5.83 (d, *J* = 5.1 Hz, 1H, 1'H), 6.78 (vbs, 1H, OH), 7.77 (s, 1H, H-2), 8.30 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{17}H_{24}N_5O_5]^+$ *m/z* = 378.19, obsd 378.23.



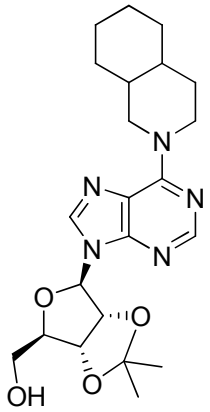
((3aR,4R,6R,6aR)-6-(6-(cycloheptylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ap)

The protected purine riboside (**4**) was reacted with cycloheptylamine as outlined in general procedure **A**, yielding **5ap** as an off-white solid (88%): m.p. = 108-120 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C$\underline{H}_3$)$_2$) 1.64 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.52-1.74 (m, 10H, cycloheptyl), 2.04-2.13 (m, 2H, cycloheptyl), 3.78 (t, *J* = 12.8 Hz, 1H, 5'H_2), 3.97 (d, *J* = 12.8 Hz, 1H, 5'H_2), 4.36 (bs, 1H, cycloheptyl), 4.52-4.54 (m, 1H, 4'H), 5.11 (dd, *J* = 5.9 Hz and 0.7 Hz, 1H, 3'H), 5.20 (t, *J* = 5.5 Hz, 1H, 2'H), 5.81 (bs, 1H, NH), 5.82 (d, *J* = 5.0 Hz, 1H, 1'H), 6.85 (bd, *J* = 11.6 Hz, 1H, OH), 7.75 (s, 1H, H-2), 8.31 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{20}H_{29}N_5O_4Na]^+$ *m/z* = 426.21, obsd 426.29.



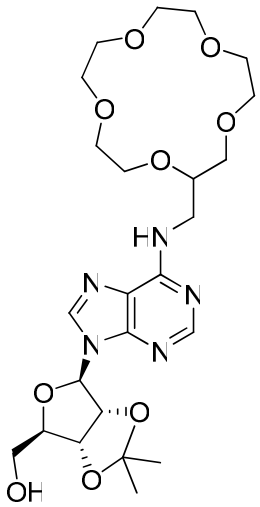
((3aR,4R,6R,6aR)-6-(6-(cyclooctylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5aq)

The protected purine riboside (**4**) was reacted with cyclooctylamine as outlined in general procedure **A**, yielding **5aq** as a white solid (91%): m.p. = 57-68 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.64 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.52-1.78 (m, 12H, cyclooctyl), 1.93-2.03 (m, 2H, cyclooctyl), 3.78 (t, J = 10.6 Hz, 1H, 5'H_2), 3.97 (dd J = 12.8 Hz and 1.3 Hz, 1H, 5'H_2), 4.40 (bs, 1H, cyclooctyl), 4.52-4.54 (m, 1H, 4'H), 5.10 (dd, J = 5.9 Hz and 0.9 Hz, 1H, 3'H), 5.19 (t, J = 5.4 Hz, 1H, 2'H), 5.82 (d, J = 5.0 Hz, 1H, 1'H), 5.88 (bs, 1H, NH), 6.88 (bs, 1H, OH), 7.76 (s, 1H, H-2), 8.30 (s, 1H, H-8); LRMS [ESI+] calcd for $[C_{21}H_{31}N_5O_4Na]^+$ *m/z* = 440.23, obsd 440.42.



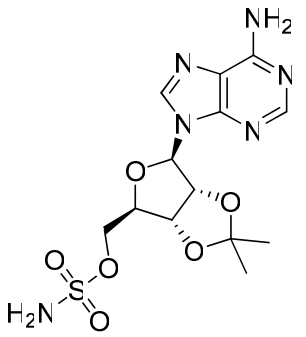
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(octahydroisoquinolin-2(1H)-yl)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5ar)

The protected purine riboside (**4**) was reacted with perhydroisoquinoline as outlined in general procedure **A**, yielding **5ar** as a clear yellow solid (98%): m.p. = 113-122 °C; δ_H (400 MHz, $CDCl_3$) 0.93-1.10 (m, 2H, perhydroisoquinoline), 1.17-1.35 (m, 6H, perhydroisquinoline), 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.62-1.80 (m, 4H, perhydroisoquinoline), 1.64 (s, 3H, C(C<u>H</u>$_3$)$_2$), 2.62 (bs, 1H, perhydroisoquinoline), 3.03 (bs, 1H, perhydroisoquinoline), 3.78 (d, J = 12.7 Hz, 1H, 5'H$_2$), 3.97 (dd, J = 12.8 Hz and 1.3 Hz, 1H, 5'H$_2$), 4.52-4.54 (m, 1H, 4'H), 5.11 (d, J = 5.9 Hz, 1H, 3'H), 3.96 (dd, J = 12.8 Hz and 1.3 Hz, 1H, 2'H), 5.11 (d, J = 5.9 Hz, 1H, 1'H), 5.46 (vbs, 2H, perhydroisoquinoline), 6.95 (bs, 1H, OH), 7.71-7.73 (m, 1H, H-2), 8.24 (m, 1H, H-8); LRMS [ESI+] calcd for $[C_{22}H_{31}N_5O_4Na]^+$ m/z = 452.23, obsd 452.45.



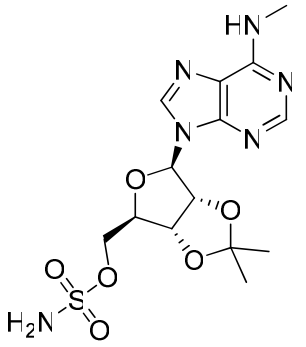
((3aR,4R,6R,6aR)-6-(6-((1,4,7,10,13-pentaoxacyclopentadecan-2-yl)methylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (5as)

The protected purine riboside (**4**) was reacted with 2-(aminomethy)-15-crown-5 as outlined in general procedure **A** with a couple of minor modifications: 1) the reaction required a total microwave-assisted reaction time of 1 hour at 105 °C and 2) the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and CH_2Cl_2/MeOH/H_2O (70/12/1). The product **5as** was obtained as a light-yellow oil (70%): δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.64 (s, 3H, C(C<u>H</u>$_3$)$_2$), 3.61-4.01 (m, 23H, HNCH_2-15-crown-5, 5H_2), 4.53-4.55 (m, 1H, 4'H), 5.10 (d, *J* = 5.9 Hz, 1H, 3'H), 5.19 (t, *J* = 5.3 Hz, 1H, 2'H), 5.81-5.95 (m, 1H, 1'H), 6.47 (vbs, 1H, NH), 6.78 (vbs, 1H, OH), 7.79 (bs, 1H, H-2), 8.32 (bs, 1H, H-8); LRMS [ESI+] calcd for $[C_{24}H_{37}N_5O_9Na]^+$ *m/z* = 562.25, obsd 562.46.



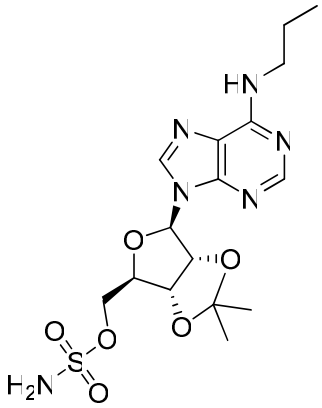
((3aR,4R,6R,6aR)-6-(6-amino-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6a)

Compound **5a** was reacted with sulfamoyl chloride as outlined in general procedure **B** yielding **5b** as an off-white solid (75%): m.p. = 62-75 °C; δ_H (400 MHz, DMSO-d_6) 1.34 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.55 (s, 3H, C(C<u>H</u>$_3$)$_2$), 4.13 (dd, *J* = 10.6 Hz and 6.4 Hz, 1H, 5'H$_2$), 4.24 (dd, *J* = 10.6 Hz and 5.3 Hz, 1H, 5'H$_2$), 4.37-4.42 (m, 1H, 4'H), 5.08 (dd, *J* = 6.2 Hz and 3.1 Hz, 1H, 3'H), 5.43 (dd, *J* = 6.2 Hz and 2.0 Hz, 1H, 2'H), 6.23 (d, *J* = 2.0 Hz, 1H, 1'H), 7.37 (s, 2H, NH$_2$), 7.61 (bs, 2H, <u>H</u>$_2$NSO$_3$), 8.17 (s, 1H, H-2), 8.30 (s, 1H, H-8); LRMS [ESI$^-$] calcd for $[C_{13}H_{18}N_6O_6S]^-$ *m/z* = 385.10, obsd 385.24.



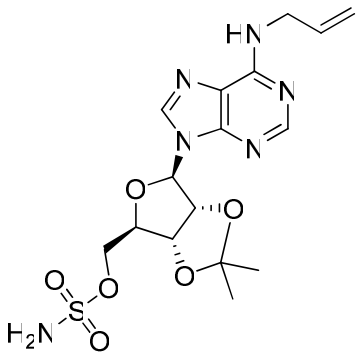
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(methylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6b)

Compound **5b** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6b** as a white solid (84%): m.p. > 200 °C (decomposes); δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.61 (s, 3H, C(C<u>H</u>$_3$)$_2$), 3.16 (bs, 3H, HNC<u>H</u>$_3$), 4.40 (dd, *J* = 11.2 Hz and 5.1 Hz, 1H 5'H_2), 4.46 (dd, *J* = 11.2 Hz and 3.7 Hz, 1H, 5'H_2), 4.52-4.57 (m, 1H, 4'H), 5.10 (dd, *J* = 6.2 Hz and 2.9 Hz, 1H, 3'H), 5.38 (dd, *J* = 6.2 Hz and 2.6 Hz, 1H, 2'H), 5.86 (bs, 2H, <u>H</u>$_2$NSO$_3$), 6.09 (d, *J* = 2.6 Hz, 1H, 1'H), 6.17 (bs, 1H, NH), 7.94 (bs, 1H, H-2), 8.36 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{14}H_{19}N_6O_6S]^-$ *m/z* = 399.11, obsd 399.29.



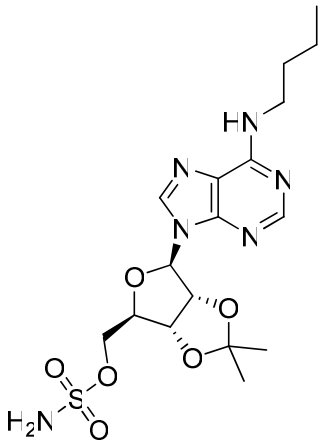
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(propylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6c)

Compound **5c** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 2.5 hours, yielding **6c** as a white solid (65%): m.p. = 89-102 °C; δ_H (400 MHz, $CDCl_3$) 1.00 (t, *J* = 7.3 Hz, 3H, HNCH$_2$CH$_2$C<u>H</u>$_3$), 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.61 (s, 3H, C(CH$_3$)$_2$), 1.69 (sextet, *J* = 7.3 Hz, 2H, HNCH$_2$C<u>H</u>$_2$CH$_3$), 3.56 (bs, 2H, HNC<u>H</u>$_2$CH$_2$CH$_3$), 4.37-4.54 (m, 3H, 5'H_2, 4'H), 5.11 (dd, *J* = 6.4 Hz and 3.1 Hz, 1H, 3'H), 5.39 (dd, *J* = 6.4 Hz and 2.8 Hz, 1H, 2'H), 5.78 (bs, 2H, <u>H</u>$_2$NSO$_3$), 5.93 (bs, 1H, NH), 6.06 (d, *J* = 2.8 Hz, 1H, 1'H), 7.87 (s, 1H, H-2), 8.34 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{16}H_{23}N_6O_6S]^-$ *m/z* = 427.14, obsd 427.24.



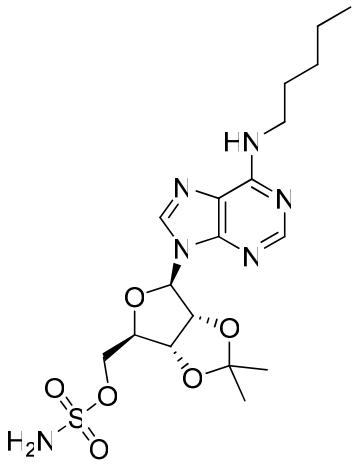
((3aR,4R,6R,6aR)-6-(6-(allylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6d)

Compound **5d** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 3.5 hours, yielding **6d** as a white solid (60%): m.p. = 71-80 °C; δ_H (400 MHz, $CDCl_3$) 1.36 (s, 3H, $C(C\underline{H}_3)_2$), 1.60 (s, 3H, $C(C\underline{H}_3)_2$), 4.25 (vbs, 2H, $HNC\underline{H}_2CHCH_2$), 4.35-4.46 (m, 2H, 5'H_2), 4.50-4.54 (m, 1H, 4'H), 5.08 (dd, *J* = 6.3 Hz and 3.0 Hz, 1H, 3'H), 5.16 (dd, *J* = 10.3 Hz and 1.5 Hz, 1H, $HNCH_2CHC\underline{H}_2$), 5.26 (dd, *J* = 17.2 Hz and 1.5 Hz, 1H, $HNCH_2CHC\underline{H}_2$), 5.36 (dd, *J* = 6.4 Hz and 2.6 Hz, 1H, 2'H), 5.92-6.02 (m, 1H, $HNCH_2C\underline{H}CH_2$), 6.01 (vbs, 2H, $\underline{H}_2NSO_3$), 6.10 (d, *J* = 2.6 Hz, 1H, 1'H), 6.14-6.21 (m, 1H, $\underline{H}NCH_2CHCH_2$), 7.94 (s, 1H, H-2), 8.34 (s, 1H, H-8); LRMS (ESI-) calcd for $[C_{16}H_{21}N_6O_6S]^-$ *m/z* = 425.12, obsd 425.30



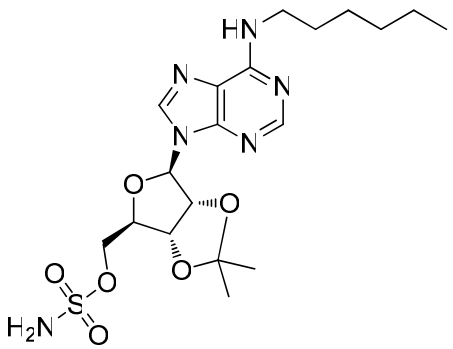
((3aR,4R,6R,6aR)-6-(6-(butylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6e)

Comound **5e** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 4 hours, yielding **6e** as a colourless oil (93%): δ_H (400 MHz, $CDCl_3$) 0.95 (t, *J* = 7.3 Hz, 3H, $HN(CH_2)_3C\underline{H}_3$), 1.38 (s, 3H, $C(C\underline{H}_3)_2$), 1.44 (sextet, *J* = 7.5 Hz, 2H, $HN(CH_2)_2C\underline{H}_2CH_3$), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 1.66 (p, 7.4 Hz, 2H, $HNCH_2C\underline{H}_2CH_2CH_3$), 3.60 (bs, 2H, $HNC\underline{H}_2(CH_2)_2CH_3$), 4.40 (dd, *J* = 11.2 Hz and 5.1 Hz, 1H, 5'H_2), 4.47 (dd, *J* = 11.2 Hz and 3.7 Hz, 1H, 5'H_2), 4.51-4.56 (m, 1H, 4'H), 5.11 (dd, *J* = 6.4 Hz and 3.1 Hz, 1H, 3'H), 5.38 (dd, *J* = 6.4 Hz, 1H, 2'H), 5.66 (bs, 2H, H_2NSO_3), 5.97 (s, 1H, NH), 6.07 (d, *J* = 2.4 Hz, 1H, 1'H), 7.91 (bs, 1H, H-2), 8.35 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{17}H_{25}N_6O_6S]^-$ *m/z* = 441.15, obsd 441.30.



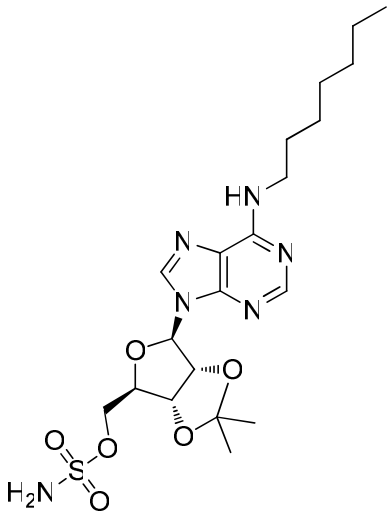
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(pentylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6f)

Compound **5f** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 4.5 hours, yielding **6f** as a white solid (68%): m.p. = 65-78 °C; δ_H (400 MHz, $CDCl_3$) 0.90 (t, *J* = 7.2 Hz, 3H, $HN(CH_2)_4C\underline{H}_3$), 1.28-1.44 (m, 4H, $HN(CH_2)_2(C\underline{H}_2)_2CH_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 1.67 (p, *J* = 7.3 Hz, 2H, $HNCH_2C\underline{H}_2(CH_2)_2CH_3$), 3.58 (bs, 2H, $HNC\underline{H}_2(CH_2)_3CH_3$), 4.39 (dd, *J* = 11.2 Hz and 5.3 Hz, 1H, 5'H_2), 4.47 (dd, *J* = 11.2 Hz and 3.7 Hz, 1H, 5'H_2), 4.51-4.54 (m, 1H, 4'H), 5.11 (dd, *J* = 6.4 Hz and 2.8 Hz, 1H, 3'H), 5.38 (dd, *J* = 6.4 Hz and 2.8 Hz, 1H, 2'H), 5.70 (bs, 2H, H_2NSO_3), 5.98 (bs, 1H, NH), 6.07 (d, *J* = 2.8 Hz, 1H, 1'H), 7.90 (s, 1H, H-2), 8.35 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{18}H_{27}N_6O_6S]^-$ *m/z* = 455.17, obsd 455.41.



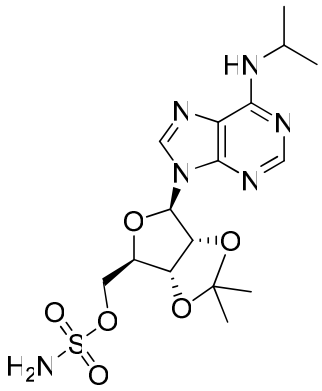
((3aR,4R,6R,6aR)-6-(6-(hexylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6g)

Compound **5g** was sulfamyl chloride as outlined in general procedure **B** for a total of 1.5 hours, yielding **6g** as a white powder (75%): m.p. = 77-85 °C; δ_H (400 MHz, $CDCl_3$) 0.88 (t, *J* = 7.06 Hz, 3H, $HN(CH_2)_5C\underline{H}_3$), 1.27-1.34 (m, 4H, $HN(CH_2)_3(C\underline{H}_2)_2CH_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.38-1.47 (m, 2H, $HN(CH_2)_4C\underline{H}_2CH_3$), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 1.66 (p, *J* = 7.41 Hz, 2H, $HNCH_2C\underline{H}_2(CH_2)_3CH_3$), 3.59 (bs, 2H, $HNC\underline{H}_2(CH_2)_4CH_3$), 4.39 (dd, *J* = 11.25 Hz and 5.13 Hz, 1H, 5'H), 4.47 (dd, *J* = 11.05 Hz and 3.65 Hz, 1H, 5'H), 4.50-4.55 (m, 1H, 4'H), 5.10 (dd, *J* = 6.55 Hz and 3.01 Hz, 1H, 3'H), 5.37 (dd, *J* = 6.45 Hz and 2.67 Hz, 1H, 2'H), 5.78 (bs, 2H, $\underline{H}_2SO_3$), 6.00 (bs, 1H, NH), 6.07 (d, *J* = 2.76 Hz, 1H, 1'H), 7.92 (s, 1H, H-2), 8.35 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{19}H_{29}N_6O_6S]^-$ *m/z* = 469.18, obsd 469.39.



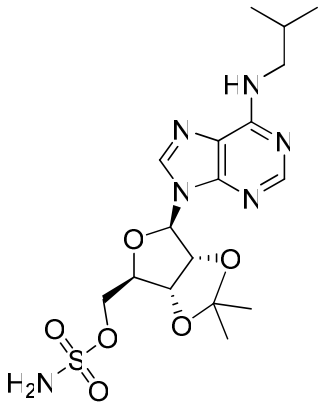
((3aR,4R,6R,6aR)-6-(6-(heptylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6h)

Compound **5h** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6h** as a colourless solid (92%): m.p. = 65-76 °C; δ_H (400 MHz, $CDCl_3$) 0.87 (t, *J* = 6.9 Hz, 3H, $HN(CH_2)_6C\underline{H}_3$), 1.18-1.48 (m, 8H, $HN(CH_2)_2(C\underline{H}_2)_4CH_3$), 1.38 (s, 3H, $C(C\underline{H}_3)_2$), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 1.67 (p, *J* = 7.3 Hz, 2H, $HNCH_2C\underline{H}_2(CH_2)_4CH_3$), 3.59 (bs, 2H, $HNC\underline{H}_2CH_2(CH_2)_4CH_3$), 4.39 (dd, *J* = 11.2 Hz and 5.1 Hz, 1H, 5'H_2), 4.47 (dd, *J* = 11.2 Hz and 3.8 Hz, 1H, 5'H_2), 4.53-4.55 (m, 1H, 4'H), 5.11 (dd, *J* = 6.4 Hz and 3.1 Hz, 1H, 3'H), 5.38 (dd, *J* = 6.4 Hz and 2.7 Hz, 1H, 2'H), 5.64 (bs, 2H, $\underline{H}_2NSO_3$), 5.96 (bs, 1H, NH), 6.07 (d, *J* = 2.6 Hz, 1H, 1'H), 7.90 (bs, 1H, H-2), 8.35 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{20}H_{30}N_5O_4]^-$ *m/z* = 483.20, obsd 483.30.



