Electronic supplementary materials *Mendeleev Commun.*, 2017, **27**, 547–549

Synthesis and antimycobacterial activity of novel purin-6-yl and 2-aminopurin-6-yl conjugates with (*S*)-aspartic and (*S*)-glutamic acids

Dmitry A. Gruzdev, Evgeny N. Chulakov, Galina L. Levit, Marionella A. Kravchenko, Victor P. Krasnov and Valery N. Charushin

1. Chemistry

General

2-Acetamido-6-chloropurine,[S1] α-*tert*-butyl *N*-Boc-(*S*)-aspartate (**6a**) and α-*tert*-butyl *N*-Boc-(*S*)-glutamate (**6b**)[S2] were obtained as described previously. 9-(2-Acetoxyethoxymethyl)-6-chloropurine (**8a**) and 2-acetamido-9-(2-acetoxyethoxymethyl)-6-chloropurine (**8b**) were synthesized by analogy with the known methods.[S3,S4] Other reagents are commercially available.

The solvents were purified according to traditional methods and used freshly distilled. Optical rotations were measured on a Perkin Elmer 341 polarimeter. The ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded on Bruker DRX-400 (400, 376, and 100 MHz, respectively) or Bruker Avance 500 (500, 470, and 125 MHz, respectively) spectrometers with TMS and hexafluorobenzene as internal references. Microanalyses were performed using Perkin Elmer 2400 II analyzer. Analytical TLC was performed using Sorbfil plates (Imid, Russia). Flash-column chromatography was performed using Silica gel 40 (230–400 mesh) (Alfa Aesar, UK). Analytical chiral HPLC of compound (*S*)-**13** was performed on a Knauer Smartline-1100 instrument using a Chiralcel OD-H column (250×4.6 mm, 5 μm); *n*-hexane–*i*PrOH–MeOH 20:0.8:0.2 mixture as an eluent, 1 ml/min flow rate, detection at 220 nm. The high-resolution mass spectra were obtained on a Bruker maXis Impact HD mass spectrometer, electrospray ionization with direct sample inlet (4 l/min flow rate).

Compounds 4a,b (general procedure). 6-Chloropurine (or 2-acetamido-6-chloropurine) (5.68 mmol) was added to a solution of *N*-Boc-1,2-ethylenediamine (2.09 g, 13.06 mmol) in EtOH (45 ml). The reaction mixture was refluxed for 8 h, cooled to room temperature and poured into water (430 ml). The precipitate was filtered off and dried *in vacuo* at 70 °C.

6-[2-(*tert*-Butoxycarbonylamino)ethyl]aminopurine (4a). Yield 1.36 g (86%). Colourless solid, mp 228 °C (decomp.) (lit.[S5] mp 225 °C). ^{1}H NMR (500 MHz, DMSO-d$_6$) (N^9–N^7 tautomers 85:15) δ: 1.30 (s, 1.35H, *t*Bu), 1.36 (s, 7.65H, *t*Bu), 3.17 (m, 2H, C$\underline{H}_2$NH), 3.52 (br. s, 1.70H, NHC$\underline{H}_2$), 3.65–4.05 (br. s, 0.30H, NHC$\underline{H}_2$), 6.49 (s, 0.15H, N$\underline{H}$CH$_2$), 6.91 (br. s, 0.85H, N$\underline{H}$CH$_2$), 7.30 (br. s,

0.15H, NHBoc), 7.59 (br. s, 0.85H, NHBoc), 8.08 (s, 0.85 H, C^8H), 8.18 (s, 0.85H, C^2H), 8.19–8.25 (br. s, 0.30H, C^8H and C^2H), 12.00 (br. s, 0.15H, N^9H), 12.90 (br. s, 0.85H, N^9H). ^{13}C NMR spectrum is identical to the published one.[S6] Found (%): C, 51.26; H, 6.58; N, 30.08. Calc. for $C_{12}H_{18}N_6O_2 \times 0.1H_2O$ (%): C, 51.45; H, 6.55; N, 30.00.

2-Acetamido-6-[2-(*tert*-butoxycarbonylamino)ethyl]aminopurine (4b). Yield 1.64 g (86%). Colourless solid, mp 258.5 °C. ^1H NMR (500 MHz, DMSO-d_6) (N^9–N^7 tautomers 9:1) δ: 1.30 (s, 0.9H, *t*Bu), 1.34 (s, 8.1H, *t*Bu), 2.22 (s, 3H, CH_3CO), 3.18 (m, 2H, CH_2NH), 3.45–3.55 (m, 2H, $NHCH_2$), 6.89 (s, 1H, $NHCH_2$), 7.62 (s, 1H, NHBoc), 7.95 (s, 1H, C^8H), 9.76 (s, 1H, NHAc), 12.74 (br. s, 1H, N^9H). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 24.61, 28.12 (3C), 38.0–41.0 (2C) (overlapped with DMSO signal), 77.49, 115.75, 138.05, 150.31, 152.58, 154.34, 155.66, 169.35. Found (%): C, 47.77; H, 6.20; N, 28.21. Calc. for $C_{14}H_{21}N_7O_3 \times 0.8H_2O$ (%): C, 48.07; H, 6.51; N, 28.03.

Compounds 5a,b (general procedure: A mixture of compound **4a** (or **4b**) (3.50 mmol), CH_2Cl_2 (12 ml) and TFA (12 ml) was stirred at room temperature for 4 h, and then evaporated to dryness under reduced pressure. The residue was treated with diethyl ether (140 ml); the precipitate was filtered off and dried *in vacuo* at 70 °C.

6-(2-Aminoethyl)aminopurine bis-hydrotrifluoroacetate (5a). Yield 1.42 g (100%). Colourless solid, mp 184–187 °C. ^1H NMR (500 MHz, DMSO-d_6) δ: 3.09 (m, 2H, CH_2), 3.77 (br. s, 2H, CH_2), 7.89 (s, 3H, NH_3^+), 8.21 (s, 1H, $NHCH_2$), 8.27 (s, 1H, C^8H), 8.34 (s, 1H, C^2H), 1 signal (N^9H) is not detectable. ^{19}F NMR (470 MHz, DMSO-d_6) δ: 88.34. ^{13}C NMR (125 MHz, DMSO-d_6) δ: 38.03, 38.53, 116.39 (q, *J* 295.4 Hz), 116.63, 141.03, 149.24, 150.34, 153.33, 158.55 (q, *J* 33.9 Hz). Found (%): C, 32.22; H, 3.18; F, 28.68; N, 20.09. Calc. for $C_7H_{10}N_6 \times 2.1CF_3CO_2H$ (%): C, 32.21; H, 2.92; F, 28.66; N, 20.12.