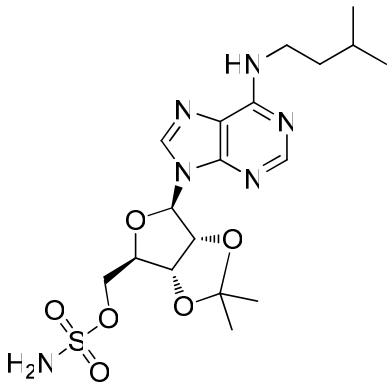
((3aR,4R,6R,6aR)-6-(6-(isopropylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6i)

Compound **5i** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 2.5 hours, yielding **6i** as a white solid (66%): m.p. > 200 (decomposes); δ_H (400 MHz, $CDCl_3$) 1.30 (d, *J* = 6.6 Hz, 6H, HNCH($C\underline{H}_3$)$_2$), 1.37 (s, 3H, C($C\underline{H}_3$)$_2$), 1.60 (s, 3H, C(CH_3)$_2$), 4.39 (dd, *J* = 11.2 Hz and 5.3 Hz, 1H, 5'H_2), 4.44-4.53 (m, 3H, 5'H_2, 4'H, HNC$\underline{H}$(CH_3)$_2$), 5.11 (dd, *J* = 6.4 Hz and 3.1 Hz, 1H, 3'H), 5.39 (dd, *J* = 6.4 Hz and 2.6 Hz, 1H, 2'H), 5.63 (bs, 2H, $\underline{H}_2NSO_3$), 5.74 (d, *J* = 7.3 Hz, 1H, $\underline{H}$NCH(CH_3)$_2$), 6.05 (d, *J* = 2.7 Hz, 1H, 1'H), 7.84 (s, 1H, H-2), 8.33 (bs, 1H, H-8). LRMS [ESI-] calcd for $[C_{16}H_{23}N_6O_6S]^-$ 427.14, obsd 427.31.



((3aR,4R,6R,6aR)-6-(6-(isobutylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6j)

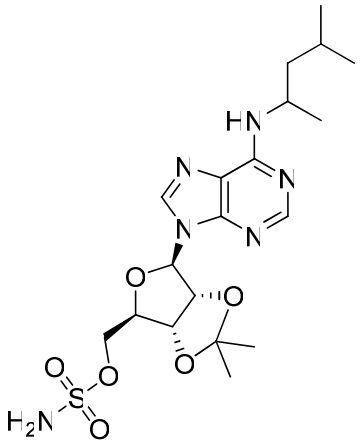
Compound **5j** was reacted with sulfamoyl choride as outlined in general procedure **B** for a total of 4.5 hours, yielding **6j** as a white solid (88%): m.p. = 92-105 °C; δ_H (400 MHz, $CDCl_3$) 0.96 (d, *J* = 6.6 Hz, 6H, $HNCH_2CH(C\underline{H}_3)_2$), 1.35 (s, 3H, $C(C\underline{H}_3)_2$), 1.58 (s, 3H, $C(CH_3)_2$), 1.93 (septet, *J* = 6.8 Hz, 1H, $HNCH_2C\underline{H}(CH_3)_2$), 3.39 (vbs, 2H, $HNC\underline{H}_2CH(CH_3)_2$), 4.34-4.45 (m, 2H, 5'$H_2$), 4.49-4.53 (m, 1H, 4'H), 5.07 (dd, *J* = 6.1 Hz and 2.6 Hz, 1H, 3'H), 5.33-5.36 (m, 1H, 2'H), 6.08 (d, *J* = 2.4 Hz, 1H, 1'H), 6.08 (bs, 1H, $\underline{H}NCH_2CH(CH_3)_2$), 6.17 (vbs, 2H, $\underline{H}_2NSO_3$), 7.87 (s, 1H, H-2), 8.31 (s, 1H, H-8); LRMS (ESI-) calcd for $[C_{17}H_{25}N_6O_6S]^-$ *m/z* = 441.15, obsd 441.30.



((3aR,4R,6R,6aR)-6-(6-(isopentylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6k)

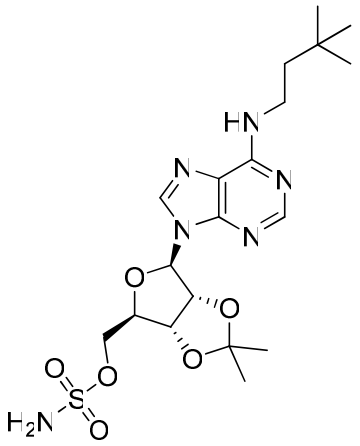
Compound **5k** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6k** as a white solid (72%): m.p. = 112-122 °C; δ_H (400 MHz, $CDCl_3$) 0.94 (d, *J* = 6.65 Hz, 6H, $HN(CH_2)_2CHC(C\underline{H}_3)_2$), 1.35 (s, 3H, $C(C\underline{H}_3)_2$), 1.54 (q, *J* = 7.3 Hz, 2H, $HNCH_2C\underline{H}_2CHC(CH_3)_2$), 1.59 (s, 3H, $C(C\underline{H}_3)_2$), 1.70 (septet, *J* = 6.7 Hz, 1H, $HN(CH_2)_2C\underline{H}C(CH_3)_2$), 3.60 (bs, 2H, $HNC\underline{H}_2CH_2CHC(CH_3)_2$), 4.35-4.45 (m, 2H, 5'$H_2$), 4.49-4.53 (m, 1H, 4'H), 5.07 (dd, *J* = 6.4 Hz

and 3.0 Hz, 1H, 3'H), 5.32 (dd, *J* = 6.4 Hz and 2.7 Hz, 1H, 2'H) 6.00 (bs, 1H, HN), 6.11 (d, *J* = 2.7 Hz, 1H, 1'H), 6.42 (bs, 2H, H_2NSO_3), 7.99 (s, 1H, H-2), 8.34 (s, 1H, H-8); LRMS (ESI-) calcd for $[C_{18}H_{27}N_6O_6S]^-$ *m/z* = 455.17, obsd 455.27.



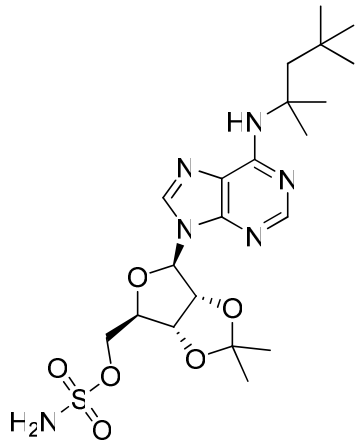
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((4-methylpentan-2-yl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6l)

Compound **5l** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 3 hours, yielding **6l** as a white solid (97%): m.p. = 72-85 °C; δ_H (400 MHz, $CDCl_3$) 0.91 (d, *J* = 3.7 Hz, 3H, $HNCH(CH_3)CH_2CH(CH_3)_2$), 0.93 (d, *J* = 3.5 Hz, 3H, $HNCH(CH_3)CH_2CH(CH_3)_2$), 1.25 (d, *J* = 6.4 Hz, 3H, $HNCH(CH_3)CH_2CH(CH_3)_2$), 1.33-1.41 (m, 1H, $HNCH(CH_3)CH_2CH(CH_3)_2$), 1.37 (s, 3H, $C(CH_3)_2$), 1.49-1.57 (m, 1H, $HNCH(CH_3)CH_2CH(CH_3)_2$), 1.61 (s, 3H, $C(CH_3)_2$), 1.66-1.75 (m, 1H, $HNCH(CH_3)CH_2CH(CH_3)_2$), 4.37-4.53 (m, 4H, 5'H_2, 4'H, $HNCH(CH_3)CH_2CH(CH_3)_2$), 5.12 (dd, *J* = 6.3 Hz and 2.8 Hz, 1H, 3'H), 5.37-5.41 (m, 1H, 2'H), 5.51 (bs, 2H, H_2NSO_3), 5.65 (bs, 1H, NH), 6.04 (d, *J* = 2.6 Hz, 1H, 1'H), 7.84 (s, 1H, H-2), 8.34 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{19}H_{29}N_6O_6S]^-$ *m/z* = 469.18, obsd 469.20.



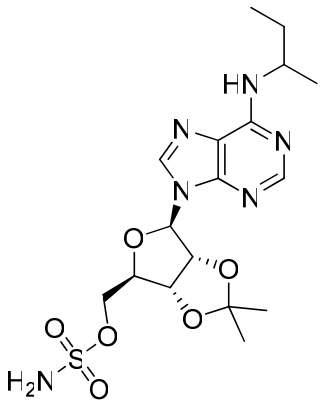
((3aR,4R,6R,6aR)-6-(6-(3,3-dimethylbutylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6m)

Compound **5m** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6m** as a colourless solid (92%): m.p. = 118-130 °C; δ_H (400 MHz, $CDCl_3$) 0.99 (s, 9H, $HN(CH_2)_2C(C\underline{H}_3)_3$), 1.39 (s, 3H, $C(C\underline{H}_3)_2$), 1.58-1.64 (m, 2H, $HNCH_2C\underline{H}_2C(CH_3)_3$), 1.61 (s, 3H, $C(CH_3)_2$), 3.62 (bs, 2H, $HNC\underline{H}_2CH_2C(CH_3)_3$), 4.39 (dd, J = 11.2 Hz and 5.1 Hz, 1H, 5'H_2), 4.47 (dd, J = 11.4 Hz and 3.5 Hz, 1H, 5'H_2), 4.52-4.57 (m, 1H, 4'H), 5.12 (dd, J = 6.4 Hz and 2.9 Hz, 1H, 3'H), 5.39 (dd, J = 6.2 Hz and 2.6 Hz, 1H, 2'H), 6.55 (vbs, 2H, $\underline{H}_2NSO_3$), 5.87 (vbs, 1H, NH), 6.08 (bs, 1H, 1'H), 7.93 (bs, 1H, H-2), 8.37 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{19}H_{29}N_6O_6S]^-$ m/z = 469.18, obsd 469.33.



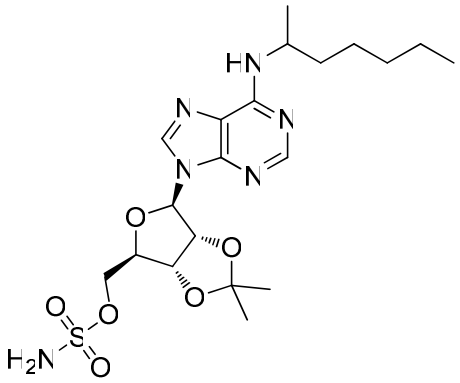
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(2,4,4-trimethylpentan-2-ylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6n)

Compound **5n** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 3 hours 40 minutes, yielding **6n** as a light-yellow oil (82%): δ_H (400 MHz, $CDCl_3$) 0.98 (s, 9H, $HNC(CH_3)_2CH_2C(C\underline{H}_3)_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.60 (bs, 6H, $HNC(C\underline{H}_3)_2CH_2C(CH_3)_3$), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 1.99-2.03 (m, 2H, $HNC(CH_3)_2C\underline{H}_2C(CH_3)_3$), 4.40 (dd, J = 12.1 Hz and 6.1 Hz, 1H, 5'H_2), 4.47-4.54 (m, 2H, 5'H_2, 4'H), 5.11 (dd, J = 6.4 Hz and 2.9 Hz, 1H, 3'H), 5.39 (dd, J = 6.4 Hz and 2.8 Hz, 1H, 2'H), 5.54 (bs, 2H, $\underline{H}_2NSO_3$), 5.80 (bs, 1H, NH), 6.04 (d, J = 2.8 Hz, 1H, 1'H), 7.89 (s, 1H, H-2), 8.34 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{21}H_{33}N_6O_6S]^-$ *m/z* = 497.22, obsd 497.28.



((3aR,4R,6R,6aR)-6-(6-(sec-butylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6o)

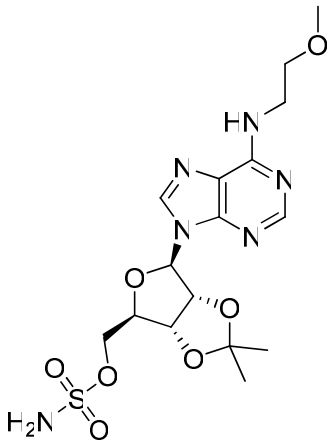
Compound **5o** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6o** as an off-white solid (82%): m.p. = 89-98 °C; δ_H (400 MHz, $CDCl_3$) 0.97 (t, *J* = 7.3 Hz, 3H, $NHCH(CH_3)CH_2C\underline{H}_3$), 1.27 (d, *J* = 6.6 Hz, 3H, $HNCH(C\underline{H}_3)CH_2CH_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.58-1.67 (m, 2H, $HNCH(CH_3)C\underline{H}_2CH_3$), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 4.32 (vbs, 1H, $HNC\underline{H}(CH_3)CH_2CH_3$), 4.37-4.53 (m, 3H, 5'$H_2$, 4'H), 5.12 (dd, *J* = 6.2 Hz and 2.9 Hz, 1H, 3'H), 5.40 (dd, *J* = 6.3 Hz and 2.8 Hz, 1H, 2'H), 5.51 (bs, 2H, $\underline{H}_2NSO_3$), 5.69 (bs, 1H, NH), 6.04 (d, *J* = 2.7 Hz, 1H, 1'H), 7.85 (s, 1H, H-2), 8.33 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{17}H_{25}N_6O_6S]^-$ 441.15, obsd 441.20.



((3aR,4R,6R,6aR)-6-(6-(heptan-2-ylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6p)

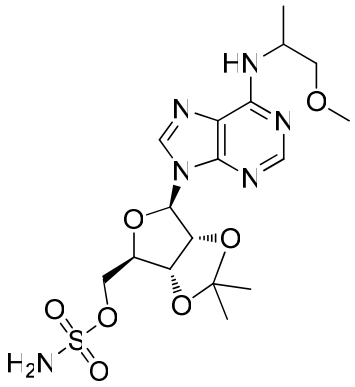
Compound **5p** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6p** as an off-white solid (63%): m.p. = 65-78 °C; δ_H (400 MHz, $CDCl_3$) 0.86 (t, *J* = 6.13, 3H, $HNCH(CH_3)(CH_2)_4C\underline{H}_3$), 1.23-1.33 (m, 9H, $HNCH(C\underline{H}_3)CH_2(C\underline{H}_2)_3CH_3$), 1.38 (s, 3H, $C(C\underline{H}_3)_2$), 1.5-1.67 (m, 2H, $HNCH(CH_3)C\underline{H}_2(CH_2)_3CH_3$), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 4.36-4.44 (m, 2H, 5'H and $HNC\underline{H}(CH_3)(CH_2)_4CH_3$), 4.46-4.54 (m, 2H, 5'H and 4'H), 5.12 (dd, *J* = 6.39 Hz and 2.75 Hz, 1H, 3'H), 5.39 (d, *J* = 6.03 Hz, 1H, 2'H), 5.50 (bs, 2H, NH_2), 5.72 (bs, 1H, NH),

6.05 (d, J = 2.63, 1H, 1'H), 7.89 (s, 1H, H-2), 8.34 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{20}H_{31}N_6O_6S]^-$ m/z = 483.20, obsd 483.18.



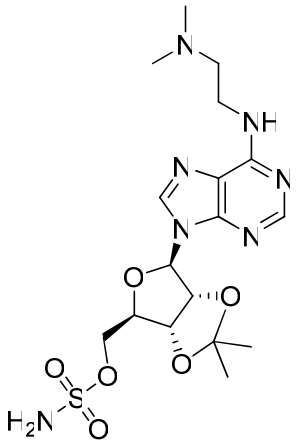
((3aR,4R,6R,6aR)-6-(6-(2-methoxyethylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6q)

Compound **5q** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 3 hours, yielding **6q** as a white solid (84%): m.p. = 52-65 °C; δ_H (400 MHz, $CDCl_3$) 1.39 (s, 3H, C($C\underline{H}_3$)$_2$), 1.62 (s, 3H, C(CH_3)$_2$), 3.39 (s, 3H, HNCH$_2$CH$_2$OC$\underline{H}_3$), 3.63 (t, J = 5.1 Hz, 2H, HNCH$_2$C$\underline{H}_2$OCH$_3$), 3.84 (bs, 2H, HNC$\underline{H}_2$CH$_2$OCH$_3$), 4.39 (dd, J = 11.2 Hz and 5.1 Hz, 1H, 5'H$_2$), 4.47 (dd, J = 11.3 Hz and 3.6 Hz, 1H, 5'H$_2$), 4.52-4.56 (m, 1H, 4'H), 5.12 (dd, J = 6.4 Hz and 3.0 Hz, 1H, 3'H), 5.41 (dd, J = 6.3 Hz and 2.7 Hz, 1H, 2'H), 5.47 (bs, 2H, $\underline{H}_2$NSO$_3$), 6.07 (d, J = 2.4 Hz, 1H, 1'H), 6.30 (bs, 1H, NH), 7.92 (s, 1H, H-2), 8.35 (s, 1H, H-8); HRMS [ESI+] calcd for $[C_{16}H_{25}N_6O_7S]^+$ m/z = 405.1186, obsd 405.1178.



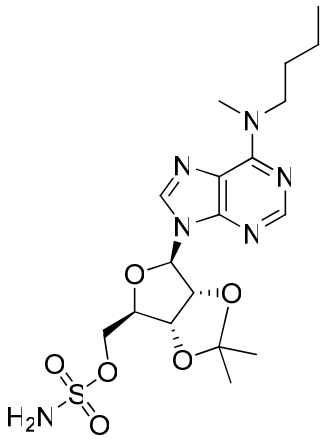
((3aR,4R,6R,6aR)-6-(6-((1-methoxypropan-2-yl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6r)

Compound **5r** was reacted with sulfamoyl chloride as outlined in general procedure **B** with a couple of modifications: 1) the reaction was stirred for a total of 3.5 hours and 2) the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and CH_2Cl_2/MeOH/NH_4OH (25/7/1). The product (**6r**) was obtained as a colourless oil (95%): δ_H (400 MHz, $CDCl_3$) 1.33 (d, *J* = 6.6 Hz, 3H, HNCH($C\underline{H}_3$)CH_2OCH_3), 1.38 (s, 3H, $C(CH_3)_2$), 1.61 (s, 3H, $C(CH_3)_2$), 3.37 (s, 3H, HNCH(CH_3)$CH_2OC\underline{H}_3$), 3.51 (d, *J* = 5.0 Hz, 2H, HNCH(CH_3)$C\underline{H}_2OCH_3$), 4.37 (dd, *J* = 11.3 Hz and 5.2 Hz, 1H, 5'H_2), 4.42-4.48 (m, 1H, 5'H_2), 4.51-4.56 (m, 1H, 4'H), 4.64 (bs, 1H, HN$C\underline{H}$(CH_3)CH_2OCH_3), 5.09-5.13 (m, 1H, 3'H), 5.37-5.42 (m, 1H, 2'H), 5.62 (bs, 2H, $\underline{H}_2NSO_3$), 6.08 (d, *J* = 2.6 Hz, 1H, 1'H), 6.20 (vbs, 1H, NH), 7.97 (bs, 1H, H-2), 8.36 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{17}H_{25}N_6O_7S]^-$ *m/z* = 457.15, obsd 457.30.



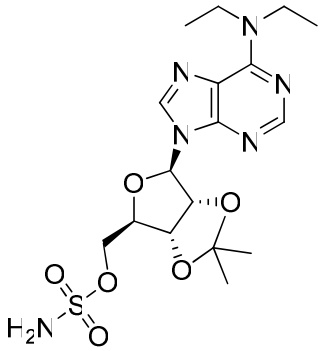
((3aR,4R,6R,6aR)-6-(6-(2-(dimethylamino)ethylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6s)

Compound **5s** was reacted with sulfamoyl chloride as outlined in general procedure **B** with a minor modification: the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and CH_2Cl_2/MeOH/NH_4OH (25/7/1). The product (**6s**) was obtained as a clear solid (30%): m.p. = 78-90 °C; δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, $C(C\underline{H}_3)_2$), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 2.39 (s, 6H, $HN(CH_2)_2N(C\underline{H}_3)_2$), 2.72 (t, *J* = 6.1 Hz, 2H, $HNCH_2C\underline{H}_2N(CH_3)_2$), 3.15-3.86 (vbs, 4H, $HNC\underline{H}_2CH_2N(CH_3)_2$, $\underline{H}_2NSO_3$), 4.36 (dd, *J* = 11.3 Hz and 5.2 Hz, 1H, 5'H_2), 4.41 (dd, *J* = 11.3 Hz and 3.6 Hz, 1H, 5'H_2), 4.51-4.55 (m, 1H, 4'H), 5.11 (dd, *J* = 6.3 Hz, 1H, 3'H), 5.45 (dd, *J* = 6.3 Hz and 2.5 Hz, 1H, 2'H), 6.10 (d, *J* = 2.4 Hz, 1H, 1'H), 6.61 (bs, 1H, $\underline{H}N(CH_2)_2N(CH_3)_2$), 7.94 (s, 1H, H-2), 8.34 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{17}H_{26}N_7O_6S]^-$ *m/z* = 456.16, obsd 456.27.



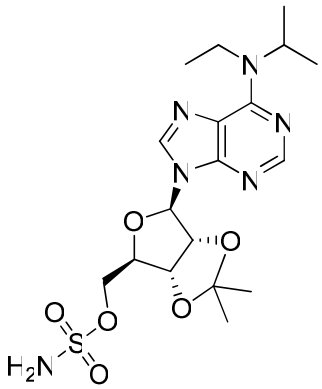
((3aR,4R,6R,6aR)-6-(6-(butyl(methyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6t)

Compound **5t** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6t** as a white solid (60%): m.p. = 75-85 °C; δ_H (400 MHz, $CDCl_3$) 0.94 (t, *J* = 7.4 Hz, 3H, $CH_3N(CH_2)_3C\underline{H}_3$), 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.37 (sextet, *J* = 7.4 Hz, 2H, $CH_3N(CH_2)C\underline{H}_2CH_3$), 1.60 (s, 3H, $C(CH_3)_2$), 1.64 (p, *J* = 7.4 Hz, 2H, $CH_3NCH_2C\underline{H}_2CH_2CH_3$), 3.40 (vbs, 2H, $CH_3NC\underline{H}_2(CH_2)_2CH_3$), 3.84-4.20 (vbs, 3H, $C\underline{H}_3N(CH_2)_3CH_3$), 4.37-4.51 (m, 3H, 5'$H_2$, 4'H), 5.12 (dd, *J* = 6.4 Hz and 3.0 Hz, 1H, 3'H), 5.38 (dd, *J* = 6.4 Hz and 2.9 Hz, 1H, 2'H), 5.65 (bs, 2H, H_2NSO_3), 6.06 (d, *J* = 2.9 Hz, 1H, 1'H), 7.86 (s, 1H, H-2), 8.29 (s, 1H, H-8); LRMS (ESI-) calcd for $[C_{18}H_{27}N_6O_6S]^-$ *m/z* = 455.17, obsd 455.28.



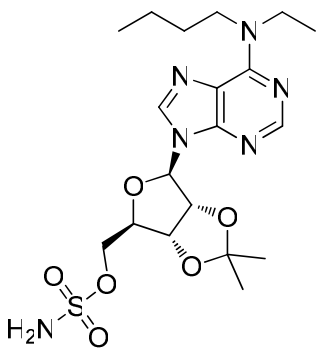
((3aR,4R,6R,6aR)-6-(6-(diethylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6u)

Compound **5u** was reacted with sulfamoyl chloride as outlined in general procedure **B** for 1.5 hours, yielding **6u** as a colourless oil (90%): δ_H (400 MHz, $CDCl_3$) 1.28 (t, *J* = 7.0 Hz, 6H, $(C\underline{H}_3CH_2)_2N$), 1.38 (s, 3H, $C(C\underline{H}_3)_2$), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 4.38-4.52 (m, 3H, 5'H_2, 4'H), 5.13 (dd, *J* = 6.4 Hz and 2.9 Hz, 1H, 3'H), 5.17 (bs, 4H, $(CH_3C\underline{H}_2)_2N$), 5.38 (dd, *J* = 6.4 Hz and 2.8 Hz, 1H, 2'H), 5.48 (bs, 2H, H_2NSO_3), 6.06 (d, *J* = 2.8 Hz, 1H, 1'H), 7.88 (s, 1H, H-2), 8.32 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{17}H_{25}N_6O_6S]^-$ *m/z* = 441.15, obsd 441.30.



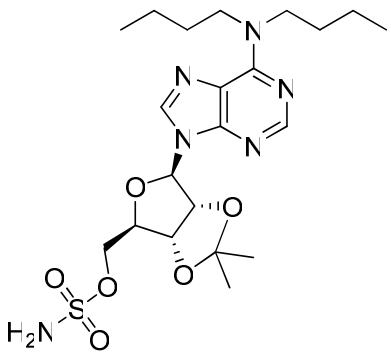
((3aR,4R,6R,6aR)-6-(6-(ethyl(isopropyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6v)

Compound **5v** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6v** as a colourless oil (92%): δ_H (400 MHz, $CDCl_3$) 1.28-1.33 (m, 9H, $(C\underline{H}_3)_2CHNCH_2C\underline{H}_3$), 1.38 (s, 3H, $C(C\underline{H}_3)_3$), 1.61 (s, 3H, $C(C\underline{H}_3)_3$), 3.82 (vbs, 2H, $(CH_3)_2CHNC\underline{H}_2CH_3$), 4.39-4.53 (m, 3H, 5'$H_2$, 4'H), 5.06 (bs, 1H, $(CH_3)_2C\underline{H}NCH_2CH_3$), 5.14 (dd, *J* = 6.4 Hz and 2.9 Hz, 1H, 3'H), 5.38 (bs, 2H, H_2NSO_3), 5.40 (dd, *J* = 6.4 Hz and 2.8 Hz, 1H, 2'H), 6.04 (d, *J* = 2.8 Hz, 1H, 1'H), 7.86 (s, 1H, H-2), 8.34 (s, 1H, H-8); LRMS [ESI-] cald for $[C_{18}H_{27}N_6O_6S]^-$ *m/z* = 455.17, obsd 455.31.



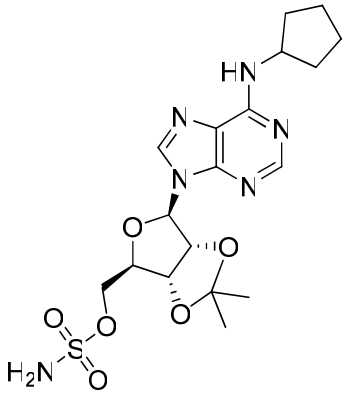
((3aR,4R,6R,6aR)-6-(6-(butyl(ethyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6w)

Compound **5w** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 3 hours, yielding **6w** as a white solid (65%): m.p. = 45-57 °C; δ_H (400 MHz, $CDCl_3$) 0.96 (t, *J* = 7.18 Hz, 3H, $(CH_2)_3C\underline{H}_3$), 1.29 (t, *J* = 6.97, 3H, $CH_2C\underline{H}_3$), 1.38 (s, 3H, $CH_3(CO_2)C\underline{H}_3$), 1.43 (m, 2H, $(CH_2)_2C\underline{H}_2CH_3$), 1.61 (s, 3H, $C\underline{H}_3(CO_2)CH_3$), 1.68 (p, *J* = 7.6, 2H, $CH_2C\underline{H}_2CH_2CH_3$), 3.96 (bm, 4H, $C\underline{H}_2CH_3$, $C\underline{H}_2(CH_2)_2CH_3$), 4.41 (m, 1H, 5'$\underline{H}_2$), 4.50 (m, 2H, 4'H, 5'$\underline{H}_2$), 5.12 (m, 1H, 3'H), 5.41 (m, 1H, 2'H), 5.43 (bs, 2H, NH_2), 6.04 (d, *J* = 2.82 Hz, 1H, 1'H), 7.87 (s, 1H, H-2), 8.36 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{19}H_{29}N_6O_6S]^-$ *m/z* = 469.18, obsd 469.26.



((3aR,4R,6R,6aR)-6-(6-(dibutylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6x)

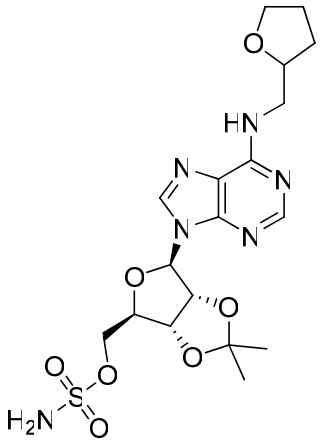
Compound **5x** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 1.5 hours, yielding **6x** as a light yellow oil (83%): δ_H (400 MHz, $CDCl_3$) 0.95 (t, *J* = 7.3 Hz, 6H, ($C\underline{H}_3CH_2CH_2CH_2)_2N$), 1.38 (s, 3H, $C(C\underline{H}_3)_2$), 1.40 (sextet, *J* = 7.4 Hz, 4H, ($CH_3C\underline{H}_2CH_2CH_2)_2N$), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 1.66 (p, *J* = 7.6 Hz, 4H, ($CH_3CH_2C\underline{H}_2CH_2)_2N$), 3.55-4.28 (vbm, 4H, ($CH_3CH_2CH_2C\underline{H}_2)_2N$), 4.37-4.54 (m, 3H, 5'$H_2$, 4'H), 5.14 (dd, *J* = 6.4 Hz and 3.1 Hz, 1H, 3'H), 5.27 (bs, 2H, H_2NSO_3), 5.41 (dd, *J* = 6.4 Hz and 2.9 Hz, 1H, 2'H), 6.01 (d, *J* = 2.9 Hz, 1H, 1'H), 7.81 (s, 1H, H-2), 8.31 (s, 1H, H-8); LRMS [ESI-] calcd for [$C_{21}H_{33}N_6O_6S$] *m/z* = 497.22, obsd 497.35.



((3aR,4R,6R,6aR)-6-(6-(cyclopentylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6y)

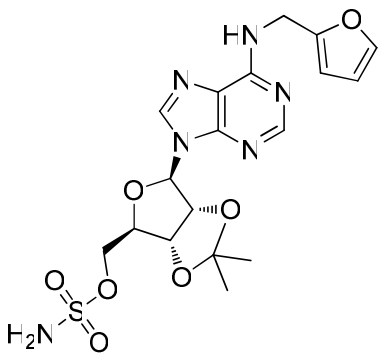
Compound **5y** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 3 hours, yielding **6y** as an off-white solid (83%): m.p. = 98-111 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, $C(C\underline{H}_3)_2$), 1.50-1.82 (m, 6H, cyclopentyl), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 2.11 (sextet, *J* = 6.3 Hz, 2H, cyclopentyl), 4.34-4.54 (m, 3H, 5'H_2, 4'H), 4.58 (bs, 1H, cyclopentyl), 5.12 (dd, *J* = 6.3 Hz and 3.1 Hz, 1H, 3'H), 5.39 (dd, *J* = 6.3 Hz and 2.7 Hz, 1H, 2'H), 5.56 (vbs, 2H,

$\underline{H_2}NSO_3$), 5.86 (bs, 1H, NH), 6.05 (d, *J* = 2.7 Hz, 1H, 1'H), 7.84 (s, 1H, H-2), 8.34 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{18}H_{25}N_6O_6S]^-$ *m/z* = 453.15, obsd 453.14.



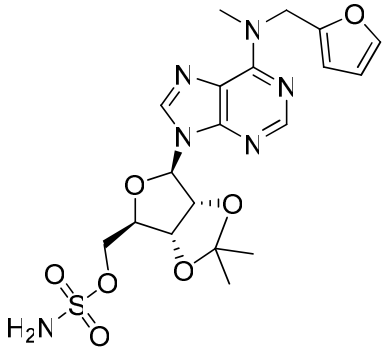
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((tetrahydrofuran-2-yl)methylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6z)

Compound **5z** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 2.5 hours, yielding **6z** as a white solid (84%): m.p. = 62-75 °C; δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, $C(C\underline{H_3})_2$), 1.58-1.68 (m, 1H, tetrahydrofuran), 1.61 (s, 3H, $C(C\underline{H_3})_2$), 1.87-1.97 (m, 2H, tetrahydrofuran), 1.98-2.08 (m, 1H, tetrahydrofuran), 3.60 (bs, 1H, tetrahydrofuran), 3.73-3.93 (m, 3H, $C\underline{H_2}$tetrahydrofuran, tetrahydrofuran), 4.10-4.17 (m, 1H, tetrahydrofuran), 4.37 (dd, *J* = 11.1 Hz and 5.2 Hz, 1H, 5'H_2), 4.44 (dd, *J* = 11.1 Hz and 3.8 Hz, 1H, 5'H_2), 4.51-4.55 (m, 1H, 4'H), 5.10 (dd, *J* = 6.2 Hz and 2.9 Hz, 1H, 3'H), 5.37-5.41 (m, 1H, 2'H), 5.79 (bs, 2H, $\underline{H_2}NSO_3$), 6.08 (d, *J* = 2.6 Hz, 1H, 1'H), 6.33 (bs, 1H, NH), 7.91 (s, 1H, H-2), 8.32 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{18}H_{25}N_6O_7S]^-$ *m/z* = 469.16, obsd 469.20.



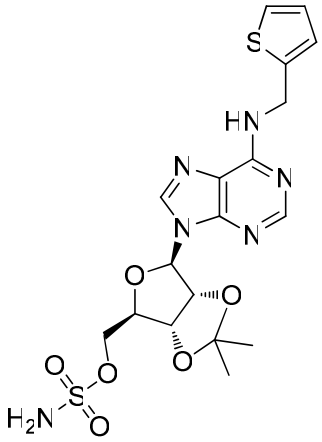
((3aR,4R,6R,6aR)-6-(6-((furan-2-ylmethyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6aa)

Compound **5aa** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 2.5 hours, yielding **6aa** as an off-white solid (69%): m.p. = 88-100 °C; δ_H (400 MHz, $CDCl_3$) 1.34 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.58 (s, 3H, C(C<u>H</u>$_3$)$_2$), 4.31-4.54 (m, 3H, 5'H_2, 4'H), 4.73-4.90 (m, 2H, HNC<u>H</u>$_2$furan), 5.05 (dd. *J* = 6.2 Hz and 2.8 Hz, 1H, 3'H), 5.31 (dd, *J* = 6.3 Hz and 2.3 Hz, 1H, 2'H), 6.1 (d, *J* = 2.3 Hz, 1H, 1'H), 6.17 (bs, 2H, <u>H</u>$_2$NSO$_3$), 6.26-6.30 (m, 2H, furan), 6.48 (bs, 1H, <u>H</u>N), 7.33 (s, 1H, furan), 7.95 (s, 1H, H-2), 8.37 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{18}H_{21}N_6O_7S]^-$ *m/z* = 465.12, obsd 465.27.



((3aR,4R,6R,6aR)-6-(6-((furan-2-ylmethyl)(methyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ab)

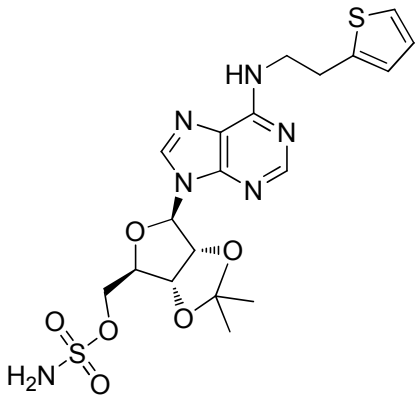
Compound **5ab** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 2.5 hours, yielding **6ab** as a white solid (79%): m.p. > 130 °C (decomposes); δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, $C(CH_3)_2$), 1.60 (s, 3H, $C(CH_3)_2$), 3.42 (bs, 3H, $C\underline{H}_3$Nfurfuryl), 4.34-4.52 (m, 3H, 5'H_2, 4'H), 5.11 (dd, *J* = 6.4 Hz and 3.1 Hz, 1H, 3'H), 5.38 (dd, *J* = 6.4 Hz and 2.8 Hz, 1H, 2'H), 5.10-5.41 (vbs, 2H, $CH_3NC\underline{H}_2$furan), 5.61 (bs, 2H, $\underline{H}_2NSO_3$), 6.09 (d, *J* = 2.8 Hz, 1H, 1'H), 6.26-6.30 (m, 2H, furan), 7.33-7.34 (m, 1H, furan), 7.92 (s, 1H, H-2), 8.35 (s, 1H, H-8); LRMS (ESI-) calcd for $[C_{19}H_{23}N_6O_7S]^-$ *m/z* = 479.13, obsd 479.27.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((thiophen-2-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ac)

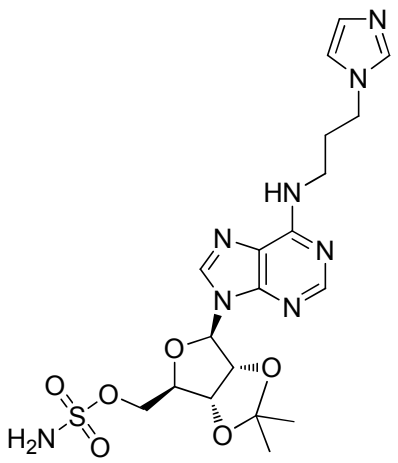
Compound **5ac** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 3 hours, yielding **6ac** as a white solid (80%): m.p. = 93-105 °C; δ_H (400 MHz, $CDCl_3$) 1.35 (s, 3H, $C(C\underline{H}_3)_2$), 1.59 (s, 3H, $C(C\underline{H}_3)_2$), 4.32 (dd, *J* = 11.2 Hz and 5.1 Hz, 1H, 5'H_2), 4.38 (dd, *J* = 11.1 Hz and 3.6 Hz, 1H, 5'H_2), 4.47-4.51 (m, 1H, 4'H), 4.97 (bs, 2H, $C\underline{H}_2$thiophene), 5.05 (dd, *J* = 6.4 Hz and 2.9 Hz, 1H, 3'H), 5.33 (dd, *J* = 6.2 Hz and 2.6 Hz, 1H, 2'H), 5.98 (bs, 2H, $\underline{H}_2NSO_3$), 6.08 (d, *J* = 2.6 Hz, 1H, 1'H), 6.63 (vbs, 1H, NH), 6.91 (dd, *J* = 5.1 Hz and 3.5 Hz, 1H, thiophene), 7.03 (d, *J* = 3.5 Hz, 1H, thiophene), 7.17 (dd, *J* = 5.1 Hz and 1.1 Hz, 1H,

thiophene), 7.89 (s, 1H, H-2), 8.38 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{18}H_{21}N_6O_6S_2]^-$ *m/z* = 481.09, obsd 481.16.



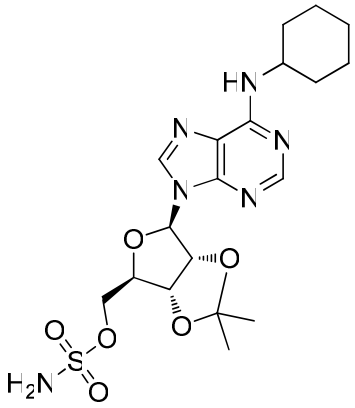
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((2-(thiophen-2-yl)ethyl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ad)

Compound **5ad** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6ad** as an off-white solid (83%): m.p. = 87-100 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.61 (s, 3H, C(C$\underline{H}_3$)$_2$), 3.19 (t, *J* = 6.8 Hz, 2H, HNCH_2C$\underline{H}_2$thiophene), 3.91 (bs, 2H, HNC$\underline{H}_2$CH_2thiophene), 4.37 (dd, *J* = 11.2 Hz and 5.2 Hz, 1H, 5'H_2), 4.44 (dd, *J* = 11.2 Hz and 3.7 Hz, 1H, 5'H_2), 4.50-4.54 (m, 1H, 4'H), 5.09 (dd, *J* = 6.3 Hz and 3.0 Hz, 1H, 3'H), 5.37 (dd, *J* = 6.4 Hz and 2.7 Hz, 1H, 2'H), 5.76 (bs, 2H, $\underline{H}_2NSO_3$), 6.08 (d, *J* = 2.6 Hz, 1H, 1'H), 6.20 (bs, 1H, $\underline{H}$NCH_2CH_2thiophene), 6.87 (d, *J* = 3.3 Hz, 1H, thiophene), 6.92 (dd, *J* = 5.0 Hz and 3.4 Hz, 1H, thiophene), 7.14 (dd, *J* = 5.2 Hz and 1.4 Hz, 1H, thiophene), 7.92 (s, 1H, H-2), 8.36 (bs, 1H, H-8). LRMS [ESI-] calcd for $[C_{19}H_{24}N_6O_6S_2]^-$ *m/z* = 495.11, obsd 495.20.



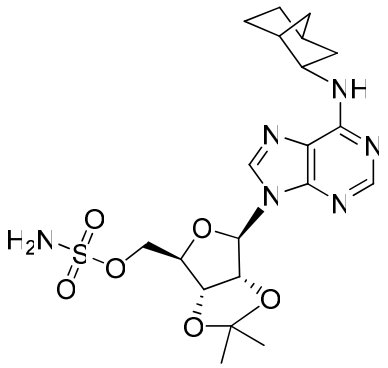
((3aR,4R,6R,6aR)-6-(6-((3-(1H-imidazol-1-yl)propyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ae)

Compound **5ae** was reacted with sulfamoyl chloride as outlined in general procedure **B** with a couple of minor modifications: 1) the reaction was carried out for a total of 4 hours and 2) the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and CH_2Cl_2/MeOH/H_2O (65/25/4)**.** The product (**6ae**) was obtained as a colourless solid (70%): m.p. = 54-68 °C; δ_H (400 MHz, MeOD) 1.39 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.60 (s, 3H, C(C$\underline{H}_3$)$_2$), 2.19 (p, *J* = 6.9 Hz, 2H, NHCH$_2$C$\underline{H}_2$CH$_2$), 3.61 (bs, 2H, NC$\underline{H}_2$(CH$_2$)$_2$), 4.18 (t, *J* = 6.9 Hz, 2H, NH(CH$_2$)$_2$C$\underline{H}_2$), 4.26 (dd, *J* = 10.7 Hz and 5.3 Hz, 1H, 5'H$_2$), 4.32 (dd, *J* = 10.8 Hz and 4.5 Hz, 1H, 5'H$_2$), 4.50-4.54 (m, 1H, 4'H), 5.13 (dd, *J* = 6.2 Hz and 2.8 Hz, 1H, 3'H), 5.43 (dd, *J* = 6.2 Hz and 2.5 Hz, 1H, 2'H), 6.24 (d, *J* = 2.4 Hz, 1H, 1'H), 7.05 (bs, 1H, imidazole), 7.25 (bs, 1H, imidazole), 7.86 (bs, 1H, imidazole), 8.23 (s, 1H, H-2), 8.27 (bs, 1H, H-8); (LRMS [ESI-] calcd for $[C_{19}H_{25}N_8O_6S]^-$ *m/z* = 493.16, obsd 493.25.