2-Acetamido-6-(2-aminoethyl)aminopurine bis-hydrotrifluoroacetate (5b). Yield 1.67 g (99%). Colourless solid, mp 218–221 °C (decomp.). ^1H NMR (500 MHz, DMSO-d_6) δ: 2.16 (s, 3H, CH_3CO), 3.09 (m, 2H, CH_2), 3.63 (br. s, 2H, CH_2), 8.02 (s, 3H, NH_3^+), 8.14 (s, 1H, C^8H), 8.26 (s, 1H, $NHCH_2$), 10.49 (s, 1H, NHAc), 1 signal (N^9H) is not detectable. ^{19}F NMR (470 MHz, DMSO-d_6) δ: 88.22. ^{13}C NMR (125 MHz, DMSO-d_6) δ: 24.22, 38.64, 39–40 (overlapped with DMSO signal), 114.30, 116.12 (q, *J* 294.1 Hz), 139.56, 149.78, 151.61, 154.15, 158.34 (q, *J* 34.8 Hz), 169.90. Found (%): C, 32.42; H, 3.56; N, 19.93. Calc. for $C_9H_{13}N_7 \times 2CF_3CO_2H \times H_2O$ (%): C, 32.44; H, 3.56; N 20.37.

Compounds 7a-d (general procedure). Ethyl chloroformate (0.11 ml, 1.09 mmol) was added to a solution of compound **6a** (or **6b**) (1.09 mmol) and *N*-methylmorpholine (NMM, 0.12 ml, 1.09 mmol) in THF (7.1 ml) under stirring at −10 °C. The reaction mixture was stirred at −10 °C for 30 min; then a solution of *N*-diisopropylethylamine (DIPEA, 0.62 ml, 3.83 mmol) in THF (5 ml) and a solution of compound **5a** (**5b**) (0.91 mmol) in water (1.4 ml) were subsequently added. The reaction

mixture was stirred at room temperature for 24 h and evaporated to dryness under reduced pressure. The residue was subjected to flash-column chromatography on silica gel ($CHCl_3$–MeOH 9:1 as an eluent). Fractions containing the target product and tertiary amine were combined and evaporated to dryness under reduced pressure. The residue was subjected to flash-column chromatography on neutral Al_2O_3 (EtOAc, then $CHCl_3$–MeOH from 99:1 to 8:2 as eluents).

***tert*-Butyl N^{α}-Boc-*N*-[2-(purin-6-yl)aminoethyl]-(*S*)-asparaginate (7a).** Yield 0.28 g (67%). Colourless solid, mp 198 °C (decomp.). $[\alpha]_D^{20}$ −10.3 (*c* 0.7, DMSO). ^{1}H NMR (500 MHz, DMSO-d_6, 100 °C) *δ*: 1.38 (s, 18H, Boc and O*t*Bu), 2.43–2.55 (m, 2H, C^3H_2, overlapped with DMSO signal), 3.33 (m, 2H, CH_2), 3.65 (m, 2H, CH_2), 4.17–4.23 (m, 1H, C^2H), 6.40 (d, *J* 7.2 Hz, 1H, NHBoc), 7.07 (br. s, 1H, N<u>H</u>CH_2), 7.71 (s, 1H, N<u>H</u>CH_2), 7.96 (s, 1H, C^8H-purine), 8.17 (s, 1H, C^2H-purine), 12.52 (br. s, 1H, N^9H-purine). ^{13}C NMR (125 MHz, DMSO-d_6) *δ*: 27.51 (3C), 28.08 (3C), 37.08, 38.65, 39–40 (overlapped with DMSO signal), 51.07, 78.09, 80.34, 118.81, 138.69, 149.48, 152.22, 154.38, 155.11, 169.26, 171.19. Found (%): C, 52.02; H, 7.10; N, 21.40. Calc. for $C_{20}H_{31}N_7O_5\times0.66H_2O$ (%): C, 52.05; H, 7.06; N, 21.24.

***tert*-Butyl N^{α}-Boc-*N*-[2-(purin-6-yl)aminoethyl]-(*S*)-glutaminate (7b).** Yield 0.372 g (88%). Colourless solid, mp 146–148 °C. $[\alpha]_D^{20}$ −9.0 (*c* 0.7, DMSO). ^{1}H NMR (500 MHz, DMSO-d_6, 100 °C) *δ*: 1.38 (s, 9H, *t*Bu), 1.40 (s, 9H, *t*Bu), 1.74–1.83 (m, 1H, C^3H_B), 1.87–1.96 (m, 1H, C^3H_A), 2.16 (t, *J* 7.7 Hz, 2H, C^4H_2), 3.33 (m, 2H, C<u>H$_2$</u>NH), 3.65 (m, 2H, C<u>H$_2$</u>NH), 3.83 (ddd, *J* 8.3, 8.2 and 5.4 Hz, 1H, C^2H), 6.48 (d, *J* 5.4 Hz, 1H, NHBoc), 7.07 (br. s, 1H, N<u>H</u>CH_2), 7.60 (br. s, 1H, N<u>H</u>CH_2), 7.97 (s, 1H, C^8H), 8.16 (s, 1H, C^2H), 12.40 (br. s, 1H, N^9H). ^{13}C NMR (125 MHz, DMSO-d_6) *δ*: 26.51, 27.58 (3C), 28.12 (3C), 31.67, 38.52, 39–40 (overlapped with DMSO signal), 53.95, 77.96, 80.19, 118.77, 138.66, 149.47, 152.21, 154.40, 155.42, 171.47, 171.50. Found (%): C, 53.60; H, 7.27; N, 20.86. Calc. for $C_{21}H_{33}N_7O_5\times0.33H_2O$ (%): C, 53.72; H, 7.23; N, 20.88.