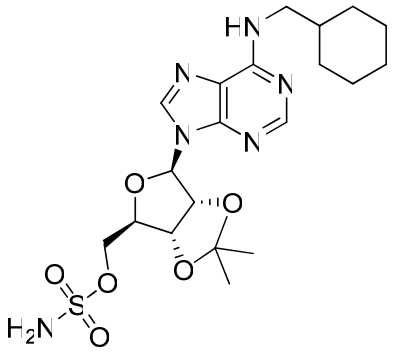
((3aR,4R,6R,6aR)-6-(6-(cyclohexylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6af)

Compound **5af** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 4 hours, yielding **6af** as an off-white solid (80%): m.p. > 220 °C (decomposes); δ_H (400 MHz, $CDCl_3$) 1.13-1.50 (m, 5H, cyclohexyl), 1.60-1.70 (m, 1H, cyclohexyl), 1.72-1.82 (m, 2H, cyclohexyl), 1.94-2.09 (m, 2H, cyclohexyl), 1.34 (s, 3H, $C(C\underline{H}_3)_2$), 1.58 (s, 3H, $C(CH_3)_2$), 4.07-4.26 (bm, 1H, cyclohexyl), 4.34-4.60 (m, 3H, 5'H_2, 4'H), 5.07 (dd, *J* = 6.4 Hz, 2.9 Hz, 1H, 3'H), 5.30 (dd, *J* = 6.3 Hz and 2.7 Hz, 1H, 2'H), 5.91 (bs, 1H, N<u>H</u>), 6.11 (d, *J* = 2.7 Hz, 1H, 1'H), 6.47 (bs, 2H, $\underline{H}_2NSO_3$), 8.01 (s, 1H, H-2), 8.33 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{19}H_{27}N_6O_6S]^-$ *m/z* = 467.17, obsd 467.25.



((3aR,4R,6R,6aR)-6-(6-((2R,4S)-bicyclo[2.2.1]heptan-2-ylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ag)

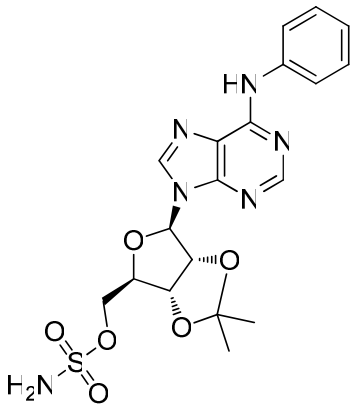
Compound **5ag** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 3 hours, yielding **6ag** as a white solid (90%): m.p. = 131-145 °C; δ_H (400 MHz, $CDCl_3$) 1.13-1.27 (m, 2H, norborane), 1.31-1.41 (m, 2H, norborane), 1.37 (s, 3H, $C(CH_3)_2$, 1.43-1.59 (m, 3H, norborane), 1.60 (s, 3H, $C(C\underline{H}_3)_2$), 1.87-1.94 (m, 2H, norborane), 2.31-2.35 (m, 1H, norborane), 4.04 (bs, 1H, norborane), 4.38 (dd, *J* = 11.2 Hz and 5.3 Hz, 1H, 5'H_2), 4.43-4.48 (m, 1H, 5'H_2), 4.52 (q, *J* = 3.9 Hz, 1H, 4'H), 5.10 (dd, *J* = 6.3 Hz and 3.0 Hz, 1H, 3'H), 5.37 (dt, *J* = 6.4 Hz and 2.1 Hz, 1H, 2'H), 5.80 (vbs, 3H, $\underline{H}_2NSO_3$, NH), 6.06 (d, *J* = 2.6 Hz, 1H, 1'H), 7.89 (s, 1H, H-2), 8.35 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{20}H_{27}N_6O_6S]^-$ *m/z* = 479.17, obsd 479.24.



((3aR,4R,6R,6aR)-6-(6-(cyclohexylmethylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ah)

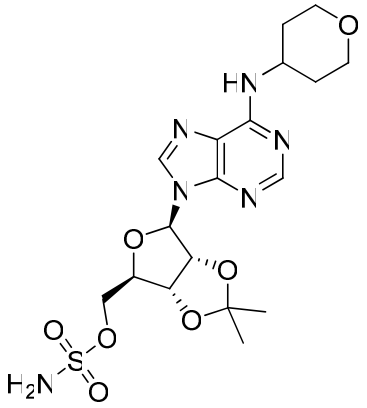
Compound **5ah** was reacted with sulfamoyl chloride as outlined in generla procedure **B** for a total of 1.5 hours, yielding **6ah** as a light-yellow oil (96%): δ_H (400 MHz, $CDCl_3$) 0.95-1.06 (m, 2H, cyclohexyl), 1.14-1.30 (m, 3H, cyclohexyl), 1.38 (s, 3H, $C(C\underline{H}_3)_2$), 1.59-1.85 (m, 6H, cyclohexyl), 1.61 (s, 3H, $C(C\underline{H}_3)_2$), 3.45 (bs, 2H, $HNC\underline{H}_2$cyclohexyl), 4.37-4.54 (m, 3H, 5'H_2,

4'H), 5.11 (dd, *J* = 6.3 Hz and 3.1 Hz, 1H, 3'H), 5.39 (dd, *J* = 6.4 Hz and 2.6 Hz, 1H, 2'H), 5.58 (bs, 2H, H_2NSO_3), 5.97 (bs, 1H, OH), 6.05 (d, *J* = 2.6 Hz, 1H, 1'H), 7.85 (s, 1H, H-2), 8.34 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{20}H_{29}N_6O_6S]^-$ *m/z* = 481.18, obsd 481.29.



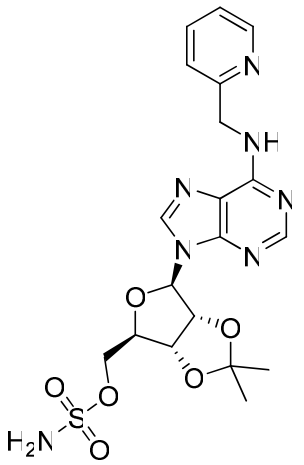
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(phenylamino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ai)

Compound **5ai** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6ai** as an off-white solid (89%): m.p. > 200°C (decomposes); δ_H (400 MHz, $CDCl_3$) 1.36 (s, 3H, $C(C\underline{H}_3)_2$), 1.59 (s, 3H, $C(C\underline{H}_3)_2$), 4.36 (dd, *J* = 11.0 Hz and 5.0 Hz, 1H, 5'H_2), 4.41 (dd, *J* = 11.0 Hz and 3.5 Hz, 1H, 5'H_2), 4.53-4.56 (m, 1H, 4'H), 5.08 (dd, *J* = 6.3 Hz and 2.8 Hz, 1H, 3'H), 5.34 (dd, *J* = 6.3 Hz and 2.3 Hz, 1H, 2'H), 5.93 (bs, 2H, $\underline{H}_2NSO_3$), 6.14 (d, *J* = 2.3 Hz, 1H, 1'H), 7.10 (t, *J* = 7.5 Hz, 1H, phenyl), 7.33 (t, *J* = 7.8 Hz, 2H, phenyl), 7.72 (d, *J* = 8.1 Hz, 2H, phenyl), 8.10 (s, 1H, H-2), 8.20 (bs, 1H, NH), 8.47 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{19}H_{21}N_6O_6S]^-$ *m/z* = 461.12, obsd 461.20.



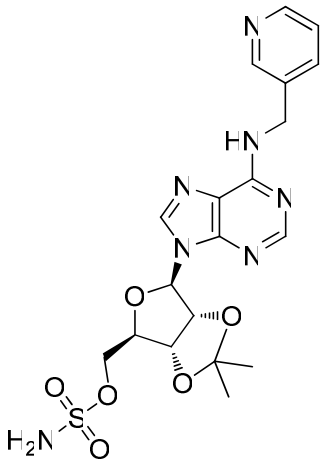
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((tetrahydro-2H-pyran-4-yl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6aj)

Compound **5aj** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 3 hours, yielding **6aj** as a white solid (76%): m.p. > 220 °C (decomposes); δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.58-1.69 (m, 2H, tetrahydropyran), 1.61 (s, 3H, C(C<u>H</u>$_3$)$_2$), 2.01-2.08 (m, 2H, tetrahydropyran), 3.57 (td, *J* = 11.7 Hz and 2.1 Hz, 2H, tetrahydropyran), 3.98-4.05 (m, 2H, tetrahydropyran), 4.37-4.55 (m, 4H, 5'H_2, 4'H, 1H-tetrahydropyran), 5.12 (dd, *J* = 6.3 Hz and 3.2 Hz, 1H, 3'H), 5.40 (dd, *J* = 6.4 Hz and 2.8 Hz, 1H, 2'H), 5.45 (bs, 2H, <u>H</u>$_2$NSO$_3$), 5.93 (bs, 1H, NH), 6.06 (dd, *J* = 2.6 Hz, 1H, 1'H), 7.87 (s, 1H, H-2), 8.34 (bs, 1H, H-8); Chemical Formula: $C_{18}H_{26}N_6O_7S$ Exact Mass: 470.16.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((pyridin-2-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ak)

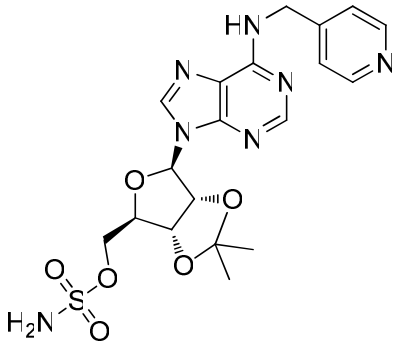
Compound **5ak** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 1.5 hours, yielding **6ak** as a white solid (84%): m.p. = 83-93 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C($C\underline{H}_3$)$_2$), 1.61 (s, 3H, C(CH_3)$_2$), 1.82 (vbs, 1H, NH), 4.36-4.45 (m, 2H, 5'H_2), 4.51-4.55 (m, 1H, 4'H), 4.90 (bs, 2H, $C\underline{H}_2$pyridine), 5.10 (dd, *J* = 6.3 Hz and 3.0 Hz, 1H, 3'H), 5.41 (dd, *J* = 6.3 Hz, 1H, 2'H), 5.95 (bs, 2H, $\underline{H}_2NSO_3$), 6.90 (d, *J* = 2.6 Hz, 1H, 1'H), 7.18 (dd, *J* = 7.5 Hz and 5.1 Hz, 1H, pyridine), 7.32 (d, *J* = 7.7 Hz, 1H, pyridine), 7.64 (td, *J* = 7.7 Hz and 1.7 Hz, 1H, pyridine), 7.89 (s, 1H, H-2), 8.33 (s, 1H, H-8), 8.53 (d, *J* = 5.0 Hz, 1H, pyridine); LRMS [ESI-] calcd for $[C_{19}H_{22}N_7O_6S]^-$ *m/z* = 476.13, obsd 476.13.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((pyridin-3-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6al)

Compound **5al** was reacted with sulfamoyl chloride as outlined in general procedure **B** with a couple of modifications: 1) the reaction was stirred for a total of 3 hours and 2) the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and CH_2Cl_2/MeOH/NH_4OH (25/7/1). The product (**6al**) was obtained as a yellow solid (72%): m.p.

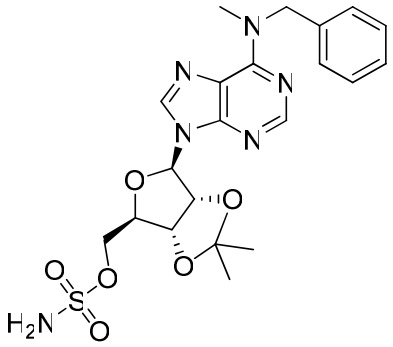
= 78-91 °C; δ_H (400 MHz, $CDCl_3$) 1.35 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.59 (s, 3H, C(C$\underline{H}_3$)$_2$), 2.33 (vbs, 2H, $\underline{H}_2NSO_3$), 4.33 (dd, *J* = 11.0 Hz and 5.1 Hz, 1H, 5'H_2), 4.39 (dd, 11.1 Hz and 3.6 Hz, 1H, 5'H_2), 4.49-4.53 (m, 1H, 4'H), 4.83 (bs, 2H, C$\underline{H}_2$pyridine), 5.06 (dd, *J* = 6.2 Hz and 2.8 Hz, 1H, 3'H), 5.35 (dd, *J* = 6.2 Hz and 2.2 Hz, 1H, 2'H), 6.11 (d, *J* = 2.6 Hz, 1H, 1'H), 6.94 (bs, 1H, NH), 7.23 (dd, *J* = 7.7 Hz and 5.0 Hz, 1H, pyridine), 7.73 (d, *J* = 7.9 Hz, 1H, pyridine), 7.90 (s, 1H, H-2), 8.33 (bs, 1H, H-8), 8.44 (d, *J* = 4.6 Hz, 1H, pyridine), 8.58 (s, 1H, pyridine); LRMS [ESI-] calcd for $[C_{19}H_{22}N_7O_6S]^-$ *m/z* = 476.13, obsd 476.25.



((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-((pyridin-4-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6am)

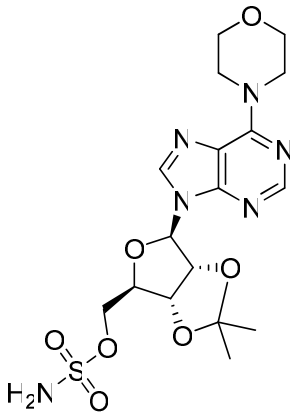
Compound **5am** was reacted with sulfamoyl chloride as outlined in general procedure **B** with a couple of minor modifications: 1) the reaction was carried out for a total of 5 hours and 2) the product was purified by silica gel column using a Biotage Isolera One set with a gradient of CH_2Cl_2 and CH_2Cl_2/MeOH/NH_4OH (25/7/1). The product (**6am**) was obtained as a beige solid (60%): m.p. > 140 °C (decomposes); δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.61 (s, 3H, C(C$\underline{H}_3$)$_2$), 4.38 (dd, *J* = 11.2 Hz and 5.3 Hz, 1H, 5'H_2), 4.44 (dd, *J* = 11.2 Hz and 3.9 Hz, 1H, 5'H_2), 4.51-4.54 (m, 1H, 4'H), 4.87 (bs, 2H, C$\underline{H}_2$pyridine), 5.11 (dd, *J* = 6.2 Hz, 1H, 3'H), 5.39 (dd, *J* = 6.2 Hz and 2.7 Hz, 1H, 2'H), 5.67 (bs, 2H, $\underline{H}_2NSO_3$), 6.08 (d, *J* = 2.6 Hz, 1H, 1'H), 6.62

(t, J = 6.2 Hz, 1H, NH), 7.24-7.27 (m, 2H, pyridine), 7.86 (s, 1H, H-2), 8.35 (bs, 1H, H-8), 8.50 (dd, J = 4.4 Hz and 1.6 Hz, 2H, pyridine); LRMS [ESI-] calcd for $[C_{19}H_{22}N_7O_6S]^-$ m/z = 476.13, obsd 467.25.



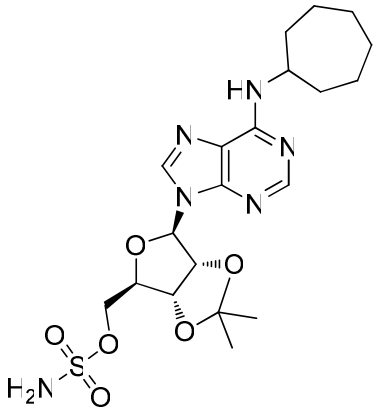
((3aR,4R,6R,6aR)-6-(6-(benzyl(methyl)amino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6an)

Compund **5an** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6an** as a white solid (93%): m.p. = 80-93 °C; δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.61 (s, 3H, C(C$\underline{H}_3$)$_2$), 3.38 (vbs, 3H, C$\underline{H}_3$NCH$_2$phenyl), 4.39 (dd, J = 11.1 Hz and 5.2 Hz, 1H, 5'H$_2$), 4.47 (dd, J = 11.1 Hz and 3.7 Hz, 1H, 5'H$_2$), 4.49-4.53 (m, 1H, 4'H), 5.06-5.62 (vbs, 2H, CH$_3$NC$\underline{H}_2$phenyl), (5.12 (dd, J = 6.4 Hz and 3.1 Hz, 1H, 3'H), 5.41 (dd, J = 6.4 Hz and 2.8 Hz, 1H, 2'H), 5.59 (bs, 2H, $\underline{H}_2$NSO$_3$), 6.08 (d, J = 2.8 Hz, 1H, 1'H), 7.23-7.34 (m, 5H, phenyl), 7.90 (s, 1H, H-2), 8.39 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{21}H_{25}N_6O_6S]^-$ m/z = 489.15, obsd 489.22.



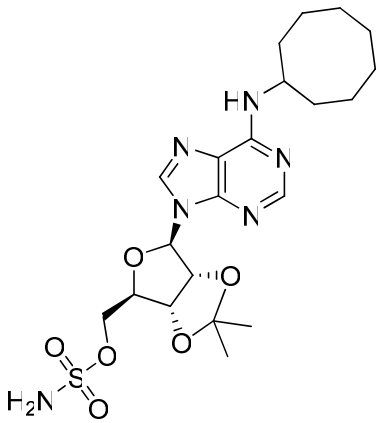
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-morpholino-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ao)

Compound **5ao** was reacted with sufamoyl chloride as outlined in general procedure **B** for a total of 3 hours, yielding **6ao** as a white solid (96%): m.p. = 89-98 °C; δ_H (400 MHz, $CDCl_3$) 1.39 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.61 (s, 3H, C(C<u>H</u>$_3$)$_2$), 3.80-3.83 (m, 4H, C<u>H</u>$_2$OC<u>H</u>$_2$ morpholine), 4.28 (bs, 4H, C<u>H</u>$_2$NC<u>H</u>$_2$ morpholine), 4.38-4.52 (m, 3H, 5'H$_2$, 4'H), 5.14 (dd, *J* = 6.4 Hz and 3.1 Hz, 1H, 3'H), 5.19 (bs, 2H, H_2NSO_3), 5.41 (dd, *J* = 6.4 Hz and 2.8 Hz, 1H, 2'H), 6.06 (d, *J* = 2.8 Hz, 1H, 1'H), 7.84 (s, 1H, H-2), 8.32 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{17}H_{23}N_6O_7S]^-$ *m/z* = 455.13, obsd 455.22.



((3aR,4R,6R,6aR)-6-(6-(cycloheptylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ap)

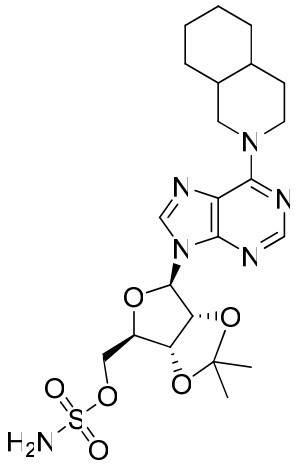
Compound **5ap** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6ap** as an off-white solid (89%): m.p. = 110-123 °C; δ_H (400 MHz, $CDCl_3$) 1.37 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.53-1.71 (m, 10H, cycloheptyl), 1.61 (s, 3H, C(C<u>H</u>$_3$)$_2$), 2.03-2.11 (m, 2H, cycloheptyl), 4.37 (bs, 1H, cycloheptyl), 4.39 (dd, *J* = 10.79 Hz and 5.15 Hz, 1H, 5'H), 4.45-4.53 (m, 2H, 5'H and 4'H), 5.12 (dd, *J* = 6.37 Hz and 3.01 Hz, 1H, 3'H), 5.40 (dd, *J* = 6.49 Hz and 2.72 Hz, 1H, 2'H), 5.51 (s, 2H, NH_2), 5.84 (d, *J* = 8.09, 1H, NH), 6.04 (d, *J* = 2.71 Hz, 1H, 1'H), 7.84 (s, 1H, H-2), 8.34 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{20}H_{29}N_6O_6S]^-$ *m/z* = 481.18, obsd 481.35.



((3aR,4R,6R,6aR)-6-(6-(cyclooctylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6aq)

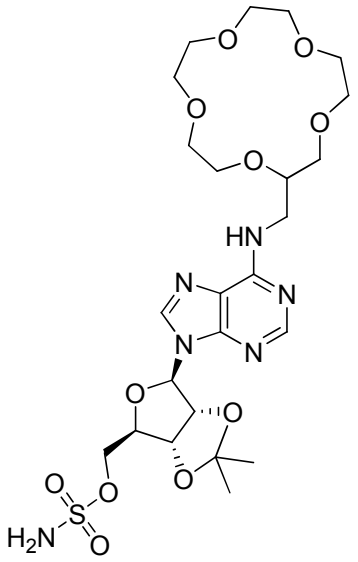
Compound **5aq** was reacted with sulfamoyl chloride as outlined in general procedure **B**, yielding **6aq** as a white solid (98%): m.p. = 94-107 °C; δ_H (400 MHz, $CDCl_3$) 1.38 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.61 (s, 3H, C(C<u>H</u>$_3$)$_2$), 1.53-1.77 (m, 12H, cyclooctyl), 1.92-2.01 (m, 2H, cyclooctyl), 4.38 (vbs, 1H,

cyclooctyl), 4.39 (dd, J = 11.2 Hz and 5.1 Hz, 1H, 5'H_2), 4.47 (dd, J = 11.2 Hz and 3.7 Hz, 1H, 5'H_2), 4.50-4.54 (m, 1H, 4'H), 5.11 (dd, J = 6.4 Hz and 3.1 Hz, 1H, 3'H), 5.39 (dd, J = 6.4 Hz and 2.8 Hz, 1H, 2'H), 5.55 (bs, 2H, H_2SO_3), 5.89 (bs, 1H, NH), 6.05 (d, J = 2.6 Hz, 1H, 1'H), 7.87 (bs, 1H, H-2), 8.34 (bs, 1H, H-8); LRMS [ESI-] calcd for $[C_{21}H_{31}N_6O_6S]^-$ *m/z* = 495.20, obsd 495.33.



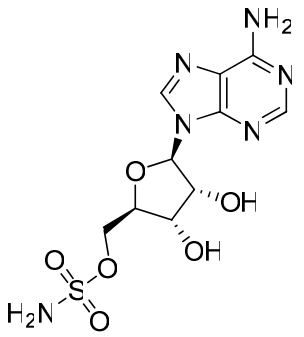
((3aR,4R,6R,6aR)-2,2-dimethyl-6-(6-(octahydroisoquinolin-2(1H)-yl)-9H-purin-9-yl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl sulfamate (6ar)

Compound **5ar** was reacted with sulfamoyl chloride as outlined in general procedure **B** for a total of 3.5 hours, yielding **6ar** as an off-white solid (76%): m.p. = 120-131 °C; δ_H (400 MHz, $CDCl_3$) 0.92-1.08 (m, 2H, perhydroisoquinoline), 1.17-1.35 (m, 6H, perhydroisoquinoline), 1.38 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.61 (s, 3H, C(C$\underline{H}_3$)$_2$), 1.63-1.79 (m, 4H, perhydroisoquinoline), 2.62 (bs, 1H, perhydroisoquinoline), 3.03 (bs, 1H, perhydroisoquinoline), 4.41 (dd, J = 12.1 Hz and 6.2 Hz, 1H, 5'H_2), 4.46-4.52 (m, 2H, 5'H_2, 4'H), 5.13 (dd, J = 6.4 Hz and 3.1 Hz, 1H, 3'H), 5.38 (bs, 2H, $\underline{H}_2NSO_3$), 5.40 (dd, J = 6.4 Hz and 2.8 Hz, 1H, 2'H), 5.05-5.60 (vbm, 2H, perhydroisoquinoline), 6.03-6.05 (m, 1H, 1'H), 7.85 (s, 1H, H-2), 8.30 (s, 1H, H-8); LRMS [ESI-] calcd for $[C_{22}H_{31}N_6O_6S]^-$ *m/z* = 507.20, obsd 507.35.



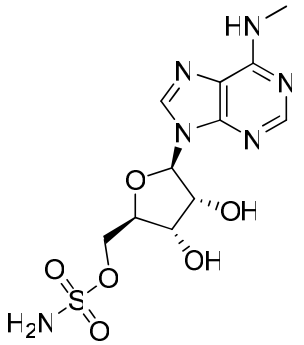
((3aR,4R,6R,6aR)-6-(6-((1,4,7,10,13-pentaoxacyclopentadecan-2-yl)methylamino)-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl (6as)

Compound **5as** was reacted with sulfamoyl chloride as outlined in general procedure **B** with some minor modifications, the reaction mixture was stirred for 3 hours after the addition of the sulfamoyl chloride and the product was purified using an eluent with a gradient of CH2Cl2 and DCM/MeOH/NH_4OH (25/7/1) yielding **6as** as a colourless solid (94%): m.p. = 62-71 °C; δ_H (400 MHz, $CDCl_3$) 1.40 (s, 3H, $C(C\underline{H}_3)_2$), 1.64 (s, , 3H, $C(C\underline{H}_3)_2$), 3.42 (bs, 2H, $HNC\underline{H}_2$-15-crown-5), 3.48-4.00 (m, 19H, $HNCH_2$-15-crown-5), 4.31-4.41 (m, 1H, 5'H_2), 4.46 (td, 11.3 Hz and 2.9 Hz, 1H, 5'H_2), 4.59-4.64 (m, 1H, 4'H), 5.04-5.13 (m, 1H, 3'H), 5.21-5.28 (m, 1H, 2'H), 6.17-6.55 (m, 3H, 1'H, $\underline{H}_2NSO_3$), 7.97-8.27 (m, 2H, H-2, NH), 8.39 (s, 1H, H-8); LRMS [ESI-] calcd for [$C_{24}H_{37}N_6O_{11}S$] *m/z* = 617.22, obsd 617.43.



((2R,3S,4R,5R)-5-(6-amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (7)

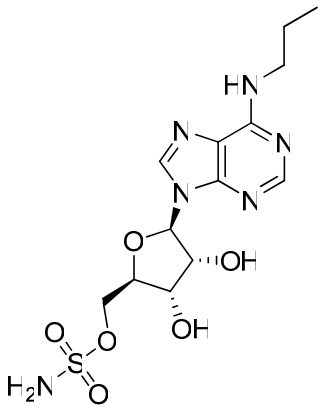
white solid (50%): m.p. = 98-112°C; δ_H (400 MHz, MeOD-d_4) 4.30-4.45 (m, 4H, 5'H_2, 4'H, 3'H), 4.66 (t, J = 5.1 Hz, 1H, 2'H), 6.08 (d, J = 5.1 Hz, 1H, 1'H), 8.24 (s, 1H, H-2), 8.34 (s, 1H, H-8); δ_C (100MHz, DMSO-d_6) 68.79, 70.40, 73.19, 81.71, 87.68, 119.13, 139.78, 149.43, 152.07, 155.62; HRMS [ESI+] calcd for $[C_{10}H_{14}N_6O_6S]^+$ *m/z* = 347.0768, obsd 347.0755; *rp*HPLC t_R: condition (I) 8.889 (II) 8.889 minutes, purity 98.37.6% and 98.23%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(methylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (8)

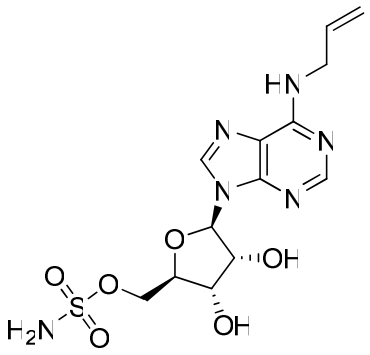
Compound **6b** was deprotected as outlined in general procedure **C**, yielding **8** as a white solid (85%): m.p. = 112-122 °C; δ_H (400 MHz, d_4-MeOD) 3.11 (bs, 3H, HNC$\underline{H}_3$) 4.29-4.44 (m, 4H, 5'H_2, 4'H, 3'H), 4.65 (t, J = 5.1 Hz, 1H, 2'H), 6.06 (d, J = 5.1 Hz, 1H, 1'H), 8.25 (s, 1H, H-2),

8.27 (bs, 1H, H-8); δ_C (100MHz, MeOD-d_4) 36.39, 78.23, 79.72, 82.42, 90.97, 97.03, 129.04, 148.61, 157.92, 162.18, 164.46; HRMS [ESI+] calcd for $[C_{11}H_{17}N_6O_6S]^+$ *m/z* = 361.0924, obsd 361.0935; *rp*HPLC t_R: condition (I) 11.533 (II) 10.195 minutes, purity 99.6% and 99.7%.



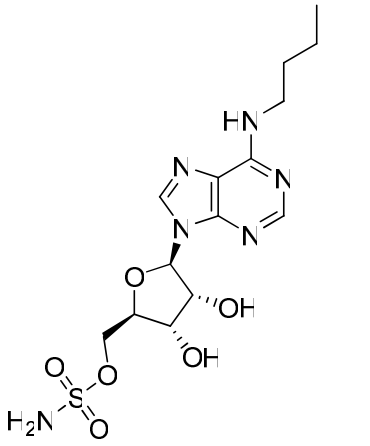
((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(propylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (9)

Compound **6c** was deprotected as outlined in general procedure **C**, yielding **9** as a white solid (93%): m.p. = 75-82 °C; δ_H (400 MHz, MeOD) 1.02 (t, *J* = 7.4 Hz, 3H, $HNCH_2CH_2C\underline{H}_3$), 1.72 (sextet, *J* = 7.3 Hz, 2H, $HNCH_2C\underline{H}_2CH_3$), 3.54 (bs, 2H, $HNCH_2C\underline{H}_2CH_3$), 4.29-4.44 (m, 4H, 5'$H_2$, 4'H, 3'H), 4.64 (t, *J* = 5.1 Hz, 1H, 2'H), 6.07 (d, *J* = 5.1 Hz, 1H, 1'H), 8.25 (bs, 1H, H-2), 8.27 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 11.60, 23.68, 43.56, 69.74, 71.82, 75.62, 83.67, 89.89, 120.65, 140.41, 149.64, 153.32, 155.67; HRMS [ESI+] calcd for $[C_{13}H_{21}N_6O_6S]^+$ *m/z* = 389.1237, obsd 389.1238; ; *rp*HPLC t_R: condition (I) 14.127 (II) 12.091 minutes, purity 99.2% and 98.4%.



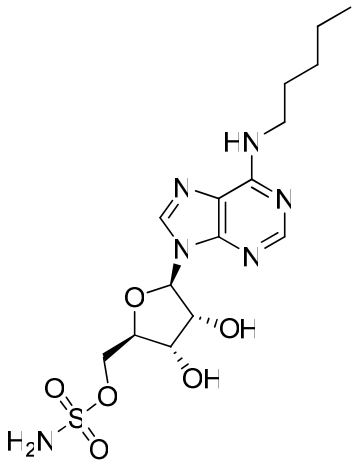
((2R,3S,4R,5R)-5-(6-(allylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (10)

Compound **6d** was deprotected as outlined in general procedure **C**, yielding **10** as an off-white solid (70%): m.p. = 64-77 °C; δ_H (400 MHz, MeOD) 4.24 (vbs, 2H, HNC$\underline{H}_2$CHCH_2), 4.30-4.44 (m, 4H, 5'H_2, 4'H, 3'H), 4.65 (t, *J* = 5.1 Hz, 1H, 2'H), 5.15 (dd, *J* = 10.3 Hz and 1.5 Hz, 1H, HNCH_2CHC$\underline{H}_2$), 5.27 (dd, *J* = 17.2 Hz and 1.7 Hz, 1H, HNCH_2CHC$\underline{H}_2$), 5.96-6.05 (m, 1H, HNCH_2C$\underline{H}$CH_2), 6.07 (d, *J* = 5.0 Hz, 1H, 1'H), 8.25 (s, 1H, H-2), 8.27 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 43.94, 69.76, 71.81, 75.59, 83.64, 89.87, 116.35, 120.69, 135.57, 140.48, 149.56, 153.53, 155.66; HRMS [ESI+] calcd for $[C_{13}H_{19}N_6O_6S]^+$ *m/z* = 387.1081, obsd 387.1086; *rp*HPLC t_R: condition (I) 13.790 (II) 11.406 minutes, purity 99.2% and 99.7%.



((2R,3S,4R,5R)-5-(6-(butylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (11)

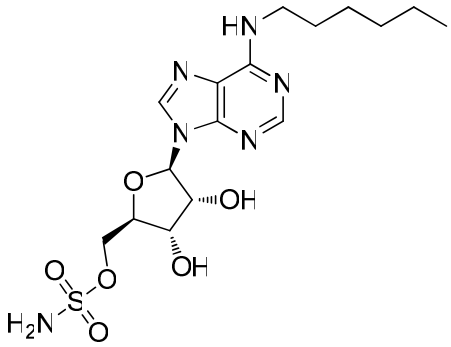
Compound **6e** was deprotected as outlined in general procedure **C**, yielding **11** as a white solid (74%): m.p. = 65-75 °C; δ_H (400 MHz, *d*$_4$-MeOD) 0.98 (t, *J* = 7.3 Hz, 3H, HN(CH$_2$)$_3$C<u>H</u>$_3$), 1.46 (sextet, *J* = 7.4 Hz, 2H, HN(CH$_2$)$_2$C<u>H</u>$_2$CH$_3$), 1.63 (p, *J* = 7.4 Hz, 2H, HNCH$_2$C<u>H</u>$_2$CH$_2$CH$_3$), 3.58 (bs, 2H, HNC<u>H</u>$_2$(CH$_2$)$_2$CH$_3$), 4.29-4.45 (m, 4H, 5'H$_2$, 4'H, 3'H), 4.64 (t, *J* = 5.1 Hz, 1H, 2'H), 6.06 (d, *J* = 5.1 Hz, 1H, 1'H), 8.23-8.26 (m, 2H, H-2, H-8); δ_C (100MHz, MeOD-*d*$_4$) 14.15, 21.07, 32.68, 41.41, 69.74, 71.83, 75.58, 83.63, 89.59, 120.73, 140.13, 149.70, 154.04, 156.20; HRMS [ESI+] calcd for $[C_{14}H_{23}N_6O_6S]^+$ *m/z* = 403.1394, obsd 403.1392; *rp*HPLC t_R: condition (I) 17.928 (II) 14.226 minutes, purity 100.0% and 99.7%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(pentylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (12)

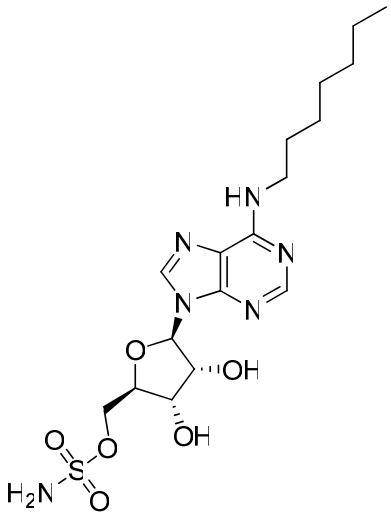
Compound **6f** was deprotected as outlined in general procedure **C**, yielding **12** as a white solid (76%): m.p. = 63-73 °C; δ_H (400 MHz, MeOD) 0.94 (t, *J* = 7.1 Hz, 3H, HN(CH$_2$)$_4$C<u>H</u>$_3$), 1.36-1.47 (m, 4H, HN(CH$_2$)$_2$(C<u>H</u>$_2$)$_2$CH$_3$), 1.70 (p, *J* = 7.3 Hz, 2H, HNCH$_2$C<u>H</u>$_2$(CH$_2$)$_2$CH$_3$), 3.57 (bs, 2H, HNC<u>H</u>$_2$(CH$_2$)$_3$CH$_3$), 4.29-4.45 (m, 4H, 5'H$_2$, 4'H, 3'H), 4.64 (t, *J* = 5.1 Hz, 1H, 2'H), 6.06

(d, J = 5.1 Hz, 1H, 1'H), 8.21-8.28 (m, 2H, H-2, H-8); δ_C (100MHz, MeOD-d_4) 14.35, 23.47, 30.17, 41.65, 69.75, 71.81, 75.59, 83.61, 89.82, 120.62, 140.12, 149.71, 154.04, 156.15; HRMS [ESI+] calcd for $[C_{15}H_{25}N_6O_6S]^+$ *m/z* = 417.1550, obsd 417.1561; *rp*HPLC t_R: condition (I) 19.426 (II) 17.326 minutes, purity 98.6% and 98.9%.



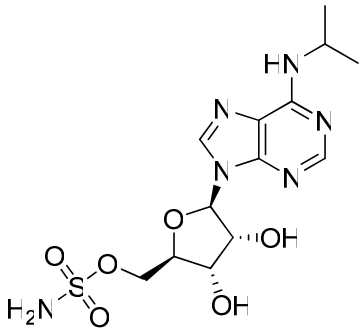
((2R,3S,4R,5R)-5-(6-(hexylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (13)

Compound **6g** was deprotected as outlined in general procedure **C**, yielding **13** as an off-white powder (75%): m.p. = 67-79 °C; δ_H (400 MHz, d_4-MeOD) 0.91 (t, J = 7.0, 3H, $HN(CH_2)_5C\underline{H}_3$), 1.32-1.39 (m, 4H, $HN(CH_2)_3(C\underline{H}_2)_2CH_3$), 1.40-1.49 (m, 2H, $HN(CH_2)_4C\underline{H}_2CH_3$), 1.69 (p, J = 7.27 Hz, 2H, $HNCH_2C\underline{H}_2(CH_2)_3CH_3$), 3.57 (bs, 2H, $HNC\underline{H}_2(CH_2)_4CH_3$), 4.29-4.45 (m, 4H, 5'$H_2$, 4'H and 3'H), 4.64 (t, J = 5.10 Hz, 1H, 2'H), 6.06 (d, J = 5.03 Hz, 1H, 1'H), 8.24 (bs, 1H, H-2), 8.25 (bs, 1H, H-8); δ_C (100MHz, MeOD-d_4) 14.34, 23.65, 27.65, 30.52, 32.73, 41.69, 69.76, 71.82, 75.59, 83.62, 89.86, 120.69, 140.15, 149.71, 154.07, 156.19; HRMS [ESI+] calcd for $[C_{16}H_{27}N_6O_6S]^+$ *m/z* = 431.1707, obsd 431.1721; *rp*HPLC t_R: condition (I) 19.618 (II) 15.913 minutes, purity 100.0 %and 100.0%.



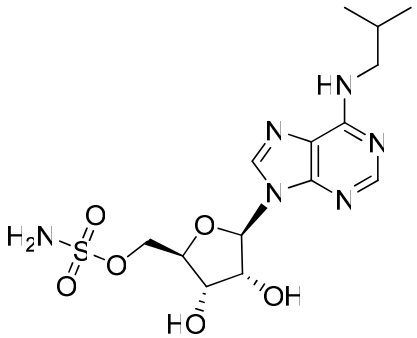
((2R,3S,4R,5R)-5-(6-(heptylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (14)

Compound **6h** was deprotected as outlined in general procedure **C**, yielding **14** as a white solid (83%): m.p. = 112-122 °C; δ_H (400 MHz, *d*$_4$-MeOD) 0.90 (t, *J* = 6.9 Hz, 3H, HN(CH$_2$)$_6$C<u>H</u>$_3$), 1.28-1.48 (m, 8H, HN(CH$_2$)$_2$(C<u>H</u>$_2$)$_4$CH$_3$), 1.69 (p, *J* = 7.4 Hz, 2H, HNCH$_2$C<u>H</u>$_2$(CH$_2$)$_4$CH$_3$), 3.57 (bs, 2H, HNC<u>H</u>$_2$CH$_2$(CH$_2$)$_4$CH$_3$), 4.29-4.45 (m, 4H, 5'H$_2$, 4'H, 3'H), 4.64 (t, *J* = 5.1 Hz, 1H, 2'H), 6.06 (d, *J* = 5.1 Hz, 1H, 1'H), 8.23-8.27 (m, 2H, H-2, H-8); δ_C (100MHz, MeOD-*d*$_4$) 14.38, 23.63, 27.93, 30.15, 30.55, 32.94, 41.65, 69.74, 71.81, 75.59, 83.60, 89.84, 120.66, 140.12, 149.70, 154.04, 156.16; HRMS [ESI+] calcd for $[C_{17}H_{29}N_6O_6S]^+$ *m/z* = 445.1863, obsd 445.1885; *rp*HPLC t_R: condition (III) 15.156 (IV) 11.663 minutes, purity 98.1% and 98.9%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(isopropylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (15)

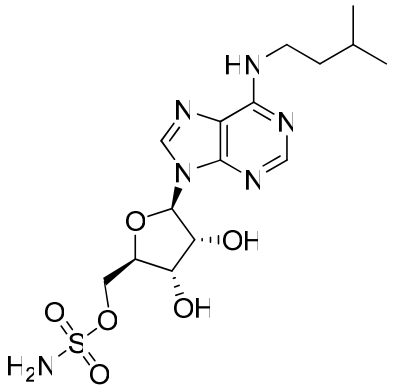
Compound **6i** was deprotected as outlined in general procedure **C**, yielding **15** as a white solid (50%): m.p. = 90-103 °C; δ_H (400 MHz, MeOD) 1.32 (d, J = 6.4 Hz, 6H, HNCH($C\underline{H}_3$)$_2$), 4.29-4.44 (m, 4H, 5'H_2, 4'H, 3'H), 4.45 (vbs, 1H, HN$C\underline{H}$($C\underline{H}_3$)$_2$), 4.64 (t, J = 5.1, 1H, 2'H), 6.06 (d, J = 5.0 Hz, 1H, 1'H), 8.24 (s, 1H, H-2), 8.24 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 22.84, 43.74, 69.74, 71.81, 75.58, 83.62, 89.83, 120.49, 140.18, 149.81, 153.82, 155.19; HRMS [ESI+] calcd for $[C_{13}H_{21}N_6O_6S]^+$ m/z = 389.1237, obsd 389.1242; *rp*HPLC t_R: condition (I) 15.055 (II) 13.351 minutes, purity 98.2% and 99.6%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(isobutylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (16)

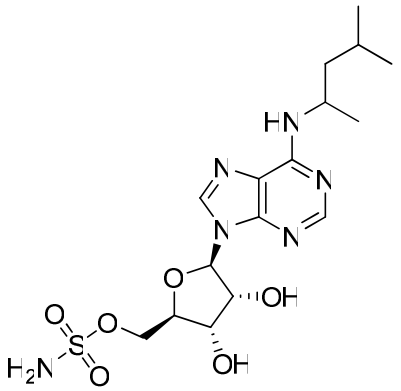
Compound **6j** was deprotected as outlined in general procedure **C**, yielding **16** as a white-solid (56%): m.p. = 90-105 °C; δ_H (400 MHz, MeOD) 1.01 (d, 6H, $HNCH_2CH(C\underline{H}_3)_2$), 1.99 (septet, J = 6.8 Hz, 1H, $HNCH_2C\underline{H}(CH_3)_2$), 3.41 (vbs, 2H, $HNC\underline{H}_2CH(CH_3)_2$), 4.30-4.45 (m, 4H, 5'$H_2$, 4'H, 3'H), 4.63-4.66 (t, J = 5.0 Hz, 1H, 2'H), 6.07 (d, J = 5.0 Hz, 1H, 1'H), 8.24 (bs, 1H, H-2), 8.27 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 20.41, 29.63, 59.59, 69.74, 71.80, 75.60, 83.64,

89.87, 120.60, 140.29, 149.66, 153.59, 156.00; HRMS [ESI+] calcd for $[C_{14}H_{23}N_6O_6S]^+$ 403.1394, obsd 403.1411; *rp*HPLC t_R: condition (I) 14.834 (II) 13.379 minutes, purity 98.1% and 98.2%.