***tert*-Butyl N^{α}-Boc-*N*-[2-(2-acetamidopurin-6-yl)aminoethyl]-(*S*)-asparaginate (7c).** Yield 0.369 g (80%). Colourless solid, mp 232−233 °C (decomp.). $[\alpha]_D^{20}$ −8.3 (*c* 0.65, DMSO). ^{1}H NMR (500 MHz, DMSO-d_6) *δ*: 1.33 (s, 9H, *t*Bu), 1.38 (s, 9H, *t*Bu), 2.20 (s, 3H, CH_3CO), 2.37 (dd, *J* 15.0 and 7.5 Hz, 1H, C^3H_B), 2.44−2.50 (m, 1H, C^3H_A, overlapped with DMSO signal), 3.27 (m, 2H, C<u>H$_2$</u>NH), 3.52 (br. s, 2H, C<u>H$_2$</u>NH), 4.03–4.19 (m, 1H, C^2H), 6.97 (d, *J* 8.1 Hz, 1H, NHBoc), 7.71 (br. s, 1H, N<u>H</u>CH_2), 7.96 (s, 1H, C^8H-purine), 8.10 (m, 1H, N<u>H</u>CH_2), 9.89 (s, 1H, NHAc), 12.77 (s, 1H, N^9H-purine). ^{13}C NMR (125 MHz, DMSO-d_6) *δ*: 24.52, 27.48 (3C), 28.08 (3C), 36.98, 39–40 (2C, overlapped with DMSO signal), 51.09, 78.08, 80.29, 115.78, 138.07, 150.30, 152.54, 154.50, 155.11, 168.98, 169.27, 170.81. HRMS (ESI) *m/z*: 507.2676 $[M+H]^+$ (calc. for $C_{22}H_{35}N_8O_6$, *m/z*: 507.2674).

***tert*-Butyl N^{α}-Boc-*N*-[2-(2-acetamidopurin-6-yl)aminoethyl]-(*S*)-glutaminate (7d).** Yield 0.343

g (72%). Colourless solid, mp 230 °C (decomp.). $[\alpha]_D^{20}$ −7.9 (*c* 0.6, DMSO). ^{1}H NMR (500 MHz, DMSO-d_6, 100 °C) *δ*: 1.37 (s, 9H, *t*Bu), 1.40 (s, 9H, *t*Bu), 1.72–1.81 (m, 1H, C^3H_B), 1.85–1.94 (m, 1H, C^3H_A), 2.15 (t, *J* 7.5 Hz, 2H, C^4H_2), 2.25 (s, 3H, CH_3CO), 3.33 (m, 2H, $C\underline{H_2}NH$), 3.62 (m, 2H, $C\underline{H_2}NH$), 3.82 (ddd, *J* 8.1, 8.0, and 5.4 Hz, 1H, C^2H), 6.45 (d, *J* 6.5 Hz, 1H, NHBoc), 7.14 (br. s, 1H, $N\underline{H}CH_2$), 7.62 (br. s, 1H, $N\underline{H}CH_2$), 7.84 (s, 1H, C^8H-purine), 9.14 (s, 1H, NHAc), 12.17 (br. s, 1H, N^9H-purine). ^{13}C NMR (125 MHz, DMSO-d_6) *δ*: 24.53, 26.51, 27.57 (3C), 28.11 (3C), 31.56, 39–40 (2C, overlapped with DMSO signal), 53.95, 77.95, 80.16, 115.76, 138.01, 150.28, 152.56, 154.49, 155.40, 169.22, 171.50 (2C). Found (%): C, 52.86; H, 7.08; N, 21.26. Calc. for $C_{23}H_{36}N_8O_6$ (%): C, 53.06; H, 6.97; N, 21.52.

Compounds 2a,b,e,f (general procedure). A mixture of compound **7** (0.77 mmol), CH_2Cl_2 (7.7 ml) and TFA (7.7 ml) was stirred at room temperature for 4 h and then evaporated to dryness under reduced pressure. The residue was treated with diethyl ether (60 ml) and kept at +4 °C overnight. The precipitate was filtered off to afford the target compound as bis-hydrotrifluoroacetate, and then dissolved in water (10 ml). 2N NaOH (0.77 ml) was added to the reaction mixture. The reaction mixture was evaporated to dryness under reduced pressure. The residue was subjected to flash-column chromatography on silica gel ($CHCl_3$–MeOH–AcOH 6:4:0.5 → $CHCl_3$–MeOH 6:4 → MeOH →MeOH–H_2O 6:4 as eluents).

***N*-[2-(Purin-6-yl)aminoethyl]-(*S*)-asparagine (2a).** Yield 0.119 g (78%). Colourless solid, mp 232–233 °C (decomp.). $[\alpha]_D^{20}$ −5.9 (*c* 0.3, H_2O). ^{1}H NMR (500 MHz, D_2O + DCl) (N^9–N^7 tautomers 8:2) *δ*: 3.03 (dd, *J* 16.9 and 4.2 Hz, 1H, C^3H_B), 3.08 (dd, *J* 16.9 and 5.3 Hz, 1H, C^3H_A), 3.57–3.68 (m, 2H, $NHC\underline{H_2}$), 3.87–3.91 (m, 1.6H, $NHC\underline{H_2}$), 3.95–4.20 (br. s, 0.4H, $NHC\underline{H_2}$), 4.40–4.42 (m, 1H, C^2H), 8.44–8.57 (br. s, 0.2H, C^8H-purine), 8.63 (s, 1H, C^2H-purine), 8.79 (s, 0.8H, C^8H-purine). ^{13}C NMR (125 MHz, D_2O + DCl) *δ*: 36.92, 40.67, 45.30, 52.16, 115.12, 145.77, 148.49, 149.19, 152.86, 173.23, 173.77. HRMS (ESI), *m/z*: 294.1306 $[M+H]^+$, (calc. for $C_{11}H_{16}N_7O_3$, *m/z*: 294.1309).

***N*-[2-(Purin-6-yl)aminoethyl]-(*S*)-glutamine (2b).** Yield 0.105 g (76%). Colourless solid, mp 208–212 °C. $[\alpha]_D^{20}$ +3.7 (*c* 0.5, H_2O). ^{1}H NMR (500 MHz, D_2O + DCl) (N^9–N^7 tautomers 75:25) *δ*: 2.08–2.25 (m, 2H, C^3H_2), 2.36–2.57 (m, 2H, C^4H_2), 3.55–3.63 (m, 2H, $NHC\underline{H_2}$), 3.84–3.92 (m, 1.5H, $NHC\underline{H_2}$), 4.09–4.12 (m, 1H, C^2H), 4.18 (br. s, 0.5H, $NHC\underline{H_2}$), 8.44 (br. s, 0.5H, C^2H and C^8H-purine), 8.50 (s, 0.75H) and 8.58 (s, 0.75H) (C^2H and C^8H-purine). ^{13}C NMR (125 MHz, D_2O + DCl) *δ*: 28.15, 33.74, 40.84, 43.81, 54.79, 116.30, 146.23, 148.60, 148.91, 153.86, 173.86, 177.32. Found (%): C, 44.29; H, 5.90; N, 29.84. Calc. for $C_{12}H_{17}N_7O_3\times H_2O$ (%): C, 44.30; H, 5.89; N, 30.14.