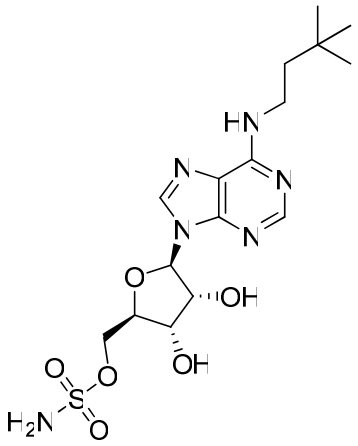
((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(isopentylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (17)

Compound **6k** was deprotected as outlined in general procedure **C**, yielding **17** as an off-white solid (60%): m.p. = 65-78 °C; δ_H (400 MHz, MeOD) 0.98 (d, *J* = 6.8 Hz, 6H, $HN(CH_2)_2CHC(C\underline{H}_3)_2$), 1.59 (q, *J* = 7.2 Hz, 2H, $HNCH_2C\underline{H}_2CHC(CH_3)_2$), 1.75 (septet, *J* = 6.7 Hz, 1H, $HN(CH_2)_2C\underline{H}C(CH_3)_2$), 3.61 (bs, 2H, $HNC\underline{H}_2CH_2CHC(CH_3)_2$), 4.29-4.44 (m, 4H, 5'$H_2$, 4'H), 4.64 (t, *J* = 5.0 Hz, 1H, 3'H), 6.06 (d, *J* = 5.0 Hz, 1H, 2'H), 8.24-8.26 (m, 2H, H-2, H-8); δ_C (100MHz, MeOD-d_4) 22.88, 26.96, 39.40, 40.06, 69.75, 71.83, 75.60, 83.66, 89.88, 120.66, 140.28, 149.70, 153.68, 155.86; HRMS [ESI+] calcd for $[C_{15}H_{25}N_6O_6S]^+$ *m/z* = 417.1550, obsd 417.1566; *rp*HPLC t_R: condition (I) 20.393 (IV) 16.387 minutes, purity 99.6% and 98.6%.



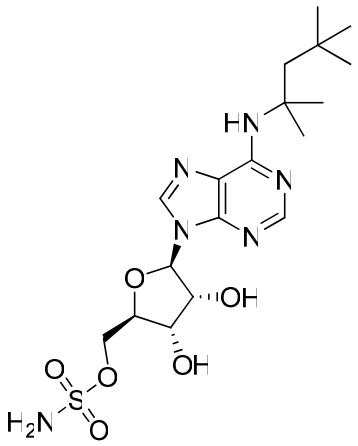
((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-((4-methylpentan-2-yl)amino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (18)

Compound **6l** was deprotected as outlined in general procedure **C**, yielding **18** as a white solid (73%): m.p. = 63-77 °C; δ_H (400 MHz, MeOD) 0.93 (d, *J* = 6.6 Hz, 3H, HNCH(CH_3)CH_2CH($C\underline{H}_3$)$_2$), 0.95 (d, *J* = 6.6 Hz, 3H, HNCH(CH_3)CH_2CH($C\underline{H}_3$)$_2$), 1.26 (d, *J* = 6.4 Hz, 3H, HNCH($C\underline{H}_3$)CH_2CH(CH_3)$_2$) 1.36-1.43 (m, 1H, HNCH(CH_3)$CH_2C\underline{H}$(CH_3)$_2$), 1.57-1.65 (m, 1H, HNCH(CH_3)$C\underline{H}_2$CH(CH_3)$_2$), 1.67-1.79 (m, 1H, HNCH(CH_3)$C\underline{H}_2$CH(CH_3)$_2$), 4.29-4.53 (m, 5H, 5'H_2, 4'H, 3'H, HNC$\underline{H}$(CH_3)CH_2CH(CH_3)$_2$), 4.62-4.66 (m, 1H, 2'H), 6.06 (d, *J* = 5.0 Hz, 1H, 1'H), 8.24 (bs, 1H, H-2), 8.25 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 21.78, 22.67, 23.31, 26.28, 45.63, 47.18, 69.74, 71.81, 75.60, 83.64, 89.87, 120.50, 140.16, 149.75, 153.86, 155.49; HRMS [ESI+] calcd for $[C_{16}H_{27}N_6O_6S]^+$ *m/z* = 431.1707, obsd 431.1716; *rp*HPLC t_R: condition (I) 18.998 (II) 16.107 minutes, purity 97.8% and 97.6%.



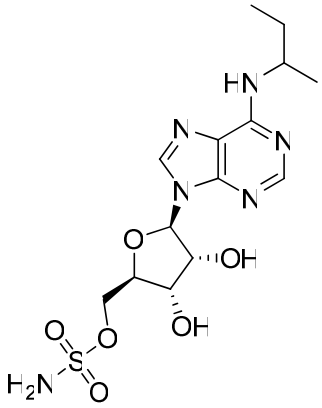
((2R,3S,4R,5R)-5-(6-(3,3-dimethylbutylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (19)

Compound **6m** was deprotected as outlined in general procedure **C**, yielding **19** as a beige solid (48%): m.p. = 66-78 °C; δ_H (400 MHz, MeOD) 1.01 (s, 9H, $HN(CH_2)_2C(C\underline{H}_3)_3$), 1.60-1.65 (m, 2H, $HNCH_2C\underline{H}_2C(CH_3)_3$), 3.60 (bs, 2H, $HNC\underline{H}_2CH_2C(CH_3)_3$), 4.29-4.44 (m, 4H, 5'$H_2$, 4'H, 3'H), 4.64 (t, J = 5.1 Hz, 1H, 2'H), 6.06 (d, J = 5.1 Hz, 1H, 1'H), 8.24 (bs, 2H, H-2, H-8); δ_C (100MHz, MeOD-d_4) 29.87, 30.76, 38.38, 44.07, 69.75, 71.82, 75.58, 83.62, 89.83, 120.70, 140.10, 149.74, 154.06, 156.06; HRMS [ESI+] calcd for $[C_{16}H_{27}N_6O_6S]^+$ m/z = 431.1707, obsd 431.1721; *rp*HPLC t_R: condition (I) 24.958 (II) 21.016 minutes, purity 97.1% and 97.5%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(2,4,4-trimethylpentan-2-ylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (20)

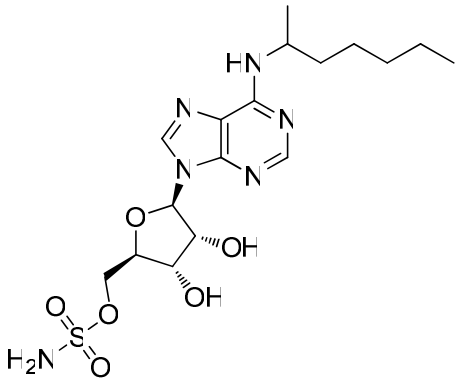
Compound **6n** was deprotected as outlined in general procedure **C**, yielding **20** off-white solid (64%): m.p. = 64-77 °C; δ_H (400 MHz, MeOD) 0.97 (s, 9H, $HNC(CH_3)_2CH_2C(C\underline{H}_3)_3$), 1.60 (s, 6H, $HNC(C\underline{H}_3)_2CH_2C(CH_3)_3$), 2.09 (s, 2H, $HNC(CH_3)_2C\underline{H}_2C(CH_3)_3$), 4.29-4.45 (m, 4H, 5'$H_2$, 4'H, 3'H), 4.63 (t, *J* = 5.1 Hz, 1H, 2'H), 6.05 (d, *J* = 5.1 Hz, 1H, 1'H), 8.24 (bs, 1H, H-2), 8.27 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 29.95, 30.39, 31.85, 32.57, 51.33, 57.07, 69.74, 71.81, 75.55, 83.63, 89.80, 120.99, 139.76, 149.47, 153.72, 155.99; HRMS [ESI+] calcd for $[C_{18}H_{31}N_6O_6S]^+$ *m/z* = 459.2020, obsd 459.2032; *rp*HPLC t_R: condition (III) 15.460 (IV) 11.920 minutes, purity 95.2 %and 95.1%.



((2R,3S,4R,5R)-5-(6-(sec-butylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (21)

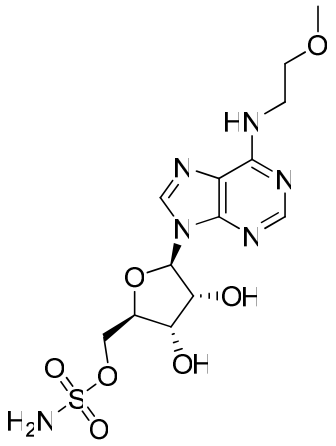
Compound **6o** was deprotected as outlined in general procedure **C**, yielding **21** as an off-white solid (70%): m.p. = 65-77 °C; δ_H (400 MHz, MeOD) 0.99 (t, *J* = 7.3 Hz, 3H, $HNCH(CH_3)CH_2C\underline{H}_3$), 1.28 (d, *J* = 6.6 Hz, 3H, $HNCH(C\underline{H}_3)CH_2CH_3$), 1.60-1.74 (m, 2H, $HNCH(CH_3)C\underline{H}_2CH_3$), 4.22-4.44 (m, 5H, 5'$H_2$, 4'H, 3'H, $HNC\underline{H}(CH_3)CH_2CH_3$), 4.65 (td, *J* =

5.0 Hz and 1.5 Hz, 1H, 2'H), 6.06 (d, J = 5.0 Hz, 1H, 1'H), 8.23 (bs, 1H, H-2), 8.25 (1H, H-8); δ_C (100MHz, MeOD-d_4) 10.76, 20.60, 30.58, 69.74, 71.81, 75.59, 83.63, 89.87, 120.51, 140.15, 149.83, 153.84, 155.64; HRMS [ESI+] calcd for $[C_{14}H_{23}N_6O_6S]^+$ m/z = 403.1394, obsd 403.1412; *rp*HPLC t_R: condition (I) 16.807 (II) 13..076 minutes, purity 99.8% and 100.0%.



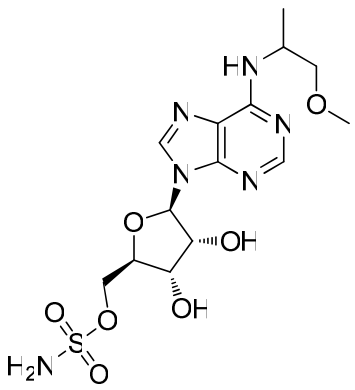
((2R,3S,4R,5R)-5-(6-(heptan-2-ylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (22)

Compound **6p** was deprotected as outlined in general procedure **C**, yielding **22** as a white solid (74%): m.p. = 65-77 °C; δ_H (400 MHz, d_4-MeOD) 0.89 (t, J = 6.92 Hz, 3H, $HN(CH_3)CH(CH_2)_4C\underline{H}_3$), 1.25-1.49 (m, 9H, $HNCH(C\underline{H}_3)(C\underline{H}_2)_4CH_3$), 1.54-1.71 (m, 2H, $HNCH(CH_3)(C\underline{H}_2)_4CH_3$), 4.29-4.45 (m, 5H, $HNC\underline{H}(CH_3)(CH_2)_4CH_3$, 5'$H_2$, 4'H and 3'H), 4.62-4.66 (m, 1H, 2'H), 6.06 (d, J = 4.99 Hz, 1H, 1'H), 8.23 (s, 1H, H-2), 8.25 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 14.34, 21.20, 23.60, 26.88, 32.88, 47.44, 54.78, 69.73, 71.80, 75.58, 83.61, 89.85, 120.51, 140.05, 149.78, 154.10, 155.76; HRMS [ESI+] calcd for $[C_{17}H_{29}N_6O_6S]^+$ m/z = 445.1863, obsd 445.1867; *rp*HPLC t_R: condition (I) 24.049 (II) 13.305 minutes, purity 99.8 %and 100.0%.



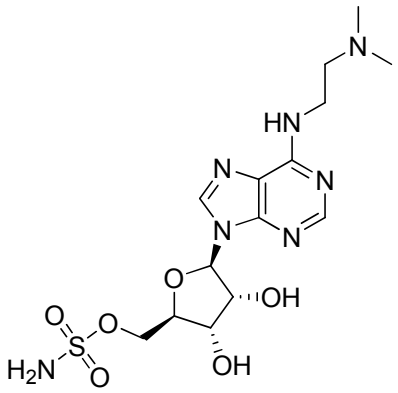
((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(2-methoxyethylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (23)

Compound **6q** was deprotected as outlined in general procedure **C**, yielding **23** as a white solid (79%): m.p. = 62-74 °C; δ_H (400 MHz, MeOD) 3.40 (3H, s, C(C<u>H</u>$_3$)$_2$), 3.64 (t, *J* = 5.4 Hz, 2H, HNCH$_2$C<u>H</u>$_2$OCH$_3$), 3.78 (bs, 2H, HNC<u>H</u>$_2$CH$_2$OCH$_3$), 4.29-4.44 (m, 4H, 5'H$_2$, 4'H, 3'H), 4.65 (t, *J* = 5.1 Hz, 1H, 2'H), 6.07 (d, *J* = 5.1 Hz, 1H, 1'H), 8.26 (s, 2H, H-2, H-8); δ_C (100MHz, MeOD-d_4) 41.39, 59.02, 69.76, 71.82, 72.06, 75.57, 83.62, 89.87, 120.72, 140.37, 149.96, 153.86, 156.04; HRMS [ESI+] calcd for [$C_{13}H_{21}N_6O_7S$] *m/z* = 405.1186, obsd 405.1178; *rp*HPLC t_R: condition (I) 13.015 (II) 11.028 minutes, purity 100.0% and 99.8%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-((1-methoxypropan-2-yl)amino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (24)

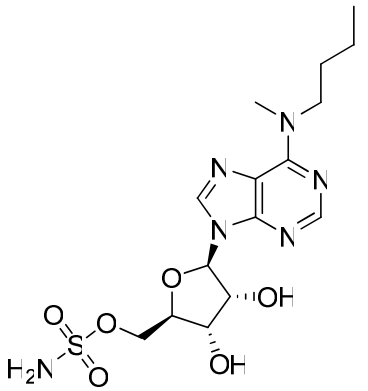
Compound **6r** was deprotected as outlined in general procedure **C**, yielding **24** as a yellow oil (55%): δ_H (400 MHz, *d*$_4$-MeOD) 1.31(d, *J* = 6.8 Hz, 3H, HNCH(C<u>H</u>$_3$)CH$_2$OCH$_3$), 3.38-3.39 (m, 3H, HNCH(CH$_3$)CH$_2$OC<u>H</u>$_3$), 3.46-3.57 (m, 2H, HNCH(CH$_3$)C<u>H</u>$_2$OCH$_3$), 4.29-4.44 (m, 4H, 5'H$_2$, 4'H, 3'H), 4.64 (t, *J* = 5.1 Hz, 1H, 2'H), 4.58 (vbs, 1H, HNC<u>H</u>(CH$_3$)CH$_2$OCH$_3$), 6.06 (d, *J* = 5.1 Hz, 1H, 1'H), 8.24-8.27 (m, 2H, H-2, H-8); δ_C (100MHz, MeOD-*d*$_4$) 40.44, 47.23, 59.28, 69.75, 71.83, 75.57, 76.73, 83.65, 89.89, 120.62, 140.29, 150.32, 154.06, 155.70; HRMS [ESI+] calcd for $[C_{14}H_{23}N_6O_7S]^+$ *m/z* = 419.1343, obsd 419.1328; *rp*HPLC t_R: condition (I) 14.801 (II) 11.778 minutes, purity 99.4% and 98.7%.



((2R,3S,4R,5R)-5-(6-(2-(dimethylamino)ethylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (25)

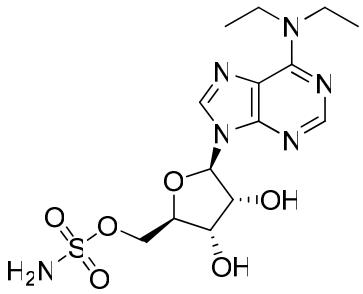
Compound **6s** was deprotected as outlined in general procedure **C**, yielding **25** as a colourless oil (88%): δ_H (400 MHz, MeOD) 3.00 (s, 6H, HN(CH$_2$)$_2$N(C<u>H</u>$_3$)$_2$), 3.47 (t, *J* = 5.7 Hz, 2H, HNCH$_2$C<u>H</u>$_2$N(CH$_3$)$_2$), 4.00 (t, *J* = 5.4 Hz, 2H, HNC<u>H</u>$_2$CH$_2$N(CH$_3$)$_2$), 4.30-4.44 (m, 4H, 5'H$_2$,

4'H, 3'H), 4.67 (t, *J* = 5.1 Hz, 1H, 2'H), 6.09 (d, *J* = 5.1 Hz, 1H, 1'H), 8.32 (bs, 1H, H-2), 8.37 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 43.96, 59.08, 69.87, 71.85, 75.61, 83.71, 89.89, 119.68, 140.97, 150.50, 153.79, 156.19; HRMS [ESI+] calcd for [$C_{14}H_{24}N_7O_6S$] *m/z* = 418.1503, obsd 418.1508; *rp*HPLC t_R: condition (I) 10.549 (II) 9.667 minutes, purity 99.5% and 99.9%.



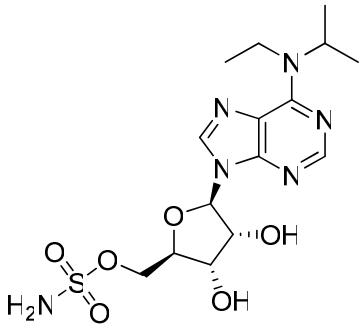
((2R,3S,4R,5R)-5-(6-(butyl(methyl)amino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (26)

Compound **6t** was deprotected as outlined in general procedure **C**, yielding **26** as a white solid (72%): m.p. = 58-71 °C; δ_H (400 MHz, MeOD) 0.97 (t, *J* = 7.3 Hz, 3H, $CH_3N(CH_2)_3C\underline{H}_3$), 1.39 (sextet, *J* = 7.5 Hz, 2H, $CH_3N(CH_2)C\underline{H}_2CH_3$), 1.69 (p, *J* = 7.6 Hz, 2H, $CH_3NCH_2C\underline{H}_2CH_2CH_3$), 3.43 (vbs, 3H, $C\underline{H}_3N(CH_2)_3CH_3$), 4.07 (vbs, 2H, $CH_3NC\underline{H}_2(CH_2)_2CH_3$), 4.29-4.44 (m, 4H, 5'$H_2$, 4'H, 3'H), 4.61 (t, *J* = 5.1 Hz, 1H, 2'H), 6.07 (d, *J* = 5.1 Hz, 1H, 1'H), 8.19 (s, 1H, H-2), 8.21 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 26.63, 29.73, 45.36, 69.09, 69.75, 71.81, 75.56, 78.97, 83.62, 89.86, 120.68, 140.35, 149.94, 153.83, 156.14; HRMS [ESI+] calcd for [$C_{15}H_{25}N_6O_6S$] *m/z* = 417.1550, obsd 417.1561; *rp*HPLC t_R: condition (I) 20.482 (II) 15.453 minutes, purity 95.6% and 96.8%.



((2R,3S,4R,5R)-5-(6-(diethylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (27)

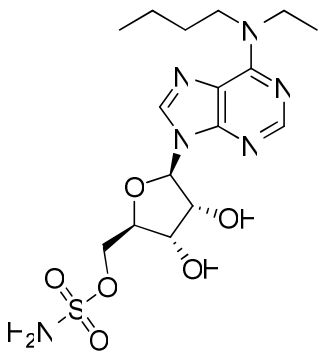
Compound **6u** was deprotected as outlined in general procedure **C**, yielding **27** as a white solid (60%): m.p. = 110-115 °C; δ_H (400 MHz, *d*$_4$-MeOD) 1.28 (t, *J* = 7.2 Hz, 6H, (C<u>H</u>$_3$CH$_2$)$_2$N), 3.99 (bs, 4H, (CH$_3$C<u>H</u>$_2$)$_2$N), 4.29-4.44 (m, 4H, 5'H$_2$, 4'H, 3'H), 4.60 (t, *J* = 5.1 Hz, 1H, 2'H), 6.07 (d, *J* = 5.1 Hz, 1H, 1'H), 8.19 (s, 1H, H-2), 8.20 (s, 1H, H-8); δ_C (100MHz, MeOD-*d*$_4$) 13.78, 44.37, 69.76, 71.81, 75.62, 83.51, 89.60, 120.76, 138.74, 151.42, 153.38, 154.95; HRMS [ESI+] calcd for $[C_{14}H_{23}N_6O_6S]^+$ *m/z* =403.1394, obsd 403.1410; *rp*HPLC t_R: condition (I) 17.568 minutes and (II) 14.226 minutes, purity 95.9% and 95.2%.



((2R,3S,4R,5R)-5-(6-(ethyl(isopropyl)amino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (28)

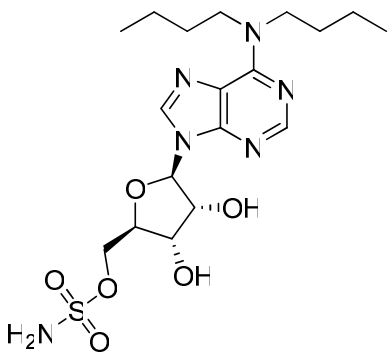
Compound **6v** was deprotected as outlined in general procedure **C**, yielding **28** as an off-white solid (73%): m.p. = 65-78 °C; δ_H (400 MHz, *d*$_4$-MeOD) 1.28-1.32 (m, 9H, (C<u>H</u>$_3$)$_2$CHNCH$_2$C<u>H</u>$_3$),

3.85 (bs, 2H, $(CH_3)_2CHNC\underline{H}_2CH_3$), 4.29-4.44 (m, 4H, 5'$H_2$, 4'H, 3'H), 4.59 (t, *J* = 5.1 Hz, 1H, 2'H), 5.73 (bs, 1H, $(CH_3)_2C\underline{H}NCH_2CH_3$), 6.08 (d, *J* = 5.1 Hz, 1H, 1'H), 8.19 (s, 1H, H-2), 8.22 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 15.96, 20.84, 38.36, 69.74, 71.79, 75.63, 83.49, 89.57, 129.93, 138.45, 151.51, 153.25, 155.22; HRMS [ESI+] calcd for $[C_{15}H_{25}N_6O_6S]^+$ *m/z* = 417.1550, obsd 417.1546; *rp*HPLC t_R: condition (I) 20.237 (II) 16.401 minutes, purity 95.1% and 95.1%.



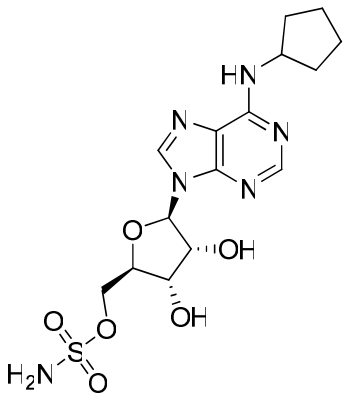
((2R,3S,4R,5R)-5-(6-(butyl(ethyl)amino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (29)

Compound **6w** was deprotected as outlined in general procedure **C**, yielding **29** as a beige solid (75%): m.p. = 109-114 °C; δ_H (400 MHz, MeOD) 0.96 (t, *J* = 7.6 Hz, 3H, $CH_3CH_2N(CH_2)_3C\underline{H}_3$), 1.25 (t, *J* = 7.6 Hz, 3H, $C\underline{H}_3CH_2N(CH_2)_3CH_3$), 1.40 (sextet, *J* = 7.6 Hz, 2H, $CH_3CH_2NCH_2CH_2C\underline{H}_2CH_3$), 1.69 (p, *J* = 7.6 Hz, 2H, $CH_3CH_2NCH_2C\underline{H}_2CH_2CH_3$), 4.0 (bs, 4H, $CH_3C\underline{H}_2NC\underline{H}_2CH_2CH_2CH_3$), 4.28-4.43 (m, 4H, 5'$H_2$, 4'H, 3'H), 4.57-4.62 (m, 1H, 2'H), 6.04-6.08 (m, 1H, 1'H), 8.16-8.21 (m, 2H, H-2 and H-8); δ_C (100MHz, MeOD-d_4) 13.69, 14.33, 21.03, 31.55, 44.74, 69.78, 71.83, 75.61, 83.53, 89.56, 120.83, 138.65, 151.41, 153.23, 155.14; HRMS [ESI+] calcd for $[C_{19}H_{29}N_6O_6S]^+$ *m/z* = 431.1707, obsd 431.1714; *rp*HPLC t_R: condition (I) 26.635 (II) 23.176 minutes, purity 97.3%and 96.0%.



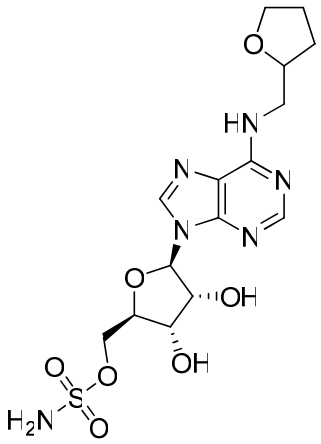
((2R,3S,4R,5R)-5-(6-(dibutylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (30)

Compound **6x** was deprotected as outlined in general procedure **C**, yielding **30** as a beige solid (94%): m.p. = 65-71 °C; δ_H (400 MHz, MeOD) 0.97 (t, *J* = 7.5 Hz, 6H, ($C\underline{H}_3CH_2CH_2CH_2)_2N$), 1.40 (sextet, *J* = 7.5 Hz, 4H, ($CH_3C\underline{H}_2CH_2CH_2)_2N$), 1.68 (p, *J* = 7.6 Hz, 4H, ($CH_3CH_2C\underline{H}_2CH_2)_2N$), 3.93 (vbs, 4H, ($CH_3CH_2CH_2C\underline{H}_2)_2N$), 4.29-4.43 (m, 4H, 5'$H_2$, 4'H, 3'H), 4.60 (t, *J* = 5.1 Hz, 1H, 2'H), 6.06 (d, *J* = 5.1 Hz, 1H, 1'H), 8.16 (s, 1H, H-2), 8.19 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 14.35, 21.02, 31.45, 69.79, 71.83, 75.58, 79.44, 83.49, 89.49, 120.91, 138.46, 151.44, 153.27, 155.46; HRMS [ESI+] calcd for $[C_{18}H_{31}N_6O_6S]^+$ *m/z* = 459.2020, obsd 459.2026; *rp*HPLC t_R: condition (I) 15.644 (II) 11.940 minutes, purity 95.2 %and 97.6%.



((2R,3S,4R,5R)-5-(6-(cyclopentylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (31)

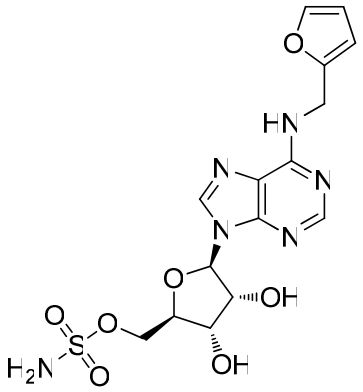
Compound **6y** was deprotected as outlined in general procedure **C**, yielding **31** as an off-white solid (60%): m.p. = 80-93 °C; δ_H (400 MHz, MeOD) 1.58-1.88 (m, 6H, cyclopentyl), 2.06-2.15 (m, 2H, cyclopentyl), 4.29-4.44 (m, 4H, 5'H_2, 4'H, 3'H), 4.53 (vbs, 1H, cyclopentyl), 4.64 (t, *J* = 5.0 Hz, 1H, 2'H), 6.06 (d, *J* = 5.0 Hz, 1H, 1'H), 8.25 (bs, 1H, H-2), 8.26 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 24.71, 33.95, 53.72, 69.73, 71.82, 75.60, 83.66, 89.90, 120.58, 140.25, 150.27, 153.71, 155.43; HRMS [ESI+] calcd for $[C_{15}H_{23}N_6O_6S]^+$ *m/z* = 415.1394, obsd 415.1391; *rp*HPLC t_R: condition (I) 16.626 (II) 13.423 minutes, purity 99.3% and 100.0%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-((tetrahydrofuran-2-yl)methylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (32)

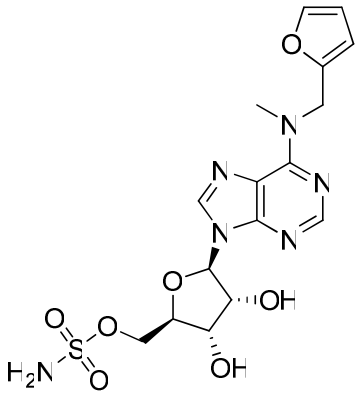
Compound **6z** was deprotected as outlined in general procedure **C**, yielding **32** as a white solid (80%): m.p. = 63-77 °C; δ_H (400 MHz, MeOD) 1.65-1.75 (m, 1H, tetrahydrofuran), 1.86-2.10 (m, 3H, tetrahydrofuran), 3.59-3.81 (bm, 2H, C$\underline{H_2}$tetrahydrofuran), 3.77 (q, *J* = 7.3 Hz, 1H, tetrahydrofuran), 3.92 (q, *J* = 7.1 Hz, 1H, tetrahydrofuran), 4.11-4.21 (m, 1H, tetrahydrofuran), 4.29-4.44 (m, 4H, 5'H_2, 4'H, 3'H), 4.65 (t, *J* = 5.0 Hz, 1H, 2'H), 6.06 (d, *J* = 5.0 Hz, 1H, 1'H),

8.23-8.29 (m, 2H, H-2, H-8); δ_C (100MHz, MeOD-d_4) 26.64, 29.73, 45.37, 69.10, 69.75, 71.83, 75.57, 79.00, 83.63, 89.88, 120.71, 140.37, 149.98, 153.87, 156.16; HRMS [ESI+] calcd for $[C_{15}H_{23}N_6O_7S]^+$ *m/z* = 431.1343, obsd 431.1333; *rp*HPLC t_R: condition (I) 14.948 (II) 12.019 minutes, purity 98.8% and 99.0%.



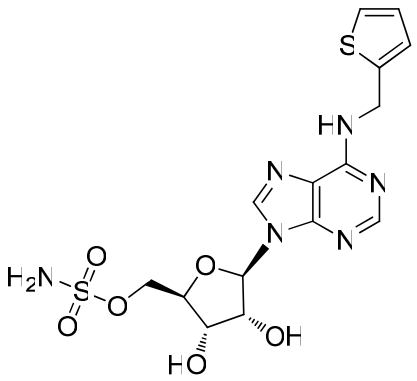
((2R,3S,4R,5R)-5-(6-((furan-2-ylmethyl)amino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (33)

Compound **6aa** was deprotected as outlined in general procedure **C**, yielding **33** as an off-white solid (61%): m.p. = 70-79 °C; (δ_H (400 MHz, MeOD) 4.30-4.45 (m, 4H, 3'H, 4'H, 5'H_2), 4.65 (t, *J* = 5.1 Hz, 1H, 2'H), 4.81 (bs, 2H, C$\underline{H_2}$furfuryl), 6.07 (d, *J* = 5.0 Hz, 1H, 1'H), 6.30-6.36 (m, 2H, furfuryl), 7.43 (s, 1H, furfuryl), 8.26 (s, 1H, H-2), 8.29 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 38.43, 69.76, 71.85, 75.57, 83.65, 89.92, 108.17, 111.37, 120.85, 140.51, 143.34, 150.37, 153.41, 153.98, 155.87; HRMS [ESI+] calcd for $[C_{15}H_{19}N_6O_7S]^+$ *m/z* = 427.1030, obsd 427.1026; *rp*HPLC t_R: condition (I) 15.801 (II) 15.801 minutes, purity 97.4% and 97.7%.



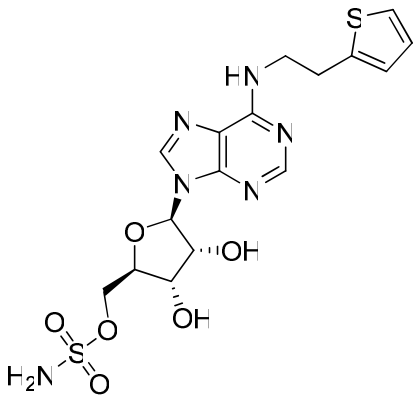
((2R,3S,4R,5R)-5-(6-((furan-2-ylmethyl)(methyl)amino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (34)

Compound **6ab** was deprotected as outlined in general procedure **C**, yielding **34** as a white solid (36%): m.p. = 65-73 °C; δ_H (400 MHz, MeOD) 3.42 (bs, 3H, C<u>H</u>$_3$Nfurfuryl), 4.30-4.45 (m, 4H, 5'H$_2$, 4'H, 3'H), 4.63 (t, *J* = 5.1 Hz, 1H, 2'H), 5.33 (bs, 2H, CH$_3$NC<u>H</u>$_2$furan), 6.09 (d, *J* = 5.0 Hz, 1H, 1'H), 6.30-6.34 (m, 2H, furan), 7.40-7.41 (m, 1H, furan), 8.23 (s, 1H, H-2), 8.26 (s, 1H, H-8); δ_C (100 MHz, MeOD-d_4) 36.70, 47.57, 69.75, 71.82, 75.59, 83.54, 89.71, 109.25, 111.28, 121.33, 138.94, 143.54, 151.62, 152.80, 153.24, 155.82; HRMS [ESI+] calcd for [$C_{16}H_{21}N_6O_7S$] *m/z* = 441.1186, obsd 441.1189; *rp*HPLC t_R: condition (I) 18.3004 (II) 13.622 minutes, purity 98.1% and 99.0%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-((thiophen-2-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (35)

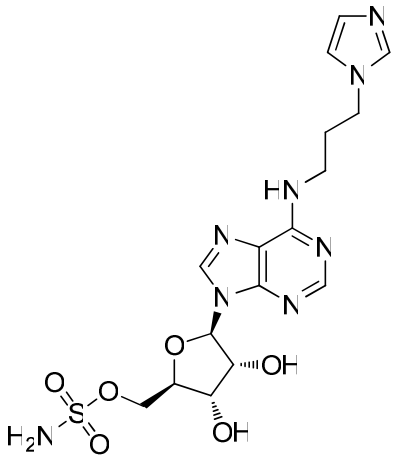
Compound **6ac** was deprotected as outlined in general procedure **C**, yielding **35** as a yellow solid (60%): m.p. = 65-78 °C; 4.30-4.45 (m, 4H, 5'H_2, 4'H, 3'H), 4.65 (t, *J* = 5.1 Hz, 1H, 2'H), 4.99 (bs, 2H, C$\underline{H}_2$thiophene), 6.07 (d, *J* = 5.1 Hz, 1H, 1'H), 6.95 (dd, *J* = 5.1 Hz and 3.5 Hz, 1H, thiophene), 7.08, *J* = 3.5 Hz and 1.1 Hz, 1H, thiophene), 7.26 (dd, *J* = 5.1 Hz and 1.3 Hz, 1H, thiophene), 8.26 (s, 1H, H-2), 8.31 (bs, 1H, H-8); δ_C (100MHz, MeOD-d_4) 40.03, 69.72, 71.79, 75.55, 83.64, 89.91, 120.80, 125.82, 126.78, 127.64, 140.47, 143.08, 150.28, 153.98, 155.66; HRMS [ESI+] calcd for $[C_{15}H_{19}N_6O_6S_2]^+$ *m/z* = 443.0802, obsd 443.0803; *rp*HPLC t_R: condition (I) 17.405 (II) 13.722 minutes, purity 96.6% and 95.6%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(2-(thiophen-2-yl)ethylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (36)

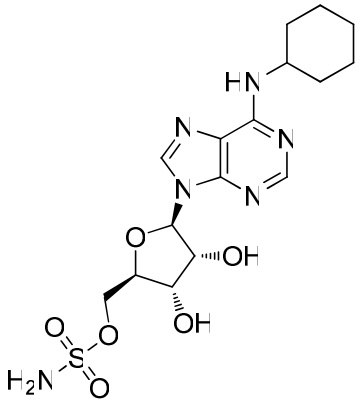
Compound **6ad** was deprotected as outlined in general procedure **C**, yielding **36** as a white solid (40%): m.p. = 58-72 °C; δ_H (400 MHz, MeOD) 3.21 (t, *J* = 7.1 Hz, 2H, HNCH_2C$\underline{H}_2$thiophene), 3.86 (bs, 2H, HNC$\underline{H}_2$CH_2thiophene), 4.30-4.45 (m, 4H, 5'H_2, 4'H, 3'H), 4.65 (t, *J* = 5.1 Hz, 1H, 2'H), 6.07 (d, *J* = 5.0 Hz, 1H, 1'H), 6.90-6.93 (m, 2H, thiophene), 7.20 (dd, *J* = 4.8 Hz and 1.6

Hz, 1H, thiophene), 8.25 (s, 1H, H-2), 8.27 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 30.72, 43.31, 69.75, 71.84, 75.57, 83.65, 89.88, 120.79, 124.71, 126.41, 127.87, 140.36, 142.52, 150.35, 153.95, 156.01; HRMS [ESI+] calcd for $[C_{16}H_{21}N_6O_6S_2]^+$ *m/z* = 457.0958, obsd 457.0965; *rp*HPLC t_R: condition (I) 18.887 (II) 15.207 minutes, purity 99.0% and 98.8%.



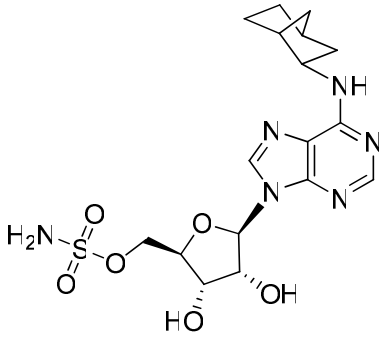
((2R,3S,4R,5R)-5-(6-((3-(1H-imidazol-1-yl)propyl)amino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (37)

Compound **6ae** was deprotected as outlined in general procedure **C**, yielding **37** as a colourless oil (55%): δ_H (400 MHz, $CDCl_3$) 2.27 (p, 1H, 7.0 Hz, 2H, $NHCH_2C\underline{H}_2CH_2$), 3.67 (bs, 2H, $C\underline{H}_2(CH_2)_2$), 4.30-4.45 (m, 6H, 5'H_2, 4'H, 3'H, $NH(CH_2)_2C\underline{H}_2$), 4.66 (t, *J* = 5.1 Hz, 1H, 2'H), 6.06 (d, *J* = 5.1 Hz, 1H, 1'H), 7.42 (1H, imidazole), 7.58 (1H, imidazole), 8.24 (s, 1H, H-2), 8.24 (s, 1H, H-8), 8.72 (s, 1H, imidazole); δ_C (100MHz, MeOD-d_4) 31.10, 38.51, 59.83, 69.97, 71.82, 75.57, 83.69, 89.68, 120.64, 121.57, 123.23,136.61, 140.39, 150.15, 153.80, 156.02; HRMS [ESI+] calcd for $[C_{16}H_{23}N_8O_6S]^+$ *m/z* = 455.1455, obsd 455.1463; *rp*HPLC t_R: condition (I) 13.509 (II) 11.282 minutes, purity 98.4% and 97.6%.



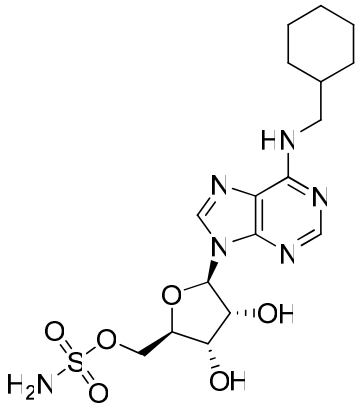
((2R,3S,4R,5R)-5-(6-(cyclohexylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (38)

Compound **6af** was deprotected as outlined in general procedure **C**, yielding **38** as an off-white solid (51%): m.p. = 153-162 °C; δ_H (400 MHz, MeOD) 1.19-1.52 (m, 5H, cyclohexyl), 1.62-1.72 (m, 1H, cyclohexyl), 1.76-1.86 (m, 2H, cyclohexyl), 1.96-2.09 (m, 2H, cyclohexyl), 4.07 (bm, 1H, cyclohexyl), 4.30-4.46 (m, 4H, 5'H_2, 4'H, 3'H), 4.64 (t, *J* = 5.0 Hz, 1H, 2'H), 6.06 (d, *J* = 5.0 Hz, 1H, 1'H), 8.21 (bs, 1H, H-2), 8.24 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 25.97, 26.69, 33.95, 50.59, 69.76, 71.82, 75.58, 83.63, 89.84, 120.50, 140.10, 150.37, 154.09, 155.34; HRMS [ESI+] calcd for $[C_{16}H_{25}N_6O_6S]^+$ *m/z* = 429.1550, obsd 429.1566; *rp*HPLC t_R: condition (I) 20.288 (II) 15.801 minutes, purity 96.9 % and 97.3%.