***N*-[2-(2-Acetamidopurin-6-yl)aminoethyl]-(*S*)-asparagine (2e).** Yield 0.174 g (61%). Pale grey solid, mp 250–253 °C (decomp.). $[\alpha]_D^{20}$ +20.6 (*c* 0.3, 1N HCl). ^{1}H NMR (500 MHz, D_2O + DCl)

(N^9–N^7 tautomers 85:15) δ: 2.09 (s, 0.45H, CH_3CO), 2.35 (s, 2.55H, CH_3CO), 2.98 (dd, *J* 17.0 and 5.0 Hz, 0.85H, C^3H_B), 3.03 (dd, *J* 17.0 and 5.8 Hz, 0.85H, C^3H_A), 3.06 (dd, *J* 16.9 and 6.0 Hz, 0.15H, C^3H_A), 3.49–3.65 (m, 2H, NHC$\underline{H}_2$), 3.78–3.88 (m, 2H, NHC$\underline{H}_2$), 4.38 (m, 1H, C^2H), 8.48 (s, 0.85H, C^8H-purine), 8.77 (s, 0.15H, C^8H-purine). ^{13}C NMR (125 MHz, D_2O + DCl) δ: 23.12, 37.01, 41.05, 43.13, 52.15, 108.23, 141.82, 145.74, 154.99, 156.54, 173.40, 173.64, 179.24. Found (%): C, 41.94; H, 5.20; N, 30.16. Calc. for $C_{13}H_{18}N_8O_4\times1.15H_2O$ (%): C, 42.08; H, 5.51; N, 30.20.

***N*-[2-(2-Acetamidopurin-6-yl)aminoethyl]-(*S*)-glutamine (2f).** Yield 0.174 g (79%). Colourless solid, mp 248–250 °C (decomp.). $[\alpha]_D^{20}$ +11.1 (*c* 0.3, 1N HCl). ^1H NMR (500 MHz, D_2O + DCl) δ: 2.11–2.24 (m, 2H, C^3H_2), 2.36 (s, 3H, CH_3CO), 2.41–2.53 (m, 2H, C^4H_2), 3.51–3.59 (m, 2H, NHC$\underline{H}_2$), 3.82–3.84 (m, 2H, NHC$\underline{H}_2$), 4.10 (t, *J* 6.5 Hz, 1H, C^2H), 8.42 (s, 1H, C^8H-purine). ^{13}C NMR (125 MHz, D_2O + DCl) δ: 23.09, 28.18, 33.79, 41.09, 43.08, 54.80, 108.02, 141.57, 145.37, 154.90, 156.50, 173.82, 177.21, 179.20. HRMS (ESI), *m/z*: 387.1502 $[M+Na]^+$, (calc. for $C_{14}H_{20}N_8NaO_4$, *m/z*: 387.1500).

Compounds 2c,d (general procedure). A solution of compound **2e** or **2f** (0.71 mmol) in 1N NaOH (5.7 ml) was stirred at room temperature for 72 h, then 4N HCl (0.9 ml) was added to the reaction mixture. The reaction mixture was evaporated to dryness. The residue was subjected to flash-column chromatography on silica gel ($CHCl_3$–MeOH–AcOH 6:4:0.5 → MeOH as eluents) and then recrystallized from aqueous ethanol.

***N*-[2-(2-Aminopurin-6-yl)aminoethyl]-(*S*)-asparagine (2c).** Yield 0.186 g (85%). Colourless solid, mp 268–271 °C (decomp.). $[\alpha]_D^{20}$ +33.8 (*c* 0.4, 1N HCl). ^1H NMR (500 MHz, D_2O) δ: 2.64 (dd, *J* 16.0 and 7.8 Hz, 1H, C^3H_B), 2.77 (dd, *J* 16.0 and 4.5 Hz, 1H, C^3H_A), 3.42–3.53 (m, 2H, NHC$\underline{H}_2$), 3.63–3.72 (m, 2H, NHC$\underline{H}_2$), 3.84 (dd, *J* 7.8 and 4.5 Hz, 1H, C^2H), 7.81 (s, 1H, C^8H-purine). ^{13}C NMR (125 MHz, D_2O) δ: 39.65, 41.88, 42.37, 54.75, 114.39, 140.90, 154.30, 157.71, 162.83, 175.27, 178.14. HRMS (ESI), *m/z*: 309.1422 $[M+H]^+$, (calc. for $C_{11}H_{17}N_8O_3$, *m/z*: 309.1418).

***N*-[2-(2-Aminopurin-6-yl)aminoethyl]-(*S*)-glutamine (2d).** Yield 0.108 g (47%). Colourless solid, mp 221–223 °C (decomp.). $[\alpha]_D^{20}$ +8.9 (*c* 0.4, 1N HCl). ^1H NMR (400 MHz, D_2O + DCl) (N^9–N^7 tautomers 9:1) δ: 2.13–2.25 (m, 2H, C^3H_2), 2.43–2.55 (m, 2H, C^4H_2), 3.37–3.40 (m, 0.2H, NHC$\underline{H}_2$), 3.48–3.57 (m, 1.8H, NHC$\underline{H}_2$), 3.76–3.85 (m, 1.8H, NHC$\underline{H}_2$), 3.86–3.97 (m, 0.1H, C^2H), 3.98–4.00 (m, 0.2H, NHC$\underline{H}_2$), 4.11 (t, *J* 6.5 Hz, 0.9H, C^2H), 8.52 (s, 0.1H, C^8H-purine), 8.60 (s, 0.9H, C^8H-purine). ^{13}C NMR (125 MHz, D_2O + DCl) δ: 28.21, 33.82, 41.15, 43.05, 54.83, 108.19, 141.82, 142.42, 145.69, 155.04, 156.51, 173.86, 177.23. HRMS (ESI), *m/z*: 323.1577 $[M+H]^+$ (calc. for $C_{12}H_{19}N_8O_3$, *m/z*: 323.1575).

Compounds 9a,b (general procedure). Compound **8a** (**8b**) (2.25 mmol) was added to a solution of *N*-Boc-1,2-ethylenediamine (0.72 g, 4.51 mmol) and TEA (0.94 ml, 6.76 mmol) in EtOH (60 ml).