((2R,3S,4R,5R)-5-(6-((2R,4S)-bicyclo[2.2.1]heptan-2-ylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (39)

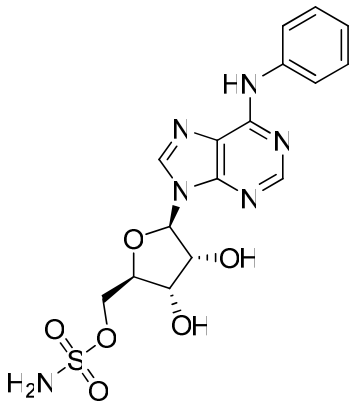
Compound **6ag** was deprotected as outlined in general procedure **C**, yielding **39** as a white solid (91%): m.p. = 105-118 °C; δ_H (400 MHz, MeOD) 1.99-1.65 (m, 7H, norborane), 1.86-1.94 (m, 1H, norborane), 2.31-2.37 (m, 2H, norborane), 4.01 (bs, 1H, norborane), 4.29-4.44 (m, 4H, 5'H_2, 4'H, 3'H), 4.64 (t, *J* = 5.0 Hz, 1H, 2'H), 6.06 (d, *J* = 5.1 Hz, 1H, 1'H), 8.24-8.28 (m, 2H, H-2, H-8); δ_C (100MHz, MeOD-d_4) 27.25, 29.31, 36.19, 37.08, 40.84, 43.63, 55.25, 69.74, 71.81, 75.58, 83.64, 89.89, 120.58, 140.16, 149.72, 153.92, 155.09; HRMS [ESI+] calcd for $[C_{17}H_{24}N_6O_6S]^+$ *m/z* = 441.1550, obsd 441.1560; ; *rp*HPLC t_R: condition (I) 22.600 (II) 18.545 minutes, purity 97.5% and 97.2%.



((2R,3S,4R,5R)-5-(6-(cyclohexylmethylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (40)

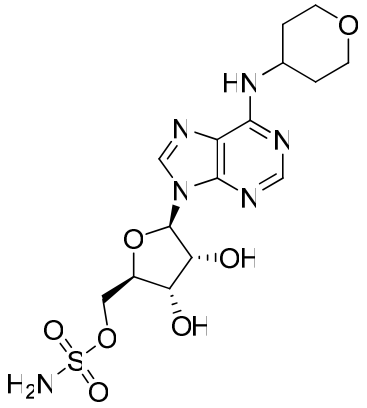
Compound **6ah** was deprotected as outlined in general procedure **C**, yielding **40** as an off-white solid (63%): m.p. = 135-147 °C; δ_H (400 MHz, MeOD) 0.98-1.10 (m, 2H, cyclohexyl), 1.16-1.35 (m, 3H, cyclohexyl), 1.64-1.88 (m, 6H, cyclohexyl), 3.42 (bs, 2H, HNC$\underline{H_2}$cyclohexyl), 4.30-4.45 (m, 4H, 5'H_2, 4'H, 3'H), 4.64 (t, *J* = 5.1 Hz, 1H, 2'H), 6.06 (d, *J* = 5.0 Hz, 1H, 1'H), 8.23 (bs,

1H, H-2), 8.25 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 27.04, 27.61, 31.93, 39.25, 47.86, 69.75, 71.84, 75.58, 83.64, 89.88, 120.68, 140.12, 149.76, 154.04, 156.37; HRMS [ESI+] calcd for $[C_{17}H_{27}N_6O_6S]^+$ *m/z* = 443.1707, obsd 443.1714; *rp*HPLC t_R: condition (I) 22.442 (II) 17.620 minutes, purity 99.4% and 98.7%.



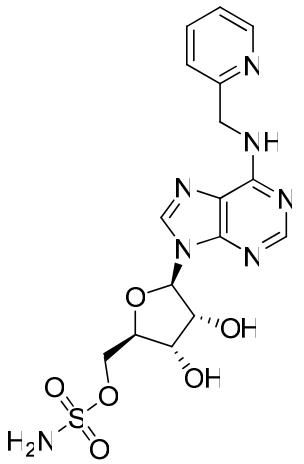
((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(phenylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (41)

Compound **6ai** was deprotected as outlined in general procedure **C** with a minor modification, the crude product was not adsorbed onto silica but instead was dissolved in minimal MeOH and added to the samplet, yielding **41** as a white solid (40%): m.p. = 99-108 °C; δ_H (400 MHz, MeOD) 4.32-4.46 (m, 4H, 5'H_2, 4'H, 3'H), 4.70 (t, *J* = 5.1 Hz, 1H, 2'H), 6.12 (d, *J* = 5.0 Hz, 1H, 1'H), 7.13 (tt, *J* = 7.3 Hz and 1.0 Hz, 1H, phenyl), 7.38 (t, *J* = 8.1 Hz, 2H, phenyl), 7.80 (d, *J* = 8.4 Hz, 2H, phenyl), 8.38 (bs, 1H, H-2), 8.40 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 69.76, 71.83, 75.56, 83.66, 89.98, 121.35, 121.98, 124.69, 129.81, 140.24, 141.14, 150.57, 153.68; HRMS [ESI+] calcd for $[C_{16}H_{19}N_6O_6S]^+$ *m/z* = 423.1081, obsd 423.1074; ; *rp*HPLC t_R: condition (I) 16.083 (II) 13.184 minutes, purity 95.2% and 96.0%.



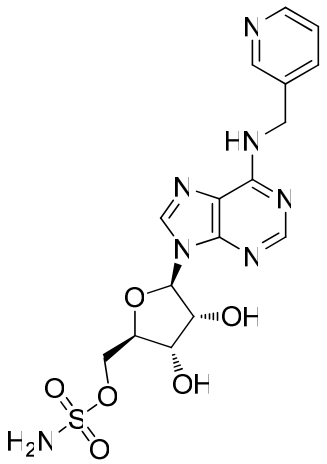
((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(tetrahydro-2H-pyran-4-ylamino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (42)

Compound **6aj** was deprotected as outlined in general procedure **C**, yielding **42** as a white solid (65%): m.p. = 85-98 °C; δ_H (400 MHz, MeOD) 1.63-1.74 (m, 2H, tetrahydropyran), 1.99-2.07 (m, 2H, tetrahydropyran), 3.49 (td, *J* = 11.6 Hz and 1.9 Hz, 2H, tetrahydropyran), 3.97-4.04 (m, 2H, tetrahydropyran), 4.29-4.45 (m, 5H, 5'H_2, 4'H, 3'H, 1H, tetrahydropyran), 4.65 (t, *J* = 5.0 Hz, 1H, 2'H), 6.07 (d, *J* = 5.0 Hz, 1H, 1'H), 8.26 (bs, 1H, H-2), 8.27 (s, 1H, H-8); δ_C (100MHZ, MeOD-d_4) 33.93, 67.74, 69.75, 71.82, 75.60, 83.66, 89.87, 120.56, 140.48, 150.07, 153.48, 154.94; HRMS [ESI+] calcd for $[C_{15}H_{23}N_6O_7S]^+$ *m/z* = 431.1343, obsd 431.1354; *rp*HPLC t_R: condition (I) 12.988 (II) 11.747 minutes, purity 100.0% and 99.7%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-((pyridin-2-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (43)

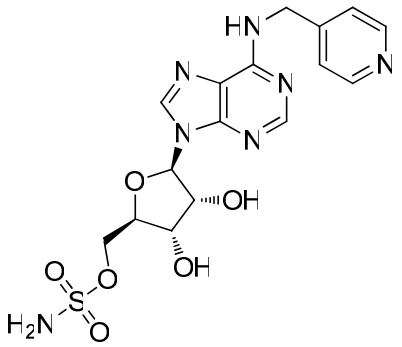
Compound **6ak** was deprotected as outlined in general procedure **C**, yielding **43** as an off-white solid (80%): m.p. = 125-138 °C; δ_H (400 MHz, MeOD) 4.30-4.45 (m, 4H, 5'H_2, 4'H, 3'H), 4.67 (t, *J* = 5.0 Hz, 1H, 2'H), 4.94 (vbs, 2H, C$\underline{H}_2$pyridine), 6.08 (d, *J* = 5.1 Hz, 1H, 1'H), 7.31 (t, *J* = 6.3 Hz, 1H, pyridine), 7.44 (d, *J* = 8.3 Hz, 1H, pyridine), 7.78 (td, 7.7 Hz and 1.7 Hz, 1H, pyridine), 8.26 (s, 1H, H-2), 8.29 (bs, 1H, H-8), 8.51 (bs, 1H, pyridine); δ_C (100MHz, MeOD-d_4) 54.40, 78.25, 79.80, 82.51, 91.10, 97.12, 125.19, 128.16, 130.19, 131.45, 146.15, 149.09, 158.25, 162.13, 164.00, 168.40; HRMS [ESI+] calcd for $[C_{16}H_{20}N_7O_6S]^+$ *m/z* = 438.1190, obsd 438.1203; *rp*HPLC t_R: condition (I) 12.903 (II) 11.437 minutes, purity 99.1% and 100.0%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-((pyridin-3-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (44)

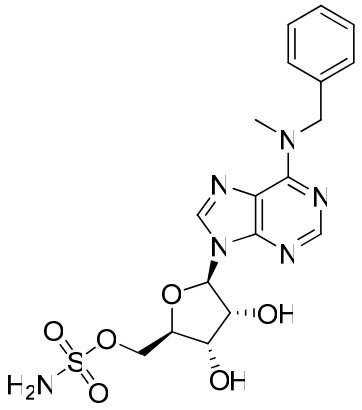
Compound **6al** was deprotected as outlined in general procedure **C**, yielding **44** as a yellow oil (60%): δ_H (400 MHz, *d4*-MeOD) 4.29-4.44 (m, 4H, 5'H_2, 4'H, 3'H), 4.66 (t, *J* = 5.1 Hz, 1H, 2'H), 4.93 (bs, 2H, C$\underline{H}_2$pyridine), 6.08 (d, *J* = 5.1 Hz, 1H, 1'H), 7.59 (dd, *J* = 7.9 Hz and 5.1 Hz, 1H, pyridine), 8.12 (d, *J* = 8.1 Hz, 1H, pyridine), 8.27-8.30 (m, 2H, pyridine, H-2), 8.48-8.56

(bm, 1H, pyridine), 8.69 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 42.57, 69.78, 71.87, 75.57, 83.70, 89.93, 126.28, 138.79, 140.75, 146.28, 146.95, 148.78, 149.17, 150.53, 153.81, 155.82; HRMS [ESI+] calcd for $[C_{16}H_{20}N_7O_6S]^+$ *m/z* = 438.1190, obsd 438.1172; *rp*HPLC t_R: condition (I) 14.415 (II) 11.740 minutes, purity 95.6% and 95.7%.



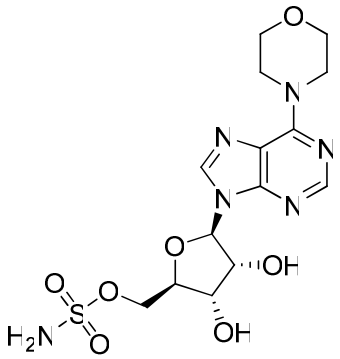
((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-((pyridin-4-ylmethyl)amino)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (45)

Compound **6am** was deprotected as outlined in general procedure **C**, yielding **45** as a yellow oil (85%): δ_H (400 MHz, d_4-MeOD) 4.30-4.44 (m, 4H, 5'H_2, 4'H, 3'H), 4.67 (t, *J* = 5.1 Hz, 1H, 2'H), 4.99-5.11 (m, 2H, C$\underline{H_2}$pyridine), 6.08 (d, *J* = 5.1 Hz, 1H, 1'H), 7.84 (d, *J* = 5.3 Hz, 2H, pyridine), 8.24 (s, 1H, H-2), 8.32 (bs, 1H, H-8), 8.56-8.70 (m, 2H, pyridine); δ_C (100MHz, MeOD-d_4) 44.32, 69.86, 71.84, 75.59, 83.70, 89.85, 119.68, 120.91, 140.80, 147.05, 150.43, 153.83, 155.86, 156.07; HRMS [ESI+] calcd for $[C_{16}H_{20}N_7O_6S]^+$ *m/z* = 438.1190, obsd 438.1206; *rp*HPLC t_R: condition (I) 14.042 (II) 11.532 minutes, purity 99.3% and 98.8%.



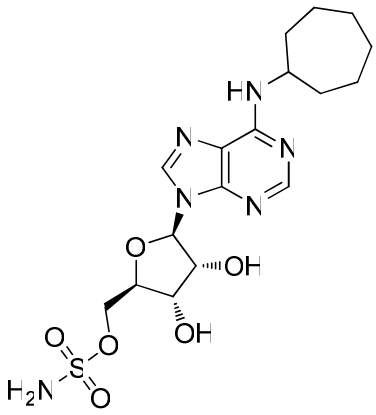
((2R,3S,4R,5R)-5-(6-(benzyl(methyl)amino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (46)

Compound **6an** was deprotected as outlined in general procedure **C**, yielding **46** as a whtie solid (81%): m.p. = 74-77 °C; δ_H (400 MHz, d_4-MeOD) 3.38 (bs, 3H, C<u>H</u>$_3$NCH$_2$phenyl), 4.30-4.44 (m, 4H, 5'H$_2$, 4'H, 3'H), 4.63 (t, J = 5.1 Hz, 1H, 2'H), 5.35 (bs, 2H, CH$_3$NC<u>H</u>$_2$phenyl), 6.10 (d, J = 5.1 Hz, 1H, 1'H), 7.22-7.37 (m, 5H, phenyl), 8.22 (s, 1H, H-2), 8.27 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 36.61, 54.53, 69.70, 71.84, 75.62, 83.59, 89.69, 121.14, 128.35, 128.63, 129.61, 138.93, 139.08, 151.70, 153.39, 156.12; HRMS [ESI+] calcd for $[C_{18}H_{23}N_6O_6S]^+$ m/z = 451.1394, obsd 451.1383; *rp*HPLC t_R: condition (I) 21.893 (II) 17.960 minutes, purity 95.5% and 97.8%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-morpholino-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (47)

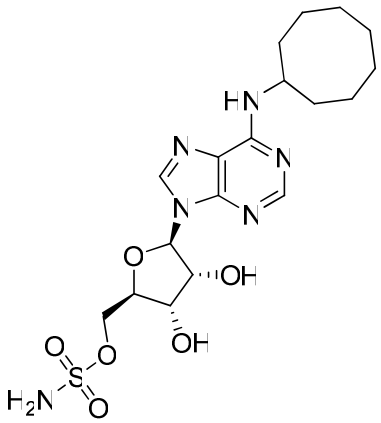
Compound **6ao** was deprotected as outlined in general procedure **C**, yielding **47** as an off-white solid (69%): m.p. = 130-141 °C; δ_H (400 MHz, MeOD) 3.79-3.82 (m, 4H, C<u>H</u>$_2$OC<u>H</u>$_2$ morpholine), 4.25-4.44 (m, 8H, C<u>H</u>$_2$NC<u>H</u>$_2$ morpholine, 5'H$_2$, 4'H, 3'H), 4.62 (t, *J* = 5.1 Hz, 1H, 2'H), 6.08 (d, *J* = 5.1 Hz, 1H, 1'H), 8.23 (s, 1H, H-2), 8.27 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 54.72, 75.63, 78.11, 79.71, 82.61, 91.01, 96.97, 128.91, 147.92, 160.08, 161.51, 162.74; HRMS [ESI+] calcd for $[C_{14}H_{21}N_6O_7S]^+$ *m/z* = 417.1186, obsd 417.1204; *rp*HPLC t_R: condition (I) 13.729 (II) 11.320 minutes, purity 99.4% and 99.8%.



((2R,3S,4R,5R)-5-(6-(cycloheptylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (48)

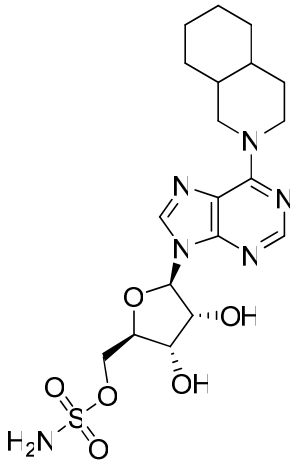
Compound **6ap** was deprotected as outlined in general procedure **C**, yielding **48** as an off-white solid (67%): m.p. = 145-158 °C; δ_H (400 MHz, *d*$_4$-MeOD) 1.55-1.80 (m, 10H, cycloheptyl), 2.02-2.11 (m, 2H, cycloheptyl), 4.29-4.45 (m, 5H, 1 H cycloheptyl, 5'H$_2$, 4'H and 3'H), 4.64 (t, *J* = 5.08 Hz, 1H, 2'H), 6.06 (d, *J* = 5.01, 1H, 1'H), 8.24 (s, 1H, H-2), 8.25 (s, 1H, H-8); δ_C (100MHz, MeOD-d_4) 25.03, 29.30, 35.91, 69.74, 71.79, 75.59, 79.44, 83.62, 89.85, 120.50,

140.12, 149.78, 153.90, 154.87; HRMS [ESI+] calcd for $[C_{17}H_{27}N_6O_6S]^+$ *m/z* = 443.1707, obsd 443.1710; *rp*HPLC t_R: condition (I) 20.669 (II) 17.237 minutes, purity 99.6 %and 99.6%.



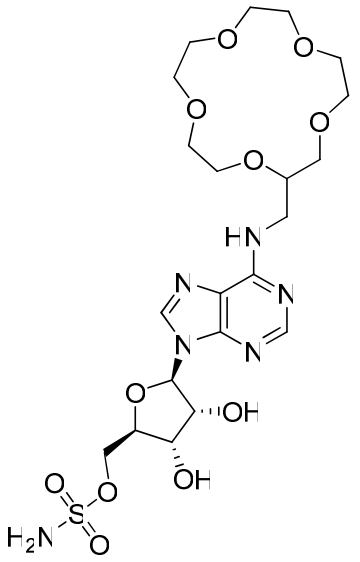
((2R,3S,4R,5R)-5-(6-(cyclooctylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (49)

Compound **6aq** was deprotected as outlined in general procedure **C**, yielding **49** as a white solid (96%): m.p. = 153-166 °C; δ_H (400 MHz, MeOD) 1.58-1.85 (m, 12H, cyclooctyl), 1.93-2.02 (m, 2H, cyclooctyl), 4.29-4.44 (m, 5H, 5'H_2, 4'H, 3'H, cyclooctyl), 4.64 (t, *J* = 5.1 Hz, 1H, 2'H), 6.06 (d, *J* = 5.0 Hz, 1H, 1'H), 8.23-8.27 (m, 2H, H-2, H-8); δ_C (100MHz, MeOD-d_4) 24.66, 26.56, 28.46, 32.92, 51.64, 69.74, 71.80, 75.59, 83.62, 89.86, 120.52, 140.03, 149.80, 154.11, 155.00; HRMS [ESI+] calcd for $[C_{18}H_{29}N_6O_6S]^+$ *m/z* = 457.0863, obsd 457.1870; *rp*HPLC t_R: condition (I) 15.011 (II) 11.525 minutes, purity 100.0% and 100.0%.



((2R,3S,4R,5R)-3,4-dihydroxy-5-(6-(octahydroisoquinolin-2(1H)-yl)-9H-purin-9-yl)tetrahydrofuran-2-yl)methyl sulfamate (50)

Compound **6ar** was deprotected as outlined in general procedure **C**, yielding **50** as an off-white solid (72%): m.p. = 77-88 °C; δ_H (400 MHz, MeOD) 0.85-1.41 (m, 8H, perhydroisoquinone), 1.66-1.83 (m, 4H, perhydroisoquinone), 2.66 (t, *J* = 11.9 Hz, 1H, perhydroisoquinone), 3.05 (t, *J* = 11.9 Hz, 1H, perhydroisoquinone), 4.29-4.44 (m, 4H, 5'H_2, 4'H, 3'H), 4.60 (t, *J* = 5.0 Hz, 1H, 2'H), 5.31 (bs, 1H, perhydroisoquinone), 5.50 (bs, 1H, perhydroisoquinone), 6.07 (d, *J* = 5.0 Hz, 1H, 1'H), 8.20, 8.21 (m, 2H, H-2, H-8); δ_C (100 MHz, MeOD-d_4) 27.07, 27.37, 31.07, 34.10, 34.20, 43.65, 43.74, 47.56, 52.67, 69.69, 71.77, 75.64, 83.50, 89.66, 120.98, 138.46, 151.64, 153.33, 154.94; HRMS [ESI+] calcd for $[C_{19}H_{29}N_6O_6S]^+$ *m/z* = 469.1863, obsd 469.1857; *rp*HPLC t_R: condition (III) 15.501 (IV) 11.856 minutes, purity 95.2 %and 96.5%.



pentaoxacyclopentadecan-2-yl)methylamino)-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl sulfamate (51)

Compound **6as** was deprotected as outlined in general procedure **C**, yielding **51** as a colourless oil (90%): δ_H (400 MHz, MeOD) 3.60-3.92 (m, 21H, 15-crown-5), 4.31-4.45 (m, 4H, 5'H_2, 4'H, 3'H), 4.66 (t, J = 5.0 Hz, 1H, 2'H), 6.08 (d, J = 5.1 Hz, 1H, 1'H), 8.27-8.31 (m, 2H, H-2, H-8); δ_C (100 MHz, MeOD-d_4) 42.00, 69.79, 69.91, 70.00, 70.14, 70.43, 70.69, 70.79, 71.23, 71.84, 75.59, 78.70, 79.45, 83.72, 89.86, 120.77, 140.62, 150.05, 153.61, 155.97; HRMS [ESI+] calcd for $[C_{21}H_{35}N_6O_{11}S]^+$ *m/z* = 579.2079, obsd 579.2066; *rp*HPLC t_R: condition (I) 15.360 (II) 12.190 minutes, purity 98.6% and 99.0%.