The reaction mixture was refluxed for 6 h, cooled to room temperature and evaporated to dryness under reduced pressure. The residue was dissolved in chloroform (50 ml) and washed subsequently 10% aqueous solution of citric acid (3 × 30 ml), saturated aqueous NaCl (2 × 30 ml), 5% $NaHCO_3$ (2 × 30 ml) and water (30 ml). Organic layer was dried (Na_2SO_4) and evaporated to dryness under reduced pressure. The residue was purified by flash-column chromatography on silica gel ($CHCl_3$–MeOH 95:5).

9-(2'-Acetoxyethoxymethyl)-6-[2-(*tert*-butoxycarbonylamino)ethyl]aminopurine (9a). Yield 0.73 g (82%). Colourless solid, mp 113–115 °C. ^{1}H NMR (500 MHz, DMSO-d_6) (N^9–N^7 tautomers 9:1) δ: 1.29 (s, 0.9H, *t*Bu), 1.36 (s, 8.1H, *t*Bu), 1.94 (s, 3H, Me), 3.15–3.19 (m, 2H, C$\underline{H_2}$NH), 3.48–3.57 (m, 2H, C$\underline{H_2}$NH), 3.68–3.72 (m, 2H, OCH_2), 4.05–4.08 (m, 2H, OCH_2), 5.58 (s, 2H, NCH_2O), 6.49 (s, 0.1H, N$\underline{H}CH_2$), 6.91 (br. s, 0.9H, N$\underline{H}CH_2$), 7.78 (br. s, 1H, N$\underline{H}CH_2$), 8.25 (s, 1H, C^{8}H-purine), 8.29 (s, 1H, C^{2}H-purine). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.45, 28.15 (3C), 39–40 (overlapped with DMSO signal), 40.43, 62.68, 66.85, 71.97, 77.55, 118.90, 140.95, 148.99, 152.77, 154.53, 155.62, 170.12. Found (%): C, 50.93; H, 6.73; N, 20.97. Calc. for $C_{17}H_{26}N_6O_5 \times 0.33H_2O$ (%): C, 50.99; H, 6.71; N, 20.99.

2-Acetamido-9-(2'-acetoxyethoxymethyl)-6-[2-(*tert*-butoxycarbonylamino)ethyl]aminopurine (9b). Yield 0.67 g (66%). Colourless solid, mp 152–153 °C. ^{1}H NMR (400 MHz, DMSO-d_6) (N^9–N^7 tautomers 9:1) δ: 1.29 (s, 0.9H, *t*Bu), 1.33 (s, 8.1H, *t*Bu), 1.94 (s, 3H, MeCOO), 2.26 (s, 3H, $\underline{Me}$CONH), 3.16–3.20 (m, 2H, C$\underline{H_2}$NH), 3.46–3.54 (m, 2H, C$\underline{H_2}$NH), 3.69–3.73 (m, 2H, 2H, OCH_2), 4.05–4.09 (m, 2H, OCH_2), 5.49 (s, 2H, NCH_2O), 6.46 (s, 0.1H, N$\underline{H}CH_2$), 6.89 (br. s, 0.9H, N$\underline{H}CH_2$), 7.40–7.60 (br. s, 0.1H, N$\underline{H}CH_2$), 7.81 (s, 0.9H, N$\underline{H}CH_2$), 8.15 (s, 1H, C^{8}H-purine), 9.88 (s, 1H, NHCOMe). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.47, 24.76, 28.11 (3C), 39–40 (overlapped with DMSO signal), 40.73, 62.69, 66.83, 71.86, 77.47, 115.74, 140.14, 149.93, 153.17, 154.64, 155.67, 169.62, 170.15. Found (%): C, 50.78; H, 6.53; N, 21.34. Calc. for $C_{19}H_{29}N_7O_6$ (%): C, 50.55; H, 6.47; N, 21.27.

Compounds 10a,b (general procedure). A solution of compound **9a** (**9b**) (0.90 mmol) in TFA (2.75 ml) was stirred at room temperature for 1.5 h, then diethyl ether (70 ml) was added to the reaction mixture. The reaction mixture was kept at −20 °C for 3 days. The precipitate was filtered off and dried *in vacuo*. Compounds **10a,b** are very hygroscopic, unstable during storage and were used immediately after preparation.

9-(2'-Acetoxyethoxymethyl)-6-(2-aminoethyl)aminopurine bis-hydrotrifluoroacetate (10a). Yield 0.46 g (97%). Colourless sticky oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.95 (s, 3H, Me); 3.04–3.12 (m, 2H, C$\underline{H_2}$NH), 3.69–3.82 (m, 4H, C$\underline{H_2}$NH and OCH_2), 4.06–4.08 (m, 2H, OCH_2), 5.60 (s, 2H, NCH_2O), 7.84 (br. s, 3H, NH_3^+), 7.99 (s, 1H, N$\underline{H}CH_2$), 8.31 (s, 1H, C^{8}H-purine), 8.36 (s, 1H, C^{2}H-purine). ^{19}F NMR (376 MHz, DMSO-d_6) δ: 88.09 (s, CF_3).

2-Acetamido-9-(2'-acetoxyethoxymethyl)-6-(2-aminoethyl)aminopurine bis-hydrotrifluoro-acetate (10b). Yield 0.40 g (96%). Colourless semisolid. ^{1}H NMR (500 MHz, DMSO-d$_6$) δ: 1.95 (s, 3H, OCOC$\underline{H}_3$), 2.18 (s, 3H, NHCOC$\underline{H}_3$), 3.10 (br. s, 2H, C$\underline{H}_2$NH), 3.63 (br. s, 2H, C$\underline{H}_2$NH), 3.70 (s, 2H, OCH$_2$), 4.08 (s, 2H, OCH$_2$), 5.52 (s, 2H, NCH$_2$O), 8.06 (s, 3H, NH_3^+), 8.26 (s, 1H, C^{8}H-purine), 8.28 (s, 1H, N$\underline{H}$CH$_2$), 10.50 (s, 1H, N$\underline{H}$Ac). ^{19}F NMR (376 MHz, DMSO-d$_6$) δ: 88.05 (s, CF_3). ^{13}C NMR (125 MHz, DMSO-d$_6$) δ: 20.48, 24.35, 38.63, 40.42, 62.65, 66.74, 72.10, 115.97 (q, J = 293.4 Hz), 116.06, 140.91, 149.94, 152.64, 155.01, 158.26 (q, J = 35.2 Hz), 169.68, 170.16.

Compounds 11a-d (general procedure). Ethylchloroformate (34 μl, 0.36 mmol) was added to a solution of compound **6a** (or **6b**) (0.36 mmol) and NMM (40 μl, 0.36 mmol) in THF (4 ml) under stirring at −10 °C. The reaction mixture was stirred at −10 °C for 30 min; then DIPEA (0.22 ml, 1.26 mmol) and a solution of compound **10a** (**10b**) (0.30 mmol) in THF (4 ml) were subsequently added. The reaction mixture was stirred at room temperature for 24 h and evaporated to dryness under reduced pressure. The residue was subjected to flash-column chromatography on silica gel (EtOAc–MeOH 96:4 as an eluent) and then treated with *n*-hexane–Et$_2$O 2:1.

***tert*-Butyl N^{α}-Boc-*N*-{2-[9-(2'-acetoxyethoxymethyl)purin-6-yl]aminoethyl}-(*S*)-asparaginate (11a).** Yield 0.16 g (93%). Colourless amorphous solid. $[\alpha]_D^{20}$ −13.3 (*c* 0.6, MeOH). ^{1}H NMR (500 MHz, DMSO-d$_6$, 100 °C) δ: 1.38 (s, 18H, Boc and *t*Bu), 1.92 (s, 3H, Me), 2.42–2.56 (br. m, 2H, C^{3}H$_2$, overlapped with DMSO signal), 3.33 (m, 2H, C$\underline{H}_2$NH), 3.66 (m, 2H, C$\underline{H}_2$NH), 3.74 (m, 2H, OCH$_2$), 4.07–4.10 (m, 2H, OCH$_2$), 4.17–4.22 (m, 1H, C^{2}H), 5.57 (s, 2H, NCH$_2$O), 6.43 (br. s, 1H, NHBoc), 7.29 (s, 1H, N$\underline{H}$CH$_2$), 7.72 (s, 1H, N$\underline{H}$CH$_2$), 8.17 (s, 1H, C^{8}H-purine), 8.23 (s, 1H, C^{2}H-purine). ^{13}C NMR (125 MHz, DMSO-d$_6$) δ: 20.45, 27.50 (3C), 27.89, 28.08 (3C), 37.07, 38.47, 51.05, 62.67, 66.84, 71.96, 78.09, 80.33, 118.91, 140.98, 148.97, 152.76, 154.49, 155.09, 169.26, 170.12, 170.77. HRMS (ESI), *m/z*: 566.2940 [M+H]$^+$ (calc. for $C_{25}H_{40}N_7O_8$, *m/z*: 566.2933).

***tert*-Butyl N^{α}-Boc-*N*-{2-[9-(2'-acetoxyethoxymethyl)purin-6-yl]aminoethyl}-(*S*)-glutaminate (11b).** Yield 0.16 g (91%). Colourless amorphous solid. $[\alpha]_D^{20}$ −6.5 (*c* 0.7, DMSO). ^{1}H NMR (500 MHz, DMSO-d$_6$, 100 °C) δ: 1.38 (s, 9H, *t*Bu), 1.40 (s, 9H, *t*Bu), 1.74–1.82 (m, 1H, C^{3}H$_B$), 1.88–1.95 (m, 1H, C^{3}H$_A$), 1.92 (s, 3H, Me), 2.14–2.17 (m, 2H, C^{4}H$_2$), 3.33 (m, 2H, C$\underline{H}_2$NH), 3.66 (m, 2H, C$\underline{H}_2$NH), 3.74 (m, 2H, OCH$_2$), 3.82 (ddd, J = 8.1, 8.1 and 5.4 Hz, 1H, C^{2}H), 4.09 (m, 2H, OCH$_2$), 5.57 (s, 2H, NCH$_2$O), 6.50 (br. s, 1H, NHBoc), 7.29 (m, 1H, N$\underline{H}$CH$_2$), 7.61 (br. s, 1H, N$\underline{H}$CH$_2$), 8.17 (s, 1H, C^{8}H-purine), 8.22 (s, 1H, C^{2}H-purine). ^{13}C NMR (125 MHz, DMSO-d$_6$) δ: 20.45, 25.90, 27.58 (3C), 28.12 (3C), 31.66, 38.38, 39.5 (overlapped with DMSO signal), 53.94, 62.68, 66.86, 71.97, 77.96, 80.20, 118.88, 140.96, 149.01, 152.77, 154.54, 155.42, 170.13, 171.49 (2C). HRMS (ESI), *m/z*: 580.3085 [M+H]$^+$ (calc. for $C_{26}H_{42}N_7O_8$, *m/z*: 580.3089).

***tert*-Butyl N^{α}-Boc-*N*-{2-[2-acetamido-9-(2'-acetoxyethoxymethyl)purin-6-yl]aminoethyl}-(*S*)-asparaginate (11c).** Yield 0.117 g (72%). Colourless amorphous solid. $[\alpha]_D^{20}$ −8.6 (*c* 0.9, DMSO).

^{1}H NMR (500 MHz, DMSO-d$_6$, 100 °C) δ: 1.36 (s, 9H, *t*Bu), 1.37 (s, 9H, *t*Bu), 1.93 (s, 3H, OAc), 2.27 (s, 3H, NHCOC$\underline{H}_3$), 2.44–2.52 (m, 2H, C^{3}H$_2$ partially overlapped with DMSO signal), 3.32–3.35 (m, 2H, NHC$\underline{H}_2$), 3.61–3.65 (m, 2H, NHC$\underline{H}_2$), 3.74–3.76 (m, 2H, OCH$_2$), 4.08–4.10 (m, 2H, OCH$_2$), 4.16–4.20 (m, 1H, C^{2}H), 5.49 (s, 2H, NCH$_2$O), 6.39–6.43 (m, 1H, N$\underline{H}$Boc), 7.34–7.38 (m, 1H, N$\underline{H}$CH$_2$), 7.77 (br. s, 1H, N$\underline{H}$CH$_2$), 8.04 (s, 1H, C^{8}H-purine), 9.32 (s, 1H, N$\underline{H}$Ac). ^{13}C NMR (125 MHz, DMSO-d$_6$) δ: 20.43, 24.59, 27.43 (3C), 28.04 (3C), 36.93, 39–40 (2C, overlapped with DMSO signal), 51.03, 62.65, 66.76, 71.85, 78.03, 80.23, 115.75, 140.22, 149.88, 153.02, 154.67, 155.06, 169.24, 169.48, 170.10, 170.76. HRMS (ESI), *m/z*: 645.2969 [M+Na]$^+$ (calc. for C$_{27}$H$_{42}$N$_8$NaO$_9$, *m/z*: 645.2967).

***tert*-Butyl N$^\alpha$-Boc-*N*-{2-[2-acetamido-9-(2'-acetoxyethoxymethyl)purin-6-yl]aminoethyl}-(*S*)-glutaminate (11d).** Yield 0.128 g (67%). Colourless amorphous solid. $[\alpha]_D^{25}$ −5.3 (*c* 0.5, DMSO). ^{1}H NMR (500 MHz, DMSO-d$_6$, 100 °C) δ: 1.37 (s, 9H, *t*Bu), 1.39 (s, 9H, *t*Bu), 1.72–1.80 (m, 1H, C^{3}H$_B$), 1.86–1.93 (m, 1H, C^{3}H$_A$), 1.93 (s, 3H, OCOC$\underline{H}_3$), 2.14 (t, *J* 7.6 Hz, 2H, C^{4}H$_2$), 2.27 (s, 3H, NHCOC$\underline{H}_3$), 3.32–3.35 (m, 2H, NCH$_2$), 3.61–3.64 (m, 2H, NCH$_2$), 3.74–3.76 (m, 2H, OCH$_2$), 3.81 (ddd, *J* 8.2, 8.1, and 5.4 Hz, 1H, C^{2}H), 4.08–4.10 (m, 2H, OCH$_2$), 5.49 (s, 2H, NCH$_2$O), 6.42–6.52 (m, 1H, N$\underline{H}$Boc), 7.33–7.37 (m, 1H, N$\underline{H}$CH$_2$), 7.63 (br. s, 1H, N$\underline{H}$CH$_2$), 8.04 (s, 1H, C^{8}H-purine), 9.29 (s, 1H, N$\underline{H}$Ac). ^{13}C NMR (125 MHz, DMSO-d$_6$) δ: 20.47, 24.67, 26.50, 27.57 (3C), 28.12 (3C), 31.55, 38–40 (2C, overlapped with DMSO signal), 53.95, 62.70, 66.81, 71.89, 77.96, 80.16, 115.76, 140.23, 149.93, 153.09, 154.69, 155.41, 169.52, 170.16, 171.52 (2C). HRMS (ESI), 637.3302 [M+H]$^+$ (calc. for C$_{28}$H$_{45}$N$_8$O$_9$, *m/z*: 637.3304).

Compounds 12a-d (general procedure). A mixture of compound **11a** (**11b-d**) (0.5 mmol) and TFA (2.3 ml, 30.0 mmol) was stirred at room temperature for 1.5 h, then diethyl ether (45 ml) was added to the reaction mixture. The reaction mixture was kept at +4 °C overnight. The precipitate (in the form of bis-hydrofluoroacetate) was filtered off, dried and dissolved in 1N NaOH (5 ml). The resulting solution was stirred at room temperature for 24 h (compounds **12a,b**) or 72 h (compounds **12c,d**), then AcOH was added to neutral pH and the reaction mixture was evaporated to drynesss under reduced pressure. The residue was subjected to flash-column chromatography on silica gel (CH$_2$Cl$_2$–MeOH–AcOH 8:2:0.5 → CH$_2$Cl$_2$–MeOH 6:4 → MeOH as eluents) and recrystallized from aqueous ethanol.

***N*-{2-[9-(2'-Hydroxyethoxymethyl)purin-6-yl]aminoethyl}-(*S*)-asparagine (12a).** Yield 0.13 g (70%). Colourless amorphous solid. $[\alpha]_D^{20}$ −5.5 (*c* 0.5, H$_2$O). ^{1}H NMR (400 MHz, D$_2$O + DCl) δ: 2.79 (dd, *J* 16.5 and 7.7 Hz, 1H, C^{3}H$_B$), 2.88 (dd, *J* 16.5 and 4.4 Hz, 1H, C^{3}H$_A$), 3.46–3.57 (m, 2H, NHC$\underline{H}_2$), 3.62–3.77 (m, 6H, O(CH$_2$)$_2$OH and NHC$\underline{H}_2$), 3.98 (dd, *J* 7.7 and 4.4 Hz, 1H, C^{2}H), 5.66 (s, 2H, NCH$_2$O), 8.20 (s, 1H, C^{8}H-purine), 8.22 (s, 1H, C^{2}H-purine). ^{13}C NMR (125 MHz, D$_2$O + DCl) δ: 37.89, 41.48, 42.76, 54.19, 62.92, 73.02, 75.76, 121.46, 144.73, 150.91, 155.50, 157.37,

174.69, 175.87. HRMS, *m/z*: 368.1677 $[M+H]^+$ (calc. for $C_{14}H_{22}N_7O_5$, *m/z*: 368.1678).

***N*-{2-[9-(2'-Hydroxyethoxymethyl)purin-6-yl]aminoethyl}-(*S*)-glutamine (12b).** Yield 0.105 g (55%). Colourless amorphous solid. $[\alpha]_D^{25}$ +5.1 (*c* 0.6, H_2O). ^1H NMR (500 MHz, D_2O) δ: 1.66–1.82 (m, 2H, C^3H_2), 2.19–2.23 (m, 2H, C^4H_2), 3.21–3.25 (m, 1H, C^2H), 3.49–3.51 (m, 2H, $NHC\underline{H}_2$), 3.60–3.90 (m, 6H, $NHC\underline{H}_2$ and $O(CH_2)_2OH$), 5.67 (s, 2H, NCH_2O), 8.22 (s, 1H, C^8H-purine), 8.24 (s, 1H, C^2H-purine). ^{13}C NMR (125 MHz, D_2O + DCl) (N^9–N^7 tautomers) δ: 27.51, 28.15, 32.11, 33.70, 40.24, 41.59, 44.35, 46.19, 54.79, 57.03, 62.85, 73.47, 76.49, 121.48, 147.17, 147.60, 149.69, 152.00, 173.94, 177.51. HRMS, *m/z*: 404.1652 $[M+Na]^+$ (calc. for $C_{15}H_{23}N_7NaO_5$, *m/z*: 404.1653).

***N*-{2-[2-Amino-9-(2'-hydroxyethoxymethyl)purin-6-yl]aminoethyl}-(*S*)-asparagine (12c).** Yield 0.136 g (63%). Colourless solid, mp 235–237 °C (decomp.). $[\alpha]_D^{20}$ −7.8 (*c* 0.4, H_2O). ^1H NMR (500 MHz, D_2O) δ: 2.77 (dd, *J* 16.4 and 7.7 Hz, 1H, C^3H_B), 2.86 (dd, *J* 16.4 and 4.4 Hz, 1H, C^3H_A), 3.43–3.54 (m, 2H, $NHC\underline{H}_2$), 3.60–3.76 (m, 6H, $O(C\underline{H}_2)_2OH$ and $NHC\underline{H}_2$), 3.98 (dd, *J* 7.7 and 4.4 Hz, 1H, C^2H), 5.50 (s, 2H, NCH_2O), 7.90 (s, 1H, C^8H-purine). ^{13}C NMR (125 MHz, D_2O) δ: 37.87, 41.84, 42.42, 54.19, 62.95, 72.71, 75.40, 115.87, 142.23, 153.04, 157.98, 162.84, 174.68, 175.83. HRMS, *m/z*: 383.1782 $[M+H]^+$ (calc. for $C_{14}H_{23}N_8O_5$, *m/z*: 383.1786).

***N*-{2-[2-Amino-9-(2'-hydroxyethoxymethyl)purin-6-yl]aminoethyl}-(*S*)-glutamine (12d).** Yield 0.113 g (57%). Colourless solid, mp 192–195 °C. $[\alpha]_D^{25}$ +2.90 (*c* 0.73, H_2O). ^1H NMR (500 MHz, D_2O) δ: 1.97–2.07 (m, 2H, C^3H_2), 2.28–2.39 (m, 2H, C^4H_2), 3.48 (t, *J* 5.6 Hz, 2H, $NHC\underline{H}_2$), 3.63–3.78 (m, 7H, C^2H, $NHC\underline{H}_2$ and $O(CH_2)_2OH$), 5.51 (s, 2H, NCH_2O), 7.92 (s, 1H, C^8H-purine). ^{13}C NMR (125 MHz, D_2O) δ: 29.06, 34.33, 41.89, 42.40, 56.88, 62.94, 72.74, 75.47, 115.85, 142.37, 152.73, 157.85, 162.47, 176.53, 177.67. HRMS, *m/z*: 419.1765 $[M+Na]^+$ (calc. for $C_{15}H_{24}N_8NaO_5$, *m/z*: 419.1762).

Acidic hydrolysis of compound 2a. A solution of ditrifluoroacetate of compound **2a** (0.096 g, 0.185 mmol) in 6N HCl (13.6 ml) containing 0.1 wt% phenol was placed in a sealed tube and then kept at 110–115 °C for 24 h. The reaction mixture was evaporated to dryness under reduced pressure, the residue was dried *in vacuo* over P_2O_5. Then, MeOH (2.5 ml) and thionyl chloride (135 μl, 1.85 mmol) were added under stirring at −5 °C. The reaction mixture was stirred at −5 to 0 °C for 15 min, at room temperature for 10 min, at 50 °C for 3 h, and then evaporate to dryness under reduced pressure. The residue was dried *in vacuo* over P_2O_5 (and KOH). Then CH_2Cl_2 (3 ml) and TEA (0.27 ml, 1.943 mmol) was added, and the reaction mixture was cooled to 0 °C. Benzoyl chloride (86 μl, 0.74 mmol) was added to the resulting solution under stirring. The reaction mixture was stirred at room temperature for 2 h, diluted with CH_2Cl_2 (15 mL) and washed subsequently with 1N HCl (3 × 12 ml), saturated aqueous NaCl (2 × 12 ml), 5% $NaHCO_3$ (2 × 12 ml), and water (2 × 12 ml). Organic layer was dried ($MgSO_4$) and evaporated to dryness under reduced pressure.

The residue was purified by flash-column chromatography on silica gel (*n*-hexane–EtOAc 6:4 as an eluent) to afford compound (*S*)-**13** (0.039 g, 75%) as a colorless solid, mp 89 °C. The ^{1}H and ^{13}C NMR spectra were identical to the published ones.[S5] *Ee* 95.5%. Analytical HPLC (Chiralcel OD-H, *n*-hexane–*i*PrOH–MeOH 20:0.8:0.2): $\tau_{(R)\text{-}\mathbf{13}}$ 28.78 min - 2.23%, $\tau_{(S)\text{-}\mathbf{13}}$ 30.62 min - 97.77%.

2. Assessment of antimycobacterial activity

To evaluate the inhibitory effect of compounds **2a-d** and **12a-d** on mycobacteria we used the following strains: *M. tuberculosis* $H_{37}Rv$, which is susceptible to all classical anti-TB drugs; *M. avium, M. terrae* and multidrug-resistant *M. tuberculosis* strain isolated from TB patients of the Ural region at the Ural Research Institute for Phthisiopulmonology (Ekaterinburg, Russia). The minimal inhibitory concentration (MIC) for mycobacteria strains for each compound was determined by the micro broth dilution method. All compounds tested were dissolved in DMSO and their 1/2 dilutions were prepared in 5 mL tubes using Löwenstein-Jensen medium. Each compound was tested at six concentrations 12.5, 6.25, 3.1, 1.5, 0.7, 0.35 μg/ml. Tubes with Löwenstein-Jensen medium (5 ml) containing tested compounds and those without them (controls) were inoculated with a suspension of appropriate mycobacteria strain and incubated at 37 °C for 10 days. The mycobacterial growth was assessed by the standard procedure: the appearance of zones of mycobacterial growth delay (more than 10 mm) indicated the presence of antimycobacterial properties of tested compounds at the studied concentrations. The value of growth retardation zone (in mm) was proportional to the antimycobacterial activity of the compounds. Growth delay (100 mm or more) is considered as a complete mycobacteria growth inhibition.

References for Supplementary Materials

S1 W. A. Bowles, F. H. Schneider, L. R. Lewis and R. K. Robins, *J. Med. Chem.*, 1963, **6**, 471.

S2 D. A. Gruzdev, G. L. Levit, V. A. Olshevskaya and V. P. Krasnov, *Russ. J. Org. Chem.*, 2017, **53**, 769 (*Zh. Org. Khim.*, 2017, **53**, 756).

S3 D. Singh, M. J. Wani and A. Kumar, *J. Org. Chem.*, 1999, **64**, 4665.

S4 G. Qu, S. Han, Z. Zhang, M. Geng and F. Xue, *Can. J. Chem.*, 2006, **84**, 819.

S5 T. Borrmann, A. Abdelrahman, R. Volpini, C. Lambertucci, E. Alksnis, S. Gorzalka, M. Knospe, A. C. Schiedel, G. Cristalli and C. E. Müller, *J. Med. Chem.*, 2009, **52**, 5974.

S6 D.-R. Hou, J. H. Reibenspies and K. Burgess, *J. Org. Chem.*, 2001, **66**, 206.